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Research Article

FORMULATION AND EVALUATION OF FAST DISPERSIBLE TABLETS OF SERTRALINE USING DIFFERENT SUPERDISINTEGRANTS

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ABSTRACT

In the present work attempts were made to prepare fast-dispersible tablets of Sertraline by direct compression method with a view to enhance patient compliance. The three superdisintegrants used in this study were Crosscarmellose sodium, Crospovidone and Sodium starch glycolate. Tablets having superdisintegrant at different concentration (8, 10 and 12 mg) level were prepared. The prepared batches of tablets were evaluated for uniformity of weight, thickness, hardness, friability, *in-vitro* dispersion time and *in-vitro* dissolution study. Tablet containing crosscarmellose sodium showed excellent in vitro dispersion time and drug release as compared to other formulations. After study, formulation N6 shows short dispersion time with maximum drug release in 40 minutes.

KEYWORDS: Sertraline, Fast dispersible tablets, *In-vitro* evaluation, Superdisintegrants.

INTRODUCTION

The tablet is the most widely used dosage form because of its convenience in terms of self-administration, compactness, and ease in manufacturing. For the past one decade, there has been an enhanced demand for more patient- friendly and compliant dosage forms. As a result, the demand for developing new technologies has been increasing annually. Since the development cost of a new drug molecule is very high, efforts are now being made by pharmaceutical companies to focus on the development of new drug dosage forms for existing drugs with improved safety and efficacy together with reduced dosing frequency, and the production of more cost- effective dosage forms[1].

Many patients find it difficult to swallow tablets and hard gelatin capsules and thus do not comply with prescription. This results in high incidence of noncompliance and ineffective therapy[2]. The proper choice of superdisintegrant and its consistency of performance are of critical importance to the formulation development of fast dispersible tablets[3]. The objective of the present study is to develop fast dispersible tablets of Sertraline and to study the effect of functionality differences of superdisintegrants on the tablet properties as well as to improve the patient compliance without compromising the therapeutic efficacy.

Sertraline is belongs to the class of SSRI (Selective serotonin reuptake inhibitors) drug but is unrelated to other SSRI's. it is chemically unrelated to tricyclic, tetracyclic depressants. The mechanism of action is inhibition of CNS neuronal uptake of serotonin (5HT). It is used as an adjuvant in the treatment of depression and anxiety disorder. However, the low aqueous solubility it is rapidly and extensively absorbed after oral administration. The absolute bioavailability is only approximately 44% due to extensive hepatic metabolism.[4] Various techniques can be used to formulate orally disintegrating tablets or fast dissolving tablets.[5] Direct compression one of the technique requires the incorporation of a superdisintegrants into the formulation the use or highly water soluble excipients to achieve fast tablet disintegration. Direct compression does not require the use of water or heat during the formulation procedure and is the ideal method for moisture and heat-labile medications. In the present study, an attempt was made to develop fast dispersible tablets of Sertraline and to improve its bioavailability.

MATERIALS AND METHODS

Sertraline was a gift from Franklin Laboratories (I) Pvt. Ltd. (Ludhiana, India). Croscarmellose sodium used was analytical reagent grade procured from Loba Chemicals, Mumbai. Crospovidone and Sodium Starch Glycolate used were procured from Merck Limited, Mumbai. All other reagents and chemicals used were of analytical grade.

Preparation of fast dispersible tablets of Sertraline

Fast dispersible tablets containing 50mg of Sertraline were prepared by direct compression method and the various formulae used in the study are shown in table 1. All the ingredients without magnesium stearate and talc were mixed uniformly followed by addition of magnesium stearate and talc. The prepared powder blend was evaluated for various parameters like bulk density, tapped density, angle of repose, compressibility index and Hausner ratio. After evaluation of powder blend the tablets were compressed with a ten-station rotary punch-tableting machine (Rimek Mini Press-1) using 8 mm flat punches set.

