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ORIGINAL ARTICLE

Formulation, Evaluation and Optimization of Herbal Emulgel using Box-Behnken Design

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ABSTRACT
The present study focuses on formulating, evaluating, and optimizing an herbal emulgel containing Ardisia solanacea leaf extract. Standard analytical techniques were used to conduct phytochemical screening and fluorescence analysis, while the antioxidant potential was assessed using a reducing power assay. The Box-Behnken design was employed to investigate the impact of Carbopol 934, propylene glycol, and Tween 20 on parameters such as spreadability, viscosity, and drug release. Phytochemical analysis indicated the presence of flavonoids, alkaloids, tannins, saponins, triterpenoids, and phenols. The antioxidant activity of the ethanolic extract of Ardisia solanacea was determined, with IC_{50} values of 79.165 µg/ml for EtAs and 77.9 µg/ml for BHT (used as a positive control). Using the Box-Behnken design, an emulgel was formulated, and among the 13 batches tested, formulation F8 exhibited optimized characteristics: pH of 6.52, spreadability of 16.871 gm.cm/sec, viscosity of 4137.7 cP, drug release of 83.704%, and drug content of 88.45%. The optimized formulation batch F8 demonstrated promising results. This suggests its potential for further development.
Keywords: *Ardisia solanacea, Box-Behnken Design, Herbal Emulgel, Reducing Power Assay, Fluorescence Analysis.*

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INTRODUCTION

The use of herbal therapy has been steadily gaining popularity among both patients and physicians, particularly in the treatment of skin diseases. Traditional Indian folk medicines, rooted in Ayurveda, have long been recognized for their efficacy in addressing a spectrum of ailments such as inflammation, leprosy, scabies, skin infections, ulcers, and wounds [1]. This renewal of interest in herbal medicine is driven by the potential of natural bioactive components found in plants, which have demonstrated significant curative benefits across various disorders [2]. The World Health Organization (WHO) notes that approximately 80% of people worldwide rely on traditional and folk medicines, highlighting the dependence on plant-based remedies [3]. Despite advancements in synthetic drug development, herbal medicines offer distinct advantages. They are often more cost-effective and exhibit better compatibility with the human body, leading to fewer side effects [4]. The rich heritage of Indian Systems of Medicine, including Ayurveda, Siddha, and Unani, highlights the profound therapeutic potential of herbal medicines, making them an area of interest for further research and exploration [5]. The plant species *Ardisia solanacea*, commonly known as Shoebutton Ardisia, belongs to the Ardisia genus and thrives in tropical and subtropical regions worldwide. Its extensive medicinal history spans over 900 years, particularly renowned in Chinese traditional medicine [6]. The genus Ardisia is rich in various compounds including polyphenols, triterpenoid saponins, coumarins, quinones, flavonoids, and alkylphenols [7]. *Ardisia solanacea* is notably valued for its medicinal properties. Traditionally, its fruits have been used to relieve conditions like dysentery and diarrhoea. Additionally, they exhibit antibacterial, antimicrobial, antioxidant, anti-spermatogenic, anti-steroidogenic, anti-inflammatory, antipyretic, stomachic, stimulant,

astringent, diuretic, and anti-diabetic properties. Conversely, the leaves of this plant possess anxiolytic, sedative, analgesic, and antibacterial effects, along with hepatoprotective, anti-inflammatory, and insect-repelling qualities [8]. Medicines are traditionally administered through various routes such as oral, parenteral, rectal, and sublingual, with oral administration being the most common. However, oral delivery presents challenges such as poor solubility and bioavailability, low patient compliance, and susceptibility to first-pass metabolism. In such cases, topical drug delivery systems offer a promising alternative by bypassing first-pass metabolism, mitigating absorption risks like gastric emptying time and pH variations, and addressing issues associated with intravenous therapy. Furthermore, they improve patient compliance and are easy to apply [9]. Topical drug delivery systems are particularly beneficial when other routes fail or for treating skin infections. However, conventional topical formulations face limitations, especially in delivering hydrophobic drugs efficiently. This limitation is addressed by emulgels, a novel combination of emulsion and gelling agents [10]. Emulgels, with their dual-phase nature (water-in-oil or oil-in-water), act as effective regulators of drug release, making them superior carriers for poorly water-soluble or hydrophobic medications. Their advantages include thixotropic behaviour, non-greasy texture, easy spreadability and washability, emollient properties, longer shelf life, environmental friendliness, transparency, and aesthetic appeal [11,12]. The preparation of emulgels involves penetration enhancers, essential oils, emulsifiers, surfactants, and gelling agents, contributing to their stability and efficacy [13].

