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Effect of natural, synthetic and co-processed excipients on drug release of fluoxetine hydrochloride immediate release drug delivery system

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Abstract
The purpose of this research was to find out the effect of natural, synthetic and co-processed excipients for the formulation of Fluoxetine hydrochloride immediate release tablet by using different super disintegrants used formulations. Fluoxetine hydrochloride is a selective serotonin reuptake inhibitor drug which is used in psychiatric disorder like depression. Immediate release tablet prepared using various concentrations (1.5%, 3% & 4.5%) of super disintegrants like *Moringa oleifera*, Crospovidone, Croscaramellose and co-processed excipients like 1:1 ratios *Moringa oleifera*, Crospovidone and *Moringa oleifera*, Croscaramellose of by wet granulation method. The pre formulation studies by FTIR confirmed no interactions between drug and polymers. The prepared formulations were evaluated for the pre-compression parameters & the values were within prescribed limits and indicated good free flowing properties. The tablets prepared by wet granulation was evaluated for physical parameters, wetting time, disintegration time, content uniformity and *In vitro* dissolution, Comparative studies with marketed product, similarity factor. The physical parameters were found to be satisfactory & within the limits. Among the all prepared formulations *Moringa oleifera* & Crospovidone 1:1 ratio at 4.5% concentration (FW_{12}) by wet granulation method was found to be best formulation as it exhibited satisfactory physical parameters, least disintegration time (30 sec.), wetting time (16 sec.) & highest % drug release (99.5%) at 30 minutes. And its having similarity factor 86 and differentiation factor 6 with marketed product.

Keywords: Immediate release tablet, Fluoxetine hydrochloride, Super disintegrants, Wet granulation method, Similarity factor.

1. Introduction
Fluoxetine hydrochloride is the first agent of the class of antidepressants known as selective serotonin-reuptake inhibitors (SSRIs). Chemical name is Benzene propanamine , IUPAC name is methyl ({3-phenyl-3-[4-(trifluoromethyl) phenoxy] propyl })amine, Emperical formula $C_{17}H_{18}F_3NO$, Molecular weight 345.79 g/mol.It's haveing melting point 179-182 ^oC, water solubility 50 mg/ ml at 25 °C, half-life 1-3 days, volume of distribution 20-45 L/Kg, protein binding 94.5%. Fluoxetine is a selective serotonin-reuptake inhibitor (SSRI), it blocks the reuptake of serotonin at the serotonin reuptake pump of the neuronal membrane, enhancing the actions of serotonin on 5HT1A auto receptors.
Depression and several other psychiatric disorders, such as OCD, may be the result of abnormally low levels of serotonin in the brain. The low levels of serotonin in turn may produce changes in select areas of the brain, producing psychiatric symptoms such as depression or anxiety. Serotonin, nor epinephrine, and dopamine are released by one neuron into the space between that neuron and the next neuron, allowing an electrical stimulus to continue down the next neuron. The antidepressants known as selective serotonin reuptake inhibitors (SSRIs) have become widely used to treat major depression and many other psychiatric disorders, including obsessive-compulsive disorder (OCD), panic disorder, generalized anxiety disorder, social anxiety disorder, posttraumatic stress disorder, eating disorders (e.g., bulimia nervosa), and premenstrual dysphonic disorder [1-4].
Immediate Release Tablets are those tablets which are designed to disintegrate and release their medication with no special rate controlling features, such as special coatings and other techniques. Recently immediate release tablets have started gaining popularity and acceptance as a drug delivery system, mainly because they are easy to administer, has quick onset of

action is economical and lead to better patient compliance [5].
Super disintegrant improve disintegrant efficiency resulting in decreased use levels when compared to traditional disintegrants Examples: Crospovidone, Croscaramellose, Sodium starch glycol ate etc. These are mainly available in three forms natural, synthetic and co-processed super disintegrants. Co-processing is defined as combining two or more established excipients by certain defined processes. Co-processing is based on the novel concept of two or more excipients interacting at the sub particle level, the objective of which is to provide a synergy of functionality improvement as well as masking the undesirable properties of individual .Co-processing of excipients could lead to the formation of excipients with superior properties compared with simple physical mixture of their components or with individual components. As such the Co-processing of super disintegrants is totally unexplored [6].
Moringa oleifera is comes under natural super disintegrant. It's common name is Moringa drum stick tree, family-Moringecaea, order - Brassicales, kingdom-plante. Its Reddish yellow color, slightly acidic nature, hygroscopic powder density 0.9032 gm cm-3. It's Partially soluble in water, most common solvents are organic solvents ,stored in airtight dry containers in cool place ,It's used as super disintegrant at concentration range of 2-5% in wet granulation and sublimation method [7, 8].

