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STUDIES ON FORMULATION AND CHARACTERIZATION OF TOPICAL EMULGEL CONTAINING MICROSPONGES OF MEFENAMIC ACID

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ABSTRACT

The objective of the present investigation was formulate & characterize the microsponge of mefenamic acid, these microsponges were prepared by quassi-emulsion method. Preformulation studies by FTIR, revealed no interaction between pure drug and the different polymers used. The prepared microsponges were characterized for their production yield, drug content, mean particle size & entrapment efficiency, Effect of formulation variable were also studied. The microsponge containing 0.5 gm of poly vinyl alcohol, 0.6 gm of ethyl cellulose and 5ml ethanol good were compared to the other formulation prepared. The best microsponges (M3, M6, M9) in cooperated into emulgel. The topical emulgel was evaluated for their organoleptic characters, viscosity, spreadability, drug content and drug release studies. From that MEG1 Shows better compared to other formulation. Permeation from mefenamic acid gel followed Higuchi model or matrix diffusion. In mefenamic acid microsponge emulgel drug seem to follow first order kinetics as it is evidenced by correlation coefficients (r^2=0.9846 to 0.974) which is better than zero order (r^2 =0.9496 o 0.9318) Higuchi's plot was also found to be linear for all formulations with regression coefficient ranging from 0.9024 to 0.7931. Hence, to confirm the exact mechanism of drug permeation from these microsponges, the data was fitted according to the Korsmeyer-Peppas model.

KEYWORDS: microsponge, mefenamic acid,ethyl cellulose, emulgel, release kinetics.

INTRODUCTION

The microsponge drug delivery system was developed by Won in 1987. The micrsponge delivery system is patented polymeric system consisting of porous microsphere. They are tiny sponge like spherical particles that consist of myriad of inter connecting void within a non-collapsible structure through which active ingredient are released in a controlled manner. Microsphere surrounded by the vehicle acts like microscopic sponges, storing the active ingredient until its release is triggered by skin application. Microspores within the spheres are employed for extensive drug retention. Release of drug into the skin is triggered by a variety of stimuli, including rubbing and higher skin temperature than ambient one. Their high degree of cross linking results in particles that are insoluble, inert and of sufficiently strong strength to withstand the high shear commonly used in creams, lotions, and powders. The active payload is protected in the formulation by the microsponge particle: it is delivered to skin via controlled diffusion. The sustained release of activities to skin over time is an effective tool to extend the efficacy and reduce the irritation commonly associated.[1,2] The microsponges were prepared by free radical suspension method or quassi emulsion solvent diffusion method. Rheumatoid arthritis and osteoarthritis treated by NSAID'S. Mefenamic acid is available as oral dosage form currently in market. Oral administration this drug has adverse effects like head ache, dizziness, G I ulcer, nausea, vomiting. Hence formulation novel drug delivery system such as microsponge drug delivery system mefenamic acid will maximize the duration of drug adherence on the skin surface and overcome problem associated with conventional preparation i.e. oral dosage form. The Microsponges are prepared by several methods utilizing emulsion system as well as suspension polymerization in a liquid-liquid system. The most common emulsion technique used is emulsion solvent diffusion method. It was shown that the drug: polymer ratio, stirring rate, volume of dispersed phase influenced the particle size and drug release behavior of the formed microsponges and that the presence of emulsifier was essential for microsponge formation.[3,4]

MATERIALS AND METHODS

Mefenamic acid pure drug was generously gifted by Camarin Pharmaceutical, kannur.Eudragit RS100 & Eudragit RL100 were gifted by Degussa India Pvt.Ltd, Mumbai.Ethyl cellulose was purchased from Lobachemei Mumbai. All other excipients used in our work were of Analytical grade.

Determination of ƛ max

Dissolve accurately weighed 100mg of mefenamic acid in 100ml of methanol in 100ml standard flask to get 1000µg/ml**.** From the stock solution of mefenamic acid, 1ml is pipette out and diluted to 100ml with methanol to get 10µg/ml. The absorption maximum of the standard solutions of mefenamic acid was scanned between 200-400nm regions on UV-visible spectrophotometer. The absorption maxima obtained with the substance being examined corresponds in position and relative intensity to those in the reference spectrum.

Preformulation Studies[5]

Pre-formulation testing was an investigation of physical and chemical properties of a drug substance alone. It is the first step in rational development of dosage form.

- **Solubility studies**

Solubility of mefenamic acid was observed in different solvent such as distilled water in acetone, methanol, 95%ethanol, sodium hydroxide, Potassium hydroxide**,** diethyl ether, chloroform, acetic acid.

- **Identification by melting point**

Melting point of drug was determined using Melting point apparatus.

- **Organoleptic properties**

Physical appearance of drug was observed and compared with the official monographs.

- **Partition Coefficient (Kp**)

The partition coefficient of the drug was determined by shaking equal volumes of organic phase (n-octanol) and the aqueous phase in a separating funnel. A drug solution of 1 mg/ml was prepared in phosphate buffer pH7.4 and 50 ml of this solution was taken in a separating funnel and shaken with an equal volume of n-octanol for 10 minutes and allowed to stand for 24 hours with intermittent shaking. Then, the concentration was determined by U V Spectra.

- **Drug-ExcipientInteractionStudies**[6]**in** order to find out the possible interactions between mefenamic acid and the polymers used in the formulation of the microsponge, Fourier transform infra-red spectroscopy (FT-IR) analysis was carried out on the pure substances and their physical mixtures.

i) FT-IR Spectra of the pure drug, ethyl cellulose, eudragit RS 100, eudragit RL 100 and the physical mixture of the drug with polymers were taken individually by KBr pellet technique between 600 to4000 cm-1. This is to ensure that there is no incompatibility between the drug and the polymers. Once spectra were recorded, the peaks of the pure drug, the polymers and the physical mixture of drug and polymers were compared for any incompatibility.

Formulation Of Mefenamic Acid Loaded Microsponges[7,8]

Microsponge were prepared by quasi-emulsion solvent diffusion method using an external phase of distilled water and polyvinyl alcohol (PVA), and internal phase consisting of drug, ethyl alcohol, polymer(ethyl cellulose, eudragit RS100 & eudragit RL 100) and Glycerol (which was added at an amount of 20% of the polymer in order to facilitate the plasticity). For preparing microsponge, the internal phase was prepared and added to the external phase at room temperature. After emulsification process is completed, the mixture was continuously stirred for 2 hours at 500 rpm. Then the microsponges were separated by filtration. The product was washed and dried under vacuum oven at 40°C for 12 hrs.

