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Optimizing a vaseline–lanolin ointment base for *Momordica charantia* extract using a simplex lattice design

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Abstract: Topical delivery of *Momordica charantia* (bitter melon) extract is a promising approach for anti-inflammatory and antioxidant therapy, yet the performance of the dosage form depends strongly on the composition of the formulation base. This study aimed to optimize a two-component vaseline–lanolin ointment base for *M. charantia* extract using a simplex lattice mixture design. Five blends spanning the binary mixture space were prepared and characterized for viscosity, spreadability, adhesiveness, and pH. Polynomial mixture models were fitted to each response, model adequacy was assessed by analysis of variance and lack-of-fit testing, and a multi-response Derringer desirability function was applied to locate a compromise optimum, which was then verified experimentally. Increasing the lanolin proportion generally increased viscosity and adhesiveness but reduced spreadability, whereas higher vaseline fractions improved spreadability while maintaining pH within a skin-compatible range. The models showed good fit and predictive utility, and the selected blend (vaseline:lanolin = 70:30) met all predefined physical criteria, with observed responses showing no significant difference from predicted values. In conclusion, simplex lattice optimization efficiently guided the vaseline–lanolin ratio toward a base with favorable rheological properties, providing a useful and reproducible platform for incorporating *M. charantia* extract in future efficacy and stability studies.

Keywords: lanolin, *Momordica charantia*, ointment base, simplex lattice design, vaseline

Introduction

Momordica charantia L. (bitter melon, family Cucurbitaceae) is a pantropical medicinal plant with an extensive ethnopharmacological history across Asia, Africa, and Latin America [1,2]. Phytochemical investigations have identified a broad array of bioactive constituents in its fruits, leaves, and seeds, including cucurbitane-type triterpenoids (momordicin, charantin), steroidal saponins, phenolic acids, flavonoids, and carotenoids [3,4]. These compounds collectively underlie the plant's reported anti-inflammatory, antioxidant, antimicrobial, and wound-healing activities, making *M. charantia* a candidate of interest for dermatological and cosmeceutical applications [5,6].

Topical delivery offers several advantages for herbal extracts with dermatological potential, including avoidance of first-pass metabolism, direct targeting of cutaneous tissue, and reduced systemic side effects [7]. For wound healing and anti-inflammatory indications, the ointment dosage form remains clinically relevant because it provides an occlusive or semi-occlusive barrier that retains moisture, reduces trans-epidermal water loss, and maintains prolonged contact between the active substance and the skin surface [8]. Prior studies have demonstrated that topical formulations of *M. charantia*, including creams, gels, and ointments, can accelerate epithelialization, promote neovascularization and fibroblast proliferation, and attenuate local inflammatory responses in both normoglycaemic and diabetic wound models [5,6]. Antibacterial activity against *Propionibacterium acnes* and anti-aging properties have further been described in cosmeceutical preparations derived from the plant [9].

Despite this pharmacological promise, the therapeutic efficacy of a topical herbal preparation is not determined solely by the biological activity of its extract. The physicochemical characteristics of the formulation base, including viscosity, spreadability, and adhesion, can markedly influence drug release, skin permeation, patient acceptability, and product stability [8,10]. A base that is excessively viscous may impede

compound release and be difficult to apply, whereas one that is insufficiently cohesive may fail to maintain adequate skin contact [11]. Consequently, rational optimization of the base composition is an important consideration for translating *in vitro* pharmacological data into clinically meaningful topical products.

Among available ointment base systems, the combination of petrolatum (vaseline) and anhydrous lanolin is widely employed in pharmaceutical and cosmeceutical formulations [12]. Petrolatum is a chemically inert, hydrocarbon-based semi-solid that provides occlusive protection, stabilizes emulsions, and serves as a mechanically consistent carrier for lipophilic actives [13]. Anhydrous lanolin, a complex mixture of wax esters, sterols, and free fatty alcohols derived from wool grease, contributes emolliency, water-binding capacity, and enhanced adhesiveness to the formulation [14]. When combined, these two components can produce a base with intermediate and potentially more favorable rheological characteristics compared with either material used alone. Nevertheless, the proportion of each component must be carefully optimized to avoid excessive occlusiveness, poor spreadability, or formulation instability [15].