2. Materials and Method

Fluoxetine Hydrochloride procured from Aurobindo Chemicals ltd, Telangana. *Moringa oleifera* is self-manufactured product from Moringa drum stick tree, Crospovidone and Croscaramellose are procured from Dr. Reddy's laboratories, Hyd, Lactose, PVP, Talc Procured from SD Fine chemicals Ltd, Mumbai, Magnesium stearate procured from NR. Chemicals Ltd, Mumbai.

3. Methods

3.1 Standard graph of Fluoxetine hydrochloride in 0.1N HCl

Principe

The calibration curve is based on the spectrophotometer. The maximum absorption of Fluoxetine hydrochloride was observed at 226 nm. It obeyed Beer's law in the concentration range of 0 -20 µg/ml.

3.2 Isolation and Purification of *Moringa oleifera* Gum [9-11]

The gum was collected from trees (injured site).It was dried, ground and passed through sieveno 80. driedgum (10 g) was stirred in distilled water (250 ml) for6-8 h at room temperature. The supernatant was obtained by centrifugation. The residue was washed with water and the washing were added to separate supernatant. The procedure was repeated four more times Finally the supernatant was made up to 500 ml and treated with twice the volume of acetone by continuous stirring .The precipitated material was washed with distilled water and dried at 50-60 °C under vacuum.

3.3 Preparation of Co-processed excipients [13]

The co-processed excipients were prepared solvent evaporation method. A blend of 1:1 ratio of *Moringa oleifera* and Crospovidone or *Moringa oleifera* and Croscaramellose were added to 10ml of ethanol .The contents of beaker was mixed thoroughly and stirred continuously till most of ethanol evaporated. The wet coherent mass was granulated through #44 meshes sieve. The wet granules were dried in a hot air oven at 60 ºC for 20 minutes. The dried granules were shifted through #44 mesh sieve stored in air tight container till further usage.

3.4 Fourier transforms infrared spectroscopy

Fourier transform infrared (FT-IR) spectral studies were conducted on FTIR Spectrophotometer (Shimadzu Instrument Corporation Inc., Japan) instrument using KBr pellets to investigate possible interactions between the respective polymers in the release media. All samples were crushed with potassium bromide. The weight ratio of a sample and potassium bromide was 2 mg to 300 mg. Crushed powders were compressed using a hydraulic compactor at approximately 20,000 pounds under vacuum for 3 min. FT-IR measurements were performed under nitrogen atmosphere at a flow rate of 50 standard cubic feet per hour. Spectral scanning was conducted from 4000 to 400 cm−1 at a resolution of 4 cm−1. Interaction studies were carried out to ascertain any interaction of the drug with the excipients used in the preparation of immediate releasing tablets.

3.5 Pre compression parameters evaluation [14, 15]

A. Angle of repose: The fixed funnel method was employed to measure the angle of repose. A funnel was secured with its tip at a given height (h), above a graph paper that is placed on a flat horizontal surface. The blend was carefully pored through the funnel until the apex of the conical pile just touches the tip of the funnel. The radius (r) of the base of the conical pile was measured. The angle of repose (θ) was calculated using the following formula:

$$\mathbf{Tan\ \theta = h/r}$$

Where; θ = Angle of repose, h = height of the cone. r = radius of the cone base.

B. Bulk Density: Bulk density is very important in the size of containers needed for handling, shipping, and storage of raw material and blend. It is also important in size blending equipment.

15 g powder blend introduced into a dry 100 ml cylinder, without compacting. The powder was carefully leveled without compacting and the unsettled apparent volume, Vo, was read. The bulk density was calculated using the following formula.

$$\rho_b = \mathbf{M / Vo}$$

Where,
ρ_b = Apparent bulk density, M = Weight of sample V = Apparent volume of powder

C. Tapped Density

After carrying out the procedure as given in the measurement of bulk density the cylinder containing the sample was tapped 500 times initially followed by an additional taps of 750 times until difference between succeeding measurement is less than 2% and then tapped volume, V_f was measured, to the nearest graduated unit. The tapped density was calculated, in gm per ml, using the following formula.

$$\boldsymbol{\rho_{tap} = M / V_f}$$

Where, ρ_{tap} = Tapped density, M = Weight of sample, V_f = Tapped volume of powder