MATERIAL AND METHODS

Chemicals and Equipment

Trichloroacetic acid (Loba Chemie, Pvt. Ltd.), Potassium Ferricyanide (Universal Laboratories Pvt. Ltd.), BHT (Cosmo chem) and other solvents used were purchased locally. Rotary Vacuum Evaporator (Modern Scientific), UV-Visible Spectrophotometer (Shimadzu, UV 1900, Japan), Digital pH meter (BioEra's pH Meter Model Adel) and Viscometer (Brookfield viscometer, Labman LVDV-60) were used.

Collection and Identification of Plant Material

Fresh leaves of *Ardisia solanacea* were sourced from Tamil Nadu, and their authenticity was verified at Sri Venkateswara University, Tirupati, under Voucher no. 0663 dated 28/08/2023.

Preparation of Extract

The freshly collected *A. solanacea* leaves were thoroughly cleaned with water, allowed to dry in the shade for a week, and then ground into a powder using a mechanical grinder. The powdered sample was extracted with petroleum ether (60-80°C) to separate fatty material. The Soxhlet extraction method was used to extract the sample with 95% ethanol, and the resulting extract was concentrated using a rotary vacuum evaporator under reduced pressure. For later use, the dried ethanolic extract of *A. solanacea* (EtAs) (Fig. 1) was kept in a sealed container in a cool (4°C), dry and dark place. The following formula was used to calculate the percentage yield of the extract:

Percentage yield = Weight of dried extract / Weight of powdered sample × 100

Fig. 1: The dried ethanolic leaves extract of *Ardisia solanacea*

Phytochemical Screening

The presence of phytochemicals in an ethanolic extract of *A. solanacea* was analysed by following standard procedures for the preliminary phytochemical screening described by Kokate *et. al* [14].

Fluorescence Analysis

Take approximately 0.5 grams of powdered sample and place it into the clean, dried test tubes. Add 5 ml of different organic solvents to each tube, including distilled water, ethanol, methanol, ethyl acetate, petroleum ether, acetone, glacial acetic acid, chloroform, FeCl3, ammonia, NaOH, iodine, conc. H2SO4,

conc. HCl, and conc. HNO3. Shake all the tubes thoroughly and allow them to stand for about 20–25 minutes. Observe the resulting solutions under visible daylight as well as short UV light (254 nm) and long UV light (365 nm) to determine any characteristic colours.

***In-vitro* Antioxidant Study by Reducing Power Assay**

The antioxidant activity of EtAs and the standard positive control BHT was assessed using the reducing power assay method described by Oyaizu in 1986. Dilutions of EtAs and BHT were prepared to achieve concentrations ranging from 2 to 20 µg/ml. For each dilution, 1 ml was combined with 2.5 ml of 0.2M phosphate buffer (pH 6.6) and 2.5 ml of 1% potassium ferricyanide solution. This mixture was then incubated at 50°C in a water bath for 20 minutes. After cooling, 2.5 ml of 10% trichloroacetic acid was added, and the resulting solution was centrifuged at 3000 RPM for 10 minutes. Next, 2.5 ml of the supernatant was withdrawn and mixed with 2.5 ml of distilled water, followed by adding 0.5 ml of 0.1% ferric chloride. The absorbance of the reaction mixture was measured at 700 nm using a UV Spectrophotometer A blank sample without any extract was also prepared. Higher absorbance values indicate greater reducing power. A plot was created showing the percentage of reduction against the concentration of the extract, from which the IC_{50} value (the concentration at which 50% inhibition occurs) was determined [15].

% Reducing activity = (Absorbance of sample − Absorbance of blank) / (Absorbance of blank) × 100

Formulation of Emulgel

1. Preparation of Gel Base:

Carbopol-934 was dispersed in distilled water with constant stirring using a mechanical stirrer. The pH of the gel was adjusted to between 6 to 7 using triethanolamine. The gel was allowed to stand overnight at room temperature to ensure proper swelling of the gel base.

2. Preparation of Emulsion:

Aqueous Phase: Purified water was mixed with Tween 20 to form the aqueous phase. Propylene glycol was used as a solvent for methyl and propylparaben, which were then added to the aqueous phase. Additionally, EtAs was incorporated into the aqueous phase.

Oil Phase: Span 20 was dissolved in light liquid paraffin to create the oil phase of the emulgel.

Both the oil and aqueous phases were heated to 70–80 °C. Subsequently, the oil phase was added to the aqueous phase with continuous stirring at 2000 RPM to achieve a thorough mixing of the two phases.

