IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

A STUDY ON DEVELOPMENT OF MATRIX MODERATED TRANSDERMAL DRUG DELIVERY SYSTEM OF MONTELUKAST SODIUM USING DIFFERENT DRUG-POLYMER COMPATIBILITY STUDIES USING FT-IR

DEVARAKONDA ANUSHA[1], D. MOUNIKA[2], D.THANUYA[2], J.SRIVALLIKA[2], P.NAZEER BASHA[2], T.SRAVANI[2]

1. **Associate Professor, Department of Pharmaceutics, Vishwa Bharathi College of Pharmaceutical Sciences, Perecherla, Guntur, A.P, Pin code: 522009**
2. **Department of Pharmaceutics, Vishwa Bharathi College of Pharmaceutical Sciences, Perecherla, Guntur, A.P, Pin code:522009**

ABSTRACT:

The montelukast is a leukotrine receptor antagonist (LTRA) used for the maintenance treatment of asthma, chronic asthma attacks and to relieve symptoms of seasonal allergies. Because of poor bioavailability of montelukast sodium by oral route, there is a need to increase its bioavailability by formulating it into buccal dosage forms.The results of swelling index between the range of 30.03 - 44.27 %, and the surface pH was in the range pH of buccal region. The results of drug content were in the prescribed range. The in vitro residence time for all the patches is in between 3.20 - 5.59 hrs. The Bursting strength of patches is in the range of 4.166 to 5.733 Kg/cm 2. In vitro release studies were conducted for montelukast loaded patches exhibited drug release in the range of 68.83 - 92.22 % in 8 hrs. FT-IR studies revealed that, there was no interaction between drug and excipients used. Release of montelukast from all patches followed zero order and mechanism was diffusion rate limited. Finally it can be concluded that F3 and F6 are the best formulation.

INTRODUCTION:

Transdermal drug delivery systems

Transdermal drug delivery systems (TDDS), also known as patches, are dosage forms designed to deliver a therapeutically effective amount of drug across a patient's skin. In order to deliver therapeutic agents through the human skin for systemic effects, the comprehensive morphological, biophysical and physicochemical properties of the skin are to be considered. Transdermal delivery provides a leading edge over injectables and oral routes by increasing patient compliance and avoiding first pass metabolism espectively. Transdermal delivery not only provides controlled, constant administration of the drug, but also allows continuous input of drugs with short biological half-lives and eliminates

pulsed entry into systemic circulation, which often causes undesirable side effects. Thus various forms of Novel drug delivery system such as Transdermal drug delivery systems, Controlled release systems, Transmucosal delivery systems etc. emerged. Several important advantages of transdermal drug delivery are limitation of hepatic first pass metabolism, enhancement of therapeutic efficiency and maintenance of steady plasma level of the drug. The first Transdermal system, Transderm-SCOP was approved by FDA in 1979 for the prevention of nausea and vomiting associated with ravel, particularly by sea. The evidence of percutaneous drug absorption may be found through measurable blood levels of the drug, detectable excretion of the drug and its metabolites in the urine and through the clinical response of the patient to the administered drug therapy. The common ingredients which are used for the preparation of TDDS are as follows.

MATERIALS AND METHODS:

Calibration curve of Montelukast Sodium in 7.4 pH Phosphate Buffer saline

Preparation of phosphate buffer saline pH 7.4 (PBS)

Disodium hydrogen phosphate 2.38 grams, 0.19 grams of potassium dihydrogen ortho phosphate, eight grams of sodium chloride was weighed accurately and transferred to 1000 mL volumetric flask and sufficient quantity of distilled water was added to produce 1000 mL and mixed it well.

Determination of λ_{max} of montelukast sodium

Standard stock solution of montelukast sodium (1000 µg/mL) was prepared by taking 25 mg of montelukast sodium in 25 mL of PBS pH 7.4 (phosphate buffer saline). One mL of stock solution was transferred into a clean and dry 10 mL standard volumetric flask and the volume was made up to the mark with the buffer, from this one mL was taken and diluted to 10mL. The resulting solution (10µg/mL) was scanned in the wavelength region of 200 – 400 nm. Maximum absorbance was seen at the wavelength of 285 nm and hence all the absorbance measurements for montelukast sodium and its formulations were carried out at this wavelength.

Preparation of Standard stock solution

Montelukast sodium, 25mg was accurately weighed and transferred into a 25mL of volumetric flask and made up with the buffer i.e phosphate buffer saline pH 7.4 to get 1mg/mL (1000µg/mL).Standard stock solution, 10mL was transferred into 100mL volumetric flask and made up to mark with the buffer to get 100 µg/mL solution which is a secondary stock solution. The absorbance of the above diluted solutions was measured at 285nm using UV spectophotometer (Elico, model SL-210) against the respective blanks. The results are tabulated in the Table 11.

A Calibration curve was constructed by plotting the absorbance against the concentration of Montelukast Sodium. The linear equation was calculated from the plot, which was used for the estimation of Montelukast Sodium in the respective media.

Drug-excipient compatibility studies by FT-IR[34]

There is always a possibility of drug-polymer interaction in the formulation due to their intimate contact. The technique employed in the present work is to study the drug-polymer interaction is Fourier Transform Infrared (FT-IR) spectroscopy.The FT-IR studied were carried out for drug (Montelukast Na), the combination of Montelukast Na and ethyl cellulose, Montelukast Na and Polyvinyl alcohol to evaluate drug polymer interaction.

