FORMULATION AND EVALUATION OF FLOATING DRUG DELIVERY SYSTEM

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Abstact:

Floating drug delivery system is enable to give prolonged and continuous release of drug to upper part of the gastrointestinal tract and improves the bioavailability of medications that are characterized by a narrow absorption window. A new strategy preferably once a daily is proposed for development of buoyant gastric dosage forms for theophylline.

The present design of the delivery system was based on controlled release formulation with floating and swelling features in order to prolong the gastric retention time of the drug.HPMC K4M, carbapol, xanthan gum were used in different concentration in order to get desired controlled release profile over period of 24 hrs. All the formulations were evaluated for drug content and *in-vitro* drug release profile.

It was found that controlled rate of formulation increased with decrease in polymer concentration. The drug release data fitted to Higuchi kinetic model.

Key words: Theophylline, HPMC, K4M, carbapol, xanthan.

INTRODUCTION:

The floating tablets can be used as alternative dosage form to minimize the problems associated with conventional dosage forms. Some common acids used in this reaction are citric, malic, and tartaric and fumaric acid and bicarbonate used in the effervescent reaction is sodium bicarbonate, potassium bicarbonate, sodium carbonate and potassium carbonate. The most common reaction for pharmaceutical purpose is the acid base reaction between sodium bicarbonate and citric acid.

Floating drug delivery systems are capable of releasing drug in a sustained manner maintaining relatively constant plasma profiles. Drug release from the delivery devices are usually sustained at the target sites for many drugs using current release technologies.

FDDS are used for gastro retention purposes and have a bulk density lower than gastric fluids and thus remains in stomach. The FDDS possesses potential advantages like simple manufacturing processes and ease of administration.

Floating drug delivery can be stimulated by change in the temperature, change in pH and change in the solvent medium, by radiation.

Theophylline is methylxanthene drug used in chronic obstructive pulmonary disease and asthma. Theophylline is xanthene derivative and is similar to theobromine and cocoa.

MATERIAL AND METHODS:

Theophylline was purchased from Yarrow Chem. Pvt. Ltd. Mumbai. HPMC was obtained from Glenmark, Mumbai. Carbapol, talc and sodium bicarbonate obtained from Lobachemie. Mumbai.

A) Preformulation study:

a) Physical characteristics of drug:

The selected drug under investigation was subjected for physical characterization parameter such as nature, color, taste, melting point etc.

b) Solubility studies:

The solubility of drug determined in distilled water using standard method procedure.

c) Melting Point:

Melting point of Theophylline determined by capillary method. A small amount of drug taken in one end and closed capillary tube placed in Thiele's tube. Melting Point of Theophylline was found to be 272^0C.While reported value was in between 270^0 C – 275^0 C.

d) Wavelength scan of drug:

50 mg of Theophylline was accurately weighed and dissolved into 50 ml methanol. Then from this 5 ml solution taken and diluted to volume 100 ml to give 50 µg/ml. From this solution 2 ml was pipetted into 100 ml volumetric flask.UV scan was taken between wavelength 200-400 nm.

e) Differential Scanning Calorimeter (DSC) studies:

Thermo grams were recorded for Theophylline, HPMC, and carbapol using DSC. Accurately weighed sample (3 mg) placed on aluminum plates and heated at constant temperature of 5ºC/min.

B) Analytical profile of Theophylline:

Calibration curve of Theophylline using UV method:

Preparation of 0.1 N HCl:

Solution of 0.1 N HCl prepared by diluting 8.5 ml of Hydrochloric acid with 1000 ml of water.

Calibration curve of Theophylline in 0.1 N HCl:

1. Preparation of stock solution I:

Theophylline (50 mg) was dissolved in 50 ml of Methanol. Then from this stock solution – I, 5 ml solution was withdrawn and diluted up to 100 ml to get 50 µg/ml concentrations.

2. Preparation of stock solution II:

From stock solution I, 1,2,3,4,5 and 6 ml withdrawn and diluted up to 10 ml to get concentrations of 5,10,15,20,25 and 30 µg/ml solutions. Absorbance recorded by using UV spectrophotometer (Lab India 3002) at 317.6 nm.

