

## **Research Article**

# **Study of Influence of Povidone and Sodium Lauryl Sulphate on Performance of Mouth Dissolving Tablets of Mirtazapine**

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**Abstract:** Mouth dissolving tablets disintegrate and/or dissolve in saliva immediately when they are placed in mouth. Their rate of disintegration and dissolution are highly influenced by the formulation and method of manufacture. In the present investigation, it was aimed to study the influence of two hydrophilic excipients viz. povidone (PVP) and sodium lauryl sulphate (SLS) on the performance of mouth dissolving tablets of mirtazapine prepared by direct compression technique. Super – disintegrants are commonly employed in mouth dissolving tablets to enhance disintegration and dissolution rates. Still higher dissolution rates might be achieved if all the formulation contains hydrophilic excipients even lubricants also. In the present work, 9 different formulations were prepared using three super – disintegrants viz. sodium starch glycolate, crospovidone and cross carmellose sodium containing alone, and combination of PVP and SLS with each disintegrant. The disintegration and dissolution tests revealed interesting findings on behavior of SLS that though it increased disintegration time, it enhanced dissolution rate. The PVP was found to be effective as binder even in dry form.

**Keywords:** Mouth dissolving tablets, Super – disintegrants, Sodium lauryl sulphate, povidone, Disintegration time, Dissolution rate.

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## **INTRODUCTION**

Recent advances in novel drug delivery systems (NDDS) aim to enhance safety and efficacy of drug molecule by formulating to achieve better patient compliance. One such approach is ‘mouth dissolving tablets’, which disintegrate or dissolve in saliva and are swallowed without water [1]. As the tablet disintegrates in mouth, this could enhance the clinical effect of drug through pregastric absorption from the mouth, pharynx, and esophagus. This leads to an increase in the bioavailability by minimizing first pass liver metabolism. Mirtazapine is an antidepressant used for the treatment of moderate to severe depression [2]. In case of severe suicidal cases it requires immediate therapy. In order to increase the bioavailability and to elicit the quick pharmacological action, preparation of mouth dissolving tablets (MDTs) by direct compression technique is an excellent approach. Benkert O *et al.* [3] and Behnke K *et al.* [4] proved that the oral disintegrating tablets of mirtazapine showed better bioavailability when compared with other antidepressants formulated as conventional and extended release dosage forms. In the present investigation, it was aimed to study the influence of

some commonly used hydrophilic excipients such as SLS and PVP on the performance of mirtazapine MDTs which facilitates to know how to enhance the bioavailability further. Even though SLS is a good water soluble material, it can coat over the other excipients and can act as lubricant in tablet dosage forms [5], so that it might interfere with the contact time of disintegrant with water. PVP also a highly hydrophilic material, it absorbs water and swells immediately which might involve in the disintegration process, thereby in dissolution.

## **MATERIALS AND METHODS**

### **Materials**

Mirtazapine, cross carmellose sodium (CCS) and cross povidone (CP) were obtained as gift samples from Capricorn Pharma, Hyderabad. Sodium starch glycolate (SSG) was purchased from Loba Chemie, Mumbai. Microcrystalline cellulose (MCC), mannitol and povidone (PVP) were purchased from obtained from CDH; sodium lauryl sulphate (SLS) was purchased from Qualigens fine chemicals. All other chemicals used are of analytical grade.

## Methods

### Construction of Standard Calibration Curve

Standard stock solution of the drug was prepared in a 100ml volumetric flask by dissolving 100 mg drug in small quantity of 0.1N HCl and the volume was made up to the mark with 0.1N HCl. From the stock solution (1000µg/ml), 5 ml was taken into a 50ml volumetric flask and further diluted to 50 ml with 0.1N HCl, thus 100µg/ml standard solution was obtained. From this standard solution, a series of dilutions ranging from 5-20 µg/ml were prepared using 0.1N HCl. The absorbance was measured by using double beam UV-Visible spectrophotometer (Elico SL 210) at an absorbance maximum of 316 nm.