Results and Discussion

Results

Table 11: Concentration vs. absorbance values of montelukast Na

S. No	Concentration (µg/ml)	Absorbances
1	5	0.0886 ± 0.0511
2	10	0.1711 ± 0.0988
3	15	0.2619 ± 0.1512
4	20	0.3614 ± 0.2086
5	25	0.4553 ± 0.2628
6	30	0.5667 ± 0.3272
7	35	0.6514 ± 0.3760
8	40	0.7429 ± 0.4289

Each value represents the Mean ± s.d. (n=3)

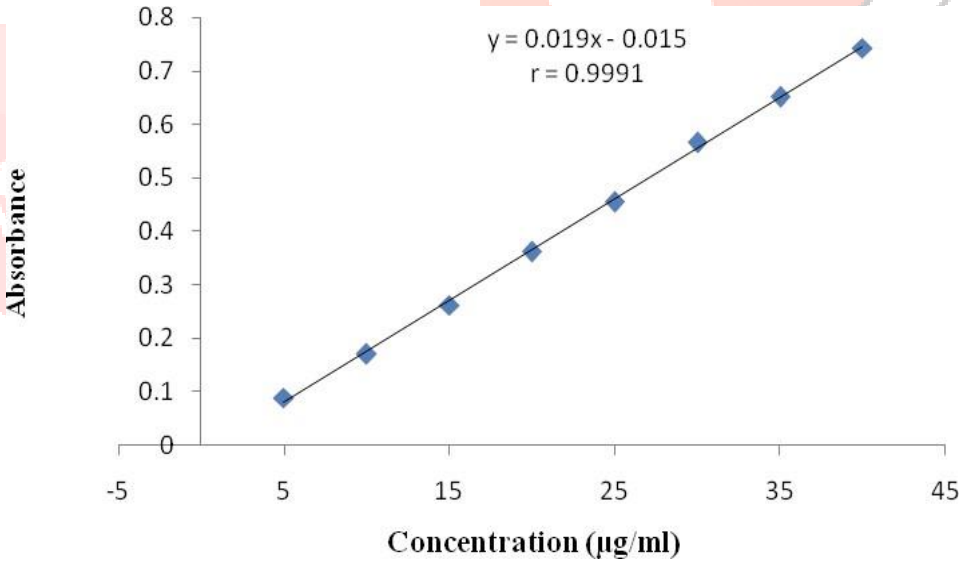


Figure 13: Calibration curve of Montelukast Sodium in 7.4pH PBS Buffer

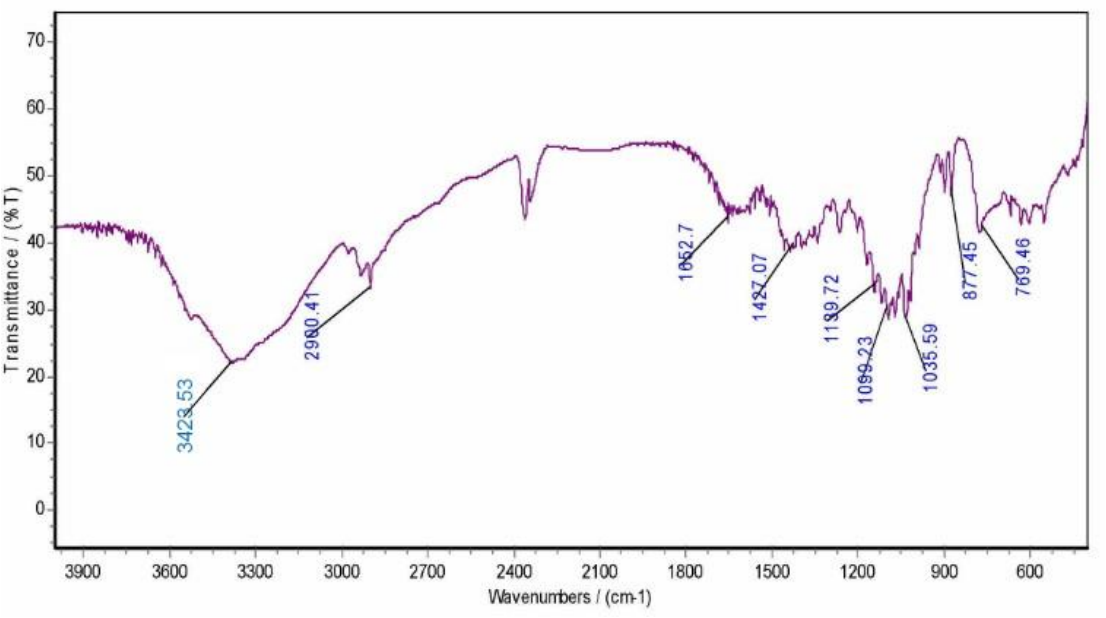


Figure 14: FT-IR of Montelukast sodium

Table 12: Interpretation of IR spectra of montelukast sodium

Wave number (cm^{-1})	Interpretation
3423.53	O-H stretching
2900.41	C-H stretching
1652.70	C=O stretching
1139.72	C-N stretching
1099.23	C-O stretching

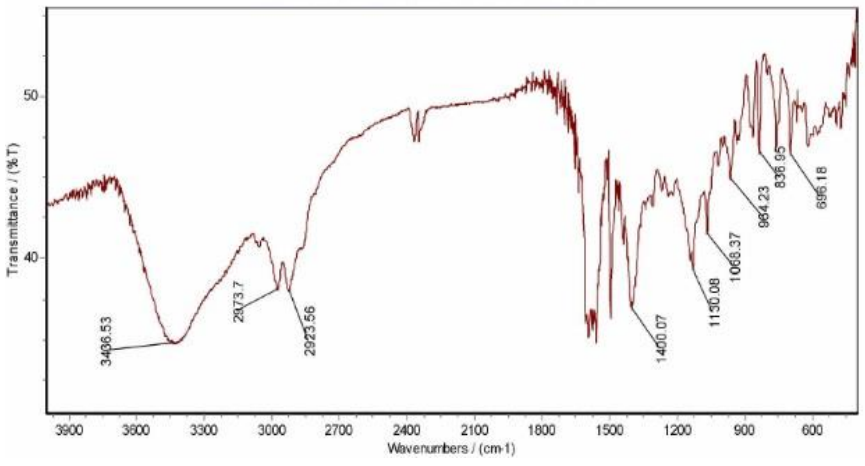


Figure 15: FT-IR spectra of combination of Montelukast sodium and ethylcellulose

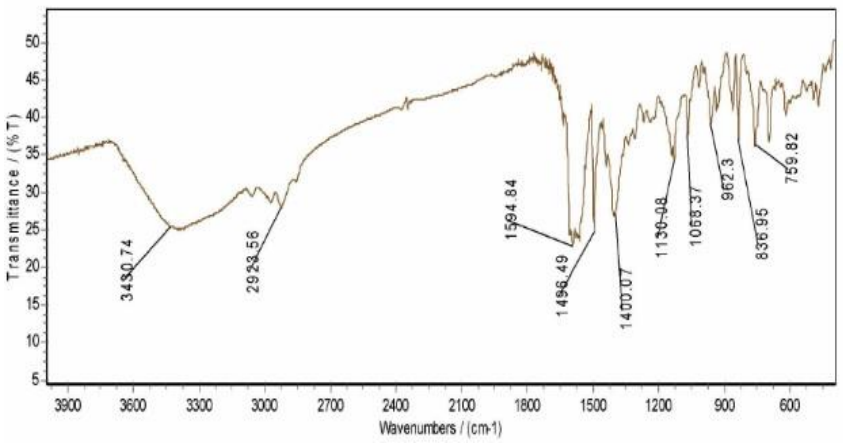


Figure 16: FT-IR spectra of combination of Montelukast sodium and Polyvinyl alcohol

