RESEARCH ARTICLE

Development and Evaluation of Emulgel Formulation of Diclofenac Sodium utilizing *Lipidium sativum* as a Gelling Agent

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ABSTRACT

Emulgels have gained recognition as an effective method for delivering non-polar drugs. The primary goal of our current research is to investigate the potential of *Lepidium sativum* seed mucilage as a gelling agent in this context. To enhance drug penetration, we have incorporated clove oil, oleic acid, and methyl salicylate. An emulsion was formulated and subsequently integrated into the gel base.

Our research encompassed a series of studies, including rheological assessments, spreading coefficient evaluations, investigations into skin irritancy, and other relevant tests. Furthermore, we conducted drug content analysis, *in-vitro* release and permeation studies, and stability assessments.

In our *in-vitro* investigations, it was observed that formulation E6 exhibited the highest drug release within a span of 180 minutes. Comparative analyses were conducted, pitting formulations E4, E5, and E6 against a commercially available emulgel preparation.

As a result of our findings, it is evident that an emulgel employing *L. sativum* mucilage can effectively function as a gelling agent in a topical drug delivery system.

Keywords: Emulgel, Emusion, Microemulsion, Gel, *Lipidium sativum.*

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INTRODUCTION

A variety of gelling agents are designed for use in diverse topical formulations. In the current investigation, *Lepidium sativum* has been ingeniously incorporated into emulgel formulations as the gelling agent of choice. Notably, there is no commercially accessible topical product featuring *L. sativum* in a gelling role, with most topical formulations relying on carbopol as their primary gelling agent.[1,2]

As expounded upon by various authors, the concept of gels involves entrapping significant quantities of water-based or hydroalcoholic liquids within a matrix of minute pores, thereby giving rise to the relatively recent family of pharmaceutical dosage forms known as gels. These gels consist of colloidal particles, comprising inorganic substances such as aluminum salts or synthetic and naturally occurring organic polymers. The adoption of gels has been driven by the promise of enhanced usability and greater patient acceptance.[3,4]

In light of the numerous advantages associated with gels, the development of emulgels has emerged as a strategic solution. Emulgels have been crafted in a manner that harnesses the unique attributes of hydrophobic substances for therapeutic purposes.[5] These substances, endowed with gelling properties, execute intricate functions, including emulsification and thickening, by mitigating surface and interfacial tension. This capability enables superior formulations with exceptional stability.[6]

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Emulgels, when applied to the skin, exhibit a host of favorable characteristics, including emollient properties, non-staining attributes, extended shelf life, non-greasiness, ease of spreadability, and eco-friendliness.[7]

The overarching objective of our study is multifaceted. Firstly, we aim to explore the potential of *L. sativum* seed mucilage as a gelling agent in emulgel formulations, incorporating a model drug. Secondly, our focus is on scrutinizing the specific properties of *L. sativum* mucilage as a gelling agent. Additionally, we endeavor to formulate emulgels characterized by exceptional stability and rheological attributes. Furthermore, we intend to scrutinize the rate of drug release from the formulated emulgel preparations. Lastly, our study involves a comparative analysis, pitting our formulated emulgels against existing market offerings.

MATERIAL AND METHODS

Diclofenac sodium was received as gift sample from Zim lab, Kalameshwar Nagpur. *L. sativum* was obtained from Loba chemicals.

Mucilage Extraction

Mucilage was extracted from *L. sativum* seed by soaking in acetone. Here, *Lipidium* seeds (100 g) were steeped for 24 hours in 800 mL of distilled water. Using a Philips HR 1453 hand blender, the soaked seeds were mixed for 15 minutes at a speed of 2000 rpm. After that, muslin cloth was used to shift the combined seeds. The same volume of acetone was introduced into the *L. sativum* gel (800 mL) to enable the perception of mucilage. The muslin cloth was used to filter the white supernatant coagulant mass that had been isolated following acetone precipitation. The extracted *L. sativum* gel was spread out on a glass slab and dried in oven for five minutes at a temperature not exceeding 60°C. Size reduction was used to turn the acquired mucilage into powder.[8-10]

Physicochemical Properties of Extracted Mucilage

Identification test

The obtained mass was subjected to various tests for confirmation of mucilage, carbohydrates, tannins, protein, reducing sugar and saponin

Characterization of L. sativum Powder[10,11]

The obtained dried powder was subjected to characterization viz., solubility, loss on drying, pH, and swelling index.

