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Development, Optimization, and evaluation of New herbal Antipsoriatic Emulgel

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A B S T R A C T

Objective: It is acknowledged that psoriasis is the most prevalent autoimmune condition brought on by the improper activation of the immune system.

the lack of possible cure and associated severe side effects in allopathic medicines have led to extensive research in natural products with antipsoriatic activity. Bearing in mind this, and based on previous studies conducted at the Medicinal and Aromatic Plant and Traditional Medicine Research Institute (MAPTMRI), in which the activity of the Aloe sinkatan plant was proven as an effective treatment for psoriasis, it was selected to formulate, optimize and evaluate a new emulgel from Aloe sinkatana plant extract used as an anti-psoriatic agent.

Method: The study included a multi-phase process that included the collecting and extraction of plants. Based on pre-formulation studies like solubility and compatibility studies, liquid paraffin, propylene glycol, Tween-20 and Span-20, alcohol, and DEMSO were selected for the forumaltion. The emulgels were designed, formulate and optimized using a 2^3 factorial design. Spreadability and viscosity were considered dependent variables, while the quantities of emulsifying agent, gelling agent and, liquid paraffin were chosen as independent formulation variables. Physical appearance and physiochemical parameters like stability, pH, viscosity, spreadability, and percentage medication content were evaluated for the produced formulations.

Results: Regression analysis showed that all three independent variables significantly affected the response variables. The formulation was optimized using a response surface plot using Design Expert software 8.0.7.1. The R^2 values for the response's viscosity and spreadability were 0.9915 and 0.9761, respectively.

Conclusion: Aloe sinkatana extract was used as an active component in the formulation of the emulgel form. Formula F3 shows good physicochemical characteristics and a higher percent of drug content than other formulations; therefore, it was selected as an optimal formula.

Keywords: Aloe sinkatana, anti-psoriatic properties, optimized formula, emulgel formulation, factorial analysis

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Introduction

The most prevalent autoimmune condition, psoriasis, is characterized by scaly, inflammatory lesions that can appear on any part of the skin and is brought on by an improper activation of the cellular immune system. [1] The National Psoriasis Foundation reports that this disease affects about One hundred and fifty million people globally, or 2-3 percent of the population [2]. Currently available synthetic drugs used to treat psoriasis have not fully met the needs of the sufferers, mostly as a result of a number of issues, such as treatment resistance following prolonged drug use and relapses following medication discontinuation following partial or satisfactory clearance. Additionally, certain treatments, such phototherapy, might cause liver problems and raise the risk of cancer [3]. Additionally, the effectiveness of the treatment may wane over time, necessitating the use of an alternative therapy. For this reason, there is currently no cure for psoriasis [3, 4].

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Based on all of the aforementioned, at MAPTMRI, we collected a large number of Sudanese medicinal plants that are traditionally used in treating psoriasis and conducted experiments to screen, evaluate, and select the most effective anti-psoriatic plants. The finding indicates that the most potent antipsoriatic plant was Aloe sinkatan. [5].

The antipsoriatic activity of the Aloe *sinkatana* plant was evaluated by studying the effect of 0.1% and 0.2% extracts of *A. sinkatana* on five groups of mice (imiquimod-induced psoriasis mice model) using dexamethasone as a control. The results show that the percent reduction of the psoriasis-like symptoms for the groups of 0.2% *A. sinkatana* extract, 0.1% A. sinkatana extract, and dexamethasone standard drug were 86%, 84%, and 68%, respectively. [5]. Furthermore, the safety of A. sinkatana was studied by conducting acute dermal toxicity by applying 2000 mg/kg of *Aloe sinkatana* extract topically on the skin of experimental animals using two groups of ten rats, and the findings demonstrate the safety and non-toxic effect of the topical use of the Aloe *sinkatana* plant, which justifies its use in traditional Sudanese medicine for the treatment of psoriasis. [5].

