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FORMULATION AND EVALUATION OF THIOCOLCHICOSIDE EMULGEL FOR ANTI-ARTHRITIC ACTIVITY

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ABSTRACT

Rheumatoid arthritis can impact places other than the joints and is an inflammatory kind of arthritis. The current study was based on the formulation and evaluation of thiocolchicoside emulgel for anti-arthritic activity. The Pre-formulation studies were done. After preparation, emulgels are evaluated for parameters i.e., physical examination, pH determination, swelling index, drug content estimation, in-vitro drug release and stability studies. Screening of anti-arthritic activity was performed through *in-vitro* models using Inhibition of protein denaturation using bovine serum albumin and Inhibition of protein denaturation using egg albumin. In results, among all the emulgel formulations, F1 showed the excellent spreadability and *in-vitro* drug release. Therefore, F1 was further utilized in the evaluation of anti-arthritic activity. thiocolchicoside based emulgel demonstrated the significant anti-arthritic activity in terms of % inhibition of protein denaturation (using BSA) as 95.4±0.6 % at the conc. of 800µg/ml. It might be tested on the animal model to confirm the safety profile of thiocolchicoside-based emulgel which could be further used clinically. It concluded that thiocolchicoside-based emulgel was found effective in the reduction of arthritis-based inflammation. The anti-arthritic effect might be due the reduction in the production and release of inflammatory cytokines. Fellow researchers are recommended to evaluate the mode of action that how thiocolchicoside emulgel treat and prevent the progression of rheumatoid arthritis.

Keywords: Rheumatoid arthritis, anti-arthritic, emulgel, thiocolchicoside.

INTRODUCTION

Rheumatoid arthritis can impact places other than the joints and is an inflammatory kind of arthritis (Klareskog et al. 2020). It is mostly brought on by environmental causes, including smoking cigarettes, and genetic predisposition (Smolen et al. 2016; Bullock et al. 2018). Typically, it affects small peripheral joints first, but if addressed, it can spread to proximal joints and become symmetric (Sparks, 2019). When inflammation erodes cartilage and pushes bone into the joint socket, degeneration of the joints results. While the symptoms of established

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RA usually manifest after the disease has been present for more than six months, those of early RA frequently manifest within the first six months of the disease's inception. Increased mortality is a result of untreated RA. as well as impairment (Pincus et al. 1999).

Drug profile

Thiocolchicoside is semi synthetic derivative of colchicoside and natural derivative of colchisine. Colchicoside and colchisine both are extracted from seeds of Gloriosa superba (Liliaceae). Thiocolchicoside is a muscle relaxant agent launched since 1959. Its good clinical efficacy has been demonstrated in several clinical trials. The tuberous roots of Gloriosa superba can be used potentially to cure snakebites, skin diseases and ulcers, or to treat inflammation. Its seeds are helpful in relieving rheumatic as well as muscle pains (Malviya et al. 2019).

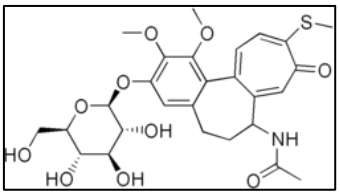

Fig 1. Structure of Thiocolchicoside

The research focuses on the formulation and evaluation of thiocolchicoside emulgel for anti-arthritic activity using suitable excipients and plasticizers. It was also evaluated for the anti-arthritic activity (in-vitro).

MATERIALS AND METHODS

Chemicals and Instruments

Thiocolchicoside, ethanol, PEG 200, carbopol, liq. paraffin, methyl paraben, tween 80, hpmc, and distilled water.

Digital weighing balance, Digital pH meter, Franz diffusion cell and UV-Spectrophotometer.

Pre-formulation study

Organoleptic properties

Thiocolchicoside was observed for their physical characteristics like colour, odour, texture of drug and compared with as reported in official monograph.

Fig 2. Thiocolchicoside drug sample

Solubility

The solubility of Thiocolchicoside is determined by placing a small quantity of polymers (about 1-2 mg) individually in a test tube, adding 5ml of solvent (water, ethanol, methanol, phosphate buffer), shaking vigorously, and holding for a while. Take note of the product's solubility in various solvents when it is at room temperature.