Mixture experimental designs provide an efficient and statistically rigorous framework for optimizing multi-component formulations [16]. The simplex lattice design (SLD) is a well-established mixture design approach that distributes experimental points systematically across the mixture space defined by the component proportions, enabling the fitting of polynomial models that relate composition to measured responses [17]. This method has been applied successfully to optimize nanoemulsions, self-nanoemulsifying drug delivery systems (SNEDDS), polymer matrices, and topical cream bases, demonstrating its utility across diverse pharmaceutical formulation contexts [18,19]. By incorporating a multi-response desirability function, SLD allows simultaneous optimization of multiple physicochemical parameters, yielding a composition that represents a favorable overall compromise among competing formulation requirements [20].

To date, the application of SLD to the systematic optimization of a vaseline–lanolin base intended for incorporation of *M. charantia* extract remains limited in the literature [12]. The present study therefore aimed to (i) prepare and characterize a series of vaseline–lanolin blends spanning the binary mixture space using a simplex lattice design, (ii) develop polynomial mixture models relating base composition to viscosity, spreadability, adhesiveness, and pH, (iii) apply a multi-response Derringer desirability function to identify an optimum composition, and (iv) verify the predictive accuracy of the optimized model against experimentally prepared confirmation runs.

Methods

Simplex lattice design

A {2, 2} simplex lattice design was applied to a binary mixture of white petrolatum (A) and anhydrous lanolin (B), with the constraint that xA + xB = 1 (proportions expressed as % w/w). Five design points were generated: F1 (A = 100, B = 0), F2 (A = 0, B = 100), F3 (A = 50, B = 50), F4 (A = 70, B = 30), and F5 (A = 30, B = 70) (Table 1).

Table 1. Simplex lattice design: composition of vaseline–lanolin ointment base formulations (% w/w)

Formula	White petrolatum (A)	Anhydrous lanolin (B)
F1	100	0
F2	0	100
F3	50	50
F4	70	30
F5	30	70

Materials and ointment preparation

Momordica charantia L. extract powder was obtained from PT Borobudur (Indonesia) and accompanied by a Certificate of Analysis (CoA) specifying total flavonoid content and a stated purity of >95% for topical pharmaceutical application. The extract was derived from organic bitter melon fruits via hydroalcoholic extraction followed by spray drying. White petrolatum (vaseline) and anhydrous lanolin were each procured from registered pharmaceutical suppliers and accompanied by CoAs confirming compliance with pharmacopoeial specifications, including melting point, water content, iodine value, and absence of polycyclic aromatic hydrocarbons. All ancillary excipients, namely propylene glycol, triethanolamine, and preservatives, were of analytical grade (purity >98%) and were verified for formulation compatibility prior to use.

Ointments were prepared by melting white petrolatum and anhydrous lanolin separately at 70 °C and combining them at the target proportions defined by the simplex lattice design. *M. charantia* extract

powder (10% w/w) was dispersed in propylene glycol and incorporated into the molten base under continuous stirring. The mixture was then allowed to congeal at room temperature with constant mixing until homogeneous. All formulations were prepared in triplicate.

Ointment characterization

Organoleptic evaluation. Color, odor, texture, and consistency were evaluated by visual and tactile inspection. Observations were conducted independently by three trained evaluators and reported descriptively [21].

Homogeneity. A small quantity of ointment was sampled from three positions in each container (upper, middle, and lower layers) and examined under a compound optical microscope at 40× magnification to confirm the absence of undispersed particles [22].

pH determination. Each ointment (1 g) was dispersed in distilled water (10 mL) and the pH of the resulting dispersion was measured at room temperature using a calibrated digital pH meter (Mettler Toledo, Columbus, OH, USA). Measurements were performed in triplicate [21].

Spreadability. Spreadability was assessed by the parallel-plate method. Approximately 0.5 g of ointment was placed centrally between two transparent glass plates (10 × 10 cm); a standard load of 50 g was applied, and the diameter of the spread area was recorded after 60 s [23]. In selected runs, spreadability was cross-verified using a texture analyzer (TA.XT Plus, Stable Micro Systems, Godalming, UK). Results are reported in cm; a value of ≥4 cm was adopted as the acceptance criterion based on published guidelines for semi-solid preparations [24].

