Formulation And Evaluation Of Emulgel For Topical Delivery Of Drug

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Abstract **- This study centers around the development and assessment of an emulgel for the topical application of thiocolchicoside, a muscle relaxant that has low oral absorption and is known to cause gastrointestinal side effects. The goal was to create a reliable, efficient and patient-friendly topical solution that improves skin absorption and delivers targeted treatment. Emulgel formulations were prepared using various concentrations of gelling agents, emulsifying agents and oils and were evaluated for physical appearance, pH, viscosity, spreadability, extrudability, drug content, and in vitro drug release. The improved formulation showed promising physical characteristics and maintained drug release for a duration of 8 hours. The formulation demonstrated excellent stability and compatibility with the skin suggesting its potential as a suitable alternative for the topical application of thiocolchicoside in the treatment of musculoskeletal conditions.**

Key word: **Thiocolchicoside, Emulgel, Topical delivery, Skin permeation, In vitro release.**

INTRODUCTION:

Due to its ability to achieve local therapeutic efficacy, topical drug delivery systems are of great interest simultaneously minimizing systemic exposure and associated side effects. Among the various topical formulations, emulsifiers combine emulsion and gel properties with improved pharmaceutical loading capacity, improved skin penetration, and better acceptance of patients. [1] relaxatives, anti-inflammatory and analgesic effects. It is often used to treat painful musculoskeletal and rheumatic conditions. [2] Despite its effectiveness, the oral and parenteral routes of administration are often associated with gastrointestinal complaints and side effects, including potential genotoxic risks at higher systemic concentrations.[3] These limitations underscore the need to investigate alternative tax routes that can improve therapeutic security and effectiveness. The low water solubility of the drug and limited skin permeability include language in effective localized systems[4]Emulgels offers a promising solution by adding hydrophobic agents to the gel matrix stabilized emulsion phase, improving solubility and skin torque.[5] The goals include optimization of formulation parameters, assessment of physicochemical properties, assessment of in-vitro-drug release and ex-vivo-skin permeational profiles. The ultimate goal is to develop stable, effective, patient-like emulsification that maximizes the therapeutic potential of thiocolchicosides while simultaneously minimizing its systemic risk.

Criteria for the selection of drug in the topical drug delivery system:[6]

Physicochemical properties:

- The drug should have a molecular weight less than approximately 1000 daltons.
- The drug should have affinity for both lipophilic and hydrophilic phases.
- Extreme partitioning characteristics are not conductive to successful drug delivery via the skin.
- The drug should have low melting point.

Biological properties:

- The drug should be potent with a daily dose of the order of a few mg/day.
- The half-life (t1/2) of the drug should be short.
- The drug must not include a cutaneous irritant or allergic response.
- Drug which degrade in the GI tract or are inactivated by hepatic first pass effect are suitable candidates for topical delivery.
- Tolerance to the drug must not develop under the near zero-order profile to topical delivery.
- Drug which have to be administered for a long period of time or which cause adverse effect to non-target tissues can also be formulated for topical delivery.
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I. ADVANTAGES OF EMULGEEL: [7]

- One way to incorporate hydrophobic medicines into the gel foundation rapidly is to use water/oil/water emulsions.
- Strength and load bearing capabilities have been increased.
- Easy for production and a low-cost method.
- Bypass the primary metabolism.
- The precise placement of drugs inside the body.
- The patient's willingness and ability to self-medicate has improved.

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II. Disadvantages of Emulgel: [8]

- Poorly soluble and poorly permeable drugs cannot be given through skin.
- Air entrapment may happen during manufacturing which leads to foam generation in the formulation.
- Drug molecule with high molecular cannot be given through emulgel.
- Drug molecule with large particle size not easily permeable through the skin.
- Skin irritation or allergic reaction may develop on contact dermatitis.

III. Challenges in development of Emulgel: [9,10]

- Risk of creaming, coalescence, flocculation and Ostwald ripening.
- Incompatibility between oil phase, surfactants, gelling agent and drug.
- Avoiding syneresis from the gel matrix.
- Difficulty in achieving uniform drug distribution.
- High water content makes emulgel prone to microbial contamination.
- Maintaining skin friendly pH [4.5-6.5] while ensuring drug stability and gelling efficiency.
- Reproducing skin condition accurately in-vitro.
- Variability in permeation data due to skin type, condition and hydration.
- Monitoring physical changes, chemical degradation and microbial growth.
- Evaluating non-greasiness, ease of application and aesthetic appeal which are subjective and difficult to quantify.

