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Evaluation of sedimentation stability in paracetamol suspensions with *Plantago ovata* mucilage as suspending agent using near-infrared transmission measurements

P. N. Murthy[1,*], M. Vimala Devi[2], Sudhir Kumar Sahoo[1], Anjan Kumar Mahapatra[1] and Madhusmruti Khandai[1]

[1]Royal College of Pharmacy and Health Sciences, Berhampur, India
[2]Auro Pharma, 77/78 Gangaimman Koil street, Vaithikuppam, Pondicherry, India

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ABSTRACT

Suspensions are one of the most important dosage forms under liquid orals. A large number of drugs are formulated as suspensions considering their therapeutic and commercial benefits. The aim of the present study is to formulate paracetamol suspensions employing Plantago ovata mucilage as a suspending agent and evaluate the sedimentation stability using near infrared transmission measurements. The mucilage extracted from Plantago ovata seeds is a natural suspending agent that can be used as an effective alternative for traditional suspending agents. Paracetamol suspensions were formulated using mucilage of Plantago ovata (POM) as suspending agent at different concentrations (0.25, 0.5, 0.75 and 1.0 %) and their infrared extinction profiles were compared to determine the corresponding sedimentation stability. The infrared (IR) spectroscopy and thermal analysis by differential scanning calorimetry (DSC), shows compatibility between paracetamol and POM, as there is no significant interaction. Physical stability of paracetamol suspensions was studied in terms of sedimenation stability employing infrared extinction profiles by using the instrument Separation analyzer (LUMiReader®). The LUMiReader® instantaneously measures the extinction profiles of the transmitted light across the entire length of a suspension sample employing STEP-Technology (Space- and Time-resolved Extinction Profiles Technology). Instability indices determined on different suspension formulations indicated that POM at 0.25% is a suitable and preferable suspending agent for the preparation of stable suspensions of paracetamol.

Key words: suspension, physical stability, mucilage of *Plantago ovata (POM)*, LUMiReader®, STEP-Technology, instability index.

INTRODUCTION

Paracetamol is N- acetyl- P- aminophenol, 4-hydroxyacetanilide, $C_8H_9NO_2$ (151.16). It is a major metabolite of phenacetin (p- ethoxy acetanilide) and an effective antipyretic and analgesic agent with mechanism similar to that of the salicylates. It produces antipyresis by acting on the hypothalamic heat- regulating centre and analgesia by elevating the pain threshold. It is useful particularly as an analgesic- antipyretic in patients who experience untoward reactions to aspirin. Unlike aspirin, acetaminophen does not antagonize the effects of uricosuric agents [1, 2]. The slight solubility of paracetamol in aqueous medium has made it a candidate for suspension which will require the inclusion of a suspending agent preferably, a natural suspending agent. Paracetamol is the most widely used and readily available antipyretic and analgesic [3]. The drug structure is shown under Figure 1.

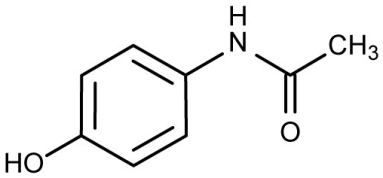


Figure1: Structure of paracetamol

Suspensions are biphasic heterogeneous coarse dispersions containing essentially the insoluble particulate matter or drug suspended with the help of suspending agent(s) in a liquid medium. The continuous or external phase is generally a liquid or semisolid. The liquid phase may be aqueous or in some instances may be organic or oily liquid for non oral use. The dispersed or internal phase is the insoluble particulate matter dispersed throughout the continuous or external phase. These are thermodynamically unstable; almost all suspension systems separate on standing. Because some products occasionally are prepared in a dry form to be placed in suspension at the time of dispensing by the addition of an appropriate liquid vehicle, this definition is extended to include these products [4, 5].

Suspending agents are generally added to the dispersion medium in order to maintain uniform suspendability or to prevent caking of the suspended particles during shelf-life. Pharmaceutical suspension is usually defined as a coarse dispersion [6].

