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Formulation And Evaluation Of Transdermal Herbal Gel Formulation Containing Ethanolic Extract Of *Zingiber Officinale*

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Abstract:

Because of widespread cultural approval. Strong acceptance by human body, and reduced occurrence of side effects, about 75-80% of the worldwide population, especially in less developed areas, continues to favor herbal remedies as their main option for fundamental healthcare. Herbal treatments comprise botanical or plant-based components and serve to address injuries, infections, and ailments. They are also employed for preventive health measures and to facilitate the recovery process. This research explored the possible therapeutic advantages of *Zingiber officinale*, commonly recognized as ginger, a naturally occurring anti-inflammatory substance with extensive culinary use. Numerous investigations have highlighted the advantages of ginger in managing conditions such as morning sickness, chronic dyspepsia, hypoglycemia, risk factors for heart disease, chemotherapy-induced nausea, and menstrual discomfort. Ginger ethanolic extract preparations in the form of transdermal gel consist of different concentrations and combinations of Carbopol 934 and Carbopol 940. All gel formulations exhibited favorable characteristics such as Spreadability, uniformity, Viscosity, and extrusion. Among these compositions, formulation F3, which contains Carbopol 934, displayed the highest release of the active ingredient in vitro and the ethanolic extract demonstrated significant anti-inflammatory effects in vitro.

KEYWORDS:-Extraction, Zingiber officinale, Transdermal gel, Anti-inflamatory activity, Gel

INTRODUCTION:-

Inflammation:

Inflammation is a multifaceted response often linked with discomfort and characterized by events like increased blood vessel permeability, protein changes, and cellular membrane modifications. This reaction occurs when the body's cells are compromised by pathogens, physical impacts, or harmful chemicals, presenting the damage as a form of stress.(1) Essentially, tissue inflammation arises as a protective mechanism against this stress. This defensive action manifests as redness, pain, warmth, swelling, and a reduction in normal functionality at the affected site. It serves as one of the body's general protective measures.

Inflammation's primary role is to neutralize, confine, or eliminate intruding harmful agents, simultaneously triggering a series of healing processes. Typical inflammation triggers include infections, burns, physical injuries, and numerous immune system reactions.(2) Inflammation can manifest in different forms:
Immediate Inflammation: This represents a brief reaction to an injury or infection, marked by indicators such as redness, warmth, swelling, discomfort, and reduced functionality. This rapid inflammatory response plays a vital role in the body's defense mechanisms, aiding in the removal of the underlying threat. Another chronic inflammation is an extended, mild reaction that persists for weeks, months, or even years. It is linked to several long-term health conditions such as arthritis, cardiovascular disease, and certain autoimmune disorders.(3)

Transdermal Drug Delivery System:
Transdermal drug delivery involves the administration of medications through the skin to attain systemic therapeutic effects. This method of delivering drugs presents various benefits, including convenience, extended drug release, and bypass the digestive system.. Here are the key aspects of transdermal drug delivery.(4)
Transdermal gel is a topical medication that is applied to the skin, and it is designed to be absorbed through the skin into the bloodstream. It is often used for the slow and controlled release of medications, providing a convenient and non-invasive way to deliver drugs into the body. This form of medication delivery is commonly used for hormone replacement therapy, pain management, and other medical treatments.
Transdermal gels, and transdermal drug delivery systems in general, offer several advantages(5):
Bypass First-Pass Metabolism: Oral medications undergo first-pass metabolism in the liver, which can significantly reduce the amount of active drug available to exert a therapeutic effect. Transdermal gels bypass the liver, allowing for a greater bioavailability of the drug.

Steady Drug Release: Transdermal gels can provide continuous and controlled drug delivery, resulting in steady plasma levels of the drug. This can reduce the peaks and troughs associated with oral or injectable dosing, potentially leading to a more consistent therapeutic effect.

Improved Patient Compliance: Transdermal gels can be more convenient for some patients, leading to better adherence to the treatment regimen. This is particularly true for medications that require frequent dosing when taken orally.

Reduced Side Effects: By maintaining steady drug levels and avoiding the gastrointestinal tract, transdermal gels might reduce the potential for certain side effects.

Non-Invasive: Transdermal gels eliminate the need for injections, reducing the potential for injection-site reactions and avoiding the complications of intravenous administration.

Versatility: The gels can be easily removed if there is an adverse reaction, or if the patient wishes to discontinue treatment. This offers a level of control that isn't present with oral or injectable forms.

Targeted Delivery: Some transdermal gels can be formulated to provide localized drug delivery, which can be beneficial for treating conditions in a specific area of the body without affecting the entire system.

Less Gastrointestinal Irritation: Since the drug does not pass through the stomach and intestines, there's often less risk of gastrointestinal side effects like nausea, vomiting, or stomach upset.

Flexibility: Transdermal gels can be formulated with various additives to modulate drug release, penetration, and stability, allowing for customization based on the needs of the patient or the specific drug.
Despite these advantages, transdermal gels are not suitable for all drugs or all patients. Factors like the drug's molecular weight, its solubility in both oil and water, and its required therapeutic concentration can influence its suitability for transdermal delivery. Additionally, some patients might experience skin irritation or allergies to components in the gel.(6)
A number of considerations, including the medication's physicochemical characteristics, the intended release profile, patient compliance, and the particular medical condition being treated, influence the choice of transdermal drug delivery method. Systems vary in their benefits and drawbacks, thus it's critical to customize the system to the drug and the patient's requirements.

