"FORMULATION AND EVALUATION OF SUSTAINED RELEASE FLOATING MICROBEADS OF KETOPROFEN"

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Abstract-
Aim: The main intention of the present study is to develop the ideal floating microbeads of Ketoprofen for prolongation of the gastric retention time in stomach and enhance the patient compliance in the treatment of pain.
Objective: Ketoprofen is a propionic acid derivative, it reversibly inhibits cyclooxygenase-1 and 2 (COX-1&2) enzymes, resultingto decrease formation of prostaglandin precursors. The elimination half-life of Ketoprofen is 2.4hrs. In the latest research workthe floating drug delivery system of Ketoprofen floating microbeads were prepared by using some polymers are sodium alginate, HPMC K100M, Carbopol 934, Methyl cellulose as a polymer and calcium carbonate used as gas forming agent.
Method: The floating microbeads were prepared by ionotropic gelation technique. By the FTIR technique the compatibility of drug and polymers were compared. The prepared microbeads were evaluated for physical characterization floating lag time, swelling index, entrapment efficiency, buoyancy studies, invitro drug release studies and SEM analysis.
Result: The formulation remains buoyant for more than 12hrs and all the formulation shows the mark increases in drug release. Formulation F2 containing HPMC K100 M shown the better result. The % yield of F2 formulation found to be 87.57%, swelling index 73%, % entrapment efficiency75.7%. SEM analysis studies shows the particles are in spherical shape. According to the obtained results, floating microbeads are good candidates for targeting to GIT.

***Key Words*: Ketoprofen, Rheumatoid arthritis, ionotropic gelation, floating microbeads, Gastric residence time, Buoyancy.**

INTRODUCTION[1-3]

The controlled release of oral medication to overcome physiological problems, such as gastric retention and gastric emptying. A unique drug delivery system was developed to address this drawback and maximize the oral absorption of a range of drugs. Mainly the drugs used for treating a selected disease or disorder at a specific part or site of the body are called a targeted drug delivery system. Oral dosage forms play an important role in treating diseases as these are easily acceptable by patients as there's no difficulty while taking an orally administered drug.

The microbeads are nearly spherical small with diameter of 0.5- 1000 micro meter. The solid and free flowing particulate carriers or containing dispersed drug particles either in solution or crystalline form allow a sustained release or multiple release profiles of treatment with various active agents without major side effect. Additionally microbeads maintain functionality under physical conditions, can incorporate the drug to deliver locally at high concentration. Ensuring therapeutic levels reduced side effects by keeping systemic concentration low and reached targeted site of action. Microbeads are produced from several polymers like cationic polymers, anionic polymers and binding components eg: chitosan, sodium alginate, gelatin, chondroitin sulfate, avidin in predominant ratio.

MATERIALS & METHODS

Table 1: List of the chemicals used

Sl. No.	Materials Used	Manufacturers
1.	Ketoprofen	Balaji chemicals, Gujrat
2.	Sodium alginate	Himedia laboratories, Mumbai
3.	HPMC K 100M	Yarrow chem, Mumbai
4.	Carbopol 934	Vasa scientific, Banglore
5.	Methyl cellulose	Karnataka fine chem, Bangalore
6.	Calcium carbonate	Karnataka fine chem, Bangalore
7.	Calcium chloride	Karnataka fine chem, Bangalore

Table 2: List of the equipment

Sl.no	Name of Equipment's/Instruments	Manufacturer/Company
1	Electronic analytical balance	Sartorius BL110S
2	FT-IR Spectrophotometer	Shimadzu
3	UV/Visible Spectrophotometer	UV-1900 Shimadzu
4	USP dissolution apparatus	DS 8000/ Lab India
5	Magnetic Stirrer	Remi instruments

PREPARATION OF FLOATING MICROBEADS OF KETOPROFEN:

Ionotropicgelation method has been widely used for microbeads preparation purpose. microbeads of Ketoprofen were prepared by weighing the required quantity of Ketoprofen is dissolved in 15ml of deionised water in a beaker. In another beaker sodium alginate(Bead core forming agent) is soaked for 3hr, in measured amount of distilled water. Weighed required quantity of HPMCK100M/ Carbopol 934/ Methyl cellulose (as rate controlling polymer as well as water swellable polymer) in different concentrations and calcium carbonate (as gas generating agent) and calcium chloride (as cross-linking agent) also weighed in required quantity, these all polymers are dissolve in separate beakers by using distilled water. Prepared Ketoprofen solution, HPMCK100M/ Carbopol 934/ Methyl cellulose solution, calcium carbonate solution added slowly to the beaker containing sodium alginate with continuous stirring by using magnetic stirrer at 500rpm maintained and the stirring is continued to obtain uniform dispersion of Ketoprofen and other polymers.If any bubbles found in the mixture, the mixture is sonicated for 30 min to eliminate air bubbles which may have been formed during the stirring process.This prepared slurry dispersion dropped through a 21G syringe into 100ml of calcium chloride solution. (table11), which was kept under stirring to improve the mechanical strength of the microbeads and to prevent aggregation of them&it is being stirred at 100 rpm for 10-15 min into the gelation medium. After 15min, microbeads are collected by filtration and washed with distilled water and dried at 40℃ overnight. The dried microbeads were doubly wrapped in an aluminium foil and kept in a desiccator till further use.

