World Applied Sciences Journal 12 (3): 364-371, 2011
ISSN 1818-4952

Study of Effect of Custard Apple Pulp Powder As an Excipient on the Properties of Acetaminophen Tablet

[1]Rahul Thube, [1]Suresh Purohit and [2]Abhijit Gothoskar

[1]Department of Pharamaceutical Sciences, Jodhpur National University, Jodhpur, 342003, India
[2]Indira College of Pharmacy, Tathwade, Pune, 411033, India

Abstract: Cost effective pharmaceutical excipients are always desirable. Pharmaceutical excipients developed from natural sources are economic. For the present study, Custard Apple Pulp Powder (CAPP) was tried as a tablet excipient. It possessed good flow characteristics. Acetaminophen tablets containing starch as a disintegrating agent and polyvinyl pyrrolidone as a binder were prepared and used as standard for comparison with the acetaminophen tablets containing CAPP. Disintegration test showed that the tablets containing CAPP in presence of PVP as a binder had two folds increase in the disintegration time. Moreover, the disintegration time for the tablets prepared by replacement of PVP with CAPP in presence of starch as a disintgrant was reduced drastically. Dissolution studies further confirmed the enhancement of binding potential of PVP and disintegrating potential of starch by CAPP. Performance of the binder and the disintgrant in the tablet has been modified by the presence of CAPP.

Key words: Disintegration · Starch · Disintegrating Agent · Binder · Tablets

INTRODUCTION

Proper design and formulation of a dosage form requires consideration of the physical, chemical and biologic characteristics of the drug substances and pharmaceutical ingredients to be used in fabricating the product. Excipients facilitate the formulation design and perform a wide range of functions to obtain desired properties for the finished drug product [1].

A generally accepted definition of pharmaceutical excipients is that they are 'the additives used to convert pharmacologically active compounds into pharmaceutical dosage forms suitable for administration to patients'. Commonly used excipients span the range of chemical types, from single chemical entities such as ethyl vanillin and chlorocresol, to complex natural product materials such as lecithin and hydrogenated vegetable oil [2]. In addition to the active ingredients, excipients are normally included in tablet and their role is to ensure that tableting operation can run satisfactorily and the tablets of specified quantity are prepared [1].

Cost effective pharmaceutical excipients are always desirable. Pharmaceutical excipients developed from natural sources are economic. Present day consumers look for natural ingredients in food, drugs and cosmetics as they believe that anything natural will be more safe and devoid of side effects [3]. Natural excipients show lack of toxicity, easy availability and economic considerations in pharmaceutical industry as compared to their synthetic counterparts. Naturally, derived excipients have shown promising results in the modification of drug release from the formulations [4].

Literature survey revealed numerous research studies related to natural excipients. Manjil Patel et. al has worked on the solubility enhancement of Lovastatin by modified Locust Bean Gum using solid dispersion techniques [5]. Gil E.C et. al developed and optimized a novel sustained release dextran tablet formulation for propranolol hydrochloride [6]. Diltiazem resin complex loaded carboxymethyl xanthan beads have been prepared and investigated by Somasree Ray *et al* [7]. Kesselhut and Bauer have developed and characterized dextran based excipients for colon-targeting [8]. Chivate et. al evaluated *Sterculia Foetida* gum as controlled release excipient [9].

Sustained release matrix tablets of highly water soluble Tramadol Hydrochloride using natural gums - xanthan gum and guar gum as cost-effective, nontoxic, easily available and suitable hydrophilic matrix systems

Corresponding Author: Rahul Thube, 16-A, Nandaraj,Chaitraban Soc, Famous Chowk, New Sangvi, Pune, 411027 India.
Tel: +9120-26442074, Fax: +9120-26442074, E-mail: rahulthube@rediffmail.com.

have been prepared and compared with the extensively investigated hydrophilic matrices i.e hydroxypropyl methylcellulose,carboxymethyl cellulose with respect to *in-vitro* drug release rate and hydration rate of the polymers [10].

