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RESEARCH ARTICLE

Formulation and Evaluation of Buspirone Oral Disintegrating Tablets Using Banana Powder

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Abstract

The present study aims to formulate and evaluate oral disintegrating tablet of buspirone. A drug that is used for the treatment of anxiety management was prepared by direct compression method using natural disintegrates. Eight formulations (F1-F8) of oral disintegrating tablets of buspirone were prepared by using natural disintegrates. The prepared tablets were evaluated for hardness, friability, thickness, drug content uniformity, water absorption, wetting time, and disintegration time and in-vitro dissolution study. Based on the results of FT-IR and DSC studies, majority of the excipients were found to be compatible with buspirone which were used for the preparation of buspirone oral disintegrating tablets. Among all the formulations F3 (containing 15mg of natural disintegrate banana powder) was considered to be the best formulation, which releases up to 98% drug in 8 minutes. From this study, we can conclude that, a formulated tablet of buspirone containing banana powder is better and effective to meet the patient compliance.

Keywords: *Orally disintegrating tablets, Buspirone, Banana powder.*

Introduction

The tablet is the most widely used dosage form existing today because of its convenience in terms of self-administration, compactness and ease in manufacturing. However, geriatric, pediatric and mentally ill patients experiences difficulty in swallowing conventional tablets, which leads to poor patient compliance (1).

To overcome these problems, scientists have developed innovative drug delivery system known as mouth dissolving/disintegrating tablets (ODTs) or fast dissolving tablets (2). The benefits of ODTs is to improve patients compliance, rapid onset of action, increased bioavailability and good stability which make these tablets popular as a dosage form of choice in the current market (3).ODT tablets were prepared by using superdisintegrants such as crosspovidone, crosacromellose sodium and sodium starch glycolate which provide rapid disintegration of the tablet in mouth.

Many techniques are provided to achieve ODT like direct compression, tablet moulding, spray drying, cotton candy process, mass extrusion and freeze drying (4). Of all these above mentioned techniques, direct compression technique is most conveniently used as it does not require any special manufacturing process (5).

In this study natural disintegrants were utilized. Natural disintegrants are safer, more biodegradable, better compressible, easier to preparation and cheaper and these advantages can boost the production of ODTs (6).Buspirone hydrochloride is a white crystalline, water soluble compound with a molecular weight of 422.0. Chemically, buspirone hydrochloride is 8-[4-[4-(2-pyrimidinyl)-1piperazinyl] butyl]-8-azaspiro [4,5] decane-7, 9-dione monohydrochloride. The empirical formula C21H31N5O2 • HCl is represented by the following structural formula: (7)

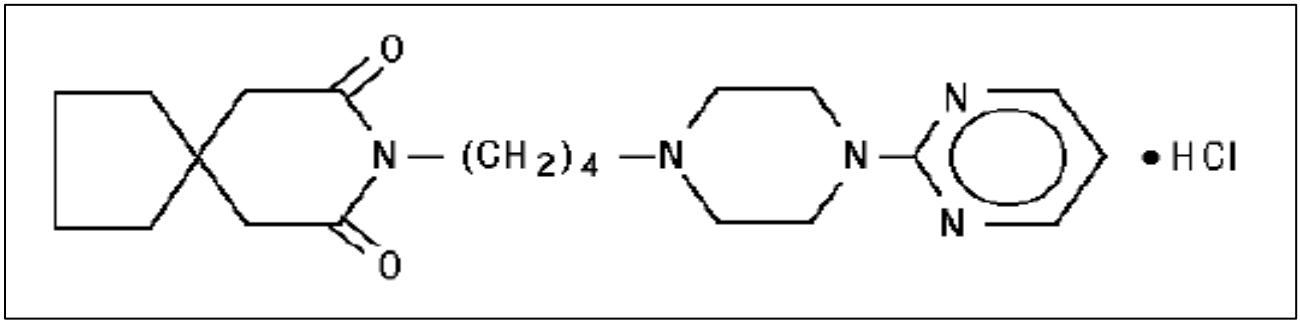

Fig. 1: Structure of Buspirone Hydrochloride

Buspirone is an anxiolytic agent and a serotonin receptor agonist belonging to the azaspirodecanedione class of compounds. Its structure is unrelated to those of the benzodiazepines, but it has an efficacy comparable to diazepam. Buspirone is used in the treatment of generalized anxiety where it has advantages over other antianxiety drugs because it does not cause sedation (drowsiness) and does not cause tolerance or physical dependence (8).

