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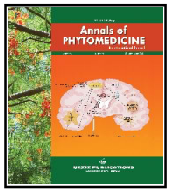

Original Article : Open Access

Formulation and evaluation of hydrogel for topical drug delivery of *Zingiber officinale* Rosc. and *Withania somnifera* (L.) Dunal to increase the bioavailability of oils for the treatment of arthritis

Dheeraj Singh Attri, Arvind Rathour, Ram Kumar Ray and Vijay Kumar◆
H.R. Institute of Pharmacy, Ghaziabad-201003, Uttar Pradesh, India

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Abstract

Medicinal plants derived drugs or formulations have been majorly contributed in maintaining the health-care system *via* targeting acute and chronic ailments. Essential oils play an important role in several skin and joint related ailments *via* exhibiting anti-inflammatory, analgesic and oxidative damage. Based in the facts, the present study is associated for development and formulation and evaluation of hydrogel for topical drug delivery of *Zingiber officinale* Rosc. and *Withania somnifera* (L.) Dunal to increase the bioavailability of oils for the treatment of arthritis. In this study, preformulation and post formulation studies were conducted to evaluate or characterised the developed formulation including stability and TEM analysis. In this study, different five formulations were developed and the outcome of the study showed that formulation one and three (F1 and F3) showed better physiochemical compatibility. The gel formulation's pH was found to be between 4.81 and 5.05 while the viscosity of F1 and F3 was found as 7220 ± 1.204 and 10340 ± 1.452. FTIR analysis showed no significant interaction between the excipients and the drugs while TEM analysis showed uniform morphology of the F1 and F3. The uniformity in the developed formulation that contributes to the uniform permeability. Hence, the formulation can be used as an effective complimentary or alternative medicine in treatment of arthritis. Although, molecular based investigation is necessary to enhance the credibility and accessibility of the developed formulation.

1. Introduction

Millions of individuals throughout the world struggle with arthritis, a common health problem. About half of all individuals with arthritis endure chronic pain, which is a major problem for patients with arthritis who battle with excruciating joint pain. There are more than 100 different kinds of arthritis. The two most prevalent kinds are rheumatoid arthritis and osteoarthritis. While having similar effects on joint structure and function, osteoarthritis and rheumatoid arthritis are not the same in terms of symptoms, aetiology, or therapies. The most prevalent form of arthritis is osteoarthritis (OA), sometimes called degenerative joint disease (*Alaaeddine et al*., 2014; Lindler *et al*., 2020). A biomechanical and inflammatory condition known as osteoarthritis (OA) is impacted by a number of variables including mechanical and obesity, oxidative stress, ageing, injury and metabolic disorders. Degeneration of the joint cartilage, alterations inside the underlying bone and synovitis are all symptoms of OA. Synovial fluid contains concentrated pro-inflammatory and pro-catabolic mediators and hydrolytic enzymes such as matrix metalloproteinases (MMPs) are associated with cartilage ageing. Breakdown of the extracellular matrix can cause an influx of immune cell cells that cause tissue damage and inflammation. OA develops slowly, frequently starting later in life and eventually results in impairment. Localized joint discomfort and pain, as well as stiffness in the morning and after periods of physical activity, are other symptoms (Holick, 2004; Shelkea *et al*., 2011). Many joints are affected by the systemic disease rheumatoid arthritis (RA), which involves immunological dysregulation and inflammation. Three variables increase the likelihood of having RA: smoking, genetics, and female gender. Seropositive or seronegative RA is determined by the presence or absence of antibodies. Seropositive individuals experience increasing inflammation and joint destruction during the duration of the illness, whereas seronegative patients initially exhibit more inflammation. In situations when the illness is severe or seropositive, extra-articular symptoms may be seen. Anti-citrullinated protein antibody (ACPA) causes pain and bone erosions while sustaining inflammation. This disease's propensity for inflammation eventually results in irreversible deformities. In general, people with RA have a high incidence of disability, with 60% of patients is unable function by at least 10 years from the beginning of the disease (Ichikawa *et al.,* 2006). RA symptoms include tightness in the morning and then after inactivity, as well as sensitive, heated and swollen joints. It is difficult to treat OA and RA effectively despite current knowledge of disease states. These suggestions for treating OA include serotonin and norepinephrine reuptake inhibitors, intra-articular corticosteroids, oral and topical non-steroidal anti-inflammatory drugs (NSAIDs), and oral analgesics. Pain and inflammation reduction are the main objective of RA therapy. Guidelines for RA vary on the stage of the illness early or advanced and the amount of disease activity. It has

Corresponding author: Mr. Vijay Kumar
Assistant Professor, Department of Pharmaceutics, H.R. Institute of Pharmacy, Ghaziabad-201003, Uttar Pradesh, India
E-mail: vijaypharma1997@gmail.com
Tel.: +91-8470052097

been previously discussed how the current medications used to treat OA and RA work (Honvo *et al*., 2019).

