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FORMULATION AND EVAUATION OF SUSTAINED RELEASE MATRIX TABLET OF IBUPROFEN

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ABSTRACT

The present work was focused to formulate and evaluate sustained release matrix tablets of ibuprofen. Sustained release matrix tablets of ibuprofen was prepared by using different concentration of hydroxypropyl methyl cellulose and ethyl cellulose are matrix polymers. Ibuprofen was slightly soluble drug. Sustained release matrix tablets was prepared by wet granulation method in different polymer concentration ratio. Preformulation studies have been performed for the active pharmaceutical ingredients. Tablets have been prepared in four different formulation(F1-F4) with change in the concentration of polymers. These tablets are evaluated for various parameters weight variation test, hardness, thickness, in- vitro dissolution studies. Higher level of polymer concentration formulation(F3) shows good in vitro drug release was 96% and all the evaluation parameters are takes place within the limit.

KEYWORD: Ibuprofen, matrix tablets, polymers, sustained release.

INTRODUCTION

Sustained release matrix tablet

Sustained release, sustained action, prolonged action, controlled release, extended action, timed release and depot dosage form as term used to identify drug delivery system that are designed to achieve prolonged therapeutic effect by continuously releasing medication over an extended period of time after administration of a single dose2.[1] A matrix system consists of active and inactive ingredients that are homogeneously dispersed and mixed in the dosage form. It is by far the most commonly used oral extended release technology and the popularity of the matrix systems can be attributed to several factors.[2]

MATERIAL AND METHOD

Materials

Ibuprofen was gifted from Strides Arcolab's Ltd**,** hydroxypropyl methyl cellulose, ethyl cellulose, IPA, Eudragit s 100, Magnesium stearate, Talc was purchased from Shree ji chemicals and N P chemicals Bombay. 0.1 N Hcl and phosphate buffer pH 7.4 were prepared as described in the Indian pharmacopoeia.

Methods[3]

Ibuprofen sustained release matrix tablets were prepared by wet granulation technique. The granules were compressed into tablets on 16 station rotary tablet compression machine using 11 mm round, biconcave punches. The compressed tablets were evaluated for various parameters viz. appearance, thickness, diameter, hardness, friability, weight variation, drug content and *in vitro* drug release studies.

composition of ibuprofen matrix tablets

Ingredients	F1	F2	F3	F4
Ibuprofen	200	200	200	200
HPMC k 100M	40	-	-	-
Ethyl cellulose	-	80	-	-
HPMC + EC	-	-	120	40
IPA +EUDRAGIT S 100	q.s	q.s	q.s	q.s
Lactose	150	110	70	150
Magnesium stearate	5	5	5	5

Talc	**5**	**5**	**5**	**5**
Total weight	**400**	**400**	**400**	**400**

Evaluation of granules

Angle of repose[4]

The angle of repose of granules was determined by the funnel method. The accurately weighed granules were taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touched the apex of the heap of the granules. The granules were allowed to flow through the funnel freely onto the surface. The diameter of the granules cone was measured and angle of repose was calculated using the following equation.

$$\tan \theta = h/r$$

Where, h and r are the height and radius of the granules cone respectively.

Loose bulk density[5]

An accurately weighed granules from each formulation was lightly shaken to break any agglomerates formed and it was introduced in to a measuring cylinder. The volume occupied by the granules was measured which gave bulk volume. The loose bulk density of granules was determined using the following formula.

Loose bulk density = Total weight of granules / Total volume of granules

Tapped bulk density

An accurately weighed granules from each formula was lightly shaken to break any agglomerates formed and it was introduced into a measuring cylinder. The measuring cylinder was tapped until no further change in volume was noted which gave the tapped volume. The TBD of granules was determined by the following formula.

Tapped bulk density = Total weight of granules/ Tapped volume

Hausner ratio[6]

Hausner ratio is the ratio between tapped density and bulk density. Hausner ratio less than 1.25 indicates good flow properties while Hausner ratio greater than 1.25 shows poor flow of granules.

Carr's compressibility index

It is a simple index that can be determined on small quantities of granules. In theory, the less compressible a material the more flowable it is. The compressibility index of the granules was determined using following formula.

Carr's compressibility index (%) = [(TBD-LBD)/ TBD] ×100

Evaluation of sustained release matrix tablets[7]

For weight variation, 20 tablets of each type of formulation were weighed individually on an electronic balance, average weight was calculated and individual tablet weight was then compared with the average value to find out the deviation in weight.

Hardness

For each type of formulation, the hardness value of 10 tablets was determined using Monsanto hardness tester.

