J. Pharm. Res. 2025;24(1):28–35

Print ISSN: 0973-7200
Online ISSN: 2454-8405

Journal of Pharmaceutical Research

RESEARCH ARTICLE

Development, Optimization, and Evaluation of New Herbal Antipsoriatic Emulgel

Azza Dawoud H Dawoud[1,*], Sali Dawoud Hussien[2], Mohammed Abdalbagi[1], Mohamed El Hassan Shayoub[3]

[1] *Medicinal and Aromatic Plants & Traditional Medicine Research Institute, National Center of Research, Sudan*
[2] *Department of Dermatology, Faculty of Medicine, Omdurman Islamic University, Sudan*
[3] *Department of Pharmaceutics, Faculty of Pharmacy, University of Khartoum, Sudan*

ARTICLE INFO

Article history:
Received 29.11.2024
Accepted 14.02.2025
Published 23.03.2025

* *Corresponding author.*
Azza Dawoud H Dawoud
azzadawoudhussien@gmail.com

https://doi.org/10.18579/jopcr/v24.i1.114

ABSTRACT

Psoriasis is recognized as the most common autoimmune disease caused by the inappropriate activation of the cellular immune system, characterized, by severe skin inflammation, epidermal hyperproliferation, the lack of possible cure and associated severe side effects in allopathic medicines has led to extensive research in natural products with antipsoriatic activity. *Aloe sinkatana* plant is a very potent antipsoriatic agent and is used traditionally to treat psoriasis. To formulate and evaluate a new emulgel from *Aloe sinkatana* plant extract used as an anti-psoriatic agent. A 2^3 factorial design was selected to formulate *Aloe sinkatana* Eumlgel. The three factors were: the amount of gelling agent X1, amount of emulsifying agent X2, and amount of liquid paraffin X3, these were selected as independent formulation variables, while the viscosity and spreadability were taken as dependent variables or response variables. The model of the formulation was considered statistically excellent with R^2 values approaching unity since, the R^2 values for both the response's viscosity and spreadability were found to be 0.9915, and 0.9761 respectively. The extract of *Aloe sinkatana* was formulated as an active ingredient in the emulgel dosage form, and formula F3 was selected as an optimal emulgel formula.

Keywords: *Aloe sinkatana*; Anti-psoriatic; Emulgel; Factorial design; Formulation

INTRODUCTION

Psoriasis is recognized as the most common autoimmune disease caused by the inappropriate activation of the cellular immune system. The National Psoriasis Foundation reports that this disease affects approximately 125 million people worldwide (2% to 3% of the total population have psoriasis)[1]. Nearly 60% of people with psoriasis reported their disease to be a large problem in their everyday life. Total healthcare costs of psoriasis for patients are calculated at $11.25 billion annually, approximately 60% of psoriasis patients miss an average of 26 days of work a year due to their illness[2]. The current available synthetic drugs used to treat psoriasis have not fully met the needs of the sufferers, largely due to several problems like resistance to treatment after long-term drug exposure and relapses upon cessation of medication after partial or acceptable clearance is obtained. Also, some treatments may increase the risk of cancer (phototherapy) and can induce disorders in the liver[3]. Furthermore, the treatment efficacy may diminish with time, and it must be replaced by another therapy. Therefore, at present, there is still no curative treatment for psoriasis.

Aloe sinkatana plant is a very potent antipsoriatic medicinal plant that grows naturally in the Eastern Sudan in the Red Sea Mountains mainly in the Sinkat area, where it is popularly used extensively by residents of the region to treat psoriasis[4,5]. Bearing in mind all this, the main task of this study is to formulate and evaluate a new safe and effective emulgel from *Aloe sinkatana* plant extract used as an anti-psoriatic agent.

Emulgel is topical drug delivery, and to date, it has less marketed product, so it is interesting and challenging to focus on emulgel. It is a combination of gels and emulsions.