Inhibition of efflux pumps is an emerging approach in cancer therapy and drug delivery. Since it has been discovered that polymeric pharmaceutical excipients such as Tweens or Pluronics can inhibit efflux pumps, various other polymers have been investigated regarding their potential efflux pump inhibitory activity. Among them are polysaccharides, polyethylene glycols and derivatives, amphiphilic block copolymers, dendrimers and thiolated polymers [11]. Gum Cordia has been studied by Biswajit Mukherjee et.al as a novel matrix forming material for enteric resistant and sustained drug delivery [12].

In the present context, the focus was the study of natural excipients. For most tablets, the first important step toward solution is breakdown of the tablets into smaller particles or granules, a process known as disintegration. Since the dissolution of a drug from the fragmented tablet appears to control its portion in the blood, disintegration is still used as a guide to the formulator in the preparation of an optimum tablet formula and as an in process control test to ensure lot to lot uniformity [13].

Disintegration test is provided to determine whether tablets disintegrate within the prescribed time when placed in liquid medium at the specific experimental condition. Complete disintegration is defined as that state in which any residue of the unit, except fragments of insoluble coating or cap shell, remaining on the screen of the test apparatus or adhering to the lower surface of the disc, if used soft mass having no palpably firm core [14].

To be absorbed, a drug substance must be in solution. The disintegration test is a measure only of the time required under a given set of conditions for a group of tablets to disintegrate into particles. This test is done as a quality control tool for conventional tablets. For compressed, uncoated tablets, the testing fluid is usually water at 37°C. Six tablets are tested.If one or two tablets fail to disintegrate; the test is to be repeated on 12 more tablets. Of the 18 tablets tested, 16 must have disintegrated within the given period of time. The conditions of the test are different for coated, buccal and sublingual tablets. For most uncoated tablets, the disintegration time is 30 minute, for enteric coated tablet up to two hours and for sublingual tablets three minutes. [15] Determination of the time of tablet to disintegrate when immersed in some test fluid has long been a requirement in most compendia. The disintegration time may be markedly affected by the amount of disintegrant used as well as tablet process condition [16].

The original rationale for tablet disintegration test was the fact that as the tablet break down into small particles, it offers a greater surface area to the dissolving media and therefore must be related to the availability of the drug to the body. The disintegration test however simply identifies the time required for the tablet to break up under the condition of the test and for all particles to pass through a 10-mesh screen. The test offers no assurance that the resultant particles will release the drug in solution at an appropriate rate. For this reason, dissolution tests and test specification have now been developed for nearly all tablets products [15].

A number of formulation and manufacturing factors can affect the disintegration and dissolution of a tablet, including particle size of the drug substance; solubility and hygroscopicity of the formulation; type and concentration of the disintegrant, binder and lubricant; manufacturing method, particularly the compactness of the granulation and compression force used in tableting; and any in-process variables. Together, these factors present a set of complex interrelated conditions that have a bearing on a product's dissolution characteristics [17].

For a drug to be absorbed, it must first be dissolved in the fluid at the site of absorption. For example, an orally administered drug in tablet form is not absorbed until drug particles are dissolved or solubilized by the fluid at some points along the gastro intestinal tract, depending on the pH solubility profile of the drug substance. Dissolution describes the process by which the drug particles dissolve. The dissolution test measures the amount of time required for a given percentage of the drug substance in a tablet to go into solution under a specified set of conditions. It is intended to provide a step towards the evaluation of the physiological availability of the substance [15].

As a drug particle undergoes dissolution, the drug molecules on the surface are the first to enter into solution, creating a saturated layer of drug solution that envelops the surface of the solid drug particle. This layer of solution is the diffusion layer. From this diffusion layer the drug molecules pass throughout the dissolving fluid and make contact with the biologic membranes and absorption ensues. As the molecules of drug continue to leave the diffusion layer, the layer is replenished with dissolved drug from the surface of the drug particle and the process of absorption continues [1].

In vitro dissolution testing of solids dosage forms guides formulation and product development toward product optimization. Dissolution studies in the early stages of a product's development allow differentiation between formulations and correlations identified with *in vivo* bioavailability data. Manufacturing may be monitored by dissolution testing as a component of the overall quality assurance program. The conduct of such testing from early product development through approval and commercial production ensures control of any variables of materials and processes that could affect dissolution and quality standards [15].

