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"FORMULATION AND EVALUATION OF HYDROGEL FOR TOPICAL DRUG DELIVERY OF *ZINGIBER OFFICINALE ROSC.* AND *WITHANIA SOMNIFERA* (L.)

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Abstract:
According to the current study, among the five formulations created, formulations 1 and 3 (F1 and F3) are the most effective, exhibiting advantageous compatibility in physicochemical qualities and causing the least skin irritation. The TEM study indicated uniformity in the synthesised composition, which improved uniform permeability. As a result, the formulation may serve as an effective additional or alternative treatment for arthritis. Molecular-based research is critical for increasing the dependability and availability of created products. Medicinal plants and their preparations have significantly improved healthcare management by providing unique therapeutic agents for both acute and chronic diseases. For the assessment of medicinal plants as pharmaceutical therapies, the essential oil of two specific Indian medicinal plants, have been used for a variety of pharmacological effects, including anti-inflammatory and antiarthritic properties, was selected for formulation development. The study discovered two formulations that outperformed others in terms of, viscosity,swelling index, and excipient-medicine compatibility. The study determined that developing a unique medical gel to treat inflammation or arthritis. According to studies, Z. officinale and W. somnifera are the most efficient Indian medicinal herbs for reducing oxidative stress and inflammation while also exhibiting antibacterial, antifungal, and anticancer properties. Medicinal herbs offer potent antioxidant and anti-inflammatory properties that minimise oxidative damage in the body.

Keywords: Arthritis, Hydrogel, Antifungal, *Zingiber officinale Rosc*, *Withania somnifera* (L.), Bioavailability.

INTRODUCTION

These systems are formed by the physical or chemical crosslinking of polymer chains, which allows them to expand yet not dissolve in water. Hydrogels, softness, biocompatibility, and drug permeability,

are suited for topical and transdermal drug delivery systems.[1,8,12]

Characteristics of Hydrogels

1. Water Absorption and Swelling.

Depending on their composition and crosslinking density, hydrogels may absorb up to 90% of their weight in water. This allows them to swell without dissolving, which is useful for long- term or controlled pharmaceutical delivery.[1,2,5]

Biocompatibility and degradability.

Many hydrogels, (e.g., chitosan, gelatin, alginate), are biocompatible and biodegradable, allowing for safe in-vivo use. Stimulus- responsiveness[15,17,21]

Some hydrogels react to environmental, and ionic strength, enabling precise medication delivery to particular target locations.

Drug Delivery System.

Hydrogels can be engineered to slowly release them over time. Their porous structure enables diffusion and swelling-controlled release mechanisms.[21,22]

- **Based on cross-linking:**

Chemically cross-linked: covalent bonding.

Physical cross-linking includes hydrogen bonds, ionic interactions, and crystallites.[13]

Applications of Hydrogels

- **Topical Drug Delivery:**

Hydrogels improve medication penetration into the skin by maintaining moisture and extending contact. Their cooling and relaxing characteristics make them great for treating arthritis, burns, and wounds. [16]

- **Wound Healing:**

These gel improves wound healing by hydration, autolytic debridement, and pain reduction. [23]

Herbal Drug Delivery Using Hydrogels

It isused to deliver herbal medicines including ginger (Zingiber officinale) and ashwagandha (Withania somnifera).[32,34]

These plant-derived oils are typically volatile or poorly soluble. Encapsulating them in hydrogels increases bioavailability, retains active molecules, and enables localised, extended release at the site of inflammation (e.g., arthritis therapy). [33]

Structure and Composition

Hydrogels may be made from natural polymers including chitosan, gelatin, alginate, and xanthan gum,. They can be chemically or physically cross-linked to improve strength.[36]

Hydrogels' porous nature allows them to absorb therapeutic substances, including hydrophobic

Mechanism of Drug Release

Hydrogel matrices is commonly accomplished by diffusion, swelling-controlled release, or erosion-controlled mechanisms, depending on the polymer

type and the drug's physicochemical characteristics. Hydrogels can offer localised, sustained release in topical therapies by extending drug residence time on the skin and enhancing absorption through the stratum corneum. [45]

