

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

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ABSTRACT

The objective of the present investigation was formulate & characterize the microsp sponge 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 microsp sponge 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 gel. The topical gel was evaluated for their organoleptic characters, viscosity, spreadability, drug content and drug release studies. From that MG2 Shows better compared to other formulation. The various release kinetics were studied from that gel have the drug release seems to follow zero order kinetics as it is evidenced by correlation coefficients ($r^2=0.9907$ to 0.9658) which is better than first order ($r^2 = 0.970$ to 0.88) in mefenamic acid microsp sponge gel. Drug permeation from mefenamic acid gel followed Higuchi model or matrix diffusion.

KEYWORDS: Microsp sponge, mefenamic acid, ethyl cellulose, gel, release kinetics.

INTRODUCTION

The microsp sponge drug delivery system was developed by Won in 1987. The microsp sponge delivery system is patented polymeric system consisting of porous microsp sphere. 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. Microsp sphere surrounded by the vehicle acts like microscopic sponges, storing the active ingredient until its release is triggered by skin application. Microsp sponges 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 microsp sponge 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 microsp sponge 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 mostcommon 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 microsp sponge 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 λ max

Dissolve accurately weighed 100mg of mefenamic acid in 100ml of methanol in 100ml standard flask to get 1000 μ g/ml. From the stock solution of mefenamic acid, 1ml is pipette out and diluted to 100ml with methanol to get 10 μ g/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.

Preparation of standard calibration curve of Mefenamic acid

A stock solution equivalent to 1 mg/ml mefenamic acid was prepared by dissolving 50 mg of pure methanol and diluting to 50 ml of calibrated flask with methanol. Different aliquots of 1 mg/ml mefenamic acid solution were accurately measured and transferred into series of 100 ml volumetric flask and volume made up to mark with methanol. Absorbance of the solutions was measured by UV/Visible spectrophotometer at 285 nm and the data were plotted against concentration. A calibration curve was plotted by taking concentration on x axis and absorbance on y axis.

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 UV Spectra.

Drug-Excipient Interaction Studies^[6]: in order to find out the possible interactions between mefenamic acid and the polymers used in the formulation of the microsp sponge, 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 to 4000 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 1: Formulation of microsponge.

Ingredients	M1	M2	M3	M4	M5	M6	M7	M8	M9
Mefenamic 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 Gel^[12,13]

Accurately weighed amount of carbopol 934 P was taken and dissolved in water using propeller. Microsponge formulations containing mefenamic acid was added to the above solution with constant stirring. This final solution was neutralized slowly adding triethanolamine with constant stirring until the gel is formed.

Table 2: Formulation of Microsponge Gel.

Ingredient	Quantity
Microsponge	1% w/w
Carbopol 934P	35g
Triethanolamine	q.s
Sodium Benzoate	50 gm
Distilled Water	10 ml

Evaluation of Mefenamic 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.

$$\text{Percentage yield (\%)} = \frac{\text{Practical weight of microsponge}}{\text{Theoretical yield (polymer + drug)}} \times 100$$

c) Drug loading efficiency

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

A sample of mefenamic 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.

$$\text{Loading efficiency (\%)} = \frac{\text{Actual drug content in microsponge}}{\text{Theoretical drug content}} \times 100$$

d) Drug content

Microsponges containing 100mg 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 microsponges were kept on the sample holder and SEM photograph was recorded using SEM (JEOL-JSM 6390, England) under vacuum at room temperature.

Characterization Of Mefenamic Acid Microsponge Gel^[14,15,16]

Gels were evaluated for their clarity, pH, viscosity, spreadability, extrudability, drug content and *in vitro* diffusion studies by using standard procedure

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

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.

Viscosity measurement

Brookfield digital viscometer was used to measure the viscosity (in cps) of the prepared gel formulations. The spindle number 64 was rotated at 20 rpm for the viscosity measurement.

Spreadability

Spreadability of the formulation was determined by using an apparatus designed and developed in the laboratory especially for the project. 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 20gm 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 50gm 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.

