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Evaluation of Methyl Paraben Content in One Branded and Two Local Lipstick Products using HPLC Quantification

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KEYWORDS

Methyl Paraben, Lipstick, High-Performance Liquid Chromatography (HPLC), Quantification, Cosmetics, Preservative.

ABSTRACT:

Methyl paraben, a member of the paraben family, is widely used as a preservative in cosmetics, pharmaceuticals, and food products due to its antimicrobial properties. Lipstick, a ubiquitous cosmetic product, often contains methyl paraben as a preservative. The presence of methyl paraben, a common preservative in cosmetic products, has raised concerns due to its potential health effects on human health, including endocrine disruption and allergic reactions. Given the frequent application of lipstick and its potential for ingestion, evaluating the concentration of methyl paraben in these products is crucial for assessing consumer exposure and ensuring product safety. In the present study, we employed High-Performance Liquid Chromatography (HPLC) to quantify the amount of methyl paraben in one branded and two local lipsticks. High Performance Liquid Chromatography (HPLC) is a powerful analytical technique used to separate, identify, and quantify components in a mixture based on their interaction with a stationary phase and a liquid mobile phase under high pressure. The results revealed varying concentrations of methyl paraben among the three lipsticks, highlighting the importance of rigorous quality control and regulatory oversight in the cosmetics industry.

Introduction:

Methylparaben, derived from the condensation of methanol with the carboxy group of 4-hydroxybenzoic acid, is a commonly utilized antimicrobial preservative found in cosmetic products. Its presence is natural in various fruits, notably blueberries, and it serves roles as a plant metabolite, antimicrobial food preservative, neuroprotective agent, and antifungal agent.[1] Methylparaben has a chemical formula of C8H8O3 with a molar mass of 152.149 g·mol−1. It appears as colorless crystals or white crystalline powder and exhibits a maximum UV-vis absorption at 255 nm in methanol. The magnetic susceptibility (χ) of methylparaben is -88.7·10−6 cm3/mol. In terms of hazards, according to NFPA 704, it is rated as 1 1 0 on the four-colored diamond scale. Methylparaben is related to other parabens such as ethylparaben, propylparaben, and butylparaben, and is also related to methyl salicylate (ortho isomer).[2] Methylparabens can be found in various products such as makeup, hair styling products, shaving cream, moisturizers, food items, and drugs. Typically, a product's packaging will indicate whether it contains methylparaben or other parabens. Presently, there remains uncertainty regarding the safety of methylparabens. While there is limited evidence indicating adverse health effects associated with methylparabens, there is also insufficient evidence to confirm their safety. The primary concerns regarding

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methylparabens pertain to their potential for causing skin irritation or corrosion, eye irritation or damage, and environmental harm, particularly to aquatic ecosystems.[3]

High Performance Liquid Chromatography (HPLC) represents a sophisticated iteration of column chromatography extensively employed for the separation, identification, and quantification of various compounds. High-performance liquid chromatography (HPLC) has become a common method for separating complex mixtures. However, the structural details of substances separated via HPLC are often limited by the type of detector used. Traditional detectors such as refractive index, UV (ultraviolet), radiochemical, fluorescence, and electrochemical provide minimal structural information. Consequently, determining the structure typically involves isolating the analyte from the matrix and then conducting off-line spectroscopic analysis. The introduction of HPLC-MS (mass spectrometry) has revolutionized this process by enabling the detection and identification of substances at low concentrations without the need for isolation. While HPLC-MS has simplified structure elucidation, there are instances where further characterization using nuclear magnetic resonance (NMR) spectroscopy is necessary. Consequently, the logical progression in instrument development would involve directly coupling HPLC and NMR, resulting in the hyphenated technique known as HPLC-NMR.[4,5,6] The primary objective of this study is to quantitatively evaluate the amount of methyl paraben present in three different lipsticks using HPLC quantification. By comparing the concentrations of methyl paraben among the three lipsticks, we aim to assess the variability in preservative content and highlight potential implications for consumer safety and regulatory compliance.

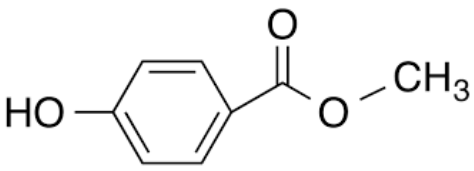

Figure 1: Methyl paraben-Molecular structure: Molecular weight: 152.15 g/mol

Methodology:

Sample Collection:

A total of three lipstick samples, one branded and two local, were purchased from local retail outlets.