Table 3: Formulation of Ketoprofen Floating microbeads

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Ketoprofen	100	100	100	100	100	100	100	100	100
Sodium Alginate	2	2	2	2	2	2	2	2	2
HPMC K100 M	50	100	150	–	–	–	–	–	–
Carbopol 934P	–	–	–	50	100	150	–	–	–
Methyl Cellulose	–	–	–	–	–	–	50	100	150
Calcium Carbonate	200	150	100	200	150	100	200	150	100
Calcium Chloride	1	1	1	1	1	1	1	1	1

Characterization of Ketoprofen

Melting point: The melting point of pure drug Ketoprofen was determined by capillary tube method.

Determination of organoleptic properties: The physical appearance of the drug was observed and compared withthepharmacopeial specifications.

Solubility: Small amount of Ketoprofen were added to 10ml of solvent (alcohol, ether, phosphate buffer & HCl) in a 25ml stoppered standard flask with vigorous shaking.

PRE-COMPRESSIONAL STUDIESBULK DENSITY

It is also called as the poured density. It is the ratio of total mass of microbeadsto the bulk volume of microbeads. It was measured by pouring the microbeads into a 100 ml measuring cylinder and initial volumewas noted. This initial volume is called the bulk volume. From this the bulk density iscalculated according to theformula mentioned below. It is expressed in g/ml and is given by

Db = M/Vb

Where, M is the mass of bead

Vb is the bulk volume of the beads[4]

TAPPED DENSITY

It is the ratio of total mass of the microbeads to the tapped volume of the beads. Volume was measured by tapping the microbeads for 100 times and tapped volume was noted. It is expressed in g/ml and is given by

Dt = M / Vt

Where, M is the mass of beads

Vt is the tapped volume of the beads.[5]

ANGLE OF REPOSE

It is defined as maximum angle possible between the surface of the pile of powder and the horizontal plane andit can be calculated by the following formula.

tan(θ) = h / r

θ = tan-1 (h / r)

Where, **θ** is the angle of repose, h is the height in cm, r is the radius in cm. The microbeads were allowed to flowthrough the funnel fixed to a stand at definite height (h). The angle of repose was then calculated by measuring the height and radius of the heap of microbeads formed. Care was taken to see that the microbeads slip and roll over each other through the sides of the funnel. Relationship between angle of repose and microbeads flow property is given as follows.[6]

Table No.4: Angle of Repose as an Indication of Flow Properties

Angle of Repose (θ)	Type of Flow
25-30	Excellent
31-35	Good
41-45	Passable
46-55	Poor
>56	Very poor

CARR'S INDEX

It indicates microbeads flow properties. It is expressed in percentage and is give

$$I = \frac{Dt - Db}{Dt} \times 100$$

Where, Dt is the tapped density of the microbeads andDb is the bulk density of the microbeads.

Table No. 5: Relationship between % compressibility and flow properties

% Compressibility	Flow character	Carr's index (%)
≤10	Excellent	1.0-1.1
11-15	Good	1.12-1.18
16-20	Fair	1.19-1.25
21-25	Passable	1.26-1.34
26-31	Poor	1.35-1.45
32-37	Very Poor	1.46-1.59
>38	Very Very poor	>1.60

HAUSNER'S RATIO

Hausner's ratio is an indirect index of ease of microbeads flow. It is calculated by the following formula.[7]

Dt Hausner's ratio = -------

Db

Where, Dt is the tapped density.Db is the bulk density.

CHARACTERIZATION OF FLOATING MICROBEADS:

DETERMINATION OF SWELLING INDEX

For determining the swelling index, the accurately weighed quantities of Ketoprofenmicrobeads were suspendedin 0.1 N HCl with pH 1.2 (simulated gastro intestinal fluids). Liquid droplets adhered to the surface of microbeadswas removed by using blotting paper and then weighed it with the help of a microbalance. The swollen microbeads were dried in oven at 60°C for 5 h or until showed the constant weight.The variation in swelling of microbeads before and after drying was used to calculate the % of swelling index. The following equation was used.[8]

Swelling index= (Mass of swollen microbeads - Mass of dry microbeads/mass of dried Beads) * 100.

ENTRAPMENT EFFICIENCY

Ketoprofen incorporation efficiency was analysed by weighing 10 mg of floatingmicrobeads then dissolved in methanol. The above solution was agitated to solubilize the drug and polymers and to extract the drug. Then solution was filtered.The drug was determined using spectrophotometerat the λmax of 259 nm. The encapsulation efficiency was determined using the following equation.

% Drug entrapment = Calculated drug concentration / Theoretical drug concentration × 100.