Drug content

Drug content of the gel was determined by dissolving an accurately weighed quantity of 1g gel in about 100 ml of methanol. 1ml 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.

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 gel was accurately weighed, and placed on membrane and attached to this assembly. The donor compartment was suspended in 50 ml of dissolution medium maintained at $37 \pm 1^\circ\text{C}$ 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.

RESULT

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

Table 3: Standard curve of mefenamic acid.

Concentration($\mu\text{g/ml}$)	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

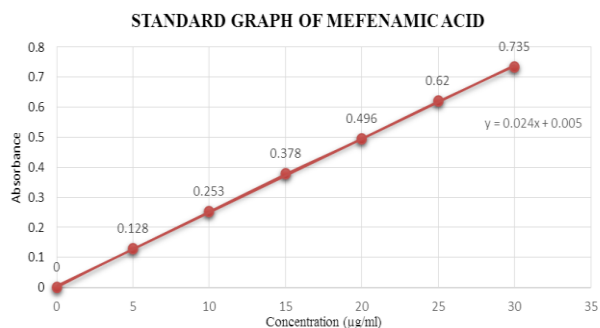


Figure 1: Calibration curve of mefenamic acid.

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 $230-231^\circ\text{C}$.
- **Organoleptic Characters:** physical appearance observed as whitish odorless powder.
- **Partition coefficient:** It determined in n-octanol – phosphate buffer 7.4 pH. was found to be 1.87.
- **Drug excipient interaction studies:** FT-IR studies of pure drug sample, polymers and physical mixtures were measured.

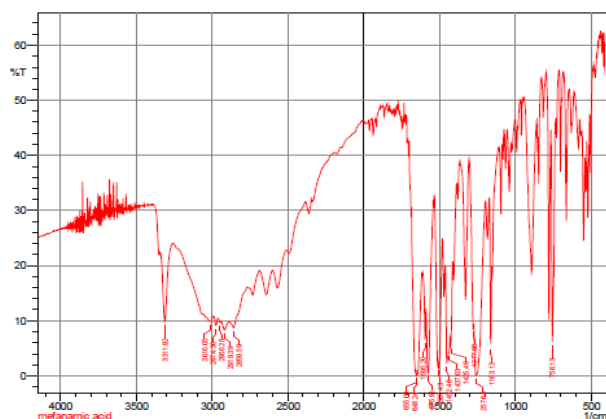


Figure 2: FTIR of mefenamic acid.

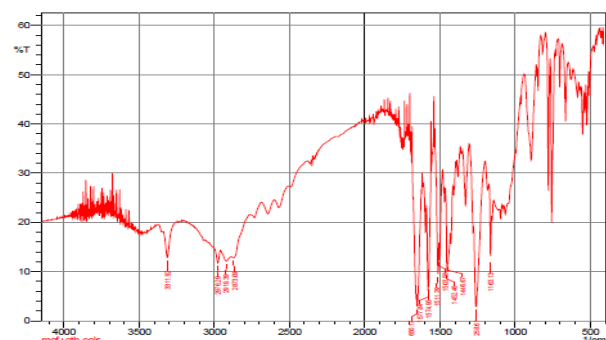


Figure 3: FT IR of mefenamic acid + ethyl cellulose.

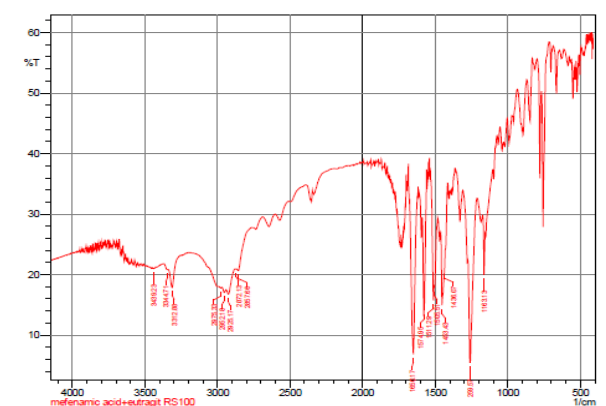


Figure 4: FT IR of mefenamic acid + eudragit RS 100.

