OPEN ACCESS Science International

ISSN 2305-1884
DOI: 10.17311/sciintl.2018.71.79

Research Article
Formulation, Development and Evaluation of a Novel Polymer-based Anti-Inflammatory Emulgel of Aceclofenac

[1]Rashmi Godbole, [1]Mihir Invally, [1]Sarika Wairkar, [2]Sukhwinder Bhullar and [1]Ginpreet Kaur

[1]Shobhaben Pratapbhai Patel School of Pharmacy and Technology Management, SVKM's NMIMS, Mumbai, Maharashtra
[2]Department of Mechanical Engineering, University of Victoria, British Columbia, Canada

Abstract

Background and Objective: Aceclofenac is a non-steroidal anti-inflammatory drug used for pain relief and inflammation in certain joint disorders. Due to the hydrophobicity (BCS class II) of aceclofenac, it's formulation into a topical gel is challenging. In this study, polymer-based emulgel formulation of aceclofenac with a microemulsion base was developed and assessed for its anti-inflammatory activity. **Materials and Methods:** Microemulsion of aceclofenac was formulated with various polymers and optimized. The optimized formulation was subjected to gelling, resulting in formulation of an emulgel. The resulting emulgel was optimized for desired pharmaceutical characteristics and later evaluated for anti-inflammatory effect in rats, comparing against the standard (most popular) marketed anti-inflammatory emulgel formulation. **Results:** The resultant microemulsion and emulgel both exhibited the desired drug release *in-vitro* and *ex-vivo*. The *in vivo* anti-inflammatory activity of topical aceclofenac emulgel on carrageenan induced paw edema model showed a time dependent response in reduction of inflammation showing the highest inhibition of 65.71%, which was significant compared with the placebo ($p<0.005$). Additionally, the activity of topical aceclofenac emulgel on croton oil induced ear edema model showed significant inhibition ($p<0.05$) of 47.86% after 4 h, compared to the placebo. **Conclusion:** The activity produced by the formulated emulgel was at par with the most marketed emulgel formulation. Thus, the microemulsion base improved the solubility of the drug and the emulgel formulation enhanced the delivery in a sustained manner. Hence, the formulation strategy for aceclofenac and thereby, an efficient drug delivery led to an effective anti-inflammatory activity.

Key words: Aceclofenac, anti-inflammatory, polymers, Carbopol, emulgel, microemulsion

Citation: Rashmi Godbole, Mihir Invally, Sarika Wairkar, Sukhwinder Bhullar and Ginpreet Kaur, 2018. Formulation, development and evaluation of a novel polymer-based anti -inflammatory emulgel of aceclofenac. Sci. Int., 6: 71-79.

Corresponding Author: Ginpreet Kaur, SPP School of Pharmacy and Technology Management, SVKM's NMIMS, V.L. Mehta Road, Vile Parle (W), 400056 Mumbai, Maharashtra, India Tel: (022) 42332000 Ext. 2035 Fax: (022) 26185422

Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Aceclofenac is a non-steroidal anti-inflammatory drug (NSAID) glycolic ester of diclofenac, used for certain joint disorders. It has a better tolerability profile as well as a better analgesic activity in comparison with diclofenac. Hence, developing formulation strategies for aceclofenac is particularly imperative[1,2].

Currently, the marketed formulation contains a tablet and a gel. However, side effects such as gastric ulcerogenicity, flatulence, indigestion and nausea, limit the utility of oral aceclofenac[1]. Hence, the topical route would be one of the ideal alternatives to enhance local delivery, bypassing these side effects. Compared with ointments and creams, gelsprovide a better feel are greaseless and easily washable. Additionally, a gel formulation aids in faster drug release in comparison to other semisolids[2].

However, a prominent drawback in formulating gels is difficulty in delivery of hydrophobic drug. To overcome this limitation, emulgel, a novel drug delivery has emerged which is a combination of gel and emulsion, where the presence of gelling agent in the water phase converts a classical emulsion into a gel. It combines dual release pattern of both gel and emulsion providing better therapeutic action and sustained release[3,4].

Microemulsion-based formulations have an advantage of improved solubility and have reported to enhance drug permeation, owing to reduced surface tension and particle size[5,6]. Microemulsions are thermodynamically stable and enhance drug permeation and release. Hence, a microemulsion of Aceclofenac was formulated, which was later formed into an emulgel.

Data regarding formulation of microemulsion-based emulgel of aceclofenac are limited and none of the previously published studies present a comparison of the aceclofenac emulgel with the currently marketed, most popular anti-inflammatory emulgel, diclofenac. Thus, the study was conducted to develop novel microemulsion-based emulgel formulations of aceclofenac, a poorly water soluble drug and evaluate its anti-inflammatory activity. The current study focused on the development and optimization of an emulgel formulation of aceclofenac and evaluation of its anti-inflammatory activity against the standard, most preferred marketed Diclofenac emulgel in experimental animals.