Materials and Methods

Buspirone and banana powder was obtained from Pharmatrain, Hyderabad. Perlitol SD 100, Avicel 200, Lactose monohydrate(flow lac 100), Starch, Vannila flavour, Citric acid, Mg.stearate were purchased from S.D. Fine chemicals, Mumbai.

Calibration Curve of Buspirone

Calibration curve of buspirone was prepared by using 0.01N HCL. The drug was analyzed spectrophotometrically (Labindia UV3000$^+$ UV-Visible Spectrophotometer) at 236 nm.

FT-IR Spectroscopic Analysis

Drug polymer interactions were studied by FT-IR spectroscopy. Ten milligrams of buspirone alone, mixture of drug and polymer were weighed and mixed properly with potassium bromide uniformly. A small quantity of the powder was compressed into a thin semitransparent pellet by applying pressure. The IR- spectrum of the pellet from 450-4000cm-1 was recorded taking air as the reference and compared to study any interference.

Differential Scanning Calorimetry (DSC)

Differential scanning calorimetry (DSC) was performed using DSC-60 (Shimadzu, Tokyo, Japan) calorimeter to study the thermal behaviors of drug alone and mixture of drug and polymer. The instrument comprised of calorimeter (DSC-60), flow controller (FCL-60), thermal analyzer (TA-60) and operating software (TA-60). The samples were heated in sealed aluminum pans under nitrogen flow (80ml/min) at a scanning rate of 10 degree centigrade/m from 25 to 450 degree centigrade. Empty aluminum pan was used as reference. The heat flow as a function of temperature was measured for the drug and drug –polymer mixture.

Preparation of Orally Disintegrating Tablet

Oral disintegrating tablets of buspirone were prepared by direct compression method according to the formulae given in table 1. All the ingredients were powdered separately and passed through # 25 mesh sieve separately. The drug and directly compressible excipient were mixed by adding small portion of each at a time and blending it for 15 minutes to get a uniform mixture and kept aside. Then the other ingredients were mixed in geometrical order, in an inflated polyethylene pouch magnesium stearate will pass through #60 mesh sieve and were added last and mixed for further five minutes. And the tablets were compressed using 6 mm flat round punches to get tablets of 100 mg weight.

Table 1: Composition of oral disintegrating tablets of Buspirone

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8
Buspirone Hcl	10	10	10	10	10	10	10	10
Pearlitol SD 100	50	44	39	36	39	71	39	54
Avicel 200	32	32	32	32	16	0	32	32
Lactose Monohydrate (Flow Lac 100)	0	0	0	0	16	0	0	0
Banana Powder	4	10	15	18	15	15	0	0
Starch	0	0	0	0	0	0	15	0
Vannila Flavour	2	2	2	2	2	2	2	2
Citric Acid	1	1	1	1	1	1	1	1
Mg. Sterate	1	1	1	1	1	1	1	1
Total	100	100	100	100	100	100	100	100

All amounts given in above table are in milligram

Pre-Compression Studies (9)

All the physical parameters namely, angle of repose, bulk density; compressibility index and Hausner's ratio were performed.

- **Bulk Density:** It is the ratio of total mass of powder to the bulk volume of powder. Required quantity of powder blend was transferred in 100 ml graduated cylinder

and the bulk density was calculated by using the formula given below:

Bulk density = weight of powder/ Bulk volume.

- **Tapped Density:** It is the ratio of total mass of powder to the tapped volume of powder. Required quantity of powder blend was transferred in 100 ml graduated cylinder which was operated for fixed number of taps until the powder bed volume has reached a minimum Tapped density using the was calculated by formula given below:

Tapped density = Weigh of powder / Tapped volume

- **Compressibility Index:** It is a simple test to evaluate bulk and tapped density of a powder .The formula for Carr's index is as below:

$$\text{Compressibility index} = 100 \times \frac{\text{Tappeddensity - Bulk density}}{\text{Tappeddensity}}$$

- **Hausner's Ratio:** Hausner's ratio is a number that is correlated to the flow ability of a powder

$$\text{Hausner's Ratio} = \frac{\text{TappedDensity}}{\text{Bulk Density}}$$

- **Angle of Repose:** It is the maximum angle possible between the surface of a pile of powder and the horizontal plane. Angle of repose was determined by the funnel method. Accurately weighed powder blend was taken in the funnel. Height of the funnel was adjusted in such a way the tip of the funnel just touched the apex of the powder blend. Powder blend was allowed to flow through the funnel freely on to the surface. Diameter of the powder cone was measured and angle of repose was calculated using the given formula.

