INTERNATIONAL JOURNAL OF PHARMACEUTICAL, CHEMICAL AND BIOLOGICAL SCIENCES

Available online at www.ijpcbs.com

Research Article

FORMULATION AND EVALUATION OF FAST DISSOLVING TABLETS OF PARACETAMOL 125 mg USING BANANA POWDER USING CO-GRINDING TECHNIQUE

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ABSTRACT

Paracetamol is a slightly water soluble drug belongs to BCS Class IV, used in various pain managements & in management of fever. The drug solubility was increased by solid dispersion method, in which two techniques namely physical mixing and co-grinding were tried at the ratios of 1:0.25, 1:0.5 & 1:0.75 for paracetamol to banana powder, a natural disintegrant. All the formulations were prepared using direct compression method, which is a conventional method of preparation. Various parameters like pre-& post compressional parameters were tested and final formula was selected based on *In-vitro* dispersion time and *In-vitro* dissolution profile. Where, all the formulations were dispersed < 40 seconds and F_6 formulation was showing 100% release at 25^{th} minute and faster compared to the marketed formulation. F_6 was prepared by co-grinding technique, at 1:0.75 paracetamol to banana powder ratio. F_6 is showing zero-order release and mechanism of release is Super case – II transport (n = 0.9832).

Keywords: Paracetamol, Disintegrant, Zero-order release.

INTRODUCTION[1-4]

Tablets are most convenient oral unit solid dosage form which made them great patient compliance. conventional tablets suffer from some disadvantages which can be masked by novel drug delivery system such as fast dissolving tablets. Now-a- days fast dissolving tablets gain great patient compliance due to their potential advantages like waterless administration of the tablets increase in bioavailability of poorly soluble drugs due to their fast disintegration etc.

Paracetamol is a BCS class II drug intended for analgesic activity and antipyretic activity. It belongs to non-steroidal anti-inflammatory agents. This drug has slight solubility in water.

Paracetamol was formulated as fast dissolving tablet using banana powder, natural disintegrating agents, which is easily to prepare abundantly available and economical in nature. These tablets were enhanced the bioavailability of paracetamol by increasing its dissolution through fast disintegration. The banana has great starch content in it, and has good disintegrating ability. Hence, the dried unripe banana powder was choosiest to prepare the fast dissolving tablets.

MATERIALS AND METHODS[5-9]

MATERIALS

Paracetamol was obtained as a gift sample from SK Health Care Formulations Pvt Ltd, Hyderabad. Micro-crystalline Cellulose, starch, Mg. Stearate, talc and other chemicals were purchased from Siri Scientifics, Rajamahendravaram.

METHODS

Analytical method development

Preparation of 0.1 N HCl solution

8.5ml of conc. HCL was place in 1000ml volumetric flask & make up to volume 1000ml by using distilled water.

Determination of λ_{max} paracetamol in 0.1 N HCl solution

100mg of paracetamol was weighed and dissolved in 0.1 N HCl and then make up to the volume of 1000ml to get 1000µg/ml concentrated stock solution (working standard). From the working standard solution 10ml was diluted to 100ml with 0.1 N HCL solution to get 100µg/ml concentrated solution (dilution1). From the dilution 1, 1ml was diluted to 10ml with 0.1 N HCl solution to get 10µg/ml concentrated solution (dilution 2). This solution was scanned at range of 200-400nm wavelength light corresponding scan spectrum curve was note. The corresponding wavelength having highest absorbance is noted as λ_{max}.

Standard calibration curve of paracetamol in phosphate 0.1 N HCl solution

100mg of paracetamol was weighed and dissolved in 10ml methanol and then make up to a volume of 100ml with 0.1 N HCl it gives 1000µg/ml concentrated stock solution (working standard). From the working standard solution 10ml was diluted to 100ml with 0.1N HCL solution to get 100µg/ml concentrated solution (dilution1). From the dilution 1, aliquots of 0.2, 0.4, 0.6, 0.8, 1 and 1.2ml of solution were pipette out in to 20ml volumetric flask. The volume was made up to the mark with phosphate buffer P^H 6.8. These dilutions give 2, 4, 6, 8, 10 and 12µg/ml concentrations of paracetamol respectively. The absorbance was measured in the UV-visible spectroscopy at 257nm using 0.1N HCL solution as blank and graph of concentration versus absorbance was plotted. The absorbance data for standard calibration curves are given in the results table.

Preparation of Banana Powder

The domestically available unripe bananas were purchased from local store and were sliced into small pieces, were dried under sunlight, grinded and passed through the sieve no. 40.

