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RESEARCH ARTICLE

Effect of Microcrystalline Cellulose as a Filler / Diluent in Tablet Formulations

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ABSTRACT

Pharmaceutical Manufacturing is an important enterprise and oral tablet Manufacturing is the most significant of all, because more drugs are made as tablets than any other dosage form. Paracetamol or also known as Acetaminophen has been very well known as analgesic and antipyretic drug. Actually, these tablets were sold as OTC drug or even prescribed by doctors with high value of prize. Don't you know, it's easy to make and all ingredients were easy and cheap to purchased Microcrystalline cellulose (MCC) is a multifunctional excipient in drug formulation. However, the dependent of most developing countries on importation of this excipient invariably increases the cost of drug production. The tablet was prepared by taking different concentration of MCC. The prepare tablets for various paracetamol contain 10%, 20%, 30% of microcrystalline cellulose. From the study, it was observed that as the concentration increase the hardness, friability, dissolution, disintegration of paracetamol tablets are also affected. From this study, it is concluded that the concentration of MCC in tablet affect the various parameters and the drug release from tablet also affected.

KEYWORDS

Paracetamol, Microcrystalline Cellulose (MCC), Friability, Dissolution, Disintegration

INTRODUCTION

Tablets are the Solid preparations each containing a single dose of one or more active ingredients and obtained by compressing uniform volumes of particles. They are used for local & systemic effect. Usually used for oral administration.

For most therapeutic agents used to produce systemic effects, the oral route still represents the preferred way of administration owing to its several advantages and high patient compliance compared to many other routes.

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The tablet dosage form accounts for approximately 50% of all dosage forms on the market. Tablets have many advantages over other dosage forms. The majority of tablets are used in the oral administration of drugs, which is the most convenient mode of drug administration.

Compressed tablets are prepared by single compression using tablet machines. After a quantity of powdered or granulated tableting material flow into a die, the upper and lower punches of the tablet machine compress the material under a high pressure (~tons/in^2).

Diluents increase the volume to a formulation to prepare tablets of the desired size. Widely used fillers are lactose, dextrin, microcrystalline cellulose (Avicel PH® from FMC Corp. and Emococel® from Mendell), starch, pregelatinized

starch, powdered sucrose, and calcium phosphate.

The filler is selected based on various factors, such as the experience of the manufacturer in the preparation of other tablets, its cost, and compatibility with other formulation ingredients. For example, in the preparation of tablets or capsules of tetracycline antibiotics, a calcium salt should not be used as filler since calcium interferes with absorption of the antibiotics from the GI tract.

Microcrystalline cellulose (MCC) is very frequently used in wet granulation, and typically these are 101 grades with median diameter of about 50 µm. In low and high shear processes, MCC allows water to be distributed evenly through the granulation and lends robustness to the process. MCC is very highly compactable and its inclusion can add strength and robustness to a tablet. Additionally, formulations containing MCC are generally relatively easy to disintegrate (when used with a superdisintegrant) leading to the potential for rapid drug dissolution. However the compactability of MCC is influenced by granulation, and factors that tend to increase the extent of granulation such as increasing amount of water, longer massing time and higher mixer speed tend to reduce the compactability of MCC. When the amount of diluent is relatively high then MCC tends to be used in conjunction with another diluent.

Advantages of tablet include-

- Ease of accurate dosing
- Good physical and chemical stability
- Competitive unit production costs
- High level of patient acceptability
- High convenience

MATERIAL AND METHODS

Material

Paracetamol E.P. (500 mg) (N-Acetyl-p-amino phenol). It is also known as an Acetaminophen (4-Acetamidophenol). Melting point is 169^{0c} to 172^{0c} and P^{H} is 5.5to 6.5. Paracetamol made by- Analab fine chemicals- Mumbai, India. Maize starch (5%w/w), croscarmillose (3%w/w), methylparaben (0.03% w/w), propylparaben (0.07% w/w), MCC (10% w/w, 20% w/w, 30% w/w), purified water (q.s.), talc (0.5%w/w), silicon dioxide colloidal (1%w/w), magnesium stearate (0.5%w/w).

Preformulation Study

Drug Characterization

Paracetamol E.P. (500 mg) (N-Acetyl-p-amino phenol). It is also known as an Acetaminophen (4-Acetamidophenol). Melting point is 169^{0}C to 172^{0}C and pH is 5.5 to 6.5. Paracetamol made by- Analab fine chemicals- Mumbai, India.