$\theta = \tan^{-1}(h/r)$ Where:

θ = angle of repose, h = height in cms, r = radius in cms

Post Compression Studies (10-18)

- **Weight Variation**: 20 tablets were selected and weighed collectively and individually. From the collective weight, average weight was calculated. Each tablet weight was then compared with average weight to assure whether it was within permissible limits or not. Not more than two of the individual weights deviated from the average weight by more than 10% for 100 mg tablets and none by more than double that percentage.

$$\%\ weight\ variation = \frac{Average\ weight - weight\ of\ eact\ tablet}{Average\ weight} * 100$$

- **Hardness Test:** Hardness of tablet is defined as the force applied across the diameter of the tablet in order to break the tablet. The hardness of the tablets was determined by diametric compression using Erweka hardness tester.
- **Thickness:** The thickness was measured by placing tablet between two arms of the vernier calipers. Five tablets were taken and their thickness was measured.
- **Friability Test**: This test was performed to determine the effects of friction and shock. Pre weighed sample of 10 tablets

was placed in the Erweka friabilator and rotated at 25 rpm for about 4 minutes. The tablets were dedusted and reweighed, and the friability percentage was calculated. Compressed tablets should not lose more than 1% of weight.

$$\% \, Friability = \frac{Initial\ weight - Final\ weight}{Initial\ weight} * 100$$

- **Wetting Time:** The wetting time of the tablets was measured using a simple procedure. Five circular tissue papers of 10-cm diameter were placed in a petridish with a 10-cm diameter. Ten milliliters of water containing eosin, a water-soluble dye, was added to the petridish. A tablet was carefully placed on the surface of tissue paper. The time required for water to reach the upper surface of the tablets was noted as the wetting time. The wetting times were measured.

- **Water Absorption Ratio**: A piece of tissue paper folded twice was placed in a small petridish (internal diameter=6.5 cm) containing 6 ml of water. A tablet was placed on the paper and the time required for complete wetting was then measured. The water absorption ratio (R) was determined using the following equation.

$$R = \frac{Wa - Wb}{Wa} * 10$$

Where, Wb is the weight of the tablet before water absorption and Wa is the weight of the tablet after water absorption.

In-Vitro Disintegration Test: The in vitro disintegration studies were carried out using a digital tablet disintegration test apparatus (Erweka ZT, Germany). One tablet was placed in each of the 6 tubes of the basket assembly and then disk was added to each tube. This assembly was then suspended in a 1-liter beaker containing water with its temperature being maintained at 37±2°C. The basket was then moved up and down through a distance of 5 to 6 cm, at the frequency of 28 to 32 cycles per minute. The time required for complete disintegration of the tablet was recorded.

Content Uniformity: Ten tablets of each batch were weighed and powdered. Aliquot of this powder containing Buspirone equivalent to 4 mg of buspirone was accurately weighed, suspended in approximately 50 ml of 0.1 N HCl and shaken for 15 minutes. Final volume was adjusted to 100 ml with 0.1 N HCl and filtered (Whatman No.1 filter paper).

From this 10 ml was diluted to 100 ml. The final volume was made by taking 2 ml of above solution and diluted to 10 ml with 0.1 N HCl. Absorbance of this solution was recorded at 236 nm using UV/Vis spectrophotometer against a reagent blank and the content was compared from a calibration curve prepared with standard buspirone in the same medium. The mean percentage drug content was calculated as an average of 3 determinations.

Dissolution Studies: The release rate of buspirone from ODTs was determined using United State Pharmacopoeia (USP) XXIV dissolution testing apparatus II (paddle method). The dissolution test was performed using 900 ml of 0.1N HCl pH 1.2 as a dissolution medium, at 37±0.5°C and 50 rpm.

A sample (5 ml) of the solution was withdrawn from the dissolution apparatus at 1, 2, 3, 4, 5, 10, 20 and 30 minutes. The samples were filtered through a 0.45 membrane filter. Absorbance of these solutions was measured at 236 nm using a Shimadzu spectrophotometer. Cumulative percentage of drug release was calculated using an equation obtained from a standard curve.

Results and Discussion

Standard Calibration Curve of Buspirone

The standard calibration curve of buspirone in 0.01N HCL (figure 2) showed good correlation with regression value of 0.9995.