MATERIALS AND METHODS

The study was conducted in the research lab of department of pharmacology, NMIMS University. The study was commenced after the relevant approvals from the concerned authorities as well as the animal ethics committee. The animal studies were conducted in the animal house, under appropriate care and precautions. The total duration of this study was approximately 5 months considering conceptualization to completion of animal studies. The study was initiated in December, 2015 and completed in May, 2016.

FORMULATION[6-8]: Preparation of microemulsion: Aceclofenac was obtained as a gift sample from FDC Limited (Mumbai, India). Polysorbate 80, isopropyl myristate, was procured from Molychem (Mumbai, India) and Loba chemie pvt limited, (Mumbai, India), respectively. All other chemicals and solvents were of analytical reagent grade.

Saturation solubility of aceclofenac in various oils, surfactants, co-surfactants was determined by saturation solubility method. Based on the results of this study, pseudo ternary phase diagram was plotted using the Tridraw software, to calculate the surfactant and co-surfactant ratio (Smix). After a number of trials, microemulsion of aceclofenac was optimized with:

- 5.74% of Isopropyl myristate
- 51.72% of polysorbate 80: ethanol mixture (Smix) in 1:1 ratio
- 42.52% of aqueous phase

Oil was mixed in the Smix for around 10 min on a magnetic stirrer. Aceclofenac was added to it in small parts until the drug completely dissolved in the solution. The optimized quantity of distilled water was then added drop by drop in the solution with constant stirring at 50rpm on a magnetic stirrer.

Emulgel was prepared by using carbopol 940 which was soaked overnight, adjusted pH with triethanolamine followed by addition of microemulsion equivalent to 1% of aceclofenac. Different concentrations of carbopol 940 were taken for trials and the optimum emulgel formulation was selected (Table 1 and Fig. 1).

Evaluation of microemulsion[4-7]

Appearance and pH: The test substance was inspected visually for color, consistency and pH (LabIndia, PICO+, Mumbai, India).

Dilution capacity: The test substance was diluted in 1:10 and 1:100 ratios with double distilled water and observed visually for cracking of the system.

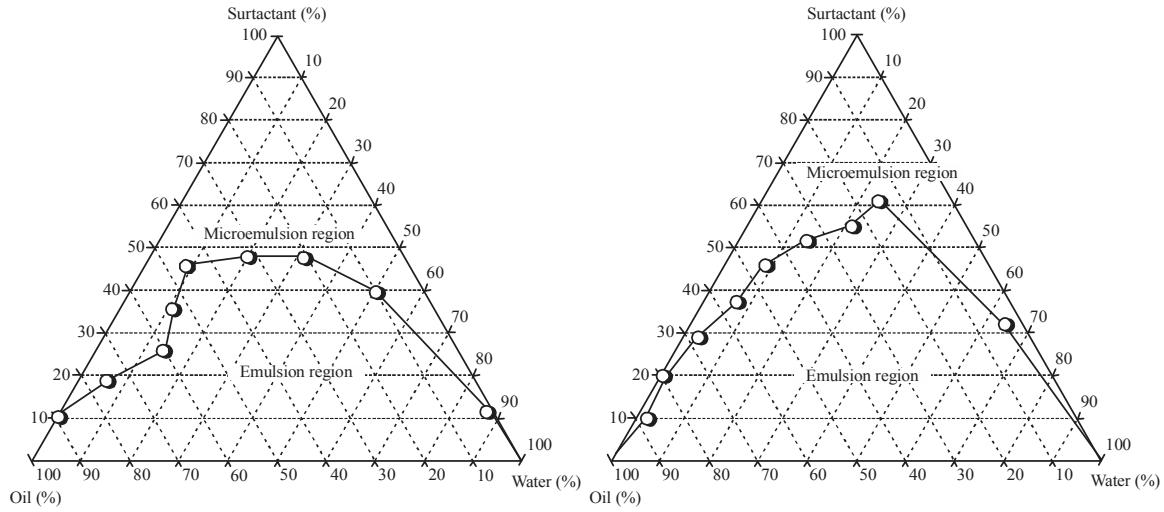


Fig. 1: Pseudo ternary phase diagram at 1:1 and 1:2 surfactants to co-surfactant ratio

Table 1: Formulation trials for emulgel

	Quantity in percentage w/w (%)			
Ingredient	F1	F2	F3	F4
Aceclofenac	1.00	1.00	1.00	1.00
Isopropyl myristate	5.74	5.74	5.74	5.74
Polysorbate 80	25.71	25.71	25.71	25.71
Ethanol	25.71	25.71	25.71	25.71
Carbopol 940	0.66	1.50	1.88	2.25
Methyl paraben	0.18	0.18	0.18	0.18
Propyl paraben	0.02	0.02	0.02	0.02
Triethanolamine	q.s*. to pH 6-6.5			
Purified water	q.s.*			

*quantity sufficient

Particles size and zeta potential: The particle size and zeta potential of the microemulsion was evaluated using nano zeta sizer.

