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Research Article

FORMULATION AND EVALUATION OF PARACETAMOL SUSPENSION BY USING NATURAL SUSPENDING AGENT EXTRACTED FROM BANANA PEELS

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Keywords: *Musa paradisica,* paracetamol, swelling index, phytochemical testing, sedimentation volume.

ABSTRACT

The present work was aimed to formulate and evaluate a new, cheap and effective natural suspending agent that can be used as an effective alternative for traditional suspending agent. The study procedure involved extraction of suspending agent from the *Musa paradisica* (Banana) fruit peels, determination of swelling index, phytochemical testing, Micromeritic properties of mucilage like Bulk density, Tapped density, Carr's index, Hausner's ratio, Angle of repose, Calibration of paracetamol, preparation of paracetamol suspensions and evaluated for pH determination, determination of sedimentation volume, redispersibility, determination of flow rate, measurement of viscosity, effect of temperature, drug content, particle size determination and *In-vitro* dissolution studies. The study showed that the extraction of suspending agent from banana fruit peels. The swelling index was found to be 40%. The photochemical test showed contains carbohydrates. As the concentration of suspending agent increases therefore viscosity of suspension increases which ultimately reduces the sedimentation of suspension.

INTRODUCTION

Taste is one of the most important parameters governing patient compliance. Undesirable taste is one of several important formulation problems that are encountered with certain drugs. Oral administration of bitter drugs with an acceptable degree of palatability is a key issue for health care providers, especially for paediatric patients. Several oral pharmaceuticals, numerous food and beverage products, and bulking agents have unpleasant, bitter tasting components. So, any pharmaceutical formulation with a pleasing taste would definitely be preferred over a competitor's product and would translate into better compliance and therapeutic value for the patient and more business and profits for the company. The desire of improved palatability in these products has prompted the development of numerous formulations with improved performance and acceptability.[1] Suspending agents also called thickening agents are used to stabilize suspensions are hydrophilic colloid i.e substances that spontaneously from colloidal dispersions with water because of an affinity between the dispersed particles and the dispersion medium.[2] They help in lowering the sedimentation rate of particles in suspension.[3,4]

Rationale of suspending agent selection

Mucilage of *Musa paradisica* can be used as Binding agent, Suspending agent, Thickening agent, Humidifying agent, Disintegrating agent, Gelling agent and Release controlling properties in medicines. In the present study, attempts shall be made to utilize dried powder of banana peel mucilage as suspending agent.

Aim: The present work was aimed to formulate and evaluation of paracetamol suspension by using a new, cheap and effective natural suspending agent from *Musa paradisica* (Banana) fruit peels.

Objective: The main objective of this extraction of suspending agent from a Banana fruit peels. Formulation development was done by using this

suspending agent in order to optimize the natural suspending agent of banana peel mucilage.

MATERIALS AND METHODS

Materials

Paracetamol were obtained from Yarrow Chem Products, Mumbai. Banana fruits were purchased from local market. Glycerin, Propyl paraben, Methyl paraben, Sodium saccharine, sodium metabisulphate and Peppermint oil were obtained from Darwin Formulations Pvt. Ltd., Vijayawada. Amaranth was obtained from Finar Limited, Vijayawada. All other solvents used were of analytical grade.

Extraction of suspending agent from *Musa paradisica* (Ripe Fruit Peels)

Initially ripe fruit peels of *Musa paradisica* were crushed and reduced in size using mill. The crushed peels were soaked in 1% sodium metabisulphite solution for 12 hrs and boiled in water bath to prepare slurry. Further slurry was cooled and allows settling down unwanted material. Upper portion was collected and concentrated in water bath and after cooling acetone was added in it with continuous stirring. The precipitate was collected and dried at room temperature for 24 hrs. The air dried material further subjected to size reduction and passed through sieve no. 60 and stored in desiccators for further evaluation.