Drug Excipient Compatibility

Paracetamol along with different excipients were subjected to accelerated stress conditions after preparing the drug and excipients admixtures and evaluated by using Infrared Spectroscopy. Results indicated that there was no incompatibility of excipients with paracetamol.

Precompression Micromeritic Properties of Tablet Powder Blend and Granules

Angle of Repose

The frictional force in a loose powder can be measured by the angle of repose θ. It is defined as, the maximum angle possible between the surface of the pile of the powder and the horizontal plane. If more powder is added to the pile, it slides down the sides until the mutual friction of particles, producing a surface at an angle θ; it is in equilibrium with the gravitational force.

Angle of repose has an indirect method of quantifying powder flow ability. The angle of repose was determined by the fixed height cone method suggested by Newman. The blend of granules was poured through a funnel that can be raised vertically until a maximum cone height (h) was obtained. Radius of heap (r) was measured and the angle of repose was calculated using the following formula.

$$\theta = tan^{-1}\frac{h}{r}$$

Where, θ = Angle of Repose

h = Height of the cone

r = Radius of cone base

Bulk Density

Density is weight per unit volume. Bulk density, is the mass of the powder divided by bulk volume and is expressed as gm/cm^3. The Bulk density of a powder primarily depends on particle size distribution, particle shape and the tendency of particles to adhere together. The particles are packed in such a way to leave large gaps between their surfaces resulting in heavy powder of high bulk density. Bulk density is very important in the size of containers needed for handling, shipping and storage of raw materials and blend. It is also important in size blending equipment. Bulk density was determined by pouring powder blend into a graduated cylinder. The bulk volume and weight of the powder was determined. The bulk density was calculated by using the following formula.

$$\text{Bulk density} = \frac{\text{Mass}}{\text{Bulk volume}}$$

Tapped density

It is the ratio of total mass of the powder to the tapped volume of powder. The volume was measured by tapping the powder for fixed time. The maximum volume occupied in the cylinder, and the weight was measured. The tapped density was calculated using the formula.

$$\text{Tapped density} = \frac{\text{Mass}}{\text{Tapped volume}}$$

Compressibility Index (Carr's Index)

The simplest method for measurement of free flow of powder is compressibility index, indication of the ease with which a material can be induced to flow is given by compressibility index which was calculated as follows.

$$\text{Carr's Index} = \frac{V_0 - V_t}{V_0} \times 100$$

Where, V0= bulk volume

Vt= tapped volume

Hausner's Ratio

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

Hausner's ratio is an indirect method to predict powder flow properties

Moisture Content / Loss of Drying

Two grams of each material was weighed and evenly distributed over the surface of a 70 mm tarred Petri-dish. The samples were placed in a dessicator containing distilled water in its reservoir (Relative Humidity=100%) at room temperature and the weight gained by the exposed samples at the end of the five day period was recorded and the amount sorbed was calculated from the weight difference as the moisture sorption capacity.

$$\text{LOD} = \frac{\text{Final weight}}{\text{Initial weight}} \times 100$$

Preparation Tablet Formulation

Wet Granulation Method

Prepare and weight all ingredients, then sieve it with mesh 20 except magnesium stearate sieve it with mesh 30.

Make Maize paste: Prepare ± 42.5 ml (aa with the maize starch). Pour it into the maize starch and stir it well. Prepare hot water ± 127.5 ml (3 x the amount of maize starch). The dissolve nipagin and nipasol using this hot water, until completely homogenous. Then, pour it together to the maize starch, stir it well until formed paste.

Wet granulation: Mix sieved paracetamol, microcrystalline cellulose 102, and croscarmellose until homogenous. Then, granulate it with maize paste. You can add purified water quantity sufficient to make a well mass. Sieve it using mesh 4.

Drying Process: Dry the mass using oven or Fluid Bed Dryer, until moisture content ± 1-2.5%. After the granule dry, sieve it again through mesh 12 and sieve it again through mesh 20.

Other Phase: Add Microcrystalline Cellulose, Talc, and Silicon Dioxide Colloidal, mix it about 10 minutes

Lubricants: Add magnesium stearate and mix it again about 3 minutes

Tablet compression: Compress the mass using rotary tablet machine, appropriate with the tablet specification.

