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Photoprotective lip formulation optimization methods: A systematic review

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ABSTRACT

Photoprotective lip preparations such as balms and tints containing natural ingredients are increasingly being developed as an alternative protection against ultraviolet radiation. The complexity of the formulation composition requires an appropriate optimization method to produce products with optimal effectiveness and stability. This review aims to analyze and compare optimization of various methods used in photoprotective lip preparations, evaluating their advantages and limitations in determining optimum conditions. This study uses a systematic review approach by searching scientific articles from databases like Google Scholar and other relevant sources within a specific time frame of years. The extracted data includes active ingredient type, optimization method, formulation variables, trial numbers, and response parameters like Sun Protection Factor (SPF), pH, and physical properties. Analysis results show that optimization methods based on experimental design, such as Response Surface Methodology (RSM), provide superior and robust capabilities in evaluating variable interactions and modeling nonlinear relationships to determine optimum conditions simultaneously. In contrast, conventional methods like one factor at a time (OFAT) combined with ANOVA still dominate but have limitations in evaluating variable interactions and generating predictive models. Most studies report that material composition variations, particularly wax bases and active ingredients, significantly influence the formulation's SPF value and physical characteristics. Experimental design-based optimization methods, particularly RSM, are strongly recommended for developing photoprotective lip formulations because they provide more efficient, accurate, and predictive results. However, their practical application is still limited. Therefore, further research is greatly needed to increase the widespread adoption of this advanced method in developing future natural product-based innovative pharmaceutical preparations.

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INTRODUCTION

The skin on the lips has a unique anatomy. Unlike most facial skin, the stratum corneum layer on the lips is very thin and contains minimal sebaceous glands or melanin. This makes them much more susceptible to damage from ultraviolet (UV) exposure. Therefore, lip cosmetics such as lip balms, lip creams, and lip tints are now required not only to provide moisturizing and coloring effects but also to act as photoprotective agents. This protection is essential to prevent photoaging and minimize the risk of more serious skin health problems caused by sun radiation.(Vatsal Modi et al., 2025).

To achieve optimal protection, researchers are exploring various types of active ingredients, both synthetic and naturally derived. Synthetic sunscreen agents, such as chemical UV-filtering compounds or ceramide analogs, are often formulated due to their good stability and directly measurable protection profile (2) (Tamura et al., 2021). On the other hand, current cosmetic trends also move towards the use of plant extracts. Natural ingredients such as asoka flower extract, rosella, teak leaves, and even beetroot are widely studied due to their secondary metabolite content, especially phenolics and anthocyanins, which have dual potential as antioxidants and increase the Sun Protection Factor (SPF) value with a lower toxicity profile (3,4) (Asari et al., 2025; Zahrotul Mungizah et al., 2025a).

However, the biggest challenge lies in the formulation process. Combining photoprotective active ingredients into a lip product base requires highly precise composition. Small changes in excipient proportions can directly affect SPF values, product stability, pH levels, and even physical characteristics such as melting point and spreadability (5) (Łusiak et al., 2025). The effectiveness of pharmaceutical and cosmetic preparations is strongly influenced by formulation variables. Previous studies on pegagan anti-inflammatory gel formulations showed that appropriate formulation design is essential to achieve desirable product characteristics and therapeutic performance, supporting the need for robust optimization strategies during product development (Fatmawati et al., 2022) In the past, finding the right formula often relied on trial-and-error methods or changing one variable at a time (One Factor at a Time). Unfortunately, this approach is inefficient, time-consuming, and often fails to detect interactions between ingredients in the formula. As a solution, many recent primary studies have turned to statistically based experimental designs. Methods such as Response Surface Methodology (RSM), Design of Experiment (DoE), Factorial Design, Mixture Design, and Simplex Lattice Design have proven to be able to guide formulators in predicting the optimum formula more systematically (3,4) (Asari et al., 2025; Zahrotul Mungizah et al., 2025).

The generation of contour plots in formulation optimization carries significant methodological implications, serving as a critical bridge between complex statistical computation and practical formulation engineering. Topographically mapping the response surface allows formulators to visually decode multifactorial interactions that are otherwise invisible in conventional single-variable analyses (Türkdoğan et al., 2026). More importantly, these 2D visual projections enable precise sensitivity analysis; the gradient density of the contour lines directly indicates formulation robustness, helping researchers predict how slight deviations in raw material scaling might impact product stability. By overlapping multiple contour plots for various physicochemical parameters such as SPF value, pH, and spreadability formulators can objectively demarcate the optimum design space. This predictive visualization ultimately eliminates the reliance on speculative trial-and-error, ensuring that the defined formulation equilibrium is not only theoretically accurate but also practically viable and robust for industrial scale-up (Clark et al., 2026).

