ISSN:0975-1459
Journal of Pharmaceutical Sciences and Research
www.jpsr.pharmainfo.in

Formulation and Evaluation of Ufasomal Topical Gel Containing Selected Non Steroidal Anti Inflammatory Drug (NSAIDs)

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Abstract

Aim

Vesicular structures are systems, which can be expected to prolong the duration of the drug in systemic circulation, and reduce the toxicity by selective uptaking. The aim of the study is to formulate and evaluate ufasomal topical gel containing etodolac by lipid film hydration method. Ufasomes enhance the drug retention properties of drugs within the cell of the skin membrane for long period of time.

Methods

Topical ufasomal gel was prepared by lipid film hydration method using oleic acid as the major component. The topical ufasomal gel formulations of all batches were evaluated for physical appearance, percentage yield, drug content, entrapment efficiency, viscosity and *in vitro* drug diffusion study.

Results

The results of FTIR analysis indicated that the characteristic peaks of the drug, etodolac are unaltered and hence it was concluded that the drug and excipients were compatible. The data of *in vitro* drug release were fitted in kinetic models. Stability studies were carried out after 30 days on all the gel formulations and were found to have good stability.

Conclusion

The study indicates that the topical ufasomal gel of etodolac can effectively improve the permeation of the drug through skin with reduced toxicity due to the presence of fatty acid in the formulation which acts as a permeation enhancer. Also, the formulation can be used for targeting of the drugs at a site using surfactants which act by decreasing the rigidity and increasing the fluidity of the vesicles.

Keywords: Etodolac; Fatty acid vesicles; Oleic acid; Transdermal drug delivery system; Ufasome.

INTRODUCTION

Proper drug selection and effective drug delivery is required for a therapeutic outcome in an optimal range. The controlled drug delivery technology has progressed immensely over the last six decades in the pharmaceutical industry. Lack of patient compliance is the major problem associated with conventional drug delivery systems.

In the past few decades, considerable attention has been paid to the development of novel drug delivery system. The basic goal of novel drug delivery system is to deliver the drug in therapeutic amount at the appropriate site in the body and to maintain the desired drug concentration over a specified term of treatment[1].

Vesicular drug delivery systems are particularly important for targeted drug delivery because of their ability to localize the activity of drug at the site of action thereby lowering its concentration at the other sites in body and simultaneously minimizing the undesirable side effects. Fatty acid vesicles have high penetration through the hydrophobic layer like skin, so they can be effectively used as carrier systems for various drugs.

Ufasomes are unsaturated fatty acid vesicles. They are suspensions of closed lipid bilayers that are composed of fatty acids, and their ionized species (soap). They have been developed to enhance penetration of drug into viable skin through stratum corneum. This carrier system appears to be promising for the efficient and targeted delivery of drugs[2].

NSAIDs taken orally are transported to all parts of the body through blood and thus high blood concentrations are needed to achieve effective tissue concentrations at the particular site of action. These high concentrations in the body can lead to a number of adverse events that can be unpleasant or potentially serious (for example, dyspepsia, gastrointestinal bleeding). Topical NSAIDs are recommended for direct application to the painful site to provide local pain-relieving effect without the systemic adverse effects associated with oral NSAIDs.

Ufasomes are vesicles of long chain unsaturated fatty acids obtained as a result of mechanical agitation of evaporated film in the presence of buffer solution. The fatty acid vesicles are colloidal suspension consisting of fatty acids and their ionized species. It provides an efficient method for delivery to the site of infection, leading to reduced drug toxicity with less adverse effects.

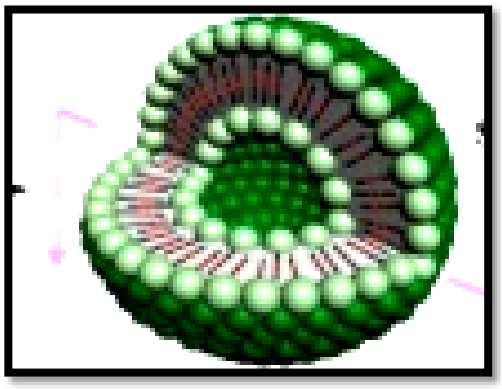

Fig 1: Structure of ufasome

In liposomes, phospholipids are used as the major component. Natural phospholipids are chemically heterogeneous and pure synthetic phospholipids are not yet available in reasonable quantities. The ready availability of fatty acids is the major advantage of ufasomes over liposomes. The fatty acid vesicles can be formed not only from unsaturated fatty acids such as oleic acid, linoleic acid, but also from saturated fatty acid such as octanoic acid and decanoic acid.

Ufasome is the new approach to enhance drug permeation through the skin. Unsaturated fatty acids like linoleic acid and oleic acids are used as natural permeation enhancers in the preparation of ufasomes. Surfactant is also used in combination with fatty acid which enhances the flexibility of skin and improves the passage of drug via skin membrane. Ufasomes enhance the drug retention properties of drugs within the cell of the skin membrane for a long period of time[4].

MATERIALS AND METHODS

The drug Etodolac was obtained from Balaji Enterprises, Gujarat, India. Oleic acid, Tween 80, Methanol, Carbopol 940, Triethanolamine were obtained from Yarrow Chem Products, Mumbai, India.

Formulation of ufasomes

Ufasomes were prepared by lipid film hydration method using rotary vacuum evaporator. Optimized concentration of oleic acid, tween 80 and etodolac was dissolved in methanol in a round bottom flask followed by evaporation of the solvent under vacuum using a rotary vacuum evaporator (600 mmHg, 100 rpm). For complete removal of any possible traces of methanol and also to prevent the formation of emulsion due to the residual organic solvent the completely dried film in rota evaporator was left overnight which was then hydrated at ambient temperature for 1 h with phosphate buffer (pH 7.4). The prepared vesicles were then sonicated to form the uniform size vesicular dispersion.