3. Preparation of Emulgel:

The emulsion obtained was combined in a 1:1 ratio with the gel phase while being moderately stirred.

Experimental design

The optimization process for the prepared emulgel formulation utilized a three-factor three-level Box-Behnken design (BBD) within Design Expert 13 software (version 8.0.0, Stat-Ease Inc., Minneapolis, Minnesota). BBD was chosen over other response surface methods like central composite and three-level full factorial design due to its superior efficiency [16]. The experimental design consisted of three factors and 13 runs (Table 1), allowing for the statistical optimization of formulation parameters and the assessment of main effects, interaction effects, and quadratic effects on spreadability, viscosity, and drug release. By employing this design, the study aimed to understand how independent variables influenced dependent variables and utilized quadratic response surfaces and contour plots to optimize processes with minimal experimental runs. The coded independent factors and their levels for this study are detailed in Table 2.

Table1: Experimental design

	Factor 1	**Factor 2**	**Factor 3**
Batches	Conc. of Carbopol-934 (gm)	Conc. of Propylene Glycol (ml)	Conc. of Tween 20 (ml)
F1	1	5	1
F2	0.75	5	1.5
F3	0.75	5	0.5
F4	1	3	1
F5	0.5	3	1
F6	0.5	5	1
F7	0.5	4	1.5
F8	0.75	4	1
F9	0.75	3	1.5
F10	0.5	4	0.5
F11	1	4	0.5
F12	1	4	1.5
F13	0.75	3	0.5

Table 2: Experimental variables in coded form.

Independent Factors	Coded levels	
	-1	+1
A = Conc. of Carbopol-934 (gm)	0.5	1
B = Conc. of Propylene Glycol (ml)	3	5
C = Conc. of Tween 20 (ml)	0.5	1.5
Dependent Factors		
Y1 = Spreadability (gm.cm/sec)		
Y2 = Viscosity (cP)		
Y3 = Drug Release (%)		

Characterization of Emulgel

1. Physical Characterization

All the formulation batches were visually examined for colour, odour, texture, homogeneity, and phase separation.

2. pH evaluation: The pH evaluation of topical dosage forms holds significant importance due to the potential for skin irritation resulting from deviations in pH levels. In this study, the pH of 13 emulgels was measured using a calibrated digital pH meter at room temperature. The pH values were determined by placing a glass electrode in contact with 1% aqueous solutions of the prepared emulgels and allowing them to stabilize for one minute before recording the pH.

3. Spreadability: The spreadability of emulgels was evaluated by using two glass slides measuring 7.5×2.5 cm each. One of the slides was affixed to a wooden frame. 1 gm of emulgel was then placed on this fixed slide, and the second slide was positioned over the emulgel. A weight of 100 gm was applied onto the top slide to remove any trapped air within the emulgel. The second glass slide was gently pulled forward until it reached a predetermined distance of 7 cm. During this process, the time taken (T in sec) and the weight (M in gm) required to move the second slide to the 7 cm (L in cm) mark were recorded. The spreadability (S) of the emulgel can be determined using the following formula:

$$S = (M \times L)/T$$

4. Viscosity: The viscosity of the emulgel was determined using a LABMAN Viscometer with the instrument set to 60 RPM and using spindle no. L4. The measurements were taken at room temperature, with the spindle groove submerged in an appropriate quantity of each emulgel formulation, and viscosity readings were recorded after 1 minute.

5. Drug Content

A formulation containing approximately 40 mg of a drug was taken and dissolved in ethanol in a 50 ml volumetric flask. The Whatman filter paper was used to filter the mixture. Next, 0.1 ml of the filtrate was pipetted out and diluted to 10 ml with ethanol [17]. The concentration of the drug in this diluted solution was then estimated spectrophotometrically using a standard calibration curve plotted at 664 nm. The drug content of the formulation was determined by using the following formula:

$$\text{Drug Content} = (\text{Concentration} \times \text{Dilution Factor} \times \text{Volume taken}) \times \text{Conversion Factor}$$

6. *In-vitro* Drug Release Studies

The drug release from all formulations was assessed using a Franz Diffusion cell operating at 100 RPM and maintained at a temperature of 37°C ±0.5°C. A phosphate buffer solution with a pH of 6.8 served as the dissolution medium. At predefined time intervals, 1 ml of the dissolution medium was withdrawn and replaced with fresh medium to maintain sink conditions. The withdrawn samples were then analyzed using a UV spectrophotometer set at 664 nm to detect the drug concentration. The percentage of drug release was determined by referencing a standard calibration curve.