Formulation of floating drug delivery system:

Theophylline passed through sieve no 60, in order to break lumps. HPMC, carbapol and sodium bicarbonate passed through sieve no.40.

The floating tablets of theophylline prepared by direct compression method. Formulation of each tablet is composed of HPMC, carbapol, sodium bicarbonate, talc and aerosil. Weight of tablet adjusted to 200 mg and each tablet contains 50 mg of theophylline.

Finally, 200 mg of each mixture fed in single punch die tablet machine (Cadmatch, Ahmadabad). Hardness of tablets adjusted at 6-6.5 kg/cm2 using Monsanto Hardness Tester (Monsanto Chemical, St. Louis, MO).

Compressed tablets then evaluated for thickness, hardness, weight variation and drug content.

Table 1: Formulation table of Theophylline floating tablets

Ingredient	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Theophylline	50	50	50	50	50	50	50	50	50	50	50	50
HPMC K4M	-	-	-	-	30	50	100	150	-	-	-	-
Carbapol	-	-	-	-	-	-	-	-	-	50	75	90
Ethyl cellulose	30	30	15	50	-	-	-	-	-	-	-	-
Sodium bicarbonate	10	30	30	40	30	40	40	40	20	20	20	20
MCC	106	-	-	-	-	-	-	-	-	-	-	-
D mannitol	-	-	-	56	86	56	6	6	51	76	51	36
Magnesium stearate	2	2	2	2	2	2	2	2	2	2	2	2
Talc	2	2	2	2	2	2	2	2	2	2	2	2

All tablets contain 50 mg Theophylline, 2 mg magnesium stearate and 2 talc. Total weight of tablet is 200 mg. All quantities are in mg.

Evaluation of Theophylline floating tablets:

- Angle of repose
- Bulk and tapped density
- Compressibility index and Hausner's ratio.
- Thickness
- Hardness
- Friability
- Weight variation
- Uniformity of drug content
- *In-vitro* dissolution studies

RESULTS:

1 Preformulation study of Theophylline:-

1.1 Description:

Color - White / Colorless

State - Powder

Taste - Odorless

1.2 Melting Point:

Melting point of Theophylline was found to be 272^0C. While reported value was in between 270^0C – 275^0C.