IV. Composition of emulgel: [11,12,13]

- Drug (Active pharmaceutical Ingredients)
- Vehicle
- Aqueous material
- Oils
- Emulsifier
- Gelling agent
- Permeation enhancer

- **Steps involved in preparation of emulgel:** [14]

- Combination oil phase and aqueous phase
- Emulsification
- o/w emulsion or w/o emulsion
- Incorporation of emulsion in gel base
- Swelling of gelling agent in aqueous medium to form gel
- Emulgel

V. Evaluation parameters of Emulgel: [15,16]

- Physical appearance
- Homogenity
- Grittiness
- pH determination
- Spreadability study
- In-vitro release kinetic study
- Extrudability study
- Swelling index
- Rheological studies
- Drug content determination
- In-vitro drug diffusion study

Methods and Material:

I. List of chemicals used

Sr. No.	Materials	Manufactures / Suppliers
1	Thiocolchicoside	Leeford Limited
2	Liquid Paraffin	Research Lab
3	Carbopol 940	Colorcon Asian Pvt. LTD
4	HPMC	Colorcon Asian Pvt. LTD
5	TWEEN 80 &60	Merck Chemicals
6	SPAN 80 & 60	Merck Chemicals
7	PEG400	Research-lab Fine Chem
8	Methyl Paraben	A.B.ENTERPRISES, Mumbai India
9	Propyl Paraben	A.B.ENTERPRISES, Mumbai India
10	Triethanolamine	Research-lab Fine Chem

II. Method

1. Preformulation Studies: [17,18]
   The melting point of Thiocolchicoside was determined using the capillary method. Solubility was assessed in various solvents and λ max was identified via UV spectroscopy in phosphate buffer (7.4). Drug-excipient compatibility was evaluated using FTIR spectroscopy.

2. Standard Curve: [19,20]
A standard calibration curve of Thiocolchicoside was prepared in phosphate buffer (pH 7.4) and absorbance was recorded at 261 nm using a UV spectrophotometer.
3. Formulation of Emulgel : [21]
For preparation of emulgel formulations, Thiocholchicoside was selected as active agent. Carbopol 940 and Tamarind Gum which is a natural novel polymer were used as gelling agent. Mineral oil / liquid paraffin was selected as oil phase. The required HLB for this was oil is in the range of 10-12 for formulation of O/W emulsion. The emulsification is achieved by using combination of emulsifying agents. Hydrophilic emulsifier and lipophilic emulsifier i.e. TWEEN 80, TWEEN 60, SPAN 80, SPAN 60 were selected respectively. PEG was incorporated as plasticizer and penetration enhancer, methyl paraben and propyl paraben as preservative.

Composition of emulgel of thiocochicoside:
Aqueous phase -

Ingredients (mg)	B1	B2	B3	B4	B5	B6
Carbopol 940	0.5g	1g	2 g			
Tamarind Gum				1g	2 g	4 g
PEG400	10 ml	10 ml	10 ml	10 ml	10 ml	10 ml
Methyl Paraben	0.25	0.25	0.25	0.25	0.25	0.25
Propyl Paraben	0.15	0.15	0.15	0.15	0.15	0.15
Triethanolamine	QS	QS	QS	QS	QS	QS
Purified Water QS to	100 ml	100 ml	100 ml	100 ml	100 ml	100 ml

Oil phase -

Ingredients	B1	B2
Thiocolchicoside	500 mg	500 mg
Liquid Paraffin	30 ml	30 ml
Tween 80	1.73	
Span 80	1.27	
Tween 60		1.52
Span 60		1.48
Methyl Paraben	0.25	0.25
Propyl Paraben	0.15	0.15
Purified Water QS to	100 ml	100 ml

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4. Evaluation of emulgel: [22,23,24]
The prepared emulgel were evaluated for physical parameters such as colour, odour, appearance, consistency, grittiness homogeneity, pH, spreadability, extrudability, swelling index, viscosity, drug content and in-vitro drug diffusion using standard protocols.
5. In-vitro drug Diffusion study: [25,26]
Drug diffusion studies were conducted using Franz diffusion cell.
6. Stability Study: [27,28]
The optimized formulation was subjected to accelerated stability testing as per ICH guidelines at 40°C and 75% RH for 3 months. Parameters such as appearance, colour, consistency, homogeneity, pH viscosity, spreadability, drug content, and drug release were re-evaluated post-storage.

