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PREPARATION AND CHARACTERIZATION OF TOPICAL HYDROGEL CONTAINING COMBINE DRUGS (COMPARATIVE STUDY) FOR TOPICAL DELIVERY

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ABSTRACT

The present study aimed to prepare and comparatively evaluate topical hydrogels containing salicylic acid, aloin, and their combination for topical drug delivery. Three hydrogel formulations were prepared using Carbopol 940 and characterized for physicochemical properties, drug content, antimicrobial activity, in vitro drug release, skin irritation, and stability. All formulations exhibited satisfactory appearance, pH, viscosity, spreadability, and drug content. The combination hydrogel (F3) showed superior performance with the highest drug content (98.65%), enhanced antimicrobial activity (18 mm zone of inhibition), and maximum cumulative drug release (96.13% in 12 h). Skin irritation studies confirmed the safety of all formulations, while accelerated stability studies demonstrated good physical and chemical stability over three months. The findings suggest that the combination hydrogel containing salicylic acid and aloin is a promising topical drug delivery system for the effective management of various dermatological conditions.

KEYWORDS: *Salicylic acid, Aloin, Topical hydrogel, Carbopol 940, Drug release, Antimicrobial activity, Topical drug delivery, Comparative study.*

1 INTRODUCTION

Topical drug delivery systems have gained considerable importance for the localized treatment of dermatological disorders due to their ability to deliver drugs directly to the affected site while minimizing systemic adverse effects. Among various topical dosage forms, hydrogels have emerged as promising carriers because of their high-water content, biocompatibility, non-greasy nature, ease of application, and ability to provide sustained drug release. Their three-dimensional polymeric network efficiently incorporates both synthetic drugs and natural bioactive compounds, making them highly suitable for the management of skin disorders. Skin diseases such as acne vulgaris, psoriasis, eczema, and hyperkeratotic conditions are commonly associated with inflammation, microbial infection, oxidative stress, and impaired wound healing. Although conventional topical therapies are effective, prolonged use often causes irritation, dryness, and poor patient compliance, highlighting the need for safer and more effective combination therapies.[1,4]

Salicylic acid is a widely used keratolytic and comedolytic agent that promotes exfoliation and exhibits mild anti-inflammatory and antimicrobial properties; however, its prolonged application may lead to skin irritation and dryness. In contrast, aloin, a natural anthraquinone glycoside obtained from *Aloe* species, possesses anti-inflammatory, antioxidant, antimicrobial, wound-healing, and skin-protective activities that can help reduce irritation and enhance tissue repair. Incorporating salicylic acid and aloin into a hydrogel may provide complementary therapeutic benefits by combining keratolytic action with anti-inflammatory and wound-healing effects while improving drug stability, skin retention, and patient acceptability. Therefore, the present study aimed to prepare and comparatively evaluate topical hydrogels containing salicylic acid, aloin, and their combination for physicochemical

characteristics and drug release performance to develop an effective and patient-friendly topical formulation for the management of dermatological disorders.[5,7]

2 MATERIALS AND METHODS

2.1 Pre-formulation studies

The pre-formulation studies included the evaluation of the organoleptic properties, solubility, pH, and melting point of salicylic acid and aloin. Organoleptic characteristics such as color, odor, and physical state were assessed through visual observation. Qualitative solubility was determined according to USP-NF (2007) guidelines by testing approximately 1 mg of each drug in methanol, ethanol, dimethyl sulfoxide (DMSO), chloroform, and water. The pH of each drug was measured using a calibrated digital pH meter following the electrochemical method. Melting point determination was carried out by the open capillary method using Thiele's tube, where the temperature at which the sample began to melt was recorded as its melting point.[8,9]

2.1.1 Determination of Lambda max and calibration curve[10,11]

Standard stock solutions (1000 µg/mL) of salicylic acid and aloin were prepared and appropriately diluted for UV spectrophotometric analysis. The λ max of each drug was determined by scanning 70 µg/mL solutions over the range of 200–400 nm. Calibration curves were constructed using salicylic acid (5–30 µg/mL) and aloin (30–80 µg/mL) at their respective λmax (305 nm and 344 nm). Both drugs showed excellent linearity within the studied concentration ranges, confirming the suitability of the method for quantitative analysis.[10,11]

2.2 Drug loaded Gel Formulation Process

Carbopol was initially dispersed in 50 ml of warm water (mixture A) and allowed to hydrate for 2 hours. The dispersion was then homogenized using a magnetic stirrer at 600 rpm to ensure uniform consistency. Meanwhile, in a separate container, carboxymethyl cellulose and methylparaben were dissolved in 50 mL of warm water (mixture B) and stirred continuously until a stiff gel was formed. Mixtures A and B were gradually combined with continuous stirring to achieve a uniform blend. Triethanolamine was added dropwise to neutralize the pH and facilitate gel formation. Subsequently, the active ingredients salicylic acid and aloin were incorporated into the neutralized gel base. Finally, propylene glycol, serving as a permeation enhancer, was added, and the entire mixture was stirred thoroughly until a smooth, homogenous gel free of lumps was obtained.[12]

Table 1: Composition of Drug loaded gel formulation.

