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Formulation And Evaluation Of Immediate Release Tablet Of Custard Apple Pulp

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An utilizing custard apple pulp powder as a model medication, an attempt has been made to manufacture quickly disintegrating oral tablets by direct compression. To increase patient compliance, immediate release tablets or instant release tablets were developed as an alternative to traditional oral dosage forms. The ingestion of traditional oral solid dosage forms is a complaint from the two extreme end age groups (paediatricand geriatric). Immediate release tablet are solid dosage forms with active chemicals or pharmaceuticals that, when pushed up against the tongue, quickly dissolve in a matter of seconds. Using the novel super-disintegrating agent Doshion, Croscarmellose Sodium, and cross povidone as super-disintegrants by direct compression method, custard apple pulp powder immediate release tablet was created. One well-known used to treat hypertension is custard apple pulp powder. Numerous characteristics, including drug content, in-vitro drug release study, disintegration time, and wetting time, were assessed for the manufactured immediate release tablets. Doshion and crospovidone demonstrated superior results in disintegration time and in-vitro drug release out of the three super-disintegrants that were tested, according to the results. After 25 minutes, the F-3 formulation with Doshion and Crospovidone demonstrated improved results in terms of maximum in-vitro drug release and disintegration time. Custard Apple pulp is applicable in High in fibre, Magnesium & Potassium, Vitamin A, good for eyes, Prevents Stomach ulcer, Oral health, Deficiency of haemoglobin.

KEYWORDS Custard Apple Pulp Powder, Immediate Release, Direct Compression, Crospovidone, Cross-Carmellose Sodium, Doshion.

INTRODUCTION

The custard apple (genus Annona) is a genus that includes approximately 170 species of tiny trees or shrubs that are native to the tropical regions of the New World and belong to the

Annonaceae family. In addition to being farmed commercially for their edible fruits, several varieties of custard apples are significant in the area for their use as traditional medicines[1]. The fruit of the common custard apple (Annona reticulata), also known as the sugar apple or bullock's-heart in the West Indies, is marked with depressions that give it a quilted appearance. The pulp is particularly soft, reddish golden, and sweet, which is how the fruit got its popular name.The custard apple pulp comprises a variety of chemical components, including the alkaloids anonaine, higenamine, roemerine, noreorydine, corydine (which exhibits anticancer action), norisocorydine, isocorydine, and glaucine. The fruit also includes vitamin C, α- and β-pinine, limonene, β-farnesene, β-sitosterol, and rutin.The ice cream business, confectionery, and some milk products are currently the only industries that process custard apple pulpBecause of its pulpy texture, custard apple fruit can make a good nectar substitute[4]. These days, sugar, acid, and other substances are added to tropical fruits like mango, litchi, guava, papaya, citrus fruits, pineapple, etc. to create nectar. It is a common misconception that fruit pulp and/or juices can be combined to enhance specific qualities including colour, flavour, scent, and nutritional content. Thus, an attempt was made to design and evaluate blended nectar using custard apple pulp as a way to give therapeutically and nutritionally important but tough to chew fruit. When compared to synthetic disintegrants, anona reticulata are less expensive, more readily available, and nontoxic.Custard Apple pulp Powder is applicable in Gain more body mass, Helps in digestion, Treats Anaemia, Vit. A, B, C & riboflavin, carbohydrates (23.5 %), minerals (0.9 %) and proteins (1.6 %). High nutritional status, Anti-microbial, Anti oxidation, Anti browning, Constipation, Hypertension. In-order to compare the efficacy of various natural and synthetic disintegrants, the rapid dissolving tablets of Custer Apple pulp were made in the current study utilizing the direct compression method[5].

