FORMULATION AND EVALUATION OF FAST DISSOLVING TABLETS OF DICLOFENAC SODIUM USING DIFFERENT SUPERDISINTEGRANTS BY DIRECT COMPRESSION METHOD

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ABSTRACT

The aim of the present work is to formulate a tablet which disintegrate and dissolve rapidly and give its rapid onset of action: analgesic, antipyretic and anti inflammatory action. Diclofenac sodium is among the most extensively used NSAIDs; employed in muscular skeletal complaints, especially arthritis. Conventional diclofenac sodium tablet available in market are not suitable where quick onset of action is required. Besides, the conventional tablets also show poor patient compliance particularly by geriatric and pediatric patients and those who are suffering from dysphegia, nausea and vomiting. In present study, an attempt had been made to formulate for FDT of diclofenac sodium by using various superdisintegrants like sodium starch glycolate, Sodium carboxymethyl cellulose followed by direct compression technique. The tablets were evaluated for weight variation, hardness, friability, disintegration time, *in vitro* dissolution studies and drug content. It was concluded that the batch which was prepared by using combination of Sodium carboxymethyl cellulose (NaCMC) and sodium starch glycolate as a superdisintegrant shows excellent disintegration time, enhance dissolution rate, taste masking and hence lead to improve efficacy and bioavaibility of drug.

Keywords: Diclofenac Sodium, Fast dissolving tablet (FDT), Superdisintegrant.

INTRODUCTION

Conventional dosage form is very popular because of ease of self administration, compact in nature, easy to manufacture and it can be delivered in accurate dose (1). One important drawback of conventional dosage form (tablet and capsule) is that it possesses higher disintegration time and pharmacological action is achieved after 30-45 min. of dosage form administration (2). To overcome this problem tablets that can rapidly disintegrate or dissolve (within one minute) in oral cavity have attracted a great deal of attention (1).

Fast disintegrating tablets are dosage form, which disintegrate in patient's mouth within a few seconds without the need of water, or chewing, providing best remedy for the patient suffering from dysphasia(3). Some

drugs are absorbed from the mouth, pharynx and oesophagus as the saliva passes down the stomach. In such cases the bioavailability is greater

than those observed for conventional dosage form (4).

Diclofenac sodium is synthetic, nonsteroidal anti-inflammatory & analgesic compound. The mechanism responsible for its anti-inflammatory / antipyretic / analgesic action is inhibition of prostaglandin synthesis by inhibition of cyclooxygenase (COX). Diclofenac may also be a unique member of the NSAIDs. There is some evidence that diclofenac inhibits the lipoxygenase pathways, thus reducing formation of the leukotrienes (also pro-inflammatory autacoids). It is well absorbed orally and shows 100% bioavailability, more than 99%

Protein bound, metabolized and excreted both in urine and bile, and plasma t is 1.2-2 hr. (5,6). Diclofenac is used for musculoskeletal complaints, especially arthritis (rheumatoid arthritis, osteoarthritis, and spondylarthritis, ankylosing spondylitis), gout attacks, and pain management in case of kidney stones and gallstones. An additional indication is the treatment of acute migraines. Diclofenac is used commonly to treat mild to moderate post-operative or post-traumatic pain, particularly when inflammation is also present, and is effective against menstrual pain - (7).

In the present study it was proposed to formulate an oral delivery device, in the form of fast disintegrating tablets by using direct compression technology (8), with the aim of reaching a high serum concentration in a short period of time (9).In this study, effort has been made to formulate fast disintegrating tablet of diclofenac potassium using super disintegrate, like Sodium Strach Glycolate and Sodium carboxy methyl cellulose was investigated for the super disintegrating property.

EXPERIMENTAL

MATERIALS USED

The used reagents were Diclofenac sodium (gift sample from Blue Cross Laboratories Limited, Mumbai), Sodium carboxy methyl cellulose (Merck), Microcrystalline cellulose (Merck), Mannitol, Magnesium Stearate, Talc and Aspartame. All other analytical grade reagents were obtained commercially and used as received.

METHODS

Preparation of blends & tablets

Fast disintegrating tablets containing 50 mg diclofenac sodium were prepared by direct compression method and the formulae for six formulations (F1 to F6) used in the study are shown in Table 1. Each tablet weigher 200mg. Different super disintegrats such as sodium starch glycolate and sodium carboxymethyl cellulose (NaCMC) was used. Mannitol was used as diluents and sodium saccharin as sweetening agent. Diclofenac sodium was mixed in geometric proportions with sweeteners, diluents, and lubricants. Blend was screened and compressed on 12 station rotary punching machine.