Name of Ingredient	Formulation I	Formulation II	Formulation III
Carbopol 940	1.5 gm	1.5 gm	1.5 gm
Carboxymethyl cellulose	1.5 gm	1.5 gm	1.5 gm
Propylene glycol	0.6ml	0.6 ml	0.6ml
Methyl paraben	0.1 ml	0.1ml	0.1ml
Salicylic acid	1 gm	----	1 gm
Aloin	----	1 gm	1 gm
Triethanolamine	q. s	q. s	q. s
Water	100 ml	100 ml	100 ml

2.3 Characterization of Drug-Loaded Gel Formulations

The prepared gel formulations were characterized for their physicochemical properties, including physical appearance, pH, viscosity, spreadability, skin irritation, and drug content. Physical appearance, color, odor, and homogeneity were assessed by visual inspection. The pH was measured using a calibrated digital pH meter, and when required, adjusted to skin pH with triethanolamine. Viscosity was determined using a Brookfield viscometer (spindle No. 62) at 100 rpm and 25°C. Spreadability was evaluated by placing 1 g of gel between two glass slides under a fixed weight, and the spreadability coefficient was calculated based on the applied weight, spreading distance, and time.[13,17]

Skin irritation was assessed by applying the gel to the shaved dorsal skin area once daily for 2–3 days and monitoring the treated site for erythema, edema, or other visible signs of irritation. Drug content was determined by dispersing a known quantity of gel in phosphate buffer (pH 7.4), followed by filtration and UV spectrophotometric analysis (250–300 nm). Drug concentration was calculated using the respective calibration curve.[18,19]

2.4 Antimicrobial activity

The antimicrobial activity of the prepared gel formulations was evaluated against *Escherichia coli* using the agar well diffusion method. Nutrient agar was prepared, sterilized by autoclaving (121°C, 15 psi, 15 min), and poured into sterile Petri plates. A standardized bacterial suspension (10^8 CFU/mL) was uniformly spread over the agar surface, and 6 mm wells were created using a sterile cork borer. Approximately 100 µL of each formulation (F1, F2, and F3) was added to the respective wells, allowed to diffuse for 30 minutes, and incubated at 37°C for 18–24 hours. Antimicrobial activity was assessed by measuring the diameter of the zone of inhibition (mm) around each well.[20]

2.5 Drug release study

Firstly, formulation was dissolved in phosphate buffer solution 7.4. Then put into the Franz diffusion cell such

that the cell's drug releasing surface remained towards the receptor compartment; which containing 50ml of phosphate buffer pH 7.4 at 37±0.5°. The cell was placed on a magnetic stirrer, and the solution in the receptor compartment was continuously stirred using magnetic bead at 50rpm at 37±0.5°C. 5ml solution was withdrawn at predefine time intervals and changed with same volume of phosphate buffer pH 7.4. Finally test solutions were quantified for drug by uv spectrophotometer.

2.6 Stability studies

The drug-loaded gel formulation was packaged and subjected to stability testing in a controlled stability chamber under accelerated conditions at 25°C ± 2°C with 60% ± 5% relative humidity (RH) and 40°C ± 2°C with 70% ± 5% RH for a period of 3 months. The formulation was periodically evaluated for key parameters such as viscosity and pH at intervals of 30, 45, 60, and 90 days. These studies were conducted following the International Conference on Harmonization (ICH) guidelines to assess the formulation's stability under accelerated storage conditions. Any changes in viscosity and pH over the testing period were recorded and analyzed.

3 RESULTS AND DISCUSSIONS

3.1 Pre-formulation study of drug

3.1.1 Organoleptic properties

Table 2: Organoleptic properties of Salicylic acid and Aloin.

Organoleptic properties	Salicylic acid	Aloin
Color	White	Brownish-yellow
Odor	Odorless	Similar to body odor
Appearance	Crystalline powder.	Yellow crystal
State	Solid	Crystaline Solid

The organoleptic properties of salicylic acid and aloin were evaluated for appearance, color, odor, and physical state. Salicylic acid was observed as a white, odorless solid, consistent with the Indian Pharmacopoeia (IP) specifications. Aloin exhibited a brownish-yellow crystalline appearance with a characteristic odor and crystalline solid state. The observed organoleptic characteristics of both drugs confirmed their identity and suitability for formulation development.