Introduction to Herbal Medicines:

Herbal medicine harnesses the therapeutic qualities of herbs, utilizing their abundant bioactive components like alkaloids, flavonoids, and essential oils for healing purposes. These compounds can have various therapeutic effects on the human body, addressing both the symptoms and underlying causes of health issues. Herbs are often prepared in the form of teas, tinctures, capsules, creams, and other remedies.(7)

The practice of herbal medicine is based on the principle of holistic health, considering the interconnectedness of the body, mind, and spirit. Natural remedies supports the body's own healing mechanisms and to promote overall well-being. Herbalists, practitioners of herbal medicine, typically take a personalized approach to treatment, considering an individual's unique constitution and specific health concerns.(8)

While herbal medicine is often viewed as an alternative or complementary approach to conventional medicine, it is worth noting that many pharmaceutical drugs have their origins in plant compoundsConsequently, there is an increasing interest in combining herbal remedies with evidence-based medical practices to offer a more inclusive and holistic approach to healthcare. Research into the safety and efficacy of herbal treatments continues to expand our understanding of their potential benefits.(9)

Applications of modern Herbal Medicines:(10)

Many modern healthcare practitioners integrate herbal medicine into their treatment plans, using herbal remedies alongside pharmaceutical drugs when appropriate. This approach is often referred to as complementary or integrative medicine and aims to provide patients with a broader range of treatment options. Modern herbal medicine is practiced by trained herbalists who have a deep understanding of the pharmacological properties of plants, as well as a thorough knowledge of human physiology and pathology. These professionals frequently create personalized treatment strategies tailored to the unique health requirements of each patient.

Many universities and institutions offer formal education and training in herbal medicine. This education includes coursework on botany, phytochemistry, pharmacology, and clinical herbalism, providing herbalists with a strong foundation in both traditional wisdom and contemporary scientific knowledge.

Modern herbalists rely on scientific research and clinical evidence to support the use of herbal remedies for specific health conditions. This evidence-based approach helps in selecting the most appropriate herbs for a given situation.

Gel:(11)

A gel is a solid or semi-solid arrangement comprising a minimum of two components, wherein a condensed mass encloses and interpenetrates a liquid. Gels and jellies are characterized by a small amount of dispersed solids in a larger liquid volume, exhibiting properties that tend to be more solid than liquid in nature.

Zingiber officinale, commonly referred to as ginger, is a flowering plant with an underground stem known as a rhizome, extensively utilized as both a spice and a traditional remedy. Belonging to the Zingiberaceae family, it shares its botanical group with turmeric and cardamom. While native to Southeast Asia, ginger is presently cultivated in various regions globally.

Key features and uses of Zingiber officinale (ginger) include:(12),(13),(14)

Culinary Uses: Ginger adds flavor to a wide variety of Asian cuisines when used fresh, dried, powdered, or as an oil or juice and is also used in baking, candy-making, and beverage preparation.

Medicinal Properties: Ginger has been used in traditional medicine for centuries. Some of its medicinal benefits are supported by modern scientific research:

Ginger can help alleviate nausea, especially morning sickness in pregnant women and nausea caused by chemotherapy. Ginger contains compounds like gingerol that have anti-inflammatory and antioxidant properties. This can be beneficial for conditions like osteoarthritis.Also reduce muscle pain and soreness.studies indicated ginger might have anti-diabetic properties.

Anti-cancer Properties: Some research, primarily in test tubes and animals, suggests that ginger might have protective effects against cancer.

Because of its anti-inflammatory and antioxidant characteristics, ginger extract is included in a variety of skincare formulations.

EXPERIMENTAL:

Methods:

1. Collection of *Zingiber officinale* and Authentication

The dried rhizomes of *Zingiber officinale* (Zingiberaceae) get purchased from Shriram Aushadhi Bhandar,

Chiplun (Dist-Ratnagiri), Maharashtra State, India. Sample of ginger get authenticated from Head of Botany Department, Sharadchandraji Pawar College of Agriculture Kharavate, Chiplun.

2. Organoleptic Characterization:(15)

Ginger typically appears as a knobby, irregularly shaped rhizome with a pale beige to light brown skin. The skin may appear slightly wrinkled or have a paper-like texture. The flesh inside can range from pale yellow to light beige. The aroma of fresh ginger is pungent and spicy. It is characterized by its unique, zesty scent that is both earthy and slightly sweet.

When ginger is cut or grated, the aroma becomes more pronounced, and its spicy notes are released, filling the air with a warm and invigorating fragrance.

3. EXTRACTION:

Preparation of Ethanolic Extract of Zingiber officinale.(16)**,**

In this study, rhizomes underwent a meticulous process of being ground into coarse powder using a mechanical grinding machine. Resulting coarse powder then was sieved through sieve no 43. Approximately 100 grams of the powdered material underwent extraction with ethanol as a solvent through maceration for 72 hours with intermittent stirring. Multiple extraction cycles were conducted to obtain a sufficient volume. The resulting extract after each extraction cycle was evaporated to dryness using an electrically heated water bath at a temperature of 60°C. Additionally, a portion of the extract was utilized for preliminary Phytochemical screening to identify various plant constituents, while the remaining extract was employed in formulating gel batches.