The Aloe sinkatana plant is a medicinal plant that grows naturally in Eastern Sudan in the Red Sea Mountains, mainly in the Sinkat area. It contains aloe-emodin and microdontin compounds. It was discovered that these two substances significantly inhibited T-cell proliferation (IC50 values of 9.2 and 7.4 mg/L, respectively), and inhibited the generation of IL-2 (IC50 values of 1.1 and 1.9 mg/L, respectively, for aloe-emodin and microdontin). [6]
One of the most important biological effects of aloe-emodin (AE), is its antiproliferative activity [7]. The growth of human keratinocytes in culture was considerably reduced by AE at a dosage of 5 μM. [8].
Ashish et al. report that When psoriatic patients applied AE topically, their skin disease symptoms decreased. [9]. These facts support and confirm the efficiency of using Aloe sinkatana extract as a cure for psoriasis since psoriasis is a disease caused by an imbalance in the immune system, and in this case, the cells have been categorized by some scientists as cancerous cells.

Bearing in mind all this, this study's main goal was to develop, obtimized, and assess a novel emulgel using plant extract from Aloe sinkatana as an anti-psoriatic treatment.

Focusing on emulgel is intriguing and difficult because it is a topical medication delivery system with fewer marketed medicines to date. It is a blend of emulsions and gels. Both gels and emulsions are in charge of regulated drug release from systems; however, gels still have trouble delivering hydrophobic medications. To get around this issue, the idea of emulgel was developed, in which the hydrophobic medications are first added to the emulsion and then to the gel [10, 11]. By incorporating the emulsion into the gel basis, Emulgel achieves the dual controlled release effect, combining the benefits of emulsions and gels [12]. Emulgel exhibits superior drug release and stability, and it can be utilized to extend the effects of medications with shorter half-lives.

Furthermore, materials used in the preparation of emulgels are available and cheaper, resulting in a reduction in emulgel production costs. [13]. Oil phase Emulsifying and, gelling agents, and are the main constituents of an emulgel [14].

The following characteristics of an emulgel make it an attractive choice for treating plaque psoriasis: easy spreadability, washable, enhanced hydrating and absorbance of drugs into the skin, increased compliance among patients because of the product's not oily, elegance aperance and smooth [15, 16]

Materials and Methods:

Materials
The standard compound

Aloe-Emodin standard compound was received as a gift from Prof. Masaki (Kobe University, Japan).

Plant Collection and Authentication

The Aloe sinkatana plants were collected, from the Sinkat area, Red Sea state, Sudan, they were authenticated by the Department of Chemistry, Medicinal & Aromatic Plants Research Institute and Traditional Medicine, National Research Center, Khartoum, Sudan.

Methods
Extraction of Aloe sinkatana:

Fresh water was used to wash Aloe sinkatana leaves that ranged in length from around seventy-five to ninety centimeters.
Inner gel is scrapped and cut into pieces. he leaves of aloe were processed using the conventional hand filleting procedure. The lower leaf base, the tapering tip at the apex of the leaf, and the small spines around the edges of the leaf were all cut off with sharp blades. Then inserting the blade into the gel layer under the green rind, and the top rind was removed. They pulled off the leaves' skin and chopped the firm, colorless gel into pieces

The epidermis of the leaves was pulled off, and the colorless, solid gel was cut into pieces. Then 250 gm of gel was loaded into a 1000ml flask and 500 ml solvent (Ethanol) was added. Ultrasound-assisted extraction was performed at 60° C for

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60 min. After that the solution was filtered and complrtly drying usuing a rotary dryer
[17].

Formulation design using 2^3 full factorial design:

To obtain the "best" or an "optimized product" eight different formulations were generated using two levels, three-factor, full factorial design.

To maximize the different response variables, a 2^3 factorial design was chosen . The quantities of liquid paraffin , gelling agent , and emulsifying agent were chosen as independent variables, and the amounts of each ingredient were appropriately coded. (Table no.1). The dependent or response variables were viscosity and spreadability. Experiments were conducted for each of the eight potential combinations (Table no.2).Throughout the study, other formulation component remained constant.[18].

Design-Expert_ DX 8 Software was used to generate and evaluate the statistical experimental design.