Formulation of carbopol gel

1% w/v of carbopol 940 was dispersed into purified water with the help of a vortex shaker and allowed to hydrate for 4-5 h. The pH value of the gel was adjusted to 7.4 using triethanolamine. During preparation of the gel, to avoid any air entrapment, the solution was agitated slowly.

Incorporation of Ufasomes in the gel base.

Under gentle mechanical mixing for 5 min, drug gel was prepared by using an equivalent amount of etodolac vesicular dispersion into the previously made carbopol gel in a 2 **:** 1 ratio.

Evaluation of Ufasomes

Shape and Surface Morphology

Morphological parameters including sphericity and aggregation of selected Etodolac loaded ufasomal dispersion were examined using Scanning Electron Microscopy (SEM). Prior to imaging, samples were dispersed in methanol and the mixture was drop casted onto a piece of silicon wafer and fixed with double sided conductive tape. Further, samples were air dried and coated with gold using a gold sputter. High resolution images of the ufosomes were visualized under high vacuum at an accelerated voltage of 20 keV.

Drug Entrapment Efficiency

The entrapment efficiency of the drug was determined by using centrifugation at 4500 rpm for 3 h at room temperature. The supernatant was separated and the drug amount was calculated by using supernatant and which carried out by detection of entrapment efficiency at 223.5 nm with UV spectroscopy. The amount of entrapment drug is determined as a percentage was estimated from the following equation:

$$\textbf{Entrapment efficiency (\%)} = \frac{\textbf{Amount of drug entrapped}}{\textbf{Total amount of drug}} * \textbf{100}$$

Where: A=Amount of drug added initially;

B=Amount of drug determined in the filtrate by spectrophotometrically

A-B=Represents the amount of drug entrapped in the formulation.

Evaluation of Ufasomal Gel

Physical Evaluation

The prepared ufasomal gels were examined for their physical properties by visual inspection of color, clarity and phase separation.

Percentage Yield

The empty container was weighed in which the gel formulation was stored then again the container was weighed with gel formulation. Then subtracted the empty container weighed with the container with gel formulation then it gives the practical yield. Then the percentage yield was calculated by the formula.

$$\textbf{Percentage yield} = \frac{\textbf{Practical yield}}{\textbf{Theoritical yield}} * \textbf{100}$$

Drug Content

Weighed 10 gm of gel formulation was transferred in 250 ml of volumetric flask containing 20 ml of alcohol and stirred for 30 min. The volume was made up to 100 ml and filtered. 1 ml of above solution was further diluted to 10 ml with alcohol and again 1 ml of the above solution was further diluted to 10 ml with alcohol. The absorbance of the solution was measured spectrophotometrically at 223.5 nm. Drug content was calculated by the following formula.

$$\textbf{Drug content} = \frac{\textbf{Absorbance}}{\textbf{Slope}} \times \textbf{Dilution factor} \times \frac{\textbf{1}}{\textbf{1000}}$$

Determination of pH

Weighed 50 gm of gel formulation was transferred into a beaker and pH measurement of the gel was carried out using a digital pH meter by dipping the glass electrode completely into the gel system to cover the electrode.

Spreadability

Two sets of glass slides of standard dimensions were taken. The gel formulation was placed over one of the slides. The other slide was placed on the top of the gel, such that the gel was sandwiched between the two slides in an area occupied by a distance of 7.5 cm along the slides. 100 g weight of gel was placed on the upper slides so that the gel between the two slides was pressed uniformly to form a thin layer. The weight was removed and the excess of gel adhering to the slides was scrapped off. The two slides in position were fixed to a stand

without slightest disturbance and in such a way that only upper slides to slip off freely by the force of weight tied on it. A 20 g weight was tied to the upper slide carefully. The time taken for the upper slide to travel the distance of 7.5 cm and separated away from the lower slide under the influence of the weight was noted. Spreadability was calculated by using the following formula:

S= m × l/t

where, S - spreadability

m - weight tied to upper slides (20 g)

l - length of the glass slide (7.5 cm)

t - time taken in sec

Homogeneity and Grittiness

A small quantity of ufasomal gel was pressed between the thumb and the index finger. The consistency of the ufasomal gel was noticed (whether homogenous or not), if there was any coarse particles appeared on fingers. Also, the homogeneity could be detected when a small quantity of the ufasomal gel was rubbed on the back of the hand. The grittiness of the prepared ufasomal gel was also observed in the same manner.

Viscosity Measurement

Viscosity of gel was determined using Brookfield viscometer (S-62, model LVDV-E) at room temperature with a spindle speed of viscometer rotated at 12 rpm.

***In Vitro* Drug Release**

In vitro drug release studies were performed on a Franz diffusion cell by applying cellophane membrane. 50 ml volume of receptor zone was maintained with phosphate buffer of pH 7.4. 1 g of gel formulation was spread on donor compartment. The temperature of receptor cell was maintained at 37º C. Equal volumes of the sample were taken at 15, 30, 60, 120, 180, 240, 300 and 360 minutes and maintained with equal volume of fresh phosphate buffer solution. Each sample was determined by spectrophotometrically at 223.5 nm and % cumulative drug release was calculated.

Kinetic Study

- **Dissolution profile modeling**

There are several linear and non-linear kinetic models to describe release mechanisms and to compare test and reference dissolution profiles which are as follows:

- **Zero order kinetics**

Drug dissolution from pharmaceutical dosage forms that do not disaggregate and release the drug slowly (assuming that area does not change and no equilibrium conditions are obtained) can be represented by the following equation:

$$W_0 - W = K_0 t$$

Where W_0 is the initial amount of drug in the pharmaceutical dosage form at time t and k is proportionality constant.