Preparation of standard calibration curve of Thiocolchicoside

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100mg of Thiocolchicoside accurately weighed and dissolved in methanol (2ml) and volume is made up to 100ml with 0.1N HCl solution thus stock solution is prepared. The 10ml of stock solution is further diluted with 0.1 N HCl (pH 1.2) in 100ml to get 100µg/ml concentration solution. Then 0.2, 0.4, 0.6, 0.8, and 1ml of solution is taken in 10ml standard volumetric flask and made the volume up to 10ml with 0.1N HCl to prepare 2µg, 4µg, 6µg, 8µg, and 10µg/ml solution. Then the absorbance is measured in a UV spectrophotometer at 270 nm against 0.1 N HCl as blank. The procedure is repeated with phosphate buffer at pH 6.8 and absorbance is measured at wavelength 270 nm (Reddy et al. 2019).

Formulation of emulgels

Preparation of emulsion

Aqueous phase

To prepare the aqueous portion of the emulsion, Tween 80 was dissolved in free, polluted water.

Oil Phase

While Thiocolchicoside was initially dissolved in ethanol, methyl paraben was dissolved in propylene glycol. Aqueous solution is supplemented with these two solutions. The aqueous and oily phases were each heated to 75°C in isolation. After that, the aqueous phase and oil phase were combined while being constantly stirred until the mixture reached room temperature (Anupama and Ashwani, 2022).

Preparation of gel

The gel bases are made by individually adding varying polymer concentrations to distilled water and continuously shaking the mixture with a mechanical shaker. Triethanolamine was used to raise each formulation's pH to 6-6.5.

Table 1. Composition of Thiocolchicoside emulgel

Ingredients	Formulation		
	F1	F2	F3
Thiocolchicoside (g)	0.5	0.5	0.5
Tween 80 (g)	0.2	0.2	0.2
Liquid Paraffin (ml)	1.0	1.5	2.0
PEG 200 (ml)	1.0	1.0	1.0
Methyl Paraben (g)	0.02	0.02	0.02
Ethanol (ml)	5	5	5
Carbopol (g)	2.0	1.5	1.0
HPMC K4M (g)	1.0	1.0	1.5
Purified Water	Qs.	Qs.	Qs.

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Fig 3. Preparation of gel

Evaluation parameters (Pani et al. 2015; Patel et al. 2013)

Physical Examination

The prepared emulgel preparations were examined for their color, homogeneity, consistency, and phase separation.

Measurement of pH

Using a digital pH meter, the pH of the emulgel formulations was examined. One gram of emulgel was dissolved in one hundred milliliters of distilled water to create an emulgel solution, which was then set aside for two hours. Each formulation's pH was measured three times, and the average results were recorded.

Swelling Index

Using porous aluminium foil, 1 gram of emulgel is taken in this technique and put into a beaker with 10 milliliters of 0.1N sodium hydroxide (NaOH). Samples were then taken out of the beakers (at various intervals) and placed in a dry location. Samples were weighed once more while they were drying.

formula-

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

Wo= Original weight of emulgel, Wt= Weight of swollen emulgel

Drug Content Estimation

After dissolving 1 g of emulgel in 50 ml of 0.1N NaOH, the mixture is let to stand for 2 hours (reaction time). Next, a UV visible spectrophotometer is used to measure the absorbance of 5 milliliters of sample at a wavelength of 276 nanometers.

***In-vitro* Drug Release**

The Franz diffusion (FD) cell uses phosphate buffer at pH scale to carry out in-vitro drug release. For diffusion, cellophane membrane is utilized as a semi-permeable membrane. 20 ml of medium are poured into the receptor compartment up until the collection limb mark. Following that, the membrane is retained on the receptor compartment.

1g of emulgel should be precisely weighed, placed between the donor and receptor compartments on the membrane, and fitted tightly. The donor compartment magnetic stirrer and the external stirrer's rotations per minute (rpm) are regulated to create laminar flow in the medium. The circulating water jacket keeps the FD cell's temperature at 37°C. 5 ml of sample is drawn from the collection limb at periodic intervals, and the same volume is then replaced

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with buffer media. The samples are then examined by a UV spectrophotometer at a wavelength of 276 nm to determine concentrations.