Figure 2: Lipstick Samples

Reagents and solvents:

Si No.	Chemicals	Make
1	Water HPLC grade	Thomas baker
2	Methanol HPLC grade	Rankem
3	Acetonitrile HPLC grade	Rankem
4	Propan-2-ol (IPA, HPLC grade)	Rankem

Preparations of Reagents/Solvents

Preparation of Mobile Phase

500 of HPLC-grade water was taken in a 0.5-liter glass bottle and 157.62mg of Ammonium Formate was added, sonicated for five minutes (ph. adjusted to 4 by 0.1% formic acid).

Preparation of Mobile Phase B

500 of Acetonitrile was taken in a 0.5-liter glass bottle and sonicated for five minutes.

Needle wash

250 mL of each, Acetonitrile, Methanol, IPA and HPLC-grade water were taken in a 1-liter glass bottle, mixed properly and sonicated for a few minutes.

Sample Preparation:

Each lipstick sample was homogenized using a mortar and pestle to ensure uniformity. A portion of the homogenized sample (200mg) was weighed and 10ml of

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methanol was added, vortexed at 1200rpm for 30mins. From the vortexed reaction mixture takeout 1ml and centrifuged at 10,000rpm for 10mins and 100µl of supernatant id submitted for HPLC Analysis.

HPLC Analysis:

HPLC analysis was performed using a Shimadzu LC 20AD. A X-bridge C18 polar, 150*4.6 mm, 3.5u column was employed for chromatographic separation, with a mobile phase consisting of 5mM Ammonium Formate: Acetonitrile (60:40 v/v). The injection volume was 10uL, and the flow rate was maintained at 0.8mL /min. Column oven temperature was 40 ± 2° C. Autosampler temperature was 10°C ± 2°C. Runtime was 20 minutes.

Calibration Curve:

A series of standard solutions containing known concentrations of methyl paraben were prepared in methanol. Calibration curves were constructed by plotting peak area against concentration for the standards.

Quantification:

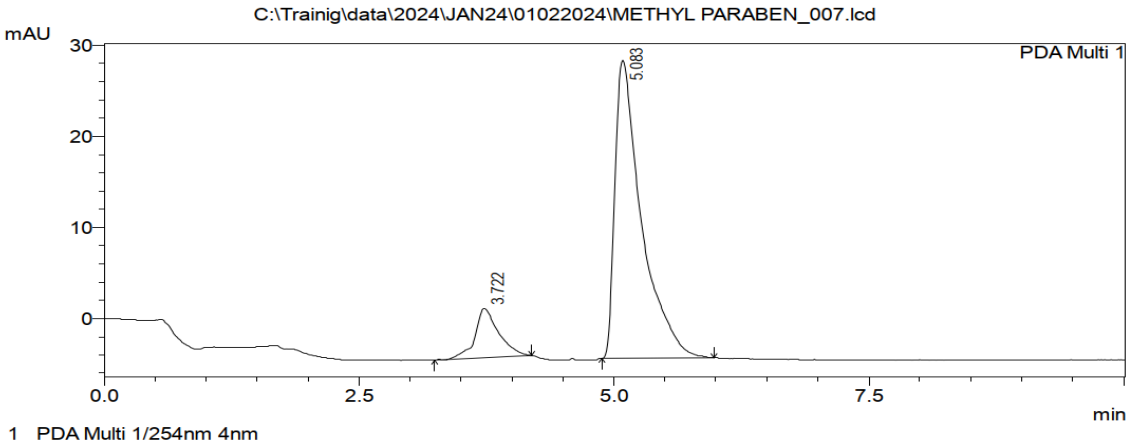
The concentration of methyl paraben in each lipstick sample was determined by comparing the peak area of the sample with the calibration curve. The analysis was performed in triplicate, and the average concentration was reported.

Results:

The results of the HPLC analysis revealed varying concentrations of methyl paraben among the three lipstick samples. Branded lipstick exhibited the highest average concentration of methyl paraben with 1627.40 µg/g, followed by local A with 547.04 µg/g and local B with 177.58 µg/g. The variability in preservative content suggests differences in formulation or manufacturing processes among the brand and local.