Table 1: Composition of tablet formulation

Sr. no.	Ingredients	B1 (mg)	B2 (mg)	B3 (mg)
1	Paracetamol	500	500	500
2	Croscarmillose	25.5	25.5	25.5
3	Maize starch	42.5	42.5	42.5
4	Methyl paraben	0.255	0.255	0.255
5	Propyl paraben	0.595	0.595	0.595
6	MCC	170	340	510
7	Purified water	q.s.to	q.s.to	q.s.to
8	MCC 102 (q.s.)	94.15	94.15	94.15
9	Talc	4.25	4.25	4.25
10	Silicon dioxide colloidal	8.5	8.5	8.5
11	Mag. stearate	4.25	4.25	4.25

Evaluation of Prepared Tablet

Weight Variation / Uniformity of Weight

Twenty tablets from each batch were selected at random and weighed individually using an electronic balance (model- PGB- 300, Made by- LC-GC, INDIA). Their mean weights and standard deviations were determined based on an official method.

Diameter

Ten tablets were taken and their thickness was recorded by a digital Vernier calliper.

Thickness

Ten tablets were taken and their thickness was recorded by a digital Vernier calliper.

Hardness

Tablet hardness was determined for a minimum of six tablets using a vertically mounted Monsanto type hardness tester.

Friability

Friability was calculated as the percentage weight loss of 20 tablets using a friabilator (LAB HOSP, INDIA) for 4 min at 25 rpm.

Content Uniformity

Weigh and powder 20 tablets weigh accurately quantity of the powder equivalent to about 0.15gm of Paracetamol & add 50 ml of 0.1 M Sodium hydroxide, dilute with 100 ml of water shake for 15 minutes and add sufficient water to produce 200 ml. Mix, filter and dilute 10 ml of the filtrate to 100 ml with water. To 10 ml of the resulting solution add 10 ml of 0.1M Sodium hydroxide dilute to 100 ml with water and mix. Measure the absorbance of resulting solution at maximum at about 257 nm, calculate the content of Paracetamol. Taking 715 as the value of A (1%, 1cm) at the maximum at about 257 nm.

Disintegration

The United States Pharmacopoeia (USP) method was adopted (USP, 2003) using the Electrolab disintegration tester. This test was carried out using 6 tablets from each batch. 900 ml of phosphate buffer (pH 6.8) was used as disintegration medium. The equipment was maintained at a temperature of 37 ± 2°C. One tablet was placed on the mesh screen at the bottom end of each of the 6 glass tubes. The basket maintained an up and down movement in and out of the medium at a frequency of 28 to 32 cycles per min. Disintegration time was noted by means of a stopwatch. All the tablet particles passed through the screen.

Dissolution

The in vitro dissolution studies were performed by USP paddle type dissolution apparatus (ELECTROLAB, INDIA) at 100 rpm. The

dissolution medium consisted of 6.8 phosphate buffer and the medium was maintained at 37˚C ± 0.5˚C. An aliquot (5 ml) was withdrawn at specific time intervals and replaced with the same volume of fresh medium at same temperature. The samples of 5 ml were withdrawn and measured spectrum mode at 243 nm by UV.

RESULTS

Microcrystalline cellulose (MCC) is a multifunctional excipient in drug formulation. However, the dependent of most developing countries on importation of this excipient invariably increases the cost of drug production. The tablet was prepared by taking different concentration of MCC. The prepare tablets for various paracetamol contain 10%, 20%, 30% of microcrystalline cellulose. From the study it was as the concentration increase the hardness, friability, dissolution, disintegration of paracetamol tablets are also affected. But does not affect the precompression parameter like bulk density, tapped density, angle of repose, hausner's ratio, and carr's index. From this study it is conclude the concentration of MCC in tablet affect the various parameter and the drug release from tablet also affected. Dissolution Study of Batch 1, 2 and 3 are given in figure.