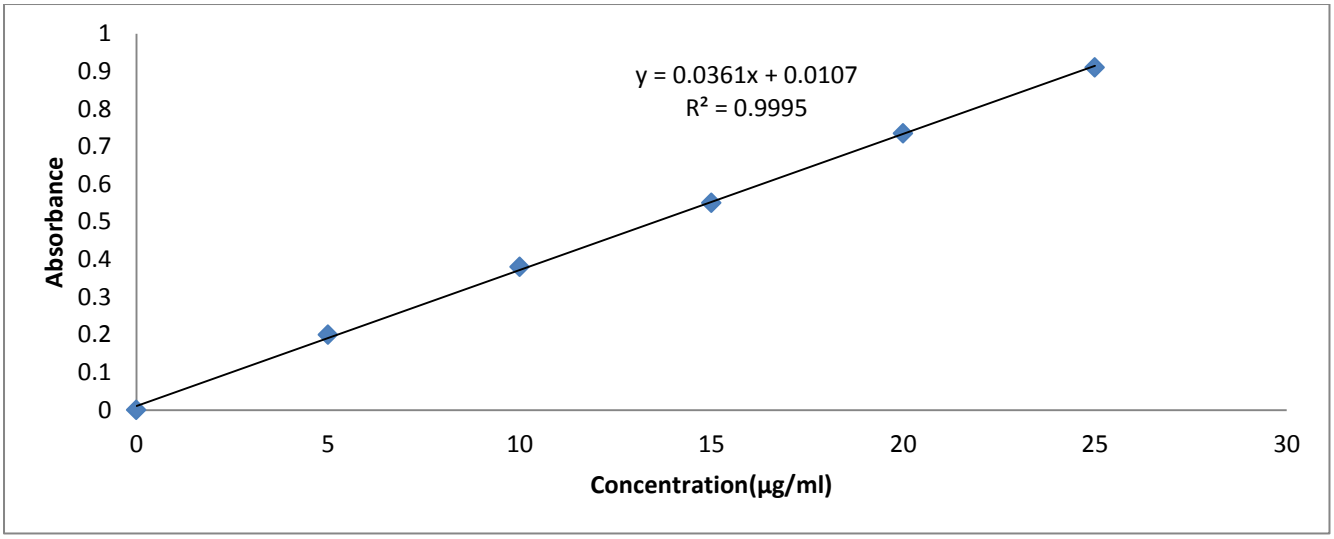

Figure 2: Standard Calibration Curve for Buspirone

FT-IR Studies

The spectral data suggests that the major peaks for drugs are obtained as nearer value and there were no considerable changes in IR peaks in all physical mixtures of drug and polymers. This indicates that the drugs were molecularly dispersed in the polymers or in drug loaded formulations thus thereby indicating the absence of any interactions as shown in figure 3, 4 and 5.

