

Formulation and Evaluation of a Polyherbal Methanolic Gel Incorporating *Plumbago auriculata*, *Calotropis gigantea*, and *Arctium lappa* for Dermatological Applications

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Abstract

The present study aimed to formulate and evaluate polyherbal methanolic gels for dermatological application using suitable gelling agents and excipients. Polyherbal extracts were incorporated into gel bases prepared with different polymers, including Carbomer 940, Carbomer 934, HPMC, and natural gums, to assess their suitability for topical delivery. The gels were prepared using a standardized method involving hydration of the polymer, incorporation of preservatives, propylene glycol, antioxidants, and polyherbal extract, followed by pH adjustment using triethanolamine. The formulated gels were evaluated for physicochemical parameters such as pH, viscosity, homogeneity, and spreadability. Stability studies, including freeze–thaw cycles, were conducted to assess formulation robustness, and flavonoid degradation was used as a marker for chemical stability. In vitro drug release studies were performed to evaluate the release profile of active constituents. Among all formulations, Carbomer-based gels exhibited superior physicochemical properties, with optimal pH (6.4–7.2), excellent homogeneity, and desirable viscosity. Formulation G8 showed the highest viscosity, minimal flavonoid degradation (12.76%), and good stability under stress conditions. In vitro release studies indicated a sustained drug release profile, with G8 exhibiting prolonged release up to 260 minutes. In contrast, formulations containing HPMC and natural polymers showed poor consistency and stability. The results suggest that Carbomer 940 is a suitable gelling agent for polyherbal topical formulations. The optimized formulation demonstrated desirable stability, controlled drug release, and potential for effective dermatological application. This study highlights the importance of formulation optimization in developing stable and efficacious polyherbal gel systems for topical therapy.

Keywords: Polyherbal gel, Carbomer 940, Topical drug delivery, Flavonoid, stability, Dermatological application, Hydrogel formulation

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Introduction

The skin, being the largest organ of the human body, serves as a primary protective barrier against environmental insults, microbial invasion, and physical injury. However, various dermatological conditions such as infections, inflammation, wounds, and acne can compromise its integrity, necessitating effective therapeutic interventions. Topical drug delivery systems have gained considerable attention in recent years due to their ability to deliver drugs directly to the site of action, thereby enhancing therapeutic efficacy while minimizing systemic side effects. Among these, gel-based formulations have emerged as a preferred dosage form owing to their ease of application, non-greasy nature, patient compliance, and ability to provide controlled drug release [1].

In recent years, there has been a growing interest in herbal and polyherbal formulations for dermatological applications. Herbal medicines have been used for centuries and are increasingly being recognized for their safety, efficacy, and minimal adverse effects compared to synthetic drugs. Polyherbal formulations

offer synergistic therapeutic effects due to the presence of multiple bioactive constituents such as flavonoids, alkaloids, tannins, and phenolic compounds. These phytoconstituents exhibit a wide range of pharmacological activities including antioxidant, anti-inflammatory, antimicrobial, and wound healing properties, making them highly suitable for topical applications [2, 3].

The development of polyherbal gels combines the advantages of herbal therapeutics with modern drug delivery systems. Gels provide a suitable matrix for incorporating hydrophilic and lipophilic herbal extracts, ensuring uniform distribution and enhanced stability of active constituents. Moreover, gel formulations facilitate better penetration of active compounds through the skin, improving bioavailability and therapeutic outcomes. Recent studies have demonstrated that polyherbal topical gels exhibit superior efficacy in managing skin disorders such as acne, wounds, and infections due to synergistic interactions among plant-derived compounds [4].

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Despite these advantages, the formulation of stable and effective polyherbal gels poses several challenges. The complex nature of herbal extracts may lead to incompatibility with excipients, instability, and degradation of active constituents. Therefore, the selection of an appropriate gelling agent plays a crucial role in determining the physicochemical properties, stability, and drug release behavior of the formulation. Carbomer-based polymers (such as Carbomer 940 and Carbomer 934) are widely used in topical gel formulations due to their excellent thickening properties, high viscosity at low concentrations, and ability to form stable hydrogel networks. These polymers also allow pH-dependent gelation, which is advantageous for maintaining skin-compatible formulations [5].

Furthermore, recent advancements in topical drug delivery have focused on enhancing the permeation and controlled release of herbal actives. Techniques such as phytosomal incorporation, nanoparticulate systems, and emulgel formulations have been explored to improve the therapeutic performance of polyherbal gels [6]. For instance, polyherbal phytosomal gels have shown improved skin permeation and sustained drug release due to enhanced encapsulation efficiency and interaction with the lipid components of the skin barrier. Similarly, emulgel systems have demonstrated improved stability and bioavailability of herbal extracts, particularly in wound healing applications.

Another critical aspect of polyherbal gel development is the evaluation of stability and drug release characteristics. Herbal constituents, especially flavonoids and phenolic compounds, are susceptible to degradation under environmental stress conditions such as temperature fluctuations and oxidation. Therefore, stability studies, including freeze-thaw analysis, are essential to ensure the integrity and efficacy of the formulation over time. Additionally, *in vitro* drug release studies provide insights into the release kinetics and help in optimizing the formulation for sustained therapeutic action [7, 8].

In the context of dermatological applications, sustained release of active constituents is particularly beneficial as it ensures prolonged contact with the affected area, enhances drug retention, and reduces the frequency of application [9]. This not only improves patient compliance but also enhances the overall therapeutic outcome. Recent research has emphasized the importance of optimizing formulation variables such as polymer concentration, viscosity, and excipient composition to achieve a balance between stability and controlled drug release [10].

Therefore, the present study aims to formulate and evaluate polyherbal methanolic gels for dermatological application using different gelling agents and excipients. The study focuses on assessing the physicochemical properties, stability, and *in vitro* drug release behavior of the developed formulations. By optimizing these parameters, the study seeks to develop a stable, effective, and patient-friendly topical herbal gel with potential therapeutic benefits for various skin disorders.

Material and Method

Preparation of carbomer based gel formulations

In a 100 ml beaker, the gelling agent was slowly mixed with 50 ml of distilled water while being constantly stirred. To allow the gel to expand, the beaker was set aside overnight. The solution was heated on a water bath (A) using 0.2 ml of 0.5 % methylparaben and 0.1 ml of 0.2% propylparaben in 5 ml of distilled water. Mixture (A) was completely combined with a separate mixture (B) containing 5 ml of 5% propylene glycol-400, 0.2 g of sodium metabisulphide, and 1% w/w polyherbal mixture after it cooled. With constant stirring, the combined A and B solutions were added to the pre-formed gel basis. Finally, the necessary pH was achieved by adding triethanolamine dropwise. Enough distilled water was added to make the gel thick enough (Fig 1).

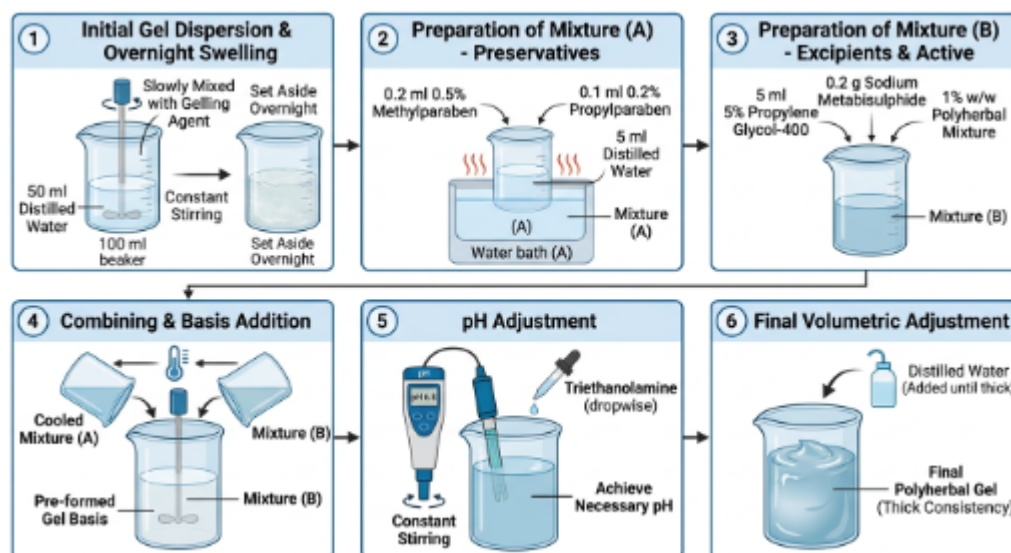


Figure 1: Preparation of carbomer based gel formulations

Preparation of oil-based gel formulations:

In a 100 ml beaker, the gelling agent was slowly mixed with 50 ml of distilled water while being constantly stirred. To allow the gel to expand, the beaker was set aside overnight. The solution was heated on a water bath (A) using 0.2 ml of 0.5 % methylparaben and 0.1 ml of 0.2% propylparaben in 5 ml of distilled water. After the first combination (A) cooled, a second mixture (B) was completely mixed with it. This second mixture contained 5 ml of 5% propylene glycol-400

and 0.2 g of sodium metabisulphide. In a premade gel basis, the final combination (A+B) was added while stirring continuously. At last, in step 4, the gel base was supplemented with a premade combination of 1% span 60, oil, and 1% polyherbal gel. Drops of triethanolamine were applied until the pH was reached. The next step was to add enough filtered water to the mixture to make a gel of the desired consistency (Fig. 2).