RESULT AND DISCUSSION

Percentage yield of the extract

The percentage yield of the ethanolic extract was found to be 7.4%.

Phytochemical Screening

The results of the phytochemical analysis are presented in Table 3 and Fig. 2, which show the presence of flavonoids, tannins, alkaloids etc.

Table 3: The results of the phytochemical analysis of ethanolic extract of *Ardisia solanacea*

Phytochemicals	Observation
Flavonoids	Present
Alkaloids	Present
Tannins	Present
Saponins	Present
Triterpenoids	Present
Phenol	Present

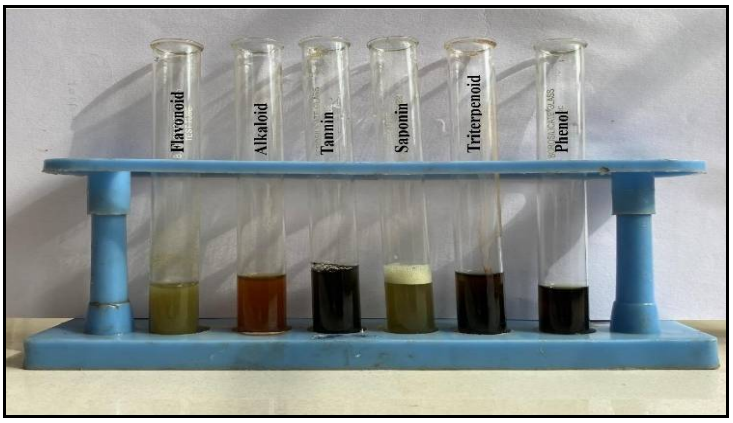

Fig 2: Phytochemical analysis of ethanolic extract of *Ardisia solanacea*

Fluorescence Analysis

Fluorescence is a significant phenomenon in plant material, where various phytoconstituents exhibit this property under ultraviolet light, even though they may not visibly fluoresce in daylight. In this study on *A. solanacea* leaf powder, different colourations were observed under visible and UV light when various chemical reagents such as distilled water, ethanol, methanol, ethyl acetate, petroleum ether, acetone, glacial acetic acid, chloroform, FeCl3, ammonia, NaOH, iodine, conc. H2SO4, conc. HCl, and conc. HNO3 were used. Notably, the plant material displayed pink fluorescence under long UV light across most solvents as described in Table 4. This fluorescence analysis is crucial for evaluating the quality and purity of drug materials, as the unique colours observed indicate the absence of adulteration. Furthermore, the presence of fluorescent compounds in the drug powder suggests the existence of a chromophore in this plant, making fluorescence analysis an essential parameter for the pharmacognostic evaluation of crude drugs.

Table 4: fluorescence analysis of ethanolic extract of *Ardisia solanacea*

Sr. No.	**Reagent**	**Colour**		
		Visible / Day Light	**Short wavelength 254 nm**	**Long wavelength 365 nm**
1	Powder	Golden Green	Pale green	Black
2	Powder + Water	Golden Green	Green	Light Pink
3	Powder + Ethanol	Dark Olive Green	Green	Fluorescent Pink
4	Powder + Methanol	Dark Olive Green	Green	Fluorescent Pink
5	Powder + Ethyl acetate	Greenish Brown	Green	Fluorescent Pink
6	Powder + Petroleum ether	Pale Yellow	Green	Fluorescent Pink
7	Powder + Acetone	Yellowish Green	Green	Fluorescent Pink
8	Powder + Glacial acetic acid	Greenish Brown	Dark Green	Fluorescent Pink
9	Powder + Chloroform	Greenish Brown	Bright Yellow Green	Faint Pink
10	Powder + FeCl3	Brown	Greenish black	Blue
11	Powder + Ammonia	Greenish Brown	Green	Blue
12	Powder + NaOH	Brown	Greenish black	Blue
13	Powder + Iodine	Dark Brown	Greenish black	Blue
13	Powder + Conc. H2SO4	Dark Brown	Dark Green	Blue
14	Powder + Conc. HCl	Olive Green	Green	Blue
15	Powder + Conc. HNO3	Brown	Green	Pinkish Blue

***In-vitro* Antioxidant Study by Reducing Power Assay**

The reducing power assay is based on substances with reduction potential, reacting with potassium ferricyanide (Fe3+) to produce potassium ferrocyanide (Fe2+), which further reacts with ferric chloride to form a ferric–ferrous complex with an absorption peak at 700 nm. The reducing power of the ethanolic extract of *A. solanacea* was determined by comparing it with that of BHT (positive control) where the yellow colour of the test solutions was changed to various shades of green. As the concentrations of the ethanolic extract and standard (BHT) increased, their reducing power (Fig 3) and potential antioxidant activity also increased. The IC_{50} values were found to be 79.165 µg/ml for EtAs and 77.9 µg/ml for BHT. Lower IC_{50} values indicate higher antioxidant potency, suggesting that the EtAs have the potential to neutralise free radicals, converting them into more stable, nonreactive forms and terminating radical chain reactions. The antioxidant activity of *A. solanacea* extract may be attributed to the phenolic and flavonoid compounds present in this plant.

