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Formulation and Evaluation of Paracetamol Tablet Using Powder of *Artocarpus heterophyllus* as Binder and Diluent

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ABSTRACT

Artocarpus heterophyllus found wild in the forest region, fruit is multiply seeded containing starch. Seeds were macerated with water then filtered to isolate starch and dried in a hot air oven. The physicochemical characteristics, phytochemical properties, powder characteristics of the seed powder were done. Granules property such as Angle of Repose, Bulk and Tapped densities, Hausner's ratio, Carr's index were studied. Paracetamol was the model drug used in the preparation of tablet. Tablets were prepared by wet granulation method. *Artocarpus heterophyllus* seed mucilage of different concentrations was used as binding agent the diluent properties of the seed powder were also studied. The compatibility of the drug with excipients was studied by FTIR spectroscopy. Tablet properties such as wetting time, water Absorption Ratio, weight uniformity, friability, disintegration time and dissolution rates using standard methods were also studied. Preparation of tablet using *Artocarpus heterophyllus* powder displayed acceptable average tablet weight, thickness, hardness, wetting time, water absorption ratio, friability, disintegration time, dissolution and potency when used as binder and diluent in tablet formulation.

INTRODUCTION:

[1]Pharmaceutical excipients are the agents other than the pharmacologically active drug or the API included in the manufacturing process. Binders are the excipients used to impart cohesive properties to the granules which help to ensure the intactness of the tablet after compression. This ensures that the granules and tablets are formed with the required mechanical strength. Starch mucilage is used as a universal binder.

Binders are used in the dry form in the powder and then moistened with a solvent to form wet lumps; binders are often added in solution form.

[2] *Artocarpus heterophyllus* found wild in the forest, fruit is multiple seeded containing starch. Starch is a mixture of polysaccharides amylopectin and amylose. Jackfruit seed contains lignans, isoflavones, saponins, all phytonutrients and their health benefits are wide ranging from anticancer to antihypertensive, antiaging, antioxidant, antiulcer, and so on. The powdered jackfruit seed have thickening and binding properties. *Artocarpus heterophyllus Lam* .belongs to the family Moraceae and is popularly known as jackfruit. It is the national fruit of Bangladesh. Commonly found in Southeast Asia and occasionally in Pacific island home gardens.

The plants of Artocarpus species have been used as traditional folk medicine against inflammation and malaria fever.

The pulp and seeds have been used as a cooling tonic. The compound isolated from the seed of A. heterophyllus, Jacalin, has potential as a therapeutic agent for cancer. Jacalin has been used as a histochemical reagent to study tissue-binding properties in benign and malignant lesions of the breast and thyroid.

The study also aims at the characterization of the Physicochemical and powder properties of the *Artocarpus heterophyllus* seed powder.

The objective of the present study is to formulate and evaluate tablet using *Artocarpus heterophyllus* seed powder as an excipient. The model drug used in this study is Paracetamol.

MATERIALS AND METHODS:

Artocarpus heterophyllus seed was collected from nearby places.

Paracetamol was supplied from Yarrow Chem Products, Mumbai. All other excipients and solvents used were of the analytical or pharmaceutical grade.

COLLECTION OF PLANT MATERIAL

The Jackfruit (*Artocarpus heterophyllus*) seed was collected from the surrounding area.

ISOLATION OF STARCH[3]

Wash seed thoroughly with water to remove adhering soil and earthy matter and reduce to fine slurry with distilled water in a blender. Pass the slurry through shaking sieves in order to remove the cell debris and other impurities. Allow the milky liquid to settle down and decant the supernatant. Wash starch 2-3 times with distilled water with constant stirring. Centrifuge the milky liquid, dry it in an oven at a low temperature or sundry the product.

CHARACTERIZATION OF ARTOCARPUS HETEROPHYLLUS SEED POWDER

Artocarpus heterophyllus powder was characterized for their physicochemical and phytochemical properties.

PHYSICOCHEMICAL CHARACTERIZATION

DETERMINATION OF ORGANOLEPTIC PROPERTIES

The physical appearance of a drug was observed.

DETERMINATION OF MELTING POINT

Melting point was determined by the capillary method.

DETERMINATION OF SOLUBILITY[4]

Small increments of *Artocarpus heterophyllus* seed powder was added to 10 ml of solvent (Coldwater, Warm water, Ethanol, Methanol, Acetone, Ether) in a 25 ml stoppered standard flask with vigorous shaking.

DETERMINATION OF pH[5]

2 g of the powder material was shaken with 100 ml of distilled water for 5 minutes and the pH of the supernatant liquid was determined using a pH meter.

PERCENTAGE MOISTURE CONTENT[6]

Dried the empty dish and lid in the oven at 105ºC for 3 h and transferred to a desiccator to cool. Weigh the empty dish and lid. Weigh about 3 g of the sample to the dish. Spread the sample with uniformity. Placed the dish with the sample in the oven. Dried for 3 h at 105ºC. After drying transferred the dish with a partially covered lid to the desiccator to cool. Reweighed the dish and its dried sample.

$$\text{Moisture (\%)} = [W1-W2] / W1*100$$

W1: Weight (g) of the sample before drying

W2: Weight (g) of the sample after drying

DETERMINATION OF SWELLING CAPACITY[7]

10 ml of distilled water and liquid paraffin was taken in two different test tubes; 3 g of powder was added to both test tubes. The dispersions were allowed to stand for12 hours. The volumes of the sediment in the tubes were recorded. The swelling index of the material was calculated using the formula

$$\text{S.I (\%)} = \frac{\text{(Volume of sediment in water} - \text{Volume of sediment in light liquid paraffin)}}{\text{Volume of sediment in light liquid paraffin}}$$

DETERMINATION OF POWDER CHARACTERISTICS

BULK DENSITY AND TAPPED DENSITY[8]

10 g of powder sample was placed into a clean dry measuring cylinder and the volume (V_0) occupied by the sample without tapping was determined. The cylinder was then dropped on to a hard wooden surface from a height of one inch at 2 seconds intervals until the powder occupied a constant volume (V_t). The bulk and tapped densities were determined from these values.