Table 1: Low and high levels for each of the variable factors for 2^3 full factorial design

Factor No.	Variable factors	Low Level (-1)	High level (+1)
Factor1-(X1)	Amount of Gelling agent(Carbopol 940)	1%	2%
Factor2-(X2)	Amount of Emulsifying agent (Tween20+Span20)	1.5%	2.5%
Factor3-(X3)	Amount of Liquid paraffin	5%	7.5%

Table 2: Formulation characteristics of full factorial design

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N.B: The Tween20 and Span20 were used as Emulsifying agent in ratio of 0.6:1 to each others

Table 3: Composition of different formulation batches (%w/w) of *Aloe sinkatana* 100ml Emulgel

	Coded formula	X1	X2	X3	X1- Amount of Gelling agent(Carbopol940)	X2- Amount of Emulsifying agent (Tween20+Span20)	X3- Amount of Liquid paraffin
1	F1	-1	-1	-1	1%	1.5%	5%
2	F2	+1	-1	-1	2%	1.5%	5%
3	F3	-1	+1	-1	1%	2.5%	5%
4	F4	+1	+1	-1	2%	2.5%	5%
5	F5	-1	-1	+1	1%	1.5%	7.5%
6	F6	+1	-1	+1	2%	1.5%	7.5%
7	F7	-1	+1	+ 1	1%	2.5%	7.5%
8	F8	+1	+1	+ 1	2%	2.5%	7.5%

Ingredients (%) Coded formula	**Role the component**	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**
Carbopol 940	Gelling Agent	1	2	1	2	1	2	1	2
Liquid Paraffin	Oil Phase	5	5	5	5	7.5	7.5	7.5	7.5
Tween20	Surfactant	0.6	0.6	1	1	0.6	0.6	1	1
Span20	Surfactant	0.9	0.9	1.5	1.5	0.9	0.9	1.5	1.5
Extract	Active Ingredient	5							
Ethanol	Co-Surfactant	2.5							
DEMSO	Permeation Enhancer	5							

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Propylene glycol	Co-Surfactant	5
Triethanolamine	Adjust pH	Q.s to Adjust pH 6-6.5
Distilled Water	Aqueous Phase	Q.S

Preparation steps of Emulgel:

Table no.3. shown the different consituents of emulgel formulations.

To prepared the gel, Carbopol 940 was first dissolved in 80 °C hot purified water, then the mixture was allowed to cool and sit overnight.
Span20 was dissolved in liquid paraffin to create the emulsion's oil phase, while Tween20 was dissolved in purified water to create the aqueous phase.
While plant extract was dissolved in DMSO, propylene glycol was dissolved in ethanol, and the two solutions were combined with the aqueous phase.
After heating the aqueous and oily phases independently to 70 to 80 °C, the oily phase was gradually introduced to the aqueous phase while being constantly stirred until it cooled to room temperature.
To prepared the final formula of the emulgel, the resulting emulsion and gel were combined in a 1:1 ratio while being gently stirred. Lastly, triethanolamine was used to change the emulgel's pH [19, 20].

The components (Excipients) were selected according to previous pre-formulation studies for the physicochemical properties and compatibility of the plant extract (active ingredient) and excipients, prior to the compounding process of the formulation.

Physical characterization

A thin coating of the emulgels was applied on glass slides, and they were inspected visually. Investigations were conducted on the color, stability, and phase separation. [21]. In order to assess the formulation's homogeneity, A tiny layer of gel was put on a microscope slide, and within two months, the Euromex model optical microscope was used to study the gel's microscopic pictures at 40x magnification. [22, 23].

Centrifugation test

One practical way to verify the stability of the created emulgel formulas is to do a centrifugation investigation. One week following the emulgels' production, these investigations were conducted. A little centrifuge was used to perform centrifugation for thirty seconds at 3000 rpm.

