Short report

Fast-disintegrating aceclofenac tablets: formulation development using simplex lattice design

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Abstract:

The poor aqueous solubility of the drug results in variable dissolution profile and hence poor bioavailability. The aim of present work was to show the effect of various super disintegrants on the disintegration time and *in vitro* drug release rate. In this study, an attempt had been made to prepare fast disintegrating tablets of the drug using different super disintegrants following wet granulation method. The sodium starch glycolate, cross carmellose sodium and pregelatinized starch (Starch 1500®) were used in different concentrations according to the simplex lattice design as the super disintegrants. The tablets were evaluated for diameter, thickness, hardness, friability, weight variation, wetting time, percentage of water absorption, disintegration time and *in vitro* dissolution studies. The disintegration time of all formulation showed less than 89 seconds. Formulation containing equal amount of Cross carmellose sodium and pregelatinized starch showed fastest disintegration than other formulations containing Starch 1500®, cross carmellose sodium and sodium starch glycolate in various proportions and the percentage drug release was 99.5 within 10 minutes.

Keywords: Aceclofenac; Fast-disintegrating; Simple lattice design; Super disintegrants

Introduction

A large number of patients may have difficulty in swallowing the conventional pharmaceutical dosage forms, particularly pediatric and geriatric. Such problems can be overcome by means of fast disintegrating/ dissolving tablets. Fast disintegrating tablets are suitable for these patients since they immediately release the active drug when they are placed on the tongue. The fast-disintegrating tablets could be prepared using various techniques such as tablet molding, spray drying, sublimation, lyophilization, solid deposition or addition of disintegrants [1-4]. The main criterion for fast disintegrating tablets is the capacity to disintegrate or dissolve rapidly in oral cavity with assessment of saliva within a minute without need of water. Thereafter this could enhance the bioavailability of drug through pregastric absorption from the mouth, pharynx and esophagus [5]. The various super disintegrants like sodium starch glycolate, cross carmellose sodium and pregelatinized starch were used for preparation of fast disintegrating tablets [6-8]. Aceclofenac, a non-steroidal anti-inflammatory drug, was selected as model drug because it is widely used in treatment of pain and inflammation. To protect mild after bitter taste of aceclofenac, sweetening agent such as sodium saccharin should be used.

A common problem in pharmaceutics occurs when the components of formulations are varied in an attempt to optimize its performance with respect to variables. Simplex lattice can be used to determine the relative proportion of ingredients that optimizes a formulation with respect to specified variables. Hence simplex lattice is used to obtain the optimum concentration of super disintegrants to formulate the fast disintegrating tablets of aceclofenac.

Materials and Methods

Materials

Aceclofenac was a gift sample from Rantus Pharma Pvt Ltd. (India). Sodium starch glycolate (SSG), cross carmellose sodium (CCS) and Starch 1500® were the gift from Merit Organic Chemicals, Sarigam, Maruti Chemicals, Ahmedabad and Colorcon Asia Pvt Ltd, Goa, respectively. All other ingredients used were of pharmaceutical grade.

Methods

Spray drying of mannitol

Spray drying can reduce the particle size of mannitol so that it is rapidly dissolved, which is necessary for the fast-disintegrating/dissolving type of formulation. In this study mannitol was spray dried using a LabUltima spray dryer. Firstly, mannitol was dissolved in water in the ratio of 10:90 and then sprayed into the drying chamber at feeding rate 2 mL/min with inlet and outlet temperature of 120 °C and 90 °C, respectively, at aspiratration speed of 40. Then the dried mannitol was collected from the cyclone separator.

Preparation of aceclofenac tablets

Tablets were made by wet granulation method using the ingredients given in Table 1. The various batches were prepared using three super disintegrants namely Starch 1500®, cross carmellose sodium and sodium starch glycolate by simplex lattice design. Disintegrants were mixed with spray-dried mannitol. Then the powder blend was mixed with purified water to obtain a coherent mass. The mass was passed through a 30 mesh. The wet granules were dried at 60°C for 1 hour in a hot air oven. The dried granules were mixed with magnesium stearate. This blend was compressed into tablets using 8 mm diameter die using KBr press (Technosearch Instruments, India). The final weight of tablets was kept at 250 mg. The hardness of the tablets was kept between 2.5 and 3 kg/cm^2. The prepared tablets were stored in airtight container before evaluation.