Fig.1:Custard Apple Pulp Extract

MATERIALS AND METHODS

MATERIALS:

Doshion was a gift sample from Doshion PVT LTD.Crospovidone was gift sample from Pallav Chemicals and Solvents Pvt. Ltd. Andheri(W), Mumbai. Croscarmellose sodium was gift sample fromVISHAL CHEM Mumbai. Polyvinyl pyrrolidone was gift sample from VISHAL CHEM Mumbai. Magnesium stearate was gift sample from Pallav Chemicals and Solvents Pvt. Ltd. Andheri(W), Mumbai. Talc was gift sample from Thomas baker, Mumbai. Mannitol Research Lab. Sodium saccharin Research Lab. Micro-crystalline cellulose Loba Chemie PVT LTD[6].

METHODS:

EXTRACTION OF ANNONA RETICULATE (CUSTARD APPLE PULP POWDER)

We bought custard apples from the nearby market. The apple pulp was carefully scraped off. The resulting pulp was sun-dried. The dried substance was passed through mesh #60 after being ground into a fine powder using a combination[3]. The pulp powder was ground into a powder using a #60 mesh screen, dried in an oven at a temperature below 60°C, weighed, and kept in a tightly sealed container until needed.

Fig.2: Annona reticulate extract

METHODOLOGY:

Analytical method development:

a) **Determination of absorption maxima:**
   A phosphatebuffer (PH 6.8) UV spectrum was used to generate a solution with a medication concentration of 100 µg/ml. obtained with a UV spectrophotometer. A 200–400 nm range was used to scan the solution.
b) **Preparation calibration curve:**

A stock solution (100 µg/ml) of Custard apple pulp was prepared in phosphate buffer (PH 6.8). From this stock solution, suitable dilutions were done so as to get solutions ranging from 100-500 µg/ml. Absorbance of each solution was recorded at max (324nm) by UV-Visible Spectrophotometer (UV-1700 Shimadzu). The calibration curves plotted as absorbance on Y-axis vs. concentration on X-axis.

Drug - Excipient compatibility studies:

Fourier- Transform Infrared Spectroscopy (FTIR):

The key component for creating a chemically stable formulation for clinical and commercial development is a research of drug excipient compatibility. To choose the best excipients, drug excipient compatibility investigations are carried out prior to preformulation. FTIR tests are conducted to determine the compatibility of drug excipients.

Presented are the infrared spectra of Custard apple pulp powder both by itself and in conjunction with super disintegrants. The Custard apple pulp powder spectrum only revealed a small variation in peak intensity rather than any visible movement in peak location. The FTIR spectra of the medication with super disintegrants did not significantly change, according to the compatibility analysis. IR spectroscopy's result demonstrates that the medication and polymer did not interact chemically. This shows how well they get along with one other.

PRE-FORMULATION PARAMETERS:

Preformulation is the stage of research and development wherein investigations are conducted to evaluate the physical and chemical properties of a therapeutic molecule with the aim of developing a stable, safe, and effective dosage form. Carr's index, Hausner's ratio, and angle of repose are used to describe the flow characteristics of powder (prior to compression). Following that, in order to ascertain:

Angle of repose:

Angle of repose was determined using fixed funnel method. The powder was poured through a funnel that can be raised vertically until a maximum cone height (h) was obtained. Radius of the heap (r) was measured and the angle of repose (e) was calculated using the formula.

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

Where, θ is angle of response, h is height and r is the radius.

Table 1: USP limits for angle of repose

Sr. No	Angle of repose	Flow property
1	25-30	Excellent
2	31-35	Good
3	36-40	Fair
4	41-45	Passable
5	46-55	Poor
6	56-65	Very poor
7	>66	Very very poor

Bulk density:
Bulk density was determined by pouring the powder into a graduated cylinder. The bulk volume (V) and weight of the powder (M) was determined. The bulk density was calculated by using the below mentioned formula

Bulk density=Mass of powder/Bulk Volume of powder

Tapped density:
The measuring cylinder containing a known mass of powder was tapped for a fixed time. The upped density was calculated using the following formula,

Tapped density=Mass of powder/Tapped volume of powder
Carr's index:
A powder's compressibility is determined by Cars Index, which takes into account both bulk and tapped densities.The formula for carr's index is as below:

Carr's index= Tapped density- Bulk density/ Bulk density x100

Hausner's ratio:
It is related to interparticle friction and could be used to predict powder flow property.