Percentage friability[8]

Friability is the measure of tablet strength. This test subjects a number of tablets to the combined effect of shock abrasion by utilizing a plastic chamber which revolves at a speed of 25 rpm, dropping the tablets to a distance of 6 inches in each revolution. A sample of preweighed tablets was placed in Roche friabilator which was then operated for 100 revolutions. The tablets were then dedusted and reweighed. A loss of less than 1 % in weight is generally considered acceptable.

In-vitro dissolution studies[3]**:** The *in-vitro* dissolution studies were performed using USP type I dissolution apparatus at 50rpm. Dissolution test was carried out for a total period of 8 hours using0.1N HCl (pH 1.2) solution (900 ml) as dissolution medium at 37 ± 0.5° for first 2 h, and pH 7.4 phosphate buffer solution (900 ml) for the rest of the period An aliquot(5ml) was withdrawn at specific time intervals and absorbance was determined by U.V. spectrophotometer at 274nm. The release studies were conducted in triplicate.

RESULT AND DISCUSSION

Melting point of sample was found to be 76°C by the Thiel's tube method which complied with IP standard, thus indicating the purity of drug. Solubility analysis of ibuprofen was done in different solvent and it was observed sparingly soluble in water, slightly soluble in methanol. Ethanol, soluble in 0.1N HCl and phosphate buffer pH 7.4. In 0.1N HCl: The absorption maximum for Ibuprofen was found to be 220.5 nm. In Phosphate buffer pH 7.4: The absorption maximum for Ibuprofen was found to be 222 nm. The blended granules of different formulation were evaluated for angle of repose, loose bulk density, tapped bulk density, compressibility index and Hausner ratio. Angle of repose ranged from 29.0±0.02 to 30.16±0.04. The results were found to be below 30^{o} and hence the blend was found to have good flowability. (Table 4.3) Bulk and tapped densities are used for the measurement of Compressibility index. (Table 4.3). The compressibility index (%) ranged from 9.07±0.99 to 10.01±0.64 (Table 4.3). The blend was found to have excellent flowing property as the result were found to be below 15%. The Hausner's ratio ranged from 5.06±1.25 to 5.49±0.68 (Table 4.3). The result indicates the free-flowing properties of the granules.

The tablets were observed visually and did not show any defect such as capping, chipping and lamination. The physical characteristic of Ibuprofen sustained release matrix tablets (F1 to F4) such as thickness, diameter, hardness, friability, weight variation and drug content were determined and results of the formulations (F1 to

F4) found to be within the limits specified in official books.

Thickness and diameter specifications may be set on an individual product basis. Excessive variation in the tablet thickness and diameter can result in problems with packaging as well as consumer acceptance. The size (diameter) of the tablets of all formulations was found to be 4.32±0.07to 4.60±0.01mm. A difference in tablet hardness reflects difference in tablet density and porosity. In which turn are supposed to result in different release pattern of the drug by affecting the rate of penetration of dissolution fluid at the surface of the tablet and formation of gel barrier. The hardness of tablets was found to be in the range of 6.32±0.03kg/cm^2 to 6.85±0.02kg/cm^2. This indicates good tablet strength. Percentage friability of all the formulations was found between 0.414±0.07 to 0.679±0.04. This indicated good handling property of the prepared SR tablet.

A tablet is designed to contain a specific amount of drug. When the average mass of the tablet is 400 mg the pharmacopoeial limit for percentage deviation is ±5%. The percentage deviation from average tablet weight for all the tablet was found to be within the specified limits and hence all formulations complied with the test for weight variation according to the pharmacopeial specifications. The content of active ingredients in the formulation was found to be between 98.86±0.07 to 99.98 ± 0.65% w/w, which is within the specified limit as per Indian Pharmacopoeia 1996 (i.e. 90-110% w/w).In vitro release behavior of all formulations is summarized table 4.4. in vitro release was performed by using 0.1 N HCL and phosphate buffer pH 7.4 as medium. The concentration of polymer in the sustained release layer was a key factor in controlling the drug release. Various sustained release formulations were formulated with HPMC K100M, ethyl cellulose, eudragit s 100 as binder and magnesium stearate as a Lubricant. In vitro release studies of formulations F1, F2, F3 and F4 prepared by HPMC K100M with respective concentration. The drug released from formulation F1 to F4 were found to be 93.7%, 93.9%, 96.2% and 94.9% for Ibuprofen respectively. The release rate of F3 was found to be higher when compared to other formulations this is due to increase in the concentration of polymer. The overall release rate of Ibuprofen from ethyl cellulose and HPMC K100M matrices are significantly higher than that from matrices; were shown in Fig no 4.3. These results are indicating that has higher drug retarding ability for long duration than ethyl cellulose and HPMC K100M.

