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Preface

We would like to present, with great pleasure, the volume-12, Issue-7, July 2026, of a scholarly journal, *International Multispeciality Journal of Health*. This journal is part of the AD Publications series *in the field of Medical, Health and Pharmaceutical Research Development*, and is devoted to the gamut of Medical, Health and Pharmaceutical issues, from theoretical aspects to application-dependent studies and the validation of emerging technologies.

This journal was envisioned and founded to represent the growing needs of Medical, Health and Pharmaceutical as an emerging and increasingly vital field, now widely recognized as an integral part of scientific and technical statistics investigations. Its mission is to become a voice of the Medical, Health and Pharmaceutical community, addressing researchers and practitioners in below areas

Clinical Specialty and Super-specialty Medical Science:

It includes articles related to General Medicine, General Surgery, Gynecology & Obstetrics, Pediatrics, Anesthesia, Ophthalmology, Orthopedics, Otorhinolaryngology (ENT), Physical Medicine & Rehabilitation, Dermatology & Venereology, Psychiatry, Radio Diagnosis, Cardiology Medicine, Cardiothoracic Surgery, Neurology Medicine, Neurosurgery, Pediatric Surgery, Plastic Surgery, Gastroentrology, Gastrointestinal Surgery, Pulmonary Medicine, Immunology & Immunogenetics, Transfusion Medicine (Blood Bank), Hematology, Biomedical Engineering, Biophysics, Biostatistics, Biotechnology, Health Administration, Health Planning and Management, Hospital Management, Nephrology, Urology, Endocrinology, Reproductive Biology, Radiotherapy, Oncology and Geriatric Medicine.

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It includes articles related to Pathology, Microbiology, Forensic Medicine and Toxicology, Community Medicine and Pharmacology.

Basic Medical Science:

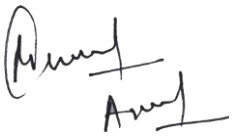
It includes articles related to Anatomy, Physiology and Biochemistry.

Spiritual Health Science:

It includes articles related to Yoga, Meditation, Pranayam and Chakra-healing.

Each article in this issue provides an example of a concrete industrial application or a case study of the presented methodology to amplify the impact of the contribution. We are very thankful to everybody within that community who supported the idea of creating a new Research with *IMJ Health*. We are certain

that this issue will be followed by many others, reporting new developments in the Medical, Health and Pharmaceutical Research Science field. This issue would not have been possible without the great support of the Reviewer, Editorial Board members and also with our Advisory Board Members, and we would like to express our sincere thanks to all of them. We would also like to express our gratitude to the editorial staff of AD Publications, who supported us at every stage of the project. It is our hope that this fine collection of articles will be a valuable resource for *IMJ Health* readers and will stimulate further research into the vibrant area of Medical, Health and Pharmaceutical Research.



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Research Area: Pediatric Surgery & Laparoscopy.

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Volume-12, Issue-7, July 2026

Antimicrobial Resistance Preparedness among Clinical Medical Students in Abuja, Nigeria: Knowledge, Attitudes and Practice Gaps

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Abstract—

Background: *Antimicrobial resistance (AMR) is a major public health challenge, and medical students require both conceptual knowledge and practical prescribing judgement to support future antimicrobial stewardship. This study assessed the knowledge, attitudes, perceptions, and self-reported antimicrobial-use practices of clinical medical students at the University of Abuja Teaching Hospital, Nigeria.*

Methods: *A cross-sectional, questionnaire-based survey was conducted among fourth, fifth, and sixth year clinical medical students at the College of Health Sciences, University of Abuja Teaching Hospital, Gwagwalada. The questionnaire assessed demographic characteristics, knowledge of antimicrobial use and resistance, attitudes toward AMR, and self-reported antimicrobial-use practices. Data were summarized using descriptive statistics, including frequencies, percentages, and proportions. Inferential analyses (chi-square tests) were conducted to examine associations between year of study and key practice indicators.*

Results: *Of 148 students invited, 108 returned usable questionnaires, giving a response rate of 73.0%. Respondents were aged 19–53 years, with most being male (76.9%). Knowledge of key consequences of inappropriate antimicrobial use was generally high, including recognition of bacterial resistance (89.8%), reduced future effectiveness (90.7%), ineffective treatment (87.0%), additional medical cost (85.2%), and prolonged illness (79.6%). Attitudes showed strong recognition of AMR as a serious issue globally (88.7%) and nationally (80.0%), although awareness of AMR as a problem within the teaching hospital was lower (62.1%). Self-reported practices were mixed: most respondents reported completing a full course (71.7%) and checking expiry dates (80.5%), but fewer reported consistently consulting a doctor before starting antimicrobials (38.9%), and some reported using antimicrobials for cough or sore throat (29.6%). Chi-square analysis revealed significant differences in antimicrobial use practices across year levels ($p<0.05$), with senior students showing slightly more appropriate practices.*

Conclusion: *The findings suggest that clinical medical students at the University of Abuja have substantial AMR awareness but important gaps in practical antimicrobial-use behaviour. Undergraduate training should place stronger emphasis on rational antimicrobial use, clinical decision-making, prescribing behaviour, and antimicrobial stewardship*

Keywords— Antimicrobial use, AMR, Clinical Medical students, Abuja, Nigeria.

Key Messages:

- Clinical medical students demonstrate good theoretical knowledge of AMR consequences
- Awareness of AMR as an institutional problem is lower than global or national awareness
- Significant gaps exist between knowledge and self-reported antimicrobial practices
- Undergraduate medical curricula should strengthen practical training in rational antimicrobial use

I. INTRODUCTION

Inappropriate antimicrobial use and insufficient knowledge of antimicrobial resistance (AMR) are major contributors to the growing burden of resistant infections. Antimicrobial resistance occurs when microorganisms adapt to antimicrobial exposure in human medicine, veterinary care, agriculture, and other settings, reducing the effectiveness of treatment. Its public health impact is substantial, with an estimated 700,000 deaths annually attributed to resistant infections worldwide.[1,2] In response to this threat, the World Health Organization designated the theme of World Health Day 2011 as "Combat Antimicrobial Resistance: No Action Today, No Cure Tomorrow."[3]

Future doctors must be able to select antimicrobials appropriately and communicate clearly with patients and other healthcare workers about their use. The WHO has emphasized the importance of undergraduate training in prudent antimicrobial prescribing, and medical students are an important group because they will become future prescribers and clinical leaders.[4] In Nigerian medical training, students are introduced to pathogenic microorganisms, infectious diseases, antimicrobial mechanisms of action, and mechanisms of resistance, but antimicrobial use and resistance are usually embedded within Pharmacology and Microbiology rather than taught as a distinct subject area.[5] A key concern is that students may acquire theoretical knowledge of AMR without developing the practical judgement needed for rational antimicrobial use in clinical settings.

Understanding clinical medical students' knowledge, attitudes, perceptions, and self-reported practices may therefore support more effective undergraduate training and inform curriculum improvements, prescribing guidelines, and interventions aimed at reducing inappropriate antimicrobial use among future doctors.[6] This study therefore aims to assess the knowledge, attitudes, and self-reported antimicrobial practices of clinical medical students at the University of Abuja.

II. SUBJECTS AND METHODS

2.1 Study Design and Setting

This was a cross-sectional, questionnaire-based study conducted at the College of Health Sciences, University of Abuja Teaching Hospital, Gwagwalada, North Central Nigeria, between [insert dates]. The University of Abuja Teaching Hospital serves as a major tertiary referral centre and training facility for medical students in the Federal Capital Territory.

2.2 Questionnaire Development and Validation

The questionnaire was developed by adapting instruments identified through a review of similar studies conducted in various settings.[7,8,9] The adaptation process involved:

1. **Content review:** Three subject lecturers with expertise in pharmacology, microbiology, and medical education reviewed the questionnaire for content relevance and comprehensiveness. Content validity was assessed using a content validity index (CVI), with items achieving a CVI of ≥0.80 retained.
2. **Pilot testing:** The questionnaire was pilot-tested with 15 medical students who were not part of the final study sample. Based on pilot results, minor modifications were made to improve clarity of wording and response options. Pilot test results were not included in the final analysis.
3. **Reliability:** Internal consistency was assessed using Cronbach's alpha, with acceptable reliability demonstrated (α = 0.78 for knowledge items, α = 0.81 for attitude items, α = 0.75 for practice items).

2.3 Ethical Considerations

Ethical approval was obtained from the University of Abuja Teaching Hospital Research and Ethics Committee (Approval Reference Number: [insert number], Date: [insert date]). All participants provided written informed consent before completing the questionnaire. Participation was voluntary, and anonymity was maintained throughout the study.

2.4 Study Population and Sampling

A total of 148 clinical medical students in the fourth, fifth, and sixth year of undergraduate medical training were invited to participate. All eligible students in these year levels were invited to ensure maximum representation. The Faculty Secretary, a non-academic senior staff member, administered the questionnaire after obtaining informed consent to reduce potential

response bias. Students who consented completed the questionnaire anonymously in a private setting and returned it within 30 minutes. Of the students invited, 108 consented and returned usable questionnaires, giving a response rate of 73.0%.

2.5 Data Collection Instrument

The questionnaire consisted of four sections:

Section 1: Demographic Information:

This section collected information on age, gender, and level of study (400, 500, or 600 level).

Section 2: Knowledge Assessment

This section assessed knowledge of antimicrobial use and resistance using true/false/uncertain response options. The results are summarized in Table 1.

Section 3: Attitudes Toward AMR

This section assessed attitudes toward antimicrobial resistance and use with five-point Likert-scale responses ranging from "strongly agree" to "strongly disagree," as shown in Table 2.

Section 4: Self-Reported Antimicrobial Practices

This section assessed self-reported antimicrobial-use practices using a five-point Likert scale with responses ranging from "always" to "never," as shown in Table 3.

2.6 Data Management and Statistical Analysis

Data were entered and analysed using Epi Info™ version 7.2.6.0 (Centers for Disease Control and Prevention, Atlanta, GA, USA, 2023).[10] For analysis, the five-point Likert responses were collapsed into three categories (agree/uncertain/disagree or yes/uncertain/no, depending on the question type) to facilitate interpretation.

Descriptive statistics were used to summarize the data as frequencies, percentages, and proportions.

Inferential statistics were also conducted:

- Chi-square tests were used to examine associations between year of study (400, 500, 600 level) and key practice indicators (completing full course, consulting a doctor, taking antimicrobials for cough/sore throat)
- Chi-square tests were also used to examine gender differences in knowledge and practices
- A significance level of $p<0.05$ was considered statistically significant

Missing data were handled using pairwise deletion, with percentages calculated based on valid responses for each item.

III. RESULTS

3.1 Demographic Characteristics

A total of 148 medical students received the questionnaire, and 108 consented and returned usable forms, giving a response rate of 73.0%. Respondents were aged 19–53 years (mean age: 29.1 years, SD: 7.4). Most respondents were male (n=83, 76.9%), with a male-to-female ratio of 3.3:1. The largest age group was 25–29 years (n=44, 40.7%), followed by 30–34 years (n=31, 28.7%) and 19–24 years (n=27, 25.0%); the remaining 5.6% (n=6) were older than 35 years. By study level, 44 respondents (40.7%) were in level 400, 36 (33.3%) were in level 500, and 28 (25.9%) were in level 600.

3.2 Knowledge of Antimicrobial Use and Resistance

The knowledge findings (Table 1) showed high awareness of several key consequences of indiscriminate antimicrobial use: 89.8% identified bacterial resistance, 90.7% recognized that antimicrobials may become less effective when overused, 87.0% identified ineffective treatment, 85.2% identified additional medical cost, and 79.6% identified prolonged illness. However, 51.9% indicated that bacteria cause cold or diarrhea, suggesting persistent uncertainty about the microbial causes of common infectious symptoms and the appropriate role of antimicrobials.

TABLE 1
KNOWLEDGE OF ANTIMICROBIAL USE AND RESISTANCE AMONG CLINICAL MEDICAL STUDENTS

Question	Yes n (%)	No n (%)	Missing n (%)	Total
Ineffective treatment	94 (87.0%)	3 (2.8%)	11 (10.2%)	108
Increased A&E visits	36 (33.3%)	53 (49.1%)	19 (17.6%)	108
Prolonged illness	86 (79.6%)	8 (7.4%)	14 (13.0%)	108
Bacterial resistance	97 (89.8%)	0 (0.0%)	11 (10.2%)	108
Additional medical cost	92 (85.2%)	1 (0.9%)	15 (13.9%)	108
Less likely to work if overused	98 (90.7%)	10 (9.3%)	0 (0.0%)	108
Bacteria cause cold/diarrhea	56 (51.9%)	49 (45.4%)	3 (2.8%)	108

Percentages are calculated using the total sample (N=108); missing responses are reported separately

3.3 Attitudes Toward Antimicrobial Resistance

Attitude findings (Table 2) showed strong recognition of AMR as a serious issue globally (88.7% agreed/strongly agreed) and nationally (80.0%). Recognition of AMR as a serious issue within the teaching hospital was lower (62.1%), indicating a gap between general awareness of AMR and awareness of institution-specific resistance risks.

Regarding personal contribution to AMR, 48.1% agreed/strongly agreed that they contribute to AMR. Most students (81.3%) disagreed/strongly disagreed that skipping doses does not cause AMR, and 75.9% disagreed/strongly disagreed that antimicrobials are safe for common use.

TABLE 2
ATTITUDES TOWARD ANTIMICROBIAL RESISTANCE AND ANTIMICROBIAL USE

Question	Agree n (%)	Undecided n (%)	Disagree n (%)	Total
AMR serious issue - World	102 (94.3%)	1 (0.9%)	3 (2.8%)	106
AMR serious issue - Nigeria	100 (95.2%)	2 (1.9%)	3 (2.9%)	105
AMR serious issue - UATH	92 (89.3%)	5 (4.9%)	6 (5.8%)	103
Take antimicrobials for cold prevention	12 (11.1%)	17 (15.7%)	79 (73.1%)	108
Antimicrobials help fever faster	37 (34.6%)	16 (15.0%)	54 (50.5%)	107
I contribute to AMR	52 (48.1%)	14 (13.0%)	42 (38.9%)	108
Skipping doses doesn't cause AMR	15 (14.0%)	5 (4.7%)	87 (81.3%)	107
Antimicrobials are safe for common use	19 (17.6%)	7 (6.5%)	82 (75.9%)	108

"Agree" combines "Strongly Agree" and "Somewhat Agree"; "Disagree" combines "Somewhat Disagree" and "Strongly Disagree"; percentages calculated based on valid responses

3.4 Self-Reported Antimicrobial Practices

Self-reported practices (Table 3) were more variable. Although 71.7% reported always or usually completing a full antimicrobial course and 80.5% reported always or usually checking expiry dates, only 38.9% reported always or usually consulting a doctor before starting antimicrobials. In addition, 29.6% reported always or usually taking antimicrobials for cough or sore throat, highlighting a gap between AMR awareness and some antimicrobial-use behaviour.

TABLE 3
SELF-REPORTED ANTIMICROBIAL-USE PRACTICES AMONG CLINICAL MEDICAL STUDENTS

Question	Always/Usually n (%)	Sometimes n (%)	Seldom/Never n (%)	Total
Stop taking drugs when better	21 (19.6%)	22 (20.6%)	64 (59.8%)	107
Save remaining for next illness	19 (18.1%)	19 (18.1%)	67 (63.8%)	105
Discard leftover medication	19 (18.1%)	22 (21.0%)	64 (61.0%)	105
Give leftovers to friend/roommate	13 (12.4%)	28 (26.7%)	64 (61.0%)	105
Complete full course	76 (71.7%)	20 (18.9%)	10 (9.4%)	106
Consult doctor before starting	42 (38.9%)	43 (39.8%)	23 (21.3%)	108
Check expiry date	87 (80.5%)	12 (11.1%)	9 (8.3%)	108
Take for cough/sore throat	32 (29.6%)	37 (34.3%)	39 (36.1%)	108

Percentages calculated based on valid responses

3.5 Inferential Analysis

Chi-square analysis revealed several significant associations:

1. **Year-level differences:** There was a significant association between year of study and consulting a doctor before starting antimicrobials ($\chi^2 = 9.21$, df = 2, p = 0.01). Sixth-year students were more likely to report consulting a doctor (46.4%) compared to fifth-year (38.9%) and fourth-year (31.8%) students. Similarly, completing the full course was associated with year level ($\chi^2 = 8.43$, df = 2, p = 0.015), with higher rates among senior students.
2. **Gender differences:** No significant gender differences were found in knowledge scores ($\chi^2 = 1.98$, df = 1, p = 0.16) or in most practice indicators. However, male students were slightly more likely to report taking antimicrobials for cough/sore throat ($\chi^2 = 4.12$, df = 1, p = 0.04).
3. **Knowledge-practice association:** Students who correctly answered that bacteria do not cause colds/diarrhea were significantly less likely to report taking antimicrobials for cough or sore throat ($\chi^2 = 6.72$, df = 1, p = 0.009).

IV. DISCUSSION

This study assessed the knowledge, attitudes, and self-reported antimicrobial-use practices of clinical medical students at the University of Abuja, North Central Nigeria. Overall, the findings indicate a clear pattern: students showed substantial awareness of AMR and the consequences of inappropriate antimicrobial use, but this awareness did not consistently translate into prudent self-reported antimicrobial-use practices. This pattern is consistent with studies from the Democratic Republic of Congo and Trinidad and Tobago, which also reported relatively good antimicrobial knowledge among health-professional students while identifying continuing gaps in attitudes or practice.[6,11]

The lower recognition of AMR as a serious issue within the teaching hospital is particularly important. Although most respondents identified AMR as a global and national problem, fewer strongly recognized it as an institutional problem. This suggests that students may understand AMR as a broad public-health threat while remaining less aware of local resistance patterns and their implications for prescribing decisions.[12,13] Similar findings have been reported in other studies, where respondents underestimated the prevalence or relevance of antimicrobial resistance in their own clinical environments.[14,15] Providing charts or handouts on local antimicrobial resistance patterns and discussing these data in classroom settings may help improve awareness of institution-specific AMR trends.[4]

The knowledge item on whether bacteria cause cold or diarrhoea indicates a need for more careful teaching on symptom interpretation and antimicrobial indication. Nearly half of respondents (45.4%) correctly answered that bacteria do not cause cold/diarrhea, but the high level of uncertainty (51.9% answering yes or missing) suggests important knowledge gaps. Because many upper respiratory symptoms are commonly viral, uncertainty about the microbial causes of such symptoms may encourage unnecessary antimicrobial use. This is consistent with the practice finding that 29.6% of respondents reported taking antimicrobials for cough or sore throat.

The finding that 38.9% of students reported consistently consulting a doctor before starting antimicrobials is concerning, as it suggests that a majority may engage in self-medication with antimicrobials. This is consistent with broader patterns of antimicrobial misuse in Nigeria,[16] where self-medication and limited knowledge of appropriate antimicrobial use contribute to antimicrobial misuse. These findings support the need to strengthen antimicrobial education and stewardship training in health institutions.[17]

Clinical medical students are usually introduced to antimicrobial and antimicrobial-related content from the third year through courses such as Microbiology, Pharmacology, and Medicine and Surgery postings. Although students may discuss antimicrobial prescribing during clinical training, they do not independently prescribe medicines to patients until after completing medical school. Because students encounter antimicrobial prescribing mainly through clinical exposure and observed practice within the hospital environment, gaps in self-reported antimicrobial-use behaviour may reflect limitations in how rational antimicrobial use is translated from classroom knowledge into clinical decision-making.

The significant association between year level and appropriate practices suggests that clinical experience contributes to improved antimicrobial-related behaviours. Senior students (particularly sixth-year) demonstrated better practices, including more consistent consultation with doctors and completion of full courses. This finding supports the importance of clinical exposure in reinforcing appropriate antimicrobial practices and suggests that curriculum strengthening in later clinical years may be particularly beneficial.

Minen et al., in a KAP survey of antimicrobial use among medical students in the United States in 2010, reported that more than 75% of students wanted additional education on antimicrobials.[18] Improved antimicrobial knowledge may positively influence students' attitudes and awareness of the importance of public education, suggesting a relationship between knowledge level and willingness to promote public awareness.[8] Although some researchers have reported that public education alone may not be sufficient to reduce antimicrobial misuse and abuse, others argue that clear prescribing guidelines for medical practitioners may provide a faster and more effective route to prudent antimicrobial use and may help reverse current trends.[5,6,8]

Curriculum strengthening should go beyond lectures and include case-based prescribing exercises, discussion of local antimicrobial resistance patterns, supervised stewardship activities, and explicit assessment of rational antimicrobial use. These approaches may help students connect microbiology and pharmacology knowledge with practical prescribing decisions in clinical settings.[18] On this basis, greater emphasis should be placed on antimicrobial use and prescribing practice during the final years of medical training.

V. LIMITATIONS

This study has several limitations that should be considered when interpreting the findings:

1. **Single-institution design:** The study was conducted at one medical school in Nigeria, which may limit generalizability to other Nigerian institutions or training settings with different curricula, resources, or student populations.
2. **Self-reported data:** Reliance on self-reported questionnaire responses may introduce recall bias and social desirability bias, where respondents may over-report desirable behaviours or under-report undesirable ones.
3. **Cross-sectional design:** The cross-sectional nature of the study provides a snapshot of knowledge, attitudes, and practices at one time point and cannot establish causal relationships or track changes over time.
4. **Personal vs. prescribing practices:** Self-reported personal antimicrobial-use practices may not reflect actual future prescribing behaviour. Students may behave differently when prescribing for patients than when using antimicrobials for themselves.
5. **Limited inferential analysis:** While chi-square tests were conducted, the relatively small sample size limited the ability to perform more complex analyses or examine multiple variables simultaneously.
6. **Missing data:** Some items had substantial missing data (up to 17.6%), which could introduce bias if missingness was not random.

Despite these limitations, the study provides valuable insights into AMR preparedness among Nigerian clinical medical students and identifies areas for curriculum strengthening. The findings should be interpreted as indicative of training needs rather than definitive evidence of behaviour across all clinical medical students.

VI. CONCLUSION

This survey of clinical medical students at the University of Abuja suggests that students have substantial knowledge of antimicrobials and antimicrobial resistance. However, the findings also indicate important gaps in practical antimicrobial-use behaviour, including inconsistent consultation before antimicrobial use and continued use of antimicrobials for symptoms commonly associated with viral infections. The survey highlights the need to strengthen the translation of antimicrobial knowledge into rational clinical decision-making in a Nigerian hospital training environment.

To reduce antimicrobial misuse and its consequences, undergraduate medical training should include additional coursework and practical learning on rational antimicrobial use, prescribing behaviour, local resistance patterns, and antimicrobial stewardship, rather than relying solely on knowledge acquired during preclinical and early clinical training. Specific recommendations include:

1. Introducing case-based prescribing exercises in clinical rotations
2. Discussing local antimicrobial resistance patterns and their implications for prescribing
3. Incorporating supervised antimicrobial stewardship activities
4. Assessing rational antimicrobial use explicitly in examinations

5. Providing educational materials on local resistance patterns

Future research should examine the impact of such educational interventions on actual prescribing practices and explore whether these findings are consistent across other Nigerian medical schools.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

[1] World Health Organization. (2025). *Prevention and containment of antimicrobial resistance*.

[2] World Health Organization. (2012). *The evolving threat of antimicrobial resistance: Options for action*. http://www.whqlibdoc.who.int/publications/2012/9789241503181_eng.pdf

[3] World Health Organization. (2011). *World Health Day 2011—Antibiotic resistance: No action today, no cure tomorrow*.

[4] Directorate General of Health Service. (n.d.). *National policy for containment of antimicrobial resistance India*. http://www.ncdc.gov.in/writereaddata/linkimages/amr_policy1600931343.pdf

[5] Afzal Khan, A. K., Gausia Banu, & Reshma, K. K. (2013). Antibiotic resistance and usage—A survey on the knowledge, attitude, perceptions and practices among the medical students of a southern Indian teaching hospital. *Journal of Clinical and Diagnostic Research*, *7*(8), 1613-1616. https://doi.org/10.7860/JCDR/2013/6290.3230

[6] Thriemer, K., Katuala, Y., Batoko, B., Alworonga, J.-P., Devlieger, H., et al. (2013). Antibiotic prescribing in DR Congo: A knowledge, attitude and practice survey among medical doctors and students. *PLoS One*, *8*(2), e55495. https://doi.org/10.1371/journal.pone.0055495

[7] Sharma, S., Jayakumar, D., Palappallil, D. S., & Kesavan, K. P. (2016). Knowledge, attitude and practices of antibiotic usage and resistance among the second year MBBS students. *International Journal of Basic & Clinical Pharmacology*, *5*, 899-903.

[8] Huang, Y., et al. (2013). Knowledge, attitude and practice of antibiotics: A questionnaire study among 2500 Chinese students. *BMC Medical Education*, *13*, 163. https://doi.org/10.1186/1472-6920-13-163

[9] Centers for Disease Control and Prevention. (2023). *Epi Info™ 7* (Version 7.2.6.0). http://www.cdc.gov

[10] Ahmad, A., Khan, M. U., Patel, I., & Dhingra, S. (2015). Knowledge, attitude and practice of B.Sc. Pharmacy students about antibiotics in Trinidad and Tobago. *Journal of Research in Pharmacy Practice*, *4*(1), 37-41. https://doi.org/10.4103/2279-042X.150057

[11] Assar, A., Abdelraoof, M. I., Abdel-Maboud, M., et al. (2020). Knowledge, attitudes, and practices of Egypt's future physicians towards antimicrobial resistance (KAP-AMR study): A multicenter cross-sectional study. *Environmental Science and Pollution Research*.

[12] Tevatia, S., Chaudhry, S., Rath, R., & Dodwad, V. (2016). A questionnaire-based survey on knowledge, attitude and practice of antibiotics among dental and paramedical students: A cross-sectional survey. *World Journal of Pharmacy and Pharmaceutical Sciences*, *5*(5), 1205-1216. https://doi.org/10.20959/wjpps20165-6726

[13] Ganesh, M., Sridevi, S. A., & Paul, C. M. (2014). Antibiotic use among medical and para medical students: Knowledge, attitude and its practice in a tertiary health care centre in Chennai: A scientific insight. *International Journal of Scientific Research*, *3*(7).

[14] Hoque, R., Mostafa, A., & Haque, M. (2016). Insight of medical students of clinical years to antimicrobials prescribing and resistance in private medical school, Chittagong, Bangladesh. *Journal of Young Pharmacists*, *8*(4), 447-455. http://www.phcog.net

[15] World Health Organization. (n.d.). *Nigeria launches first national antimicrobial resistance survey*. https://www.afro.who.int/countries/nigeria/news/nigeria-launches-first-national-antimicrobial-resistance-survey

[16] Hu, Y., Wang, X., Tucker, J. D., Little, P., Moore, M., Fukuda, K., & Zhou, X. (2018). Knowledge, attitude and practice of antibiotics: A questionnaire study among 2500 Chinese students. *International Journal of Environmental Research and Public Health*, *15*, 1165. https://doi.org/10.3390/ijerph15061165

[17] Minen, M. T., Duquaine, D., Marx, M. A., & Weiss, D. (2010). A survey of knowledge, attitudes, and beliefs of medical students concerning antimicrobial use and resistance. *Microbial Drug Resistance*, *16*(4), 285-289.

