RESEARCH PAPER

Formulation and Evaluation of Polyherbal Gel Containing Hydroalcoholic Extracts of *Cressa cretica* L., *Fagonia indica* Burm.f., and *Plantago major* L.

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Abstract:
Topical herbal formulations have gained increasing attention as safer alternatives to conventional antimicrobial agents owing to their broad spectrum of biological activities, reduced adverse effects, and improved patient acceptability. The present study was undertaken to formulate and evaluate a polyherbal antimicrobial gel containing hydroalcoholic extracts of *Cressa cretica* L. (Rudanti), *Fagonia indica* Burm.f. (Dhamasa), and *Plantago major* L. (Greater Plantain). These medicinal plants have long been utilized in traditional systems of medicine and are reported to possess antimicrobial, anti-inflammatory, antioxidant, and wound-healing properties attributed to their rich content of phenolics, flavonoids, tannins, terpenoids, and other bioactive phytoconstituents. Hydroalcoholic extracts of the selected plants were incorporated into topical gel formulations using Carbopol 940, hydroxypropyl methylcellulose (HPMC K100M), and combinations of both polymers. Thirty formulations were prepared and evaluated for physicochemical characteristics including appearance, homogeneity, pH, viscosity, spreadability, washability, extrudability, total phenolic content, in vitro release, bioadhesive strength, swelling index, gel erosion, and accelerated stability according to ICH guidelines. The optimized formulation was selected on the basis of its rheological properties, extract incorporation efficiency, sustained release characteristics, and overall stability. Combination polymer formulations exhibited superior physicochemical performance compared with single-polymer gels. Among all formulations, formulation F25 demonstrated optimum viscosity, satisfactory spreadability, excellent bioadhesion, high extract recovery, controlled swelling, minimal gel erosion, sustained release of phenolic constituents, and acceptable stability during accelerated storage. The balanced interaction between Carbopol 940 and HPMC K100M contributed to improved gel consistency and prolonged retention of phytoconstituents. The findings suggest that the optimized polyherbal gel provides an appropriate topical delivery system for medicinal plant extracts and may serve as a promising natural antimicrobial formulation. Further pharmacological and clinical investigations are warranted to establish its therapeutic efficacy and safety.

Keywords: Polyherbal gel; *Cressa cretica*; *Fagonia indica*; *Plantago major*; Carbopol 940; HPMC K100M; Topical formulation; Herbal gel; Physicochemical evaluation.
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1. Introduction

Skin is the largest organ of the human body and serves as a protective barrier against microbial invasion, physical injury, and environmental insults. Wound healing is a complex biological process involving inflammation, tissue formation, and remodelling. Wound infection and delayed healing remain important clinical concerns, while antimicrobial resistance increases the need to investigate alternative and complementary antimicrobial agents[1, 2]

Topical gels are widely investigated for localized drug delivery because they are generally easy to apply, can be spread over the affected area, and may provide suitable release characteristics depending on their composition. The physical properties of a topical semisolid, including rheology and spreadability, influence its application and performance[3, 4] Medicinal plants contain diverse phytoconstituents, including flavonoids, phenolic compounds, tannins, and glycosides, some of which have demonstrated antioxidant, antimicrobial, or anti-inflammatory activities in experimental studies [5]

Polyherbal formulations combine extracts from two or more medicinal plants with the aim of obtaining complementary biological effects. However, any synergistic effect must be demonstrated experimentally rather than assumed from the use of multiple extracts[6,7]

Cressa cretica L. (Convolvulaceae) is a halophytic medicinal plant traditionally used for several conditions. Published literature describes its phytochemical constituents and reports various biological activities, including antimicrobial and anti-inflammatory effects.[8] Fagonia indica Burm.f. (Zygophyllaceae), commonly known as Dhamasa, has

been investigated for its phytochemical composition and pharmacological properties. Reported constituents include flavonoids, saponins, tannins, and glycosides, while reported activities include antioxidant and anti-inflammatory effects.[9] Similarly, Plantago major L. (Plantaginaceae) contains flavonoids, phenolic acids, iridoid glycosides, and polysaccharides. Experimental and review literature describes its potential wound-healing, anti-inflammatory, and antimicrobial properties. [10, 11, 12]

Plant-derived flavonoids have been investigated for antimicrobial activity through mechanisms that may include effects on microbial membranes, biofilm formation, and cellular processes. These findings support further investigation of plant extracts but do not establish the antimicrobial efficacy of a particular polyherbal gel without formulation-specific testing[5]

The selection and concentration of gelling agents are important in developing topical formulations with suitable viscosity, spreadability, and release characteristics. Carbopol polymers form viscous gels following appropriate neutralization, while hydroxypropyl methylcellulose (HPMC) is used as a viscosity-modifying and gel-forming polymer. The properties of the final formulation depend on polymer grade, concentration, neutralization, and interactions with other ingredients. [3], [13]

Topical gel formulations therefore require systematic evaluation of their physicochemical and performance characteristics, including appearance, pH, viscosity, homogeneity, spreadability, extrudability, and in vitro release. Additional tests, such as bioadhesion, swelling, gel erosion, and stability, should be selected according to the formulation and the intended purpose of the study. Stability testing can be designed with reference to applicable pharmaceutical stability guidance, while recognising that the scope of ICH Q1A(R2) is pharmaceutical drug substances and products [4], [14]

Although the individual medicinal properties of Cressa cretica, Fagonia indica, and Plantago major have been reported, further formulation-specific investigation is needed to establish the physicochemical properties and in vitro performance of their combined hydroalcoholic extracts in a topical gel. Therefore, the present study aimed to formulate and evaluate a polyherbal gel containing these three plant extracts using different combinations of Carbopol 940 and HPMC K100M, with particular emphasis on physicochemical characteristics, in vitro release, bioadhesive properties, swelling behaviour, gel erosion, and accelerated stability.

2. Materials and Methods:

2.1 Materials: Fresh whole plants of *Cressa cretica* L. (Rudanti, Family: Convolvulaceae), *Fagonia indica* Burm.f. (Dhamasa, Family: Zygophyllaceae), and *Plantago major* L. (Greater Plantain, Family: Plantaginaceae) were collected from different regions of Rajasthan, India, during their flowering season. The plant materials were taxonomically authenticated by a qualified taxonomist/Pharmacognosist. Carbopol 940, Hydroxypropyl Methylcellulose (HPMC K100M), propylene glycol, glycerin, triethanolamine, methyl paraben, propyl paraben, ethanol, and other analytical-grade chemicals were procured from certified chemical suppliers. Double-distilled water was used throughout the study.