Emulsions are controlled release systems containing two immiscible phases in which the internal phase is dispersed into external, with the use of an emulsifying agent to stabilize the system. Emulsions are of oil-in-water or water-in-oil type, where the active agent particle entrapped in the internal

KRUPANIDHI COLLEGE OF PHARMACY

phase passes through the external phase,[6,7] USP defines gel as a semisolid system consisting of dispersions made up of either small inorganic particles or large organic molecules enclosing and interpenetrated by liquid. The gel contains a larger amount of aqueous liquid in a cross-linked network of colloidal solid particles where it captures small drug particles and maintains the controlled release of the drug. The emulsion and gel both are responsible for the controlled drug release from the systems[8], gels have still limitations in the delivery of hydrophobic drugs so to overcome this limitation the concept of emulgel was introduced where the hydrophobic drugs are incorporated in emulsion and then to gel[9,10]. Emulgel combines the advantage of emulsion and gels, gaining the dual controlled release effect, where the emulsion is gelled by incorporation in the gel base[11], emulgel shows good stability and better release of drugs, also it can be used to prolong the effect of drugs having shorter t1/2. Furthermore, materials used in the Preparation of emulgels are available, and cheaper, resulting in, a reduction in emulgels production costs[12–14].

The most important constituent of emulgels is an aqueous phase (water, alcohol, etc), oil phase (eg mineral oils liquid paraffin, propylene glycol, isopropyl myristate, isopropyl palmitate, castor oil, olive oil, balsam oil, wool wax, soyabeen oil, cotton seed oil, oleic acid, maize oil, arachis oil, etc.), emulsifying agent (e.g. Polyethylene glycol, Span 80, Tween 80, Stearic acid, Sodium stearate, etc.), gelling agent (e.g. Carbopol 934, 940, xanthan gum, etc.) and permeation enhancer (e.g. Oleic acid, Menthol, Clove oil, Lecithine, Isopropyl myristate, Urea, Linoleic acid, Cinnamon, etc.)[15–17].

MATERIAL 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

Mature, healthy, and fresh leaves of *Aloe sinkatana* having a length of approximately 75 to 90 cm were washed with fresh water.

The inner gel is scrapped and cut into pieces. A traditional hand filleting method of processing Aloe leaves was used. In this method, the lower leaf base, the tapering point at the leaf top, and the short spines located along the leaf margins were removed by sharp blades. The blade was then introduced into the mucilage layer below the green rind avoiding the vascular bundles, and the top rind was removed. The epidermis of the leaves was peeled off, and the colorless, solid mucilaginous 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 60 min. After that the solution was filtered and the solvent was removed under reduced pressure in a Rotary evaporator until it became completely dry[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.

A 2^3 factorial design for three factors at two levels each was selected to optimize the varied response variables. The three factors, amount of gelling agent X1, amount of emulsifying agent X2, and amount of liquid paraffin X3 were selected as independent formulation variables, and the factor levels were suitably coded (Table 1). Viscosity and Spreadability were taken as dependent variables or response variables. Experimental trials were performed at all 8 possible combinations (Table 2). All other formulation variables and processing variables were kept invariant throughout the study[18].

Design-Expert_DX 8 Software was used for the generation and evaluation of 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%

Preparation of Emulgel

The composition of emulgel formulations is shown in Table 3.

First, the gel was prepared by dispersing Carbopol 934 in heated purified water (80 °C), and the dispersion was cooled and left overnight. The oil phase of the emulsion was prepared by dissolving Span20 in liquid paraffin while the aqueous phase was prepared by dissolving Tween20 in purified water.

Table 2: Formulation characteristics of full factorial design

Run	Coded values				Actual values		
	Coded formula	X1	X2	X3	X1- Amount ofGelling agent (Carbopol940)	X2- Amount ofEmulsifying 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%

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

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

Ingredients (%) Coded formula	F1	F2	F3	F4	F5	F6	F7	F8
Carbopol 940	1	2	1	2	1	2	1	2
Liquid Paraffin	5	5	5	5	7.5	7.5	7.5	7.5
Tween20	0.6	0.6	1	1	0.6	0.6	1	1
Span20	0.9	0.9	1.5	1.5	0.9	0.9	1.5	1.5
Extract	5							
Ethanol	2.5							
DEMSO	5							
Propylene glycol	5							
Triethanolamine	Q.s to Adjust pH 6-6.5							
Distilled Water	Q.S							

Propylene glycol was dissolved in ethanol whereas plant extract was dissolved in DMSO, and both solutions were mixed with the aqueous phase. Both the oily and aqueous phases were separately heated to 70 to 80 °C then the oily phase was added to the aqueous phase with continuous stirring until cooled at room temperature. The obtained emulsion was mixed with the gel in a 1:1 ratio with gentle stirring to obtain the emulgel. Finally, the pH of the emulgel was adjusted by using triethanolamine[19,20].