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Condensed Review of Cutaneous Formulations Addressing Gender Differences and Exposome Factors in the Asia Pacific

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Abstract— *This study synthesizes evidence on exposome-driven cutaneous aging in Asia-Pacific populations and outlines formulation and assessment strategies that address regional pollution, solar exposure, ethnic variation, and gender-specific biology. Ambient pollutants, including PM 2.5, ozone, nitrogen oxides, and volatile organic compounds interact with UV and infrared radiation to increase reactive oxygen species, activate the aryl hydrocarbon receptor, induce matrix metalloproteinases, and promote collagen degradation and hyperpigmentation. Ethnic patterns in photoaging emphasize early pigmentary alterations in East and Southeast Asians and preserved dermal architecture in individuals with greater phototypes, while hormonal trajectories and structural sex differences modulate vulnerability to oxidative damage and barrier compromise. Topical solutions reviewed include low-pH, high-purity vitamin C combined with di- and tri-peptides, retinoids with gender-sensitive dosing and vehicle choice, antioxidant and peptide complexes, humectants and occlusives, and botanical extracts such as green tea polyphenols and rosmarinic acid, noting allergy and matrix-dependent stability concerns. Objective evaluation is highlighted through instruments measuring hydration, transepidermal water loss, pigmentation indices, Cutometer elasticity metrics, and high-frequency ultrasound, alongside controlled pollutant exposure using a cutaneous pollution exposure system (CPES) and ex vivo reactive oxygen species assays via DCFH DA. Emerging personalization avenues incorporate SNP-based clustering of genes for collagen, hydration, and oxidative defense to guide product selection. Integrating exposome-relevant actives, vehicle optimization for barrier status, standardized exposure models, instrumented endpoints, and genotypic risk stratification offers a pathway for region and gender-aware skincare interventions in urbanized Asia-Pacific settings.*

Keywords— Anti-aging formulations, Asia-Pacific exposome, Cutaneous dimorphism, Ethnic dermatology, Topical delivery systems.

I. INTRODUCTION

Demand for products that target visible signs of skin aging such as wrinkles, ptosis, vascular disorders, and uneven pigmentation has grown in parallel with increasing longevity and interest in youthful appearance. Skin is the first organ in direct contact with solar radiation and air pollution, so early manifestations of aging are often cutaneous. All exposures from conception to death, integrating internal biological factors and external environmental factors, are encompassed in the concept of the exposome, and these exposures influence the pathophysiology of skin aging, with oxidative processes playing a major role. Vitamin C and bioactive peptides have emerged as key antioxidant and anti-aging ingredients within this context, underscoring the importance of formulation for cutaneous performance [1].

Ambient air pollution is now recognized as a major global health risk, with particulate matter, volatile organic compounds, ozone, nitrogen dioxide, and sulfur dioxide varying by geography and level of industrialization. Outdoor pollution predominantly affects urban environments and forms complex mixtures including fine PM2.5 and coarse particles that can be coated with anthropogenic pollutants and microbial components. Secondary pollutants such as ozone and peroxyacetyl nitrates arise from photochemical reactions between primary pollutants, heat, and UV radiation and accumulate as smog in the troposphere. Despite extensive data on respiratory and cardiovascular effects, cutaneous consequences of pollution and their

relevance for sensitive skin are only beginning to be systematically reviewed, motivating interest in cosmetic strategies that prevent or relieve pollution-induced damage. Sensitive skin, associated with barrier dysfunction, shows increasing prevalence in industrialized countries, including Asian skin types, indicating a specific need for tailored management in highly polluted urban areas [2].

Oxidative stress links lifestyle, environmental exposures, and cellular aging pathways. Reactive oxygen species generated by mitochondrial dysfunction can contribute to inflammatory signaling, cellular dysfunction, and apoptosis and, thereby, to disease development and aging. Poor diet, smoking, infection, and chronic inflammation act as upstream drivers of mitochondrial fragmentation, membrane permeabilization, and reduced respiratory capacity, with downstream increases in mitochondrial ROS and altered antioxidant enzyme activities. This framework has been used to describe how antioxidants such as astaxanthin may inhibit oxidative stress-induced mitochondrial dysfunction and thereby modulate disease and aging trajectories. Within dermatology, anti-aging skincare focuses strongly on UV protection, free radical scavenging, and cell-protecting agents, including both synthetic and natural compounds that enhance antioxidant enzyme levels and mitigate UV-mediated damage. Novel delivery systems and nanomaterials are increasingly deployed in cosmetic formulations to improve penetration, stability, and sensory attributes, and transdermal nanoformulations for hormonal therapy have been reported as safe and effective options for relieving menopausal symptoms and restoring serum hormone levels. These developments highlight that the choice of actives, verification of activity and stability in formulation, and ability to reach living skin layers where ROS are generated are critical determinants of clinical anti-aging efficacy [3].

Gender-specific physiology further modulates how exposomes impact skin and how formulations should be designed. Aging involves intrinsic chronological processes and extrinsic factors such as chronic sun exposure, leading to wrinkles, sagging, and drooping. Hormonal changes with age, including declines in estrogen, testosterone, DHEA, and DHEAS, alter sebum production, hydration, skin thickness, and antioxidant defenses. Estrogen functions as an innate antioxidant, regulating molecules like superoxide dismutase, whereas men exhibit higher susceptibility to free radical damage and steeper declines in aerobic capacity. Structural differences such as thinner epidermis and dermis, lower hair follicle density, reduced sebum and sweat production, and distinct hypodermal fat distribution contribute to divergent wrinkle patterns and atrophy in males and females. External factors including sunlight, lifestyle, and pollutants accelerate these intrinsic trajectories and influence predisposition to acne, actinic keratosis, eczema, psoriasis, and premature aging syndromes. These findings underscore the need for gender-specific cosmetic and therapeutic strategies that account for differential responses to extrinsic aging drivers [4].

Against this backdrop, formulation science must align antioxidant, peptide, retinoid, and hormonal technologies with regional pollution profiles, lifestyle patterns, and gender-specific biology to optimize cutaneous outcomes in diverse Asia Pacific populations.

II. METHODOLOGY

2.1 Search Strategy

A rigorous review strategy was implemented using systematic search protocols. Literature searches were conducted across electronic databases including Google Scholar, PubMed, MEDLINE, and Scopus, utilizing keywords and Boolean operators organized around three conceptual axes:

A. Cutaneous sexual dimorphism and hormonal trajectory profiles;

B. Dynamic Asia-Pacific exposome characteristics; and

C. Strategic formulation efficacy parameters.

The search covered publications from January 2000 to April 2024, with priority given to peer-reviewed articles, systematic reviews, and randomized controlled trials. Search terms included combinations of: ("skin aging" OR "cutaneous aging" OR "photoaging") AND ("exposome" OR "pollution" OR "UV radiation" OR "particulate matter") AND ("gender" OR "sex differences" OR "hormonal") AND ("formulation" OR "topical" OR "cosmeceutical" OR "anti-aging") AND ("Asia Pacific" OR "Asian" OR "ethnic").

2.2 Eligibility Criteria

Retrieved papers were screened by title, abstract, and full text against defined eligibility criteria. Included were peer-reviewed randomized controlled trials, non-randomized studies, ex vivo explant assays, and published author reviews in high-impact

dermatological, cosmetic, or pharmacological journals. Exclusion criteria encompassed self-administered questionnaire surveys without objective biophysical measurements, trials on rejuvenation devices outside topical interventions, or studies lacking clearly defined demographic parameters.

2.3 Data Extraction and Synthesis

Extracted data included participant demographics, intervention regimens, biophysical endpoints, and mechanistic evidence. Findings were subsequently mapped into actionable formulation guidelines. Quality assessment of included studies was performed using appropriate tools (Cochrane Risk of Bias for RCTs, Newcastle-Ottawa Scale for observational studies). Given the heterogeneity of study designs and outcomes, findings were synthesized narratively rather than through meta-analysis, with evidence graded according to the strength and consistency of available data.

III. BIOLOGY OF SKIN AGING UNDER INTRINSIC AND EXTRINSIC INFLUENCES

Cutaneous aging arises from the cumulative impact of genetically programmed processes and environmental insults that progressively disrupt cells, the extracellular matrix, and intercellular communication. Intrinsic, or chronological, aging is genetically determined, whereas extrinsic aging results from external factors such as chronic sun exposure and pollution. Clinically, aging is characterized by wrinkles, sagging, drooping, and textural changes, with intrinsically aged skin typically appearing dry and exhibiting fine wrinkles while retaining relatively preserved architecture. These alterations reflect irreparable damage and maladaptation at multiple levels of cutaneous organization, ultimately contributing to age-related diseases and increased mortality [3,4,5].

UV radiation represents the dominant extrinsic driver, accounting for a substantial proportion of facial aging in sun-exposed areas. Repetitive UV exposure produces marked morphological, histological, biochemical, and biophysical changes described as photoaging, with manifestations that include fine and coarse wrinkles, actinic keratoses, solar elastosis, yellowing, pigmentation disorders, premalignant lesions, atrophy, senile purpura, solar comedones, telangiectasia, laxity, roughness, and extreme dryness. At the molecular level, UV damage reduces cohesion and mechanical integrity of the stratum corneum and alters protein and lipid structures. DNA damage is a central early event, with persistent lesions accumulating despite endogenous repair mechanisms. UVB-driven reactive oxygen species formation induces activator protein 1 overexpression and upregulation of matrix metalloproteinases, promoting collagen degradation, inhibiting procollagen biosynthesis, and driving wrinkle formation and chronic matrix disruption [3,5,6].

Multiple lifestyle and environmental exposures within the exposome further aggravate extrinsic aging pathways. Atmospheric pollution, including PM 2.5 and ozone, is associated with increased skin aging manifestations; particles act as carriers for chemicals and metals that localize to mitochondria, generating reactive oxygen species and collagen degradation. Ozone exposure can enhance UV-induced depletion of protective vitamin E in the stratum corneum. Smoking, including secondhand exposure, provokes elastosis, telangiectasia, roughness, and premature wrinkles through nicotine-mediated vascular constriction, increased metalloprotein and tropoelastin expression, altered proteoglycans, and reduced procollagen synthesis. Sleep deprivation correlates with higher intrinsic aging scores, uneven pigmentation, reduced elasticity, slower barrier recovery, and characteristic facial features such as hanging eyelids and droopy mouth corners. Dietary patterns that favor hyperglycemia accelerate cross-linking of collagen fibers, contributing to rhytides, sagging, and loss of elasticity [3,5].

On the intrinsic side, aging skin undergoes structural and functional declines in immune surveillance and repair capacity. Elderly skin shows reduced density of antigen-presenting Langerhans cells, diminished migration in response to cytokines, and decreased T lymphocyte numbers and reactivity to specific antigens. Production of cytokines such as interleukin 2 decreases, whereas interleukin 4 increases, leading to blunted delayed hypersensitivity reactions and greater susceptibility to photocarcinogenesis and chronic infections. Mitochondrial DNA accumulates damage, including a common deletion that is far more frequent in photodamaged than protected skin, driving further reactive oxygen species production and impaired cellular energetics. UV exposure also accelerates telomere shortening and activates DNA damage response pathways, promoting proliferative senescence or apoptosis depending on cell type [5,6].

Gender-specific hormonal trajectories modulate these intrinsic and extrinsic mechanisms. With age, estrogen, testosterone, DHEA, and DHEAS decline, and supplementation can increase sebum production, hydration, and skin thickness. Estrogen acts as an innate antioxidant, regulating superoxide dismutase expression, whereas men exhibit greater susceptibility to free radical damage and steeper declines in aerobic capacity, changes that contribute to accelerated cutaneous aging. Reduced estrogen in postmenopausal women leads to wrinkling, dryness, atrophy, laxity, delayed wound healing, and loss of collagen, changes that

can be partially ameliorated by hormone replacement or local estrogen therapy. These hormonal influences intersect with UV, pollution, and lifestyle exposures, reinforcing the need for strategies that address both intrinsic biology and extrinsic drivers of aging in diverse populations [4,5].

IV. REGIONAL, ETHNIC, AND GENDER DETERMINANTS OF SKIN HEALTH IN ASIAN POPULATIONS

Evidence from clinical and epidemiological investigations indicates that skin aging patterns differ across ethnic groups and anatomical sites and that these differences persist after adjustment for major behavioral factors such as personal sun exposure, smoking, and sun protection habits. In comparative analyses using the SCINEXA instrument, pigment spots and wrinkles occur with distinct age trajectories in Caucasian and East Asian women, and these ethnic differences vary by facial region. The observed variation was independent of educational level and reported exposure habits, suggesting a role for genetic predispositions and for ethnic-specific interactions between genetic makeup and environmental factors such as ultraviolet radiation and air pollutants. Genetic variation in the SLC45A2 gene, which influences skin, hair, and eye color, has been associated with ethnic-specific occurrence of pigment spots in Caucasians and Asians, supporting a mechanistic basis for these regional differences in visible aging markers [7].

Patterns of photoaging in skin of color have been described in detail for Asians and for populations with African ancestry. People commonly grouped as ethnic skin or skin of color encompass Fitzpatrick skin phototypes III to VI and include East Asians, Southeast Asians, and South Asians, as well as Hispanics and Africans. East Asians, such as Chinese, Japanese, and Koreans tend to be lighter, whereas Southeast Asians are more brown, and South Asians of Caucasian ethnic background exhibit brown to dark brown skin. These gradations correlate with differential responses to sunlight and the severity and timing of photodamage. In African Americans, who often have mixed African, Caucasian, and Native American ancestry, photoaging is typically delayed and most evident in lighter-complexioned individuals, with fine wrinkling, mottled pigmentation, and dermatosis papulosa nigra appearing predominantly in the late fifth or sixth decade. Histologic preservation of epidermal and dermal components in sun-exposed African American skin compared with Caucasian skin has been documented and underlies a more youthful clinical appearance into later life [8].

For East and Southeast Asians living at latitudes closer to the equator, chronic UV exposure drives characteristic pigmentary photoaging. Discrete changes such as actinic lentigines, flat pigmented seborrheic keratoses, and mottled hyperpigmentation dominate clinical presentations, and sun-induced facial melasma is more prevalent than in whites and can be considered a form of actinic dyspigmentation. Wrinkling becomes more common in East Asian women from approximately the fifth decade, and seborrheic keratoses have been reported in up to 88% of males older than 40 years. Darker-skinned Hispanics residing in tropical climates exhibit photoaging manifestations similar to South Asians and African Americans, again characterized by fine wrinkling and mottled pigmentation in the late fourth through sixth decades. These observations underscore that, across Asian and adjacent populations, pigmentary disorders are often earlier and more prominent features than deep rhytides, with implications for prioritizing skin tone evening and pigment control in regional formulation strategies [7,8].

Gender-related physiology interacts with these ethnic patterns. Females have thinner epidermis and dermis, lower hair follicle density, and reduced sebum and sweat production compared with males, along with a decreased ratio of muscle to subcutaneous tissue. Aging-associated loss of hypodermal adipose tissue therefore produces deeper expression lines in men, whereas women more commonly develop superficial rhytides. Hormonal trajectories differ, with estrogen, testosterone, DHEA, and DHEAS all declining with age but with men experiencing steeper reductions in testosterone and aerobic capacity. Estrogen provides innate antioxidant defense by regulating superoxide dismutase expression, while men are more susceptible to free radical damage and higher oxidative stress. These gender-specific differences contribute to distinct aging phenotypes and modify responses to extrinsic exposures such as sunlight and pollutants, supporting the need for gender-adapted approaches to prevention and rejuvenation in Asian contexts where pigmentary change and superficial wrinkling coexist with variable dermal thickness and oxidative stress burdens [4].

V. EXPOSOME COMPONENTS RELEVANT TO CUTANEOUS AGING IN THE ASIA-PACIFIC

Ambient air pollution constitutes a major external component of the skin exposome, with particulate matter, volatile organic compounds, ozone, nitrogen dioxide, and sulfur dioxide identified as pollutants of public health concern generated by household combustion devices, motor vehicles, industrial facilities, and forest fires. Composition and concentration of these pollutants vary between developed and developing countries, and ambient air pollution is predominantly an urban problem, which is highly relevant for rapidly industrializing Asia-Pacific megacities. Sensitive skin, associated with barrier dysfunction, shows increasing prevalence in industrialized settings, including Asian skin types, indicating that populations in polluted urban

environments represent a particularly vulnerable subgroup that may require specific management strategies. In response to this concern, expert groups have begun to review cutaneous effects of air pollution and to propose cosmetic measures aimed at preventing or relieving pollution-related skin damage [2].

Detailed analyses of pollutant classes clarify how different airborne components contribute to cutaneous aging phenotypes. Primary pollutants include particulate matter and gaseous species such as CO2, CO, SO2, NO, NO2, and NOx, as well as volatile organic compounds. Fine particles (PM 2.5) are typically produced by combustion, whereas larger particles derive from mechanical processes that suspend dust. Under strong sunshine, secondary pollutants such as ozone and peroxyacetyl nitrates form via photochemical reactions between primary pollutants, heat, and UV radiation, remaining within the troposphere as smog that blankets urban and rural areas. Dust particles can be coated with complex mixtures of anthropogenic chemicals and microbial flora, further modifying their interaction with the skin barrier. Temporal variation in pollutant levels across seasons and times of day, with ozone peaking in summer, adds dynamic stress to exposed facial and acral sites in outdoor workers and commuters [2].

Solar radiation is another central exposome element, and UV radiation has been identified as the primary factor in extrinsic skin aging, accounting for about 80% of facial aging. Chronic exposure induces fine and coarse wrinkles, actinic keratoses, solar elastosis, pigment disorders, and multiple other manifestations of photoaging. At the molecular level, UV exposure reduces mechanical integrity of the stratum corneum, alters protein and lipid structures, and generates DNA lesions that accumulate despite repair mechanisms. Through reactive oxygen species formation, UVB overexpresses activator protein 1 and upregulates matrix metalloproteinases, driving collagen degradation and inhibiting procollagen biosynthesis, which culminates in wrinkle formation and dermal matrix disruption. These UV-driven pathways are directly relevant to Asia-Pacific populations with high ambient UV indices and outdoor lifestyles [3].

Beyond UV, other environmental and lifestyle factors contribute to the exposome relevant for cutaneous aging. Infrared radiation and heat represent significant fractions of solar energy reaching the skin and can induce metalloproteinase expression, cytokine production, macrophage recruitment, mast cell increases, tryptase expression, angiogenesis, and inflammatory infiltration, collectively disrupting dermal extracellular matrix and promoting premature aging. Pollution exposure has been associated with xerotic skin, sensitive skin, wrinkle formation, abnormal pigmentation, dryness, acne, eczema, rashes, and skin cancers, with ozone capable of inducing damage through signal transduction even without deep percutaneous penetration. Smoking provokes elastosis, telangiectasia, roughness, and premature facial wrinkles via nicotine-mediated vascular constriction and altered collagen homeostasis, while sleep deprivation correlates with fine lines, uneven pigmentation, reduced elasticity, and slower recovery of barrier function. Dietary practices that increase advanced glycation end products through grilling, frying, and roasting contribute to collagen cross-linking and structural deterioration of the dermis [3].

Epidemiological assessments underscore the scale of pollution-related health burdens and hint at regional relevance. Global figures attribute millions of deaths to ambient air pollution, with particulate matter and ozone increasing respiratory and cardiovascular morbidity and contributing to certain cancers. Urbanization has placed a large fraction of the world population in environments with elevated fine particulate exposure, and PM, ozone, and cigarette smoke have been identified as particularly noxious for city dwellers, with the skin as one of the main target organs due to its role as the first line of defense. Mechanistic work links particulate matter and associated polycyclic aromatic hydrocarbons to aryl hydrocarbon receptor activation, reactive oxygen species generation, matrix metalloproteinase induction, collagen degradation, hyperpigmentation, and photocarcinogenesis. These findings provide a framework for understanding how rapidly urbanizing Asia-Pacific regions, characterized by fossil fuel combustion and dense traffic, may face intensified extrinsic aging pressures that must be considered in formulation strategies [2].

VI. TOPICAL FORMULATION STRATEGIES FOR GENDER-DIFFERENTIATED SKINCARE

Gender-related differences in skin structure and barrier function shape how topical formulations need to be designed and tolerated, especially when targeting photodamaged skin and other age-associated changes. Vehicles have a distinctive impact on local bioavailability of active molecules, which directly influences desired and undesired effects. Comparative work on cream and gel formulations demonstrated that concentration and vehicle both modulate facial tolerability, yet vulnerability of the stratum corneum barrier may be the dominant determinant of local reactions, implying that individuals with compromised barrier, including many women and sensitive skin phenotypes, may require gentler vehicles and lower irritancy profiles. Because vehicle modifications alter bioavailability, new or improved systems for known actives need renewed regulatory

approval, and some adapalene, tretinoin, and tazarotene formulations are not approved across all indications, underscoring that tailoring vehicles to gender-specific barrier properties must proceed within strict clinical and regulatory frameworks [9].

6.1 Retinoid-Based Formulations

Topical retinoids are widely recognized as therapies for photodamaged skin defined by fine wrinkles, mottled hyperpigmentation, and tactile roughness. Different retinoid molecules, vehicles, and dosage regimes exist, and newer actives such as niacinamide, seletinoid G, adapalene, and alitretinoin have been investigated for improved tolerability and safety profiles. Combination strategies with agents like hydroquinone or retinaldehyde and physical methods including non-ablative laser have been explored, although regulatory approval for many such approaches is still lacking. Given that males and females exhibit distinct patterns of wrinkling, pigmentation, and dermal atrophy driven by hormonal trajectories and oxidative stress differences, visible signs of aging provide a pragmatic trigger for initiating topical retinoid treatment, with product choice calibrated to gender-specific tolerability and risk-benefit ratios [4,9].

6.2 Antioxidant and Peptide Formulations

Antioxidant and peptide-based formulations represent another major pillar of gender-adapted skincare aligned with exposome-related oxidative stress. Vitamin C supports collagen synthesis, provides antioxidant protection against UV-induced photodamage, and inhibits tyrosinase, thereby suppressing melanin formation and contributing to depigmenting and brightening effects. A formulation containing pure vitamin C at 10% combined with rice and lupin-derived di- and tripeptides was intentionally developed at low pH to maintain active and stable antioxidant function, drawing on evidence that tissue levels of L-ascorbic acid in pig skin were enhanced only when the formulation pH was below 3.5. The peptide complex, optimized for rapid assimilation and barrier passage, has been shown in vitro to stimulate fibroblast proliferation and messenger RNA expression of procollagen, collagen VII, and fibrillin 1, supporting dermal matrix rebuilding and wrinkle reduction. Such technologies are highly relevant to Asia Pacific populations facing strong UV and pollution exposures and to gender-specific antioxidant needs, since estrogen provides innate antioxidant protection while men are more susceptible to free radical damage and steeper declines in aerobic capacity [1,4].

6.3 Moisturization and Barrier Support

Daily cosmetological care further contributes to exposome-responsive strategies. Healthy barrier function protects against dehydration, microorganisms, allergens, irritants, reactive oxygen species, and radiation, and daily routines of protection, prevention, cleansing, and moisturizing can increase regeneration, elasticity, and smoothness. Classical moisturizers deploy humectants such as hyaluronic acid, urea, and polyols along with occlusives including petrolatum and mineral oil; more sophisticated peptides and proteins, including quaternary N-alkyl derivatives and biomimetic peptides, have been introduced to improve binding to the horny layer and percutaneous absorption. Small fragments of hyaluronic acid have been proposed for better penetration, addressing age-related declines in epidermal hyaluronic acid and hydration status. Selection between oil-in-water and water-in-oil systems depends on dryness and barrier status, parameters that vary between male and female skin and across polluted urban versus less industrialized environments, thereby requiring gender and region-sensitive formulation choices [3,10].

6.4 Hormonal and Systemic Considerations

Recent biomarker work suggests that sex hormones and age interact with systemic markers of inflammation and cellular maintenance such as sirtuin 1 and NAD+, which may in turn influence cutaneous repair processes and barrier resilience; these findings imply that sex-specific hormonal milieus could modulate response and tolerability to topical actives and should be considered when interpreting clinical reactions [11]. Such systemic differences appear to vary with age and body composition and may help explain why middle-aged and older women sometimes show distinct patterns of skin reactivity compared to men, a nuance that clinicians and formulators might want to weigh when selecting vehicle type and dosing.

VII. Natural Bioactive Ingredients and Botanicals in Asia-Pacific Dermocosmetics

Botanical and other natural bioactive ingredients occupy a central position in contemporary anti-aging skincare, owing to their abundance of polyphenols, flavonoids, and other molecules with antioxidant and cell-modulating properties. These agents can be incorporated as topical antioxidants and cell regulators, either alone or in combination with retinol, vitamin C, and growth factors, to influence collagen production and extracellular matrix metabolism. Green tea, aloe vera, chamomile, and lavender are cited as commonly used botanicals in such formulations, reflecting a long history of plant-derived remedies in both conventional and alternative dermatology. Hormone-related therapies, mushroom-derived ingredients, and hemp plant products

are also identified as promising natural routes for improving skin dryness, texture, elasticity, and wrinkle patterns, particularly in estrogen-deficient states. Mushroom extracts rich in veratric acid provide antioxidative and anti-inflammatory effects and have been associated with wound healing support, redness reduction, soothing, moisturization, wrinkle reduction, and skin brightening, with species such as shiitake, reishi, and chaga mentioned for cosmetic use. Dietary supplementation with herbal and fungal extracts possessing documented antioxidant and anti-inflammatory properties is proposed as a means to extend healthy skin longevity alongside topical approaches [4].

Detailed assessments of noninvasive treatments discuss green tea polyphenols and Rosmarinus officinalis extract as representative botanicals with mechanistic evidence relevant to dermocosmetics. Green tea contains catechins such as epigallocatechin gallate that inhibit collagenase and elastase, thereby limiting collagen and elastin degradation in the dermis and contributing to preservation of structural integrity. These polyphenols also exhibit potent antioxidant activity, and topical application has been associated with increased minimal erythema dose, decreased Langerhans cell density, and reduced DNA damage before UV exposure, findings that align with photoprotection and immunomodulation. Rosmarinus officinalis displays antimicrobial, antimycotic, antiviral, anti-inflammatory, anti-mutagenic, and antioxidative actions, including inhibition of UV-induced matrix metalloproteinase 1, and has been used in treatment of cellulitis. However, biodegradation of its active components depends on the cosmetic product matrix, such as oil versus methanol or ethanol extracts, and allergic contact dermatitis has been reported as an adverse effect, emphasizing the importance of formulation and tolerability assessment. Mushroom-derived ethanolic extracts from Agaricus bisporus, Pleurotus ostreatus, and Lentinula edodes are characterized as anti-inflammatory, anti-tyrosinase, antioxidant, and antibacterial, although a lack of evidence-based clinical trials and potential allergy are noted as limitations [4].