Dividing this equation by W_0 and simplifying:

$$F_t = k_0 t$$

Where F_t = 1- (W_t/W_0) and F_t represents the fraction of drug dissolved in time t and k_0 the apparent dissolution rate constant or zero order release constant.

- **First order kinetics**

This type of model to analyze the drug dissolution study was first proposed by Gibaldi and Feldman and later by Wagner. The relation expressing this model:

$$\text{Log } Q_t = \text{Log } Q_0 + \frac{k1t}{2.303}$$

Where, Q_t = amount of drug released in time t, Q_0 is initial amount of drug in the solution and K_1 first order release rate constant.

- **Korsmeyer peppas model**

Korsmeyer developed a simple, semi empirical model, relating exponentially the drug release to the elapsed time (t).

$$\frac{Qt}{Qa} = Kt^n$$

Where 'K' is a constant incorporating structural and geometric characteristic of the drug dosage form and 'n' is the release exponent.

The release exponent can be obtained from the slope and the constant (K) obtained from the intercept of the graphical relation between logarithmic versions of left side of the equation versus log t.

- **Higuchi model**

$$Q_t = K_H t^{1/2}$$

Where Q_t = the amount of drug released at time 't'

K_H = Higuchi release rate

This is the most widely used model to describe drug release from pharmaceutical matrices. A linear relationship between the square roots of time versus concentrations indicates that the drug release follows strict fickian diffusion.

Storage Stability Studies

The stability studies of gel formulation were determined at 40±2°C, 30±2°C and 5±2°C in glass container for 30 days. The gel formulations were checked in the change in physical appearance and drug content was analyzed by applying a spectrophotometrically at 223.5 nm and phosphate buffer used as blank.

RESULTS AND DISCUSSION

Drug - Excipient Compatibility Studies

The FTIR studies were carried out for pure drug, drug polymer mixture and drug excipient mixtures. Spectrum of drug and excipients in figure 2, 3, 4, 5, 6, 7 and 8 showed the prominent peaks with respect to functional groups. The spectrum of physical mixture of drug with polymer and drug with excipients concluded that there is no significant interaction between the drug, polymer and excipients. In the spectrum of drugs polymer mixture, the characteristic peak of drug was not altered.