Specifications of the zeta sizer:

- Make: Malvern
- Model: ZS 90, Particle size range: 3 nm to 10 µm

***In vitro* diffusion studies:** *In vitro* diffusion studies were done with the help of modified Franz diffusion cell (Sumati sales corporation, Mumbai, India). Microemulsion containing 15 mg of aceclofenac was evenly applied onto the surface of dialysis membrane along with aceclofenac suspension in water for comparison. The dialysis membrane was attached between the donor and the receptor chamber of diffusion cell. The receptor chamber was filled with freshly prepared phosphate buffer (pH 6.8). The receptor chamber was stirred by magnetic stirrer. The aliquots (1 mL) were collected at time intervals of 1 h up to 8 h. Samples were analyzed for drug content by UV-Vis spectrophotometer after appropriate dilutions. Cumulative corrections were made to obtain the total amount of drug release at each time interval.

Evaluation of emulgel[7-11]

Optimization: F1 and F2 with 0.66 and 1.5% concentration of carbopol 944, respectively, on addition of microemulsion, formed a gel with low viscosity. Hence, F3 with 1.88% of carbopol 940 was finalized for formulation of emulgel.

Appearance and pH: The test substance was inspected visually for color, consistency and pH (LabIndia, PICO+, Mumbai, India).

***In vitro* diffusion studies:** These studies were conducted in the same way as that described for microemulsion, but by using the emulgel in the place of microemulsion.

***Ex-vivo* diffusion studies:** *Ex-vivo* studies were done in the same manner as that of *in vitro* diffusion studies where the dialysis membrane was replaced with rat skin. The average cumulative amount of drug permeated per unit surface area of the skin was plotted versus time.

Drug content determination: Aceclofenac content in emulgel was measured by dissolving known 0.5 g of emulgel in methanol by sonication. Absorbance was measured after suitable dilution at 277 nm using UV-Vis spectrophotometer.

Animal studies: The protocol designed for animal studies was compliant with the CPCSEA guidelines and was approved by the institutional animal ethics committee. Ethics committee approval number: 1830/PO/Re/S/15/CPCSEA.

Skin irritation test (patch test)[7-10]: A set of nine rats was used in the study. The emulgel was applied on the properly shaven skin of rat. Undesirable skin changes, i.e., change in color, change in skin morphology were checked for a period of 24 h.

Anti-inflammatory studies by carrageenan induced paw edema model: A total of 6 rats were used in each group, for placebo, marketed gel and aceclofenac formulated emulgel, amounting to 18 rats in total.

The anti-inflammatory activity of aceclofenac emulgel was evaluated using carrageenan induced paw edema in rats by a method described by Gerald *et al*. Female wistar rats weighing 150-200 g were divided into three groups. Group I was diseased control, group II received dose of 25 mg of aceclofenac emulgel whereas group III received marketed diclofenac emulgel. Edema was induced in rats using 0.1 mL of 1% carrageenan solution in 0.9% saline solution into the sub plantar region of right hind paw of the rat. The swelling in the paw of each rat was measured by plethysmometer by volume displacement method at baseline and every h till the 6th h[11]. Percentage inflammation was calculated as under:

$$\text{Inflammation (\%)} = \frac{\text{Vt-Vo}}{\text{Vo}} \times 100$$

Where:

Vt = Paw thickness at each time interval

Vo = Initial paw thickness

The average paw swelling in the drug treated rats was compared with that of control rats and the% inhibition of edema was calculated as:

$$\text{Inflammation (\%)} = \frac{\text{Ec-Et}}{\text{Ec}} \times 100$$

Where:

Ec = Edema rate of control group

Et = Edema rate of the treated group

Anti-inflammatory studies by croton oil induced ear edema: The anti-inflammatory activity of aceclofenac emulgel was evaluated using croton oil induced ear edema against acute inflammation. Ear edema was induced by topical application of 8% croton oil in mixture of solvents (percentage, croton oil: Ethanol: Pyridine: Diethyl ether = 8: 10: 20: 62) on the outer and inner surfaces of the right ear of each rat. Wistar rats (150-200 g) were divided randomly into three groups. Group I was taken as disease control. Group II received aceclofenac emulgel equivalent to 2.5 mg of drug whereas group III received marketed voltaren emulgel equivalent to 2.5 mg of drug. The inflammation in the ear of each rat was noted using Vernier caliper at 1st, 2nd, 3rd and 4th h of treatment. The percentage change in inflammation was calculated by the same formula as mentioned above.

Statistical analysis: Experimental values were expressed as Mean±SD. The data were analyzed by one way analysis of variance (ANOVA) followed by Bonferroni's multiple comparison test. A value of $p<0.05$ was considered as significant.