1.3 INFRARED SPECTROSCOPY:

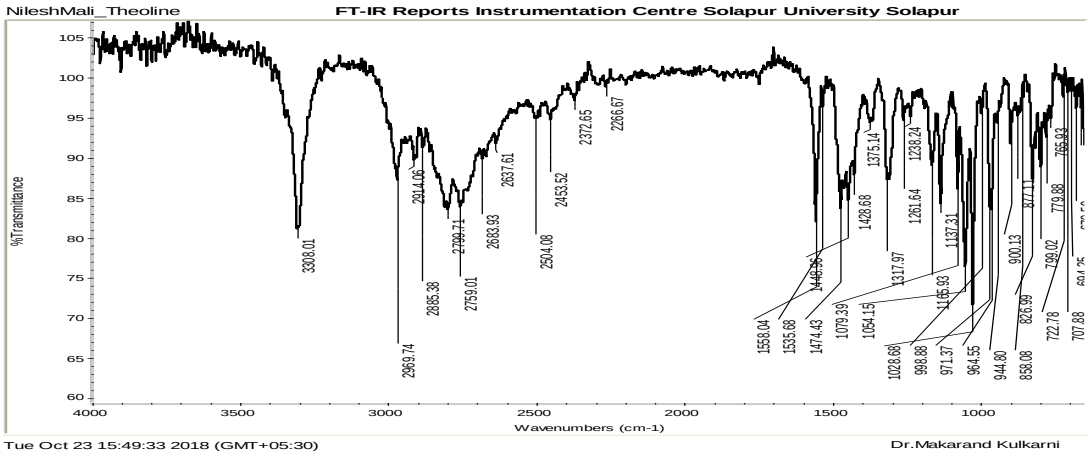

Fig 1. IR Spectra of Theophylline

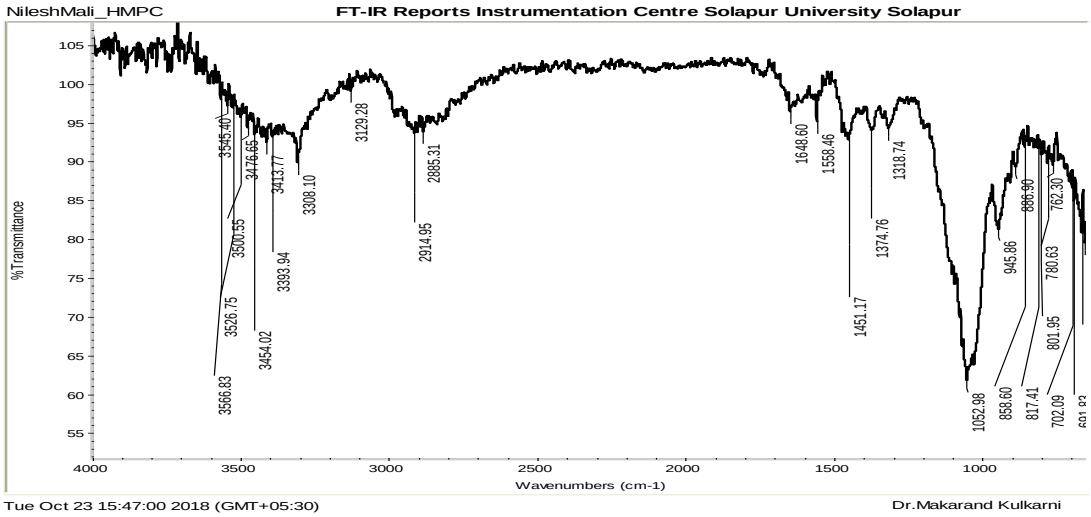

Fig. 2 IR Spectra of HPMC

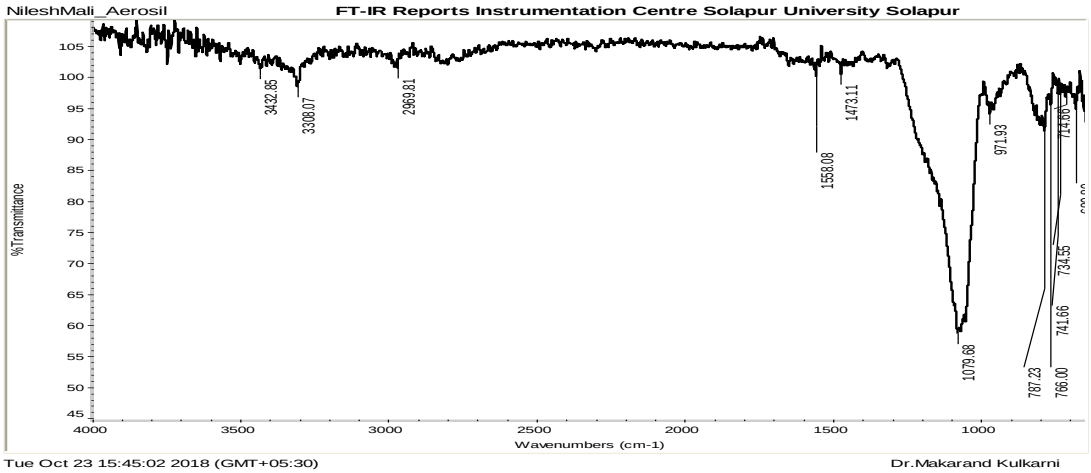

Fig.3 IR spectra of Aerosil

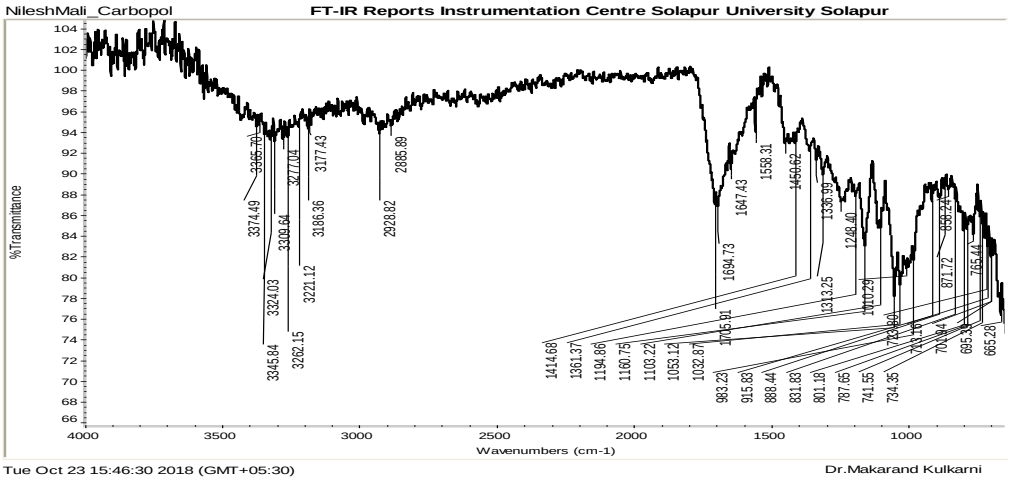

Fig. 4 IR specra of Carbapol

1.4 DSC Study:

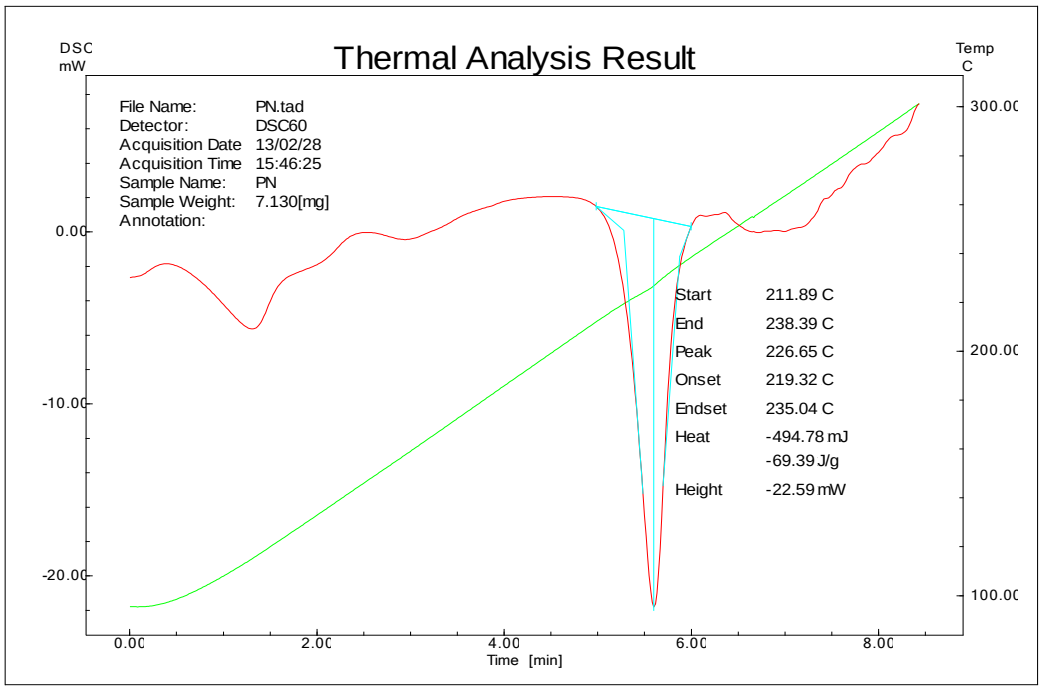

Fig.5 DSC of Pure Drug

Table 1: *In-vitro* drug release of Formulation 10

Sr. No	Time	Concentration(mg/ml)		Cum. Loss (mg/ml)	Cum.Conc. (mg/ml)	% Cum. DR
		1ml	900ml			
1	0	0	0	0	0	0
2	1	0.099	89.41	0	89.41	22.44±0.57
3	2	0.192	173.68	0.099	173.77	43.61±0.74
4	4	0.281	253.51	0.291	253.80	63.70±0.93
5	6	0.311	280.09	0.572	280.67	70.45±0.75
6	12	0.435	392.38	0.883	393.26	98.70±1.12