Table 4.1: Standard calibration curve of Ibuprofen in 0.1N HCl.

S. NO	Conc in µg/ml	Absorbance at 220.5 nm			Standard Deviation (S.D)
		Trail 1	Trail 2	Trail 3	
1	0	0	0	0	0
2	2	0.0930	0.0972	0.0894	0.0932±0.03
3	4	0.1765	0.1835	0.1995	0.1865±0.04
4	6	0.2737	0.2893	0.2763	0.2797±0.01
5	8	0.341	0.337	0.441	0.373±0.01
6	10	0.459	0.470	0.468	0.4662±0.07

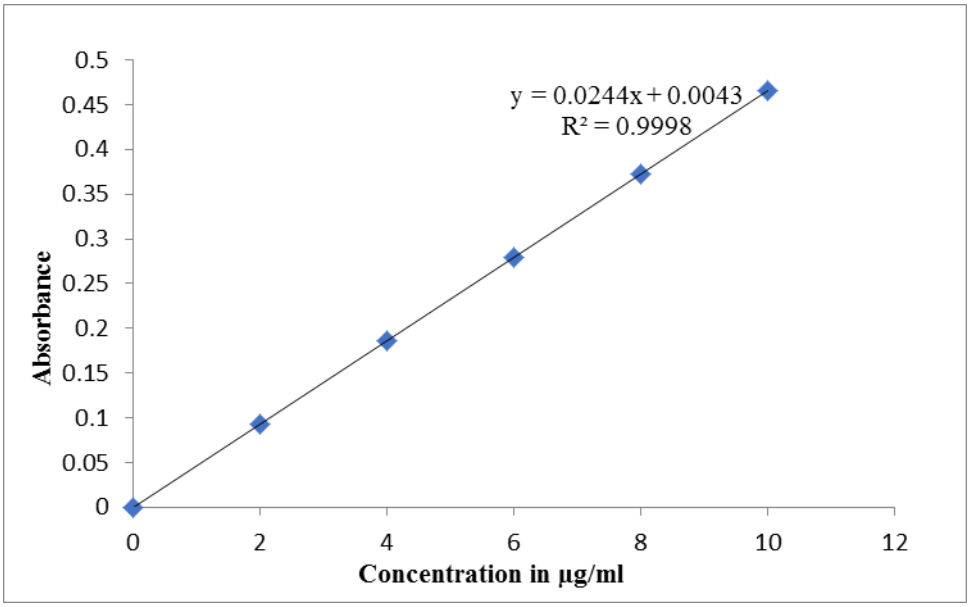

Figure 4.1: Calibration Curve of Ibuprofen in 0.1N HCl.

Table 4.2: Standard calibration curve of Ibuprofen in Phosphate buffer pH 7.4.

S.No	Con (µg/ml)	Absorbance at 272.5 nm			Standard deviation (SD)
		Trial 1	Trail 2	Trail 3	
1	0	0	0	0	0
2	4	0.146	0.163	0.129	0.146±0.02
3	8	0.297	0.273	0.303	0.291±0.06
4	12	0.425	0.460	0.411	0.432±0.06
5	16	0.560	0.525	0.640	0.575±0.08
6	20	0.718	0.701	0.729	0.715±0.01

