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PREPARATION AND EVALUATION OF ORAL EXTENDED RELEASE TABLET OF IBUPROFEN FOR BETTER EFFICACY

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ABSTRACT

Sustained-release matrix tablets of Ibuprofen was developed that help in releasing only small quantities of drug over a prolonged period of time,with the use of various hydrophilic polymers for their sustaining effect. Preparation of garnual and then after tablet preparation we find that there is good behaviour shown by the formulation and the best result is evaluated further for the study.

Introduction

Oral medication conveyance is the most broadly appropriate route among every single other route, for example, nasal, ophthalmic, rectal, transdermal and parenteral routes. It has been investigated for systemic transport of drug through different pharmaceutical products of a dissimilar dosage form. The oral course is viewed as most regular, uncomplicated, advantageous and safe because of its simplicity of administration, and patient consistence. Dominant part of the pharmaceutical items intended for oral conveyance are prompt discharge or conventional release system for fast medicine captivation [1].Controlled drug

delivery system has been established which are able to controlling the rate of drug delivery, supporting the extent of therapeutic activity or potentially focusing on the delivery of medication to a tissue [2]. Controlled drug delivery or altered drug delivery systems are suitably partitioned into four classes: delayed release, sustained release, site-specific targeting, receptor targeting.Ibuprofen is a Biopharmaceutics Classification System (BCS) class II drug with low solubility at pH 1.2 and 4.5 and high solubility at pH 6.8 and has a pKa value of 4.5 & it is poorly soluble in water (0.078 µg/ml). [3]. Ibuprofen is selected for the development of once daily sustained release matrix tablets because it is reported to have a short biological half-life (3.4 ± 0.7 h) requiring it to be administered in 100mg twice daily [4]. The basic goal of therapy is to achieve a steady state blood or tissue level that is therapeutically effective and non-toxic for an extended period of time. Sustained release drug delivery systems, with an aim of improved patient compliance, better therapeutic efficacy, less side effects and reduced dosage regimen with less toxicity for treatment for many acute and chronic disease.

Materials

Ibuprofen, HPMCK15M, Guar Gum, Lactose, PVP K30, IPA, Talc, Magnesium stearate, etc. all chemicals are procured from sigma Aldrich and they are of synthesis grade.

Methodology

Different parameters involved in developing sustained release matrix tablet are described in this section.

Preparation method of tablet

The constant amount of drug was weighed and passed through sieve no.40. The equivalent amounts of polymers (HPMC/ guar gum), lactose was weighed, screened through screen

sieve no.40. The screened mass was transferred into a clean and dry mortar and mixed gently for 5 min and alcoholic solution (IPA) of PVP K 30 (5% w/v) was gradually added to the powder mixture and blended to form a wet mass. The wet mass was passed through sieve no. 10 to form granules and resulting granules were placed on a tray for drying into the oven at 50 ^{o}C for 10 min. The dried granules were passed through sieve no. 18. corresponding amount of magnesium stearate and talc were weighed and mixed with granules for 3 min. The evaluation of granules showed excellent flow properties. 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. [5].

Table 1 Composition of the sustained release matrix tablets containing Aceclofenac.

Ingredients (mg)	**Formulation code**								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Ibuprofen	250	250	250	250	250	250	250	250	250
HPMCK15M	60	110	160	210	-	-	-	-	-
Guar Gum	-	-	-	-	60	120	160	210	110
Lactose	210	160	110	60	210	160	110	60	60
PVP K30	30	30	30	30	30	30	30	30	30
IPA	q. s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
Talc	25	25	25	25	25	25	25	25	25
Magnesium	10	10	10	10	10	10	10	10	10

Micromeretic characterization of granules

Determination of bulk density

Mass (M) of the powder divided by the bulk volume (Vb) gives Bulk density which expressed as g/cm3 and depends on particle size distribution, particle shape and particles adhere. Apparent bulk density (ρb) was determined by pouring the blend into a 10 ml graduated cylinder [6]. The bulk density was calculated using folowing formula:

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

Determination of tapped density

Tapped density was measured by a measuring cylinder containing a known mass (M) of powder blend and was tapped 100 times using density apparatus. The minimum volume (Vt) occupied by the powder in the cylinder was measured. The tapped density (ρt) was calculated using the formula [7]:

Tapped density = Total weight of granules/ Tapped volume.