Evaluation of extracted powder

1. Determination of Swelling Index
2. Phytochemical Screening of Mucilage
3. Micromeritic Properties of Mucilage

a. Bulk density
b. Tapped density
c. Carr's Compressibility Index
d. Hausner's ratio
e. Angle of repose

1. Determination of Swelling Index

500 mg of isolated mucilage was taken in a Petri dish and then 10 ml of distilled water was added and the mixture was shaken and allowed to stand for 1 hour. After 1 hour the remaining water in Petri dish was discarded and the weight increase of the isolated mucilage was determined. [7]

Swelling Index % (SI) = (W2 – W1/W2) x 100

W1= Weight of compact at time '0'

W2= Weight of compact t at time 't'

2. Phytochemical Screening of Mucilage

Preliminary tests were performed to confirm the nature of mucilage obtained. The chemical tests that were conducted are: Molisch's test, Ninhydrin test, Wagner's test, Ruthenium red test, Iodine test, Shinoda test, Keller-Killaini test and Ferric chloride test. [7]

3. Micromeritic Properties of Mucilage

a & b: Bulk density and Tapped density: [8, 9]

Loose bulk density and Tapped bulk density was calculated by the following formula

$$\textit{Bulk density} = \frac{\textit{Mass of powder}}{\textit{Bulk volume of the powder}}$$

$$\textit{Tapped density} = \frac{\textit{Mass of powder}}{\textit{Tapped volume of the powder}}$$

c. Carr's Compressibility Index

% Carr's Index can be calculated by using the following formula

$$\textit{Carr's index}(\%) = \frac{\textit{Tapped density} - \textit{Bulk density}}{\textit{Tapped density}} x\ 100$$

d. Hausner's ratio

Hausner ratio is an indirect index of ease of measuring the powder flow. It is calculated by the following formula

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

e. Angle of repose

Angle of repose (θ) can be calculated from the following formula

$$Tan\theta = \frac{h}{r} \text{ (or) } \theta = tan^{-1}\frac{h}{r}$$

H = height of pile and r = radius of the base of pile

Table 1: Physical characterization of the extracted powder

S. No.	Angle of repose	Carr's index	Hausner's ratio	Flow property
1.	25-30	5-12	1.00-1.11	Free flowing
2.	30-35	12-16	1.12-1.18	Good
3.	35-40	18-21	1.19-1.25	Fair
4.	40-55	23-35	1.35-1.45	Poor
5.	55-65	33-38	1.46-1.59	Very poor
6.	>65	>40	>1.60	Extremely poor

Estimation of Paracetamol

Determination of λmax of Paracetamol in Phosphate buffer pH 5.8

Stock solution: Standard stock solution was prepared by dissolving 100 mg drug in pH 5.8 and make up with pH 5.8 to get concentration of 100 µg/ml.

Method development: From the above stock solution, 1 ml was transferred into a 10 ml volumetric flask and volume was adjusted to 10 ml that corresponded to 100 µg/ml solution. From that solution different aliquots of 0.2, 0.4, 0.6, 0.8 and 1 ml were transferred to 10 ml volumetric flask, volume was adjusted with pH 5.8 phosphate buffer, which gave a concentration of 2, 4, 6, 8 and 10 µg/ml of the final standard. A standard curve was plotted by taking absorbance of secondary stock solutions in UV double beam spectrophotometer at 257nm.

Formulation development

Design: F1, F2, F3, F4, F5and F6were designed to optimize the ratios of paracetamol and banana peel mucilage and to study the effect of mucilage in ratios.

Chemicals used in formulation:

Table 2: List of chemicals used in study and their manufacturers

S. No.	Chemicals	Manufacturer	Purpose
1	Paracetamol	Yarrow chem products, Mumbai	API
2	Banana peel mucilage	Isolated product	Suspending agent
3	Glycerin	Darwin, Vijayawada	Protect API from natural suspending agent
4	Propyl paraben	Darwin, Vijayawada	preservative
5	Methyl paraben	Darwin, Vijayawada	preservative
6	Sodium saccharine	Darwin, Vijayawada	Sweetening agent
7	Peppermint oil	Darwin, Vijayawada	Flavoring agent
8	Amaranth	Finar, Vijayawada	Coloring agent
9	Purified water	Institutional supply	Solvent

