WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 5.990
Volume 4, Issue 12, 1542-1552. Research Article ISSN 2277– 7105

COMPARATIVE STUDY ON EFFECT OF NATURAL AND SYNTHETIC SUPERDISINTEGRANT IN FORMULATION OF FAST DISINTEGRATING TABLETS OF DICLOFENAC SODIUM

Priyanka Shrivastav*[1], Abhay Kumar Verma[2] and Vandana Sethi[3], Arun Kumar Singh[4]

[*1,3]Department of Pharmaceutics, Lloyd Institute of Management & Technology, Greater Noida, U.P., India.

[2]Department of Pharmaceutical Chemistry, Magadh University, Bodh Gaya, Bihar, India.

[4]Department of Pharmaceutical Chemistry, Magadh University, Bodh Gaya, Bihar, India.

Article Received on
19 Oct 2015,

Revised on 09 Nov 2015,
Accepted on 29 Nov 2015

***Correspondence for Author**
Priyanka Shrivastav
Department of Pharmaceutics, Lloyd Institute of Management & Technology, Greater Noida, U.P., India.

ABSTRACT

Diclofenac is a NSAID (Non steroidal ant inflammatory drug) which is generally taken to reduce inflammation and as an analgesic. In this study an attempt has been made to formulate a dosage form of diclofenac sodium using natural superdisintegrant Guargum to show that this natural superdisintegrant will show better disintegrating property than the synthetic superdisintegrant like sodium starch glycolate in the formulation of Fast disintegrating tablet (FDT) of diclofenac sodium. Fast disintegrating tablet prepared by direct compression technique using natural & synthetic superdisintegrant in different concentration & evaluated. Among all G2 is an optimized formulation of guargum that releases the drug above 90% with in 60 min. as compared to S2 which is a sodium starch glycolate preparation.

KEYWORDS: Diclofenac, Fast disintegrating tablets, Superdisintegrant.

INTRODUCTION

With the increase demand of novel drug delivery, the fast disintegrating drug delivery system has become one of the mile stone of present investigations. Tablets produced by these technologies have sufficient mechanical strength, disintegration and dissolution profile. An FDT is "a solid dosage form containing medicinal substances, which disintegrates rapidly, usually within a matter of seconds when placed upon tongue.[1] Fast dissolving tablets are also applicable when local action in the mouth is desirable such as local anesthetic for

toothache, oral ulcers, cold sores, or teething.[2] They do not require water for administration, thus are good alternative for travelers and for bed ridden patients.[3] Difficulty in swallowing is experienced by patients such as geriatric & pediatric patients, disabled and mentally ill.[4]

MATERIAL AND METHOD

All the chemicals procured from Central Drug House (P.) Ltd, New Delhi. The λmax of Diclofenac sodium was scanned on UV visible spectrophotometer - Shimadzu 1700 Japan. The dissolution apparatus used was HICON, USP/BP/IP(PDA-65). Guargum was available commercially.

Preparation of Fast dissolving tablets

Each tablet containing 50mg of Diclofenac sodium was prepared by using Direct compression technique. The superdisintegrants sodium starch glycolate (5%, 10%, 15%) and Guargum (5%, 10%, 15%) were used in different proportion and in different combinations. 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, superdisintegrant, mannitol, microcrystalline cellulose were 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. Four batches were prepared.

Table 1. Batch-1 S-1 (Diclofenac sodium+SSG (5%)

S.NO.	INGREDIENTS	mg/Tablets
1.	Diclofenac sodium	50
2.	SSG	10
3.	MCC	125
4.	Talc	5
5.	Mg. stearate	6
6.	Mannitol	4
	Total Weight	200

Table 2. Batch-2 S-2(10%)

S.NO	INGREDIENTS	mg/tablets
1.	Diclofenac sodium	50
2.	SSG	20
3.	MCC	115
4.	Talc	5
5.	Mg.stearate	6
6.	Mannitol	4
	Total weight	200

Table 3. Batch-3 G-1(5%)

S.NO	INGREDIENT	mg/tablets
1.	Diclofenac sodium	50
2.	Guargum	10
3.	MCC	125
4.	Talc	5
5.	Mg.stearate	6
6.	Mannitol	4
	Total weight	200