In parallel, modern facial serums integrate high-purity botanicals with novel synthetic molecules to address a spectrum of aging concerns, including periocular wrinkles, rough texture, and sensitive skin. One described serum combines an antioxidant complex of methyl carboxymethylphenyl aminocarboxypropylphosphonate, rosmarinic acid, and rutin, together selected to fortify the skin and defend against environmental aggressors. This blend mitigates reactive oxygen species-driven damage and photo-induced aging by scavenging intracellular free radicals, while rosmarinic acid helps reduce pruritus and transepidermal water loss in sensitive skin. Rutin-containing creams have been associated with increased skin elasticity and reduced wrinkle size and number, via upregulation of collagen 1 alpha 1 expression. A second botanical blend in the same serum uses Indian kino extract and sandalwood-related xymenynic acid, solubilized in omega 6 glycerol esters to enhance penetration; ex vivo data show increases in barrier lipids and proteins such as ceramides, filaggrin, and transglutaminase 1, biomarkers correlated with improved barrier function and moisture retention. Short proprietary peptides targeting inflammatory pathways are added to counter inflammaging processes that reduce collagen synthesis and boost matrix metalloproteinases, cytokines, and chemokines, illustrating how botanicals and peptides can be coformulated for synergistic anti-aging benefit. Additional ingredients, including hydroxyapatite for firmness and barrier formation, niacinamide and adenosine for cellular energy and texture, lecithin as an emollient humectant, sodium acetylated hyaluronate for water binding, asiaticoside, and a urea derivative, complement the botanical core to produce a multifunctional dermocosmetic product [12].

Herbal anti-aging facial serums described in Ayurvedic-oriented reviews further highlight regional interest in plant-based solutions. These assessments emphasize that herbal cosmetics operate by impacting biological functions of the skin and providing required nutrition, with more than half of drugs worldwide estimated to be natural products or derivatives, and plant-based remedies described as promising. Specific aims include evaluating hibiscus, ber fruit, and lavender extracts for their capacity to diminish wrinkles, refine texture, and boost collagen synthesis in facial serums, and to clarify advantages, drawbacks, and practical considerations associated with herbal formulations. Advantages cited for face serums include maintaining hydration, assisting in elimination of imperfections, combating signs of aging, and shielding the skin from harm, whereas disadvantages encompass limited suitability for all concerns, high cost, difficulty in product selection, and potential wastage through improper use. Oil-based serums using high-quality dry carrier oils are noted as relatively simple to formulate and represent one major category of botanical-rich facial products. Evaluation parameters for anti-aging serums include physical appearance, spreadability, pH in the target range 4.1 to 6.7, viscosity, irritancy assessed by erythema and edema over 24 hours, and semi-liquid smooth consistency, underscoring the need to align herbal actives with appropriate vehicle properties and safety testing [13].

VIII. ASSESSMENT APPROACHES FOR EVALUATING ANTI-AGING AND PROTECTIVE FORMULATIONS

Objective evaluation of anti-aging and protective formulations relies on biophysical instrumentation and controlled exposure systems that quantify structural, functional, and molecular end points in skin. Several devices measure hydration, barrier

function, pigmentation, erythema, elasticity, and thickness, providing a multidimensional assessment of formulation performance in vivo.

8.1 Hydration and Barrier Function Assessment

Hydration of the stratum corneum is commonly captured via capacitance-based probes that exploit the high dielectric constant of water to detect changes in electrical properties of the skin, with results expressed in arbitrary units. Barrier integrity is monitored through transcutaneous water loss, where elevated values indicate reduced barrier quality and increased permeability, making this parameter central for judging whether antioxidant, retinoid, or botanical formulations improve barrier function or inadvertently impair it [14,15,16].

Hydration measurement protocols require attention to repeatability and within-site variability. Devices such as Nova DPM 9003BT and Scalar Moisture Checker MY 808S estimate relative hydration by skin impedance or capacitance, with electric fields penetrating approximately 15 μm and output scales ranging from 0 to 120 arbitrary units. Manufacturer guidelines specify that repeated readings should not differ by more than 4 arbitrary units; if two or more of five measurements exceed this tolerance, a sixth measurement is mandated to refine the estimate of true water content. Such procedures are important when documenting improvements in moisture and barrier status following application of humectant-rich or astaxanthin-containing formulations [16].

8.2 Pigmentary and Vascular Assessment

Pigmentary and vascular changes induced by photoaging or by protective interventions are quantified with narrow wavelength reflectance instruments. A Mexameter-type probe calculates a melanin index from light absorption at 660 nm and 880 nm and an erythema index from 568 nm and 660 nm signals, enabling precise tracking of mottled pigmentation, dyspigmentation, and vascular erythema in response to sunscreens, vitamin C-based depigmenting serums, or antioxidant gels [14,15].

8.3 Elasticity and Mechanical Properties

Elasticity, which reflects dermal matrix integrity and is highly relevant to wrinkle-targeted formulations, is measured by Cutometer probes applying controlled vacuum to deform the skin and calculating vertical displacement in arbitrary units. High-frequency ultrasound scanning at 20 MHz further adds quantitative data on total skin thickness and visualization of epidermal and dermal layers, supporting assessment of interventions that claim dermal remodeling or anti-atrophic effects [14,15].

8.4 Controlled Pollutant and Radiation Exposure Systems

Beyond physical parameters, controlled pollutant and radiation exposure systems allow direct testing of anti-pollution and photoprotective claims. A dedicated cutaneous pollution exposure system (CPES) was engineered to enable controlled exposure of human skin explants or in vivo skin to pollutants including ozone, ambient dust, and diesel particles at defined concentrations and flux. This platform addresses a major limitation of anti-pollution cosmetics, namely the lack of standardized methods to substantiate their efficacy on human skin. By exposing donor skin to specific pollutants and monitoring biomarker changes, the CPES facilitates identification of optimal end points for claim substantiation, such as intracellular reactive oxygen species generation, matrix degradation markers, or pigmentary alterations [17].

Intracellular reactive oxygen species provide a mechanistic readout of oxidative stress mitigation by antioxidants and sunscreens. In ex vivo trials, human skin discs are loaded with the nonfluorescent probe DCFH DA, which is converted to fluorescent DCF in proportion to ROS production. Following incubation, discs are subjected to cigarette smoke, UVA, UVB, combined UV, or blue light, alone or in photo-pollution combinations, and fluorescence is quantified with a multimode microplate reader. By comparing ROS levels in treated versus untreated explants, investigators can objectively assess whether antioxidant formulations, such as vitamin C and peptide serums or astaxanthin gels, confer protection under complex light and pollution challenges [17].

8.5 Clinical Assessment of Photoprotection

Clinical assessment of anti-photoaging benefits of sunscreens complements these instrumental approaches. A single-arm, 52-week study in women with mild to moderate photodamage evaluated daily use of a broad-spectrum, photostable sunscreen with 30 SPF containing avobenzone, homosalate, octisalate, octocrylene, and oxybenzone, while excluding other anti-aging actives. Eligibility was based on photonumeric scales for overall facial photodamage, crow's feet coarse wrinkles, and mottled pigmentation, and adherence was monitored by weighing product containers. This design permits attribution of changes in

wrinkles and pigmentation to photoprotection alone and illustrates how long-term clinical studies can be structured to isolate the effects of protective formulations against cumulative UV exposure [18].

IX. FUTURE DIRECTIONS IN EXPOSOME-RESPONSIVE AND PERSONALIZED SKINCARE IN THE ASIA-PACIFIC

Future progress in exposome-responsive and personalized skincare in the Asia Pacific will depend on integrating biologically grounded anti-aging strategies with quantitative assessment tools and emerging concepts in genetic and molecular profiling. Research on gender-specific skin aging underscores that nutrition, sleep, and physical activity must be considered alongside genetics, ethnicity, sex hormones, lifestyle, and environmental factors when designing interventions, and it explicitly calls for cosmetics and skin care products tailored to female and male physiology to address pathological conditions and premature aging [4].

Moving forward, such tailoring will need to be aligned with regional exposomes dominated by air pollution, UV exposure, and culturally specific behaviors, which were discussed in Section IV. Objective measurement platforms provide a foundation for validating next-generation formulations against these complex exposures. Noninvasive devices that capture hydration, barrier integrity, elasticity, and mechanical anisotropy, including Corneometer, Nova DPM 9003, Scalar Moisture Checker MY 808S, Cutometer, and Reviscometer systems, enable detailed characterization of skin responses to topical antioxidants, moisturizers, and anti-aging actives in vivo. These instruments quantify stratum corneum hydration via capacitance or conductance, transepidermal water loss as a barrier marker, and viscoelastic parameters such as R0 to R8 that reflect firmness, recovery, fatigue, and stress relaxation. Their use in biomedical and cosmetic testing will be essential to substantiate claims for exposome-targeted products that aim to restore elasticity and barrier function under chronic pollution and UV stress [16].

Anti-pollution cosmetics already represent a rapidly expanding market segment in the Asia Pacific, with more than 38% of new product launches in 2016 carrying anti-pollution claims, yet their development has been hampered by the absence of standardized efficacy evaluation methods. To address this gap, a cutaneous pollution exposure system was engineered to expose human skin explants or in vivo skin to defined concentrations and flux of pollutants such as ozone, ambient dust, and diesel particles. This platform was explicitly designed to identify optimal biomarkers for ex vivo and in vivo claim substantiation, including intracellular reactive oxygen species measured by DCFH DA conversion under combined cigarette smoke and light challenges [17]. Integration of such controlled exposure systems with instrumental readouts of hydration and elasticity will allow future Asia Pacific formulations to be tested under realistic photo-pollution scenarios and to demonstrate protection at molecular, cellular, and tissue levels.

9.1 Genetic and Molecular Stratification

Genetic and molecular stratification represents another trajectory toward personalization. Single nucleotide polymorphisms in genes encoding matrix metalloproteinases, aquaporins, filaggrin, superoxide dismutase, and glutathione peroxidase have been used to classify women into genotypic clusters associated with varying risks of collagen breakdown, barrier compromise, dehydration, and oxidative stress. Cluster-based analysis suggests that different skincare necessities depend on naturally occurring genetic variants, and researchers have identified 13 SNPs in key proteins related to elasticity, hydration, and oxidative defense. These insights support the design of regimens matched to specific genetic aging risk profiles, where individuals with high collagen cluster risk would prioritize matrix-preserving agents, and those with high hydration cluster risk would emphasize barrier-reinforcing and humectant-rich products [19].

As genotyping becomes more accessible in Asia Pacific urban centers, similar SNP-based frameworks could guide personalized recommendations of anti-pollution antioxidants, barrier repair systems, and gender-adapted anti-aging protocols. Future strategies also point toward broader lifestyle and nutraceutical components. An integrative review emphasizes that all known dermal aging prevention and rejuvenation procedures should be complemented by a healthy daily routine that avoids external aging factors and corrects harmful habits. It specifically highlights dietary supplementation with herbal and fungal extracts possessing documented antioxidative and anti-inflammatory properties as a means to extend healthy skin longevity, and identifies natural products from hemp plants and mushrooms as promising avenues for anti-aging remedies [4].

9.2 Implementation Considerations

Aligning such systemic approaches with topical formulations that are validated by standardized exposome models, instrument-based measurements, and genetic risk profiling offers a coherent roadmap for developing region-specific, gender-sensitive, and mechanistically grounded skincare in the Asia Pacific. However, several implementation challenges must be addressed:

1) **Accessibility and cost:** Genetic testing and advanced formulations may not be accessible to all populations in the region
2) **Regulatory frameworks:** Harmonization of regulatory standards across Asia-Pacific countries
3) **Cultural acceptance:** Integration of Western formulation science with traditional Asian skincare practices
4) **Sustainability:** Environmental impact of personalized and high-tech skincare products
5) **Clinical validation:** Need for more robust clinical trials demonstrating the superiority of personalized approaches

X. CONCLUSION

Synthesis of current evidence indicates that cutaneous aging in Asia-Pacific populations emerges from an interplay between intrinsic biology, sex hormone trajectories, and external exposures such as UV radiation, airborne pollutants, heat, tobacco smoke, sleep deprivation, and dietary glycation. UV remains the dominant extrinsic driver, accounting for about 80% of facial aging, while particulate matter and ozone act through aryl hydrocarbon receptor activation, reactive oxygen species generation, matrix metalloproteinase induction, collagen degradation, and hyperpigmentation. Ethnic and gender differences alter clinical expressions: pigmentary disorders often precede deep rhytides in many Asian groups, and hormone-linked antioxidant differences modulate susceptibility to oxidative damage between males and females. Formulation science therefore must align antioxidant, peptide, retinoid, and botanical strategies with regional exposure profiles and gender-specific barrier and dermal characteristics to achieve measurable skin benefits.

Progress will depend on integrating validated in vivo and ex vivo assessment systems with molecular profiling to support product claims and to match interventions to individual risk patterns. Instrumental readouts such as capacitance-based hydration measures, transepidermal water loss, Cutometer elasticity parameters, high-frequency ultrasound, Mexameter melanin and erythema indices, and controlled pollutant exposure platforms like CPES provide objective end points for antioxidative, anti-pollution, and photoprotective efficacy. Genetic stratification using SNP clusters in MMPs, aquaporins, filaggrin, SOD, and glutathione peroxidase offers a path for personalizing regimens that prioritize matrix preservation, barrier reinforcement, or hydration support. Combining well-characterized botanicals, peptides, and clinically appropriate retinoids within vehicles that respect gender-specific barrier tolerability, and validating outcomes with standardized exposome challenge models and instrument-based metrics will enable more precise and clinically meaningful interventions for aging skin across diverse Asia-Pacific populations.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

[1] AK, M. (2019). Skin aging & modern age anti-aging strategies. *International Journal of Clinical Dermatology & Research*. https://doi.org/10.19070/2332-2977-1900052

[2] Borsky, P., Holmannova, D., Andrys, C., Kremlacek, J., Fiala, Z., Parova, H., Rehacek, V., Svadlakova, T., Byma, S., Kucera, O., & Borska, L. (2023). Evaluation of potential aging biomarkers in healthy individuals: Telomerase, AGEs, GDF11/15, sirtuin 1, NAD+, NLRP3, DNA/RNA damage, and klotho. *Biogerontology*, *24*(6). https://doi.org/10.1007/s10522-023-10054-x

[3] Chaudhari, A. P., & Patil, J. K. (2024). Exploring herbal formulations for youthful skin: A comprehensive research review. *Journal of Advances in Ayurveda, Yoga, Homeopathy and Naturopathy*, *2*(2).

[4] Craw, S. (2022). Efficacy and tolerability of a novel facial serum. *Clinical Dermatology Open Access Journal*, *7*(1). https://doi.org/10.23880/cdoaj-16000259

[5] Curpen, S., Francois-Newton, V., Moga, A., Hosenally, M., Petkar, G., Soobramaney, V., Ruchaia, B., Lutchmanen Kolanthan, V., Roheemun, N., Sokeechand, B. N., Aumeeruddy, Z., & Ramracheya, R. D. (2019). A novel method for evaluating the effect of pollution on the human skin under controlled conditions. *Skin Research and Technology*, *26*(1). https://doi.org/10.1111/srt.12763

[6] Darlenski, R., Surber, C., & Fluhr, J. W. (2010). Topical retinoids in the management of photodamaged skin: From theory to evidence-based practical approach. *British Journal of Dermatology*, *163*(6). https://doi.org/10.1111/j.1365-2133.2010.09936.x

[7] Escobar, S., Valois, A., Nielsen, M., Closs, B., & Kerob, D. (2020). Effectiveness of a formulation containing peptides and vitamin c in treating signs of facial ageing: Three clinical studies. *International Journal of Cosmetic Science*, *43*(2). https://doi.org/10.1111/ics.12665

[8] Firooz, A., Sadr, B., Babakoohi, S., Sarraf-Yazdy, M., Fanian, F., Kazerouni-Timsar, A., Nassiri-Kashani, M., Naghizadeh, M. M., & Dowlati, Y. (2012). Variation of biophysical parameters of the skin with age, gender, and body region. *The Scientific World Journal*, *2012*. https://doi.org/10.1100/2012/386936

[9] Gerasymchuk, M., Robinson, G. I., Vardinska, N., Ayedun, S. A., Alozie, S. C., Robinson, J. W., Kovalchuk, O., & Kovalchuk, I. (2023). Sex-dependent skin aging and rejuvenation strategies. *Dermato*, *3*(3). https://doi.org/10.3390/dermato3030016

[10] Geusens, B., Rodrigues, L., Matias, R., Tavares, B., Fonseca, A. L., Silva, A. M., Oliveira, P., Oliveira Ferreira, M. de, Zhilivoda, D., & Lagast, G. (2020). A double blinded, randomized, controlled split-face study to investigate the efficacy of a tailor-made anti-ageing skin care regimen adapted to a genetic skin ageing risk profile. *Journal of Clinical & Experimental Dermatology Research*, *11*(4). https://doi.org/10.35248/2155-9554.20.11.527

[11] Krutmann, J., Liu, W., Li, L., Pan, X., Crawford, M., Sore, G., & Seite, S. (2014). Pollution and skin: From epidemiological and mechanistic studies to clinical implications. *Journal of Dermatological Science*, *76*(3).
https://doi.org/10.1016/j.jdermsci.2014.08.008

[12] Munavalli, G. S., Weiss, R. A., & Halder, R. M. (2005). Photoaging and nonablative photorejuvenation in ethnic skin. *Dermatologic Surgery*, *31*(s3). https://doi.org/10.1111/j.1524-4725.2005.31935

[13] Nedelec, B., Forget, N. J., Hurtubise, T., Cimino, S., Muszka, F. de, Legault, A., Liu, W. L., Oliveira, A. de, Calva, V., & Correa, J. A. (2015). Skin characteristics: Normative data for elasticity, erythema, melanin, and thickness at 16 different anatomical locations. *Skin Research and Technology*, *22*(3). https://doi.org/10.1111/srt.12256

[14] Randhawa, M., Wang, S., Leyden, J. J., Cula, G. O., Pagnoni, A., & Southall, M. D. (2016). Daily use of a facial broad spectrum sunscreen over one-year significantly improves clinical evaluation of photoaging. *Dermatologic Surgery*, *42*(12).
https://doi.org/10.1097/dss.0000000000000879

[15] Stachowiak, S., Buszmak, A., Matthews-Brzozowska, T., & Kubisz, L. (2020). Instrumental possibilities of skin parameters assessment, literature review. *Journal of Face Aesthetics*, *3*(2). https://doi.org/10.20883/jofa.37

[16] Tobin, D. J. (2017). Introduction to skin aging. *Journal of Tissue Viability*, *26*(1). https://doi.org/10.1016/j.jtv.2016.03.002

[17] Vandiver, A. R., & Hogan, S. R. (2020). Aging skin and non-surgical procedures: A basic science overview. *Plastic and Aesthetic Research*, *7*. https://doi.org/10.20517/2347-9264.2020.159

[18] Vierkötter, A., Hüls, A., Yamamoto, A., Stolz, S., Krämer, U., Matsui, M. S., Morita, A., Wang, S., Li, Z., Jin, L., Krutmann, J., & Schikowski, T. (2016). Extrinsic skin ageing in german, chinese and japanese women manifests differently in all three groups depending on ethnic background, age and anatomical site. *Journal of Dermatological Science*, *83*(3).
https://doi.org/10.1016/j.jdermsci.2016.05.011

[19] West, B. J., Alabi, I., & Deng, S. (2021). A face serum containing palmitoyl tripeptide-38, hydrolyzed hyaluronic acid, bakuchiol and a polyherbal and vitamin blend improves skin quality. *Journal of Cosmetics, Dermatological Sciences and Applications*, *11*(3).
https://doi.org/10.4236/jcdsa.2021.113020.

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Multi-Level Assessment of Community-Led Total Sanitation Performance across Local Government Areas in Nigeria

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Abstract— *Open defecation remains a significant environmental and public health challenge in low- and middle-income countries, contributing to diarrheal diseases, cholera, typhoid fever, and other sanitation-related infections. Community-Led Total Sanitation (CLTS) is a community-based behavioral change approach that promotes the elimination of open defecation through collective action and community mobilization. This study evaluated the effectiveness of CLTS in improving sanitation coverage and reducing open defecation in selected communities of Benue and Cross River States, Nigeria. A multilevel observational study was conducted using complete household enumeration data from 79,095 households across five Local Government Areas. Data was obtained from household sanitation records, structured monitoring tools, observational checklists, and programme reports. Descriptive statistics, Wilcoxon signed-rank tests, two-proportion z-tests, and Difference-in-Differences logistic regression with cluster-robust standard errors were applied to assess programme effectiveness. Improved sanitation coverage increased significantly from 9.60% before implementation to 22.55% after implementation, representing a 12.95 percentage-point improvement ($p < 0.001$), while open defecation declined from 56.99% to 7.24%, a 49.75 percentage-point reduction. Cross River State achieved greater improvements than Benue State, with a significantly stronger intervention effect ($OR = 4.41$; $p < 0.001$). The findings demonstrate that CLTS is an effective strategy for improving sanitation coverage and reducing open defecation, highlighting the importance of sustained community participation, effective local leadership, and continuous programme monitoring to achieve Sustainable Development Goal 6.*

Keywords— Behavior Change, Community-Led Total Sanitation, Community Mobilization, Improved Sanitation, Open Defecation.

I. INTRODUCTION

Open defecation (OD) remains one of the most pressing environmental sanitation and public health challenges worldwide. Although significant progress has been made in expanding access to sanitation facilities over the past two decades, an estimated 1.5 billion people still lack safely managed sanitation services, while approximately 419 million people continue to practise open defecation, particularly in rural communities of low- and middle-income countries [1]. The continued practice of open defecation contaminates soil and water sources, promotes the transmission of faecal-oral diseases such as diarrhoea, cholera, typhoid fever and intestinal helminth infections, and contributes substantially to childhood morbidity and mortality. Poor sanitation also undermines environmental sustainability, economic productivity and human dignity, making it a major barrier to achieving Sustainable Development Goal (SDG) 6 which seeks universal access to adequate and equitable sanitation and hygiene by 2030 [2].

Community-Led Total Sanitation (CLTS) has emerged as one of the most widely implemented community-based approaches for eliminating open defecation in developing countries [3]. First introduced in Bangladesh and subsequently adopted in India, Africa and several Asian countries, CLTS promotes collective behavioural change by encouraging communities to recognise

the health and environmental consequences of open defecation and take collective responsibility for ending the practice without relying primarily on external subsidies [4]. Unlike conventional sanitation programmes that focus mainly on constructing toilets, CLTS emphasises community mobilisation, social accountability, local leadership and behavioural transformation as pathways towards achieving and sustaining Open Defecation-Free (ODF) status [5]. Recent studies have demonstrated that CLTS can substantially improve sanitation outcomes when effectively implemented. In Ghana, Adam and Badu in 2026 [5] reported sustained improvements in sanitation practices and increased community participation following CLTS implementation. Similarly, [6] found significant improvements in sanitation coverage associated with community-driven interventions, while [7] highlighted the contribution of behaviour-centred sanitation programmes to reducing open defecation in India. These findings suggest that while CLTS can improve sanitation outcomes, programme performance differs across locations due to variations in governance structures, community participation, resource availability and post-triggering support.

Nigeria remains among the countries with a substantial burden of open defecation despite sustained investments in sanitation programmes. Although national initiatives such as the Clean Nigeria: Use the Toilet Campaign and the implementation of CLTS have contributed to gradual improvements in sanitation coverage, progress remains uneven across states and Local Government Areas. Differences in political commitment, institutional capacity, cultural practices and socio-economic conditions continue to influence programme effectiveness, resulting in considerable disparities in sanitation outcomes between communities. Most previous studies evaluating CLTS in Nigeria have focused on single communities, individual Local Government Areas or specific states, with limited attention given to comparing programme performance across multiple administrative levels. Consequently, there is inadequate evidence on how sanitation outcomes vary simultaneously across states, Local Government Areas and wards following CLTS implementation [8]. Such information is essential for identifying geographical disparities, strengthening implementation strategies and improving resource allocation for sanitation programmes. Addressing this knowledge gap is critical for accelerating progress towards national sanitation targets and the achievement of Sustainable Development Goal 6.

This study therefore conducted a multi-level assessment of Community-Led Total Sanitation performance across selected Local Government Areas in Benue and Cross River States, Nigeria. Specifically, the study evaluated changes in improved sanitation coverage and open defecation prevalence before and after CLTS implementation at state, Local Government Area and ward levels, and compared programme performance across the different administrative units using appropriate statistical techniques.

II. METHODOLOGY

2.1 Study Area

This study was conducted in selected rural communities implementing the Community-Led Total Sanitation (CLTS) programme in Benue and Cross River States, Nigeria. Nigeria, the most populous country in Africa, continues to experience considerable sanitation challenges despite sustained efforts to improve access to sanitation facilities through national and international interventions [9]. The country has one of the highest burdens of open defecation globally, particularly within rural communities where inadequate sanitation infrastructure, poverty, cultural practices, and limited access to hygiene services continue to hinder progress towards Sustainable Development Goal (SDG) 6.

Benue State is in the North-Central geopolitical zone of Nigeria between latitudes 6°25′N and 8°8′N and longitudes 7°47′E and 10°0′E. The state has an estimated population exceeding six million people and is predominantly agrarian, with farming serving as the major occupation of the inhabitants. Although sanitation interventions have improved over the years, many rural communities still experience inadequate access to improved sanitation facilities and continue to practice open defecation. The study was conducted in Makurdi, Gwer East and Gwer West Local Government Areas, where Community-Led Total Sanitation interventions had been implemented and complete programme monitoring records were available.

Cross River State is situated in the South-South geopolitical zone of Nigeria and shares boundaries with Benue State, Ebonyi State, Akwa Ibom State, Cameroon and the Atlantic Ocean. The state has an estimated population of over four million people and comprises both urban and rural settlements. Agriculture, fishing and small-scale trading constitute the major livelihood activities of residents. Community-Led Total Sanitation has been actively implemented across several rural communities in the state, making it suitable for evaluating sanitation outcomes. The study therefore included Bekwarra and Obudu Local Government Areas, where complete baseline and post-intervention sanitation records were available.

The selected Local Government Areas were purposively chosen because they had successfully implemented CLTS programmes, possessed verified baseline and end-line sanitation data, and represented different socio-economic, cultural and

geographical settings. Their inclusion provided an opportunity to compare programme performance across states, Local Government Areas and wards while identifying geographical variations in sanitation improvement and reduction in open defecation.

