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ORAL EXTENDED RELEASE DRY SUSPENSION OF PARACETAMOL LOADED MICROSPHERES

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Keywords:

Paracetamol, Ethyl cellulose, Microspheres, Dry suspension

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ABSTRACT: Background: A novel reconstitutable suspension of Paracetamol loaded microspheres was prepared using ethyl cellulose as a release controlling polymer and by solvent evaporation technique for the relief of osteo-arthritic pain. **Objective:** The formulation was developed to enhance patient compliance of population suffering from dysphagia or have difficulty in swallowing oral solid dosage forms like tablets and capsules. **Method:** Microspheres were evaluated for percent yield, drug loading, and entrapment efficiency, in vitro drug release profile and particle size. The microspheres were formulated as a dry oral suspension which has to be reconstituted at the time of use. **Result:** The particle size of microspheres was in the range of 550 -700 μm. The entrapment efficiency was in the range of 82.95- 95.56% and the yield obtained was 91.13-98.76%. The dissolution studies of selected trial showed a percent cumulative drug release of not less than 85% at the end of 3 hours. Formulation trial P5containing 4% xanthan gum, 5% purified talc and 6 mg sucralose gave a suspension having good flow property, viscosity, sedimentation value, redispersibility and palatability. The dissolution studies showed a 92.43% cumulative drug release in 3 hours. Comparative dissolution profile with marketed preparation gave a similarity factor of 78. **Conclusion:** The objective of developing a novel patient-compliant oral suspension for patients having difficulty in swallowing solid dosage forms was achieved.

INTRODUCTION: Oral drug delivery is the most preferred route of drug administration because of its administration ease; formulation stability and enhanced patient compliance [1]. Attempts have been taken to develop novel technologies to enhance performance, patient compliance and quality.

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Patient compliance depends on the ease with which the drug is delivered into the body without causing any effect on its efficacy and patient inconvenience [2]. Among oral solid dosage forms, tablets and capsules being the major portion have one important drawback- dysphagia or difficulty in swallowing [3]. This problem is particularly faced by geriatric patients who have difficulty in swallowing. A significant administration challenge of solid dosage forms is also seen in other patient groups such as children, mentally challenged, bed ridden and uncooperative patients [3]. The swallowing ability defines the acceptability of any

conventional medication. To cater the needs of such population, an oral pharmaceutical suspension presents a novel means of circumventing the potential problems that are associated to administration of such solid dosage systems [4]. Suspension has been one of the most favourable dosage form for pediatric and geriatric patient group or for patients who are not able to tolerate solid dosage forms.

Microencapsulation of drugs has been suggested to control drug release [4] and microspheres formulated and developed as a reconstituted oral suspension allow swallowing ease and flexibility in dose adjustment. Additionally, incorporation of micro-spheres as a dispersed phase in a suspension has been proposed earlier since these systems may spread out more uniformly in gastrointestinal tract thereby reducing the local irritation as compared to single unit dosage forms [5]. The dry suspension which is formed has to be reconstituted with water before use.

Osteoarthritis (OA) is a musculoskeletal disease affecting weight bearing joints, peripheral and axial articulations. It is a very common rheumatic complaint with prevalence of 22% to 39% in India [6]. Osteoarthritis of knee is the leading cause of disability making everyday activities like standing and walking difficult. Age is the strongest predictor of the development and progression of radiographic arthritis. Treatment options primarily focused on reducing the pain and other symptoms maintain and/or improve joint mobility and limit functional disability with overall management goal of improving patient's quality of life [7].

Pain management begins with non-pharmacologic interventions following pharmacologic means and ultimately surgical interventions [8]. The simple analgesic, Paracetamol has been found to be effective in alleviating pain in patients with osteoarthritis and evidence suggests that non-steroidal anti-inflammatory drugs (NSAIDs) offer no additional symptomatic benefit over simple analgesics like paracetamol for many OA patients. Paracetamol is considered as a core treatment in the first recommendations from European League against Rheumatism (EULAR), OA Research Society International (OARSI) and the American college of Rheumatology (ACR) because of its supposed efficacy and good safety profile [9]. Based on the overall efficacy, toxicity profile and cost, the pharmacologic management guidelines suggests that paracetamol should be considered as first line drug of choice for management of OA pain. Extended release dosage form will release an adequate amount of drug to bring about necessary blood concentration for the immediate relief from pain and the remaining drug amount to maintain the blood levels for the desired period of time.