2.2 Preparation of Plant Extracts

The collected plant materials, namely Cressa cretica whole plant, Fagonia indica aerial parts, and Plantago major roots, were washed to remove adhering impurities and shade-dried at room temperature for 10–15 days. The dried materials were coarsely powdered separately using a mechanical grinder and passed through sieve No. 40. For extraction, 100 g of each powdered plant material was separately macerated with hydroalcoholic solvent (ethanol:water, 80:20 v/v) at a solvent-to-drug ratio of 10:1. The mixtures were kept in tightly closed containers for 15 days at room temperature with intermittent shaking to facilitate extraction of phytoconstituents. After maceration, the extracts were filtered through muslin cloth followed by Whatman No. 1 filter paper. The filtrates were concentrated under reduced pressure using a rotary evaporator at a temperature below 45°C and further dried to obtain semisolid masses. The dried extracts were weighed, transferred into airtight containers, and stored at 4°C until further use. Each plant material was extracted separately to maintain the identity of each extract and allow independent evaluation of its phytochemical characteristics [15,16,17]

2.3 Determination of percentage yield

The percentage yield of each extracts will be calculated by using following formula:

$$\text{Percentage yield} = \frac{\text{Weight of Extract}}{\text{Weight of powder drug Taken}} \times 100$$

2.4 Formulation, Evaluation, and Optimization of Polyherbal Gel

2.4.1 Selection of Polyherbal Extract Concentration

A polyherbal mixture comprising hydroalcoholic extracts of *Cressa cretica*, *Fagonia indica*, and *Plantago major* roots was selected for topical gel development. A concentration of 5% w/w polyherbal extract was incorporated into the formulations as the target extract loading. The concentration was selected for formulation development, subject to confirmation through preliminary trials and evaluation of the physicochemical properties of the prepared gels.

2.4.2 Selection of Excipients

Carbopol 940 and hydroxypropyl methylcellulose (HPMC K100M) were selected as gelling agents to investigate their effects on viscosity, spreadability, and formulation characteristics. Propylene glycol and glycerin were used as humectants, while methyl paraben and propyl paraben were incorporated as preservatives. Triethanolamine was used to neutralize Carbopol and adjust the formulation pH. Distilled water served as the aqueous vehicle. The selection of excipients was based on established pharmaceutical formulation principles. [18]

2.4.3 Preparation of Polyherbal Gel

The required quantities of Carbopol 940 and/or HPMC K100M were gradually dispersed in distilled water with continuous stirring and allowed to hydrate adequately. Separately, the polyherbal extract was mixed with propylene glycol and glycerin to facilitate uniform incorporation. The preservatives were dissolved in a suitable solvent and added to the formulation. The extract mixture was then gradually incorporated into the hydrated polymer dispersion under continuous stirring until a uniform preparation was obtained. Triethanolamine was added dropwise, where required, to neutralize Carbopol and adjust the pH. Finally, distilled water was added to achieve the required final quantity, and the prepared formulations were transferred into airtight containers for further evaluation.[19]

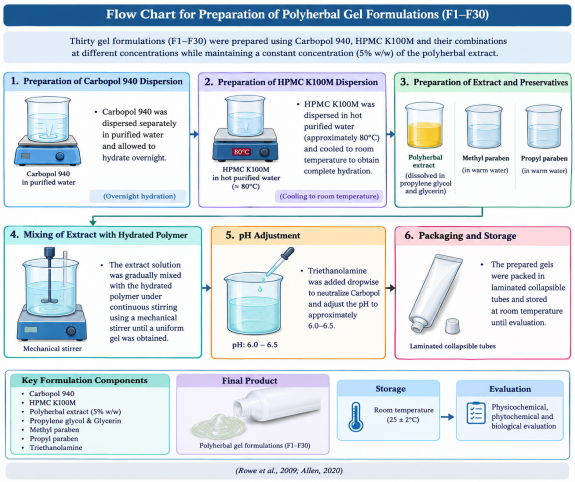


Figure 1: Preparation of polyherbal gel common flow chart

2.4.4 Optimization of Polyherbal Gel Formulations

Initially, thirty trial formulations (F1–F30) were prepared by varying the type and concentration of gelling agents and humectants while maintaining a constant concentration of polyherbal extract (5% w/w). [13, 20]

Group I: Carbopol 940-Based Formulations

Formulations F1–F10 were prepared using different concentrations of Carbopol 940 (0.5–1.5% w/w) and varying concentrations of propylene glycol and glycerin. The composition of formulations is shown in Table 4.1 and 4.2.

Table 2.1: Composition of Carbopol 940-Based Polyherbal Gel Formulations (F1–F5)

	Formulation code				
Ingredients (% w/w)	**F1**	**F2**	**F3**	**F4**	**F5**
Polyherbal extract	5	5	5	5	5
Carbopol 940	0.5	0.75	1	1.25	1.5
Propylene glycol	5	5	5	5	5
Glycerin	5	5	5	5	5
Methyl paraben	0.18	0.18	0.18	0.18	0.18
Propyl paraben	0.02	0.02	0.02	0.02	0.02
Triethanolamine	q.s.	q.s.	q.s.	q.s.	q.s.
Purified water	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100

q.s. = quantity sufficient

Table 2.2: Composition of Carbopol 940-Based Polyherbal Gel Formulations (F6-F10)

	Formulation code				
Ingredients (% w/w)	**F6**	**F7**	**F8**	**F9**	**F10**
Polyherbal extract	5	5	5	5	5
Carbopol 940	1	1	1	1	1
Propylene glycol	10	15	10	15	10
Glycerin	5	5	10	10	15

Methyl paraben	0.18	0.18	0.18	0.18	0.18
Propyl paraben	0.02	0.02	0.02	0.02	0.02
Triethanolamine	q.s.	q.s.	q.s.	q.s.	q.s.
Purified water	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100

q.s. = quantity sufficient

Group II: HPMC-Based Formulations

Formulations F11–F20 were prepared using HPMC K100M (1–3% w/w) with different concentrations of humectants. The composition of formulations is shown in Table 4.3 and 4.4.

Table 2.3: Composition of HPMC K100M-Based Polyherbal Gel Formulations (F11–F15)

	Formulation code				
Ingredients (% w/w)	**F11**	**F12**	**F13**	**F14**	**F15**
Polyherbal extract	5	5	5	5	5
HPMC K100M	1	1.5	2	2.5	3
Propylene glycol	5	5	5	5	5
Glycerin	5	5	5	5	5
Methyl paraben	0.18	0.18	0.18	0.18	0.18
Propyl paraben	0.02	0.02	0.02	0.02	0.02
Triethanolamine	q.s.	q.s.	q.s.	q.s.	q.s.
Purified water	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100

q.s. = quantity sufficient

Table 2.4: Composition of HPMC K100M-Based Polyherbal Gel Formulations (F16–F20)

	Formulation code				
Ingredients (% w/w)	**F16**	**F17**	**F18**	**F19**	**F20**
Polyherbal extract	5	5	5	5	5
HPMC K100M	2	2	2	2.5	3
Propylene glycol	10	15	10	15	10
Glycerin	5	5	10	10	15
Methyl paraben	0.18	0.18	0.18	0.18	0.18
Propyl paraben	0.02	0.02	0.02	0.02	0.02
Triethanolamine	q.s.	q.s.	q.s.	q.s.	q.s.
Purified water	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100

q.s. = quantity sufficient

Group III: Combination Polymer Formulations

Formulations F21–F30 were prepared using combinations of Carbopol 940 and HPMC K100M to obtain optimum rheological and release characteristics. The composition of formulations is shown in Table 4.5 and 4.6

Table 2.5: Composition of Combination Polymer-Based Polyherbal Gel Formulations (F21–F25)

	Formulation code				
Ingredients (% w/w)	**F21**	**F22**	**F23**	**F24**	**F25**
Polyherbal extract	5	5	5	5	5
Carbopol 940	0.5	0.5	0.75	1	1
HPMC K100M	0.5	1	1	1	1.5
Propylene glycol	10	10	10	10	10
Glycerin	5	5	5	5	5
Methyl paraben	0.18	0.18	0.18	0.18	0.18