Table 4. Batch-4 G-2(10%)

S.NO	INGREDIENTS	mg/tab
1.	Diclofenac sodium	50
2.	Guargum	20
3.	MCC	115
4.	Talc	5
5.	Mg.stearate	6
6.	Mannitol	4
	Total weight	200

Table 5. Percent drug content of all batches

FORMULATION	% DRUG CONTENT
S1	88.4
S2	90.6
G1	94.3
G2	95.6

Precompression parameters

1. Bulk density

It was determined by pouring blend into a graduated cylinder. The bulk volume(V_0) and weight of powder (M) was determined. The bulk density was calculated by using the formula.[5]

$$\text{Bulk density} = \frac{\text{Weight of powder (M)}}{\text{Volume of packing } (V_0)}$$

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.

$$\text{Tapped density} = \frac{\text{Weight of powder (M)}}{\text{Volume of packing } (V_t)}$$

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.[6,7]

tan (q)= h/r

q=tan-1 (h/r)

where, q is the angle of repose

h is the height in cms

r is the radius in cms

4. Carr's index/ % Compressibility

It indicates the powder flow properties. The simplest way for measurement of free flow of powder is compressibility, a 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 gives rise to good flow properties whereas above 25% indicates poor flow ability which is calculated by following formula.[8]

%C.I = pt-pb/pt x100

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 ratiless 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.[9]

Hausner ratio = Dt / Db, Where, Dt is the tapped density

Db is the bulk density

Lower hausner ratio(<1.25) indicates better flow properties than higher ones(1.25)

Table 6. Physical characteristics of active ingredients

Formulation	Bulk density(gm/cm^3)	Tapped density(gm/cm^3)	Angle of repose	Carrs index(%)	Hausner Ratio
S1	0.520	0.67	22.23	21.12	1.35
S2	0.532	0.68	21.55	20.35	1.36
G1	0.617	0.74	27.21	19.20	1.40
G2	0.620	0.78	28.21	20.14	1.38

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.[10]

2. Friability

The pharmacoepial 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 FDT product keeping hardness at its lowest possible level in order to achieve a minimum possible disintegration time.[11]

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 37^0C for 24 h. The tablets were then 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 superdisintegrant) was kept to assess the moisture uptake due to other excipients. Tablets were weighed and the percentage increase in weight was recorded.[12]

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.[13]

Table 7. Weight variation as per I.P

Average Weight of Tablet	%Deviation
80mg or less	+10
More than 80mg but less than 250mg	+7.5
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 petridish 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.[14]

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 time of FDTs is measured using the disintegration test for conventional tablets that is described in the Pharmacoepia. European Pharmacoepia has set the limit of 3min for disintegration time of FDTs 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.[15,16]

Disintegration Test using Modified Dissolution Apparatus

Bi et al 1999 suggested the use of a modified dissolution apparatus, instead of the disintegration apparatus. In this experiment 900ml of water maintained at 37^0C s the disintegration fluid and a paddle at 100rpm as stirring element were used. Disintegration time was noted when the tablet disintegrated and passed completely through the screen of the sinker (3-3.5mm in height and 3.5-4mm in width, immersed at a depth of 8.5cm from the top with the help of a hook). This method was useful in providing differences among batches which was not possible with the conventional disintegration apparatus.

Table 8. Physical Evaluation of FDT of batches

Formulation	Weight (mg)	Hardness (kg/cm^2)	Thickness (mm)	Friability	D.T (sec)	Wetting time (s)	Water absorption ratio(%)
S1	201±2.3	4.67±0.23	4.0±0.017	0.431	75	90	61±0.43
S2	200±2.2	4.65±0.25	4.3±0.22	0.290	70	80	75±0.40
G1	198±1.4	4.54±0.24	4.2±0.22	0.293	50	50	82±0.22
G2	201±2.4	4.53±0.23	4.3±0.023	0.290	45	55	85±0.69

7. Dissolution Test

Dissolution conditions for drugs listed in a pharmacopeia monograph, is a good place to start with scouting runs for a bioequivalent FDT. Other media such as 0.1N HCl and buffers (pH

4.5 and 6.8) should be evaluated for FDT. 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 FDT 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.[17]

