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FORMULATION & COMPARATIVE EVALUATION OF RAPID DISINTEGRATING TABLETS OF DICLOFENAC SODIUM USING SODIUM STARCH GLYCOLATE AS A SYNTHETIC SUPERDISINTIGRANT

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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 musculoskeletal complaints, especially arthritis. Conventional diclofenac sodium tablet available in market are not suitable where quick onset of action is required. In present study, an attempt had been made to formulate for RDT of diclofenac sodium by using various superdisintigrant like sodium starch glycolate, followed by direct compression technique to develop formulations of diclofenac sodium Rapid dispersing tablets, in the present study it was propose to formulate an oral delivery system, in the form of Rapid dispersing tablet of diclofenac sodium, sodium starch glycolate and their combinations in different ratios.

Introduction

Conventional oral drug products are formulated to release the active pharmaceutical principle immediately after oral administration to obtain rapid and systemic absorption. Oral route of drug administration is the most appealing, convenient, significant and popular route for the delivery of drugs owing to ease of swallowing, self-medication, and most economic. Tablets are the most popular and preferred oral formulation available in the market because of its ease of manufacturing, convenience in administration, accurate dosing, stability compared with oral liquids and because it is more tamperproof than capsules RDT'sare designed to disintegrate rapidly on contact with saliva and enable oral administration without water or chewing. significant progress in terms of clinical efficacy and patient compliance. One important drawback of conventional dosage form (Tablet and capsule) is that it possesses higher disintegration time so patient obtained pharmacological effect after 30-45 min. of dosage form administration. To overcome these problem tablets that can rapidly disintegrate or dissolve (within one minute) in oral cavity have attracted a great deal of attention.

An attempt had been made to formulate for FDT of diclofenac sodium by using various superdisintegrants like sodiumstarch glycolate, croscarmellose sodium and crosspovidone (polyplasdone XL) followed by direct compression technique.The tablets were evaluated for weight variation, hardness, friability, disintegration time, wetting time, in vitro dissolutionstudies and drug content. It was concluded that the batch which was prepared by using combination of crosspovidone andsodium starch glycolate as a superdisintigrant shows excellent disintegration time, enhance dissolution rate, taste maskingand hence lead to improve efficacy and bioavaibility of drug[1]. The Diclofenac sodium is a non-steroidal-anti-inflammatorydrug. Itcomprises a large family of weak acidic drugs whose pharmacologicaleffects result primarily from the inhibition of cyclooxygenase (COX)an enzyme that catalyzes the first step in the synthesis of prostaglandinsfrom arachidonic acid and other precursor fatty acids. Since itssolubility is very high in upper G.I. and need of fast releasing action in case of acute pain it is formulated as fast dissolving tablet[2]. The methods commonly employed for achieving effective taste masking include various physical and chemical methods that prevent the drug substance from interaction with the taste buds[3].Fast dissolving tablets ofdiclofenac sodium using 3 different superdisintegrants like Sodium starch glycolate, croscarmellose sodium, andcrospovidone by direct compression technique using 3 different concentrations of each superdisintigrant[4].

Material and Method

Diclofenac sodium was purchased sample from Swapnroop Drugs &Pharmaceuticals, Aurangabad, India. All other ingredients such as sodium starch glycolate, Methyl Cellulose, Mannitol, magnesium stearate and talc were obtained from Departmental Lab B.A.M.U., Aurangabad, India. All ingredients used were of analytical grade.

Preparation of Rapid Disintegrating Tablets

Each tablet containing 50mg of Diclofenac sodium was prepared by using direct compression technique. The superdisintigrant sodium starch glycolate was used in different proportion and in different combination. All the ingredients were passed through sieve no.60 and kept in hot air oven at 600C to make anhydrous and accurately weighed. The drug, superdisintigrant, mannitol, microcrystalline cellulose was mixed to improve drug distribution and content uniformity and triturated in mortar. After then talc and magnesium stearate were passed through sieve no 80 mixed and blended well with the previous mixture. Then the mixture was compressed using single punching machine to produce tablet weighing 200mg. Two batches were prepared.