Density= Weight of powder (w)/volume of powder

Bulk density= Weight of powder (w)/Bulk volume of powder (V_0)

Tapped density= Weight of powder (w)/Tapped volume of powder (V_t)

CARR'S INDEX[9]

Carr's index or the compressibility index of the Artocarpus seed powder was calculated using the equation

Carr's Index= [(Tapped density-Bulk density)/Tapped density] * 100

HAUSNER RATIO[10]

Hausner Ratio was calculated using the formula

Hausner Ratio=Tapped density/Bulk density

POWDER POROSITY[10]

Powder porosity can be derived from the values of true density and bulk density as follows

Porosity= [1-(Bulk density/True density]*100

ANGLE OF REPOSE[10]

An angle of repose was determined by using the funnel method. The powder was poured through a funnel that can be raised vertically until a maximum cone height (h) was obtained. The inverse tangent of this ratio is the angle of repose. The radius of the heap(r) was measured and the angle of repose (Θ) was calculated using the formula.

$$\Theta = \tan^{-1} (h/r$$

Table 1: Flow property based on the angle of repose

Angle of Repose (degrees)	Flow
<25	Excellent
25-30	Good
30-40	Passable
>40	Very poor

PHYTO-CHEMICAL CHARACTERIZATION[11]

CHEMICAL IDENTIFICATION TESTS

TESTS FOR ALKALOIDS

WAGNER'S TEST: Crude extract was mixed with 2 ml of Wagner's reagent. Reddish brown colored precipitate indicates the presence of Alkaloids.

MAYER'S TEST: To about 2 ml of crude extract, a few drops of Mayer's reagent was added. Formation of precipitate indicates the presence of Alkaloids.

DRAGENDORFF'S TEST: To about 3 ml of crude extract, a few drops of Dragendorff's reagent was added. Brownish fluorescent precipitate indicates the presence of Alkaloids.

TEST FOR CARBOHYDRATES

MOLISCH'S TEST: 2-3 drops of the beta-naphthol solution was added to 2ml of the test solution. Very gently add 1 ml of Conc. H_2SO_4 along the side of the test tube. A deep violet coloration is produced at the junction of two layers which indicates the presence of carbohydrates.

FEHLING'S TEST: About 2 ml of sugar solution is added to about 2 ml of Fehling's solution taken in a test-tube. It is then boiled for 10 min. A red precipitate is formed which indicates the presence of reducing sugars.

BENEDICT'S TEST: To 5 ml of Benedict's solution, add 1 ml of the test solution and shake each tube. Place the tube in a boiling water bath and heat for 3 minutes. Remove the tubes from the heat and allow them to cool. Formation of a green, red, or yellow precipitate indicates the presence of reducing sugars.

TEST FOR SAPONINS

Foam test was performed to test the presence of Saponins. To 2 ml of extract was added

6 ml of water in a test tube. The mixture was shaken vigorously and observed for the formation of persistent foam that confirms the presence of Saponins.

TEST FOR PROTEINS

NINHYDRIN TEST

Ninhydrin test was employed to detect the presence of proteins. Crude extract when boiled with 2 ml of 0.2% solution of ninhydrin, the violet color appeared suggesting the presence of amino acids and proteins.

PREFORMULATION STUDIES

Preformulation testing is the first step in the rational development of a dosage form of the drug substance. The overall objective of the study is to generate information that is useful in developing stable dosage forms. The following preformulation studies were carried out.

DETERMINATION OF ORGANOLEPTIC PROPERTIES

The physical appearance of the drug was observed and compared with the pharmacopoeial specifications.

DETERMINATION OF MELTING POINT

The melting point of Paracetamol and *Artocarpus heterophyllus* seed powder was determined by the capillary method. Fine powder of Paracetamol was filled in glass capillary tube (previously sealed at one end). The capillary tube was inserted into the melting point apparatus and observed the temperature at which drug started to melt by using the thermometer which was already immersed into the liquid paraffin in the apparatus.

DETERMINATION OF pH[12]

pH of Paracetamol drug was determined using a pH meter.

SOLUBILITY[13]

Solubility test was done for Paracetamol to confirm the theoretical reported values of solubilities. Small increments of Paracetamol were added to 10 ml of solvent (coldwater, ethanol, acetone, and methanol) in a 25 ml stoppered standard flask with vigorous shaking. Visually observed the solution, if the solution was clear and no undissolved particles were observed if it was insoluble again another increment of particular solvent was added and the procedure was continued until undissolved Paracetamol was found.

