Available online at www.ijpcr.com
International Journal of Pharmaceutical and Clinical Research 2009; 1(2): 82-84

Research Article ISSN 0975 1556

Formulation and Characterization of Fast-Dissolving Tablet of Nimesulide

Chopra VS*, Singhai SK

Ranbaxy Laboratories Limited, Industrial area- 3, Dewas 455001, Madhya Pradesh, India

ABSTRACT
Fast dissolving tablets (FDT) of Nimesulide were prepared by direct-compression method after incorporating superdisintegrants like Ac-Di-Sol & Sodium Starch Glycolate (SSG). The study was performed by incorporating the superdisintegrants in 2 % & 4 % concentration for each and 2 % - 2 % in combination of both superdisintegrants. Five formulations having superdisintegrants at different concentration levels were prepared to assess their efficiency. Different types of evaluation parameters for tablets were used. Tablets containing superdisintegrants in combination showed excellent *in vitro* dispersion time and drug release as compared to other formulations.

Key words: Direct compression, Nimesulide, superdisintegrants.

INTRODUCTION

Nimesulide (4-nitro-2-phenoxymethanesulfoanilide) is a selective COX-2 nonsteroidal anti-inflammatory drug. This compound, a derivative of p-nitrophenylmethane-sulfonamide, is structurally a unique nonsteroidal anti-inflammatory drug. It belongs to selective COX-2 inhibitors, with a potent anti-inflammatory and analgesic activity, when administered orally, rectally, or topically. Due to its analgetic and antipyretic properties, nimesulide is widely used for the treatment of various inflammatory processes. Besides, its better tolerated and causes fewer adverse effects than other currently used nonsteroidal anti-inflammatory drugs. It also shows less severe gastrointestinal side effects. This compound is structurally different from other new classes of COX-2 inhibitors named coxibes. The literature data suggests pK_a values, (from 5.9 to 6.56) of nimesulide. This compound is freely soluble in organic polar solvents, while its solubility in water was reported to be 0.01 mg ml but it depends on the pH of the aqueous solution. Its main impurities are C (2-phenoxyaniline) and D (2-phenoxy-4-nitroaniline). [1] This fast dissolving technology of nimesulide is convenient for administration and patient compliance for disabled, bedridden patient and for travelers and busy people, who do not always have access to water. And also the risk of choking or suffocation can also be avoided. These dosage forms dissolve in the oral cavity within a minute without the need of water or chewing. This technology also offers new business opportunity like product differentiation, product promotion, and patent extension. [2]

***Corresponding author: Mr. Vikram Singh Chopra,**
Ranbaxy Laboratories Limited, Industrial Area-3
Dewas 455001, M.P, India
Email: Vikram.chopra@ranbaxy.com

The fast dissolving tablets of nimesulide contains superdisintegrants, which accelerates the disintegration of tablets by virtue of their ability to absorb large amount of water when exposed to aqueous environment. This rapid disintegration of FDTs is due to penetration of saliva into the pores, which lead to the swelling of superdisintegrants to create enough hydrodynamic pressure for quick and complete disintegration of the tablets. This increase bioavailability / rapid absorption through pre-gastric absorption of drugs from mouth, pharynx & esophagus as saliva passes down. [3]

The objective of this study was to enhance the efficacy of drug molecule, achieve better compliance, enhance onset of action, and provide stable dosage form.

MATERIALS AND METHODS

Nimesulide, croscaramellose sodium, sodium starch glycolate, microcrystalline cellulose, D-mannitol, aspartame, talc, and magnesium stearate was received as a gift sample from Schon Pharmaceutical limited (Indore). All reagents and solvents used were analytical grade.

Preparation of blends and tablets

The superdisintegrants (Croscaramellose sodium, Sodium starch glycolate) in varying concentration (02 % & 04 %) and in combination (Croscaramellose sodium, Sodium starch glycolate) (02-02 %) were used to develop the tablets. All the ingredients (shown in Table 1) were passed through mesh # 60. All the ingredients were co-ground in a pestle motor for 5 min. The mixed blend of excipients was compressed using single punch on Karnawati, Rimek, Minipress II MT machine to produce convex faced tablets with upper punch embossed with 'SDS' and 'breakline' on lower punch weighing 200 mg each, with thickness of 2.9 ± 0.2 mm and diameter of 8.0 mm (Fig. 1). For all the formulations approximate 100 tablets were compressed. [3]

Table 1: Formulation of fast dissolving tablets of Nimesulide

Formulation ingredients	F 1	F 2	F 3	F 4	F 5
Nimesulide	100	100	100	100	100
Croscaramellose sodium	4	8	-	-	2
Sodium starch glycolate	-	-	4	8	2
Micro crystalline cellulose	50	50	50	50	50
D-Mannitol	30	26	30	26	30
Aspartame	10	10	10	10	10
Talc	4	4	4	4	4
Magnesium Stearate	2	2	2	2	2

Evaluation of blends

In solid dosage forms the physiochemical properties of blend rules the tablet quality. The mixing step if not properly optimized can effect the characteristics of blend and thereby tablet produced. The blends were characterized by mass-volume relationship (bulk density, tapped density, Hausner's ratio, compressibility index) and flow properties (static angle of repose). [3]

Evaluation of tablets

Prepared tablets were evaluated for hardness (Dr Schulzner hardness tester), friability (Roche friabilator), weight variation, disintegration time, wetting time, water absorption ratio, *In-vitro* dispersion time, and drug content.