Present study was undertaken to determine the potential of Custard Apple Pulp Powder (CAPP) as a tablet excipient. Its botanical name is *Annona squamosa Lin*. Custard Apple was selected for the study because it is easily and economically available in India. In particular, the focus was to check the effect of CAPP on the disintegration and dissolution pattern of acetaminophen tablets and assess the competency of the formulated tablets by comparing them with standard formulation.

Experimental:

Preparation of Custard Apple Pulp Powder (CAPP): Custard Apples were purchased from the local market. The pulp of the fruits was scraped off gently. The pulp obtained was dried in sunlight. The dried mass was grinded in mixture to get fine powder. The pulp powder was subjected to further testing.

Evaluation of CAPP: [1, 19] CAPP was subjected to evaluation of micromeritic properties. It included determination of Bulk density, Tapped density, Hausner's ratio, Compressibility index and Angle of repose.

Bulk Density: 10 g powder was placed in a 50 ml measuring cylinder. Volume occupied by the powder was noted without disturbing the cylinder and bulk density was calculated by the following equation:

$$D_b = M / V_b$$

Where, D_b is the bulk density, M is mass of the drug, V_b is Volume of bulk drug.

Tapped Density: Powder weighing 10 g was placed in 50 ml measuring cylinder. The cylinder was then subjected to a fixed number of taps [50] until the powder bed had reached the minimum. The final volume was recorded and the tap density was calculated by the following equation:

$$D_t = M / V_t$$

Where, D_t is the tapped density, M is mass of the drug, V_t is Volume of bulk drug on tapping.

Hausner's Ratio: Hausner's ratio was calculated using the formula;

$$\text{Hausner's ratio} = D_t / D_b$$

Where, D_t is the tapped density, D_b is the bulk density.

Compressibility Index: The compressibility index was calculated using the formula;

$$\text{Compressibility index} = (D_t - D_b / D_t) \times 100$$

Where, D_t is the tapped density, D_b is the bulk density.

Angle of Repose: The angle of repose was determined by fixed funnel method. The accurately weighed wheat bran powder was taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touched the apex of the heap of the powder. The powder was allowed to flow through the funnel freely onto the surface. The height and diameter of the powder cone was measured and angle of repose was calculated.

$$\text{Angle of repose } (\theta) = \tan^{-1} (2h/d)$$

Where, h is height of the pile and d is the diameter of the pile.

Preparation of Acetaminophen Tablets: [20] Acetaminophen tablets were prepared as per Remington's formula. The batch size was 30 tablets for each batch. The batch B1 consisted of Standard Acetaminophen tablets containing Starch as the disintegrating agent and PVP as the binder. The batch B2 was prepared with an intention to determine the disintegration potential of CAPP. Table 1 depicts the composition of batch B1 and batch B2.

The batch B1 contained Standard Acetaminophen Tablets and was used as a control for comparison with the successive batch B2 which contained Acetaminophen Tablets prepared by using CAPP. During the formulation process for the batch B1, all the ingredients were weighed accurately. Acetaminophen, PVP and Lactose were blended together. The blend was passed through sieve no. 40. Sufficient alcohol was added till a coherent mass was formed. It was passed through sieve no. 18. Granules

Table 1: Formula for Acetaminophen Tablets

Ingredients	B1	B2
Acetaminophen	300 mg	300 mg
PVP	22.5 mg	22.5 mg
Lactose	61.75 mg	61.75 mg
Alcohol	4.5 ml	4.5 ml
Stearic acid	9 mg	9 mg
Talc	13.5 mg	13.5 mg
Starch	43.25 mg	--
CAPP	--	43.25 mg

were obtained and dried at 50°C. Stearic acid, Talc and Starch were passed through sieve no. 16 and then blended with the granules. The granules were compressed with tablet compression machine (Cadmach Single Press) to get uncoated tablets. The batch B2 was prepared by similar procedure as that of the batch B1. Batch B2 was prepared by replacing the disintegrating agent, starch by CAPP. These tablets so prepared were subjected to comparative evaluation tests.