Table 13: Interpretation of FT-IR spectras of Drug (MS) with polymers

Group	Drug (cm^{-1})	Drug + EC (cm^{-1})	Drug + PVA (cm^{-1})
O-H stretching	3423.53	3436.53	3430.73
C-H stretching	2900.41	2923.56	2923.56
C=O stretching	1652.70	1646.32	1618.80
C-N stretching	1139.72	1130.08	1130.08
C-O stretching	1099.23	1068.37	1068.37

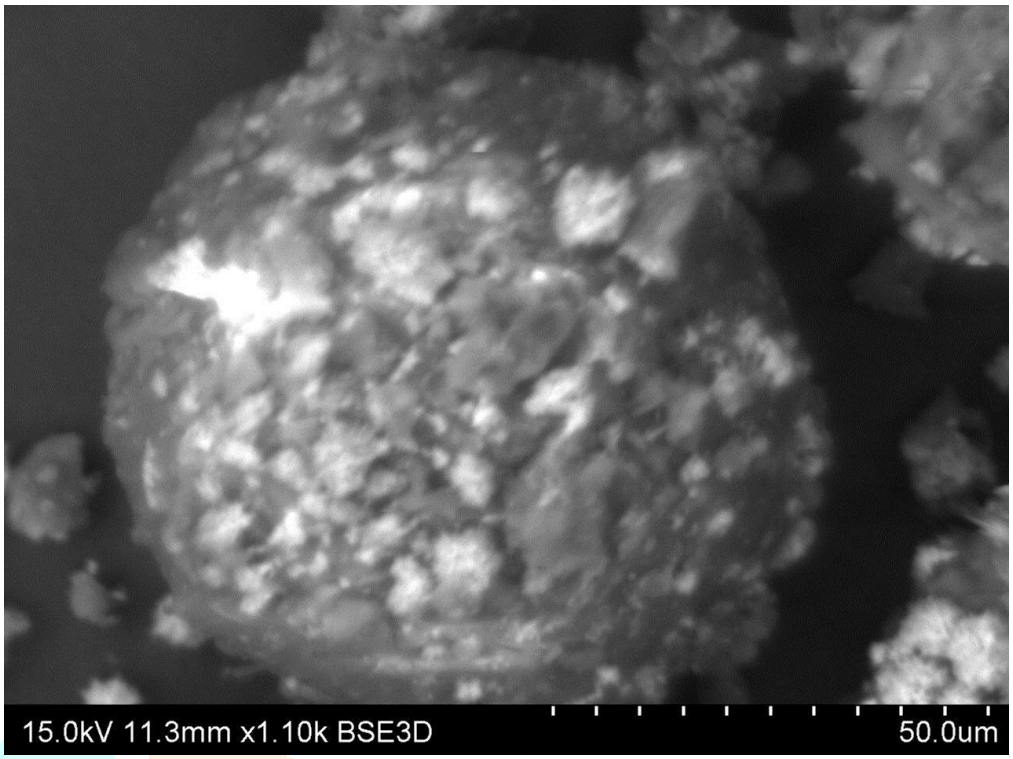
EC, Ethyl cellulose; PVA, Polyvinylacohol;

Table 14: Particle size and polydispersity index (PDI) values of prepared microsponges

Formulation	Component ratio (MS:EC:PVA)	PDI	Size (µm)
M1	1:1:1	0.508	18.4 ± 1.20
M2	1:2:1	0.527	39.4 ± 2.60
M3	1:1:2	0.482	30.1 ± 2.70
M4	1:2:2	0.449	47.8 ± 1.18
M5	1:3:2	0.404	55.9 ± 2.15
M6	1:2:3	0.326	50.7 ± 1.76
M7	1:3:3	0.478	83.4 ± 3.80

Size values represents the Mean ± s.d. (n=3)

a)



b)