Previous reviews on cosmetic formulations have mostly discussed active ingredients or SPF performance, while comparative methodological evaluations of optimization strategies remain underexplored. Although numerous original studies have reported the success of these optimization methods, there has been no comprehensive literature review directly comparing their performance in the development of photoprotective lip preparations. Each statistical method naturally has a different modeling approach and level of efficiency. Therefore, this systematic review was conducted to map and compare various formulation optimization methods for photoprotective lip preparations, both those using synthetic chemical active ingredients and natural ingredients.

This review specifically evaluates original research articles by focusing on three main comparative aspects: (1) the number of experimental variables used in each study, (2) the number of experiments (runs) required to assess the operational efficiency of the method, and (3) the level of accuracy of the mathematical modeling in predicting the parameters of the resulting preparation (including SPF value, stability, pH, and physical characteristics). The results of this comparison are expected to be a practical and objective reference for researchers in determining the most efficient and accurate optimization method for the development of photoprotective lip cosmetics in the future.

RESEARCH METHOD

Study Design

This study is a systematic literature review that aims to compare the efficiency and accuracy of various optimization methods in photoprotective lip cosmetic formulations, both those using synthetic chemical active ingredients and natural plant extracts. The literature search, selection, and synthesis process were carried out strictly in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) reporting guidelines. This approach was applied to ensure transparency of the search, ensure study reproducibility, and minimize bias.

Literature Search Strategy

A comprehensive and systematic literature search was conducted in four major academic databases: PubMed, Scopus, ScienceDirect, and Google Scholar. The search was limited to articles published within the last 10 years to capture the latest trends in formulation and optimization technology. The search strategy used specific keyword combinations, including: ("lip formulation" OR "lip balm" OR "lip tint") AND ("photoprotective" OR "UV protection" OR "SPF") AND ("optimization" OR "Response Surface Methodology" OR "Design of Experiment" OR "Simplex Lattice") AND ("plant extract" OR "synthetic"). Initial selection was conducted by scanning the suitability of the title and abstract. Articles deemed relevant were then proceeded to the full-text review stage.

Inclusion and Exclusion Criteria

Inclusion criteria included original research articles focusing on lip dosage formulations (solid or semi-solid) containing photoprotective agents and explicitly applying experimental optimization methods. Conversely, observational studies without finished product formulation data, review articles, and studies using a purely conventional approach without further statistical analysis were excluded.

Data Extraction

The data extraction process was carried out systematically on all studies that met the inclusion criteria. To accommodate the comparative research objectives, the collected data were divided into two focus groups. The first focus was related to basic formulation aspects, including the source of the active ingredient (plant/synthetic material), solvent and extraction method (if natural material), concentration in the formula, and in vitro SPF measurement methods (such as UV-Vis spectrophotometry) and their values. The second focus extracted optimization method metrics, which included the type of statistical design method used, the number of independent variables or excipients tested, the total number of trials (runs) executed, and the accuracy parameters of the mathematical model (such as the coefficient of determination or prediction error).

Data Analysis and Risk of Bias Assessment

The extracted data were then analyzed qualitatively and comparatively. Comparisons were conducted to evaluate the efficiency of each optimization method (as measured by the ratio of the number of variables to the number of runs) and the accuracy of their mathematical modeling in predicting the final response of the photoprotective lip preparation.

To ensure the validity of the findings of this systematic review, a risk of bias assessment was performed on the included literature. This assessment considered the clarity of the optimization design, the transparency of the extraction and formulation procedures, the validity of the SPF response measurements, the use of controls/comparators, and the completeness of analytical data reporting. The results of this risk of bias assessment were then used as a basis for interpreting the strength and accuracy of the scientific evidence for each reported optimization method.