Hausner's ratio= Tapped density/ Bulk density
Lower Hausner's ratio (<1.25) indicates better flow properties than higher ones (>1.25)

Table 2: USP limits forHausner's ratio

Sr.no	Hausner's ratio	Flow property
1	1.00-1.11	Excellent
2	1.12-1.18	Good
3	1.19-1.25	Fair
4	1.26-1.34	Passable
5	1.35-1.45	Poor
6	1.46-1.59	Very poor
7	>1.60	Very very poor

FORMULATIONS OF CUSTARD APPLE PULP POWDER TABLETS

Fast dissolving tablets of Custer Apple pulp Powder were prepared by direct compression method, using polymer Crospovidone (CP) and croscarmellose Na as a synthetic super disintegrant in different ratios and directly compressible mannitol as diluent to enhance the mouth feel[7]. All the ingredients were passed through #60mesh separately. The drug and mannitol were mixed by small portion of both each time and blending it to get a uniform mixture and kept aside. Then the ingredients were weighed and mixed in geometrical order

and tablets were compressed at 8 mm size to get a tablet of 250 mg weight using a (Clit pilot press 10 station rotary tablet compression machine[2]. The tablets were prepared according to the formulae as shown in Table 3.

Table 3: Formulation of custard apple pulp powder immediate release tablet by direct compression method

Ingredients (mg)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**
Drug	150	150	150	150	150	150
Doshion	18.75	18.75	18.75	18.75	18.75	18.75
Crospovidone	5	8.75	12.5	-	-	-
Cross-Caremellose Sodium	-	-	-	5	8.75	12.5
PVP	7.5	7.5	7.5	7.5	7.5	7.5
Magnesium Stearate	5	5	5	5	5	5
Talc	5	5	5	5	5	5
Mannitol	25	25	25	25	25	25
MCC	33.75	30	26.25	33.75	30	26.25

Evaluation

Weight Variation

10 Tablets Were Selected Randomly And Average Weight Was Determined. The Individual Tabletwasweighted And Was Compared With Average Weight. The Comparison Variation Within The I.P Limits, It Passes The Weight Variation Test.

Hardness

Tablet Crushing Strength Or Hardness, The Force Required To Break A Tablet In A Diametric Compression, Was Measured Using Monsanto Tablet Hardness Tester.

Friability

In general, friability refers to the weight of the tablets in the containers decreasing as a result of the particles being removed from the tablet surface. Friability sometimes signifies a lack of cohesiveness among the components of a tablet. A Roche Friabilator was filled with ten weighted tablets, and the starting weight of the pills was noted. The tablets were then rotated at a speed of 25 rpm for 100 revolutions[8]. Subsequently, the tablets were taken out of the Friabilator, the particles were wiped off, and the weight was measured once more and noted. The following formula was used to determine the percentage friability:

$$\% \text{ Friability} = \frac{\text{Initial weight of the tablets} - \text{Final weight of the tablets}}{\text{Initial weight of the tablets}} \times 100$$

Tablet Thickness

The thickness of individual tablets was measured using Vernier calliper, which permits accurate measurements and provides information of the variation between tablets.

Wetting Time & Water Absorption Ratio

A little Petri dish with six ml of water was filled with a piece of tissue paper that had been folded twice. The amount of time needed to completely wet a tablet was measured after it was placed on the paper. The tablet was then moistened and weighed using the formula shown in Table 6.

Water absorption ratio 'R' was determined using following equation:

$$R = 100 \times (Wa-Wb/Wb)$$

Where,

Wa = weight of tablet before water absorption,

Wb = weight of tablet after water absorption

In vitro disintegration time

Tablet was added to 10 ml of phosphate buffer solution, pH 6.8 at 37±0.5 °C. Time required for complete dispersion of a tablet was measured as given in Table 6.