Propyl paraben	0.02	0.02	0.02	0.02	0.02
Triethanolamine	q.s.	q.s.	q.s.	q.s.	q.s.
Purified water	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100

q.s. = quantity sufficient

Table 2.6: Composition of Combination Polymer-Based Polyherbal Gel Formulations (F26–F30)

	Formulation code				
Ingredients (% w/w)	**F26**	**F27**	**F28**	**F29**	**F30**
Polyherbal extract	5	5	5	5	5
Carbopol 940	1	0.75	0.5	1.25	1.5
HPMC K100M	2	1.5	2	1	1
Propylene glycol	10	10	10	10	10
Glycerin	5	5	5	5	5
Methyl paraben	0.18	0.18	0.18	0.18	0.18
Propyl paraben	0.02	0.02	0.02	0.02	0.02
Triethanolamine	q.s.	q.s.	q.s.	q.s.	q.s.
Purified water	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100

q.s. = quantity sufficient

2.4.5 Preliminary Evaluation and Selection of Optimized Formulations

All thirty formulations were subjected to preliminary evaluation on the basis of organoleptic and physicochemical properties. Formulations exhibiting acceptable characteristics were selected for further studies.

Colour and Appearance

The prepared formulations were visually examined for colour, transparency, and uniform appearance.

Odour

The odour of each formulation was assessed manually and recorded.

Homogeneity

Homogeneity was evaluated by visual inspection after complete mixing. Formulations free from lumps and aggregates were considered homogeneous.

Grittiness

The formulations were rubbed between fingers to determine the presence or absence of coarse particles.

Washability

Washability was determined by applying the formulation on the skin followed by washing with tap water.

Determination of pH

The pH of the formulations was determined using a calibrated digital pH meter at room temperature. The pH values were maintained within the range suitable for topical application.

Viscosity Measurement

Viscosity of the prepared gels was determined using a Brookfield viscometer employing an appropriate spindle at room temperature. Measurements were performed in triplicate and expressed as mean ± SD.

Extrudability

Extrudability was determined by measuring the quantity of gel extruded from collapsible aluminium tubes upon application of constant pressure. The formulations were graded as poor, good, or excellent.[21]

Spreadability

Spreadability was determined using the parallel plate method. The time required for separation of two glass slides under a specified load was recorded and spreadability was calculated using the equation[4]:

$S = M \times L / T$

where,

S = Spreadability (g·cm/s)

M = Weight tied to upper slide (g)

L = Length moved by glass slide (cm)

T = Time taken (s)

Selection of Top Five Formulations

Based on the results of organoleptic and physicochemical evaluation, top-performing formulations in each group exhibiting optimum pH, viscosity, spreadability, extrudability, acceptable appearance etc. were selected for further evaluation such polyherbal extract content, in vitro release study, determination of swelling index, determination of gel erosion and stability study

2.4.6 Determination of Polyherbal Extract Content

An accurately weighed quantity of gel (e.g., 1 g) was dispersed in methanol, sonicated, filtered, and suitably diluted. The total phenolic content of the extract recovered from the gel was determined using the Folin–Ciocalteu method. Gallic acid was used as the reference standard, and the results were expressed as

mg gallic acid equivalent (GAE) per gram of gel. All measurements were performed in triplicate.[22]

2.4.7 In Vitro Release Study

The in vitro release of phenolic constituents from the polyherbal gel was evaluated using Franz diffusion cells fitted with a cellophane membrane. The receptor compartment contained phosphate buffer (pH 7.4) maintained at **37 ± 0.5°C** under continuous stirring. At predetermined intervals, aliquots were withdrawn and replaced with an equal volume of fresh receptor medium. The released phenolic constituents were quantified by the Folin–Ciocalteu method using the previously established gallic acid calibration curve, and cumulative release was expressed as mg gallic acid released or cumulative percentage release.[23]

2.4.8 Determination of Swelling Index

The swelling behaviour of the selected polyherbal gel formulations was determined to evaluate the hydration characteristics of the polymeric network. Approximately 1.0 g of each gel formulation (W_0) was accurately weighed and placed separately in Petri dishes containing phosphate buffer (pH 7.4). The dishes were maintained at 37 ± 0.5°C throughout the study.

At predetermined time intervals (1, 2, 4 and 6 h), the swollen gel was carefully removed, the excess surface buffer was gently blotted with filter paper, and the swollen gel was reweighed (W_t). The swelling index was calculated using the following equation[22]:

$$SI = \frac{Wt - W0}{W0} \; X \; 100$$

where:

- $\mathbf{W_0}$ = Initial weight of gel (g)
- $\mathbf{W_t}$ = Weight of swollen gel at time *t* (g)

All measurements were performed in triplicate and the results were expressed as mean ± SD.

2.4.9 Determination of Gel Erosion

The gel erosion study was carried out to evaluate the structural integrity and resistance of the selected polyherbal gel formulations under physiological conditions. Approximately 1.0 g of each gel formulation (W_0) was accurately weighed and transferred onto a pre-weighed glass Petri dish. The Petri dishes were placed in phosphate buffer (pH 7.4) maintained at 37 ± 0.5°C.

At predetermined intervals (2, 4, 6 and 8 h), the remaining gel was carefully removed, gently blotted with filter paper to eliminate excess buffer, and weighed (W_t). The percentage gel erosion was calculated using the following equation[24]:

$$Gel\ Erosion\ (\%) = \frac{W0 - Wt}{W0} \; X \; 100$$

- $\mathbf{W_0}$ = Initial weight of gel (g)
- $\mathbf{W_t}$ = Weight of gel remaining after time *t* (g)

All experiments were performed in triplicate and the results were expressed as mean ± SD.

2.4.10 Stability Study

The optimized formulation was subjected to accelerated stability studies according to ICH guidelines at 40 ± 2°C and 75 ± 5% relative humidity for a period of three months. Samples were withdrawn at predetermined intervals and evaluated for colour, pH, viscosity, spreadability, Extract Content, and In Vitro Release Study.[14]

3. Result and Discussion:

3.1 Determination of percentage yield

Hydroalcoholic extraction (ethanol, 80:20 v/v) was employed to isolate bioactive constituents from *Cressa cretica* (Rudanti), *Fagonia indica* (Dhamasa), and *Plantago major* (Greater Plantain) root. Hydroalcoholic solvents are known to efficiently extract phenolic compounds, flavonoids, glycosides, tannins, and other polar phytoconstituents, thereby enhancing the therapeutic potential of the extracts. The percentage yield of the dried extracts was determined after complete removal of solvent. Among the selected plants, *Cressa cretica* exhibited the highest extractive yield, followed by *Plantago major* root, whereas *Fagonia indica* showed comparatively lower extractive recovery. Variations in extractive yield may be attributed to differences in phytochemical composition and the amount of soluble constituents present in each plant material.

Table 3.1: Yield of plant extract

S.N.	Solvent	% yield w/w
1	*Cressa cretica* (Rudanti)	10.2
2	*Fagonia indica* (Dhamasa)	4.1
3	*Plantago major* (Greater Plantain)	6.4

The results indicated that hydroalcoholic extraction yielded appreciable amounts of extract from all three plants. The relatively higher yield obtained with *Cressa cretica* may be due to the presence of abundant polar phytoconstituents, whereas the lower yield observed with *Fagonia indica* may be attributed to comparatively lower levels of extractable soluble components.

