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Research Article

ALGINATE BEADS OF IBUPROFEN FOR ORAL SUSTAINED DRUG DELIVERY: AN IN VITRO EVALUATION

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ABSTRACT

An investigation into the suitability of alginate beads of microspheres for oral delivery of Ibuprofen is presented. Alginate beads microspheres were formulated under different conditions of polymer concentration at constant speed. The microspheres were evaluated according to particle size, drug content, percentage yield, moisture content by Karl Fischer titration, bulk density, tapped density, Carr's index. In vitro release of Ibuprofen from the microspheres was studied in simulated intestinal fluid (SIF, pH 7.4). The release data was fitted into two release models to investigate the mechanism of Ibuprofen release from the microspheres. All the microspheres showed good swelling characteristics in distilled water. The investigation revealed that the microspheres produced with 2.5% (W/V) sodium alginate had the optimum prolonged release pattern. The microspheres produced using 2% (W/V) Sodium alginate had the highest delayed release of the incorporated drug, whereas other ratios of drug polymer had the fastest release. The Invitro dissolution studies appeared to have adequately described the release process as about 8 to 10 hours. The Scanning Electron Microscopic study revealed the spherical shape and the presence of pores which is effective for loading of the dose. The X-Ray diffraction study showed a normal graph which represents no drug polymer interaction. Differential Scanning Calorimeter, Thermo gravimetric analysis and FTIR spectroscopy also reveals no possibility of interaction between drug and polymers used in the study. This implies that formulations of Ibuprofen-sodium alginate microspheres are likely to offer a reliable means of delivering Ibuprofen by the oral route.

Keywords: Microsphere, DSC, XRD study, Scanning Electron Microscopy.

INTRODUCTION

Rheumatoid arthritis is an auto immune disease, which is chronic, affecting the people of all ethnic groups worldwide. Even though various categories like immuno suppresants, NSAID, steroidal anti inflammatory drugs are being used till now, the development of new anti rheumatic drugs is aimed towards the discovery of safe, potent drugs with minimal side effects. Here present study reveals the formulation and evaluation of alginate beads of Ibuprofen as an sustained release anti rheumatic drug delivery system.

To improve the sustained release activity of Ibuprofen, the author tries to give it a form of novel drug delivery system by forming micro spheres in ion gelation technique. The in-vivo dissolution study and other parameters testing by

different studies like Scanning Electron Microscope, Differential Scanning Calorimeter, X-Ray Diffraction etc helps to prove it a sustained release anti rheumatic drug delivery system[1-30].

EXPERIMENTAL METHODS

1. Collection of drug and polymer

The pure drug of Ibuprofen was collected from Dr.Reddy's lab, Hyderabad. The sodium alginate used was Lobachem grade and all other chemicals used are in the Merck grade of lab reagent.

2. Formulation of alginate beads of Ibuprofen

1%, 1.5 %, 2% & 2.5% w/v aqueous solution of sodium alginate was by a REMI stirrer of speed 500rpm to form a homogeneous polymer solution. The drug sample was dispersed in an appropriate proportion i.e. 1:1, 1:2 & 1:3 ratios and stirring was continued for one to two hours to allow complete dispersion. The dispersion was drop from a glass van syringe having 18-G hypodermic needle to the magnetically stirred calcium chloride water solution at a rate of 1ml per minute at stirring speed of 800 rpm. The beads are collected followed by washing and drying at 25ºc and relative humidity 30% [2].

3. Qualitative Evaluation

The formulations were quantitatively evaluated for different parameters like drug content, percentage yield, moisture content by Karl Fischer titration, bulk density, tapped density, Carr's index were evaluated.

4. Scanning Electron Microscopic (SEM) Study

Scanning electron photo micro graphs of Ibuprofen micro spheres were taken. A small amount of micro spheres were spread on glass stub [6]. After wards the stub containing the sample was placed in the in scanning electron microscope JSM 5610 LV SEM, JEOL, Datum Ltd (Japan) Chamber at accelerated voltage of 20kv, chamber pressure 0.6mm hg at different magnification[17].