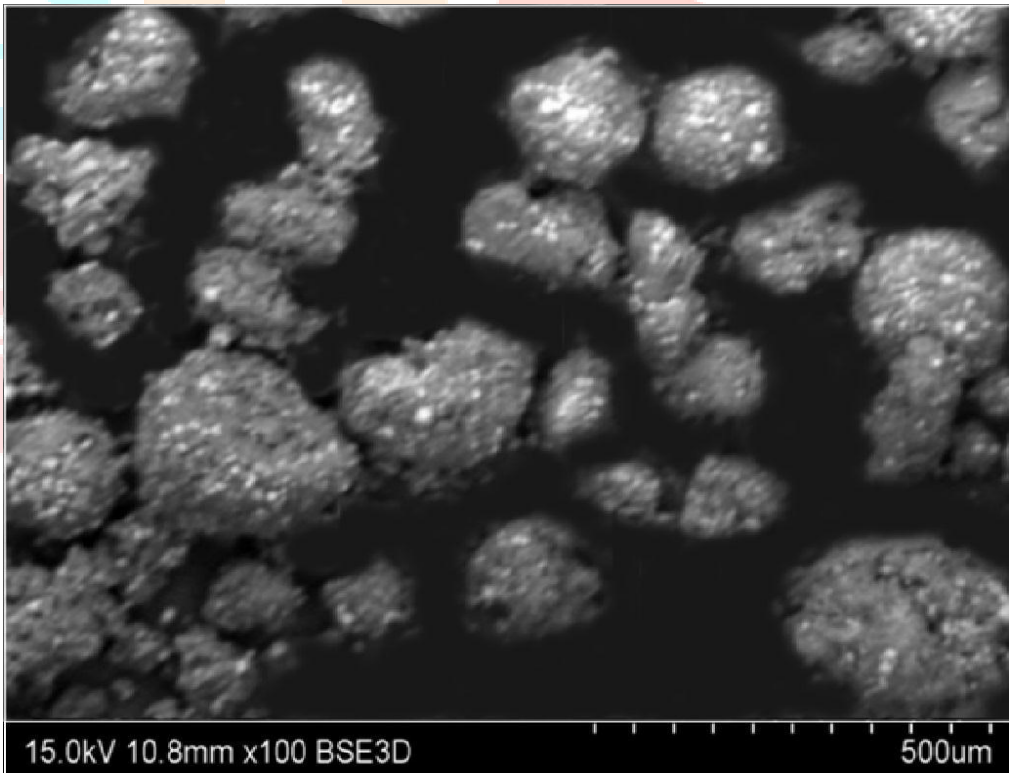


Figure 17: Scanning electron micrographs of montelukast sodium microsponges

Surface view b) full view

Table 15: Fundamental rheological properties of montelukast sodium microsponges

Formulation code	Angle of Repose	Flow property
M1	46.58	very poor
M2	38.65	passable
M3	40.83	poor
M4	33.74	fair
M5	27.92	excellent
M6	29.68	excellent
M7	22.36	excellent

Table 16: Derived rheological properties of montelukast sodium microsponges

Formulation code	Bulk density	Tapped density	Hausner's ratio	Flow property	Carr's index	Flow property
M1	0.42 ± 0.04	0.62 ±0.02	1.476	very poor	32.25	very poor
M2	0.67 ± 0.03	0.86 ± 0.03	1.283	passable	22.09	passable
M3	0.6 ± 0.02	0.78 ± 0.03	1.317	passable	27.85	poor
M4	0.56 ± 0.03	0.68 ± 0.01	1.214	fair	17.64	fair
M5	0.46 ± 0.02	0.5 ± 0.04	1.086	excellent	8	excellent
M6	0.47 ± 0.01	0.52 ± 0.01	1.106	excellent	9.61	excellent
M7	0.77 ± 0.02	0.8 ± 0.01	1.038	excellent	3.75	excellent

Each bulk and tapered density value represents the Mean ± s.d. (n=3)

Table 17: Entrapment efficiencies of montelukast sodium microsponges

Formulation Code	Entrapment Efficiency (%)
M1	68.5 ± 0.59
M2	76.8 ± 0.40
M3	72.9 ± 0.50
M4	84.7 ± 0.75
M5	90.3 ± 0.36
M6	90.1 ± 0.12
M7	94.28 ± 0.26

Each value represents the Mean ± s.d. (n=3)