Determination of angle of repose

Angle of repose was determined using funnel method, powder blend was poured through a funnel which raised vertically a maximum cone height (h) [8]. Radius of the heap (r) was measured and angle of repose (θ) was calculated using the formula:

$$\boldsymbol{tan}\theta = \boldsymbol{h/r}$$

The values of angle of repose indicating flow properties have been recommended as <25 indicating excellent flow, 25-30 indicating good flow, 30-40 indicating passable, and value >40 indicated very poor flow of the powered material.

Determination of compressibility index

Compressibility index is the simplest way for measurement of flow property of powder to determine its compressibility. It is an indication of the ease with which a material can persuaded to flow which is calculated using following equation:

Carr's compressibility index (%) = [(Tapped Density -Bulk Density)/ Tapped Density] ×100

The values of compressibility index indicating flow properties have been recommended as <12 indicating excellent flow, 12 – 16 indicating good flow, 18 – 21 indicating fair to passable, 25 – 35 indicating poor, 33 – 38 indicating very poor, and value > 40 indicated extremely poor flow of the powered material.

Evaluation of tablets

Examination of tablet appearance

Randomly twenty tablets of each preparation were taken and studied for physical or surface roughness in the tablets [9].

Determination of tablet thickness

Tablet thickness is an important parameter in reproducing appearance and also in counting by suing filling equipment, many tablet filling/ packaging equipment utilizes the uniform thickness of the tablets as a counting mechanism [10]. In present study, 10 tablets were randomly selected and their thickness was recorded using micrometer (Mityato, Japan).

Determination of uniformity of weight

The weight variation method of determining the drug content uniformity would be satisfactory, U.S.P procedure for uniformity of weight was followed. The allowed weight variation limits are 10%, 7.5% and 5% for tablets having weight 130 mg or less, 130-324 mg and > 324 mg, respectively. 20 tablets were taken & weighed individually using a digital weighing balance and average weight of one tablet was determined from the collective weight [11].

Determination of tablet hardness

The resistance of tablet to chipping, abrasion or breakage under condition of storage, transportation, and handling before use depends on its hardness or strength [12]. Hardness of tablet is the force applied across the diameter of the tablet in order to break it, 10 tablets from each batch were randomly selected and hardness was determined using Monsanto tablet hardness tester.

Determination of tablet friability

Friability of the prepared tablets was determined using Roche friabilator. Tablets were subjected to the combined effect of abrasions and shock in a plastic chamber revolving at 25 rpm and dropping the tablets at a height of 6 inch in each revolution. 20 tablets were weighed earlier & placed in the friabilator subjected to 100 revolutions . Tablets were de-dusted using a soft muslin cloth and re-weighed, percentage friability was determined using following formula [13]:

$$\%F = 1 - \frac{Wo}{W} \times 100$$

where, initial weight(Wo) is weight of the tablets before the test, final weight(W) is the weight of the tablets after test.

Determination of drug content

From each batch six tablets were weighed and finely powdered using clean and dry mortar and pestle. Powder equivalent to the weight of one tablet was transferred to volumetric flask of 100 ml and shake with 60 ml of phosphate buffer (pH 6.8) for 10 min. The volume of resulting solution was made up to 100 ml and kept for 24 h. After 24 h, the content was filtered, an aliquot of 1.0 ml from the filtrate was diluted to 100 ml with phosphate buffer pH 6.8 in volumetric flask and then further 1 ml from this solution were diluted up to 10 ml with phosphate buffer (pH 6.8) [14]. The sample was analyzed by a UV spectrophotometer (LabIndia 3000+, Mumbai, India) at 273 nm.