5. X-Ray Diffraction (PXRD) study

The X-Ray diffraction study is important from the point of any conversion of crystallinity of the drug to the amorphous form which was carried out in Department of Instrumentation Science, Jadavpur University Calcutta.

6. Differential Scanning Calorimeter (DSC) Study

To study the drug polymer interaction in different ranges temperature, the author analyzed the formulation by Differential Scanning Calorimeter, carried out in Institution, Science, Jadavpur University which shows no interaction in form of independent graphs.

7. In-vitro dissolution study

In-vitro dissolution rate studies of the micro spheres were performed using USP XX type-II (electro lab TDP- 06T) apparatus[21]. Drug release was studied in 900ml of 7.2 pH phosphate buffer 37± 0.5ºC at 100 rpm. 1ml sample was withdrawn at regular intervals and the same quantity of pre warmed fresh dissolution medium was replaced. The samples withdrawn were assayed spectro photo metrically at 320nm using shimadzu 1700 UV visible spectrophotometer.

RESULTS AND DISCUSSION

The prepared Ibuprofen micro spheres by ion gelation technique were discrete, spherical and free flowing having a good percentage yield. Scanning electron microscopy images demonstrated spherical shaped micro particles and presence of pores which gives the relevant idea of better drug absorption. Thermal behavior of Ibuprofen micro spheres with sodium alginate by DSC shows no peak indicating no drug polymer interaction. The x-ray diffraction pattern of the pure 320drug shows peaks that are sharp and intense signifying its crystalline nature[10]. But its mixture with sodium alginate reduce the number of peaks and peak heights which suggest that the crystallinity converted to amorphous form and it is in good agreement with enhanced solubility. The in-vitro release data were plotted graphically by taking cumulative percent drug release versus time and the plots were found to obey kinetics of Higuchi model[5] gives a very good bench marking anti rheumatic formulation of sustained release action[4].

Table 1: Formulation design of micro particles

Sl.no.	%w/v of formulation	Ratio (Drug: Sod. Alginate)	Distilled Water in ml.	Sodium Alginate (gm)	Drug(gm)
1	1	1:1	25	0.125	0.125
2	1	1:2	25	0.083	0.167
3	1	1:3	25	0.062	0.187
4	1.5	1:1	25	0.187	0.187
5	1.5	1:2	25	0.125	0.250
6	1.5	1:3	25	0.093	0.281
7	2	1:1	25	0.25	0.25
8	2	1:2	25	0.166	0.334
9	2	1:3	25	0.125	0.375
10	2.5	1:1	25	0.312	0.312
11	2.5	1:2	25	0.208	0.417
12	2.5	1:3	25	0.156	0.469

Table 2: Determination of % yield of Ibuprofen

Sl. No.	Formulations	% w/v	Ratio (D:P)	% yield	Melting point in °C	% incorporation	% Moisture content
1	Pure Ibu.	-	-	-	172	-	1.1
2	Ibu:Sod.alg	1	1:1	68.8	152	8.1	2.1
3	Ibu:Sod.alg	1	1:2	73.2	149	7.2	2.5
4	Ibu:Sod.alg	1	1:3	80.4	155	6.2	2.4
5	Ibu:Sod.alg	1.5	1:1	82.133	156	7.1	2.2
6	Ibu:Sod.alg	1.5	1:2	83.466	163	6.6	3.3
7	Ibu:Sod.alg	1.5	1:3	87.2	165	5.7	3.1
8	Ibu:Sod.alg	2	1:1	91.8	167	6.6	1.9
9	Ibu:Sod.alg	2	1:2	94.4	163	5.6	2.3
10	Ibu:Sod.alg	2	1:3	97.8	162	4.9	2.2
11	Ibu:Sod.alg	2.5	1:1	94.88	164	5.8	2.5
12	Ibu:Sod.alg	2.5	1:2	96.16	167	3.4	2.6
13	Ibu:Sod.alg	2.5	1:3	97.28	165	3.5	2.4