API- Active Pharmaceutical Ingredient

Equipments used in formulation

Table 3: List of instruments used in study and their manufacturers

S. No.	Equipment	Manufacturer
1	Electronic balance	Shimadzu, Mumbai.
2	Mechanical sieve shaker	Darwin, Vijayawada
3	Tap density tester	Delta, Vijayawada
4	Dissolution apparatus USP2	Lab India DS 8000, Mumbai
5	Hot air oven	KEMI, Ernakulam, Kerala
6	U.Vspectrophotometer	Shimadzu, Mumbai.
7	P^H meter	Darwin, Vijayawada
8	Ostwald viscometer	Darwin, Vijayawada
9	Brookfield's viscometer	Asian Scientific Instruments, Hyderabad
10	Microscope	Magnus Analytics, New Delhi

Formulation of suspension

Formulation of suspension was prepared as per formula given in Table 4. Extracted banana peel powder was taken in mortar to which methyl and propyl paraben were added and triturated for some time along with water to make paste. In beaker paracetamol was mixed well with glycerin. This mixture was further added to the above paste and triturated for 20 min. Then colouring agent i.e. Amaranth and

flavouring agent i.e. Peppermint oil were added mixed well in suspension. Volume made up with water up to 50 ml and further homogenized of suspension.

Optimization of formulation ingredients in preparation

Table 4: Optimization of formulation ingredients

S. No.	Ingredients	F1	F2	F3	F4	F5	F6
1.	Paracetamol (g)	2.5	2.5	2.5	2.5	2.5	2.5
3.	Banana peel mucilage (g)	0.25	0.5	1	2	3	4
4.	Glycerin (ml)	5	5	5	5	5	5
5.	Propyl paraben (g)	0.1	0.1	0.1	0.1	0.1	0.1
6.	Methyl paraben (g)	0.15	0.15	0.15	0.15	0.15	0.15
7.	Sodium saccharine (g)	0.05	0.05	0.05	0.05	0.05	0.05
8.	Peppermint oil (ml)	1	1	1	1	1	1
9.	Amaranth (g)	0.01	0.01	0.01	0.01	0.01	0.01
10.	Purified water (m1)	50	50	50	50	50	50

Characterization of formulated suspensions: [8, 9]

i. pH determination of suspension

The pH of all developed formulations was measured using digital pH meter.

ii. Sedimentation volume

Sedimentation volume is determined by following equation,

$$F = \frac{\text{Hu}}{\text{Ho}}$$

Where, Hu is ultimate or final height of sediment as suspension settles, Ho is original height of suspension.

iii. Redispersibility

Fixed volume of each suspension (50 ml) was kept in calibrated tubes which were stored at room temperature for various time intervals (1, 5, 10, 15, 20, 30, 45 days). At regular interval one tube was removed and shaken vigorously to redistribute the sediment and the presence of deposit if any was recorded.

iv. Flow rate (F)

The time taken for 10ml sample of suspension to flow through a 10ml pipette was determined and the flow rate calculated using the following equation:

$$F = \frac{\text{Volume of pipette (ml)}}{\text{Flow time (sec)}}$$

v. Determination of viscosity

The viscosity of suspension samples was determined using the Brookfield viscometer at 100 rpm. All determinations were carried out in at least triplicates and results obtained were expressed as the mean values.

vi. Degree of flocculation

Degree of flocculation (β) was determined using following equation.