[24]

pH Measurement

A pH meter (Max Instruments Chandigarh, India) calibrated before each reading was used to test the pH of 1% aqueous solutions of the produced A.sinkatana emulgel using buffered solutions at pH 4.0 and 7.0. After washing the pH meter electrode with distilled water, 1g of the emulgel was dissolved in the water, and the volume adjusted to 100 ml (1% of the formulated emulgel).
Each formulation's pH was measured three times, and the average results were computed. [25,26,27]. Since pH directly affects how well the emulgel works with the physiology of the skin, it is essential to understand it. In addition to potentially compromising the integrity of skin cells, an acidic or too alkaline pH may also result in less than ideal antibacterial action. To guarantee biocompatibility, the formulations were designed to replicate the pH of normal skin, which is between 4.5 and 6.5.[28]

Viscosity Test

Using the Viscometer VR 3000 (Viscotech, Spain), viscosity was measured at room temperature with the proper spindle number (L4) and rpm (100 rpm). Before the measurement was made, a suitable quantity of each emulgel formulation was placed in a beaker and let to settle for 30 minutes at the test temperature (25±1 °C). Next, making sure the spindle did not contact the jar's bottom, the spindle groove was dropped perpendicularly into the middle of the emulgel. It was then spun for ten minutes at 50 rpm. After one minute, the viscosity of each formulation was determined by measuring the data obtained from the first viscosity tests [29, 30].
Viscosity has a significant impact on the emulgel's flow characteristics and may serve as a predictor of its long-term stability. Phase separation may result from lower viscosity; however, the therapeutic efficacy may be impacted by increased viscosity as it may hinder easy spread ability. One can forecast the spreadability over a vast skin surface area and the possibility of prolonged release of the active component by assessing this characteristic. [31]

Spreadability test

After a minute, the spreading diameter of 1g of emulgel between two horizontal plates (30cm x 30cm) was measured using the commonly used parallel plate method to estimate the spreadability. [32].

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Determination of emulsion type

Either water or oil is used to dilute the emulsion. Since water is the external phase, an o/w type emulsion diluted with water will stay stable; nevertheless, if diluted with oil, the emulsion would seperate since water and oil are incompatible. While water in oil emulsion may be diluted with an oily liquid, oil in water emulsion can be readily diluted with an aqueous solvent. [33]

Quantitative analysis

Calibration curve of standard Aloe-emodin compound

Based on previous studies, the Aloe sinkatan's λ max was determined. [5] For this purpose, 0.01g of the standard Aloe-emodin material was put into a 100 ml volumetric flask and dissolved with methanol using an ultrasonic shaker to create a standard solution (stock solution) of 100µg/ml.
. A UV spectrophotometer was used to measure the absorbance of several dilutions when a stock solution with different concentrations (2 µg/ml, 4 µg/ml, 6 µg/ml, 8 µg/ml, 10 µg/ml, and 12 µg/ml) was prepared. By charting the absorbance versus the concentration, the calibration curve was established.

Determination of Aloe Emodin content in Aloe sinkatana extract

0.5gm of dried extracts were dissolved by ultrasonic shaker in 100ml of methanol (0.5%). The absorbance of the resultant solution was read at wavelength 430 nm using a UV spectrophotometer.

Determination of Drug Content:

For determination of the aloe emodin compound content in the different formulas of Aloe, sinkatana extract was weighted 5gm of emulgel formula and dissolved by ultrasonic shaker in 50ml of methanol (10%). A UV spectrophotometer was used to measure the absorbance of the resulting solution at 430 nm. The drug content as a percentage was determined.

Statistical analysis

Design-Expert program (version: Design Expert software 8.0.7.1) was used to optimize the emulgel formulation. Multiple linear regression analysis was used to create polynomial models with interaction and quadratic components for each response variable. To ascertain how each variable affected the formulation's properties, equations were computed. Analysis of variance (ANOVA) was used to determine the model's statistical validity, and Design-Export software was used to create the 3D response graphs. [34]

Results

Physical characterization

For two months, the Aloe sinkatana emulgel formulations' physical properties were assessed. After two months, the emulgel formulations' glossy reddish-brown look persisted without changing color. Because emulgel is a pharmaceutical form, it was smooth and didn't feel sticky, gritty, or greasy. Two months of optical microscopy were employed to evaluate potential morphological and homogeneity changes. The results showed that the spherical droplets were well-dispersed and had comparable morphologies (Table No. 4).
The prepared emulgels passed the pharmaceutical quality grade approval since they looked excellent. [21, 35].