### Compatibility Studies by FT – IR

The physicochemical compatibility between mirtazapine & super – disintegrants (sodium starch glycolate, cross povidone and cross carmellose sodium) used in the research were carried out by subjecting to IR spectral studies using Perkin Fourier Transform infrared Spectrophotometer, Shelton, USA. The samples were prepared by mixing the drug with the super – disintegrants at the ratio used in the preparation of the tablets. These samples were scanned under diffuse reflectance mold and plotted the graph by KBr pellet method and spectra were recorded in wave length region between 4000cm<sup>-1</sup> to 400cm<sup>-1</sup>. The spectra obtained for pure drug was compared with that of the physical mixtures of the drug with super – disintegrants.

### Preparation of Mirtazapine Mouth Dissolving Tablets

**Table 1: Formulae for Mirtazapine MDTs of all formulations**

Sl. No.	Ingredients	Quantities in mg per one tablet								
		F <sub>1</sub>	F <sub>2</sub>	F <sub>3</sub>	F <sub>4</sub>	F <sub>5</sub>	F <sub>6</sub>	F <sub>7</sub>	F <sub>8</sub>	F <sub>9</sub>
1	Mirtazapine	30	30	30	30	30	30	30	30	30
2	Sodium starch glycolate (SSG)	3	3	3	-	-	-	-	-	-
3	Cross povidone (CP)	-	-	-	3	3	3	-	-	-
4	Cross carmellose sodium (CCS)	-	-	-	-	-	-	3	3	3
5	Micro crystalline cellulose (MCC)	89.5	92.5	95.5	89.5	92.5	95.5	89.5	92.5	95.5
6	Mannitol	20	20	20	20	20	20	20	20	20
7	Polyvinyl pyrrolidone (PVP)	3	-	-	3	-	-	3	-	-
8	Sodium lauryl sulphate (SLS)	3	3	-	3	3	-	3	3	-
9	Talc	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5

In this present work, a mirtazapine mouth dissolving tablets (MDTs) were prepared as three batches with 2% concentration of three different super – disintegrants. With each super – disintegrant three different formulae were made as one with combination of PVP and SLS; second one with only SLS and the third one without both PVP and SLS.

The mirtazapine MDTs were prepared by direct compression technique as the weighed amounts of mirtazapine, the super – disintegrant (sodium starch glycolate (SSG)/ crospovidone (CP)/ croscarmellose sodium (CCS)) and PVP were taken after sieved (through #80) according to the formulae mentioned in the table 1, and were triturated thoroughly. Then the weighed quantities of other excipients such as MCC, mannitol, SLS and talc were added and mixed thoroughly. This mixture was compressed to tablets of 150 mg each using 12 stage rotary tablet punching machine (Shakthi Tablet Press – 1 GMP).

### Characterization Studies [6-8]

#### Micromeritic properties of the blend

The physical blends of API with all other excipients of all formulations were subjected to various micromeritic Properties.

#### Bulk density

Blend was weighed and transferred to a measuring cylinder. Then bulk volume was noted. Bulk density was calculated by using the following formula

$$\text{Bulk density} = \frac{\text{Mass of the powder}}{\text{Bulk volume}}$$

#### Tapped density

Blend was weighed, transferred to a measuring cylinder and subjected to 100 tapings. Then volume was noted as tapped volume. Tapped density was measured by using the following formula

$$\text{Tapped density} = \frac{\text{Mass of the powder}}{\text{Tapped volume}}$$

#### Carr's index

Carr's index was calculated by using the following formula

$$\text{Carr's index} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

#### Hausner's ratio

$$\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

**Angle of repose**

Required quantity of blend was taken and poured into a hollow cylinder which was placed on a graph sheet. Then the cylinder was slowly lifted. Then height and diameter of the heap formed were noted down. The angle of repose ( $\theta$ ) was calculated by the formula

$$\text{Angle of repose, } \theta = \tan^{-1} \frac{h}{r}$$

**Characterization of mirtazapine MDTs****Average weight**

Five tablets were selected and were weighed collectively and individually. From the collective weight, average weight was calculated.