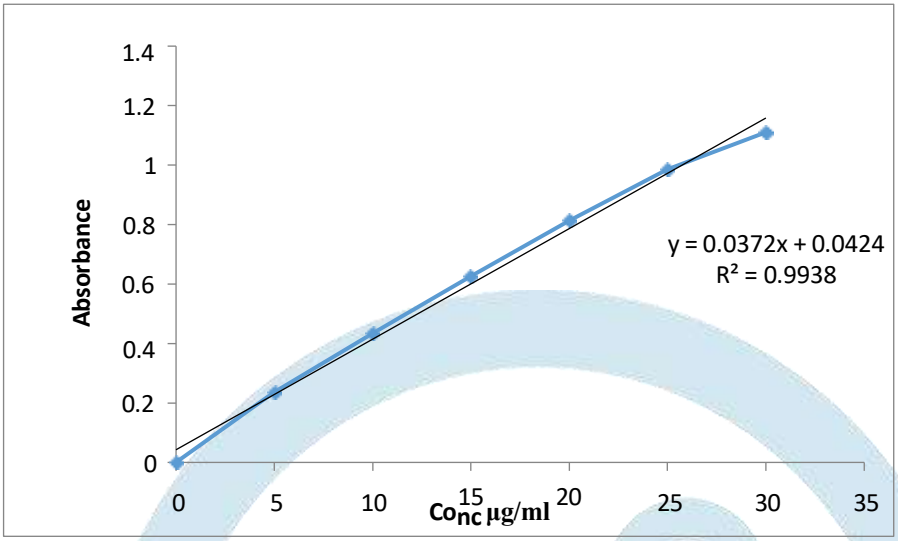
RESULT AND DISCUSSION:

I. PREFORMULATION STUDIES:

Thiocolchicoside exhibited a melting point between 194°C–196°C, confirming its purity. It was found to be very soluble in water and slightly soluble in ethanol & methanol and insoluble in benzene. The λmax was observed at 261 nm in phosphate buffer (pH 7.4) consistent with reported values.

II. STANDARD CALIBRATION CURVE:

The delivery system is supposed to release the drug in the dermal region, so the standard curves was prepared in buffers pH 7.4. Standard Curve was prepared by dissolving 100 mg of drug in 100 ml of buffer (1 mg/ml); one ml of this solution was further diluted to 10 with buffer (100 µg /ml). This solution was further used to prepare final solutions of 5 µg /ml to 30 µg /ml. The solutions were finally filtered using Whatman's filter paper. Absorbance was recorded at 261 nm.