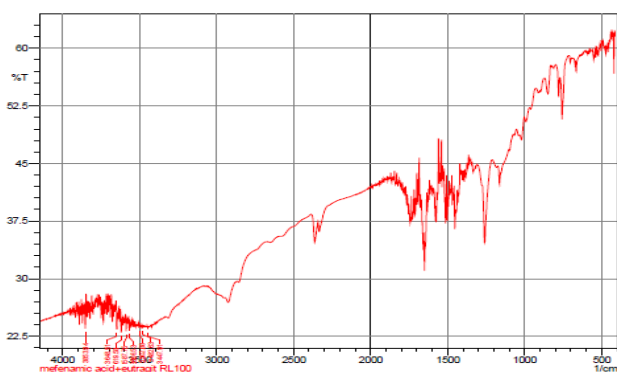


Figure 5: FT IR of mefenamic acid + Eudragit RL100.

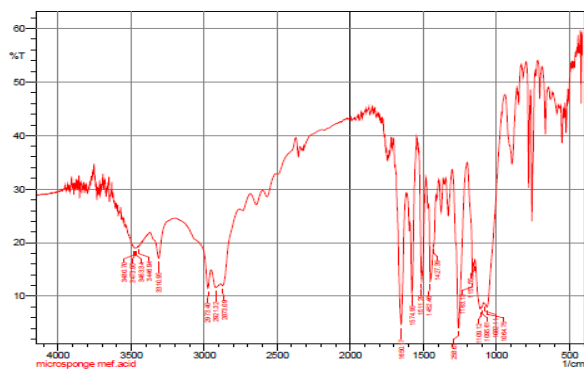


Figure 6: FT IR of mefenamic acid microspunge.

- 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 Microspunge

Nine microspunge 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 Microspunge

Effect of Internal phase Composition on Mefenamic acid Microspunge

Table 4: Effect of internal phase on mefenamic acid microspunge.

INGREDIENTS	M1	M2	M3	M4	M5	M6	M7	M8	M9
Mefenamic 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 particlediameter (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 microspoon**Table 5: Effect on polymer on mefanamic acid microspoon.**

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 microspoon**Table 6: Effect on emulsifying agent on Mefanamic acid microspoon.**

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 mefenamic acid microspoon formulations 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 microspoon 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.

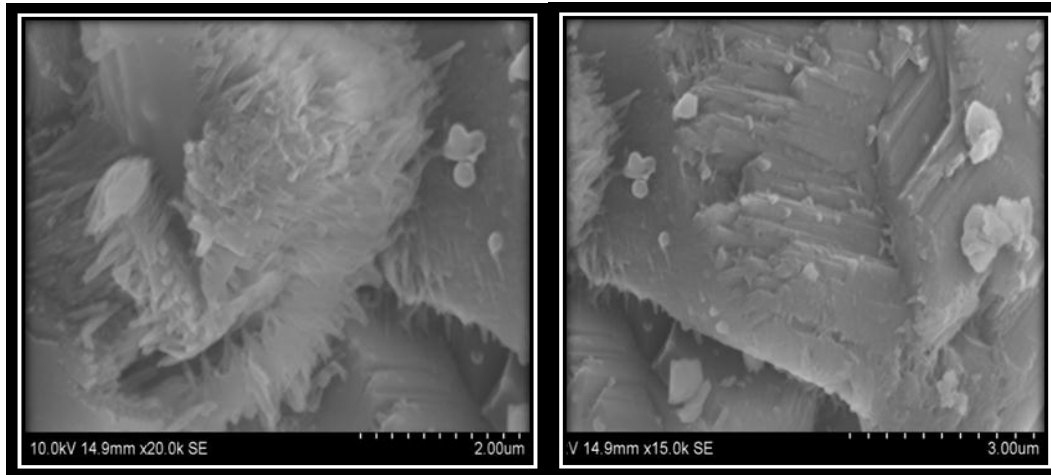


Figure 7: SEM Images of microspunge containing Ethyl cellulose.