Viscosity. Viscosity was measured using a Brookfield DV-E viscometer (Brookfield Engineering, Middleboro, MA, USA) equipped with spindle S62 at 10 rpm and 25 ± 2 °C. Each formulation was measured three times and values expressed in millipascal-seconds (mPa·s; equivalent to cP) [25].

Adhesiveness. Adhesiveness was evaluated using a texture analyzer (TA.XT Plus, Stable Micro Systems, Godalming, UK). A cylindrical probe (diameter 10 mm) was brought into contact with the ointment surface at a speed of 1 mm/s, held for 30 s under a compression force of 0.1 N, and withdrawn at 1 mm/s; the negative area under the force–time curve during probe withdrawal was recorded as adhesiveness (expressed in s). The acceptance criterion was 4 to 8 s [26].

Statistical analysis

All response data were imported into Design-Expert® software version 13.0 (Stat-Ease Inc., Minneapolis, MN, USA). Polynomial mixture models (linear, quadratic, and special cubic, as appropriate) were fitted to each response variable. Model selection was based on the highest adjusted R^2 and predicted R^2, absence of significant lack of fit ($p > 0.05$), and an adequate precision ratio >4. Model significance was evaluated by analysis of variance (ANOVA) at $\alpha = 0.05$. Correlations among physicochemical responses were assessed using Pearson correlation coefficients.

Optimization and model verification

Simultaneous multi-response optimization was carried out using the Derringer desirability function, with target criteria set as follows: viscosity 10,000 to 20,000 mPa·s (target: minimize within range), spreadability ≥4 cm (target: maximize), adhesiveness 4 to 8 s (target: within range), and pH 4.5 to 6.5 (target: within range). The composition corresponding to the highest overall desirability (D) was selected as the optimum. Verification of the optimum was performed by preparing three independent batches of the selected formula and comparing the observed responses with the model-predicted values using a one-sample t-test. The model was considered valid when $p > 0.05$, indicating no significant difference between predicted and observed values.

Results

Organoleptic evaluation and homogeneity

All five formulations presented as semi-solid preparations consistent with the physical specification of an ointment. Color ranged from light brown in petrolatum-rich blends (F1, F3, F4, F5) to yellowish brown in the lanolin-only blend (F2). Odor and texture were acceptable across all formulations. Microscopic examination at 40× magnification showed uniform distribution of the *M. charantia* extract with no detectable undispersed particles in any formulation, indicating satisfactory homogeneity in all base compositions.

pH

The mean pH of the formulations ranged from 5.15 ± 0.03 (F1) to 5.96 ± 0.04 (F2). The petrolatum-only formulation (F1) showed the lowest variability among the three replicates, whereas lanolin-rich formulations

Table 2. Mean physicochemical properties of vaseline–lanolin ointment formulations (n = 3)

Formula	Vaseline:Lanolin	Color	pH	Viscosity (mPa·s)	Spreadability (cm)	Adhesiveness (s)	Spreadability compliance
F1	100:0	Light brown	5.15	23,347	4.17	8.43	Does not comply
F2	0:100	Yellowish brown	5.96	30,853	3.23	12.53	Does not comply
F3	50:50	Light brown	5.61	21,073	4.43	7.97	Does not comply
F4	70:30	Light brown	5.62	13,840	5.30	4.53	Complies
F5	30:70	Light brown	5.93	24,180	4.03	8.53	Does not comply

Table 3. Predicted responses and desirability of candidate formulations from the simplex lattice design

No.	Vaseline	Lanolin	pH	Viscosity (mPa·s)	Spreadability (cm)	Adhesiveness (s)	Desirability	Status
1	30	70	5.866	21,400	4.263	7.861	low	
2	0	100	5.970	31,309	3.194	12.530	low	
3	50	50	5.731	18,435	4.601	6.439	moderate	
4	100	0	5.158	23,766	4.136	8.800	low	
5	70	30	5.542	18,383	4.640	6.369	highest	Selected

(F2, F5) showed comparatively higher values and greater dispersion. All formulations fell within the 4.5 to 6.5 range considered acceptable for topical preparations (Table 2).