Macroscopic evaluations

The 8 batches of the emulgel formulae were viewed under a microscope to study their color, texture, homogeneity, consistency, and phase separation[21,22].

Centrifugation study

Centrifugation study is a useful means to check the stability of the prepared emulgel formulae. These studies were performed one week after the preparation of emulgels. Centrifugation was carried out using a Mini centrifuge at 3000 rpm for 30 minutes[23].

Measurement of pH

The pH value of 1% aqueous solutions of the prepared *A. sinkatana* emulgel was measured using a pH meter (Max Instruments Chandigarh, India), which was calibrated before each reading, with buffered solution at pH4.0 and 7.0. The measurement of the pH of each formulation was done in triplicate and average values were calculated.[24–26]

Viscosity Test

Measurements of viscosity were done by Viscometer VR 3000 (Viscotech, Spain) by choosing the appropriate spindle number (L4) and rpm (100 rpm) at room temperature. An appropriate amount of each emulgel formulation was kept in a suitable beaker, the spindle groove was dipped, and the rpm was set. Viscosity measurements were started, and the readings were measured after 1 minute, and the viscosity of each formulation was calculated[27,28].

Spreadability test

The Spreadability was determined by the parallel plate method, which is widely used, by measuring the spreading diameter of 1gm of emulgel between two horizontal plates (30cm x 30cm) after one minute[29].

Determination of the emulsion type formed (Dilution test)

The emulgel formulae were diluted either with oil or water. If the emulsion of the emulgel is o/w type and it is diluted with water, it will remain stable as water is the dispersion medium but if it is diluted with oil the emulsion will break as oil and water are not miscible with each other[30].

Quantitative analysis

Calibration curve of standard Aloe-emodin compound

Accurately weighed Aloe-emodin standard material (0.01g) was, transferred to a 100 ml volumetric flask and dissolved by ultrasonic shaker with methanol to get a standard solution of 100μg/ml (stock solution). Various concentrations (2 μg

/ml, 4 μg / ml, 6 μg /ml, 8 μg /ml, 10 μg /ml, and 12 μg /ml) of stock solution were made and the absorbance of various dilutions was taken at wavelength 430 nm using a UV spectrophotometer. The calibration curve was determined by plotting the absorbance, against the concentration.

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%). The absorbance of the resultant solution was read at wavelength 430 nm using a UV spectrophotometer. The percentage drug content was calculated.

Statistical analysis

The data obtained was statistically analyzed by Design-Expert_ DX 8 Software statistical program.

RESULTS

Table 4: Results of macroscopic evaluations of formulation batches

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

$$Y = 0.046 \times X - 0.027 \quad (1)$$

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	6.44 ± 0.15	28191 ± 10.2	23.4 ± 1.43
F3	Stable	6.39 ± 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	6.40 ± 0.17	28089 ± 14.3	23.7 ± 2.6
F7	Stable	6.48 ± 0.52	27096 ± 13.0	24.9 ± 0.05
F8	Stable	6.40 ± 0.21	28250 ± 11.4	23.2 ± 3.5

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

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
6	10	0.435
7	12	0.545

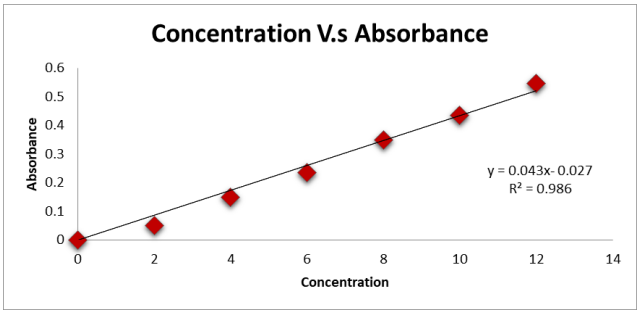

Fig. 1: Calibration curve of absorption of various concentrations of Aloe Emodin standard compound at 430nm