Preformulation Study

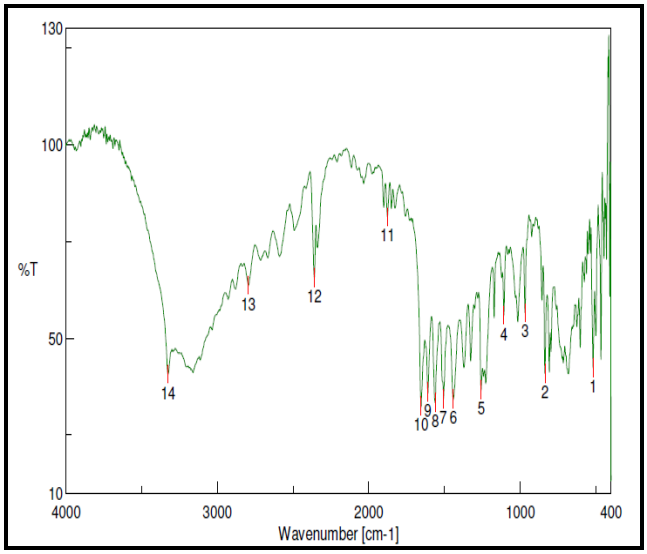

Figure 1: Infrared spectroscopy of pure drug

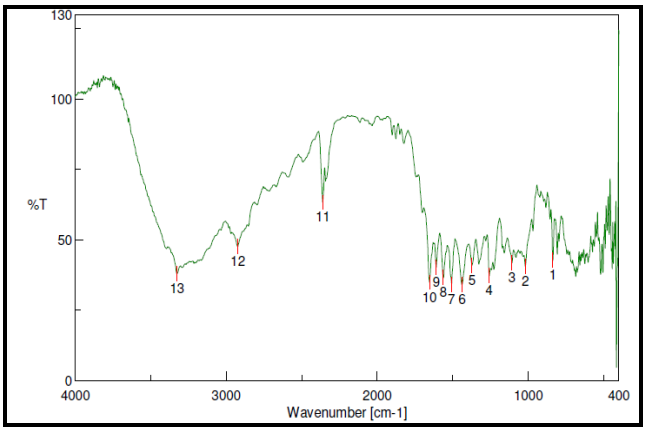

Figure 2: Infrared spectroscopy of granules (drug + excipients)

Precompression Study

Table 2: Precompression property of powder blend

Test	B1	B2	B3
Bulk density (gm/cc)	0.4	0.38	0.41
Tapped density (gm/cc)	0.53	0.50	0.55
Angle of repose (oc)	26.02	24.55	29.01
Carr's index (%)	24.52	24.00	25.24
Hausner's ratio	1.325	1.315	1.341

Table 3: Precompression property of granules

Test	B1	B2	B3
Bulk density(gm/cc)	0.34	0.35	0.33
Tapped density(gm/cc)	0.38	0.40	0.37
Angle of repose	16.06	15.74	15.90
Carr's index	10.52	12.50	10.81
Hausner's ratio	1.117	1.142	1.120

Evaluation of Tablets

Table 4: Evaluation of tablets of different batches

Sr. no.	Test	B1	B2	B3
1.	Shape	Round	Round	Round
2.	Weight variation / uniformity of weight (mg)	745.60	748.17	778.69
3.	Diameter (mm)	0.473 ± 0.0016	0.469 ± 0.0026	0.476 ± 0.0040
4.	Thickness (mm)	0.261 ± 0.0017	0.262 ± 0.0028	0.271 ± 0.0018
5.	Hardness (kg/cm^2)	3 ± 0.5	3.5 ± 0.5	4.5 ± 0.5
6.	Friability (%)	0.8026	0.8647	0.9541
7.	Content Uniformity (%)	97.90	98.45	98.26

Table 5: Disintegration time (in second) of tablet formulation

Sr. No.	Tablet	B1	B2	B3
1.	Tablet 1	28	34	50
2.	Tablet 2	32	36	46
3.	Tablet 3	30	38	48
4.	Tablet 4	28	38	46
5.	Tablet 5	32	40	48
6.	Tablet 6	30	42	50
7.	**Mean**	**30**	**38**	**48**