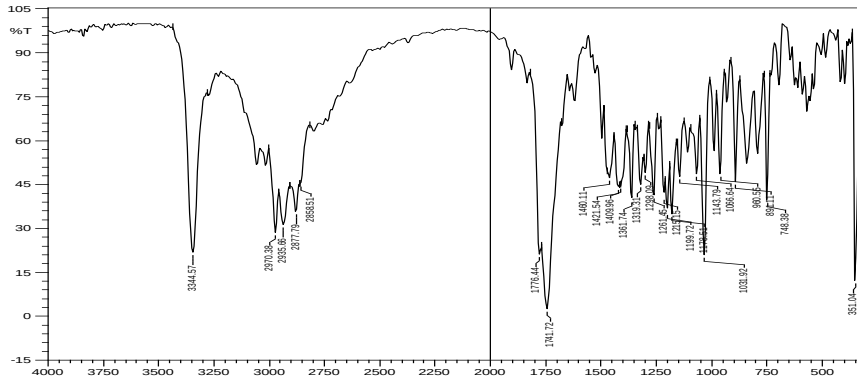

Fig 2: FTIR spectrum of Etodolac

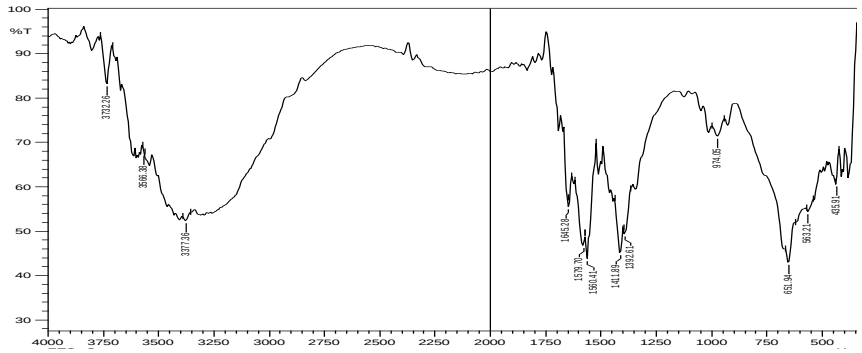

Fig 3: FTIR spectrum of Etodolac and Oleic acid

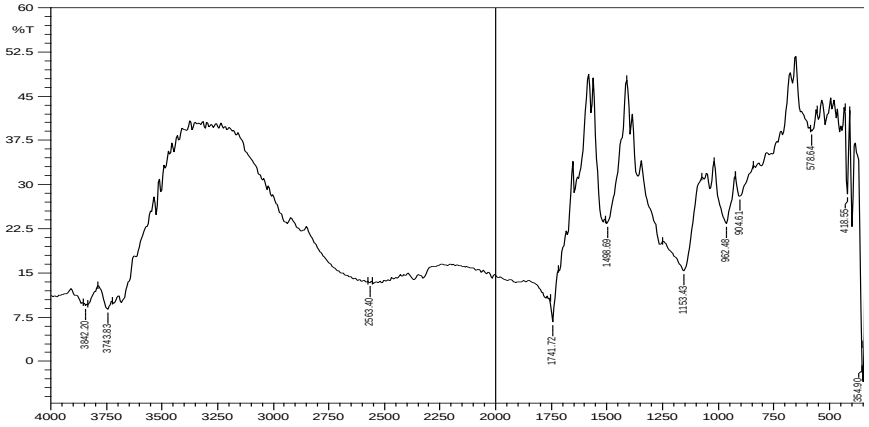

Fig 4: FTIR spectrum of Etodolac and Tween 80

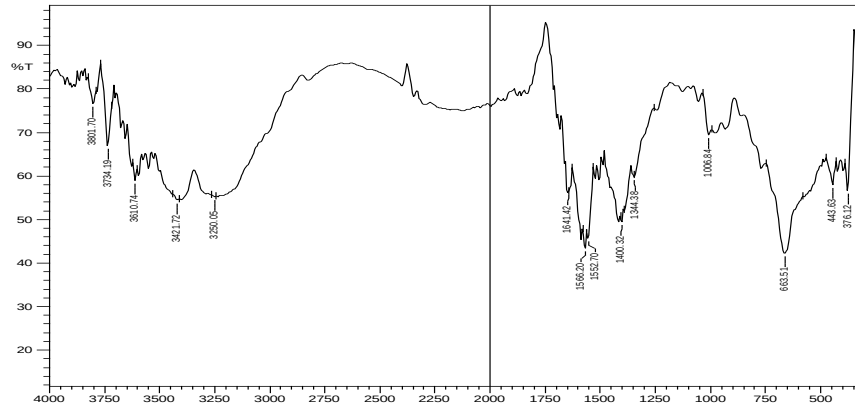

Fig 5: FTIR spectrum of Etodolac and Methanol

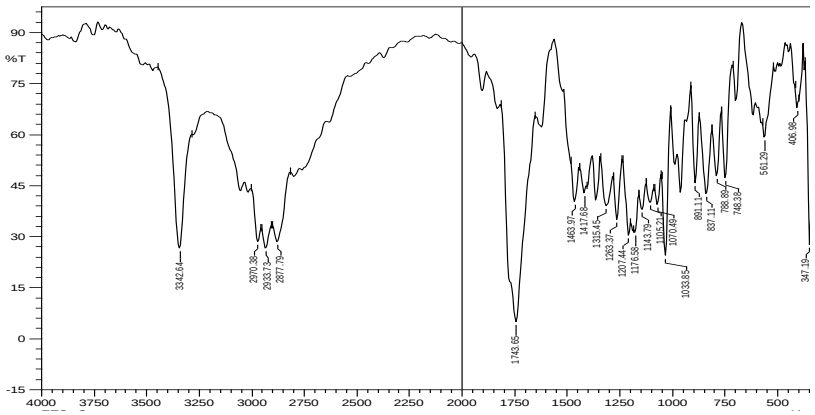

Fig 6: FTIR spectrum of Etodolac and Carbopol 940

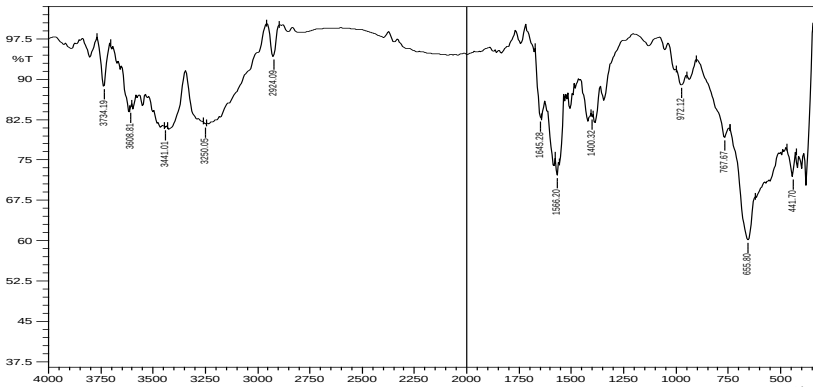

Fig 7: FTIR spectrum of Etodolac and Triethanolamine

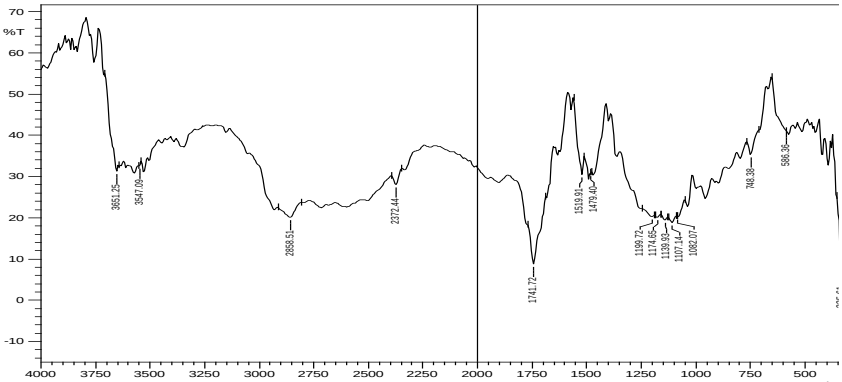

Fig 8: FTIR spectrum of drug and excipients

Formulation Development

Fig 9: Ufasomal dispersion of Etodolac

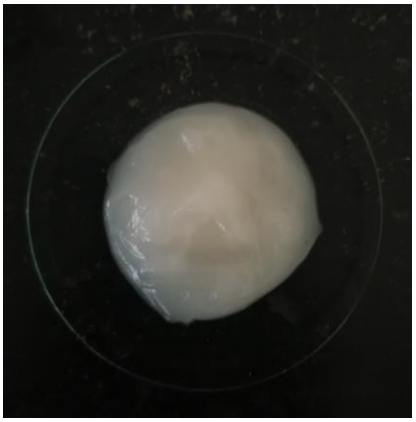

Fig 10: Ufasomal gel of Etodolac

Evaluation of Ufasomes

Shape and Surface Morphology

The external and internal morphology of ufasomal dispersion were studied by SEM. SEM photograph of ufasomal dispersion is shown in the Fig 11 and 12, in which the prepared ufasomal dispersion were spherical with roughly smooth surface.