Table1. Batch (Diclofenac sodium+ SSG (5%))

Sr. NO.	INGREDIENTS	mg/Tablets			
		S1	S2	S3	S4
1.	Diclofenac sodium	50	50	50	50
2.	SSG	10	20	30	40
3.	MCC	125	115	105	95
4.	Talc	5	5	5	5
5.	Mg. stearate	6	6	6	6
6.	Mannitol	4	4	4	4
Total Weight		200	200	200	200

Table No.2: Equipment used for Evaluation Diclofenac Sodium RDT

Sr. No.	Test	Equipment
01	Weight variation	High Precision Balance
02	Hardness	Monsanto Hardness Tester
03	Thickness	Vernier Caliper
04	Friability	RocheFriabilator
05	Dissolution	USP Type II Dissolution Apparatus

Pre-compression parameters

1. Bulk density

It was determined by pouring blend into a graduated cylinder. The bulk volume (V0) and weight of powder (M) was determined. The bulk density was calculated by using the formula.

Bulk density = Weight of powder (M) / Volume of packing (V0)

2. Tapped density (Dt)

It is the ratio of total mass of powder o the tapped volume of powder. The minimum volume (Vt) occupied in the cylinder and weight of powder blend (M) was measured. It was calculated by the formula.

Tapped density = Weight of powder (M) / Volume of packing after tapings (Vt)

3. Angle of Repose (q)
It was determined by fixed funnel method. The blend was poured through a funnel that can be raised vertically until a maximum cone height (h) was obtained. Radius (r) of the heap was measured and angle of repose was measured using formula.

Angle of Repose = tan (q)= h/r
q =tan-1 (h/r),
where, q is the angle of repose
h is the height in cm.
r is the radius in cm.

4. Carr's index/ % Compressibility
It indicates the powder flow properties. The simplest way for measurement of free flow of powder is compressibility, an indication of the ease with which a material can be induced to flow is given by compressibility index. The value below 15% indicates a powder which givesrise to good flow properties whereas above 25% indicates poor flow ability which is calculated by following formula.

%C. I. = Dt-Db/Dt × 100
Where, Dt =Tapped density
Db = Bulk density

5. Hausner Ratio
It is an indirect index of ease of powder flow. Hausner ratio is the ratio of tapped density to bulk density. Lower the value of Hausner ratio better is the flow property. Powder with Hausner Ratio less than 1.18, 1.19, 1.25, 1.3- 1.5 and greater the 1.5 indicate excellent, good, passable, and very poor, respectively. It is calculated by following formula.

Hausner ratio = Dt / Db
Where, Dt =Tapped density
Db = Bulk density

Table 3. Physical characteristics of active ingredients

Formulation	Bulk density (gm/cm3)	Tapped density (gm/cm3)	Angle of repose	Carrs index (%)	Hausner Ratio
S1	0.509	0.686	10.75	25.80	1.347
S2	0.532	0.725	10.73	26.62	1.362
S3	0.423	0.648	11.03	34.72	1.500
S4	0.464	0.632	10.52	26.58	1.362

Post compression parameters
1. Measurement of Tablet Tensile Strength
For measuring the hardness of the tablets, the plunger of the hardness tester is driven down at a speed of 20mm/min. Tensile strength for crushing (T) is calculated using following equation.

T=2F/ dt, Where F is the crushing load d and t denote the diameter and thickness of the tablet respectively.

2. Friability
The pharmacopeia limit of friability test for a tablet is not more than 1% using tablet friability apparatus, carried out at 25rpm for 4min. However, it becomes a great challenge for a formulator to achieve friability within this limit for RDT product keeping hardness at its lowest possible level in order to achieve a minimum possible disintegration time.

3. Moisture Uptake Studies
It should be conducted to assess the stability of the formulation. Ten tablets from each formulation were kept in a desiccator over calcium chloride at 370C for 24 h. The tablets werethen weighed and exposed to 75% relative humidity at room temperature for 2 weeks. Required humidity was achieved by keeping saturated sodium chloride solution at the bottom of the dessicator for 3 days. One tablet as control (without superdisintigrant) was kept to assess the moisture uptake due to other excipients. Tablets were weighed and the percentage increase in recorded.

4. Weight Variation
In this 20 tablets were selected randomly from the lot and weighed individually to check for weight variation. Weight variation as per I.P. is shown in table below.

Table 4. Weight variation as per I.P Average

SR. NO.	Weight of Tablet	%Deviation
01	80mg or less	+10
02	More than 80mg but less than 250mg	+7.5
03	250mg or more	+5.0

5. Wetting time and Water Absorption Ratio

Study on wetting time and water absorption ratio reported the use of a piece of double folded tissue paper placed in a petri-dish containing 6ml of water. One tablet was placed on this paper and the time for complete wetting of tablet was noted as wetting time. The wetted tablet was then weighed and the water absorption ratio R, was determined according to equation.