RESULTS AND DISCUSSIONS

Table 1. Study characteristics and optimization methods of photoprotective lip formulation

Reference	Active Ingredients	Form Preparation	Optimization Method	Variables Independent	Amount Experiment (Efficiency)	Accuracy / Results
(Iskandar et al., 2025)	Extract strawberry	Lip tint	RSM (BBD)	Variables: tween 80 & propylene concentration glycol	17 formula	Influence significant to the parameters important in lip tint formulation, namely ph, power spread, and power sticky.
(Asari et al., 2025)	Red beet extract & extract leaf hibiscus	Lip tint	RSM (CCD)	Variables: ratio extract, speed homogenization, & time homogenization	16 formulations (trial)	In a way significant influence pigment concentration and performance SPF
(Endriyatno et al., 2024)	Extract skin fruit pomegranate black	Lip balm	Conventional	Variation concentration of beeswax and carnauba wax as a base	4 formulations	Difference the concentration of beeswax and carnauba wax affects organoleptic, viscosity, power spread, power stick to lip balm extract skin pomegranate.
(Wahid Suleman et al., 2022)	Extract skin Dragon fruit	Lip balm	Conventional analysis One way anova	Variation concentration extract skin dragon fruit & addition oil olive as emollient	3 formulations	Concentration extract skin red dragon fruit in each lip balm preparation has an effect to mark SPF stock
(Risnayanti et al., nd)	Extract fruit watermelon	Lip balm	Conventional	Variation concentration carnauba wax	3 formulations	Show existence difference significant from results ph test evaluation, power

Reference	Active Ingredients	Form Preparation	Optimization Method	Variables Independent	Amount Experiment (Efficiency)	Accuracy / Results
						spread and power sticky. Have content SPF of 20 where including ultra category so safe For used
(Kresnawati et al., 2024)	Extract leaf gotu kola	Lip balm	Conventional Anova analysis	Variation concentration extract leaf gotu kola	3 formulations	Concentration extract leaf pegagan in each lip balm preparation has an effect to mark SPF stock
(Safitri et al., 2020)	Extract leaf shoots red	Lip balm	Conventional analysis SPSS	Variation concentration extract leaf shoots red	3 formulations	Concentration extract leaf shoots The red color on each lip balm preparation has an effect to mark SPF stock
(Nugrahaeni Ayuningtyas et al., 2025)	Extract wood sappanwood	Lip balm	Conventional analysis One way anova	Variation concentration extract wood sappanwood	3 formulations	Variation concentration show activity antioxidants and value spf that significant.
(Hilmia Lukman et al., 2025)	Extract tubers carrot	Lip balm	Conventional	Variation concentration tubers carrot	3 formulations	Variation concentration own activity very powerful antioxidant and value significant spf
(More et al., 2025)	Extract cherry leaves	Lip balm	Conventional	Activity test (antioxidant & screen) solar) and stability	3 formulations	Variation concentration extract own activity antioxidants and stability Good as well as mark significant spf
(Nareswari et al., 2022)	Combination oil coconut pure and oil palm oil raw .	Lip balm stick	(anova One direction) is done with using prism graphpad 9.0	Variation concentration VCO and CPO	5 formulations	Concentration VCO own activity curtain solar analysis activity curtain surya lip balm stick, increasingly tall content cpo, increasingly tall mark spf produced.
(Dewi & Senda, 2025)	Nanoparticles red beet extract	Lip balm	Conventional analysis Conventional	Comparison between use red beet extract conventional with extract red beet nanoparticles and variations concentration extract	Extract (f1-f3) nanoparticles beetroot extract (f4-f6) basic formula (f7)	Lip balm formulation based on nanoparticles beetroot extract shows improvement activity curtain significant solar compared to with formula without nanoparticles
(Salsabila et al., 2025)	Butterfly pea flower	Lip oil	Conventional analysis SPSS	Combinations and variations	3 formulation	Combination butterfly pea flower