There are many synthetic drugs used as conventional treatments for rheumatoid arthritis, but these treatments have side effects that may hinder curative treatment, increasing the likelihood that herbal plants will be employed instead. This article reviews the medicinal plants used to treat rheumatoid arthritis (Ali *et al*., 2022; Dhama *et al*., 2022).

The bark and gummy-oleo resins of the *Boswellia serrata* Linn. have anti-inflammatory, antiarthritic, astringent, stimulant, expectorant, and antimicrobial properties. It is also known to restore the integrity of blood vessels of joints after injury or spasm. *Boswellia serrate* extract contains naturally occurring anti-inflammatory cytokines and mediators, which starts the process. Non-steroidal anti-inflammatory medicines (NSAIDs) can break down glycosaminoglycan production, which, by turning off pro-inflammatory, can speed up the articular injury in arthritic activities at places where chronic inflammation is prevalent (Sharma *et al*., 2009; Siddiqui, 2011).

Since history, medicinal plants have been used for several acute and chronic disorders, traditionally (Mehrotra, 2020; Rana *et al*., 2021). Black pepper is used as an aromatic, stimulant, stomachic and carminative. It boosts the production of gastric juices. Moreover, it makes several medications more bioavailable. Separation of piperine from black pepper (Dosoky *et al*., 2019; Lee *et al*., 2020).

Z. officinale and *W. somnifera* are the most common Indian medicinal plants that have been used for many acute and chronic ailments for treatment various acute and chronic disease such as inflammation, oxidative stress, unwanted cellular proliferation, skin infection, kidney dysfunction, brain disorders, *etc*., traditionally. Steroids, terpenes, phenols, glycosides, alkaloids are the common phytochemical in each plants that exhibits pharmacological response and thus showed multi-mechanistic and therapeutic effect against various diseases and disorders (Bahall, 2017; Birla *et al*., 2019; Biswas *et al*., 2017; Boskabady *et al*., 2020; Singh *et al*., 2010). It is beneficial for things like wound healing, hepatoprotection, and neuroprotection. It has antispasmodic, antimicrobial, anticancer, and antimutagenic qualities (Daily *et al*., 2016; Kocaadam and Anlier, 2017). Taking all these factors into consideration, the present study is associated to develop and evaluate hydrogen containing *Z. officinale* and *W.* somnifera for treatment of arthritis.

2. Material and Methods

2.1 Chemicals and instrumentations

Ginger oil, Ashwagandha oil, Carbopol 940, Propylene glycol, Span 80, Distilled water and Triethanolamine were purchased from Sisco Research Laboratories Pvt. Ltd. (SRL) India. The instrumentations such as Weighing balance (Shimadzu, Japan), pH meter (Hanna instruments, India), Magnetic stirrer (REMI, India), Transmission electron microscopy (Hitachi; H-7500), Refrigerator (LG, India) and Humidity chamber (Navyug, India).

2.2 Preformulation study

According to the definition, it is a study of the chemical and physical characteristics of the active component in drugs, both by itself and in conjunction with an excipient. To design the optimum drug delivery system, the physicochemical properties of the drug substance are defined using biopharmaceutical principles during preformulation. Prior research was conducted in this case before other dosage forms were developed. A foot forward is worth nine steps back, therefore the preformulation studies of such new product can avoid disasters from occurring in the first place.

2.2.1 Morphology study of ginger oil and ashwagandha oil

It refers to the analysis of the drug's appearance, including its size, colour, flavour and other sensory attributes including touch and texture. By virtue of the physical characteristics of medications, morphological studies enable us to comprehend several aspects of them. It is described as the study of the physical and chemical characteristics of a drug component, both by itself and in combination with a stimulant (Adhikari and Paul, 2018; Dandiya and Bapna, 1974).

2.2.2 Solubility study of ginger oil and ashwagandha oil

The capacity of a material to dissolve in an amount of fluid to create a concentrated solution at a specific temperature and pressure is known as solubility. To assess the quantitative and crude solubility of the medication, a known quantity (1 mg) was suspended in a variety of solvents at room temperature and shaken on a shaker for two hours. Crude solubility was assessed only by visual inspection. The drug's discovered solubility profile is tabulated (Chaurasia, 2016; Verma and Mishra, 2016).