Where, (Vu) floc is ultimate sedimentation volume in flocculated suspension and (Vu) defloc is ultimate sedimentation volume in deflocculated suspension.

$$F = \frac{\text{(Vu) floc}}{\text{(Vu) defloc}}$$

vii. Drug content

5 ml of suspension (250mg/ml) was accurately measured and transferred into 100 ml volumetric flask. And volume made up with P^H 5.8. Further from above suspension 1 ml was withdrawn and added to 10 ml flask, volume made with P^H 5.8. Absorbance was measured using UV-Visible double beam spectrophotometer at λ max 257 nm. Drug content was calculated by comparing the absorbance with standard curve.

viii. Particle size measurement

Particle size determination is carried out by optical microscopy method using motic microscope. Suspension was spread on slide & observed under microscope. Diameters of 50 particles were measured.

ix. *In-vitro* dissolution studies

Dissolution study of formulated suspensions was carried out in USP type II dissolution test apparatus in 500 ml of water for 30 min (37 ± 0.5°C and 25rpm). USP type II dissolution test apparatus although mainly designed for tablets and capsules, this apparatus has also been used by several investigators to study the dissolution behaviour of suspensions.

5 ml suspension was introduced carefully into the bottom of the apparatus. 5 ml aliquots were withdrawn at interval of 5 min for analysis and replenished by equivalent amount of blank. The aliquots were filtered through Whatman filter paper and further analyzed at respective

wavelength by double beam UV visible spectrophotometer. [10]

To study the drug release kinetics, the data obtained from in vitro drug release studies were plotted in various kinetic models such as a first order equation.

x. First order kinetics: To study the first order release kinetics the release data was fitted into the following equation.

$$DQ/d_t = K_1Q$$

Where Q is amount of drug unreleased
K_1 is first order release rate constant
t is release time

The graph is plotted percentage log% cumulative drug unreleased v/s time

RESULTS AND DISSCUSSION

Evaluation of extracted powder

1. Determination of swelling index

Result: Swelling index of banana peel mucilage was found to be 40% at end of 1hrs.

Discussion: Result shows that the swelling index was found to be increased with time. Swelling index was increased, because weight gain by mucilage was proportional to rate of hydration. The direct relationship was observed between swelling index and mucilage concentration. As the mucilage concentration increases swelling index increases.

2. Phytochemical screening of mucilage

Table 5: Phytochemical screening of mucilage

S. No.	Identification test	Name of the test	Observation
1.	Test for carbohydrates	Molisch's test	Positive
2.	Test for proteins	Ninhydrin test	Negative
3.	Test for alkaloids	Wagner's test	Negative
4.	Test for mucilage	Ruthenium red test	Positive
5.	Test for starch	Iodine test	Negative
6.	Test for flavonoids	Shinoda test	Negative
7.	Test for glycosides	Keller Killani test	Negative
8.	Test for tannins	Ferric chloride test	Negative

Discussion

Phytochemical test carries out on banana peel mucilage confirmed the absence of alkaloids, glycosides, starch and tannins. Treatment of mucilage with ruthenium red showed red coloration confirms the obtained product as mucilage. A violet ring was formed at the junction of two liquids on reaction with Molisch's reagent indicates presence of carbohydrates. The results are shown in Table 5.

3. Micromeritic properties of mucilage

Table 6: Micromeritic properties of mucilage

S. No.	Parameters	Valve
1.	Bulk density	0.75g\ml
2.	Tapped density	0.80g\ml
3.	Hausner's ratio	1.06
4.	Carr's compressibility index	6.25
5.	Angle of repose	29

Discussion: Values of Carr's compressibility index showed that mucilage powder has excellent flow properties. Values of Angle of repose and Hausner's ratio showed that mucilage powder has good flow properties. The flow properties results are shown in Table 6.