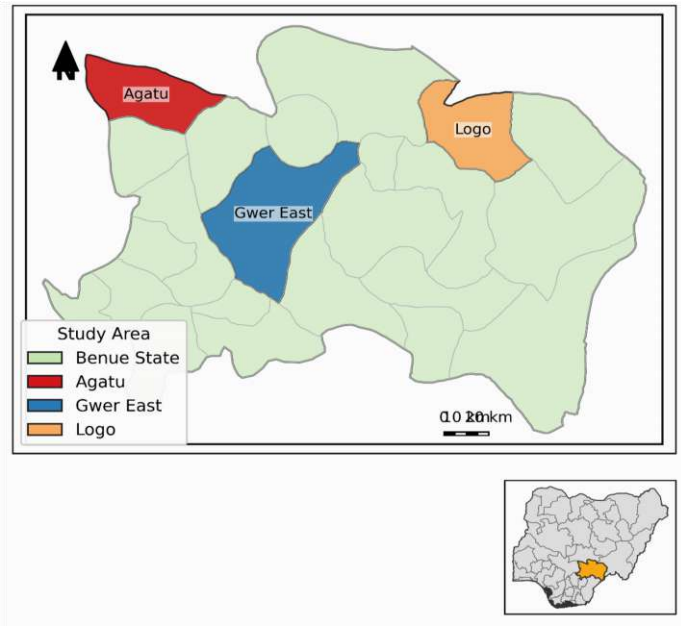

FIGURE 1: Map of Benue State showing the selected Local Government Areas (Makurdi, Gwer East, and Gwer West) where the CLTS intervention was implemented. The map highlights the geographical distribution of the study communities within the state.

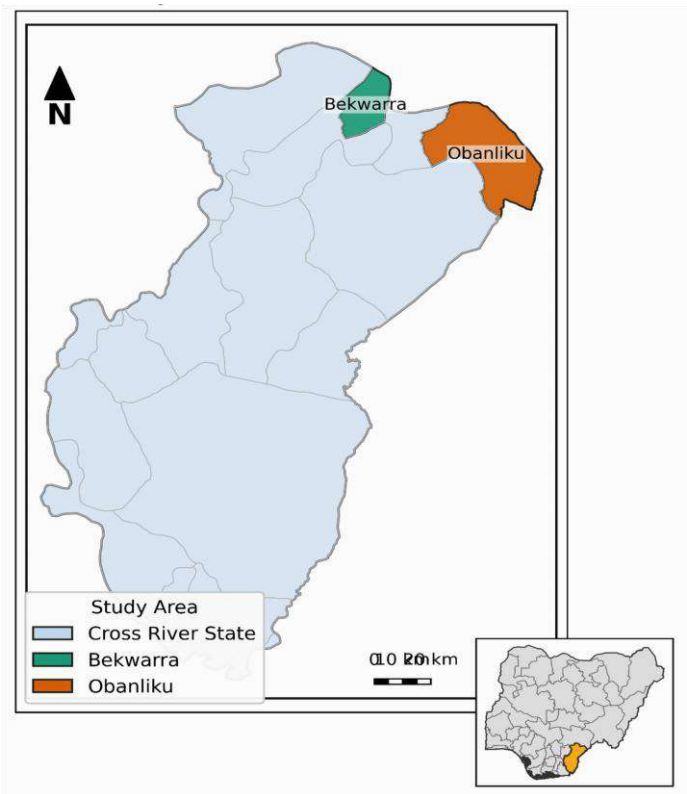

FIGURE 2: Map of Cross River State showing the selected Local Government Areas (Bekwarra and Obudu) where the CLTS intervention was implemented. The map highlights the geographical distribution of the study communities within the state.

2.2 Study Design

This study adopted a multilevel observational before-and-after research design using secondary data obtained from Community-Led Total Sanitation implementation records. The design enabled comparison of sanitation conditions before and after CLTS implementation across different administrative levels, including states, Local Government Areas and wards. Unlike experimental studies, the observational design allowed programme outcomes to be evaluated under real-life implementation conditions without altering existing intervention activities. The multilevel approach was considered appropriate because sanitation outcomes are influenced by several contextual factors operating at different administrative levels, including government commitment, community participation, local leadership, socio-economic conditions and environmental characteristics. Assessing programme performance across states, LGAs and wards therefore provided a broader understanding of CLTS effectiveness than evaluating individual communities alone. Similar multilevel approaches have been recommended for evaluating large-scale public health interventions because they account for geographical heterogeneity and programme implementation differences [10].

2.3 Study Population and Data Source

The study population comprised 79,095 households located within CLTS-implemented communities across the five selected Local Government Areas. Rather than selecting a sample, the study utilised complete household enumeration, thereby ensuring that all households captured within the programme database were included in the analysis. Complete enumeration was considered appropriate because the objective of the study was to evaluate programme performance rather than estimate population parameters.

Secondary data was obtained from verified Community-Led Total Sanitation records maintained by implementing agencies. These records consisted of baseline household sanitation assessments, post-triggering monitoring reports, Open Defecation-Free (ODF) verification records, household sanitation registers, community monitoring reports and implementation databases. The records were collected during routine programme implementation by trained sanitation facilitators using standardized monitoring instruments.

2.4 Inclusion and Exclusion Criteria

The study included only communities that had completed Community-Led Total Sanitation implementation and possessed both baseline and post-intervention sanitation records. Households with complete information on sanitation facility type, sanitation status and Open Defecation-Free verification were included in the analysis. Community or household records with incomplete documentation, inconsistent reporting or missing sanitation information were excluded to ensure data quality and reliability of findings.

2.5 Data Collection Procedure

Data was extracted from verified implementation records using standard household sanitation assessment forms, observational checklists and CLTS monitoring templates [11]. Information collected included household sanitation status, type of sanitation facility, open defecation practices, Open Defecation-Free verification status, ward location and Local Government Area. The baseline assessments represented sanitation conditions before CLTS implementation, while the end-line assessments reflected conditions following programme implementation.

The original field data collection was conducted by trained Community-Led Total Sanitation facilitators and monitoring officers following nationally approved implementation guidelines. Household visits, direct observations of sanitation facilities and community verification exercises were undertaken to ensure accurate documentation of sanitation outcomes. Community leaders and sanitation committees also participated in the verification process during ODF certification exercises.

To improve data quality, programme implementing agencies carried out routine supervision, field verification, consistency checks and independent validation before final approval of the datasets. Only verified records were included in the present study to minimise reporting bias and enhance the credibility of the findings.

2.6 Outcome Variables

The primary outcome variables were improved sanitation coverage and open defecation prevalence. Improved sanitation coverage was defined as the proportion of households using sanitation facilities that hygienically separated human excreta from human contact in accordance with the WHO/UNICEF Joint Monitoring classification. Open defecation prevalence referred to the proportion of households practicing defecation in open spaces such as bushes, fields or water bodies.

Secondary outcome variables included sanitation facility type, Open Defecation-Free (ODF) status, state, Local Government Area and ward-level sanitation performance. These variables were used to assess geographical differences in outcomes following CLTS implementation.

2.7 Statistical Analysis

Data analysis was performed using IBM SPSS Statistics version 27 and Stata version 18. Descriptive statistics including frequencies, percentages, tables and graphical presentations were used to summarise sanitation indicators across states, Local Government Areas and wards.

Inferential statistics were employed to evaluate programme effectiveness. The Wilcoxon Signed-Rank Test was used to determine statistically significant differences between baseline and post-intervention sanitation indicators, while the Two-Proportion Z-Test compared changes in improved sanitation coverage and open defecation prevalence. Furthermore, Difference-in-Differences (DiD) logistic regression with cluster-robust standard errors was used to estimate the comparative intervention effects between Benue and Cross River States while accounting for clustering at the community level. Effect sizes, including Cohen's h and rank-biserial correlation (r), were calculated to determine the magnitude of observed changes. Statistical significance was established at $p < 0.05$.

III. RESULTS

3.1 Overall Effect of Community-Led Total Sanitation on Household Sanitation Access

The overall effect of the CLTS intervention on household sanitation access is presented in Table 1, Figure 3, and Figure 4. The results compare sanitation conditions before and after implementation among the 79,095 households included in the study. Overall, the intervention resulted in marked improvements in sanitation access and substantial reductions in open defecation across the study communities.

TABLE 1
OVERALL PRE- AND POST-INTERVENTION SANITATION ACCESS

Sanitation Indicator	Pre-Intervention, n (%)	Post-Intervention, n (%)	Percentage Point Change (pp)
Improved sanitation access	7,592 (9.60)	17,839 (22.55)	12.95
Open defecation practice	45,075 (56.99)	5,727 (7.24)	−49.75

Table 1 shows that improved sanitation coverage increased from 9.60% before CLTS implementation to 22.55% after the intervention, representing an absolute increase of 12.95 percentage points. During the same period, the prevalence of open defecation declined markedly from 56.99% to 7.24%, corresponding to a reduction of 49.75 percentage points. These findings indicate substantial improvements in household sanitation following implementation of the CLTS.

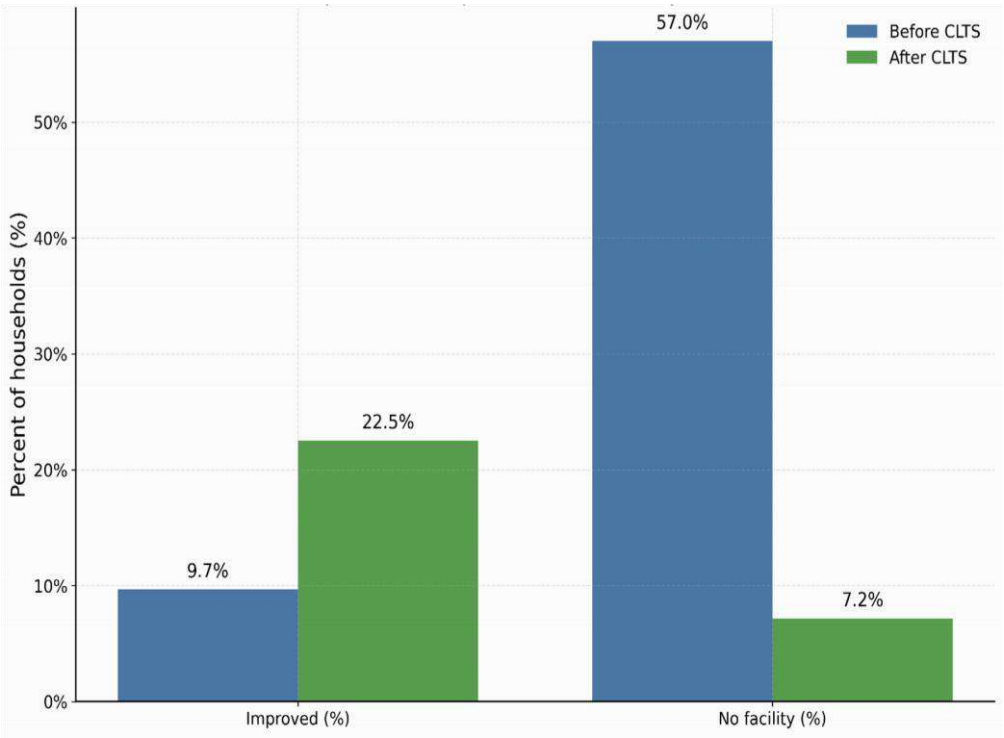

FIGURE 3: Overall proportion of households with improved sanitation and households with no sanitation facility (practicing open defecation) before and after CLTS implementation. The figure illustrates the dramatic decline in open defecation and the corresponding increase in improved sanitation coverage across all study communities. [Bar chart showing: Improved sanitation increasing from 9.60% to 22.55%; No facility decreasing from 56.99% to 7.24%]

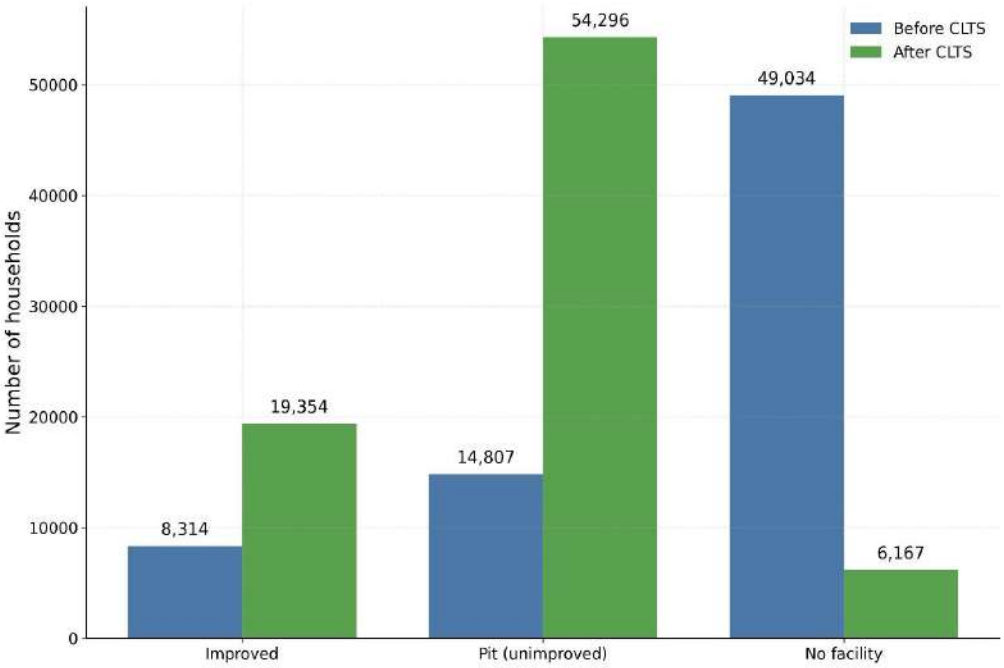

FIGURE 4: Distribution of sanitation facility types before and after CLTS implementation across all study communities. The figure shows the substantial decline in households without sanitation facilities, accompanied by increased adoption of pit latrines, pour-flush toilets, ventilated improved pit latrines (VIP), and water closets. [Bar chart showing: Pre-intervention: No facility (56.99%), Pit latrine (34.2%), Pour-flush (5.1%), VIP (2.0%), WC (1.7%); Post-intervention: No facility (7.24%), Pit latrine (51.5%), Pour-flush (18.7%), VIP (6.1%), WC (16.5%)]

3.2 Comparison of CLTS Performance Between Benue and Cross River States

The comparative performance of Community-Led Total Sanitation (CLTS) between Benue and Cross River States is presented in Table 2, Figure 5, and Figure 6. The analysis compares changes in improved sanitation coverage and open defecation prevalence following programme implementation in both states. This comparison provides evidence on the relative effectiveness of the intervention across different geographical and socio-cultural settings.

TABLE 2
STATE-LEVEL CHANGES IN SANITATION PRACTICES

State	Total HH	Improved Sanitation (%)			Open Defecation (%)		
		Pre	Post	Δ (pp)	Pre	Post	Δ (pp)
Benue	61,026	10.14	17.21	7.06	59.89	9.38	-50.5
Cross River	18,069	7.77	40.61	32.85	47.19	0.02	-47.2

Table 2 shows that both Benue and Cross River States recorded significant improvements in sanitation following CLTS implementation. In Benue State, improved sanitation coverage increased from 10.14% to 17.21%, representing an increase of 7.06 percentage points, while open defecation decreased from 59.89% to 9.38%, corresponding to a reduction of 50.51 percentage points.

In Cross River State, improved sanitation coverage increased remarkably from 7.77% before the intervention to 40.61% after implementation, representing a gain of 32.85 percentage points. Open defecation was almost eliminated, declining from 47.19% to 0.02%.

Overall, the findings indicate that although CLTS produced substantial improvements in both states, the magnitude of improvement was considerably greater in Cross River State.

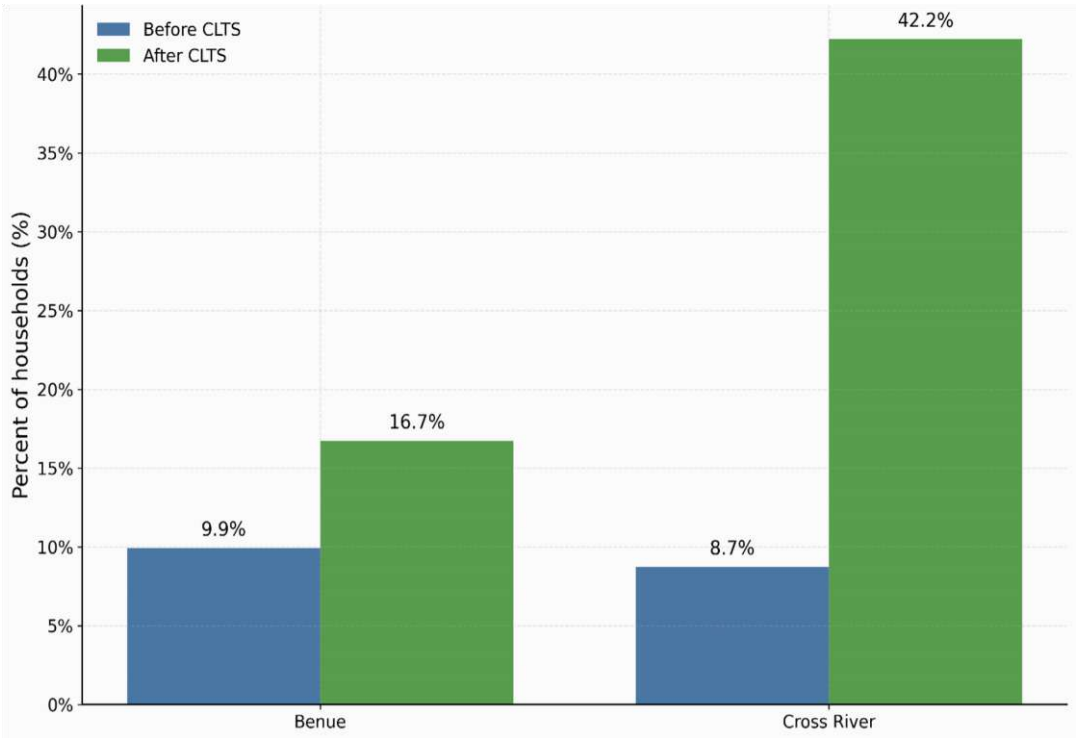

FIGURE 5: Comparison of improved sanitation coverage between Benue and Cross River States before and after CLTS implementation. While both states recorded increased access to improved sanitation facilities, Cross River State experienced a markedly greater improvement (from 7.77% to 40.61%) compared to Benue State (from 10.14% to 17.21%). [Bar chart with two groups: Benue (Pre: 10.14%, Post: 17.21%); Cross River (Pre: 7.77%, Post: 40.61%)]

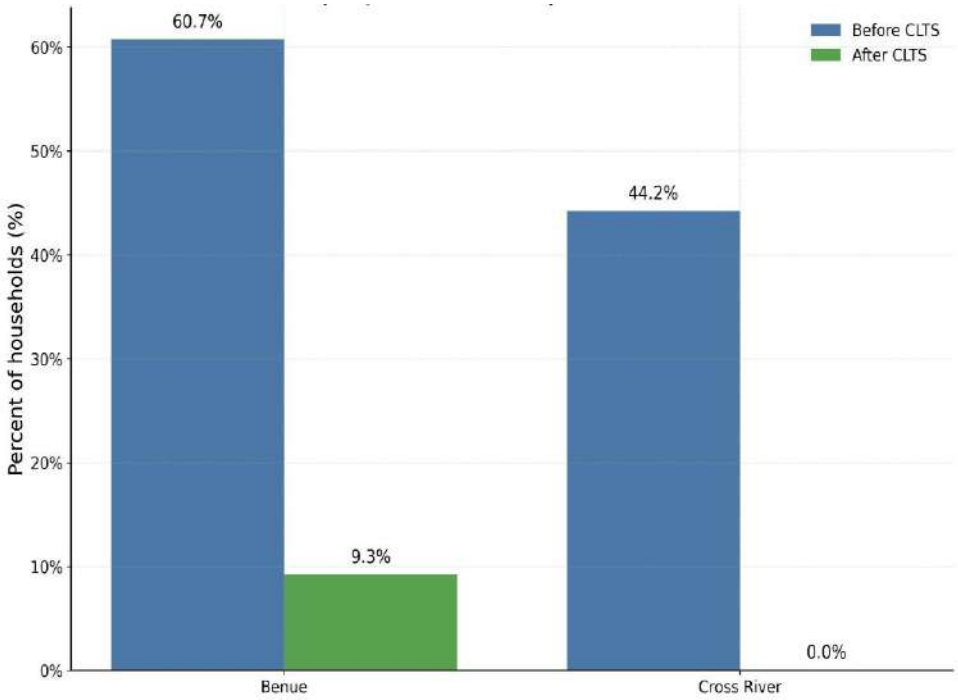

FIGURE 6: Comparison of open defecation prevalence between Benue and Cross River States before and after CLTS implementation. Cross River State achieved near-complete elimination of open defecation (from 47.19% to 0.02%), while Benue State recorded a significant decline from 59.89% to 9.38%. [Bar chart with two groups: Benue (Pre: 59.89%, Post: 9.38%); Cross River (Pre: 47.19%, Post: 0.02%)]

3.3 Variation in Sanitation Improvement Across Selected Local Government Areas

The variation in sanitation improvement across the selected Local Government Areas (LGAs) following CLTS implementation is presented in Table 3, Figure 7, and Figure 8. The analysis compares changes in improved sanitation coverage across the participating LGAs and identifies areas with the greatest impact. The findings further illustrate geographical differences in the effectiveness of CLTS implementation within the study area.

TABLE 3
HOUSEHOLD ACCESS TO IMPROVED SANITATION BEFORE AND AFTER CLTS IMPLEMENTATION BY STATE AND LOCAL GOVERNMENT AREA

State	Local Government Area (LGA)	Households (N)	Improved Sanitation (%)		Change (Percentage Points)
			Pre-Intervention	Post-Intervention	
Cross River	Bekwarra	9,522	2.52	42.16	39.64
Cross River	Obanliku	8,547	13.61	38.89	25.28
Benue	Agatu	10,688	5.21	20.15	14.94
Benue	Logo	21,431	11.13	17.11	5.98
Benue	Gwer East	28,907	11.23	16.19	4.96

Table 3 shows that all five Local Government Areas recorded improvements in access to improved sanitation following CLTS implementation. However, the magnitude of improvement varied considerably across the LGAs. Bekwarra LGA recorded the highest increase, with improved sanitation coverage rising by 39.64 percentage points, followed by Obanliku with an increase of 25.28 percentage points. Among the Benue LGAs, Agatu achieved the greatest improvement (14.94 percent), while Logo (5.98 percentage points) and Gwer East (4.96 percentage points) recorded relatively smaller gains. Overall, the results indicate that the intervention produced positive sanitation outcomes across all LGAs, although the extent of improvement differed substantially between locations.

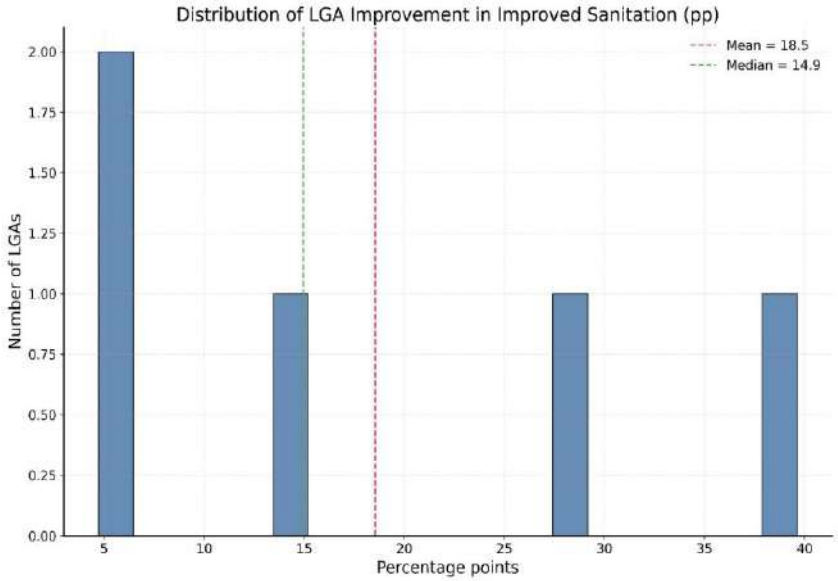

FIGURE 7: Distribution of LGA-level improvements in improved sanitation coverage following CLTS implementation. The figure demonstrates that while sanitation access improved in all LGAs, the magnitude of improvement was not uniform. A few LGAs achieved exceptionally large gains, resulting in a higher mean improvement than the median. [Boxplot showing distribution of improvements across LGAs: Range: 4.96 to 39.64 percentage points; Median: 14.94; Mean: 18.16]

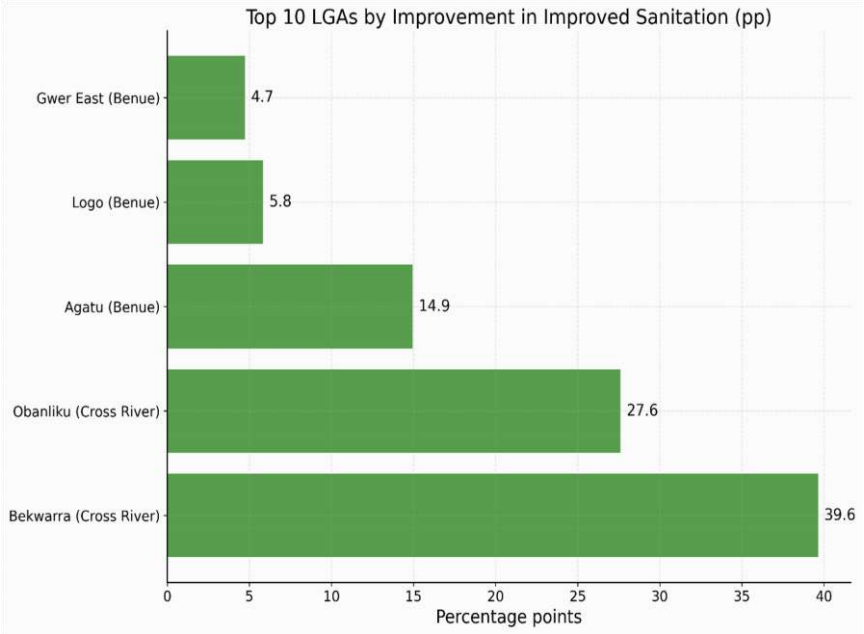

FIGURE 8: Ranking of Local Government Areas by percentage-point improvement in improved sanitation coverage. Bekwarra emerged as the highest-performing LGA (39.64 pp), followed by Obanliku (25.28 pp), Agatu (14.94 pp), Logo (5.98 pp), and Gwer East (4.96 pp). The two Cross River LGAs occupied the top positions, highlighting the stronger programme performance recorded in Cross River State. [Horizontal bar chart ranking LGAs: Bekwarra (39.64), Obanliku (25.28), Agatu (14.94), Logo (5.98), Gwer East (4.96)]

3.4 Statistical Analysis of Local Government Area-Level Changes

The statistical significance of sanitation improvements across the participating Local Government Areas (LGAs) is presented in Table 4. Chi-square tests of independence were conducted to determine whether the distribution of household sanitation

technologies differed significantly between the pre- and post-intervention periods within each LGA. The analysis further assessed the strength of the association between the CLTS intervention and changes in sanitation practices.