Evaluation of powder blends [6-9]

Bulk density

Apparent bulk density (ρb) was determined by placing presieved drug excipients blend into a graduated cylinder and measuring the volume (Vb) and weight (M) "as it is".

$$\rho b = M/Vb$$

Tapped density

The measuring cylinder containing a known mass of blend was tapped for a fixed number of taps. The minimum volume (Vt) occupied in the cylinder and the weight (M) of the blend was measured. The tapped density (ρt) was calculated using following formula.

$$\rho t = M/ Vt$$

Angle of repose

Angle of repose (θ) was determined using funnel method. The blend was poured through a funnel that can be raised vertically until a maximum cone height (h) was obtained. The radius of the heap (r) was measured and angle of repose was calculated.

$$\theta = \tan^{-1} h/r$$

Compressibility index

The simplest way of measurement of free flow property of powder is compressibility, an indication of the ease with which a material can be induced to flow is given by % compressibility which is calculated as follows:

$$C = (\rho t - \rho b) / \rho t \times 100$$

ρt - Tapped density, ρb - Untapped bulk density

Hausner's ratio

Hausner's ratio is an index of ease of powder flow; it is calculated by following formula.

$$\text{Hausner's ratio} = \rho t \backslash \rho b$$

ρt - Tapped density, ρb -Untapped bulk density

Evaluation of Sertraline fast dispersible tablets[10-12]

Weight variation test

Weight variation test was done by weighing 20 tablets individually, by using Sartorious balance (Model CP- 224 S). Calculating the average weight and comparing the individual tablet weight to the average weight.

Tablet thickness

The thickness was measured by placing tablet between two arms of the Varnier calipers. 5 tablets were taken and their thickness was measured.

Tablet hardness

The tablet hardness, which is the force required to break a tablet in a diametric compression force. The hardness tester used in the study was Monsanto hardness tester, which applies force to the tablet diametrically with the help of an inbuilt spring.

Tablet friability

The friability of the tablets was measured in a Roche friabilator (Camp-bell Electronics, Mumbai). Tablets of a known weight (Wo) or a sample of 20 tablets are dedusted in a drum for a fixed time (100 revolutions) and weighed (W) again. Percentage friability was calculated from the loss in weight as given in equation as below. The weight loss should not be more than 1 %. Determination was made in triplicate.

$$\% \text{ Friability} = 100 (Wo - W) / Wo$$

***In-vitro* dispersion time**

Tablet was added to 10 ml of phosphate buffer solution (pH 6.8) at 37±0.5°C. Time required for complete dispersion of a tablet was measured.

***In-vitro* dissolution study**

The release rate of Sertraline from fast dispersible tablets was determined using United State Pharmacopoeia (USP) XXIV dissolution testing apparatus II (paddle method). The dissolution test was performed using 900 ml of phosphate buffer pH 6.8 as a dissolution medium, at 37±0.5^{0}C and 50 rpm. A sample (5 ml) of the solution was withdrawn from the dissolution apparatus at 5, 10, 15, 20, 25, 30, 35 and 40 minutes. The samples were filtered through a 0.45µ membrane filter. Absorbance of these solutions was measured at 270 nm using a Shimadzu UV-1700 UV/VIS spectrophotometer. Cumulative percentage of drug release was calculated using an equation obtained from a standard curve.

RESULTS AND DISCUSSION

For each designed formulation, blend of drug and excipients was prepared and evaluated for micromeritics properties shown in table 2. Bulk density was found to be between 0.422–0.457 gm/mi and tapped density between 0.475–0.528 gm/ml for all formulations. Hausner's ratio was found below 1.2 and carr's compressibility index between 10-16 for all formulations. The angle of repose is known to be a measure of flowability and the angle of repose of all formulations was found between 23.13^0-25.19^0 it indicate good flow properties of powder.

All batches of the tablets were evaluated for various physical parameters shown in table 3. the weight variation of all the tablets were within the ranges of 198-203 mg. The hardness of the tablets were within the range of 3.4-3.8 kg/cm2. The friability of all tablets below 1% and the dispersion time was found Sodium starch glycolate ≤ Croscarmellose sodium ≤ Crospovidone. The influence of superdisintegrants on the dissolution of Sertraline from the tablets is shown in Fig. 1, 2&3. The drug release increased with increase in the level of superdisintegrants. Out of nine formulations N6 formulation shows best drug release 99.81% in 40 minutes.

CONCLUSION

It can be concluded that disintegration time and dissolution rate of Sertraline can be enhanced to a great extent by direct compression technique with the addition of superdisintegrants. Further investigations are needed to confirm the *in-vivo* efficiency.