3.1.2 Solubility study

Table 3: Solubility study of Salicylic acid and Aloin.

Solvents	Observation/Inference	Aloin
Water	Soluble	Soluble
Ethanol	Freely soluble	Freely soluble
Methanol	Freely soluble	Freely soluble
Chloroform	Soluble	Very slightly soluble
DMSO	Freely soluble	Soluble

The solubility of salicylic acid and aloin was evaluated in various solvents to assess their suitability for formulation development. Salicylic acid was found to be freely soluble in methanol, ethanol, and dimethyl sulfoxide (DMSO), and soluble in water and chloroform. Similarly, aloin exhibited good solubility in methanol, ethanol, water, and DMSO, but showed only very slight solubility in chloroform. These findings indicate that both drugs possess favorable solubility in aqueous and polar organic solvents, making them suitable for hydrogel formulation.

3.1.3 pH determination

Table 4: pH of Salicylic acid and Aloin.

S. No	Drugs	Observed
1.	Salicylic acid	3.0
2.	Aloin	4.3

The digital pH meter used to determine the pH of a substance. The pH of the Salicylic acid and Aloin was found to be 3.0 and 4.3, which is well within the limits of the drug specification.

3.1.4 Melting point

Table 5: Melting point of Salicylic acid and Aloin.

Drugs	Observed	References
Salicylic acid	157°C	155°C-160°C
Aloin	148 °C	148°C - 149°C

The capillary method is used to determine the melting point of a substance. The melting point of the Salicylic acid and Aloin was found to be 157ºC and 148^{o}C, which is well within the limits of the drug specification.

3.1.5 Lambda max Salicylic acid

Table 6: Lambda max Salicylic acid.

S. No	Drug	UV absorption maxima (Lambda max)
1.	Salicylic acid	235.5 nm

Double beam UV visible spectrophotometer (Shimadzu-1700) was used to determine the lambda max (absorption maxima) of a substance. The lambda max of the Salicylic acid was found to be 235.5 nm. This is well within the limits of the drug specification.

Lambda max of Aloin

Table 7: Lambda max aloin.

S. No	Drug	UV absorption maxima (Lambda max)
1.	Aloin	297.0 nm

The lambda max of the Aloin was found to be 297.0 nm. This is well within the limits of the drug specification.

Lambda max of Salicylic acid and Aloin

Table 8: Lambda max (overlay).

S. No	Drug	UV absorption maxima (Lambda max)
1.	Salicylic acid and Aloin	290.0nm

The lambda max of each drug was found to be 290.0nm. This is well within the limits of the drug specification.

Calibration curve of Salicylic acid

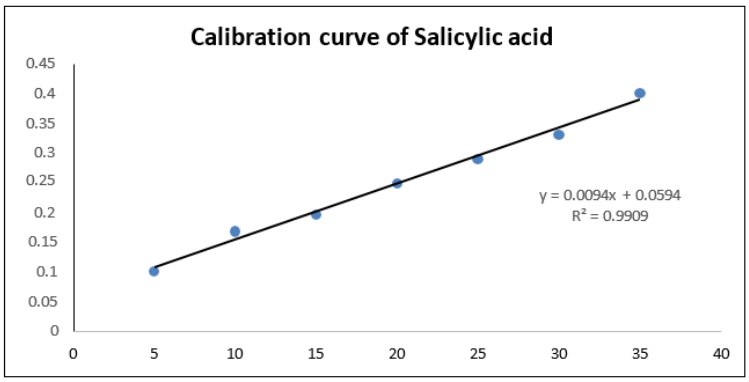

Figure 4: Calibration curve of Salicylic acid.

The linearity of the proposed method was established by least squares linear regression analysis of the calibration curve. The regression equation for Salicylic acid was obtained by plotting absorbance versus concentration of Salicylic acid in the range of 5-35µg/mL.