Table 4: Results of Physical characterization of emulgels of formulation batches

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Formula code	Color	Texture	Appearance	Phase separation
F1	Reddish Brown	Smooth	Glossy	Stable
F2	Reddish Brown	Smooth	Glossy	Stable
F3	Reddish Brown	Smooth	Glossy	Stable
F4	Reddish Brown	Smooth	Glossy	Stable
F5	Reddish Brown	Smooth	Glossy	Stable
F6	Reddish Brown	Smooth	Glossy	Stable
F7	Reddish Brown	Smooth	Glossy	Stable
F8	Reddish Brown	Smooth	Glossy	Stable

Centrifugation study

Emulsion and other semisolid formulations may be evaluated and their shelf life predicted with the use of centrifugation. In terms of phase separation, the centrifugation test, also known as stress testing, is typically performed to assess the physical stability of semisolid formulations held at various temperatures [36]. Table 5 shows the outcomes. demonstrates that all of the formulas retained their homogeneity and consistency after 30 minutes of centrifugation, with the exception of formula F5, which showed phase separation after 25 minutes, which may have been caused by the low concentration of gelling and emulsifying agents.

Measurement of pH

One important consideration when making skin care products is pH, which has to be assessed [37, 38]. A reasonable pH value should be utilized for topical application since formulations with extremely high or low pH might harm the skin [29]. Because psoriatic patients' skin is sensitive, the ideal pH for creating topical formulations was chosen to be near neutral in order to lower the possibility of adverse effects [40]. Table 5 demonstrates that the formulations' pH values fall between 6.36 and 6.48, which is deemed suitable to reduce the possibility of skin irritation when applied (within the pH range of human skin). Triethanolamine was used to achieve this.

Viscosity and spreadability test

Viscosity is a crucial metric to assess since it primarily determines the uniformity of the medication content release and dose form [41]. Brook field viscometers were used to measure the viscosities of all formulations. Values are listed in Table 5. The viscosity varied from 26734 to 28510 Cps, and the test results indicated that the viscosity rose as the amount of gelling agent and surfactant increased and vice versa.

While the results of spreadability ranged between 23.2 to 25.1cm

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Table 5: Results of centrifugation, pH, viscosity, and spreadability tests of formulation batches.

Formula code	Centrifugation test	pH	Viscosity(Cps.)	Spreadability(cm.)
F1	Stable	6.42 ± 0.02	26956± 12.3	24.5± 0.5
F2	Stable	6.٤4 ± 0.15	28191± 10.2	23.4±1.43
F3	Stable	6. ٣٩± 0.04	27422± 21.5	24.2±0.12
F4	Stable	6.36 ± 0.11	28510± 11.4	23± 0.9
F5	Phase separation	6.38 ± 0.02	26734± 9.1	25.1± 1.3
F6	Stable	6.٤0 ± 0.17	28089± 14.3	23.7± 2.6
F7	Stable	6.48 ± 0.52	27096± 13.0	24.9± 0.05
F8	Stable	6.٤0 ± 0.21	28250 ± 11.4	23.2± 3.5

All values represent means ±S.D. of the mean (n=3)

Determination of the emulsion type formed

All formulations were diluted with oil to determine the type of emulsion; no phase separation occurred upon dilution (stable); nevertheless, the emulgel of all recipes split into two phases when water was used for dilution, indicating that the emulsions were W/O type.

Quantitative analysis

The absorbance for the concentration of Aloe Emodin standard compound is shown in Table No.6, and the calibration curve is illustrated in Figure No.1.

With a regression value of 0.986, the standard graph of the aloe emodin compound demonstrates strong linearity and complies with Beer's-Lambert's Law in the concentration range of 0-100 µg/ml.