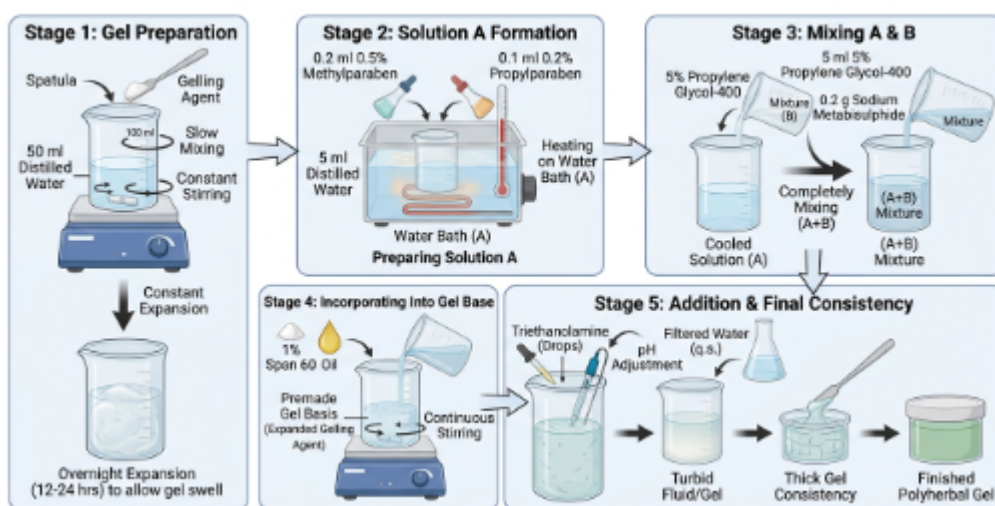


Figure 2: Preparation of oil-based gel formulations

Optimization/ Development of Gel formulation:

The physicochemical features of the excipients were considered when making their selection. In order to meet the specified and intended physicochemical and stability criteria for polyherbal gel formulation, the formulations shown in Tables 1 to 14 were refined and improved. Choosing and adjusting the ratio of various excipients used in various feed compositions allowed for the optimization of the formulations. Characterization and analysis of all formulations were conducted using several assessment parameters, including viscosity, extrudability, spreadability, and pH.

Table 1 Formulation of Gel using HPMC

CONTENTS	G1	G2	G3	G4
Sodium metabisulphide (gm)	0.200	0.200	0.200	0.200
Propylene glycol- 400 (5%)	5ml	5ml	5ml	5ml
HPMC (gm)	2.0	4.0	6.0	8.0
PHME (1% w/v)	1	1	1	1
Triethanolamine (ml)	QS	QS	QS	QS
Methyl Parabeen (0.5%)	0.2ml	0.2ml	0.2ml	0.2ml
Propyl parabeen (0.2%)	0.1ml	0.1ml	0.1ml	0.1ml
Distill water Upto 100ml	QS	QS	QS	QS

Table 2 Formulation of Gel using Carbomer-940

CONTENTS	G5	G6	G7	G8
Sodium metabisulphide (gm)	0.200	0.200	0.200	0.200
Propylene glycol- 400 (5%)	5ml	5ml	5ml	5ml
Carbomer-940 (gm)	0.5	1.0	1.5	2.0
PHME (1% w/v)	1	1	1	1
Triethanolamine (ml)	QS	QS	QS	QS
Methyl Parabeen (0.5%)	0.2ml	0.2ml	0.2ml	0.2ml

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Propyl parabeen (0.2%)	0.1ml	0.1ml	0.1ml	0.1ml
Distill water Upto 100ml	QS	QS	QS	QS

Table 3 Formulation of Gel using Carbomer-934

CONTENTS	G9	G10	G11	G12
Sodium metabisulphide (gm)	0.200	0.200	0.200	0.200
Propylene glycol- 400 (5%)	5ml	5ml	5ml	5ml
Carbomer-934 (gm)	0.5	1.0	1.5	2.0
PHME (1% w/v)	1	1	1	1
Triethanolamine (ml)	QS	QS	QS	QS
Methyl Parabeen (0.5%)	0.2ml	0.2ml	0.2ml	0.2ml
Propyl parabeen (0.2%)	0.1ml	0.1ml	0.1ml	0.1ml
Distill water Upto 100ml	QS	QS	QS	QS

Table 4 Formulation of Gel using Sodium CMC

CONTENTS	G13	G14	G15	G16
Sodium metabisulphide (gm)	0.200	0.200	0.200	0.200
Propylene glycol- 400 (5%)	5ml	5ml	5ml	5ml
PHME (1% w/v)	1	1	1	1
Sodium CMC (gm)	1.0	2.0	3.0	4.0
Triethanolamine (ml)	QS	QS	QS	QS
Methyl Parabeen (0.5%)	0.2ml	0.2ml	0.2ml	0.2ml
Propyl parabeen (0.2%)	0.1ml	0.1ml	0.1ml	0.1ml
Distill water Upto 100ml	QS	QS	QS	QS

Table 5 Formulation of Gel using Carbomer-940 with Chitosan and Sodium Alginate

CONTENTS	G17	G18	G19	G20
Sodium metabisulphide (gm)	0.200	0.200	0.200	0.200
Propylene glycol- 400 (5%)	5ml	5ml	5ml	5ml
Carbomer-940 (gm)	0.5	1.0	1.5	2.0
Chitosan (gm)		0.2	0.1	0.1
Sodium Alginate (gm)	1.5		0.75	0.1
PHME (1% w/v)	1	1	1	1
Triethanolamine (ml)	QS	QS	QS	QS
Methyl Parabeen (0.5%)	0.2ml	0.2ml	0.2ml	0.2ml
Propyl parabeen (0.2%)	0.1ml	0.1ml	0.1ml	0.1ml
Distill water Upto 100ml	QS	QS	QS	QS

Table 6 Formulation of Gel using Carbomer-934 with Chitosan and Sodium Alginate

CONTENTS	G21	G22	G23	G24
Sodium metabisulphide (gm)	0.200	0.200	0.200	0.200
Propylene glycol- 400 (5%)	5ml	5ml	5ml	5ml
Carbomer-934 (gm)	0.5	1.0	1.5	2.0
Chitosan (gm)		0.2	0.1	0.1
Sodium Alginate (gm)	1.5		0.75	0.1
PHME (1% w/v)	1	1	1	1
Triethanolamine (ml)	QS	QS	QS	QS
Methyl Parabeen (0.5%)	0.2ml	0.2ml	0.2ml	0.2ml
Propyl parabeen (0.2%)	0.1ml	0.1ml	0.1ml	0.1ml
Distill water Upto 100ml	QS	QS	QS	QS

Table 7 Formulation of Gel using Carbomer-940 with Nutmeg oil

CONTENTS	G25	G26	G27	G28
Sodium metabisulphide (gm)	0.200	0.200	0.200	0.200
Propylene glycol- 400 (5%)	5ml	5ml	5ml	5ml

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Carbomer-940 (gm)	0.5	1.0	1.5	2.0
Span-60	1ml	1ml	1ml	1ml
Nutmeg oil (%)	0.2	0.4	0.6	0.8
PHME (1% w/v)	1	1	1	1
Triethanolamine (ml)	QS	QS	QS	QS
Methyl Paraben (0.5%)	0.2ml	0.2ml	0.2ml	0.2ml
Propyl paraben (0.2%)	0.1ml	0.1ml	0.1ml	0.1ml
Distill water Upto 100ml	QS	QS	QS	QS

Table 8 Formulation of Gel using Carbomer-940 with Coconut oil

CONTENTS	G29	G30	G31	G32
Sodium metabisulphide (gm)	0.200	0.200	0.200	0.200
Propylene glycol- 400 (5%)	5ml	5ml	5ml	5ml
Carbomer-940 (gm)	0.5	1.0	1.5	2.0
Span-60	1ml	1ml	1ml	1ml
Coconut oil (%)	0.2	0.4	0.6	0.8
PHME (1% w/v)	1	1	1	1
Triethanolamine (ml)	QS	QS	QS	QS
Methyl Paraben (0.5%)	0.2ml	0.2ml	0.2ml	0.2ml
Propyl paraben (0.2%)	0.1ml	0.1ml	0.1ml	0.1ml
Distill water Upto 100ml	QS	QS	QS	QS