Mucilages are polysaccharide macro molecules that dissolve more or less upon contact with water and form colloidal solutions. In recent years, plant gums and mucilages have evoked tremendous interest due to their diverse applications in pharmacy in the formulation of both solid and liquid dosage forms as thickeners, water retention agents, emulsion stabilizers, suspending agents, binders and film formers [7].

Stability study of suspensions is a very important aspect to enable the patient to receive the intended amount of the drug(s) in the dose administered. Physico-chemical stability of suspensions is important for maintaining the quality of the product. Physical stability of suspensions may be defined as the condition in which the particles do not aggregate and in which they remain uniformly distributed throughout the dispersion. Because this ideal situation is seldom realized, it is appropriate to add that if the particles do settle, they should be easily resuspended by a moderate amount of agitation [8].

Physical stability testing of paracetamol suspensions

Different procedures have been suggested in the past for evaluating the physical stability of suspensions [9-12]. Some of these are experiential in the sense that they have no mathematical base. Some methods currently being used are so drastic that they destroy the structure of the suspension.

The evaluation methods used may well be classified into:
(1) Sedimentation methods, (2) Rheological methods, (3) Electro-kinetic methods and
(4) Micromeritic methods.

Under sedimentation methods, measurement of the sedimentation volume and its ease of re-dispersion, form two of the most common basic evaluation procedures. Rheological methods help in predicting the settling pattern and can also provide evidences to vehicle particle structure. Data collected on samples stored for various periods can give useful information about the stability of the suspension. Electro-kinetic methods measure the surface electric charges or zeta potential which is instrumental in deciding the stability of disperse systems. Micromeritic methods deal with the particle size changes. The stability of a suspension is inter-related to the size of particles constituting its disperse phase. A growth in the particle size is a pointer towards its instability since such an occurrence can ultimately result in the formation of aggregates or cake destroying the physical structure of a suspension and rendering it useless. Hence, an appreciation of change in particle size with passage of time can provide an insight into the stability aspect of a suspension. Changes in absolute particle size, particle size distribution, crystal habit etc. can be worked out by microscopy, Coulter counter etc.

Normally there is a need to carry out a quick assessment of particle size change since no formulator can afford to wait for the normal shelf storage periods to study such changes. Hence, suspensions are subjected to artificial stress conditions in the form of freezing and thawing. Such a treatment is known to promote particle growth and can be used to predict future behaviours. However, an important point to remember is that sometimes hydrocolloids which are usual additives in suspensions can themselves get affected by freezing and thawing leading to caking of suspensions. Hence, observations may not be quite correlated to shelf-life of the products.

STEP-Technology (Space- and Time-resolved Extinction Profiles Technology)

STEP-Technology stands as acronym for Space and Time Resolved Extinction Profiles Technology. It can be used to measure the infrared extinction profiles of the transmitted light across the entire length of a suspension sample from top to bottom instantaneously [13]. By using an instrument called LUMiReader® which operates on STEP-Technology, it is possible to observe and understand different stability/instability phenomena of a suspension concurrently; e.g., creaming, sedimentation, coalescence, aggregation and flocculation at original product concentration. Basing on these phenomena the instability index is generated by the software SEPview installed in the instrument. Depending on the instability index measured for different suspension samples prepared with various suspending agents and other excipients, an ideal suspending agent and its concentration required to get a stable suspension can be selected.

Different program components are provided in a LUMiReader® for the qualitative and quantitative analysis of the samples, e.g.,

1. The Front Tracking for settling, creaming and consolidation (separation velocity)
2. The Integral Transmission for the clarification speed
3. The PSA-Module for the calculation of the particle size distribution.
4. Stability analysis for determination of instability index and for comparison of stability of different samples.

Separation analyser LUMiReader®

The Separation analyser LUMiReader® PSA-453 manufactured by LUM GmbH, Germany was used in the present work to carry out physical stability studies on paracetamol suspensions formulated with mucilage of *Plantago ovata as* suspending agent. The sample cell in a LUMiReader® is illuminated by a multi-colour light source I_0, including one near infrared wavelength (870 nm). Behind the sample cell the transmitted light I is detected using a CCD-line detector. The detector contains about 6434 elements, with a detector resolution of 9 µm and detection length of 45 mm. Transmission is converted into extinction by In (I_0/I).

