
Characterization of Ibuprofen Loaded Microcapsules Prepared by Ionotropic Gelation

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Calcium-induced freeflowing, spherical, smooth surfaced alginate microcapsules of ibuprofen were prepared by ionotropic gelation method. The preparation is based on dispersion of sodium alginate-ibuprofen mixture in liquid paraffin followed by incuring coating process by calcium chloride as curing agent. Sodium alginate concentrations influenced the mean diameter, recovery, encapsulation efficiency, wall thickness, size distribution and release characteristics of the microcapsules. SEM, Polarising microscopy, powder x-ray analysis and IR spectral analysis of microcapsules were also conducted.

MICROENCAPSULATION has become a common technique in the production of controlled release dosage forms. A great deal has been written by scientists concerning current applications and future possibilities for altering activities action and stabilities of drug substances by packing in microcapsules.¹⁻²¹ When preparing microcapsules one must take into account the total system involving the original capsule, the mechanism of release and the ultimate fate of all ingredients. By optimizing the positive qualities and minimizing the deficiencies of the system, one may design a viable composition.

In the present study attempt was made to prepare calcium induced alginate microcapsules of ibuprofen by ionotropic gelation procedure.

EXPERIMENTAL

Materials: Ibuprofen I.P. (Kee Pharma), Sodium alginate I.P., Light liquid paraffin (18 cps at 30°C), Calcium chloride I.P. and Dipotassium hydrogen phosphate I.P.

PREPARATION OF MICROCAPSULES

Method: Four batches of microcapsules (MCI, MCII, MCIII, MCIV) were prepared. To 100 ml of

Sodium alginate (1-4% w/v) in distilled water at 25°C, 2.0g of ibuprofen was added and thoroughly mixed. The mixture was kept at 25°C. Separately 200 ml of Light liquid paraffin was placed in silicone treated round bottom flask and kept at 25°C. Sodium alginate ibuprofen (86.90 µm) suspension was poured into the Liquid paraffin and stirred with a four bladed propeller at 2000 rpm for 10 minutes. To this dispersion 100 ml of 3% w/v solution of calcium chloride was added slowly. Stirring was continued at 25°C for 20 minutes. Solidified microcapsules were recovered by filtration, washed with petroleum ether followed by water and dried under vacuum. Various size fractions were separated by sieving.

Ibuprofen content: Microcapsules (50 mg) accurately weighed were suspended in 100 ml phosphate buffer (pH 7.2) and the suspension was homogenized. Ibuprofen content in the filtrate was analyzed spectrophotometrically at 221 nm after proper dilution.

Dissolution studies: *In vitro* release profiles of ibuprofen from microcapsules were examined in phosphate buffer (pH 7.2) by rotating basket method specified in USP XXII at 100 rpm using 900 ml of test fluid maintained at 37°C ± 1°C. Microcapsules

containing a given amount of Ibuprofen were accurately weighed and placed in the fluid. At suitable intervals, 3 ml aliquot was removed. Then 3 ml of fresh test fluid was added to maintain the original volume. Concentrations of Ibuprofen were determined spectrophotometrically at 221 nm. Dissolution results are reported in the table.

Micromeritics Studies: Microcapsules were investigated for particle size, mean diameter and wall thickness. The particles' size and their distribution were measured by a sieve method. Results are reported in the table.

Infrared Spectroscopy: IR spectra of microcapsules (MCII) as KBr pellets were recorded using infrared spectrophotometer, SHIMADZU (Fig.2).

Power X-ray Diffractometry: Powder X-ray diffraction patterns of microcapsules (MCII) were recorded using X-ray diffractometer, PHILIPS PH1130/00 in 2 theta range of 10° - 40° at scanning speed of 1° /minute. Chart speed 10 mm/minute and range 1×10^3 cps. Diffractograms are shown in Fig.3 (a-c)

Polarising Microscopy: Photomicrographs of microcapsules were taken at magnification eyepiece 12.5 x lens 2.5 and camera factor 0.32X.

