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Preparation and evaluation of Ibuprofen Micro spheres by using Co-acervation phase separation technique

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Abstract: Aim of our present study was to formulate the Ibuprofen Micro spheres by using Co-acervation phase separation technique to improve the bioavailability of drug. We were used the Ibuprofen as a model drug, it has a biological half-life of 2hrs. Ibuprofen Micro spheres were formulated by using different drug: gelatine-carbopol in 6 batches was F1, F2, F3, F4, F5 & F6. Ibuprofen Micro spheres were performed by evaluation tests such as particle size analysis, morphology (SEM), angle of repose and bulk density. Further Ibuprofen Micro spheres were investigated by in-vitro dissolution studies using phosphate buffer (PH 7.4) to know the drug release.

Key words: Ibuprofen, Micro spheres, gelatine, carbopol, optical microscope, Uv-visible Spectrometers & dissolution apparatus.

Introduction

Advancement in drug delivery could come from innovative improvement to existing drug delivery system. Because of reducing frequency of administration, sustained release dosage form and ambulatory patient compliance .Micro sphere technology has been studied extensively for the sustained delivery of therapeutic agents[1-5].One is recovery of the solid from slurry and having the final products in a dry form. This becomes increasingly difficult as the size of the micro particulate decreases. The standard methods such as centrifugation and filtration, followed by vacuum or freeze-drying, involves several transfer steps resulting in loss of product and risk of contamination, the latter being quite serious when an aseptic process is required[6].Control release system include any drug delivery system that releases the drug over an extended period of time. If it is unsuccessful in this but only extents the duration of actions. If the system is successful in maintaining a constant drug level in the blood or target tissue[7,8]. Ibuprofen has prominent analgesic, anti-inflammatory and pyretic actions. Ibuprofen has similar potency in regard to aspirin but it is less potent than naproxen or indomethacin.Previous studies were done by using ibuprofen with polystyrene, ethyl cellulose shows good drug release characters [9, 10]. Ibuprofen –loaded ethyl cellulose micro spheres were studied by higuchi model and analysis of the matrix were studied structure by thermal analysis [11, 12]. In-vitro release studies of ibuprofen Micro spheres using cannuaba wax by melt dispersion technique shows good drug release characters [13].

Materials and Methods

Materials: Ibuprofen (Micro labs Ltd, Pondicherry), Gelatine IP grade (Ranbaxy Laboratory Ltd, India), Carbopol C940 grade (Mclareu Bio-tech (P) Ltd, Hosur), formaldehyde, Isopropyl alcohol (S.D.Fine chemicals ltd, India).

Method of Preparation:

Gelatine and gelatine-carbopol mixture containing ibuprofen Micro spheres were prepared by co-acervation phase separation technique utilising temperature chance.

Gelatine was dissolved in 10ml of water which was previously heated to 50˚ C, to this ibuprofen was added and stirred approximately at 300 rpm with the help of magnetic stirrer for 15 mins to get a stable dispersion. The dispersion was poured drop wise into the 10ml of sunflower oil which was also previously heated to 50˚ C on a water bath. The mixture was stirred with a help of magnetic stirrer for 2 hrs at 300rpm at room temperature. At the end of 2 hrs cross-linking agent such as formaldehyde 0.5ml was added to the dispersion medium and stirring was continued for next 30 mins. Finally it was kept in refrigerator for 24 hrs to ensure the rigidization of Micro spheres. This Procedure was followed to prepare 6 batches of ibuprofen Micro spheres with different ratios of gelatine and gelatine-carbopol mixtures. The core: coat ratio, amount of drug and polymers used were given in table-1.

Result & Discussions:

Evaluation of Ibuprofen Micro spheres:

Particle size analysis:

The Particle size analysis was carried out by using optical microscopy. About 200 Micro spheres were selected randomly and their size was determined by using optical microscope fitted with standard micrometer scale. The particle size of Micro spheres was given in table-2.

Scanning Electron Microscopy:

Scanning Electron microscopy [Crystal Growth Centre Anna University, Chennai] was carried out to study the morphological characteristics of Ibuprofen Microspheres.Scanning Electron micrographs were also taken and shown in fig 1.

Determination of angle of repose:

The angle of repose was determined by funnel method. The angle of repose was calculated by $\theta = \tan^{-1}(h/r)$.The angle of Micro spheres was given in table 3.

Table 1 Composition of Ibuprofen Micro spheres.

S.no	Batch no	Core: coat ratio	Amount of drug (gm)	Amount of gelatine(gm)	Amount of Carbopol(gm)
1	F1	1:1	1	1	-
2	F2	1:1.5	1	1.5	-
3	F3	1:2	1	2	-
4	F4	1:1	1	0.75	0.25
5	F5	1:1	1	0.50	0.50
6	F6	1:1	1	0.25	0.75

Table 2 The particle size of Ibuprofen Micro spheres.

S.no	Batch no	Average particle size (µm)
1	F1	62.3
2	F2	70.8
3	F3	78.5
4	F4	60.8
5	F5	64.6
6	F6	71.2

Table 3 The angle repose values of Ibuprofen Micro spheres.