Comparative Evaluation of Tablets: [1, 13, 15, 21] The batches B1 and B2 were subjected to various comparative tests. These tests included determination of Diameter, determination of Thickness, Hardness Test, Uniformity of weight, Friability Test, Disintegration Test and Dissolution Test.

Hardness: Hardness of the tablets was determined by Monsanto Hardness tester. The tablet was placed vertically between jaws of the tester. The two jaws placed under tension by a spring and screw gauge. By turning the screw, the load was increased and at collapse, the applied pressure from the spring was measured in kg/cm^2. The test was performed on three tablets.

Uniformity of Weight: 20 tablets were weighed at random and average weight was calculated. Not more than two of the individual weights should deviate from the average weight by more than 5%.

$$\text{Average Weight} = \frac{\text{Weight of 20 tablets}}{20}$$

Friability Test: Friability test measures the tablet strength. Friabilator (Electrolab - USP- EF 2) was used for testing the friability of tablets. Twenty tablets were weighed and placed in the tumbling apparatus that revolves at 25 rpm dropping the tablets through a distance of six inches with each revolution. After revolutions, the tablets were weighed and the percentage loss in tablet weight was determined. Friability values of 1% or less are usually acceptable. Following is the formula used for calculations.

Friability (%) = ((Initial wt. of tablets – Final wt. of tablets) / Initial wt. of tablets)X 100

Disintegration Test: Disintegration pattern of tablets was studied by following disintegration test as per USP. Standard disintegration test apparatus was used for the test. One tablet was placed in each of the six tubes of the apparatus. The apparatus was operated using water as the dispersion fluid maintained at 37±2°C. At the end of every ten minutes, the basket was lifted from the fluid and the tablets were observed for any residue of the unit, except fragments of insoluble coating or cap shell, remaining on the screen of the test apparatus or soft mass having no palpably firm core [14].

Dissolution Test: Dissolution pattern of tablets was studied by following dissolution test as per USP. The amount of acetaminophen ($C_8H_9NO_2$) was determined in comparison with a standard having known concentration of acetaminophen by employing U.V absorption at the wavelength of maximum absorbance at 243 nm on filtered portion of the solution under test. The medium used was 900mL pH 5.8 phosphate buffer and the apparatus used was USP type-2 (Paddle Type) at 50 rpm [14].

pH 5.8 phosphate buffer was prepared by placing 50 ml of the 0.2M Monobasic Potassium Phosphate solution in a 200 ml volumetric flask. 3.6 ml of 0.2 M NaOH solution was added. Then water was added to volume. 0.2 M Monobasic Potassium Phosphate required to prepare pH 5.8 Phosphate Buffer was prepared by dissolving 27.22 g of Monobasic Potassium Phosphate (KH_2PO_4) in water and diluting with water to 1000 ml [14].

Procedure: 900 mL of pH 5.8 phosphate buffer as the dissolution medium was placed in the vessel of apparatus 2 (Paddle Type). The dissolution medium was equilibrated to 37°C and the thermometer was removed. One tablet was placed in the apparatus taking care to exclude air bubble from the surface of the dosage unit. After every ten min, a specimen was withdrawn from a zone midway between the surface of the dissolution medium and the top of the rotating paddle not less than 1cm from the vessel wall the aliquots withdrawn were replaced for analysis with equal volume of fresh dissolution medium at 37°C.

The analysis was performed as directed in the monograph for acetaminophen tablets by employing U.V absorption at the wavelength of maximum absorbance at 243 nm on filtered portion of the solution under test [14].

Preparation of Batch B3: [20] The results of Disintegration Tests and Dissolution Tests prompted us to determine the binding potential of CAPP. Hence another batch of tablets as B3 was prepared. It was prepared by replacing the exact quantity of the binder, PVP by CAPP in the standard formula for B1. Rest of all the ingredients and method of preparation was similar to that of the batch B1. These tablets so prepared were subjected to evaluation tests.

RESULTS

Micromeritic evaluation of CAPP showed results given in Table 2.

For CAPP, the Compressibility Index value is less than 10 and the Hausner's ratio is in the range of 1.00 to 1.11. Hence, it is evident that it possesses excellent flow character [22].