The aloe-emodin concentration in Aloe sinkatana extract and then the drug content was estimated from equation no.1 of the calibration curve. The final concentration of Aloe-emodin in the plant extract was found to be equal to 4 µg /5mg = 0.08%

Table 6: The absorbance data of serial concentration of Aloe Emodin

No.	Concentration (µg /ml)	Absorbance at 430nm in Methanol
1	0	0
2	2	0.05
3	4	0.148
4	6	0.235
5	8	0.349

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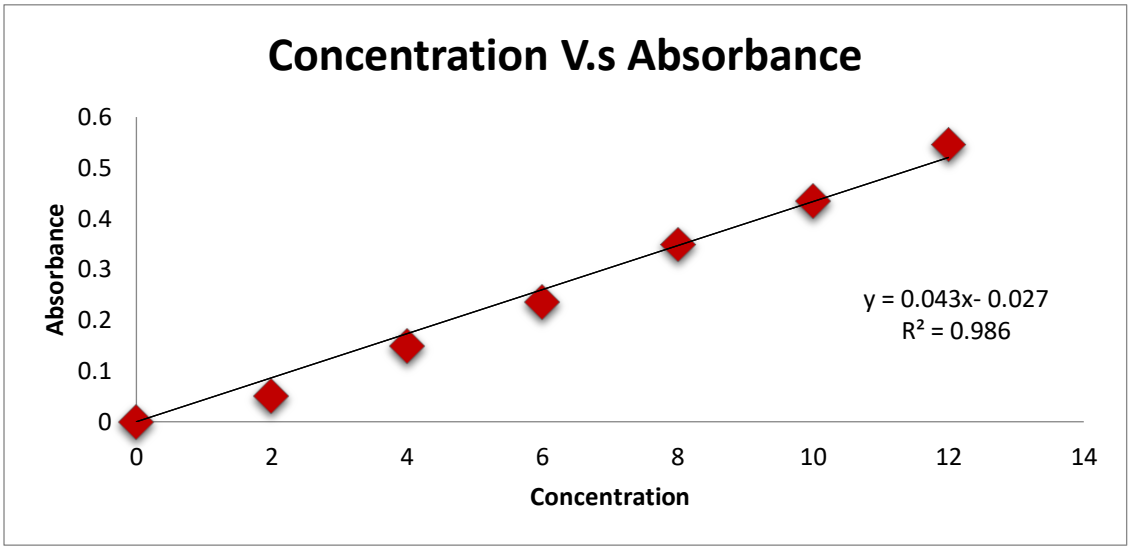
6	10	0.435
7	12	0.545

Figure 1: Calibration curve of absorption of various concentrations of Aloe Emodin standard compound at 430nm



Y= 0.046× **X** - 0.027……Eq.1.

Table 7 represent the result of drug content of the 8 formulae that ranged between 92.34% & 99.48, while the (F3) formula shows the highest percent of drug content

Table 7: Aloe Emodin content in the drug formulas

Formula	Absorbance of Emulgel Formula at 430nm	The practical concentration of Aloe-emodin in the drug formula	The practical concentration of Aloe-emodin in the drug formula %	Theoretical Concentration of Aloe-emodin in drug formula	Drug content= Practical Concentration/ Theoretical Concentration
F1	0.132	3.69 µg /100g	0.00369%	0.0040%	92.25%
F2	0.141	3.90 µg /100g	0.00390%	0.0040%	97.95%
F3	0.144	3.97 µg /100g	0.00397%	0.0040%	99.48%
F4	0.143	3.95 µg /100g	0.00395%	0.0040%	98.97%
F5	0.136	3.79 µg /100g	0.00379%	0.0040%	94.75%

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F6	0.130	3.65 µg /100g	0.00365%	0.0040%	91.25%
F7	0.135	3.76 µg /100g	0.00376%	0.0040%	94%
F8	0.132	3.69 µg /100g	0.00369%	0.0040%	92.25%

Optimization Study

Viscosity and spreadability analysis of variance (ANOVA) based on response data (Y1&Y2) is displayed in Tables Nos. 8 and 9.

All P-values listed on tables no. 8 & 9, showed that the independent factors (X1, X2, and X3) had a significant impact on the responses (Viscosity and Spreadability).