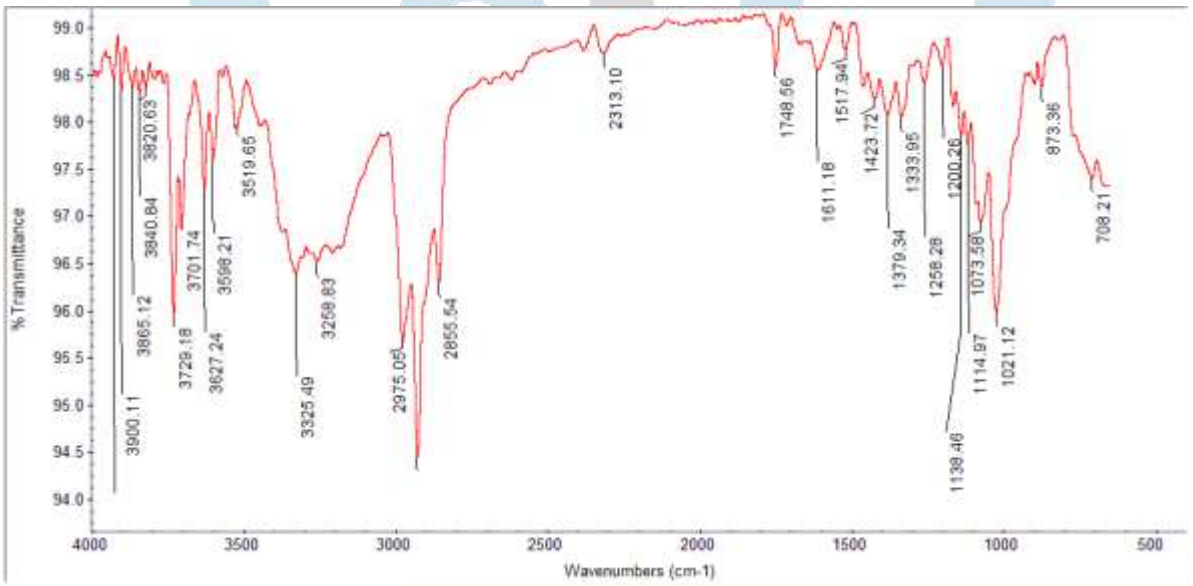


Standard Calibration Curve of Thiocolchicoside

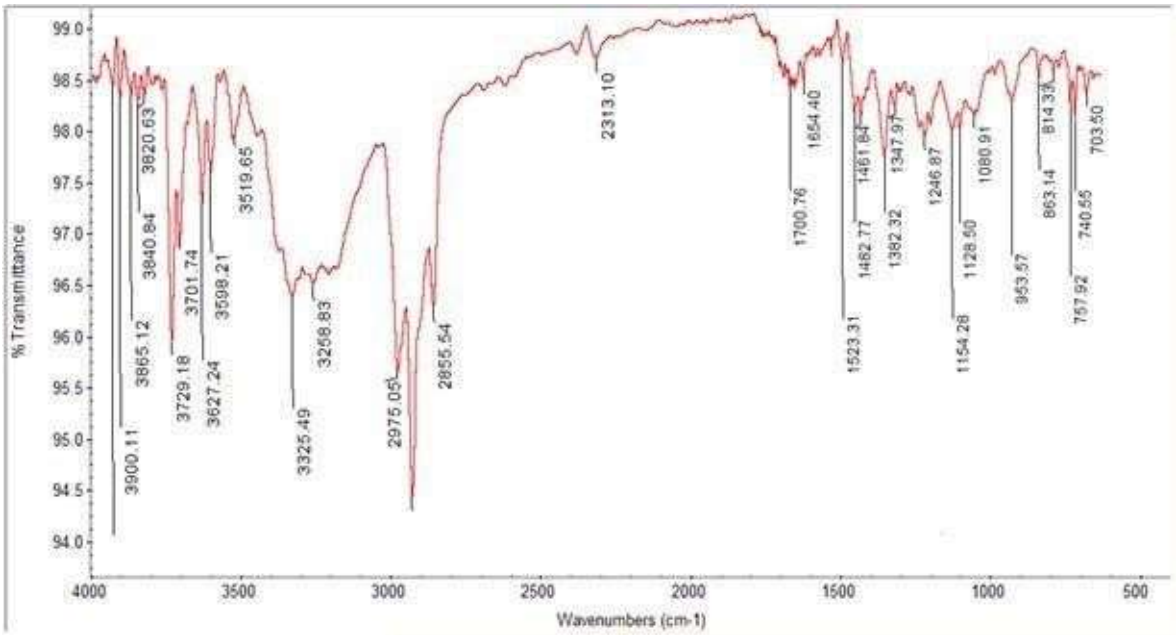
III. Compatibility Studies:

FTIR analysis revealed no significant interaction between Thiocolchicoside and the excipients, confirming their compatibility for formulation.

IR spectra of pure drug Thiocolchicoside:



IR Spectra of drug and excipient mixture:



IV. EVALUATION OF EMULGEL:

All six batches (b1–b6) showed acceptable physical properties. The transparency of carbapol emulgels was comparatively more than the tamarind gum gels. All the formulations were found to possess uniform homogeneity. As the concentration of carbapol increases the consistency, viscosity of the product increases. The Emulgels prepared with the tamarind gum showed comparatively lesser viscosity as compared to the carbapol emulgels. The gelling effect of Carbapol was pH dependent where no such relationship was found with the tamarind gum gels. The gelling effect was due to swelling of the polymeric chains of the gums.