Evaluation of tablets

Prepared tablets were evaluated for diameter, thickness, hardness, friability, weight variation, wetting time, percentage of water absorption, disintegration time and *in vitro* dissolution studies (n=3). The diameter and thickness were measured using Mitutoyo Digimatic Caliper (CD-6" CSX, Kawasaki, Japan). Hardness was

measured using Monsanto hardness tester (Technosearch Instruments, India). Friability was determined by Roche friabilator by evaluating 20 tablets of each formulation (Lab Hosp, India).

Wetting time was determined by placing a piece of tissue paper folded twice in a small petridish containing 6 mL water. A tablet was placed on the tissue paper and small amount of amaranth powder was placed on upper surface of tablet. The time required for development of a red color on the upper surface of the tablet was recorded as wetting time [4].

A piece of tissue paper folded twice was placed in a small petridish containing 6 mL of water. A tablet was kept on paper and time required for complete wetting was measured. Then wetted tablet was weighed and percentage of water absorption was determined using the following equation [9]:

$$R = Wb\text{-}Wa/Wa \times 100$$

where, Wa is weight of tablet before water absorption
Wb is weight of tablet after water absorption
R is water absorption ratio.

In vitro disintegration time was determined using a disintegration test apparatus (Lab Hosp, India). This test was carried out at 37 ± 2°C in 900 mL of distilled water. *In-vitro* dissolution studies were carried out using USP apparatus type II at 50 rpm. The dissolution medium used was a phosphate buffer pH 6.4 (900 mL) maintained at 37 ± 0.5°C. 5 mL of sample was withdrawn and replaced with fresh dissolution medium at different time intervals and the concentration of aceclofenac was measured by determining absorbance at 275 nm using UV spectrophotometer (Jasco V530, Japan).

Results and Discussion

The average weight of the prepared tablets was in between 258.22 and 260.34 mg. The average thickness and diameter of tablets were found to be 3.45 mm and 8.00 mm, respectively. The hardness of prepared tablets was between 2.5 to 3.5 kg/cm^2. The friability of all the formulations was less than 1% indicating the ability of tablet to withstand abrasion in handling packaging and shipment. The weight variation of prepared tablets was within limits. The wetting time of formulation F4 was 35 seconds containing Starch 1500® and cross carmellose sodium in equal proportion, which was lower than other formulations. The percentage of water absorption was between 67.35 to 99.72. The disintegration time of the tablets varied from 17 to 89 seconds. The tablet containing equal proportion of Starch 1500® and cross carmellose sodium disintegrates faster than tablets prepared with other formulations as shown in Table 2. The *in vitro* drug release from tablets containing Starch 1500® and cross carmellose sodium was 99.5% and drug release of tablets containing only sodium starch glycolate was 86.12% while tablets formulated using

Table 1 Formulation (F1-F7) of tablets

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7
Aceclofenac	100	100	100	100	100	100	100
SSG	25	12.5	-	-	-	12.5	8.33
CCS	-	12.5	25	12.5	-	-	8.33
Starch 1500	-	-	-	12.5	25	12.5	8.33
MS	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Mannitol	106.25	106.25	106.25	106.25	106.25	106.25	106.25
Lactose	15	15	15	15	15	15	15
SS	1.25	1.25	1.25	1.25	1.25	1.25	1.25

SSG = Sodium starch glycolate; CCS = Cross carmellose sodium; MS = Magnesium stearate
SS = Sodium saccharin; F= Formulation

sodium starch glycolate and Starch 1500® could release the drug of 88.7% within 10 minutes. The drug release profiles of all prepared tablets are shown in Figure 1.

This rapid disintegration of fast disintegrating tablets was due to the penetration of saliva into the pores of the tablets, which lead to the swelling and wicking of super disintegrants to create enough hydrodynamic pressure for quick and complete disintegration of the tablet. The optimum formulation which showed rapid disintegration contained equal proportion of pregelatinized starch and cross carmellose sodium.