MATERIALS AND METHODS:

Materials: Paracetamol was received as a gift sample from Simzen Pharmachem Pvt. Ltd, Mumbai. Ethyl cellulose was obtained as a gift sample from Dow Chemicals, India and Eudragit E100 from Evonik Industries, India. Xanthan gum and Purified talc were purchased from Loba Chemie, Mumbai and Sucralose was procured from Gangwal Chemicals Pvt. Limited, Mumbai. All other chemicals and reagents used during the study were of analytical grade. Deionised distilled water was used throughout the study. The study was carried out in the year 2016 at VES College of Pharmacy, Mumbai.

Preparation of Paracetamol Microspheres: Microspheres were prepared by solvent evaporation technique. Briefly, weighed amount of ethyl cellulose and Paracetamol were dissolved in acetone under constant magnetic stirring to obtain a homogenous drug-polymer solution to which dichloromethane was added. The resultant drug-polymer solution was then poured as a thin stream into liquid paraffin (light grade) used as a continuous phase. The system was kept under constant stirring with a lab stirrer (Remi Enterprises) at 1300 rpm for about 2 hours or until all the organic solvent was evaporated. Microspheres formed were collected by filtration and washed with n-hexane followed by washings with warm distilled water to remove traces of n-hexane and liquid paraffin. Microspheres were air dried for 24 hours at room temperature and stored in a dry container. Several batches were prepared varying drug: polymer ratio keeping all other parameters constant. The ingredients/parameters used for formulation trials F1 to F4 are given in **Table 1**.

TABLE 1: FORMULATION TRIALS VARYING DRUG: POLYMER RATIO

Ingredient / Parameter	F1	F2	F3	F4
Paracetamol	1	1	1	1
Ethyl cellulose	1	0.5	0.75	0.25
Acetone: Dichloromethane	2:1	2:1	2:1	2:1
Volume of organic phase (ml)	30	30	30	30
Volume of oil phase (ml)	100	100	100	100
Stirring speed (rpm)	1300	1300	1300	1300
Temperature	RT	RT	RT	RT

(RT = Room Temperature)

Prepared batches were evaluated for production yield, drug loading, entrapment efficiency and *in vitro* drug release and the release profile was compared to the dissolution limits of Acetaminophen Extended Release Tablets USP. To develop a formulation having an initial immediate release, the unit dose of Paracetamol (650 mg) was divided into two parts- one part of unit dose was added directly as an Active Pharmaceutical Ingredient (API) to get an initial immediate drug release while the remaining part of dose was given as microspheres. Dissolution trials (**Table 2**) were carried out by varying the percentage of directly added Paracetamol and as drug loaded microspheres.

TABLE 2: DISSOLUTION TRIALS WITH MICROSPHERES AND DIRECTLY ADDED PARACETAMOL

Trial	Drug: Polymer ratio in microspheres	Ratio of percent of drug added as microspheres: percent added directly as API
F5	1:0.75	70%: 30% of unit dose
F6	1:0.75	65%: 35% of unit dose
F7	1:0.75	55%: 45% of unit dose
F8	1:0.75	50%: 50% of unit dose
F9	1:0.75	50%: 50% of unit dose

Standard Calibration Curve for Paracetamol:

Calibration Curve of Paracetamol in 0.1 M Sodium Hydroxide: Five different concentrations were prepared in the range of 2-10 ppm using suitable dilutions of stock solution and the absorbance was determined at 257 nm using UV-Vis Spectrophotometer. A calibration curve of absorbance versus concentration was plotted and correlation coefficient was determined.

Calibration Curve of Paracetamol in Simulated Gastric Fluid (TS) without Enzyme: Dissolve 2 grams of sodium chloride and 7 ml of concentrated hydrochloric acid and sufficient water to make 1000 ml. This test solution has pH 1.2. Five different concentrations were prepared from the stock solution in the range 2-10 ppm and their absorbance was recorded at 243 nm using UV-Vis Spectrophotometer. A calibration curve of absorbance versus concentration was plotted and correlation coefficient was determined.

Characterisation of Microspheres:

Production Yield Determination: Percent production yield for each batch of microspheres was calculated by dividing the weight of obtained dried microspheres to the total solid material added in the dispersed phase. Yield was calculated using the formula:

$$\text{Yield (\%)} = \frac{\text{Weight of microspheres}}{\text{Total weight of drug and polymer}} \times 100$$

Entrapment Efficiency and Drug Loading Determination: Paracetamol-loaded microspheres (200mg) were weighed and crushed in a mortar and suspended in a 250 ml volumetric flask containing 100 ml distilled water and 50 ml of 0.1 M sodium hydroxide. The above solution was sonicated for 2 hours for complete extraction of the drug. Sample was filtered and the drug concentration was determined spectrophotometrically at 257 nm using UV-Vis Spectrophotometer. Percent entrapment efficiency and percent drug loading was calculated using the formula:

$$\text{Entrapment efficiency (\%)} = \frac{\text{Practical drug content}}{\text{Theoretical drug content}} \times 100$$

$$\text{Drug loading (\%)} = \frac{\text{Weight of drug in microspheres}}{\text{Weight of microspheres}} \times 100$$