4. INITIAL PHYTOCHEMICAL ANALYSIS:(17)**,**(18)

The alcoholic extract underwent a qualitative chemical analysis. The subsequent methods were employed to examine the existence of different phytochemical components in the extract. Table No 1

1. Test for Tannin: Combining 0.5 mL of plant extract with 2 mL of water, the mixture was heated in a water bath. After filtration, 1 mL of a 10% FeCl3 solution was introduced to the filtrate.
2. Test For Saponins-Foam Test: Placed a small quantity of the extract in a test tube along with a minimal amount of water. The mixture was vigorously shaked.
3. Test for Reducing Sugar: Combined 0.2 mL of the extract with 2 mL of distilled water, and shaked the mixture thoroughly in a test tube. Added 1 mL of both Fehling solutions A and B to the mixture.
4. Test for Phlobatannins: Mixed 0.2 mL of the extract with 2 mL of a 10% aqueous hydrochloric acid solution and heated the mixture to boil.
5. Test for Anthraquinones: Combined 0.2 mL of plant extract with 5 mL of chloroform, shaked the mixture for 5 minutes, and then filtered it. Added 2.5 mL of a 10% ammonium hydroxide solution to the resulting filtrate.
6. Test for Volatile Oil: Mixed 0.2 mL of plant extract with 2 mL of ethanol, and introduced a few drops of ferric chloride solution to the mixture.
7. Test for Steroids (Salkowski test): Combined 0.2 mL of plant extract with 2 mL of chloroform, and then 2 mL of concentrated sulfuric acid added to create a layered structure.
8. Test for Balsam: Mixed 0.2 mL of plant extract with 2 mL of ethanol and add two drops of alcoholic ferric chloride solution.
9. Test for Chalcone: Combined 0.2 mL of plant extract with 2 mL of 1% ammonium hydroxide...
10. Test for Glycoside: 0.2 ml of plant extract and 2.5 mL of dilute H_2SO_4 were mixed and boiled for 15 minutes, cooled, and, neutralized with 5 mL each of Fehling solutions A and B. The formation of brick red precipitate confirms glycoside.
11. Test for Amino Acid (Protein): 0.2 ml of extract and 5 ml of distilled water was mixed together and left for 3 hr. The mixture was later filtered to 2 ml of the filtrate 0.1 ml Million reagent was added. A yellow precipitate indicated the presence of protein (amino acid).
12. Test for Resin: In the concentrated ginger extract, 4 ml Ethyl alcohol was added to the test tube. The resins are observed in the test tube.

13. TEST FOR ALKALOIDS

- Dragendroff's test: Dissolved extract of the herbal drug in chloroform. Evaporate chloroform and acidify the residue by adding few drops of Dragendroff's reagent (Potassium Bismuth Iodide).
- Wagner's test: 2-3 ml of filtrate with few drops of Wagner's reagent

5. In-vitro anti-inflammatory study of extract(19)

• Inhibition of albumin denaturation

The investigation into the anti-inflammatory activity of the ethanolic extract of ginger and optimized gel formulations utilized the protein denaturation method. The reaction mixture comprised the test extract and a 1% aqueous solution of the albumin fraction, with the pH adjusted using a small quantity of 1 N HCl. The sample extracts were incubated at 37°C for 20 minutes, followed by heating to 51°C for an additional 20 minutes. After cooling the samples, turbidity was measured at 660 nm. The experiment was conducted in triplicate, and the percentage inhibition of protein denaturation was calculated accordingly.

Percentage inhibition= (abs Control-Abs Sample) /Abs control × 100

6. Drug-Excipients compatibility study:-

To investigate the interaction between the drug and excipients, samples of the ethanolic extract of ginger, Carbalpol 934, Carbapol 940, propylene glycol, and a physical mixture of the drug and excipients were analyzed using FTIR at Shivaji University, Kolhapur.

7. Experimental design:(20)

During formulation two gelling agents Carbopol 934, Carbapol 940 were used at two different concentrations, resulting total nine batches prepared. Carbopol 934 (at concentration 1% and 1.5%) Carbapol940 (at concentration 1% and 1.5%) and a combination

Preparation of Gel:

Table No. 01: Formulation composition of ginger gel formulation

Composition	F1	F2	F3	F4	F5	F6	F7	F8	F9
Ginger extract	5	5	5	5	5	5	5	5	5
Carbopol 934	0.5	0.25	0.75	-	-	-	-	-	-
Carbapol 940	-	-	-	0.5	0.25	0.75	-	-	-
Carbapol (934+940)	-	-	-	-	-	-	0.5+0.5	0.25+0.50	0.50+0.25
Propylene glycol	10	10	10	10	10	10	10	10	10
Albumin	1	1	1	1	1	1	1	1	1
Triethanolamine	Ph 7	Ph7	Ph7	Ph7	Ph7	Ph7	Ph7	Ph7	Ph7
Sodium benzoate	0.025	0.025	0.025	0.025	0.025	0.025	0.025	0.025	0.025
Purified water	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.

7.1. Preparation of gel with Carbopol 934: In a beaker, accurately weighed Carbopol 934 was dispersed in 50 ml of distilled water. The beaker was set aside for Carbopol to swell for half an hour, followed by manual stirring for an additional 30 minutes. In a separate container, 5 ml of propylene glycol and the necessary amount of extract were combined. Another beaker containing 5 ml of propylene glycol had weighed quantities of propyl paraben and methyl paraben added, and the mixture was stirred thoroughly. Once Carbopol was completely dispersed, 1 gm of extract and the preservative solutions were introduced with continuous stirring. The final volume was adjusted to 100 ml by adding the remaining distilled water, and Triethanolamine was gradually added to the formulations for pH adjustment to the required skin pH (6.8-7) and to achieve the desired gel consistency.