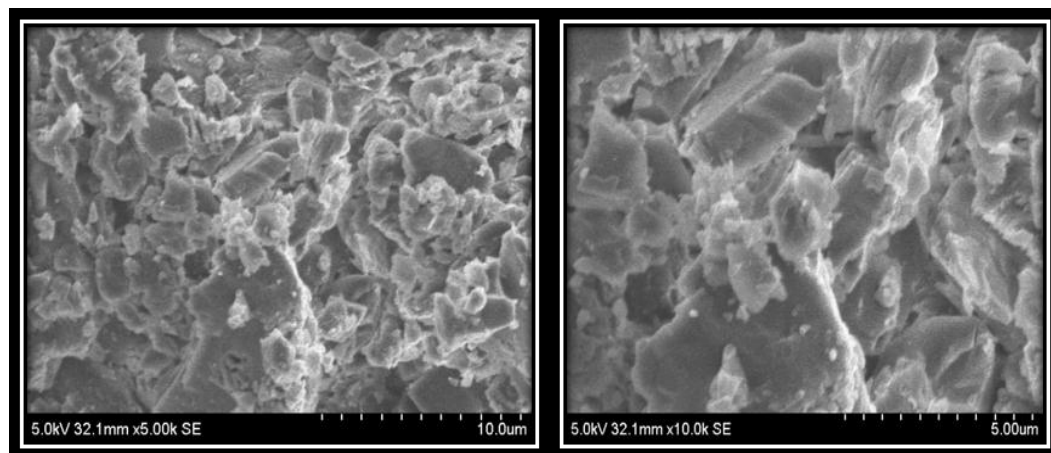


Figure 8: SEM Images of Microspunge containing Eudragit RS 100.

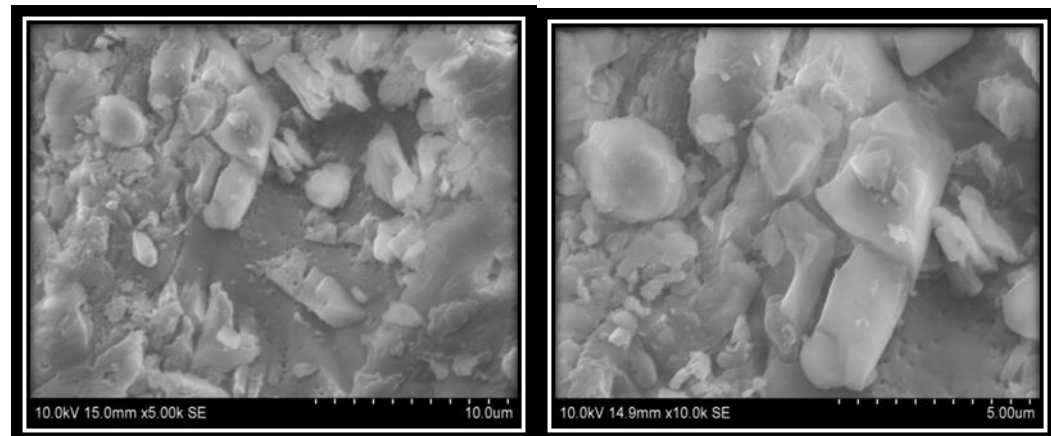


Figure 9: SEM Images of Microspunge containing Eudragit RL 100.

Evaluation of Microspunge Gel

Formulation code	Colour	Homogeneity	Grittiness	pH:	Extrudability
MG1	Clear	Homogenous	No	6.8±0.10	1.1±0.20
MG2	Clear	Homogenous	No	6.5±0.17	1.2±0.128
MG3	Clear	Homogenous	No	6.7±0.11	1.15±0.079

Spreadability of Microsponge Gel

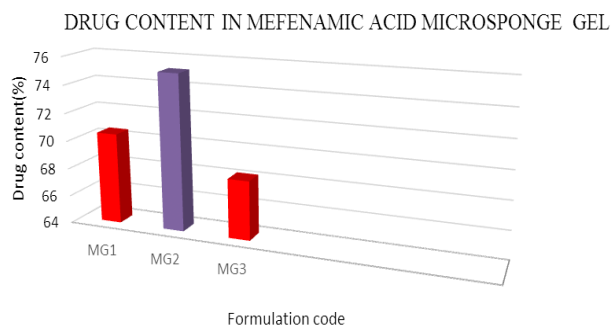
Formulation code	M(gm)	L(cm)	T(Sec)	spreadability
MG1	50	6	22	13.633±0.39
MG2	50	6	23	13.092±0.33
MG3	50	6	20	15±0.91