IR studies

Here dried, purified mucilage was made as a potassium bromide disc, and infrared spectra were captured between 4000 and 400 cm^{-1}.

Drug excipients compatibility studies (IR spectra of diclofenac sodium and L. sativum mucilage)

When dried pure mucilage and diclofenac sodium were combined on a potassium bromide disc, infrared spectra between 4000 and 5000 nm were observed.

Preparation of emulgel[12]

L. saivum mucilage was dissolved in purified water while being constantly stirred at a reasonable speed to create the gel in the formulations. To adjust the pH to a range of 6 to 6.5, triethanolamine (TEA) was next utilized. Tween 20 mixed with water to create the aqueous constituents of the emulsion, including Span 20 and light liquid paraffin. were combined to create the oil phase. Methyl and propyl parabens were separately dissolved in propylene glycol, and the medication was dissolved in ethanol. Subsequently, both solutions were combined with the aqueous phase and was heated at 70 to 80°C, mixed and agitated constantly, and cooled to room temperature. Mix the gel with emulsion in an exact ratio to produce the emulgel. The composition is given in Table 1.

Characterization of Emulgel[13]

Physical examination

Visual examinations were conducted to assess the emulgel formulations like color, homogeneity, constancy, and possible phase parting.

Rheology

Stickiness of emulgels was assessed at 25°C by employing a cone and plate viscometer fitted with spindle 52. This instrument was connected to a thermostatically regulated circulating water bath to maintain the temperature at 25°C. A beaker with a thermostatic jacket on it received the formulation whose viscosity was to be measured.

Spreading coefficient

The spreadability of a formulation is a critical factor influencing its medicinal effectiveness. Here spreadability of both emulgel and commercial gel by placing them between two glass plates under a specific weight. One glass plate contained a precisely measured quantity (350 mg) of the emulgel or gel, and the other plate was released from a 5 cm height, resulting in the formation of a spread emulgel circle and measuring the diameter of this spread emulgel circle.

Table 1: Composition of emulgel (using various gelling agent)

Ingredient	*Formulation code*						
	E1	*E2*	*E3*	*E4*	*E5*	*E6*	*E7*
Carbopol (g)	0.5	-	-	1	-	-	-
L. sativum mucilage (g)	-	0.5	-	-	1	-	2
Carbopol: *L. sativum* mucilage (g)	-	-	0.5:0.5	-	-	1:1	-
Tween 20 (mL)	0.5	o.5	0.5	0.5	0.5	0.5	0.5
Span 20 (mL)	1	1	1	1	1	1	1
Light liquid paraffin (mL)	5	5	5	5	5	5	5
Propylene glycol (mL)	5	5	5	5	5	5	5
API (%)	1	1	1	1	1	1	1

In each formulation: Propyl paraben (g): 0.03, Methyl paraben (g): 0.05, Ethanol and water : Quantity Sufficient

Extrudability study

An empirical test is often performed to conclude the amount of force needed to drive out matter from a tube. The procedure involving the level of applied shear within the rheogram's domain." where the yield value is found is determined surpassed, causing a blockage in the flow. The amount of extruded emulgel and emulgel in %upon application of weight in grams necessary to extrude from lacquered aluminum collapsible tube. The technique utilized in the current study is based on emulgel ribbons that are at least 0.5 cm long and applied for 10 seconds. Evaluate the extrudability of the emulgel formulation. Greater extrudability volume enhances extrudability. Three measurements of the extrudability of each formulation yield an average of given.

Extrudability = applied "grams per square centimetre (g/cm^2) for emulgel extrusion from a tube

Swelling index: A quantity of 1 gram of emulgel was applied onto porous aluminum foil and then submerged in individual beakers, each containing 10 mL of a 0.1 N NaOH solution. This procedure was carried out to assess the emulgel swelling index. At specified time intervals, emulgel samples were taken out from the beakers, positioned on a dry surface, and weighed again. These measurements were utilized to calculate the swelling index, employing the following formula:

$$\text{Swelling Index (SI)\%} = [(wt - wo)/wo] \times 100$$

Where (SI)% : equilibrium swelling percentage, wt: weight of the swollen emulgel at time t, and wo: weight of the emulgel at the beginning.