Table no 1: Formulation of microsponge.

INGREDIENTS	M1	M2	M3	M4	M5	M6	M7	M8	M9
Mefanamic acid(gm)	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Ethyl cellulose(gm)	0.2	0.4	0.6	-	-	-	-	-	-
EudragitRS 100(gm)	-	-	-	0.2	0.4	0.6	-	-	-
Eudragit RL100(gm)	-	-	-	-	-	-	0.2	0.4	0.6
Polyvinyl alcohol(gm)	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Ethanol (ml)	5	5	5	5	5	5	5	5	5
Distilled water(ml)	100	100	100	100	100	100	100	100	100

In this experiment and effect of different variables such as external phase volume, internal phase volume, stirring speed, and drug: polymer ratio was observed. The formed microsponges were evaluated for their physical characteristics, % entrapment efficiency,drug content and particle size.

Formulation Of Mefenamic Acid Microsponge Emulgel

Gel Formation

The gel were prepared by dispersing gelling agent (HPMC) in purified water with continuous stirring at moderate speed to this add microsponge, then the p^H adjusted to 6-6.5 using Triethanolamine.

Emulsion Formation

The oil phase of emulsion were prepared by dissolving span 20 in light liquid paraffin while aqueous phase were

prepared by dissolving Tween 20 in purified water. Methyl paraben and propyl paraben was dissolved in ethanol and both solution was mixedwith aqueous phase were separately heated to 70-80°C, then oily phase was added to the aqueous phase and to this added required quantity of clove oil as penetration enhancer, continue the stirring until cool to room temperature.

Emulgel Formation

Mix the gel and emulsion in the ratio of 1:1 to obtain emulgel.

The formulation component of microsponge emulgel is mentioned in table no: 2

Table No.2: Formulation of Mefenamic acid Microsponge Emulgel.

Sl no	Ingredients	Quantity
1	Mefenamic aciid micropsponge	0.1g
2	Hydroxy propyl methyl cellulose	2.5g
3	Light liquid paraffin	7.5ml
4	Span 20	0.5ml
5	Tween 20	0.5ml
6	Propylene glycol	5ml
7	Ethanol	5ml
8	Methyl paraben	0.01g
9	Propyl paraben	0.03g
10	Clove oil	2 ml
11	Purified water	q.s

Evaluation of Mefanamic Acid Loaded Microsponges.[9,10, 11]

a) Particle size

Particle size was determined using an optical microscope under 40X magnification. The microscope was fitted with a stage micrometer to calibrate the eyepiece micrometer.

b) Determination of Percentage yield

The percentage yield of the microsponge can be obtained by calculating accurately the initial weight of the solid raw materials and the last weight of the microsponge obtained after drying.

$$\text{Percentage yield (\%)} = \frac{\text{Practicalweightofmicrosponge}}{\text{Theoreticalyield (polymer+ drug)}} \times 100$$

c) Drug loading efficiency

The drug content in microsponges was determined spectrophotometrically at 285nm.

A sample of mefanamic acid microsponge (10mg) was dissolved in 100 ml of solution. The drug content was expressed as actual drug content in microsponge. The loading efficiency (%) of the microsponge was calculated according to following equation

$$\text{Loading efficiency (\%)} = \frac{\text{Actualdrugcontentinmicrosponge}}{\text{Theoreticaldrugcontent}} \times 100$$

d) Drug content

Microsponges containing100mg of drug from all batches were accurately weighed and dissolved in Methanol in 100 ml standard flask and made up to the volume.From the above solution 1ml was taken and diluted to 100ml with Methanol. Then the amount of drug was detected by UV spectrophotometric method at 285 nm.

e) Surface morphology of microsponges by Scanning Electron Microscopy (SEM)

The morphology of microsponge formulation was observed by scanning electron microscope operating at 10kV. Prepared microsponges were coated with platinum by ion sputtering using auto fine coater. The microspoges were kept on the sample holder and SEM photograph was recorded using SEM (JEOL-JSM 6390, England) under vacuum at room temperature.

Characterization Of Microsponge Emulgel[12,13,14]

1) Clarity

The clarity of various formulations was determined by visual inspection under black and white background and it was graded as follows: turbid, clear, very clear

2) Homogeneity

All developed gels were tested for homogeneity by visual inspection after the gels have been set in the container for their appearance and presence of any aggregate.

3) pH

1g of gel was accurately weighed and dispersed in 100 ml of distilled water. The pH of dispersion was measured by using digital pH meter.

4) Viscosity measurement

Brookfield digital viscometer was used to measure the viscosity (in cps) of the prepared emulgel formulations. The spindle number 62 was rotated at 50 rpm for the viscosity measurement.

5) Spreadability[15]

Spreadability of the formulation was determined by using an apparatus designed and developed in the laboratory especially for the project and diagram of the apparatus is shown in fig.12. Two rectangular glass plates of standard dimension were selected.500mg of the sample was placed on one of the glass plate. Second plate was placed over the other one to sandwich sample between plates. A 20 gm weight was placed on the top of upper plate to provide a uniform thin film of the sample between the plates. Weight was removed; excess of the gel sample was scrapped off from the edges. The top plate was then subjected to pull by using string to which 50 gm weight was applied. The time required by the upper plate to travel a distance of 6cm and separate from the lower plate was noted. A shorter interval indicates better spreadability.

Experiment was repeated and averages of three attempts were calculated for each formulation using following formula.

$$\text{Spreadability} = (\mathbf{M}x)/T$$

M = weight tied to the upper side

L = length of the glass slide

6) Extrudability

The developed formulations were filled in collapsible metal tubes and crimped at one end. After removing the cap tube is pressed to extrude the product from the tube.

7) Drug content

Drug content of the emulgel was determined by dissolving an accurately weighed quantity of 1g gel in about 100 ml of methanol. 2ml of this solution was diluted to 10ml with methanol Solutions were then filtered and spectrophotometrically analyzed for drug content at 285nm. Drug content was determined from the standard curve of mefenamic acid.