Scanning Electron Microscopy: The surface topography of microcapsules was investigated with scanning electron microscopy using PHILIPS instrument (Model 515) after coating micro capsules with Palladium/Gold with following conditions: Potential applied 10.1 KV, Magnification:300X and measuring scale 0.1 mm.

RESULTS AND DISCUSSION

Chemical reaction between Sodium alginate and Calcium chloride to form calcium alginate was utilized for the microencapsulation of of Ibuprofen core material. Preliminary work on preparation of

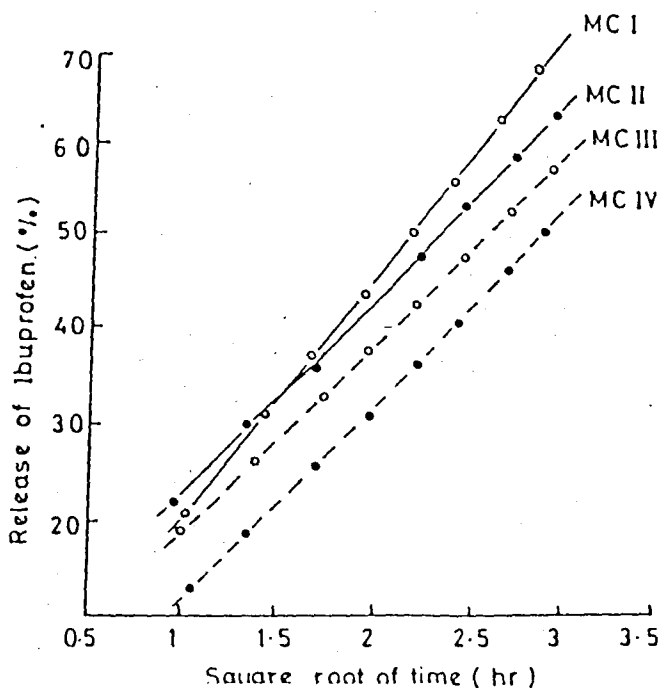


Fig. 1: Higuchian plot of % Ibuprofen released as a function of square root of time.

microcapsules revealed that stirring speed and time greatly affected the size of microcapsules. Stirring at 2000 rpm for 20 minutes formed small spherical microcapsules and was maintained throughout the preparation of microcapsules.

It was found that sodium alginate concentration influence the microcapsules size, average diameter, recovery, encapsulation efficiency, wall thickness, size distribution and the release characteristics. The total yields of microcapsules obtained were between 89.65% to 95.62%. Microcapsules with particle size of 40 to 450 μm accounted for about 81.30 to 94.35% of the total product prepared by this microcapsulation procedure. Results of particle-size distribution (Table) show that microcapsules prepared in this study are distributed in a relatively narrow range of diameter (40 to 450 μm). Average diameter was between 165.8 to 260.85 μm .

The drug entrapment in microcapsules was found to be good (Range 87.2 to 95.3%) with all concentrations of Sodium alginate. The mean diam-

Table : FORMULATION, MICROMERITICS & DISSOLUTION PROPERTIES OF MICROCAPSULES

Batch No.	Ibuprofen (g)	Sodium Alginate (g)	Mean Particle Dia (μm)	Wall Thickness (μm) of Microcapsules in the size range 40-450 μm	Percent yield of Microcapsules range 40-450 μm	Drug Incorporation efficiency (%)	Dissolution percent ibuprofen released	
							After 1hr	After 8 hr
MC I	2	1	165.8	19.43	90.25	92.72	23.45	68.36
MC II	2	2	189.51	24.74	94.35	95.30	21.421	62.80
MC III	2	3	212.71	36.81	85.45	94.00	20.32	57.35
MC IV	2	4	260.85	54.48	81.30	87.20	14.35	51.25
PURE DRUG (Ibuprofen)	—	—	86.90	—	—	—	—	—
					SD \pm 3.09			SD \pm 0.73