Table 9. In vitro dissolution study of batches containing SSG

Formulation		% Drug Release	
		S1	S2
Time	5(min)	18.32	22.27
	10(min)	30.40	34.45
	15(min)	38.52	43.56
	20(min)	42.86	51.34
	30(min)	60.12	65.13
	45(min)	70.23	76.12
	60(min)	79.79	86.12

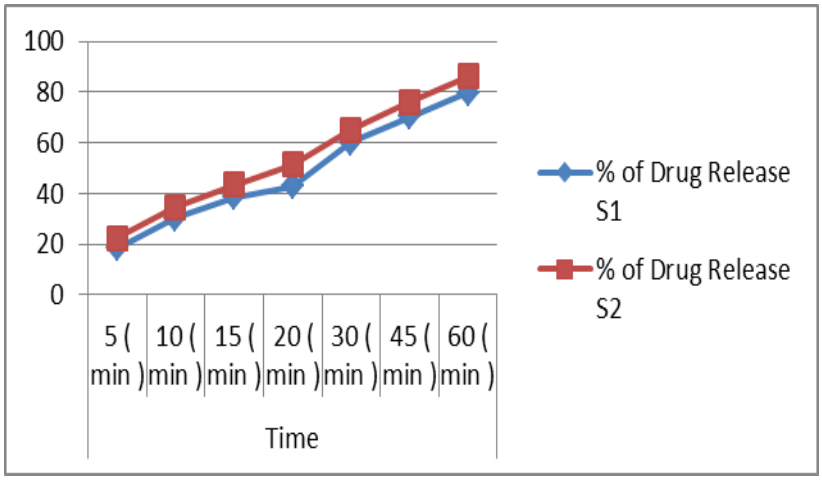

Fig 1. showing dissolution profile of S1 & S2

The attempt of using SSG in earlier formulation was not upto mark, so there was a need to formulate the tablets by using natural superdisintegrant like guargum. Two batches like that of SSG were prepared namely G1,G2. Their drug release pattern was studied and then compared with the synthetic superdisintegrant batch.

Table 10. In vitro dissolution study of batches containing Guargum

Formulation		%Drug Release	
		G1	G2
Time	5(min)	22.16	25.27
	10(min)	34.25	36.49
	15(min)	45.70	48.57
	20(min)	51.76	60.36
	30(min)	71.16	74.17
	45(min)	82.26	88.18
	60(min)	88.69	94.70

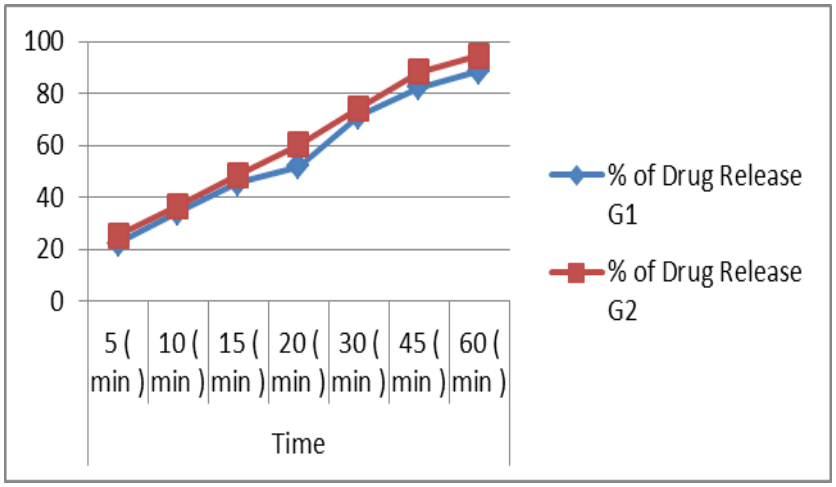

Fig 2. showing dissolution profile of G1 & G2

Disssolution profile of batches G1 & G2 : The tablets of G1 and G2 have shown 88.69% and 94.70% of drug release in 60 minutes which is better as compared to the formulation S1 and S2 which shows 79.79% and 86.12% of drug release in 60 minutes

Table 11. Comparative dissolution between batches of S2 and G2

Formulation		%Drug Release	
		S2	G2
Time	5(min)	22.7	25.27
	10(min)	34.45	36.49
	15(min)	43.56	48.57
	20(min)	51.34	60.36
	30(min)	65.13	74.17
	45(min)	76.12	88.18
	60(min)	86.12	94.70

Comparative dissolution between batches of S2 and G2 : The dissolution profile of both the S2 and G2 preparation can be compared which clearly shows that G2 shows better drug

release of 94.70% in 60 min. It shows that natural superdisintegrant are much better as compared to synthetic disintegrant.