DRUG CONTENT

Drug content ofKetoprofen floating microbeads with sodium alginate, HPMC K100M, Carbopol 934, Methyl cellulose, Calcium Carbonate. Calcium chloride was estimated UV-Spectrophotometric method. An accurately weight quantity of floating microbeads (equivalent to 10 mg of Ketoprofen) was taken and dissolved in 100 mlof 0.1N Hcl, from the solution 1ml of solution was diluted to 10 ml and assayed for drug content at 259nm.[9]

% Drug content = (Actual amount of drug in floating microbeads /Theoretical amount of drug in floatingmicrobeads) X100

PERCENT PRACTICAL YIELD (PY)

Practical yield (%) was calculated to know about percent yield or efficiency. Floating microbeads were collectedand weighed to determine practical yield (PY) from the following equation.[10]

PY (%) = [Practical Mass / Theoretical Mass (Drug + Carrier)] × 100

BUOYANCY STUDIES

Buoyancy test was carried out by weighing 100 mg of the microbeads and transferred to a USP type II dissolution test apparatus containing 900 ml of simulated gastric fluid (0.1N HCl) at 37°C.Then microbeadswere separated at different time intervals and dried until a constant weight obtained.[11]

The % of buoyancy is calculated by using following equation.

$$\text{Buoyancy (\%)} = \frac{\text{weight of floating microbeads} \times 100}{\text{Initial weight of floating microbeads}}$$

IN VITRODRUG RELEASE STUDIES

Ketoprofen floating microbead release studies of were conducted in 900 ml of simulated gastric fluid (0.1N HClpH 1.2) at 37 ± 0.5°C by using USP dissolution apparatus II. Accurately weighed quantity of 100 mg floating microbeads was transferred into 900 ml of 0.1N HCl medium and stirring at 100 rpm.Aliquots of samples were withdrawn at specific time intervals, filtered and diluted with similar medium finally assayed at259 nm using double beam spectrophotometer.The samples withdrawn were replaced with same dissolution medium and all the samples were analysed in triplicate.[12]

RELEASE ORDER KINETICS

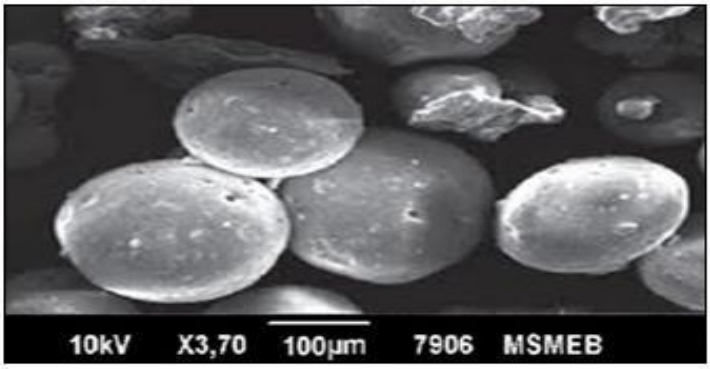
Drug release data of optimized floating microbead formulation were fitted to various kinetic models to revealthe drug release mechanism from the Beads. Those consist of Zero order, first order, Higuchi model and Korsmeyer-Peppas exponential equation and R2 values were determined.[13]

1) Zero Order Kinetics Model – Cumulative % drug release versus Time T.
2) First Order Kinetics Model - Log cumulative percent drug remaining versus Time T.
3) Higuchi's model – cumulative percent drug released versus square root of Time T.
4) Korsmeyer equation / Peppa's model - Log cumulative percent Drug released versus log time.

SCANNING ELECTRON MICROSCOPY (SEM)

Morphologicalexamination of the surface and internal structure of the dried microbeads of formulation F2 was performed using a scanning electron microscope (SEM). The samples are gold coated prior to the scanning. Forexamination of the internal structure

of the microbeads, they were cut in half with a steel blade.



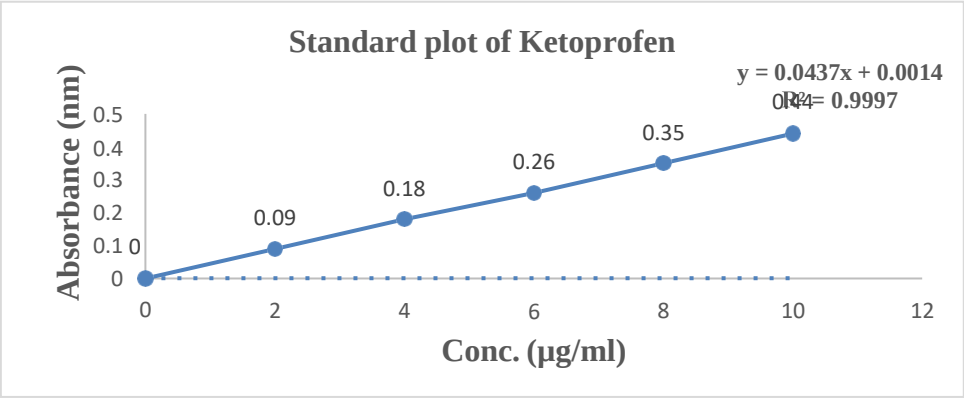
RESULTS:

PREFORMULATION STUDIES OF KETOPROFEN

Standard calibration plot of Ketoprofen: The λmax of Ketoprofenin 0.1 N Hcl buffer was found to be 259nm.The absorbance values are tabulated in the table. Ketoprofenobeyed Beer Lamberts law in the concentration range of 2-20 µg/ml with regression co-efficient 0.9997.