Drug content determination

- Begin by taking 1-gram of emulgel and introducing an appropriate solvent.
- Mix the solvent thoroughly with the emulgel.
- Filter the resulting solution to achieve a clear and transparent solution.
- Utilize a UV spectrophotometer to measure the absorbance of the solution.
- Establish drug standard plots using the same solvent. This will allow for the determination of concentration and drug content by comparing the measured absorbance value to drug standard plot.

Drug content: volume consumed x conversion factor x (concentration x dilution factor)

Skin irritation test (Patch test)

A human volunteer's skin is adequately prepped before the preparation is applied, and any negative effects or observations, such as alterations in color, should be continuously monitored for a duration of up to six hours. Test is considered successful when no irritations are observed.

In-vitro release/permeation studies

The phosphate buffer 7.0 was applied to the dialysis membrane pre-treated with NaOH. The donor and receptor compartments of the Franz diffusion cell were placed on opposite sides of the treated dialysis membrane. On the dialysis membrane, 0.5 g of gel was added to the formulation. To prevent the diffusion layer effect. A magnetic stir bar was consistently stirred within the diffusion medium. The removed sample was examined using a UV spectrophotometer.

Table 2: Emulgel formulation with different penetration enhancer

S. No	*Penetration enhancers (ml)*	*Formulation Code*		
		E1	*E2*	*E3*
1	Clove oil	2	2	2
2	Oleic acid	2	2	2
3	Methyl salicylate	2	2	2

Stability studies

The prepared emulgel formulations were placed into collapsible aluminum tubes. (5 grams), and kept for 15 days and then it was subjected to an evaluation. The details of penetration enhancers are given in Table 2.

RESULT AND DISCUSSION

Organoleptic Characteristics

Organoleptic characteristics are shown in Figure 3.

Solubility of mucilage

The solubility behavior of LSM mucilage indicated showed speedy solubility. The presence of mucilage is confirmed by identification test as shown in Table 3 and 4.

Loss on drying

The weight loss after drying reveals the quantity of moisture present in the substance that is available to interact with other materials.

Swelling index

The swelling index observed was 300 cm. Water retention capacity was 10 cm. Results indicated that the mucilage has excellent swelling properties.

Ash value and pH determination

The analysis of LSM mucilage revealed total ash and acid-insoluble ash content of 7.36% and 0.75% w/w, respectively.

Table 3: Organoleptic characteristics of *Lipdium sativum* seed mucilage

S. No.	*Parameter*	*Result*
1	Appearance	Amorphous
2	Color	Light brown
3	Odor	Odorless
4	Taste	Tasteless

Table 4: Identification test of mucilage

S. No.	*Parameter*	*Result*
1	Presence of mucilage	+
2	Presence of carbohydrate	+
3	Presence of tannins	-
4	Presence of protein	-
5	Presence of reducing sugar	-
6	Presence of saponin	-

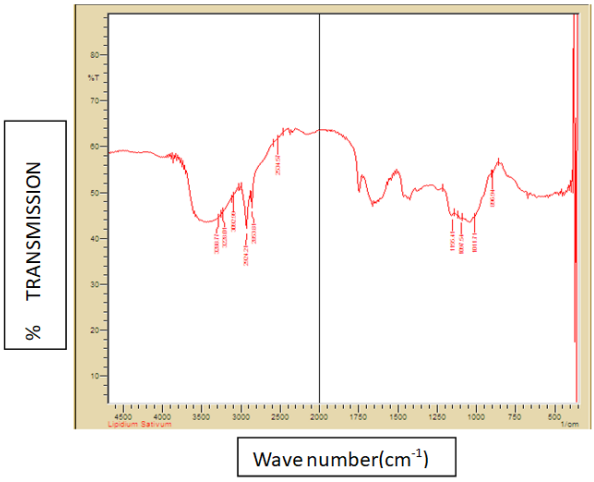

Figure 1: IR spectrum of mucilage

Table 5: FTIR spectrum analysis of mucilage

Absorption peak	*Functional group*
3530,3200	0-H stretching
2361.94	C=O stretching
1597	C=C stretching
1140, 655	C=H stretching