7.2 Preparation of gel with Carbopol 940: Precisely measured Carbopol 940 was placed in a beaker and dispersed in 50 ml of distilled water. The beaker was set aside to allow Carbopol to swell for half an hour, followed by manual stirring for an additional 30 minutes. In a separate container, 5 ml of propylene glycol and the necessary amount of extract were combined. Another beaker containing 5 ml of propylene glycol had weighed quantities of propyl paraben and methyl paraben added, and the mixture was stirred thoroughly. Once Carbopol was completely dispersed, 1 gm of extract and the preservative solutions were introduced with

continuous stirring. The final volume was adjusted to 100 ml by adding the remaining distilled water, and Triethanolamine was gradually added dropwise to the formulations for the adjustment of the required skin pH (6.8-7) and to achieve the desired gel consistency.

8. Preparation of gel with combination of Carbapol 934 and Carbopol 940: Accurately measured amounts of Carbapol 934 and Carbopol 940 were placed in a beaker and dispersed in 50 ml of distilled water. The beaker was set aside to allow the Carbopol to swell for half an hour, followed by manual stirring for an additional 30 minutes. In another beaker, 5 ml of propylene glycol and the necessary quantity of extract were combined. Additionally, 5 ml of propylene glycol in a separate container had a weighed amount of propyl paraben and methyl paraben added, and the mixture was stirred thoroughly. Once the Carbopol was fully dispersed, 1 gm of extract and the preservative solutions were added with continuous stirring. The final volume was adjusted to 100 ml by adding the remaining distilled water, and Triethanolamine was gradually added dropwise to the formulations for the adjustment of the required skin pH (6.8-7) and to achieve the gel of the desired consistency.

8. Physicochemical evaluations:(21)

8.1 Physical appearance:

The gel formulations, which included the ethanolic extract of ginger, were visually examined for aspects such as color, homogeneity, consistency, and the absence of phase separation.

8.2 Determination of pH:

The pH of the formulated gels was assessed using a digital pH meter. One gram of gel was dissolved in 100 ml of distilled water and allowed to stand for two hours. The pH measurements for each formulation were conducted in triplicate, and the average values were calculated.

8.3 Spreadability:

Spreadability was assessed using a device consisting of a wooden block equipped with a pulley at one end. The evaluation was based on the slip and drag characteristics of the gels. Approximately 2 grams of the gel under examination were placed on a ground slide within this apparatus. The gel was then positioned between this slide and another glass slide with dimensions matching the fixed ground slide and featuring a hook. A one-kilogram weight was placed on top of the two slides for 5 minutes to eliminate air and create a uniform gel film between them. Excess gel was removed from the edges. The top plate was then subjected to an 80-gram pull with the assistance of a string attached to the hook, and the time (in seconds) required for the top slide to cover a distance of 7.5 cm was recorded. A shorter interval suggests better spreadability. Spreadability was calculated using the formula: $S = M \times L / T$, where S is spreadability, M is the weight in the pan (attached to the upper slide), L is the length moved by the slide, and T is the time (in seconds).

8.4 Rheological Examination:

The viscosity of the formulated gel compositions was assessed using a Brookfield viscometer (Brookfield viscometer RVT) equipped with spindle No. 7.

8.5 Extrudability Assessment:

The gel formulations were packaged into standard capped collapsible aluminum tubes and sealed by crimping at the end. The weights of the tubes were recorded. Placing the tubes between two glass slides, they were securely clamped. A 500 gm weight was applied over the slides, and then the cap was removed. The amount of extruded gel was collected and weighed. The percentage of the extruded gel was computed (extrudability >90%: excellent, >80%: good, >70%: fair).

8.7 In-vitro Drug Release Investigation: (22)

For the assessment of drug release, Franz diffusion cells were utilized in the study of all formulations. The diffusion cell apparatus had a height of 100 mm and a diffusion area of 3.8 cm2. A phosphate buffer with a pH of 7.4 served as the receptor medium. A freshly isolated egg membrane was employed as the dialysis membrane, affixed to the diffusion cell (donor cell) with the outer side in direct contact with the release surface of the formulation. Prior to mounting on the diffusion cell, an isotonic phosphate buffer solution with a pH of 7.4 (100 mL) was introduced into a donor compartment. A specific quantity of the formulation, equivalent to 1 g of gel, was applied to the egg membrane and slightly immersed in 100 mL of continuously stirred receptor medium. The entire system was maintained at a temperature of 37±1 ºC.

At specified time intervals up to 2 hours, a 1 mL aliquot was withdrawn and spectrophotometrically analyzed at 280 nm. Following each withdrawal, the diffusion medium was replaced with an equal volume of fresh diffusion medium. The cumulative percent release calculated for each time point**.**

8.6 Optimization Process:
The batches underwent optimization through a comprehensive assessment, including the study of physical properties such as pH, viscosity, spreadability, and extrudability for all formulation batches. Upon evaluating these parameters across all batches, the F3 gel formulation was identified and selected as the optimized batch.

In-vitro anti-inflammatory activity of prepared herbal gel:(22)
The reaction mixture (5 mL) was composed of 0.2 mL of egg albumin (extracted from fresh hen's egg), 2.8 mL of phosphate-buffered saline (PBS, pH 6.4), and 2 mL of gel solution, resulting in final concentrations of 31.25, 62.5, 125, 250, 500, and 1000 µg/mL. Double distilled water of a similar volume was used as the control. Subsequently, the mixtures were incubated at 37±2°C in a BOD incubator for 15 minutes and then heated at 70°C for five minutes. After cooling, their absorbance was measured at 660 nm, with the vehicle serving as a blank. Diclofenac sodium at final concentrations of 78.125, 156.25, 312.5, 625, 1250, and 2500 µg/mL was employed as the reference drug and subjected to the same procedures for absorbance determination. The percentage inhibition of protein denaturation was calculated using the formula: % inhibition = 100 × (Vt/Vc - 1), where Vt is the absorbance of the test sample and Vc is the absorbance of the control.