2.3 Development of formulations

The gel created using the direct dispersion technique. In this initial step, carbopol-940 was continuously mixed with distilled water in a beaker using a magnetic stirrer set at 800 rpm (70°C). The carbopol 934 was left in the beaker overnight to expand for 24 h until it solidified into a homogenous mass. Propylene glycol (PEG) was added once the mix had cooled and solidified and it was thoroughly combined before ginger and ashwagandha essential oils, 100 ml of water and triethanolamine were added. The mixture was then carefully stirred till a clear gel had formed. As stated in Table 1, there were five different types of gel formulations created with different concentrations of carbopol 940, ginger oil and ashwagandha oil (Kurniawan *et al*., 2022).

Table 1: Composition of prepared gel formulation

Drug	F1	F2	F3	F4	F5
Carbopol 940	0.75 g	1 g	1.5 g	2 g	2.5 g
Ginger oil	1 ml	1.5 ml	2 ml	2.5 ml	3 ml
Ashwagandha oil	3 ml	1.5 ml	3 ml	3 ml	3 ml
Propylene glycol	2 ml	2 ml	2 ml	2 ml	2 ml
Triethanolamine	Q.s.	Q.s.	Q.s.	Q.s.	Q.s.
Distilled water	Upto 100 ml	Upto 100 ml	Upto 100 ml	Upto 100 ml	Upto 100 ml

2.4 Evaluation of gel

2.4.1 Measurement of pH

The glass electrode was fully submerged into the gel system to completely cover it and the pH of the gel was measured to use a digital pH metre (Satpathy *et al*., 2011).

2.4.2 Determination of homogeneity

The homogeneity of each generated gel was checked after it had been placed in the container using a visual inspection. They underwent inspections to check for aggregates and for outward signs of appearance (Satpathy *et al*., 2011).

2.4.3 Determination of viscosity

The Brookfield viscometer was used to determine the apparent viscosity of the gels in centipoises while maintaining a constant temperature of 25°C. Spindle No. 64 was rotated at 10 revolutions per minute (Mashinchian *et al*., 2014).

2.4.4 Determination of spreadability

The spreading ability of the gel was assessed by applying 0.5 g of the gel to a circle that was first formed on a glass plate and then using a second glass plate. A 500 g weight was allowed to rest on the upper glass plate for 5 min. When the gel had spread, the circumference of the circle was measured. This formula was used to determine the gel's spreadability (Dantas *et al*., 2016).

$$\text{Spreadability} = M \times L/T$$

where, S = spreadability

M = mass applied on the glass slide,

L = length of the diameter of spreaded gel,

T = time noted after weight applied.

2.4.5 Determination of swelling index

According to a study on the topical gel's swelling index, the polymer would expand in direct proportion to its ionic strength, concentration, and water content. In order to determine the swelling index of the manufactured topical gel, 1g of the gel was first placed separately in a 50 ml beaker containing 10 ml of 0.1 N NaoH. The samples were then removed from the beakers at different intervals and set down on a dry surface until being reweighed (Kumar and Verma, 2010). Following is the calculation of the swelling index:

$$\text{Swelling index (SW)} \% = [(Wt - Wo) / Wo] \times 100$$

where, SW % = equilibrium percent swelling

W = weight of swollen gel after time t

Wo = original weight of gel at zero time.

2.4.6 Extrudability study

The objective of the gel formulations research is to ascertain the amount of force or pressure required to extrude gel from a tube in the study of extrudability. A greater amount of extruded gel guarantees improved extrudability. This technique is based on the proportion of gel that emerges from a collapsible tube when finger pressure is applied. Using a universal tube filing machine, 10 g of gel was placed within an aluminium collapsible tube, which was then held between fingers. Finger pressure was used to compress the tube and the quantity of gel that was extruded in percentage after compression was used to gauge the formulation's extrudability (Riaz *et al*., 2017; Shivathaya *et al*., 2022).

2.4.7 FTIR spectra study

The FTIR spectra of both the methanol extract and the herbal gel formulation were obtained and compared in order to explore any potential interactions between the extract and excipients. For a formulation, the gel excipients need to work well with the drug extract (Dantas *et al*., 2016).

2.4.8 Stability studies

The stability study involves a number of tests to guarantee the stability of a therapeutic product. Gel stability investigations were carried out in accordance with standardised recommendations from the International Conference on Harmonization (ICH). All of the chosen formulations underwent a 3 month stability test at room temperature and under accelerated (40 ± 2°C/75 ± 5% RH) humidity and temperature conditions. The pH by technique established previously was used to analyse the variation in appearance in all of the chosen formulations (Kumar *et al*., 2022; Sharma, 2019)

2.4.9 Skin irritation test

In order to identify any irritation issues that would render the chosen gels inappropriate for topical application, skin irritancy tests for the gels were carried out on human volunteers. On three volunteers, skin irritancy tests for each gel were conducted. On the hand, close to the wrist, 1 g of gel was topically placed over a two square inch region, as well as any lesions and irritation/redness were noted (Shukr and Metwally, 2013).