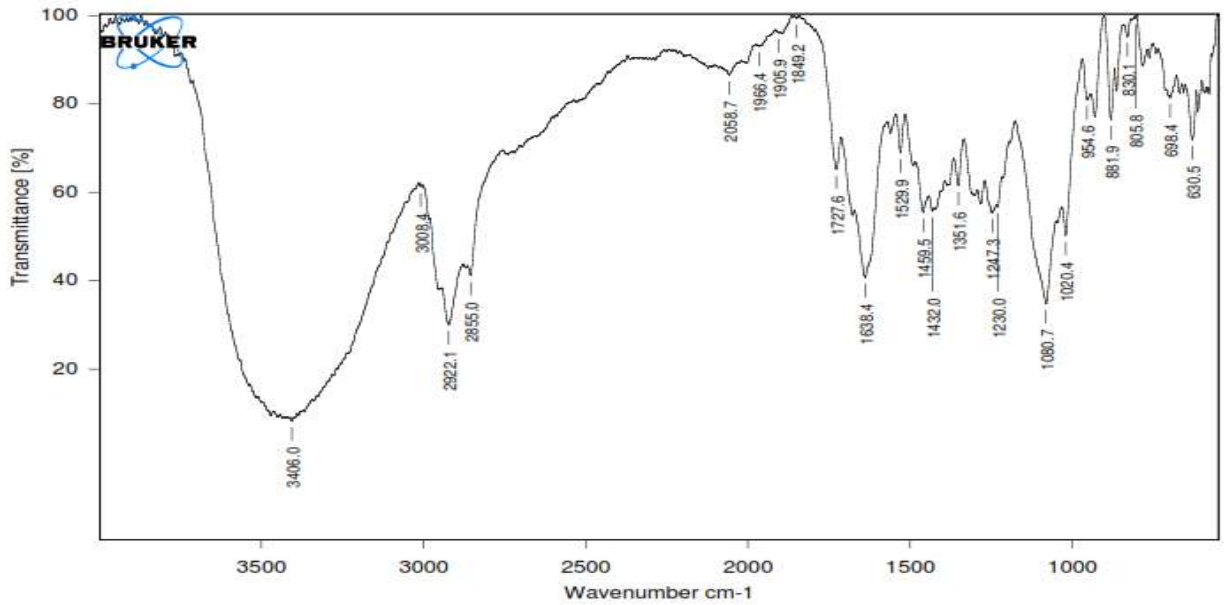

Figure 3: FTIR graph for Buspirone

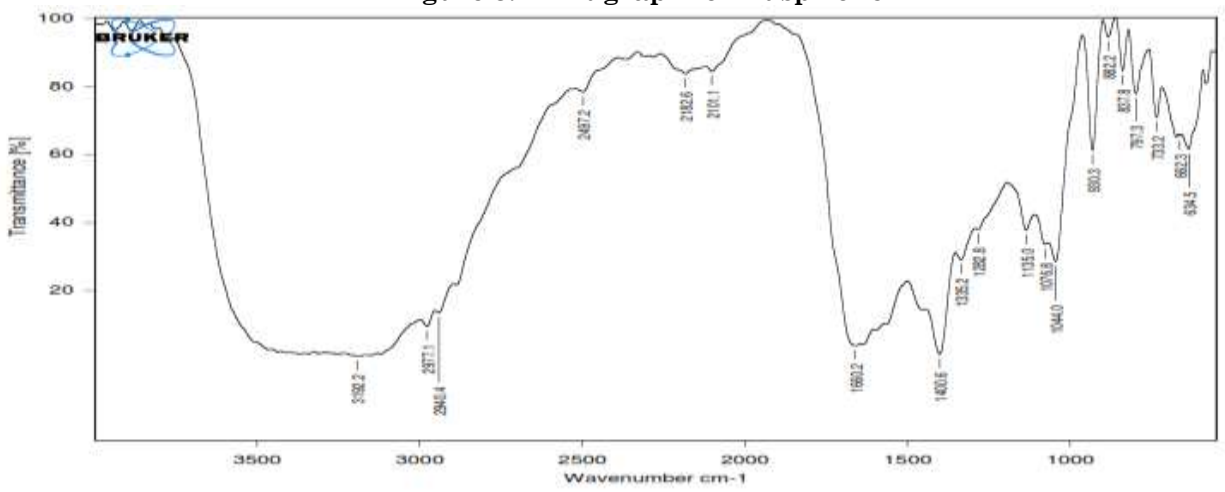

Figure 4: FTIR graph for Banana powder

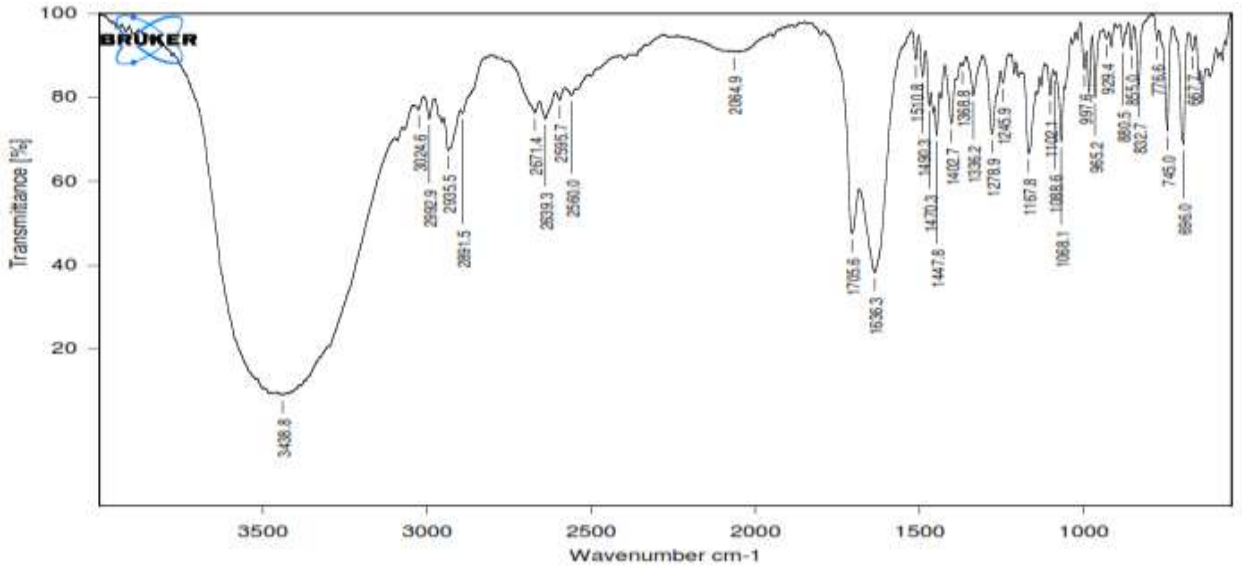

Figure 5: FTIR graph for Buspirone + Banana powder

Differential Scanning Calorimetry (DSC)

DSC studies (figure 6 and 7) show the peak value corresponds to standard melting point. All the characteristic test of pure drug confirms the purity of buspirone.