For example, oils strong in gingerols (from ginger) or withanolides (from Ashwagandha) can be combined with hydrogels to gently release these compounds at the site of inflammation, retaining effective medicine levels and minimising the need for recurrent application.[47]

Advantages in Topical Herbal Drug Delivery

1) Hydrogels enhance drug retention and stability by entrapping herbal oils in a polymeric matrix, preventing environmental deterioration such as oxidation and volatilization. [41]
2) Hydrogels improve skin permeability by hydrating and softening the stratum corneum, allowing active molecules to penetrate more effectively. [51]
3) Hydrogels are non-greasy and easy to apply, reducing residue and enhancing patient compliance. [46,23]
4) Compatible with Herbal Extracts: Hydrogels enable the inclusion of various phytochemicals, volatile oils, and essential extracts without affecting their activity or stability. [22]

These polymers can be modified to produce hydrogels with particular mechanical strength, rheology, and release kinetics based on the therapeutic requirement.

Challenges and Considerations

Despite its potential, hydrogel compositions confront some limitations, including:

- Some synthetic polymers and preservatives might cause skin sensitivity.
- High water content leads to microbial infection, requiring preservatives.
- These constraints can be overcome using nanoemulsion-based gels, bioadhesive polymers, or natural preservatives such as neem extract or vitamin E.[26]

Topical Hydrogels

Topical hydrogels are semi-solid systems composed of a network of hydrophilic polymers floating in water or aqueous solvents that are applied to the skin or mucous membranes to deliver targeted therapeutic effects. They are beneficial for medication administration because they retain moisture, offer cooling effects, and increase drug absorption across the epidermal barrier.

Herbal Drug-Loaded Topical Hydrogels

Hydrogels have been used to deliver herbal oils and extracts with anti-inflammatory and analgesic properties, such as Zingiber officinale (ginger) and Withania somnifera (ashwagandha). Encapsulating them in a hydrogel matrix improves their skin permeability and absorption at the site of inflammation, such as arthritis or joint disorders.[2]

2. DRUG AND EXCIPIENT PROFILE

2.1 Carbopol 940 [23]

Parameter	Details
Category	Synthetic polymer and gelling agent
Cemical stucture	COOH | ...-CH2-CH--CH2-CH-COOH--CH2-CH-... | COOH
Function	Constitutes the hydrogel matrix, imparting viscosity and stability.
Appearance	White, fluffy, dry powder
Solubility	Water expands, forming a gel upon neutralization.
Concentration	Typically 0.5–1.5% w/w
Mechanism	Expands following hydration and neutralization with TEA to create a gel matrix.
Role in Formulation	Regulates medication release, enhances spreadability, and increases retention on the skin.
Advantages	Non-irritating, non-greasy, facilitates prolonged medication release

2.2. Ginger Oil (*Zingiber officinale*) [25]

Parameter	Details
Category	Herbal active ingredient / Essential oil
Chemical structure	HO | OCH3—[[Benzene Ring]]—CH2—CH2—CO—CH2—CH(OH)—(CH2)4—CH3
Key Phytoconstituent	6-Gingerol, shogaols
Function	Provides anti-inflammatory, analgesic, and antioxidant effects
Solubility	Oil-soluble
Concentration	2–5% w/w (varies with formulation)
Mechanism	Reduces pro-inflammatory mediators (e.g., TNF-α, IL-6), inhibits COX-2
Role in Formulation	Main therapeutic agent for joint inflammation relief
Advantages	Natural origin, effective at low concentrations, skin-permeable

2.3. Ashwagandha Oil (*Withania somnifera*) [26]

Parameter	Details
Category	Herbal active ingredient / Medicinal oil
Chemical structure	O / \ Steroid backbone — Epoxy ring | OH (C-4) | Long lactone side chain
Key Phytoconstituent	Withaferin A, withanolides
Function	Anti-inflammatory, immunomodulatory, anti-arthritic effects
Solubility	Oil-soluble

Concentration	2–5% w/w (formulation dependent)
Mechanism	Modulates inflammatory pathways, reduces joint stiffness
Role in Formulation	Enhances therapeutic action synergistically with ginger oil
Advantages	Well-tolerated, herbal origin, bioactive delivery through skin