***In vitro* Drug Release:** *In vitro* drug release profile of Paracetamol loaded microspheres was performed using Dissolution Apparatus USP Type I (Basket) containing 900 ml of simulated gastric fluid TS (without enzyme). Weighed quantity of Paracetamol microspheres equivalent to unit dose of paracetamol were placed in the basket and rotated at 50 rpm. Aliquots were removed at 15 minutes, 1 hour and 3 hours and replenished with equal amount of fresh medium to maintain the sink conditions. Filtered sample was analysed spectro-photometrically at 243 nm and the amount of drug release was calculated.

TABLE 3: ACETAMINOPHEN EXTENDED RELEASE TABLETS USP

Time	Amount dissolved
15 minutes	Between 45% and 65%
1 hour	Between 60% and 85%
3 hours	Not less than 85%

Particle Morphology: Prepared microspheres were observed under biological microscope to understand particle shape and uniformity. Microspheres were also observed after carrying out dissolution studies.

Particle Size Analysis: Particle size of microspheres was determined by optical microscopy. Eye piece was calibrated with the help of stage micrometer. Microspheres were viewed under microscope and their diameter was measured to find out the particle size range.

Taste Masking of Directly Added Paracetamol for Immediate Release: Paracetamol being bitter in taste, the part of the unit dose added directly as an API to get an immediate release needs to taste masked. Eudragit E100, a cationic polymer having pH dependent solubility is being specifically used for taste masking and it also favours drug release in acidic pH [10]. It is soluble in the gastric fluid upto pH 5.0 and is an effective taste masking agent. Therefore when Eudragit E100 coated drug is consumed by patients, it does not interact with the taste receptors as it is insoluble at salivary pH thus masking the bitter taste of drug. The moment the Eudragit E100 coated drug reaches the stomach, the acidic pH of stomach favours dissolution and the drug is released. Paracetamol: Eudragit E100 in the ratio of 1:1 was used to prepare polymer coated drug. Polymer was dissolved in acetone under continuous magnetic stirring to obtain a clear polymer solution. Weighed quantity of paracetamol was taken in a dry crucible and was coated with the Eudragit E100 solution under constant stirring in a water bath. The obtained molten mass of polymer coated drug was kept overnight for complete evaporation of acetone and the dry lump was crushed and sieved to obtain polymer coated drug. The drug release profilewas checked using Eudragit E100 coated paracetamol.

TABLE 4: DISSOLUTION TRIAL USING EUDRAGIT E100 COATED PARACETAMOL

Trial	Drug: Polymer ratio in microspheres	Ratio of percent of drug added as microspheres: percent added directly as API
F10	1:0.75	50% (325 mg): 50%(325 mg)

Formulation of an Oral Dry Suspension: Microspheres of optimized drug: polymer ratio i.e. 1:0.75 and Eudragit E100 coated paracetamol were formulated and developed into an oral dry suspension which has to be reconstituted during use. Dry suspension was formulated as per following formula (**Table 5**). Weighed amount of xanthan gum, purified talc and sucralose were added to weighed quantity of paracetamol micro-spheres and Eudragit E100 coated paracetamol. All ingredients were mixed thoroughly in a small mixing bag for uniform mixing. Formulation trials were conducted varying the quantities of added excipients so as to develop a suspension which will have good flow property, viscosity, sedimentation rate and which will be easily redispersible and palatable. To prepare the reconstituted suspension, 30 ml of water was added to unit dose of dry suspension [11] and stirred with spoon until a homogenous product was obtained.

TABLE 5: COMPOSITION FOR ORAL RECONSTITUTABLE DRY SUSPENSION

Sr No.	Ingredients	P1	P2	P3	P4	P5	P6
1.	Microspheres + Eudragit E100 coated drug equivalent to Paracetamol	650 mg	650 mg	650 mg	650 mg	650 mg	650 mg
2.	Xanthan gum	2%	2%	4%	4%	4%	4%
3.	Purified talc	5%	10%	5%	10%	5%	10%
4.	Sucralose	4 mg	4 mg	4 mg	4 mg	6 mg	6 mg

Evaluation of Dry Suspension:

Angle of Repose: Angle of repose was evaluated by funnel method. The height and radius of pile was measured and angle of repose (Θ) was calculated using formula:

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

Where, h = height of pile; r = radius of pile

Rheological Studies: The rheological profile of each formulation after constitution, in terms of viscosity was determined. The settling behaviour of suspension, viscosity of formulated suspension was checked using Brookfield digital rotational viscometer equipped with spindle (No. LV 62). The prepared suspension was poured in a beaker and the spindle was lowered perpendicularly. The spindle was rotated in the suspension at increasing shear rates 2.5, 4, 5, 6, 10, 12 and 20 rpm. At each speed, the corresponding dial reading was noted. All viscosity measurements were carried out at ambient temperature.