Table 9 Formulation of Gel using Carbomer-940 with Lemon oil

CONTENTS	G33	G34	G35	G36
Sodium metabisulphide (gm)	0.200	0.200	0.200	0.200
Propylene glycol- 400 (5%)	5ml	5ml	5ml	5ml
Carbomer-940 (gm)	0.5	1.0	1.5	2.0
Span-60	1ml	1ml	1ml	1ml
Lemon oil (%)	0.2	0.4	0.6	0.8
PHME (1% w/v)	1	1	1	1
Triethanolamine (ml)	QS	QS	QS	QS
Methyl Paraben (0.5%)	0.2ml	0.2ml	0.2ml	0.2ml
Propyl paraben (0.2%)	0.1ml	0.1ml	0.1ml	0.1ml
Distill water Upto 100ml	QS	QS	QS	QS

Table 10 Formulation of Gel using Carbomer-934 with Nutmeg oil

CONTENTS	G37	G38	G39	G40
Sodium metabisulphide (gm)	0.200	0.200	0.200	0.200
Propylene glycol- 400 (5%)	5ml	5ml	5ml	5ml
Carbomer-934 (gm)	0.5	1.0	1.5	2.0
Span-60	1ml	1ml	1ml	1ml
Nutmeg oil (%)	0.2	0.4	0.6	0.8
PHME (1% w/v)	1	1	1	1
Triethanolamine (ml)	QS	QS	QS	QS
Methyl Paraben (0.5%)	0.2ml	0.2ml	0.2ml	0.2ml
Propyl paraben (0.2%)	0.1ml	0.1ml	0.1ml	0.1ml
Distill water Upto 100ml	QS	QS	QS	QS

Table 11 Formulation of Gel using Carbomer-934 with Coconut oil

CONTENTS	G41	G42	G43	G44
Sodium metabisulphide (gm)	0.200	0.200	0.200	0.200
Propylene glycol- 400 (5%)	5ml	5ml	5ml	5ml
Carbomer-934 (gm)	0.5	1.0	1.5	2.0
Span-60	1ml	1ml	1ml	1ml
Coconut oil (%)	0.2	0.4	0.6	0.8

PHME (1% w/v)	1	1	1	1
Triethanolamine (ml)	QS	QS	QS	QS
Methyl Parabeen (0.5%)	0.2ml	0.2ml	0.2ml	0.2ml
Propyl parabeen (0.2%)	0.1ml	0.1ml	0.1ml	0.1ml
Distill water Upto 100ml	QS	QS	QS	QS

Table 12 Formulation of Gel using Carbomer-934 with Lemon oil

CONTENTS	G45	G46	G47	G48
Sodium metabisulphide (gm)	0.200	0.200	0.200	0.200
Propylene glycol- 400 (5%)	5ml	5ml	5ml	5ml
Carbomer-934 (gm)	0.5	1.0	1.5	2.0
Span-60	1ml	1ml	1ml	1ml
Lemon oil (%)	0.2	0.4	0.6	0.8
PHME (1% w/v)	1	1	1	1
Triethanolamine (ml)	QS	QS	QS	QS
Methyl Parabeen (0.5%)	0.2ml	0.2ml	0.2ml	0.2ml
Propyl parabeen (0.2%)	0.1ml	0.1ml	0.1ml	0.1ml
Distill water Upto 100ml	QS	QS	QS	QS

Table 13 Formulation of Gel using Guar gum and Sodium alginate

CONTENTS	G49	G50	G51	G52
Sodium metabisulphide (gm)	0.200	0.200	0.200	0.200
Propylene glycol- 400 (5%)	5ml	5ml	5ml	5ml
Guar gum	2	2.5	3	3.5
Sodium alginate	0.75	1.5	2.25	3.0
PHME (1% w/v)	1	1	1	1
Triethanolamine (ml)	QS	QS	QS	QS
Methyl Parabeen (0.5%)	0.2ml	0.2ml	0.2ml	0.2ml
Propyl parabeen (0.2%)	0.1ml	0.1ml	0.1ml	0.1ml
Distill water Upto 100ml	QS	QS	QS	QS

Table 14 Formulation of Gel using Tragacanth and Sodium alginate

CONTENTS	G53	G54	G55	G56
Sodium metabisulphide (gm)	0.200	0.200	0.200	0.200
Propylene glycol- 400 (5%)	5ml	5ml	5ml	5ml
Tragacanth	2	2.5	3.0	3.5
Sodium alginate	0.75	1.5	2.25	3.0
PHME (1% w/v)	1	1	1	1
Triethanolamine (ml)	QS	QS	QS	QS
Methyl Parabeen (0.5%)	0.2ml	0.2ml	0.2ml	0.2ml
Propyl parabeen (0.2%)	0.1ml	0.1ml	0.1ml	0.1ml
Distill water Upto 100ml	QS	QS	QS	QS

Evaluation Parameters of the formulated Gels

a. Measurement of pH

The digital pH meter was used to find the pH of different gel compositions. After dissolving the gel (1 gram) in 100 ml of distilled water using the correct stirring technique, it was let to sit at room temperature for two hours. Each formulation's pH was measured three times, with the average readings being computed.

b. Viscosity study

A Brookfield Viscometer was used to measure the gel's viscosity after it was made. The gels were spun at three different speeds: 0.3, 0.6, and 1.5 revolutions per minute. The dial reading was recorded for each speed.

To find the gel's viscosity, we multiplied the dial reading by the usual value.

c. Spreadability

An equipment that had been modified inside was used to ascertain the spreadability. A wooden block is fastened to a pulley at one end to make it. This technique relied on the gels' "slip" and "drag" properties to determine the value. This block served as a mounting base for the ground glass slide. This ground slide was used to hold the excess gel, which weighed approximately 2 g. The gel was subsequently placed between two identically sized glass slides using a hook. For 5 minutes, a 100 g weight was put on top of each slide to press out air and ensure that the gel was

evenly distributed between them. The excess gel was removed by scraping it off the edges. The next step was to tie a line to the hook and draw a weight of 20 g on the top plate. The time it took for the top slide to travel 4.5 cm was then recorded in seconds. The spreadability is better when the interval is shorter. When applied to the skin or afflicted region, it reveals the maximum surface area that the gel may spread to. When two slides are subjected to a specific force, the spreadability is measured by the amount of time (in seconds) it takes for the gel between the slides to slide off. The better the spreadability, the shorter the time it takes for the top slide to cover the 4.5 cm distance across the bottom slide. A formulation's therapeutic potency is proportional to its spreading value.

It is calculated by using the formula:

$S = M \cdot L / T$ where, M = wt. tied to upper slide

L = length of glass slides

T = time taken to separate the slides

d. Stability study:

The stability study for the topical herbal gel formulation was done as per ICH guidelines in a stability chamber for a period of 6 months. The temperature and relative humidity:

25°C ± 2°C/60% ± 5% RH,

32°C ± 2°C/60% RH ± 5% RH

40°C ± 2°C/75% RH ± 5% RH.

Samples were withdrawn at an initial, first, second, third and sixth months and evaluated for change in color, odor, homogeneity, pH and viscosity [11].

e. Freeze thaw study

Phase one of the investigation involved defrosting the formulations at 25 °C for 24 hours after keeping them at 4 °C in 25 ml sintered glass bottles for 24 hours. The samples were defrosted at 40 °C for 1.5 hours after being stored at 4 °C for a further 24 hours in the second part of the investigation. Last but not least, after letting the samples settle at room temperature for an hour, they were examined for their contents [12].

In Vitro Drug release Study

Using a modified Franz diffusion cell, in vitro drug release studies were conducted on certain gel compositions. A diffusion membrane, similar to an egg

membrane, separated the cell's two compartments, the donor and the receptor. The donor chamber had an inner diameter of 24 mm and was open at one end, meaning it was exposed to the environment. The receptor chamber was designed to allow sampling. Phosphate buffer solution, with a pH of 5.8, was utilized as the diffusion medium. With the drug release membrane separating the donor compartment from the receptor compartment and the egg membrane separating the two, 1 gram of polyherbal gel was added to the donor compartment. Earlier, the egg membrane was immersed in PBS for a period of 24 hours. A clamp was used to keep the donor and receptor chambers together. To ensure that the egg membrane comes into contact with the diffusion medium, the donor compartment was positioned such that it does. A magnetic stirrer held the whole system in place. The 100 mL of PBS-filled receptor compartment was set on a magnetic stirrer that was regulated by a thermostat. The temperature was kept at 37 ± 0.5 °C and it was regularly swirled at 50 rpm. The drug content was examined using a UV Spectrophotometer at 285 nm after samples were taken at specific intervals of 0, 5, 10, 20, 30, 60, 90, 120, 180, and 240. Following each sample removal, the receptor phase was restocked with phosphate buffer in an identical amount [13].