2.4.10 Grittiness

All of the formulations were examined under a light microscope for the appearance of any detectable particle debris. As a result, it is clear that the gel preparation satisfies the criteria of being devoid of specific substance and from gritty feeling as sought for any topical preparation (Kaur and Guleri, 2013).

2.5 Transmission electron microscopy (TEM) for samples F1 and F3 for analysis

TEM analysis was conducted based on the basis of a pH, viscosity and stability study. A drop of gel was applied on a 300-mesh copper grid that had been coated with carbon to create the samples. The solution was allowed to adhere to the carbon substrate for around two minutes so that extra liquid could be sucked out using the filter paper. Thereafter, for 35 seconds, a drop of a 2 % (w/v) uranyl acetate-containing aqueous solution was administered for contrast enhancement. Again, any surplus solution was scraped off with the tip of the filter paper. After drying by air, the material was examined under a microscope (PU Chandigarh) Hitachi (H-7500) 120 KV (Londono-Calderon *et al*., 2019).

2.6 Statistical analysis

The data was represented as Mean ± SD using one way: Anova test followed by t-test. The significance level of the samples was considered at $p<0.05$ and statistical summary was represented as $*p<0.05$.

3. Results

3.1 Preformulation study

3.1.1 Morphology study of ginger oil and ashwagandha oil

The ginger oil had a light-yellow colour and had a strong aroma, while ashwagandha oil was brown in colour, had a light aroma that was distinctive and tasted bitter as shown in Figure 1 and the results are tabulated in Table 2.

3.1.2 Solubility of ginger oil and ashwagandha oil

Different solvents solubility profiles for ginger and ashwagandha oil was performed successfully. In this analysis, based on the visual investigation, the solubility of oils was determined. The medication's observed solubility profile was documented in a table and solubility indicators were compared using the different solvents including methanol, ethanol, chloroform, isopropyl alcohol and water as shown in the Tables 3 and 4.

Table 2: Morphological features of ginger oil and ashwagandha oil

S. No.	Ginger oil		Ashwagandha oil	
	Morphological feature	Results	Morphological feature	Results
1	Colour	Pale yellow	Colour	Brown
2	Odour	Aromatic	Odour	Characteristic
3	Taste	Pungent	Taste	Bitter

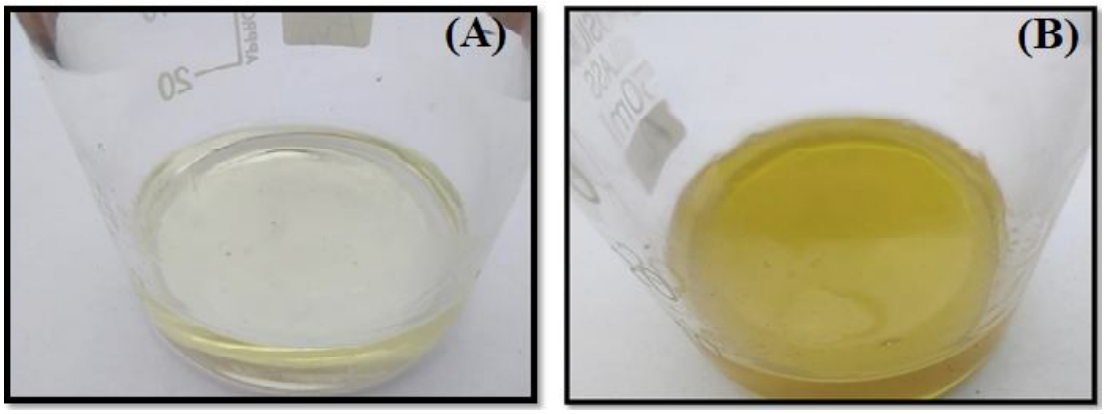

Figure 1: Morphology of ginger oil (A) and ashwagandha oil (B).

Table 3: Solubility profile of ginger oil

S. No.	Solvent	Ginger oil		Ashwagandha oil	
		Solubility	Sign	Solubility	Sign
1	Water	Slightly soluble	++	Slightly soluble	++
2	Methanol	Sparingly soluble	+++	Sparingly soluble	+++
3	Chloroform	Freely soluble	+++++	Freely soluble	+++++
4	Isopropyl alcohol	Soluble	++++	Soluble	++++

Table 4: Solubility indicators

S. No.	Solubility	Sign	Range
1	Slightly soluble	++	1-10
2	Sparingly soluble	+++	10-30
3	Freely soluble	+++++	30-100
4	Soluble	++++	100-1000

3.2 Development and evaluation of formulations

The formulations were developed as per the referenced protocol. The developed formulation according to Vijay *et al*. (2020), the unique and fragrant flavour of ginger and ashwagandha could be detected in all of the gel formulations, which were discovered to be creamy white in colour shows in Figure 2.