Determination of Redispersibility: The redispersibility of a suspension was evaluated qualitatively. The test consisted out manually shaking the cylinder. The prepared suspension was allowed to settle in a measuring cylinder. The mouth of cylinder was closed and inverted through 180° and the number of inversions required to restore a homogenous suspension were counted. If the homogeneity was attained in one inversion, then suspension is considered to be 100% redispersible. Every additional inversion causes a decrease in % redispersibility ease by 5% [4].

Sedimentation Value: The reconstituted suspension was kept in a measuring cylinder undisturbed at room temperature. To understand the sedimentation rate of the suspension, sedimentation volume (V_s) of the formulation was determined using following formula. Height of the sediment was noted at particular time intervals. The Hu/Ho ratio was obtained and plotted as ordinate taking time as abscissa. Formulation was chosen by comparing the plots, best one producing lines that are more horizontal and/or less steep.

$$V_s = H_u / H_o$$

Where, H_u = Ultimate height of the sediment; H_o = Initial height of the total suspension.

Evaluation of Taste: Paracetamol being a bitter drug, the palatability of prepared suspension was checked by panel method. A panel of 6 volunteers were selected and were asked to taste the suspension. Each volunteer was asked to hold the suspension in the mouth for 30 seconds and then spit out. The scale used was (a) 0 Tasteless, (b) 1- Slightly bitter, (c) 2- Bitter, (d) 3- Very bitter. Volunteer's opinion for bitterness value was noted and based on their opinion; amount of sweetening agent was optimised.

***In vitro* Drug Release:** The dry suspension was tested for *in vitro* drug release. The protocol is tabulated below (**Table 6**).Unit dose of suspension containing unit dose paracetamol was placed in a basket and dissolution studies were performed. Aliquots were removed at 15 minutes, 1 hour and 3 hours and replenished with equal amount of fresh dissolution media. Filtered sample was analysed by UV spectrophotometer at 243 nm and the amount of drug release was calculated.

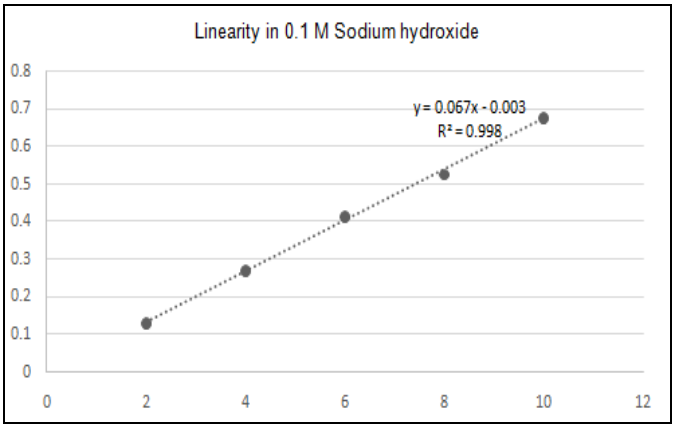
TABLE 6: PROTOCOL FOR *IN VITRO* DRUG RELEASE OF PARACETAMOL

Medium	Simulated gastric fluid TS (without enzyme); 900 ml
Apparatus	Dissolution apparatus USP Type I
Speed	50 rpm
Time points	15 minutes, 1 hour and 3 hours
λ_{max}	243 nm

Comparison with Marketed Formulation: *In vitro* drug release profile of prepared suspension and marketed preparation was compared and the similarity factor was found. The protocol followed was same as tabulated in **Table 6**.