Standard curve of Paracetamol

Table 7: Series of concentrations and their absorbance

Concentration (µg/ml)	Absorbance
0	0
2	0.163
4	0.308
6	0.464

8	0.597
10	0.755

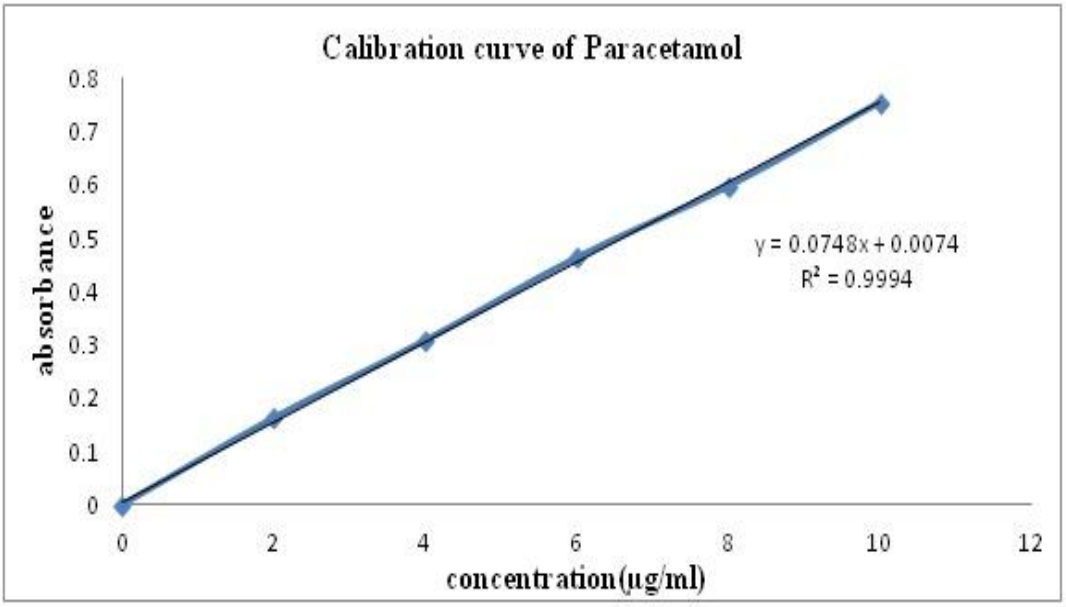

Fig. 1: Calibration curve of Paracetamol

Discussion: It has been inferred that API shows linearity in concentration range of 2-10µg/ml. the regression coefficient of calibration curve was found to be 0.999. The linearity results were shown in Table. 7 and calibration curve were shown in Fig. 1.