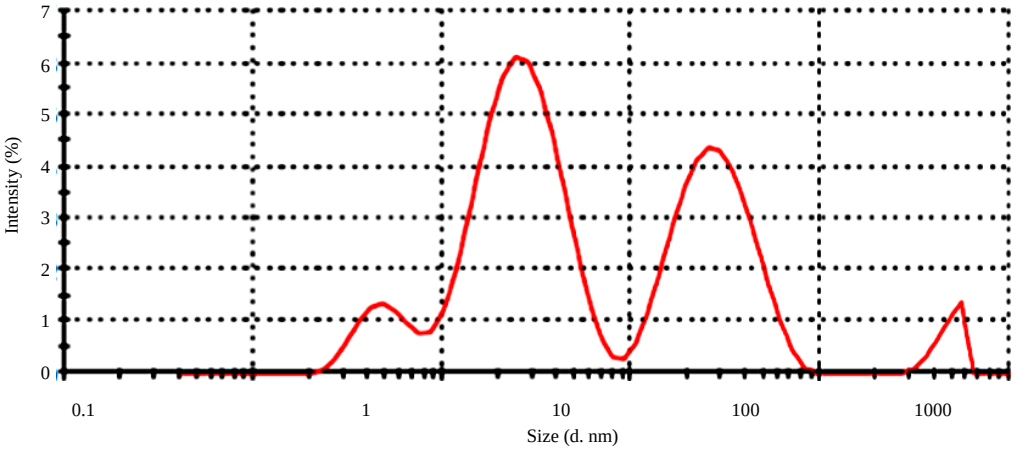
RESULTS

Optimization of microemulsion: The solubility of aceclofenac in different oils, surfactants and co-surfactants was determined since it is the most important criteria for microemulsion preparation (Table 2).

The solubilization capability of aceclofenac in different oils, surfactant and co surfactant was shown in the Table 1. Isopropyl myristate showed best solubility amongst all the oils, polysorbate 80 showed two times better solubility than other surfactants and Ethanol showed the 5 times better solubility amongst co-surfactants. Based on the results of solubility studies, Isopropyl myristate, Polysorbate 80 and Ethanol were chosen as oil, surfactant and co-surfactant, respectively.

Table 2: Solubility of aceclofenac in various oils, surfactants and co-surfactants

Name of the excipient	Results (mg mL^{-1})
Oils	
Corn oil	9.77
Sesame oil	13.09
Peppermint oil	3.84
Eucalyptus oil	3.56
Clove oil	19-33
Oleic acid	6.47
Castor oil	13.31
Isopropyl myristate	20.59
Surfactants	21.24
Polysorbate 80	10.87
Polysorbate 20	8.54
Sorbitan oleate	19.52
Polyoxyl 35 castor oil	28.04
Co-surfactants	
Polyethylene glycol	4.92
Lutreol E 400	4.92
Lutreol E 600	4.60
Propylene glycol	4.56



		Size (d.nm…	Intensity (%)	St Dev (d.n…
Z-average (d.nm): 31.36	Peak 1:	28.22	53.1	14.31
Pdl: 0.747	Peak 2:	295.2	35.9	134.2
Intercept: 0.853	Peak 3:	4.947	7.5	1.385
Result quality Refer to quality report				

Fig. 2: Particle size analysis report by nano zetasizer

Pseudo ternary phase diagram was constructed by varying Polysorbate 80 and ethanol in 1:1 and 1:2 ratios (Fig. 1).

The microemulsion region obtained in 1:1 ratio was more as compared with that of 1:2 ratio of Smix. The particle size of 1:1 ratio of Smix was found to be 31.36 nm whereas that for 1:2 ratios was found to be 57.57 nm. Hence, 1:1 ratio of Smix (Polysorbate 80: Ethanol) was chosen for further studies. The microemulsion which had highest amount of drug solubility and water uptake in the pseudo ternary phase diagram was chosen for trials on microemulsion. A formulation yielding clear and transparent appearance and the one not cracking when observed for 24 h was selected for further studies.

Evaluation of microemulsion

Appearance and pH: The aceclofenac microemulsion was transparent yellow colored solution with a pH of 5.52.

Dilution capacity: The microemulsion when diluted in 1:10 and 1:100 ratios with double distilled water, clear solution was obtained which had a slight bluish tinge, no breaking of the system was observed.

Particle size and Zeta potential analysis: The particle size of the microemulsion was found to be 31.36 nm (Fig. 2) and zeta potential of the microemulsion was found to be 0.00835 (Fig. 3).

***In vitro* diffusion studies:** The drug release was found to be 94.46 and 47.38% of aceclofenac microemulsion and plain dispersion aceclofenac, respectively in 6 h (Fig. 4).

Formulation, development and evaluation of emulgel: Emulgel was prepared by using carbopol 940 which was soaked overnight, adjusted pH with triethanolamine followed by addition of microemulsion equivalent to 1% of aceclofenac. Different concentrations of carbopol 940 were taken for trials and the optimum emulgel formulation (F3) was selected, (Table 1 and Fig. 1). F1 and F2 with 0.66 and 1.5% concentration of carbopol 944, respectively, on addition of microemulsion, formed a gel with low viscosity. Hence, F3 with1.88% of carbopol 940 was finalized for formulation of emulgel.

Appearance and pH: The aceclofenac emulgel obtained was a white translucent gel with a pH of 6.72.