Table 1: Formulation design of Diclofenac Sodium tablet (F1 to F6)

TABLETS INGREDIENTS (mg)	F1	F2	F3	F4	F5	F6
Diclofenac sodium	50	50	50	50	50	50
Mannitol	130	130	120	120	120	140
Sodium starch glycolate	-	10	5	15	10	-
NaCMC	10	-	15	5	10	-
Saccharin sodium	5	5	5	5	5	5
Talc	3	3	3	3	3	3
Magnesium stearate	2	2	2	2	2	2

Characterization &Evaluation of formulation :

Precompression parameter

1. Bulk density

The accurate weighed amounts of granules were taken in 25 ml measuring cylinder. Volume of granule packing was recorded before doing tapping there after measuring cylinder containing granule was tapped 50 times on a plane hard wooden surface and tapped volume of packing recorded. Both loose bulk density (LBD) and tapped bulk density (TBD) were calculated by the following formula:

LBD (Loose bulk density) = Mass of Powder/Volume of Packing

TBD (Tapped bulk density) = Mass of Powder/ Tapped Volume of Packing (10)

2. Compressibility index

Percent compressibility of powder mix was determined by Carr's compressibility index calculated by the formula. Carr's index % =TBD-LBD/TBD*100(10).

EVALUATION OF TABLET

1. General Appearance

The general appearance of a tablet, its visual identity and over all "elegance" is essential for consumer acceptance. Include in are tablet's size, shape, colour, presence or absence of an odour, taste, surface texture, physical flaws and consistency and legibility of any identifying marking.

2. Size and Shape

The size and shape of the tablet can be dimensionally described, monitored and controlled

3. Uniformity of weight

I.P. procedure for uniformity of weight was followed, twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. The weight variation test would be a satisfactory method of determining the drug content uniformity.

4. Tablet hardness

Hardness of tablet is defined as the force applied across the diameter of the tablet in the order to break the tablet. The resistance of the tablet to chipping, abrasion or breakage under condition of storage transformation and handling before usage depends on its hardness. Hardness of the tablet of each formulation was determined using Monsantro Hardness tester.

5. Friability

It is measured of mechanical strength of tablets. Roche fribaiator was used to determine the friability by following procedure. A preweighed tablet was placed in the fribaiator. Fribaiator consist of a plastic-chamber that revolves at 25 rpm, dropping those tablets at a distance of 6 inches with each revolution. The tablets were rotated in the friabalator for at least 4 minutes. At the end of test tablets were dusied and reweighed, the loss in the weight of tablet is the measure of friability and is expressed int x 100.

In Vivo Disintegration test

The test was carried out on 6 tablets using the apparatus specified in I.P.-1996 distilled water at 37ºC ± 2ºC was used as a disintegration media and the time in second taken for complete disintegration of the tablet with no palable mass remaining in the apparatus was measured in seconds.

Dissolution Studies

Dissolution was carried out by using Electro lab dissolution apparatus (USP XXI) by paddle method using 900ml of 1%w/v SLS as the medium and rotating the paddle at 50 rpm for 10 minutes. The temperature of dissolution medium was maintained at 37±20C. Aliquots were withdrawn at different time intervals of 0, 2, 4, 6, 8 and 10 minutes. And it was replaced by adding equal volumes of fresh dissolution medium. The samples were suitably diluted and absorbance of the solution was determined at 276 nm by using UV-visible spectrophotometer.

RESULT AND DISCUSSION

The compositions of different formulations are presented in (Table 1). The preformulation studies and evaluation parameters like weight variation, friability, hardness, thickness, and disintegration time and dissolution rate for drug were found to be satisfactory and the results were presented in (Table 2 & 3).

Table 2: Preformulation studies of blends

Parameters	F1	F2	F3	F4	F5	F6
Bulk density (gm/ml)	0.52	0.50	0.51	0.50	0.50	0.48
Tapped density(gm/ml)	0.62	0.62	0.61	0.63	0.62	0.58
Compressibility index (%)	16.1	19.4	16.4	20.6	19.4	20.5
Angle of repose	25°	28°	24°	25°	25°	25°

Table 3: Evaluation of fast dissolving tablet of sodium diclofenac of different blends

Parameters	F1	F2	F3	F4	F5	F6
%wt variation	1.8	2.3	2.4	2.2	1.9	2.1
Thickness(mm)	2.71	2.68	2.7	2.75	2.77	2.84
Friability (%)	0.54	0.26	0.58	0.47	0.62	0.65
Hardness (kg/cm_2)	4.53	4.96	4.60	4.80	4.41	4.50
Disintegration Time (sec)	70	62	47	43	30	74