Table 6: Absorbance of Ketoprofenin 0.1 N Hcl buffer at 259nm

Concentration (µg/ml)	Absorbance
0	0
2	0.09±0.002
4	0.18±0.005
6	0.26±0.004
8	0.35±0.009
10	0.44±0.003

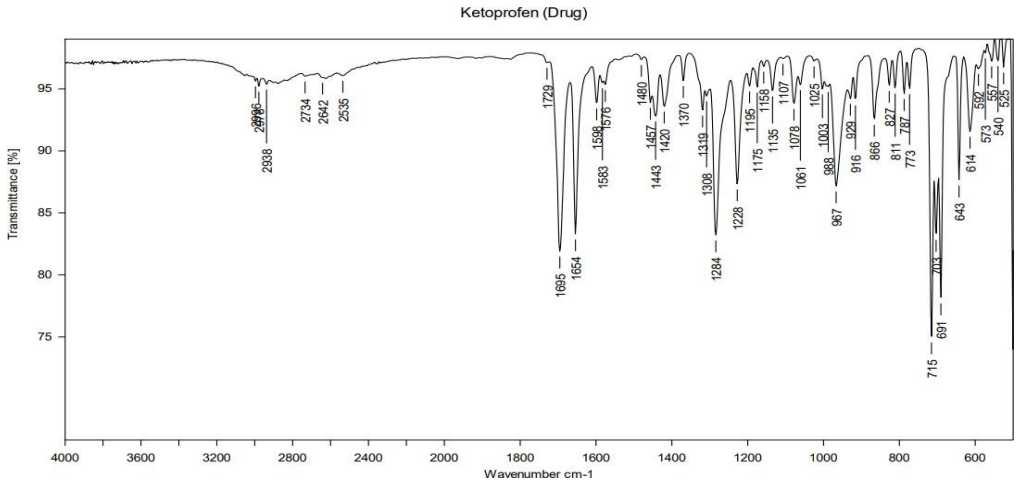


Graph 1: Standard curve of Ketoprofen in 0.1N HCl

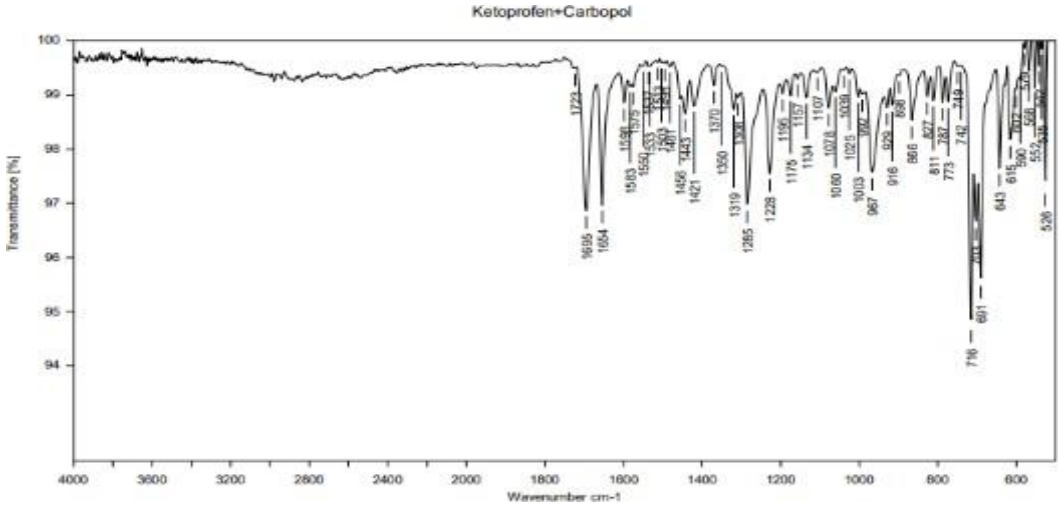
Drug-Polymer Compatibility Studies:

Drug and polymers used to prepare solid dispersions and inclusion complexes were checked for compatibility by carrying out FTIR spectroscopy. FTIR spectra obtained for pure drug and drug-polymer mixtures from 4000 to 400 cm^{-1} are given as follows:

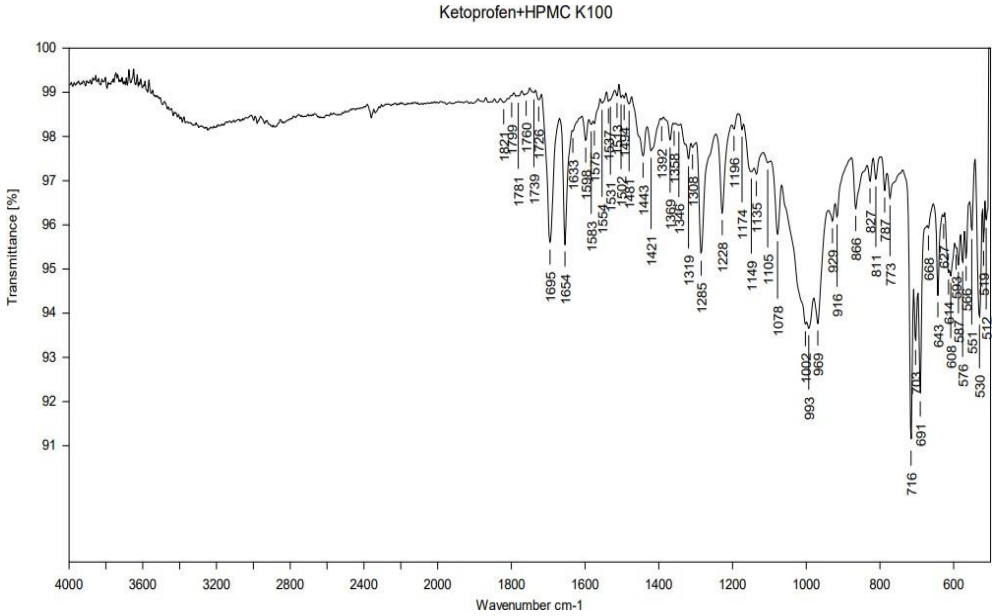
Drug and polymer compatibility studies



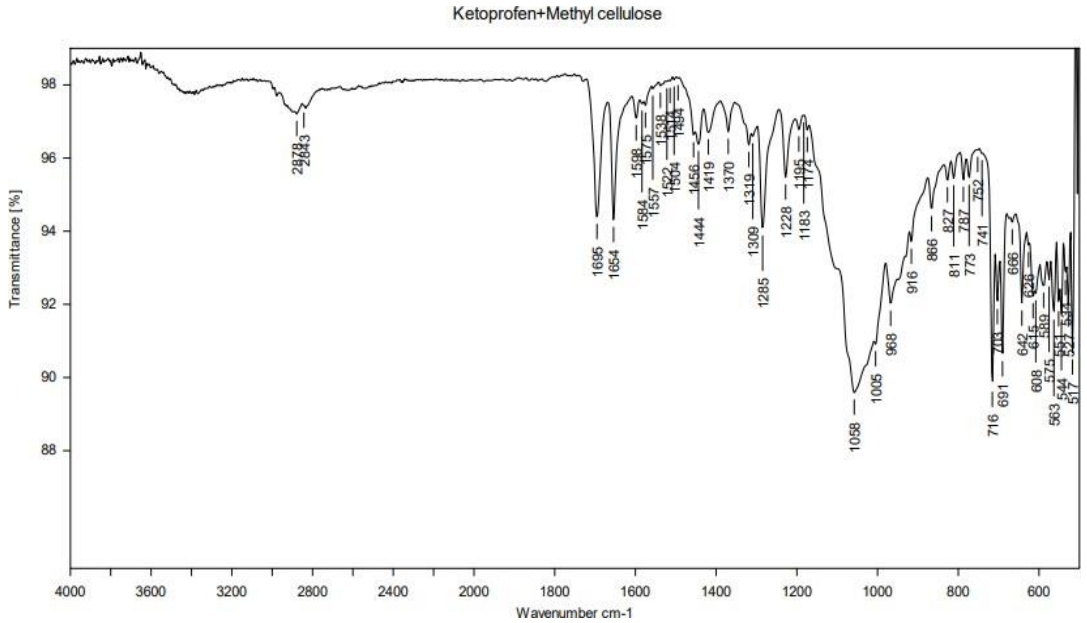
Graph 2: FTIR Analysis of Pure Drug (Ketoprofen)



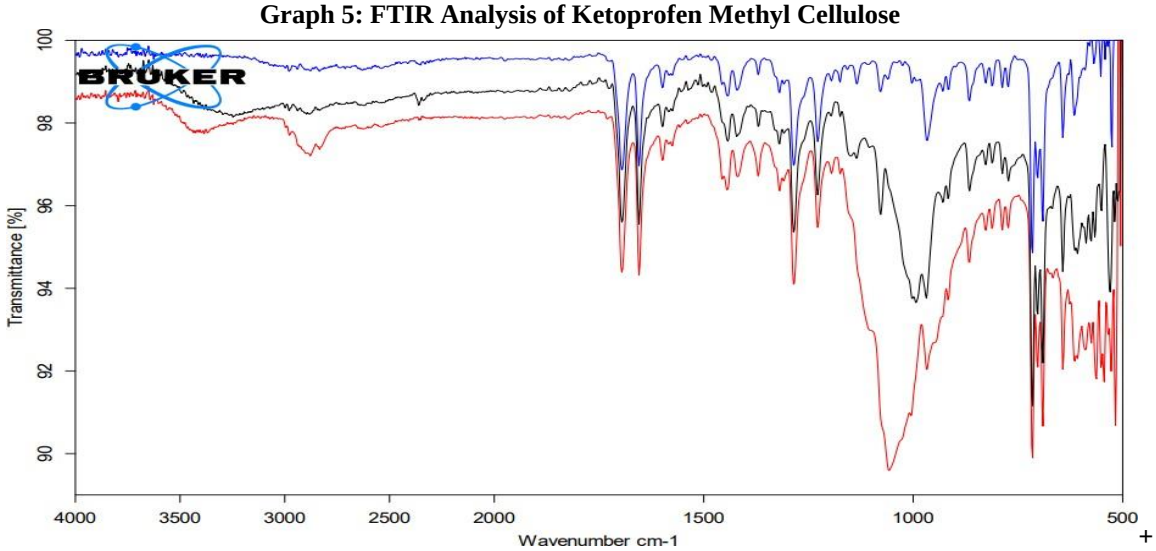
Graph 3: FTIR Analysis of Ketoprofen + Carbopol 934