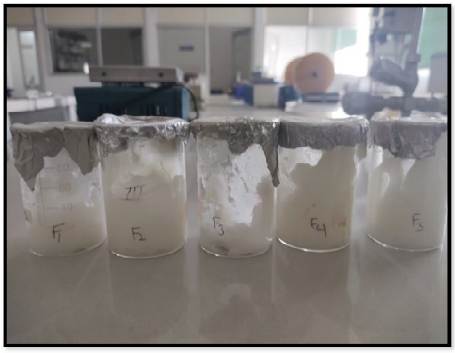

Figure 2: Visual appearance of different formulation of hydro-gel using ginger oil and ashwagandha oil.

3.2.1 pH of the gel formulation

The pH of the composition of the gel was measured using a digital pH metre. The gel formulation's pH was found to be between 4.81 and 5.05. Although, the physiological pH range of human skin is 4.5 to 5.5, topical formulations for sensitive skin regions have a slightly acidic but not neutral pH. The pH is changed by adding triethanolamine, which ranges from 4.5 to 5.5 shows Figure 3 and Table 5.

Table 5: pH of the different formulation of gel

S. No.	Formulation	pH
1	F1	5.05 ± 0.124
2	F2	5.03 ± 0.023
3	F3	5.01 ± 0.114
4	F4	4.86 ± 00.05
5	F5	4.81 ± 0.118

Figure 3: Visual appearance of pH reading different formulation of gel.

3.2.2 Appearance and homogeneity

The appearance and homogeneity of the inspection, it was determined that every gel formulation was satisfactory in terms of homogeneity, nice look, consistency and free of aggregates.

3.2.3 Viscosity of the formulation

The viscosity of the different formulation using for Brookfield DV-E Viscometer using spindle 64 was used to test the viscosity of the produced hydrogel. The dial's corresponding reading was recorded while the gels were spun at speed of 30 rpm at each speed. The findings demonstrate the viscosity of carbopol gel at different concentrations and pH tabulated in the Table 6.

Table 6: Viscosity of the different formulation of gel

S. No.	Formulation	Viscosity (Pa·s)
1	F1	7220 ± 1.204
2	F2	14080 ± 2.337
3	F3	10340 ± 1.452
4	F4	15500 ± 3.214
5	F5	18180 ± 2.148

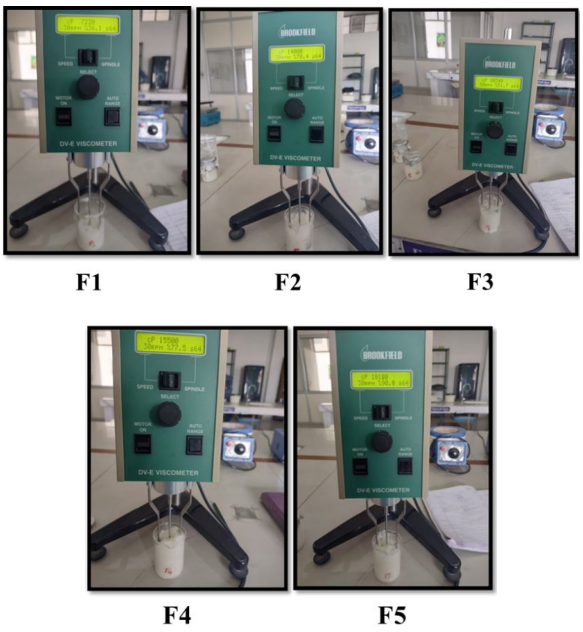

Figure 4: Visual appearance of viscosity reading different formulation of gel.

3.2.4 Determination of spreadability

According to Vijay *et al.* (2020), the gels that were created using various polymers at various concentrations were spreadable. The formulations first shown their greatest spreadability. The spreadability measurements showed that the gels could be spread with only a minimal amount of shear. The results are summarised in Table 7.

Table 7: Spreadability results of different formulation of gels

S. No.	Formulation	Spreadability (g.cm/sec)
1	F1	9.16
2	F2	8.30
3	F3	6.33
4	F4	7.50
5	F5	7.83

3.2.5 Determination of swelling index

Gels have a swelling capacity that is thousands of times greater than their dry weight. The behaviour of the swelling determines how quickly the medication is released from gel particles. The network holes open as the gel expands, allowing the medication to be released. Gel swelling research was conducted as a dynamic equilibrium study. The findings are reported in table number and visually shown in Figure 6. one may argue that the formulation's capacity to swell grew along with the amount of polymer present (Pasparakis and Bouropoulos, 2006).