Stability studies

Stability studies are carried out by keeping the optimized formulations in the glass container. It is sealed by heat at the end for one month at room temperature. The films are taken at different time intervals like 0 to 4th week and are analyzed for its appearance, swelling index and drug content.

Evaluation of anti-arthritic activity

- **Inhibition of protein denaturation using bovine serum albumin**

The anti-arthritic activity of emulgel is evaluated using method of bovine serum albumin denaturation. The reaction mixture (0.5ml) contained 0.45 ml BSA (5% aqueous solution) and 0.05ml of different concentrations (12.5, 25, 50, 100, 200, 400, 800µg/ml) of emulgel, fractions and indomethacin (reference drug), correspondingly. Each solution was attuned to pH 6.3 by 1 N HCl. The samples were incubated at 37°C for 20 min and heated at 57°C for 30 min. Then phosphate buffer (2.5 ml) was added and absorbance was measured at 660nm via spectrophotometer. For test control 0.05ml distilled water was used while product control lacked BSA (Pandey, 2010). The percentage inhibition of protein denaturation was deliberated by following formula:

Percentage inhibition= [Abs control–Abs test sample/Abs Test Control] × 100

Abs = Absorbance.

- **Inhibition of protein denaturation using egg albumin**

The reaction mixture (5 ml) included egg albumin (0.2 ml), phosphate buffered saline, 2.8 ml (pH 6.4) and 2ml of emulgel and diclofenac sodium at various concentrations (12.5, 25, 50, 100, 200, 400 and 800µg/ml), respectively. Equal volume of double-distilled water served as control. The mixtures are incubated at 37±2°C in a biochemical oxygen demand (BOD) incubator for 15min and then heated at 70°C for 5 min. Their absorbance is measured at 660nm (Pandey, 2010). The percentage inhibition of protein denaturation is appraised using undermentioned formula:

Percentage inhibition = [Abs control–Abs test sample/Abs Test Control] × 100

Abs = Absorbance.

RESULTS AND DISCUSSION

Pre-formulation studies

Organoleptic properties

Drug sample of Thiocolchicoside was observed as pale yellow, crystalline powder with its characteristics order. Carbopol as white powder with Characteristics order. PEG 200 was found as colorless liquid, while Tween 80 as yellow liquid.

Table 2. Organoleptic properties of Thiocolchicoside emulgel

Ingredients	Organoleptic characteristics		
	Appearance	Colour	Odor

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Thiocolchicoside	Crystalline Powder	Pale yellow	Characteristics
Carbopol	Powder	White	Characteristics
HPMC 4KM	Powder	Off-White	Odourless
PEG 200	Liquid	Colourless	Characteristics
Tween 80 (ml)	Liquid	Yellow	Characteristics
Ethanol	Liquid	Clear	Wine-like

Solubility

Thiocolchicoside solubility in the different solvents was assessed. Thiocolchicoside demonstrated free solubility in Tween 80, ethanol and distilled water. It was found soluble in chloroform, and phosphate buffer solution.

Table 3. Solubility of Thiocolchicoside

Solvent	Thiocolchicoside
Tween 80	Freely Soluble
Ethanol	Highly Soluble
Distilled water	Highly soluble
Chloroform	Soluble
Phosphate Buffer Solution	Soluble

Preparation of Std. Calibration curve of Thiocolchicoside

Thiocolchicoside showed the absorption maxima (λmax) at 260nm when determined in the conc. range of 2 µg/ml- 10 µg/ml.

Table 4. Std. Calibration curve of Thiocolchicoside

Conc. (µg/ml)	Absorption (λmax 260 nm)
2	0.19
4	0.34
6	0.59
8	0.76
10	0.93

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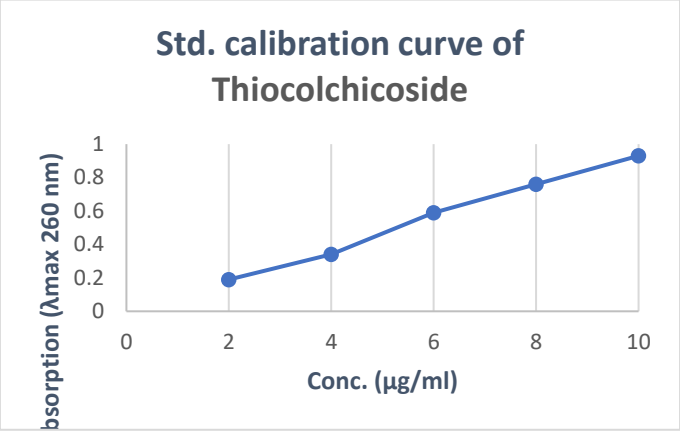