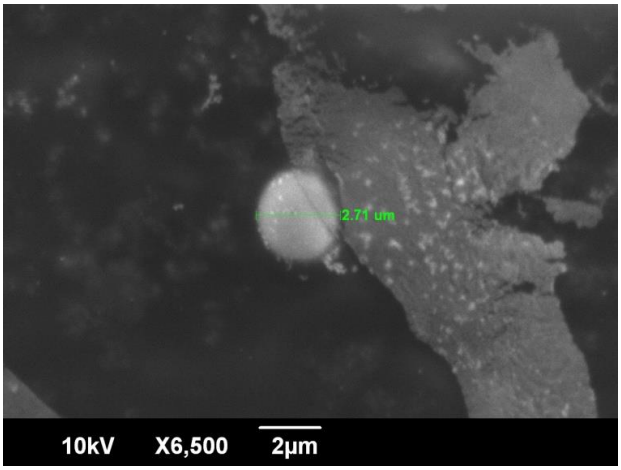

Fig 11: SEM image of ufasomal dispersion

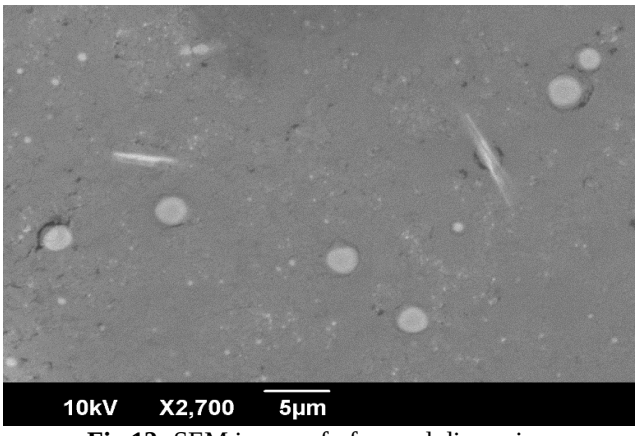

Fig 12: SEM image of ufasomal dispersion

Drug Entrapment Efficiency

Drug entrapment effieciency of different formulations was calculated and the percentage entrapment of etodolac loaded ufasomes was found in the range of 74.33% and 83.57% as given in Table a. The results were depicted as a graph in Fig 13. The entrapment efficiency was found to be higher in F4 formulation which is 83.57 %.

Sl. No.	Formulation Code	Entrapment Efficiency (%)(* ± SD)
1	F1	74.33 ± 0.16
2	F2	76.54 ± 0.18
3	F3	78.19 ± 0.19
4	F4	83.57 ± 0.13
5	F5	80.44 ± 0.05
6	F6	81.44 ± 0.11

*Average of 6 determinants, SD = Standard deviation

Table a: Entrapment efficiency of ufasome

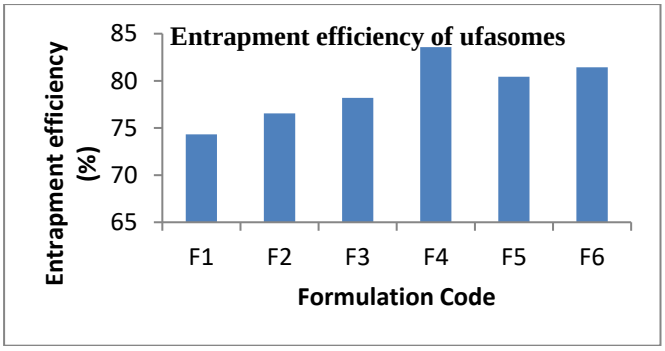

Fig 13: Entrapment efficiency of ufasomes

Evaluation Of Ufasomal Gel

Physical Evaluation

The physical evaluation of ufasomal gel was evaluated and the results were tabulated in Table b. From the analysis of the results, the physical appearance of the ufasomal gels were found to be clear, white and translucent.

Sl.No.	Formulation Code	Colour	Clarity	Appearance
1	F1	White	Clear	Translucent
2	F2	White	Clear	Translucent
3	F3	White	Clear	Translucent
4	F4	White	Clear	Translucent
5	F5	White	Clear	Translucent
6	F6	White	Clear	Translucent

Table b: Physical evaluation of ufasomal gel

Percentage Yield

The percentage yield of all ufasomal formulations were performed. The values obtained were in the range of 87.52% and 99.53% were summarized in Table c. The results were depicted as a graph in Fig 14. The percentage yield was found to be higher in F4 which was 99.53%.

Sl. No.	Formulation Code	Perecentage yield (%)(*± SD)
1	F1	93.33 ± 0.23
2	F2	99.46 ± 0.11
3	F3	93.32 ± 0.15
4	F4	99.53 ± 0.07
5	F5	94.6 ± 0.13
6	F6	87.52 ± 0.31

*Average of 6 determinants, SD = Standard deviation

Table c: Percentage yield of ufasomal gel formulations

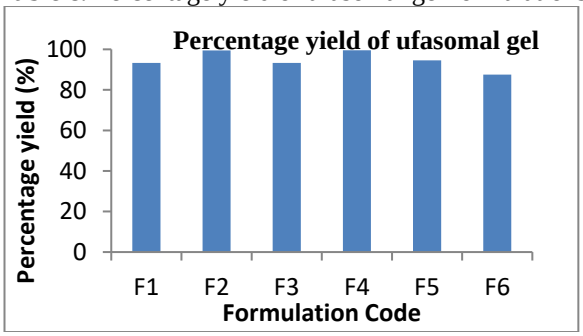

Fig 14: Percentage yield of ufasomal gel

Drug Content

The drug content of different formulations was determined by UV spectroscopic method at a wavelength of 223.5 nm. The values obtained were in the range of 84.39% and 99.32% as given in the Table d. The drug content was found to be higher in F4 which was 99.32%.