Frequently optical particle size measurement techniques are used to determine the volume weighted particle size distribution. For this purpose the size and material dependent extinction coefficient is needed which can be calculated with Mie-theory using the complex refractive index of the particles. In this case strong assumptions have to be made like spherical homogeneous particles. However, the determination of the refractive index can be very difficult especially in the submicron range and for heterogeneous particles. No standard measurement methods are available up to now. The way out could be the evaluation of space and time resolved extinction profiles [14,15] at different wavelengths for sedimenting or creaming particles in gravitational or centrifugal field.

Illuminating the dispersion across its entire sample height, and by having many thousand detectors, LUMiReader® can measure the light source extinction profile instantaneously; even the smallest changes in concentration can be detected. The instrument measures the extinction profiles over the whole sample length during physically accelerated separation. Changes in the extinction profile are representative for the changes in particle concentration and allow to determine the velocity of individual particle classes with no assumptions regarding particle properties. Particle size distribution is obtained based on Stokes' law [13]. Mostly 2 mm cells made of polycarbonate are used for measurements (sample volume 0.4 cm^3). For samples with very low turbidity 10 mm cells (sample volume 2 cm^3) are used alternatively.

MATERIALS AND METHODS

Materials: Paracetamol IP was procured from SS Pharmachem, Cuttack, India. *Plantago ovata* mucilage (POM) was extracted from the seeds of *Plantago ovata* purchased from local market following the procedure described by Kulkarni et al. [16]. The seeds were soaked in distilled water for 48 hours and boiled for 10 minutes thereafter. The resulting viscous gel mass was pressed through a muslin cloth. The filtrate so isolated was treated with equal volume of acetone which resulted in precipitation of the mucilage. The isolated precipitate was dried at 40 °C for 2 hours. The dried mass was subjected to size reduction which yielded a powder mass. The powder was finally passed through sieve number 80 and stored in desiccators for further analysis and use. The yield was found to be around 30 % w/w.

All other chemicals, solvents and reagents used in the study were of analytical grade.

Compatibility studies

Compatibility studies were carried out to investigate the incompatibilities between paracetamol and the suspending agent (POM) by using differential scanning calorimetry (DSC) and Fourier transform infrared (FT-IR) spectroscopy.

Sample preparation: Drug to excipient ratio of 1:1 provides maximum possibilities of interaction between the drug and suspending agent thus enabling easy detection of any incompatibility. Therefore, homogeneous 1:1 physical mixtures of paracetamol and suspending agent (POM) were prepared by trituration in a clean and dry glass mortar and pestle [11,17]. These mixtures were stored in glass vials in a stability chamber at 25 ± 2 °C for four weeks after which they were subjected to DSC and FT-IR studies using differential scanning calorimeter, DSC-4000 and FT-IR, model IR Affinity-1, Shimadzu Corporation, Japan.

Preparation of paracetamol suspensions

Paracetamol suspensions were prepared with four different concentrations of the suspending agent POM as described hereunder. The suspending agent was used in four concentrations at 0.25 %, 0.5 %, 0.75 % and 1.0 % as shown in **Table 1**.

Table 1. Formulation of paracetamol suspensions

Formulation code	Amount of paracetamol (g)	Sodium benzoate (mg)	Suspending agent used	Amount of suspending agent (g)	Purified water to (ml)
F1	4	100	POM	0.25	100
F2	4	100	POM	0.50	100
F3	4	100	POM	0.75	100
F4	4	100	POM	1.00	100

POM- Plantango ovata mucilage

Procedure

The suspending agent was kept in contact with about 90 ml of water containing 100 mg of sodium benzoate for 12 hours to allow swelling of the suspending agent. The dispersion was thoroughly mixed with a laboratory stirrer (REMI) for 30 minutes at an average speed of 200 rpm to get a uniform dispersion. Paracetamol was then added to the dispersion under stirring and stirring continued for another 30 minutes and made up to volume. The prepared suspensions were stored at room temperature until further studies.

Physical stability determination

Separation analyser LUMiReader® PSA 453 manufactured by LUM GmbH, Germany was employed for stability determinations.