Preparation of Solid Dispersion Using Co-Grinding Method

1 gram of paracetamol was placed in a mortar and 0.25 or 0.5 or 0.75 grams of oats powder was added and grinded by sprinkling a little amount of water to moisten the powder mix. The resultant dispersion was passed sophisticatedly through sieve no. 40 and dried in a hot air oven at 60^0c for 30 minutes. This dispersion equivalent to 125mg was used to prepare paracetamol 125mg fast dissolving tablets.

Preparation of paracetamol fast disintegrating tablets

Fast disintegrating tablets of paracetamol were prepared by direct compression method. All the ingredients (as shown in table) were powered separately and passed though the sieve no. 40 separately. The drug and directly compressible excipient were mixed by adding small portion of each at a time and blending it to get uniform mixture and kept aside. Then the other ingredients were mixed in geometrical order, in an inflated polyethylene pouch magnesium stearate and talc were added last and mixed for further two minutes and the tablets were compressed using 8-12 mm flat round punches to get tablets of 250mg weight.

Table 1: Formulation table for paracetamol 125 mg fast dissolving tablets

Ingredients	Physical Mixture			Co-grinding method		
	F1	F2	F3	F4	F5	F6
Paracetamol dispersion (equivalent to 125mg)	156.25	187.5	218.75	156.25	187.5	218.75
Microcrystalline cellulose	68.75	37.5	6.25	68.75	37.5	6.25
Starch	20	20	20	20	20	20
Mg. stearate	2.5	2.5	2.5	2.5	2.5	2.5
Talc	2.5	2.5	2.5	2.5	2.5	2.5
Total weight	250	250	250	250	250	250

Evaluation of Oral Fast Disintegrating Tablets of Paracetamol 125 mg

Evaluation of blends

The powder blend was evaluated for bulk density, tapped density, carr's index, hausner's ratio and angle of repose.

Bulk density (D_b)

Is the total mass of powder to the bulk volume of powder. It was measured by pouring the weighed powder into a measuring cylinder and the initial volume was noted the initial volume is called the bulk volume. From this, the bulk density is calculated according to the formula obtained below. It expressed in g/cc and is given by:

$$D_b = \frac{M}{V_O}$$

Where, M is the mass of the powder, V_o is the bulk volume of the powder.

Tapped density (D_t)

It is the ratio of total mass of powder to the tapped volume of powder. The volume was measured by tapping the powder for 500 times. Then the tapping was done for 750 times and the tapped volume was noted (the difference between these two volumes should be less than 2%). If it is more than 2%, tapping is continued for 1250 times and tapped volume was noted. It is expressed in g/cc and is given by:

$$D_t = \frac{M}{V_1}$$

Where, M is the mass of powder, V_t is the tapped volume of the powder.

Carr's index (%)

The bulk density is the measurement of weight to the volume of the sample. Tapped density is determined as the measurement of weight of the sample to the volume after tapping the measuring cylinder for 500 times form a height of 2 inches. The percentage compressibility (carr's index) was calculated as 100 times the ratio of the difference between tapped density and the bulk density to the tapped density.

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

Hausner's ratio

Hausner's ratio of tapped density to bulk density. Lower the value of hauser's ratio better is the flow property. The powder with hausner's ratio less than 1.18, 1.19-1.25, 1.3-1.5 and greater than 1.5 indicates excellent, good, passable and very poor flow properties, respectively.

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

Angle of repose (θ)

It is defined as the maximum angle possible between the surface of a pile of powder and the horizontal plane.

$$\theta = tan^{-1}\left(\frac{h}{r}\right)$$

Where, θ is the angle of repose, h is the height in cms, r is the radius in cms.

The powder mixture was allowed to flow through the funnel with its tip fixed to stand at a definite height from a graph paper placed on a horizontal surface. The angle of repose was then calculated by measuring the height and radius of the heap of powder formed. A value for angle of repose ≥ 40^0 suggests poorly flowing material.

EVALUATION OF TABLETS

Weight variation

Twenty tablets were selected at random and average weight was determined. Then individual tablets were weighted and the individual weight was compared with an average weight. The results are shown in tables.

Hardness and friability

Friability of the tablets was checked by using Roche friabilator. The device subjects a number of tablets to the combined effect of abrasions and shock by utilizing a plastic chamber that revolves at 25rpm dropping the tablets from a height of 6 inches with each revolution.

Pre-weighed sample tablets were placed in the friabilator, which was then operated for 100 revolutions. Tablets were dusted ad reweighed. The results are shown in table.