D. Carr's Index (%)

The Compressibility index (Carr's index) is a measure of the propensity of a powder to be compressed. It is determined from the bulk and tapped densities. In theory, the less compressible a material the more flowable it is. As such, it is measures of the relative importance of inter particulate interactions. In a free flowing powder, such interactions are generally less significant, and the bulk and tapped densities will be closer in value. For poorer flowing materials, there are frequently greater inter-particle interactions, and a greater difference between the bulk and tapped densities will be observed.

$$\text{Compressibility index} = \frac{(\rho_{tap} - \rho_b)}{\rho_{tap}} \times 100$$

Where, ρ_b = Bulk Density, ρ_{tap} = Tapped Density

E. Hausner's Ratio

Hausner's ratio is an indirect index of ease of powder flow. It is calculated by the following formula.

$$\text{Hausner's Ratio} = \frac{\text{Tapped density } (\rho_t)}{\text{Bulk density } (\rho_b)}$$

3.6 Preparation of Fluoxetine hydrochloride immediate release tablets by Wet granulation method

Fluoxetine hydrochloride raw material and all excipients were passed through sieve no. #60 before granulation and lubrication. The required quantity of Fluoxetine hydrochloride and other excipients (except lubricants and glidants) were weighed and mixed uniformly. Then the mixture was made to a damp mass using methanol. Then the prepared mass was passed through sieve no. #16. The prepared granules were dried in an oven at a temperature of 35 °C for one hour. The granules obtained were lubricated by adding and mixing with talc, magnesium stearate. The lubricated granules were evaluated and punched into tablets with an average weight of 100 mg; using Shakhty tableting machine. The composition of formulations is shown in Table. No 1 and 2.

Table 1: Formulation composition of immediate release tablets of Fluoxetine hydrochloride

Ingredients	FW_1 (mg)	FW_2 (mg)	FW_3 (mg)	FW_4 (mg)	FW_5 (mg)	FW_6 (mg)	FW_7 (mg)	FW_8 (mg)	FW_9 (mg)
Drug (Fluoxetine. HCl)	10	10	10	10	10	10	10	10	10
Lactose	59.5	58	56.5	59.5	58	56.5	59.5	58	56.5
Starch	20	20	20	20	20	20	20	20	20
Moringa oleifera	1.5	3	4.5	-	-	-	-	-	-
Crospovidone	-	-	-	1.5	3	4.5	-	-	-
Croscaramellose	-	-	-	-	-	-	1.5	3	4.5
Poly vinyl pyrolidine	5	5	5	5	5	5	5	5	5
Aspartame	3	3	3	3	3	3	3	3	3
Magnesium stearate	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Talc	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Total Wt.	100	100	100	100	100	100	100	100	100

Table 2: Formulation composition of immediate release tablets of Fluoxetine hydrochloride with co-processed excipients.

Ingredients	FW_{10} (mg)	FW_{11} (mg)	FW_{12} (mg)	FW_{13} (mg)	FW_{14} (mg)	FW_{15} (mg)
Drug (Fluoxetine. HCl)	10	10	10	10	10	10
Lactose	54.5	53	51.5	54.5	53	51.5
Starch	20	20	20	20	20	20
Moringa + Crospovidone (1:1)	1.5	3	4.5	-	-	-
Moringa + Croscarmellose (1:1)	-	-	-	1.5	3	4.5
Poly vinyl pyrollidine	5	5	5	5	5	5
Aspartame	3	3	3	3	3	3
Magnesium stearate	0.5	0.5	0.5	0.5	0.5	0.5
Talc	0.5	0.5	0.5	0.5	0.5	0.5
Total Wt.	100	100	100	100	100	100

3.7 Post formulation Evaluations

1. Tablet thickness

The thickness in millimeters (mm) was measured individually for 10 pre weighed tablets by using venire calipers.

2. Weight variation

Twenty tablets were randomly selected from each batch and individually weighed. The average weight and standard deviation of three batches were calculated, It was calculated on an electronic weighing balance.

3. Tablet hardness

Hardness of tablet is defined as the force applied across the diameter of the tablet in order to break the tablet, For each formulation, the hardness of 6 tablets was determined using Pfizer Hardness tester and the average is calculated and presented with standard deviation.

4. Friability

The friability values of the tablets were determined using a Roche-type friabilator. Accurately weighed six tablets were placed in Roche friabilator and rotated at 25 rpm for 4 min.

The tablets were then dusted and re-weighed to determine the loss in weight. Friability was then calculated as percent weight loss from the original tablets. Percentage friability was calculated using the following equation.

$$\text{Friability} = \frac{[\,w_O - w]}{w_O} \times 100$$

Where,
w_O = weight of the tablet at time zero before revolution.
w = weight of the tablet after 100 revolutions.

