ScienSage

Journal of Advanced Scientific Research

Available online through http://www.sciensage.info/jasr

ISSN
0976-9595
Short Communication

FORMULATION AND EVALUATION OF FAST DISSOLVING TABLET OF PARACETAMOL

Bulet Kumar Gupta*, Anuj Moral, Sultan Ahmed, Md. Asraf, Aman Sharma

Department of Pharmaceutics, Kalka Institute for Research & Advanced Studies, Partapur By-Pass Meerut NH-58 (U.P.), India

**Corresponding author: bulletkumar37069@gmail.com*

ABSTRACT

Fast dissolving tablets (FDTs) are novel types of tablets that disintegrate or disperse in saliva within few seconds without water. Paracetamol was used as a model drug in this formulation. Paracetamol is widely prescribed antipyretic and analgesic drug for all age groups. 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 F6 formulation was showing 100% release at 25 minute and faster, compared to the marketed formulation and the formulation was found to be stable.

Keywords: *Fast dissolving tablets, Acetaminophen, Direct compression.*

1. INTRODUCTION

The fast dissolving tablet is most important single unit solid dosage form for particularly used for pediatric and geriatric population who has difficulty in swallowing. This is most extensively utilized oral route of administration, its products are designed for oral delivery and easily available in the market on the prescription and over the counter drug, which disintegrate or dissolve rapidly orally, without chewing. Fast dissolving tablets are prepared for immediate release of drugs for high absorption and completely solubilization of tablet through surface erosion, leading to elimination of lag time for disintegration thereby offering high absorption and rapid onset of action. These tablets disintegrate instantaneously when placed on the tongue, and active pharmaceutical drug starts releasing that dissolve in saliva. The disintegrated mass can slide down smoothly along the oesophagus with the help of saliva, so even people who have swallowing or chewing difficulties can take it with ease [1]. The acetaminophen (Paracetamol) is an important Non-steroidal anti-inflammatory drugs (NSAIDs) which gives analgesic and antipyretic effects; most NSAIDs are weak organic acids, once absorbed they get bound to serum albumin. Due to increased vascular permeability in localized sites of inflammations, the primary effect of NSAIDs is to inhibit COX enzyme, thereby blocking the transformation of arachidonic acid to prostaglandins, prostacyclin and thromboxane [2]. The fast dissolving tablet of paracetamol are uncoated tablets intended to be placed in the mouth where they disperse rapidly before swallowed. These tablets disintegrate within 3 min., when examined by the test for disintegration of tablets and capsules [3]. Paracetamol is used in various pain & fever treatment alone or in combination with other anti- inflammatory drug, it is slightly soluble in water and having low bioavailability; hence frequency of administration is high. The quick dissolving tablets are prepared by direct compression method [4]. The main side effects of the paracetamol tablet have nausea or vomiting, allergic skin reaction, gastric/mouth ulcer, anaemia and fatigue. These tablets are formulated with the help of active pharmaceutical ingredients (API) and following type of excipients such as diluents, granulating agents, binding agents, disintegrating agents, lubricants, colouring agents, flavouring agents, and sweetening agents [5]. Acetaminophen; used as an analgesic and antipyretic having bitter taste, the acetaminophen absorbed orally only about 1/3 or (10-25%) is protein bound in plasma and uniformly distributed in the body, plasma half-life is 1-4 hours. The bioavailability of paracetamol tablet is 63-80%, the onset of action by mouth, buccal, and intravenous is 37 min., 15 min., and 8 min., respectively [6]. The contraindications of paracetamol tablets are allergy, analgesic nephropathy (kidney disease) and severe liver impairment. This medicine should be used with extreme caution in patients with chronic alcohol use due to the increased risk of serious liver injuries, while the medicines is safe to use during breastfeeding. However, it is advised to consult your doctor before taking this medicine [7]. The following types of advantage present in the quick

dissolving tablets-No water needed, no chewing needed, improve stability & have a pleasing mouth feel [8].

2. MATERIAL & METHOD

2.1. Material used

Acetaminophen was obtained as a gift sample from Central Drug House (CDH) private limited in Delhi and Croscarmellose Sodium, PEG-400, Acacia, Talc, Lactose, and Magnesium Stearate were obtained as a gift sample from CDH.

2.2. Direct compression method

There are a few crystalline substances, such as acetaminophen that may be compressed directly in a tablet machine without need of granulation. For chemicals lacking this quality, special pharmaceutical excipients may be used to impart the necessary qualities for production of tablet by direct compression. These excipients include lactose, microcrystalline cellulose, acacia, talc, magnesium stearate and PEG-400 [1]. These medicaments are passed through sieve no. 20, 40 or any other specified sieve and then mixed with any additional excipients [2]. The capping, splitting, or laminating of tablets is sometimes related to air entrapment during direct compression, capping also may be caused by punches that are not immaculately clean and perfectly smooth or by a granulation with too much fines, or fine powder. Fine powder, which results when a dried granulation is sized, is generally 10 to 20% of the weight of the granulation. Some fine powder is desired to fill the die cavity properly. However, an excess can lead to tablet softness and capping [3].