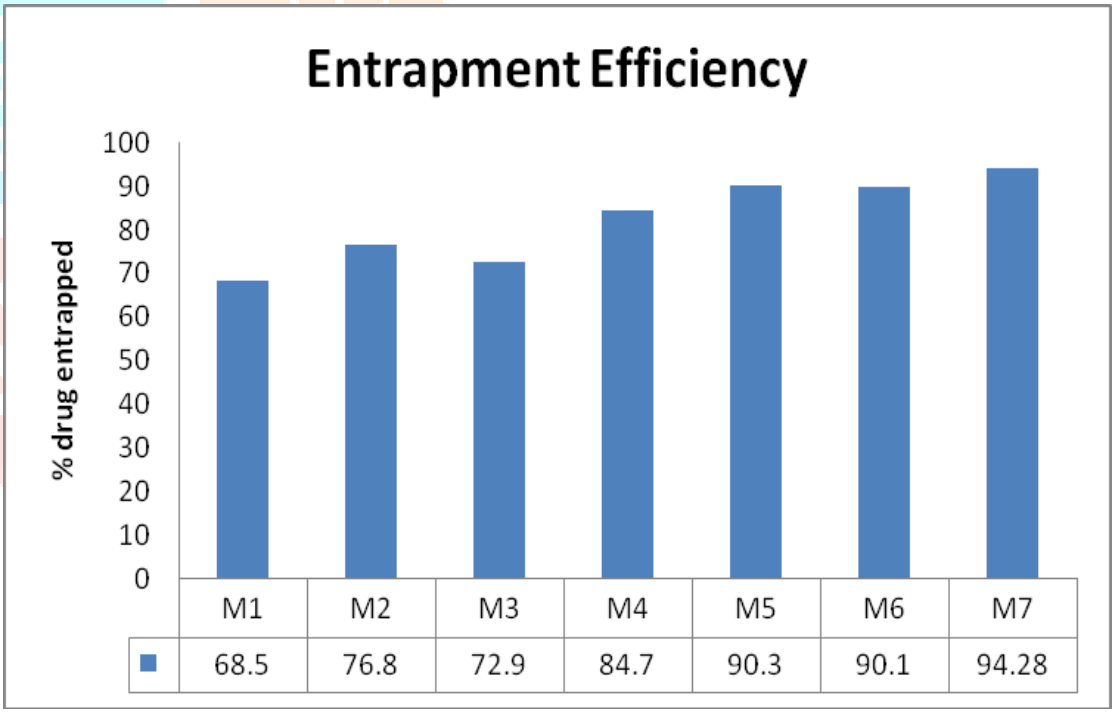


Figure 18: Entrapment efficiency of formulations M1 to

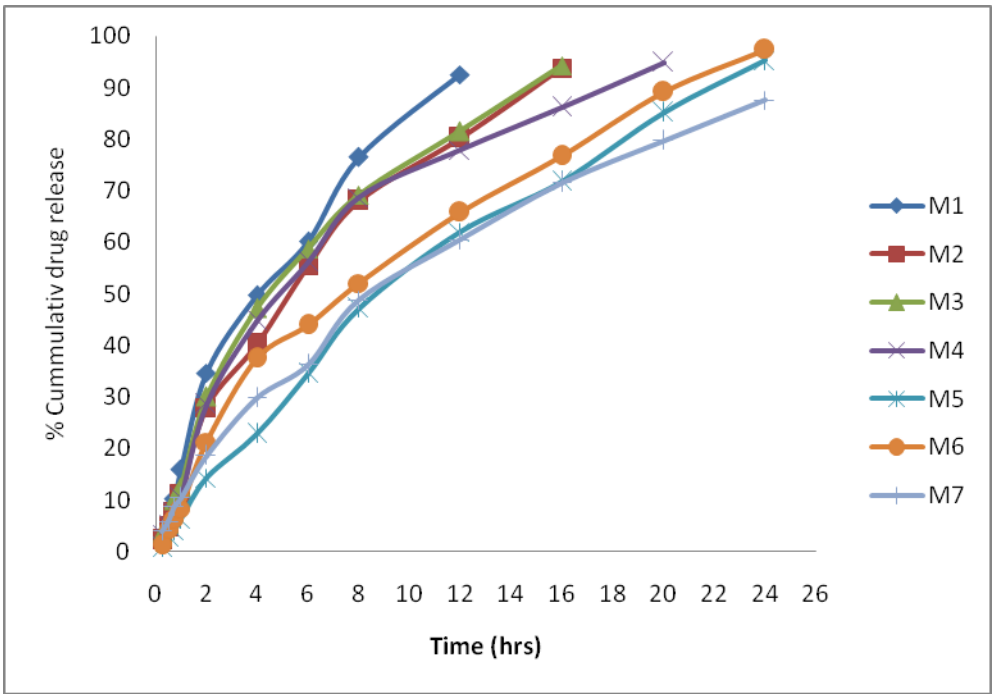
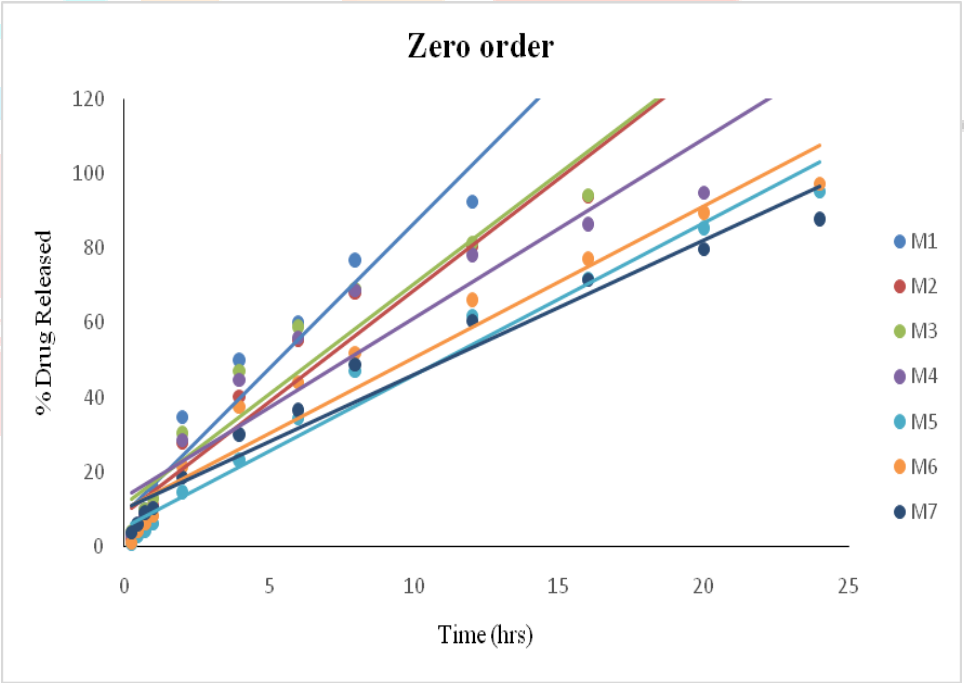
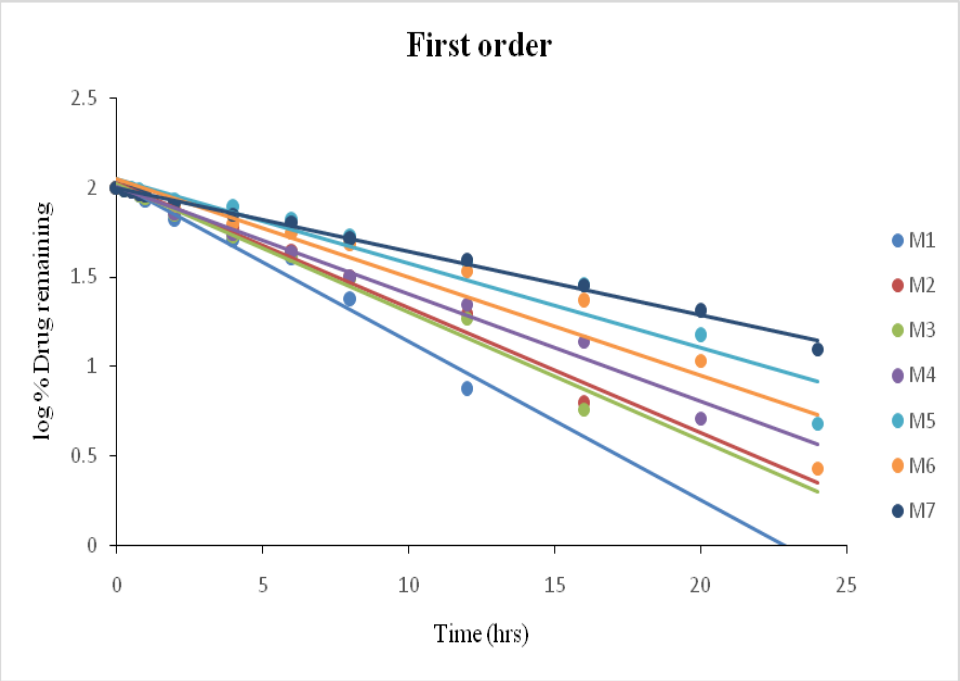