5. Content uniformity
From each batch of prepared tablets, ten tablets were collected randomly and powdered. A quantity of powder equivalent to weight of one tablet was transferred in to a 100 ml volumetric flask, to this 10 ml of 0.1N HCl was added and then the solution was subjected to sonication for about 1 hours. The solution was made up to the mark with 0.1N HCl. The solution was filtered and suitable dilutions were prepared with medium. The drug content was estimated by recording the absorbance at 226 nm by using UV-Visible spectrophotometer.

6. Disintegration time
Disintegration test was performed for the prepared tablets at 37±2 ºC by using USP disintegration apparatus. Time was noted with a digital Chronometer. Triplicate readings were taken and average was computed.

7. Wetting time
Wetting time corresponds to the time taken for the tablet to disintegrate when kept motionless on the tissue paper in a Petri dish. This method will duplicate the *in vivo* disintegration. Wetting time was measured by placing a tablet on a piece of tissue paper folded twice, and was placed in a small Petri dish containing 6 ml of water, and the time for complete wetting was measured. Three tablets from each batch were used.

8. Dissolution Study of tablets
In this studies USP XXIII, type 2 apparatus (paddle method) with 50rpm speed maintained, in 0.1 N HCl medium ,the volume of medium was 900 ml in and temperature 37± 0.5 °C.

Procedure The tablet was placed inside the dissolution vessel. Samples of 5ml were withdrawn at time intervals of 5, 10, 15, 20, 30, 45 and 60 minutes. The volume of dissolution fluid adjusted to 900 ml by replacing 5ml of fresh dissolution medium after each sampling. The release studies were conducted with 3 tablets, & the mean values were plotted versus time. Each sample analyzed at 226 nm using double beam UV and Visible Spectrophotometer against reagent blank. All dissolution runs were performed in triplicate. Finally optimized formulation results were compared with marketed product dissolution results.

9. Similarity factor
A model-independent method for comparison of two dissolution profiles is based on determination of difference factor f1 and similarity factor f2 which are calculated using following formulae.

$$f_1 = \frac{\sum_{t=1}^{n} (R_t - T_t)}{\sum_{t=1}^{n} R_t} 100$$

$$f_2 = 50 \log \left\{ \left(1 + 1/n \sum_{t=1}^{n} (R_t - T_t)^2 \right)^{-0.5} 100 \right\}$$

Where,
n = number of dissolution time,
R_t = dissolution value of the reference drug product at time t,
T_t = dissolution value of the test drug product at time t

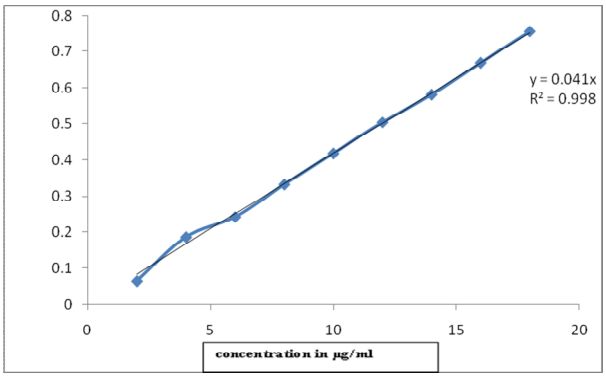
Comparison of Dissolution Profile

Difference factor f_1	Similarity factor f_2	Inference
0	100	Dissolution profile are identical
≤15	≥50	Similarity or equivalence of two profiles

The evaluation of similarity between dissolution properties is based on following conditions-

- Minimum of three dissolution time points are measured
- Number of drug products tested for dissolution is 12 for both test and reference.
- Not more than one mean value of > 85% dissolved for each product.
- Standard deviation of mean of any product should not be more than 10% from second to last dissolution time point.

4. Results and Discussion
4.1 Physicochemical characterization of the gum



Slope=0.042; Intercept= 0.004; Regression=0.998

Fig 1: Calibration graph of Fluoxetine hydrochloride

Fig 1: represents the λ_{max} of Fluoxetine hydrochloride in 0.1N HCl was scanned and found to have the maximum absorbance at 226 nm. Standard graph of Fluoxetine hydrochloride in 0.1N HCl was plotted by taking concentration ranging from 2 to 20 µg/ml and then finding the corresponding absorbance values by spectrophotometrically at 226 nm. The slope and intercept values were found to be 0.042 and 0.004 and the Coefficient of Correlation (r^2) was found to be 0.998.