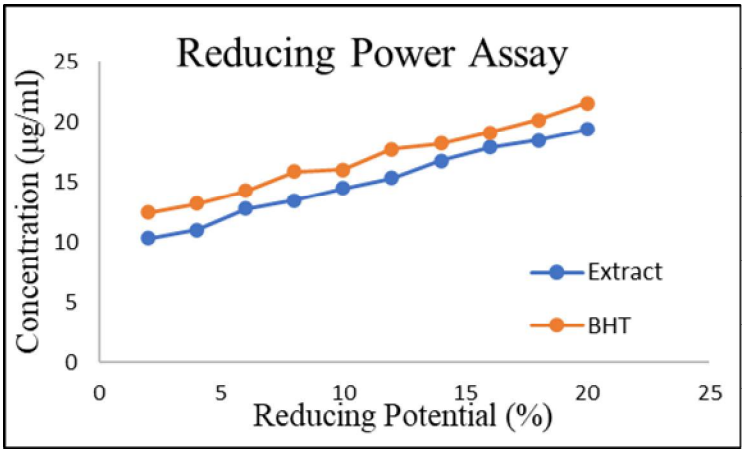

Fig. 3: *In-vitro* antioxidant study by reducing power assay

Characterization of Emulgel

1. Physical Characterization of Emulgel

The physical properties of the formulated emulgels were assessed visually, covering aspects such as colour, odour, texture, homogeneity, and phase separation. Table 5 displays the results obtained from the physical characterization. The formulated herbal emulgels exhibited smooth and homogeneous textures, with a characteristic odour of extract used. The colour of the emulgels ranged from 'light green' to 'moss green'. All formulations demonstrated stability and did not exhibit any phase separation.

Table 5: Physical Characterization of Emulgel

Batches	Colour	Odour	Texture	Homogeneity	Phase Separation
F1	Moss Green	Characteristic odour	Smooth	Homogeneous	No separation
F2	Light Green	Characteristic odour	Smooth	Homogeneous	No separation
F3	Moss Green	Characteristic odour	Smooth	Homogeneous	No separation
F4	Moss Green	Characteristic odour	Smooth	Homogeneous	No separation
F5	Moss Green	Characteristic odour	Smooth	Homogeneous	No separation
F6	Moss Green	Characteristic odour	Smooth	Homogeneous	No separation
F7	Moss Green	Characteristic odour	Smooth	Homogeneous	No separation
F8	Moss Green	Characteristic odour	Smooth	Homogeneous	No separation
F9	Moss Green	Characteristic odour	Smooth	Homogeneous	No separation
F10	Moss Green	Characteristic odour	Smooth	Homogeneous	No separation
F11	Moss Green	Characteristic odour	Smooth	Homogeneous	No separation
F12	Moss Green	Characteristic odour	Smooth	Homogeneous	No separation
F13	Moss Green	Characteristic odour	Smooth	Homogeneous	No separation

2. pH evaluation:

The pH of each formulation was measured and is detailed in Table 6. The pH values of the formulated emulgels ranged from 5.21 to 6.79. The ideal pH range for emulgels intended for skin application is typically between 5 to 7. This pH range ensures that the emulgel can be comfortably applied to the skin without causing any discomfort or irritation. Therefore, based on the pH analysis, the formulated emulgels are suitable for skin application.

3. Spreadability

Spreadability measurements for all emulgels were conducted and are detailed in Table 6. Spreadability is a crucial parameter for evaluation, as an ideal emulgel should exhibit good spreadability. A topical formulation's ability to spread over the skin directly impacts patient compliance and the therapeutic effects achieved. It's noteworthy that all formulations demonstrated adequate spreadability. Specifically, batch F13 had the lowest spreadability at 10.28 gm.cm/sec, while batch F2 showcased the highest spreadability with a value of 19.743 gm.cm/sec.