Formulation	Appearance	Color	Odour
B 1	Semisolid Emulgel	Brownish -Yellow	Characteristics like Colchicin
B 2	Semisolid Emulgel	Brownish -Yellow	Characteristics like Colchicin
B 3	Semisolid Emulgel	Brownish -Yellow	Characteristics like Colchicin
B 4	Semisolid Emulgel	Brownish -Yellow	Characteristics like Colchicin
B 5	Semisolid Emulgel	Brownish -Yellow	Characteristics like Colchicin
B 6	Semisolid Emulgel	Brownish -Yellow	Characteristics like Colchicin

Formulation	Consistency	Grittiness	Homogeneity
B 1	Low	Non Gritty Smooth	Uniform
B 2	Good	Non Gritty Smooth	Uniform
B 3	Higher	Non Gritty Smooth	Uniform
B 4	Low	Non Gritty Smooth	Uniform
B 5	Low	Non Gritty Smooth	Uniform
B 6	Intermediate	Non Gritty Smooth	Uniform

Determination of pH

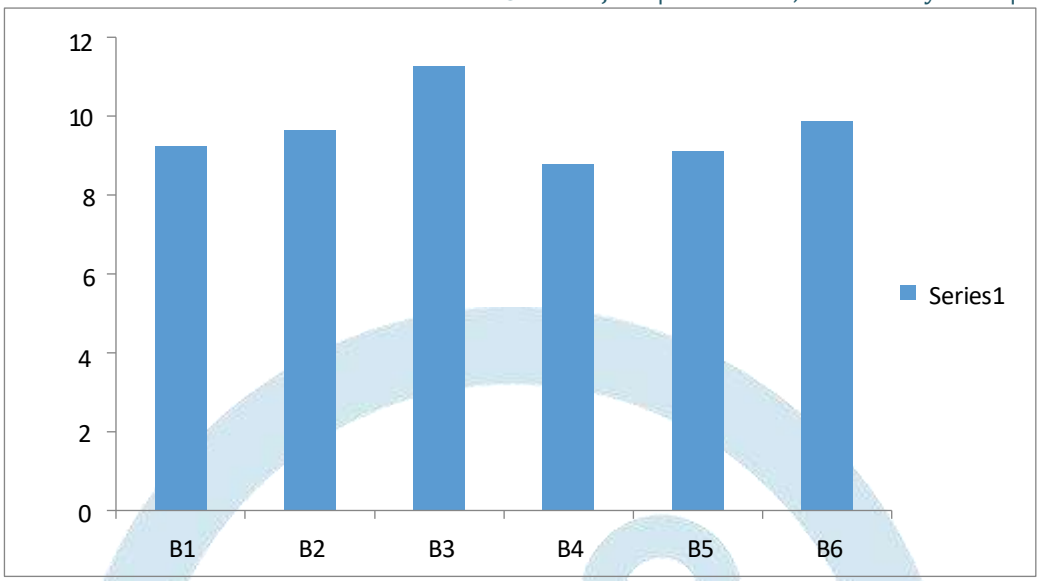
The pH of the prepared gel formulations was determined by utilizing a digital pH meter. The pH of all the formulations B1, B2, B3 were found to be in the of 6.8 to 7.1, whereas gels formulated with the tamarind gum shown the pH values from 6.5 and 6.6.

Sr. No	Formulation	pH
1	B1	7.1
2	B2	6.9
3	B3	6.8
4	B4	6.6
5	B5	6.6
6	B6	6.5

Spreadability Study

Spreadability is measured using this method based on the gel's 'Slip' and 'Drag' qualities. As the concentration of polymer increases the value of spreadability coefficient increases indicating decrease in the spreading ability.