Table 8: Percentage swelling index of different formulation

Time (h)	F1	F2	F3	F4	F5
0	0	0	0	0	0
1	6	22	24	27	32
2	11	32	37	41	47
3	21	41	45	53	58
4	45	54	59	65	75
5	60	67	75	81	88

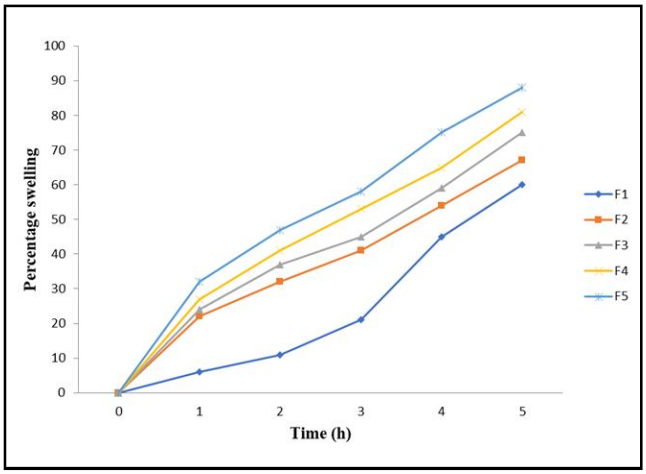

Figure 5: Percentage swelling index vs. time for formulations F1, F2, F3, F4 and F5.

3.2.6 Extrudability study

The gel to be applied and be accepted by the patient, the tube must be extruded of the gel. It is necessary to have an appropriate consistency for the gel to extrude from the tube since high consistency gels might not do so, whilst low consistency gels might flow easily. Carbopol 940-prepared formulations demonstrated good extrudability. Results are shown in Table 9 (Gupta *et al.*, 2015).

Table 9: Extrudability observation results of different formulation of gels

S.No.	Formulation	Extrudability observation
1	F1	Good (70.5 %)
2	F2	Good (73.3 %)
3	F3	Good (71.9 %)
4	F4	Good (71.6 %)
5	F5	Good (74.9 %)

3.2.7 FTIR spectroscopy

Herbal FTIR is evaluated in the 4000-400 range. As the peaks in the IR spectra of ginger oil, ashwagandha oil and their physical mixing with carbopol 934 were found to be the same, it was concluded from the FTIR interpretation that there was no interaction between the medication and the polymer employed. The physical mixing of a medication and the polymers F1 and F3 as well as the FTIR spectrum pictures of ginger and ashwagandha oils, carbopol 940 are shown in Figure 7 (Renuka and Jeyanthi, 2021).

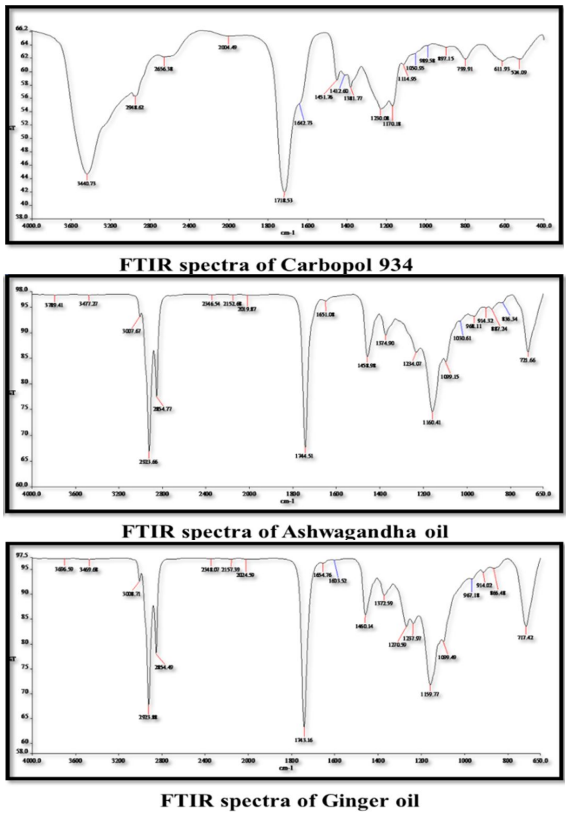

Figure 6: FTIR spectra of carbopol 934, ashwagandha oil and ginger oil.

3.2.8 Stability studies

The created gel formulation was tested for stability by storing it at 4°C, 25°C and 45°C for 90 days to determine how the 5 prepared formulations would fare under different environmental circumstances.