Sl. No.	Formulation Code	Percentage drug content (%) (* ± SD)
1	F1	84.39 ± 0.19
2	F2	98.44 ± 0.24
3	F3	87.11 ± 0.22
4	F4	99.32 ± 0.09
5	F5	91.52 ± 0.11
6	F6	95.48 ± 0.33

*Average of 6 determinants, SD = Standard deviation

Table d: Percentage drug content of ufasomal gel formulation

Determination of pH

The pH values of all the formulations were determined as per the procedure. The values were in the range of 7.22 and 7.42 and is summarized in Table e.

Sl. No.	Formulation Code	pH (* ± SD)
1	F1	7.22 ± 0.02
2	F2	7.35 ± 0.10
3	F3	7.32 ± 0.09
4	F4	7.22 ± 0.01
5	F5	7.42 ± 0.16
6	F6	7.28 ± 0.06

*Average of 6 determinants, SD = Standard deviation

Table e: pH of ufasomal gel formulations

Spreadability

The spreadability of all the formulations were determined as per the procedure. The values were in the range of 19.64 and 28.33 and is summarized in Table f. The formulation F4 is found to have highest spreadability which is 28.33g/cm/sec. This indicates that the formulation F4 will easily spread on the skin which will enhance the absorption of the drug through stratum corneum.

Homogeneity and Grittiness

The homogeneity and grittiness of all the formulations were determined as per the procedure. The values are summarized in Table g. All the formulation of ufasomal gel was found to be homogenous without any grittiness.

Sl. No.	Formulation Code	Spreadability (g/cm/sec) (*± SD)
1	F1	23.80 ± 1.68
2	F2	22.61 ± 1.69
3	F3	19.64 ± 1.25
4	F4	28.33 ± 2.35
5	F5	20.53 ± 1.26
6	F6	26.66 ± 2.36

*Average of 6 determinants, SD=Standard deviation

Table f: Spreadability of ufasomal gel formulations

Sl. No.	Formulation Code	Homogeneity	Grittiness
1	F1	Homogenous	No
2	F2	Homogenous	No
3	F3	Homogenous	No
4	F4	Homogenous	No
5	F5	Homogenous	No
6	F6	Homogenous	No

Table g: Homogeneity and grittiness of ufasomal gel formulations

Viscosity Measurement

The viscosity of all the ufasomal gel formulations was found using Brookfield viscometer. The results were summarized in the Table h.

Sl. No.	Formulation Code	Viscosity (cps) (* ± SD)
1	F1	1886.33 ± 0.47
2	F2	1885.66 ± 0.94
3	F3	1891 ± 0.81
4	F4	1873 ± 0.81
5	F5	1880.66 ± 0.94
6	F6	1891.33 ± 1.24

*Average of 6 determinants, SD = Standard deviation

Table h: Viscosities of ufasomal gel formulations

The viscosity of all batches of etodolac ufasomal gel was tested. The viscosity of all the formulations were evaluated using Brookfield programmable DV-E viscometer by using spindle no: 62. Viscosity of various formulated gels were found in the range of 1873 to1891 centipoises.

***In Vitro* Drug Release**

Time (min)	Percentage of drug release (%)(*± SD)					
	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
15	8.4 ± 0.16	12.26 ± 1.53	4.96 ± 0.38	14 ± 0.98	9.66 ± 0.79	8.56 ± 0.61
30	13.32 ± 0.67	25.33 ± 1.02	16.26 ± 1.37	21.2 ± 1.21	15.6 ± 0.98	17.6 ± 0.78
60	26.2 ± 0.55	34.86 ± 2.36	23.06 ± 2.17	35.53 ± 0.97	22.16 ± 0.66	35.26 ± 1.58
120	38.45 ± 0.90	46.13 ± 2.63	43.53 ± 2.29	57.13 ± 1.93	45.01 ± 1.39	45.13 ± 1.47
180	47.06 ± 1.30	57.04 ± 2.27	55.60 ± 1.15	64.86 ± 1.05	62.86 ± 2.12	54.73 ± 1.06
240	55.40 ± 2.93	69.36 ± 1.35	59.13 ± 2.36	73.56 ± 1.67	73.86 ± 2.26	64.1 ± 1.74
300	61.56 ± 0.81	75.68 ± 0.88	65.80 ± 0.86	86.26 ± 2.41	83.76 ± 1.37	67.13 ± 1.34
360	65.68 ± 0.87	82.8 ± 2.40	68.86 ± 2.00	91.01 ± 1.69	86.1 ± 2.22	77.73 ± 1.58

*Average of 6 determinants, SD = Standard deviation

Table i: *In vitro* drug release study of etodolac ufasomal gel.

The *in vitro* drug release of the ufasomal gel was carried out using franz diffusion cell apparatus with phosphate buffer 7.4 for 6 h. The results obtained were tabulated in Table i. The plot of percentage cumulative drug release v/s time (min) was plotted and depicted as shown in Fig 15 and 16. *In vitro* drug release study was conducted on the formulations for 6 h and the highest drug release of 91.01% was observed with formulation F4.