8) In vitro drug release of mefenamic acid microsponge Emulgel[16,17]

i) Activation of Egg membrane

Activation of egg membrane was carried out by soaking the membrane sodium chloride saline solution to use. It was then mounted on the diffusion cell and equilibrated with receptor fluid for 15 minutes and used for drug release studies.

ii) Drug Release studies

The in vitro release of mefenamic acid microsponges from the formulations were studied using modified Keshary-Chien apparatus which was fabricated in our laboratory and used for the release study. The dissolution medium used was Phosphate buffer 7.4 pH.1 gm of the formulated emulgel was accurately weighed, and placed on membrane a and placed in membrane and attached to this assembly. The donor compartment was suspended in 50 ml of dissolution medium maintained at 37± 1°C so that the membrane just touched the receptor medium surface. The medium was stirred at 50 rpm using magnetic stirrer. Aliquots, each of 1ml volume, were withdrawn at hourly intervals and replaced by an equal volume of the receptor medium. The aliquots were diluted to 10ml with the receptor medium and analyzed by UV-Visible spectrophotometer at 285 nm and % cumulative drug release was calculated.

iii**) Kinetics of drug release** to examine the drug release kinetics and mechanism, the cumulative release data were fitted to models representing zero order, first, Higuchi's plot and Korsemeyer Peppas plot respectively.

RESULT

- **Determination of ƛ max**: Scanned in between 200-400 nm methanol as solvent maximum absorbance at 285 nm.
- **Standard curve of mefenamic acid**:

Table no: 3 Standard curve of mefenamic acid.

Concentration(µg/ml)	Absorbance
5	0.128±0.0015
10	0.253±0.0010
15	0.378±0.0021
20	0.496±0.0020
25	0.620±0.00208
30	0.735±0.00152

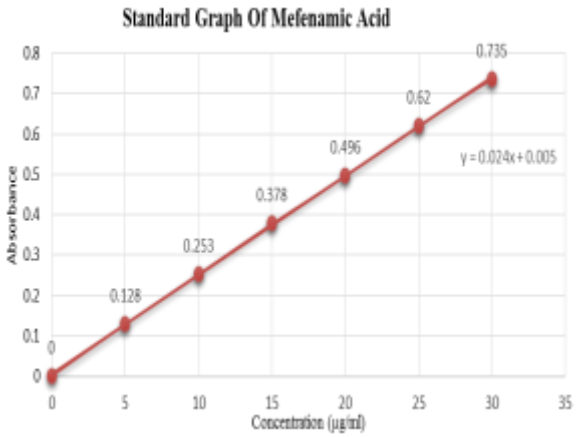

Figure no 1: Calibration curve of mefenamic acid.

Preformulation Studies

- Solubility studies: Solubility observed different solvents as water, acetone, methanol. Ethanol, chloroform, sodium hydroxide & it was found as mefenamic acid soluble in alkali hydroxide and 95% soluble in ethanol.
- Melting point: Determined by melting point apparatus and it was found to be 230-231°C.
- Organoleptic Characters**:** physical appearance observed as whitish odorless powder.
- Partition coefficient: It determined in n-octanol – phosphate buffer7.4 pH.was found to be 1.87.
- Drug excipient interaction studies: FT-IR studies of pure drug sample, polymers and physical mixtures were measured.

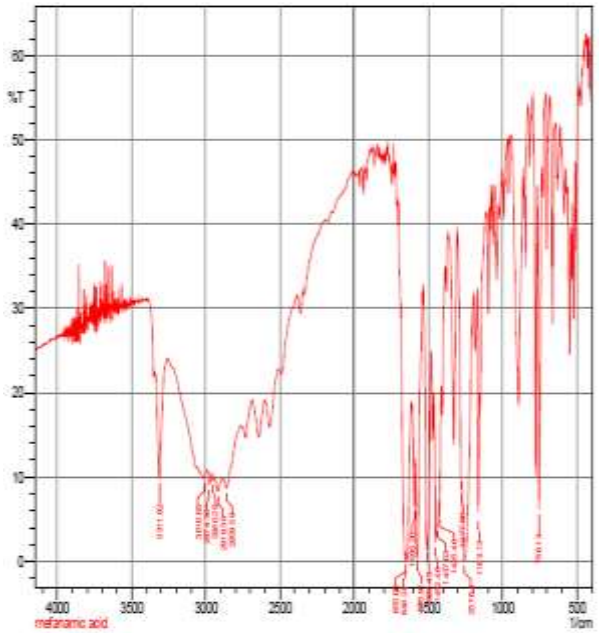

Figure no: 2 FTIR of mefenamic acid.

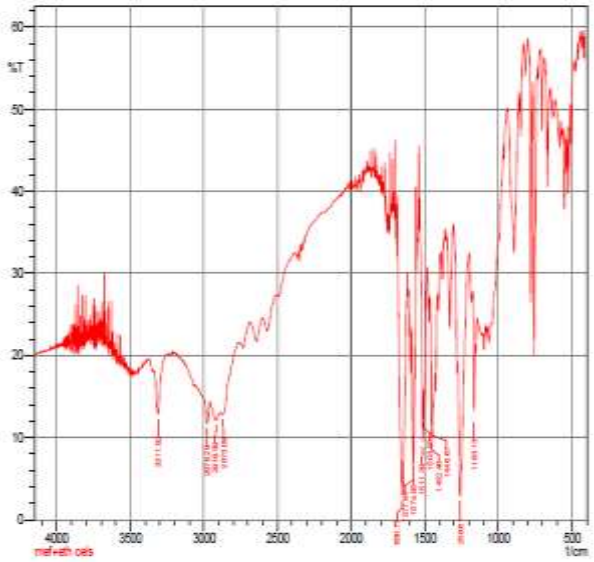

Figure no: 3 FT IR of mefeamic acid+ethyl cellulose.

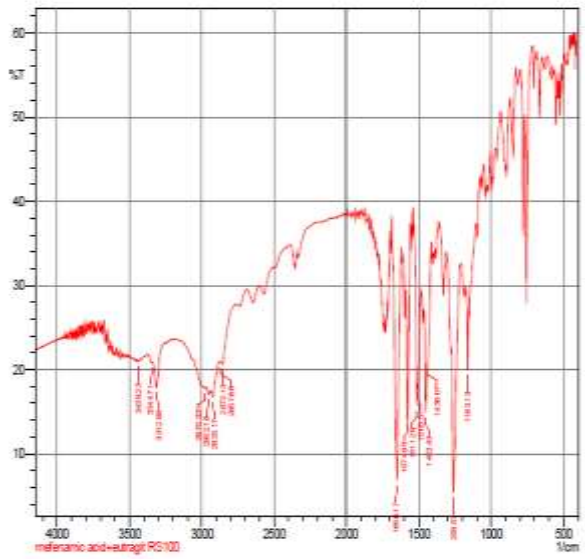

Figure no: 4 FT IR of mefenamic acid+ eudragit RS 100.

