FORMULATION AND EVALUATION OF MATRIX TABLET OF IBUPROFEN

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ABSTRACT

The purpose of the study was to prolong the gastric residence time and increase the bioavailability of Ibuprofen by designing its matrix tablets and to study the influence of different polymers on its release rate. The tablets were prepared by wet granulation technique, using different polymers such as hydroxy propyl methyl cellulose (HPMC K4M and ethyl cellulose and other standard excipients. The physical characteristics of tablets were evaluated viz. hardness, thickness, weight variation tablets were evaluated for *in-vitro* drug release characteristics for 9 hr.

KEYWORDS: Ibuprofen, HPMC K4M, Ethyl cellulose.

INTRODUCTION

Drug delivery system is become increasingly sophisticated as pharmaceutical scientists acquire a better understanding of physicochemical and biological parameters pertinent to their performances. The oral route of drug administration is the most important method of drug administration. Parenteral route is routinely used for self administration of medication. Topical route of administration is limited in its ability to allow effective drug absorption for system drug action. It is probable that at least 90% of all drugs used to produce systemic effect are administered by oral route. When new drug is discovered, one of the first question a pharmaceutical company, ask is whether or not the drug can be effectively administered for its intended effect by the oral route. If patient self medication cannot be achieved the market requirement will be low. Among the drugs administered orally solid oral dosage form is preferred choice of class of product. Most common solid dosage forms are tablet and capsule.

Nonsteroidal anti-inflammatory agents are one of the most widely used groups of therapeutic agents. The estimated 70-100 million prescriptions are written annually for NSAIDs with over the counter use accounting for an additional use which may be up to seven times higher. Approximately 7 million Indian suffer from arthritis which is about 15% of the total population. A growing proportion of elderly patients suffer from diseases like osteoarthritis or rheumatoid arthritis and they require nonsteroidal anti-inflammatory drugs (NSAIDs) therapy for its treatment.

Ibuprofen is chiral propionic acid derivative belonging to the class of non-steroidal anti-inflammatory drugs (NSAIDs). Due to its analgesic, antipyretic and anti inflammatory actions it is used in the treatment of inflammatory condition such as rheumatoid arthritis. Osteoarthritis, ankylosing spondylitis, mild and moderate pain, dysmenorrheal, vascularheads and fever. Ibuprofen is one of the safest and most potentnon-steroidal anti-inflammatory drug in market. It may be tolerated better than other NSAIDs. Due to rapid excretion of ibuprofen in urine, Large amount of drug is required for conventional dosage form. However it is suffers From limited aqueous solubility, gastrointestinal side effects and hardening of the tablets on aging2,3. Due to short half-life of ibuprofen (about 2 hours) and rapid excretion from urine For prevention of drug fluctuation in blood, ibuprofen must be administered frequently4.

Ibuprofen is a more active and is usually well tolerated analgesic and non-steroidal anti-inflammatory drug (NSAID), anti-pyretic properties with potent inhibitors of platelet aggregation currently available, used to treat gout, osteoarthritis, rheumatoid arthritis and sunburn. Most commonly used method of modulating the drug release is to include it in a matrix system. Because of their flexibility, hydrophilic polymer matrix systems are widely used in oral controlled drug delivery to obtain a desirable drug release profile, cost effectiveness and broad regulatory acceptance. hence, in the present work and attempt has been made to develop once-dailysustained release matrix tablets of Ibuprofen using hydrophilic matrix materials andhydrophobic material such as hydroxypropylmethylcellulose (HPMC), Ethyl Cellulose(EC) and PEG 600. The sustained release matrix of Ibuprofen were prepared by wet granulation technique in differ matrix polymers ratio.

Plasma concentration of a drug administered with an immediate release (IR) dosage form generally raises quickly, peaks and then declines The elimination of the drug is fast, this results in only a short period during which the plasma concentration of the drug is within the therapeutic window and required frequent dosing, patient have to be take several times a day as to maintain a therapeutically effective plasma level of the drug, which is a major drawback in terms of patient compliance.
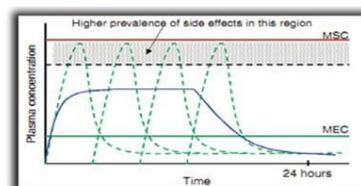
Oral controlled release (CR) formulations overcome many of the drawbacks of conventional IR dosage forms. Contrary to conventional IR dosage forms, CR tablets are not associated with alternating periods of toxic levels and sub-therapeutic concentrations, thereby improving the therapeutic efficacy and avoiding toxic side effects. The reduced side effects and lower frequency of administration of CR tablets represents increased comfort and improved patient compliance and more reliable tablet intake, which is especially important for patients which are subject to a chronic medication regimen. Furthermore, controlled release formulations have the potency to prevent night time dosing, reduce hospitalization costs, since self-administration is relatively easy.[2]

1. The extended release formulations reduce dosing frequency of drugs.
2. The extended release formulations may maintain therapeutic concentrations.
3. Reduce the toxicity by slowing drug absorption.
4. The use of these formulations avoids the high blood concentration.
5. Extended releaseformulations have the potential to improve the patient compliance and convenience.
6. Minimize the local and systemic side effects.
7. Increase the stability by protecting the drug from hydrolysis or other degradative changes in gastrointestinal tract.
8. Improvement in treatment efficacy.
9. Minimize drug accumulation with chronic dosing.
10. Improve the bioavailability of some drugs.
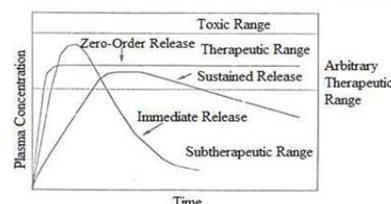12. Improve the ability to provide special effects.