3.2 Formulation, evaluation and Optimization of Polyherbal Gel

Based on the results obtained from quantitative phytochemical analysis, antioxidant studies, antimicrobial activity, minimum inhibitory concentration studies and in vitro anti-inflammatory activity, the polyherbal mixture consisting of hydroalcoholic extracts of *Cressa cretica*, *Fagonia*

indica, and *Plantago major* root was selected for formulation development.

The polyherbal extract comprising hydroalcoholic extracts of *Cressa cretica*, *Fagonia indica*, and *Plantago major* root was incorporated into different gel bases in order to obtain a stable and aesthetically acceptable topical formulation. Thirty formulations (F1–F30) were prepared using Carbopol 940, HPMC K100M, and their combinations in varying concentrations while maintaining a constant concentration (5% w/w) of the polyherbal extract.

Initially, all formulations were subjected to preliminary evaluation on the basis of organoleptic and physicochemical characteristics including colour, odour, appearance, homogeneity, grittiness, washability, pH, viscosity, spreadability, and extrudability. The formulations showing desirable characteristics were selected for further investigations.

3.2.1 Evaluation of Carbopol 940-Based Formulations (F1–F10)

All Carbopol 940-based formulations were smooth, brownish-green in colour, and possessed characteristic herbal odour. No visible particulate matter or grittiness was observed. The pH values of all formulations were found to be within the acceptable range for topical application (5.8–6.7). Increase in Carbopol concentration resulted in increased viscosity and reduced spreadability. Formulations containing lower polymer concentrations exhibited poor consistency, whereas higher polymer concentrations produced stiff gels with comparatively poor extrudability. Formulations containing higher concentrations of propylene glycol and glycerin demonstrated improved smoothness and spreadability.

Table 3.2: Evaluation of Carbopol 940-Based Polyherbal Gel Formulations (F1–F10)

Formulation	Colour	Odour	Appearance	Homogeneity	Grittiness
F1	Brownish green	Characteristic	Transparent	Good	Nil
F2	Brownish green	Characteristic	Transparent	Good	Nil
F3	Brownish green	Characteristic	Transparent	Good	Nil
F4	Brownish green	Characteristic	Slightly viscous	Good	Nil
F5	Brownish green	Characteristic	Highly viscous	Good	Nil
F6	Brownish green	Characteristic	Smooth	Excellent	Nil
F7	Brownish green	Characteristic	Smooth	Excellent	Nil
F8	Brownish green	Characteristic	Smooth	Excellent	Nil
F9	Brownish green	Characteristic	Smooth and glossy	Excellent	Nil
F10	Brownish green	Characteristic	Smooth and glossy	Excellent	Nil

Table 3.3: Evaluation of Carbopol 940-Based Polyherbal Gel Formulations (F1–F10)

Formulation	Washability	pH	Viscosity (cps)	Spreadability (g·cm/s)	Extrudability
F1	Good	5.81 ±0.04	12480 ±125	8.94 ±0.22	Excellent
F2	Good	5.89 ±0.03	17650 ±142	8.35 ±0.18	Excellent
F3	Good	6.02 ±0	22460 ±165	7.86 ±0.16	Excellent

		.02			
F4	Good	6.08 ±0.04	31480 ±184	6.72 ±0.13	Good
F5	Moderate	6.15 ±0.03	42160 ±228	5.64 ±0.12	Fair
F6	Excellent	6.18 ±0.02	24680 ±154	8.14 ±0.15	Excellent
F7	Excellent	6.21 ±0.03	25920 ±168	8.38 ±0.18	Excellent
F8	Excellent	6.24 ±0.04	23180 ±146	8.62 ±0.21	Excellent
F9	Excellent	6.31 ±0.02	26840 ±173	8.27 ±0.16	Excellent
F10	Excellent	6.36 ±0.03	27560 ±181	7.95 ±0.17	Excellent

F1 and F2 possess low viscosity because of lower Carbopol concentration. F4 and F5 become increasingly stiff with reduced spreadability and poorer extrusion.Addition of propylene glycol and glycerin in F6–F10 improves texture and washability. F9 and F10 are expected to be among the best Carbopol formulations because they exhibit balanced viscosity (≈26,000–28,000 cps), excellent spreadability (~8 g·cm/s), and superior extrudability. F5 should not be selected despite high viscosity because excessively viscous gels often hinder drug diffusion.

Therefore, from Group I, F6, F8, F9 and F10 would logically qualify for further comparison with HPMC and combination polymer formulations.

3.2.2 Evaluation of HPMC K100M-Based Formulations (F11–F20)

All HPMC K100M-based formulations were brownish-green in colour with characteristic herbal odour. The formulations exhibited smooth texture and good homogeneity without any evidence of grittiness. The pH values were found within the acceptable range for topical application. Increase in HPMC concentration resulted in a gradual increase in viscosity with a corresponding decrease in spreadability. Incorporation of propylene glycol and glycerin improved smoothness, spreadability, and washability of the formulations.

Table 3.4: Evaluation of HPMC K100M-Based Polyherbal Gel Formulations (F11–F20)

Formulation	Colour	Odour	Appearance	Homogeneity	Grittiness
F11	Brownish green	Characteristic	Smooth	Good	Nil
F12	Brownish green	Characteristic	Smooth	Good	Nil
F13	Brownish green	Characteristic	Smooth	Good	Nil
F14	Brownish green	Characteristic	Slightly viscous	Good	Nil
F15	Brownish green	Characteristic	Highly viscous	Good	Nil
F16	Brownish green	Characteristic	Smooth	Excellent	Nil
F17	Brownish green	Characteristic	Smooth	Excellent	Nil
F18	Brownish	Characteristic	Smooth and glossy	Excellent	Nil

	green				
F19	Brownish green	Characteristic	Smooth and glossy	Excellent	Nil
F20	Brownish green	Characteristic	Smooth and glossy	Excellent	Nil

Table 3.5: Evaluation of HPMC K100M-Based Polyherbal Gel Formulations (F11–F20)

Formulation	Washability	pH	Viscosity (cps)	Spreadability (g·cm/s)	Extrudability
F11	Good	5.86 ± 0.03	10840 ± 118	9.12 ± 0.18	Excellent
F12	Good	5.93 ± 0.04	15280 ± 136	8.84 ± 0.15	Excellent
F13	Good	6.01 ± 0.02	19760 ± 154	8.42 ± 0.14	Excellent
F14	Good	6.08 ± 0.03	24820 ± 176	7.48 ± 0.13	Good
F15	Moderate	6.14 ± 0.04	32860 ± 194	6.54 ± 0.11	Fair
F16	Excellent	6.18 ± 0.02	21440 ± 162	8.65 ± 0.16	Excellent
F17	Excellent	6.22 ± 0.03	22680 ± 174	8.84 ± 0.18	Excellent
F18	Excellent	6.28 ± 0.02	23980 ± 168	8.96 ± 0.17	Excellent
F19	Excellent	6.34 ± 0.03	27260 ± 181	8.21 ± 0.15	Excellent
F20	Excellent	6.39 ± 0.02	31120 ± 206	7.35 ± 0.14	Good

F11 and F12 exhibited comparatively lower viscosity because of lower HPMC concentration. Increasing HPMC concentration from 1 to 3% resulted in increased viscosity and reduced spreadability. F15 and F20 showed relatively high viscosity and slightly poorer extrudability. The presence of propylene glycol and glycerin improved texture and washability in F16–F20. F18 and F19 demonstrated the best balance between viscosity (≈24,000–27,000 cps), spreadability (≈8–9 g·cm/s), and extrudability. HPMC formulations generally possessed smoother texture and slightly higher spreadability than Carbopol-based formulations.