Content uniformity test

Ten tablets were weighed and powdered, a quantity of powder equivalent to 100mg of paracetamol was transferred to a 100ml volumetric flask and 10ml methanol is added. The drug is extracted in methanol by vigorously shaking the stopped flask for 15 minutes. Then the volume adjusted to the mark with 0.1ml volumetric flask and makes up to mark with 0.1N HCL. The paracetamol content was determined by measuring the absorbance a 257 nm after appropriate dilution in UV-spectrophotometer.

The drug content was calculated using the standard calibration curve. The mean percent

drug content was calculated as an average of three determinations.

***In-vitro* disintegration time**

The *in-vitro* disintegration test was performed by placing tablet in one of the disintegrating basket which was dipped in 1 liter of 0.1 N HCl solution maintained at 37^0C and the time required for disintegration was observed. The test is repeated for total 3 tablets and average value was considered as disintegration time for the tablet

***In-vitro* dissolution data**

Dissolution rate studies were performed in 900ml of 0.1 N HCl solution at 37±0.5^{0}C, using 8-station USP type-II (paddle) apparatus with paddle rotating at 50rpm. 250mg of paracetamol fast disintegrating tablets was placed in dissolution basket. At fixed time intervals, samples withdrawn were filtered and spectrophotometrically analyzed for the drug content at 257nm.

$$\%\textbf{Drug dissolved} = \left(\frac{A_t}{A_s}\right) \times \left(\frac{D_s}{D_t}\right) \times 100$$

Where, A_t- test absorbance, A_s- standard absorbance, D_s- standard dilution & D_t- test dilution.

RESULTS AND DISCUSSIONS

Construction of Standard calibration curve of Paracetamol in 0.1 N HCl

The absorbance of the solution was measured at 257nm, using UV spectrometer with 0.1N HCl solution as blank. The values are shown in below table. A graph of absorbance Vs concentration was plotted which indicated in compliance to beer's law in the concentration range 2-10µg/ml as shown in figure 1.

Table 2: Construction of Standard calibration curve of Paracetamol in 0.1 N HCl

Concentration (µg/ml)	Absorbance
2	0.2722
4	0.4076
6	0.5449
8	0.6917
10	0.8235
12	0.9773

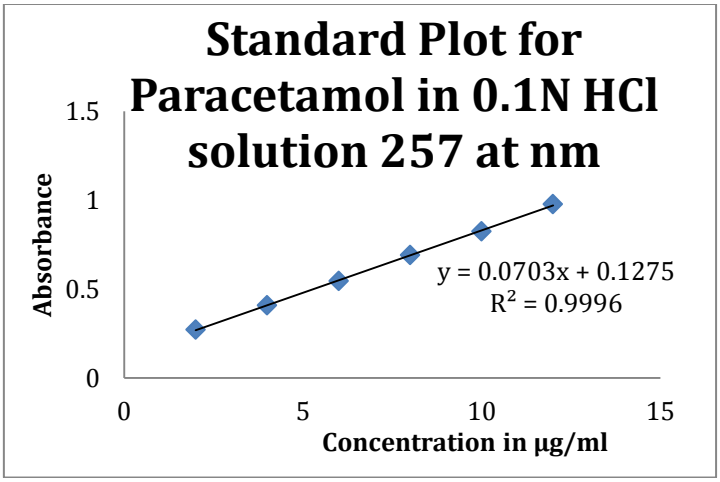

Fig. 1: Standard Plot for Paracetamol in 0.1N HCl solution 257 at nm

The calibration curve of Paracetamol in 0.1 N HCl showed good correlation with regression value of 0. 999.

Pre-compressions studies

Table 3: Pre-compression parameters for paracetamol 125mg fast dissolving tablet mix

Formulation Code	Angle of repose (o)	Bulk density (g/cc)	Tapped density (g/cc)	Carr's Index (%)	Hausner's Ratio
F1	29.13	0.40	0.48	16	1.20
F2	26.21	0.41	0.50	13.0	1.15
F3	25.83	0.50	0.58	13	1.16
F4	31.34	0.39	0.47	17.0	1.16
F5	32.11	0.37	0.41	9.75	1.10
F6	24.25	0.43	0.52	17.3	1.14

The bulk density and the tapped density for all formulations were found to be almost similar. The Carr's index and Hausner's ratio were found to be in the range of ≤ 18 % and 1.10 to 1.20 respectively, indicating good flow and compressibility of the blends. The angle of repose for all the formulations was found to be 29.25 to 32.11^0 indicating passable flow.