4.2 Physicochemical characterization of the gum

Moringa oleifera gum insoluble in water, partially soluble in ethanol, acetone and chloroform. Its having 12.02% loss on drying, total ash 12%, acid in soluble ash 3%, true density 1.7118± 0.53, bulk density of powder 0.667± 01.24 ,tapped density 0.854± 1.82, compression index 22.2± 1.33 ,angle of repose 42.76± 1.82, pH of gum was 6.8-6.9.

4.3 Pre formulation Studies

Fourier Transform Infrared Spectroscopy (FTIR)

Observed frequencies in the FTIR spectra of pure drug (fluoxetine hydrochloride) and physical mixture with their assignments.

Table 3: FTIR frequencies of Fluoxetine hydrochloride

Frequency observed in IR spectrum (cm^{-1})	Assignments
3440.7 1070.1	Amines stretching vibration (N-H) (N-C) stretching
2960.3	Alkane (C-H stretching)
3014.5 1518.2	Aromatic (C-H stretching) (C=C stretching)
1242	Phenoxy stretching vibration (C-O-Aromatic group)
1331	Halide stretching vibration (C-F)
1108,1050,842,699,588,526	Fingerprint absorption bands

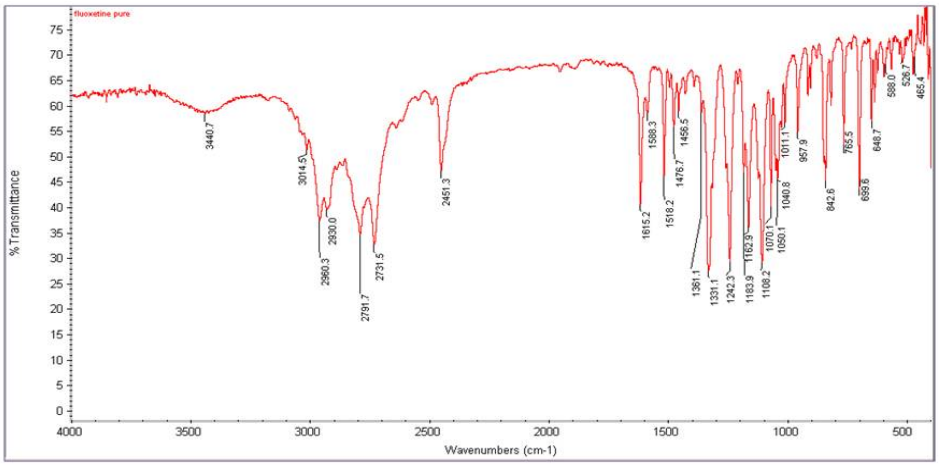


Fig 2: FTIR spectra of pure drug

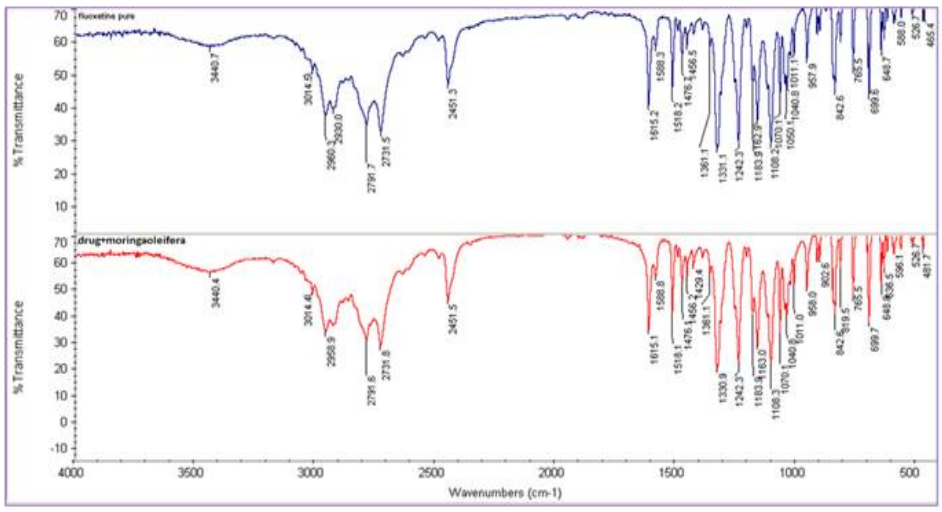


Fig 3: FTIR spectra of formulation containing cross povidone sodium

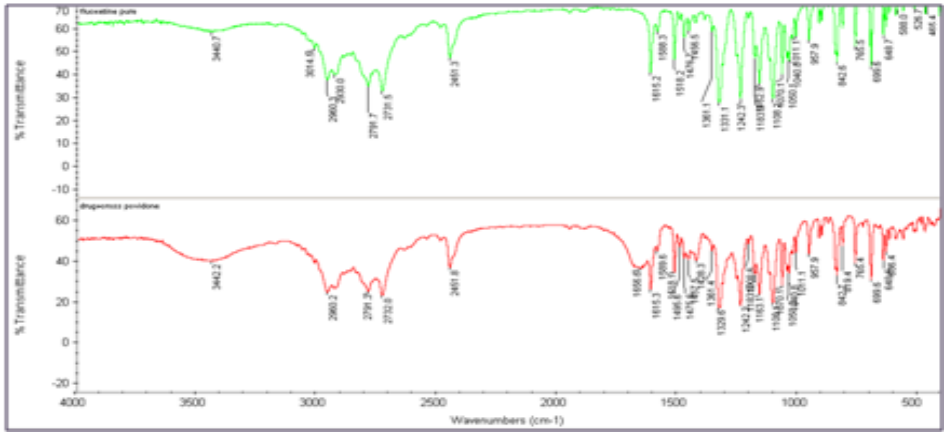


Fig 4: FTIR spectra of formulation containing *Moringa oleifera*

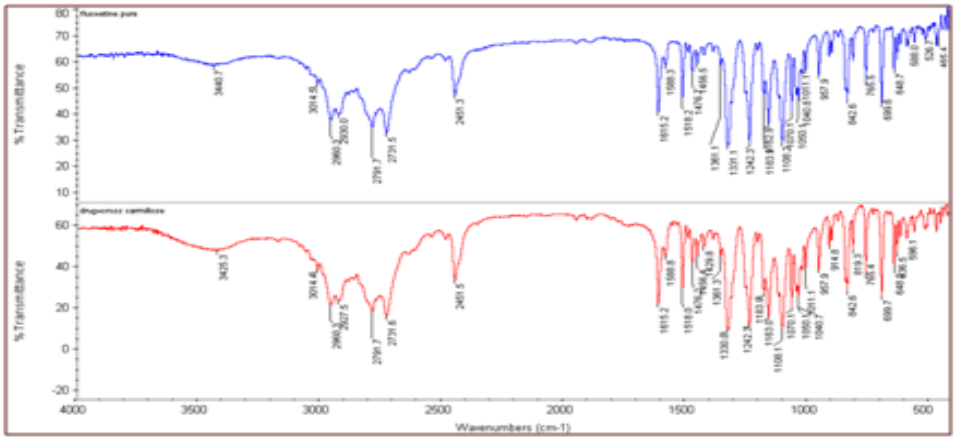


Fig 5: FTIR spectra of formulation containing *Moringa oleifera* + Cross povidone