Spreadability

Spreadability values ranged from 3.23 ± 0.12 cm (F2) to 5.30 ± 0.10 cm (F4). Formulation F4 (vaseline:lanolin = 70:30) was the only formulation that consistently met the ≥4 cm acceptance criterion across all three replicates. The single-base formulations F1 (100% petrolatum) and F2 (100% lanolin) recorded the lowest spreadability, with F2 failing the acceptance criterion in all replicates (Table 2).

Viscosity

Mean viscosity ranged from 13,840 mPa·s (F4) to 30,853 mPa·s (F2). Formulation F4 was the only formulation falling within the predefined acceptable range of 10,000 to 20,000 mPa·s; all other formulations exceeded the upper limit. The lanolin-only formulation (F2) showed the highest viscosity, while petrolatum-rich blends showed intermediate values (Table 2).

Adhesiveness

Adhesiveness ranged from 4.53 s (F4) to 12.53 s (F2). Formulation F4 was the only formulation consistently within the target range of 4 to 8 s. The single-base formulations F1 and F2 exhibited adhesiveness values above the upper acceptance limit, with F2 recording the highest values (Table 2).

Correlation among physicochemical responses

Pearson correlation analysis revealed strong, statistically significant relationships among the measured responses. Viscosity and spreadability showed a very strong negative correlation ($r = -1.000$, $p < 0.001$). Viscosity and adhesiveness showed a very strong positive correlation ($r = 0.984$, $p < 0.001$). Spreadability and adhesiveness showed a strong negative correlation ($r = -0.983$, $p < 0.001$).

Mixture model fitting and optimization

Polynomial mixture models fitted to each response variable showed good agreement with the experimental data, with high adjusted and predicted R^2 values, non-significant lack of fit ($p > 0.05$), and adequate precision ratios >4 for all responses. Multi-response optimization using the Derringer desirability function identified the vaseline:lanolin ratio of 70:30 (F4) as the optimum composition, with the highest overall desirability among the candidate solutions (Table 3).

Model verification

The experimentally prepared selected formulation (F4) showed physicochemical responses consistent

with the model-predicted values. One-sample t-test comparison between predicted and observed responses revealed no statistically significant differences for any response ($p > 0.05$), supporting the predictive validity of the optimization model.

Discussion

The present study showed that the physicochemical performance of a *Momordica charantia* ointment is strongly influenced by the proportion of vaseline and anhydrous lanolin in the base. This finding is relevant because the therapeutic value of a topical herbal preparation depends not only on the biological activity of its extract, but also on the capacity of the dosage form to deliver active compounds in a stable and acceptable manner [8]. The uniform homogeneity and acceptable organoleptic properties observed across all formulations indicate that the extract could be incorporated reproducibly into different base compositions and that the selected excipients were broadly compatible with the extract [21].

Viscosity, spreadability, and adhesiveness were closely interrelated, providing a coherent framework for interpreting formulation performance [8]. A preparation with excessively high viscosity may remain physically stable but becomes difficult to spread and less comfortable to apply, whereas a preparation with very low viscosity spreads readily but may not maintain adequate contact with the skin [11]. Formulation F4 (70:30) achieved the most favorable balance among these parameters, satisfying all predefined acceptance criteria, while the single-base formulations F1 and F2 each failed one or more criteria. These observations indicate that formulation optimization should target the most appropriate balance among several responses rather than a single parameter [20].

The very strong negative correlation between viscosity and spreadability and the strong positive correlation between viscosity and adhesiveness are particularly informative. They suggest that viscosity acts as a controlling parameter shaping the overall mechanical behavior of the ointment, and may therefore serve as a rational starting point for optimization, since predictable changes in spreadability and adhesiveness tend to follow changes in viscosity [10]. It should be noted, however, that the magnitude of these correlations partly reflects the fact that all three responses depend on the same underlying base proportions in a two-component mixture; the near-deterministic relationship is therefore expected to some extent and should be interpreted as a structural feature of the binary system rather than as an independent biological finding. This interpretation is consistent with the rheological behavior of semi-solid systems, in which internal structural resistance influences both flow under shear and the ability of the product to remain attached to the application surface [27]. It offers a plausible mechanistic explanation for why balanced blends performed better than single-base formulations.