Preparation of optimized Polyherbal Methanolic Gel

In a 100 ml beaker, 2 grams of carbopol-940 were mixed with 50 ml of distilled water while being stirred continuously. The carbopol was allowed to expand overnight in the reserved beaker. In a separate container, 5 millilitres of distilled water were heated with 0.2 millilitres of 0.5 percent methylparaben and 0.1 millilitres of 0.2% propylparaben. The correct amount of polyherbal combination (2 g for 2% gel and 5 g for 5% gel) was combined with 5 ml of 5% propylene glycol-400 and 0.2 g of sodium metabisulphide when it cooled. With constant stirring, the resulting liquid was added to a carbopol gel basis that had already been prepared. Drops of triethanolamine were applied until the pH was reached. Finally, enough distilled water was added to make the gel thick enough (Fig. 3).

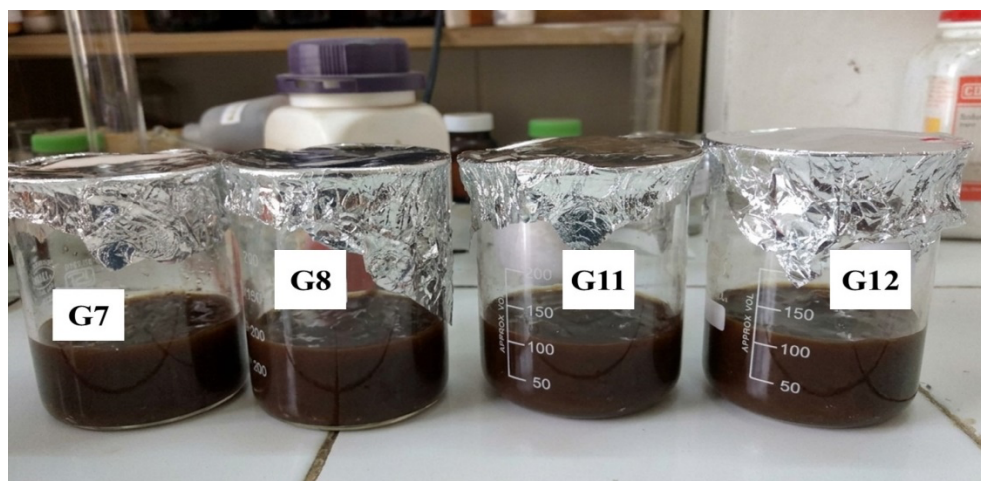


Figure 3: PHME gel with carbomer 940 (G7 and G8) and Carbomer 934 (G11 and G12).

Result

Physical evaluation parameters of formulated Gels

The formulations containing HPMC were not included for further investigation due to their uneven gel

structure and lumps. Nevertheless, physical qualities such as grittiness, homogeneity, stickiness, spreadability, and viscosity were assessed for the formulations (G5 to G56) (Table 15 to 27).

Table 15 Physical evaluation parameters of formulated Gels using Carbomer-940

Code	pH	Grittiness	Homogeneity	Stickiness	Spreadability	Viscosity(cP)
G5	6.6	-	+++	-	++	7456
G6	7.2	-	+++	-	+++	13254
G7	7.1	-	+++	-	++	9270
G8	7.2	-	+++	-	+++	25145

Table 16 Physical evaluation parameters of formulated Gels using Carbomer-934

Code	pH	Grittiness	Homogeneity	Stickiness	Spreadability	Viscosity(cP)
G9	6.5	-	+++	-	+	4565
G10	7.2	-	+++	-	+	6654
G11	7.0	-	+++	-	++	10235
G12	6.8	-	+++	-	++	12458

Table 17 Physical evaluation parameters of formulated Gels using Sodium CMC

Code	pH	Grittiness	Homogeneity	Stickiness	Spreadability	Viscosity(cP)
G13	6.4	-	+++	-	+	635
G14	7.0	-	+++	-	+	565
G15	6.8	-	+++	-	+	478
G16	6.8	-	+++	-	+	897

Table 18 Physical evaluation parameters of formulated Gels using Carbomer-940 with Chitosan and Sodium Alginate

Code	pH	Grittiness	Homogeneity	Stickiness	Spreadability	Viscosity(cP)
G17	6.8	-	+++	-	+	2040
G18	6.9	-	++	-	+++	16720
G19	6.7	-	++	-	+	9080
G20	6.8	-	++	-	+++	16200

Table 19 Physical evaluation parameters of formulated Gels using Carbomer-934 with Chitosan and Sodium Alginate

Code	pH	Grittiness	Homogeneity	Stickiness	Spreadability	Viscosity(cP)
G21	6.7	-	+++	-	+	1575

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G22	6.9	-	++	-	++	10225
G23	6.8	-	++	-	+	6325
G24	6.9	-	++	-	++	14235

Table 20 Physical evaluation parameters of formulated Gels using Carbomer-940 with Nutmeg oil

Code	pH	Grittiness	Homogeneity	Stickiness	Spreadability	Viscosity(cP)
G25	7.0	-	+++	-	++	12322
G26	7.1	-	+++	-	+++	16254
G27	7.0	-	+++	-	+++	30126
G28	7.0	-	+++	-	+++	24528

Table 21 Physical evaluation parameters of formulated Gels using Carbomer-940 with Coconut oil

Code	pH	Grittiness	Homogeneity	Stickiness	Spreadability	Viscosity(cP)
G29	6.9	-	+++	-	++	11040
G30	6.8	-	+++	-	+++	17040
G31	7.0	-	+++	-	+++	22920
G32	7.0	-	+++	-	+++	20400

Table 22 Physical evaluation parameters of formulated Gels using Carbomer-940 with Lemon oil

Code	pH	Grittiness	Homogeneity	Stickiness	Spreadability	Viscosity(cP)
G33	6.9	-	+++	-	+	6588
G34	6.7	-	+++	-	+++	13254
G35	7.0	-	+++	-	+++	18254
G36	7.0	-	+++	-	+++	20458

Table 23 Physical evaluation parameters of formulated Gels using Carbomer-934 with Nutmeg oil

Code	pH	Grittiness	Homogeneity	Stickiness	Spreadability	Viscosity(cP)
G37	6.8	-	+++	-	+	6587
G38	7.0	-	+++	-	++	10325
G39	6.8	-	+++	-	++	12365
G40	7.0	-	+++	-	++	15587

Table 24 Physical evaluation parameters of formulated Gels using Carbomer-934 with Coconut oil

Code	pH	Grittiness	Homogeneity	Stickiness	Spreadability	Viscosity(cP)
G41	6.9	-	+++	-	+	5600
G42	7.2	-	+++	-	+	7852
G43	6.8	-	+++	-	++	10265
G44	7.0	-	+++	-	++	12365

Table 25 Physical evaluation parameters of formulated Gels using Carbomer-934 with Lemon oil

Code	pH	Grittiness	Homogeneity	Stickiness	Spreadability	Viscosity(cP)
G45	7.0	-	+++	-	+	8658
G46	7.0	-	+++	-	+	10325
G47	6.9	-	+++	-	++	11257
G48	7.1	-	+++	-	++	12368

Table 26 Physical evaluation parameters of formulated Gels using Guar gum and Sodium alginate

Code	pH	Grittiness	Homogeneity	Stickiness	Spreadability	Viscosity(cP)
G49	6.8	-	+++	-	+	865
G50	6.7	-	+++	-	+	758
G51	6.9	-	+++	-	+	4236
G52	6.8	-	+++	-	+	8698

Table 27 Physical evaluation parameters of formulated Gels using Tragacanth and Sodium alginate

Code	pH	Grittiness	Homogeneity	Stickiness	Spreadability	Viscosity(cP)
G53	6.9	-	+++	-	+	758
G54	6.7	-	+++	-	+	569

G55	6.8	-	+++	-	+	3256
G56	6.9	-	+++	-	+	7569

Stability study of formulated gels

Freeze thaw studies

Before the freeze-thaw trials began, all of the samples were tested for flavonoid content. Because the amounts of extract used were diverse, the flavonoid concentration also differed between these formulations. In the initial cycle, the mixtures were frozen in 25 ml glass bottles and stored at 4 °C for 24 hours before being thawed at 25 °C for the same amount of time. During the second cycle, the samples were frozen at 4 °C for 24 hours before being thawed at 40 °C for 1.5 hours. Afterwards, the samples were left to equilibrate for one hour at room temperature before being examined for their content and other related investigations. A total 24 formulations were found to be unstable during the stability testing. Gels containing HPMC (G1 to G4) and Sodium CMC (G13 to G16) (Table 5.8) were found to have improper gel structure and hence discarded. Gels containing Carbomer 940

with Chitosan and Sodium alginate (G17 to G20) were discarded because of Clumped formation (Table 17). Fungal growth were observed gels containing Carbomer-934 with Chitosan and Sodium Alginate (G-21 to G-24) (Table 19). While separation of oil was observed within one month of study in samples containing Carbomer-940 with Coconut oil (G-29 to G-32) (Table 21) and Carbomer-934 with Coconut oil (G-41 to G-44) (Table 24). Gels containing Guar gum and Sodium alginate (G-49 to G-52) (Table 26) and Gels using Tragacanth and Sodium alginate (G-53 to G-56) were found to possess inadequate viscosity in terms of gelling property (Table 27). The Remaining 24 samples (G5-G12, G25-G28, G33-G40, G-45 to G48) appeared stable and normal with little variation in their physical properties. The graphical representation of changes in flavonoid content before and after the freeze thaw are shown in Figures 1 to 6.