**Thickness**

Thickness of the prepared tablets was measured by using screw – gauge.

**Drug content**

Twenty tablets were powdered, and 10 mg mirtazapine equivalent weight of tablet powder was accurately weighed and transferred into a 100 ml volumetric flask. Then it was dissolved in 0.1N HCL and volume was made up to 100ml with 0.1N HCL. The solution in the volumetric flask was filtered, diluted suitably and analyzed spectrophotometrically at 316 nm.

**Disintegration Time**

The disintegration time was determined in distilled water at  $37 \pm 0.5^\circ \text{C}$  using disintegration test apparatus USP ED-2L.

**Friability**

Roche Friabilator was used to determine the friability. 6 Pre – weighed tablets were placed in friabilator and rotated at a speed of 25 rpm for 4 minutes or up to 100 revolutions. The tablets are dropped from a distance of 6 inches in each revolution. The tablets were then reweighed after removal of fines and the percentage of weight loss was calculated.

$$\% \text{ Friability} = \frac{\text{Initial weight} - \text{Final Weight}}{\text{Initial Weight}} \times 100$$

**Hardness**

Hardness of the tablet was determined using the Monsanto hardness tester. The lower plunger was placed in contact with the tablet and a zero reading was taken. The plunger was then forced against a spring by tuning threaded bolts until the tablet fractured. Then the final reading was recorded as hardness.

**Wetting time and Water absorption ratio**

A piece of paper folded twice was kept in a Petri dish containing 6 ml of purified water. A tablet having a small amount of Rosaline dye powder on the upper surface was placed on the tissue paper. The time

required to develop a red color on the upper surface of the tablet was recorded as the wetting time. The same procedure without Rosaline dye powder was followed for determining the water absorption ratio (R) and was calculated according to the following equation.

$$R = [(W_a - W_b)/W_b] \times 100$$

Where,  $W_b$  and  $W_a$  were the weights of the tablet before and after water absorption.

**Measurement of tablet porosity**

The mercury penetration porosimeter can be used to measure the tablet porosity which is a relative assessment of degree of water penetration in the formulation, responsible for its fast disintegration. Otherwise, tablet porosity can be calculated using the following equation.

$$\varepsilon = 1 - [m/(\rho_t/v)]$$

where,  $\rho_t$  is the true density,  $m$  and  $v$  are weight and volume of tablet, respectively.

**Dissolution studies**

Dissolution studies for mirtazapine mouth dissolving tablets were performed in 0.1 N HCl using DISSO 8000 (Lab India) dissolution test apparatus with a paddle stirrer. The paddles were allowed to rotate at speed of 100 rpm. The dissolution medium was maintained at a temperature of  $37 \pm 0.5^\circ \text{C}$  and samples were withdrawn at an interval of every 5 min. and the volume of the withdrawn samples were replaced by fresh medium in order to keep the volume of the dissolution medium as constant. The withdrawn samples were filtered and absorbance was measured at a wavelength of 316 nm using double beam UV- Visible spectrophotometer (ELICO SL 210).

**RESULTS AND DISCUSSION**

The opted method for the construction of standard calibration curve showed good linearity and reproducibility. The compatibility studies between mirtazapine and the excipients used in the preparation were studied by FT – IR and the obtained spectra for pure drug and physical mixtures were compared. The presence of the mirtazapine characteristic peaks at same positions in the spectra of physical mixtures as like in the pure mirtazapine indicated that there is no incompatibility.

The results of micromeritic properties of all formulations were shown in table 2. The results of angle of repose, Hausner's ratio and Carr's index indicated that all the precompression blends have good flowability [9]. The significant difference between bulk and tapped densities indicated that all the formulations have good compressibility so that they are suitable for direct compression.