The disintegration time was determined using USP tablet disintegration test apparatus (ED 2L, Electrolab, India) using 900 ml of distilled water without disk at room temperature.

In weight variation test twenty tablets were selected at random and average weight was determined using an electronic balance (Shimadzu AX200, Japan). Tablets were weighed individually and compared with average weight.

Wetting time was carried out by using the method given by Bi et al. (1996). In this method a piece of tissue paper folded twice in a small culture dish (internal diameter = 6.5 cm) containing 6 ml of water. A tablet is placed on the paper and the time for complete wetting is measured. The wetted tablet is then weighed and the water absorption ratio was calculated using eq. (1)

$$R = (W_b - W_{a)} / W_a \quad \text{.....1}$$

Where Wa and Wb are the weights before and after water absorption, respectively. [4-5]

For the determination on in vitro dispersion time (Fig 2 a & 2 b), one tablet was placed in a beaker containing 10 ml of pH 6.8 phosphate buffer at 37 ± 0.5 ºC and the time required for complete dispersion was determined.

For assay, mobile phase used was, phosphate buffer (pH6.8): ACN in 60:40 ratio. Column used was C18 4.6 × 250 mm (5 mm packing) at a flow rate of 1.0 ml min^{-1}.The UV detection was performed at 254 nm. Injected volume was 20 µL.

In vitro dissolution studies of optimized batch tablets were performed by using type USP type-II apparatus in 6.8 pH phosphate buffer (900 ml)with 1 % SLS at 37 ± 2 ºC at speed of 50 ± 5 rpm. [6-9]

RESULTS AND DISCUSSION

The use of superdisintegrants for preparation of fast dissolving tablets is highly effective and commercially useful. Prepared fast dissolving tablets gets dispersed in the mouth quickly and release the drug early as compared to its formulated conventional tablets. The superdisintegrants croscaramellose sodium, sodium starch glycolate alone in varying concentration and both in combination were studies for achieving faster dispersion of tablets.

Since, the flow properties of the powder mixture are important for the uniformity of mass of tablets, the flow of the powder mixture was analyzed before compression of tablets.

All the formulation were analyzed for bulk density,tapped density, compressibility index, hausner's ratio, and angle of repose (Table 2) As the tablet powder was free flowing, tablets produced were of uniform weight with acceptable weight variation (≤ 0.483 %) due to uniform die-fill