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%
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%

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 freedom	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
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

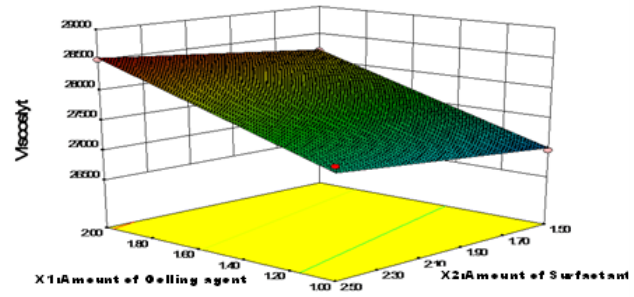

Fig. 2: 3D Surface Plot of Linear Model of the Viscosity

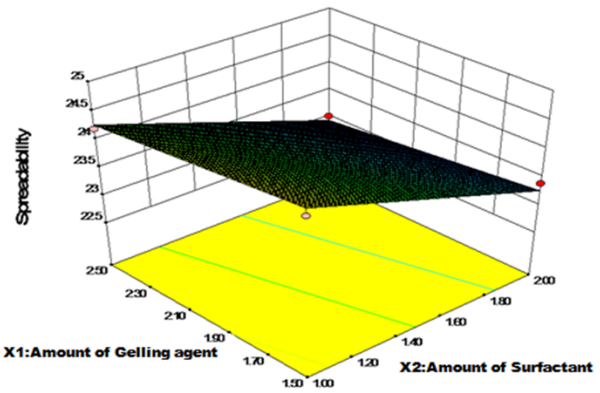

Fig. 3: 3D Surface Plot of Linear Model of the spreadability

DISCUSSION

The emulgel formulas are glossy, reddish brown in color; all formulations are homogeneous, stable, and smooth in texture, as shown in Table 4.

The centrifugation test, measured pH, viscosity and spreadability values of the prepared emulgel formulations are given in Table 5. Centrifugation is an important tool for evaluating and predicting the shelf life of semisolid formulations like emulsion. The centrifugation test (stress testing) is usually used to evaluate the physical stability of semisolid formulation stored at different temperatures in terms of phase separation[31], the results show that all the formulas maintained their consistency and homogeneity after 30 minutes of centrifugation and no phase separation was detected, except the formula F5 showing phase separation after 25 minutes of centrifugation and this may be due to the low concentration of emulsifying agent and gelling agent

The pH values of the formulations range from 6.36 to 6.48, which is considered acceptable to avoid the risk of irritation upon application to the skin (within the pH range of the human skin). This was achieved by the incorporation of triethanolamine. The physiologic role of an acidic skin surface historically was thought to be a defense mechanism against invading organisms. More recently, it has been demonstrated that several key enzymes involved in the synthesis and maintenance of a competent skin barrier are largely impacted by pH. Hence, a broader view of the importance of pH in the function and integrity of the skin is emerging[32].

Results of the viscosity test showed that the viscosity increased as the amount of gelling agent and a surfactant increased and vice versa, the viscosity ranged between 26734 to 28510 Cps. While the results of spreadability ranged between 23.2 to 25.1cm.

To determine the emulsion type, all prepared formulas were diluted with oil and there was no phase separation upon dilution (stable), however, when water was used for dilution the emulgel of all formulas was separated into two phases, and this result indicated that the emulsions were W/O type.

The absorbance for the concentration of Aloe Emodin standard compound is shown in Table 6, and the calibration curve is illustrated in Figure 1. The standard graph of Aloe Emodin compound shows good linearity with an R2 value of 0.986, which indicates that it obeys 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 (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%

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

Analysis of variance (ANOVA) according to the data of the responses (Y1&Y2) for both viscosity and spreadability is shown in Tables 8 and 9. All P-values listed on Tables 8 and 9, indicated a significant effect of the independent factors (X1, X2 & X3) 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.