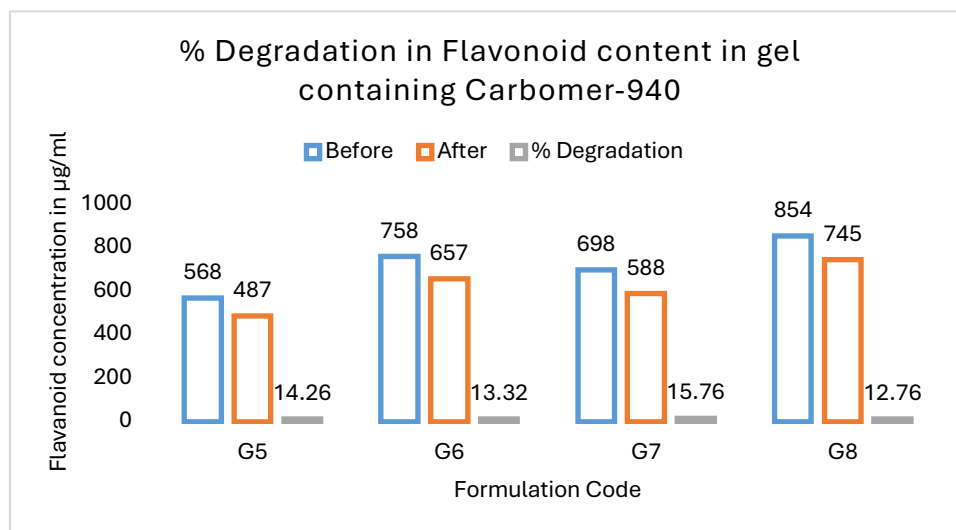


Figure 4 Flavonoid content in formulation containing carbomer-940

Sample G8 showed a minimum degradation of 12.76% of flavonoid after freeze thaw in comparison to sample G5 to G7 which showed a degradation of 14.26, 13.32 and 15.76% respectively (Fig. 4). It can be concluded

that increase in concentration of carbomer 940 results in increased stability with decreased flavonoid degradation.

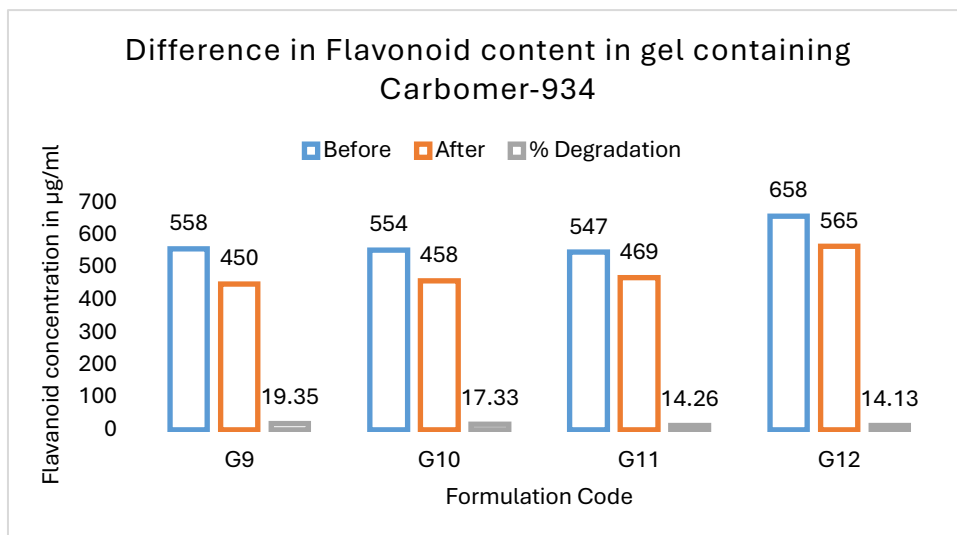


Figure 5 Flavonoid content in formulation containing carbomer-934

Sample G12 shows a minimum flavonoid degradation of 14.13% after freeze thaw while G9, G10 and G11 shows degradation of 19.35, 17.33 and 14.26 %

respectively (Fig. 5). The increased concentration of Carbomer-934 in the formulation favors the better stability with least flavonoid degradation.

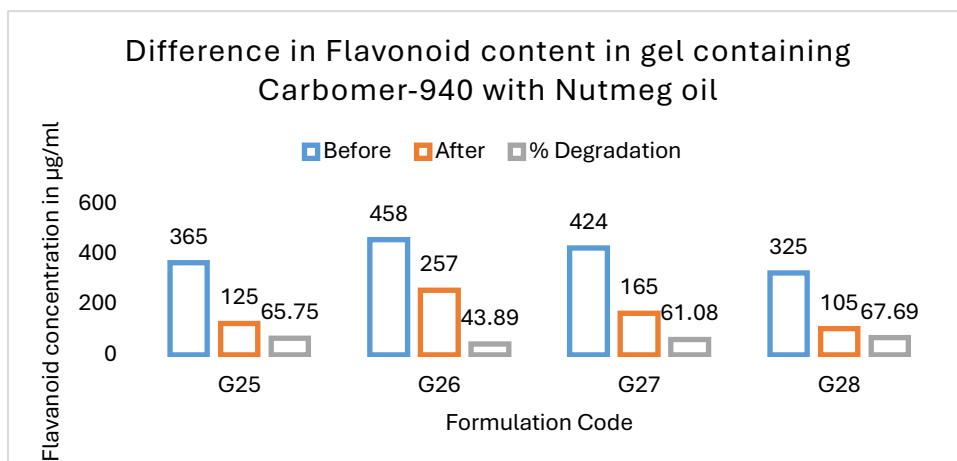


Figure 6 Flavonoid content in formulation containing Carbomer-940 with Nutmeg oil

Sample G26 showed a minimum flavonoid degradation of 43.89% after freeze thaw while G25, G27 and G28 showed 65.75, 61.08 and 67.69% respectively (Fig. 6). This shows that an optimized carbomer 940 and Nutmeg oil concentration favored better stability with

least flavonoid degradation. Furthermore, increased carbomer 940 and Nutmeg oil concentration (G27 and G28) reduced the formulation stability with increased flavonoid degradation.

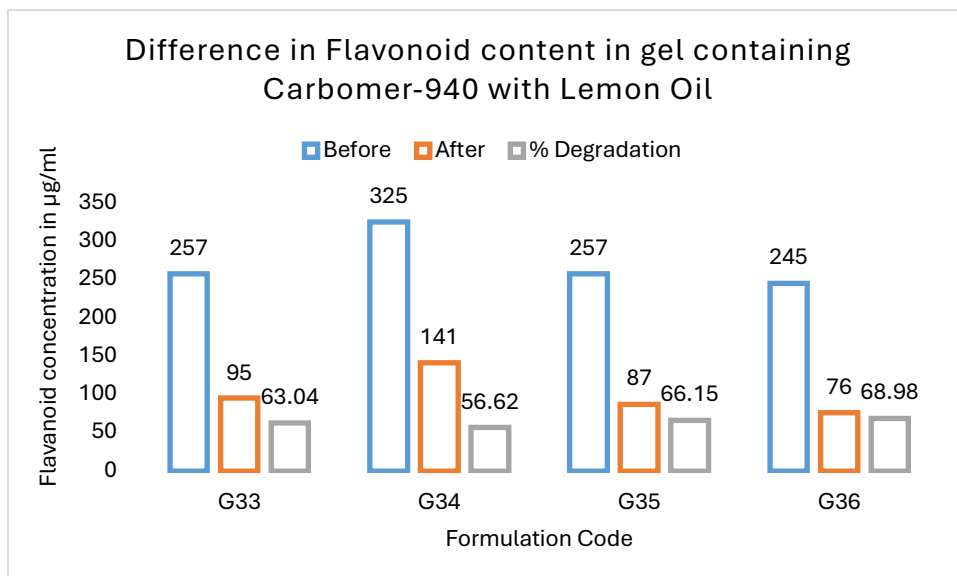


Figure 7 Flavonoid in formulation containing Carbomer-940 with Lemon oil

Sample G34 showed a minimum flavonoid degradation of 56.62% after freeze thaw while G33, F35, and G36 showed 63.04, 66.15 and 68.98% respectively (Fig. 7).