Post compression studies

Table 4: Post-compression parameters for paracetamol 125mg fast dissolving tablets

Formulation Code	Avg. wt (mg) (n=20)	Thickness (mm) (n=3)	Hardness (kg/cm^2) (n=3)	% Friability	%Drug content (n=3)	Disintegration Time (sec.)
F1	252.8	3.61	3.6	0.43	100.23	27.5
F2	251.6	3.76	3.5	0.52	101.87	33.5
F3	248.3	3.68	3.7	0.64	99.83	39.5
F4	253.0	3.94	3.7	0.59	100.25	29
F5	248.2	3.59	3.4	0.38	99.68	34.5
F6	251.4	3.58	3.2	0.46	100.54	38.5

Table 5: *In-vitro* dissolution studies of Paracetamol tablets in 0.1N HCl solution

Time (min)	Marketed Formulation	F1	F2	F3	F4	F5	F6
5	12	12	10	14	15	17	17
10	25	21	23	27	28	31	42
15	41	33	38	34	47	52	65
20	59	46	59	61	64	74	84
25	82	62	75	83	86	93	100
30	95	79	90	95	98	100	-

The weight variation of tablets was within the range of ±7.5% complying with pharmacopoeia specifications of IP. The thickness of tablets was found to be between 3.58 to 3.94 mm. The hardness for different formulations was found to be between 3.2 to 3.7 kg/cm^2, indicating satisfactory mechanical strength. The friability was < 1.0% W/W for all the formulations, which is an indication of good mechanical resistance of the tablet. The drug content
found to be within limits 99 to 102%.

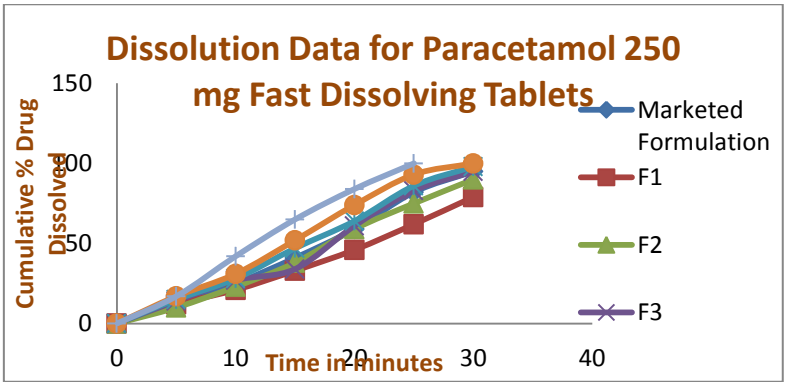

Fig. 2: *In-vitro* dissolution studies of Paracetamol 125 mg fast dissolving tablets in 0.1N HCl solution

Kinetic Data

Table 6: Release kinetic data for **Paracetamol 125 mg fast dissolving tablets in 0.1N HCl solution**

FORMULATION CODE	R^2 values	
	Zero Order	First Order
Marketed Formulation	0.9907	0.8353
F1	0.9893	0.9011
F2	0.9916	0.8839
F3	0.9775	0.8325
F4	0.9954	0.7953
F5	0.9902	0.8284
F6	0.9953	0.7854

The highest concentration of polymer was shown faster dissolution and lowest concentration shown slower dissolution. From the above dissolution data, it was observed that dissolution enhancement in the following order

Co-grinding > Physical Mixing

Among the formulations F6 formulation showed very fast dissolution i.e. 100% at 25th minute. From the kinetic data, it was observed that F6 was following zero-order kinetics. F6 formulation was formulated using banana powder as disintegrating agent at 1: 0.75 ratios.

CONCLUSION

Suitable analytical method based on UV-Visible spectrophotometer was developed for Paracetamol. λ_{max} of 257 nm was identified in 0.1N HCl solution. Paracetamol-Banana dispersion was tried at 1: 0.25, 1:0.5 & 1:0.75 concentrations (drug: polymer) using physical mixture and co-grinding methods.500 mg equivalent weight to Paracetamol the Paracetamol-Banana dispersion was used to prepare directly compressed tablets. F1, F2 & F3 tablets are prepared by physical mixture method and F4, F5 & F6 are prepared by co-grinding method. The evaluation parameters like hardness, friability, weight variation and drug content indicate that values were within permissible limit for all formulations. Disintegration time for all the formulations were < 40 seconds which is less than marketed formulation (83 seconds), comparatively it is very less for F1 formulation. *In vitro* drug release study was carried out in 0.1 N HCl solution using USP II (Lab India Disso 8000) for 30 minutes; F-6 was identified as the best formulation among all the formulations, selected based on *in-vitro* dissolution data. F6 was prepared using co-grinding technique has shown better release profile compared to physical mixing technique. Thus, we are able to achieve our objective of preparing fast dissolving tablets of Paracetamol with natural excipients and simple method of manufacture to enhance the dissolution of the drug.

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