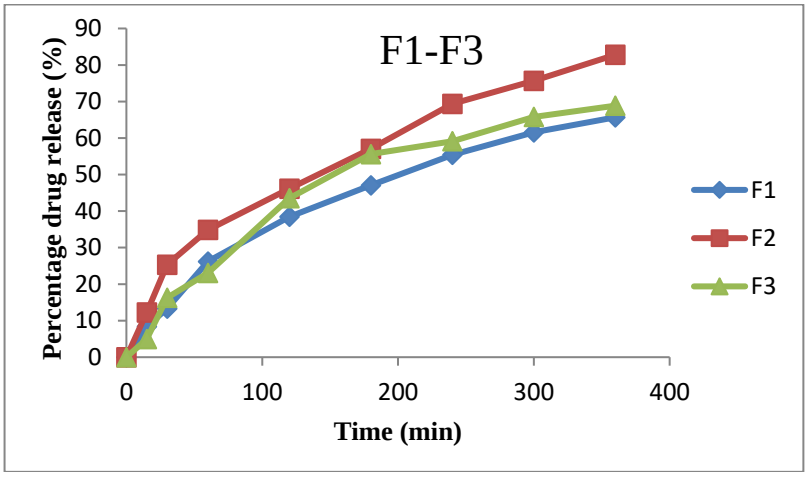

Fig 15: *In vitro* drug release of formulation F1-F3

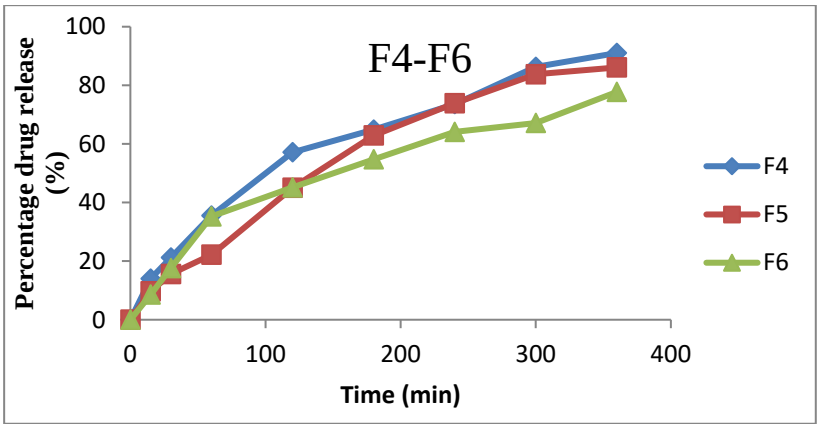

Fig 16: *In vitro* drug release of formulation F4-F6

Kinetic Modelling

Time (min)	cum % drug released	% drug remaining	Square root time	log Cum % drug remaining	log time	log Cum % drug released	% Drug released	Cube Root of % drug Remaining (Wt)	Wo-Wt
0	0	100	0.000	2.000	0.000	0.000	100	4.642	0.000
15	14	86	3.873	1.934	1.176	1.146	14	4.414	0.228
30	21.2	78.8	5.477	1.897	1.477	1.326	7.2	4.287	0.355
60	35.53	64.47	7.746	1.809	1.778	1.551	14.33	4.010	0.632
120	57.13	42.87	10.954	1.632	2.079	1.757	21.6	3.500	1.142
180	64.86	35.14	13.416	1.546	2.255	1.812	7.73	3.275	1.367
240	73.56	26.44	15.492	1.422	2.380	1.867	8.7	2.979	1.663
300	86.26	13.74	17.321	1.138	2.477	1.936	12.7	2.395	2.247
360	91.01	8.99	18.974	0.954	2.556	1.959	4.75	2.079	2.563

Table j: Pharmacokinetic values of the study

Formulation	Kinetic models			
F4	Zero order	First order	Korsmeyer-peppas model	Higuchi model
R^2 values	0.926	0.914	0.970	0.990