Dissolution Study

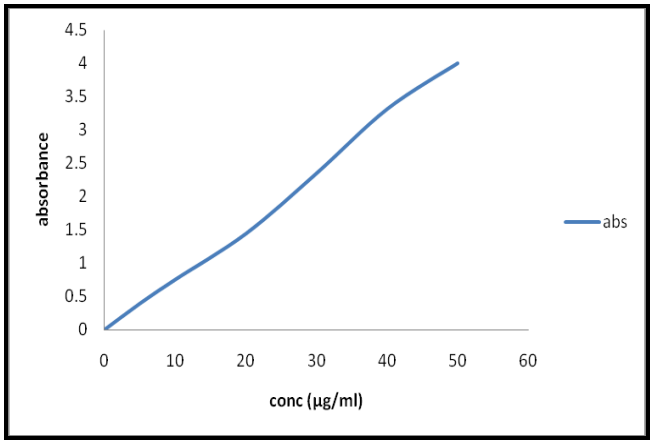

Figure 3: Calibration curve of paracetamol

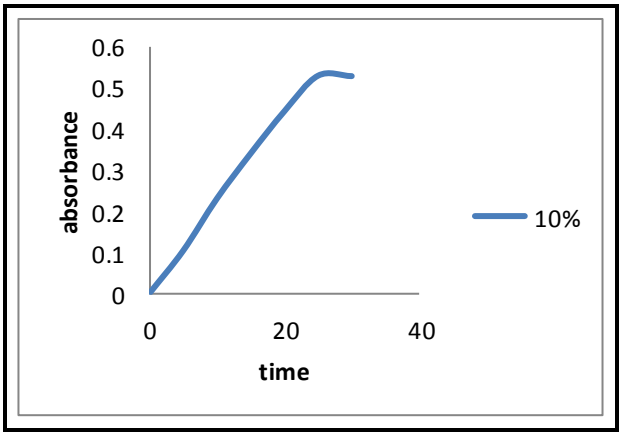

Figure 4: Dissolution study of batch 1

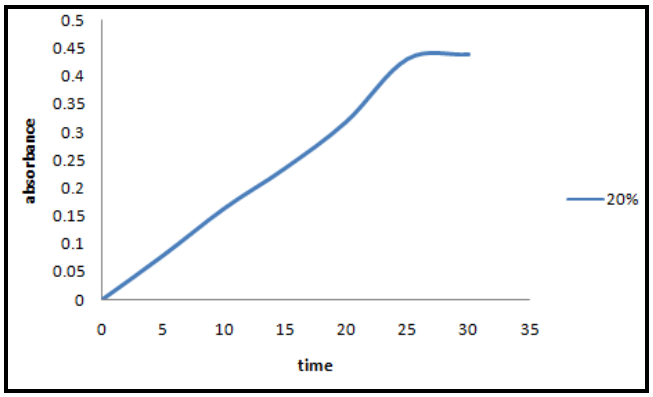

Figure 5: Dissolution study of batch 2

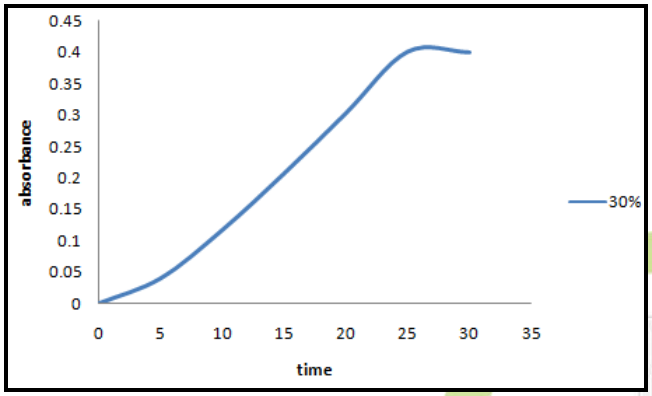

Figure 6: Dissolution study of batch 3

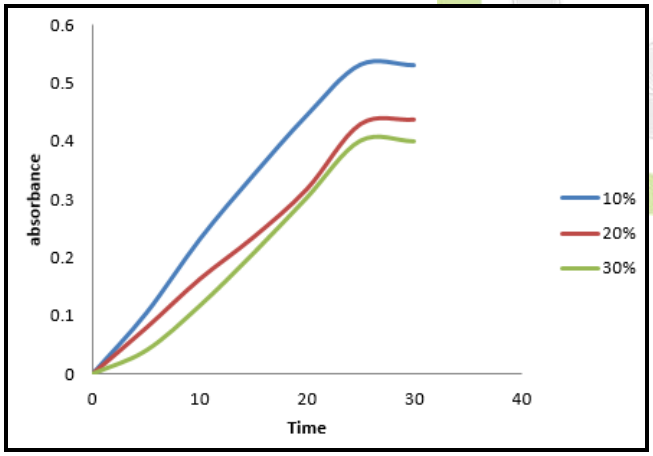

Figure 7: Dissolution study of batch 1, batch 2 and batch 3

CONCLUSION

The tablets were prepared by taking different concentration of MCC. The prepare tablets for various paracetamol contain 10%, 20%, 30% of microcrystalline cellulose. From the study it was as the concentration increase the hardness, friability, dissolution, disintegration of paracetamol tablets are also affected. From this study it is conclude the concentration of MCC in tablet affect the various parameter and the drug release from tablet also affected.

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