Table 3: Determination of flow properties of Ibuprofen

Formulation	% w/v	Ratio (D:P)	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index	Packing factor
Pure Ibu.	-	-	0.4312	0.5504	21.65	1.276
Ibu:Sod.alg	1	1:1	0.4217	0.6606	36.13	1.565
Ibu:Sod.alg	1	1:2	0.4314	0.6609	34.71	1.531
Ibu:Sod.alg	1	1:3	0.4227	0.6507	35.02	1.539
Ibu:Sod.alg	1.5	1:1	0.4195	0.6009	30.15	1.431
Ibu:Sod.alg	1.5	1:2	0.3998	0.5012	20.23	1.253
Ibu:Sod.alg	1.5	1:3	0.4718	0.6210	24.02	1. 316
Ibu:Sod.alg	2	1:1	0.4277	0.5890	27.36	1.376
Ibu:Sod.alg	2	1:2	0.4104	0.5995	31.49	1.459
Ibu:Sod.alg	2	1:3	0.5002	0.6989	28.42	1.397
Ibu:Sod.alg	2.5	1:1	0.4812	0.6019	20.03	1.250
Ibu:Sod.alg	2.5	1:2	0.4514	0.6089	25.88	1.349
Ibu:Sod.alg	2.5	1:3	0.4117	0.5993	31.31	1.456