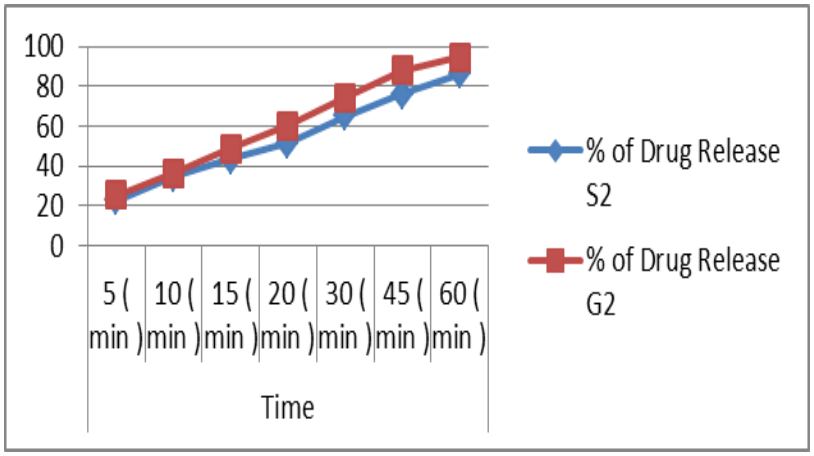

Fig 3. showing comparative dissolution profile of S2 & G2

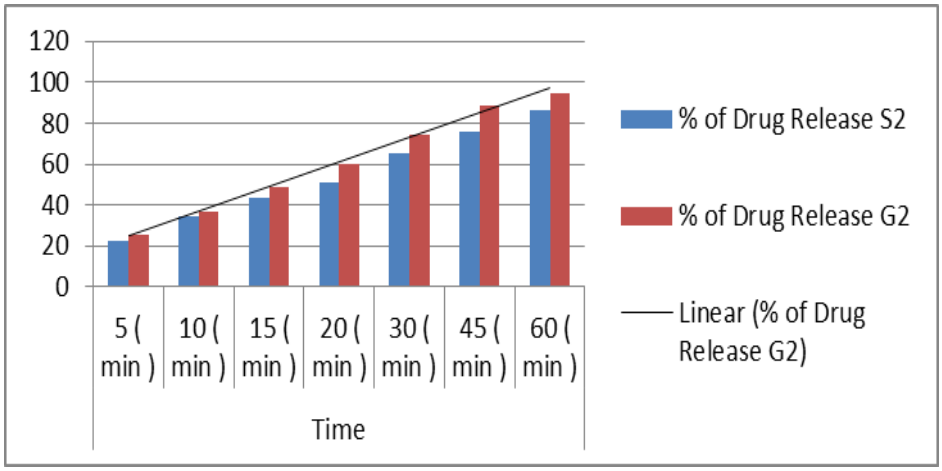

Fig 4. showing graph of dissolution profile of optimized formulation

RESULTS AND DISCUSSION

The present study was undertaken to formulate fast 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 invitro release of diclofenac sodium tablets which were prepared from two superdisintegrants one was natural (guargum) and other was synthetic(sodium starch glycolate). Guargum have been used as disintegrant because of its tendency to swell in water. It showed good disintegration characteristics. So, here guargum shows the best disintegrating property as compared to sodium starch glycolate. In vitro study that was conducted showed that guargum has better dissolution at 10% as compared to dissolution of SSG at 10% as shown in table 11 as it releases the drug more than 90% in 60min. as compared to SSG.