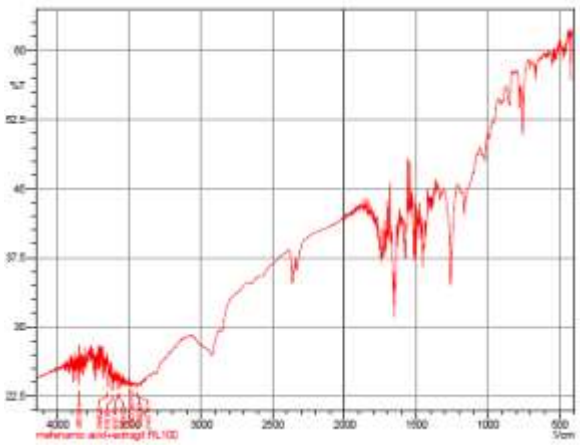

Figure no: 5 FT IR of mefenamic acid+ Eudragit RL1000.

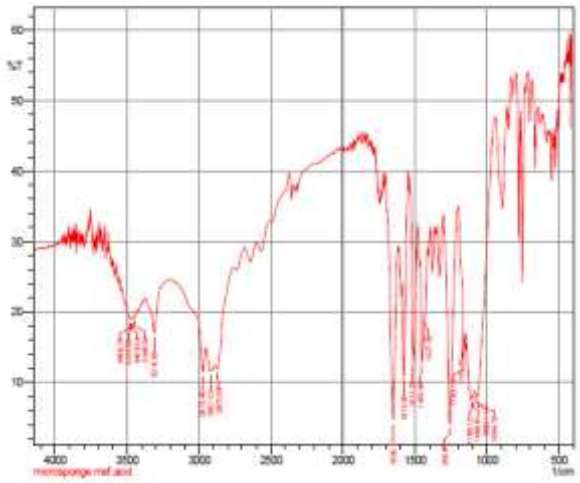

Figure no: 6 FT IR of mefnamic acid microsponge.

- The FT-IR spectrums of pure drug, polymers and physical mixture of drug and polymers shows that no interaction took place between drug and polymer.
- Some additional peaks were observed with physical mixtures, which could be due to the presence of polymers.
- These results suggest that there is no interaction between the drug and polymers used in the study. Thus indicating that the drug and polymer are compatible with each other.

Effect Formulation Variables for the Formulation of Mefenamic Acid Microsponge

Nine microsponge formulations (M1 -M9) were prepared at 0.2, 0.4 and 0.6gm of polymers, ethanol concentration as 5, 10 and 15 ml & emulsifying agents as 0.5, 0.75 and 01 gm keeping all the other variables constant. The formed microsponges were then evaluated for particle size and percentage yield, loading efficiency and drug content in order to find out the optimum polymer, ethanol and emulsifying agent composition

Characterization of Microsponge

Effect of Internal phase Composition on Mefanamic acid Microsponge.

Table no 4: Effect of internal phase on mefenamic acid microsponge.

INGREDIENTS	M1	M2	M3	M4	M5	M6	M7	M8	M9
Mefanamic acid(gm)	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Ethyl cellulose(gm)	0.2	0.4	0.6	-	-	-	-	-	-
EudragitRS 100(gm)	-	-	-	0.2	0.4	0.6	-	-	-
Eudragit RL100(gm)	-	-	-	-	-	-	0.2	0.4	0.6
Polyvinyl alcohol(gm)	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Ethanol (ml)	5	10	15	5	10	15	5	10	15
Distilled water(ml)	100	100	100	100	100	100	100	100	100
Production yield(%)	56.3±1.36	62.2±1.51	74.8± 2.01	52.5±1.65	69.9±2.83	73.4±2.92	51.3±1.70	64.2±0.90	66.76±1.80
Loading Efficiency(%)	69.34±1.6	74.1±0.90	81.2±1.37	64.5±1.35	71.54±1.82	79.3±1.37	61.24±2.41	67.8±1.45	73.2±0.79
Drug content(%)	53.9±1.40	57.8±1.57	62.7±0.60	51.3±0.90	54.7±2.94	56.4±2.66	51.6±1.15	52.8±1.44	54.2±1.35
Mean particle diameter(µm)	28.6±2.00	30.3±0.74	34.7±1.66	29.4±0.97	32.9±1.10	35.4±1.07	28.1±1.35	29.8±1.71	31.5±0.77

Effect on polymer on mefanamic acid microsponge

Table no:5 Effect on polymer on mefanamic acid microsponge.

INGREDIENTS	M1	M2	M3	M4	M5	M6	M7	M8	M9
Mefanamic acid(gm)	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Ethyl cellulose(gm)	0.2	0.4	0.6	-	-	-	-	-	-
EudragitRS 100(gm)	-	-	-	0.2	0.4	0.6	-	-	-
Eudragit RL100(gm)	-	-	-	-	-	-	0.2	0.4	0.6
Polyvinyl alcohol(gm)	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Ethanol (ml)	5	5	5	5	5	5	5	5	5
Distilled water(ml)	100	100	100	100	100	100	100	100	100
Production yield(%)	74.81±2.0	68.05±1.90	61.24±1.75	73.4±2.42	71.7±1.40	69.4±1.45	66.7±1.80	65.1±1.32	64.8±1.07
Loading efficiency (%)	81.2±1.75	79.3±1.45	77.8±1.47	79.3±1.15	76.8±2.23	75.2±1.25	73.2±1.32	72.9±2.02	71.1±1.36
Drug content (%)	62.7±1.00	61.4±1.79	59.4±1.83	56.4±2.07	54.9±2.05	53.5±1.83	54.2±1.15	53.3±1.73	52.6±1.00
Meanparticle diameter(µm)	34.7±1.00	33.1±1.45	32.5±2.47	35.4±1.73	33.6±0.85	32.8±1.25	31.5±1.67	30.6±1.00	29.5±1.68

Effect on emulsifying agent on Mefanamic acid microsponge

Table no: 6 Effect on emulsifying agent on Mefanamic acid microsponge.