Seven points calibration curves were obtained in a concentration range from 5-35 µg/ml for drug. The response of the drug was found to be linear in the investigation concentration range and the linear regression equation was y = 0.009x + 0.0594with correlation coefficient R^2 = 0.990**.**

Calibration curve of Aloin

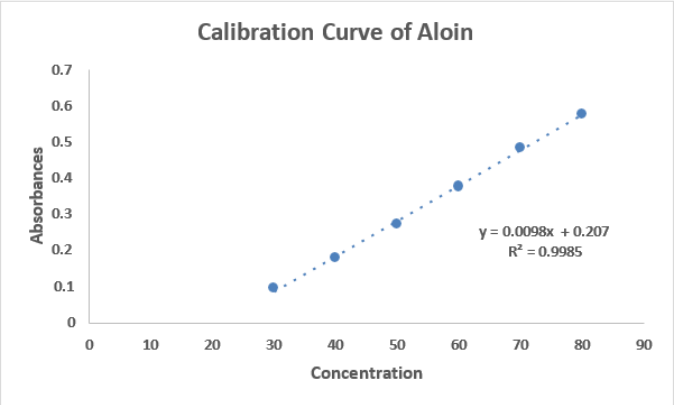

Figure 5: Calibration curve of Aloin.

The linearity of the proposed method was established by least squares linear regression analysis of the calibration curve. The regression equation for Aloin was obtained by plotting absorbance versus concentration of Aloin in the range of 30-80 µg/mL. Seven points calibration curves were obtained in a concentration range from 30-80 µg/ml for drug. The response of the drug was found to be linear in the investigation concentration range and the linear regression equation was y = 0.098x + 0.207 with correlation coefficient R^2 = 0.998.

3.2 Evaluation parameter of gel formulation

3.2.1 Organoleptic properties

Table 9: Organoleptic properties gel formulation.

S. No	Parameters	Results
1.	Physical appearance	Semisolid gel
2.	Colour	Slightly yellowish gel
3.	Homogeneity	Absence of aggregates

An evaluation of the gel, including colour, appearance and homogeneity, was conducted. Gel was discovered to have a slightly yellowish colour to it when tested. Gel exhibited the same colour, and Appearance as the I.P. requirements for these characteristics and the results were listed in Table No. 9.

3.2.2 Measurement of pH

Table 10: pH.

S. No	Formulation	Results
1.	F1 (Salicylic acid gel)	5.5
2.	F2 (Aloin gel)	6.6
3.	F3 (salicylic acid and Aloin gel)	6.7

The pH of all prepared formulation ranged from 5.5- 6.7. The pH of the prepared gel formulation was considered to be acceptable to avoid the risk of irritation upon application to the skin. The results were shown in Table No.10.

3.2.3 Determination of Viscosity

Table 11: Viscosity determination.

S. No	Formulation	Results (cps)
1.	F1 (Salicylic acid gel)	5527±0.26
2.	F2 (Aloin gel)	5597±0.79
3.	F3 (salicylic acid and Aloin gel)	5612±0.89

Viscosity is an important property of fluids which describes a liquids resistance to flow and is related to the internal friction within the fluid. This rheological property helps in determining consistency and also the diffusion rate of drug from gel. The measurement of viscosity of the prepared gel was done with Brookfield viscometer with spindle no: 62. The results were shown in Table no.11.

3.2.4 Spreadability

Table 12: Spreadability test.

S. No	Formulation	Results (gm.cm/sec)
1.	F1 (Salicylic acid gel)	21.46
2.	F2 (Aloin gel)	25.32
3.	F3 (salicylic acid and Aloin gel)	26.17

Spreadability denotes the extent of area to which the gel readily spreads on application to skin or the affected part. Spreadability of different gel formulation was studied. The formulations produced good spreadability and the results were shown in Table no. 12.

3.2.5 Acute skin irritation study

Table 13: Skin irritation study.

S. No	Formulation	Results
1.	F1 (Salicylic acid gel)	Not irritant observed
2.	F2 (Aloin gel)	Not irritant observed
3.	F3 (salicylic acid and Aloin gel)	Not irritant observed

Results of skin irritation test indicate that prepared gels were not produce irritation, redness, or edema on application and free from dermatological reaction.

3.2.6 Drug content

Table 14: Drug content.

S. No	Formulations	Results
1.	F1 (Salicylic acid gel)	96.56%
2.	F2 (Aloin gel)	97.13%
3.	F3 (salicylic acid and Aloin gel)	98.65%

3.3 Antimicrobial activity of Gel formulation

Table 15: Antimicrobial activity of all formulation (F1, F2 and F3 formulation).

S. No	Sample name	Zone of Inhibition (mm)
1	F1 (Salicylic acid gel)	9 mm
2	F2 (Aloin gel)	10 mm
3	F3 (salicylic acid and Aloin gel) (1mg/ml)	15 mm
4	F4 (salicylic acid and Aloin gel) (2mg/ml)	18 mm

Figure 6: Antimicrobial Activity of All Formulation (F1, F2 And F3 Formulation).