METHODS:

Compatibility studies using FT-IR Spectroscopy[14]

The pure drug, drug, and polymer were prepared and scanned from 1500-800 cm-1 in FTIR spectrophotometer. The FT-IR spectrums of the obtained sample of the drug were compared with the standard functional group frequencies of Paracetamol. The compatibility between the drug, polymer was evaluated using FTIR peak matching method.

PREPARATION OF STANDARD CALIBRATION CURVE OF PARACETAMOL

Preparation of stock solution[15]

A stock solution of Paracetamol was prepared by dissolving the required amount in a Small amount of ethanol and made up to volume with Phosphate buffer. Standard solutions of the analyte (2-10 µg/ml) were prepared by serial dilution of the stock solution.

Procedure for preparing the calibration curve

- Weighed accurately 100 mg of Paracetamol and dissolved in 2ml ethanol and made up to 100 ml with Phosphate buffer.
- From stock solution 10 ml was pipetted out and made up to 100 ml with Phosphate buffer to get the solution of concentration 100µg/ml. (Second stock solution).
- From the Second stock solution 2 ml, 4 ml, 6 ml, 8 ml and 10 ml aliquots were withdrawn and diluted to 100 ml with Phosphate buffer to get the solution of concentration 2-10 µg/ml.
- Absorbance was recorded at 246 nm in UV/visible spectrophotometer using Phosphate buffer as Blank.

FORMULATION AND EVALUATION OF PARACETAMOL TABLET USING POWDER OF ARTOCARPUS HETEROPHYLLUS AS BINDER AND DILUENT

The properties of *Artocarpus heterophyllus* seeds as an excipient were studied using Paracetamol as the model drug**.**

PREPARATION OF BINDER SOLUTION

The binder solution was prepared by dissolving the starch of *Artocarpus heterophyllus* in water.

PREPARATION OF PARACETAMOL TABLETS BY WET GRANULATION METHOD

Five formulations were prepared by wet granulation method. Three different concentrations of *Artocarpus heterophyllus* seed mucilage were used for the preparation of first three batches and starch was used as diluent. The fourth batch was prepared using starch mucilage as a binder. The fifth batch was prepared using *Artocarpus heterophyllus* seed powder as a tablet diluent and in all the formulations Paracetamol was used as model drug Magnesium stearate and talc was used as anti-frictional agents.

Drug and diluent were weighed and mixed thoroughly. It was then granulated using binder mucilage and passed through number 10 mesh screen. The granules were dried at 60^0 c. Dried granules were passed through number 20 mesh screen. Talc and magnesium stearate were added and mixed. It was then compressed in a 16-station Karnavati Rotary Tablet Machine.

Table 2: Formulation of Paracetamol tablet

INGREDIENTS	F1	F2	F3	F4	F5
Paracetamol(mg)	300	300	300	300	300
Starch (mg)	185	185	185	-	185
A: heterophyllus Seed mucilage	4%w/w q.s	6%w/w q.s	8%w/w q.s	-	-
Starch mucilage	-	-	-	q.s	q.s
A:heterophyllus seed powder	-	-	-	185	-
Magnesium stearate(mg)	5	5	5	5	5
Talc(mg)	10 mg	10 mg	10 mg	10 mg	10 mg

PRECOMPRESSION PARAMETERS

BULK DENSITY[16]

The bulk density of a powder is the ratio of the mass of an untapped powder sample and its volume including the contribution of the interparticulate void volume

Apparent bulk density (ρ_b) was determined by pouring the blend into a graduated cylinder. The bulk volume (V_b) and weight of the powder(M) were calculated using the formula.

$$\rho_b = M/V_b$$

TAPPED DENSITY[16]

. The tapped density is obtained by mechanically tapping a graduated measuring cylinder or vessel containing the powder sample. The minimum volume (V_t) occupied in the cylinder and the weight (M) of the blend was measured. The tapped density (ρ_t) was calculated by using formula.

$$\rho_t = M/V_t$$

ANGLE OF REPOSE (θ)[17]

For determination of the angle of repose (θ), the blend was poured through the walls of a funnel, which was fixed at a position such that its lower tip was at a height of exactly 2.0 cm above the hard surface. The blends were poured till the time when upper tip of the pile surface touched the lower. The radius of the heap(r) was measured and the angle of repose (Θ) was calculated using the formula,

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

Table 3: Flow property based on the angle of repose

Angle of Repose (degrees)	Flow
<25	Excellent
25-30	Good
30-40	Passable
>40	Very poor

Compressibility Index (I)[17]

The Carr index or Carr's Compressibility Index is an indication of the compressibility of a powder. It is named after the scientist Ralph J. Carr, Jr. The Carr index is calculated by the formula,

$$C = 100[(V_b - V_t)/V_b]$$

Table 4: Flow property based on compressibility index

Compressibility index	Flow property
<10	Excellent
11-15	Good
16-20	Fair –aid not needed
21-25	Passable
26-31	Poor
32-37	Very poor
>38	Very very poor

Hausner ratio (H_R)[17]

The Hausner ratio is a number that is correlated to the flowability of a powder or granular material. It is named after the engineer Henry H. Hausner. The Hausner ratio is calculated by the formula.

$$H_R = \rho_t/\rho_b$$

Lower Hausner ratio (<1.25) indicates better flow property than higher ones (>1.25).

POST COMPRESSIONAL PARAMETERS

PHYSICAL APPEARANCE

The shape of the tablet can be dimensionally described, monitored and controlled.