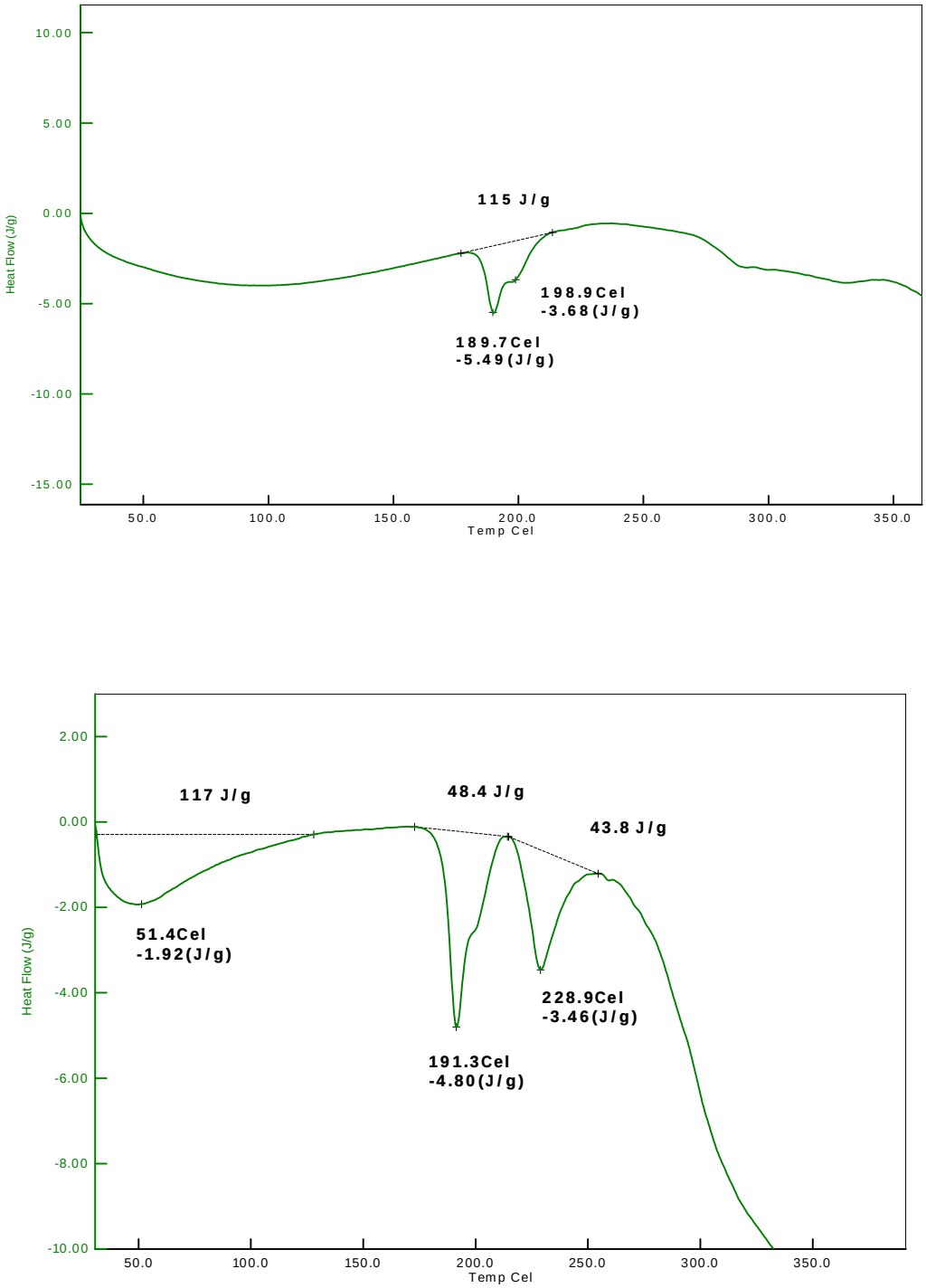

Fig. 1: DSC Photography of Ibuprofen Pure drug & Microspheres

Fig. 2: SEM Photography of Ibuprofen Microspheres

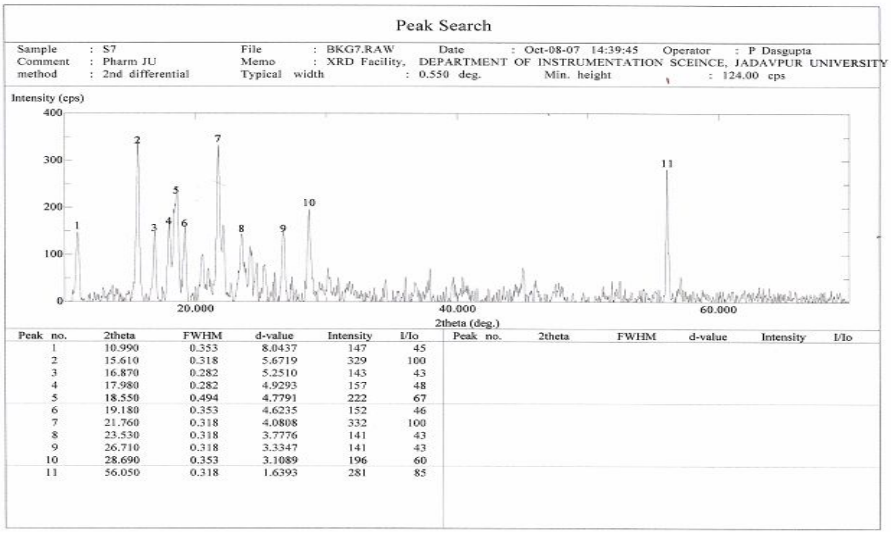

Fig. 3: X-RD Photography of Ibuprofen Microspheres

Table 4: Dissolution Profile of Ibuprofen Microspheres (2.5 %, 1:2)