Sr. No	Formulation	Spreadability g cm/sec
1	B1	9.23
2	B2	9.65
3	B3	11.28
4	B4	8.78
5	B5	9.10
6	B6	9.88

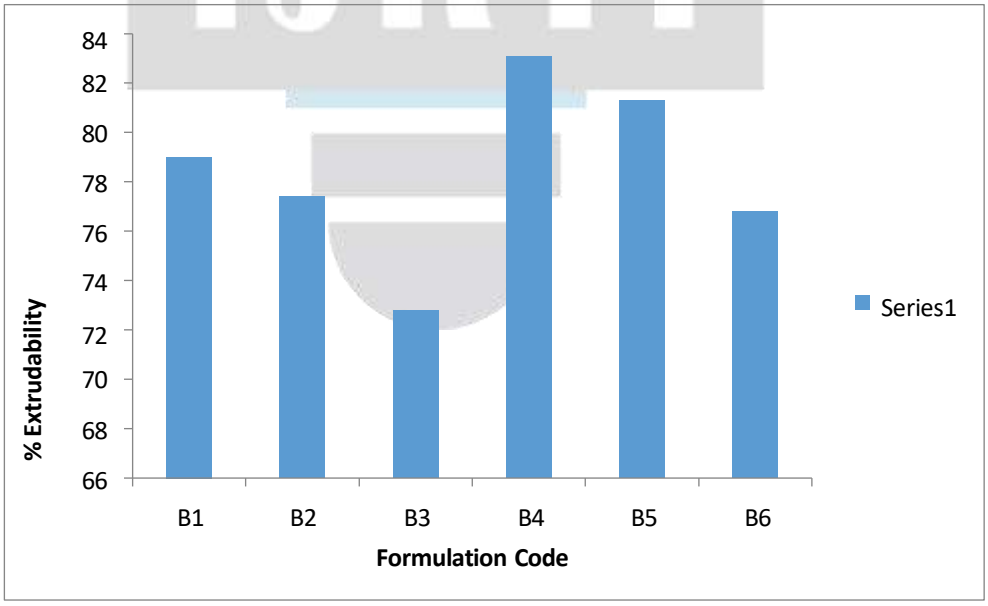


Spreadability of Formulations

Extrudability study

Extrudability is indicative of ease with which product could be easily removed from the collapsible tube. The effect of polymer concentration and consistency were observed on the extrudability of the product. The extrudability was found to be in the range of 69-75 % for the Carbapol gels where as from 76.8 to 84.2 for the tamarind gum gels.

Formulation	Extrudability (% gel Extruded)	Grade
B 1	79	Fair
B 2	77.4	Fair
B 3	72.8	Fair
B 4	83.1	Good
B 5	81.3	Good
B 6	76.8	Good

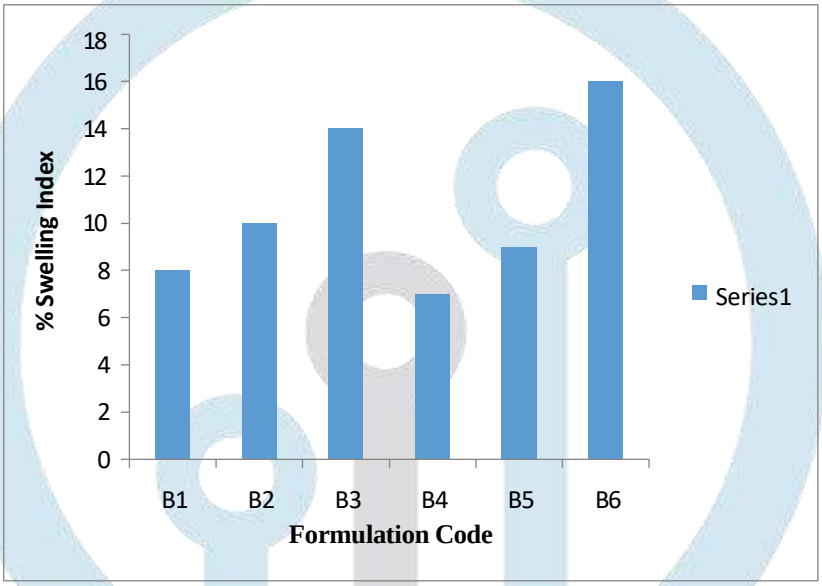


Extrudability Study

Swelling Index

Swelling studies were performed for all the formulations. The swelling index was found to be in the range of 7.8 % to 13.8 % and 7.1 % to 15.8 % for Batch B1 to B3 and B4 to B6 respectively. The results of swelling index suggest the higher swelling properties of the tamarind gum based emulgels whereas the carbapol based emulgels swells comparatively lesser.