**Table 2: Results of micromeritic properties of pre – compressed blends of all formulations**

Sl. No.	Formulation	Bulk density (g/cc) (Avg. ± S.D.)*	Tapped density (g/cc) (Avg. ± S.D.)*	Carr's index (%) (Avg. ± S.D.)*	Hausner's ratio (Avg. ± S.D.)*	Angle of repose (Avg. ± S.D.)*
1.	F1	0.53 ± 0.01	0.63 ± 0.02	15.87 ± 0.11	1.19 ± 0.01	25.8 ± 0.16
2.	F2	0.50 ± 0.01	0.58 ± 0.01	13.79 ± 0.12	1.16 ± 0.01	22.1 ± 0.13
3.	F3	0.52 ± 0.01	0.62 ± 0.02	16.13 ± 0.13	1.19 ± 0.01	26.2 ± 0.19
4.	F4	0.54 ± 0.01	0.63 ± 0.02	14.28 ± 0.11	1.17 ± 0.01	24.6 ± 0.16
5.	F5	0.57 ± 0.02	0.66 ± 0.01	13.64 ± 0.12	1.16 ± 0.01	22.5 ± 0.18
6.	F6	0.55 ± 0.01	0.65 ± 0.01	15.38 ± 0.13	1.18 ± 0.01	27.2 ± 0.16
7.	F7	0.59 ± 0.02	0.69 ± 0.02	14.49 ± 0.11	1.67 ± 0.02	24.3 ± 0.18
8.	F8	0.59 ± 0.02	0.67 ± 0.01	13.43 ± 0.11	1.14 ± 0.01	20.1 ± 0.16
9.	F9	0.58 ± 0.01	0.69 ± 0.01	15.94 ± 0.12	1.19 ± 0.01	25.7 ± 0.19

\*n (number of trials) = 3

The results of various physical characterization studies performed on Mirtazapine MDTs were shown in table 3. All the prepared tablets were checked for weight variation test and it was observed that all formulations were passed the test in the first trial only. The thickness was measured for the tablets of all formulations and was found to be within the acceptable range. The hardness for the tablets of all formulations was adjusted to 2.5 kg/cm<sup>2</sup> so that the effect of super – disintegrant, PVP and SLS on the dissolution rate could be evaluated accurately. The tablets of all formulations have shown good friability within the acceptable range.

This good friability was attributed to the presence of microcrystalline cellulose.

The wetting times of formulations containing PVP i.e. F1, F4, F7 were high when compared to the other formulations in the respective batches. This might be because of the tight binding nature of the PVP; it took more time for the water to penetrate. The wetting times of formulations containing only SLS i.e. F2, F5, F8 were low when compared to the respective formulations without SLS i.e. F3, F6, F9. This might be attributed to the wetting enhancement nature of the SLS.