3.4 Drug release study of all formulations (F1 to F3)

Table 16: Drug release study of all formulations (F1 to F3).

S. No	Time (Hr)	% drug released (F1)	% drug released (F2)	% drug released (F3)
1.	**0**	0	0	0
2.	**1**	20.11	12.45	23.18
3.	**2**	45.36	17.36	36.09
4.	**4**	47.46	46.86	43.63
5.	**6**	53.86	57.8	57.6
6.	**8**	61.88	60.31	66.13
7.	**10**	72.47	65.23	77.56

8.	**11**	79.63	74.22	82.45
9.	**12**	92.01	76.96	96.13

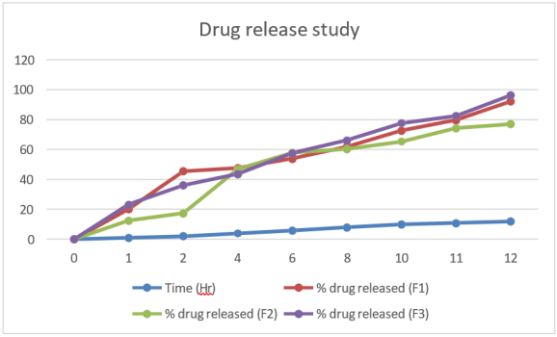

Figure 7: Graphical representation of Drug Release study of all formulation.

3.5 Stability studies

Table 17: Stability Study of formulation (Gel).

S. No	Time (Days)	25^{0}C±2 ^{0}C and 60 ± 5% RH		40^{0}C±2 ^{0}C and 70 ±5% RH	
		Viscosity	pH	Viscosity	Ph
1.	0	5612	6.1	5612	6.1
2.	30	5615	6.3	5618	6.4
3.	45	5621	6.5	5623	6.9
3.	60	5628	6.8	5629	7.2
4.	90	5632	7.1	5635	7.5

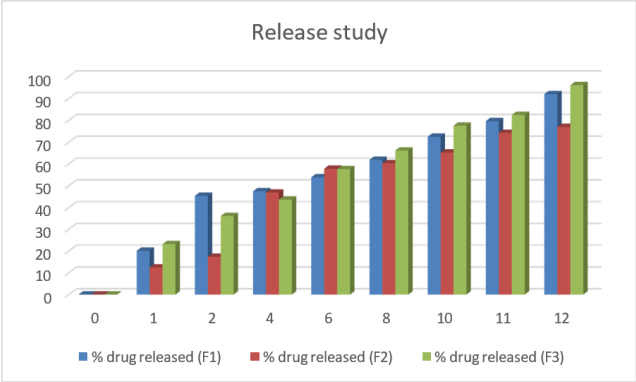

Figure 8: Stability study of viscosity.

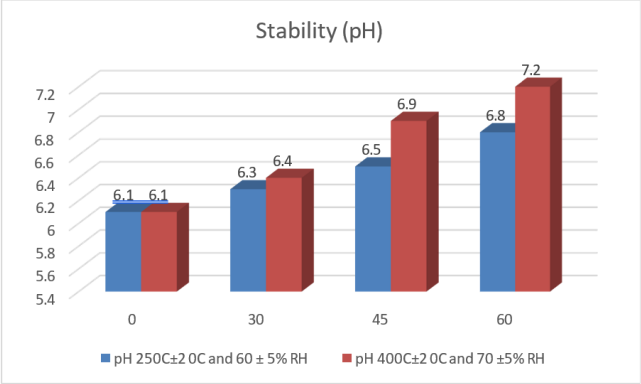

Figure 9: Stability of Ph.

Formulation was found to be stable, both physically and chemically, for a period of 3 months at accelerated stability conditions (25^{0}C±2 ^{0}C and 60 ± 5% RH) and (40^{0}C±2 ^{0}C and 70 ±5% RH). Evaluation parameters including viscosity and pH studies were not altered significantly. Results of assay and other evaluation criteria at periodic time points of stability studies are summarized in Table 17. The result of accelerated stability studies of gel formulation is shown in above table. No major changes were observed.

4. CONCLUSION

The study successfully formulated and characterized topical hydrogels containing salicylic acid, aloin, and their combination. All formulations exhibited acceptable physicochemical properties, good drug content, and excellent stability. Among them, the combination hydrogel (F3) demonstrated superior antimicrobial activity, highest drug release, better spreadability, and good skin compatibility. These findings indicate that the combined salicylic acid–aloin hydrogel is a stable, safe, and effective topical formulation with potential application in the treatment of acne and other inflammatory skin disorders.

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