Table 2: *In-vitro* drug release of Formulation F11

Sr. No	Time	Concentration(mg/ml)		Cum. Loss (mg/ml)	Cum.Conc. (mg/ml)	% Cum. DR
		1ml	900ml			
1	0	0	0	0	0	0
2	1	0.099	89.26	0	89.26	22.37±0.41
3	2	0.204	183.76	0.099	183.85	46.07±1.05
4	4	0.289	260.80	0.303	261.11	65.54±0.92
5	6	0.321	289.06	0.616	289.68	72.60±0.94
6	12	0.434	391.45	0.991	392.44	98.35±0.87

Table 3: *In-vitro* drug release of Formulation F12

Sr. No	Time	Concentration(mg/ml)		Cum. Loss (mg/ml)	Cum.Conc. (mg/ml)	% Cum. DR
		1ml	900ml			
1	0	0	0	0	0	0
2	1	0.075	67.64	0	67.64	17±0.95
3	2	0.166	150.01	0.075	150.05	37.71±0.45
4	4	0.260	234.39	0.241	234.62	58.97±1.13
5	6	0.287	259.14	0.501	259.65	65.27±1.02
6	12	0.425	282.79	0.802	383.65	96.43±0.97

***In vitro* Dissolution study:**

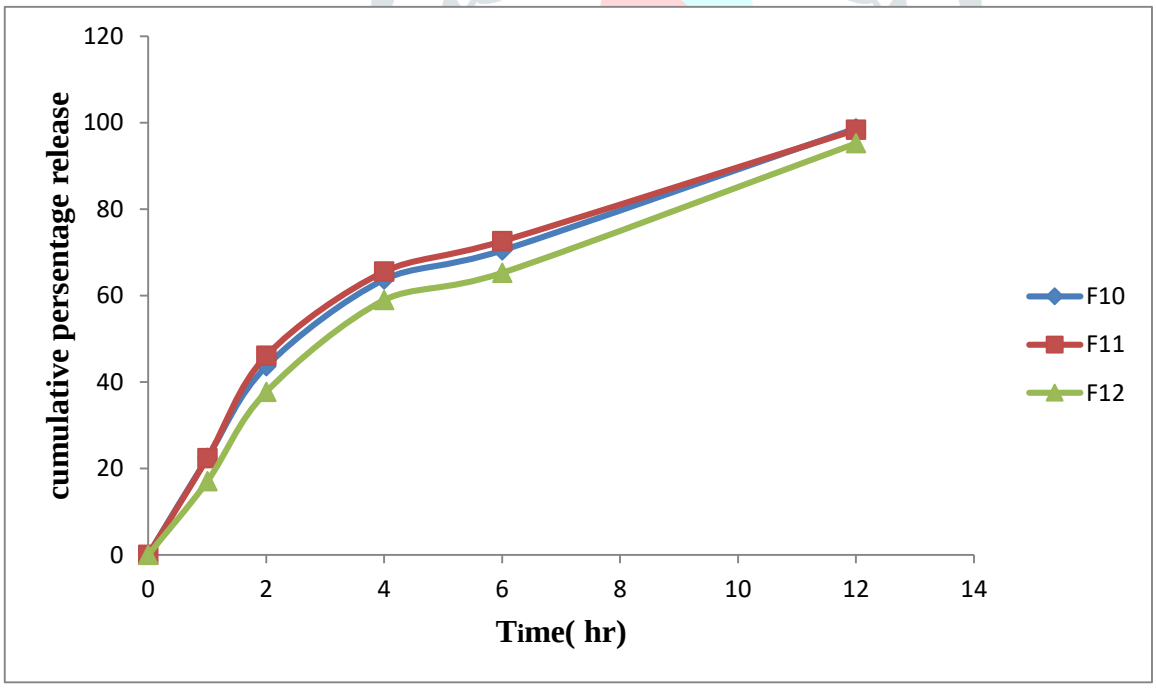

Fig. 6 *In-vitro* drug release of Formulation F10, F11 & F12

DISCUSSION:

In this study, floating tablets of Theophylline prepared by using HPMC, carbapol, MCC, aerosil, magnesium stearate, talc etc.