Graph 4: FTIR analysis of Ketoprofen + HPMC K 100

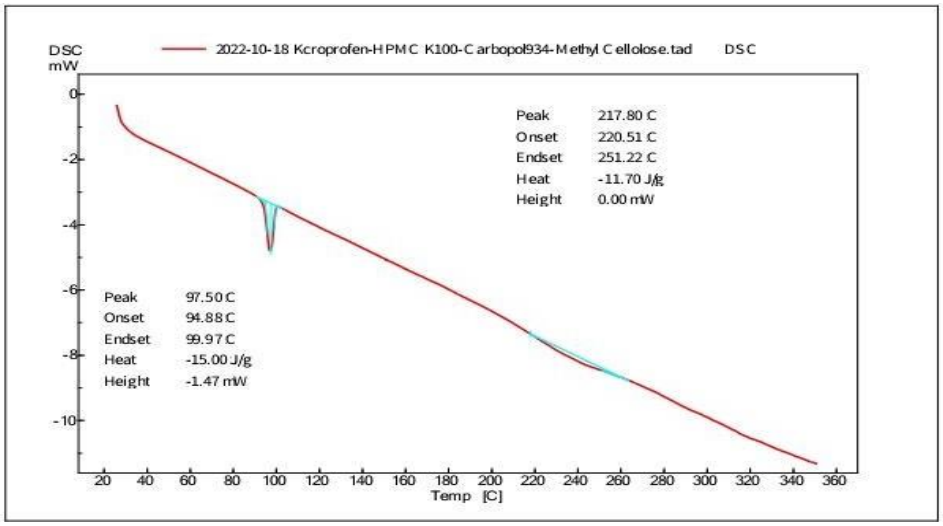


Graph 5: FTIR Analysis of Ketoprofen Methyl Cellulose



Graph 6: FTIR Analysis of Drug + Methyl Cellulose + HPMC K 100 + Carbopol 934

DIFFERENCIAL SCANNING CALORIMETRY (DSC) ANALYSIS



The melting point of Ketoprofen was found to be 93°C. In DSC 97.50°C and drug shows melting point in physical mixture alsowithin the range.

Table No. 7: Pre compression study of formulations

Formulation	Particle size(µm)	Bulk densityg/ml	Tappeddensity g/ cm3	Carr's index	Hausner'sratio	Angle ofrepose
F1	385.0±0.9	0.31±0.002	0.35±0.006	11.42±1.7	1.12±1.21	25.52°±3.40
F2	448.0±0.6	0.3±0.004	0.34±0.009	11.76±0.8	1.13±0.70	22.20°±1.20
F3	457.0±0.5	0.32±0.005	0.38±0.007	15.78±1.1	1.18±1.00	22.10°±0.77
F4	482.0±0.0	0.31±0.001	0.34±0.004	10.60±0.9	1.11±1.30	25.90°±1.30
F5	480.0±.0.8	0.34±0.006	0.35±0.005	11.76±1.8	1.02±1.30	25.89°±1.56
F6	520.0±0.6	0.31±0.007	0.33±0.004	11.42±1.3	1.06±0.91	25.30°±0.48
F7	478.8±0.7	0.31±0.002	0.34±0.006	10.42±0.9	1.19±0.70	23.50°±1.76
F8	531.6±0.6	0.32±0.009	0.34±0.003	10.16±1.2	1.92±1.20	26.20°±1.64
F9	360.0±0.9	0.34±0.005	0.37±0.007	11.24±0.7	1.10±0.40	24.60°±1.76

Table 8:Percent yield, Drug content, Floating lag time, swelling index, Buoyancy %, Entrapment efficiency % Evaluation parameter for Floating microbeads.

Sl.no	Formulation	Buoyancy %	Percent yield (%)	Swelling index %	Drug content (%)	Floatinglag time(sec.)	Floating time (hrs)
1	F1	81.00±0.06	87.5±1.57	47±0.05	95.22±2.59	50±3.01	≥12
2	F2	93.70±0.02	80.7±1.32	48±1.79	97.85±0.44	33±4.55	≥12
3	F3	66.60±0.10	79.0±0.96	73±1.06	94.74±4.86	41±6.13	≥12
4	F4	52.44±0.05	84.0±1.29	32±1.22	96.43±1.66	49±6.02	≥12
5	F5	61.20±0.08	85.0±1.48	36±0.10	95.46±1.77	40±3.53	≥12
6	F6	75.00±0.07	80.7±2.00	36±0.22	95.46±3.78	40±14.02	≥12
7	F7	71.40±0.09	78.5±1.66	51±0.09	94.03±2.88	43±8.44	≥12
8	F8	60.00±0.06	79.0±1.59	52±1.70	94.03±1.97	47±6.07	≥12
9	F9	51.72±0.04	83.6±1.80	53±1.49	94.03±3.53	43±8.06	≥12