2.3. Evaluation of oral fast dissolving tablets of paracetamol 125 mg.

2.3.1. Evaluation of blends

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

2.3.1.1. Bulk density (Db)

It is the ratio of total mass of the powder to bulk volume of powder, it was measured by pouring the weighed powder (passed through standard sieve #20) 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 given below. It is expressed in g/cc and is given by:

$$D_b = M/V_o$$

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

2.3.1.2. Tapped density (Dt)

It is the ratio of total mass of powder to the tapped volume of powder. The volume was measured by tapping the powder repeatedly, then the tapping was done after sometimes, and the tapped volume was noted (the difference between these two volume should be less than 2%) if it is more than 2%, tapping is continued for some more time and tapped volume was noted. It is expressed in g/cc and is given by:

$$Dt = M/V1$$

Where, M is the mass of powder, V1 is the tapped volume of powder.

2.3.1.3. Carr's index (%)

The bulk density is the measurement of weight to the volume of sample. Tapped density is determined as the measurement of weight of the sample to the volume after tapping the measuring cylinder for sometimes from 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 bulk density upon tapped density.

Carr's index= (Tapped density - bulk density / Tapped density) x 100.

2.3.1.4. Hausner's ratio

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

Hausner's ratio = Tapped density / Bulk density

2.3.1.5. Angle of repose (ϴ)

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

$$\text{Tan}\theta = h / r, \text{ then } \theta = \tan^{-1}(h/r)$$

Where, ϴ is the angle of repose, h is the height in cm; r is the radius in cm.

The powdered mixture was allowed to flow through the funnel with its tip fixed to stand at a definite height (h) 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 degree suggest a poorly flowing material.

2.4. Evaluation of Tablets

2.4.1. Weight variation test

In the test, 10 tablets were weighed individually and the average weight was calculated. The tablets were assayed and the content of active ingredient in each of the 10 tablets was calculated assuming homogeneous drug distribution.

2.4.2. Content uniformity Test

Ten (10) tablets were weighed and powdered, a quantity of powder equivalent to 100 mg of paracetamol was transferred to a 100 ml of volumetric flask and 10 ml of methanol was added. The drug was extracted in methanol by vigorously shaking the stoppered flask for 15 minutes. Then the volume was adjusted to the mark with 0.1N HCl. The paracetamol content was determined by measuring the absorbance at 257 nm after appropriate dilution in UV spectrophotometer. The drug content was calculated using the standard calibration curve.

2.4.3. Tablet Thickness

The thickness of tablet was determined by the diameter of the die, the amount of fill permitted to enter the die, the compaction characteristics of the filled material, and the force or pressure applied during compression. The degree of pressure affects not only thickness but also hardness of the tablets. Tablet thickness may be measured by hand gauge during production, Vernier caliper or by automated equipment.

2.4.4. Hardness test

Tablet hardness testing is a laboratory technique used by the pharmaceutical industry to test the breaking point and structural integrity of a tablet. Placed the paracetamol tablet in the Monsanto hardness tester, and then rotated the screw till break point of the tester. The procedure was repeated 8 to 10 times for average reading. Observation was recorded the in inspection sheet and attached in BMR.

2.4.5. Friability

Friability of the tablets was checked by using Roche friabilator. The device subjects the no. of tablets to be combined effect of abrasions and shock by utilizing a plastic chamber that revolves at 25 rpm dropping the tablets from a height of 6 inches with each revolution. Pre-weighed sample tablets were placed in a friabilator, which was then operated for 100 revolutions. Tablets was dusted and reweighed.

2.4.6. In-vitro disintegration time

The *in-vitro* disintegration test was performed by placing the tablets in a tube of disintegrating basket which were dipped in 1 litre of 0.1N HCl solution and maintained temperature at 37°C and the time required for disintegration was observed. The test was repeated for total 3 tablets and average value was considered as disintegration time for the tablets.

2.4.7. In-vitro dissolution data

Dissolution rate studies were performed in 900 ml of 0.1N HCl solution at 36.5 to 37.5 °C, using USP type-2 (paddle) apparatus with paddle rotating at 50 rpm. The quick dissolving tablets of paracetamol were placed in dissolution basket. At fixed time intervals, samples withdrawn were filtered and spectrophotometrically analysed for the drug content at 257nm.

$$\% \text{ Drug dissolved} = (At/As) \times (Ds/Dt) \times 100$$

Here, At= test absorbance, As= standard absorbance, Ds= standard dilution & Dt= test dilution.