S.no	Batch no	Angle of repose	Comments
1	F1	25º 40’	Good flow
2	F2	27º 28’	Good flow
3	F3	26 º44’	Good flow
4	F4	23 º48 ‘	Good flow
5	F5	25º 34’	Good flow
6	F6	24º 30’	Good flow

Fig 1 Electron micrographs of Ibuprofen Micro spheres.

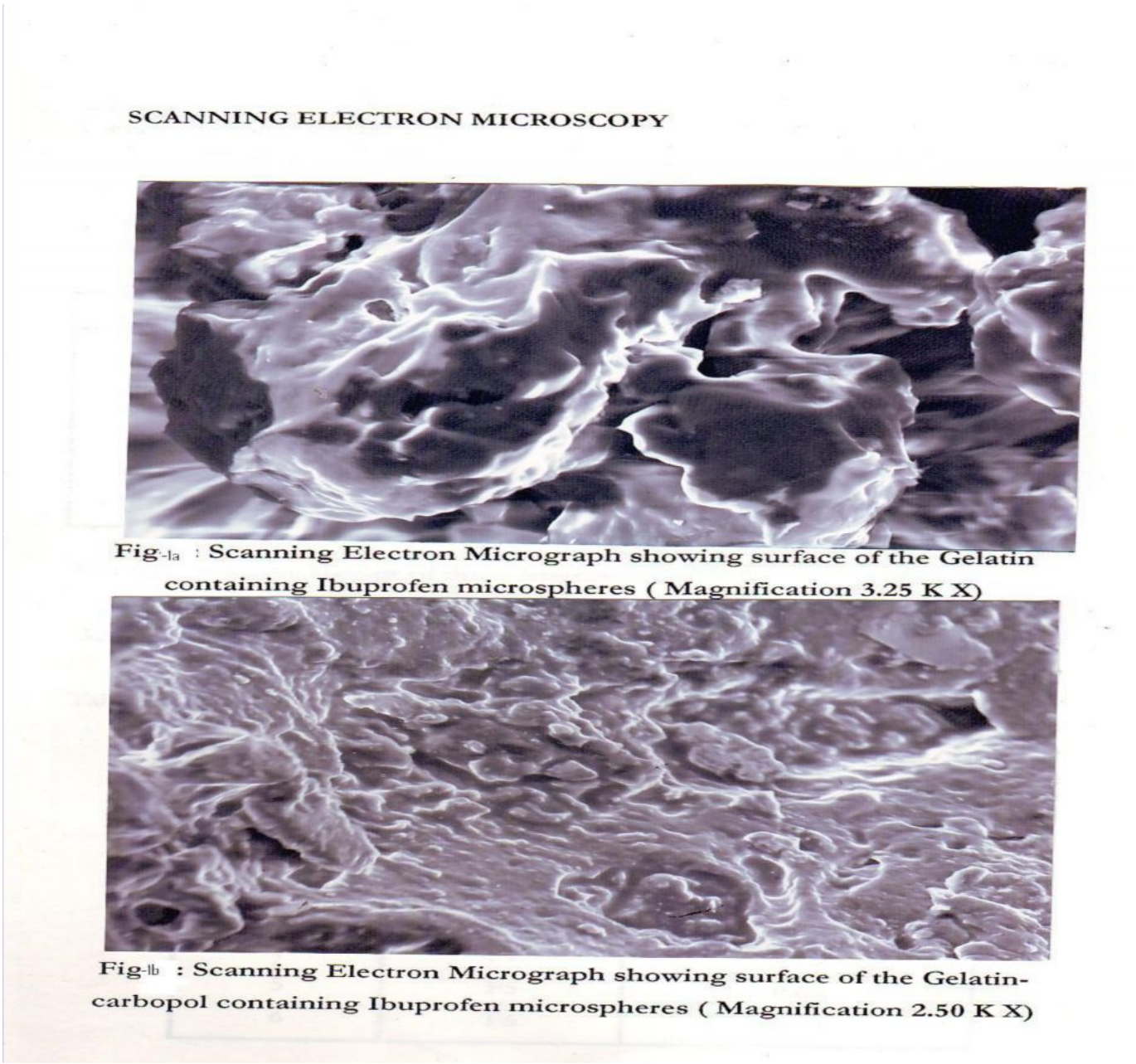


Fig-Ia : Scanning Electron Micrograph showing surface of the Gelatin containing Ibuprofen microspheres (Magnification 3.25 K X)

Fig-Ib : Scanning Electron Micrograph showing surface of the Gelatin-carbopol containing Ibuprofen microspheres (Magnification 2.50 K X)

Table 4 The bulk density of Ibuprofen Micro spheres.

S.no	Batch no	Bulk density (gm/ml)
1	F1	0.68
2	F2	0.73
3	F3	0.84
4	F4	0.75
5	F5	0.66
6	F6	0.93

Table 5 The dissolution study of Ibuprofen Micro spheres.