From the spectrums of fig 2 to fig 5 and table no1 it was observed that observed frequencies in the FTIR spectra of pure drug remained same in the spectra obtained using formulations, which shows that there were no interaction of the drug with the other excipients used in the formulation of the immediate release tablets.

4.4 Evaluation

Table 4: Pre compression characterization of immediate release granules

Formula code	Bulk density (gm/cm^3)	Tapped density(gm/cm^3)	Carss index (%)	Angle of repose	Hausner's ratio
FW_1	0.341±0.04	0.422±0.04	12.46±1.87	27°.11′±0.065	1.14±0.01
FW_2	0.357±0.03	0.423±0.06	**9.50±1.23**	**26°.12′±0.043**	1.10±0.03
FW_3	0.365±0.12	0.405±0.06	**12.75±1.98**	28°.21′±0.032	1.14±0.01
FW_4	**0.333±0.32**	0.403±0.02	11.11±0.05	28°.32′±0.05	1.12±0.03
FW_5	0.371±0.05	0.417±0.05	13.08±0.42	27°.09′±0.06	1.15±0.02
FW_6	0.370±0.06	0.467±0.09	12.69±0.05	29°.12′±0.03	**1.15±0.03**
FW_7	0.364±0.06	**0.467±0.16**	10.61±0.76	27°.34′±0.07	1.14±0.06
FW_8	0.369±0.09	0.428±0.14	10.73±0.32	30°.20′±0.04	1.11±0.02
FW_9	0.375±0.05	0.408±0.31	12.55±0.64	26°.10′±0.08	1.12±0.03
FW_{10}	0.378±0.01	0.403±0.87	11.21±0.46	27°.22′±0.03	1.14±0.05
FW_{11}	0.369±0.15	0.431±0.24	11.13±0.1	**31°.41′±0.08**	**1.08±0.01**
FW_{12}	0.381±0.21	0.418±0.65	11.28±1.09	29°.28′±0.09	1.12±0.02
FW_{13}	**0.384±0.06**	0.422±0.06	11.57±1.65	28°.21′±0.04	1.21±0.05
FW_{14}	0.344±0.25	0.413±0.07	11.75±0.05	29°.08′±0.03	1.32±0.02
FW_{15}	0.362±0.14	**0.395±0.03**	12.53±0.06	27°.11′±0.05	1.14±0.05

Data represents mean ± SD (n=3)

From the above readings table no: 2 the pre-compression parameters & the values were within prescribed limits and indicated good free flowing properties. The physical parameters were found satisfactory & within the limits.