ORGANOLEPTIC PROPERTIES

It includes the color and odor of the prepared tablet.

WEIGHT VARIATION[18]

Weight variation was carried out to ensure that, each of tablets contains the proper amount of drug. The test was carried out by weighing the 20 tablets individually using analytical balance, then calculating the average weight, and comparing the individual tablet weights to the average. The percentage of weight variation is calculated by using the following formula.

$$\% \text{ Deviation} = \frac{Averageweight - Individualweight}{Averageweight} * 100$$

Table no 5: Weight variation specification as per USP

S. No.	The average weight of tablets (mg)	Maximum percentage difference allowed
1	130 or less	±10.0
2	130-324	±7.50
3	More than 324	±5.0

HARDNESS TEST[19]

The hardness of the tablet is defined as the force applied across the diameter of the tablet in order to break the tablet. The resistance of the tablet to chipping, abrasion or breakage under the condition of storage, transportation, and handling before usage depends on its hardness.

The tablet was placed between two anvils; the force applied to the anvils, and the crushing strength that just causes the tablet to break was recorded.

THICKNESS[20]

Tablet thickness is an important characteristic in reproducing appearance and also in counting by using the filling equipment. Some filling equipment utilizes the uniform thickness of the tablets as a counting mechanism. The thickness of the tablets was measured using Vernier calipers. It is expressed in mm. Tablet thickness should be within a ±5% variation of a standard value.

FRIABILITY[21]

It is the phenomenon whereby tablet surfaces are damaged and/or show evidence of lamination or breakage when subjected to mechanical shock or attrition. Roche friabilator is the equipment which is used for the determination of friability. It is expressed in percentage.

Note down the initial weight of the tablets individually (W initial). Tablets are placed in a plastic chamber which revolves at 25 rpm and they are subjected to fall from a height of 6 inches in the friabilator for about 100 revolutions. Then measure the weight of the tablet (W final) and observe any weight difference before and after the friabilator processing. Limits: loss in weight less than 0.5 to 1% of the initial weight of the tablet should be considered as acceptable limits. Percentage of friability is calculated as:

$$F= \{(W_i)- (W_f)/ (W_i)\}\times 100.$$

Where; F= friability,

W_i= initial weight

W_f= final weight

WETTING TIME[22]

This method was performed to determine the wetting time of a tablet. A piece of tissue paper which is folded twice is kept in a Petri dish containing 6 ml of water and place the tablet on the tissue paper. Observe the time taken for complete wetting of the tablet. Following procedure should follow three times (three trial) for each batch and the standard deviation is also calculated from the obtained results.

WATER ABSORPTION RATIO[23]

A piece of tissue paper folded twice was placed in a small Petri dish (Internal Diameter = 6.5 cm) containing 6 ml of water. A tablet was placed on the paper and the time required for complete wetting was then measured.

The water absorption ratio (R) was determined using the following Equation

$$\text{Water absorption ratio (R)} = \frac{Wa - Wb}{Wa} * 100$$

Where Wb is the weight of the tablet before water absorption and Wa is the weight of the tablet after water absorption.

CONTENT UNIFORMITY[24]

Five tablets were weighed and powdered. The powder equivalent to 100mg Paracetamol content was determined by measuring the absorbance at 246nm after appropriate dilution.

***IN-VITRO* DISINTEGRATION TEST[25]**

The process of breakdown of a tablet into smaller particles is called as disintegration. The *in-vitro* disintegration time of a tablet was determined using the disintegration test apparatus. Place one tablet in each of the 6 tubes of the basket. Add a disc to each tube and run the apparatus using pH 6.8 maintained at 37°±2°C as the immersion liquid. The assembly should be raised and lowered between 30 cycles per minute in the pH 6.8 maintained at 37°±2°C. The time in seconds taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus measured and recorded.

INVITRO DISSOLUTION STUDY[26] :

- **Preparation of phosphate buffer (pH 6.8)**

Dissolved28.80gm of Disodium hydrogen phosphate and 11.45gm of Potassium dihydrogen phosphate in sufficient water to produce 1000 ml.

- **Procedure for dissolution:** The release rate of Paracetamol Tablet was determined using United State Pharmacopoeia (USP) dissolution testing apparatus II (paddle method). The dissolution test was performed using 900 ml of pH 6.8 phosphate buffer, at 37± 0.50^0C and 50 rpm. A sample (2ml) of the solution was withdrawn from the dissolution apparatus at 5,10,15,20,25,30,45 and 60 min. The samples were replaced with fresh dissolution medium of the same quantity. The absorbance of these solutions was measured at 246nm using a Shimadzu UV/Vis double beam spectrophotometer. Cumulative percentage of drug release was calculated using an equation obtained from a standard curve.