Stability study:(20)
The optimized gel formulations were formulated, filled into aluminum collapsible tubes, and underwent stability assessments at 40°C/75% RH for a duration of 3 months following ICH Guidelines. Samples were retrieved at monthly intervals, and their physical appearance, pH, rheological properties, spreadability, extrudability, drug content, and in-vitro drug release were evaluated.

RESULTS AND DISCUSSION

The present work aimed to formulate and evaluate transdermal gel containing ethanolic ginger extract with Carbopol 934, Carbapol 940. The prepared formulations were characterized for physical appearance, pH, spreadability,Extudability, viscosity, In vitro drug release and in-vitro anti-inflammatory study.

Table No.01: Preliminary Phytochemical investigation

Sr.no	Chemical test	observation	Inference
1	Test for Tannin	Blue Black Colour	+
2	Test for Saponin Foam Test Lieberman burchard test	 Foam not formed Color not changes	 - -
3	Test for Reducing Sugar	A brick-red precipitate	+
4	Test for Phlobatannins	A deposition of red precipitate	+
5	Test for Anthraquinones	A bright pink colour at the upper layer	+
6	Test for Volatile Oil	A green coloration	+
7	Test for Steroids	The formation of a violet ring at the interface	+
8	Test for Balsam	A dark green coloration	+
9	Test for Chalcone	Appearance of red color	+
10	Test for Glycoside	The formation of brick red precipitate	+
11	Test for Amino Acid	A yellow precipitate	+
12	Test for Resin	The resins are observed in the test tube.	+
13	Test or alkaloid Dragondroff's test Wagner's reagent	 Formation of orange brown ppt Formation of reddish brown ppt	 + +
14	Test for flavonoid Lead acetate test	 Yellow colored ppt formation	+
15	Test for protein Biuret test	Blue color is not produced	-
16	Test for Phenol	Deepbluish-green coloration	+

In-vitro Anti inflammatory study of Ginger extract:-

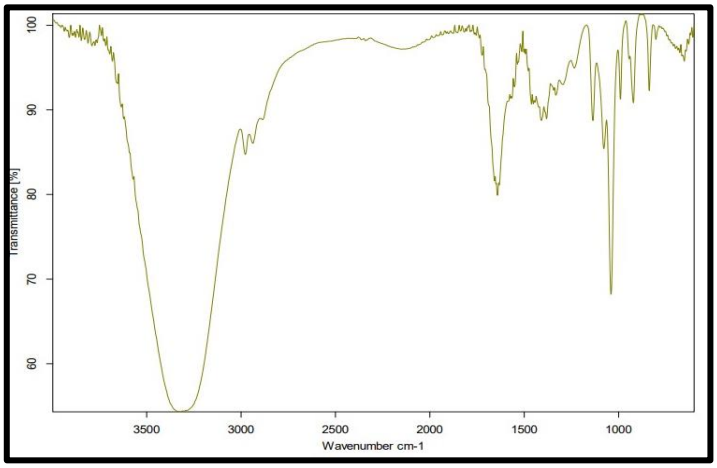
In this study, the protein/albumin denaturation bioassay was chosen for the in vitro evaluation of the anti-inflammatory properties of the herbal extract from Zingiber officinale. As a component of the investigation into the mechanism of the anti-inflammatory activity, the extract's ability to inhibit protein denaturation was examined. The current findings demonstrated a concentration-dependent inhibition of protein (albumin) denaturation by Zingiber officinale extract across the concentration range of 100 to 500 µg/mL. Diclofenac, at a concentration of 100 µg/mL, served as a reference drug and also displayed concentration-dependent inhibition of protein denaturation.

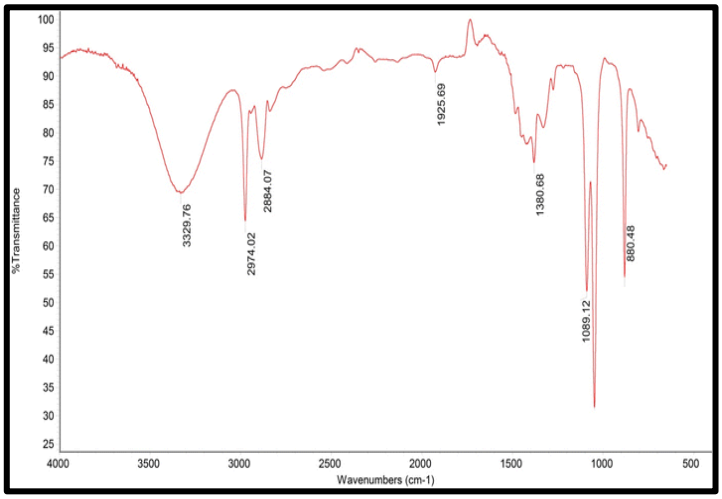
Table No.02: In vitro anti-inflammatory test of extract by albumin denaturation method

Ginger ethanolic extract conc(µg/ml)	absorbance	% inhibition
Control	0.3905	-
100	0.2731	30.06
200	0.2243	42.56
300	0.1610	58.77
400	0.1287	67.04
500	0.1129	71.08
Diclofenac	0.1014	74.03

FTIR Analysis for excipient compatibility:-

The examination of FT-IR spectra for Ginger ethanolic extract and Physical mixture of ingredients of herbal gel verified the absence of any interaction between the extract and excipients. The excipients were determined to be compatible with the ethanol extract.