Fig 5. Std. Calibration curve of Thiocolchicoside

Evaluation of formulations

Physical appearances

Three different emulgels were developed and assessed based on their physical characteristics, including color, consistency, and phase separation. It demonstrated that emulgels are in pale yellow color. Phase separation was not found in these formulations, with optimum consistency.

Table 6. Physical appearance

Formulation	Color	Consistency	Phase separation
F1	Pale yellow	Optimum	Not found
F2	Pale yellow	Optimum	Not found
F3	Pale yellow	Optimum	Not found

Estimation of pH

The pH level was determined to maximize the solubility and absorption. pH was estimated as 6.7±0.5 (F1). While pH for F2 and F3 was measured as 6.9±0.3 and 6.5±0.7, respectively. Therefore, all the formulations showed pH range in slight acid environment which exhibit better solubility.

Table 7. Estimation of pH

Formulation	pH range
F 1	6.7±0.5
F 2	6.9±0.3
F 3	6.5±0.7

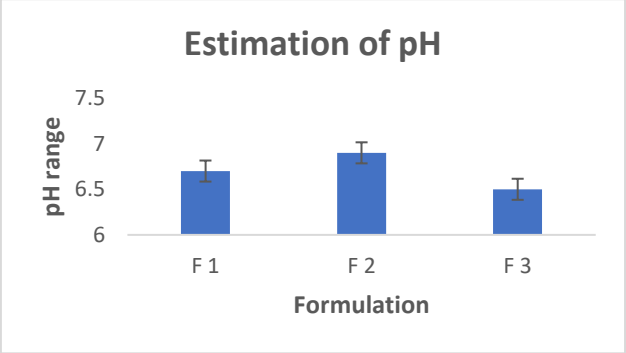

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Fig 6. Graphicald data of measurements of pH

Determination of viscosity

Every emulgel's viscosity is a quality factor that guarantees its homogeneity and consistency. It makes the formulation more flowable, which improves availability. The highest viscosity was estimated in F1 as 571.11±0.29. However, formulation F2 revealed a viscosity of 549.24±0.32. While, F3 has shown viscosity as 562.16±0.40. High viscosity exhibits a better adhere and absorption property.

Table 8. Determination of viscosity

Formulation	Viscosity
F1	571.11±0.29
F2	549.24±0.32
F3	562.16±0.40

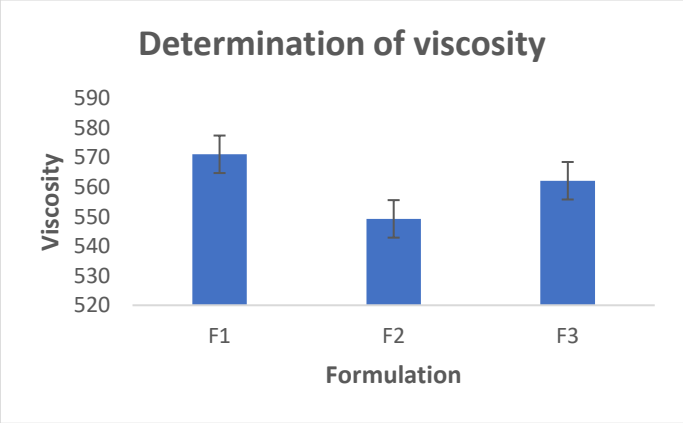

Fig 7. Graphical data of determination of viscosity

Spreadability

Spreadability refers the absorption capacity through the better uniformity of contents. The spreadability data showed a specific flowability of the formulations developed. Emulgel (F1) demonstrated highest spreadability as 17.56±0.81 g.cm/s. When observed F2 and F3 were shown spreadability as 14.18±0.26 g.cm/s and 13.61±0.53 g.cm/s, respectively.