RESULTS:

Standard Calibration Curve of Paracetamol:



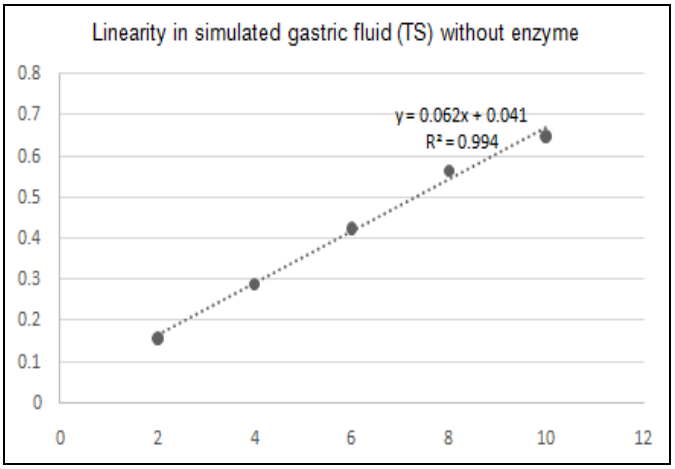


FIG. 1: STANDARD CALIBRATION CURVE IN SODIUM HYDROXIDE AND SIMULATED GASTRIC FLUID (TS) WITHOUT ENZYME

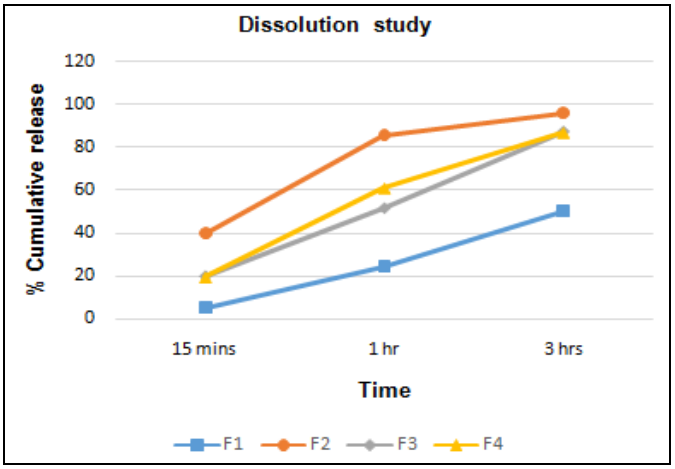


FIG. 2: GRAPH SHOWING *IN VITRO* DRUG RELEASE PROFILE OF FORMULATION TRIALS

Evaluation of Paracetamol Loaded Microspheres: The aim of formulation development was to develop paracetamol microspheres having optimum yield, drug loading, entrapment efficiency and whose *in vitro* drug release profile is within dissolution limits of Acetaminophen Extended Release Tablets USP. Four different formulations of microspheres were formulated varying drug: polymer ratio which gave following results.

TABLE 7: RESULTS OF FORMULATION TRIALS VARYING DRUG: POLYMER RATIO

Parameters		F1	F2	F3	F4
% Yield		93.46 ± 0.981	98.76 ± 0.587	94.298 ± 0.424	91.133 ± 0.756
% Drug loading		47.947 ± 0.4077	55.68 ± 1.416	54.475 ± 1.445	70.568 ± 1.121
% Entrapment efficiency		95.561 ± 0.008	82.955 ± 0.054	93.153 ± 0.051	89.20 ± 0.067
In vitro drug release	15 mins	4.916 ± 0.467	39.638 ± 2.712	19.785 ± 1.789	19.527 ± 0.261
	1 hour	24.004 ± 1.347	85.504 ± 1.128	51.579 ± 0.551	61.203 ± 1.307
	3 hours	50.221 ± 1.051	96.072 ± 0.649	87.412 ± 1.241	87.124 ± 0.168

Trial F1 to F4 was designed to check the effect of drug: polymer ratio on *in vitro* drug release. Results showed that the drug release for all the above formulation trials did not fall within the USP limits. Therefore, further trials were continued. Acetaminophen Extended Release Tablets USP states that the amount of drug release at 15 minutes should be between 45% and 65% *i.e.* there should be an initial immediate release of paracetamol to get an immediate relief from pain. Hence the unit dose of Paracetamol was divided into two parts-one part of unit dose was added directly as an API to obtain an immediate drug release while the remaining part was given as microspheres to get the later drug effect. Drug release profile was checked by varying the percentage of directly added drug and drug added as microspheres. The release profile is enclosed in **Fig. 3**.

Particle Morphology and Particle Size: Microscopic images of prepared Paracetamol microspheres checked before and after dissolution using biological microscope showed that the prepared microspheres were spherical in shape. The particle size was found in the range of 550 µm -700 µm.