KINETICS OF INVITRO DRUG RELEASE[27]

The results obtained from *in-vitro* release studies were attempted to fit into various mathematical models as follows:

1) Cumulative percent drug released Vs. Time (Zero order kinetics)

2) Log cumulative percent drug retained Vs. Time (First order kinetics)

3) Cumulative percent released Vs. The square root of Time (Higuchi model)

4) Log cumulative percent drug released Vs. Log Time (Korsmeyer- Peppas model)

Table 6: Interpretation of diffusional release mechanism

Release exponent	Diffusion release mechanism
0.45	Fickian diffusion
0.45<n<0.89	Anomalous (non – fickian) diffusion
0.89- 1.0	Case II transport (Zero order release)
>1.0	Super case II transport

STABILITY STUDIES[28]:

Stability testing plays a crucial role in the drug development process. The purpose of stability testing is to provide evidence on how the quality of drug product varies with time under the influence of a variety of environmental factors, such as temperature, humidity, and light so as to recommending shelf life for the drug product and recommended storage conditions. Stability studies were conducted according to ICH guidelines 40˚C ± 2˚C/ 75% ± 5% RH to test the physical and chemical stability of the developed formulations. Throughout the study, m tablet formulation was stored in well-closed containers. The stored formulations were evaluated for hardness, drug content, disintegration time and *in-vitro* drug release at a predetermined time intervals.

RESULTS AND DISCUSSION:

CHARACTERIZATION OF ARTOCARPUS HETEROPHYLLUS SEED POWDER

PHYSICOCHEMICAL CHARACTERIZATION

ORGANOLEPTIC PROPERTIES

Table 7: Physicochemical characterization of *Artocarpus heterophyllus* seed powder

Colour	White
Odor	Pungent
Taste	Mucilaginous
Melting point	148 ˚C
pH	6.8
Moisture Content	2.68
Swelling Index	48

Table 8: Powder characteristics of *Artocarpus heterophyllus* seed powder(N=3)

A: Heterocycles Seed Powder	**Bulk Density**	**Tapped Density**	**Carr's Index**	**Hausner Ratio**	**Powder Porosity**	**Angle Of Repose**
	0.39±0.20	0.44±0.34	11.36 ±0.24	1.12 ±0.04	0.1137 ±0.19	25.26 ±39

Table 9: Solubility characteristics of *Artocarpus heterophyllus* seed powder

SOLVENT	**SOLUBILITY**
Cold Water	Sparingly soluble
Warm Water	Quickly Soluble
Ethanol	Soluble
Methanol	Soluble
Acetone	Insoluble
Ether	Insoluble

Table 10: Phytochemical characterization of *Artocarpus heterophyllus* seed powder

	TEST	RESULT
ALKALOIDS	Wagner's Test	Negative
	Mayer's Test	Negative
	Dragendorff's Test	Negative
CARBOHYDRATES	Molish's Test	Positive
	Fehling's Test	Positive
	Benedict's Test	Positive
SAPONINS	Foam Test	Positive
PROTEINS	Ninhydrin Test	Negative

PREFORMULATION STUDIES

Table 11: Properties of paracetamol powder

Colour	White
Odor	characteristic
Melting point	169˚C
pH	6

Table 12: Solubility of paracetamol in various solvents

SOLVENT	SOLUBILITY
Cold Water	Insoluble
Ethanol	Soluble
Methanol	Soluble
Acetone	Soluble

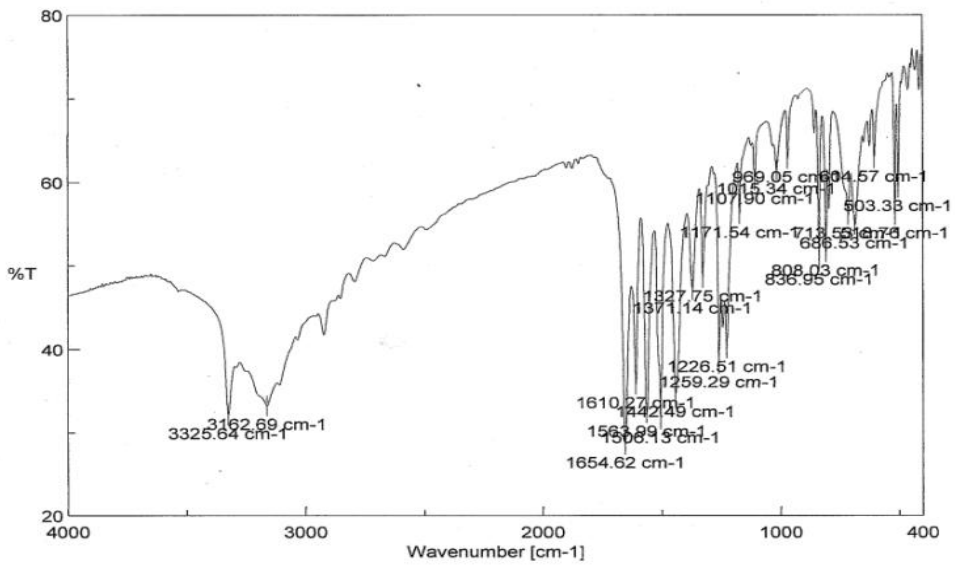

Figure 1: FTIR Spectrum of Paracetamol

Table 13: IR frequencies of Paracetamol

Functional group	Characteristic wave number	Paracetamol observed wave number
Para- disubstituted aromatic ring	850-750	836.95 cm^{-1}
Amide II band	1570-1515	1563.99 cm^{-1}
C=O stretching	1655-1620	1654.62 cm^{-1}
N-H stretching	3500-3100	3162.69 cm^{-1}
O-H stretching	3400-3200	3325.64 cm^{-1}

Compatibility between drug and polymer

The FTIR spectrum paracetamol with *Artocarpus heterophyllus* seed powder are shown in figure