Table 10: Stability investigation after 15 days of various formulations

S. No.	Storage condition	F1	F2	F3	F4	F5
RT (25-28°C)	NC	NC	NC	NC	NC	NC
HC (40-45°C)	NC	NC	NC	NC	NC	NC
ReT 4°C	NC	NC	NC	NC	NC	NC

*Room temperature (RT), Humidity chamber (HC), Refrigeration temperature (ReT), No change (NC)

Table 11: Stability investigation after 30 days of various formulations

S. No.	Storage condition	F1	F2	F3	F4	F5
RT (25-28°C)	NC	NC	NC	NC	NC	CA
HC (40-45°C)	NC	NC	NC	NC	NC	CA
ReT 4°C	NC	NC	NC	NC	NC	NC

*Room temperature (RT), Humidity chamber (HC), Refrigeration temperature (ReT), No change (NC)

Table 12: Stability investigation after 45 days of various formulations

S. No.	Storage condition	F1	F2	F3	F4	F5
RT (25-28°C)	NC	NC	NC	NC	NC	CA
HC (40-45°C)	NC	NC	NC	NC	NC	CA
ReT 4°C	NC	NC	NC	NC	NC	NC

*Room temperature (RT), Humidity chamber (HC), Refrigeration temperature (ReT), No change (NC), Change in appearance (CA)

Table 13: Stability investigation after 60 days of various formulations

S. No.	Storage condition	F1	F2	F3	F4	F5
RT (25-28°C)	NC	NC	CA	NC	NC	CA
HC (40-45°C)	NC	NC	CA	NC	NC	CA
ReT 4°C	NC	NC	NC	NC	NC	NC

*Room temperature (RT), Humidity chamber (HC), Refrigeration temperature (ReT), No change (NC), Change in appearance (CA)

Table 14: Stability investigation after 90 days of various formulations

S. No.	Storage condition	F1	F2	F3	F4	F5
RT (25-28°C)	NC	NC	CA	NC	NC	CA
HC (40-45°C)	NC	NC	CA	NC	NC	CA
ReT 4°C	NC	NC	NC	NC	NC	NC

*Room temperature (RT), Humidity chamber (HC), Refrigeration temperature (ReT), No change (NC), Change in appearance (CA)

After 15 days of keeping them at room temperature in a humidity chamber, *etc*., the created gel compositions still appear the same. The formulations F2 and F5 alter their appearance after 30 to 90 days in various storage conditions, whilst the other formulations remain constant. Stability data was shown in the Tables 11, 12, 13, 14 and 15.

3.2.9 Skin irritation test

According to Kanikkannan and Singh (2022), skin irritation experiments of the chosen gel were performed on human patients and no redness/irritation was discovered on the treated surface, confirming that the created formulation was entirely safe for use on human skin (Kanikkannan and Singh, 2002).

Table 15: Skin irritation study of the different formulation of gel

S. No.	Formulation	Skin irritation study
1	F1	No irritation
2	F2	No irritation
3	F3	No irritation
4	F4	No irritation
5	F5	No irritation

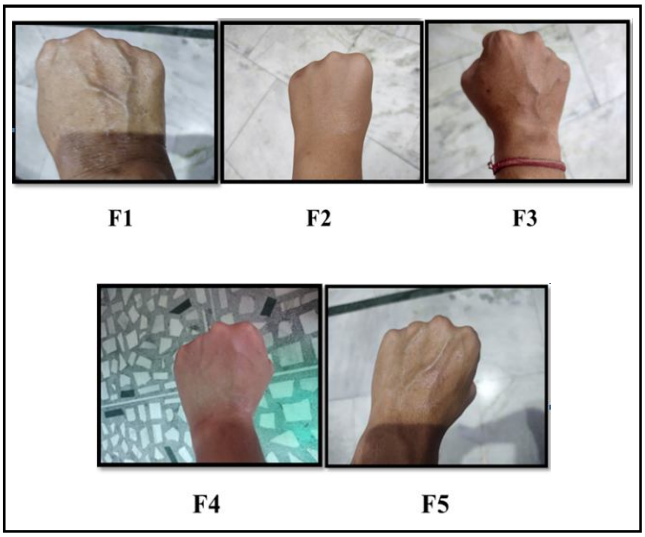

Figure 7: Visual appearance of viscosity reading different formulation of gel.

3.2.10 Grittiness

The different formulations were examined under a microscope to check for the presence of any discernible particle debris. The gel compositions lacked grittiness and particle debris (Imai *et al*., 1995).

3.3 Morphological characterization using TEM study

TEM examinations were used to conduct morphological evaluations for various formulations. For a variety of morphological investigations, the TEM equipment Hitachi (H-7500) was employed. On a copper grid with a mesh size of 300, a droplet of gel was applied to prepare the samples. The suspension was allowed to cling to the carbon substrate at around 2 min in order to give it time to sink into the carbon layer. After that, any extra liquid was removed using the filter paper's tip. The contrast was then improved for 35 sec with a drop of 2 % (w/v) hydrophilic uranyl acetate solution and once more, any extra solution was sucked off using the tip of the filter paper. The samples were dried by air and examined using a transmission electron microscope (at SAIF, PU Chandigarh) at 120 kV as shown in Figure 8 (Kumar *et al*., 2020).