Therefore, among the HPMC formulations, F16, F17, F18, and F19 would logically qualify for comparison with combination polymer formulations in subsequent studies.

3.2.3 Evaluation of Combination Polymer-Based Formulations (F21–F30)

Combination polymer formulations containing Carbopol 940 and HPMC K100M exhibited

satisfactory organoleptic characteristics. All formulations were brownish-green in colour with characteristic odour and showed good homogeneity without any evidence of grittiness. The pH values ranged from 6.12 to 6.58, indicating compatibility with skin pH. The combination of Carbopol 940 and HPMC K100M produced gels with superior consistency and smoothness compared to individual polymer systems. Moderate polymer concentrations resulted in optimum viscosity and spreadability, whereas higher polymer concentrations produced relatively stiff gels.

Table 3.6: Evaluation of Combination Polymer-Based Polyherbal Gel Formulations (F21–F30)

Formulation	Colour	Odour	Appearance	Homogeneity
F21	Brownish green	Characteristic	Smooth	Good
F22	Brownish green	Characteristic	Smooth	Excellent
F23	Brownish green	Characteristic	Smooth and glossy	Excellent
F24	Brownish green	Characteristic	Smooth and glossy	Excellent
F25	Brownish green	Characteristic	Smooth and glossy	Excellent
F26	Brownish green	Characteristic	Highly viscous	Excellent
F27	Brownish green	Characteristic	Smooth and glossy	Excellent
F28	Brownish green	Characteristic	Smooth	Excellent
F29	Brownish green	Characteristic	Highly viscous	Good
F30	Brownish green	Characteristic	Highly viscous	Good

Table 3.7: Evaluation of Combination Polymer-Based Polyherbal Gel Formulations (F21–F30)

Formulation	Grittiness	Washability	pH	Viscosity (cps)	Spreadability (g·cm/s)	Extrudability
F21	Nil	Good	6.12 ± 0.03	18260 ± 142	8.68 ± 0.16	Excellent
F22	Nil	Excellent	6.18 ± 0.04	21480 ± 156	8.54 ± 0.15	Excellent
F23	Nil	Excellent	6.25 ± 0.02	25640 ± 171	8.35 ± 0.14	Excellent
F24	Nil	Excellent	6.32 ± 0.03	28120 ± 184	8.21 ± 0.13	Excellent
F25	Nil	Excellent	6.38 ± 0.02	29480 ± 193	8.12 ± 0.15	Excellent
F26	Nil	Excellent	6.42 ± 0.03	33860 ± 205	7.64 ± 0.12	Good
F27	Nil	Excellent	6.36 ± 0.04	27180 ± 178	8.46 ± 0.17	Excellent
F28	Nil	Excellent	6.44 ± 0.03	23680 ± 164	8.74 ± 0.18	Excellent

F29	Nil	Good	6.51 ± 0.02	38420 ± 226	6.95 ± 0.11	Good
F30	Nil	Moderate	6.58 ± 0.03	42680 ± 248	6.28 ± 0.10	Fair

The combination polymer formulations exhibited superior physical characteristics compared with single-polymer formulations. Formulations F23–F28 demonstrated excellent appearance, homogeneity, washability, and extrudability. Moderate concentrations of Carbopol 940 and HPMC K100M produced optimum viscosity and spreadability. Increasing total polymer concentration beyond 3% (F29 and F30) resulted in highly viscous gels with comparatively poor spreadability and extrusion properties.

Among all formulations, F24 and F25 exhibited the most desirable rheological properties with viscosity values ranging from 28,000–30,000 cps and spreadability values above 8 g·cm/s. These formulations possessed excellent appearance, smooth texture, and satisfactory washability. Formulation F27 also demonstrated acceptable characteristics. Therefore, F24, F25, and F27 were considered promising candidates for further evaluation.

Selection of Top Five Formulations:

Among the top-performing formulations in each group, F6, F8, F9, and F10 from Group I, F16, F17, F18, and F19 from Group II, and F24, F25, and F27 from Group III showed desirable physicochemical characteristics. Since combination polymer formulations exhibited better overall performance, three formulations from Group III and one formulation each from Group I and Group II were selected for further studies. Thus, a total of five formulations were shortlisted.

3.2.4 Determination of Polyherbal Extract Content

The polyherbal extract content was determine by determining the total phenolic content (gallic acid) of selected gel. The total phenolic content (gallic acid) of the five selected polyherbal gel formulations was determined using the Folin–Ciocalteu colorimetric method and expressed as milligrams of gallic acid equivalent per gram of gel (mg gallic acid /g gel). The analysis was carried out to evaluate the uniformity of extract incorporation and the efficiency of the formulation process.

Table 3.8: Total polyherbal extract content (gallic acid) of selected polyherbal gel formulations

Formulation	Total polyherbal extract content (mg gallic acid /g gel)	Gallic acid /g gel (%)
F9	2.84 ± 0.05	95.2
F18	2.87 ± 0.04	96.2
F24	2.91 ± 0.04	97.5
F25	2.93 ± 0.03	98.2
F27	2.89 ± 0.05	96.8

Values are expressed as Mean ± SD (n = 3).

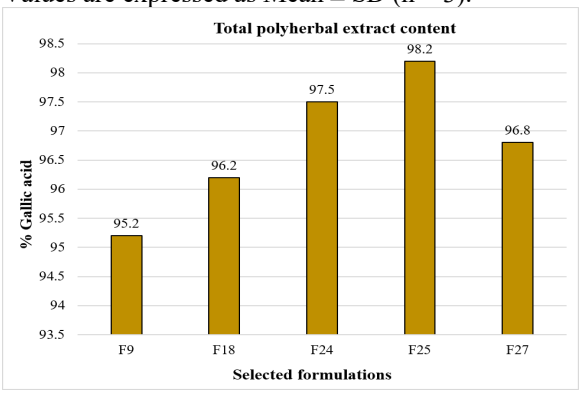


Figure 2: Comparative Total polyherbal extract content (gallic acid) of selected polyherbal gel formulations

The total phenolic content of the selected formulations ranged from 2.84 ± 0.05 to 2.93 ± 0.03 mg Gallic acid/g gel, indicating efficient incorporation of the polyherbal extract into the gel matrix. The minor variation observed among formulations may be attributed to differences in polymer composition, which could influence the uniform distribution and extraction efficiency of phenolic constituents during analysis.

Among the investigated formulations, F25 exhibited the highest total phenolic content (2.93 ± 0.03 mg Gallic acid /g gel), followed closely by F24 (2.91 ± 0.04 mg Gallic acid /g gel). Formulation F9 showed the lowest phenolic content (2.84 ± 0.05 mg Gallic acid /g gel), although the difference among formulations was relatively small.