Batch No.	MSR in μm	Cumulative percent (oversize) frequency per mean size range (MSR)		
		(43.5)	(101.5)	(159.5)
MC I	6.25	28.75	75.0	88.0
MC II	6.25	16.25	59.25	80.5
MC III	8.75	19.27	34.25	66.75
MC IV	3.75	11.25	21.25	41.75
PURE DRUG (Ibuprofen)	MSR in μm	(85)	(87)	(116)
	11.25	30.0	71.50	89.0
				(145)
				100.0
				100.0
				100.0
				93.75
				86.25
				—
				—

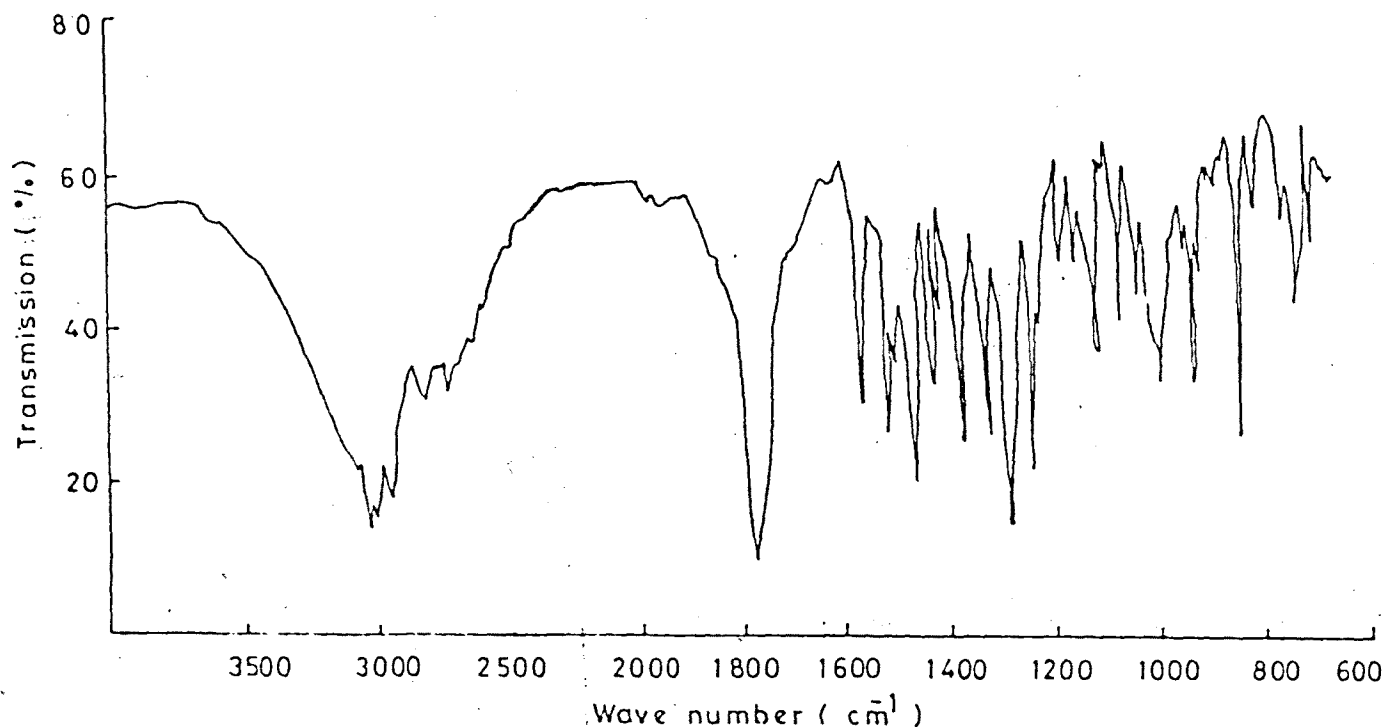


Fig. 2: Infrared spectra of microcapsules

eter and wall thickness of microcapsules increased with the increase in concentration of Sodium alginate (Table).