For example, Morning relief of arthritis through bed time dosing

Figure 1. Plasma drug concentration profiles for conventional tablet formulation, sustained release formulation and a zero order controlled release formulation.

Figure 2. Drug level vs. time profile showing the relationship between sustained release and conventional release.

MATERIAL AND METHODS

Tablets were prepared by wet granulation, using 200mg of ibuprofen per tablet, magnesium stearate as lubricant, IPA as binder, talc glidant, lactose as a diluents, HPMC-K4Methyl cellulose as a polymer in sufficient quantities to obtain a final mass. The composition of the tablets is described in Table 1All the ingredients, except lubricant magnesium stearate, glidant talc and binder polyvinylpyrrolidone (PVP), were manually blended homogeneously in a mortar by way of geometric dilution. The mixture was moisturized with PVP solution in isopropyl alcohol and granulated through sieve No. 18(aperture size 1000 μm, US Standard) to obtain the desired consistency of the mass . The granulated blend was dried in a hot air oven at 40 oC for sufficient time (3 to 4 hours) so that the moisture content of the granules reached 3–5%. The dried granules were passed through sieve No. 26.

(aperture size 710 μm, US Standard) and blended with talc and magnesium stearate. The homogeneous blend was then compressed into tablets (300 mg each) using 9-mm diameter, deepconcave punches. The compression force was adjusted to give tablets with approximately 7 kg cm2 hardness on a tablet hardness tester. A constant compression force was obtained by using the same distance between the upper and lower punches.

Table 6.2 Formulation of matrix tablets of Ibuprofen

Ingredients	F-1	F-2	F-3	F-4
Drug	200	200	**200**	200
HPMC-K4M	30	60	30	60
Ethyl cellolose	40	40	120	120
Lactose	120	90	40	10
Magnesium sterate	5	5	5	5
Talc	5	5	5	5
Total weight of tablet= 400 mg				

EVALUATION OF MATRIX TABLET OF IBUPROFEN

A. Pre compression study

5.1.1 Organolepic Properties

Colour
Small quantity of drug powder was taken on butter paper and viewed in well illuminated place. Colour was the drug observed.

Taste
Very less quantity of drug was used to get the taste.

Odour
Very less quantity of drug was taken and smelled for determination of its odour.

State
With the help of light microscope state of drug was observed.

Organoleptic and physical properties of drug

Sr. No.	Test	Observation
1.	Colour	White powder
2.	Odor	odorless
3.	Taste	Tasteless
4	State	Crystalline

5.1 Physical Characteristics

Solubility Analysis
Solubility-Determination of quantitative solubility was done by adding a solvent with small incremental amount to a test tube containing fixed quantity of solute (Drug) or vice versa. After each addition the system was vigorously shaken and visually observed

Melting Point
For melting point determination of the drug sample, small quantity of powder was placed into a fusion tube. That tube was placed in the melting point determining apparatus. The temperature gradually increased automatically and temperature at which powder started to melt was recorded and the temperature when all the powder gets melted was also recorded.
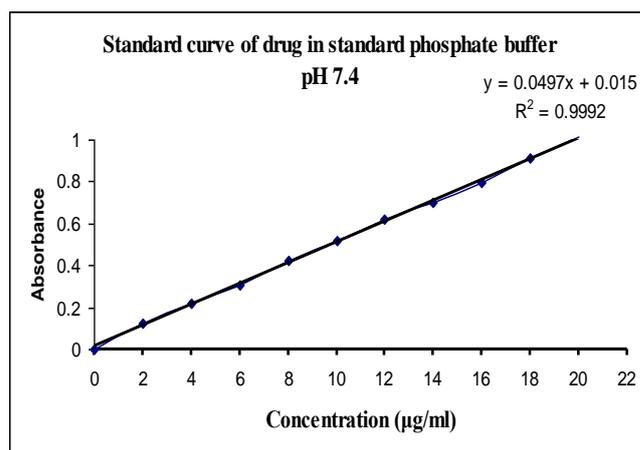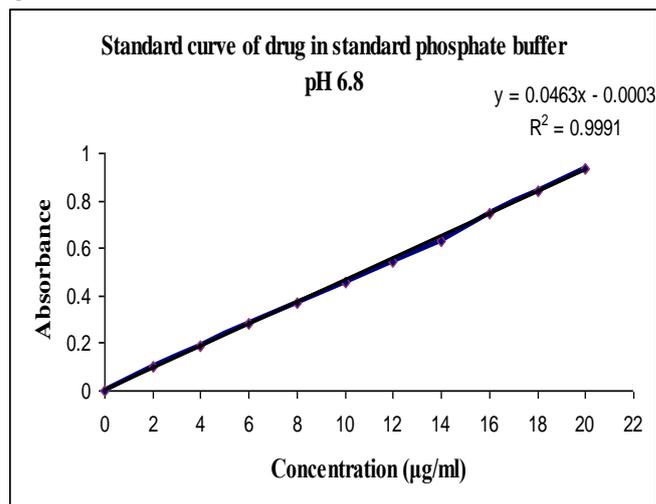
Table 4: Solubility profile of drug