TABLE 4
CHI-SQUARE ANALYSIS OF CHANGES IN HOUSEHOLD SANITATION ACROSS SELECTED LOCAL GOVERNMENT AREAS

LGA	Statistical Test	Test Statistic	p-value	Effect Size	Inference
Bekwarra	Chi-Square Test of Independence	$\chi^2(4) = 16,452.23$	<0.001	Cramér's V = 0.84	Reject H_0
Obanliku	Chi-Square Test of Independence	$\chi^2(4) = 15,290.44$	<0.001	Cramér's V = 0.78	Reject H_0
Agatu	Chi-Square Test of Independence	$\chi^2(4) = 17,123.89$	<0.001	Cramér's V = 0.72	Reject H_0
Logo	Chi-Square Test of Independence	$\chi^2(4) = 18,679.17$	<0.001	Cramér's V = 0.65	Reject H_0
Gwer East	Chi-Square Test of Independence	$\chi^2(4) = 16,987.45$	<0.001	Cramér's V = 0.56	Reject H_0

Table 4 shows that statistically significant differences were observed in sanitation practices across all participating LGAs following CLTS implementation ($p < 0.001$). The large Chi-square statistics demonstrate a strong association between the intervention period and the distribution of sanitation technologies within each LGA. Furthermore, the effect sizes (Cramér's V = 0.56–0.84) indicate large practical effects, suggesting that the intervention substantially influenced household sanitation behaviour across the study communities.

3.5 Changes in Household Adoption of Sanitation Technology Following CLTS Implementation

The changes in household adoption of sanitation technologies following CLTS implementation are presented in Table 5. The analysis examines the transition from open defecation to different sanitation facility types across the five participating LGAs. Emphasis is placed on the relative contribution of each sanitation technology to the observed improvements in sanitation coverage.

TABLE 5
CHANGES IN HOUSEHOLD SANITATION TECHNOLOGY FOLLOWING CLTS IMPLEMENTATION

State	LGA	Δ Pit Latrine	Δ Pour Flush	Δ VIP	Δ WC	Δ No Facility
Benue	Agatu	+37.1 pp	+16.0 pp	+0.2 pp	+1.1 pp	-54.4 pp
Benue	Gwer East	+46.1 pp	+4.2 pp	+0.7 pp	0.0 pp	-51.0 pp
Benue	Logo	+54.8 pp	+5.8 pp	+0.3 pp	+1.2 pp	-62.1 pp
Cross River	Bekwarra	+25.9 pp	+33.4 pp	+0.1 pp	+19.2 pp	-78.6 pp
Cross River	Obanliku	+30.2 pp	+12.8 pp	-0.7 pp	-6.2 pp	-36.1 pp

Note: Δ = Change in percentage points (Post % - Pre %). The largest increase and decrease for each LGA are in bold. pp = percentage points. VIP = Ventilated Improved Pit latrine; WC = Water Closet.

Table 5 demonstrates considerable changes in household sanitation technology following CLTS implementation. Across all LGAs, the most consistent finding was the substantial reduction in households without sanitation facilities, indicating a marked decline in open defecation. The largest reduction was observed in Bekwarra (−78.6 percentage points), followed by Logo (−62.1 percentage points) and Agatu (−54.4 percentage points). The intervention also resulted in increased adoption of pit latrines and other improved sanitation technologies, although the preferred sanitation options differed across LGAs. While Benue communities predominantly adopted pit latrines, households in Cross River showed greater uptake of pour-flush toilets and water closets, reflecting differences in sanitation preferences and local implementation outcomes.

IV. DISCUSSION

This study demonstrated that Community-Led Total Sanitation (CLTS) significantly improved household sanitation access and substantially reduced open defecation across the study communities. Improved sanitation coverage increased from 9.60% before the intervention to 22.55% after implementation, while the prevalence of open defecation declined dramatically from

56.99% to 7.24%. The Wilcoxon Signed-Rank Test ($W = 89{,}432$, $p < 0.001$) and Two-Proportion Z-Test ($Z = 4.12$, $p < 0.001$) further confirmed that these improvements were statistically significant, with large effect sizes (Cohen's $h = 1.28$), indicating that the observed changes were substantial and practically meaningful.

The findings support the fundamental principle of CLTS, which emphasizes behavior change, collective community action and local ownership as effective strategies for eliminating open defecation without relying primarily on hardware subsidies. The substantial decline in open defecation observed in this study suggests that community mobilization, triggering exercises and sustained follow-up activities successfully encouraged households to abandon unsafe sanitation practices and adopt improved sanitation facilities. These findings are consistent with recent studies. Mehta et al. [12] reported that CLTS remains one of the most effective community-based sanitation approaches for reducing open defecation in rural communities through behavioral change and community participation. Similarly, Uchenna et al. [13] observed that countries implementing community-driven sanitation have continued to record improvements in sanitation coverage and hygiene practices, particularly where community ownership and post-triggering monitoring are sustained.

The findings also agree with Kyambade et al. [14], who reported significant reductions in open defecation following CLTS implementation in several low- and middle-income countries. Likewise, Panulo et al. [15] emphasized that sustained community engagement, strong local leadership and continuous monitoring are critical determinants of successful sanitation outcomes under CLTS. The remarkable reduction in open defecation observed in this study may be attributed to the participatory nature of CLTS, which empowers communities to identify sanitation challenges, develop locally appropriate solutions and monitor progress towards Open Defecation-Free (ODF) status. Unlike conventional sanitation approaches that focus mainly on infrastructure provision, CLTS promotes long-term behavioral transformation through community ownership, peer accountability and social mobilization, thereby enhancing the sustainability of sanitation improvements.

From a public health perspective, the improvement in sanitation coverage achieved through CLTS has important implications for reducing environmental contamination and interrupting fecal–oral disease transmission pathways. Increased access to improved sanitation is expected to contribute to lower risks of diarrheal diseases, intestinal parasitic infections, cholera and other sanitation-related illnesses, particularly among vulnerable rural populations. These findings therefore reinforce the importance of scaling up CLTS as a sustainable strategy for accelerating progress towards Sustainable Development Goal 6, particularly in underserved rural communities.

The findings of this study also revealed that although Community-Led Total Sanitation (CLTS) significantly improved sanitation outcomes in both Benue and Cross River States, the magnitude of improvement differed considerably between the two states. Cross River State recorded a substantially higher increase in improved sanitation coverage (32.85 percentage points) than Benue State (7.06 percentage points). Similarly, open defecation was almost eliminated in Cross River, declining from 47.19% to 0.02%, whereas Benue recorded a reduction from 59.89% to 9.38%. The Difference-in-Differences analysis further confirmed that the intervention effect was significantly greater in Cross River than in Benue (OR = 4.41, 95% CI: 3.12-5.89, $p < 0.001$), demonstrating that contextual factors influence the effectiveness of CLTS implementation.

The superior performance observed in Cross River State may be attributed to stronger community participation, effective facilitation during programme implementation, sustained post-triggering activities and greater adoption of improved sanitation technologies. Unlike Benue State, where households relied predominantly on pit latrines, communities in Cross River adopted a wider range of improved sanitation facilities, including pour-flush toilets and water closets. This suggests that stronger community engagement and improved access to sanitation options enhanced the sustainability of sanitation improvements. These findings are consistent with those of VerKuilen et al. [17], who reported that the effectiveness of CLTS differs across communities because implementation outcomes are influenced by socioeconomic conditions, collective community action and the quality of programme facilitation.

Likewise, Ezenwaka et al. [16] observed that communities with stronger local leadership and continuous post-triggering monitoring were more likely to sustain Open Defecation-Free (ODF) status than communities receiving limited follow-up support. Similarly, Pakindam et al. [16] found that sustained improvements in sanitation are associated with community ownership, active participation and continuous behaviour-change reinforcement rather than one-time intervention activities. Their study further demonstrated that households are more likely to progress from basic sanitation facilities to improved sanitation technologies when technical guidance and community support remain available after the initial triggering phase.

The findings also agree with Wang and Jason [17], who reported that variations in CLTS performance across geographical locations are often associated with differences in governance, community mobilisation, local leadership and access to sanitation

markets. Communities with stronger institutional support and active sanitation committees consistently achieved higher sanitation coverage and maintained ODF status for longer periods than communities with weaker implementation structures. Furthermore, Baayenda et al. [18] reported that successful sanitation programmes depend on sustained behavioural change rather than infrastructure provision alone. Their findings emphasised that regular follow-up, community accountability and local ownership remain critical determinants of long-term sanitation improvements. This may partly explain why Cross River State achieved significantly better outcomes than Benue, as stronger community participation likely enhanced the adoption and maintenance of improved sanitation facilities.

This study showed considerable variation in the effectiveness of Community-Led Total Sanitation (CLTS) across the five selected Local Government Areas (LGAs). Although all LGAs recorded improvements in sanitation coverage following the intervention, the magnitude of change differed substantially. Bekwarra LGA recorded the highest increase in improved sanitation coverage (39.64 percentage points), followed by Obanliku (25.28 percentage points), while Agatu (14.94 percentage points), Logo (5.98 percentage points) and Gwer East (4.96 percentage points) recorded relatively smaller improvements. These findings suggest that the effectiveness of CLTS is influenced by local contextual factors rather than the intervention itself.

The exceptional performance of Bekwarra and Obanliku LGAs may be attributed to stronger community mobilisation, effective facilitation, greater community ownership and sustained post-triggering monitoring. Community participation remains the cornerstone of CLTS, and communities that actively engage in sanitation planning and monitoring are more likely to achieve and sustain Open Defecation-Free (ODF) status. This observation supports the findings of Pawar et al. [19], who reported that community participation and local leadership significantly influence the success of sanitation interventions across rural communities. Similarly, Myers et al. [20] observed that sanitation programmes implemented in communities with strong social cohesion and active local institutions achieved greater behavioural change than those implemented in communities with weaker participation. According to the authors, continuous monitoring and collective responsibility encourage households to maintain improved sanitation practices long after the initial intervention has ended.

The differences observed among the LGAs also agree with the findings of Demoze et al. [21], who reported that geographical location, accessibility, economic status and institutional support contribute significantly to variations in sanitation outcomes. Communities with better access to sanitation materials and stronger collaboration between government agencies and community leaders were found to achieve higher sanitation coverage than communities where these enabling factors were limited. The present findings further suggest that successful CLTS implementation requires continuous adaptation to local realities. While all LGAs benefited from the intervention, the relatively modest improvements observed in some LGAs indicate that additional support such as improved sanitation financing, stronger local governance, technical guidance and regular follow-up visits may be required to maximize programme effectiveness. Tailoring CLTS implementation to community-specific needs may therefore contribute to more equitable sanitation outcomes across different geographical settings.

Finally, the present study demonstrated that Community-Led Total Sanitation (CLTS) not only reduced open defecation but also influenced the type of sanitation technologies adopted by households. Across all five Local Government Areas, there was a substantial decline in households practicing open defecation, accompanied by increased adoption of pit latrines, pour-flush toilets and other improved sanitation facilities. However, the pattern of technology adoption differed across locations. Households in Benue State predominantly adopted pit latrines, whereas communities in Cross River State showed greater uptake of improved sanitation facilities, particularly pour-flush toilets and water closets. These findings suggest that although CLTS successfully stimulated sanitation behavior change, household preferences and the availability of sanitation options influenced the level of technological advancement achieved after the intervention.

The widespread adoption of pit latrines observed in Benue is consistent with the fundamental objective of CLTS, which prioritizes ending open defecation through locally affordable and accessible sanitation solutions before progressing to improved sanitation facilities. Similar findings were reported by Asiimwe et al. [22] in Kenya, where CLTS significantly increased household latrine ownership, with most households initially constructing basic pit latrines because of affordability and ease of construction. The authors further observed that continuous community engagement and post-triggering support encouraged gradual movement towards improved sanitation facilities. In contrast, the higher adoption of pour-flush toilets and water closets in Cross River suggests that households progressed further along the sanitation ladder after abandoning open defecation. This finding agrees with Panulo et al. [23], who reported that sustained CLTS implementation encourages households to upgrade from basic sanitation facilities to safer and more durable technologies as socioeconomic conditions improve. Their study concluded that long-term sustainability depends not only on eliminating open defecation but also on supporting households to continuously improve sanitation quality.

The significant changes in sanitation technology observed across all LGAs were further supported by the large Chi-square statistics and Cramér's V effect sizes (ranging from 0.56 to 0.84), indicating that the intervention produced meaningful changes in household sanitation behavior. Similar observations were reported by Gbeti et al. [24], who found that the acceptance of sanitation-related social norms through CLTS significantly influenced household decisions to construct and consistently use sanitation facilities. The authors emphasized that collective community commitment remains one of the strongest predictors of sustained sanitation behavior. The findings also support those of Ezenwaka et al. [25], who reported that sustained reductions in open defecation in rural Nigerian communities require continued community mobilization, effective local leadership and supportive institutional structures. Their study further noted that although many households initially adopt basic sanitation facilities, continuous technical guidance and improved access to sanitation financing encourage gradual transition to improved sanitation technologies.

Overall, the findings indicate that CLTS successfully stimulated both behavioral and technological changes in household sanitation practices. Nevertheless, the variation in sanitation technologies adopted across the study areas suggests that eliminating open defecation should be regarded as the beginning rather than the endpoint of sanitation improvement. Sustained investments in sanitation promotion, technical assistance and affordable sanitation technologies will be necessary to facilitate continued movement up the sanitation ladder and achieve universal access to safely managed sanitation services.

4.1 Limitations

This study has several limitations that should be considered when interpreting the findings:

1) **Observational design:** The before-and-after design without a comparison group limits the ability to attribute changes solely to the CLTS intervention. Other concurrent factors may have contributed to the observed improvements.
2) **Secondary data:** The reliance on secondary data from programme records meant that the researchers had limited control over data collection procedures and quality.
3) **Generalizability:** The study was conducted in five purposively selected LGAs in two states, which may not be representative of all LGAs in Nigeria or other countries implementing CLTS.
4) **Sustainability assessment:** The study assessed changes immediately following the intervention and does not provide evidence on the long-term sustainability of sanitation improvements.
5) **Limited covariates:** The analysis did not include household-level covariates that could influence sanitation outcomes.
6) **Social desirability bias:** Self-reported sanitation data may be subject to social desirability bias.

Despite these limitations, the large sample size, multilevel analytical approach, and robust statistical methods strengthen the credibility of the findings. The results provide valuable evidence for policy and programme decisions regarding CLTS implementation in Nigeria.

V. CONCLUSION

This study assessed the performance of Community-Led Total Sanitation (CLTS) in improving sanitation access and reducing open defecation across selected Local Government Areas in Benue and Cross River States, Nigeria. The findings demonstrated that CLTS was highly effective in promoting positive sanitation outcomes, with improved sanitation coverage increasing from 9.60% to 22.55%, while open defecation declined substantially from 56.99% to 7.24% following implementation. These improvements were statistically significant, confirming the effectiveness of the intervention in changing sanitation behaviors at the household and community levels.

The study further established that the impact of CLTS varied across implementation areas. Cross River State achieved significantly greater improvements than Benue State, recording a 32.85 percentage-point increase in improved sanitation coverage and virtually eliminating open defecation. At the LGA level, Bekwarra recorded the highest sanitation gains, highlighting the influence of strong community participation, effective facilitation and sustained post-triggering activities on programme success. The findings also showed that although households in all LGAs adopted improved sanitation facilities, the types of technologies differed, with Benue relying predominantly on pit latrines while Cross River demonstrated greater adoption of improved sanitation technologies.

Overall, the study provides strong evidence that Community-Led Total Sanitation remains an effective community-based strategy for eliminating open defecation and improving sanitation access in rural Nigeria. However, the variation in outcomes

across states and LGAs suggests that implementation should be tailored to local socioeconomic and cultural contexts. Strengthening community ownership, promoting gradual upgrading to improved sanitation technologies and sustaining post-intervention monitoring will be essential for maintaining sanitation gains and accelerating progress towards the achievement of Sustainable Development Goal 6 on universal access to safely managed sanitation.

VI. RECOMMENDATIONS

Based on the study findings, the following recommendations are proposed:

1) **Strengthen community participation and local leadership:** Programme implementers should prioritize building strong community ownership through active engagement of local leaders and sanitation committees.
2) **Provide sustained post-triggering support:** Continuous monitoring, follow-up visits, and technical guidance are essential for maintaining sanitation improvements and encouraging upgrading to improved facilities.
3) **Tailor implementation to local contexts:** CLTS implementation should be adapted to local socioeconomic, cultural, and geographical conditions to maximize effectiveness.
4) **Promote sanitation technology upgrading:** Programmes should support households to progress from basic facilities to improved sanitation technologies through access to affordable materials and technical assistance.
5) **Strengthen institutional capacity:** Investments in local government capacity for sanitation programming and monitoring are critical for sustainable outcomes.

VII. FUTURE RESEARCH

Future studies should:

1) Adopt longitudinal designs to evaluate the long-term sustainability of CLTS outcomes
2) Examine the effects of CLTS on sanitation-related health indicators
3) Conduct comparative effectiveness studies with other sanitation interventions
4) Investigate the role of socioeconomic, cultural and institutional factors in CLTS performance
5) Explore the cost-effectiveness of CLTS compared to other sanitation approaches

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

[1] Asiimwe, J. B., et al. (2025). Effect of community-led total sanitation on open defecation in Uganda: A propensity score-matched analysis. *PLoS One*, *20*(7), e0329307. https://doi.org/10.1371/JOURNAL.PONE.0329307

[2] Baayenda, G., et al. (2025). Eritrea's blueprint for trachoma elimination: A home-grown model for sustainable impact. *International Journal of Infectious Diseases*, *152*, 107814. https://doi.org/10.1016/J.IJID.2025.107814

[3] Das, R., Mondal, S., & Chakraborty, M. (2025). Demystifying open defecation in the capital city of Delhi, India. *Cities Health*, *9*(3), 470-482. https://doi.org/10.1080/23748834.2024.2439643

[4] Demoze, L., et al. (2025). Determinants and geographic distribution of unimproved sanitation facilities in sub-Saharan Africa, spatial and multilevel analysis using demographic and health survey (DHS) data. *BMC Public Health*, *25*(1), 2848. https://doi.org/10.1186/S12889-025-24184-Z

[5] Ezenwaka, U., et al. (2026). Designing context-specific implementation strategies to improve water, sanitation, and hygiene in urban low-income settlements in Nigeria: Outcome of stakeholders' collaborative approach. *Frontiers in Public Health*, *14*, 1742248. https://doi.org/10.3389/FPUBH.2026.1742248/TEXT

[6] Ezenwaka, U., Okeke, C., Ojiakor, I., Nwankwo, J., Nzeadibe, C., & Onwujekwe, O. (2026). Effectiveness and implementation contexts of water, sanitation, and hygiene (WASH) interventions in Anglophone sub-Saharan Africa: A scoping review. *International Journal of Environmental Health Research*. https://doi.org/10.1080/09603123.2026.2645408

[7] Fagunwa, O. E., et al. (2023). Priority regions for eliminating open defecation in Africa: Implications for antimicrobial resistance. *Environment, Development and Sustainability*, *27*(1), 2675-2699. https://doi.org/10.1007/S10668-023-03992-6

[8] Garga Mu'azu, U. (n.d.). *Understanding sanitation practices in Nigeria: Exploring the relationship of socioeconomic factors, demographics and environmental contexts*. https://doi.org/10.17028/RD.LBORO.30776036.V1

[9] Gbeti, C., Donkor, I. A., & Wumbei, A. (2026). Predictors of open defecation amidst community-led total sanitation approach. *Discover Public Health*, *23*(1), 685. https://doi.org/10.1186/S12982-026-01975-2

[10] Jacob, D. E. (2026). Education and behavioral changes for safe water usage. *Springer Water*, *Part F1314*, 217-244. https://doi.org/10.1007/978-3-032-10602-5_8/SAVE-RESEARCH

[11] Khatun, S., Alam, A., & Biswas, S. (2026). Unlocking SDG-6: Accelerating WASH for health and equity in developing countries: A comprehensive systematic review with a focus on India. In *The impact of water scarcity and malnutrition on rural women's health* (pp. 265-289). https://doi.org/10.1007/978-3-032-10887-6_13

[12] Kim, D., et al. (2026). Waterborne diseases burden, determinants and health system gaps in Eastern Uganda: A mixed-methods baseline study in the Busoga region. *Frontiers in Public Health*, *14*, 1808626. https://doi.org/10.3389/FPUBH.2026.1808626/TEXT

[13] Kyambade, M., Mwesigwa, R., Alinda, K., Tumwine, S., & Lwanga, F. (2026). A qualitative exploration of social sustainability performance in health and sanitation projects. *Sustainable Development*. https://doi.org/10.1002/SD.71104

[14] Makita, A., & Calanzani, N. (2026). Community-based interventions addressing open defecation in Sub-Saharan Africa: A scoping review. *Global Health Action*, *19*(1). https://doi.org/10.1080/16549716.2026.2655033

[15] Mehta, L., et al. (2026). Urban community-led total sanitation: Opportunities, barriers and lessons from Nanded, India. *World Development*, *205*, 107336. https://doi.org/10.1016/J.WORLDDEV.2026.107336

[16] Myers, J., Tembe, É., Hutchings, P., Bartram, J., & Evans, B. (2026). Does peer learning improve local government capacity to improve sanitation? A contribution analysis in rural Mozambique. *International Journal of Hygiene and Environmental Health*, *271*, 114701. https://doi.org/10.1016/J.IJHEH.2025.114701

[17] Napoleon Kobhamologi, O., Kalagbor, I., Bealo, B., & Cookey, E. (2025). Impact of community-led total sanitation on the eradication of open defecation in Nigeria: A systematic review. *Journal of Nwashdev*, *1*(2), 288-303.

[18] Ologunagba, M. M., Ogunbode, T. O., & Owoeye, O. M. (2025). Public perception of environmental sanitation regulations on solid waste management in Owo and Akure cities, Ondo State, Nigeria. *Scientific Reports*, *15*(1), 37799. https://doi.org/10.1038/s41598-025-21714-y

[19] Pakin dam, D., et al. (2024). *Evaluation of the community-led total sanitation in Bongo District, Ghana*. https://doi.org/10.37432/jieph-d-25-00293

[20] Panulo, M., et al. (2026). Community-led total sanitation implementation in Malawi: Process evaluation of a sanitation and hygiene intervention. *Global Public Health*, *21*(1). https://doi.org/10.1080/17441692.2026.2638018

[21] Pawar, S., Chougule, M., & Channaveer, R. M. (2025). Human capital and stakeholder engagement intervention: A women empowerment pathway to achieve sustainable community development in water, sanitation, and hygiene at Vaijapur Village of Karnataka, India. *Frontiers in Sustainability*, *6*, 1562033. https://doi.org/10.3389/FRSUS.2025.1562033/TEXT

[22] Wang, R., & Spicer, J. (2026). "All roads lead to Rome?" Performance evaluation across different types of community land trusts based on a large-scale survey. *Journal of Urban Affairs*, *48*(1), 20-41. https://doi.org/10.1080/07352166.2024.2371400

[23] Yang, Y., Han, H., Li, S., Fu, J., Su, X., & Fan, C. (2026). A multilevel regression model to explain disparities in residential cooling infrastructure across heat-threatened regions. *Applied Geography*, *189*, 103939. https://doi.org/10.1016/J.APGEOG.2026.103939.

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Peptide-Based Approaches for Extracellular Matrix Remodeling, Senescence Modulation, and Topical Delivery in Adult and Aging Skin

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Abstract**—** *This study synthesizes current knowledge on bioactive peptides for adult and aging skin, integrating skin structure, aging biology, peptide classes, formulation science, preclinical models and clinical evaluation to inform evidence-based topical strategies. Skin architecture and ageing mechanisms are summarized to contextualize peptide interventions that target epidermal renewal, dermal extracellular matrix, pigmentation and inflammation. Peptide categories covered include signal peptides that promote collagen, elastin and glycosaminoglycan synthesis, carrier peptides that deliver trace metals such as copper, neurotransmitter-modulating peptides for expression lines, and enzyme-inhibiting sequences that reduce MMP and tyrosinase activity. Case examples describe Pal-KTTKS, Pal-GHK, Cu-GHK, tripeptide-10 citrulline, SA1-III (KP1) and Pep 14, highlighting modes of action from collagen fibrillogenesis control and MMP activity reduction to modulation of PP2A/AKT and senescence-associated signaling. Formulation considerations examine physicochemical constraints on cutaneous delivery, lipidation strategies, nanocarriers, cell-penetrating peptides, stability challenges and vehicle design that balance penetration with safety. Mechanistic assays spanning fibroblast and keratinocyte monolayers, 3D skin equivalents and ex vivo human skin are presented alongside clinical and instrumental endpoints including profilometry, ultrasound, histology and DNA methylation age metrics. Safety, sensitization, regulatory labeling and claim frameworks are discussed with recommendations for rigorous trial design, standardized measurements and population-specific risk assessment for aging skin. Practical guidance addresses regimen sequencing, combination with retinoids and procedures such as laser, microneedling and fillers, emphasizing controlled evaluation to optimize matrix remodeling, repair and tolerability in mature skin.*

Keywords— Anti-aging, Dermatology, Peptide, Skincare, Extracellular Matrix, Senescence.

I. INTRODUCTION

Adult and aging skin comprises discrete yet tightly interconnected layers with specialized cell populations and extracellular matrices that are directly relevant to peptide-based interventions. The outer compartment, the epidermis, is a stratified epithelium populated primarily by keratinocytes. Its innermost portion contains proliferating basal keratinocytes, above which lie three differentiated strata: stratum spinosum, stratum granulosum and stratum corneum. The most superficial stratum corneum consists of anucleate corneocytes embedded in a lipid-rich matrix, a configuration that is central to barrier function and to the limitation of transcutaneous penetration of many hydrophilic molecules [1].