Figure 19: Diffusion profile of Montelukast microsponge formulations

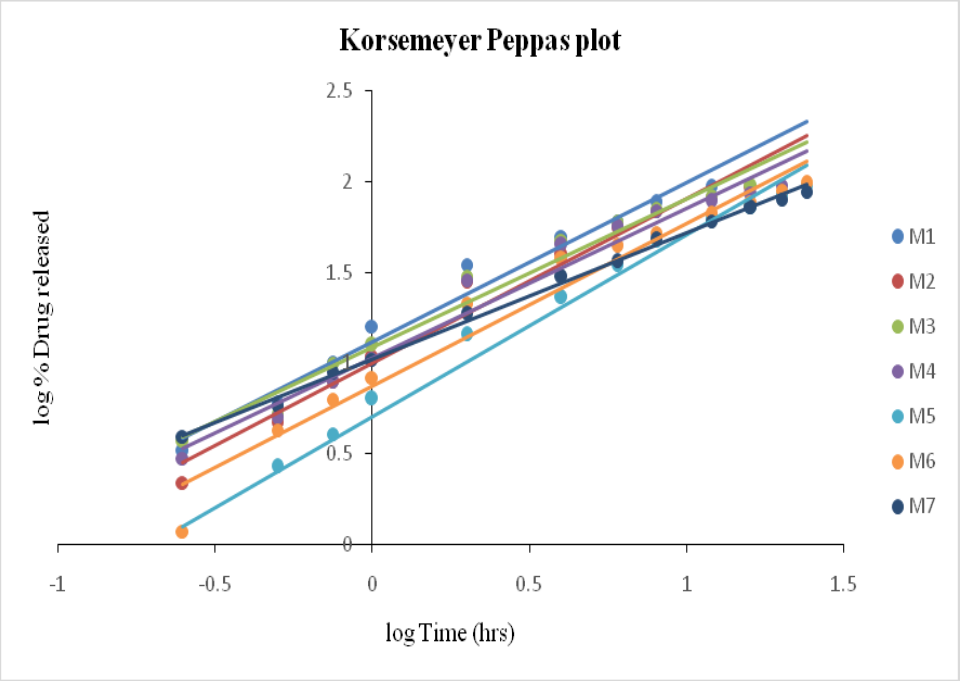
a)



b)


First order
log % Drug remaining
Time (hrs)
M1
M2
M3
M4
M5
M6
M7

c)


Korsemeyer Peppas plot
log % Drug released
log Time (hrs)
M1
M2
M3
M4
M5
M6
M7

d)

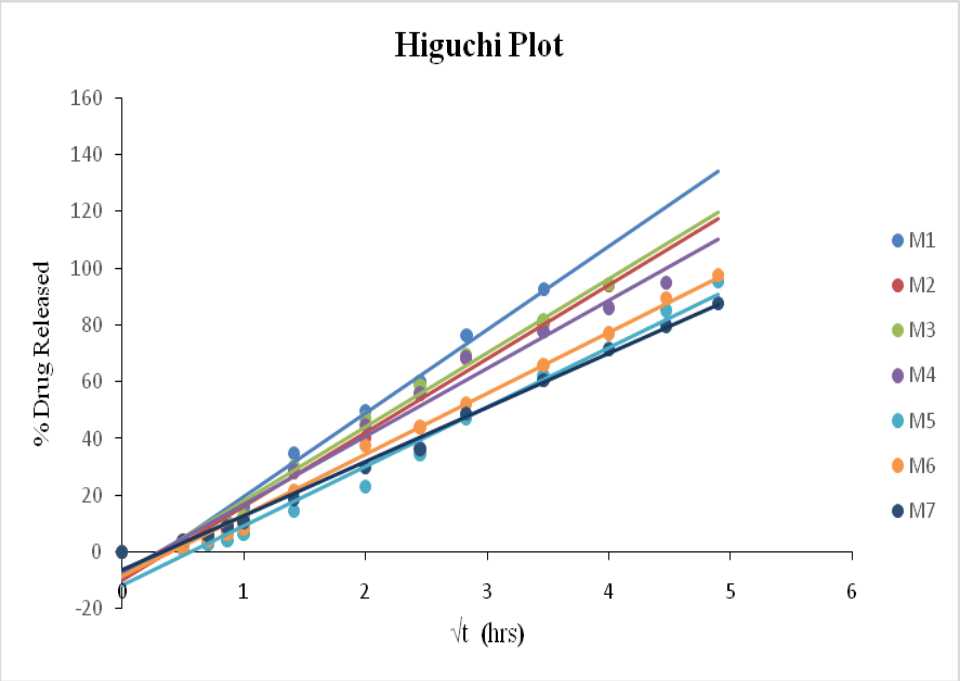


Figure 20: Linear Correlation plots of Kinetic models of montelukast Na microsponges

a) zero order b) first order c) Peppas d) Higuchi

Table 21: Physico chemical parameters of montleukast microsponge incorporated hydrogels

Formulation code	pH	% Drug Content
H1	6.54	91.86± 0.49
H2	5.47	93.91 ± 0.36
H3	4.82	90.62 ± 0.92
H4	5.51	94.36 ± 0.76

Each value represents the Mean ± s.d. (n=3)

Table 22: cumulative percentage of drug permeation values of montelukast sodium microspongesincorporated hydrogels

Time (hrs)	Cumulative percentage of drug permeated			
	H1	H2	H3	H4
0.25	0.52	1.86	1.94	2.16
0.5	1.53	3.78	2.92	3.81
0.75	3.96	5.69	8.07	8.97
1	5.38	7.11	12.49	12.55
2	18.23	20.6	28.72	29.68
4	29.65	34.83	37.69	38.46
6	38.75	40.61	50.38	52.79
8	44.73	49.83	61.42	64.98
12	50.5	60.77	70.08	73.81
16	61.8	71.47	81.96	84.76
20	70.2	84.9	89.42	90.22
24	86.65	93.71	94.74	96.82