The increased in carbomer-940 and lemon oil from G35 and G36 doesn't favors the stability with increased flavonoid degradation.

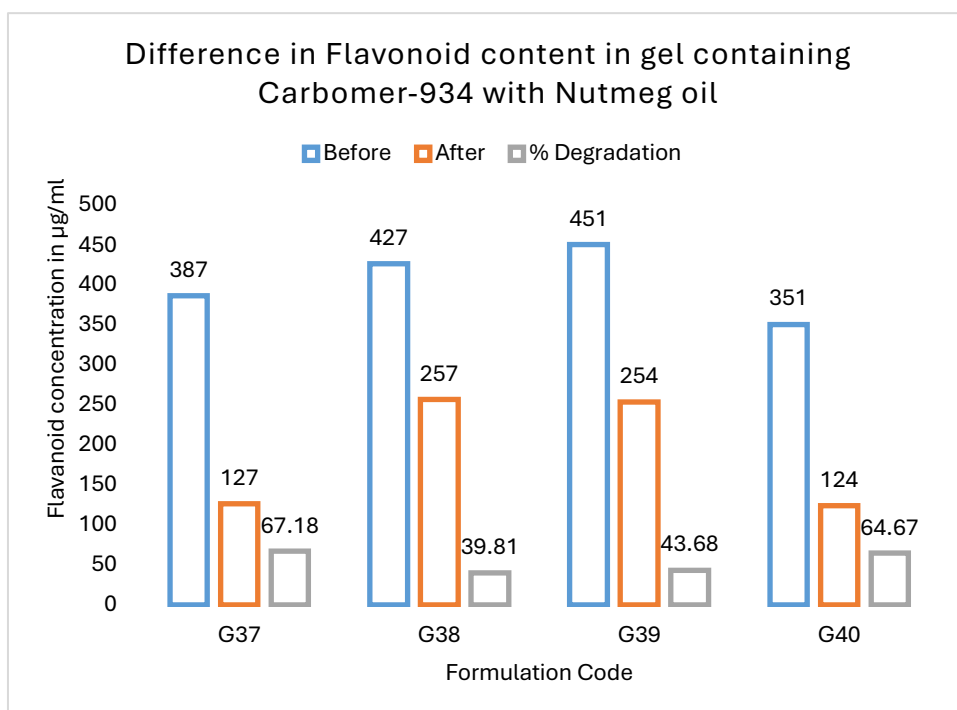


Figure 8 Change in concentration of flavonoid in formulation containing Carbomer-934 with Nutmeg oil

Sample G38 showed a minimum flavonoid degradation of 39.81% after freeze thaw while F37, F39 and F40 showed 67.18, 43.68 and 64.67% respectively (Fig. 8). However, further increase in carbomer 934 and

Nutmeg oil concentration (G39-G40) doesn't favored stability in the formulation and increased flavonoid degradation was found.

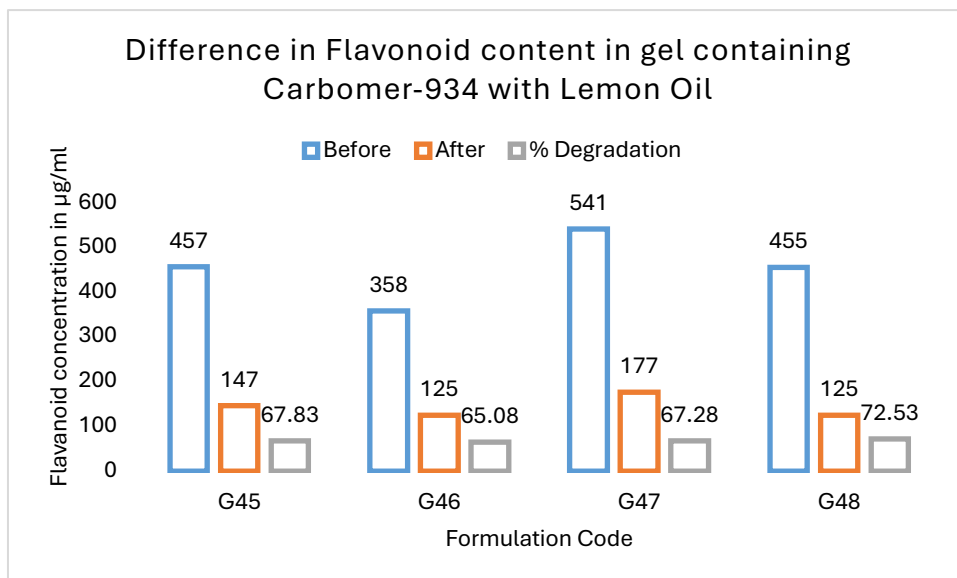


Figure 9 Flavonoid content in formulation containing Carbomer-934 with lemon oil

Sample G46 showed a minimum flavonoid degradation of 65.08% after freeze thaw while to G45, G47, and G48 showed 67.83, 67.28 and 72.53% respectively (Fig. 9). However, increased percentage of carbomer-934 and lemon oil in F47 and F48 imparts poor stability with increased flavonoid degradation.

It was found that the minimum %degradation value of 12.76% of flavonoid was found in G8 after freeze thaw as compared to other formulations. *In vitro* Drug release study was performed for selected gel formulations

having less than 20% degradation (G5 to G12) by modified franz diffusion method.

5.8. Estimation of Drug release profile of selected PHMG

Release of drug from gels were studied at various time intervals at pH 6.8 to pH 7.0. Samples were analyzed for the presence of flavonoid (Rutin) and amount released at various time intervals were interpreted. (Fig. 09 to 16). The sample G8 exhibited greater stability and extended release up to 260 min. out of from the 08 formulations.