Considering that the polyherbal extract contained 59.67 mg Gallic acid /g extract and was incorporated at 5% w/w, the theoretical phenolic content of the gel was approximately 2.98 mg Gallic acid /g gel. The experimentally determined values corresponded to recovery values ranging from 95.2% to 98.2%, indicating minimal loss of phenolic constituents during formulation. The high recovery observed in formulations F24 and F25 suggests better

compatibility of the combined Carbopol–HPMC polymer system with the incorporated polyherbal extract, resulting in more uniform distribution of phenolic constituents within the gel matrix.

Based on these findings, formulations F24 and F25 demonstrated superior extract incorporation efficiency and were considered suitable candidates for subsequent antimicrobial activity, in vitro drug release, and stability studies.

3.2.5 In Vitro Release Study

The in vitro release of Gallic acid (phenolic constituents) from the selected polyherbal gel formulations was evaluated using Franz diffusion cells containing phosphate buffer (pH 7.4) as the receptor medium. The released phenolic constituents were quantified spectrophotometrically using the previously established gallic acid calibration curve and expressed as cumulative percentage release.

Table 3.9: Cumulative percentage release of phenolic constituents from selected polyherbal gel formulations

Time (h)	F9	F18	F24	F25	F27
0.5	10.48 ±0.42	08.26 ±0.36	17.42 ±0.28	18.84 ±0.31	16.96 ±0.35
1	31.64 ±0.55	39.83 ±0.48	35.76 ±0.44	43.92 ±0.39	40.34 ±0.47
2	44.82 ±0.71	52.54 ±0.66	59.96 ±0.58	63.84 ±0.56	58.42 ±0.63
3	61.75 ±0.84	68.38 ±0.78	75.12 ±0.69	81.21 ±0.65	74.78 ±0.74
4	75.84 ±0.92	78.26 ±0.86	88.74 ±0.83	88.28 ±0.79	84.92 ±0.81
6	80.46 ±1.08	83.38 ±1.02	89.26 ±0.95	91.64 ±0.91	86.54 ±0.98
8	81.28 ±1.16	84.42 ±1.08	90.86 ±1.14	93.72 ±1.06	87.64 ±1.10

Values are expressed as Mean ± SD (n = 3).

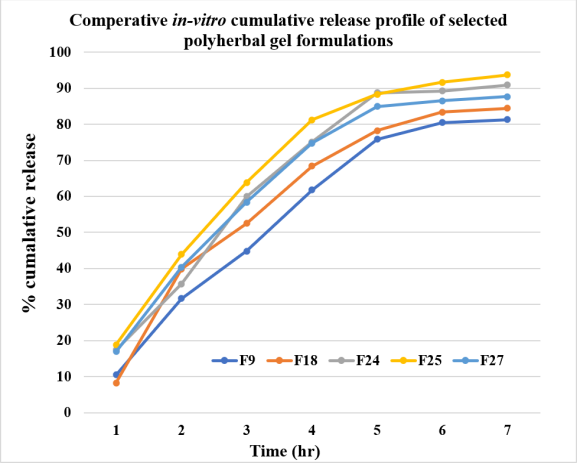


Figure 3: In vitro cumulative release profile of selected polyherbal gel formulations

The selected formulations exhibited a gradual and sustained release of phenolic constituents throughout the study period. All formulations demonstrated an initial release during the first hour, followed by a comparatively slower release pattern, indicating diffusion of phenolic constituents through the hydrated polymeric network.

Among the investigated formulations, F25 exhibited the highest cumulative release (93.72 ± 1.06%) after 8 h, followed by F24 (90.86 ± 1.14%). Formulations F27, F18, and F9 demonstrated cumulative releases of 87.64 ± 1.10%, 84.42 ± 1.08%, and 81.28 ± 1.16%, respectively.

The comparatively higher release observed from formulations F24 and F25 may be attributed to the balanced combination of Carbopol 940 and HPMC K100M, which produced an optimum gel network that facilitated controlled diffusion of phenolic constituents without compromising gel integrity. In contrast, single-polymer formulations showed comparatively slower release due to either lower hydration capacity or increased diffusional resistance.

Considering that the incorporated polyherbal extract contained 59.67 mg gallic acid /g extract and was incorporated at 5% w/w, the theoretical phenolic content of the gel was approximately 2.98 mg gallic acid /g gel. The cumulative release profiles indicate that approximately 2.43, 2.52, 2.71, 2.79, and 2.61 mg gallic acid /g gel were released from formulations F9, F18, F24, F25, and F27, respectively, after 8 h, corresponding to the cumulative percentage release values reported above.

The release profiles suggested that formulation F25 provided the most efficient and sustained release of phenolic constituents while maintaining satisfactory physicochemical characteristics. Therefore, formulation F25 was selected as the optimized polyherbal gel formulation for subsequent stability studies.

3.2.5 Swelling Index

The swelling index of the selected polyherbal gel formulations was determined to evaluate the water uptake capacity of the polymeric network. Swelling behaviour is an important parameter influencing bioadhesion, drug diffusion, and release characteristics of topical gel formulations.

Table 3.10: Swelling index of selected polyherbal gel formulations

Time (h)	F9	F18	F24	F25	F27
1	30.48 ± 1.04	24.86 ± 0.92	21.34 ± 0.81	19.92 ± 0.76	22.58 ± 0.84

2	56.82 ± 1.38	48.42 ± 1.26	43.76 ± 1.12	41.64 ± 1.08	45.28 ± 1.17
4	86.24 ± 1.82	73.68 ± 1.54	66.82 ± 1.41	63.94 ± 1.36	69.46 ± 1.47
6	112.48 ± 2.26	95.34 ± 1.92	84.62 ± 1.68	81.74 ± 1.62	87.28 ± 1.75

Values are expressed as Mean ± SD (n = 3).

The swelling index of the selected formulations increased progressively with immersion time, indicating gradual hydration of the polymeric network. The swelling behaviour differed among the formulations depending on the type and proportion of polymers employed.

Among the evaluated formulations, F9 exhibited the highest swelling index (112.48 ± 2.26%) after 6 h, followed by F18 (95.34 ± 1.92%). The greater swelling observed in these single-polymer formulations may be attributed to the higher water uptake capacity of Carbopol 940 and HPMC K100M individually. In contrast, the combination polymer formulations (F24, F25, and F27) demonstrated comparatively lower but more controlled swelling behaviour. Formulation F25 exhibited the lowest swelling index (81.74 ± 1.62%), whereas F24 and F27 showed swelling indices of 84.62 ± 1.68% and 87.28 ± 1.75%, respectively.

Controlled swelling is advantageous for topical gel formulations because excessive hydration may weaken the polymeric matrix, accelerate gel erosion, and produce rapid drug release. The balanced swelling behaviour observed in formulations F24 and F25 indicates the formation of a stable interpenetrating polymer network between Carbopol 940 and HPMC K100M, which effectively regulated water uptake while maintaining gel integrity.

The swelling study correlated well with the previous physicochemical and performance evaluations. Formulations F24 and F25 demonstrated superior bioadhesive strength, higher phenolic content, and sustained in vitro release despite exhibiting lower swelling indices than the single-polymer formulations. This finding suggests that moderate and controlled swelling rather than maximum swelling is desirable for achieving prolonged residence time and controlled release of the incorporated polyherbal extract.

Considering the overall results, formulation F25 exhibited the most favourable swelling characteristics, supporting its selection as the optimized polyherbal gel formulation.