Table 1: Methyl paraben quantification

Sl.No.	Sample	RT	Area	Concentration (µg/ml)	Concentration (µg/g)
1	Std_10ppm	5.08	591436		
2	sample 1	5.19	1925005	32.55	1627.40
3	sample 2	5.37	647074	10.94	547.04
4	sample 3	5.22	210055	3.55	177.58



PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %
1	3.722	86713	5396	12.787
2	5.083	591436	32711	87.213
Total		678150	38107	100.000

Figure 3: Chromatograms of Methyl paraben standard_10ppm

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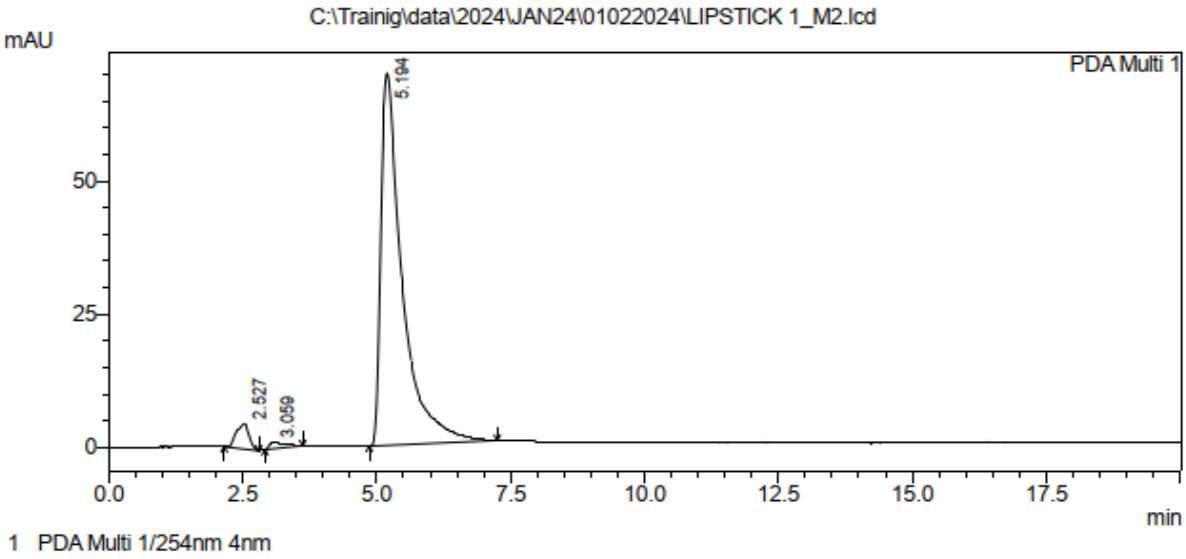
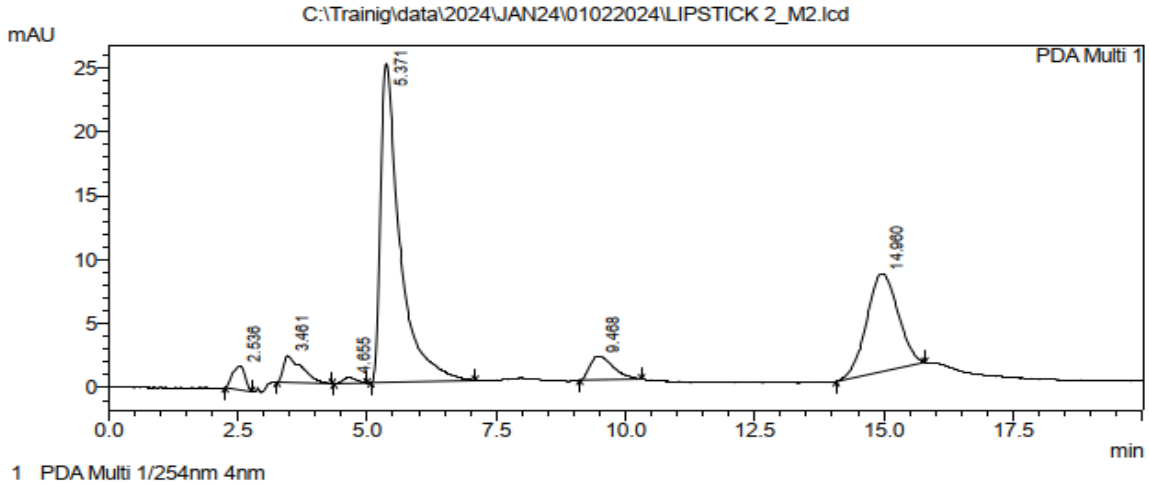


PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %
1	2.527	77112	4732	3.800
2	3.059	27197	1269	1.340
3	5.194	1925005	69807	94.860
Total		2029313	75809	100.000

Figure 4: Chromatograms of Lipstick sample-1



PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %
1	2.536	30997	1876	2.768
2	3.461	51439	2072	4.594
3	4.655	7708	440	0.688
4	5.371	647074	24887	57.794
5	9.468	58522	1866	5.227
6	14.960	323889	7673	28.928
Total		1119629	38813	100.000

Figure 5: Chromatograms of Lipstick sample-2

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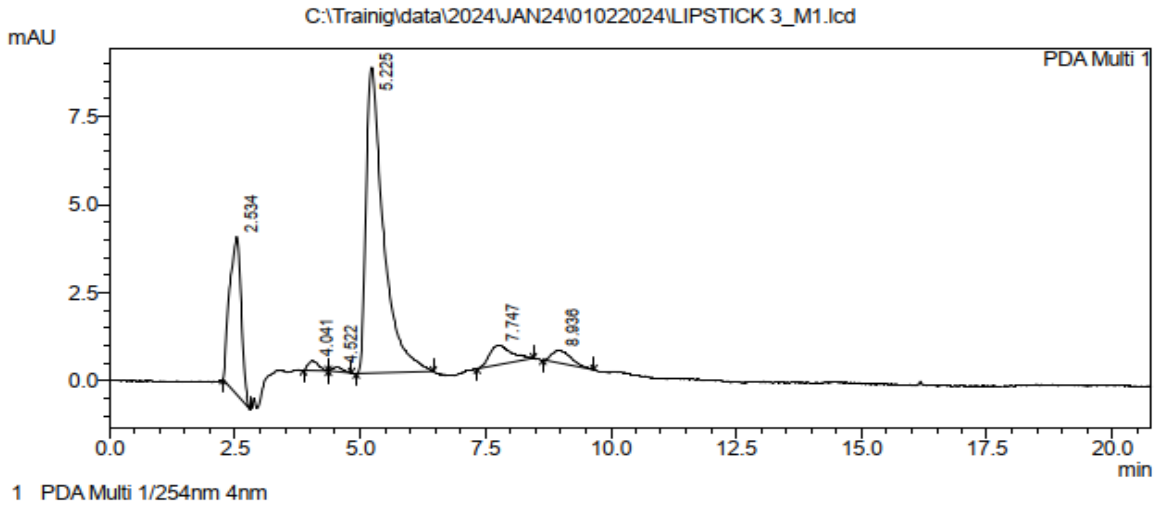

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %
1	2.534	71261	4465	22.742
2	4.041	3812	280	1.217
3	4.522	1687	122	0.538
4	5.225	210055	8667	67.037
5	7.747	16863	550	5.382
6	8.936	9663	375	3.084
Total		313341	14458	100.000

Figure 6: Chromatograms of Lipstick sample-3

Discussion:

The study by Özcan S et al., aimed to develop a high-performance liquid chromatographic (HPLC) method for the quantitative determination of various paraben derivatives commonly used as antimicrobial preservatives in foods, cosmetics, and pharmaceuticals. The method was designed to be simple, selective, and cost-effective, utilizing a C18-bonded core-shell silica particle column and a photodiode array detector set at 254 nm wavelength. The results demonstrate successful chromatographic separation of seven paraben derivatives, including methylparaben, ethylparaben, n-propyl paraben, isopropyl paraben, n-butyl paraben, isobutyl paraben, and benzyl paraben. The method exhibited a wide linear range of detection (250-2000 ng/mL) and high recovery rates ranging from 99.95% to 113.84%, with a maximum relative standard deviation (RSD) of 3.95%. The validated method was then applied to analyze various pharmaceutical and cosmetic samples, including syrups, suspensions, oral sprays, and gels. Notably, at least one paraben derivative was detected quantitatively in six out of sixteen samples tested, with methylparaben being the most commonly found compound, reaching a maximum concentration of 321.7 ng/mL.[7] The study by Khansari N et al., presented a new method for the extraction and determination of methylparaben in infant formulas using an HPLC method with a UV detector. The findings of the study suggest that the developed method offers good recovery rates and decreases interferences between methylparaben and other ingredients in infant formulas, as evidenced by improved chromatograms. The average recoveries for methylparaben were within an acceptable range (88–108%), indicating the effectiveness of the extraction procedure. The limits of detection (LOD) and quantitation (LOQ) for methylparaben were determined to be 0.2 and 0.5 µg/mL, respectively, indicating the sensitivity of the method. Moreover, the method demonstrated good reproducibility, with low relative standard deviations (RSD) for both within-day and between-day analyses, further confirming its reliability. The linear range of detection (0.5–20 µg/mL) suggests that the method is suitable for quantifying methylparaben over a wide concentration range commonly found in infant formulas. Interestingly, among the twenty real infant formula samples analyzed, methylparaben was detected only in one sample at a concentration of 0.3