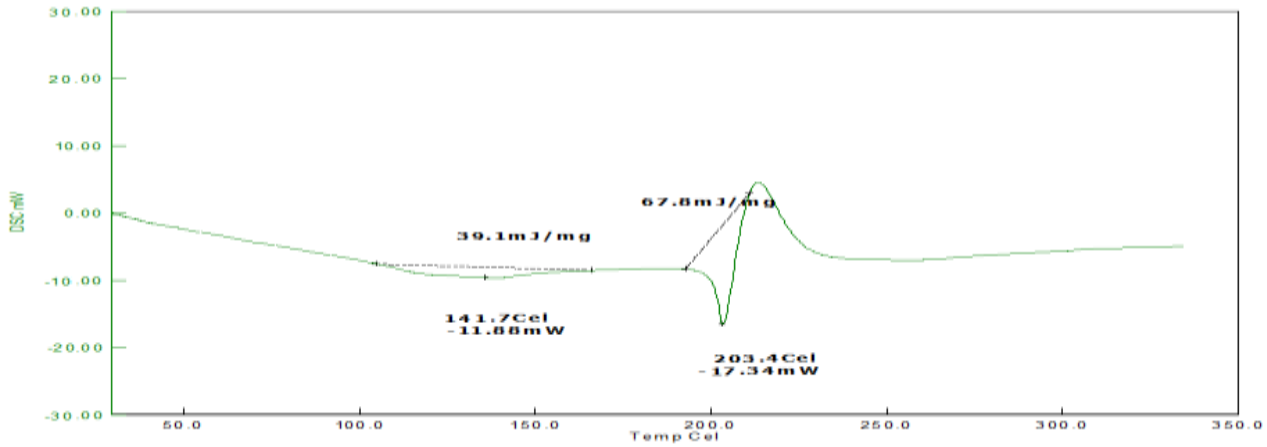

Figure 6: DSC graph for Buspirone

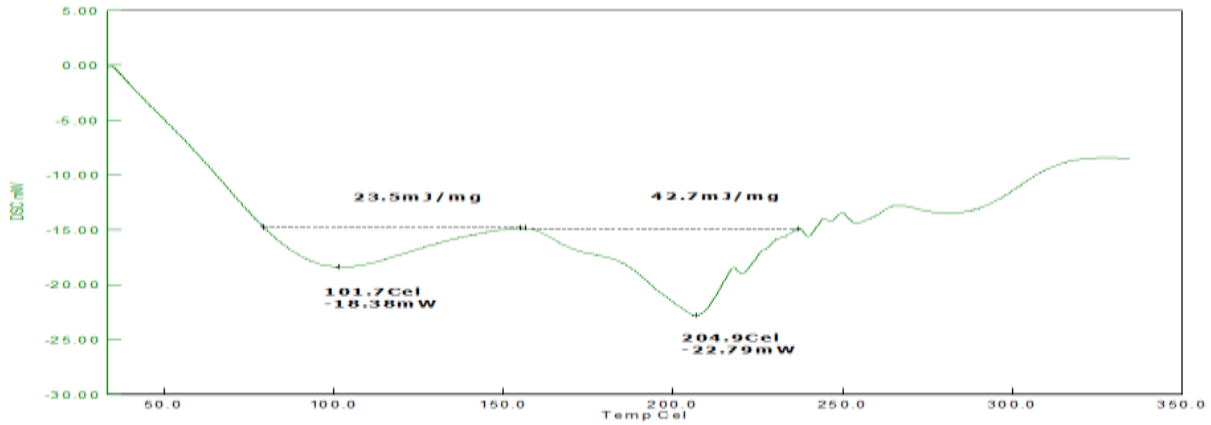

Figure 7: DSC graph for Buspirone + Banana powder

Pre Compression Studies

- **Evaluation of Blend**

Physical properties such as bulk density, tapped density, percent compressibility index, Hausner ratio, angle of repose were determined (Table 2) for the prepared tablet blend. The tablet blend batches in which microcrystalline cellulose was used as diluent, the angle of repose is between 27.5° to 34.8°, this indicated the passable flow

ability. This property may be attributed due to the presence of microcrystalline cellulose having filamentous particles as diluent. Also, the Carr's index and Hausner's ratio were found to be in the range of ≤ 18 and 1.08 to 1.17 respectively, indicating good flow and compressibility of the blends.