Sample cells: LUM 10 mm, PC, synthetic cells were used for separation studies basing on the sample properties like freedom from organic solvents, viscosity of the suspensions etc., as recommended by the manufacturer of the instrument.

Selection of tilt angle and temperature

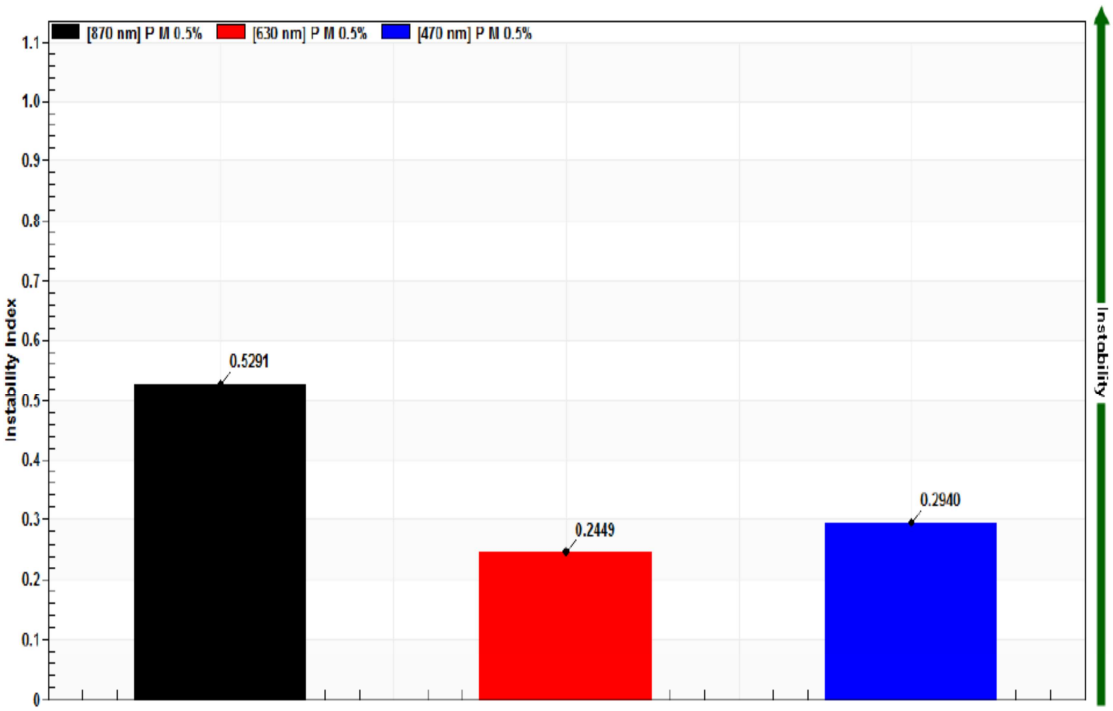
The instrument has a provision for measurements from 0 to 30˚ tilt allowing the sample to remain in upright or inclined position depending on the angle of tilt selected. Tilting the sample from its normal upright position allows an increase in the separation rate at gravity without any additional external forces. The magnitude of acceleration (upto 10 times) depends on geometric factors, such as tilt angle, vial dimensions, and sample type. The LUMiReader® has a provision to maintain the temperature between ambient temperature to 60 °C. Measurements were carried out at 0˚ tilt at 30 °C, 30˚ tilt at 30 °C and 30˚ tilt at 60 °C for the suspension samples. A sample volume of about 2 ml was used in the determinations.

Procedure

The suspension sample of about 2 ml was filled in the sample cell. The instrument was switched on and the SOP was programmed by selecting various parameters like the tilt angle, temperature, number of profiles, interval, number of cycles etc. Once, the instrument was ready with normalization and base line correction applied, a message appeared to insert the sample. The sample tube was gently shaken to disperse the sample and inserted into the sample holder. The instrument started recording the profiles as per the set SOP once the sample holder lid is closed by sliding in the direction shown on the instrument. The extinction profiles were recorded at three wavelengths i.e., 470 nm (blue), 630 nm (red) and 870 nm (NIR) with the help of the software SEPView® installed in the instrument. The profiles were automatically saved in the instrument [13]. The extinction profiles of 870 nm (near infrared) wavelength were taken into account for determination of sedimentation stability in the present work. Different suspension samples were analyzed as per the set parameters discussed above.