**Table 3: Results of various physical evaluation parameters of Mirtazapine MDTs of all formulations**

Sl. No.	Parameter	F1 (Avg. ± S.D.)*	F2 (Avg. ± S.D.)*	F3 (Avg. ± S.D.)*	F4 (Avg. ± S.D.)*	F5 (Avg. ± S.D.)*	F6 (Avg. ± S.D.)*	F7 (Avg. ± S.D.)*	F8 (Avg. ± S.D.)*	F9 (Avg. ± S.D.)*
1	Weight (mg)	147.5 ± 0.8	149.4 ± 0.6	150.7 ± 0.5	148.9 ± 0.6	151.8 ± 0.7	150.9 ± 0.4	149.8 ± 0.4	150.5 ± 0.3	152.1 ± 0.8
2	Thickness (mm)	2 ± 0.05	2 ± 0.05	2 ± 0.05	2 ± 0.05	2 ± 0.05	2 ± 0.05	2 ± 0.05	2 ± 0.05	2 ± 0.05
3	Hardness (kg/cm <sup>2</sup> )	2.5 ± 0.2	2.5 ± 0.2	2.5 ± 0.2	2.5 ± 0.2	2.5 ± 0.2	2.5 ± 0.2	2.6 ± 0.2	2.5 ± 0.2	2.5 ± 0.2
4	Friability (%)	0.4 ± 0.05	0.5 ± 0.02	0.5 ± 0.03	0.6 ± 0.06	0.7 ± 0.05	0.5 ± 0.03	0.7 ± 0.05	0.8 ± 0.07	0.8 ± 0.03
5	Wetting time (sec)	42.2 ± 0.4	16.5 ± 0.6	24.4 ± 0.5	30.4 ± 0.6	15.5 ± 0.8	20.4 ± 0.4	23.5 ± 0.2	14.1 ± 0.1	19.3 ± 0.2
6	Water absorption ratio	42.3 ± 0.2	34.1 ± 0.3	36.2 ± 0.7	38.5 ± 0.3	31.1 ± 0.5	33.2 ± 0.7	38.5 ± 0.2	29.7 ± 0.2	34.1 ± 0.3
7	Tablet porosity (%)	2.18 ± 0.03	4.22 ± 0.02	11.72 ± 0.02	1.56 ± 0.05	2.28 ± 0.04	8.53 ± 0.03	1.24 ± 0.02	1.26 ± 0.03	2.34 ± 0.02
8	Disintegration time (min:sec)	11.40 ± 0.53	2.11 ± 0.11	0.23 ± 0.03	6.31 ± 0.48	0.28 ± 0.12	0.19 ± 0.04	1.52 ± 0.13	0.15 ± 0.03	0.15 ± 0.01
9	Assay (%)	99.1 ± 0.9	99.4 ± 1.0	102 ± 0.9	100.5 ± 0.9	101 ± 0.8	104.0 ± 0.5	98.9 ± 0.9	97.2 ± 0.6	99.4 ± 0.8

\*n (number of trials) = 3

The water absorption ratios of formulations containing PVP i.e. F1, F4, F7 were high when compared to those of other formulations in the respective batches since PVP is a hydrophilic colloid

and it can absorb water. Assay was performed by using UV – Visible spectrophotometer at 316 nm and the results for all the formulations were within the acceptable limits. From the results of porosity it was

observed that the formulations containing PVP had less porosity which might be attributed to the high binding nature of the PVP.

The disintegration times of the mirtazapine MDTs of batch 3 (croscarmellose sodium) were low when compared to those of other batches. The increasing order of effectiveness of super – disintegrants with respect to the disintegration time was found to be

Sodium starch glycolate < crospovidone < croscarmellose sodium

This might be due to the long fibrous structure of the croscarmellose sodium and it acts by both swelling and wicking mechanism [5]. Again in each batch, formulations containing PVP i.e. F1, F4 and F7 showed greater disintegration times than those of other formulations in the same batches. This might be because of the high binding capacity of the PVP. The disintegration times of the formulations containing SLS were high when compared to those in the formulations without SLS. As a lubricant SLS was coated over the surface of other particles including super – disintegrant which might delay the contact of later with water thereby enhancing the disintegration times.

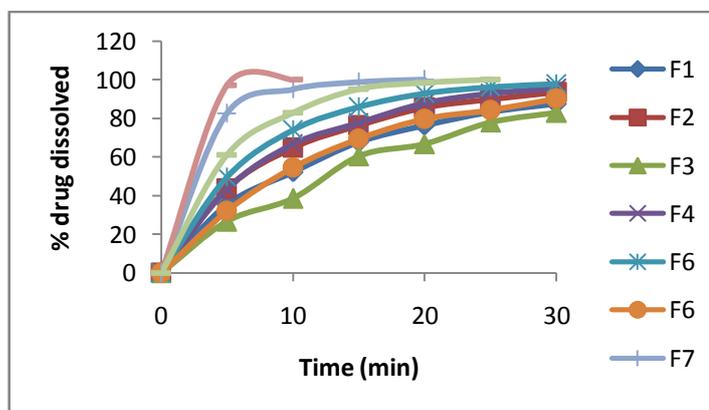
**Table 4: Results of dissolution studies of Mirtazapine MDTs of all formulations**