Table 5: Post compression evaluation immediate release tablets

Formula code	Weight variation(mg)	Hardness (Kg/cm^2)	Thickness (mm)	Friability (%)	Drug content (%)
FW_1	99.4±0.6	3.1±0.1	2.20 ± 0.01	0.41±0.03	95.9±0.07
FW_2	98.9±0.81	3.2±0.12	2.22±0.03	0.57±0.04	98.6±0.06
FW_3	100.05±0.85	3.3±0.15	2.23±0.035	0.47±0.02	98.1±0.05
FW_4	99.6±0.37	3.1±0.13	2.12±0.03	**0.34±0.035**	97.6±0.02
FW_5	100.3±0.53	3.2±0.14	2.20±0.015	0.42±0.03	97.8±0.07
FW_6	99.5±0.97	**3.4±0.1**	**2.11±0.03**	0.35±0.015	99.1±0.02
FW_7	100.3±0.88	3.2±0.17	2.28±0.035	0.46±0.034	**95.4±0.04**
FW_8	99.7±0.51	3.1±0.1	2.30±0.03	0.57±0.015	96.4±0.05
FW_9	98.8±0.88	3.2±0.15	2.29±0.04	**0.66±0.026**	97.1±0.052
FW_{10}	98.8±1.23	2.8±0.2	2.25±0.036	0.5±0.026	99.1±0.045
FW_{11}	99.2±0.19	2.7±0.21	2.31±0.03	0.54±0.03	98.1±0.061
FW_{12}	98.7±0.89	3.1±0.32	2.24±0.07	0.44±0.032	98.3±0.042
FW_{13}	**100.3±1.21**	**2.7±0.08**	2.45±0.06	0.61±0.03	96.9±0.061
FW_{14}	**98.01±1.46**	2.8±0.16	**2.51±0.03**	0.65±0.04	97.6±0.04
FW_{15}	100.3±0.78	2.7±0.17	2.49±0.04	0.61±0.031	97.8±0.05
PROZAC10mg	100±0.12	3.0±0.12	2.1±0.01	0.40±0.012	**99.9±0.1**

Data represents mean ± SD (n=3)

From the above results shown in table 3 represents the weight variation for all formulation was tested and found that they are in the ranged (98.01-100.3 mg), the Hardness of the tablets for all the formulation (FW1-FW9)) of wet granulation method with simple super disintegrants values are in ranged 3.1-3.4 kg/cm2 and all the formulation (FW10-FW15) of wet granulation method with co-processed super disintegrants values are in ranged 2.1-2.8 kg/cm2 , The results showed that the hardness of the tablets of wet granulation method with co-processed super disintegrants formulation having less hardness values than the simple super disintegrants contained formulation. Because in the co-processed super disintegrants are less adhered nature than the simple super disintegrants. The thickness of immediate release tablets of all the formulation ranged from 2.11 to 2.49 mm and linearly correlated with the weight of the tablets. Drug content uniformity in all formulations was calculated and the percent of active ingredient ranged from 95.4% to 99.9%.

Table 6: Disintegration and Wetting time of immediate release tablets

Formula code	Disintegration time in seconds	Wetting time in seconds
FW_1	66±4.35	62±2.3
FW_2	59±2.51	59±3.1
FW_3	45±1.5	45±2.45
FW_4	59±1.4	59±3.54
FW_5	45±1.15	38±4.12
FW_6	40±3.6	30±1.23
FW_7	63±4.09	**64±5.2**
FW_8	55±3.6	52±3.21
FW_9	49±3.65	32±1.8
FW_{10}	40±3.05	23±1.54
FW_{11}	35±1.08	19±2.32
FW_{12}	**30±1.5**	**16±1.23**
FW_{13}	**76±3.7**	55±1.24
FW_{14}	64±4.3	45±1.45
FW_{15}	45±3.6	30±2.34
PROZAC10mg	46±3.6	29±2.36

Data represents mean ± SD (n=3)

From the results shown in table no 4 the least disintegration time of 13±1.5 sec. was obtained in tablets prepared by wet granulation method with 4.5% concentration of *Moringa oleifera*+ crospovidone as a co-processed super disintegrant. And this value less than that of markedly available formulation PROZAC 10 mg. The probable reason for rapid disintegration of tablet with *Moringa oleifera* + Crospovidone might be due to solvent intake in to the

matter by capillary action, by the increasing of concentration of super disintegrants wetting time also decreased. This formulation having 4.5% concentration range of co-processed super disintegrant *Moringa oleifera* & Crospovidone with 1:1 ratio havening least wetting time 10±1.23 compare to other formulations and marketed product.