Evaluation of formulated suspensions

i. pH

Table 8: pH values data for F1, F2, F3, F4, F5 and F6

Formulation	F1	F2	F3	F4	F5	F6
pH	7.01	7.1	7.15	7.19	7.29	7.24

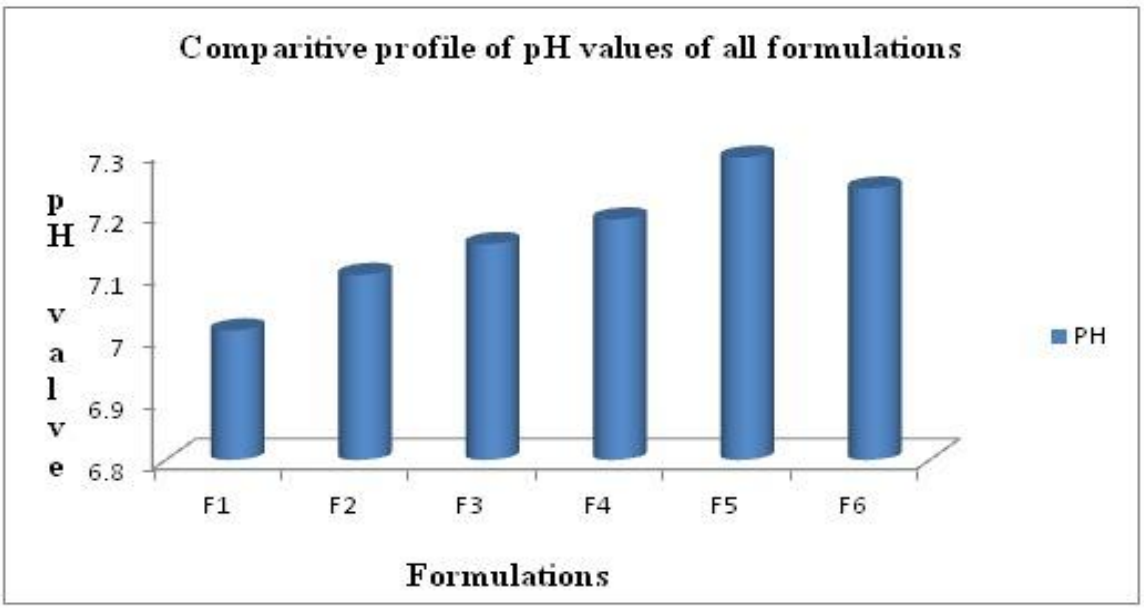

Fig. 2: Comparative profiles of pH values of all formulations

Discussion: pH of all formulation was found to be in the range of 7.01 to 7.29. All the pH values are within the limits. The pH values were shown in Table. 8 and Comparative profiles of pH of all batches were shown in Fig. 2.

ii. Sedimentation volume

Table 9: Sedimentation volume values for F1, F2, F3, F4, F5 and F6

S. No.	Time (Days)	F1	F2	F3	F4	F5	F6
1.	0	0	0	0	0	0	0
2.	1	0.44	0.65	0.7	0.75	0.8	0.99
3.	2	0.40	0.54	0.67	0.7	0.76	0.95
4.	3	0.35	0.5	0.6	0.65	0.72	0.89
5.	4	0.30	0.4	0.54	0.64	0.66	0.82
6.	5	0.25	0.36	0.49	0.56	0.62	0.78
7.	10	0.20	0.35	0.42	0.51	0.54	0.72
8.	20	0.15	0.34	0.36	0.48	0.49	1.67
9.	30	0.126	0.32	0.35	0.45	0.45	0.62
10.	45	0.10	0.3	0.34	0.39	0.4	0.60

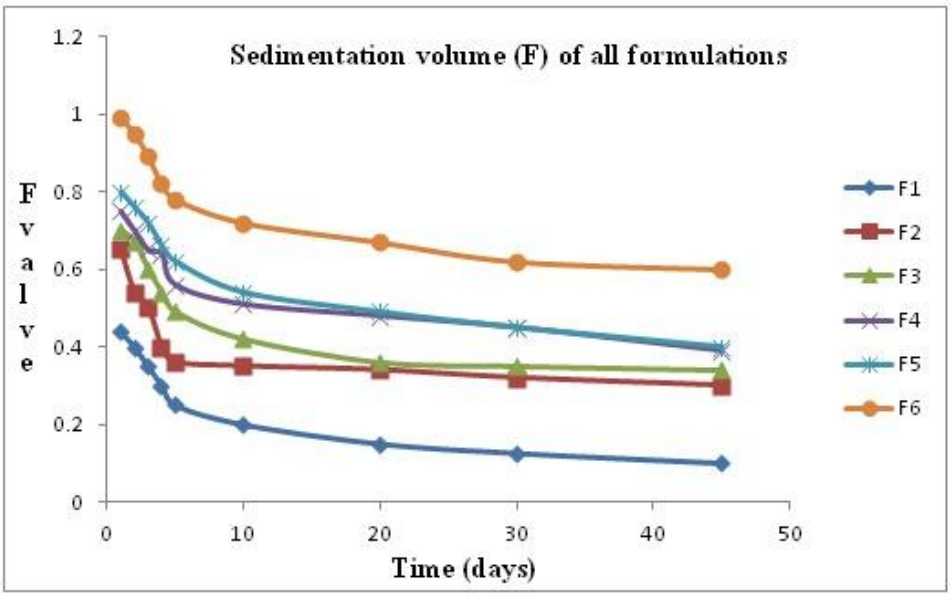

Fig. 3: Comparative profiles of sedimentation volume of all formulations

Discussions: sedimentation volumes were found to be decreased at the end of 5 days. Batch F6, was found to be stable and dispersed at the end of 45 days. The dispersed particle were sediment at faster rate in suspension containing lower concentration of suspending agent compared to containing higher amount. The sedimentation volume values were shown in Table 9 and Comparative profiles of sedimentation volume of all batches were shown in Fig. 3.