Table 6: FTIR Spectrum Analysis of Diclofenac Sodium

Absorption peak	*Functional group*
3385 cm^{-1}	NH – stretching of secondary amine
1574 cm^{-1}	C=O stretching (carbonyl ion)
1557 cm^{-1}	C=C RING stretching
746 CM^{-1}	C-Cl stretching

Low values showed minimal contamination during collection and handling. pH was found to be 6.0

Infrared Spectrum

The mucilage revealed the presence of hydroxyl, carboxyl and alkane groups which are typical characteristic groups of carbohydrates as shown in Table 5 and Figure 1.

IR spectra of diclofenac sodium

Structure analysis of diclofenac sodium was done by taking IR spectrum of mucilage. The diclofenac sodium revealed the presence of a secondary amine, carboxyl ion as shown in Table 6 and Figure 2.

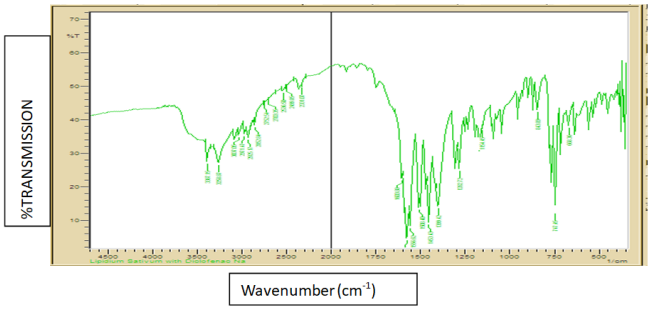

Figure 2: IR Spectrum of diclofenac sodium and *L. sativum* mucilage

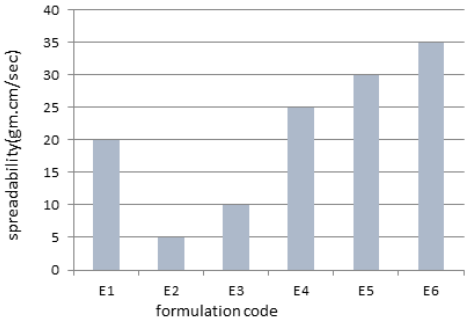

Figure 3: Spreading coefficient

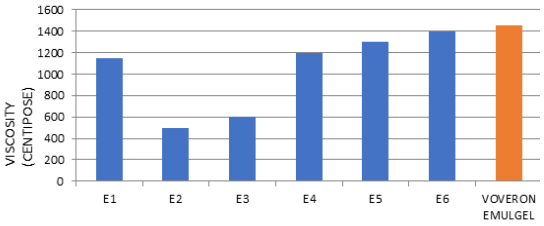

Figure 4: Viscosity study

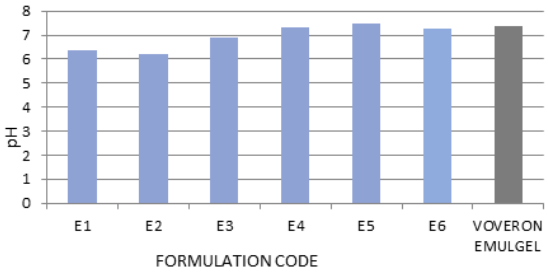

Figure 5: pH of emulgel formulation

Table 7: Evaluation parameter of various emulgel formulations (E1 TO E6)

Parameters	*E1*	*E2*	*E3*	*E4*	*E5*	*E6*
Appearance	White	Creamish	Off creamish	White	Creamish	Off creamish
Easily washable	Yes	Yes	Yes	Yes	Yes	Yes
Spreadability (g.cm/sec)	20	5	10	25	30	35
Extrudability	Excellent	Good	Good	Excellent	Good	Excellent
Viscosity (centipose)	1150	500	600	1200	1300	1400
pH	6.39 ± 0.5	6.20 ± 0.8	6.90 ± 0.32	7.32 ± 0.43	7.50 ± 0.32	7.25 ± 0.34