Epidermal renewal depends on distinct epidermal stem cell populations distributed within the basal layer and the hair follicle. These stem cells support continuous regeneration of the epidermis on top of the collagen-rich dermal extracellular matrix (ECM). The dermis lies beneath the basal epidermal layer and contains vasculature and adnexal structures within an ECM produced by dermal fibroblasts, which are terminally differentiated cells of mesenchymal origin. Collagen and elastin fibers within this matrix provide mechanical integrity, firmness and tensile strength, and are key targets of aging-associated

degradation processes. Histologic and molecular analyses of photoaged skin show dermal loss of collagen and elastin accompanied by increased dermal inflammation and elevated gene expression of matrix metalloproteinases (MMPs), with concomitant decreases in ECM components such as collagen and elastin [1,2,3].

Extrinsic aging driven by ultraviolet (UV) radiation particularly affects epidermal and dermal structure. UVB, with higher energy and shorter wavelength, primarily damages the epidermis through direct absorption by chromophores including nucleic acids and amino acids, leading to the formation of cyclobutane pyrimidine dimers and photoproducts. These lesions interfere with RNA transcription, activate p53, and induce keratinocyte apoptosis. Photosensitization mechanisms further generate reactive oxygen species (ROS) and reactive nitrogen species that penetrate nuclei and induce oxidative DNA damage and strand breaks. Downstream, oxidative stress activates inflammatory pathways and upregulates MMPs such as MMP-1, MMP-3 and MMP-9, which degrade collagen and elastin, with clinical consequences including wrinkle formation, loss of elasticity, hyperpigmented lesions and impaired barrier function [3].

Within the dermal ECM, fragmented collagen acquires a central role in propagating aging-related signaling. Photoaging is strongly associated with collagen degradation initiated by UV-induced increases in MMP secretion from basal keratinocytes and dermal fibroblasts, linked to activation of AP-1 signaling. In vitro, dermal fibroblasts cultured on synthetically degraded collagen exhibit increased ROS generation, elevated MMP secretion and reduced collagen production. Co-culture experiments show that MMP expression in fibroblasts decreases regenerative capacity and longevity of overlying epidermal stem cells, highlighting bidirectional communication between dermal ECM and epidermal progenitors. These interactions position ECM composition and integrity as critical determinants of both structural and functional aspects of skin aging, including barrier maintenance and repair potential [1].

Structural differences between intrinsically aged and photoaged skin further clarify how tissue architecture underlies clinical phenotypes. Intrinsic aging typically presents with fine wrinkles, some deepening of surface markings, modest loss of elasticity, and relatively smooth but sagging skin. Photoaged skin, in contrast, shows nodular, leathery surfaces, coarse wrinkles, severe loss of elasticity, yellowish mottled pigmentation and a reddened appearance. At the epidermal level, intrinsic aging involves thinning with lower cell growth and minor keratinocyte irregularities, while photoaging is characterized by marked acanthosis followed by cellular atrophy, high basal keratinocyte irregularity, a compact stratum corneum and loss of rete pegs in both states. In the dermis, intrinsic aging features a thinner reticular dermis with decreased fibroblasts and collagen fibers, whereas photoaging produces a thickened dermis with elastosis, increased and hyperactive fibroblasts and mast cells, excessive and disorganized elastin, collagen fiber thickening followed by wear, and formation of a grenz zone associated with solar elastosis. Collagen bundles are thick but disoriented in intrinsic aging, and markedly decreased in photoaging, while glycosaminoglycans are slightly decreased versus markedly increased, respectively. Microvascular loss is moderate in intrinsic aging but pronounced, abnormal and telangiectatic in photoaging [2].

These structural and functional characteristics of epidermis, dermis and ECM set the biological context in which signaling peptides must operate, including constraints imposed by the stratum corneum barrier and the central role of fibroblast–matrix–stem cell interactions in maintaining adult skin homeostasis and responding to injury and photoinduced damage [1,2,3].

Cosmetic use of peptides has expanded markedly, with a wide variety of structures now incorporated into anti-aging formulations targeted to adult and aging skin. These compounds are generally short chains of amino acids, often chemically synthesized or obtained by biotechnology, and are selected or modified to display specific biological activities relevant to skin appearance and function. Within topical products, peptides can be present as isolated molecules, as components of protein hydrolysates categorized as Generally Recognized as Safe (GRAS) by regulatory authorities, or embedded in complex mixtures whose individual contributions to efficacy are not always clear [4,5].

A central conceptual framework classifies cosmetic peptides by their predominant mechanism of action. Signal peptides stimulate production of extracellular matrix molecules such as collagen, elastin, proteoglycans, glycosaminoglycans and fibronectin, and may enhance cell growth and other metabolic functions. Carrier peptides facilitate transport or stabilization of trace elements like copper and manganese inside cells. Neurotransmitter-inhibiting peptides target expression wrinkles by modulating acetylcholine release or related neuronal mechanisms, whereas enzyme-inhibiting peptides reduce the activity of proteases involved in skin aging, including matrix metalloproteinases and tyrosinase [4,6,7,8].

This mechanistic categorization underpins formulation choices for specific clinical indications such as wrinkles, sagging, hyperpigmentation and photo-damage. Signal peptides are particularly relevant for aging skin because they modulate collagen turnover and broader matrix homeostasis. Examples include palmitoyl pentapeptide Pal-KTTKS, a fragment of procollagen I that stimulates collagen types I, III and VI, fibronectin, elastin and glucosaminoglycan production, and is frequently used as an anti-wrinkle and anti-aging topical agent. Palmitoyl tripeptide-1 (Pal-GHK) and its unconjugated form GHK act as collagen-modulating signal peptides, increasing collagen and glycosaminoglycan synthesis in vitro and in vivo. Palmitoyl tripeptide-3/5 mimics a thrombospondin I sequence to activate transforming growth factor-β and thereby promote collagen formation, and is formulated as a firming, moisturizing and anti-wrinkle agent, including for stretch marks. Tripeptide-10 citrulline, a decorin-mimetic, regulates collagen fibrillogenesis and controls fibril diameter and placement, conferring firming and anti-aging effects and utility as a sun protection agent. Synthetic acetyl tetrapeptides such as AcTP1 and AcTP2 further exemplify signal peptides that stimulate collagen I, lumican, keratinocyte growth and syndecan-1 synthesis, with anti-aging and firming applications [6,7,8,9].

Carrier peptides conceptually combine signaling and metal delivery functions. The copper tripeptide complex Cu-GHK, derived from the Gly-His-Lys sequence, is a well-examined example that stabilizes and transports copper while acting as a signal peptide. It supports tissue remodeling by promoting regular synthesis of collagen, elastin, proteoglycans and glycosaminoglycans, enhancing growth and migration of multiple cell types, and exerting anti-inflammatory and antioxidant responses. Topically, Cu-GHK is used in anti-aging, anti-wrinkle, after-sun and skin renewal products, moisturizers and hair growth stimulators. Clinical and experimental studies report increased keratinocyte proliferation, improved skin firmness, elasticity, thickness, wrinkle reduction and diminished hyperpigmentation, as well as stimulation of dermal procollagen synthesis superior to vitamin C or retinoic acid in comparative trials [4,7,9].

Neurotransmitter-inhibiting peptides in cosmetic formulations conceptually target dynamic expression lines by modulating neuromuscular signaling without the invasiveness of injectable toxins. Acetyl hexapeptide-3 (also known as acetyl hexapeptide-8) inhibits SNARE complex formation and catecholamine release, leading to reduced muscle contraction and is marketed for periorbital wrinkles, skin moisturization and improved firmness and tone. Pentapeptide-18 mimics enkephalin mechanisms to inhibit neuronal activity and catecholamine release, and pentapeptide-3 acts as a competitive antagonist at acetylcholine receptors as an alternative to botulinum toxin for expression wrinkles. These molecules illustrate how peptide design can exploit neuromodulatory pathways while remaining within cosmetic claim boundaries focused on appearance [4,5,9].

Despite an extensive catalog of peptide ingredients, research sources note that in vivo efficacy data for many cosmetic peptides remain limited, and mixtures in commercial formulations complicate attribution of clinical effects to individual molecules. Consequently, conceptual discussions emphasize the need to define modes of action, optimize study designs and clarify mechanistic and receptor-level interactions for peptides intended for adult and aging skin care [4,6,7].

TABLE 1
CLASSIFICATION OF PEPTIDES IN SKINCARE

Peptide Class	Mechanism of Action	Key Examples	Primary Indications
Signal Peptides	Stimulate ECM production (collagen, elastin, GAGs)	Pal-KTTKS, Pal-GHK, Palmitoyl tripeptide-3/5, Tripeptide-10 citrulline, AcTP1, AcTP2	Wrinkles, sagging, loss of firmness
Carrier Peptides	Transport trace metals (Cu, Mn) with signaling functions	Cu-GHK (Copper tripeptide)	Tissue remodeling, wound healing, anti-aging
Neurotransmitter-Inhibiting Peptides	Modulate neuromuscular signaling	Acetyl hexapeptide-3/8, Pentapeptide-18, Pentapeptide-3	Expression lines, periorbital wrinkles
Enzyme-Inhibiting Peptides	Reduce MMP and tyrosinase activity	SA1-III (KP1), Rice-derived peptides	Collagen preservation, pigmentation control

Source: Compiled from [4,6,7,8,9]

II. METHODOLOGY

2.1 Search Strategy

A comprehensive literature search was conducted using systematic protocols. Electronic databases searched included PubMed, Google Scholar, MEDLINE, Scopus, and Web of Science. The search covered publications from January 2000 to April 2024. Search terms were organized around the following conceptual axes:

A. Peptide types and mechanisms: ("bioactive peptides" OR "signal peptides" OR "carrier peptides" OR "neurotransmitter-inhibiting peptides" OR "enzyme-inhibiting peptides" OR "cosmetic peptides" OR "anti-aging peptides")

B. Skin biology and aging: ("skin aging" OR "cutaneous aging" OR "photoaging" OR "extracellular matrix" OR "collagen" OR "elastin" OR "senescence" OR "fibroblast" OR "keratinocyte")

C. Formulation and delivery: ("topical delivery" OR "formulation" OR "nanocarrier" OR "lipidation" OR "cell-penetrating peptide" OR "stratum corneum" OR "permeation")

D. Evaluation and clinical studies: ("clinical trial" OR "in vitro" OR "ex vivo" OR "profilometry" OR "ultrasound" OR "methylation age" OR "safety" OR "irritation")

Boolean operators (AND, OR) were used to combine search terms. Reference lists of included articles were also screened for additional relevant publications.

2.2 Eligibility Criteria

Retrieved papers were screened by title, abstract, and full text against defined eligibility criteria. Included were:

- Peer-reviewed original research articles (randomized controlled trials, non-randomized studies, in vitro and ex vivo studies)
- Systematic reviews and meta-analyses
- Authoritative reviews in dermatological, cosmetic, or pharmacological journals
- Studies published in English
- Exclusion criteria encompassed:
- Studies on injectable or systemic peptide therapies (outside topical applications)
- Studies on peptides for non-cutaneous indications
- Conference abstracts without full text
- Studies lacking clearly defined methodology or outcomes
- Self-administered questionnaire surveys without objective measurements

2.3 Quality Assessment

Quality assessment of included studies was performed using appropriate tools: Cochrane Risk of Bias for randomized controlled trials, Newcastle-Ottawa Scale for observational studies, and a custom quality checklist for in vitro and ex vivo studies. Evidence was graded according to the strength and consistency of available data, with priority given to well-designed clinical trials and studies with objective, validated endpoints.

2.4 Data Extraction and Synthesis

Extracted data included: peptide characteristics (type, sequence, concentration, vehicle), study design (in vitro, ex vivo, clinical), participant demographics (where applicable), intervention regimens, outcome measures, and key findings. Given the heterogeneity of study designs, peptide types, and outcome measures, findings were synthesized narratively. Evidence was organized thematically according to the main areas of investigation: peptide classification, mechanisms of action, formulation strategies, evaluation methods, and clinical applications.

III. BIOLOGY AND PATHOPHYSIOLOGY OF SKIN AGING

3.1 Intrinsic Aging Mechanisms

Intrinsic aging in adult skin is characterized by coordinated structural and molecular changes affecting epidermis, dermis, vasculature and adnexal structures. Clinically, intrinsic aging presents with skin thinning, dryness, loss of elasticity and fine wrinkling, accompanied by impaired barrier function, delayed wound healing, cutaneous immunosenescence, dysregulated vasomotor responses, altered glandular secretions, sensory changes and reduced capacity for vitamin D synthesis. Histologic correlation includes thinning and flattening of the dermoepidermal junction, which decreases the contact surface area between epidermis and dermis and contributes to the fragile skin phenotype described as dermatoporosis, cutaneous insufficiency or skin failure. This phenotype reflects compromised regenerative capacity and structural maintenance in advanced intrinsic aging [3].

At the molecular level, telomere shortening is a central mechanism of chronological skin aging. Telomeres at chromosome termini prevent degradation and fusion, and their progressive shortening signals malfunction of this protective system. Shortened telomeres activate the DNA damage response pathway and downstream cyclin-dependent kinase inhibitors p16 and p21, leading to cell cycle arrest and cellular senescence. Intrinsic aging-induced senescence arising from repeated cell division is therefore directly attributed to gradual telomere erosion in cutaneous cells, with specific relevance to fibroblast and keratinocyte populations that support tissue homeostasis [1,3].

Oxidative stress represents another key driver. Reactive oxygen species generated during mitochondrial aerobic metabolism influence chronological aging by disrupting transmembrane signaling, inducing DNA damage and increasing expression of tumor necrosis factor alpha and matrix metalloproteinases. These zinc-containing metalloproteinases degrade extracellular matrix molecules and diminish collagen synthesis. Elevated ROS levels also oxidize cellular lipids, proteins and DNA, producing cellular dysfunction and oxidative protein damage as a primary biomarker of aging. In photodamaged epidermis, accumulation of lipofuscin, a redox-active aggregate, forms age spots and promotes cycles of free radical generation and proteasome inhibition that further favor protein aggregation [2,3].

Genetic determinants modulate intrinsic aging trajectories. Specific genes regulate cellular repair, responses to oxidative stress and synthesis of structural proteins such as collagen and elastin, and many exhibit pleiotropy, influencing multiple phenotypic traits. Single-nucleotide polymorphisms cluster within a set of central pleiotropic genes and pigmentation-associated genes, several located in chromosomal band 16q24.3. Transcriptomic analyses show that most aging-related genes are differentially expressed with age, linking gene expression profiles to cutaneous aging [3].

Hormonal alterations overlay these genetic influences. Declining estrogen during menopause affects skin because of nuclear estrogen receptor isoforms expressed in sebaceous and eccrine glands, dermal fibroblasts, sebocytes, adipocytes, melanocytes and keratinocytes. Reduced estrogen correlates with decreased collagen synthesis, diminished hydration and increased wrinkle formation, leading to dryness, thinning and elasticity loss in postmenopausal skin. In men, age-related testosterone decline similarly reduces skin thickness and sebum production, contributing to drier, less elastic skin, albeit generally less pronounced than estrogen-related changes. Additional hormones such as growth hormone and dehydroepiandrosterone also decrease with age, reducing cellular regeneration, repair and sebum production, and thereby increasing dryness, elasticity loss, impaired tissue regeneration and diminished UV protection [3].

Locally produced insulin-like growth factor 1 is reduced in senescent dermal fibroblasts, promoting connective tissue atrophy and aged skin phenotype. IGF-1 deficiency decreases epidermal proliferation and differentiation, impairs barrier function and relieves inhibition on matrix metalloproteinases, further favoring ECM degradation. Metabolic slowing augments these processes by limiting energy and nutrient supply, impairing cellular function and regenerative capacity, and delaying waste removal. Accumulation of damaged proteins and lipids and formation of advanced glycation end products cross-link collagen fibers, stiffen the matrix and reduce elasticity [3].

3.2 Extrinsic Aging and Photoaging Mechanisms

Extrinsic aging encompasses environmentally driven alterations in skin structure and function, with chronic solar radiation as a principal determinant. Ultraviolet radiation constitutes a small but biologically potent fraction of solar energy, comprising UVA (320–400nm) and UVB (280–320nm), which reach the Earth's surface, while UVC is largely absorbed by the ozone

layer. Immediately adjacent to UVA lies visible blue light (400–490nm), originating from sunlight and artificial sources such as LEDs and electronic screens, and increasingly scrutinized because of its cumulative facial exposure. Wavelength and energy profile govern penetration depth and target structures: UVA penetrates more deeply into the dermis and is strongly implicated in photoaging, while the higher-energy, shorter-wavelength UVB primarily affects the epidermis [3].

UV photons damage skin through direct absorption by chromophores and through photosensitization mechanisms. In direct absorption, nucleic acids and amino acids such as tryptophan and tyrosine act as chromophores that convert UV energy into molecular events, notably formation of cyclobutane pyrimidine dimers and 6-4 photoproducts in DNA. These lesions interfere with RNA transcription, activate p53, and drive keratinocyte apoptosis. Photosensitization generates reactive oxygen species and reactive nitrogen species from endogenous or exogenous sensitizers, leading to oxidative DNA damage and strand breaks. Resulting oxidative stress initiates inflammatory signaling and upregulates matrix metalloproteinases, particularly MMP-1, MMP-3 and MMP-9, which degrade collagen and elastin, reducing skin firmness and disturbing the extracellular matrix. Clinically, these processes manifest as loss of elasticity, wrinkle formation, hyperpigmented lesions and impaired barrier function, and underlie the morphological, histologic and biochemical changes collectively termed photoaging [2,3].

Visible blue light shares several mechanistic features with UVA. In vitro, blue light within 450–490nm exerts cytotoxic effects on human dermal fibroblasts and keratinocytes at high intensities, acting through chromophores such as flavin adenine dinucleotide and flavoproteins that trigger UVA-like photoreactions. At lower intensities, blue light reduces antimicrobial peptide expression, slows epidermal regeneration, compromises skin integrity, decreases cell viability and increases epidermal inflammatory markers. Blue light also stimulates melanogenesis through the G-protein-coupled receptor opsin-3; in darker phototypes, sustained tyrosinase activity and associated protein complexes produce prolonged hyperpigmentation. UVA1 further contributes to pigmentary change via immediate and persistent pigment darkening and delayed tanning, with visible light implicated in rapid, photochemical pigmentation and delayed neomelanogenesis. These pigmentary responses intersect with oxidative stress, as α-melanocyte-stimulating hormone reduces UV-induced hydrogen peroxide in melanocytes, suggesting a coupling between melanogenesis and ROS modulation [3].

Repetitive UV exposure leads to characteristic clinical features of photoaging, including fine and coarse wrinkles, solar elastosis, pigmentation disorders, lentigines, actinic keratoses, telangiectasia, laxity, roughness, extreme dryness and premalignant lesions. Histologically, solar lentigines show basal layer hyperpigmentation and irregular melanosome distribution driven by melanocytic hyperplasia induced by UV, visible light and other environmental factors. Solar elastosis reflects dermal thickening with abnormal elastotic material, associated with chronic ROS generation and MMP-9 and MMP-12 activation. Telangiectasias represent dilated superficial capillaries; proposed mechanisms include UV-induced downregulation of angiogenesis inhibitors such as thrombospondin-1 and increased nitric oxide production that perpetuates vasodilation [2,3].

3.3 Broader Exposome Contributions

Extrinsic aging is further shaped by the broader exposome, including pollution, smoking, diet, sleep and additional radiation sources. Environmental pollutants such as nitrogen dioxide, particulate matter and traffic-related emissions correlate with wrinkles and lentigines, likely through synergistic enhancement of ROS with UV. Ozone, despite limited penetration, oxidizes stratum corneum lipids and proteins, depletes antioxidants including vitamins C and E, activates NF-κB and increases interleukin-8, MMP-9 and COX-2, thereby reducing type I and III collagen and accelerating aging. Smoking delivers thousands of toxic compounds and is dose-dependently linked to premature wrinkling, solar elastosis-like elastic fiber changes, upregulation of MMP-1 and MMP-3, reduced transforming growth factor-β1 signaling, microvascular constriction, DNA mutations and chronic oxidative stress [2,3].

Dietary habits modulate collagen and elastic fibers, with processed sugars promoting abnormal glycation and cross-linking of collagen, and excessive lipid intake fostering a pro-inflammatory milieu with elevated tumor necrosis factor alpha and inflammasome activation. In contrast, omega-3 and omega-6 polyunsaturated fatty acids show anti-inflammatory and photoprotective effects in vitro, and vitamins C and E jointly support antioxidant defense, collagen synthesis and reduction of UV-induced lipid oxidation [2,3].

IV. MOLECULAR ACTIONS OF PEPTIDES IN CUTANEOUS TISSUES

Regulation of the extracellular matrix in aging skin can be directly modulated by several classes of bioactive peptides that act on collagen turnover, fibrillogenesis and metalloproteinase activity. Signal peptides derived from collagen or decorin sequences are particularly relevant, as they engage dermal fibroblasts to adjust production and organization of matrix components. Palmitoyl pentapeptide Pal-KTTKS, a fragment of procollagen I, stimulates synthesis of collagen types I, III and VI, as well as fibronectin, elastin and glucosaminoglycans, thereby addressing the age-related decline in these structural proteins and contributing to firmer, smoother skin with reduced fine lines and wrinkles [6,7,9].

Palmitoyl tripeptide-1 (Pal-GHK) similarly promotes collagen and glycosaminoglycan synthesis in vitro and in vivo, supporting its use as an anti-aging, anti-wrinkle, firming and moisturizing ingredient. Palmitoyl tripeptide-3/5 mimics a thrombospondin I tripeptide sequence, binds the inactive form of transforming growth factor-β and induces its activation, which in turn promotes collagen formation and is exploited in formulations targeting stretch marks and dermal firmness [6,7,9].

Beyond stimulating collagen production, some peptides modulate the qualitative architecture of fibrils. Tripeptide-10 citrulline, designed as a decorin-mimetic, binds collagen fibrils, regulates fibrillogenesis and influences fibril diameter and placement, which translates into firming and anti-aging effects and additional utility as a sun protection agent. By impacting fibril uniformity and growth, this peptide addresses changes in collagen organization that accompany aging and photo-damage [6,7,9].

Synthetic acetyl tetrapeptides also intervene in matrix homeostasis: acetyl tetrapeptide-9 (AcTP1) stimulates collagen I and lumican synthesis, whereas acetyl tetrapeptide-11 (AcTP2) increases keratinocyte growth and syndecan-1 synthesis, effects that enhance dermal structure and epidermal-dermal cohesion in anti-wrinkle and firming applications. These molecules belong to a broader group of matricins or collagen stimulators released from or modeled on extracellular matrix fragments that trigger signaling cascades leading to increased collagen, elastin, proteoglycan, glycosaminoglycan and fibronectin production, with downstream reductions in pigmentation of photo-damaged skin and improvement of wrinkles and elasticity [6,7,9].

Carrier peptides add a complementary layer of dermal remodeling by combining metal delivery with signaling functions. The copper tripeptide complex Cu-GHK (copper Gly-His-Lys) is described as both a signal and carrier peptide that promotes regular synthesis of collagen, elastin, proteoglycans and glycosaminoglycans, while providing anti-inflammatory and antioxidant responses relevant to matrix preservation under oxidative stress. In vitro experiments show that Cu-GHK increases collagen and glycosaminoglycan synthesis and other extracellular matrix molecules, and placebo-controlled clinical trials demonstrate stimulation of dermal procollagen synthesis that is significantly superior to vitamin C, tretinoin or melatonin. In a comparative study, topical Cu-GHK increased collagen in 70% of treated women, compared with 50% for vitamin C and 40% for retinoic acid, and longer-term applications in aged and sun-damaged skin improved density, thickness, elasticity, humidity and wrinkle smoothing via enhanced collagen synthesis. More generally, GHK and related complexes degrade extra-large collagen aggregates in scars, support regular collagen synthesis in normal skin, and promote elastin, proteoglycan and glycosaminoglycan production, alongside growth and migration of multiple cell types and anti-inflammatory and antioxidant activities. These properties directly support tissue remodeling and barrier reinforcement in adult and aging skin [4,7,9].

A distinct strategy for extracellular matrix regulation involves modulating collagen degradation rather than biosynthesis. SA1-III (KP1), a decapeptide derived from the C-terminal portion of serpin A1, has been characterized as a collagen turnover modulating peptide. In human dermal fibroblast cultures, SA1-III increases extracellular soluble collagen levels to an extent comparable with L-ascorbic acid and transforming growth factor-β1. Mechanistic analysis using Western blot and gelatin zymography demonstrates that this increase arises primarily from reduced collagen degradation, with minimal effect on biosynthesis or cell proliferation. Specifically, SA1-III decreases activity of MMP-2 and MMP-9 in cell-conditioned media without altering gene expression of inflammatory mediators in resting or lipopolysaccharide-stimulated fibroblasts. Acting at low concentrations and across fibroblasts from individuals of different ages, SA1-III thus protects collagen from enzymatic breakdown while avoiding pro-proliferative or pro-inflammatory effects, positioning it as a candidate for preserving matrix integrity in aging dermis [6].

TABLE 2
KEY PEPTIDES AND THEIR MECHANISMS OF ACTION

Peptide	Class	Sequence/Structure	Mechanism	Key Effects
Pal-KTTKS	Signal	Palmitoyl-Lys-Thr-Thr-Lys-Ser	Procollagen I fragment	Stimulates collagen I, III, VI, fibronectin, elastin, GAGs
Pal-GHK	Signal	Palmitoyl-Gly-His-Lys	Collagen fragment	Stimulates collagen and GAG synthesis
Cu-GHK	Carrier/Signal	Copper-Gly-His-Lys	Copper delivery + signaling	Stimulates collagen, elastin, GAGs; anti-inflammatory
Tripeptide-10 citrulline	Signal	Decorin-mimetic	Regulates fibrillogenesis	Controls fibril diameter and placement
AcTP1	Signal	Acetyl tetrapeptide-9	Lumican synthesis	Stimulates collagen I and lumican
AcTP2	Signal	Acetyl tetrapeptide-11	Syndecan-1 synthesis	Stimulates keratinocyte growth
SA1-III (KP1)	Enzyme-inhibiting	Serpin A1-derived	MMP-2/9 inhibition	Reduces collagen degradation
Acetyl hexapeptide-3/8	Neurotransmitter-inhibiting	Acetyl-Glu-Glu-Met-Gln-Arg-Arg	SNARE inhibition	Reduces muscle contraction

Source: Compiled from [4,6,7,9]

V. TYPES AND SOURCES OF PEPTIDES FOR SKINCARE FORMULATIONS

Synthetic and bioengineered peptides used in skincare are typically short amino acid chains whose sequences and chemical modifications are designed to achieve specific cutaneous functions, including improved skin penetration, receptor binding, stability and solubility. Modern approaches allow tailoring of these properties so that peptides can better traverse the stratum corneum, particularly in dry or aged skin, and interact with defined molecular targets in the epidermis and dermis [5,7].