Comparative Evaluation of Tablets: The batches B1 and B2 were subjected to various comparative tests. These tests included, Determination of dimensions, Hardness Test, Uniformity of weight, Friability Test, Disintegration Test. The results of these tests are summarized in Table 3.

Observations for Hardness Test, Uniformity of Weight and Friability Test indicate that the values are within the desirable limits.

Disintegration Test: The Disintegration Test results are markedly varying. Herein, the batch B2 tablets i.e. Acetaminophen Tablets containing CAPP as disintegrating agent required 40 min to get disintegrated while the batch B1 tablets i.e. Acetaminophen Tablet containing starch as the disintgrant required 19 min to get disintegrated.

Dissolution Test: Dissolution pattern of tablets was studied by following dissolution test as per USP. U.V absorption at the wavelength of maximum absorbance at 243 nm on filtered portion of the solution under test was employed. The medium used was 900mL pH 5.8 phosphate buffer and the apparatus used was USP type-2 (Paddle Type) at 50 rpm [14]. Table 4 depicts the Absorbance values for batch B1 Tablet at various time intervals.

Table 2: Micromeritic properties of CAPP

Parameter	Results
Bulk density	0.581 ±0.02 g/ml
Tapped density	0.632 ±0.02 g/ml
Hausner ratio	1.08
Compressibility index	8.06%
Angle of repose	31°±1.6°

Table 3: Comparative evaluation of tablets

Parameter	B1	B2
Diameter	12.08 mm±0.00577	12.08 mm±0.00577
Thickness	3.56 mm	3.57 mm
Uniformity of weight	0.442 gm	0.446 gm
Friability Test	F = 0.90%±0.01	F = 0.69%±0.02
Hardness Test	5.5 kg/cm^2 ±0.15275	3.8 kg/cm^2±0.20817
Disintegration Time	19 min. ±1.52753	40 min±2.08167

(Standard Deviation, n = 3)

Table 4: Absorbance values for Batch B1 during dissolution test

Time (min)	Absorbance
5	0.133
15	0.18
25	0.17
35	0.189
45	0.176
55	0.176
65	0.411
75	0.18
85	0.182
95	0.173
105	0.184

Table 5: Absorbance values for Batch B2 during dissolution test

Time (min)	Absorbance
5	0.057
15	0.042
25	0.049
35	0.051
45	0.077
55	0.068
60	0.072
75	0.074
85	0.096
95	0.077
105	0.084

The absorbance values of formulation B1 at various time intervals depicted in Table 4 treated with PCP Disso, a Graphical Model Software, reveal the release profile in terms of percentage drug release. The release profile for standard Acetaminophen tablets is shown in Figure 1.

Table 5 depicts the absorbance values for B2 at various time intervals.

The absorbance values of B2 depicted in Table 5 treated with PCP Disso software reveal the release profile in terms of percentage drug release w.r.t. time. The release profile for batch B2 is shown in Figure 2.