The goodness of fit of the model was considered statistically excellent with R2 values approaching unity. The values for the responses Y1, and Y2 were found 0.9915 to 0.9761. Therefore, the model was found statistically excellent for both responses Y1 and Y2.

To validate the predictive ability of the hypothesized model for each response, the agreement between predicted and observed responses was verified; the experimental and predicted values were within the confidence interval for each response, the "Predicted R squared" of 0.9652 is in reasonable agreement with the "Adjusted R Squared" of 0.9848 in case of viscosity while the value "Predicted R squared" of 0.9652 is in reasonable agreement with the "Adjusted R Squared" of 0.9582in case of spreadability. These

results indicate that the viscosity and spreadability both are strongly affected by the variables selected for the study. Consequently, we can conclude that the statistical model is mathematically valid. The resulting equations for dependent variables—Y1 (Viscosity), and Y2 (spreadability) in terms of coded factors are presented below.

$$Y1 = +27769.75 + 604.00 \times X_1 + 163.50 \times X_2 - 227.50 \times X_3 \quad (2)$$

$$Y_2 = +23.78 - 0.68 \times X_1 - 0.18 \times X_2 + 0.45 \times X_3 \quad (3)$$

where:

Y= Dependant factor

b0 ,b_1 ,b_2, b_3=intercept

X_1 = Amount of gelling agent

X_2 = Amount of surfactant

X_3 = Amount of liquid parrafin

The regression Equations (2) and (3) presented in Figures 2 and 3 show the influence of independent variables X1, X2, and X3 on the viscosity (Y1) and spreadability (Y2). It was clear that the three independent variables had a significant influence 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 -X1 and amount of surfactant-X2 have 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, that mean when viscosity is very high, the formulation becomes rigid and the spreadability decreases. So, it is necessary to choose the optimum amount of variables to get good viscosity. Formulation variables, e.g. gelling agent, surfactant, emulsifying agent, and oil phase influence the rheological properties of the formulation.

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).

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. It was finally concluded that the developed formulation F3 was found to be a more promising topical herbal emulgel as it shows good physicochemical characteristics highest percent of drug content. Future Research works can be done to get better results.

Statements and Declarations

- **Funding support:** This research was funded by the Ministry of Higher Education and Scientific Research.
- **Authors' contributions :** The investigation, data collection Writing an original draft, Writing review, & editing: Azza Dawoud; editing, and data analysis: Sali Dawoud Hussien & Mohammed abdalbagi, Supervision: Mohamed El Hassan Shayoub.
- **Competing interests:** The authors declare there is no competing interests.