Table k: R^2 values of kinetic model

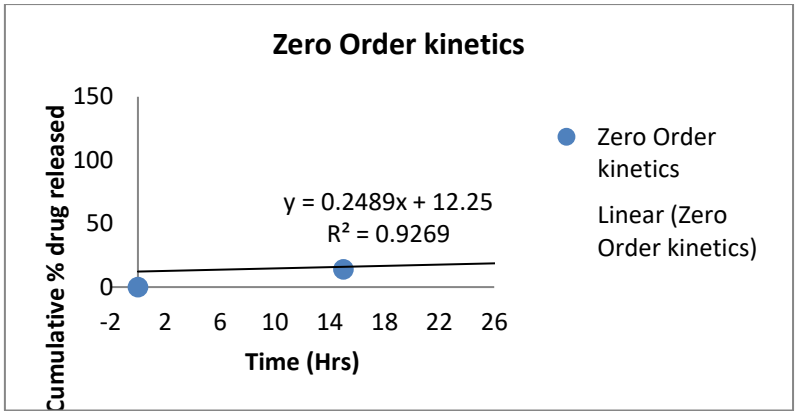

Fig 17: Zero order plot

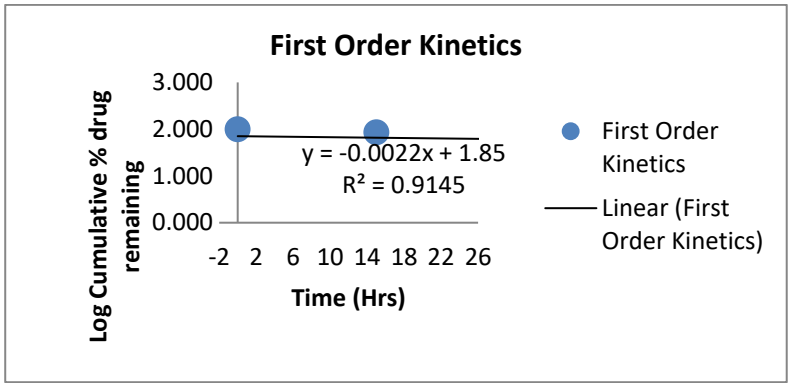

Fig 18: First order plot

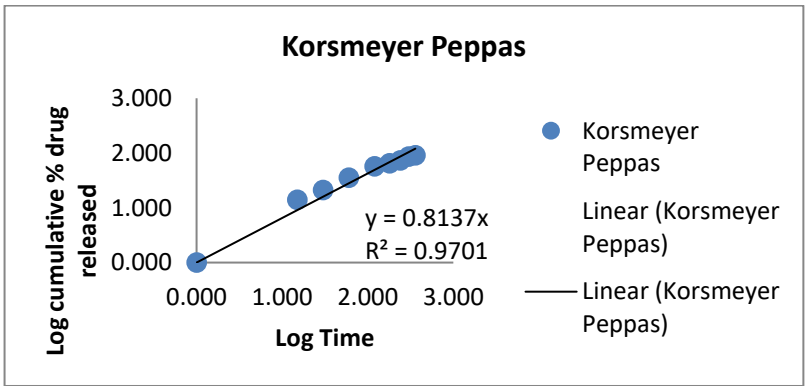

Fig 19: Korsemeyer peppas plot

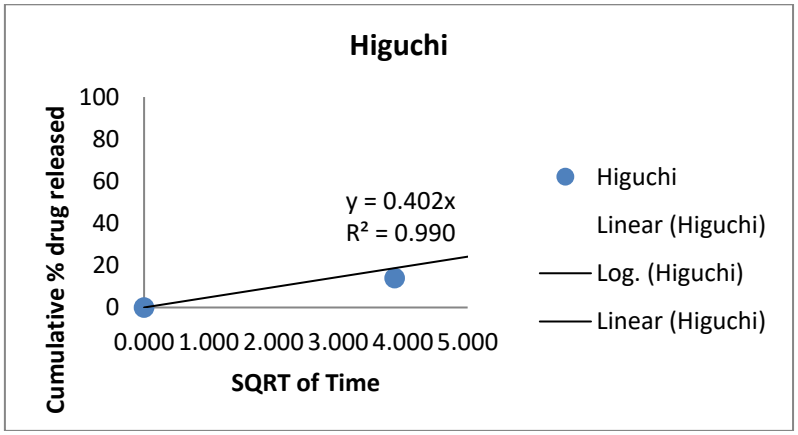

Fig 20: Higuchi plot

The diffusion profile of optimized formulation F4 was fitted to zero order, first order, Korsmeyer – peppas model and Higuchi model to ascertain the kinetic modelling of the drug release mechanism shown in Fig 17 to 20. The correlation coefficient (R^2) for the formulation using different kinetics equation is listed in Table k. It was found that the *in vitro* drug release of the optimized batch F4 was best explained by Higuchi plot as the plot show highest linearity (R^2 = 0.990). The R^2 value was used to evaluate the accuracy of fit. The formulation F4 provide best fit to the Higuchi model.

Storage Stability Studies

The stability study of the optimized formulation (F4) was carried out for 30 days at 40±2°C, 30±2°C and 5±2°C in glass container. After prolonged storage, the ufasomal gel of formulation F4 were evaluated for various parameters like physical appearance, pH, drug content and percentage drug release.

Days	Physical appearance	pH (*±SD)	Drug content (*±SD)	*In vitro* drug release (%) (*±SD)
0	Clear and colourless	7.22 ± 0.01	99.32 ± 0.09	91.01 ± 1.69
30	Clear and colourless	7.20 ± 0.15	99.24 ± 0.02	90.92 ± 0.09

*Average of 6 determinants, SD = Standard deviation

Table l: Stability study at 5±2°C

Days	Physical appearance	pH (*±SD)	Drug content (*±SD)	*In vitro* drug release (%) (*±SD)
0	Clear and colourless	7.22 ± 0.01	99.32 ± 0.09	91.01 ± 1.69
30	Clear and colourless	7.24 ± 0.15	99.24 ± 0.07	90.98 ± 0.08

*Average of 6 determinants, SD = Standard deviation

Table m: Stability study at 30±2°C

Days	Physical appearance	pH (*±SD)	Drug content (*±SD)	*In vitro* drug release (%)(*±SD)
0	Clear and colourless	7.22 ± 0.01	99.32 ± 0.09	91.01 ± 1.69
30	Clear and colourless	7.24 ± 0.12	99.31 ± 0.45	90.85 ± 0.42

*Average of 6 determinants, SD = Standard deviation

Table n: Stability study at 40±2°C

Formulation F4 after 30 days of storage shows there is no major change in the formulation after the storage as initial. The study shows no major difference before and after the storage and all are in the satisfactory range. Therefore formulation remains stable for sufficient time after the storage of 30 days.

CONCLUSIONS

In the present study, an attempt was made to prepare topical ufasomal gel of etodolac. The ufasomal gel was prepared using lipid film hydration method using different concentration of the penetration enhancer, oleic acid and surfactant, tween 80. Formulation F4 contains the optimized fatty acid and surfactant concentration based on entrapment efficiency, drug content and drug release kinetics. Hence, formulation F4 was selected as the best formulation. From the studies conducted, the following conclusions were drawn. As per pre-established objectives, the physico-chemical characterizations of the formulations were performed and satisfactory results were obtained. Also, the *in vitro* drug release of ufasomal gel was found to be the highest in the formulation F4 which is 91.01% ± 1.69 which proves its ability to enhance the bioavailability through its longer residence time and increased permeation of the drug through skin.

Acknowledgements

I express my deep gratitude to Prof. (Dr.) Shaiju S Dharan (Principal, Ezhuthachan College of Pharmaceutical Sciences) for his kind considerations on number of occasions throughout my project work. I am also thankful to Mrs. Deepa Manohar R (Asst. Professor, Ezhuthachan College of Pharmaceutical Sciences) for her guidance, encouragement and suggestions rendered for the successful completion of my project work. I am also indebted to Dr. Mathan S (Head, Department of Pharmaceutics), Prof. Janeera Beevi S (Head, Department of Pharmaceutical Chemistry), Dr. Merlin N. J (Director of PG Studies) for their guidance and support. I express my sincere gratitude to Ezhuthachan College of Pharmaceutical Sciences, KUHS, Thiruvananthapuram, India, for the constant support throughout.

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