Dissolution of Ibuprofen from microcapsules after 1 hr and 8 hrs are tabulated in the Table. Results of investigation revealed that drug release rate from microcapsules is controlled by wall thickness. Release of Ibuprofen from microcapsules after 1 hr and 8 hrs decreased with the increase in wall thickness. Release of Ibuprofen from microcapsules after 1 hr and 8 hrs is between 14.35% to 23.45% and 51.24% - 68.36% respectively. $T_{50\%}$ release is between 7.80 to 5.85 hrs. The data reported according to Higuchi model for microcapsules showed linear relationship over a wide range. (Fig.1)

Powder X-ray analysis and infrared analysis of microcapsules indicated that Ibuprofen was unchanged in its physico chemical properties such as crystalline form and crystallinity without interaction between Ibuprofen and Sodium alginate (Fig.3)

Polarising photomicrographs of microcapsules revealed the crystalline form of Ibuprofen and

microcapsules surface. Microcapsules were nearly spherical. The surface topography of microcapsules was investigated by SEM. The microcapsules were nearly spherical and their surface was rough up to drug content of 95.30%. With increasing concentration of Sodium alginate the surface of microcapsules becomes smooth.

CONCLUSION

In conclusion the proposed method is simple, rapid and can directly produce controlled release microcapsules. It allows high drug loading and does not change the physical properties of drug. The method can easily control the diameter of microcapsules as desired irrespective of size and shape of crystal of drug to be encapsulated.

From the investigation of results it was concluded that MCI batch is most satisfactory microcapsules with regard to recovery (95.62%), encapsulation efficiency (94.35%) mean diameter (189.51 μm) and release rate (62.80%) after 8 hours.

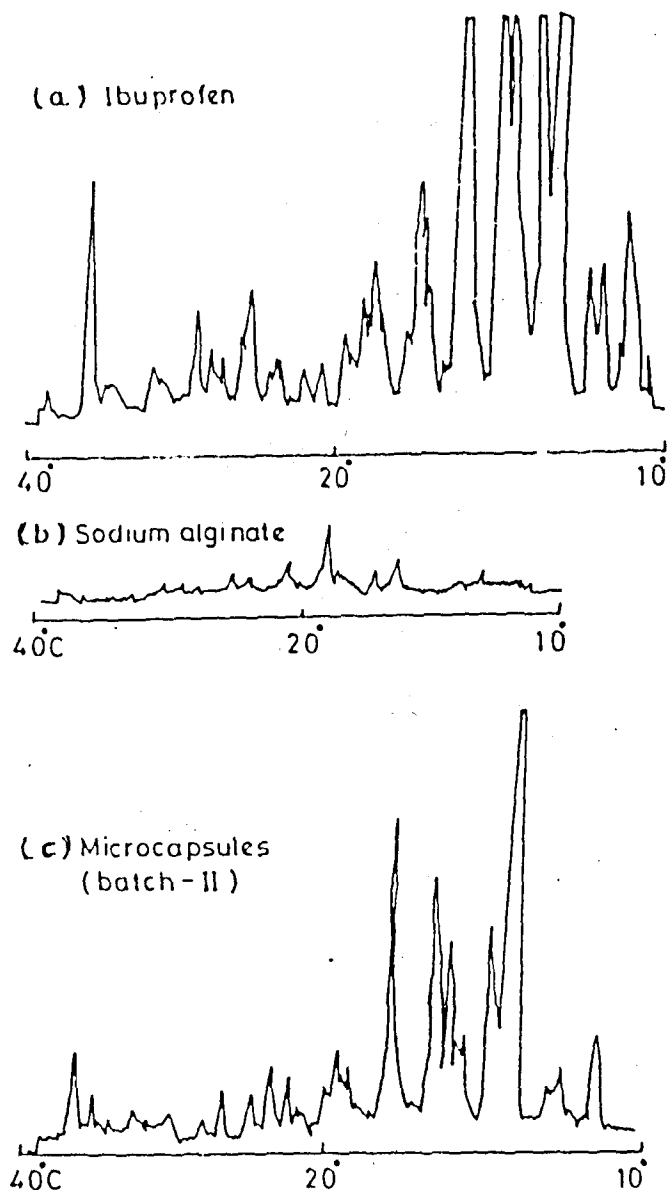


Fig. 3(a-c): x-ray diffractogram of (a) Ibuprofen, (b) sodium alginate and (c) microcapsules (batch-II)

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