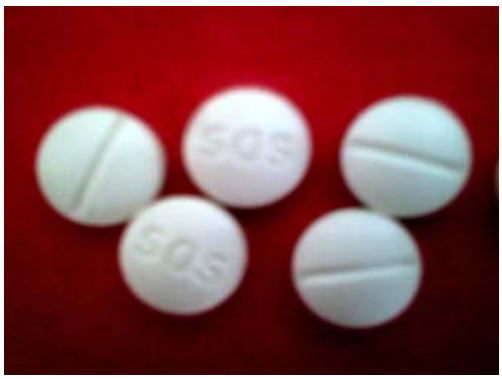

Fig. 1: Nimesulide FDDT's

Fig. 2 (a): *In-vitro* dispersion time of F5

Fig. 2 (b): *In-vitro* dispersion time of F5

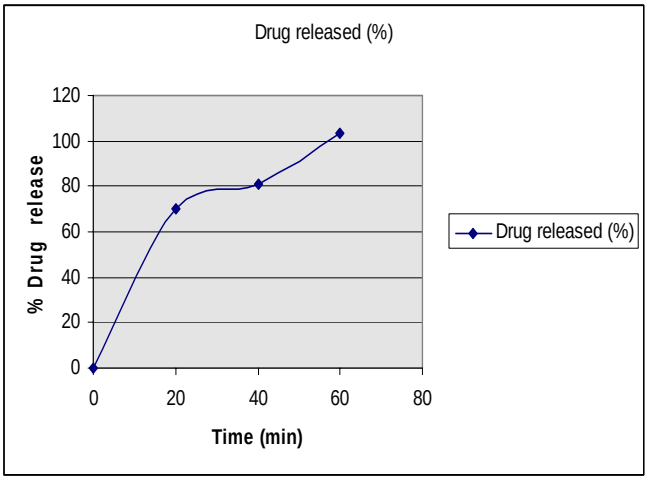

Fig. 3: *In-vitro* dissolution profile of F5

Table 2: Evaluation of fast-dissolving tablet of nimesulide

Formulation parameters	F 1	F 2	F 3	F 4	F 5
Bulk density (gm/cm ^{3})	0.416	0.476	0.476	0.472	0.476
Tapped density (gm/cm ^{3})	0.588	0.700	0.700	0.694	0.661
Compressibility index (%)	29.25	31.97	32.00	31.98	28.00
Hausner's ratio	1.413	1.47	1.47	1.47	1.39
Static angle of repose (θ)	35º 52'	31º 00'	30º 54'	30º 75'	31º 21'
Weight variation (mg)	200.28 ± 0.882	200.23 ± 0.659	200.2 ± 0.574	200.64 ± 0.856	200.53 ± 0.967
Hardness (kg / cm ^{2})	4.14 ± 0.250	4.18 ± 0.361	4.36 ± 0.372	4.24 ± 0.409	3.97 ± 0.275
Friability (%)	0.26	0.25	0.32	0.60	0.58
Disintegration time (sec)	47.67 ± 2.517	23.0 ± 2.646	46.0 ± 1.732	29.33 ± 1.555	12.67 ± 1.155
Wetting time (sec)	80	20	32	25	20
Water absorption ratio (%)	80.57	91.0	74.35	83.59	86.21
In-vitro dispersion time (sec)	29.33 ± 1.155	16.67 ± 1.528	28.0 ± 2.0	25.0 ± 2.0	18.67 ± 1.528
Assay (%)	98.96	99.12	96.67	101.23	100.05

Table 3: Dissolution values for formulation F 5

Dissolution (by UV) Formulation F5	Drug Released (%)
20 min	69.86 %
40 min	80.96 %
60 min	103.03 %

- Tablets prepared by direct compression method were found to be good, without any chipping, capping and sticking.
- The most important parameter of fast dissolving tablets is the disintegration time. In the present study all tablets disintegrated in ≤ 47.67 seconds fulfilling the official requirements (≤ 3 minutes) for dispersible tablets. Formulation F5 showed disintegration of 12.67 seconds.
- The hardness of tablets was found to be in range of 3.9 – 4.4 kg/cm^2.
- The friability of all formulation was below 1 % was an indication of good mechanical resistance of tablets.
- Drug content was found to be in range of 98 – 101 %.
- The formulation F5 has displayed good water absorption ratio of about 86.21 % which indicates better and faster swelling ability of the superdisintegrants in presence of little amount of water.
- The formulation F5 has displayed wetting time of 20 seconds, which facilitates their faster dispersion in mouth.
- The dissolution study of the formulation F5 showed that complete drug was released in 60 minutes. (Fig. 3)

Thus it can be concluded that disintegration of nimesulide can be enhanced to a great extent by direct compression technique with the addition of combination of superdisintegrants

REFERENCES

1. Tubic B, Ikovic B, Zecevic M, Vladimirov S. Simaltaneous determination of nimesulide and its impurities in pharmaceutical formulations by reversed phase HPLC. Acta Chim Slov 2007; 54: 583-590.
2. Bhandari S, Mitapalli RK, Gannu R, Rao YM. Orodispersible tablets: An Overview. Asian Journal of Pharmaceutics 2008; 2-11.
3. Sharma S, Gupta GD, Formulation and characterization of fast dissolving tablets of Promethazine theoclate. Asian Journal of Pharmaceutics 2008; 70-72.
4. Kundu S, Sahoo PK. Recent trends in the developments of orally disintegrating technology. Pharma Times 2008; 40(4): 11-15.
5. Chakraborthy S, Khandai M, Singh SP. Patra N. Comparitive study on effect of natural and synthetic superdisintegrant in the formulation of fast dissolving tablets; International Journal of Green Pharmacy 2008; 22-25.
6. Swamy PV, Areefulla SH, Shirsand SB, Gandra S, Prashanth B. Orodispersible tablets of Meloxicam using disintegrants blends for improved efficacy. Indian J Pharm Sci 2007; 69(6): 836-840.
7. Jacob S, Shirwaikar AA, Joseph A, Sriniwasan KK. Novel co-processed excipients of mannitol and microcrystalline cellulose for preparing fast dissolving tablets of glipizide. Indian J Pharm Sci 2007; 69(5): 633-639.
8. Setty MC, Prasad DVK, Gupta RM, Sa B. Development of of fast dispersible Aceclofenac tablets: Effect of functionality of superdisintegrants. Indian J Pharm Sci 2008; 70(2): 180-185.
9. Zade PS, Kwatikwar PS, Sakarkar DM, Formulation evaluation and optimization of fast dissolving tablets containing tizanidine hydrochloride. International Journal of Pharm Tech Research 2009; 1(1): 34-42