Several families of synthetic signal peptides have been developed to stimulate extracellular matrix production. Palmitoyl pentapeptide Pal-KTTKS is a pro-collagen I fragment that stimulates collagen types I, III and VI, fibronectin, elastin and glucosaminoglycan production, and is frequently used as an anti-wrinkle and anti-aging topical agent. Its design includes five amino acids linked to a 16-carbon aliphatic chain, which improves permeability through the lipid matrix of the skin [6,7,9].

Palmitoyl tripeptide-1 (Pal-GHK) consists of the Gly-His-Lys collagen fragment conjugated to palmitic acid and has been shown in vitro and in vivo to stimulate collagen and glycosaminoglycan synthesis, supporting anti-aging, anti-wrinkle, firming and moisturizing actions in cosmetic products. Palmitoyl tripeptide-3/5 mimics a thrombospondin I tripeptide, binds inactive transforming growth factor-β and promotes its activation, thereby enhancing collagen formation; it is formulated as a firming, moisturizing and anti-wrinkle agent, including for stretch marks [6,7,9].

Tripeptide-10 citrulline, a decorin-mimetic peptide, regulates collagen fibrillogenesis and influences fibril diameter and placement, conferring anti-aging, firming and sun-protection properties. Synthetic acetyl tetrapeptides such as AcTP1 and AcTP2 further exemplify signal peptides: AcTP1 stimulates collagen I and lumican synthesis, while AcTP2 stimulates keratinocyte growth and syndecan-1 synthesis, with both used as anti-wrinkle and firming ingredients [6,7,9].

Carrier peptides represent another important synthetic class. Copper tripeptide complex Cu-GHK (copper Gly-His-Lys) is a well-examined molecule that acts both as signal and carrier peptide. It promotes regular synthesis of collagen, elastin, proteoglycans and glycosaminoglycans, and provides anti-inflammatory and antioxidant responses. Experimental work shows that Cu-GHK increases collagen, glycosaminoglycans and other extracellular matrix molecules in vitro. Placebo-controlled clinical trials demonstrate that topically applied Cu-GHK stimulates dermal procollagen synthesis significantly more than vitamin C, tretinoin or melatonin, with one study reporting increased collagen production in 70% of women treated with Cu-GHK versus 50% with vitamin C and 40% with retinoic acid. Additional studies in aged and sun-damaged skin showed improved density and thickness, elasticity, humidity, wrinkle smoothing and overall appearance after Cu-GHK cream application [4,7,9].

Synthetic neurotransmitter-inhibiting peptides are designed to act on neuromuscular signaling to reduce expression lines. Acetyl hexapeptide-3 (Acetyl hexapeptide-8, Argireline) inhibits SNARE complex formation and catecholamine release, and is used particularly for periorbital wrinkles, skin moisturization and improved firmness and tone. Pentapeptide-18 (Leuphasyl) mimics enkephalin mechanisms to inhibit neuronal activity and catecholamine release, while pentapeptide-3 (Vialox) functions

as a competitive antagonist at acetylcholine receptors and is positioned as a topical alternative to botulinum toxin for expression wrinkles. These peptides exemplify rational design of synthetic sequences to target specific neuronal pathways within the constraints of cosmetic indications [7,9].

Bioengineered peptides produced by biotechnological processes complement chemically synthesized molecules. Peptamide-6, generated by Saccharomyces yeast fermentation, is a firming signal peptide that increases collagen synthesis and upregulates growth factors, transmembrane, matrix and cell-shock proteins, making it suitable for face, body and eye creams. Recombinant human growth hormone is another biotechnological peptide classified as a signal peptide; it increases IGF-1 production, enhances fibroblast and keratinocyte activity and sebum production, and is used in anti-aging, anti-wrinkle and post-resurfacing formulations. More broadly, protein hydrolysates containing bioactive peptides are recognized as safe and are employed for skin moisturization and anti-aging applications, while biomimetic peptides produced in transformed bacteria systems have been explored to modulate dermal repair markers such as type I procollagen and AP-1 in vitro and in vivo [4,7,10].

Naturally derived peptides for skincare originate from plant, marine and animal sources, often obtained by controlled digestion or hydrolysis of structural or storage proteins. These peptide mixtures and isolated sequences can display anti-aging, antioxidant, whitening, moisturizing and repair-promoting activities that are relevant for adult and aging skin, but available data are uneven and frequently limited to small studies or in vitro models [2,7,11].

Plant-derived peptides include soybean, rice and cereal peptides. A pseudo-randomized in vivo/in vitro study in 10 women reported that a soybean peptide significantly increased glycosaminoglycan and collagen synthesis, supporting its anti-aging potential; this peptide is classified as an enzyme-inhibitor in cosmetic taxonomy, although the detailed mechanism is not fully defined. Rice-derived peptides have been studied in several forms. After special processing of rice bran protein, low molecular weight peptides of less than 3000Da, including black rice oligopeptides around 1300Da, were identified. These oligopeptides inhibited matrix metalloproteinase activity and stimulated hyaluronan synthase 2 gene expression in human keratinocytes in a dose-dependent manner, indicating potential to support extracellular matrix integrity and hydration. Three newly identified rice bran protein peptides with C-terminal tyrosine residues showed significant inhibitory effects against tyrosinase-mediated monophenolase reactions; one sequence, CT-2 (Leu-Gln-Pro-Ser-His-Tyr), potently inhibited melanogenesis in mouse melanoma cells without cytotoxicity, positioning rice bran protein as a potent source of tyrosinase-inhibitory peptides for melanin-related skin conditions [7].

In a separate cosmetic formulation, a biological peptide complex comprising di- and tri-peptides from rice and lupin proteins was optimized for rapid assimilation by skin cells and passage through the barrier; previous in vitro work showed that rice-derived di- and tri-peptides stimulate fibroblast proliferation and messenger RNA expression of procollagen, collagen VII and fibrillin-1, supporting dermal matrix rebuilding in anti-aging applications [11].

Silk fibroin peptide represents a marine-adjacent animal-derived ingredient obtained from the silkworm Bombyx mori. Experimental data demonstrate that silk fibroin peptide can inhibit inflammation and enhance the anti-inflammatory activity of tTAT-superoxide dismutase, which penetrates cells and tissues and exerts antioxidative activity in a mouse inflammation model. Despite these promising anti-inflammatory and antioxidant properties, no human in vivo efficacy data are currently available, emphasizing the need for translational studies before firm conclusions about cosmetic benefit can be drawn [7].

Keratin-based peptides illustrate animal-derived structural protein digestion applied directly in topical skincare. Formulations containing keratin-based peptides of molecular weight less than 1000Da have been described as hemostatic, moisturizing, repair-promoting and potentially radio-protective. In a placebo-controlled in vivo study with nine healthy females with dry skin types III to V, a 3% keratin-based peptide hand cream improved water-holding capacity, hydration and elasticity relative to deionized water and untreated areas, and appeared to prevent some damaging effects associated with surfactant exposure. Additional studies in six and 16 healthy females tested 3% keratin-based peptide in aqueous solution and internal wool lipid liposome suspension; both formulations improved skin barrier integrity and water-holding capacity, and combining keratin-based peptide with internal wool lipids led to further beneficial effects. These studies are limited by low participant numbers and lack of mechanistic detail, yet they support the concept that short keratin-derived peptides can enhance barrier function and hydration in dry, possibly aging skin [7].

Within daily moisturization strategies, sophisticated peptides and protein derivatives from wheat, rice, silk, soybean and oat are already used as humectant and film-forming agents. Quaternary N-alkyl derivatives of proteins or small polypeptides with long side chains increase lipophilicity, promote binding to the stratum corneum and improve percutaneous absorption, while

biomimetic small peptides that mimic collagen or enzyme sequences have been proposed as moisturizers with enhanced surface smoothing and hydration [2,5,7].

TABLE 3
SOURCES OF BIOACTIVE PEPTIDES FOR SKINCARE

Source	Examples	Key Activities	Evidence Level
Synthetic	Pal-KTTKS, Pal-GHK, Cu-GHK, Acetyl hexapeptide	ECM stimulation, neuro-modulation, copper delivery	Strong (clinical trials)
Bioengineered	Peptamide-6, Recombinant growth hormone	Collagen synthesis, growth factor stimulation	Moderate
Plant-Derived	Soybean peptides, Rice peptides, Lupin peptides	Collagen synthesis, MMP inhibition, tyrosinase inhibition	Moderate-Limited
Animal-Derived	Silk fibroin, Keratin peptides	Anti-inflammatory, barrier support, hydration	Limited

VI. FORMULATION SCIENCE OF PEPTIDE-BASED SKINCARE

Physicochemical constraints of peptides strongly influence their topical delivery and must be accounted for in formulation design. Successful transdermal molecules generally have molecular weight below 500Da, moderate lipophilicity with logP between 1 and 3, melting point below 200°C and reasonable aqueous solubility above 1 mg/mL. Diffusivity in the stratum corneum decreases with increasing size and number of hydrogen-bonding groups, and is maximal for small, non-hydrogen-bonding molecules. Peptides and proteins contain multiple amide bonds that act as hydrogen bond donors and acceptors, are often charged at physiological pH, and therefore intrinsically hydrophilic. These features drastically lower their diffusivity through the lipophilic stratum corneum, making this outer barrier the dominant obstacle for peptide penetration and necessitating delivery-enhancing strategies [9].

Several approaches exploit physicochemical modification and external energy to improve dermal access. Chemical penetration enhancers such as esters, fatty alcohols and fatty acids have been used to increase permeation of actives like melatonin across skin, although enhancement is dependent on enhancer structure and can be limited by local toxicity or irritation. Physical methods including electroporation, iontophoresis, sonophoresis and laser microporation can transiently disrupt barrier properties and have enabled delivery of large molecules such as insulin and cyclosporine A; however, these techniques require specialized equipment and their feasibility and reproducibility in routine cosmetic use remain challenging [9].

Conjugation of peptides to hydrophobic moieties such as fatty acids is another strategy to increase lipophilicity and stratum corneum partitioning. For example, a palmitoyl derivative of interferon α penetrated human skin 5- to 6-fold more efficiently than the unconjugated peptide, and topical palmitoyl KTTKS (palmitoyl pentapeptide-4) showed significantly greater clinical improvement in facial skin compared with the non-palmitoylated sequence. These data illustrate that tuning partition coefficient and charge through lipidation can markedly alter cutaneous bioavailability while preserving biological activity [9,12].

Nanotechnology-based carriers further address peptide stability and delivery requirements. Solid lipid nanoparticles are composed of physiological lipids and can encapsulate actives to protect them from enzymatic and chemical degradation, reduce transepidermal water loss, and provide controlled, sustained release that enhances therapeutic effect. Nonetheless, their relatively ordered solid matrices may limit drug loading and promote expulsion during storage. To reduce internal crystallinity and increase payload capacity, nano lipid crystal systems combine solid and liquid lipids, improving solubility of actives in the oil phase and minimizing expulsion. These particles share occlusive properties with solid lipid nanoparticles, forming films that enhance hydration and residence time on the skin surface. Importantly, several studies show that such lipid nanoparticles usually remain localized in the stratum corneum and appendages and do not readily cross into deeper epidermis, which restricts direct delivery to dermal targets unless additional permeation strategies are employed [12,13].

Cell penetrating peptides and related carriers provide complementary solutions by mediating translocation of nanocarriers and cargo across cellular membranes. Positively charged sequences rich in arginine and lysine, such as TAT, have been conjugated to solid lipid nanoparticles and liposomes to enhance deposition into deeper epidermal layers. In experimental systems, coating nanoparticles with TAT facilitated their movement from the stratum corneum into the viable epidermis, with depth profiling revealing fluorescence up to 120μm when occlusive film formation allowed progressive penetration. Mechanistically, early binding of the cationic peptide to the stratum corneum, water evaporation from the formulation, and occlusive lipid film formation precede CPP-guided movement into deeper layers. However, high cell-penetrating activity of some CPPs raises

safety concerns that drugs could be transported beyond intended layers into deeper tissues, underscoring the need to balance penetration enhancement with spatial control of distribution. Alternative CPPs with restricted exocytosis have been proposed to confine entry to epidermal cytosol while maintaining barrier integrity in reconstructed human epidermis models [12,14].

Peptide-containing creams and emulsions must also maintain molecular stability against environmental stress at the skin surface. Water-in-oil or oil-in-water formulations can create microenvironments that protect labile peptides, prolong residence time and slightly enhance transepidermal passage without disrupting barrier function. For tested CPP formulations, standard cosmetic vehicles provided sufficient stability and allowed penetration into epidermal layers while preserving cell viability, supporting their suitability for cosmeceutical applications [5,14].

Vehicles and dosage forms for peptide-based skincare must balance physical stability, controlled release and appropriate skin tolerability while maintaining peptide integrity. Emulsions are commonly employed, with oil and aqueous phases heated and combined under stirring to yield homogenous systems. An example is an argireline-containing lotion in which isopropyl myristate, glycerin monostearate, paraffin, cetyl alcohol, canola oil, non-ionic surfactants, humectants and preservatives are processed at 80°C before cooling and quality control testing. This formulation exhibited uniform white appearance, microscopic homogeneity of internal phases, a pH of 5.85±0.18 within the physiological skin range, and resistance to centrifugal stress and freeze–thaw cycling, indicating robustness against mechanical and thermal challenges typical of cosmetic storage and use conditions [15].

Dosage-form performance is further characterized by in vitro release and rheological behavior. For the argireline lotion, a 6-hour release study showed non-Fickian diffusion, interpreted as a combination of diffusion and erosion-controlled processes, with Higuchi kinetics providing the best fit (R^2=0.9949), consistent with diffusion-driven release from a semi-solid matrix. Rheological assessment reported a viscosity of 480rpm (instrument parameter), supporting suitable spreadability for topical application. Stability studies across different temperatures over 28 days revealed no changes in physical appearance, organoleptic properties or argireline content, and a skin irritation test in healthy volunteers showed no erythema or edema, underscoring the feasibility of such lotions as peptide delivery vehicles in routine skincare regimens [15].

Vehicle selection also interacts with peptide chemical stability. Work on acetyl hexapeptide-8 (Argireline) has shown that peptides can undergo substantial oxidation in complex cream or serum matrices, with oxidation often complete depending on formulation and sample handling. Accelerated stability testing demonstrated that Argireline content remained stable at 25°C but decreased to 59% and 41% after 24 hours at 40°C and 60°C, respectively. These observations highlight that process and storage temperatures are critical parameters in dosage-form design for bioactive peptides. Because methionine and other oxidation-prone residues can be converted to sulfoxides or sulfones during production, purification and storage, resulting in loss of function, reduced stability or increased aggregation, analytical characterization of peptide-containing vehicles is required to monitor side-chain modifications and ensure cosmeceutical potency over shelf life [16].

Beyond conventional emulsions, nanotechnology-based vehicles provide alternative dosage forms compatible with antioxidant and vitamin co-actives. Solid lipid nanoparticles encapsulate active ingredients within physiological lipids to protect against enzymatic degradation, prevent transepidermal water loss and deliver controlled, prolonged release, thereby enhancing therapeutic effect. Nano lipid crystal systems with mixed solid and liquid lipids further increase loading capacity and minimize drug expulsion during storage, while retaining occlusive film-forming properties on the skin surface. In cosmeceutical contexts these nanocarriers have been used for vitamins and antioxidants, such as liposomal sodium ascorbyl phosphate, to improve epidermal penetration and stability of otherwise labile molecules. Encapsulation can thus support compatibility between peptides and co-formulated antioxidants by shielding each component from degradative interactions and modulating their release profiles [5,12,17].

Nanoparticle-based dosage forms also have defined spatial distribution and penetration characteristics that bear on safety and compatibility. Studies with solid lipid nanoparticles and nano lipid crystals report that these particles generally do not cross the stratum corneum barrier; instead, they reside within this outer layer and release their cargo into the epidermis, aided by occlusive film formation that enhances hydration and residence time. When combined with cell-penetrating peptides such as TAT, lipid nanoparticles and liposomes can be guided into deeper epidermal layers, raising the possibility of co-delivering peptides with other actives like melatonin or cyclosporine. However, high translocation capability of some CPPs introduces a risk that actives might be transported beyond intended cutaneous targets, so compatibility assessments must consider not only chemical interactions between ingredients but also the depth and distribution of delivery achieved by the chosen vehicle and enhancer combination [12,14].

Compatibility with other topical anti-aging agents, notably retinoids and acids, depends on maintaining barrier function and minimizing irritation. Evidence on topical therapies shows that retinol, retinaldehyde, glycolic acid and azelaic acid improve epidermal turnover, dermal collagen, pigmentation and inflammation but can be irritative, particularly at higher concentrations or in sensitive skin. At the same time, humectant- and emollient-rich formulations containing glycerin or hyaluronic acid help preserve barrier integrity and hydration, enhancing tolerance to active ingredients. Incorporating peptides into vehicles that already contain humectants, emollients and barrier-restoring agents may therefore support their use alongside retinoids and acids, provided that pH, temperature and oxidative environment are controlled to protect peptide structure while maintaining the established efficacy and safety profiles of co-formulated actives [2,3,5,17].

TABLE 4
DELIVERY SYSTEMS FOR PEPTIDE-BASED SKINCARE

Delivery System	Mechanism	Advantages	Limitations
Chemical Penetration Enhancers	Disrupt lipid organization	Simple, cost-effective	Potential irritation
Lipidation (Palmitoylation)	Increase lipophilicity	Enhanced partitioning	Requires synthesis
Solid Lipid Nanoparticles	Encapsulation, occlusive film	Protection, controlled release	Limited loading capacity
Nano Lipid Crystals	Mixed solid/liquid lipids	Higher loading, reduced expulsion	Complex formulation
Cell-Penetrating Peptides (CPPs)	Transmembrane translocation	Enhanced epidermal penetration	Safety concerns
Emulsions (O/W, W/O)	Solubilization, skin hydration	Good tolerability, stable	Limited penetration

Source: Compiled from [5,9,12,13,14]

VII. EVALUATION OF PEPTIDE-CONTAINING SKINCARE PRODUCTS

Mechanistic assessment of peptide-based skincare relies heavily on in vitro and ex vivo models that recapitulate key features of adult and aging skin while allowing controlled manipulation of cellular pathways. Several studies have implemented culture systems of human dermal fibroblasts, keratinocytes, three-dimensional (3D) reconstructed skin equivalents and ex vivo biopsies to dissect peptide effects on collagen turnover, senescence, inflammation and barrier-related parameters [6,18,19].

For collagen-modulating peptides such as SA1-III (KP1), primary human dermal fibroblast cultures have been central. In one study, soluble collagen levels in culture media were quantified using an in-house sandwich enzyme-linked immunosorbent assay after SA1-III treatment, demonstrating increases comparable to positive controls L-ascorbic acid and transforming growth factor-β1. Follow-up mechanistic work combined Western blot analysis of type I collagen in cell lysates and conditioned media with gelatin zymography to profile matrix-degrading enzymes. These experiments showed that SA1-III elevates extracellular collagen predominantly by reducing degradation, with minimal influence on biosynthesis or fibroblast proliferation. Activity of MMP-2 and MMP-9 decreased in conditioned media, and gene expression of inflammatory mediators remained unchanged in resting and lipopolysaccharide-stimulated fibroblasts, indicating that collagen preservation occurred without pro-inflammatory signaling. Importantly, SA1-III was effective at reasonably low concentrations and across fibroblasts derived from donors spanning a wide age range, supporting its relevance for aging dermis [6].

Broader serpin A1-derived constructs have also been probed in vitro. Wound-healing models using monolayers of a kidney epithelial line and primary human skin fibroblasts showed that natural serpin A1, the synthetic C-terminal peptide A1-C26, and a serpin A1–insulin-like growth factor fusion protein all reduced wound size. A1-C26 significantly enhanced collagen I production in fibroblasts, whereas the chimera promoted fibroblast proliferation and thymidine incorporation. In primary keratinocytes, only the chimera reduced wound size, illustrating cell-type-specific responses and the utility of parallel fibroblast and keratinocyte assays to map peptide actions on repair processes [6].

Senotherapeutic evaluation of Pep 14 has used an integrated platform of human skin cells, 3D skin equivalents and ex vivo human skin biopsies. In multiple senescence-inducing models that mimic intrinsic chronological aging, Hutchinson–Gilford progeria syndrome (HGPS) and extrinsic stresses such as UVB and etoposide, Pep 14 treatment reduced cellular senescence and inflammation markers while enhancing cellular resilience and DNA repair. Single-cell RNA sequencing of HGPS fibroblasts revealed diverse subpopulations of senescent and non-senescent cells; pseudotime analysis showed that Pep 14 increased non-senescent and early-senescent cells and reduced late-senescent cells by supporting DNA repair and preventing

progression into advanced senescence. Across clusters, Pep 14 consistently lowered CDK2AP1 mRNA, leading to CDK2 activation and a transient cell cycle arrest that facilitates repair and limits accumulation of SASP-secreting late-senescent cells. Notably, apoptosis and autophagy-related mRNAs were not induced, indicating a senomorphic rather than senolytic mode of action [18,19].

Ex vivo human skin models have extended these mechanistic insights to tissue-level outcomes directly relevant to topical application. Treatment of ex vivo skin biopsies with Pep 14 formulated to deliver up to 2% of the peptide into the dermis led to improved histological scores, reduced mRNA expression of senescence markers such as p16, decreased IL-8 and TYR, and increased expression of keratins and collagen. A skin-specific DNA methylation clock (MolClock) was applied to quantify biological age; Pep 14 decreased methylation age by an average of 2.6 years, with similar reductions observed using other established clocks. In comparative ex vivo experiments, rapamycin reduced p16 and IL-8 expression but did not improve epidermal area or DNA methylation age, and in some parameters worsened tissue phenotype, highlighting that senescence marker reduction alone may not translate into global skin rejuvenation. Topical retinol, used as an anti-aging reference, induced stratum corneum peeling but increased CDKN2A and CXCL-8 mRNAs in both epidermis and dermis, changes plausibly associated with irritation and heightened senescence markers. These ex vivo data underscore the value of combined histologic, transcriptional and epigenetic readouts for mechanistic assessment of peptide formulations in human skin [1,18,19].

Collectively, fibroblast and keratinocyte monolayer assays, 3D skin equivalents and ex vivo biopsies provide complementary mechanistic information on peptide effects in collagen turnover, wound repair, senescence modulation and inflammation. Such models allow rigorous comparison of peptide candidates with established actives like retinoids and rapamycin under controlled conditions, and are essential for linking molecular pathways to functional rejuvenation markers before clinical evaluation [1,6,18,19].

Clinical and instrumental evaluation in human subjects is essential for determining whether peptide-containing formulations deliver meaningful anti-aging benefits beyond in vitro and ex vivo findings. Several trials have examined facial and periorbital wrinkles, hydration, elasticity and skin surface topography using standardized imaging and biophysical tools [7,11,20].

Palmitoyl pentapeptide pal-KTTKS has been evaluated in multiple placebo-controlled, double-blind human studies focused on periorbital wrinkles. In one trial, a 0.005% pal-KTTKS formulation applied twice daily for 28 days to the periocular region produced quantitative reductions in fold depth, fold thickness and skin rigidity by 18%, 37% and 21%, respectively, as measured by optical profilometry. These improvements were reproduced in two additional double-blind studies enrolling women with moderate to distinct periorbital wrinkles. A split-face, left–right randomized trial in 93 subjects further demonstrated significant enhancement in fine lines and wrinkles compared with vehicle, using wrinkle volume, wrinkle depth, skin roughness, elastin fiber density and collagen IV regulation at the dermal–epidermal junction as endpoints. These data illustrate how profilometry and histologically inferred matrix changes can be combined to substantiate clinical efficacy of signal peptides in vivo [7,9].

Clinical investigation of palmitoyl tripeptide-3/5 has similarly relied on instrumental wrinkle analysis. In vivo results with a cream containing 10–25ppm palmitoyl tripeptide-3/5 demonstrated dose-dependent wrinkle reduction quantified by PRIMOS surface topography. In an 84-day efficacy study with 60 Chinese volunteers, twice-daily application reduced skin roughness more effectively than control and placebo creams, and outperformed pal-KTTKS-containing formulations. These findings, based on objective surface profiling, support the concept that peptides which both stimulate collagen synthesis and interfere with MMP-1 and MMP-3 mediated collagen degradation can yield measurable improvements in wrinkle metrics in human subjects [7].

Cu-GHK has been the subject of several controlled trials examining dermal remodeling and global appearance. A non-randomized, four-arm active-controlled study compared creams containing GHK-Cu, tretinoin, vitamin C and melatonin applied to the thighs for one month. Immunohistological assessment of biopsies showed increased procollagen synthesis in 7/10 patients with GHK-Cu versus 4/10, 5/10 and 5/10 for tretinoin, vitamin C and melatonin, respectively. Additional studies over 8 and 12 weeks used visual evaluation and ultrasound to document improved skin laxity, clarity, fine lines, wrinkles, mottled hyperpigmentation, density and thickness, together with enhanced viscoelastic properties and keratinocyte proliferation, all without significant irritation. These trials integrate subjective scoring with quantitative imaging and histology to characterize the clinical performance of a carrier–signal peptide complex in photodamaged facial skin [7,9].

Other peptide-based formulations have been assessed with sophisticated instrumental approaches. A vitamin C serum containing rice-derived di- and tri-peptides, hyaluronic acid and mineralizing water was tested using Quantirides evaluation of

crow's-foot replicas and Toposurf 3D fringe projection analysis of wrinkle "peaks" and "valleys". After 29 days of use, the number, surface and length of crow's-foot wrinkles decreased, and topographic parameters indicated smoothing of the skin surface, findings that aligned with investigator clinical scoring and subject self-assessment of fine wrinkle improvement. Dansyl chloride labelling of the stratum corneum showed accelerated desquamation and epidermal renewal relative to untreated skin, supporting a rejuvenation effect at the tissue level, although the contribution of individual ingredients could not be disentangled. These methods exemplify how non-invasive optical and fluorescence techniques can capture changes in epidermal turnover and wrinkle morphology following peptide-containing treatments [11].

Formulation-focused clinical studies also provide information on safety and instrumentally measured performance. An argireline (acetyl hexapeptide-8) lotion formulated as an emulsion was assessed for stability and tolerability in human volunteers. Physical characterization showed homogenous appearance, appropriate pH and robust resistance to centrifugal and freeze–thaw stress. A 6-hour release study indicated non-Fickian diffusion governed by Higuchi kinetics, and skin irritation testing revealed no erythema or edema. Complementary work on argireline oxidation in creams and serums underscored that peptide content can decline markedly at elevated temperatures, highlighting the need to control storage conditions to maintain clinical efficacy. These observations link vehicle design, peptide stability and dermatological safety in the context of human use [15,16].

More broadly, clinical and instrumental approaches recommended for cosmeceutical evaluation include randomized controlled trials with defined inclusion and exclusion criteria, standardized measurements of hydration, elasticity, wrinkles and pigmentation, and use of non-invasive imaging such as dermoscopy and digital photography, alongside dermatological irritation and sensitization testing and appropriate statistical analysis. Such frameworks have been proposed to systematically assess peptide-based formulations within cosmeceutical practice [20].