Preformulation study:

A) Description and Melting point :

Theophylline is white crystalline, odorless powder and having melting point 272^0C.While reported value was in between 270^0C-275^0C.

B) Determination of λ max of Theophylline:

On the basis of preliminary identification test it was observed that the drug complies the preliminary identification parameters. After scanning of drug, it was found that the drug has λ max of 276 nm.

C) Preparation of standard calibration curve of Theophylline:

From the standard curve of Theophylline it is observed that the drug obeys beer's law in concentration range of 2-10 µg/ml.

D) Drug Excipient Compatibility Studies:

The interaction between drug and excipients determined after specific time of period by using suitable analytical techniques like IR, DSC.

a) FTIR:

FTIR spectra of pure Theophylline blend of polymers with drug were determined.

Theophylline shown IR peaks 3308.01, 2969.74, 2914.06, 2885.38, 2799.71, 2759.01, 2683.93, 2637.61, 2504.08, 2453.52, 2372.65 and 2266.67.

HPMC K4M shown IR peaks 3545.40, 3566.83, 3526.75, 3500.55, 3476.65, 3454.02, 3393.94, 3413.77, 3308.10, 3129.28, 2914.95 and 2885.31.

Aerosil shown IR peaks 3432.85, 3308.07 and 2969.81.

Carbapol shown IR peaks 3374.49, 3365.70, 3345.84, 3324.03, 3309.64, 3262.15, 3277.04, 3221.12, 3186.36, 3177.43, 2928.82 and 2885.89.

Evaluation of tablets:

1. Tablet dimensions:

Thickness of tablets ranging from 2.52± 0.11 to 2.64±0.16 mm. The thickness of the tablet is depends upon the diameter of die and force applied during compression.

2. Hardness :

Hardness of all formulations found to be in the range of 5.1±0.28kg/cm2 to 6.3±0.76 kg/cm2.

3. Weight variation test:

Weight variation test revealed that the tablets of all formulations were within the range of Pharmacopoeial specifications.

4. Friability:

Friability below 1% is an indication of good mechanical resistance of the tablets. Friability of all formulations ranges from 0.10 to 0.22. Formulations F1, F2, F3 showed friability 0.14, 0.12, 0.10 respectively. Formulations F4, F5, F6 showed friability 0.21, 0.24, 0.12 respectively. Formulations F7, F8, F9 showed friability 0.17, 0.22, 0.11 respectively. Formulations F10, F11, F12 showed friability 0.22, 0.14, 0.16 respectively.

5. Drug content:

Percentage drug content of Theophylline determined by UV method and found in the range of 98.80±0.97 to 99.80±0.74.

6. *In-vitro* drug release study:

The results of *in-vitro* cumulative % amount of drug released at different time intervals plotted against time to obtain the release profiles. All the Formulations F1, F2, F3, F4, F5, F6, F7, F8, F9, F10, F11 and F12 showed cumulative % DR 99.89±0.73%,98.50±0.92%,96.50±1.12%,99.18±0.36%,97.65±0.45%,95.27±0.71%,95.54±0.73%, 91.45±0.72%, 87.65±0.77% respectively.

Summary and Conclusion:

Summary:

The purpose of this investigation was to design floating tablets of Theophylline. Theophylline gets well absorbed through GIT and stomach. Theophylline has short biological half-life (5-8 hrs.) and high bioavailability (100 %) hence selected as a model drug. The data of *in-vitro* drug release were fitted into Higuchi kinetic model. All formulations were evaluated for their pre-formulation studies. Compatibility study was carried out by using IR and DSC.