Evaluation of suspensions like particle size, degree of flocculation, flow rate, redispersibility, drug content and viscosity:

Table 10: Evaluation of suspensions for F1, F2, F3, F4, F5 and F6

Formula	Particle size (µm)	Degree of flocculation	Flow Rate	Redispersibility	Drug content (%)	Viscosity
F1	68.2	2.57	0.50	5	96.09	1.18
F2	71.2	2.99	0.30	6	97.8	1.93
F3	65.8	3.10	0.12	8	95.96	3.28
F4	66.5	3.31	0.08	9	98.36	4.48

F5	64.5	3.55	0.067	10	97.97	5.94
F6	67.2	4.01	0.046	11	99.12	7.10

iii. Particle size (µm): Particle size of 50 particles of all formulated suspensions was determined and valves are reported. Which is acceptable and within limits. The particle size values were shown in Table 10.

iv. Degree of flocculation: Degree of flocculation was determined for all formulation suspensions using different concentration of banana peel mucilage. The values of degree of flocculation for all formulated suspension have been shown in above Table were found to be increased at higher concentration of suspending agent, due to higher viscosity of suspension at higher concentration which ultimately reduces the sedimentation of suspension. The degree of flocculation values were shown in Table 10.

v. Flow rate: Flow rate was found to be decreased as concentration of suspending agent and viscosity of suspension increased found in the range of 0.5 to 0.046. The flow rate values were shown in Table 10.

vi. Redispersibility: Since the suspension sediment on storage it must be readily dispersible so as to ensure a more uniform dosage administration of medicament after shaking. All the suspension was found to be easily redispersible after maximum 11 shakings after 45 days. Redispersibility was found to be faster for suspension with lower amount of suspending agent comparing to higher concentration. The redispersibility values were shown in Table 10.

vii. Drug content (%): Drug content for all batches was found to be in the range of 95.96 to 99.12%. The drug content values were shown in Table 10.

viii. Viscosity (poise): Viscosity was found to be increased as concentration of suspending agent increased. It found in the range of 1.18 to 7.10. The viscosity values were shown in Table 10.

ix. *In-vitro* Dissolution:

Table 11: Dissolution data for F1, F2, F3, F4, F5 and F6

S. No.	Time (mins)	F1	F2	F3	F4	F5	F6
1.	0	0	0	0	0	0	0
2.	5	60	58	58	56	58	58
3.	10	65	60	60	65	68	68
4.	15	66	68	68	73	78	76
5.	20	70	76	68	78	86	84
6.	25	82	86	80	80	90	92
7.	30	90	90	92	92	98	99