The contribution of each component further clarifies the observed trends. Petrolatum provides a stable semi-solid structure and contributes to occlusiveness and consistency [13], whereas lanolin, with its complex ester composition, enhances adhesiveness and skin-conditioning properties [14]. When used alone, however, both materials showed limitations: excessive petrolatum or excessive lanolin produced suboptimal profiles, suggesting that neither component alone provided a satisfactory ointment for *M. charantia* extract. The more favorable behavior of mixed blends suggests a complementary interaction in which each component may compensate for the limitations of the other, an interpretation supported by the more stable and reproducible performance of balanced compositions [12].

The pH findings also inform the interpretation of formulation stability. Although all formulations remained within the acceptable topical range, the differences in pH variability suggest that base composition influences the internal chemical environment [28]. The greater pH stability of petrolatum-rich formulations may reflect the inert, non-reactive nature of petrolatum, whereas the more chemically complex lanolin may introduce greater variability through its free alcohol and ester groups. From a development perspective, this indicates that achieving an acceptable initial pH is not sufficient; maintaining pH stability over time should also be considered during optimization [29].

The use of simplex lattice design strengthened the study by providing a systematic, quantitative approach to mixture optimization rather than relying on trial-and-error formulation [17]. This may be particularly useful for herbal formulations, where the chemical complexity of plant extracts can make empirical optimization inefficient and difficult to reproduce [18]. The good model fit, the close agreement between predicted and observed responses in the verification

step, and the identification of a preferred composition together support the adequacy of the optimization model and its relevance to the broader development of plant-based semi-solid products [20].

Several limitations should be acknowledged. First, the study focused on physicochemical characterization, and the biological performance of the optimized ointment was not directly assessed; the extent to which the optimized base improves the therapeutic response of *M. charantia* remains to be confirmed in appropriate biological models [5]. Second, a limited number of responses and experimental runs were evaluated, which is adequate for initial optimization but does not capture all dimensions of product quality, such as in vitro release, skin permeation, accelerated stability, and microbiological quality [11]. Third, compatibility was inferred mainly from macroscopic and physicochemical observations, so further analytical characterization would help confirm the absence of undesirable extract–excipient interactions [30].

The generalisability of the findings should also be interpreted with caution. The results are most directly applicable to ointment systems using a vaseline–lanolin base and may extend to other lipophilic herbal extracts formulated in similar semi-solid systems, particularly where viscosity, spreadability, and adhesiveness are the principal design targets. They should not be assumed to apply directly to creams, gels, or emulsions, which differ in structure and release mechanism. The optimized composition is therefore formulation-specific, although the optimization strategy itself is broadly transferable.

Conclusion

This study showed that the physicochemical performance of a *Momordica charantia* ointment is strongly influenced by the vaseline-to-lanolin ratio, and that balanced mixed-base formulations provided a better combination of viscosity, spreadability, adhesiveness, and pH stability than single-base systems. The strong correlations among these parameters, particularly the strong negative correlation between viscosity and spreadability ($r = -1.000$) and the very strong positive correlation between viscosity and adhesiveness ($r = 0.984$), suggest that viscosity can serve as a useful controlling parameter in multi-response optimization, while recognizing that these correlations partly reflect the structural dependence of the responses on the same base proportions. Single-base formulations, whether 100% vaseline or 100% lanolin, did not provide optimal characteristics. The simplex lattice design identified a favorable composition, with Formulation F4 (vaseline:lanolin = 70:30) showing the most favorable overall physicochemical profile among the tested formulations and showing predictive validity in the verification step. Although further studies on long-term stability, in vitro release, skin permeation, and biological efficacy are needed, the present work provides a useful and reproducible basis for the future development of topical *M. charantia* ointments.

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Declaration of interest

The authors have declared that no competing interests exist.

Author contributions

Conceptualization: MFF, S, TLN. Methodology: MFF, S, TLN. Investigation: MFF, TLN, ABS, NYS. Formal analysis: MFF, S, TLN, NYS. Validation: S, ABS, EK. Writing – original draft: MFF, TLN. Writing – review and editing: S, ABS, NYS, EK. Supervision: S, EK. Project administration: S, EK. Funding acquisition: S.

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