Conclusion:

The aim of this study was to formulation and evaluation of Theophylline floating tablets by using HPMC and carbapol as polymers.

The following conclusions can be drawn from the results obtained,

1) Preformulation study on Theophylline performed in accordance with the reported literature limits.

2) The floating tablets were found to be uniform consistency.

3) The drug content was within acceptable range which insured dose uniformity in the formulation.

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References:

1. Riyaz AM, Osmani , Nagesh h. Aloorkar , Bharati u. Thaware ,Parthasarathi k. Kulkarni , Afrasim moin et al , Microsponge based drug delivery system for augmented gastroparesis therapy: Formulation development and evaluation, Asian j. of pharmaceutical sci. 2015 442–451

2. Patil SV, Ratnaparakhi DU., Patil SS., Formulation and Evaluation of Microsponge of Benzyol Peroxide by Quasi Emulsion Solvent Diffusion Method, Int. J. of Pharmaceutical Research, 2015, Vol 7, Issue 2. 38-43

3. Mohan kumar V, Veena N M, Manjula B P.,Formulation And Evaluation Of Microsponges For Topical Drug Delivery Of Mupirocin Int. Journal of PharmTech Res, 2013, Vol.5, No.3, 1434-1440

4. Jain V and Singh R, Dicyclomine-loaded Eudragit®-based Microsponge with Potential for Colonic Delivery: Preparation and Characterization" Tropical J Pharmaceutical Res. 2010; 9:1. 67-72

5. Mahajan A, Jagtap LS, Chaudhari AL, Swami Sima P, Mali PR , formulation and evaluation of Microsponge drug delivery system using indomethacin " Int. Research journal of Pharmacy 2011,2(10) 64-69

6. Nevine S Abdelmalak, Shahira F El-Menshawe, A new topical fluconazole microsponge loaded hydrogel: preparation and characterization "Int. Journal of Pharmacy and Pharmaceutical Sci. Vol 4, Suppl 1, 2012. 460- 468

7. RishabhS,DK, Pathaka K, Colonic luminal surface retention of meloxicam microsponges delivered by erosion based colon-targeted matrix tablet Int. Journal of Pharmaceutics 427 (2012) 153– 162

8. Srivastava R Tansel C¸ omog˘lu, Nurs¸in Go¨nu, Tamer Baykara , Preparation and in vitro evaluation of modified release ketoprofen microsponges., Il Farmaco 58 (2003) 101/106

9. Nokhodchi A Jelvehgari M. , Siahi-Shadbad MR., AzarmiS. , Gary P., The microsponge delivery system of benzoyl peroxide: preparation, characterization and release studies, international journal of pharmaceutics 308 (2006) 124–132

10. Simonoska MC, Dimitrovska A, Nadica S, Mladenovska K, Renata et al., Implementation of quality by design principles in the development of microsponges as drug delivery carriers: Identification and optimization of critical factors using multivariate statistical analyses and design of experiments studie, Int. Journal of Pharmaceutics 489 (2015) 58–72

11. Mahesh Kumar, Ghosh A., Development and evaluation of metronidazole loaded microsponge based gel for superficial surgical wound infections. Journal of Drug Delivery Science and Tech. 30 (2015) 15-29

12. Arya P, Pathak K.,Assessing the viability of microsponges as gastro retentive drug delivery system of curcumin: Optimization and pharmacokinetics" Int. Journal of Pharmaceutics (2014) 1– 12

13. Mine O, Erdal C, Ahmet A., Design and evaluation of colon specific drug delivery system containing flurbiprofen microsponges. Int. Journal of Pharmaceutics 318 (2006) 103–117

14. Shah H, Patel K, U.M.U padhyay.,Formulation and evaluation of controlled release colon targeted micro sponge of Aceclofenac" The Pharma Innovation Journal 2014; 3(10): 81-87

15. Sonali, Pratap R and Kumar P., Formulation and evaluation of prednisolone loaded microsponges for colon drug delivery: in-vitro and pharmacokinetic study. Int. Journal of Pharmaceutical Sciences and Research 2014; Vol. 5(5): 1994-2005.