The linear model was selected for both responses (viscosity and spreadability) with Model F-value 151.88, P- value is 0.0001 and F-value 54.54, P- value is 0.0011, respectively.

With R2 values close to unity, the model's goodness of fit was deemed statistically great. Based on the values for the response Y1 and Y2, which ranged from 0.9915 to 0.9761, the model was deemed statistically excellent for both responses.

The agreement between expected and observed answers was checked to confirm the hypothesized model's predictive power for each response; the experimental and predicted values for each response fell within the confidence interval, when it comes to viscosity, the "Predicted R squared" of 0.9652 is reasonably consistent with the "Adjusted R Squared" of 0.9848, and when it comes to spreadability, the "Predicted R squared" of 0.9652 is reasonably consistent with the "Adjusted R Squared" of 0.9582. These findings suggest that the factors used for the study had a significant impact on both viscosity and spreadability. As a result, we can say that the statistical model has mathematical validity. The resulting equations for dependent variables—Y1 (Viscosity), and Y2 (spreadability) in terms of coded factors are presented below.

$$Y1= +27769.75+604.00\times X1+163.50\times X2-227.50 \times X3 \quad \text{Eq. 2}$$

$$Y2 = +23.78-0.68 \times X1-0.18 \times X2+0.45\times X3 \quad \text{Eq. 3}$$

where:

Y= Dependant factor

b0 ,b1 ,b2, b3=intercept

X1 = Amount of gelling agent

X2 = Amount of surfactant

X3 = Amount of liquid parrafin

The regression equations no. 2 & 3 presented in Figures no. 2 & 3 show the effect of independent variables X1, X2, and X3 on the viscosity(Y1) and spreadability (Y2). It was clear that the three independent variables had a strong impact on Y1 and Y2 but the most important (highest) effect occurred by factor X1 which is the amount of gelling agent (P- value < 0.0001 & 0.0003 respectively)

Both variables (Amount of gelling agent and Amount of surfactanthave a positive effect (synergistic effect) on viscosity and a negative effect (antagonistic effect) on the spreadability. The variable (amount of liquid paraffin -X3) has a direct relationship with spreadability and an inverse relationship with viscosity, Formulation variables, such as gelling agent, surfactant, emulsifying agent, and oil phase, influence the rheological properties of the formulation; therefore, it is important to choose the ideal number of variables to achieve good viscosity. Conversely, when viscosity is very high, the formulation becomes rigid and the spreadability decreases.

The model graph for the viscosity is given in Figure (2). The figure showed the viscosity increased as the amount of a gelling agent and a surfactant increased and vice versa.

The graphical result in Figure (3) showed that the spreadability is indirectly proportional to the amount of a gelling agent and a surfactant, and directly proportional to the amount of liquid paraffin (linear model).

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Table 8: Analysis of variance (ANOVA) results of multiple regression analysis summary statistics for viscosity response

Source	Sum of square	Degree of freedom	Mean square	F value	p-value Prob> F
Model	3.236E+006	3	1.079E+006	151.88	0.0001
X1	2.919E+006	1	2.919E+006	410.95	< 0.0001
X2	2.139E+005	1	2.139E+005	30.11	0.0054
X3	1.035E+005	1	1.035E+005	14.58	0.0188
Residual	28407.50	4	7101.87		
Cor Total	3.264E+006	7			

Std. Dev.	84.27	R-Squared	0.9913
Mean	27656.00	Adjusted R-Squared	0.9848
C.V. %	0.30	Predicted R-Squared	0.9652
PRESS	1.136E+005	Adequate Precision	29.577

Table 9: Analysis of variance (ANOVA) results of multiple regression analysis summary statistics for spreadability response

Source	Sum of square	Degree of fredum	Mean square	F value	p-value Prob> F
Model	4.30	3	1.43	54.54	0.0011
X1	3.65	1	3.65	138.86	0.0003
X2	0.25	1	0.25	9.33	0.0378
X3	0.40	1	0.40	15.43	0.0171