Table 8: Emulgel formulation with different penetration enhancers

S. No.	*Penetration enhancer in ml*	*Formulation code*		
		E4	*E5*	*E6*
1	Clove oil	2.5	2.5	2.5
2	Oleic acid	2.5	2.5	2.5
3	Methyl salicyalte	2.5	2.5	2.5

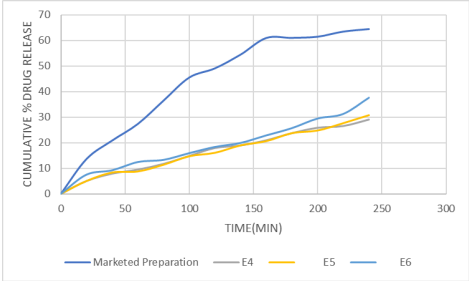

Figure 6: Emulgel formulation with clove oil penetration enhancer

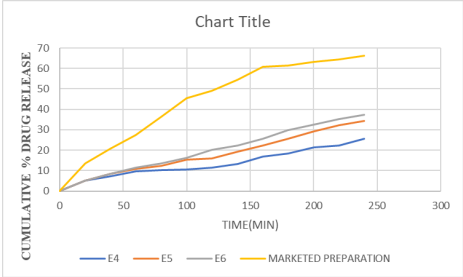

Figure 7: Emulgel formulation with oleic acid penetration enhancer

Drug compatibility study

A compatibility study of diclofenac sodium and L. *sativum mucilage* was done by taking IR spectrum of mucilage. Peaks of L. *sativum* and diclofenac sodium are retained.

The R^2 values for diclofenac sodium calibration curves were found to be 0.999 in water respectively.

The spreadability value for each prepared emulgel was shown in Table 7. The formulation E6, which has a viscosity of 1400 centipoise, has a high spreading coefficient of 35 g.cm/s. It shows that the formulation spreads well as viscosity decreases as shown in Figure 3.

Viscosity

The viscosity of all the prepared emulgel formulation are shown in Figure 4. The findings indicated that emulgel formulation E6 exhibited the highest viscosity at 1400 centipoise and the lowest viscosity at 500 centipoise.

pH

The pH of all the prepared emulgel was depicted in Table 5. All the emulgel formulation was in a normal range of skin pH. The highest pH value is E5 as shown in Figure 5..

From above all the results, 3 emulgel were selected (E4, E5, E6) for further studies because it shows good spreadability, viscosity, pH etc.

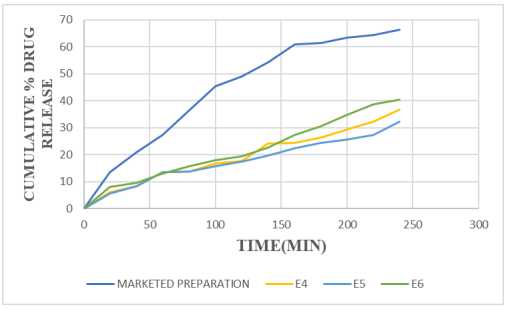

Figure 8: Emulgel formulation with methyl salicylate penetration enhancer

Table 9: Studies of various parameters

S. No	*Parameter*	*Formulation code*			
		E4	*E5*	*E6*	*Marketed preparation*
1	Swelling index (Sw)%	80	75	95	97
2	Drug content%	79	75	80	98.3
3	Skin irritation	-Ve	-Ve	Ve	-Ve

Table 10: Stability studies

S. No.	*Period (*Month*)*	*Drug content (%)*	*pH*
1	0	77.34% ± 0.04	7.10 ± 0.02
2	1	74.36% ± 0.026	7.00 ± 0.12
3	2	71.32% ± 0.49	6.76 ± 0.21

In-vitro drug release study of E4, E5, E6 and compared with marketed preparation

The permeation abilities of the E4, E5, E6 were analyzed by *in-vitro* permeation tests. Permeation study was carried out by using the 3 different types of penetration enhancers as shown in figure 6,7,8. (Clove oil, oleic acid, methyl salicylate). The permeation profile of clove oil, oleic acid, methyl salicylate. A consistent growth in drug concentration within the receptor chamber was noted over time.