Result and discussions

Micromeritic properties

The flow property of prepared granules was estimated based on different micromeritic properties. The bulk density and tapped density was determined using USP bulk density apparatus and the results were represented in Table 1.

Formulation code	Bulkdensity (g/cm^3)	Tapped density(g/cm^3)	Compressibility Index(%)	Angleofrepose (□)
F1	0.538±0.004	0.613±0.008	14.2±0.36	34.50±0.576

F2	0.628±0.006	0.597±0.003	14.60±0.638	35.00±0.137
F3	0.567±0.029	0.362±0.03	19.66±1.531	26.05±0.230
F4	0.581±0.090	0.661±0.016	14.92±0.130	26.40±0.43
F5	0.611±0.005	0.544±0.005	12.84±0.138	25.10±0.134
F6	0.423±0.029	0.529±0.012	12.0±1.012	29.48±0.910

Evaluation of tablet

The tablets were evaluated for weight variation, thickness, hardness, friability drug content and *in vitro* drug release profiles. Weight variation data indicates no significant difference in individual tablet weight from the average weight (550.333±0.577 to 552.33±0.577). Tablet hardness was observed within the range of 3.73±0.115 to 3.92±0.200 kg/cm^2 with uniform thickness ranges from 3.38±0.004 to 3.41±0.008. Friability of all the formulations was below 1%, which indicates good mechanical strength of the tablets. Table 2.

Formulation code	**Weight(mg)**	**Thickness(mm)**	**Hardness(kg/cm^2)**	**Friability (%)**	**Drug Content (%)**
F1	550.33±0.577	3.38±0.035	3.82±0.115	0.41	98.89
F2	551.67±0.535	3.39±0.010	3.74±0.200	0.53	99.53
F3	550.67±1.528	3.40±0.005	3.85±0.115	0.73	96.02
F4	552.33±0.577	3.39±0.006	3.92±0.200	0.65	98.09
F5	550.68±0.438	3.38±0.008	3.90±0.115	0.43	97.30

F6	551.33±1.155	3.40±0.012	3.73±0.120	0.59	100.01

Determination of *in-vitro* dissolution profile

The *in vitro* dissolution studies were carried out in USP tablet dissolution test apparatus, Type 1 (Basket type) using Phosphate buffer (pH 6.8) 900 ml, as dissolution medium, temperature of dissolution medium was maintained at 37±0.5□C, rotation 75 rpm and studies were carried out for 24 h. Sample (5 ml) was withdrawn at a predetermined interval for 24 h & sink condition was maintained by adding same volume of fresh dissolution medium after each sampling. The samples were diluted with phosphate buffer (pH 6.8) at suitable volume and the absorbance was recorded at 273.5 nm using UV-VIS spectrophotometer (LabIndia 3000^{+}, Mumbai, India) [14].

Estimated values of diffusional exponent (n) and correlation coefficient (r^2) from the dissolution data of Ibuprofen in phosphate buffer, pH 6.8. Table 3.

Formulation	Zero Order (r^2)	First Order(r^2)	Higuchi's model (r^2)	Peppas' model	
				(r^2)	n
F1	0.9711	0.9118	0.9973	0.9813	0.612
F2	0.9709	0.8666	0.9964	0.9674	0.598
F3	0.9687	0.8412	0.9959	0.9784	0.632
F4	0.9770	0.8204	0.9957	0.9809	0.618

F5	0.9771	0.8070	0.9934	0.9712	0.545
F6	0.9718	0.8296	0.9950	0.9778	0.625

Discussion

In this work an attempt was made to formulate and evaluate sustained release matrix tablets of Ibuprofen to maintain the plasma drug concentration constant for the whole day. It also helps in decreasing the dosing frequency by which the patient compliance increases. Iuprofenhas a very short half life ($t_{1/2}$ □ 1.8 h), so in case of conventional tablets ibuprofen dosing frequency is more. Plasma drug concentration can't be maintained at the therapeutic levels for a longer period of time of drugs with short half -life, to decrease the dosing frequency and increase the patient compliance sustained release matrix tablets were formulated.

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