Table 9. Measurements of Spreadability

Formulation	Spreadability (g.cm/s)
F1	17.56±0.81
F2	14.18±0.26
F3	13.61±0.53

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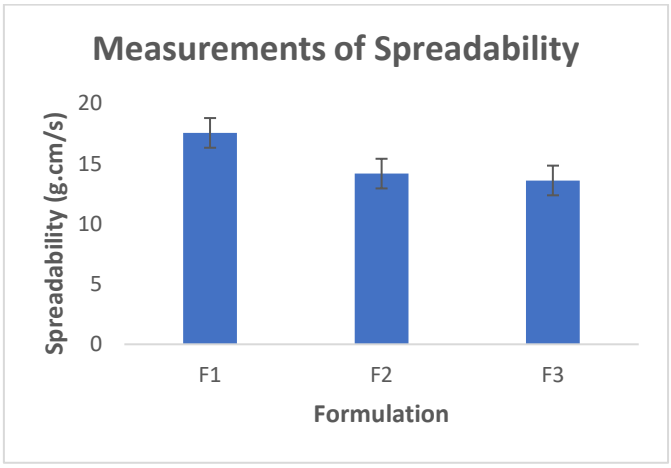

Fig 8. Graphical data of measurements of spreadability

Swelling index

Each emulgel was weighed 12g. When observed, it has shown an amazing swelling property. F1 showed a minimum swelling index of 14.29±0.41 g. While, F2 and F3 showed nearly identical swelling indices of 15.64±0.12 and 15.19±0.27, respectively. The concentration of polymers employed in the emulgel formulation is displayed by the swelling index. It prevents the compositions from flaking off or creaming.

Table 10. Swelling index determination

Formulation	Weight (g)	Weight g (after swelling)
F1	12	14.29±0.41
F2	12	15.64±0.12
F3	12	15.19±0.27

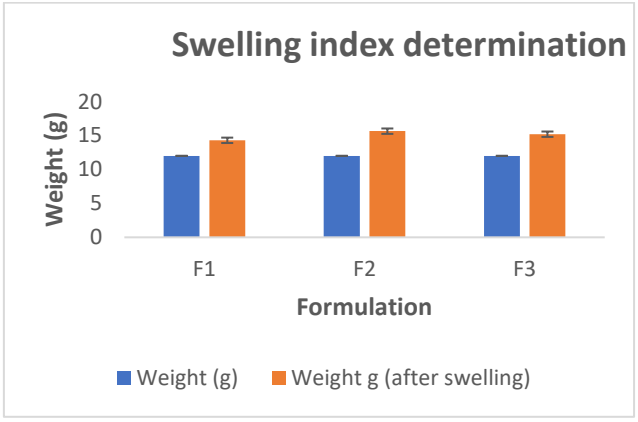

Fig 9. Graphical data of swelling index estimation

Determination of % Drug content

The emulgels exhibited superior drug content in terms of both concentration and flowability, also known as rheological characteristics. Emulgel F1 had a maximum drug content as 87.19±0.36 %. On the other hand, F2 and F3 displayed higher drug content percentages of 84.35±0.21 % and 86.20±0.64 %, respectively.

Table 11. Determination of % drug content

Formulation	% Drug content

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F1	87.19±0.36
F2	84.35±0.21
F3	86.20±0.64

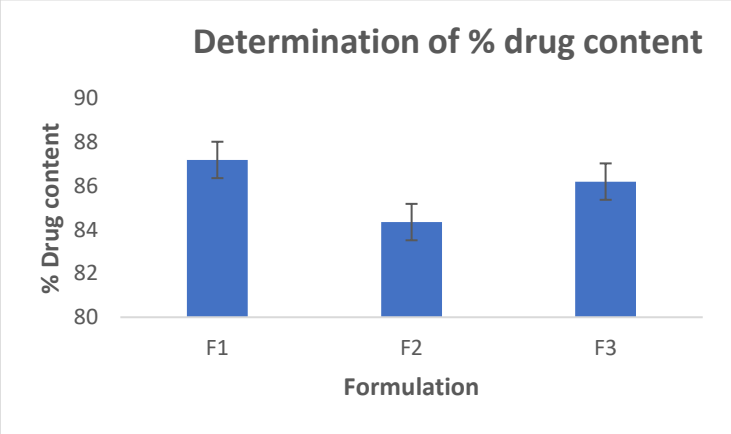

Fig 10. Graphical data of determination of % Drug content

Determination of *in-vitro* drug release

After 12 hours, % *in-vitro* drug release was estimated as 97.18±0.36, 94.12±0.13 and 95.24±0.19 in F1, F2 and F3, respectively. The drug release was observed almost similar in all the 3 formulations. It was found in ascending order i.e., drug release increases as time increase highest effect was observed at 12 hours.