Reference	Active Ingredients	Form Preparation	Optimization Method	Variables Independent	Amount Experiment (Efficiency)	Accuracy / Results
	extract and lavender oil		version 25	butterfly pea flower extract and lavender oil	s	extract and lavender oil show activity curtain solar low until moderate. There is effect significant from variation concentration material active to mark spf.
(Rahmawati et al., 2025)	Combination butterfly pea flower extract and lemon oil	Lip cream	Conventional One-way ANOVA analysis	Combinations and variations butterfly pea flower extract and lemon oil	5 formulations	Combinations and variations extract influential significant to mark SPF
(Sukamdi et al., 2025)	Combination extract pineapple skin and skin carrot	Lip balm	Conventional analysis SPSS 16	Combinations and variations extract pineapple skin and skin carrot	3 formulations	Combinations and variations at optimal concentrations, meet condition For good lip balm formulation and has mark SPF give "ultra" protection
(Winarti et al., 2024)	Concentration oil bitter melon seeds and titanium dioxide	Lip cream	Design expert 11 with simplex lattice design method	Variations and combinations concentration oil bitter melon seeds and titanium dioxide	5 formulations	Optimal formula for lip cream tabir preparation solar energy obtained from simplex lattice design, namely with concentration oil bitter melon seeds 4.5%, and titanium dioxide 1.5% and increasing mark SPF
(Wisudyaningsih et al., 2025)	Concentration of quercetin and zinc oxide	Lipstick	Design expert 13.0	Concentration quercetin and zinc oxide,	4 formulations	Concentration of quercetin and zinc oxide in a way significant influence SPF
(Nahda & Amelia, 2025)	Beeswax and oil coconut	Lip balm	Conventional	Addition physical (spf) agent, namely zinc oxide	2 formulations	The addition of zinc oxide significant increase mark SPF to 15.2.
(Ristia Rahman et al., 2025)	Extract skin fruit tampoi	Lip balm	Conventional	Variation concentration surfactant tween 80	3 formulations	The best formula reach mark spf 9.67 with category protection maximum
(Zahrotul Mungizah et al., 2025)	Teak leaf extract and carnauba Wax Base	Lip cream	Simplex Lattice Design	Adjustment proportions on a mixed basis between extract teak leaves and Carnauba wax.	5 formulations	Implementation method optimization ensure compound This function optimally as antioxidants at a time increase external photoprotective

Reference	Active Ingredients	Form Preparation	Optimization Method	Variables Independent	Amount Experiment (Efficiency)	Accuracy / Results
						without trigger instability in the wax phase of the preparation.
(Warapsari et al., 2025)	Extract mulberry fruit	Lip balm	Conventional	Mixed base ratio wax (beeswax and carnauba wax).	4 formulations	Physical properties SPF preparation and levels are influenced base proportion.
(Ramayani et al, 2024)	Butterfly pea flower extract	Lip tint	Conventional	Variation concentration extract	3 formulations	Concentration extract 15% reaches SPF value 6.12 is categorized protection extra.
(Jannah et al., 2020)	Nanoextract beetroot (Beta vulgaris) and rosella flowers	Lip balm	Observational parametric	Use technology nanoparticles in the extract a mixture of rosella flowers and beetroot.	3 formulations	Nano rosella extract distributes effectiveness protection curtain in a way more evenly.

A synthesis of data from 23 literature reviews confirms a methodological paradigm shift in the design of photoprotective lip preparations. Formula development, which initially relied on an empirical, trial-and-error approach, is now beginning to be integrated with precise statistical modeling. Lip cosmetic formulation practices over the past decade have generally been polarized into two main spectrums: the conventional One-Factor-at-a-Time (OFAT) method and experimental optimization based on Design of Experiments (DoE).

The importance of formulation optimization is not limited to photoprotective products. Previous studies on peel-off gel masks containing Eucheuma cottonii and kefir whey demonstrated that formulation composition significantly affected physicochemical characteristics and biological activity, highlighting the need for systematic optimization to obtain products with desirable quality attributes and functional efficacy (Fatmawati et al., 2020)

Based on various optimization methods used in formulation research, Response Surface Methodology (RSM) demonstrates superiority in simultaneously determining optimum conditions compared to conventional methods such as trial and error. However, this method requires more complex statistical analysis. Meanwhile, factorial design is simpler and suitable for the initial screening stage, but is less optimal in determining specific optimum conditions. Therefore, the choice of optimization method must be tailored to the research objectives and the complexity of the formulation system being studied.

RSM is able to evaluate interactions between variables as in research. (Iskandar et al., 2025), such as the concentration of Tween 80 and propylene glycol on pH, spreadability, and adhesion. With a relatively efficient number of experiments (17 runs), it still produces a predictive model while still being mathematically modeled to determine optimum conditions. This approach is quite accurate and valid because it describes a nonlinear relationship between variables. For example, in the variable "use of Tween 80," where too little use causes the emulsion to become unstable. When too much Tween is used, the emulsion becomes unstable. When optimal use of Tween is used, the emulsion is stable and the SPF value is high. These variables do not work alone but interact with each other, resulting in a curve that is almost always nonlinear.