Conclusion

The result of simplex lattice design revealed that the combination of disintegrants significantly affect the wetting time, disintegration time, drug release. The formulation containing Starch 1500® and cross carmellose sodium in equal proportion showed the fast disintegration as compared to the other formulations. It is thus concluded that by selecting proper amount and combination of disintegrants in tablets formulation, tablet with fast disintegration can be produced.

Table 2 Evaluation of tablet formulations (F1-F7)

Properties	F1	F2	F3	F4	F5	F6	F7
Thickness (mm)	3.45 ± 0.02	3.47 ± 0.05	3.45 ± 0.03	3.44 ± 0.02	3.45 ± 0.06	3.45 ± 0.05	3.46 ± 0.06
Diameter (mm)	8.01 ± 0.09	7.98 ± 0.12	8.00 ± 0.03	8.00 ± 0.09	8.02 ± 0.03	8.02 ± 0.01	8.00 ± 0.07
Hardness (kg/cm^2)	2.80 ± 0.04	3.20 ± 0.03	3.00 ± 0.09	2.70 ± 0.04	2.70 ± 0.11	2.80 ± 0.10	2.90 ± 0.09
Friability (%)	0.580 ± 0.002	0.410 ± 0.012	0.400 ± 0.031	0.670 ± 0.004	0.620 ± 0.011	0.600 ± 0.002	0.580 ± 0.015
Weight variation (%)	1.63 ± 0.12	2.03 ± 0.43	1.86 ± 0.08	1.95 ± 0.05	3.09 ± 0.09	2.58 ± 0.05	2.97 ± 0.08
Wetting time (sec)	214.00 ± 0.95	97.00 ± 1.04	175.00 ± 0.84	35.00 ± 1.48	46.00 ± 0.65	124.00 ± 1.17	87.00 ± 0.53
% Water absorption	94.73 ± 0.99	67.35 ± 1.16	84.77 ± 0.35	99.72 ± 0.92	84.35 ± 0.43	77.32 ± 0.84	88.27 ± 0.12
Disintegration time (sec)	89.00 ± 1.03	54.00 ± 0.39	75.00 ± 0.34	17.00 ± 0.89	23.00 ± 1.15	74.00 ± 1.02	32.00 ± 0.93
% Drug release (10 min)	86.12 ± 0.83	91.73 ± 0.76	89.99 ± 1.52	99.50 ± 0.91	93.70± 0.58	88.70 ± 0.42	87.75 ± 0.35

*All readings were taken in triplicate ± Standard Deviation.

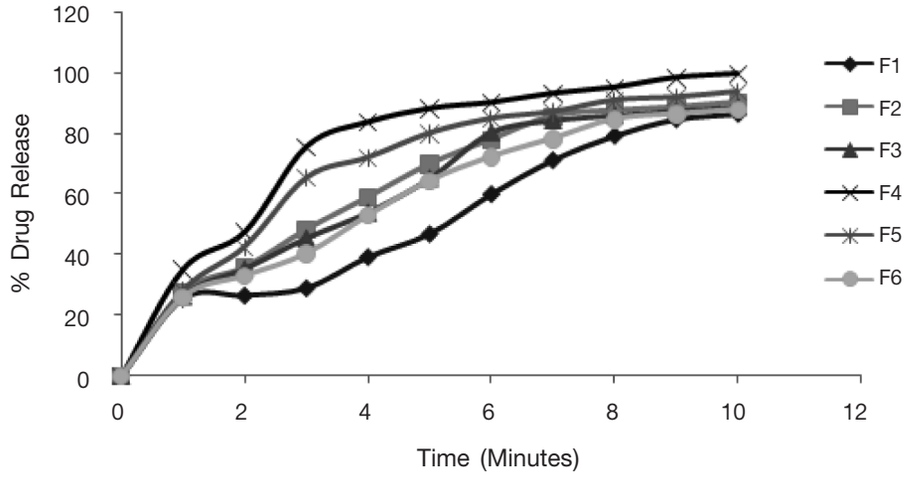

Figure 1 Drug release profile (n=3)

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