Table 12. Estimation of *in-vitro* drug release

Formulation	***In-vitro* drug release (hr)**					
	1	**2**	**4**	**8**	**10**	**12**
F1	18.20±041	32.12±0.4	39.21±0.11	51.39±0.40	69.26±0.39	97.18±0.36
F2	14.27±0.72	30.27±0.16	37.36±0.18	49.12±0.84	67.20±0.14	94.12±0.13
F3	26.18±0.35	31.16±0.19	38.14±0.16	50.39±0.17	65.82±0.29	95.24±0.19

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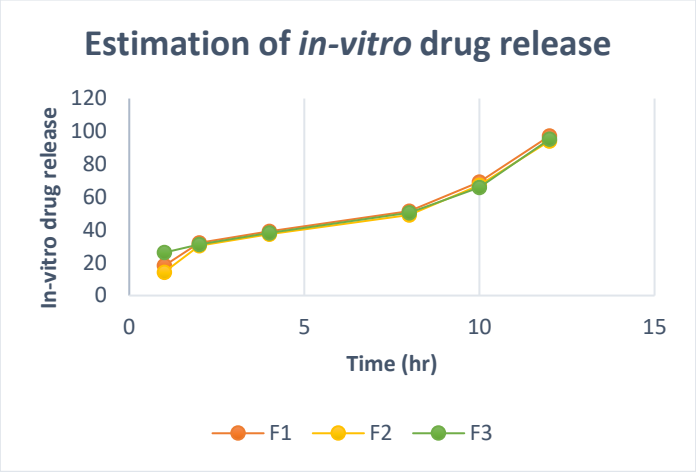

Fig 11. Graphical data of estimation of % Drug release

Evaluation of anti-arthritic activity

Inhibition (%) of protein denaturation through bovine serum albumin

The inhibition (%) of protein denaturation through bovine serum albumin (BSA) was estimated at different concentrations i.e., 12.5 µg/ml, 25 µg/ml, 50 µg/ml, 100 µg/ml, 200 µg/ml, 400 µg/ml, and 800 µg/ml, respectively.

The optimized Thiocolchicoside emulgel (F1) demonstrated the % inhibition of protein denaturation using BSA as 59.4±0.2 % and 95.4±0.6 % at the conc. of 12.5 µg/ml and 800 µg/ml respectively.

Table 5.13 Inhibition (%) of protein denaturation through bovine serum albumin of emulgel

Treatment	Inhibition (%) of protein denaturation [Conc. (µg/ml)]						
	12.5	25	50	100	200	400	800
F1	59.4±0.2	67.3±0.5	74.4±0.6	78.2±0.6	83.4±0.1	87.6±0.3	95.4±0.6

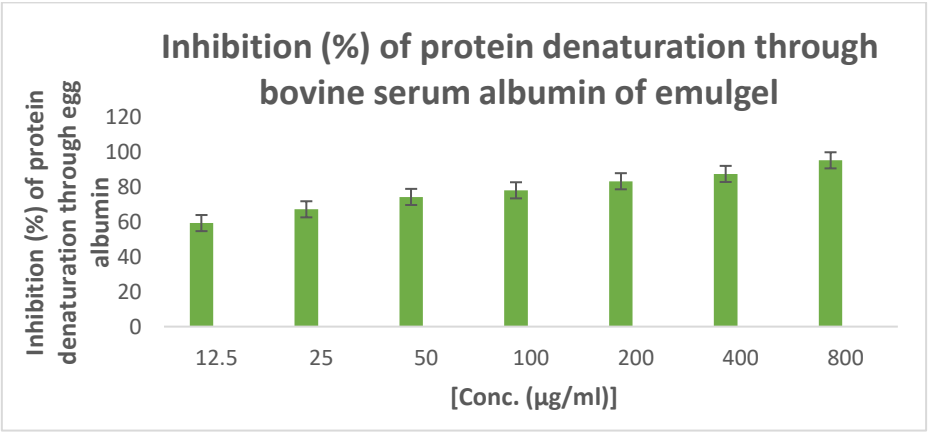

Fig 12. Determination of inhibition (%) of protein denaturation through bovine serum albumin of emulgel