4. Viscosity

The viscosity of each formulation was measured using spindle no. L4 at 60 RPM, and the viscosity values for all formulations are documented in Table 6. The viscosity values for the formulations ranged from 3555.4 to 4359.3 cP. It was observed that the viscosities of the formulations fall within a relatively narrow range, indicating consistency in viscosity across the different batches. This range, from 3555.4 to 4359.3 cP, suggests that the emulgels possess a desirable viscosity for their intended application,

5. *In-vitro* drug release studies

The release of a drug from a pharmaceutical dosage form is crucial for its therapeutic efficacy. *In-vitro* drug release studies were conducted using Franz diffusion cells, and the resulting data is displayed in Table 6. The cumulative drug release was plotted against time, as depicted in Fig. 4. The percentage of drug release ranged from 58.36% to 85.758%. This indicates differences in the formulation's ability to release the drug over time, which is essential for achieving the desired therapeutic effect.

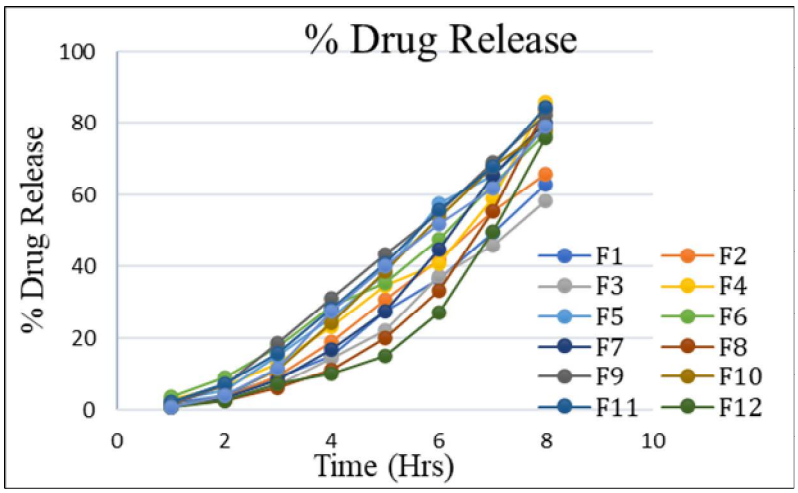

Fig. 4: Drug release studies of formulated batches

6. Drug Content

The drug content analysis for all formulations was conducted following the specified procedure, resulting in values ranging from 77.23% to 90.67%, as detailed in Table 6. This variability could be attributed to factors such as formulation techniques, ingredient concentrations, and manufacturing processes.

Table 6: Evaluation parameters for Emulgel

Batches	pH	Spreadability (gm.cm/sec)	Viscosity (cP)	Drug Release (%)	Drug Content (%)
F1	5.43	17.54	3723.1	63.122	78.89
F2	5.21	19.743	3555.4	65.924	80.45
F3	6.34	15.354	3822.3	58.36	77.23
F4	6.08	16.177	4035.2	85.758	89.56
F5	6.12	16.58	3910.9	78.69	82.78
F6	5.92	16.86	3962.3	75.842	90.67
F7	6.39	16.385	3829.8	80.014	85.12
F8	6.52	16.871	4137.7	83.704	88.45
F9	6.75	14.65	4152.4	82.36	79.12
F10	5.61	13.941	4218.6	77.941	86.11
F11	6.58	11.623	4327.1	84.29	92.56
F12	6.79	14.021	4148.2	76.008	84.34
F13	6.47	10.28	4429.3	79.1167	81.67

7. Formulation Optimization using Box-Behnken Design

13 emulgel batches were prepared by blending emulsion with gel base at a 1:1 ratio under moderate stirring conditions. A Box-Behnken Design was employed to optimize the concentrations of Carbopol 934, propylene glycol, and Tween 20 to achieve optimal spreadability, viscosity, and drug release. The study revealed that the concentrations of Carbopol 934, propylene glycol, and Tween 20 significantly influenced the spreadability, viscosity, and drug release of the emulgels. Among the formulations, batch F8 demonstrated satisfactory outcomes in terms of spreadability, viscosity, and drug release.

Analysis of data using Box–Behnken design

Effect on Spreadability

The coded equation for the spreadability of a formulation is:

$$Y1 = +7.73316-2.20250A+1.47625B+3.40025C$$

The concentration of Carbopol 934 exhibited a negative effect on spreadability, indicating that higher levels of cross-linking in Carbopol 934 hindered the formulation's ability to evenly distribute on the skin. Conversely, increasing the concentrations of propylene glycol and Tween 20 had a positive impact on spreadability, with Tween 20 showing a greater influence in improving spreadability compared to propylene glycol. The statistical analysis shows that the model and its terms are significant ($p < 0.0500$), indicating a strong relationship between the independent factors and spreadability. As shown in Fig. 5, The interaction between independent factors was significant, suggesting that their combined effects play a crucial role in determining the spreadability of the formulation.