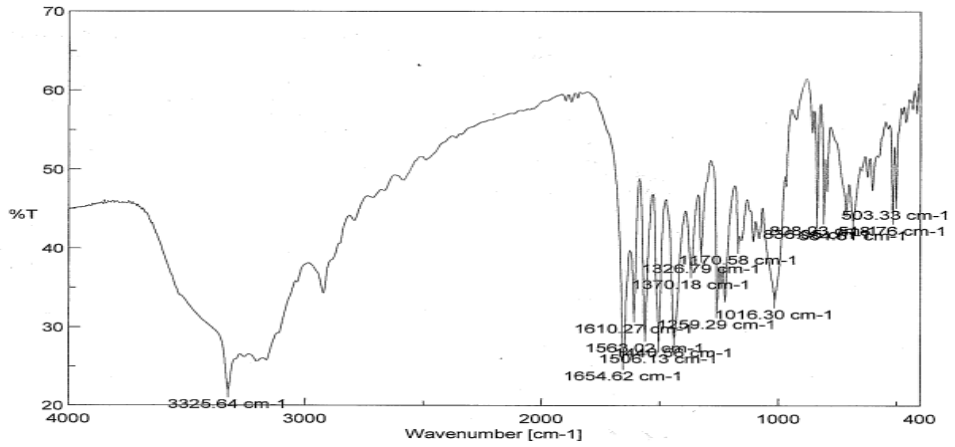

Figure 2: FTIR Spectrum of Paracetamol and *Artocarpus heterophyllus* seed powder

Table 14: IR frequencies of Paracetamol – *Artocarpus heterophyllus* powder mixture

Functional group	Characteristic wave number	Paracetamol observed wave number	Para – Arto heterophyllus powder mixture
Para- disubstituted aromatic ring	850-750	836.95 cm^{-1}	836.65 cm^{-1}
Amide II band	1570-1515	1563.99 cm^{-1}	1563.02 cm^{-1}
C=O stretching	1655-1620	1654.62 cm^{-1}	1654.62 cm^{-1}
O-H stretching	3400-3200	3325.64 cm^{-1}	3325.64 cm^{-1}

The compatibility between drug-seed powder was carried out by using FT-IR peak matching method. All major peaks present in the spectrum of the pure drug were observed in the spectrum of the drug-seed powder mixture. This suggests that the drug remains in its normal structure and hence this confirmed the absence of any chemical interaction or complexation between drug and polymers.

Preparation of standard calibration curve Paracetamol

The calibration curve was found to be linear in the range of 2-10 µg/ml at λmax at 246 nm.

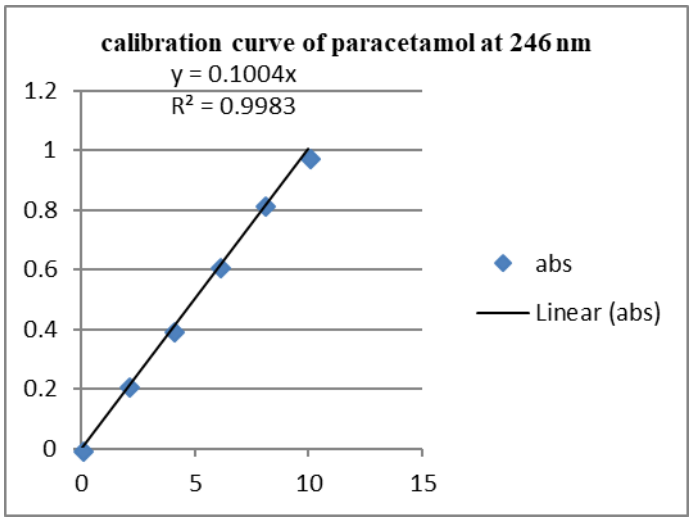

Figure 3: Standard calibration curve of paracetamol in phosphate buffer pH 6.8

FORMULATION OF PARACETAMOL TABLET

Paracetamol tablets were prepared using wet granulation method.

- **Precompression parameters**

Table 15: Physical characteristics evaluation of powder mixture (n=3)

Formulation code	Bulk density (gm/cm^3)	Tapped density (gm/cm^3)	The angle of repose (°)	Compressibility index (%)	Hausner's ratio
F1	0.39±0.002	0.45±0.001	28.28±0.25	13.33±0.33	1.15±0.002
F2	0.38±0.004	0.43±0.005	27.55±0.21	11.62±0.45	1.13±0.004
F3	0.35±0.10	0.39±0.002	27.03±0.35	10.25±0.54	1.11±0.007
F4	0.40±0.005	0.46±0.004	27.94±0.24	13.04±0.44	1.15±0.008
F5	0.42±0.005	0.47±0.005	28.19±0.33	10.63±0.14	1.11±0.005

Table 16: Physicochemical evaluation of Paracetamol tablet (n=3)

Formulation code	Average weight (gm)	Thickness (mm)	Hardness (kg/cm^2)	%Friability	Wetting time (sec)	Water absorption ratio (%)	Content uniformity (%)	Disintegration time(sec)
F1	0.504±0.3	2.62±0.01	6.08±0.07	0.80±0.12	46sec±0.05	81.88±0.11	95.68±0.24	44±0.08
F2	0.499±0.02	2.58±0.08	6.08±0.08	0.70±0.15	43sec±0.06	82.20±0.14	97.28±0.14	40.20±0.09
F3	0.501±0.05	2.60±0.09	6.10±0.09	0.65±0.18	39sec±0.01	86.50±0.17	98.77±0.04	38.16±0.08
F4	0.496±0.05	2.74±0.07	6.13±0.05	0.79±0.09	48sec±0.02	81.63±0.24	97.59±0.05	46.01±0.01
F5	0.503±0.08	2.63±0.09	6.05±0.06	0.75±0.15	73sec±0.08	85±0.14	96.95±0.05	70±0.01