Inhibition (%) of protein denaturation through egg albumin

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Inhibition (%) of protein denaturation using egg albumin was estimated at different concentrations i.e., 12.5 µg/ml, 25 µg/ml, 50 µg/ml, 100 µg/ml, 200 µg/ml, 400 µg/ml, and 800 µg/ml respectively.

The optimized Thiocolchicoside emulgel (F1) demonstrated the % inhibition of protein denaturation using egg albumin as 44.7±0.1 % and 93.6±0.1 % at the conc. of 12.5 µg/ml and 800 µg/ml respectively.

Table 5.14 Inhibition (%) of protein denaturation through egg albumin of emulgel

Treatment	Inhibition (%) of protein denaturation [Conc. (µg/ml)]						
	12.5	25	50	100	200	400	800
F1	44.7±0.1	53.2±0.1	63.4±0.2	71.4±0.9	76.3±0.1	86.4±0.2	93.6±0.1

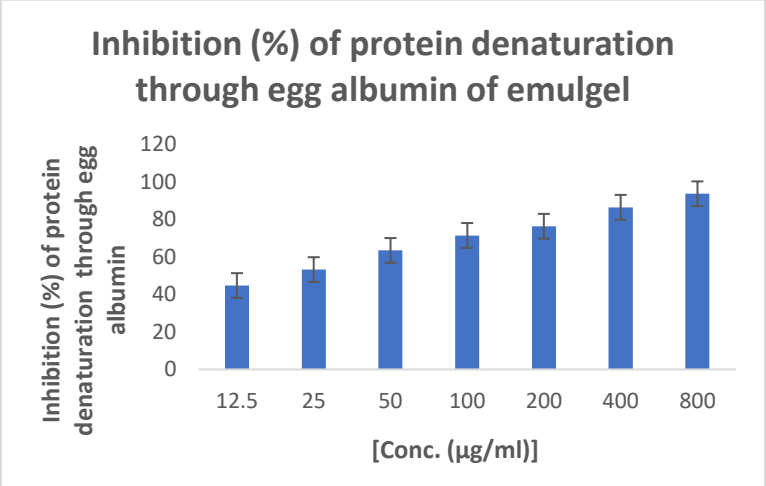

Fig 13. Inhibition (%) of protein denaturation through egg albumin of emulgel

Formulation scientists need to find a way to distribute hydrophobic medicines-which are notoriously difficult to dissolve in water-in order to increase therapeutic bioavailability. Since forty percent of pharmaceuticals are hydrophobic, it is challenging for the body to absorb them. Among the several topical formulation processes, emulgel has been found to be especially significant in improving the topical dispersion of hydrophobic medications. Because gel contains an emulsion, it has a dual control release mechanism. In addition, problems like phase separation and creaming are resolved and the emulsion's stability is improved. The primary problem with emulgel is drug permeability because to its large particle size; however, by using the NEG technique, this can be resolved by adding nanoemulsion to the gel foundation.

It is possible to extrapolate the results of the in vitro antiarthritic membrane stabilization approach to the impact of *B. calliobotrys* that prevent muscular atrophy. Similarly, hypermetabolism mediated by cytokines is considered to be the cause of rheumatoid cachexia. Previous studies have also suggested that the gut of rats has a decrease in the absorption of 14C-glucose and 14C-leucine when it is inflamed, and that this reduction can be restored by anti-inflammatory medications. The current study's findings indicate that the aqueous fractions of B, n-bustanol fraction, and methanolic extract. Rats with arthritis benefit greatly from calliobotrys' protective effect on body weight. Additionally, it was determined by histological

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slides of the ankle joints that the treatment with B. When comparing the medication-treated groups to the negative control, no degeneration of the ankle joint was seen. Thus, the antiarthritic action of B has been established by histological studies. Calliobotrys by reducing the inflammatory response, potentially as a result of its inhibition of the cyclooxygenase enzyme and pro-inflammatory cytokines. Numerous plants in the genera Berberis and Coptis contain the pharmacologically powerful isoquinoline alkaloid berberine. In a number of autoimmune disorders, berberine has been demonstrated to have immunosuppressive and anti-inflammatory properties through the suppression of Th17 and dendritic cell responses. Furthermore, by blocking the most common variables associated with arthritis, berberine also helps to reduce joint inflammation and severe pain (Yang et al. 2013).