The % cumulative drug release for all emulgel formulations was determined at the end of a three-hour period. The findings revealed that emulgel formulation E6 exhibited the highest release rate when compared to E4 and E5. The maximum observed release was 7.32%.

In the formulation E6 40%, the maximum drug release was seen. It was concluded that formulation E4, E5, E6 by formula containing clove oil in their high rate of drug permeation as compared to others.

Stability studies

All the emulgel formulations stored for two months and later on minor changes were observed as shown in Table 10.

Determination of saturation solubility of diclofenac sodium

The saturation solubility of diclofenac sodium was determined in prepared microemulsions by adding excess amount of drug to each sample, mixed, and equilibrating. Then saturated

microemulsions were centrifuged at 3000 rpm for 15 minutes take 1-mL of supernatant and suitably dilute in dimethyl sulphoxide and then transfer 1-mL of the supernatant and suitably diluted in 10 mL dimethyl sulphoxide and then transfer 1-mL of the solution from this to 50 mL volumetric flask and make the volume with the 7.4 phosphate buffer and take the absorbance at 276 nm for determining content of diclofenac sodium. The result indicated that the maximum solubility was observed in the formulation

DISCUSSION

A fascinating alternative to conventional systemic drug delivery is provided by topical formulation. The parenteral route is preferred over oral route, because it may cause nausea, vomiting, limited bioavailability, and bypass the hepatic first part metabolism of this innovative medicine. Skin condition and exterior quality are assessed.[14,15] Despite the fact that gel has several benefits, one of its main limitations is the delivery of hydrophobic drugs. Even a hydrophobic person can benefit from the unique qualities of gel and emulgel when they are combined into one dose, which is called emulgel.[16,17] This is accomplished by using an emulsion-based technique. The objective of this study was to investigate the potential utilization of *L. sativum* seed mucilage as a gelling agent in the development of emulgel, microemulgel-based hydrogel, and gel formulations.[18] In contrast to previous mucilage-isolation techniques, the method used for *L. sativum* seed provides the highest overall yield by precipitating the soaked and blended seed in acetone. For physicochemical studies of extracted material confirm the presence of mucilage with good swelling index and high viscosity suitable for pharmaceutical excipients in pharmaceutical preparation as a gelling agent. Properties of mucilage as a gelling agent in emulgel formulation were evaluated.[19,20] In these we were used different type of gelling like carbopol, *L. sativum* mucilage and carbopol: *L. sativum* mucilage in 1:1. Formulation codes E1, E2, E3, E4, E5, and E6 were developed employing various gelling agents as shown in Table 8 and subsequently assessed for their visual appearance, pH, and spreadability, rheological study, extrudability, etc from all of this three formulation were selected E4, E5, E6 for further study because it has shown the good viscosity and spreadability. And then we were used different type of penetration enhancers in the formulations E4, E5, E6. Penetration enhancer clove oil, oleic acid, methyl salicylate. *In-vitro* drug release study was carried out by this we observed that the penetration enhancer (clove oil) showed the maximum drug release as compared to the oleic acid and methyl salicylate.[21] The maximum drug release show in the E6 formulation in which clove oil penetration are used. After that we evaluated the evaluation parameters like swelling index (Table 9), drug content, and stability study. In the swelling index E6 show the maximum swelling property and efficient amount of drug entrapped in the internal phase and stability study for 2 months. After 2 month there were no changes in formulation.[22,23]

CONCLUSION

Here a topical emulgel and an *L. sativum* gel were developed, utilizing *L. sativum* mucilage as a gelling agent. These formulations underwent a series of physical and chemical analyses, including rheological assessments, spreadability evaluations, and *in-vitro* release studies, among others.

The *in-vitro* release experiments were conducted to investigate the release of the drug from the emulgel formulations. Among these formulations, E6 displayed the most significant drug release over a 180-minute duration. Additionally, formulations E4, E5, and E6 were compared to commercially available preparations.

Based on the *in-vitro* results, it was evident that emulgel formulations utilizing *L. sativum* mucilage as a gelling agent hold promise for use in topical drug delivery systems.

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