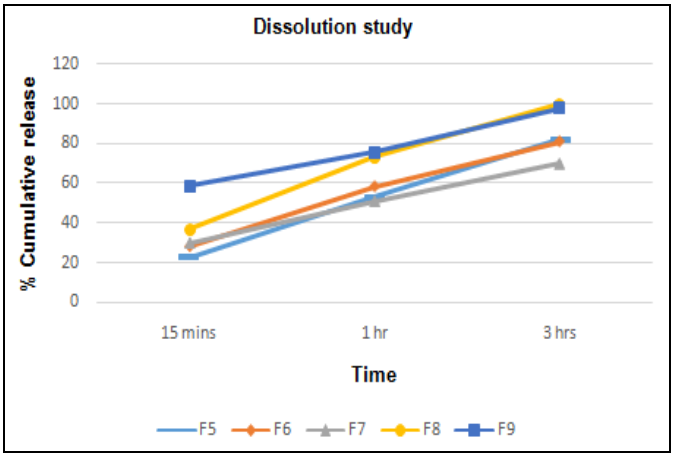


FIG. 3: *IN VITRO* DRUG RELEASE PROFILE OF TRIAL F5 TO F9

FIG. 4: MICROSPHERE BEFOREDISSOLUTION

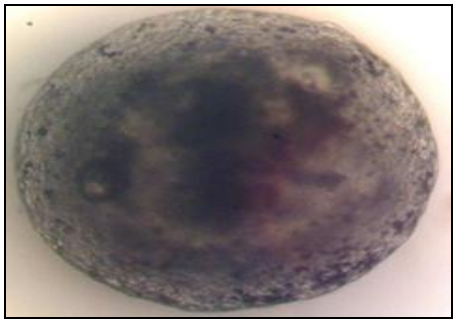


FIG. 5: MICROSPHERE AFTER DISSOLUTION

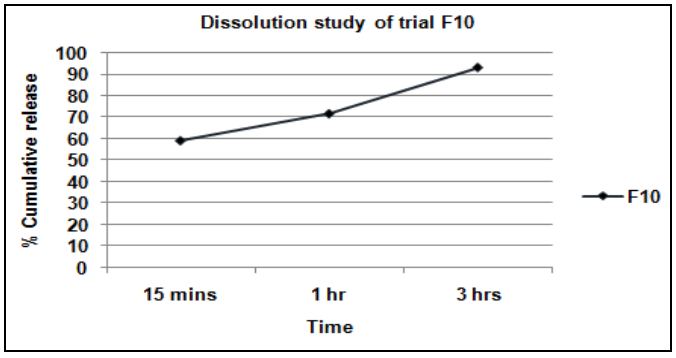


FIG. 6: *IN VITRO* DRUG RELEASE USING EUDRAGIT E100 COATED PARACETAMOL

The dissolution study carried out using Eudragit E100 coated paracetamol gave the drug release within desired limits.

Evaluation of Oral Dry Suspension:

Angle of Repose:

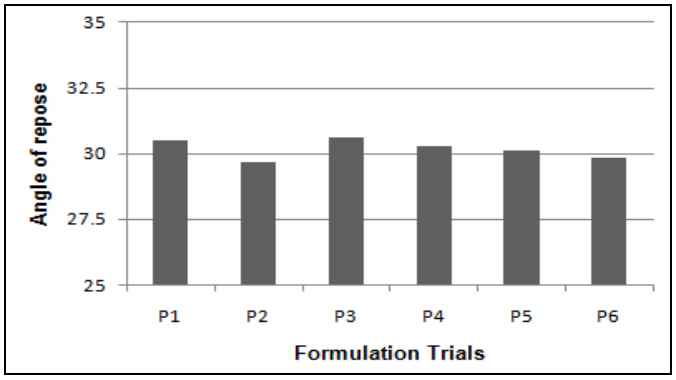


FIG. 7: ANGLE OF REPOSE FOR FORMULATION TRIALS P1 TO P6

Rheology Study:

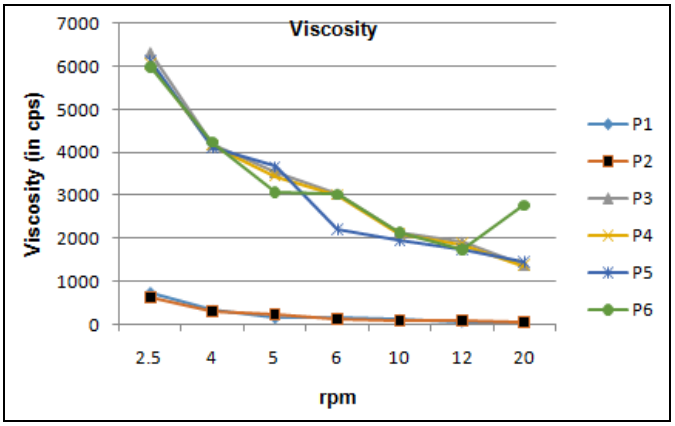


FIG. 8: RHEOLOGICAL STUDY OF FORMULATION TRIALS

Redispersibility:

TABLE 8: REDISPERSIBILITY OF FORMULATION TRIALS

Trial	P1	P2	P3	P4	P5	P6
Number of shakes required for complete redispersibility	2	2	1	1	1	1

Sedimentation Value:

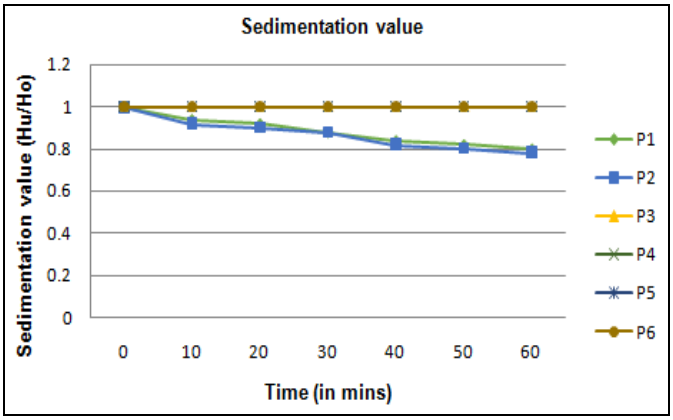


FIG. 9: GRAPH SHOWING SEDIMENTATION VALUE FOR FORMULATION TRIALS

Evaluation of Taste:

TABLE 9: EVALUATION OF TASTE

	Volunteer's opinion					
Volunteer	**P1**	**P2**	**P3**	**P4**	**P5**	**P6**
A	1	1	1	1	0	0
B	1	1	1	1	0	0
C	1	1	1	1	0	0
D	1	1	1	1	0	0
E	1	1	1	1	0	0
F	1	1	1	1	0	0

(SCALE: (a) -0 Sweet, (b) 1- Slightly bitter, (c) 2- Bitter, (d) 3- Very bitter)

***In vitro* Release Study:**

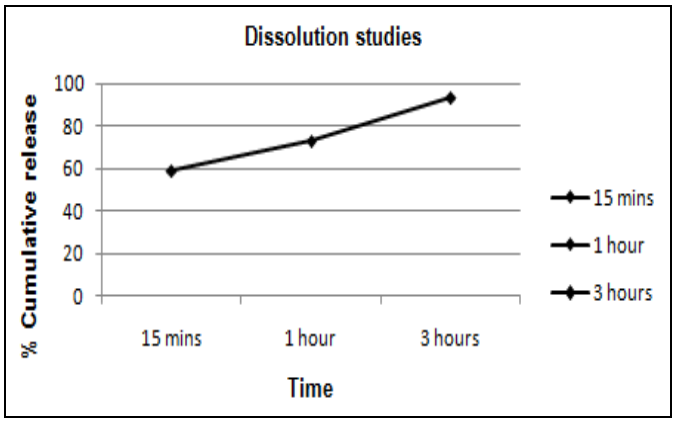


FIG. 10: GRAPH SHOWING *IN VITRO* DRUG RELEASE PROFILE OF SUSPENSION

Comparison of Prepared Suspension with Marketed Preparation:

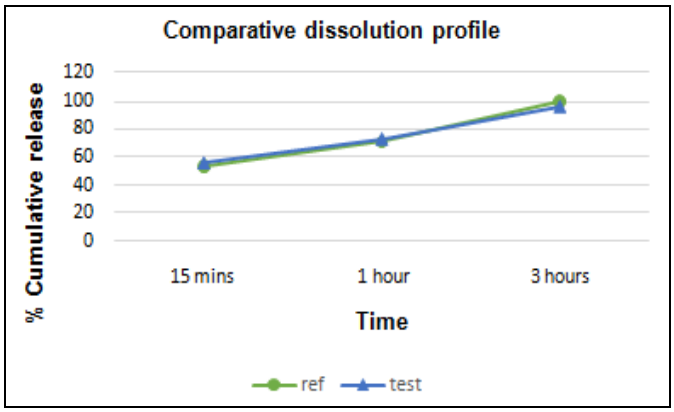


FIG. 11: COMPARATIVE DISSOLUTION PROFILE

DISCUSSION: The present study was carried out to develop a patient-compliant oral dry suspension of Paracetamol microspheres which has to be reconstituted at the time of use. The solvent evaporation technique has attracted most of the attention because of its ease of use and scale-up and lower residual solvent potential compared to other techniques [12]. Also, the technique requires milder conditions such as ambient temperature and constant stirring. Preliminary studies were performed varying paracetamol and ethyl cellulose ratio to obtain microsphere with good production yield, entrapment efficiency and *in vitro* drug release profile.