Table 4: % drug released of fast dissolving tablet of sodium diclofenac of batch F4and F5

Time(in min)	F4	F5
0	0	0
2	43.76	50.98
4	72.20	80.42
6	90.13	94.24
8	95.63	98.29
10	97.54	99.53

For each designed formulation, blend of drug and excipients was prepared and evaluated. Bulk density was found between 0.48 to 0.52 gm/cm^3 and tapped density between 0.58 – 0.63 gm/cm^3. For density data, %compressibility was calculated. Flowability of the material was found to excellent as indicated by compressibility-flowability correlation data. Angle of repose was found in the range of 22°-28°. As it below 30° it indicates good flow property of blend.

Tablets were prepared by direct compression method. As the material was a free flowing, tablets were obtained of uniform weight due to uniform die fill, with acceptable variation as per I.P. Drug content was found in acceptable limit. Hardness of the tablet for each formulation was 4.41-4.91 kg/cm^2. Friability was below than1.0% shows an indication of good mechanical strength resistance of the tablet. (Table 3)

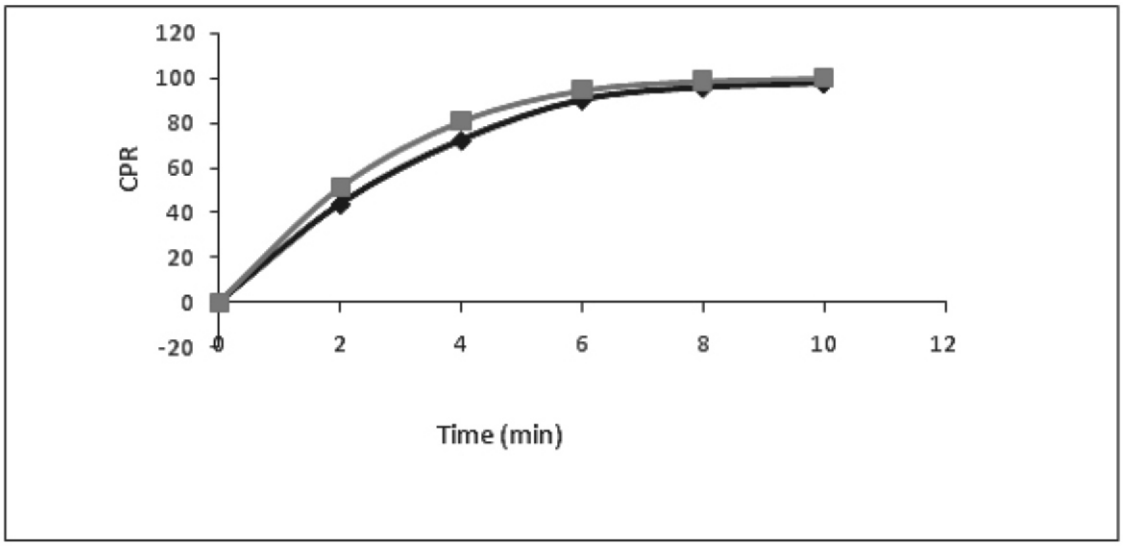

Figure 1 : CPR of F4 and F5

CPR- Cumulative percentage release

The formulation containing NaCMC and Sodium Starch Glycolate shows sufficiently decrease in disintegration time (i.e. 30 sec.) among all the formulation. When NaCMC and Sodium Starch Glycolate were used alone in the formulations, disintegration time was noticed more than 1 min. furthermore. When combination of these superdisintigrant was used, significant decrease in a disintegration time was achieved. Two formulation (F4 & F5) was taken as they shows minimum disintegration time. *In vitro* dissolution rate study shows that after 10 min formulation F4 – F5 % drug release 97.54% and 99.98% respectively.. As fast dissolution formulation F5 shows satisfactory % drug release and disintegrating time as shown in (Fig. 1). Thus the formulation batch F5 can be said as best combination of superdisintigrant for fast dissolving tablet of diclofenac sodium.

CONCLUSION

From the present study it may be concluded that fast dissolving tablet of diclofenac sodium can be formulated by direct compression method by using suitable superdisintigrant Sodium Carboxy methyl cellulose, Sodium Starch Glycolate). The combination of these was found to be best among the different combination of superdisintigrant. The proposed fast dissolving formulations possess ideal and reproducible characteristics of disintegration time and enhanced dissolution and thus give better patient compliance compare to conventional tablet of diclofenac sodium.

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