In results, among all the emulgel formulations, F1 showed the excellent spreadability and *in-vitro* drug release. Therefore, F1 was further utilized in the evaluation of anti-arthritic activity. Thiocolchicoside based emulgel demonstrated the significant anti-arthritic activity in terms of % inhibition of protein denaturation (using BSA) as 95.4±0.6 % at the conc. of 800µg/ml. It might be tested on the animal model to confirm the safety profile of Thiocolchicoside-based emulgel which could be further used clinically.

CONCLUSION

It would be a great step towards allopathic externally applied drugs that can help millions of people live more comfortably. Cost-effective mass production of this material may also be verified. Stability of the prepared emulgel would be much improved.

It concluded that Thiocolchicoside-based emulgel was found effective in the reduction of arthritis-based inflammation. The anti-arthritic effect might be due the reduction in the production and release of inflammatory cytokines. Fellow researchers are recommended to evaluate the mode of action that how Thiocolchicoside emulgel treat and prevent the progression of rheumatoid arthritis.

CONFLICT OF INTEREST

Authors declare for none conflict of interest.

FUNDING

Nil.

BIBLIOGRAPHY

1. Anupama S, Ashwani K. 2022. Preparation and Evaluation of Mefenamic Acid Emulgel. *Nov Appro Drug Des Dev.,* 6(3): 555690.
2. Bullock J, Rizvi SAA, Saleh AM, Ahmed SS, Do DP, Ansari RA, Ahmed J. Rheumatoid Arthritis: A Brief Overview of the Treatment. Med PrincPract. 2018;27(6):501-507.
3. Klareskog L, Ronnelid J, Saevarsdottir S, Padyukov L, Alfredsson L. The importance of differences; On environment and its interactions with genes and immunity in the causation of rheumatoid arthritis. J Intern Med. 2020 May;287(5):514-533.
4. Malviya VR, Pande SD, Bobade NN., 2019. Preparation and evaluation of sustained release beads of zolmitriptan hydrochloride. *Research Journal of Pharmacy and Technology,* 12(12), 5972-6.

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5. Pandey S., 2010. Various Techniques for The Evaluation of Anti Arthritic Activity In Animal Models. *J Adv Pharm Technol. Res.,* 1(2), 164-171.
6. Pani P C Sathya Keerthi, C Haranath, C Suryaprakash Reddy, A Chaitanaya Kumar, M Kiran Kumar, D Rushi Kumar Reddy, V Umapathi, B Yamuna, R Raviprakash Reddy, 2015. Emulgel: A Novel Approach for Enhancing Topical Delivery of Aceclofenac, 1, 1-5.
7. Patel CJ, Tyagi S, Gupta AK, Sharma P, Prajapati PM, Potdar MB. Emulgel: A combination of emulsion and gel. J Drug Discov Ther 2013;1(6):72-6.
8. Pincus T, O'Dell JR, Kremer JM. Combination therapy with multiple disease-modifying antirheumatic drugs in rheumatoid arthritis: a preventive strategy. Ann Intern Med. 1999 Nov 16;131(10):768-74.
9. Reddy Yella Thirupathi, Rohit Saraswat, Reddy Sunil, 2019. Design and Characterization of Buccal Patches of Atomoxetine. *International Journal of Pharmaceutical Sciences Review and Research,* 56(1), 96-102.
10. Smolen JS, Aletaha D, McInnes IB. Rheumatoid arthritis. Lancet. 2016 Oct 22;388(10055):2023-2038.
11. Sparks JA. Rheumatoid Arthritis. Ann Intern Med. 2019 Jan 01;170(1):ITC1-ITC16.
12. Yang Y, Qi J, Wang Q, et al. Berberine suppresses Th17 and dendritic cell responses. Invest Ophthalmol Vis Sci. 2013; 54: 2516-22.