For weight variation test, twenty tablets were randomly selected from each formulation and evaluated. The average weight of each formulation values are almost uniform and was within the specifications. Thus all the formulations passed the test for weight variation. The thickness value of tablet ranges from 2.58-2.74 mm. The hardness values range from 6.08-6.15 kg/cm^2. The friability values of tablets ranged from 0.65-0.80 %. All the values are below 1% indicating that the tablets of all formulations are having good friability property. Wetting time of formulations are ranged from 43sec to 73sec. The water absorption ratio of the formulations ranges from 81.63 to 86.50 % respectively. The content uniformity of the prepared formulations values ranged from 95.68 to 98.77 %. The disintegration time of formulations values ranged from 38.16 to 70sec

***In vitro* dissolution studies**

Table 17: Percentage cumulative drug release data for formulations F1-F5, n=3

Time (min)	F1 %CDR	F2 %CDR	F3 %CDR	F4 %CDR	F5 %CDR
5	30.92±0.05	33.30±0.02	36.12±0.07	34.93±0.08	33.89±0.07
10	38.20±0.04	39.25±0.01	45.19±0.08	47.39±0.09	43.38±0.08
15	45.34±0.02	44.89±0.02	62.12±0.04	53.81±0.02	55.15±0.09
20	53.22±0.05	56.74±0.05	73.74±0.02	69.71±0.05	61.10±0.05
25	57.39±0.02	60.50±0.04	81.32±0.09	78.05±0.04	66.75±0.05
30	68.39±0.04	72.55±0.02	89.94±0.02	84.89±0.04	71.95±0.09
45	79.09±0.03	86.68±0.05	96.48±0.03	94.85±0.03	89.49±0.06
60	88.90±0.08	91.13±0.04	99.05±0.09	98.57±0.02	95.74±0.06

Kinetics of *in vitro* drug release

The *in vitro* drug release data of all the paracetamol tablet formulations were subjected to the goodness of fit test by linear regression analysis according to zero order and first order kinetic equations, Higuchi's and Korsmeyer–Peppas models to ascertain the mechanism of drug release.

Table 18: Kinetic study of formulations

Formulation code	Release Kinetics				
	Zero-order R^2	First order R^2	Higuchi R^2	Peppas	
				R^2	N
F1	0.875	0.988	0.993	0.986	0.444
F2	0.866	0.985	0.985	0.966	0.447
F3	0.762	0.995	0.951	0.989	0.444
F4	0.799	0.990	0.970	0.971	0.448
F5	0.847	0.982	0.991	0.995	0.432