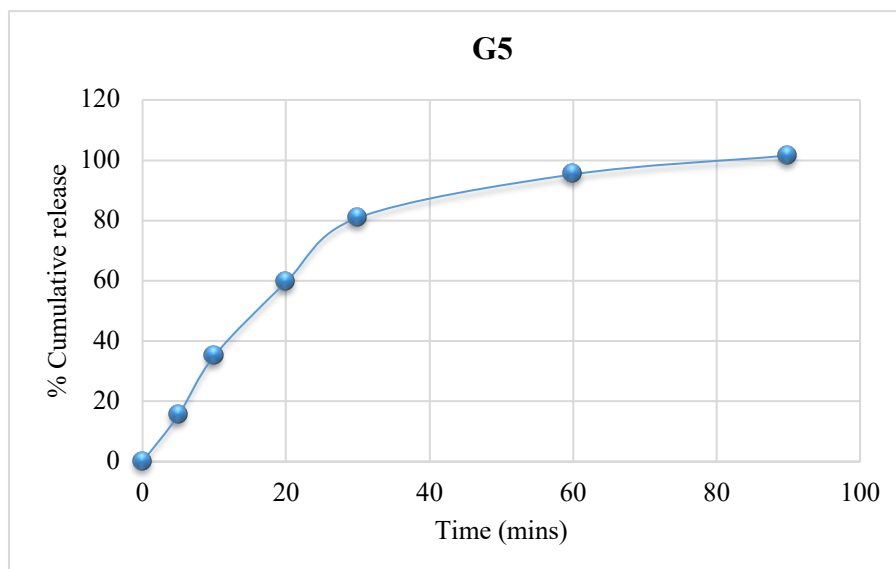


Figure 10 Drug Release profile for Formulation G5

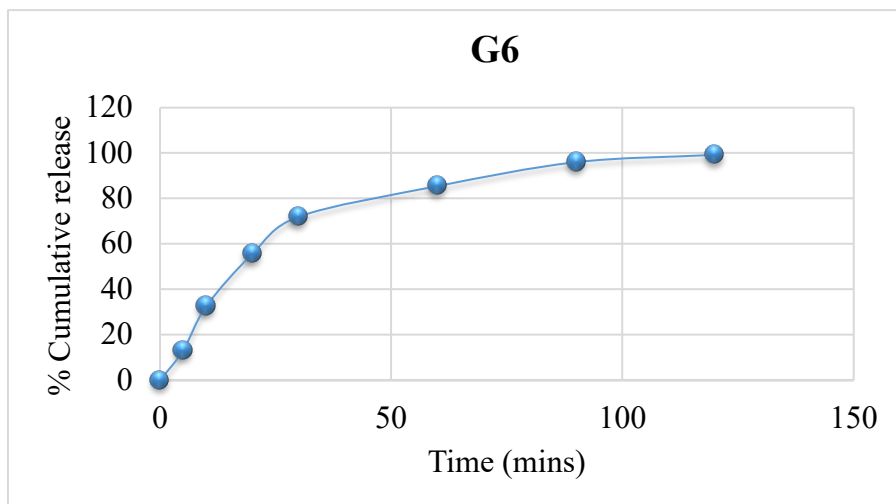


Figure 11 Drug Release Profile of formulation G6

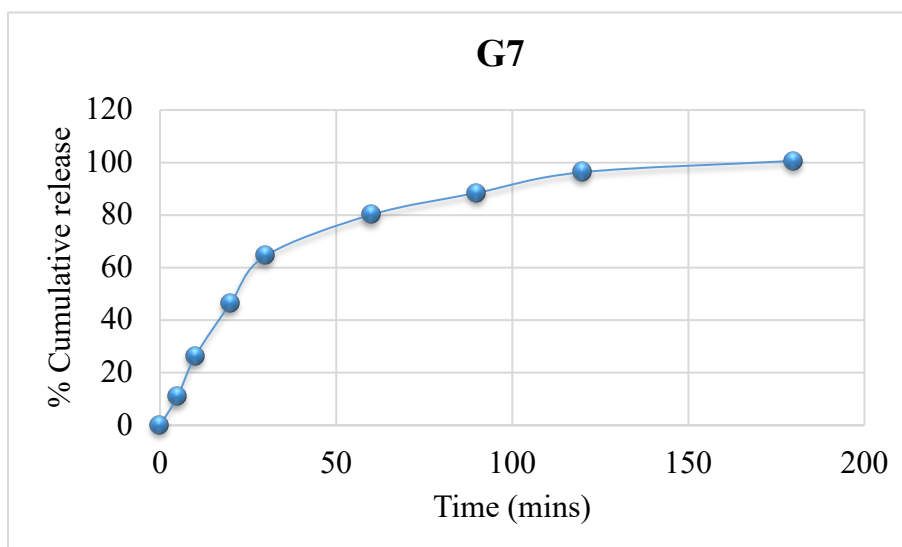


Figure 12 Drug Release Profile of formulation G7

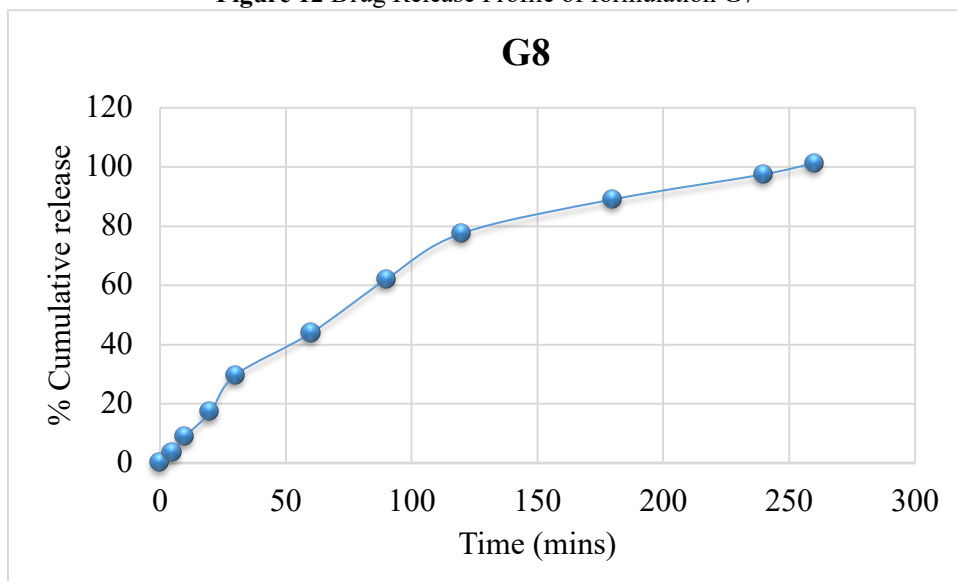


Figure 13 Drug Release Profile of Formulation G8

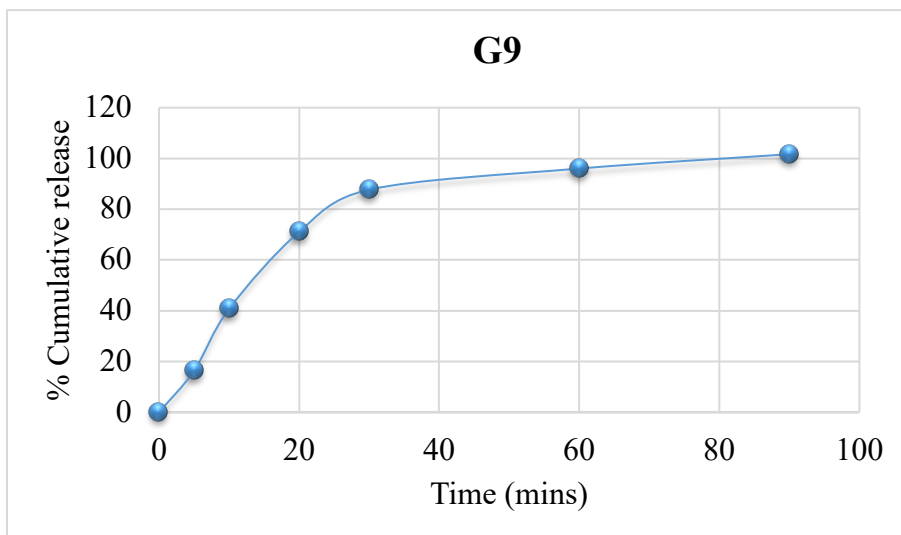


Figure 14 Drug Release Profile of formulation G9

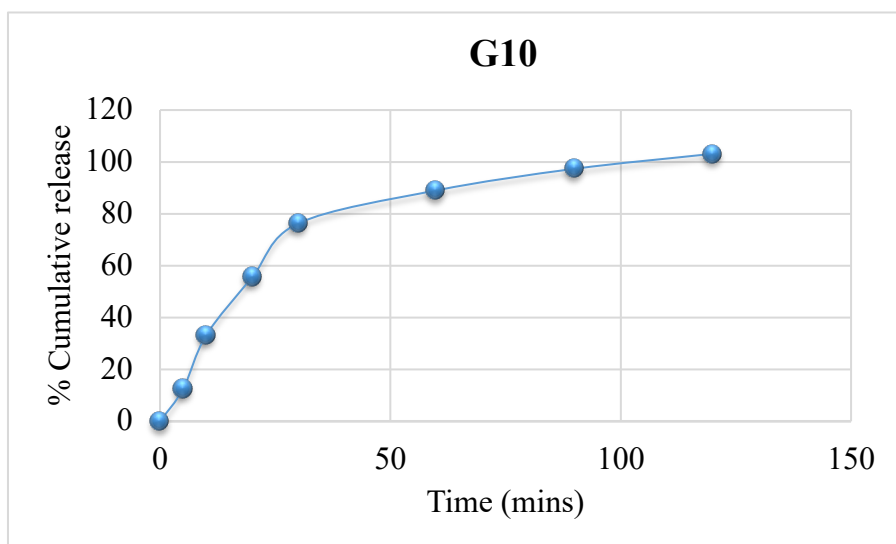


Figure 15 Drug Release Profile of Formulation G10

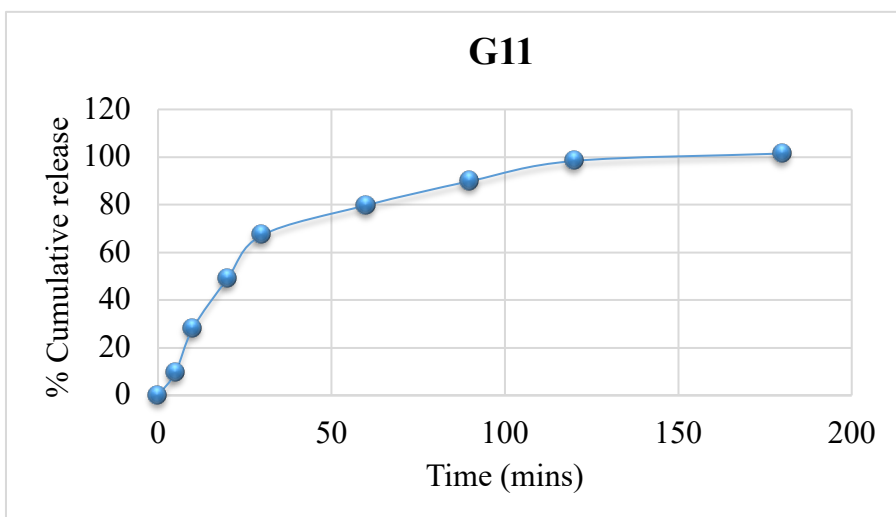


Figure 16 Drug Release Profile of Formulation G11

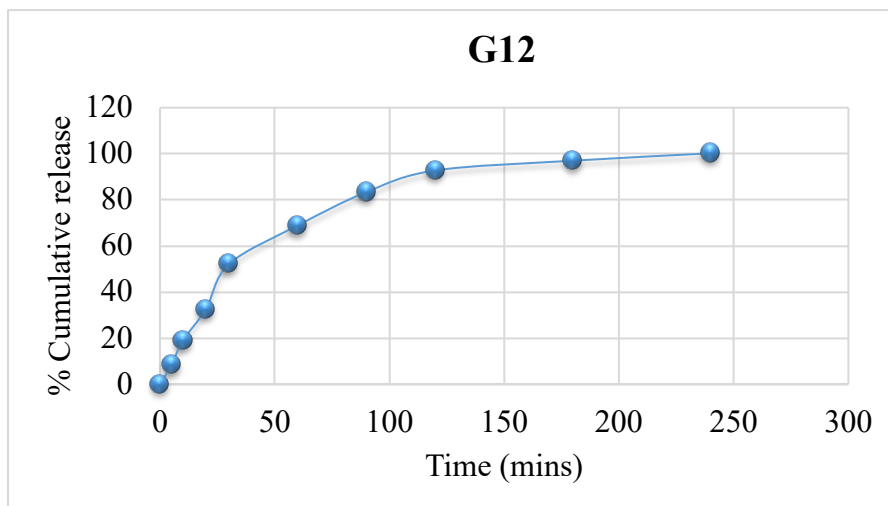


Figure 17 Drug Release Profile of Formulation G12

The G8 formulation demonstrated an extended drug release profile, sustaining the release for up to 260 minutes (Fig 13), indicating its potential for prolonged therapeutic action at the site of application. This extended release can enhance the drug's efficacy by maintaining a consistent concentration over time, reducing the need for frequent applications. Additionally, the G8 formulation exhibited optimal viscosity, which is critical for ensuring better adhesion and retention on the wound area. This enhanced viscosity facilitates prolonged contact with the wound surface, promoting localized drug availability and improving the overall wound healing process. The drug release characteristics, stability and physicochemical properties favor the selection of PHMG formulation G8 for further studies like *in-vivo* skin irritation study, *in-vivo* anti-inflammatory and wound healing activity.

Discussion

The present investigation focused on the formulation, optimization, and evaluation of polyherbal methanolic gels intended for dermatological applications. The results obtained from physicochemical evaluation, stability studies, and *in vitro* drug release collectively demonstrate the critical influence of polymer selection, excipient compatibility, and compositional balance on the performance of topical herbal gel systems [14]. The preliminary screening revealed that gels formulated using HPMC exhibited poor structural integrity, characterized by lump formation and non-uniform consistency, leading to their exclusion from further studies. This observation aligns with recent findings indicating that although HPMC is widely used as a gelling agent, its compatibility with complex polyherbal extracts is often limited due to phase separation and poor hydration behavior in the presence of phytoconstituents [15-17]. In contrast, Carbomer-based formulations (Carbomer 940 and Carbomer 934) demonstrated superior gel characteristics, including excellent homogeneity (+++), absence of grittiness, and desirable spreadability. The pH of all developed formulations ranged between 6.4 and 7.2, which is

considered ideal for topical application as it closely matches the physiological skin pH, thereby minimizing irritation potential. Similar pH ranges have been reported as optimal in recent dermatological gel formulations to ensure patient compliance and safety [18-20]. Viscosity plays a crucial role in determining the retention time and spreadability of topical formulations. Carbomer 940-based gels (G5–G8) exhibited higher viscosity (7456–25145 cP) compared to Carbomer 934 and other polymer systems, indicating better gel network formation and structural stability. Notably, formulation G8 showed the highest viscosity (25145 cP), which contributed to improved consistency and adhesion. This is in agreement with recent studies highlighting Carbomer 940 as a preferred polymer for topical gels due to its high thickening efficiency and ability to form stable hydrogel matrices [21-24]. On the other hand, formulations containing Sodium CMC and natural polymers such as guar gum and tragacanth showed significantly lower viscosity and weaker gel structures, which may compromise drug retention and therapeutic efficacy. These findings corroborate earlier reports suggesting that natural polymers, although biocompatible, often lack the mechanical strength required for stable topical formulations unless combined with synthetic polymers [25-26]. The incorporation of essential oils (nutmeg, coconut, and lemon oil) significantly influenced the physicochemical properties of the gels. Carbomer 940 formulations containing nutmeg oil (G25–G28) and lemon oil (G33–G36) maintained good homogeneity and spreadability, whereas coconut oil-containing formulations exhibited phase separation during stability studies. This may be attributed to the immiscibility of coconut oil with the aqueous gel matrix and inadequate emulsification, leading to instability. Similarly, combinations of Carbomer with chitosan and sodium alginate resulted in clumping and reduced homogeneity, indicating incompatibility between polymers. Such interactions may lead to altered rheological properties due to ionic crosslinking or polymer-polymer interactions, as supported by recent literature [27-29]. Stability is a