2.4. Propylene Glycol [28]

Parameter	**Details**
Category	Humectant / Solvent / Penetration enhancer
Chemical structure	OH | CH3—CH—CH2—OH
Function	Solubilizes oils, enhances dermal penetration of actives
Solubility	Miscible with water and alcohols
Concentration	5–15% w/w
Mechanism	Increases stratum corneum permeability by disrupting lipid structure
Role in Formulation	Improves delivery of ginger and ashwagandha oils across skin
Advantages	Non-toxic, improves stability and skin absorption of actives

2.5. Triethanolamine (TEA) [32]

Parameter	**Details**
Category	Neutralizing agent / pH adjuster
Chemical structure	HOCH2CH2 | HOCH2CH2—N—CH2CH2OH
Function	Neutralizes Carbopol to form a stable gel
Solubility	Miscible with water
Concentration	0.5–1.0% w/w
Mechanism	Raises pH to allow Carbopol cross-linking and gel formation
Role in Formulation	Ensures gel consistency and skin-compatible pH
Advantages	Mild, non-irritant, commonly used in topical preparations

3. MATERIALS AND METHODS

3.1 Chemicals and instrumentations:

Sisco Research Laboratories Pvt. Ltd. (SRL) in India supplied ginger oil, ashwagandha oil, carbopol 940, propylene glycol, span 80, distilled water, and triethanolamine. 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).

3.1.1 Preformulation study:

According to the definition, it is the study of hydrogel active ingredient in medications, both alone and in combination with an excipient. Preformulation uses biopharmaceutical principles to A foot forward is worth nine steps back, therefore preformulation studies for such novel products help prevent disasters from arising in the first place. [38]

3.1.2 Morphology study of ginger oil and ashwagandha oil:

It refers to the examination of the drug's appearance, including size, color, flavor, and other sensory characteristics such as touch and texture. Morphological studies allow us to understand numerous features of drugs based on their physical qualities.

3.1.3 Solubility study of ginger oil and ashwagandha oil

Solubility refers to a material's ability to dissolve in a certain amount of fluid to form a concentrated solution at a given temperature and pressure. To study of quantitative and crude solubility, a known quantity (1 mg) was suspended in several solvents at room temperature and shaken on a shaker for two hours. Visual inspection was the only method used to measure crude solubility. The drug's found solubility profile is listed. [22]

1.1 Development of formulations:

The gel was generated utilizing the direct dispersion technique. In this first phase, carbopol-940 was constantly combined with distilled water in a beaker with a magnetic stirrer set to 800 rpm (70°C). The carbopol 934 was left in the beaker overnight to expand for 24 hours before solidifying into a homogeneous mass. Propylene glycol (PEG) was added when the mixture had cooled and solidified, and properly mixed before adding ginger and ashwagandha essential oils, 100 mL of water, and triethanolamine. The mixture was gently mixed until a clear gel formed. Aa see in figure Table, five distinct gel formulations were developed using varying quantities of carbopol 940, ginger oil, and ashwagandha oil.

1.1.1 FTIR spectra study

The FTIR spectra of the methanol extract and the herbal gel formulation were collected and compared to identify any potential attechments between the extract and the excipients. The gel excipients in a formulation must be Suitable with the drug extract.

1.1.2 Stability studies

The stability study to ensure the stability of a therapeutic substance. Gel stability studies were conducted in accordance with the International Conference on Harmonization's (ICH) standardized standards. The formulations were tested for stability over three months at room temperature and under accelerated humidity and temperature conditions (40 ± 2°C/75 ± 5% RH). The previously described pH approach was utilized to analyze the variation in appearance in all of the chosen formulations.

1.1.3 Skin irritation test

Skin irritancy tests on human volunteers were conducted to discover any irritation issues that would make the chosen gels unacceptable for topical application. On the hand, around the wrist, 1 g of gel was topically put across a two square inch region, and any lesions, irritation, or redness were documented .

1.1.4 Grittiness

All formulations were checked under a light microscope for the presence of identifiable particle debris. As a result, it is obvious that the gel preparation meets the criterion of being free of specific substances and having a gritty texture, as desired for any topical preparation.