Sl. No.	Time (min)	% Drug dissolved (Avg. ± S.D.)*								
		F1	F2	F3	F4	F5	F6	F7	F8	F9
1	5	35.14 ± 0.25	43.51 ± 0.32	26.58 ± 0.23	43.38 ± 0.39	49.54 ± 0.32	31.93 ± 0.24	82.51 ± 0.54	97.22 ± 0.36	61.19 ± 0.47
2	10	52.25 ± 0.41	64.85 ± 0.53	38.49 ± 0.31	66.59 ± 0.53	73.88 ± 0.53	54.61 ± 0.38	95.03 ± 0.67	100.00 ± 0.68	82.83 ± 0.41
3	15	67.65 ± 0.52	76.29 ± 0.71	60.38 ± 0.42	77.77 ± 0.62	85.72 ± 0.68	69.31 ± 0.51	98.72 ± 0.72	-	95.15 ± 0.76
4	20	76.29 ± 0.46	85.45 ± 0.78	66.66 ± 0.43	87.73 ± 0.35	92.78 ± 0.46	79.68 ± 0.74	100.00 ± 0.53	-	98.43 ± 0.34
5	25	83.29 ± 0.70	89.82 ± 0.56	77.87 ± 0.74	92.85 ± 0.73	96.06 ± 0.59	84.12 ± 0.68	-	-	100.00 ± 0.59
6	30	87.42 ± 0.66	93.58 ± 0.81	82.94 ± 0.62	95.51 ± 0.81	97.85 ± 0.58	90.10 ± 0.76	-	-	-

\*n (number of trials) = 3

**Table 5: Dissolution kinetics of Mirtazapine MDTs of all formulations**

S. No.	Formulation	Regression values (R <sup>2</sup> )		T <sub>50</sub> (min.)	T <sub>90</sub> (min.)	First – order dissolution rate constant, k (min. <sup>-1</sup> )
		Zero – order	First - order			
1.	F1	0.7941	0.9956	9.8	32.2	0.0713
2.	F2	0.6651	0.994	7.4	24.6	0.0935
3.	F3	0.9104	0.9921	11.6	39.4	0.0584
4.	F4	0.6782	0.9986	6.6	22.0	0.1043
5.	F5	0.5638	0.9994	5.3	17.8	0.1294
6.	F6	0.8133	0.9973	9.0	29.9	0.0769
7.	F7	0.4081	0.9922	2.3	7.7	0.2968
8.	F8	0.725	1.0	0.9	3.2	0.7162
9.	F9	0.542	0.9923	3.2	11.4	0.2003



**Fig. 1: Dissolution profiles of Mirtazapine MDTs of all formulations**

Finally, the dissolution test (results were shown in table 4 & 5 and fig 1) showed that the dissolution rates of mirtazapine MDTs of batch 3 (croscarmellose sodium) were high when compared to those of other batches. The increasing order of dissolution rates of mirtazapine MDTs of various batches was found to be

Batch 1 (sodium starch glycolate) < Batch 2 (crospovidone) < Batch 3 (croscarmellose sodium)

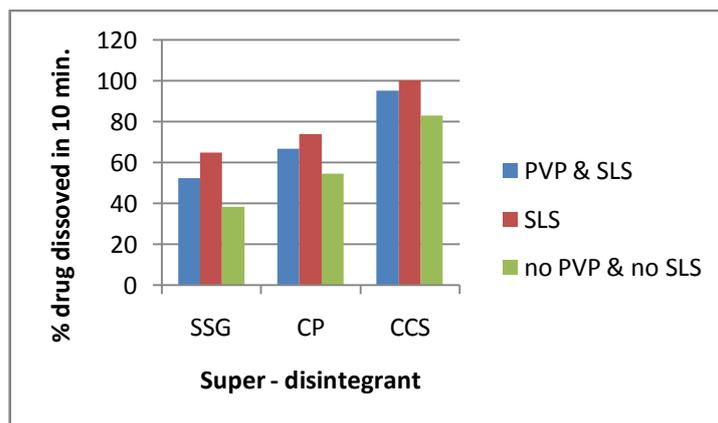


Fig 2: Comparison of different formulations according to the % drug dissolved in 10 min