These analytical weaknesses can be effectively addressed through the implementation of Response Surface Methodology (RSM), which demonstrates superior modeling performance, particularly for preparations with dynamic rheological characteristics such as lip tint. The application of Box-Behnken Design (BBD) to the strawberry extract lip tint formulation (Iskandar et al., 2025)proves that 17 experimental designs (runs) are sufficient to construct a precise polynomial function. This model successfully maps the physical interactions between the concentrations of surfactant (Tween 80) and solvent (propylene glycol), which simultaneously dictate the pH stability, spreadability, and adhesiveness of the final preparation.

The validity of RSM is further strengthened through the application of Central Composite Design (CCD) on a lip tint combination of red beet extract and hibiscus leaves (Asari et al., 2025). Through 16 runs, this modeling breaks through conventional limitations by integrating formulation variables (active ingredient ratio) with machine mechanical variables (homogenization speed and time). These parameters are crucial to control, considering that anthocyanin pigments and natural phenolic compounds are very unstable and easily degraded by thermal exposure due to high-speed rotor friction. The assistance of analytical software in this RSM method has been proven to be able to mitigate the level of damage to active ingredients during the mixing process, so that the photoprotective capacity of the product is not reduced.

The OFAT approach has been identified as still dominating early-stage research (screening), particularly in exploratory studies of phytochemical efficacy. This method works by sequentially modifying a single parameter while holding other variables constant. Results are evaluated using One-Way ANOVA. This method is effective for early identification of the influence of a single variable, but has fundamental limitations such as: inability to evaluate interactions between variables, partial optimization, not global optimum conditions, and low predictive validity because it does not produce a mathematical model. As a result, optimization results are often only applicable to limited conditions and are less robust for further scale-up development.

The high level of operational efficiency is the main reason for the persistence of this method; the majority of successful studies obtained prototype preparations after only 3 to 5 trials. This is seen in lip balm formulations with various wax bases (beeswax and carnauba wax) in black pomegranate (Endriyatno et al., 2024b)and mulberry fruit extracts (Warapsari et al., 2025), each of which limited its design to 4 test formulations. Equivalent empirical efficiency patterns are also widely adopted in the development of red dragon fruit extract (Wahid Suleman et al., 2022), gotu kola leaves (Kresnawati et al., 2024), red shoot leaves. (Jannah et al., 2020), sappan wood (Nugrahaeni Ayuningtyas et al., 2025), carrot tubers (Hilmia Lukman et al., 2025), cherry leaves (More et al., 2025), a mixture of pineapple and carrot skin (Sukamdi et al., 2025), and carrier optimization in butterfly pea flower extract (Rahmawati et al., 2025; Salsabila et al., 2025).

Although operationally very efficient, the OFAT method has a fundamental deficiency in its predictive validity. Evaluation of physical stability and UV protection metrics is generally based only on basic inferential statistics such as One-Way ANOVA. Although this approach can confirm the significance of differential outcomes such as achieving the "ultra" protection category (SPF 20) in watermelon extract preparations (Risnayanti et al., 2022), or the maximum category (SPF 9.67) in Tween 80 surfactant-based tampoi rind extract, (Ristia Rahman et al., n.d.)a single analysis of variance does not have the capacity to calculate the effects of multifactorial interactions. Modification of a single excipient (e.g., escalating the dosage of virgin coconut oil and crude palm oil (Nareswari et al., 2022)) will directly affect the physical stability and balance between excipients in the preparation. The absence of mapping the interactions between these variables makes the determination of the optimum point of the preparation partial and less reliable for manufacturing transition scales. The dominance of these conventional methods carries systemic implications that are detrimental to the final quality of the formulation. The fundamental blind spot of this approach is its inability to detect and evaluate multifactorial interactions between raw materials. Consequently, the optimization achieved is merely partial and often fails to locate the global optimum of a preparation. Furthermore, the absence of a valid predictive model results in formulations with low reproducibility and a high vulnerability to instability during the transition to a production scale-up. Ultimately, continued reliance on these conventional methods carries a high risk of producing cosmetic products with suboptimal quality and protective efficacy.