CONCLUSION

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 guargum as a natural superdisintegrant and sodium starch glycolate as synthetic superdisintegrant. Also micromeritic 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 with in 30-60minutes. Guargum shows the good disintegrated property. In vitro dissolution studies conducted for both guargum and SSG, table revealed that G2 is an optimized formulation that releases the drug above 90% with in 60 min. as compared to S2 which is a SSG preparation. So, we can say that instead of using synthetic superdisintegrant use of natural ones like guargum should be used.

REFERENCES

1. Mehta K, Garala K, Basu B, Bhalodia R, Joshi B, Charylu R.N. An emerging trend in oral drug delivery technology: Rapid disintegrating tablet. Journal of Pharmaceutical Sciencs Technology. 2010; 318-329.
2. Kumar R, Patil S, Patil M B, Patil SR, Paschapur M S. Isolation and evaluation disintegrate properties of fenugreek seed mucilage. International Journal of Pharm Tech Research 2009; 1(4): 982-996.
3. Shu T, Suzuki H, Hironaka K and Ito K.” Studies of rapidly disintegrating tablets in oral cavity using coground mixture of mannitol with crospovidone. Chem. Pharm. Bull.2004; 50; 193-198.
4. Seagre,H Drug delivery product and zydis Fast dissolving form.J.Pharm, Pharmacol, 1998; 50(4): 375-382.
5. Lachman A, Lieberman, H.A, Kanig J.L(1990), Banker, G.S, Anderson, N.R. In: The Theory and Practice of Industrial Pharmacy 3rd ed,.Mumbai, Varghese Publishing House : 296-302.
6. Rockville, M.D, United States of Pharmacoepia-National Formulary,USP30-NF25, vol-1,The United States Pharmacoepial Convention: 2007; 635-645.
7. Mukesh.P.,Ratnaparkhi,.Mohanta,G.P.,Upadhaya,L., Review on : Fast Dissolving tablet, Journal of Pharmacy Research, 2009; 2(1): 5-12.

8. D. Bhowmik et al, Fast Dissolving Tablet: An Overview; Journal of Chemical and Pharmaceutical Research, 2009; 163-177.
9. Patel D M, Prajapati D G, Patel N M Seed mucilage of Ocimum americanum linn. As disintegrate in tablet: separation and evaluation. Indian Journal of Pharmaceutical Sciences. 2007; 69(3): 431-435.
10. Bi Y., Sunada H., Yonezawa Y., Danjo K., Otsuka A., Iida K., Preparation and evaluation of compressed tablet rapidly disintegrating in oral cavity. Chem. Accuracy Pharm. Bull. 1996; 44: 2121-2127.
11. Dali Shukla, Subhashis Chakraborty, Sanjay Singh, Brahmeshwar Mishra,Mouth Dissolving Tablets II: An Overview of Evaluation Techniques.Scientia Pharmaceutica, 2008; 329.
12. Mahaveer Pr Khinchi, Orally disintegrating tablets: A future prospectus, International Journal of Pharm Sciences Bio, 2010; 71-79.
13. Ratnaparkhi Mukesh P, Mohanta G.P, Upadhyay Lokesh: Review On: Fast Dissolving Tablet. Journal of Pharmacy Research 2009; 2(1): 5-12.
14. Sunada H, Bi Y. Preparation, evaluation and optimization of rapidly disintegrating tablets. Powder Technol 2002; 122(23): 188-198. and Pharmacotherapeutics, 19th ed., Popular Prakashan Pvt.Ltd, Mumbai, India, 2005; 665.
15. Koizumi K, Watanabe Y, Monita K, Utosuchi N. New method of preparing high porosity rapidly saliva soluble compressed tablets using mannitol with camphor, a subliming material. Int J Pharm. 1997; 152: 127–31.
16. R. Narazaki , Harada, T. Uchida, M. Yoshida, Y. Kobayashi, T. Ohwaki : A new method for evaluating the bitterness of medicines in development using a taste sensor and a disintegration testing apparatus, Chem Pharm bull, 2010; 58: 1009-1014.
17. Khan I.R , A. Marjina, H. Razibul, Khan I.M, R.Mominur, S.Mohammad : Design, Physicochemical Evaluation and In Vitro Dissolution Studies of Transdermal Patches Containing Aceclofenac, International Journal of Drug Development & Research, 3: 236.