FTIR studies interpreted no interaction observed in physical mixture of extract and other exicipents indicating stretching or bending peaks in similar regions as that of FTIR spectra of Extract

Sr No	Peak (Extract)	Peak (Mixture)	Range	Functional Group	Stretching/ Bending
1	3329.76	3300	3250-3650	O-H Phenol	Stretching
2	2974.02	2900	2800-3000	C-H Alkane	Stretching
3	2884.07	2850	2500-3300	O-H Acid	Stretching
4	1925.69	1650	1600-1980	C=C Aromatic	Stretching
5	1089.12	1100	1050-1150	C-O Alcohol	Stretching

Physicochemical Assessment:

1 Physical Characteristics:

All batches of formulations were observed to be homogeneous light green gel preparations.

2 pH Measurement:

The pH values of all the formulated preparations fell within the range of 6-7, which is considered acceptable to minimize the risk of skin irritation upon application, given that the pH of adult skin is 5.5.

Table No.04 : pH of gel formulation.

Formulation	pH
F1	**7.1**
F2	**7.1**
F3	**6.9**
F4	**8.0**
F5	**8.1**
F6	**7.6**
F7	**8.3**
F8	**8.2**
F9	**8.5**

3 Rheological Examination:

Viscosity measurements of the prepared gel were conducted using a Brookfield viscometer from Brookfield Engineering Laboratories. Among all the formulations, the highest viscosity was observed in batches F3 and F9

Table No 7 Rheology Study

Batches	Viscosity(Cps)
F1	**30001 ±0.11**
F2	**20532 ±0.43**
F3	**34224 ±0.21**
F4	**31308 ±0.69**
F5	**36047 ±0.58**
F6	**33305 ±0.25**
F7	**32482 ±0.54**
F8	**32906 ±0.75**
F9	**34004 ±0.98**

4. Extrudability:

The expulsion of the gel from the tube plays a crucial role in its application and overall patient acceptance. Gels with high viscosity might face challenges in extrusion, while low-viscosity gels may flow too rapidly. Therefore, achieving an optimal consistency is essential to facilitate the smooth extrusion of the gel from the tube. The Xanthan gum gel formulations demonstrated good extrudability, while the Carbopol 934 gels exhibited satisfactory extrudability.

Table No.6: Extrudability of root extract gel formulations

batches	wt.of formulation	Wt.of gel extrudded	Extrudability amount	appearance
F1	**16.65**	**14.83**	**86.06**	++
F2	**17.02**	**15.18**	**89.18**	++
F3	**17.51**	**14.30**	**81.66**	++
F4	**16.85**	**14.53**	**86.23**	+
F5	**17.43**	**15.86**	**90.99**	++
F6	**17.39**	**15.42**	**88.67**	++

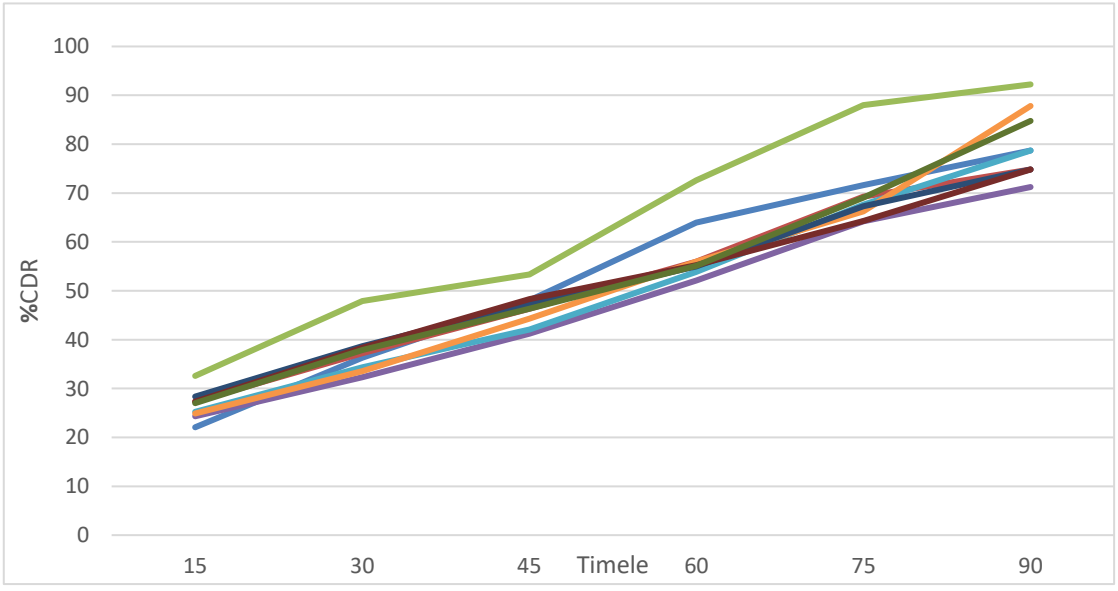
Note: + fair, ++ good, +++ excellent

In-vitro drug release Study:-

In vitro drug release studies were carried out for all gel formulations for 2 h and amount of polyphenolic content released were estimated which is shown in table no. Gel formulation F3 showed higher percentage release of phenolic content (88.02%) after 2 h than other formulations Gels prepared with combination of carbopol-934 as gelling agent showed better release of polyphenolic content when to compare to other formulations. Amount of drug permeated through unit area of the membrane was determined on the basis of in vitro drug release data. For all formulations, average flux was maximum in the first one hour of drug release and thereafter flux decreased gradually with time which is shown in table 4. It is also observed that among the gel formulations, average flux values were greater for F3 containing of carbopol 934.