Viscosity of mefenamic acid microsponge gel

Formulation Code	Spindle number	Revolution per min (RPM)	Torque (%)	Viscosity (Cp)
MG1	S62	20	87.5	1266±22.50
MG2	S62	20	91.2	1342±22.05
MG3	S62	20	89	1150±33.56

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

Formulation Code	Drug Content (%)
MG1	70.5±1.35
MG2	75.16±0.69
MG3	68.20±1.51



In vitro drug release of mefenamic acid microsponge Gel

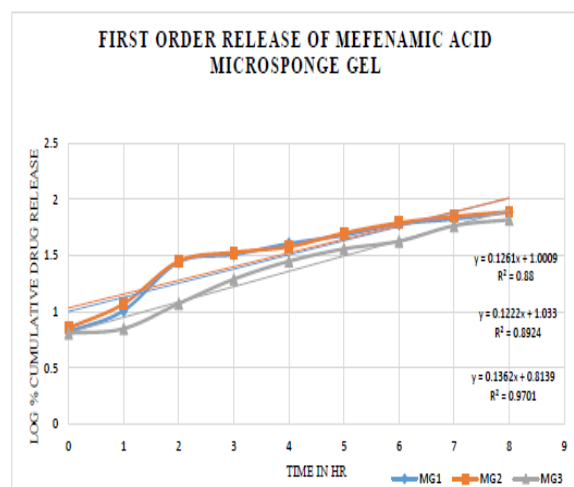
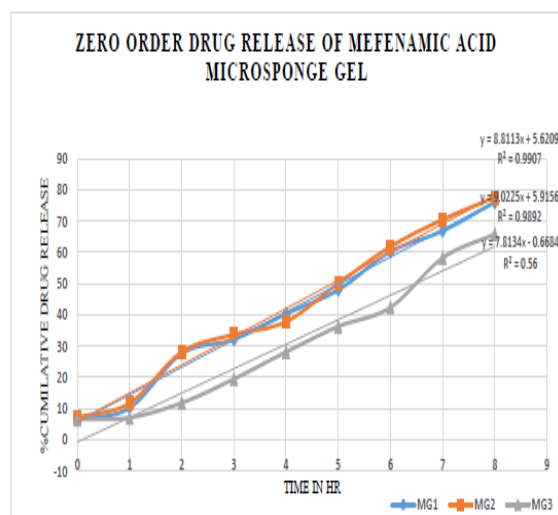
- Modified Keshary-Chien apparatus
- The dissolution medium used was phosphate buffer pH7.4
- Analyzed by UV-Visible spectrophotometer at 285 nm and % cumulative drug release was calculated.

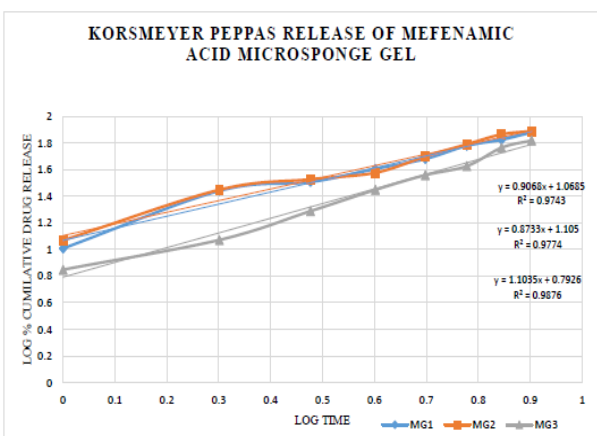
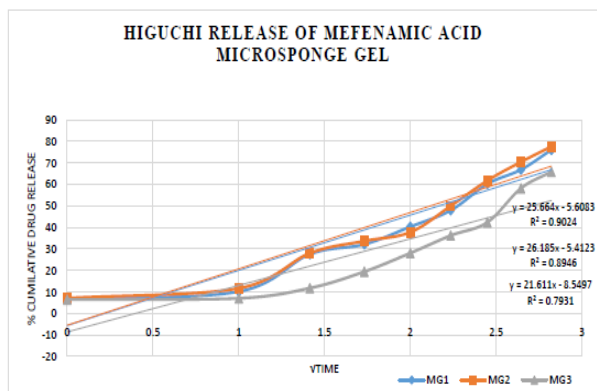
In vitro drug release mefenamic acid microsponge gel