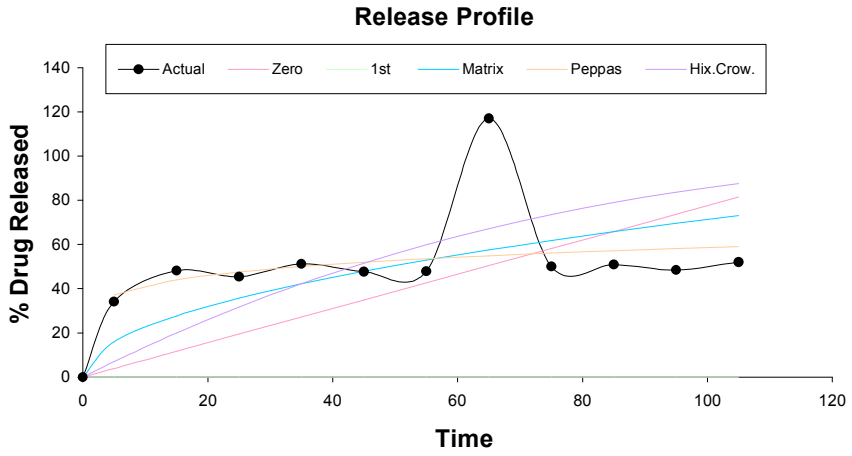

Fig. 1: Dissolution profile for Batch B1

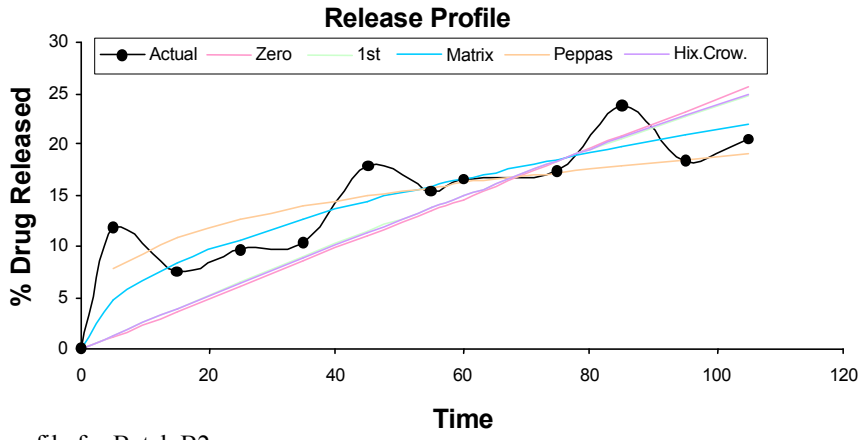

Fig. 2: Dissolution profile for Batch B2

It can be observed from figure 1 that, for B1 i.e. Standard Acetaminophen Tablet, approximately 50% drug is released in initial 15 min. Fig. 2 reveals the fact that, for B2 i.e. Acetaminophen Tablet containing CAPP, approximately 10% drug is released in initial 15 min.

Need for batch B3: During the preparation of batch B2, CAPP was used with an intention to perform as a disintegrant but instead of that, it prolonged the disintegration time. The results of Disintegration Tests and Dissolution Tests prompted the preparation of batch B3 to determine the binding potential of CAPP. To evaluate CAPP as a binder for tablet, batch B3 was prepared by replacing the exact quantity of the binder, PVP by CAPP in the standard formula for B1. The tablets so prepared were subjected to evaluation tests. The results of these tests are summarized in Table 6.

Hardness Test, Uniformity of Weight and Friability Test for batch B3 indicate that the values are within the desirable limits.

Table 6: Evaluation of B3 tablets

Parameter	Observation
Diameter	12.07 mm±0.00565
Thickness	3.56 mm
Uniformity of weight	0.444 gm
Friability Test	F = 0.92%±0.01
Hardness Test	3.2 kg/cm^2 ±0.2867
Disintegration Time	20 sec. ±0.0624

(Standard Deviation, n = 3)

Table 7: Absorbance values for Batch B3 during dissolution test

Time (min)	Absorbance
5	0.17
15	0.18
25	0.178
35	0.205
45	0.204
55	0.25
65	0.2
75	0.144
85	0.502
95	0.203
105	0.207

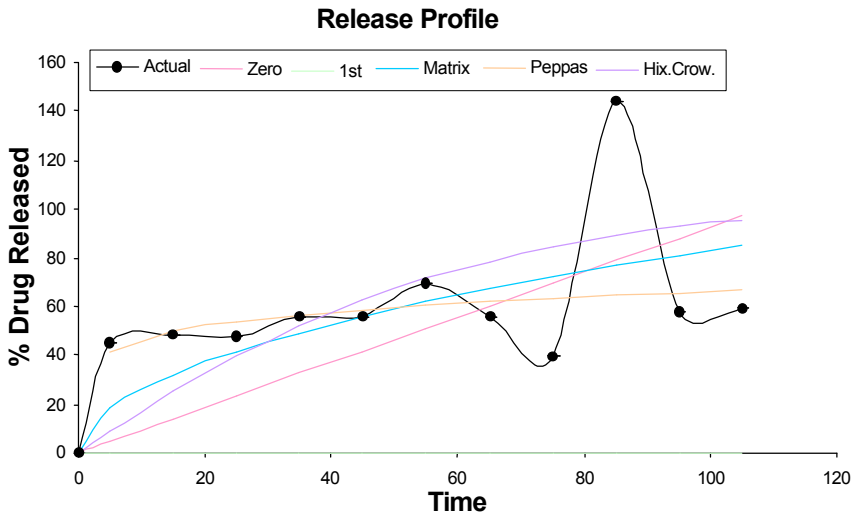

Fig. 3: Dissolution profile for Batch B3

The Disintegration Test for batch B3 results is noticeable. Herein, the batch B3 tablets i.e. Acetaminophen Tablets containing CAPP as a binder required only 20 seconds to get disintegrated.