Table No 8: In vitro release study

Sr. No	Time (min)	%Cumulative drug release (with SD)								
		F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
1	15	9.2 ±0.016	9.49 ±0.051	11.78±0.043	8.21±0.11	8.38±0.64	8.21±0.046	10.42 ±0.032	9.89 ±0.042	10.21 ±0.012
2	30	15.57 ±0.091	18.39 ±0.089	21.7.5±0.041	18.35±0.023	13.23 ±0.041	12.34 ±0.032	12.21±0.042	13.21 ±0.034	14,21 ±0.043
3	45	22.07 ±0.047	27.37 ±0.121	32.58±0.032	24.32±0.069	25.23 ±0.042	24.89 ±0.054	28.35 ±0.032	27.32±0.043	27.01±0.034
4	60	36.32 ±0.012	37.24 ±0.12	47.9 ±0.052	32.32 ±0.012	34.32 ±0.023	33.56 ±0.034	38.67 ±0.043	38.32 ±0.024	37.89 ±0.023
5	75	48.05 ±0.082	46.30±0.071	53.37±0.049	41.21±0.023	42.05 ±0.082	44.30±0.031	47.30±0.043	48.30 ±0.087	46.30±0.071
6	90	63.94 ±0.016	55.96±0.092	72.62±0.0524	52.12±0.043	53.84 ±0.016	55.96±0.042	54.96±0.031	55.26 ±0.032	55.12±0.022
7	105	71.63 ±0.014	69.27±0.011	88.02±0.061	64.21±0.067	67.63 ±0.014	66.27±0.016	67.27 ±0.021	64.27 ±0.016	69.05 ±0.08
8	120	78.70 ±0.012	74.82±0.023	92.23±0.041	71.23±0.045	78.70 ±0.012	87.82 ±0.023	74.82 ±0.023	74.82 ±0.023	84.76 ±0.021



10. Optimization of Batch:

Upon analyzing all formulation batches for parameters such as pH, viscosity, spreadability, and

extrudability, formulation batch F3 containing ginger ethanolic extract exhibited favorable results. All formulations showed good viscosity, spreadability, and extrudability. Furthermore, F3 demonstrated excellent spreadability and in-vitro drug release. So optimized F3 formulation was selected for further assessments, including in-vitro anti-inflammatory studies and stability studies

Table no 9 : In vitro anti-inflammatory Activity of Gel Formulation F3

Formulation F3	abs	% inhibition
Control	0.2410	-
100	0.1831	24.02
200	0.1443	39.61
300	0.1367	42.44
400	0.1029	56.57
500	0.0705	70.71
Diclofenac gel	0.0615	73.53

11.Stability studies:

Accelerated stability studies indicated that the physical appearance, rheological properties, extrudability, spreadability in the prepared gel remained unchanged upon storage for 1 month. The pH observed of prepared gel through 1 month storage was in between 6-7. Rheological properties and extrudability was obtained uniformly. Gel formulation was maintaining drug level after 3 months of accelerated stability.

Table No 10 Stability Study

Evaluation Parameter	initial	After 1 Month	After 2 months	After 3 Months
pH	6.8	6.8	6.8	6.8
Viscosity(CPs)	34224 ±0.21	34224 ±0.21	34424 ±0.42	34624 ±0.34
Spreadability (gm.cm/sec)	22.16	22.14	23.61	23.60
Extrudability (%)	91.71	91.60	90.99	90.82
In vitro drug Release				

SUMMARY:

Gel-based drug delivery systems have gained popularity for enhancing the therapeutic effectiveness of topically applied drugs. Zingiber officinale, a traditional anti-inflammatory agent with analgesic and anti-oxidative properties, was chosen for transdermal delivery to minimize gastrointestinal irritation and optimize drug concentration at the targeted site. The transdermal delivery faces challenges due to skin barrier properties, necessitating the inclusion of penetration enhancers in the formulation. This study aimed to formulate and evaluate transdermal gels of Zingiber officinale**.**

In the preliminary investigation, Zingiber officinale underwent standardization for purity and identity. Authentication and taxonomical identification were conducted by the Principal at Sharadchndraji Pawar College of Agriculture, Kharavte, Tal: Chiplun, Dist Ratnagiri. Preformulation studies, including identification, phytochemical evaluation, physicochemical evaluation, extraction, and solubility, were carried out. A drug extract-excipient study confirmed the compatibility of the drug extract with both polymers, Carbopol 934 and Carbapol 940.

The developed gels underwent comprehensive evaluation for physicochemical properties such as appearance, pH values, rheological properties, spreadability, extrudability, skin irritation, stability, and anti-inflammatory activity. The pH range of Carbopol 934 and Carbapol 940 gels was found suitable for transdermal application. Viscosity measurement using a Brookfield Viscometer at room temperature indicated comparable results among the selected gels. Extrudability of Carbapol 934 gel showed better results than Carbopol 940 gels and was comparable to a marketed gel (Diclofenac Sodium Gel).

Anti-inflammatory activity assessment was conducted using an in-vitro anti-inflammatory method, specifically the inhibition of albumin denaturation. Ginger ethanolic extract as well as optimized formulation F3gels exhibited similar percentages of inhibition, comparable to the marketed gel. Stability studies were carried out for three months according to ICH norms at a temperature of 40°C ± 2°C and 75% ± 5% RH. Analysis for changes in appearance, pH, spreadability, viscosity and in vitro drug release revealed no

significant variations with respect to evaluation parameters. The results indicated that the Zingiber officinale gel formulation remained stable, suggesting promising outcomes for the treatment of inflammation.