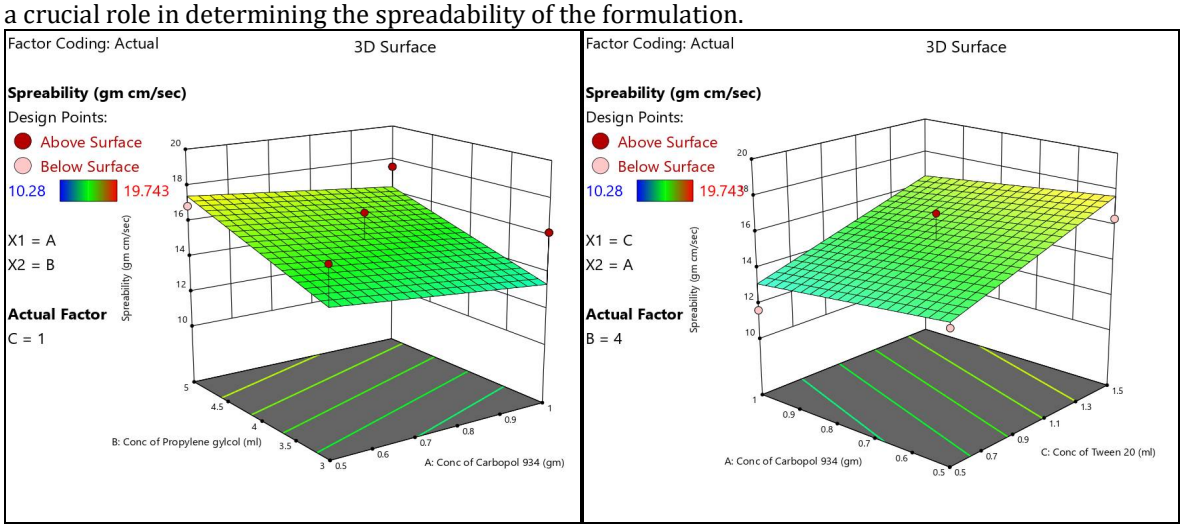

Fig. 5: 3D Surface response plot of spreadability

Effect on Viscosity

The coded equation for the viscosity of a formulation is:

$$Y2 = +4854.74808+156.0A-174.33750B-260.37500C$$

The concentration of Carbopol 934 exhibited a significantly positive effect on viscosity, with higher concentrations leading to increased viscosity. This is attributed to Carbopol 934 acting as a gelling agent that forms a rigid gel network through cross-linking with the solvent, thereby trapping solvent molecules and imparting resistance to force and pressure. On the other hand, increasing concentrations of propylene glycol and Tween 20 had a negative impact on viscosity, with propylene glycol showing a more pronounced effect in reducing viscosity compared to Tween 20. The statistical analysis shows that the model and its terms are significant ($p < 0.0500$), indicating a strong relationship between the independent factors and viscosity. As shown in Fig. 6, The interaction between independent factors was found to be significant, suggesting that their combined effects play a crucial role in determining the viscosity of the formulation.