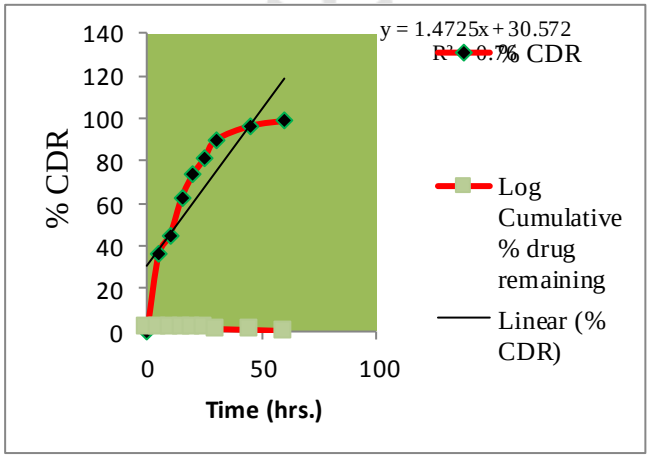

Figure 4: Zero-order release kinetics profile of optimized formulation F3

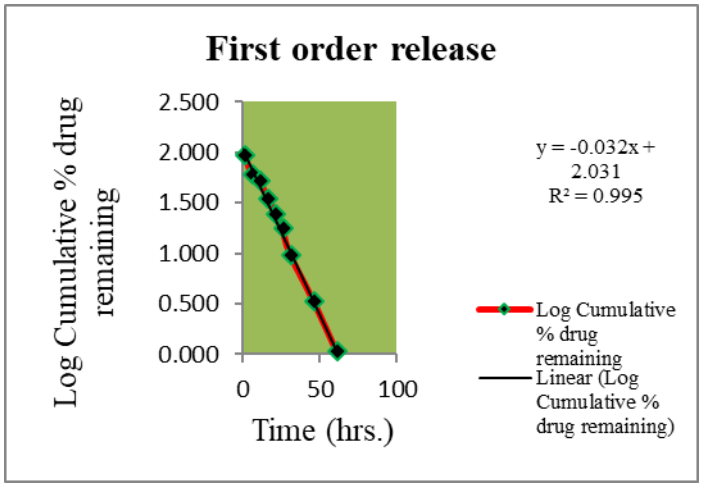

Figure 5: First order release kinetic profile of optimized formulation F3

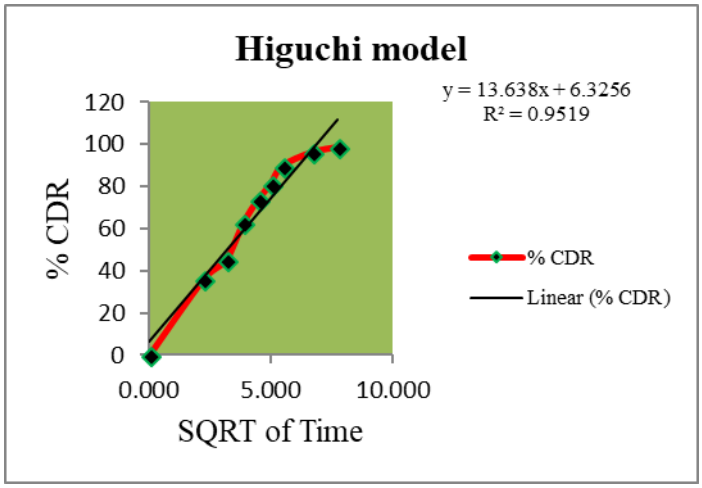

Figure 6: Higuchi release kinetics profile of optimized formulation F3

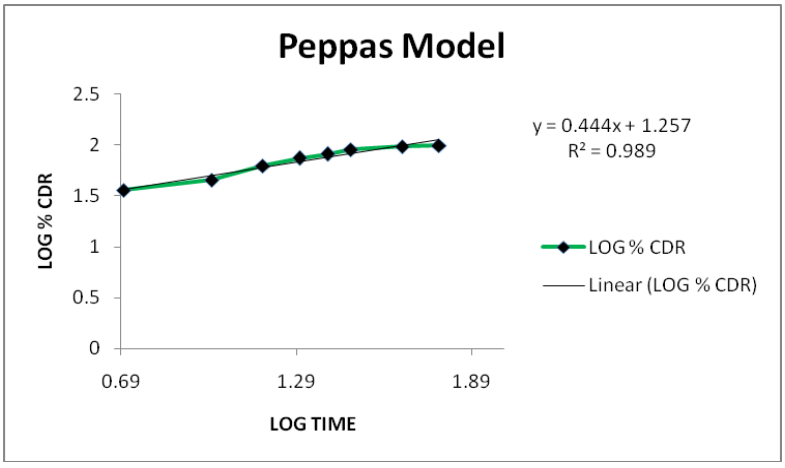

Figure 7: Peppas release kinetics profile of optimized formulation F3

From the above data, it was concluded that the formulation F3 follows first-order kinetics with R^2 value 0.995. The *in vitro* drug release data as log % CDR versus time were fitted to Korsmeyer equation in order to understand the mechanism by which Paracetamol was released from this formulation. Value of exponent 'n' was found to be 0.43-44. The Korsmeyer-Peppas model yields 'n' values <0.45 indicating that the diffusion mechanism from the formulation followed Quasi-Fickian diffusion.

Stability studies

Stability studies were carried out on formulation F3 for a period of 1 and 3 month and comparison of the parameters before and after stability studies was represented in the table

Table 19: comparison of parameters before and after stability

Parameters	Before stability studies(F3)	Stability study after 1 month (F3)	Stability study after 3 months (F3)
Physical changes	White, standard convex shape	No change	No change
Wetting time	39sec	37sec	35sec
Disintegration time(sec)	38.16	37.08	36.88
%drug content	98.77	98.64	98.55

Table 20: drug release determination after stability

Time(min)	Before stability %CDR	Stability study after 1 month (F3) %CDR	Stability study after 1 month (F3) %CDR
5	36.12±0.07	36.02±0.05	35.85±0.08
10	45.19±0.08	45.10±0.06	44.81±0.05
15	62.12±0.04	61.99±0.04	61.54±0.09
20	73.74±0.02	73.65±0.02	73.24±0.07
25	81.32±0.09	81.09±0.08	80.98±0.06
30	89.94±0.02	89.75±0.09	89.75±0.05
45	96.48±0.03	96.38±0.05	96.18±0.04
60	99.05±0.09	98.95±0.05	98.87±0.07

The stability of the optimized formulation was known by performing stability studies for 1 to 3 month at accelerated conditions of 40ºC ± 75 % RH. The formulation was found to be stable with no physical changes and shows a slight decrease in disintegration time and also shows a slight decrease in drug content and in- vitro drug release pattern after the stability

period. From the stability studies, it was confirmed that the formulation remains stable at accelerated stability conditions.

CONCLUSION:

Utilization of fruit by-product offers a potential solution to minimizing the economic and environmental problems produced by their wastes. Jackfruit have diverse medicinal uses especially antioxidant, anti-inflammatory, antimicrobial, anti-cancer and anti-fungal activity. Jackfruit is considered to be an underutilized fruit where most of the fruits get wasted due to ignorance, lack of post-harvest technology and gaps in supply chain systems. Jackfruit contains more protein, calcium, iron, vitamins and other essential nutrients when compared to the common fruits

The compatibility of the drug in the formulation was performed by FTIR spectroscopy. Each batch of the formulations was subjected to pre-compression and post compression evaluation techniques. Accelerated stability studies of the optimized (F3) formulation were also conducted.

Preparation of tablet using *Artocarpus heterophyllus* powder displayed acceptable average tablet weight, thickness, hardness, wetting time, water absorption ratio, friability, disintegration time, dissolution when used as binder and diluent in tablet formulation

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