In each batch the formulations containing only SLS i.e. F2, F5 and F8 showed greater dissolution rates in spite of their high disintegration times when compared to the formulations containing without SLS and PVP i.e., F3, F6 and F9. This might be because of presence of SLS, which is added at critical micellar concentration, exhibited its wetting property in dissolution and enhanced the dissolution rates of formulations. The formulations containing both PVP and SLS F1, F4 and F7 showed higher dissolution rates when compared to formulations containing without SLS and PVP i.e., F3, F6 and F9 because here even though there is PVP, its binding action is overwhelmed by the wetting property of SLS this might be the reason behind the enhanced dissolution rates of formulations containing PVP and SLS. Finally, the increased order of dissolution rates (shown in fig 2) of formulations was found to be

Formulations without SLS and PVP (F3, F6 and F9) < Formulations with both PVP and SLS (F1, F4 and F7) < Formulations with only SLS (F2, F5 and F8)

The difference in the order of disintegration and dissolution rates indicated that the dissolution might be started before complete disintegration of tablets, this might be because of the presence of PVP and SLS, the highly hydrophilic excipients.

## CONCLUSION

Mirtazapine MDTs, formulated with various super – disintegrants, have showed different

Croscarmellose sodium swells 4-8 folds in less than 10 seconds and it has excellent swelling properties and its unique fibrous nature gives it excellent water wicking capabilities. Croscarmellose sodium provides superior drug dissolution and disintegration characteristics, thus improving bioavailability of formulations, so it showed increased rates of dissolution when compared to other two super disintegrants SSG and crospovidone.

disintegration times and different dissolution rates. PVP was found to have good binding characteristics even in the dry form as it reduced porosity and enhanced wetting and disintegration times. SLS was found to show quite different influence on disintegration and dissolution that though it delayed disintegration by acting as lubricant, it enhanced dissolution rates by its excellent wetting characteristics. Among the nine formulations, F8 with cross carmellose sodium and only SLS showed excellent disintegration and dissolution rate.

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## REFERENCES

1. Fu Y, Yang S, Jeong SH, Kimura S, Park K; Orally fast disintegrating tablets: Developments, technologies, taste-masking and clinical studies. Crit Rev Ther Drug Carrier Sys., 2004; 21(6): 433-476.
2. Hardman JG, Limbird LE; Goodman & Gilman's The Pharmacological Basis of Therapeutics. McGraw – Hill, 10<sup>th</sup> edition, 2001: 451 – 462.
3. Benkert O, Szegedi A, Philipp M, Kohnen R, Heinrich C, Heukels A *et al.*; Mirtazapine Orally Disintegrating Tablets versus Venlafaxine

Extended Release: A Double-Blind, Randomized Multicenter Trial Comparing the Onset of Antidepressant Response in Patients with Major Depressive Disorder. *Journal of Clinical Psychopharmacology*, 2006; 26(1): 75-78.

4. Behnke K, Sogaard J, Martin S, Bäuml J, Ravindran AV, Agren H *et al.*; Mirtazapine Orally Disintegrating Tablet versus Sertraline: A Prospective Onset of Action Study. *Journal of Clinical Psychopharmacology*, 2003, 23(4): 358-364.
5. Rowe RC, Sheskey PJ, Owen SC; Handbook of Pharmaceutical Excipients. 5<sup>th</sup> edition, American Pharmacists Association, Pharmaceutical Press, London, 2006: 211 – 213.
6. Indian Pharmacopoeia 2007, Volume 3, Monographs on Dosage Forms, The Indian Pharmacopoeia Commission, Ghaziabad, 2007.
7. USP 27/NF 22, Asian edition, General Test Procedures, U.S. Pharmacopoeial Convention, Rockville MD, 2000.
8. Suresh B, Kumar MR, Ramesh G, Rao YM; Orodispersible Tablets: An Overview. *Asian Journal of Pharmaceutics*, 2008; 2(1): 2-11.
9. Aulton ME; Aulton's Pharmaceutics: The Design and Manufacture of Medicines. Churchill Livingstone, 3<sup>rd</sup> edition, 2007: 175 – 177.