R=100 (Wa-Wb)/Wb,
Where, Wa and Wb are the weight of tablet before and after water absorption.

6. Disintegration Time
At present, the disintegration time of RDTs is measured using the disintegration test for conventional tablets that is described in the Pharmacopeia. European Pharmacopeia has set the limit of 3min for disintegration time of RDTs using conventional disintegration apparatus. The conventional test employs a relatively huge volume of test solution (900ml) compared to the volume of saliva in human buccal activity. The result so obtained from the conventional disintegration test do not reflect the actual disintegration rate in the human mouth which usually ranges from 5-30 sec. To overcome these issues, several new methods have been proposed, which are reviewed here.

Table 5. Physical Evaluation of RDT of batches

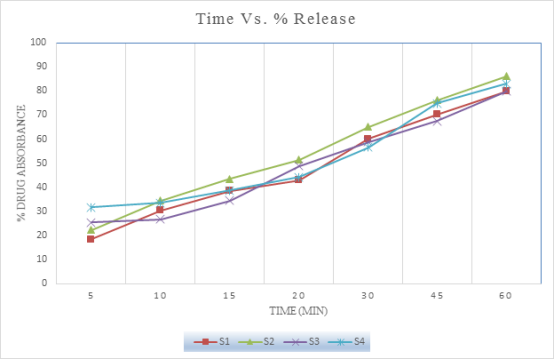
Sr. No.	Formulation	Weight (mg) (mean)	Hardness (kg/cm2)	Friability	D.T (sec)	Wetting time (s)
1	S1	202	4	0.431	75	90
2	S2	200	4	0.290	70	80
3	S3	201	3	0.547	72	85
4	S4	202	4	0.475	68	76

7. Dissolution Test
Dissolution conditions for drugs listed in a pharmacopeia monograph, is a good place to start with scouting runs for a bioequivalent RDT. Other media such as Phosphate buffer (pH 7.5) should be evaluated for RDT. USP dissolution apparatus 1 and 2 can be used. USP 1 basket apparatus may have certain applications but sometimes tablet fragments or disintegrated tablet masses may become trapped on the inside top of the basket. Kancke proposed USP 2 Paddle apparatus which is the most suitable and common choice for RDT with a paddle speed of 50rpm commonly used. The USP 2 Paddle apparatus at 50-100rpm is suitable for dissolution testing of taste masked drug as well.

Table 6. Formulation, Development, Evaluation Parameters of all batches

Formulation		% Drug Release			
		S1	S2	S3	S4
Time	5(min)	18.32	22.27	25.43	31.68
	10(min)	30.40	34.45	26.63	33.47
	15(min)	38.52	43.56	34.53	38.65
	20(min)	42.86	51.34	48.75	44.16
	30(min)	60.12	65.13	58.71	56.63
	45(min)	70.23	76.12	67.44	74.80
	60(min)	79.79	86.12	79.92	82.96

Graph 1. Time × % Drug release:



Result and Discussion

The present study was undertaken to formulate Rapid disintegrating tablet of Diclofenac sodium with a view to deliver the drug in rapid manner. The objective of the study is to carry out the comparative in-vitro release of diclofenac sodium tablets which were prepared from synthetic superdisintigrant (sodium starch glycolate).

It showed good disintegration characteristics. So, here S2 shows the best disintegrating property as compared to S1, S3 & S4. In vitro study that was conducted showed that sodium starch glycolate has better dissolution at 10% as compared to other as shown in as it releases the drug more than 80% in 60min. as compared to other SSG preparation.

This study involves preformulation studies, compatibility with excipients, formulation and evaluation of tablets. Literature review showed that Diclofenac sodium is a NSAID drug which act as a NSAIDS. Preformulation study was done and batches of diclofenac sodium were also prepared using sodium starch glycolate as synthetic superdisintigrant. Also micrometric properties were calculated like bulk density, tapped density, angle of repose, hausners ratio. All the formulation had showed good blend properties. The tablets were prepared by using Direct compression technology.

All the formulation disintegrated within 30-60 minutes. In vitro dissolution studies conducted for both SSG preparation, table revealed that S2 is an optimized formulation that releases the drug above 80% within 60 min. as compared to S1, S3, S4 which is alsoa SSG preparation. So, we can say that sodium starch glycolate as a superdisintigrant should be used for better dissolution.

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