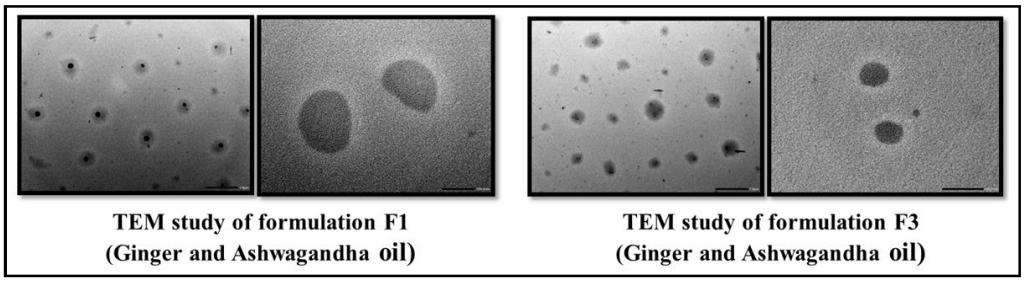

Figure 8: Morphological characterization using of TEM study of formulation 1 and formulation 3.

4. Discussion

Medicinal plants and formulation that are derived from medicinal plants have been actively playing an important role in managing healthcare system *via* contributing novel therapeutic agents for treating acute and chronic ailments (Gaurav, 2022; Gautam, 2022). For assessment of medicinal plants as the pharmaceutical's regimen, the essential oil of two different Indian medicinal plants that has been used traditional for several pharmacological activities including anti-inflammatory and antiarthritis activity, were taken for development of the formulation (Dhama *et al*., 2022; Rana *et al*., 2021).

Preformulation and post formulation studies were conducted as per the standard protocol and the study were carried out with proper SOPs as well as the suitability of chemicals and instrumentations. In preformulation studies, the parameters such as morphology and solubility of the of both oils were determined. The outcome suggest that both the samples are sparingly soluble in chloroform. Furthermore, different formulation was prepared to optimize a better formulation based on the content of drug, drug and excipient compatibility, spreadability and many physiochemical parameters.

The finding suggests that among different developed formulation, two formulation were found better that were optimized based on the pH value, viscosity, spreadability, swelling index, and excipient and drug compatibility. The study showed that formulation F1 and formulation F3 were found well optimized formulations for development of an alternative pharmaceutical gel formulation for treating inflammation or arthritis. It has been reported that *Z. officinale* and *W. somnifera* are the most active Indian medicinal plants that have been used for oxidative stress, inflammation, antibacterial, antifungal, anticancer, *etc*. (Li *et al*., 2022; Mbaveng and Kuete, 2017), (Ichikawa *et al*., 2006; Mayola *et al*., 2011; Priyanka *et al*., 2020; Zahiruddin *et al*., 2022). Medicinal plants are a good source of antioxidant and anti-inflammatory activity and thus reduced the oxidative damage in the body (Khan *et al*., 2022a, 2022b).

Nahain *et al*. (2014) reported that the plant *Z. officinale*, which is a member of the *Zingiberaceae* family, has historically been used as a complementary therapy in various nations to treat rheumatoid arthritis (RA). Many phytochemical components found in the rhizomes of this plant offer medicinal advantages, including RA relief. This review makes an effort to list those phytochemical components with their known mechanisms of action. These phytochemicals may serve as the basis for the development of novel medications that not only treat RA symptoms but also perhaps prevent bone loss caused by the disease. More studies should be conducted to clarify the molecular mechanisms underlying RA and the development of medications that can halt or reverse these processes by ginger phytoconstituents because the development of RA is a complex process (Al-Nahain *et al*., 2014).

Considering the facts and outcomes of the study, it has been suggested that the developed formulation can be the better choice of pharmaceutical for alleviating arthritis or its associated complications. The developed formulation can be the best alternatives for not only healthcare system as well as sustainable development of the Nation.

5. Conclusion

The present study concludes that out of five developed formulation 1 and 3 (F1 and 3) are considered as the most optimised formulation that showed well compatibility in physiochemical characteristic as well as showed no skin irritation. TEM analysis showed the uniformity in the developed formulation that contributes to the uniform permeability. Hence, the formulation can be used as an effective complimentary or alternative medicine in treatment of arthritis. Although, molecular based investigation is necessary to enhance the credibility and accessibility of the developed formulation.

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Conflict of interest

The authors declare no conflict of interest relevant to this article.

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