On the other hand, the design of solid or semi-solid lipid-based preparations (such as lip balms, lip creams, and lipsticks) is bound by mixture experiment regulations, where the accumulated proportions of all base excipients must absolutely reach 100%. Under these phase equilibrium conditions, mathematical mixture design such as Simplex Lattice Design (SLD) becomes the most rational optimization instrument. Optimization of bitter melon seed oil and titanium dioxide-based lip cream (Winarti et al., 2024)proved that SLD is able to extract reliable predictive equations through only 5 tests. This approach successfully locked the formulation equilibrium point at 4.5% bitter melon seed oil and 1.5% titanium dioxide, which was shown to be positively correlated with the UV inhibition profile enhancement.

Visual projections in the form of contour plots generated by the SLD model facilitate formulators in simulating the functional balance between the photoprotective agent and the wax base without triggering double-phase instability (syneresis). The selection and combination of these wax bases are crucial factors that directly dictate the physical profile, thermodynamics, and user experience of the preparation. The characteristics of solid lip cosmetics rely heavily on the equilibrium ratio between soft and hard waxes. Beeswax, functioning as a natural emollient, is inherently softer; its dominant concentration significantly increases the product's adhesiveness to the lip mucosa and provides excellent spreadability for smooth application. However, due to its relatively lower melting point, excessive use of beeswax reduces the thermal stability of the preparation, making it susceptible to melting or deformation in warmer environments (Apurva Vinodkumar et al., 2019; Hidayah et al., 2026). In contrast, carnauba wax, recognized as one of the hardest natural plant waxes, possesses a very high melting point. Its incorporation into the formula matrix provides a rigid structure that increases overall thermal stability, preventing the product from breaking or "sweating" (syneresis) during storage. Yet, its rigid and brittle nature means that excessive addition lowers product plasticity, which risks decreasing spreadability and causing a dragging sensation during application (Endriyatno et al., 2024; Muslim & Fitriani, n.d.). Consequently, combining beeswax and carnauba wax requires a highly precise equilibrium. If the mixed base is too hard from excess carnauba, the product loses flexibility, spreads poorly, and releases pigments unevenly. Conversely, if the matrix is too soft from excess beeswax, it loses structural integrity, becomes highly unstable, and is prone to phase separation (Apurva Vinodkumar et al., 2019).

The selection of an optimization design is fundamentally dependent on the physicochemical profile of the sunscreen active ingredient used. The incorporation of an inorganic UV filter such as zinc oxide into a conventional beeswax matrix (Nahda & Amelia, 2025)can linearly increase the SPF value of the preparation by up to 15.2. The technical challenges in this inorganic system are more focused on preventing solid particle agglomeration, so dispersant optimization is the primary focus. Conversely, the phytochemical lability of temperature- and pH-sensitive botanical extracts requires advanced formulation engineering. The incorporation of nanoparticle delivery system technology into beetroot extract (Dewi & Senda, 2025)and a beetroot-roselle nano-extract mixture (Jannah et al., 2020)confirms the expansion of the specific surface area that significantly increases the UV protection value. The thermodynamic dynamics of such cosmetic nano-suspensions make a statistical approach (DoE) an absolute prerequisite to prevent matrix phase coagulation during storage.

A comprehensive analysis of the literature underscores the urgency of a methodological transition towards statistical computation-assisted pharmaceutical formulation. RSM is positioned as the operational standard for liquid lip preparations or fluid systems susceptible to distortion by mechanical variables, where the accuracy of its predictive function compensates for the time commitment of 15-17 test sets. For pure lipid-modified preparations governed by the law of 100%

excipient mixing, SLD provides precise empirical justification, capable of minimizing extensive laboratory testing, without compromising the validity of the collected physicochemical data.

CONCLUSION

Although conventional methods still dominate research into natural ingredient-based lip balm formulations, these approaches tend to result in less comprehensive optimizations. In contrast, DoE-based methods such as RSM have demonstrated advantages in producing more robust and predictive formulation models. However, the use of RSM remains limited, likely due to the need for specialized statistical skills and software. This indicates a research gap, where more sophisticated optimization methods have not yet been widely adopted in the development of natural ingredient-based photoprotective lip balms. To address this gap, future research should prioritize: (1) expanding the application of advanced DoE methods (such as RSM and SLD) specifically for complex botanical extract formulations; (2) validating these computationally optimized formulas through in vivo clinical trials to confirm real-world photoprotective efficacy and safety; and (3) testing the robustness of these predictive models under industrial scale-up conditions, such as mechanical shear and thermal cycling. Furthermore, developing accessible, standardized DoE guidelines is highly recommended to bridge the statistical knowledge gap for cosmetic researchers.

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