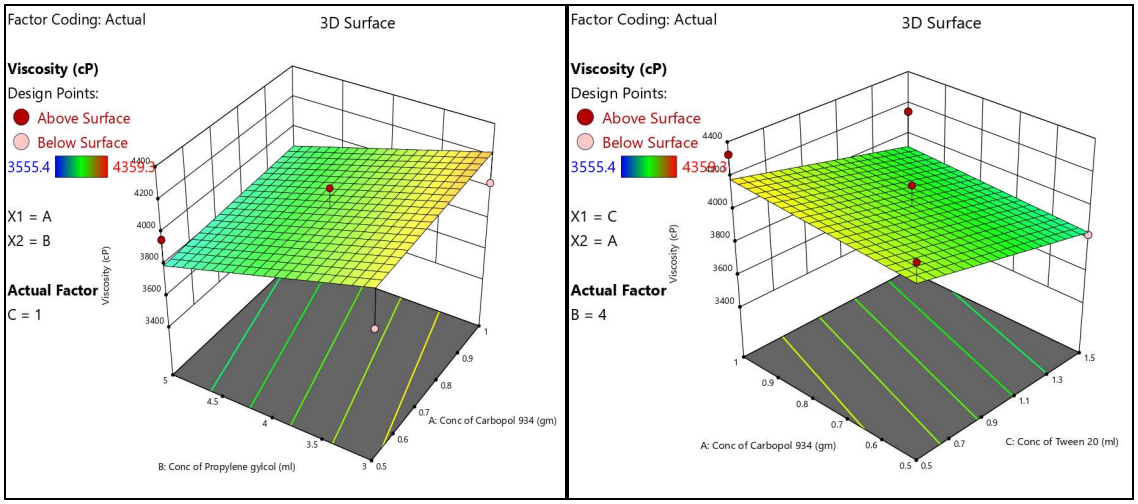

Fig. 6: 3D Surface response plot of viscosity

Effect on Drug Release

The coded equation for the drug release of a formulation is:

$$Y3 = +107.67040 - 1.65450A - 7.83459B + 1.14957C$$

The concentration of Carbopol 934 and propylene glycol showed negative coefficients, indicating a reduction in drug release at higher concentrations. This reduction is attributed to Carbopol 934 creating a more intricate gel network, resulting in longer diffusion pathways for the drug to permeate the membrane [18]. Similarly, propylene glycol's concentration also contributed to decreased drug release. Conversely, the concentration of Tween 20 exhibited a positive effect on drug release, with higher concentrations correlating with increased drug release from the formulation. The statistical analysis shows that the model and its terms are significant ($p < 0.0500$), indicating a strong relationship between the independent factors and drug release. As shown in Fig. 7, The interaction between independent factors was significant, suggesting that their combined effects play a crucial role in determining the percentage of drug release of the formulation.

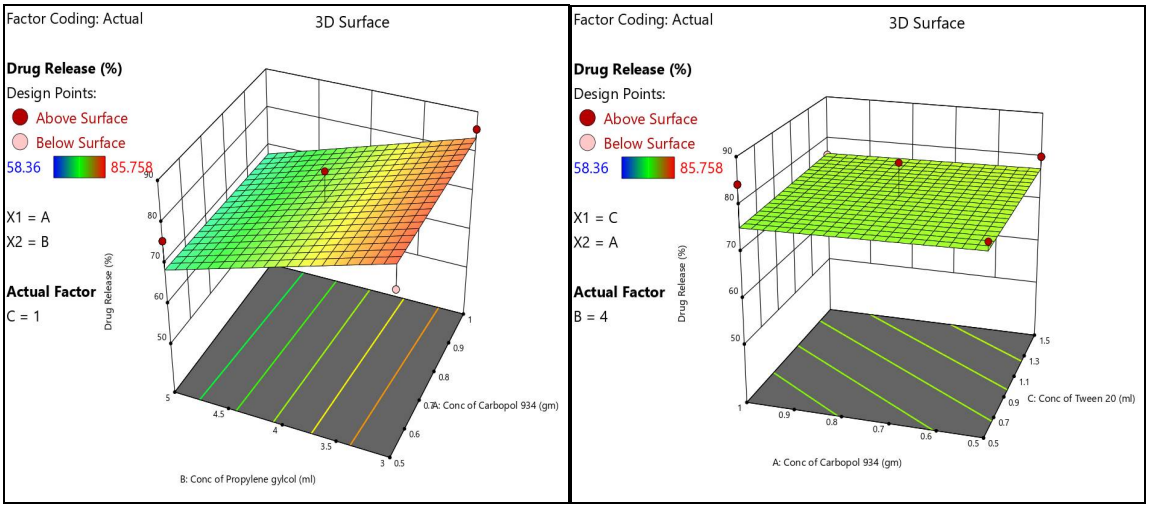

Fig. 6: 3D Surface response plot of drug release

CONCLUSION

In this study, the ethanolic extract of *Ardisia solanacea* was successfully obtained using the Soxhlet extraction method. Phytochemical screening revealed the presence of important compounds such as flavonoids, alkaloids, tannins, saponins, triterpenoids and phenols. The powder sample exhibited a distinctive pink fluorescence with most of the solvents, at longer wavelengths. Furthermore, the antioxidant potential of the ethanolic extract was determined through a reducing power assay, which demonstrated satisfactory antioxidant activity. Additionally, utilizing the Box-Behnken design, 13 batches of emulgels were formulated and extensively evaluated for various parameters including physical

characteristics, pH, spreadability, viscosity, drug release, and drug content. Among these formulations, batch F8 stood out with satisfactory results across multiple parameters, indicating its potential as an optimized formulation for further development.

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