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Table 1: Formulation of Sertraline FDT

Ingredients	Formulation Code								
	N1	N2	N3	N4	N5	N6	N7	N8	N9
Sertraline	50	50	50	50	50	50	50	50	50
Croscarmellose sodium	8	10	12	--	--	--	--	--	--
Crospovidone	--	--	--	8	10	12	--	--	--
Sodium starch glycolate	--	--	--	--	--	--	8	10	12
Microcrystalline cellulose	35	35	35	35	35	35	35	35	35
Mannitol	92	90	88	92	90	88	92	90	88
Aspartame	9	9	9	9	9	9	9	9	9
Magnesium stearate	3	3	3	3	3	3	3	3	3
Talc	3	3	3	3	3	3	3	3	3
(Total) mg	200	200	200	200	200	200	200	200	200

Table 2: Pre compression parameters data for Sertraline powder blend

Parameters	Formulation Code								
	N1	N2	N3	N4	N5	N6	N7	N8	N9
Bulk density (gm/ml)	0.443	0.457	0.434	0.439	0.445	0.449	0.422	0.427	0.431
Tapped density (gm/ml)	0.493	0.510	0.520	0.501	0.517	0.528	0.475	0.496	0.505
Hausner's ratio	1.1128	1.1159	1.1981	1.1412	1.1617	1.1759	1.1255	1.1615	1.1716
Carr's index (%)	10.1419	10.3921	16.5384	12.3752	13.9264	14.9621	11.1579	13.9112	14.6534
Moisture content	3.0	3.0	3.0	3.0	3.5	3.0	3.0	3.0	3.0
Angle of repose (θ)	23.39	23.24	24.05	23.13	24.23	24.15	24.34	25.19	25.11

Table 3: Evaluation of Sertraline FDT

Formulation parameters	Formulation Code								
	N1	N2	N3	N4	N5	N6	N7	N8	N9
Weight variation (%)	202 ±1.21	199 ±1.15	198 ±2.10	201 ±2.30	203 ±1.12	200 ±2.11	202 ±2.15	201 ±1.34	199 ±1.46
Thickness (mm)	3.2	3.1	3.1	3.0	3.1	3.0	3.1	3.2	3.0
Hardness (kg/cm2)	3.5 ±0.26	3.4 ±0.32	3.8 ±0.17	3.4 ±0.37	3.5 ±0.29	3.5 ±0.27	3.5 ±0.11	3.5 ±0.21	3.5 ±0.12
Friability (%)	0.36	0.31	0.31	0.35	0.38	0.47	0.41	0.39	0.46
Dispersion time (min)	34.27	33.12	30.15	30.44	28.45	25.23	38.24	37.38	32.56
% Drug release (after 40 min)	85.68	91.41	95.18	87.42	93.24	99.81	84.13	90.23	93.44