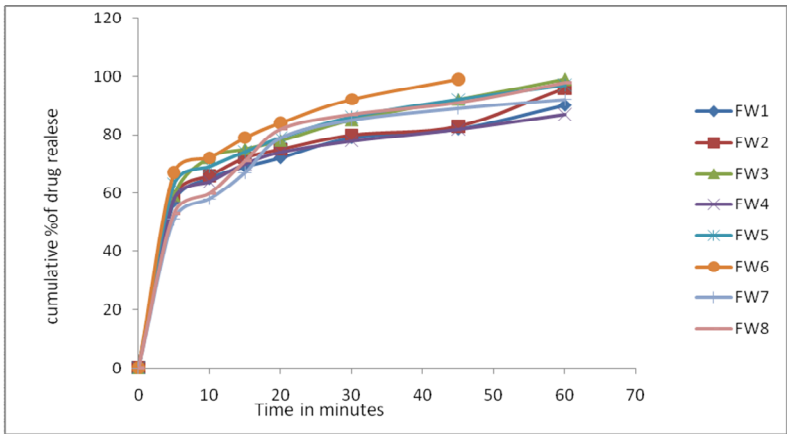


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Fig 6: Dissolution profile of formulations FW1 to FW8 immediate release tablets

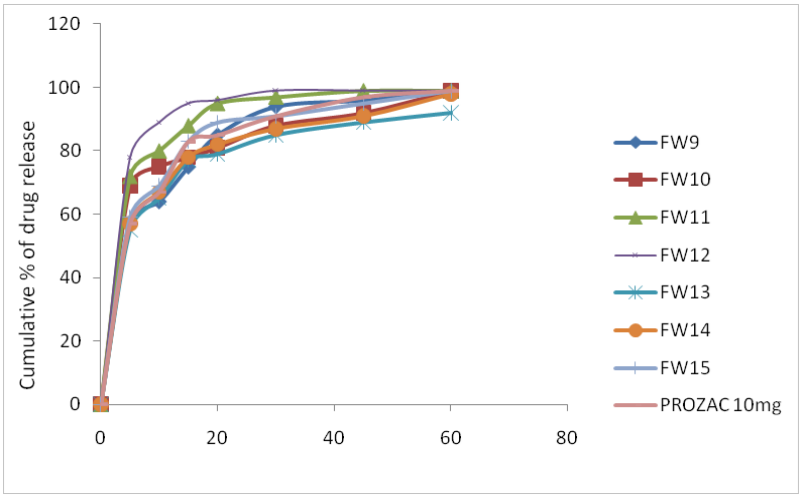

Fig 7: Dissolution profile of formulations FW9 to FW 15 with Marketed Immediate release tablets.

From the fig no 6 and 7 shows that cumulative % drug release indicated that with increase in polymer concentration the drug release was also increased release because this polymer shows capillary action for solvent intake for disintegration , optimized formulation FW12 was observed to be 99.5±0.95 in 30 minutes respectively, its incorporated with1:1 ratio of *Moringa oleifera* & Crospovidone as co-processed super disintegrant in 4.5% concentration, comparatively Markedly available PROZAC 10 mg formulation take 60 minutes time for 99.1±0.01% of drug release**.**

4.5 Similarity factor

Similarity factor f_2 for marketed product and formulation FW_{12} and is 86 and Differentiation factor f_1 for marketed product and formulation FW_{12} and is 6.

4.6 Conclusion

The tablets prepared with the 1:1 ratios of *Moringa oleifera* and Crospovidone at 4.5% concentration (FW_{12}) by wet granulation method was found to be best formulation as it exhibited satisfactory physical parameters, least disintegration time (30 sec.),wetting time (16 sec.) & highest % drug release (99.5%) in 30 minutes. Its having similarity factor 86 and differentiation factor 6 with marketed product PROZAC 10mg so it's having identical dissolution properties.

From the present work I concludes that the co-processing of excipients could lead to the formation of excipients granules with superior properties such as better flow, superior compressibility and rapid disintegrating ability compared with individual super disintegrants.

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