INGREDIENTS	M1	M2	M3	M4	M5	M6	M7	M8	M9
Mefanamic acid(gm)	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Ethyl cellulose(gm)	0.2	0.4	0.6	-	-	-	-	-	-
EudragitRS 100(gm)	-	-	-	0.2	0.4	0.6	-	-	-
Eudragit RL100(gm)	-	-	-	-	-	-	0.2	0.4	0.6
Polyvinyl alcohol(gm)	0.25	0.5	0.75	0.25	0.5	0.75	0.25	0.5	0.75
Ethanol (ml)	5	5	5	5	5	5	5	5	5
Distilled water(ml)	100	100	100	100	100	100	100	100	100

Production yield(%)	74.81±0.84	72.4±1.7	69.2±1.0	73.4±1.33	70.9±0.79	67.8±1.32	66.7±1.76	63.9±0.96	62.18±3.4
Loading efficiency(%)	82.7±1.20	81.9±1.79	81.2±1.22	82.3±1.05	81.49±1.30	79.3±1.16	75.2±0.90	74.8±1.55	75.2±1.77
Drug content(%)	62.7±1.35	61.4±0.97	59.6±1.96	56.4±1.30	53.7±1.72	52.1±0.76	54.2±1.01	52.8±0.95	49.7±1.40
Meanparticle diameter(µm)	34.7±0.9	35.6±1.2	37.9±1.0	35.4±0.75	36.1±0.90	38.2±1.21	31.5±1.01	32.9±1.01	34.6±0.71

From the characterization study of mefenanic acid microsponge formulatons M3,M6,M9 were found to be good, so these formulations are converted into gel and emulgel.

Surface morphology by **scanning electron microscopy**, assume that the microsponge formed is spherical in shape and it has a porous surface. This may be due to rapid escape of volatile solvent (ethanol) during the formulation procedure.

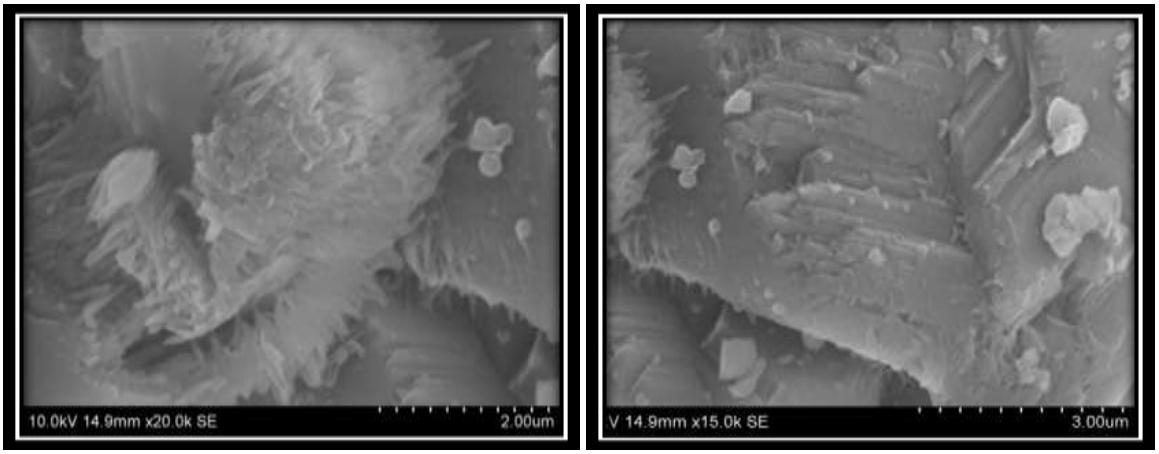

Figure no: 7. SEM Images of microsponge containing Ethyl cellulose.

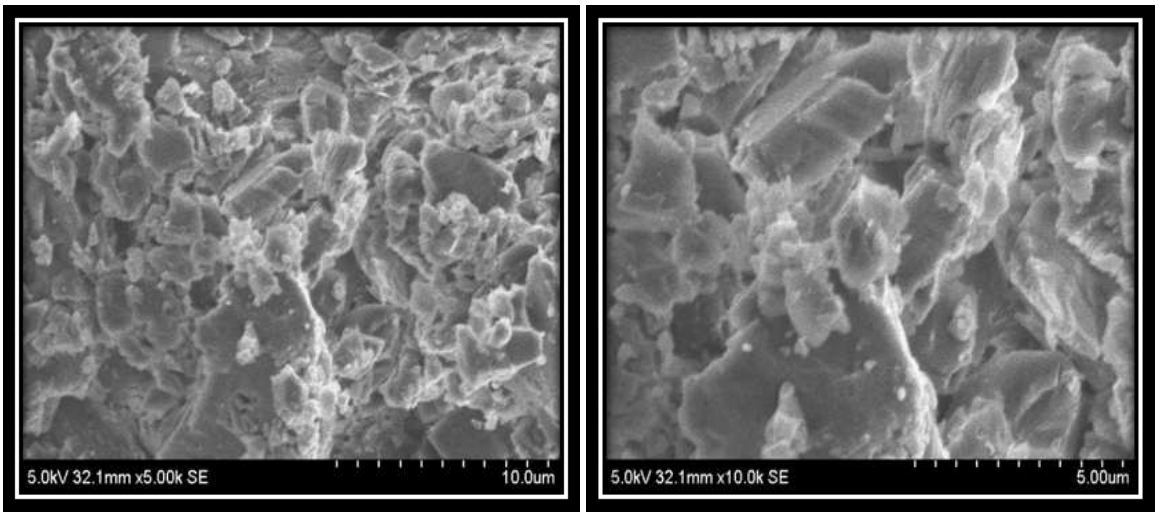

Figure no: 8 SEM Images of Microsponge containing Eudragit RS 100.