In Vitro dissolution study

In vitro dissolution of Custer Apple pulp Powder fast dissolving tablets was studied in USP XXII type-II dissolution apparatus (Electro lab USP TDT-06T) employing a paddle stirrer. 900 ml of phosphate buffer pH 6.8 was used as dissolution medium. The stirrer was adjusted to rotate at 50 rpm. The temperature of dissolution media was previously warmed to 37±0.5 °C and was maintained throughout the experiment. One tablet was used in each test, 5 ml of sample of dissolution medium were withdrawn by means of syringe fitted with pre-filter at known intervals of time and analysed for drug release by measuring the absorbance at 324 nm. The volume withdrawn at each time interval was replaced with fresh quantity of dissolution medium.

RESULTS AND DISCUSSION

In this study, Annona reticulata, crospovidone, and croscarmellose were produced as fast-dissolving custard apple pulp powder tablets using the direct compression method. Not asto improve the mouthfeel, mannitol is used as a diluting agent when utilizing a syntheticsuper disintegrant in varying ratios. Ten formulations in total were created, together with a control formulation FCo. Table 2 displays the blends' respective IP limits. All blends were found to be free-flowing, with an angle of repose less than 25°, a Carr's index less than 20%, a tapped density of 83.33, a bulk density of 62.5, and a Hausner's ratio less than 1.25.The tablets produced had a consistent weight because of the homogeneous die fill, and the allowable variance fell within the IP requirements, specifically less than ±7.5%. There were two variables: drug content, hardness, water absorption ratio, and wetting timefound to be, as indicated in Table 6, within the following ranges: 2 kg/cm, 36 to 46sec. The produced tablets were found to have a friability rating of less than 1%, which indicates that the tablets had

strong mechanical resistance. It was determined that the formulation F3, which contains 8% w/w of Annona reticulata, was the most promising of all the created formulations. The times of dispersion, wetting, and water absorption ratio in vitro of Table 6 revealed that the F3 values were 36 seconds to 46seconds, in that order according to the experimental data, Annona reticulate Pulp powder yields superior outcomes than traditional commercial formulations.

1) CALIBRATION CURVE:

A stock solution (100 µg/ml) of Custard apple pulp was prepared in phosphate buffer (PH 6.8). From this stock solution, suitable dilutions were done so as to get solutions ranging from 100-500 µg/ml. Absorbance of each solution was recorded at max (324nm) by UV-Visible Spectrophotometer (UV-1700 Shimadzu). The calibration curves plotted as absorbance on Y-axis vs. concentration on X-axis.

Table 4: construction of calibration curve

Sr no.	Concentration	absorbance
1	100	0.4506
2	200	0.6921
3	300	0.9084
4	400	1.1727
5	500	1.3821