Table 9: *IN-VITRO* DRUG DISSOLUTION DATA & CURVE OFF1– F9

Time (h)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	19.11±0.78	20.83±0.77	19.78±0.92	16.12±0.96	14.31±0.82	17.16±0.89	18.55±0.66	18.87±0.85	19.24±0.54
2	33.26±0.82	31.94±0.45	31.18±0.62	27.24±0.76	23.56±0.76	22.20±0.78	33.20±0.64	32.92±0.87	32.69±0.73
3	40.14±0.93	40.67±0.64	39.24±0.54	33.34±0.82	31.63±0.78	30.15±0.76	39.52±0.86	40.76±0.49	38.74±0.62
4	44.93±0.68	49.58±0.78	42.29±0.32	38.56±0.65	36.13±0.53	37.87±0.85	44.14±0.58	42.85±0.77	42.96±0.74
5	48.72±0.59	55.73±0.95	45.93±0.54	43.77±0.48	42.32±0.48	43.13±0.56	48.64±0.90	48.33±0.76	46.67±0.55
6	54.68±0.44	61.14±0.86	48.62±0.83	47.23±0.07	49.28±0.77	50.10±0.90	52.54±0.62	51.05±0.54	49.33±0.78
7	60.30±0.89	69.23±0.58	53.75±0.63	52.14±0.90	55.10±0.69	57.41±0.62	59.48±0.68	56.81±0.42	56.54±0.71
8	68.85±0.76	76.18±0.66	64.53±0.68	63.46±0.90	61.35±0.75	62.22±0.59	69.33±0.76	67.51±0.59	65.66±0.66
9	82.39±0.64	82.09±0.45	77.48±0.78	71.09±0.91	72.49±0.86	70.00±0.44	81.37±0.82	78.83±0.87	78.03±0.1
10	87.00±0.48	89.80±0.76	80.12±0.88	78.16±0.83	81.00±0.74	82.42±0.90	81.27±0.56	83.63±0.73	82.19±0.64
11	95.40±0.32	92.79±0.90	84.36±0.95	83.51±0.65	86.34±0.79	87.17±0.66	89.47±0.74	88.40±0.85	88.25±0.68
12	96.01±0.67	97.77±0.34	96.11±0.76	92.61±0.57	94.01±0.67	95.09±0.72	93.43±0.96	90.09±0.76	95.69±0.72

n=3±Std

Graph 6: *IN-VITRO* DISSOLUTION CURVE OF DILTIAZEM HYDROCHLORIDE OF FORMULATIONF1-F9

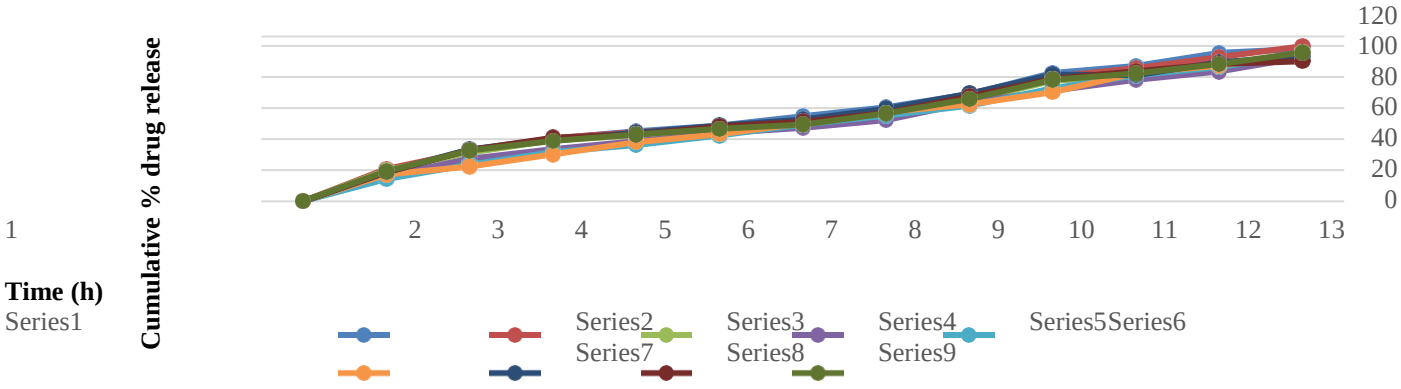


Table No.10: different kinetic models for Ketoprofen of floating microbeads

Code	Zero order	First order	Higuchi	Peppas		Best fitmodel
	R^2	R^2	R^2	R^2	n	
F1	0.979	0.809	0.966	0.942	1.612	**Zero order Higuchi model**
F2	0.981	0.872	0.946	0.968	1.299	**Zero order Peppas model**
F6	0.975	0.790	0.941	0.962	1.285	**Zero order Peppas model**
F4	0.979	0.809	0.906	0.942	1.612	**Zero order Peppas model**
F5	0.973	0.824	0.979	0.960	8.630	**Zero order Higuchi model**
F6	0.971	0.775	0.952	0.970	1.277	**Zero order Peppas model**
F7	0.975	0.891	0.979	0.963	13.87	**Zero order Higuchi model**
F8	0.960	0.925	0.960	0.973	1.289	**Zero order Peppas model**
F9	0.973	0.824	0.979	0.960	8.630	**Zero order Higuchi model**