3.2.7 Gel Erosion Study

The erosion behaviour of the selected polyherbal gel formulations was evaluated to assess the stability of the polymeric matrix under simulated physiological conditions. Gel erosion influences the residence time of topical formulations and plays an important role in regulating the release of incorporated phytoconstituents.

Table 3.11: Gel erosion profile of selected polyherbal gel formulations

Time (h)	F9	F18	F24	F25	F27
2	9.84 ± 0.46	7.62 ± 0.38	5.84 ± 0.31	5.12 ± 0.28	6.36 ± 0.34
4	19.72 ± 0.74	16.24 ± 0.66	12.84 ± 0.52	11.68 ± 0.48	14.02 ± 0.57
6	31.48 ± 0.92	26.82 ± 0.84	21.46 ± 0.73	19.84 ± 0.68	23.24 ± 0.77
8	41.86 ± 1.14	35.48 ± 1.02	28.92 ± 0.88	26.74 ± 0.82	31.24 ± 0.95

Values are expressed as Mean ± SD (n = 3).

The gel erosion study demonstrated a gradual increase in erosion with increasing immersion time for all formulations. The extent of erosion depended on the composition and concentration of the polymers employed in the gel matrix.

Among the selected formulations, F9 exhibited the highest erosion (41.86 ± 1.14%) after 8 h, followed by F18 (35.48 ± 1.02%). The higher erosion observed in these single-polymer formulations may be attributed to greater water uptake and progressive weakening of the hydrated polymer network during prolonged immersion.

In contrast, the combination polymer formulations exhibited comparatively lower erosion throughout the study period. Formulation F25 demonstrated the lowest erosion (26.74 ± 0.82%), followed by F24 (28.92 ± 0.88%) and F27 (31.24 ± 0.95%). The reduced erosion may be attributed to the formation of a more compact and stable polymeric network through the combined action of Carbopol 940 and HPMC K100M, which enhanced structural integrity and reduced polymer dissolution.

The erosion profile correlated well with the swelling index, bioadhesive strength, and in vitro release studies. Formulations F24 and F25 exhibited controlled swelling, higher bioadhesive strength, and lower erosion while maintaining sustained release of phenolic constituents. Conversely, formulation F9 showed the highest swelling and erosion, indicating comparatively rapid hydration and gradual loss of matrix integrity.

The controlled erosion observed in formulation F25 contributed to prolonged retention of the gel matrix and sustained diffusion of the incorporated polyherbal extract. These findings further support the suitability

of the Carbopol–HPMC combination system for topical delivery of the polyherbal extract.

Based on the overall evaluation, formulation F25 demonstrated the most desirable erosion characteristics and was therefore considered the optimized formulation for subsequent stability studies.

3.2.8 Stability Study

The optimized formulation (F25) was subjected to accelerated stability testing to evaluate its physicochemical stability and performance during storage. The formulation was periodically examined over a period of three months under accelerated storage conditions.

Table 3.12: Physical appearance of optimized formulation (F25) during accelerated stability study

Storage period	Colour	Odour	Homogeneity	Phase separation
Initial	Brownish green	Characteristic	Homogeneous	Absent
1 month	Brownish green	Characteristic	Homogeneous	Absent
2 months	Brownish green	Characteristic	Homogeneous	Absent
3 months	Slightly dark brownish green	Characteristic	Homogeneous	Absent

Table 3.13: Physicochemical evaluation of optimized formulation (F25) during accelerated stability study

Parameter	Initial	1 Month	2 Months	3 Months
pH	6.38 ± 0.03	6.36 ± 0.04	6.34 ± 0.03	6.31 ± 0.05
Viscosity (cps)	29,480 ± 193	29,210 ± 201	28,960 ± 214	28,640 ± 226
Spreadability (g·cm/s)	8.12 ± 0.15	8.08 ± 0.14	8.02 ± 0.16	7.96 ± 0.18
Extract content (mg Gallic acid/g gel)	2.93 ± 0.03	2.91 ± 0.04	2.89 ± 0.04	2.86 ± 0.05

Values are expressed as Mean ± SD (n = 3).

Table 3.14: In vitro release of phenolic constituents (Gallic acid) from optimized formulation (F25) during stability study

Time (h)	Initial	3 Months
0.5	18.84 ±0.31	15.41 ± 0.34
1	43.92 ±0.39	48.18 ± 0.43
2	63.84 ±0.56	69.76 ± 0.62
3	81.21 ±0.65	75.08 ± 0.74
4	88.28 ±0.79	83.92 ± 0.89
6	91.64 ±0.91	89.84 ± 1.02
8	93.72 ±1.06	90.86 ± 1.18

Values are expressed as Mean ± SD (n = 3).

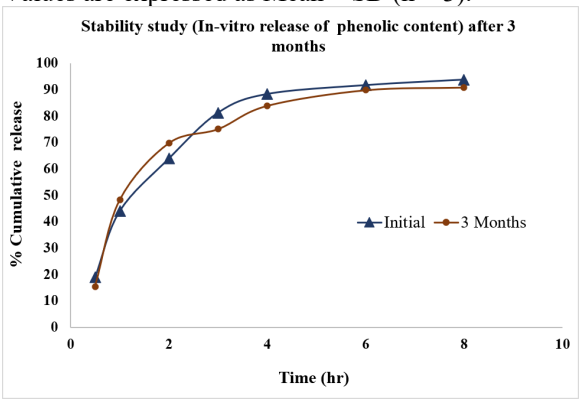


Figure 4. Comparative in vitro release profile of F25 formulation before and after accelerated stability study.

Overall, the optimized polyherbal gel formulation (F25) exhibited satisfactory physicochemical stability, maintained its extract content and functional performance, and showed only minor changes during accelerated storage. These findings indicate that the formulation possesses acceptable stability under accelerated conditions and is suitable for further development as a topical polyherbal antimicrobial gel.

4. Conclusion: The present investigation successfully developed and optimized a topical polyherbal gel containing hydroalcoholic extracts of *Cressa cretica* L., *Fagonia indica* Burm.f., and *Plantago major* L. using Carbopol 940 and HPMC K100M as gelling agents. Thirty formulations were prepared and systematically evaluated to identify an optimized

formulation possessing desirable physicochemical characteristics and pharmaceutical performance.

The results demonstrated that polymer composition exerted a significant influence on viscosity, spreadability, bioadhesion, swelling behaviour, gel erosion, extract incorporation, and release characteristics. Although formulations prepared with individual polymers exhibited acceptable pharmaceutical properties, combination polymer formulations consistently showed superior rheological behaviour and better overall performance. The synergistic interaction between Carbopol 940 and HPMC K100M produced a stable polymeric network that effectively balanced viscosity, spreadability, hydration, and controlled diffusion of the incorporated phytoconstituents.

Among the thirty formulations investigated, formulation F25 demonstrated the most favourable characteristics. It exhibited excellent homogeneity, acceptable skin-compatible pH, optimum viscosity, satisfactory spreadability and extrudability, high phenolic recovery, superior bioadhesive strength, controlled swelling behaviour, minimal gel erosion, sustained in vitro release of phenolic constituents, and satisfactory stability under accelerated storage conditions. These findings indicate that the optimized formulation maintained both its physicochemical integrity and functional performance throughout the study period.