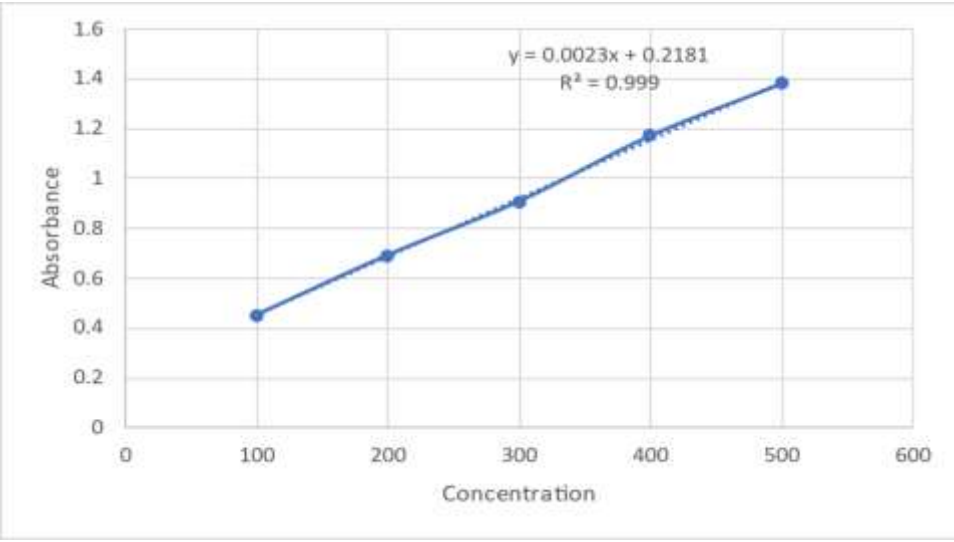

Fig.3: calibration curve of API

2) FT-IR (FOURIER TRANSFORM INFRARED SPECTROSCOPY)

The key component for creating a chemically stable formulation for clinical and commercial development is a research of drug excipient compatibility. To choose the best excipients, drug excipient compatibility investigations are carried out prior to preformulation. FTIR tests are conducted to determine the compatibility of drug excipients. Presented are the infrared spectra

of Custard apple pulp powder both by itself and in conjunction with super disintegrant. The Custard apple pulp powder spectrum only revealed a small variation in peak intensity rather than any visible movement in peak location. The FTIR spectra of the medication with super disintegrant did not significantly change, according to the compatibility analysis. IR spectroscopy's result demonstrates that the medication and polymer did not interact chemically. This shows how well they get along with one other.

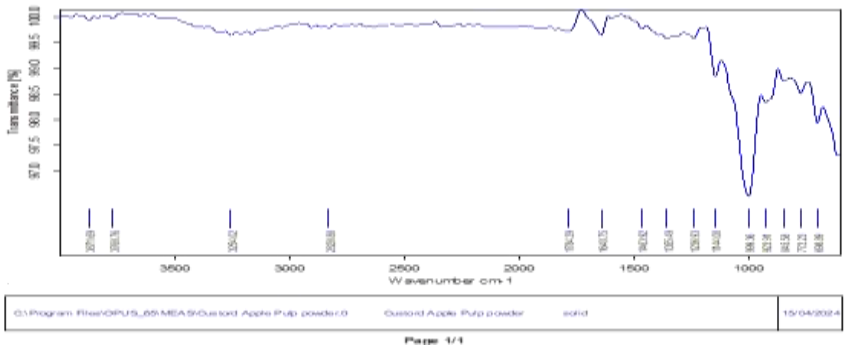

Fig.4: FT-IR of Custard apple pulp powde

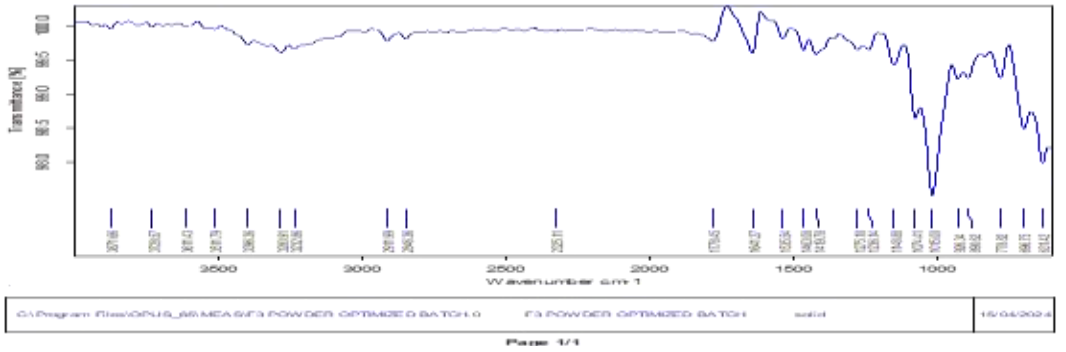

Fig.5: FT-IR of F3optimized batch powder

3) PRECOMPRESSION PARAMETERS:

The Precompression parameters have been performed as per Indian pharmacopeia & its specifications, so all the observation of the parameter has complied with the standard. So consider that all formulations of mixture powder has good flowability & packing capacity as per the given table no. 5.