Time in hr.	% Cumulative Drug release		
	MG1	MG2	MG3
0	6.6±0.30	7.142±0.49	6.42±0.65
1	10.20±0.85	11.73±0.71	7.048±0.92
2	27.55±1.72	28.06±1.43	11.78±1.23
3	32.14±1.40	33.67±1.09	19.43±1.84
4	40.30±0.96	37.75±1.22	28.06±1.17
5	47.95±0.91	50±1.65	36.22±0.77
6	60.20±1.35	61.75±1.74	42.34±1.94
7	66.83±0.98	70.40±1.53	58.16±1.88
8	76.02±1.07	77.55±1.41	65.81±1.39

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
- Korsmeyer Peppas model





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 °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-IR spectra 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 be 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 results 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 of emulsifying agent. The increase in the amount of emulsifying agent resulted in larger microsponges. This could be due to increased viscosity. The increased amount of emulsifying agent decreased the production yield, 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 Gel

Physical appearance

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

pH measurement

pH values of formulation MG1, MG2 and MG3 is 6.8, 6.5 and 6.7 respectively. The values are acceptable where it avoids risk of irritation upon application to the skin because skin pH is 5.5.

Viscosity

The rheological behaviour of all formulated gels was studied using Brookfield viscometer at a speed of 20 rpm and spindle no.64 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 formulations was determined. It was found that the formulation MG3 has excellent extrudability with low viscosity.

Spreadability

Spreadability of various formulated microsponge gels was determined and it was found that the microsponge

good spreadability to microspunge gel MG1 has spreadability 15g.cm/sec. which indicates that it spreads easily by the application of small shear. Values of spreadability were ranges from 19-25 g.cm/sec. It was found that the spreadability increased with decreased viscosity.

Drug content

Drug content of the formulated gels was estimated by UV spectrophotometer at λ_{max} 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 microspunge gel MG1, MG2 and MG3 is 70.5%, 75.16% and 68.20

In vitro Drug release studies

In vitro drug release studies of MG1, MG2 and MG3 as microspunge gel. The release profiles obtained mefenamic acid From the drug release profiles the mefenamic acid microspunge gel it as found that the formulation containing eudragit RS 100 (MG2) as polymer showed good cumulative % drug release (75.16%)

Drug Release kinetics

The cumulative percentage of drug released when plotted against time, the figure shows the drug release seems to follow zero order kinetics as it is evidenced by correlation coefficients ($r^2=0.9907$ to 0.9658) which is better than first order ($r^2 = 0.970$ to 0.88) in mefenamic acid microspunge gel. Therefore it was ascertained that the drug permeation from these formulations could follow nearly zero order kinetics. In this study the correlation coefficient (r^2) of Korsmeyer-Peppas model was found to be closer to 1 and slope values (n) was ranging from 0.9068-08733 for MG1 & MG2 ,this suggests that the drug permeation from mefenamic acid gel followed Higuchi model or matrix diffusion

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 microspunge 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. microspunge with ethanol 5ml as internal phase and 0.5 g of emulsifying agent shows better microspunge. The developed formulations were in cooperated into gel. Mefenamic acid microspunge good to gel as their

viscosity, spreadability, drug content and *in vitro* release was found better than that of mefenamic acid microspunge gel. Mefenamic acid containing eudragit RS100 produced good gel (MG2) showed the better result in term of drug content and *in vitro* drug release.

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