- **Transmission electron microscopy (TEM) for samples F1 and F3 for analysis:**

  A pH, viscosity, and stability investigation served as the foundation for TEM examination. on make the samples, a drop of gel was placed on a 300-mesh copper grid coated with carbon. The solution was allowed to cling to the carbon substrate for approximately two minutes so that any excess liquid could be sucked off using filter paper. A drop of a 2% (w/v) uranyl acetate aqueous solution was then injected for 35 seconds to increase contrast. Again, any excess solution was scraped off with the tip of the filter paper. After air drying, the material was inspected using a microscope (PU Chandigarh) Hitachi (H-7500) 120 KV.

- **Statistical analysis:**

The data was displayed as Mean ± SD using the Anova test followed by a t-test. Samples were considered significant at $p < 0.05$.

2. RESULTS AND DISCUSSION

4.1. PREFORMULATION STUDIES

4.1.1 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.

4.1.2 Solubility of ginger oil and ashwagandha oil

Different solvent solubility characteristics for ginger and ashwagandha oil were successfully tested. The solubility of oils was tested in this examination via a visual inspection. The medication's observed solubility profile was reported in a table, and solubility indicators were compared using various solvents (Tables 4.2 and 4.3).

Table 4.2: Solubility profile of ginger oil

Sn.	Solvent	Ginger Solubility	Sign	Ashwagandha 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	+++ +

S.n.	Solubility Term	Sign	Range (parts solvent per part solute)
1.	Slightly soluble	++	1–10
2.	Sparingly soluble	+++	10–30
3.	Freely soluble	++++	30–100
4.	Soluble	+++ +	100–1000

Table 4.3: Solubility indicators

4.2 Development and evaluation of formulations

The formulations were created in accordance with the referenced protocol. The unique and fragrant flavour of ginger and ashwagandha could be recognized the result.

pH of the gel formulation

The pH of the gel composition was determined by pH meter. The pH ranged from 4.81 to 5.05. Although the physiological pH range of human skin is 4.5 to 5.5, topical treatments for sensitive skin regions have a slightly acidic, rather than neutral, pH. The pH is adjusted by adding triethanolamine, which ranges from 4.5 to 5.5

Table 4.4 : pH of the different formulation of gel

S. No.	Formulation	pH (Mean ± SD)
1	F1	5.05 ± 0.124
2	F2	5.03 ± 0.023
3	F3	5.01 ± 0.114
4	F4	4.86 ± 0.050
5	F5	4.81 ± 0.118

4.2.1 Appearance and homogeneity

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

4.2.2 Viscosity of the formulation

The viscosity measured by using a Brookfield DV E Viscometer with spindle 64 to determine the viscosity. The dial's corresponding reading was recorded while the gels were spun at 30 rpm for each speed. The results show the viscosity of carbopol gel at various concentrations and pH levels, as shown in Table 4.5 .

Table 4.5 :

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

4.2.3 Determination of spreadability

The gels made with various polymers at different concentrations were spreadable. The formulations initially shown their highest spreadability. The spreadability measurements revealed that the gels could be spread with a minimum of shear. The findings are summarized in Table 4.6 .

Table 4.6 : Spreadability results of different different formulation of gel

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

Table 4.8 : Extrudability observation results of 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%)

4.2.4 Determination of swelling index

Gels can swell thousands of times their dry weight. The swelling's conduct dictates how quickly the drug is released from the gel particles.. Gel swelling research was carried out as a dynamic equilibrium study. The see in table format and visually in Figure 4.5 . One may claim that the formulation's ability to swell increased with the amount of polymer present.

4.2.5 Extrudability study

To apply the gel and have it approved by the patient, the gel must be extruded from the tube. It is vital to have a suitable consistency for the gel to extrude from the tube, since high consistency gels may not do so, while low consistency gels may flow freely. Carbopol 940-prepared formulations showed good extrudability. Table 7.8 shows the results.