Time(T)(hr)	Log [con^n]	SQRT	%CDR	W01/3-W1/3
0		0	0	0
0.5	1.483637	5.477226	30.45349	0.529222608
1	1.55377	7.745967	35.7907	0.637233113
2	1.689061	9.486833	48.87209	0.93006143
3	1.736582	10.95445	54.52326	1.072178678
4	1.800781	12.24745	63.2093	1.315662126
5	1.877679	13.41641	75.45349	1.735359196
6	1.906798	14.49138	80.68605	1.958569964
7	1.951202	15.49193	89.37209	2.442973522
8	1.979262	16.43168	95.33721	2.970952302
9	1.995176	17.32051	98.89535	3.607855824
10	1.951202	15.49193	89.37209	2.442973522

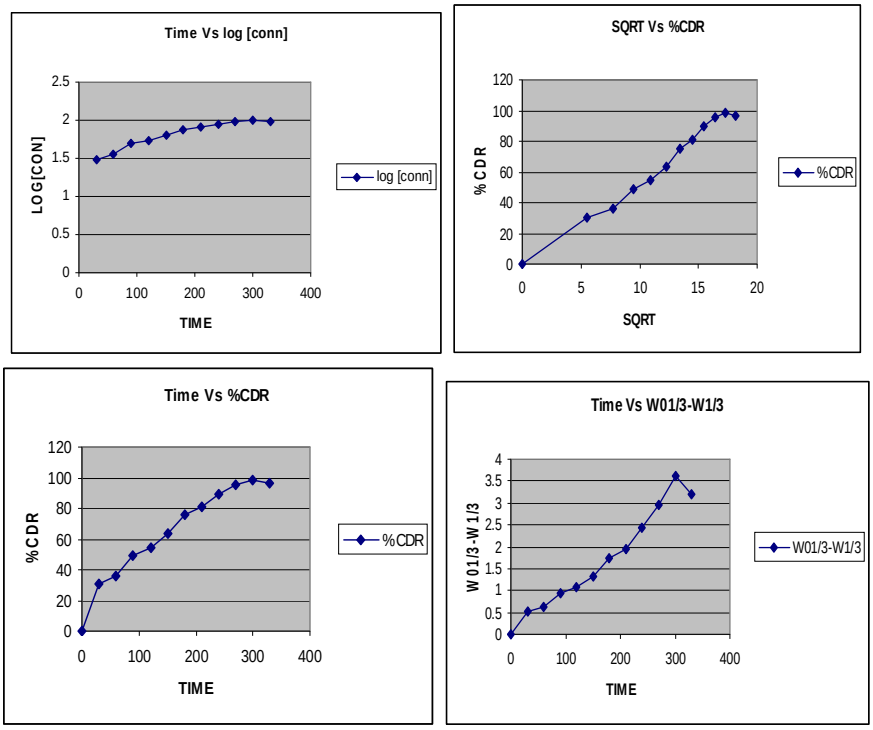

Fig. 4: Dissolution Profile of Ibuprofen Microspheres (2.5 %, 1:2)

CONCLUSION

It could be concluded that the sustained release alginate beads of Ibuprofen evaluated by qualitative method gave effective data's.

Extensive and intensive experimental datas with regard to the percentage yield, drug content, melting point, moisture content by auto Karl Fischer titration and flow ability obtained such that the physiability of pilot plant study with regard to scale of technique is quite encouraging.

The surface topography by SEM under high magnification shows nearly circular shape with several surface pores through which the drug find a gateway for releasing to the dissolution media or in-vivo gastric fluid.

From the Differential Scanning Calorimeter pattern of thermal degradation of compound reveals no interaction as evidenced by their appearance of new peaks. The In-vitro dissolution study conducted for a period of 12hours in continuous monitoring process shows diffusion rate controlled kinetics following Higuchi model.

The In-vitro dissolution release pattern follows Higuchi model and their activity is sustained over a maximum period of 10 hours which shows 2 times administration of the formulation would be ideal for pain management of rheumatoid arthritis. Similarly the SEM, X-Ray Diffraction studies and Differential Scanning Calorimeter studies also helped for showing no drug polymer interaction and spherical shape of the micro sphere.

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