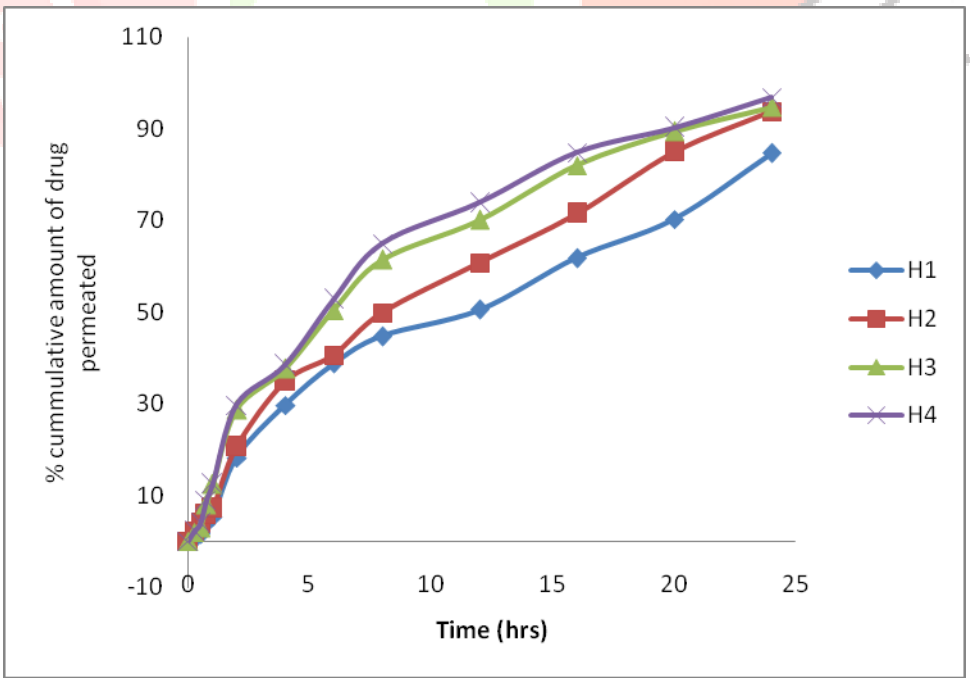
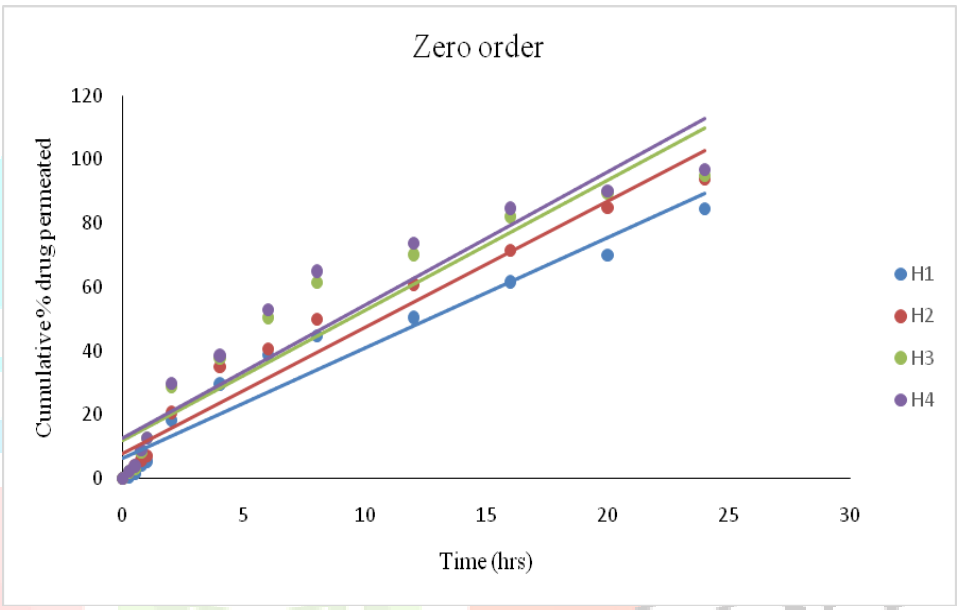


Figure 21: Time vs percent cumulative drug permeated from montelukast microspongeincorporated hydrogels

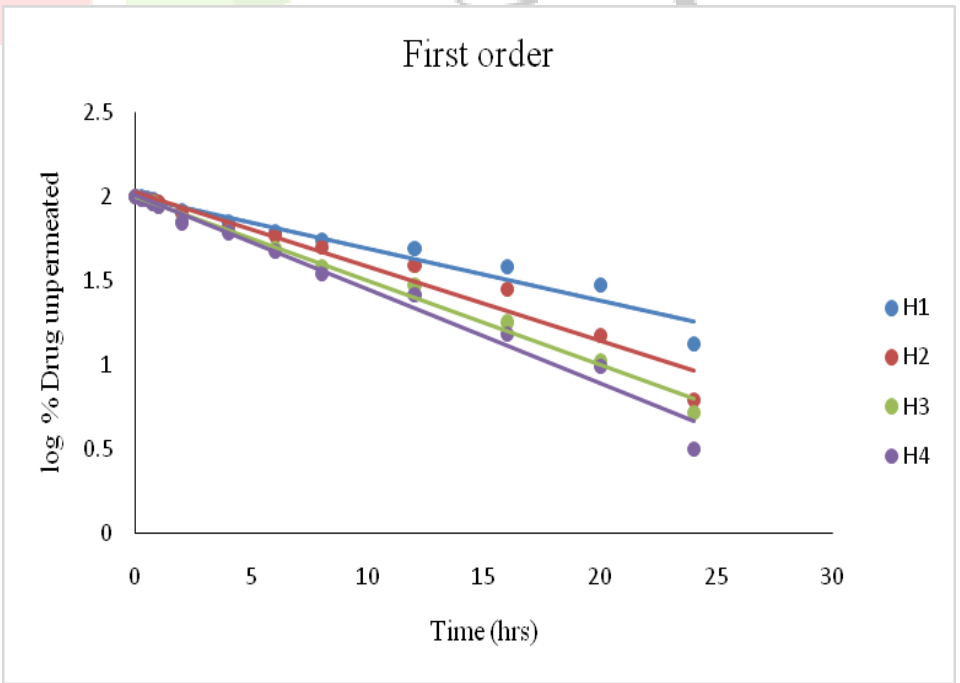
Table23: Maximum Flux values shown by Microsponge incorporated hydrogel.

Formulation	Flux (µg/cm^2/hr)
H1	577.02
H2	700.36
H3	968.60
H4	1226.25

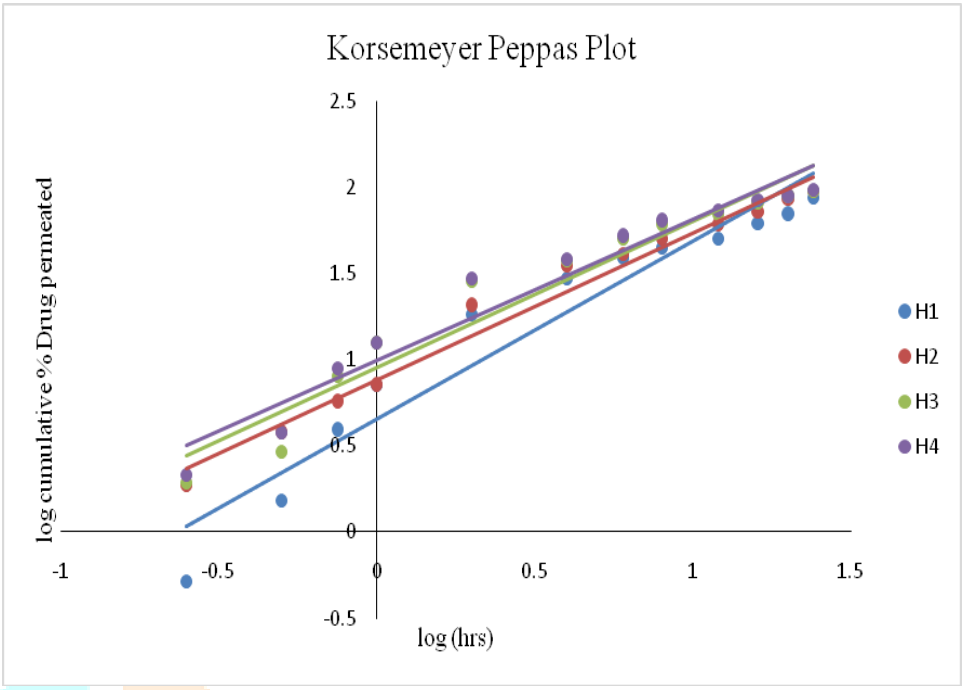
a)