Stability studies:

Table No. 11: Stability Studies of F6 Formulation at Room temperature

S.N	Para-meters	Observation			
		Initial	1 month	2 month	3 month
			Room temperature	Room temperature	Rooom temperature
1	Nature	Compactsolid	Compact solid	Compact solid	Compactsolid
2	Color	Yellowish	Yellowish	Yellowish	Yellowish
3	Buoyancy(%)	91.12	90.32	90.01	89.14
4	Swellingindex (%)	48	46	45	43
5	Floatingtime(%)	>12 h	>12 h	>12 h	>12 h

Table No.12: *In vitro* drug release study for Stability testing of formulation F2 at Room temperature

S.N	Time(h)	Room temperature
		90th Day cumulative % drug release
1	1	18.25±0.67
2	2	28.23±0.32
3	3	37.67±0.24
4	4	45.18±0.28
5	5	52.12±0.47
6	6	58.14±0.58
7	7	67.13±0.38
8	8	73.32±0.14
9	9	79.09±0.25
10	10	87.80±0.76
11	11	90.79±0.11
12	12	94.17±0.24

DISCUSSION

Evaluation parameters

Pre-compression parameters play an important role in important role in improving the flow properties of pharmaceuticals especially in microbeads formulation. These include angle of repose, bulk density, Carr's index and Hausner's ratio. Before formulation of microbeads the drug was evaluated for all the above said parameters and it was found that all the observations were within the prescribed limits of IP. The results of above pre- compression parameters are given in table.10

- Angle of repose of all the formulations (F1to F9) was found to be 22.10°±0.77 to 26.20°±1.64 which is good.
- Bulk density of all the formulations (F1 to F9) was found to be 0.3±0.004 to 0.34±0.00
- Carr's index of all the formulation (F1 to F9) was found to be 10.16±1.2 to 15.78±1.1 which is good.
- Hausner's ratio of all the formulations (F1 to F9) was found to be 1.02 to 1.92.

Post- compression parameters: Formulations (F1-F9) were evaluated for microbeads properties like buoyancy, percent yield, swelling index, drug content uniformity, floating lag time and floatinf time. The results of above post compression parameters are given in table.7 (b)

- Formulations (F1 to F9) buoyancy was found to range from 51.72 to 93.70 %.
- Formulations (F1 to F9) pecentage yield was found to range from 78.5 to 87.5%.
- Formulations (F1 to F9) swelling index was found to range from 32 to 73 %.
- Formulations (F1 to F9) floating lag time was found range from 33 to 50 sec.
- Formulations (F1 to F9) drug content was found to be in range from 94.03 to 97.85 %.
- Formulations (F1 to F9) floating time was found to be $\geq$ 12 h.
- ***In-vitro* dissolution study:** Formulation F1, F2 and F3, which contain sodium alginate with HPMC K100M and Calcium carbonate, released 99.67%, 99.77% and 96.11%of drug respectively at the end of 12hrs. Formulation F4, F5and F6 which contain Carbapol along with Sodium alginate and calcium carbonate, released 96.62%, 96.33% and 98.67% of the drug at the end of 12hrs. Formulation F7, F8 and F9 which contain sodium alginate along with Methyl cellulose and calcium carbonate, released 89.47%, 88.40% and 89.01% of the drug at the end of 12hrs. respectively. AsHPMC K100M is better water swellable polymer than Carbapol934 and Methyl cellulose. The microbeads in 0.1N Hcl, exhibited a release profile when evaluated for drug release as an initial rapid drug release phase followedby slower and sustained, increasing drug release phase.

CONCLUSION

Ketoprofen is a cyclooxygenase-1 and 2 (COX-1&2) enzymes inhibitor. It is prescribed in rheumatoid arthritis. Floating microbeadswere prepared by ionotropic gelation method by using different ratio of drug and carrier.

From the research work carried out, following conclusions can be drawn:

- FTIR spectra led to the conclusion that there was no interaction between drug and polymers; hence they are compatible.
- The microbeads were spherical in nature and evaluation of the microbeads are carried out to know the performance of themicrobeads.
- The drug is combined with different grades of HPMC K100M, Carbopol 934, Methyl cellulose in various ratios.

- The microbeads showed instantaneous and excellent buoyancy and remained a float on dissolution medium throughout the studyperiod.
- The percentage yield of different formulations was found to be in the range of 78.5% to 87.57%
- The *In-vitro* release study showed that all the formulations gave better drug release.
- The entrapment efficiency of drug and HPMC K100M gave higher release than other formulations.
- In formulation F2 showed highest drug release i.e., 99.77% in 12 hrs. as compared to other formulations.
- Thus, the objective of the present work of formulating a dosage form for Ketoprofen using sodium alginate, HPMC K100M, Carbopol 934, Methyl cellulose as rate controlling polymer, calcium carbonate as gas generating agent, calcium chloride has been achieved with the success.

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