TABLE 5
SUMMARY OF CLINICAL EVIDENCE FOR KEY PEPTIDE FORMULATIONS

Peptide	Study Design	Key Findings	Assessment Methods
Pal-KTTKS	Double-blind, placebo-controlled	18-37% reduction in fold depth, thickness, rigidity	Optical profilometry
Cu-GHK	Active-controlled (4-arm)	70% showed increased procollagen synthesis	Immunohistology, ultrasound
Palmitoyl tripeptide-3/5	84-day RCT (n=60)	Dose-dependent wrinkle reduction	PRIMOS surface topography
Vitamin C + Rice Peptides	29-day clinical study	Reduced crow's-foot wrinkles, smoother surface	Quantirides, Toposurf 3D
Acetyl hexapeptide-8	Stability and tolerability	No irritation, stable formulation	Skin irritation testing

VIII. SAFETY, REGULATORY AND ETHICAL CONSIDERATIONS

Dermatological safety of peptide-containing skincare must be considered in the broader context of cutaneous responses to topical agents, particularly in adult and aging populations with fragile skin and frequent polypharmacy. Elderly individuals exhibit increased susceptibility to adverse reactions because of chronic use of topical and systemic medications, cumulative environmental exposures and structural skin changes that compromise barrier integrity. Stronger medications are recommended only when the expected therapeutic benefit justifies the associated risk, underscoring the need for cautious selection and monitoring of any bioactive ingredient used on aged skin [21].

Contact dermatitis represents a key safety concern. Allergy-type reactions remain common among older adults despite an age-related reduction in delayed-type hypersensitivity responses, which arises from decreased numbers of Langerhans cells, diminished T-cell populations and reduced vascular reactivity. These immunological changes would be expected to lower individual susceptibility to allergic contact sensitivity, yet decades of potential sensitization and increased exposure to topical preparations sustain a significant burden of allergy in geriatric patients. Topical medications are identified as the most frequent culprits, with reports that up to 81% of patients treated for chronic leg ulcers exhibit allergic reactions to these agents. In this context, patch testing prior to the introduction of new topical medications is advocated for high-risk groups, such as those with dermatitis or ulceration of the lower extremities, with test panels including medicaments, dressings, dental prostheses and ocular medications. Generalized allergic rashes in the aged are far more often attributed to medicines than to food, and agents may additionally provoke phototoxic or photoallergic responses by increasing sensitivity to sunlight [21].

Against this background, available data on cosmetic peptides are relatively reassuring but remain incomplete. A survey of proteins and peptides used in cosmetics notes that some proteins are linked to skin allergy, including contact dermatitis, yet no evidence was found that peptides currently employed in cosmetic formulations raise specific safety concerns of this type. Furthermore, protein hydrolysates that contain bioactive peptides are categorized as Generally Recognized as Safe by the FDA, providing a regulatory indication of acceptable systemic and dermatologic risk under normal conditions of use. Nonetheless, this evaluation emphasizes the diversity of peptide structures and acknowledges that many cosmetic trials assess formulations containing peptides together with multiple other active ingredients, making it difficult to clearly attribute observed benefits or adverse effects to peptides alone. These limitations highlight the need for well-controlled safety assessments that isolate peptide contributions to cutaneous responses, particularly in vulnerable aging skin [4,14].

Immunological and inflammatory aspects are also central to peptide safety. Some bioactive peptides derived from food proteins show anti-inflammatory and immunomodulatory properties in systemic models. For example, pea protein hydrolysate significantly reduces lipopolysaccharide/interferon-γ-induced nitric oxide production and suppresses TNF-α and IL-6 in macrophages, while maintaining cell viability, and enhances phagocytic activity and beneficial cytokine profiles in mice. Fermented milk-derived peptides similarly decrease proinflammatory TNF-α and IL-6 and increase IL-10 in tumor models, suggesting anti-inflammatory and potential anticancer activities. Although these findings are based on oral administration and systemic outcomes, they illustrate that peptides can interact with immune pathways in ways that may theoretically influence cutaneous inflammation, underscoring the importance of characterizing immunological effects when adapting such molecules or related sequences for topical use in adult and aging skin [22].

Methodological frameworks for cosmeceutical evaluation provide practical guidance for structuring safety investigations. Recommended approaches include dermatological assessments of irritation and sensitization, systematic monitoring of adverse reactions and side effects, and adherence to ethical and regulatory requirements. Clinical trial designs call for clear inclusion and exclusion criteria, standardized measurement of parameters such as hydration, elasticity, wrinkles and pigmentation, and use of non-invasive imaging modalities to complement subjective questionnaires. Safety assessment protocols emphasize the need to document severity and frequency of cutaneous events and to interpret data within the context of existing scientific evidence on active ingredients, including peptides. These structured methods are particularly relevant for peptide-based formulations intended for aging populations, where immunological shifts, comorbidities and concurrent medications may modify both risk and benefit profiles [20].

Regulatory framing of peptide-containing products determines how they can be marketed, what evidence is required, and which claims are permissible. Cosmeceuticals are defined as topical products, typically creams, lotions, serums and ointments, that are designed to improve the appearance of aging skin but are generally not tested or approved as drugs that alter cellular functions. Their presence on the market is often justified by theoretical benefits derived from in vitro studies of active ingredients rather than by formal drug-level clinical evaluation. Regulations governing concentration of components and the scope of activity claims differ across countries and organizations, which creates heterogeneous standards for peptide-based formulations and complicates cross-jurisdictional comparison of products [16].

Within this framework, peptides are one category of active ingredients among retinoids, antioxidants and growth factors that are incorporated into cosmeceuticals to target specific skin concerns such as aging, hyperpigmentation and acne. Methodological guidance for evaluation of such products stresses that active ingredients and formulations should be linked to clearly defined skin conditions and mechanistic targets, and that scientific evidence must support claims of efficacy and safety. Recommended procedures include comprehensive literature review, identification of key actives, in vitro and in vivo experimentation, randomized controlled trials, and structured safety assessment, all conducted under ethical and regulatory oversight. These steps are intended to align peptide-containing cosmeceuticals with standards that bridge cosmetics and pharmaceuticals, even though formal drug approval pathways may not be pursued [20].

Labeling practices for cosmetic peptides operate within ingredient nomenclature systems and claim restrictions. In Europe, a dedicated glossary of common ingredient names for cosmetic labeling lists hundreds of entries containing the word "peptide," reflecting the diversity of sequences used in anti-aging products. Anti-aging cosmetics are selected for analysis when labels contain terms such as anti-wrinkle, anti-aging, wrinkle repair, regenerator, aging, anti-slackening or firming, indicating that peptide-related claims are typically framed around improvement of appearance rather than treatment of disease. Exploratory analysis of multinational anti-aging products emphasizes that claims of "anti-wrinkle" or "firming" are tied to the presence of signal peptides, carrier peptides, neurotransmitter-inhibiting peptides or enzyme-inhibiting peptides, but also notes that many formulations combine peptides with other actives, complicating attribution of labeled benefits to specific molecules [4,7].

Safety-related aspects of regulatory status intersect with labeling in several ways. Protein hydrolysates containing bioactive peptides are categorized by the FDA as Generally Recognized as Safe, which provides a baseline regulatory acceptance for their use in cosmetic contexts. At the same time, surveys of cosmetic peptides report that, although some proteins are linked to contact dermatitis, no evidence has been found that peptides used in cosmetics raise specific allergy concerns. These observations support current practice in which peptide-containing products are labeled and marketed without special allergen warnings beyond standard cosmetic requirements, but they also underscore that safety data often derive from heterogeneous sources and that individual peptide contributions are rarely isolated in clinical trials [4,7].

Claims regarding penetration, activity and "cosmeceutical" status increasingly involve nanotechnology-based vehicles and cell-penetrating peptides. Research on nanoemulsions, nanoparticles and peptide-enhanced creams shows improved penetration of vitamins, antioxidants and biofunctional peptides, and these findings are cited in support of claims about enhanced delivery and bioavailability in labeled products. However, such studies frequently acknowledge that clinical trials using formulations with multiple actives do not clearly differentiate peptide effects from those of other ingredients. Methodology papers therefore call for standardized clinical trial designs, clear inclusion and exclusion criteria, objective endpoints such as hydration, elasticity, wrinkles and pigmentation, and detailed safety monitoring to substantiate marketing claims for peptide cosmeceuticals within regulatory constraints [12,14,20].

TABLE 6
SAFETY CONSIDERATIONS FOR PEPTIDE-BASED SKINCARE

Consideration	Key Points	Recommendations
Contact Dermatitis	Potential for sensitization in aging skin	Patch testing in high-risk groups
Irritation	Generally well-tolerated	Monitor for erythema, edema
Photoallergy	Limited evidence	Sun protection advised
Immunological Effects	Theoretical immune modulation	Characterize immunological effects
Regulatory Status	GRAS for hydrolysates	Follow local regulations
Polypharmacy	Interactions with other topicals	Cautious introduction

IX. PRACTICAL INTEGRATION OF PEPTIDE FORMULATIONS INTO SKINCARE ROUTINES

Designing peptide-inclusive skincare regimens for adult and aging skin requires coordinated attention to cleansing, treatment layering, moisturization and photoprotection, together with appropriate clinical evaluation of outcomes. Structured protocols for integrating cosmeceuticals begin with gentle cleansing tailored to skin type, followed by targeted treatment steps using serums, and completion with moisturizers and broad-spectrum sunscreens. Cleansers remove dirt, oil and makeup, toners can help rebalance pH, and treatment serums deliver active ingredients such as peptides to address concerns including fine lines, hyperpigmentation and acne. Moisturizers then hydrate and seal in water, while sunscreens protect against ultraviolet damage and premature aging, with reapplication during sun exposure to preserve benefits from cosmeceutical actives [2,20].

Adult and aging skin often exhibits increased dryness, barrier fragility and cumulative photo-damage, making daily barrier care central to regimen design. Regular use of moisturizers containing humectants such as glycerin, hyaluronic acid, urea, lactic acid and amino acid derivatives, together with occlusives like petrolatum, mineral oil and lanolin, improves water-holding capacity of the stratum corneum and reduces transepidermal water loss. More sophisticated peptides and proteins, including lipophilic quaternary N-alkyl derivatives of proteins or small polypeptides, are already used as moisturizers to bind the horny layer and enhance percutaneous absorption. Biomimetic small peptides that mimic collagen or enzyme sequences have been proposed for surface smoothing and hydration, and protein derivatives from wheat, rice, silk, soybean and oat contribute humectant and film-forming properties that are particularly useful in dry, photoaged skin. Selecting oil-in-water or water-in-oil formulations according to dryness severity further adapts regimens to skin profiles, with richer creams preferred for marked xerosis [2].

Integration of peptide-based treatments into these routines benefits from methodologically robust assessment frameworks. Recommended protocols call for in vitro studies of cell proliferation, collagen synthesis and antioxidant activity, followed by in vivo trials in human volunteers to measure hydration, elasticity, wrinkles and pigmentation using standardized techniques. Subsequent randomized controlled trials should employ clear inclusion and exclusion criteria, cover diverse age groups, skin types and ethnicities, and combine subjective questionnaires with objective imaging such as dermoscopy and digital photography. Dermatological safety assessments, including irritation and sensitization tests with systematic monitoring of adverse reactions, are essential when regimens for aging skin incorporate potent actives like peptides alongside retinoids, acids

or antioxidants. Statistical analysis comparing treatment and control arms allows clinicians and pharmacists to interpret regimen performance and refine product combinations for specific adult and elderly profiles [20].

Day-to-day implementation for aging skin emphasizes sequencing and layering that maximize penetration while limiting irritation. Evidence indicates that cosmeceuticals achieve better efficacy when applied to clean, dry skin, starting with the thinnest products, such as toners or serums, and gradually moving to thicker creams or ointments, allowing each layer to absorb before the next is added. Consistency and patience are highlighted; sustained use over weeks to months is necessary before measurable improvements in skin texture, wrinkles and elasticity become apparent. Sunscreen use every morning, with reapplication, protects against UV-driven oxidative stress that would otherwise undermine peptide-induced collagen synthesis and barrier repair. These practical rules are supported by research on penetration enhancement, photoprotection and long-term outcomes of topical antiaging strategies [3,20].

Adult and aging skin regimens that incorporate peptides must also account for broader therapeutic choices. Topical retinoids such as retinol and retinaldehyde, glycolic acid and azelaic acid possess strong evidence for improving epidermal renewal, dermal collagen and pigmentation, but are associated with irritation risks, especially in sensitive or older phototypes. Combining these actives with humectant- and emollient-rich bases helps maintain barrier integrity, and regimented introduction (for example, alternating nights or lower initial concentrations) can be guided by clinical monitoring of tolerability. Concurrent use of peptide-containing products within such regimens should be evaluated through well-designed trials that document changes in wrinkles, hydration and pigmentation, while safety assessments track sensitization or irritant reactions and support ethical, evidence-based optimization of peptide-centric routines for varied adult and aging skin profiles [2,3,20].

Integration of peptide-containing skincare with office-based dermatologic procedures requires understanding how professional interventions remodel skin structure and signaling, creating windows in which topical actives may exert enhanced or altered effects. Energy-based devices such as intense pulsed light (IPL) use non-coherent, broad-spectrum light filtered between 500 and 1200nm to target melanin and hemoglobin, treating dyschromia, telangiectasias, lentigines and texture irregularities via selective photothermolysis. IPL stimulates dermal fibroblasts, increases collagen synthesis through sublethal thermal injury and activation of transforming growth factor-β signaling, and yields improved elasticity, reduced fine lines and smoother skin tone, typically after three to six sessions spaced at 3–4 week intervals with maintenance every 6–12 months. Side effects are generally mild, but pigmentary risk is higher in Fitzpatrick IV–VI phototypes, where strict photoprotection and cautious parameter selection are essential. These fibroblast-stimulating and collagen-inducing effects suggest that peptide formulations designed to support extracellular matrix homeostasis could be logically positioned in post-IPL regimens that already rely on barrier-restoring humectants, emollients and ceramide-containing products to maintain hydration and protect against transepidermal water loss [3].

Laser resurfacing approaches, including fractional ablative CO_2 and non-ablative modalities, induce wound repair responses with collagen remodeling and elastin synthesis. Ablative lasers vaporize epidermal and dermal structures by targeting water as chromophore, achieving robust correction of moderate-to-severe photoaging at the cost of longer recovery and higher risks of post-inflammatory hyperpigmentation and infection. Fractional ablative CO_2 lasers create microscopic zones of ablation surrounded by intact tissue and are regarded as a gold standard for balancing efficacy and safety; expert consensus emphasizes individualized parameters and structured post-procedural skincare to mitigate complications. Non-ablative lasers such as Nd:YAG, Er:Glass and diode systems act via dermal coagulation without epidermal disruption, offering reduced downtime but requiring more sessions. Meta-analyses show comparable overall wrinkle reduction and patient satisfaction between ablative and non-ablative lasers, with ablative systems trending toward superior improvement in severe photoaging [3].

In this context, layering peptide-containing formulations after laser resurfacing should account for altered barrier integrity, heightened inflammatory signaling and the concurrent use of agents like retinoids or niacinamide that modulate collagen, elastin and immune pathways [3]

Mechanical rejuvenation techniques also create opportunities for synergistic use of topical peptides. Microdermabrasion removes the stratum corneum using abrasive crystals or diamond-tipped devices and vacuum, inducing increased cell turnover, fibroblast activation and neocollagenesis with improvements in smoothness, tone and radiance, while remaining limited to superficial photoaging and mild dyschromia. Microneedling generates controlled microinjuries with dermarollers or motorized pens, upregulating collagen types I and III and extracellular matrix remodeling, effectively improving texture, fine wrinkles and scars such as atrophic acne scars. Emerging microneedle patch technologies employ dissolvable or hydrogel arrays that deliver antioxidants, extracellular vesicles, mRNA or stem-cell-derived products directly into the dermis to combat photoaging at a molecular level. Preclinical work with patches loaded with adipose-derived extracellular vesicles demonstrates collagen

remodeling, reduced oxidative stress and enhanced epidermal structure, positioning microneedle-based delivery as a promising platform for transdermal administration of peptides, proteins and other biomolecules. Broader microneedle arrays fabricated from biocompatible polysaccharides like hyaluronic acid, chondroitin sulfate, alginate and chitosan can create reversible microchannels, bypass stratum corneum resistance, and enable sustained release profiles with low toxicity, supporting their use for cosmetic indications including aging, wrinkles and depigmentation [3,13].

When peptide-based products are combined with such mechanical or microneedle procedures, regimen planning must consider timing relative to injury and repair phases, penetration depth, and the potential for enhanced bioavailability that might amplify both desired matrix effects and any irritation or sensitization risks already recognized for actives like glycolic and azelaic acids, retinoids and niacinamide [3].

Injectable and minimally invasive procedures further shape the milieu in which topical peptides act. Botulinum toxin type A selectively inhibits acetylcholine release at the neuromuscular junction, softening dynamic wrinkles in glabellar lines, forehead creases and crow's feet. Hyaluronic acid fillers restore volume and re-establish youthful facial proportions, with some formulations also stimulating neocollagenesis. Biostimulatory approaches such as calcium hydroxylapatite fillers and absorbable polydioxanone or poly-lactic acid sutures promote collagen I and III production, tissue contracture and improved vasculature in animal and tissue culture models, with benefits that may decline or persist depending on thread type and time course. Platelet-rich plasma delivers concentrated growth factors including TGF-β, PDGF, FGF and IGF, with modest but documented benefit for aging skin, especially as an adjuvant to laser resurfacing. These professional interventions alter extracellular matrix composition, fibroblast signaling and vascular architecture; topical peptide regimens introduced alongside or following them should be structured using evidence-based methodologies that integrate objective measures of wrinkles, elasticity and pigmentation, standardized inclusion criteria and safety monitoring, as proposed for cosmeceutical trials [3,20].

X. CONCLUSION

This synthesis highlights how short bioactive peptides interact with key cutaneous compartments to modify extracellular matrix turnover, cell signaling and repair pathways. Signal and carrier sequences such as palmitoyl-conjugated collagen fragments, Cu-GHK and decorin-mimetic tripeptides have demonstrable effects on collagen, elastin and glycosaminoglycan dynamics, while modulators like SA1-III can reduce proteolytic collagen loss by attenuating MMP activity. Senotherapeutic sequences exemplified by Pep 14 influence PP2A/AKT and FoxO-related networks to reduce late-stage senescence markers and support DNA repair without triggering apoptosis, producing favorable ex vivo tissue responses including increased epidermal thickness and reduced methylation age metrics.

Delivery constraints imposed by the stratum corneum demand physicochemical modification, lipidation, nanoparticulate encapsulation or transient barrier disruption for deeper dermal targeting; each approach alters spatial distribution and bioavailability and therefore must be matched to the intended molecular target and safety profile. Translational pathways benefit from a staged evaluation framework that integrates molecular, cellular and tissue models with rigorous clinical and instrumental endpoints. In vitro and ex vivo assays clarify mechanism of action and off-target signals, three-dimensional skin equivalents connect cellular responses to organ-level outcomes, and randomized human trials with profilometry, ultrasound and biochemical readouts validate functional benefits such as wrinkle depth reduction, elasticity improvement and increased procollagen synthesis.

Safety assessment should prioritize irritation, sensitization and potential photoallergic effects in older, barrier-compromised cohorts, and regulatory labeling must reflect the level of evidence supporting claims. Future work should refine delivery systems to balance epidermal versus dermal exposure, expand controlled comparative trials that isolate peptide effects within complex formulations, and apply standardized endpoints including epigenetic clocks and objective imaging to establish durable, reproducible benefits for adult and aging skin.

CONFLICT OF INTEREST

The author declare no conflict of interest.

REFERENCES

[1] AK, M. (2019). Skin aging & modern age anti-aging strategies. *International Journal of Clinical Dermatology & Research*. https://doi.org/10.19070/2332-2977-1900052

[2] Aluko, R. (2012). Bioactive peptides. In *Functional foods and nutraceuticals* (Food Science Text Series). Springer. https://doi.org/10.1007/978-1-4614-3480-1_3

[3] Arab, H., Sadeghi, S., Shahtalebi, M. A., Siadat, A. H., Tahvilian, B., & Mofid, M. R. (2025). Anti-wrinkle effect of an emulsion based on the hexapeptide argireline. Pilot study. *Aesthetic Cosmetology and Medicine*, *14*(4). https://doi.org/10.52336/acm.2025.030

[4] Escobar, S., Valois, A., Nielsen, M., Closs, B., & Kerob, D. (2020). Effectiveness of a formulation containing peptides and vitamin c in treating signs of facial ageing: Three clinical studies. *International Journal of Cosmetic Science*, *43*(2). https://doi.org/10.1111/ics.12665

[5] Farage, M. A., Miller, K. W., Elsner, P., & Maibach, H. I. (2007). Structural characteristics of the aging skin: A review. *Cutaneous and Ocular Toxicology*, *26*(4). https://doi.org/10.1080/15569520701622951

[6] Ferreira, M. S., Magalhães, M. C., Sousa-Lobo, J. M., & Almeida, I. F. (2020). Trending anti-aging peptides. *Cosmetics*, *7*(4). https://doi.org/10.3390/cosmetics7040091

[7] Fu, T.-K., Kuo, P.-H., Lu, Y.-C., Lin, H.-N., Wang, L. H.-C., Lin, Y.-C., Kao, Y.-C., Lai, H.-M., & Chang, M. D.-T. (2020). Cell penetrating peptide as a high safety anti-inflammation ingredient for cosmetic applications. *Biomolecules*, *10*(1). https://doi.org/10.3390/biom10010101

[8] Gazitaeva, Z., Drobintseva, A., Chung, Y., Polyakova, V., & Kvetnoy, I. (2017). Cosmeceutical product consisting of biomimetic peptides: Antiaging effects in vivo and in vitro. *Clinical, Cosmetic and Investigational Dermatology*, *Volume 10*. https://doi.org/10.2147/ccid.s97573

[9] Gorouhi, F., & Maibach, H. I. (2009). Role of topical peptides in preventing or treating aged skin. *International Journal of Cosmetic Science*, *31*(5). https://doi.org/10.1111/j.1468-2494.2009.00490.x

[10] Kluczyk, A., Ludwiczak, J., Modzel, M., Kuczer, M., Cebrat, M., Biernat, M., & Bąchor, R. (2021). Chemical and biological properties of anti-wrinkle peptide argireline. *Aesthetic Cosmetology and Medicine*, *10*(3). https://doi.org/10.52336/acm.2021.10.3.05

[11] Moazzam, M., Mehboob, T., Bashir, I., Aslam, R., Tabassam, N., & Jamshaid, M. (2018). Constituents of cosmeceuticals and implication of nanotechnology in cosmetics. *RADS Journal of Pharmacy and Pharmaceutical Sciences*, *6*(4).

[12] Naharro-Rodriguez, J., Bacci, S., Hernandez-Bule, M. L., Perez-Gonzalez, A., & Fernandez-Guarino, M. (2025). Decoding skin aging: A review of mechanisms, markers, and modern therapies. *Cosmetics*, *12*(4). https://doi.org/10.3390/cosmetics12040144

[13] Patlolla, R. R., Desai, P. R., Belay, K., & Singh, M. S. (2010). Translocation of cell penetrating peptide engrafted nanoparticles across skin layers. *Biomaterials*, *31*(21). https://doi.org/10.1016/j.biomaterials.2010.03.010

[14] Rovero, P., Malgapo, D. M. H., Sparavigna, A., Beilin, G., Wong, V., & Lao, M. P. (2022). The clinical evidence-based paradigm of topical anti-aging skincare formulations enriched with bio-active peptide SA1-III (KP1) as collagen modulator: From bench to bedside. *Clinical, Cosmetic and Investigational Dermatology*, *Volume 15*. https://doi.org/10.2147/ccid.s374295

[15] Sánchez, A., & Vázquez, A. (2017). Bioactive peptides: A review. *Food Quality and Safety*, *1*(1). https://doi.org/10.1093/fqs/fyx006

[16] Schagen, S. (2017). Topical peptide treatments with effective anti-aging results. *Cosmetics*, *4*(2). https://doi.org/10.3390/cosmetics4020016

[17] Singh, S., Singh, V., & Patel, S. (2024). Cosmeceuticals; the fusion of cosmetics and pharmaceuticals. *Journal of Community Pharmacy Practice*, *42*. https://doi.org/10.55529/jcpp.42.16.27

[18] TATARINGA, G., & ZBANCIOC, A. M. (2021). Antirid peptides in cosmeceutical formula. *Romanian Journal of Pharmaceutical Practice*, *14*(3-4). https://doi.org/10.37897/rjphp.2021.3.1

[19] Umeyor, C. E., Shelke, V., Pol, A., Kolekar, P., Jadhav, S., Tiwari, N., Anure, A., Nayak, A., Bairagi, G., Agale, A., Raut, V., Bahadure, S., Chaudhari, A., & Patravale, V. B. (2023). Biomimetic microneedles: Exploring the recent advances on a microfabricated system for precision delivery of drugs, peptides, and proteins. *Future Journal of Pharmaceutical Sciences*, *9*(1). https://doi.org/10.1186/s43094-023-00553-6

[20] Vandiver, A. R., & Hogan, S. R. (2020). Aging skin and non-surgical procedures: A basic science overview. *Plastic and Aesthetic Research*, *7*. https://doi.org/10.20517/2347-9264.2020.159

[21] West, B. J., Alabi, I., & Deng, S. (2021). A face serum containing palmitoyl tripeptide-38, hydrolyzed hyaluronic acid, bakuchiol and a polyherbal and vitamin blend improves skin quality. *Journal of Cosmetics, Dermatological Sciences and Applications*, *11*(3). https://doi.org/10.4236/jcdsa.2021.113020

[22] Zonari, A., Brace, L. E., Al-Katib, K. Z., Porto, W. F., Foyt, D., Guiang, M., Cruz, E. A. O., Marshall, B., Salgueiro, W. G., Inan, M. D., Rahman, M., Anupom, T., Vanapalli, S., Mori, M. A., Franco, O. L., Oliveira, C. R., Boroni, M., & Carvalho, J. L. (2020). *Senotherapeutic peptide reduces skin biological age and improves skin health markers*. https://doi.org/10.1101/2020.10.30.362822

[23] Zonari, A., Brace, L. E., Al-Katib, K., Porto, W. F., Foyt, D., Guiang, M., Cruz, E. A. O., Marshall, B., Gentz, M., Guimarães, G. R., Franco, O. L., Oliveira, C. R., Boroni, M., & Carvalho, J. L. (2023). Senotherapeutic peptide treatment reduces biological age and senescence burden in human skin models. *npj Aging*, *9*(1). https://doi.org/10.1038/s41514-023-00109-1.

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