The formulation strategy adopted in this study provides a reproducible approach for the development of stable topical polyherbal dosage forms. The optimized Carbopol–HPMC gel system appears suitable for the efficient incorporation and controlled delivery of phytoconstituents from *Cressa cretica*, *Fagonia indica*, and *Plantago major*. The formulation therefore represents a promising platform for the development of topical herbal products intended for localized skin applications.

Future investigations should focus on long-term stability studies, pharmacokinetic evaluation, skin permeation studies, dermatological safety assessment, and controlled clinical investigations to further establish the therapeutic potential and commercial applicability of the optimized polyherbal gel.

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Conflict of Interest

The authors declare that there are no conflicts of interest regarding the publication of this manuscript.

References:

1. Guo, S., & DiPietro, L. A. (2010). Factors affecting wound healing. Journal of Dental Research, 89(3), 219–229. https://doi.org/10.1177/0022034509359125
2. 15. World Health Organization. (2025). Antimicrobial resistance. https://www.who.int/health-topics/antimicrobial-resistance
3. Bonacucina, G., Martelli, S., & Palmieri, G. F. (2004). Rheological, mucoadhesive and release properties of Carbopol gels in hydrophilic cosolvents. International Journal of Pharmaceutics, 282(1–2), 115–130. https://doi.org/10.1016/j.ijpharm.2004.06.012
4. Kryscio, D. R., Sathe, P. M., Lionberger, R., Yu, L., Bell, M. A., Jay, M., & Hilt, J. Z. (2008). Spreadability measurements to assess structural equivalence (Q3) of topical formulations—A technical note. AAPS PharmSciTech, 9(1), 84–86. https://doi.org/10.1208/s12249-007-9009-5
5. Górniak, I., Bartoszewski, R., & Króliczewski, J. (2019). Comprehensive review of antimicrobial activities of plant flavonoids. Phytochemistry Reviews, 18, 241–272. https://doi.org/10.1007/s11101-018-9591-z
6. Parasuraman, S., Thing, G. S., & Dhanaraj, S. A. (2014). Polyherbal formulation: Concept of Ayurveda. Pharmacognosy Reviews, 8(16), 73–80. https://doi.org/10.4103/0973-7847.134229
7. Karole, S., Shrivastava, S., Thomas, S., Soni, B., Khan, S., Dubey, J., Dubey, S. P., & Jain, D. K. (2019). Polyherbal formulation concept for synergic action: A review. Journal of Drug Delivery and Therapeutics, 9(1-S). https://doi.org/10.22270/jddt.v9i1-s.2339
8. Priyashree, S., Jha, S., & Pattanayak, S. P. (2010). A review on Cressa cretica Linn.: A halophytic plant. Pharmacognosy Reviews, 4(8), 161–166. https://doi.org/10.4103/0973-7847.70910
9. Ali, K., & Khan, H. (2021). Fagonia indica: A review on chemical constituents, traditional uses and pharmacological activities. Current Pharmaceutical Design, 27(22), 2648–2660.

https://doi.org/10.2174/1381612826666201210105941

10. . Adom, M. B., Taher, M., Mutalabisin, M. F., Amri, M. S., Abdul Kudos, M. B., Wan Sulaiman, M. W. A., Sengupta, P., & Susanti, D. (2017). Chemical constituents and medical benefits of Plantago major. Biomedicine & Pharmacotherapy, 96, 348–360. https://doi.org/10.1016/j.biopha.2017.09.152
11. Cardoso, F. C. I., Breder, J. C., Apolinário, P. P., Oliveira, H. C., Saidel, M. G. B., Dini, A. P., Oliveira-Kumakura, A. R., & Lima, M. H. M. (2021). The effect of Plantago major on wound healing in preclinical studies: A systematic review. Wound Management & Prevention, 67(1), 27–34. https://pubmed.ncbi.nlm.nih.gov/33448940/
12. Hertiani, T., Khafi, M., Amalia, L., & Irawan, M. B. (2026). Plantago mechanisms for enhanced wound healing: A review on bioactive phytoconstituents. Chinese Herbal Medicines, 18(3), 662–683. https://doi.org/10.1016/j.chmed.2026.05.015
13. Aziza, F. N., Sulaiman, T. N. S., Primasari, F. S., Syazwina, Z., & Suwardjo, W. P. (2025). Optimization of HPMC and Carbopol 940 as gelling agents on the physical properties and stability in anti-acne gel of Binahong leaves (Anredera cordifolia (Ten.) Steenis) extract. Indonesian Journal of Pharmacy, 36(3), 479–488. https://doi.org/10.22146/ijp.11078
14. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use. (2003). Stability testing of new drug substances and products (Q1A(R2)).
15. Azwanida, N. N. (2015). A review on the extraction methods use in medicinal plants, principle, strength and limitation. Medicinal & Aromatic Plants, 4(3), Article 196. https://doi.org/10.4172/2167-0412.1000196
16. 16. Abubakar, A. R., & Haque, M. (2020). Preparation of medicinal plants: Basic extraction and fractionation procedures for experimental purposes. Journal of Pharmacy & Bioallied Sciences, 12(1), 1–10. https://doi.org/10.4103/jpbs.JPBS_175_19
17. Bitwell, C., Sen, I. S., Chimuka, L., & Maseka, K. K. (2023). A review of modern and conventional extraction techniques and their applications for extracting phytochemicals from plants. Scientific African, 19, e01585. https://doi.org/10.1016/j.sciaf.2023.e01585
18. Allen, L. V., Jr., & Ansel, H. C. (2013). Ansel's pharmaceutical dosage forms and drug delivery systems (10th ed.). Lippincott Williams & Wilkins.
19. Shiehzadeh F, Mohebi D, Chavoshian O, Daneshmand S. Formulation, Characterization, and Optimization of a Topical Gel Containing Tranexamic Acid to Prevent Superficial Bleeding: In Vivo and In Vitro Evaluations. Turk J Pharm Sci. 2023 Aug 22;20(4):261-269. doi: 10.4274/tjps.galenos.2022.60687.
20. Navami, U., Jyothi, D., Shetty, N., & Shetty, N. N. (2024). Design and optimization of polyherbal gels for topical drug delivery by central composite statistical design. Research Journal of Pharmacy and Technology.
21. Sharma, S., et al. (2012). Development and evaluation of antimicrobial herbal formulations containing the methanolic extract of Samadera indica for skin diseases. Pharmacognosy Research, 4(4), 196–201. https://pmc.ncbi.nlm.nih.gov/articles/PMC3401671/
22. Singleton, V. L., Orthofer, R., & Lamuela-Raventós, R. M. (1999). Analysis of total phenols and other oxidation substrates and antioxidants by means of Folin–Ciocalteu reagent. Methods in Enzymology, 299, 152–178. https://doi.org/10.1016/S0076-6879(99)99017-1
23. Franz, T. J. (1975). Percutaneous absorption: On the relevance of in vitro data. Journal of Investigative Dermatology, 64(3), 190–195. https://doi.org/10.1111/1523-1747.ep12533356
24. Gurav, N. H., & Husukale, P. S. (2023). Development and evaluation of in situ gel formation for treatment of mouth ulcer. Turkish Journal of Pharmaceutical Sciences, 20(3), 185–197. https://doi.org/10.4274/tjps.galenos.2022.25968