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µg/mL.[8] The study Agnieszka Zgoła-Grześkowiak et al., developed a straightforward HPLC method with fluorescence detection for quantifying methylparaben, ethylparaben, propylparaben, and butylparaben in cosmetics, adhering to EU regulations. The method's high sensitivity and selectivity, coupled with simple sample preparation, allowed for accurate analysis using basic laboratory equipment. Results from over 20 cosmetic samples confirmed compliance with established limits. Additionally, HPLC analysis with mass spectrometric detection validated the findings.9 The study by Gao Xun Xu Kai Chi et al, employed a two-step extraction approach involving IL-DLLME and MSPE combined with HPLC for selective enrichment and trace determination of four benzoate preservatives in cosmetics. The optimized method proved efficient, accurate, and environmentally friendly, free from matrix interference. Compared to traditional DLLME, [C8MIM][PF6] ILs offered higher sensitivity and a broader linearity range. The method demonstrated acceptable accuracy, linearity, precision, and detection limits for real samples.[10] The study by Ning XP et al., introduced a novel method based on solid-phase extraction (SPE) coupled with high-performance liquid chromatography (HPLC) for the determination of seven paraben preservatives in various food products, specifically oyster sauce, shrimp sauce, and fish sauce. This method addresses limitations of previous techniques, such as the use of toxic reagents and limited detection scope. By optimizing the pretreatment method and device parameters, the proposed approach enables the detection of more compounds and expands its applicability across different food types. The method's efficacy was demonstrated through good linearity, low limits of detection and quantification, and high recoveries in spiked samples. Comparison with liquid-liquid extraction methods showed improved purification effects and higher recovery rates. The successful application of this method to analyze 135 food products further validates its effectiveness in determining the presence of paraben preservatives, including methyl p-hydroxybenzoate and ethyl p-hydroxybenzoate, in soy sauce, vinegar, and pickles.[11]

Methyl paraben, a widely used antimicrobial preservative, exhibits low toxicity and negligible accumulation in the body. While considered non-carcinogenic, non-mutagenic, and non-teratogenic, it may cause contact dermatitis and allergic reactions in sensitive individuals, particularly when applied to damaged skin. Its mechanism of action involves mitochondrial failure, potentially linked to membrane permeability transition and ATP depletion.[12] Parabens, a group of PHBA esters widely used in cosmetics, exhibit low toxicity and minimal accumulation in the body. While generally non-carcinogenic and non-mutagenic, they may affect male reproductive toxicity at high concentrations. Despite reports of skin sensitization, clinical data show minimal adverse effects, particularly on intact skin. Cosmetic products containing parabens are considered safe, with margins of safety exceeding exposure levels, as evaluated by the Cosmetic Ingredient Review Expert Panel.[13] The study by Petric Z et al., discusses the ongoing debate surrounding the toxicity of parabens, which are widely used as antimicrobial agents in various products. While animal and in vitro studies have reported toxicity, their relevance to human health is questioned due to unrealistic exposure scenarios. Despite concerns, evidence of teratogenicity, mutagenicity, and carcinogenicity in humans is lacking, leading to the general acceptance of methyl-, ethyl-, and propylparaben as safe within recommended doses. Exploring alternatives to parabens is ongoing, but any substitution would require rigorous testing for toxicity and safety.[14] The study of Matwiejczuk N et al., on the safety of dermal application of parabens in cosmetics emphasizes their potential health hazards, particularly their estrogenic potential and the risk of adverse health outcomes. While single cosmetics containing parabens may not pose a significant hazard, excessive use of products containing these compounds could lead to negative health effects. The absorption of parabens into the body and their retention in intact form raises concerns about their systemic exposure and potential toxicity. Additionally, evidence suggesting the negative impact of methylparaben on skin cells underscores the importance of considering the cumulative effects of paraben exposure from multiple cosmetic products. Given the real risk of estrogenic effects associated with paraben exposure, caution is advised against simultaneous use of numerous cosmetic products containing these preservatives to mitigate potential health risks.[15] The study by Herrera-Cogco E et al., examined the potential health hazards of two common parabens, methylparaben (MPB) and butylparaben (BPB), often found in cosmetics and food products. Despite concerns about their link to infertility due to their impact on hormone production and mitochondrial damage, the study found that neither MPB nor BPB significantly affected basal steroidogenesis in human granulosa cells. While BPB did show some impact on mitochondrial health at high concentrations, overall, the evidence suggests that these