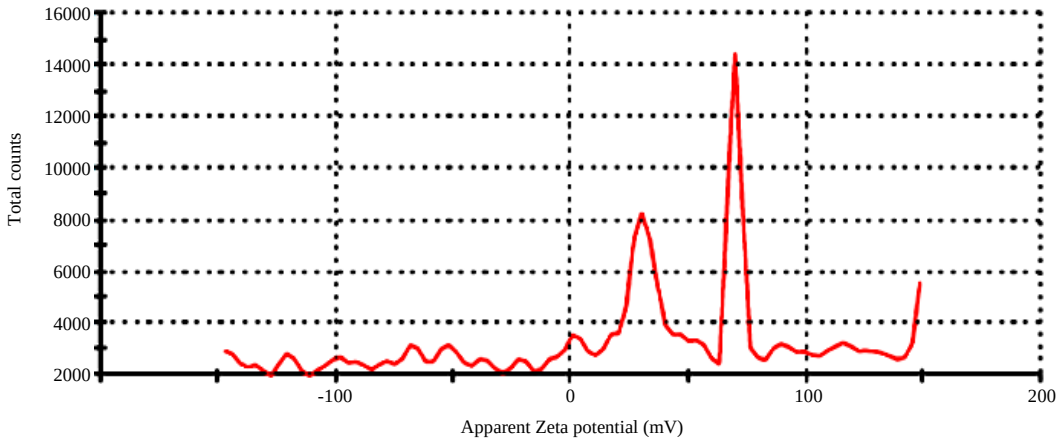
***In vitro* diffusion studies:** The *in vitro* drug release of emulgel was found to be 83.54% in 8 h (Fig. 5).

***Ex-vivo* diffusion studies:** *Ex-vivo* drug release of emulgel was found to be 71.88% in 8 h (Fig. 6).

***In vivo* studies**

Skin irritation test: No allergic symptoms like inflammation, redness, irritation appeared on rats up to 24 h.

Carrageenan induced paw edema model: In case of control, inflammation showed an increase till 4 h, followed by a slight reduction. Animals treated with aceclofenac emulgel showed a significant reduction in the paw volume ($p<0.05$) compared to control by 64%, at the end of 6 h. Inflammation increased



		Mean (mV)	Area (%)	St Dev (mV)
Zeta potential (mV): 0.00835	Peak 1:	30.5	17.6	10.5
Zeta deviation (mV): 123	Peak 2:	70.9	12.3	4.93
Conductivity (mS/cm): 0.0853	Peak 3:	-1.86	7.4	8.08
Result quality Refer to quality report				

Fig. 3: Zeta potential analysis report by nano zetasizer

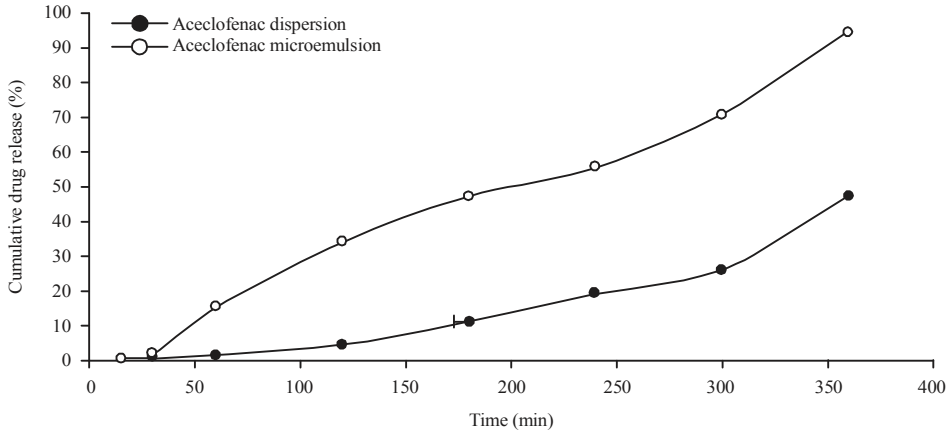


Fig. 4: Plot of comparative cumulative drug release

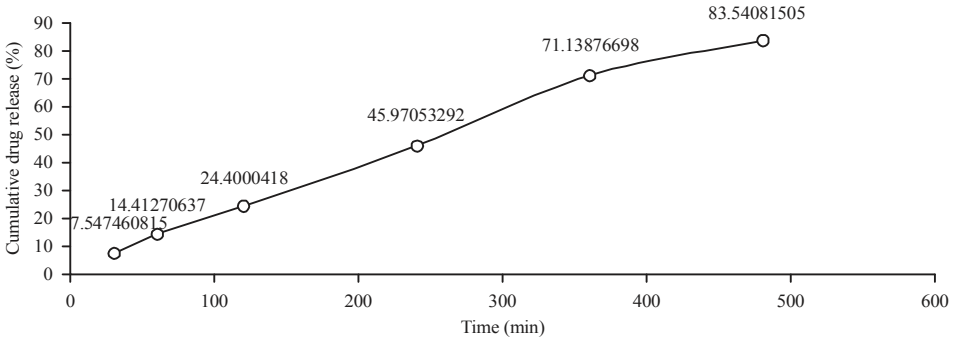


Fig. 5: *In vitro* diffusion studies

for the first 2 h, followed by gradual reduction, an observation starkly distinct from the control. Voltaren emulgel produced maximum inhibition of 77.74% by the end of 6 h (Table 3).