Table 2: Pre compression studies

Formulation code	bulk density	Tapped density	Cars index	Hausner's ratio	Angle of repose
F1	0.49	0.56	12.50	1.14	32.7
F2	0.52	0.61	14.75	1.17	34.8
F3	0.51	0.55	7.27	1.08	27.5
F4	0.55	0.61	9.84	1.11	29.7
F5	0.45	0.52	13.46	1.16	33.5
F6	0.59	0.67	11.94	1.14	31.9
F7	0.55	0.62	11.29	1.13	31.6
F8	0.49	0.57	14.04	1.16	33.8

Post Compression Studies

- The data obtained of post-compression parameters such as hardness, thickness, friability, weight variation, amount of drug content, disintegration time and water absorption ratio are shown in (Table 3).

  Tablets obtained were of uniform weight (due to uniform die fill) with acceptable variation. The percentage drug content of all the tablets were found in the range of 98% to 102% of buspirone, which was within the acceptable limits. Hardness of the tablets was found to be 3.54 to 3.81 kg/cm^2, indicating satisfactory mechanical strength. The thickness of tablets was found to be 3.11 – 3.19 mm. The result revealed that the tablets of all the formulations showed uniform thickness. In all the formulations, the friability values were less than 1% w/w.

  The results of *in vitro* disintegration time of all the formulations were found to be within the prescribed limits and satisfied the criteria of fast dissolving tablets. The values were found to be in the range of 17 to 28 Seconds. The water absorption ratio for all formulations was found to be in the range of 81 to 95 %.

Table 3: Post compression studies

Formulation code	Weight variation	Hardness	Thickness	Friability	wetting time	water absorption ratio	Disintegration time (sec)	Drug content uniformity
F1	Pass	3.73	3.17	0.42	35	82	22	98.94
F2	Pass	3.59	3.12	0.37	37	87	28	100.62
F3	Pass	3.81	3.19	0.24	31	95	17	99.65
F4	Pass	3.67	3.15	0.27	35	91	24	99.83
F5	Pass	3.79	3.18	0.31	37	85	21	100.12
F6	Pass	3.63	3.14	0.28	32	90	25	99.43
F7	Pass	3.54	3.11	0.41	38	89	28	98.12
F8	Pass	3.75	3.18	0.38	30	81	22	98.43

- ***In Vitro* Dissolution Study**

The in vitro dissolution profile indicated faster and maximum drug release from formulations F3 and F4 (figure8, 9). Formulation F3 and F4 showed 98% w/v and 99% w/v respectively drug release at the end of 8 min when compared with other formula. The rapid drug dissolution might be due to easy breakdown of particles due to porous structure formation rapid absorption of drugs into the dissolution medium.

Table 4: In-vitro dissolution studies for Buspirone orally disintegrating tablets

Time in mints	F1	F2	F3	F4	F5	F6	F7	F8
0	0	0	0	0	0	0	0	0
2	11	23	34	32	25	31	17	7
4	26	45	68	66	48	61	34	14
6	42	76	88	90	71	85	55	29
8	58	89	98	99	86	97	69	41
10	73	97			97	99	81	57
12	89						91	69
15	94						96	81