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parabens do not pose a significant risk to human health in terms of altering hormone production in granulosa cells. However, further research may be needed to fully understand the potential long-term effects of paraben exposure on human health.[16] The study by Ishiwatari S et al., investigated the potential health hazards associated with daily use of methylparaben (MP) in dermatological formulations. It found that MP, a commonly used preservative, persisted in the outermost layer of human skin (stratum corneum) even after daily applications for one month. This persistence may lead to accumulation of MP in the skin. The study also revealed that MP exposure decreased the proliferative ability of keratinocytes, altered cell morphology, and affected the expression of certain genes and proteins involved in skin aging and differentiation. These findings suggest that long-term exposure to MP through dermatological formulations could potentially influence the aging process and differentiation of keratinocytes, raising concerns about its health hazards on human skin.[17]

The study by Al-Saleh I et al., assessed the safety of inexpensive cosmetic brands sold in Saudi Arabia, focusing on lead content in lipsticks and eye shadows. Lead was detected in all samples, with some exceeding the FDA's limit for lead impurities in color additives. While the median lead levels were below the FDA limit, a few brands had concentrations above 20 PPM, posing a potential risk of lead poisoning, especially with daily or frequent use. Pregnant and nursing mothers are particularly vulnerable to lead exposure, as it can affect fetal and infant development. The findings emphasize the need for regular testing of cosmetics imported into Saudi Arabia to mitigate excessive lead exposure and protect consumer health.[18] The study by Fu PP et al., highlights the unique ways in which the skin interacts with and responds to retinyl palmitate (vitamin A), specifically retinoids. While the skin shares similarities with other organs in how it absorbs and metabolizes vitamin A, its anatomical location and specialized functions make it distinct. Retinoids influence cellular division and differentiation in the epidermis, impacting processes like dermal aging, immune defense, and wound healing. Despite considerable knowledge about how retinoids affect skin responses, there is still much to be understood. Interest in the effects of retinoids on skin health and appearance, driven by the potential for improved dermatologic and cosmetic products, underscores the need for ongoing research into their health hazards and benefits.[19] The study Almukainzi M et al., evaluated the quality and safety of common cosmetic products through microbial load, heavy metal content, and organoleptic properties assessment. Microbial contamination was found in a significant portion of the products, with *Staphylococcus aureus* and *Bacillus* species being commonly isolated. Additionally, most products showed metal impurities, notably toothpaste with high concentrations of various metals. Continuous use of such products could pose serious health risks. Therefore, ensuring the quality of cosmetics is crucial, and regulatory authorities must enforce strict legislation to assess and guarantee product safety before reaching consumers. This underscores the importance of ongoing monitoring and regulation to mitigate potential health hazards associated with cosmetic use.[20]

Conclusion:

The HPLC quantification method employed in this research effectively measured the levels of methyl paraben in three different lipsticks. Through meticulous analysis, it was found that Branded contained the highest concentration of methyl paraben, followed by local lipsticks. These findings underscore the importance of vigilant monitoring and regulation within the cosmetics industry to ensure consumer safety and awareness regarding the presence of potentially harmful chemicals in everyday products. Further research could explore additional brands and formulations, as well as investigate the long-term effects of prolonged exposure to methyl paraben through lipstick use. Ultimately, this study contributes to the ongoing dialogue surrounding cosmetic safety and serves as a valuable resource for consumers, manufacturers, and regulatory agencies alike.

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