Croton oil induced ear edema: The trend in inflammation and reduction was similar as observed with the first model, in the respective groups. Aceclofenac emulgel demonstrated

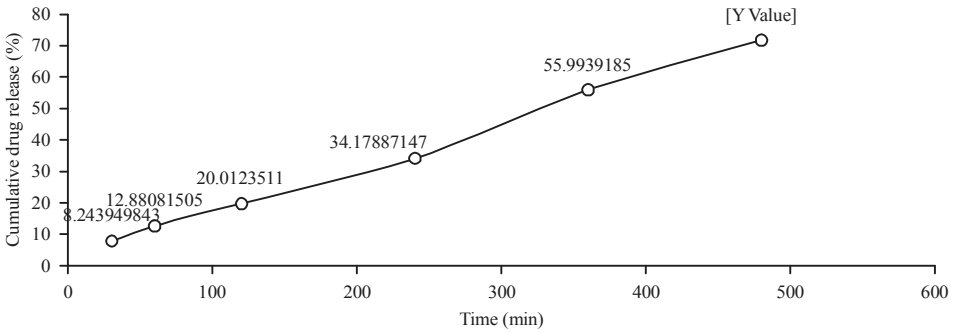


Fig. 6: *Ex vivo* diffusion studies

Table 3: Results of carrageenan induced Paw Edema model

	Group I	Group II		Group III	
Time (h)	Inflammation (%)	Inflammation (%)	Inhibition (%)	Inflammation (%)	Inhibition (%)
1	27.84±3.40	16.08±2.28	42.22	17.56±2.85	36.92
2	39.21±6.64	34.74±2.26	11.39	15.93±1.89	59.35
3	45.48±13.75	26.93±9.23	40.92	27.25±0.46	40.21
4	55.64±8.37	25.54±5.74	54.09	32.29±4.05	41.95
5	43.96±9.17	15.07±4.65	65.71	15.34±1.38	65.10
6	21.68±6.41	7.76±6.07	64.19	4.82±3.29	77.74

Table 4: Results of croton oil induced Ear Edema model

	Group I	Group II		Group III	
Time (h)	Inflammation (%)	Inflammation (%)	Inhibition (%)	Inflammation (%)	Inhibition (%)
1	29.94±1.56	16.78±7.09	43.94	23.20±2.60	22.50
2	40.46±1.61	27.50±4.57	32.03	16.37±2.02	59.52
3	36.21±6.18	21.75±2.02	39.93	19.03±6.44	47.43
4	23.06±3.62	12.02±8.46	47.86	11.09±5.53	51.88

significant ($p<0.05$, nearly half) reduction in inflammation by end of the 4th h compared to the control (Table 4) Voltaren emulgel presented maximum inhibition of 55.8% in 4 h.

The anti-inflammatory activity was numerically more in voltaren emulgel as compared to aceclofenac emulgel. However, these differences were not statistically significant.

DISCUSSION

In this investigation, a microemulsion-based emulgel of aceclofenac was successfully formulated, which lead to improved solubility and drug release of aceclofenac. Moreover, the improvement in solubility and drug release translated into an effective biological activity, when tested in animal models of inflammation, the formulated microemulsion-based emulgel brought about an effective anti-inflammatory activity, reducing the inflammation by more than 50% compared to placebo alone, 55.8 and 64% in paw edema and ear edema animal models, respectively. Most remarkable finding was that the anti-inflammatory activity exhibited by aceclofenac microemulsion-based emulgel.

The dual novel technique viz. microemulsion formulation, further incorporation into a gel and its influence on the anti-inflammatory activity is not reported elsewhere in the previous literature. Microemulsion formulation aids in improving the drug solubility owing to reduced particle size, improved surface tension and better permeation. Additionally, microemulsions have improved stability[12-14].

Previous studies have attempted formulation of aceclofenac in emulgels and gels, however, the data regarding formulation of microemulsion-based emulgel of aceclofenac and head-to-head comparison of anti-inflammatory activity with the most popular marketed emulgel is not reported in the literature[15-18].

In an earlier study conducted by Pani *et al.*[15], aceclofenac was attempted in an emulgel formulation, using mentha oil as a penetration enhancer. The study revealed that the formulation with carbopol 934 shown better release profile than HPMC K4M, depicting carbopol 934 as the better choice of polymer for aceclofenac emulgel. In another study by

Shah *et al.*[16], a microemulsion base for aceclofenac was formulated using isopropyl myristate 5%, labrasol/plurol oleique 45% (4:1) and water, which yielded an *ex vivo* release of 95%.