REFERENCES

1. Gelfand JM, Stern RS, Nijsten T, Feldman SR, Thomas J, Kist J, et al. The prevalence of psoriasis in African Americans: results from a population-based study. *Journal of the American Academy of Dermatology*. 2005;52(1):23–26. Available from: https://doi.org/10.1016/j.jaad.2004.07.045.
2. Horn EJ, Fox KM, Patel V, Chiou CF, Dann F, Lebwohl M. Association of patient-reported psoriasis severity with income and employment. *Journal of the American Academy of Dermatology*. 2007;57(6):963–971. Available from: https://doi.org/10.1016/j.jaad.2007.07.023.
3. Kormeili T, Lowe NJ, Yamauchi PS. Psoriasis: immunopathogenesis and evolving immunomodulators and systemic therapies; U.S. experiences. *British Journal of Dermatology*. 2004;151(1):3–15. Available from: https://doi.org/10.1111/j.1365-2133.2004.06009.x.
4. Almahdi RA. Pharmacovigilance of Herbal Products. *Sudan Journal of Rational Use Medicine*. 2016;11:29–29.
5. Hussien AD. Formulation and Evaluation of Aloe sinkatana Gel as Anti-psoratic Agent. . Available from: https://scholar.google.com/scholar?cluster=7732684696030835252&hl=en&oi=scholarr.
6. Single V, Saini S, Joshi B, Rana AC. Emulgel: a new platform for topical drug delivery. *International Journal of Pharma and Bio Sciences*. 2012;3(1):P485–P498. Available from: https://www.ijpbs.net/abstract.php?article=MTI1OA==.
7. Mohamed MI. Optimization of chlorphenesin emulgel formulation. *AAPS Journal*. 2004;6(3):81–87. Available from: https://doi.org/10.1208/aapsj060326.
8. Mulye SP, Wadkar KA, Kondawar MS. Formulation development and evaluation of Indomethacin emulgel. *Der pharmacia sinica*. 2013;4(5):31–45. Available from: https://www.imedpub.com/articles/formulation-development-and-evaluation-of-indomethacin-emulgel.pdf.
9. Mona A, Yogesh A, Prakash I, Arun P, Jayshree V, Amruta K. Phytochemical and HPTLC studies of various extracts of Annona squamosa (Annonaceae). *International Journal of Pharm Tech Research*. 2012;4(1):364–368. Available from: https://www.researchgate.net/publication/267943673_Phytochemical_and_HPTLC_Studies_of_Various_Extracts_of_Annona_squamosa_Annonaceae.
10. Basheer H, Krishnakumar K, Dineshkumar B. Emulgel Formulation: Novel Approach for Topical Drug Delivery System. *International Journal for Pharmaceutical Research Scholars*. 2016;5(1):227–230. Available from: https://www.ijprs.com/article/emulgel-formulation-novel-approach-for-topical-drug-delivery-system/.
11. Caddeo C, Sales OD, Valenti D, Saurí AR, Fadda AM, Manconi M. Inhibition of skin inflammation in mice by diclofenac in vesicular carriers: liposomes, ethosomes and PEVs. *International Journal of Pharmaceutics*. 2013;443(1-2):128–136. Available from: https://doi.org/10.1016/j.ijpharm.2012.12.041.
12. Panwar AS, Upadhyay N, Bairagi M, Gujar S, Darwhekar GN, Jain DK. Emulgel: A Review. *Asian Journal of Pharmacy and Life Science*. 2011;1(3):333–340. Available from: https://shop.tarjomeplus.com/UploadFileEn/TPLUS_EN_3952.pdf.