4.2.6 FTIR spectroscopy

The 4000-400 spectral range is used to analyze herbal FTIR. The FTIR analysis showed that there was no interaction between the medicine and the polymer utilized because the peaks in the IR spectra of ginger oil, ashwagandha oil, and their physical mixing with carbopol 934 were the **Stability studies.**

The gel storing it at 4°C, 25°C, and 45°C for 90 days to see how the five prepared formulations would perform under various environmental conditions**.**

S. No.	Storage Condition	F1	F2	F3	F4	F5
1	RT (25–28°C)	NC	NC	NC	NC	NC
2	HC (40–45°C)	NC	NC	NC	NC	NC
3	ReT (4°C)	NC	NC	NC	NC	NC

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

Table 4.10 : Stability investigation after 30 days of various formulations

S. No.	Storage Condition	F1	F2	F3	F4	F5
1	RT (25–28°C)	NC	NC	NC	NC	NC
2	HC (40–45°C)	NC	NC	NC	NC	CA
3	ReT (4°C)	NC	NC	NC	NC	NC

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

Table 4.11: Stability investigation after 45 days of various formulations

S. No.	Storage Condition	F1	F2	F3	F4	F5
1	RT (25–28°C)	NC	NC	NC	NC	NC
2	HC (40–45°C)	NC	NC	NC	NC	CA
3	ReT (4°C)	NC	NC	NC	NC	NC

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

Table 4.12: Stability investigation after 60 days of various formulations

S. No.	Storage Condition	F1	F2	F3	F4	F5
1	RT (25–28°C)	NC	NC	NC	NC	CA
2	HC (40–45°C)	NC	CA	NC	NC	CA
3	ReT (4°C)	NC	NC	NC	NC	NC

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

Table 4.13: Stability investigation after 90 days of various formulations

S. No.	Storage Condition	F1	F2	F3	F4	F5
1	RT (25–28°C)	NC	CA	NC	NC	CA
2	HC (40–45°C)	NC	NC	NC	CA	NC
3	ReT (4°C)	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 being kept at room temperature in a humidity chamber, etc., the gel compositions generated remain unchanged. The formulas F2 and F5 change appearance after 30 to 90 days in various storage circumstances, whilst the other formulations remain stable. Tables 11, 12, 13, 14, and 15 presented stability data.

4.2.7 Skin irritation test

Skin irritation studies of the chosen gel were done on human patients, and no redness/irritation was observed on the treated surface, demonstrating that the formulation was suitable ,better for use on human skin .

Table 4.14: 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

4.2.8 Grittiness

The different formulations were examined under a microscope to identify of any discernible particle debris. These are lacked grittiness and particle debris.

4.3 Morphological characterization using TEM study

TEM examinations was beneficial to conduct morphological evaluations for various formulations. For morphological investigations, the TEM equipment Hitachi (H-7500) was employed. On a copper grid with a mesh size of 300, a droplet of gel were useful to prepare the samples. The suspension was placed 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 gels were dried by air and seen using a transmission electron microscope at 120 kV.

SUMMARY AND CONCLUSION

The study selects formulations 1 and 3 (F1 and F3) as the best candidates for creating a new medicinal gel to treat inflammation

or arthritis. These formulations have favourable physicochemical properties, little skin irritation, and a consistent composition, making them a suitable supplemental or alternative therapy for arthritis. Molecular-based research is critical for increasing the credibility and accessibility of the developed product. The study developed formulations with the essential oils of two Indian medicinal herbs, Z. officinale and W. somnifera. Preformulation and postformulation experiments were carried out to assess the

treating diabetes problems. More study is needed to establish the precise mechanism behind the extract's antidiabetic effect.

structure and solubility of the oils. The studies revealed a restricted solubility in chloroform. Other formulations were created to improve drug content, compatibility with excipients, spreadability, and other physicochemical qualities. The study discovered that Z. officinale and

W. somnifera are the most effective Indian medicinal herbs for reducing oxidative stress and inflammation, as well as possessing antibacterial, antifungal, and anticancer activities.

The extract's antidiabetic action was investigated in preclinical tests on STZ-induced diabetic rats, and it showed insulin mimetic activity and blood sugar control equivalent to the reference medication, glibenclamide, at 10 mg/kg. Finally, the extract is both safe and beneficial in

treating diabetes problems. More study is needed to establish the precise mechanism behind the extract's antidiabetic effect.

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