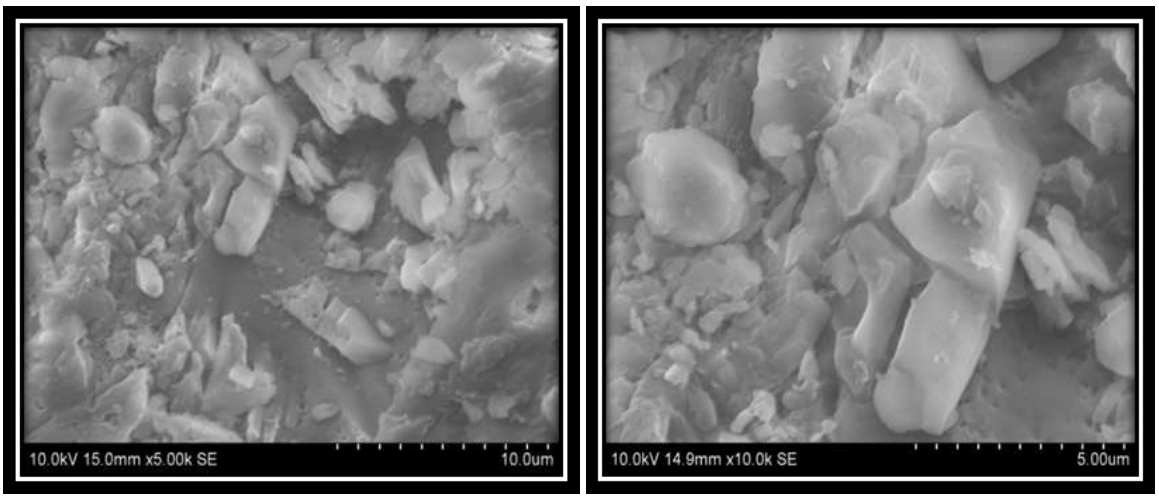

Figure no. 9.SEM Images of Microsponge containing Eudragit RL.

Evaluation of Mefenamic Acid Microspone Emulgel

Table no: 7. General evaluationof microsponge emulgel containing mefenamic acid.

Formulation code	Colour	Homogenity	Grittiness	pH:	Extrudability
MEG1	Clear	Homogenous	No	6.57.±0.10	1.2±0.20
MEG2	Clear	Homogenous	No	6.46±0.17	1.15±0.128
MEG3	Clear	Homogenous	No	6.38±0.11	1.1±0.079

Spreadability of Microsponge Emulgel

Table no: 8. Spreadability microsponge emulgel containing mefenamic acid.

FORMULATION CODE	M(gm)	L(cm)	T(Sec)	spreadability
MEG1	50	6	11	27.22±0.39
MEG2	50	6	13	23.07±0.33
MEG3	50	6	12	25.2±0.91

Viscosity of mefenamic acid microsponge emulgel

Table no: 9. Viscosity of microsponge emulgel containing mefenamic acid.

Formulation Code	Spindle number	Revolution per min (RPM)	Torque (%)	Viscosity (Cp)
MEG1	S63	50	82.5	1642±26.50
MEG2	S63	50	85.6	1379±40.58
MEG3	S63	50	88.2	1581±33.56

Drug content: 1g emulgel in about 100 ml of methanol& diluted to 10ml with methanol Solutions were then filtered and spectrophotometrically analyzed for drug content at 285nm.

Table no: 10. Drug content of microsponge emulgel containing mefenamic acid.

Formulation Code	Drug Content (%)
MEG1	89.59
MEG2	87.34
MEG3	82.05

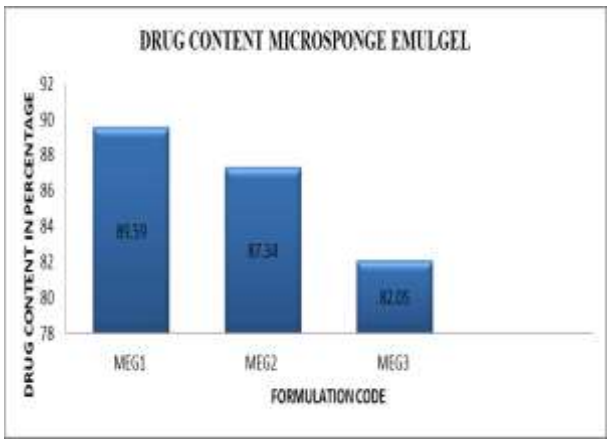

Figure no. 10: Drug content microsponge emulgel containing mefenamic acid.

***In vitro* drug release of mefenamic acid microsponge Emulgel**

- Modified Keshary-Chien apparatus
- The dissolution medium used was phosphate buffer pH7.4
- Analyzed by UV-Visible spectrophotometer at 285 nm and % cumulative drug release was calculated.

Table no: 11. In vitro drug release microsponge emulgel containing mefenamic acid.

Time in hr.	% Cumulative Drug release		
	MEG1	MEG2	MEG3
0	7.65±0.30	8.1±0.49	6.63±0.65
1	9.183±0.85	9.69±0.71	8.67±0.92
2	12.24±1.72	10.71±1.43	11.7±1.23
3	19.89±1.40	18.36±1.09	15.81±1.84
4	31.12±0.96	27.55±1.22	24.84±1.17
5	47.44±0.91	41.32±1.65	40.30±0.77
6	63.32±1.35	61,22±1.74	53.06±1.94
7	78.06±0.98	74.4±1.53	68.36±1.88
8	84.18±1.07	80.61±1.41	77.9±1.39

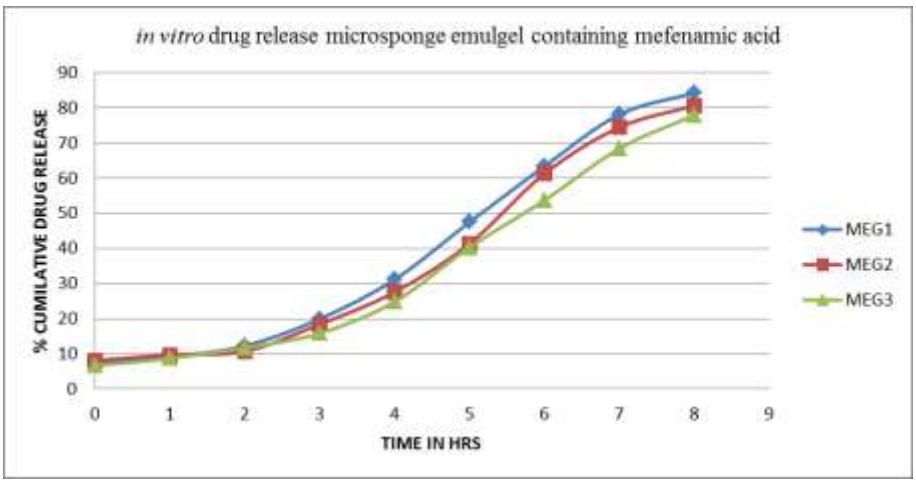

Figure no. 11. *In vitro* drug release microsponge emulgel containing mefenamic acid.