critical parameter for topical formulations, particularly those containing herbal extracts prone to degradation. The freeze–thaw studies revealed that out of 56 formulations, 24 were unstable due to issues such as clumping, fungal growth, phase separation, and inadequate viscosity. These findings emphasize the importance of selecting appropriate preservatives, polymers, and formulation conditions. Formulations containing Carbomer 940 and Carbomer 934 (G5–G12, G25–G28, G33–G40, G45–G48) exhibited satisfactory stability with minimal changes in physical properties. The stability of Carbomer-based gels can be attributed to their robust cross-linked polymeric structure, which resists environmental stress conditions such as temperature fluctuations. Flavonoid degradation was used as a marker for chemical stability. Among all formulations, G8 demonstrated the lowest degradation (12.76%) after freeze–thaw cycles, indicating superior stability. A clear trend was observed where an optimal concentration of Carbomer enhanced stability, whereas excessive polymer concentration or oil content led to increased degradation. This phenomenon may be explained by restricted molecular mobility within the gel matrix at optimal viscosity, which protects active constituents from degradation [30]. Conversely, formulations containing essential oils showed significantly higher flavonoid degradation (up to ~70%), suggesting that volatile components or oxidation processes may compromise stability. This observation is consistent with recent reports indicating that essential oils can accelerate degradation of phenolic compounds under stress conditions unless properly stabilized [31]. The in vitro drug release studies provided valuable insights into the performance of selected stable formulations (G5–G12). The release studies were conducted at pH 6.8–7.0, simulating physiological skin conditions. Among all formulations, G8 exhibited the most favorable release profile, sustaining drug release up to 260 minutes. The extended-release behavior of G8 can be attributed to its optimal viscosity and well-formed gel network, which controls drug diffusion. According to Fick's law of diffusion, drug release from a gel matrix is inversely proportional to viscosity; however, an optimal balance is necessary to ensure both sustained release and adequate drug diffusion. G8 appears to achieve this balance effectively. Other formulations showed comparatively faster release profiles, likely due to lower viscosity or weaker gel structures. These findings are in line with contemporary studies demonstrating that Carbomer-based gels can provide controlled drug release by modulating polymer concentration and crosslinking density [32]. The presence of flavonoids such as rutin further contributes to therapeutic efficacy due to their well-documented antioxidant, anti-inflammatory, and wound healing properties. Sustained release of such bioactive compounds enhances their bioavailability at the site of application, thereby improving clinical outcomes [33]. A strong correlation was observed between viscosity, stability, and drug release behavior. Formulations with

optimal viscosity (such as G8) demonstrated enhanced stability (minimal flavonoid degradation), improved spreadability and homogeneity and sustained drug release profile. This indicates that viscosity is a key determinant in designing effective topical gel systems. Excessively high viscosity may hinder drug release, while low viscosity may reduce retention time and stability [34-35]. Therefore, careful optimization of polymer concentration is essential.

Based on comprehensive evaluation, formulation G8 was identified as the optimized formulation due to ideal pH (7.2), suitable for skin application, excellent homogeneity and absence of grittiness, highest viscosity ensuring better retention with minimum flavonoid degradation (12.76%) indicating superior stability that impart sustained drug release up to 260 minutes. These attributes make G8 a promising candidate for further in vivo studies, including skin irritation, anti-inflammatory, and wound healing assessments. The developed polyherbal gel demonstrates significant potential for dermatological use due to its favorable physicochemical properties and sustained release profile [36-37]. Herbal formulations are increasingly preferred due to their safety, biocompatibility, and therapeutic versatility. The incorporation of flavonoid-rich extracts enhances antioxidant and anti-inflammatory effects, which are crucial for treating skin disorders such as wounds, inflammation, and infections. Recent advancements in herbal topical delivery systems emphasize the importance of polymer selection and formulation optimization to overcome challenges such as poor stability and inconsistent drug release [38]. The present study successfully addresses these challenges by identifying an optimized Carbomer-based gel system.

Conclusion

Overall, the study highlights the critical role of formulation variables in determining the quality and performance of polyherbal gels. Carbomer 940 emerged as the most suitable gelling agent, providing optimal viscosity, stability, and drug release characteristics. The optimized formulation G8 demonstrated superior performance and holds promise for effective dermatological application. Future studies should focus on in vivo evaluation and clinical validation to establish its therapeutic efficacy.

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