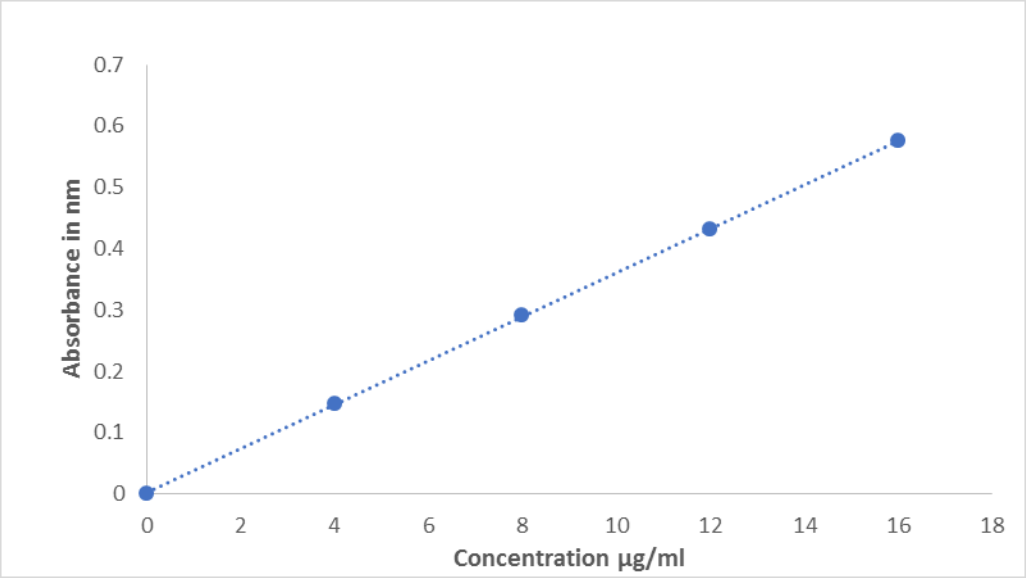

Figure 4.2: Calibration Curve of Ibuprofen phosphate buffer pH7.4.

Table 4.3: Flow properties of granules.

F code	Angle of repose (°)*	Loose bulk density (g/ml)*	Tapped bulk density (g/ml)*	Carr's index (%)*	Hausner's ratio*
F1	30.16±0.04	0.26±0.19	0.29±0.19	9.717±0.22	5.44±0.19
F2	30.22±1.76	0.61±0.50	0.53±0.36	10.01±0.64	5.49±0.68
F3	29.31±1.32	0.55±0.20	0.40±0.27	9.167±0.56	5.26±1.26
F4	29.0±0.02	0.53±0.54	0.35±0.23	9.072±0.99	5.06±1.25

Table 4.4: Physico-Chemical Characterization of Ibuprofen SR Tablets.

F code	Thickness (mm)*	Hardness (kg/cm^2)*	Friability (%)	Weight variation (mg)	Drug content (%w/w)**
F1	4.44±0.02	6.32±0.03	0.679±0.04	398.25±0.04	99.86±0.02
sF2	4.54±0.05	6.54±0.01	0.514±0.05	397.06±0.08	99.65±0.01
F3	4.32±0.07	6.85±0.02	0.414±0.07	398.55±0.03	99.98±0.06
F4	4.60±0.01	6.36±0.09	0.655±0.01	396.55v0.08	98.86±0.07

Table 4.5: Invitro dissolution study of F1-F4.

Time in (h)	F1	F2	F3	F4
0	0	0	0	0
2	15.2	28.4	30.1	28.9
4	57.2	53.2	45.6	44.2
6	93.1	74.6	64.7	69.8
8	93.4	93	77.2	94.7
10	93.7	93.9	96.2	94.9

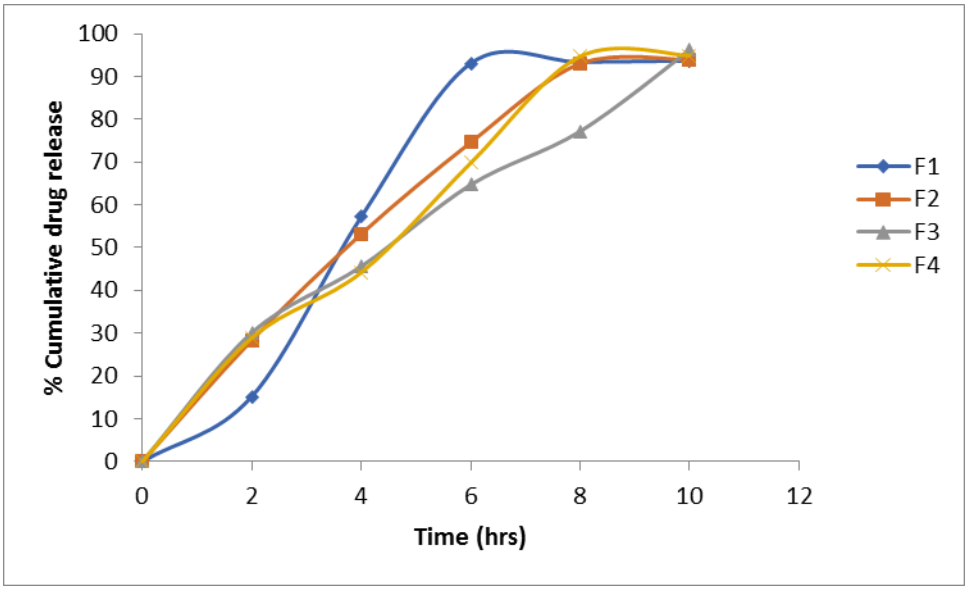

Fig.4.3: % cumulative drug release of formulation F1-F4.

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