Dissolution test for batch B3 was performed in the same manner as that of the B1 and B2. Table 7 depicts the Absorbance values for batch B3 Tablets at various time intervals.

The absorbance values treated with PCP Disso, the Graphical Model Software, reveal the release profile in terms of percentage drug release w.r.t. time.. The release profile for batch B3 is shown in Figure 3.

It can be observed from figure No.3 that, for batch B3 i.e. Acetaminophen Tablet containing CAPP as a binder approximately 50% drug is released in initial 5 min.

DISCUSSION

Micromeritic studies of CAPP explain the fact that it possesses excellent flow properties. Hardness Test, Uniformity of Weight and Friability Test results for all the three batches i.e. B1, B2 and B3 were in desirable limits.

The Disintegration Test results, in particular, are markedly varying. The batch B2 which contained CAPP, required double time as compared to the standard formulations B1 containing starch to disintegrate. This indicates the fact that CAPP increased the D.T of tablets markedly. The intention was to test CAPP as a disintegrating agent but it no longer performed as a disintegrant. The disintegration test reveals its potential as a probable binding agent.

This fact is further ascertained by the Dissolution Test results. Dissolution profiles of both the tablet batches under consideration differ markedly. The percentage drug release is affected for the tablet batch containing CAPP i.e. B2. CAPP has substantially slowed down the drug release. Slow disintegration due to CAPP has significantly contributed to the extent of dissolution leading to a 40% reduction in the cumulative percentage drug release in initial 15 min for the standard tablet containing starch as the disintegrant. This may be contributed to the binding potential of CAPP.This explains the fact that CAPP has performed like a binder rather than a disintgrant in comparison with starch in the process of dissolution of Acetaminophen tablet.

As CAPP, did not show promising results as a disintegrant, the third batch B3 was prepared to check the binding potential. The results for batch B3 were extremely unexpected. The tablets got disintegrated in just 20 seconds. It is further justified by the results of Dissolution Test. According to it; approximately 50% drug was released in initial 5 min. The tablets of batch B3 show initial rapid dissolution on account of short disintegration time due to the presence of CAPP.

The standard acetaminophen tablets contained starch as a disintgrant and PVP as a binder. When starch was replaced in the formula by CAPP, it prolonged the disintegration time and slowed down the dissolution of the drug. So it was thought that CAPP acts like a binder. Hence tablets were prepared by replacing the binder in the standard formula by CAPP. The results were unexpected. The tablets got disintegrated ultra rapidly and showed very fast dissolution of the drug for initial time interval.

It is observable that CAPP extended the disintegration time and hence dissolution in presence of the binder PVP. It markedly reduced the disintegration time for the tablet in presence of Starch as a disintgrant. It assisted the functions of the excipients substantially.

CONCLUSIONS

Custard Apple Pulp Powder possessed excellent flow characteristics and hence it can be used as a tablet excipient. The disintegration tests revealed the fact that Custard Apple Pulp Powder enhanced the binding properties of PVP and markedly added to the disintegration potential of Starch. These facts are further confirmed with dissolution profiles of the formulations. It is found that the performance of the binder and the disintgrant in the tablet has been modified by the presence Custard Apple Pulp Powder.