S.no	Time intervals (hr)	Percentage release of drug					
		F1	F2	F3	F4	F5	F6
1	0.5	11.3	9.2	8.8	13.8	11.3	12.5
2	1	25.0	18.3	12.5	21.3	20.0	16.3
3	2	55.0	44.5	31.3	43.8	45.0	33.8
4	3	71.3	63.7	53.8	66.3	68.8	56.3
5	4	78.8	67.3	58.8	76.3	73.8	62.5
6	5	81.3	72.5	61.3	80.0	75.0	65.0
7	6	82.5	76.0	62.5	81.3	76.3	66.3
8	7	83.8	78.3	65.0	82.5	77.5	67.5
9	8	85.0	81.5	66.3	83.8	80.0	68.8

Determination of bulk density:

Bulk density was determined by transferring known quantity of Micro spheres to 50ml measuring cylinder and tapping 100 times from 1 inch at 2 sec interval. The bulk density of Micro spheres was given in table 4.

In-vitro release study:

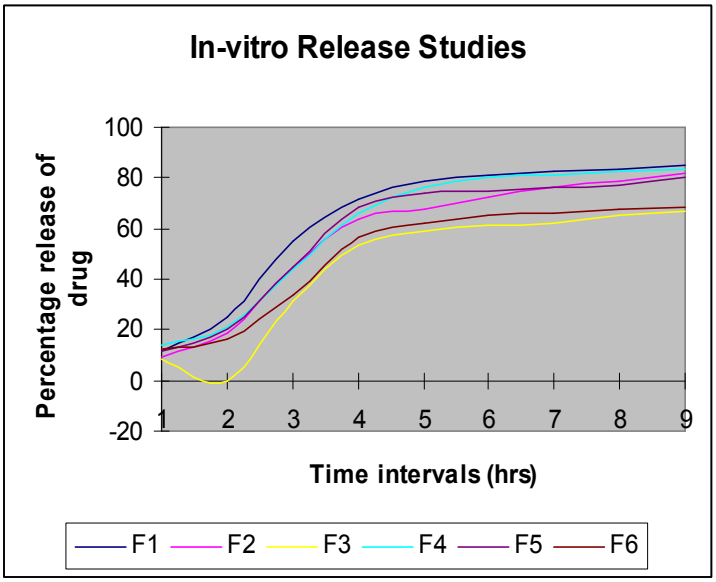
In-vitro release study was carried out by using basket method of dissolution at 50 rpm in 37º ± 0.5º C using phosphate buffer (PH 7.4) as dissolution medium. The samples were estimated at 264nm by using Uv-visible spectrometer, the amount of drug released was interpreted from the calibration curve. The results were given in table 5 & the plots were shown in fig 2.

Discussion:

The particle size of Micro spheres were ranged between 60.8µm-78.5µm.It was mentioned in table2.The shape of the Micro spheres shows rough surface and presence of drug particles even on this surface. It was evidenced from Scanning Electron micrographs (SEM). It was shown in fig 1.The prepared Ibuprofen Micro spheres were subjected to the measurement of flow properties by determining angle of repose and the results indicate good flow property. The results was shown in table 3.The prepared Ibuprofen Micro spheres were subjected to bulk density test and the results indicates good packing property. The results were given in table 4.The in-vitro

dissolution profile of gelatine containing Ibuprofen Micro spheres in Phosphate buffer PH7.4 showed that Micro spheres with low amount of gelatine released 85.0%(F1) of Ibuprofen after 8hrs while Micro spheres prepared with high amount of gelatine released only 66.3%(F3)0f Ibuprofen. The in-vitro dissolution profile of gelatine-carbopol containing Ibuprofen Micro spheres in Phosphate buffer PH7.4 showed that Micro spheres with high amount of carbopol were most effective in showing down the drug release 68.8%(F6),while the Micro spheres containing high amount of gelatine were released 83.8%(F4) of Ibuprofen.

Fig 2 Dissolution Profile of Ibuprofen Micro spheres at 37ºC in Phosphate buffer (PH 7.4).



Conclusion:

The Micro encapsulation of Ibuprofen with gelatine and gelatine –carbopol by co-acervation phase separation technique utilizing temperature change and cross linking with formaldehyde, was able to sustain the drug release efficacy. The Micro spheres having core: coat ratios (F1&F4) provides the best sustained release formulations and other formulations (F2, F3, F5 & F6) may be suitable for prolonged action formulations. These studies compared the release behaviour of gelatine and gelatine –carbopol controlled release system of Ibuprofen. The gelatine (F1) Micro spheres preparation had exhibited suitable pronounced sustained release effect with in this period of time. The F3 & F6 formulations had less pronounced sustained release effects compared with other formulations. The two carbopol formulations (F4 & F5) displayed almost similar release behaviour, while gelatine formulation displayed a different and most distinct behaviour, finally all the Micro spheres were able to control the drug release, but Micro spheres containing gelatine (F3) and gelatine – carbopol mixture (F6) was most effective in slowing down the drug release.

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