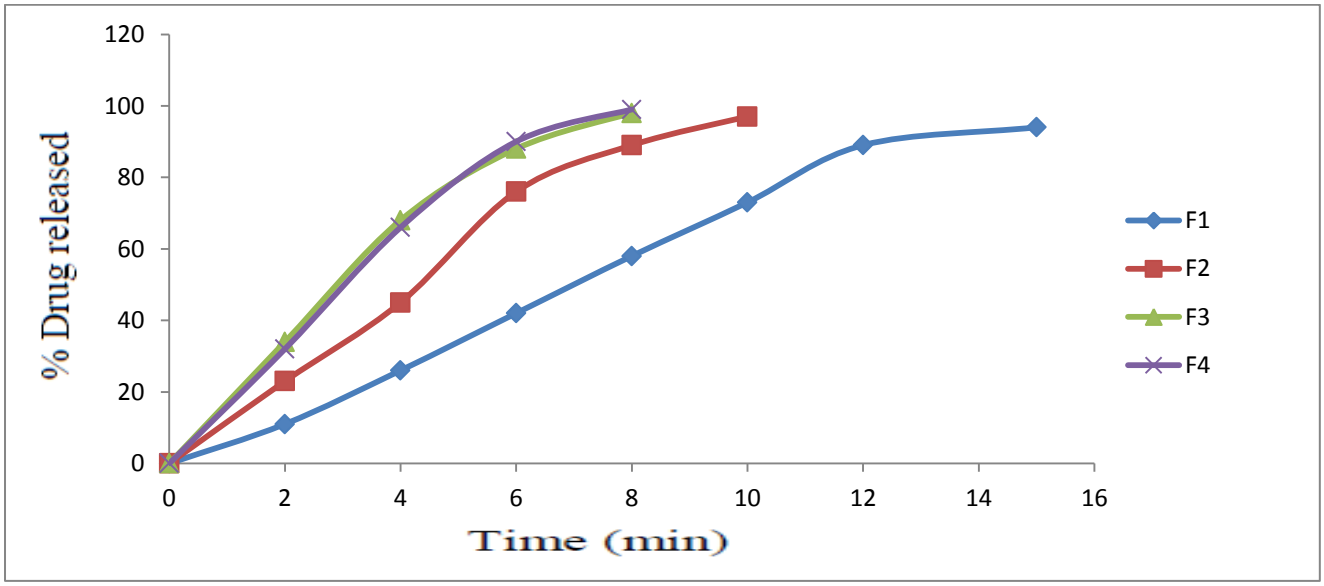

Figure 8: Comparative dissolution profile for F1, F2, F3 and F4 formulations

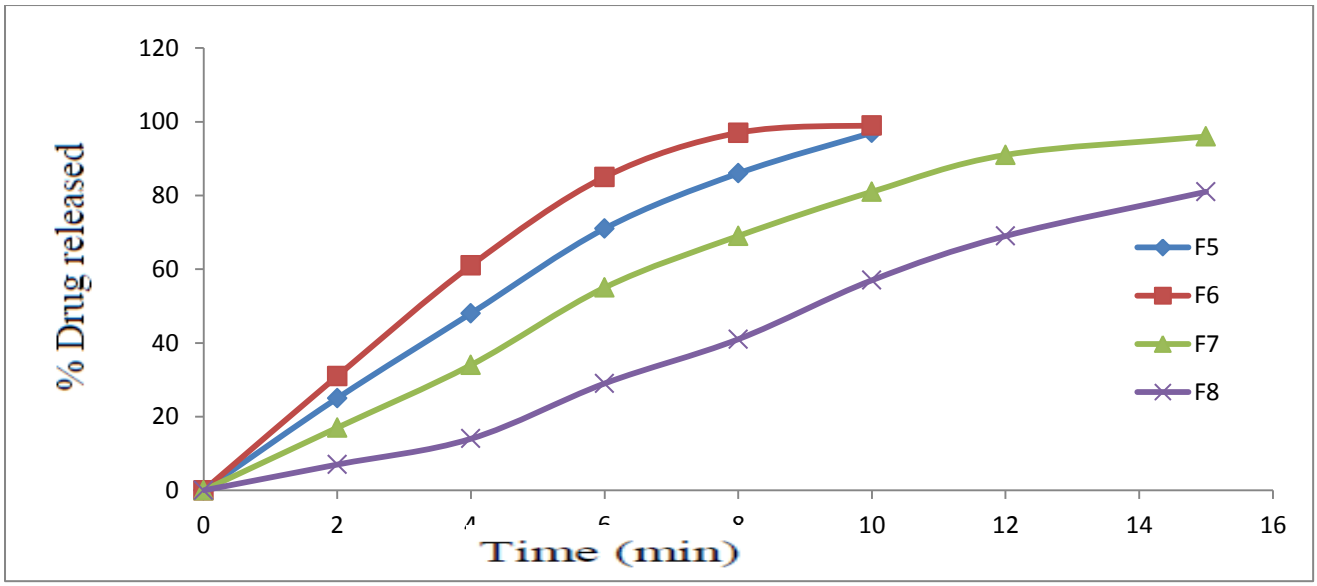

Figure 9: Comparative dissolution profile for F5, F6, F7 and F8 formulations

Conclusion

In the present work, an attempt has been made to develop orally disintegrating tablets of buspirone. The IR spectra revealed that, there was no interaction between disintegrants and drug. The result of physical parameter of all formulations by direct compression showed good flow property. Formulation F3 was the optimized formulation having least disintegration time as well as other parameters within acceptable range. In-vitro release of optimized formulation of buspirone orally disintegrating tablets of F3 was found to be 98% drug release within 8 minutes with in vitro disintegration time being 17sec. From this observation it was concluded that the

formulated tablets of buspirone (F3) were superior and effective in achieving patient compliance.

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