b)



c)



d)

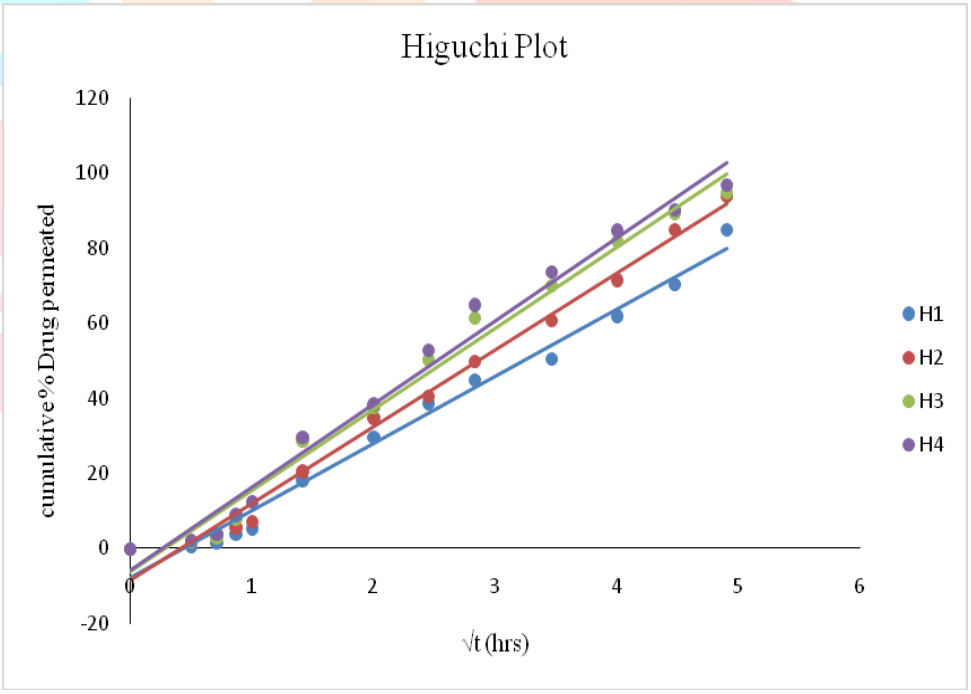


Figure 22: Linear Correlation plots of Kinetic models of montelukast Na microsponges basedhydrogels

a) zero order b) first order c) Peppas d) Higuchi

CONCLUSION

The present work focused on the development of montelukast sodium loaded microsponge based hydrogels which serve as vehicles for sustaining the drug release for transdermal drug delivery system. As the drug has low bioavailability (because of first pass metabolism) and half-life, the transdermal drug delivery systems helps in surpassing the first pass metabolism and problems with montelukast sodium (slight numbness on oral administration) and we can also decrease the dose and dosing frequency, as we prepare a sustain relaease formulation.

To check the interactions between the drugs and various components of formulation, FT-IR studies were performed. Confirming the compatibility, the studies were continued with those excipients. The montelukast loaded microsponges were formulated and evaluated. The microsponges were evaluated for PDI, particle size, rheological properties, Entrapment Efficiency and *in vitro* release studies. Among all the formulations based on the above parameters formulation M6 was selected. Finally, the optimized formulation was incorporated into the hydrogel.

The montelukast sodium loaded microsponge based hydrogels were evaluated for drug content, visual inspection, pH, and permeation studies. Based on these parameters the best formulation was selected which sustained the drug release for 24hrsthat served the criteria.

Thus by this work, we could conclude that microsponge based hydrogels can be used for increasing the bioavailability and as effective means for sustaining the release of drug. The studies revealed that the microsponge based hydrogels can be used as a potential carrier for topical drug delivery for montelukast sodium.

REFERENCES

1. Bellantone N.H., Rim S., Rasadi B., Enhanced percutaneous absorption via Iontophoresis I. Evaluation of an in-vitro system & transport of model compound., Int. J. Pharm., 30, 1986, 63-72.
2. Gros L., Clark W.E. “The structure of skin” in “ The tissue of the body” Le Gros & Clark W. E.(editors) edition VI, ELBS and Oxford University Press, London, 1980; 29-313.
3. Chien Y.W. ”Systemic delivery of pharmacologically active molecules across skin” in “Targeted drug delivery” Radolph L., Juliano(Editor) Springer- Verlag, Berlin, 1991; 182-230.
4. Charro B.D., Guy R.H. “Transdermal drug delivery” in “Drug delivery & targeting” Hillery A. M., Lloyd A.W., Swarbrilk J. edition I., Published by Taylor & Francis. NY, US, 2001; 216-217.
5. Jain Amit K, A systematic review on transdermal drug delivery system, International Journal of Pharmaceutical Studies and Research, January-March, 2011; II(I): 122-132
6. Selvamuthukumar S,. Nanosponges: A Novel Class of Drug Delivery System- Review. J Pharm Pharmaceut Sci. 2012; 15(1): 103-111.
7. Kamla Pathak, Evaluation of Kinetics and Mechanism of Drug Release from Econazole nitrate Nanosponge Loaded Carbapol Hydrogel, Ind J Pham Edu 2011; 45(1): 25-31.
8. David F. Nanosponge drug delivery system more effective than direct injection. www.physorg.com 2010.
9. Trotta F, Ultrasound-assisted synthesis of Cyclodextrin-based nanosponges. EP 2007; 1: 786 – 841.