3. RESULTS & DISCUSSION

The formulation of different batches is described in table 1. The pre-compression study and evaluation parameter like- angle of repose, bulk density, tapped density, carr's index, hausner's ratio & weight variation, thickness, hardness, friability, disintegration & dissolution rate and assay for drug content were found to be satisfactory and result were presented in table no. 2, 3 & 4.

In this formulation containing microcrystalline cellulose and sodium starch glycolate show sufficiently decrease in disintegration time (average time 30 to 32 seconds) among all the formulation. In-vitro dissolution rate study show that after 15 min. formulation F4-F6 % drug release 64%, 74% and 84% respectively. And pre-compression studies such as angle of repose of this formulation blends of F4-F6 was found to be 31.34, 32.11 and 24.25 respectively. The flow was graded as excellent, good, fair and passable for angle of repose is 25-30, 31-35, 36-40 and 41-45 respectively. The fast dissolving tablets show uniform thickness throughout, in the range of 3.7mm, 3.4mm and 3.2mm respectively. Thus the formulation of batch F6 was prepared by direct compression method has shown better profile.

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

Ingredients	F1	F2	F3	F4	F5	F6
Acetaminophen	125	125	125	125	125	125
Microcrystalline Cellulose	51	52	53	54	55	56
Starch	5	5	5	5	5	5
Magnesium	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
Lactose	39	38	37	36	35	34
Sodium starch	25	25	25	25	25	25
Total	250	250	250	250	250	250

Table 2: Pre compression parameters for fast dissolving tablets of paracetamol (125 mg)

Formulation code	Angle of repose (θ)	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	1.15
F3	25.83	0.50	0.58	13	1.16
F4	31.34	0.39	0.47	17	1.16
F5	32.11	0.37	0.41	9.75	1.10
F6	24.25	0.43	0.52	17.3	1.14

Table 3: Post compression parameters for fast dissolving tablets of paracetamol (125 mg)

Formulation code	Avg. Wt. (mg) n=20	Thickness (mm) n=3	Hardness (Kg/cm^2) n=3	% Friability	% Drug Content	Disintegration time (Sec.)
F1	251.6	3.76	3.5	0.52	101.87	33.5
F2	252.8	3.61	3.6	0.43	100.23	38.5
F3	248.3	3.68	3.7	0.64	99.83	39.5
F4	253	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	27.5

Table 4: *In vitro* dissolution studies for paracetamol tablets in 0.1 NHCl solution

Time	Marketed	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	79	83	86	93	96
30	95	79	90	95	98	100	100

The weight variation of tablets was within the range of±7.5 % complying with pharmacopoeia specification of IP. The thickness of tablets was found to be between 3.58 to 3.94 mm. The hardness of 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 formulation, which is an indication of good mechanical resistance of the tablets. The drug content found to be within limits 99 to 102%.

4. CONCLUSION

The goal of this investigation has been achieved by preparing fast dissolving tablet of paracetamol with the pharmaceutical aid of super disintegrating agent (sodium starch glycolate and microcrystalline cellulose). Six batches *i.e.* F1, F2, F3, F4, F5 and F6 were prepared by direct compression method. The evaluation parameters like Hardness, friability, weight variation and drug content indicate that value were within permissible limit for all formulations. Disintegration time for all the formulation were <40 seconds, which is less than marketed formulations (80 seconds), comparatively it is very less for F2 formulation. *In-vitro* drug release study was carried out in 0.1 N HCl solution using USPII (Lab India Disso 8000) for 30 minutes. F6 formulation was identified as the best formulation among all the formulations, selected based on *In-vitro* dissolution data. F6 was prepared by using direct compression method and showed better release profile. Thus, we are able to achieve our objective of preparing fast dissolving tablets of paracetamol with excipients and simple method of manufacturing to enhance the dissolution of the drug.

5. REFERENCES

1. Sujitha V, Sayani Bhattacharya, Geetha T. *Der Pharmacia letter*, 2014; **6(2):**82-89.
2. Anil Kumar Sahdev, Somya Purwa. *Asian journal of research in pharmaceutical science (AJPS Ci),* 2018; **8(4):**203-209.
3. *British pharmacopoeia,* British Pharmacopoeia Commission, *6755,* 2014; 2144.
4. Chowdary KPR, Aishwarya KVNR. *Journal of Global Trends in Pharmaceutical sciences*, 2013; **4(4):**1329-1334.
5. Mehta RM. *Pharmaceutics-I,* Vallabh Prakashan, Delhi, 2017; Page no -259.
6. Jhansi Saranya M, Suma Devi E, Naresh BSV, Phani Kumar CHS, and Vidyadhar KN. *International Journal of Pharmaceutical, Chemical & Biological Sciences.*, 2017; **7(3):**245-252.
7. Mourya AK, Prajapati SK, Jain SK. *International Journal of Pharmaceutical Science & Research*, 2012; 3(2):610-614.
8. Ansel, Howard C, Popovich, Nicholas GA, Loyd V. Lippincott Williams & Willcins, 7th Edition, 1999; 245.