- **Kinetics of drug release** was studied to examine the drug release kinetics and mechanism, the cumulative release data were fitted to models representing zero order, first order, Higuchi's plot and Korsemeyer Peppas model.

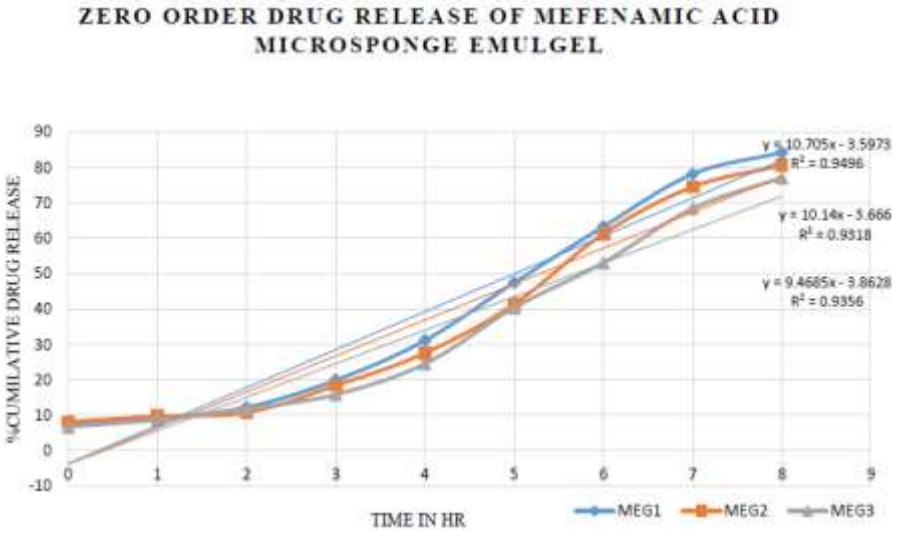

Figure no.12. Zero order drug release microsponge emulgel containing mefenamic acid.

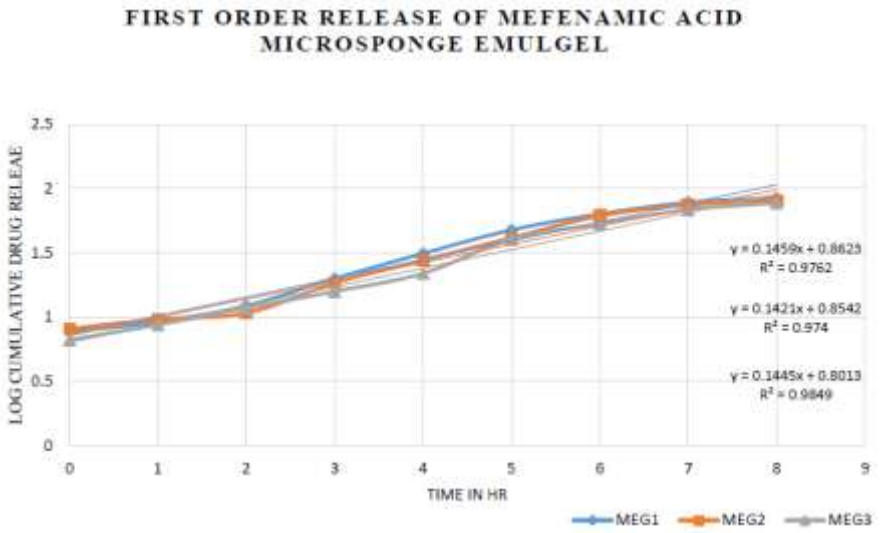

Figure no.13. First order drug release microsponge emulgel containing mefenamic acid.

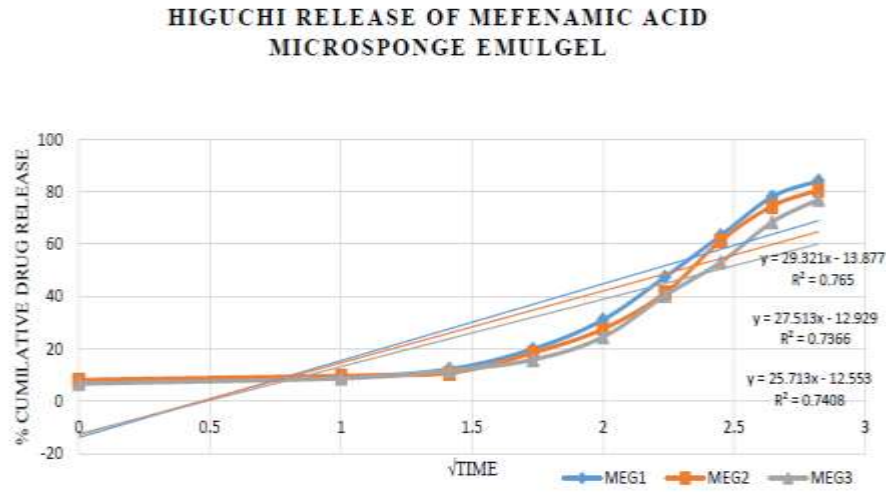

Figure no.14. Higuchi model drug release microsponge emulgel containing mefenamic acid.

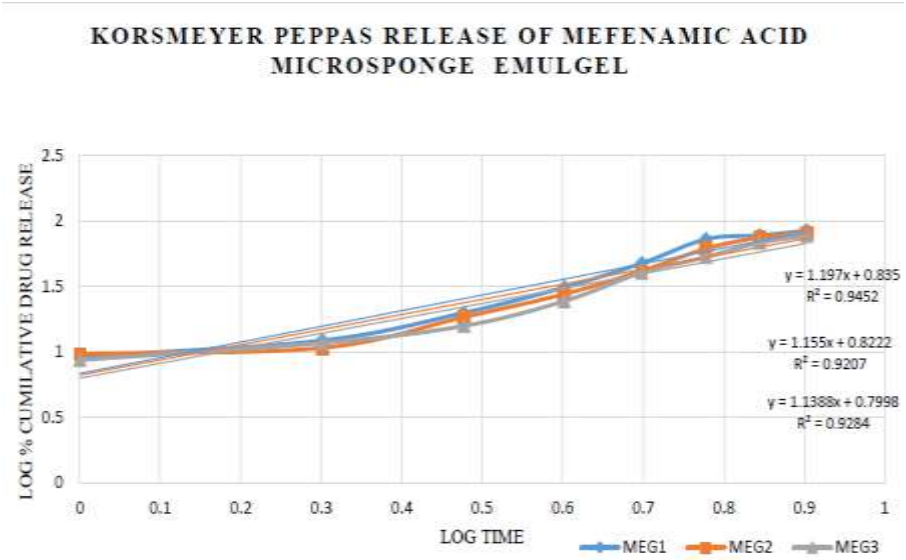

Figure no.15. Kosmeyer peppas drug release microsponge emulgel containing mefenamic acid.