Additionally, a study conducted by Patel *et al.*[17] analyzed the effect of various gelling agents on the release profile of aceclofenac, among all the gel formulations, carbopol exhibited superior drug release than followed by Na CMC, HPMC and sodium alginate. Similar investigation by Pottalaswathi and Vema[18], reiterated these findings that incorporation of Carbopol in an emulgel of aceclofenac improves its penetration[18]. Herein, no further evaluation and animal studies were done to assess the implications of the formulation *in vivo*. Hence, we addressed the issues of previously published studies, presenting a novel research. In view of the foregoing, we attempted to formulate a microemulsion based emulgel of aceclofenac and tested the efficacy of the formulation in animal models of inflammation. Moreover, we compared our formulation with the most commonly preferred anti-inflammatory emulgel brand, VOLTAREN.

The micro emulsion formulation developed in this maneuver was found to be satisfactory in terms of physical characteristics like clarity, particle size as well and *in vitro* drug diffusion (Fig. 1-4) compared with the simple aqueous dispersion of the drug. This is indicative of the improved solubility brought about by the microemulsion formulation. Testing for the drug release from the micro emulsion itself is critical prior to designing an emulgel. Hence, the micro emulsion was considered optimum in terms of these pharmaceutical characteristics.

The objective to formulate an emulgel using non-irritating and pharmaceutically acceptable ingredients was achieved. The emulgel was studied in terms of physical characteristics, particle size, skin irritation test and drug release and was found satisfactory, achieving more than 75% drug release at the end of 8 h. Thus, the formulated emulgel was considered optimum, based on the pharmaceutical characteristics and further subjected to animal testing for anti-inflammatory activity using two animal models viz. Carrageenan induced paw edema and croton ear edema model.

Carrageenan induced paw edema and croton induced ear edema model have been frequently used to assess the edematous effect of the contribution of mediators involved in vascular changes associated with acute inflammation. Both of these models differ in terms of underlying pathways of the inflammatory cascade. An effective anti-inflammatory drug is purported to act via both the pathways, thus mitigating inflammation. In this regard, the activity of aceclofenac in alleviating inflammation was evaluated as measure of the efficiency of the formulation and thereby, the drug release. In both the models, animals treated with aceclofenac emulgel showed inflammation reversal in 2 h of application, resulting in improved inhibition of inflammation with an effect lasting up to 6 h. These results were concordant with the study conducted by Fathalla *et al.*[5]. A similar effect was observed with the marketed diclofenac formulation, which reinforces the proof of efficiency of the marketed gel in delivering diclofenac and reducing inflammation. On the contrary, in the placebo group inflammation persisted till the 4th h and later showed a decline which was statistically insignificant compared to the treated groups, which reinstates the efficacy of aceclofenac, lack of any activity attributed to excipients and effective delivery of the drug. In both the models, the inflammatory edema reached its maximum level at the 4h and later started declining. The late phase of the inflammatory response has been shown to be due to potentiating effect of bradykinin on mediator release and prostaglandins, producing edema after mobilization of the leukocytes as studied by Necas and Bartosikova[19] and Siqueira *et al.*[20]. Hence, the study yields valuable insights into improving the solubility of a BCS class II drug, through a microemulsion based emulgel. Moreover, the effectiveness of the formulation in delivering the drug as manifested *in vitro* and *ex vivo* studies, was transposed into significantly mitigating inflammation in animal models. Although, the pharmacological evidence presented herein, shows a quantitatively higher activity for the marketed preparation, the designed formulation was at par with the marketed one with significantly better activity demonstrated against the placebo. Aceclofenac exhibits a better tolerability profile compared to diclofenac when taken orally. However, the implications of this phenomenon, when the drugs are administered topically remain a question to be addressed in future studies. Secondly, relevance of this fact is even more when the respective drugs are taken life-long in chronic conditions like arthritis. In this regard, the study provides a preliminary comparative efficacy data for both the drugs, providing a foundation for a robust clinical evaluation in future studies.

CONCLUSION

Thus, the microemulsion based aceclofenac emulgel showed promising results as an effective anti-inflammatory topical drug delivery system, in this preliminary investigation. Moreover, the reduction in inflammation was comparable to that of the most consumer preferred anti-inflammatory emulgel brand of diclofenac. Thus, manifesting a comparable

activity and a better tolerability profile of aceclofenac to that of diclofenac, the former may provide an edge over the latter, for topical activity. However, further research is warranted focusing on formulation stability and more *in vivo* studies to substantiate the potential of the emulgel formulation as robust and efficacious topical based drug delivery system of aceclofenac.

SIGNIFICANCE STATEMENT

The study yields novel insights into the formulation strategies for designing a water soluble novel drug delivery system of an anti-inflammatory, low-solubility drug aceclofenac. The study also highlights preclinical analysis, that aceclofenac and diclofenac show equal efficacy when used topically. The findings of the study may yield further avenues for researchers as well as formulation scientists to design further studies on aceclofenac emulgel formulations, using the optimized microemulsion techniques.