REFERENCES

1. Aulton, M.E., 2007. design and manufacture of medicines in Aulton's Pharmaceutics. Third Edition, Churchill-Livingstone: Elsevier. pp: 113-137, 201,315-320, 417-419,449-454.
2. Norwood, D.L. and F. Qiu, 2010. Strategies for the analysis of Pharmaceutical Excipients and their trace level impurities, American Pharmaceutical Review. Available at: http:// americanpharmaceuticalreview/ ViewArticle.aspx? ContentID =76. Accessed on 19 October 2010.
3. Patel, D.B. *et al*., 2009. Natural Excipient in controlled Drug Delivery Systems. J. Pharmacy Res., 2(5): 900-907.
4. Shirwaikar, A., A. Shirwaikar, S.L. Prabhu and G.A. Kumar, 2008. Herbal Excipient in Novel Drug Delivery Systems. IJPS, 70, (4): 415-422.
5. Patel, M., A. Tekade, S. Gattani, S. Surana, M. Patel, A. Tekade, S. Gattani and S. Surana Dec, 2008. Solubility Enhancement of Lovastatin by Modified Locust Bean Gum Using Solid Dispersion Techniques. AAPS Pharm. Sci. Tech., 9(4): 1262-1269.
6. Gill, E.C., A.I. Colarte, B. Bataille, J.L. Pedraz, F. Rodriguez and J. Heinamaki, 2006. Development and optimization of a novel sustained-release dextran tablet formulation for propranolol hydrochloride. International J. Pharmaceutics. 317(1): 32-9. Epub 2006 Apr 11.
7. Ray, S., S. Maiti and B. Sa, 2008. Preliminary Investigation on the Development of Diltiazem Resin Complex Loaded Carboxy methyl Xanthan Beads. AAPS Pharm. Sci. Tech., 9(1): 295-301.
8. Bauer, K.H., 1995. Development and characterization of water soluble dextran fatty acid esters as excipients for colon targeting. Pharmazie, 50(4): 263-9.
9. Chivate, A.A., S.S. Poddar, S. Abdul and G. Savant, 2008. Evaluation of Sterculia Foetida gum as controlled release excipient. AAPS Pharm. Sci. Tech., 9(1): 197-204.
10. Varshosaz, J., N. Tavakoli and F. Kheirolahi, 2006. AAPS Pharm. Sci. Tech., 7(1): E168-E174.
11. Werle, M., 2008. Natural and Synthetic Polymers as Inhibitors of Drug Efflux Pumps. Pharmaceutical Res., 25(3): 500-511.
12. Mukherjee, B., S. Dinda and B. Barik, 2008. Gum Cordia: A Novel Matrix Forming Material for Enteric resistant and Sustained Drug Delivery - A Technical Note. AAPS Pharm. Sci. Tech., 9 (1): 330-333.
13. Lachman, H.A. Lieberman and J.L Kanig, 1990. The Theory and Practice of Industrial Pharmacy, Third edition Lea and Febiger, Philadelphia, pp: 296-303: 336-342.
14. USP 30, Asian Edition, Volume-2, 2007 pp: 276-277, 807, 1269-1270.
15. Allen, L.V., N.G. Popovich and H.C. Ansel, 2008. Pharmaceutical Dosage Forms and Drug Delivery Systems. Eighth Edition, Wolters Kluwers Lippincott Willam and Wilikins. Philadelphia, pp: 148-50: 227-259.
16. Bankar, G.S. and C.T. Rhodes, 1996. Modern Pharmaceutics, Third Edition revised and expanded, Marcel Dekker. New York, pp: 385.
17. Jain, N.K., 2006. Pharmaceutical Product Development. First Edition, CBS Publishers and Distributors, New Delhi and Bangalore, Reprint 2008, pp: 100.
18. Kokate, C.K., A.P. Purohit and S.B. Gokhale, 2007. Pharmacognosy, 38th Edition, Nirali Prakashan, pp: 160-162.
19. Hadkar, U.B., 2008. Handbook of practical Physical Pharmacy and Physical Pharmaceutics. Nirali Prakashan, pp: 85(88): 92-93.
20. Gennaro, A.R., 1995. Remington. The science and practice of Pharmacy, Volume-II, Nineteenth Edition, Mack Publishing Company, pp: 1635.
21. The Indian Pharmacopoeia. Volume I, the Controller of Publications, Ministry of Health and Family Welfare, Government of India, 2007 pp: 175-184.
22. http:// www.pharmacopoeia.cn/ v29240/ usp29n24s0_ c1174.html, Accessed on 17 October 2010.