Table 5: Pre-compression parameters of formulations prepared by direct compression method

Parameters	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**
Bulk Density(gm/cc)	62.5	50	62.5	62.5	50	62.5
Tapped Density(gm/cc)	83.33	62.5	83.33	83.33	62.5	83.33

Hausner's Ratio	1.33	1.25	1.33	1.33	1.25	1.33
Carr's Index (%)	24	20	24	24.99	20	24.99
Angle of Repose (°)	29	27	25	27.47	27	26

4)POSTCOMPRESSION PARAMETERS:

Weight variation data of the tablets shows no significant difference in the weight of individual tablet from the average value. The thickness of all formulations was in the range 1-1.8 mm. The hardness ranged from 2-5 kg/cm², All formulations passed the USP requirements for friability and uniformity of weight. In vitro disintegration was found in the range 34-58 sec.

Table 6: Post-compression parameters of formulations prepared by direct compression method

Parameters	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**
Hardness (Kg/cm2)	2 ±5	2 ±5	2 ±5	2 ±5	2 ±5	2 ±5
Thickness(mm)	1.8	1.8	1.8	1.8	1.8	1.8
Friability (%)	±0.3 0.5	0.2 ±0.5	0.2 ±0.5	0.2 ±0.5	0.5 ±0.5	0.4 ±0.5
Disintegration Time(sec)	57	46	34	58	46	45
Wetting Time(sec)	45	41	36	46	42	37
Dissolution Time	93.19	95.24	99.33	90.56	93.44	96.05
Weight Variation	(247 to 250mg) within IP limits of ± 0.5%					

5) Wetting Time

A little Petri dish with six ml of water was filled with a piece of tissue paper that had been folded twice. The amount of time needed to completely wet a tablet was measured after it was placed on the paper. The tablet was then moistened and weighed using the formula shown in Table 3.

Table 7: wetting time observations

Sr. No.	**Formulation code**	**Time (sec)**
1	F1	45
2	F2	41
3	F3	36
4	F4	46
5	F5	42

6	F6	37

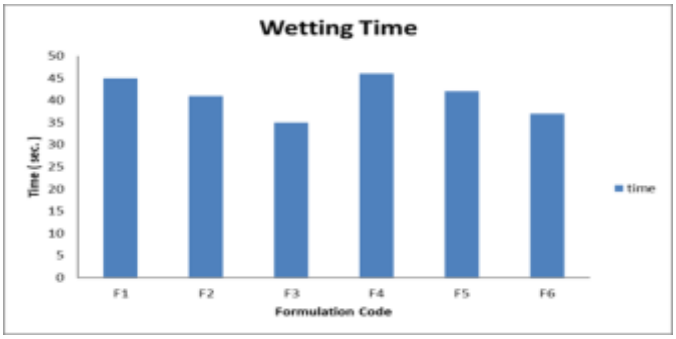

Fig 6: Wetting Time

6) **In Vitro Disintegration Time**

Tablet was added to 10 ml of phosphate buffer solution, pH 6.8 at 37±0.5 °C. Time required for complete dispersion of a tablet was measured as given in Table 8.