Sr. No.	Solvents	Solubility
1.	Water	Partially soluble
2.	Acetone	Freely soluble
3.	chloroform	Freely soluble
4.	Ethanol	Freely soluble
5.	0.1 N NaoH	Slightly soluble

Table 5: Melting point of drug

Material	Observation
Ibuprofen	78.0^0C

Quantitative Estimation

Standard curve of drug in standard phosphate buffer pH 6.8

$y = 0.0463x - 0.0003$
$R^2 = 0.9991$

Standard curve of drug in standard phosphate buffer pH 7.4

$y = 0.0497x + 0.015$
$R^2 = 0.9992$

B. Post compression parameters

1. Bulk density (BD)

It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weighed powder in to a measuring cylinder and the volume was noted. It is expressed in gm/ml is given by

LBD = M/Vo

Where,
M = The mass of powder
Vo = The bulk volume of powder

2. Tapped bulk density (TBD)

It is the ratio of total mass of powder of the tapped volume of powder. A quantity of 2 g of powder from formula, previously lightly shaken to break any agglomerates formed, was introduced into a 10 mL measuring cylinder. After the initial volume was observed, the cylinder was allowed to fall under its own weight onto a hard surface from the height of 2.5 cm at 2-second intervals. The tapping was continued until no further change in volume was noted. TBD were calculated using the following formulas,

TBD = M/Vt

Where,
M = The mass of powder
Vt = The tapped volume of powder

3. Angle of repose (θ)
The frictional force in a loose powder can be measure by angle of repose (Φ). This is the maximum angle responsible between the surface of a pile of powder and the horizontal plane is used to determine the flow property of granules.

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 powder cone was measured and angle of repose was calculated using the following equation:
tan Φ = h/r
Φ = tan^{-1} (h/r)

Where h= the height of the pile of powder
r= the radius of the pile of powder
Powder Flow Properties: The flow properties were determined by;

1. Carr's index (I)
The compressibility index of the granules was determined by Carr's compressibility index
Carr's index (%) = [(TBD – LBD) *100]/TBD

Where,
TBD = Tapped density of the powder
LBD = Bulk density of the powder

2. Hausner's Ratio
This value was calculated by making use of LBD and TBD
Hausner's Ratio = TBD∕LBD

Where,
TBD = Tapped density of the powder
LBD = Bulk density of the powder

Lower Hausner's ratio (<1.25) indicates better flow properties than higher ones (>1.25).

Preformulation is the first phase about a new drug molecule. It provides information regarding physiochemical properties of drug, its interaction with excipients and stability profile. Drug molecule should be physically and chemically characterized before the formulation.

1. Thickness
The dimensions of tablets are thickness and diameter. Thickness and diameter of a tablet were measured by venire caliper.

2. Hardness
Tablets require a certain amount of strength to withstand the mechanical shocks of handling in manufacture, packaging, and shipping. The strength of the tablet was determined by Monsanto hardness tester. The lower plunger was placed in contact with the tablet, and a zero reading was taken. The upper plunger is then forced against a spring by turning a threaded bolt until the tablet fractures. The force of fracture was recorded, and the zero force reading was deduced from it. It is expressed in Kg/cm^2.

3. Friability
Friability of the tablet was determined using Roche friabilator. Friability test was performed to assess the effect of friction and shock which may often cause tablets to chip, cap or break. Weighed tablets sample was placed in the chamber and the Roche friabilator was operated for 100 revolutions (at 25 rpm) and the tablets were then dusted and reweighed again. The tablets that losses less than 0.5-1.0% of their weights are generally considered acceptable.
% F = {1-(W_t/W)} ×100

Where, % F = friability in percentage
W = Initial weight of tablet, W_t = weight of tablets after revolution

EVALUATION PARAMETER OF MATRIX TABLET OF IBUPROFEN

S.NO	Physical parameter	F1	F2	F3	F4
1.	Bulk density	0.575	0.547	0.588	0.499
2.	Tapped density	0.862	0.875	0.981	0.898
3.	Hausner's ratio (%)	1.27	1.17	1.15	1.16
4.	Carr's index (%)	18	16	13	61
5.	Angle of repose	38	37	32	33
6.	Thickness (mm)	0.2	0.2	0.3	0.3
7.	Hardness (kg/cm^2)	1.2	1.2	1.3	1.3
8.	Friability (%)	0.98	0.96	0.95	0.93

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