CONCLUSION:

The current study implies that the effective design and development of a transdermal drug delivery system hinge upon careful selection of polymers for the drugs. The outcomes of physical compatibility assessments indicate that the chosen polymers, namely Carbopol 934 and Carbapol 940, exhibit compatibility with the drug Zingiber Officinale. The manipulation of polymer concentrations was observed to impact gel properties such as viscosity and spreadability. Gel formulations incorporating Carbapol 934 and Carbapol 940 demonstrated favorable characteristics, including homogeneity, stability, and anti-inflammatory activity. Formulation F3 proved better spredability as well as drug release.

References:

1. Smith C, Kruger MJ, Smith RM, Myburgh KH. The Inflammatory Response to Skeletal Muscle Injury Illuminating Complexities. 2008.
2. Medzhitov R. Origin and physiological roles of inflammation. Nature. 2008;454(7203):428–35.
3. Ahmed AU. An overview of inflammation: Mechanism and consequences. Front Biol China. 2011;6(4):274–81.
4. Ghulaxe C, Verma R. A review on transdermal drug delivery system. 2015;4(1):37–43.
5. Shingade GM, Ameer Quazi, Sabale PM, Grampurohiy ND, Gadhave MV, Jadhav SL GD. Review on: Recent Trend on Transdermal Drug Delivery System. J Drug Deliv Ther. 2012;2(1):66–75.
6. Rastogi V, Yadav P. Transdermal drug delivery system : An overview. Asian J Pharm. 2012;July(September):161–70.
7. Afrin S, Jahan I, Hasan AHMN, Deepa KN. Novel Approaches of Herbal Drug Delivery. J Pharm Res Int. 2018;21(5):1–11.
8. Saraf S. Fitoterapia Applications of novel drug delivery system for herbal formulations. Fitoterpia. 2010;81:680–9.
9. Verma H, Prasad SB, Singh H. Herbal Drug Delivery System : A Modern Era Prospective Herbal Drug Delivery System : A Modern Era Prospective. Int J Curr Pharm Rev Res. 2013;4(3):88–101.
10. Murti Y, Gupta J, Gupta R. A Review on Novel Herbal Drug Delivery System and its Application. Curr Tradit Med. 2023;9(April):43–55.
11. Jamadar MJ, Shaikh RH. Preparation and evaluation of herbal gel formulation. J Pharm Res Educ. 2017;1(2):201–24.
12. Otari AD, Patil RA. Exploring Therapeutic Potential of Ginger : Preclinical and Clinical Review. Indian J Nutr Diet. 2023;60(June):293–304.
13. Mekuriya W, Mekibib B. Review on the Medicinal Values of Ginger for Human and Animal Ailments. J Vet Sci Technol. 2018;9(2):9–12.
14. Taylor P, Baliga MS, Haniadka R, Pereira MM, Souza JD, Pallaty PL, et al. Update on the Chemopreventive Effects of Ginger and its Phytochemicals Update on the Chemopreventive Effects of Ginger and its. Crit Rev Food Sci Nutr. 2011;51(6):499–523.
15. Achour L, Cheikh H Ben. Journal of Coastal Life Medicine rhizomes , and antioxidant properties of their ethanolic and aqueous extracts. J Coast Life Med. 2017;5(2):70–6.
16. Lidiia Eberle,Alona Kobernik AA and IK. Optimization of extraction methods for total Polyphenolic Compounds otained from rhizoes of Zingiber officinale. Trends Phytochem Res (TPR). 2018;2(1):37–42.
17. Arawande JO, Akinnusotu A, Alademeyin JO. Extractive Value and Phytochemical Screening of Ginger (zingiber officinale) and Turmeric (curcuma longa) Using Different Solvents. Int J Tradit Nat Med. 2018;8(1):13–22.
18. Sharma S, Kumar R. ANTIOXIDANT ACTIVITY , TLC AND PHYTOCHEMICAL ANALYSIS OF GINGER (ZINGIBER OFFICINALE L .) RHIZOME. Plant Arch. 2018;18(special issue):210–4.
19. Ezzat SM, Ezzat MI, Okba MM, Menze ET, Abdel-naim AB. The hidden mechanism beyond ginger (Zingiber o ffi cinale Rosc .) potent in vivo and in vitro anti-in fl ammatory activity. J Ethnopharmacol [Internet]. 2018;214(December 2017):113–23. Available from: https://doi.org/10.1016/j.jep.2017.12.019
20. Surve, Chaitrali, Tawde, Salonee, Gawde Kinjial,Mahind Deepak, Mhaprolkar Chetan, Sawant Kirti.

GINGEL : Development and Evaluation of Anti- Arthritic Gel Containing Ginger (Zingiber officinale). Int J Innov Sci Res Technol. 2020;5(7):1147–53.
21. Laksmi SVVNSM, Guglothu Suryam, Mohanty Chandan, Senthilkumar S R, Venkatachalam T, Nayak Chandan krishna M. DEVELOPMENT AND EVALUATION OF ANTI-INFLAMMATORY GEL CONTAINING ZINGER OFFICINALE . Neroquantology [Internet]. 2022;20(12):1030–7. Available from: http://www.cibtech.org/jms.htm
22. Padmanabhan P, Jangle SN. Evaluation of in-Vitro Anti-Inflammatory Activity of Herbal Preparation, a Combination of Four Medicinal Plants. Int J Basic Appl Med Sci [Internet]. 2012;2(1):109–16. Available from: http://www.cibtech.org/jms.htm