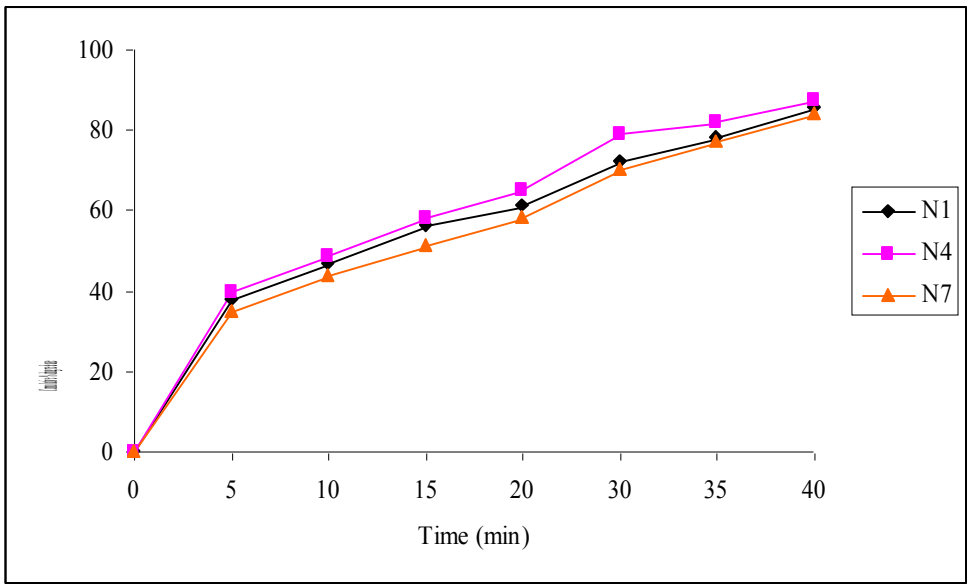

Fig. 1: Drug release profile of Sertraline FDT N1, N4 and N7 formulations

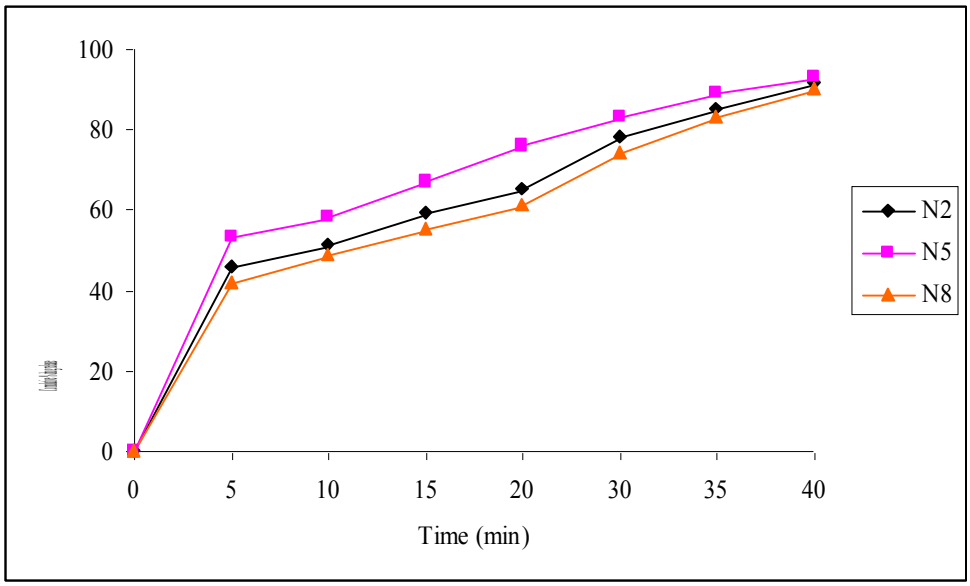

Fig. 2: Drug release profile of Sertraline FDT N2, N5 and N8 formulations

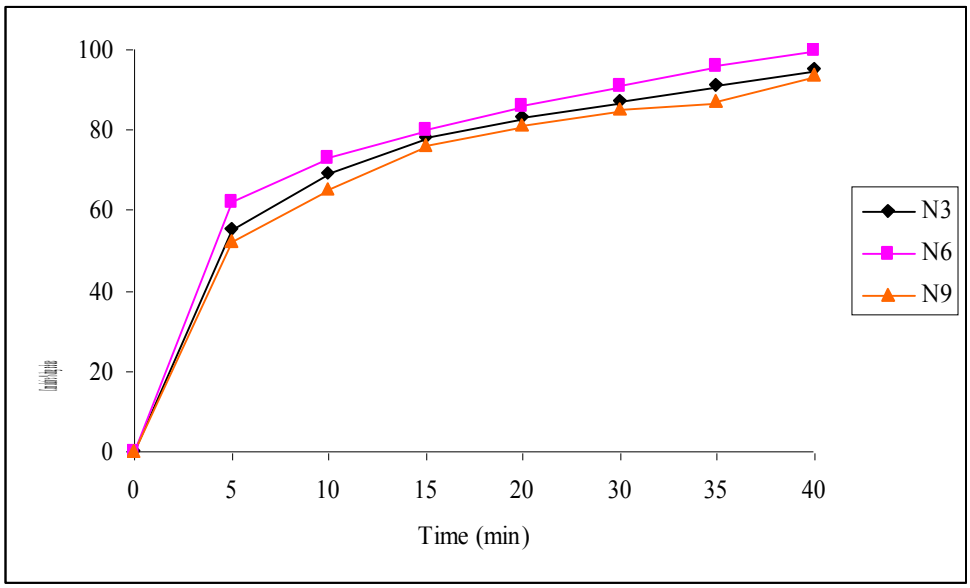

Fig. 3: Drug release profile of Sertraline FDT N3, N6 and N9 formulations

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