ACKNOWLEDGMENTS

We acknowledge SPPSPTM, SVKM's NMIMS, Mumbai for providing funding and facilities to execute the study.

REFERENCES

1. Mahalingam, R., X. Li and B.R. Jasti, 2012. Semisolid Dosages: Ointments, Creams and Gels. In: Pharmaceutical Sciences Encyclopedia, Gad, S.C. (Ed.)., Vol. 9, John Wiley & Sons, Inc., UK., pp: 1-46.
2. Sharma, G., J. Singh, D. Anand, M. Kumar, K. Raza, A. Pareek and O.P. Katare, 2017. Aceclofenac: Species-dependent metabolism and newer paradigm shift from oral to non-oral delivery. Curr. Topics Med. Chem., 17: 107-119.
3. Hardenia, A., S. Jayronia and S. Jain, 2014. Emulgel: An emergent tool in topical drug delivery. Int. J. Pharm. Sci. Res., 5: 1653-1660.
4. Jha, S.K., R. Karki, D.P. Venkatesh and A. Geethalakshami, 2011. Formulation development and characterization of microemulsion drug delivery systems containing antiulcer drug. Int. J. Drug Dev. Res., 3: 336-343.
5. Fathalla, D., A. Abdel-Mageed, F. Abdel-Hamid and M. Ahmed, 2014. *In vitro* and *in vivo* evaluation of niosomal gel containing aceclofenac for sustained drug delivery. Int. J. Pharm. Sci. Res., Vol. 1. 10.15344/2394-1502/2014/105.
6. Syed, H.K. and K.K. Peh, 2014. Identification of phases of various oil, surfactant/co-surfactants and water system by ternary phase diagram. Acta Polonniae Pharm. Drug Res., 71: 301-309.
7. Ajazuddin, A. Alexander, A. Khichariya, S. Gupta, R.J. Patel, T.K. Giri and D.K. Tripathi, 2013. Recent expansions in an emergent novel drug delivery technology: Emulgel. J. Controlled Release, 171: 122-132.
8. Arunothayanun, P., J.A. Turton, I.F. Uchegbu and A.T. Florence, 1999. Preparation and *in vitro*/*in vivo* evaluation of Luteinizing Hormone Releasing Hormone (LHRH) loaded polyhedral and spherical/tubular niosomes. J. Pharm. Sci., 88: 34-38.
9. Biswal, B., N. Karna, J. Nayak and V. Joshi, 2014. Formulation and evaluation of microemulsion based topical hydrogel containing lornoxicam. J. Applied Pharm. Sci., 4: 77-84.
10. Khullar, R., D. Kumar, N. Seth and S. Saini, 2012. Formulation and evaluation of mefenamic acid emulgel for topical delivery. Saudi Pharm. J., 20: 63-67.
11. Gerhard, H.G., 2002. Vogel Drug Discovery and Evaluation Pharmacological Assays. 2nd Edn., Springer, Berlin Heidelberg, pp: 757-760.
12. Lawrence, M.J. and G.D. Rees, 2000. Microemulsion-based media as novel drug delivery systems. Adv. Drug Delivery Rev., 45: 89-121.
13. Jha, S.K., S. Dey and S. Karki, 2011. Microemulsions-potential carrier for improved drug delivery. Asian J. Biomed. Pharm. Sci., 1: 5-9.
14. Kawakami, K., T. Yoshikawa, T. Hayashi, Y. Nishihara and K. Masuda, 2002. Microemulsion formulation for enhanced absorption of poorly soluble drugs: II. *In vivo* study. J. Controlled Release, 81: 75-82.
15. Pani, P.S.K., C. Haranath, C.S. Reddy, A.C. Kumar and M.K. Kumar *et al*., 2015. A novel approach for enhancing topical delivery of aceclofenac. Inventi Rapid, Vol. 2015.
16. Shah, R.R., C.S. Magdum, S.S. Patil and N.S. Niakwade, 2010. Preparation and evaluation of aceclofenac topical microemulsion. Iran. J. Pharm. Res., 9: 5-11.
17. Patel, J., B. Patel, H. Banwait, K. Parmar and M. Patel, 2011. Formulation and evaluation of topical aceclofenac gel using different gelling agent. Int. J. Drug Dev. Res., 3: 156-164.
18. Pottalaswathi and K. Vema, 2015. Formulation and evaluation of aceclofenac topical emulgel. Int. J. Adv. Pharm. Sci. Innovat. Res. Dev., 3: 52-56.
19. Necas, J. and L. Bartosikova, 2013. Carrageenan: A review. Vet. Med., 58: 187-205.
20. Siqueira, Jr., J.M., R.R. Peters, A.J. de Brum-Fernandes and R.M. Ribeiro-do-Valle, 2003. Effects of valeryl salicylate, a COX-1 inhibitor, on models of acute inflammation in mice. Pharmacol. Res., 48: 437-443.