Formulation	Swelling Index %
B 1	7.8
B 2	9.9
B 3	13.8
B 4	7.1
B 5	9.1
B 6	15.8



Swelling Index Chart

Rheological Studies

All the preparation was studied for the rheological characters. Viscosity is one of the important characteristic property of liquid and semisolid dosage form. The emulgels during the storage and usage by the patient or any user are exposed to various stress conditions leading to changes in the flow behavior of the formulation. The results of rheological studies suggest the carbapol concentration based changes in the viscosity of the product. As the concentration of carbapol increases the viscosity of the formulation increases. The tamarind gum based emulgels have lower viscosity as compared to formulation B1, B2, and B3.

Formulation	Viscosity in CPS
B 1	1220
B 2	1630
B 3	2210
B 4	1010
B 5	1150
B 6	1360

Drug Content Determination

The amount of drug present was determined using 1 gm of the gel.

Formulation	%Drug Content
B 1	98.7 %
B 2	97.9 %
B 3	98.2 %
B 4	98.6 %
B 5	99.2%

V. In-Vitro Drug Diffusion Study

The drug diffusion studies were conducted using the Franz diffusion cell.

Time (Min)	Cumulative Percent Release of Thiocolchicoside					
	B 1	B 2	B 3	B 4	B 5	B 6
0	0	0	0	0	0	0
5	4.12	3.98	3.88	4.6	4.5	4.5
10	10.16	8.2	7.9	9.2	8.9	8.4
15	20.8	18.6	17.4	22.6	20.9	19.8
20	28.6	25.4	24	30.6	28.8	27.6
30	38.2	35	34.2	40.8	38.8	37.4
60	64.1	58.6	54.8	60.6	62.1	60.6
120	78.2	74.2	73.8	84.2	82.8	78.2
240	80	81.2	79.6	85.6	86.2	82.8

Cumulative Percent Drug Release of Thiocolchicoside

VI. Stability Study:

Batch B5 was studied for stability characteristics. The batch does not show major variations.

Characteristics	Before study	After study
Appearance	Semisolid emulgel	No change
Color	Brownish-yellow	No change
Consistency	Low	No change
Grittiness	Non gritty smooth	Non gritty smooth
Homogeneity	Uniform	Uniform
PH	6.6	6.6
Spreadability	9.10	9.5
Extrudability	81.3	81.2
Viscosity	1150	1140
Drug content	99.2%	99.1%

CONCLUSIONS:

From the current study, it can be concluded that, Thiocolchicoside emulgel was successfully developed using carbopol and tamarind gum as gelling agents. The emulgels were further evaluated spredability studies, the results of the suggest that as the concentration of the polymer increases the spredability is reduced. Moreover, the emulgels with the tamarind gum are having good spreadability characteristics.

The emulgels show good extrudability indicating ease of use by the user. The extrudability value increases at lower concentration, however there is no major difference in the emulgels formulated with two polymers.

The formulated gels show swelling characteristics on exposure to the moisture. The swelling was observed to higher extent in the tamarind gum gels as compared to the carbapol gels, this can be attributed to higher water entrapment and holding of the polysaccaharide chains of the gum.

The emulgels were studied for rheological properties using Brookfield's Viscometer. The viscosity studies revealed that the carbapol containing emulgels were having comparatively higher viscosity as compared to tamarind gum containing gels. The drug content was estimated using 1gm of the gel, it was found to be in the acceptable limits.

The drug diffusion studies done using Franz Diffusion cell and membrane shown that the drug diffusion from all the formulations was good. The drug diffusion from formulation B 5 was highest 86.2 % at the end of four hours.

Batch B 5 was accepted as the optimized batch due its good consistency, non-grittiness, soothness in texture etc. The spredability, extrudability was also good for this formulation.

Overall it can be concluded that emulgels offer variety of the advantages for the topical delivery of the hydrophilic as well as hydrophobic agents. Stable emulsions can be formulated using the concept of RHLB. The emulsions can be well incorporated in the gelling agent. The tamarind gum which is newer polymer can be further explored for the pharmaceutical applications.

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