Table 8: Disintegration time observations

Sr. No.	**Formulation code**	**Time (sec)**
1	F1	57
2	F2	46
3	F3	34
4	F4	58
5	F5	46
6	F6	45

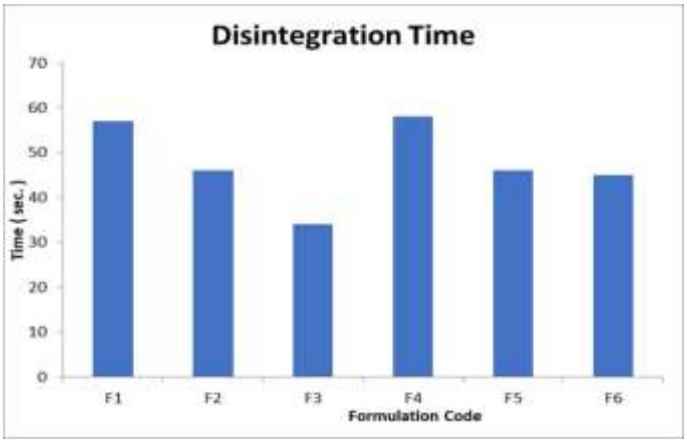

Fig.7: Invitro disintegration time

7) In Vitro Drug Release Study

In this study by using a paddle stirrer, the USP XII type-II dissolution apparatus (Electro lab USP TDT-06T) was used to study the in vitro dissolution of Custer Apple pulp Powder fast dissolving tablets. The dissolve medium employed was 900 ml of pH 6.8 phosphate buffer. A 50-rpm rotation was set for the stirrer. Throughout the experiment, the temperature of the dissolving media was kept at 37±0.5 °C, which was pre-heated. For each test, one tablet was utilized. Five ml of the dissolving medium sample were taken using a syringe equipped with a pre-filter at predetermined intervals, and the absorbance at 324 nm was used to measure the drug release. A new volume of dissolving liquid was added to the volume removed at each time interval.

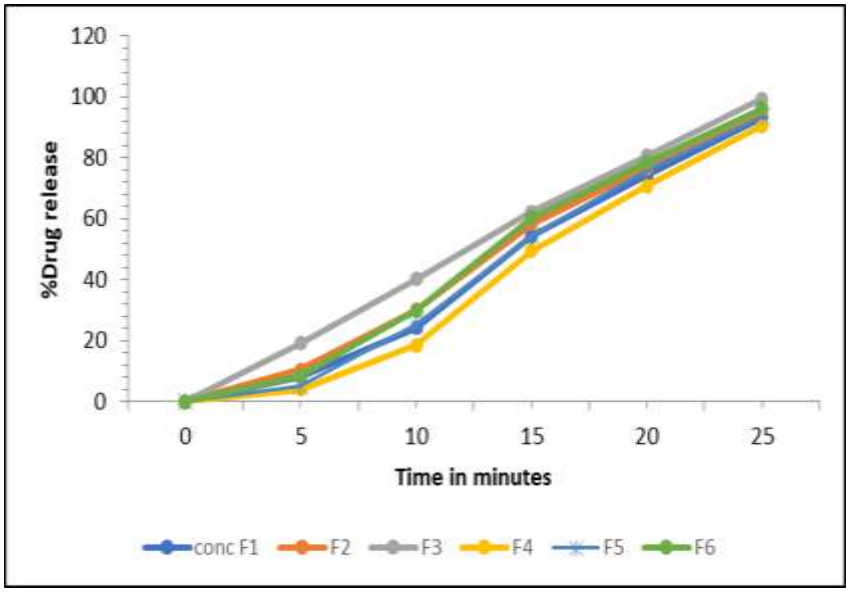

Fig.8: Percentage of drug release

CONCLUSION

According to the result of this study, it can be concluded that immediate release tablets of custard apple pulp powder (Annona reticulata) prepared by using doshion and crospovidone shows better drug release and disintegration time as compared to tablets prepared from other natural and synthetic disintegrants. Disintegration time of formulation F3 was found to be 34 seconds and the drug release was found to be 99.33 within 25 minutes. Based on observation for disintegration time the efficiency of super disintegrants was found in the following order: Doshion> Crospovidone > Croscarmellose Sodium

Since this immediate release tablet complies with the requirements for disintegration time i.e., disintegration time must be less than 1 min, it will improve the patient's compliance.

Here we concluded that the formulation F3 containing crospovidone shows the desirable immediate Release.

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