Percent Yield: The percent yield for all the formulations were in the range 91.13% to 98.76% as tabulated in **Table 7**. This showed that the process is efficient for preparation of drug loaded microspheres.

Drug Entrapment Efficiency: The entrapment efficiency was found to be in the range of 82.95% to 95.56% and the drug loading was found to be in the range between 47.95% and 70.57% exhibiting good encapsulation efficiency of ethyl cellulose.

***In vitro* Drug Release:** The release profile of trials F1 to F4 were not within the dissolution limits of Acetaminophen Extended Release Tablets USP. Hence further trials were continued by dividing the unit dose of Paracetamol into two parts- one part of unit dose as directly added API to get an initial immediate drug release while the remaining part of dose as microspheres. Microspheres prepared using 1:0.75 drug to polymer ratio were taken for all further trials. With increase in the percentage of directly added paracetamol, the drug release at 15 minutes was found to increase.

Formulation trial carried out with 50% (325 mg) directly added paracetamol and remaining 50% (325 mg) paracetamol as microspheres gave drug release profile that was not within the dissolution limits at 15 minutes time point. To enhance drug dissolution, surfactants are added [13]. Hence, 1% sodium lauryl sulphate was added and the dissolution studies were performed. Trial F9 carried out using sodium lauryl sulphate gave drug release profile within the USP limits.

Taste Masking with Eudragit E100: The part of drug added directly as API was taste masked with Eudragit E100 and the drug release profile was evaluated. Eudragit E100 being soluble at pH 1.2, the release profile was within the limits indicating that the drug release did not get affected by Eudragit E100 and taste masking was also achieved.

The Paracetamol loaded microspheres and Eudragit coated Paracetamol was developed into an oral dry suspension which has to be reconstituted at the time of use. Trial formulations P1 to P6 were prepared and evaluated to optimise the quantity of xanthan gum, sucralose and purified talc.

Angle of Repose: All the formulation trials P1 to P6 were evaluated for its flow property and angle of repose was calculated. With increase in the quantity of purified talc, the flow property of suspension was improved.

Rheological Study: Formulation containing 2% xanthan gum when reconstituted gave less viscous suspension leading to fast sedimentation. With increasing the quantity of xanthan gum to 4% in the formulation, the prepared suspension was viscous and the particles were well suspended.

Redispersibility: The number of shakes required for complete redispersibility of all formulation trials showed that the formulation containing 4% xanthan gum gave 100% redispersibility in one shake showing good redispersibility.

Sedimentation Value: A comparative graph showing sedimentation value of all the formulation trials showed that the formulation trials P3 to P6 gave a horizontal line. This suggests that the particles were well suspended.

Evaluation of Taste: Based on the opinion of the panel, it was found that the trials containing 4 mg of sucralose gave a slight bitter taste. Increase in the amount of sucralose to 6 mg, the bitter taste was masked and the formulation was found to be palatable. Based on the obtained results, it was found that the formulation containing 4% xanthan gum, 5% purified talc and 6 mg of sucralose gave a formulation having good flow property, viscosity, sedimentation value, redispersibility and palatability.

***In vitro* Drug Release:** The drug release profile of the suspension was found to be within the dissolution limits. The *in vitro* release profile developed formulation was compared with the marketed preparation which gave a similarity factor of 78.

CONCLUSION: In the present study, Paracetamol loaded microspheres were successfully prepared by solvent evaporation technique with good yield, entrapment efficiency and *in vitro* drug release profile within the dissolution limits of Acetaminophen Extended Release Tablets USP. The part of unit dose added directly as an API was successfully coated with Eudragit E100 polymer to mask the bitter taste of Paracetamol. The selected combination of Paracetamol microspheres and Eudragit E100 coated Paracetamol was developed into an oral dry suspension which has to reconstitute at the time of use. Different formulation trials were taken to develop a suspension having good flow property, viscosity, sedimentation value, redispersibility and palatability. Based on the results obtained for various evaluation parameters, suspension F5 was selected and the *in vitro* drug release profile was checked. The suspension gave drug release profile within the dissolution limits. The developed suspension compared with marketed tablet formulation gave a similarity factor of 78. Thus, a novel oral dry suspension containing Paracetamol microspheres and Eudragit E100 coated Paracetamol was successfully formulated and developed. The objective of developing a patient-compliant dosage form was achieved. This novel formulation would be helpful for patients who suffer from dysphagia or those who have difficulty in swallowing solid oral dosage forms.

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