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Residual	0.10	4	0.026		
Cor Total	4.40	7			
Std. Dev.	0.16	R-Squared		0.9761	
Mean	24.00	Adjusted R-Squared		0.9582	
C.V. %	0.68	Predicted R-Squared		0.9045	
PRESS	0.42	Adequate Precision		18.767	

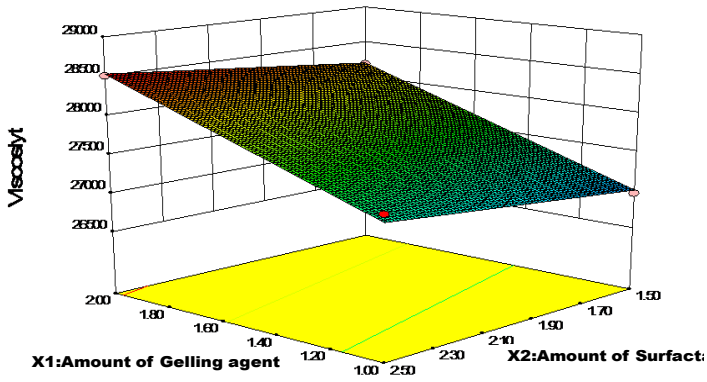

Fig. 2: 3D Surface Plot of Linear Model of the Viscosity

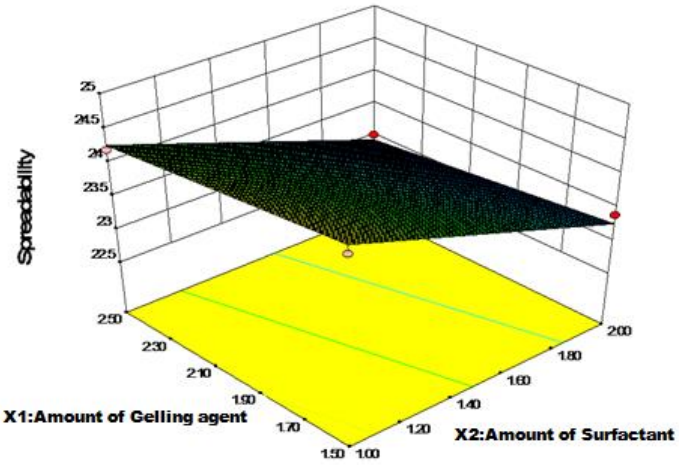

Fig. 3: 3D Surface Plot of Linear Model of the spreadability.

Discussion

The emulgel formulations are described as reddish-brown, shiny, homogeneous, stable, and with good spreadability. The physical properties seem suitable for to be used topicall. Emulgel's nature allows for more penetration and retention into the skin, which is desirable in psoriasis, given that psoriatic skin is dry and covered with plaque. It also increases skin hydration, which is a crucial component of psoriasis care. Additionally, because it is smooth, elegant, non-greasy, non-sticky, and easy to apply to the skin's surface, it improves patient compliance.

The pH of the formulations is kept between 6.36 and 6.48, which is a skin-friendly range. Given that it is applied to irritated skin, such as that of psoriasis, its consistency is crucial for preventing skin irritation.

While the formulation has been scientifically tested for physicochemical stability, clinical testing would be necessary to confirm the effectiveness of Aloe sinkatana emulgel against psoriasis symptoms.

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Conclusion

Aloe-emodin has been determined as one of the active constituents of Aloe sinkatana as a marker compound. The antipsoriatic emulgel has been formulated from Aloe sinkatana extract using 2^3 factorial design which fulfills all standard requirements. Finally, it was determined that the produced formulation F3 had good physiochemical features,and highest percent of drug content making it a more promising topical herbal emulgel. Future Research works can be done to get better results

Statements and Declarations

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Competing interests

The authors affirm that there are no Competing interests.

Authors' contributions

The Data collection investigation, editing, Writing an original draft and review: Azza Dawoud; editing, and analysis of data: Sali Dawoud Hussien & Mohammed abdalbagi, Supervision: Mohamed El Hassan Shayoub

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