DISCUSSION

Identification of drug & Compatibility studies

Drug identification was done by performing melting point determination and FT-IR studies. From the result the melting point of drug was found to be 230 ^{0}C which complies with official standard indicating the purity of the sample. FT-IR studies peak of mefenamic acid obtained at 3311.92cm^{-1}, 2974.36cm^{-1}, 1648cm^{-1}, 1595.2 cm^{-1},1575.91 cm^{-1}, 1507cm^{-1}, 1257 cm^{-1}, 1163 cm^{-1},756.13 cm $^{-1}$ showed that the peaks are identical to reference indicating the identity of drug. The FT-IRspectrums of pure drug, polymers and physical mixture of drug and polymers. (figure 2,3,4,5) shows that no interaction took place between drug and polymer.However,some additional peaks were observed with physical mixtures, which could be due to the presence of polymers. These results suggest that there is no interaction between the drug and polymers used in the study. Thus indicating that the drug and polymer are compatible with each other.

Effect of Formulation Variables Microsponges

Effect of polymer content on microsponges

It was observed that on the increase of polymer ratio to 0.2-0.6 gm production yield, loading efficiency and particle size increase and drug content decreased on increasing polymer ratio. From this study formulation containing ethyl cellulose (0.6gm) [M3] was found to be good microsponges as shown in table no.4

Effect of volume of Internal Phase on Microsponges

It was observed that on increasing the volume of internal phase 5 to 10 ml microsponge were not formed. This may due to the decrease in the viscosity of internal phase. In this study observed that particle size, production yield and drug content decreased on increasing internal phase. These result suggest that the amount of ethanol need to be controlled within an appropriate range to affect not only the formation of quasi emulsion but also the solidification of drug and polymer in the droplets. The good microsponges were produced as better when 5 ml of ethanol was used as shown in table no. 5.

Effect of Amount of Emulsifying agent on Microsponge

The production yield and mean particle size were greatly affected by the amount emulsifyingagent. The increase in the amount emulsifying agent resulted in larger microsponges. This couldbe due to increased viscosity. The increased amount of emulsifying agent decreased the productionyield, drug content and loading efficiency, with increased and mean particle size also as shown in table no.6.

Surface morphology by scanning electron microscopy

From figure 7, 8 and 9 we can assume that the microsponge formed is spherical in shape and it has a porous surface. This may be due to rapid escape of volatile solvent (ethanol) during the Formulation procedure.

Characterization of Microsponge Emulgel

Physical appearance

The prepared mefenamic acid microsponge emulgel was evaluated visually for their clarity and homogeneity. All the 3 formulations had good clarity and homogeneous with absence of lumps.

pH measurement

pH values of formulation MEG1, MEG2 and MEG3 is 6.57, 6.46 and 6.38 respectively. The values are acceptable where avoids risk of irritation upon application to the skin because skin pH is 5.5.

Viscosity

The rheological behaviour of all formulated Emugels was studied using Brookfield viscometer at a speed of 50 rpm and spindle no.63 was used. And it was found that

all the formulations exhibit plastic flow which is a desirable property for topical gel

Extrudability
Extrudability of all the formulation was determined. It was found that the formulation MEG1 has Excellent extrudability with low viscosity.

Spreadability
Spreadability of various formulated microsponge emulgel was determined and it was found that the microsponge good spreadability to microsponge emulgel MEG1 has spreadability 27.22g.cm/sec. which indicates that it spreads easily by the application of small shear. Values of spreadability were ranges from 23-27 g.cm/sec. It was found that the spreadability increased with decreased viscosity.

Drug content
Drug content of the formulated emulgels was estimated by UV spectrophotometer at λmax 285nm and Drug content was calculated from calibration curve. Drug content of the formulations showed that the drug was uniformly distributed in to gels and the drug content values of the three microsponge Emulgel MEG1, MEG2 and MEG3 is 89.59.18%, 87.34% and 82.05%.

***In vitro* Drug release studies**
In vitro drug release studies of MEG1, MEG2 and MEG3 as microsponge Emulgel. The release profiles obtained mefenamic acid from the drug release profiles the mefenamic acid microsponge emulgel it as found that the formulation containing Ethylcellulose (MEG1) as polymer showed good cumulative % drug release (84.18%).

Drug Release kinetics
The cumulative percentage of drug released when plotted against time, the figure shows the drug Release seems microsponge emulgel drug seem to follow first orderkinetics as it is evidenced by correlation coefficients (r2=0.9846 to 0.974) which is better than zero order(r2 =0.9496 o 0.9318) Higuchi's plot was also found to be linear for all formulations with regression coefficient ranging from 0.9024 to 0.7931. Hence, to confirm the exact mechanism of drug permeation from this microsponge, the data was fitted according to the Korsmeyer- Peppas model. In mefenamic acid microsponge emulgel the n value shows above 1(1.13-1.197) then it shows case II transport.

CONCLUSION
Mefenamic acid is anthranilic acid derivative of NSAID'S; it appears to be first antiphlogistic,analgesic discovered since aminopyrine. Rheumatoid and osteo arthritis are treated by NSAID'S, mefenamic acid is used tablets orally as currently. Oral administration this drug has adverse effects like head ache, dizziness, G I ulcer, nausea, vomiting. Hence formulation novel drug delivery system such as microsponge drug delivery system mefenamic acid will maximize the duration of drug adherence on the skin surface and overcome problem associated with conventional preparation i.e. oral dosage form.

Mefenamic acid loaded microsponges were successfully developed by quasi emulsion technique. microsponge with ethanol 5ml as internal phase and 0.5 g of emulsifying agent shows better microsponge. The developed formulations were in cooperated into emulsion for formation of emulgel emulgel. Mefenamic acid microsponge good to emulgel as their viscosity, spreadability, drug content and *in vitro* release was found better than that of mefenamic acid microsponge gel. Mefenamic acid containing ethyl cellulose produced good gel (MEG1) showed the better result in term of drug content and *in vitro* drug release.

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