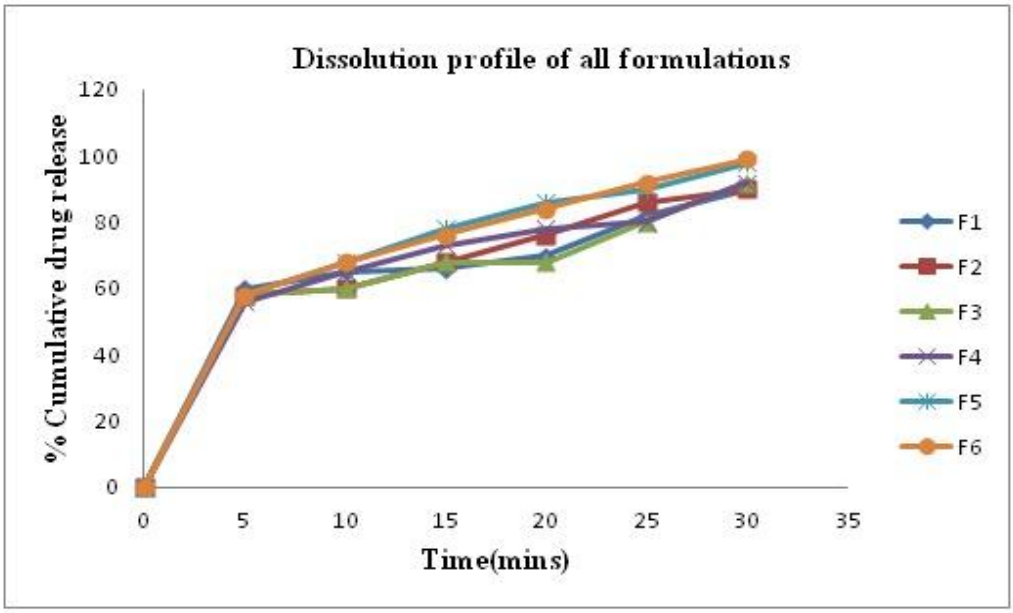

Fig. 4: Comparative dissolution profiles for F1, F2, F3, F4, F5 and F6

Discussion: Results shows that all formulations drug release was almost 90 to 99% at the end of 30 min. For most of the batches, the release kinetics of Paracetamol suspensions appeared to follow first order release kinetics. The dissolution values were shown in Table. 11 and Comparative profiles of dissolution values of all batches were shown in Fig. 4.

x. First order kinetics for dissolution profiles

Table 12: Regression co-efficient (R^2) values for F1, F2, F3, F4, F5 and F6

Formulation	F1	F2	F3	F4	F5	F6
R^2 Valve	0.90	0.94	0.86	0.91	0.90	0.963

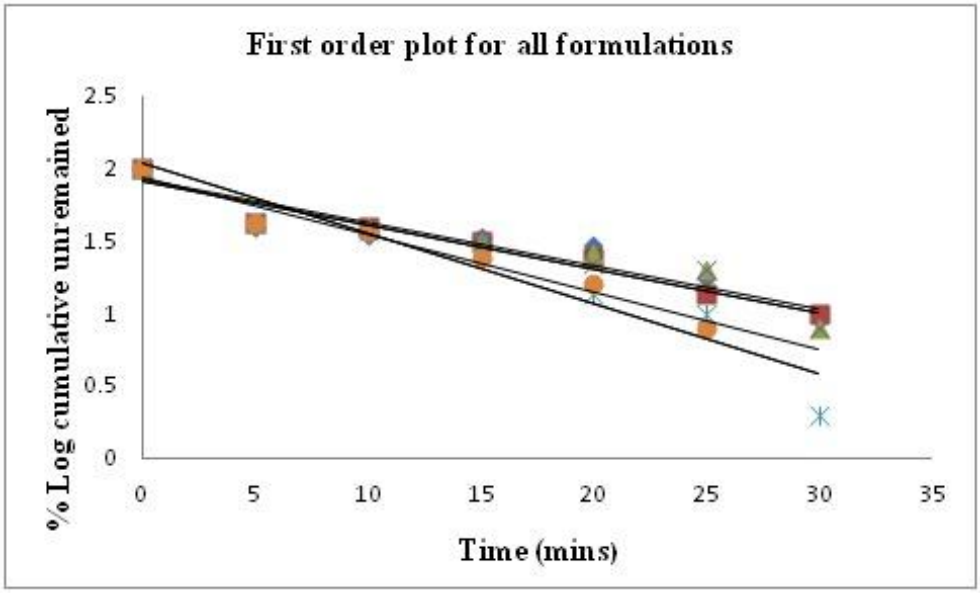

Fig. 5: First order kinetics for dissolution profiles

Discussion: Regression co-efficient values were closer to unity in case of first order hence, release is apparently first order. As clearly indicated the release of the drug followed first order release kinetics and regression value indicates fair of linearity in the data. This shows that the release is dependent on the concentration of drug. The first order values were shown in Table 12 and Comparative profiles of first order values of all batches were shown in Fig. 5.

CONCLUSION

We can conclude that this formulation development was used to optimize the natural suspending agent of banana peel mucilage. The result generated in this study showed that all the evaluation values within the limits and were optimized formulation according to the sedimentation volume. As the concentration of suspending agent increases viscosity of suspension increases this ultimately reduces the sedimentation volume of suspension.

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