13. Wang M, Fang L. Percutaneous absorption of diclofenac acid and its salts from emulgel. *Asian journal of pharmaceutical sciences*. 2008;3(3):131–141. Available from: https://www.researchgate.net/publication/228625806_Percutaneous_absorption_of_diclofenac_acid_and_its_salts_from_emulgel.
14. Veni NK, Yashwanthi P, Hemalatha B, Padmalatha K. A Review on Emulgels as a Novel Approach for Topical Drug Delivery. *Asian Journal Of Research In Pharmaceutical Sciences*. 2022;12(02):163–168. Available from: https://doi.org/10.52711/2231-5659.2022.00028.
15. Jain A, Gautam SP, Gupta, Jain S. Development and characterization of Ketoconazole emulgel for topical drug delivery. *Der Pharmacia Sinica*. 2010;1(3):221–231. Available from: https://www.researchgate.net/publication/285798718_Development_and_characterization_of_ketoconazole_emulgel_for_topical_drug_delivery.
16. Ajazuddin AA, Khichariya A, Gupta S, Patel RJ, Giri TK, Tripathi DK. Recent expansions in an emergent novel drug delivery technology: Emulgel. *Journal of Controlled Release*. 2013;171(2):122–132. Available from: https://doi.org/10.1016/j.jconrel.2013.06.030.
17. Ashara KC, Paun JS, Soniwala MM, Chavada JR, and NMM. Micro-emulsion based emulgel: a novel topical drug delivery system. *Asian Pacific Journal of Tropical Disease*. 2014;4(Supplement 1):S27–S32. Available from: https://doi.org/10.1016/S2222-1808(14)60411-4.
18. Kumar L, Reddy MS, Managuli RS, Pai KG. Full factorial design for optimization, development and validation of HPLC method to determine valsartan in nanoparticles. *Saudi Pharmaceutical Journal*. 2015;23(5):549–555. Available from: https://doi.org/10.1016/j.jsps.2015.02.001.
19. Khullar R, Kumar D, Seth N, Saini S. Formulation and evaluation of mefenamic acid emulgel for topical delivery. *Saudi Pharmaceutical Journal*. 2012;20(1):63–67. Available from: https://doi.org/10.1016/j.jsps.2011.08.001.
20. Yılmaz G, Tanrıverdi ST, Aksu B, Yeğen G, Özer O. Preparation and in vitro characterization of etofenamate emulgels using quality by design. *Journal of Research in Pharmacy*. 2019;23(6):1033–1039. Available from: https://doi.org/10.35333/jrp.2019.67.
21. Ambala R, Vemula SK. Formulation and Characterization of Ketoprofen Emulgels. *Journal of Applied Pharmaceutical Science*. 2015;5(7):112–117. Available from: https://dx.doi.org/10.7324/japs.2015.50717.
22. Plumb AP, Rowe RC, York P, Brown M. Optimisation of the predictive ability of artificial neural network (ANN) models: A comparison of three ANN programs and four classes of training algorithm. *European Journal of Pharmaceutical Sciences*. 2005;25(4-5):395–405. Available from: https://dx.doi.org/10.1016/j.ejps.2005.04.010.
23. Vasiljevic D, Parojcic J, Primorac M, Vuleta G. An investigation into the characteristics and drug release properties of multiple W/O/W emulsion systems containing low concentration of lipophilic polymeric emulsifier. *International Journal of Pharmaceutics*. 2006;309(1-2):171–177. Available from: https://dx.doi.org/10.1016/j.ijpharm.2005.11.034.
24. Kamble A, Adnaik R, Bhutkar M. Formulation and Evaluation of Itraconazole Emulgel For Topical Drug Delivery. *International Journal Of Universal Pharmacy and Bio sciences*. 2014;3:37–45.
25. Mohite S, Salunkhe A. Formulation and evaluation of Emulgel containing Coriandrum sativum seeds oil for Anti-inflammatory activity. *Journal of Drug Delivery and Therapeutics*. 2019;9(3-s):124–130. Available from: https://dx.doi.org/10.22270/jddt.v9i3-s.2808.
26. Burki IK, Khan MK, Khan BA, Uzair B, Braga VA, Jamil QA. Formulation Development, Characterization, and Evaluation of a Novel Dexibuprofen-Capsaicin Skin Emulgel with Improved In Vivo Anti-inflammatory and Analgesic Effects. *AAPS PharmSciTech*. 2020;21(6). Available from: https://dx.doi.org/10.1208/s12249-020-01760-7.
27. Yapar EA, Ýnal Ö, Erdal MS. Design and in vivo evaluation of emulgel formulations including green tea extract and rose oil. *Acta Pharmaceutica*. 2013;63(4):531–544. Available from: https://dx.doi.org/10.2478/acph-2013-0037.
28. Shelke O, Kulkarni A. Formulation, Development and Evaluation of Nifedipine Emulgel for Treatment of Anal Fissures Using Polymeric Emulsifiers. *Indian Journal of Pharmaceutical Education and Research*. 2019;53(2s):s74–s81. Available from: https://dx.doi.org/10.5530/ijper.53.2s.51.
29. Goyal S. Novel Anti-Inflammatory Topical Herbal Gels Containing Withania somnifera and Boswellia serrata. *International Journal of Pharmaceutical & Biological Archive*. 2011;2(4):1087–1094. Available from: http://www.ijpba.info/ijpba/index.php/ijpba/article/view/339.
30. Ashara KC, Paun JS, Soniwala MM, Chavada JR, Mori NM. Micro-emulsion based emulgel: a novel topical drug delivery system. *Asian Pacific Journal of Tropical Disease*. 2014;4:S27–S32. Available from: https://dx.doi.org/10.1016/s2222-1808(14)60411-4.
31. Coneac G, Vlaia V, Olariu I, Muţ AM, Anghel DF, Ilie C, et al. Development and evaluation of new microemulsion-based hydrogel formulations for topical delivery of fluconazole. *AAPS PharmSciTech*. 2015;16(4):889–904. Available from: https://doi.org/10.1208/s12249-014-0275-8.
32. Ali SM, Yosipovitch G. Skin pH: from basic science to basic skin care. *Acta Dermato-Venereologica*. 2013;93(3):261–267. Available from: https://doi.org/10.2340/00015555-1531.