Some of the representative profiles recorded are shown in Figure 2, Figure 3 and Figure 4. The relevant data is shown in Table 2.

Figure 2: Extinction profiles for paracetamol suspension containing 0.5% of POM as suspending agent measured at 30º tilt and 60 ºC temperature: Stability analysis – Instability index



Results:

Sample Name	Time in s	Instability Index	Mean RCA in g	Mean	StdDev
[870 nm] P M 0.5%	8,998	0.5291	-x-	0.4230	0.1787
[630 nm] P M 0.5%	8,938	0.2449	-x-	0.2076	0.0839
[470 nm] P M 0.5%	8,939	0.2940	-x-	0.2501	0.1070

Figure 3. Extinction profiles for paracetamol suspension containing 0.5% of POM as suspending agent measured at 30º tilt and 60 ºC temperature: Extinction ratio 470 nm/870 nm

LUM

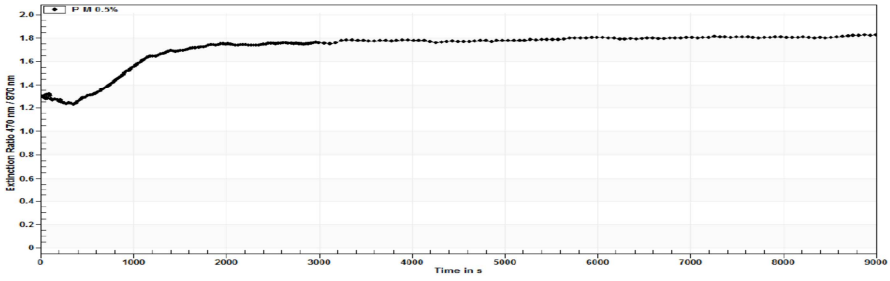
MWL Extinction Ratio

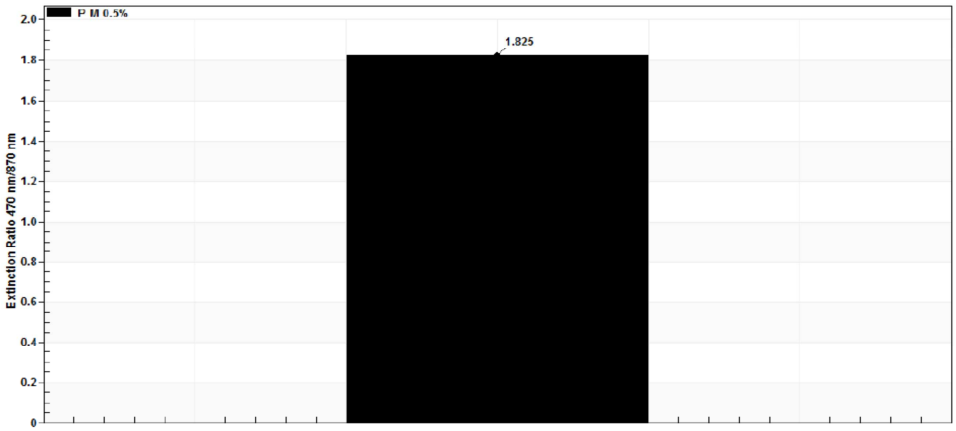
Analysis Summary

Title of Analysis:	P M 0.5% Sample 2(c) 300x10/100x60 30°/30° 1/1 60 20150211 15:46:01
Saved:	Analysis not saved
Wavelengths:	470nm / 870nm
Extinction Type:	Extinction
User:	admin
Samples:	P M 0.5%
Normalization:	Normalization applied, dynamic baseline correction
Smoothing:	Moving Average (9 points)
Notes:	

Data Range Analysed:

Sample Name	Range from in mm	Range to in mm	Range in mm	Time in s
P M 0.5%	1.28	44.28	43.00	8,998.50

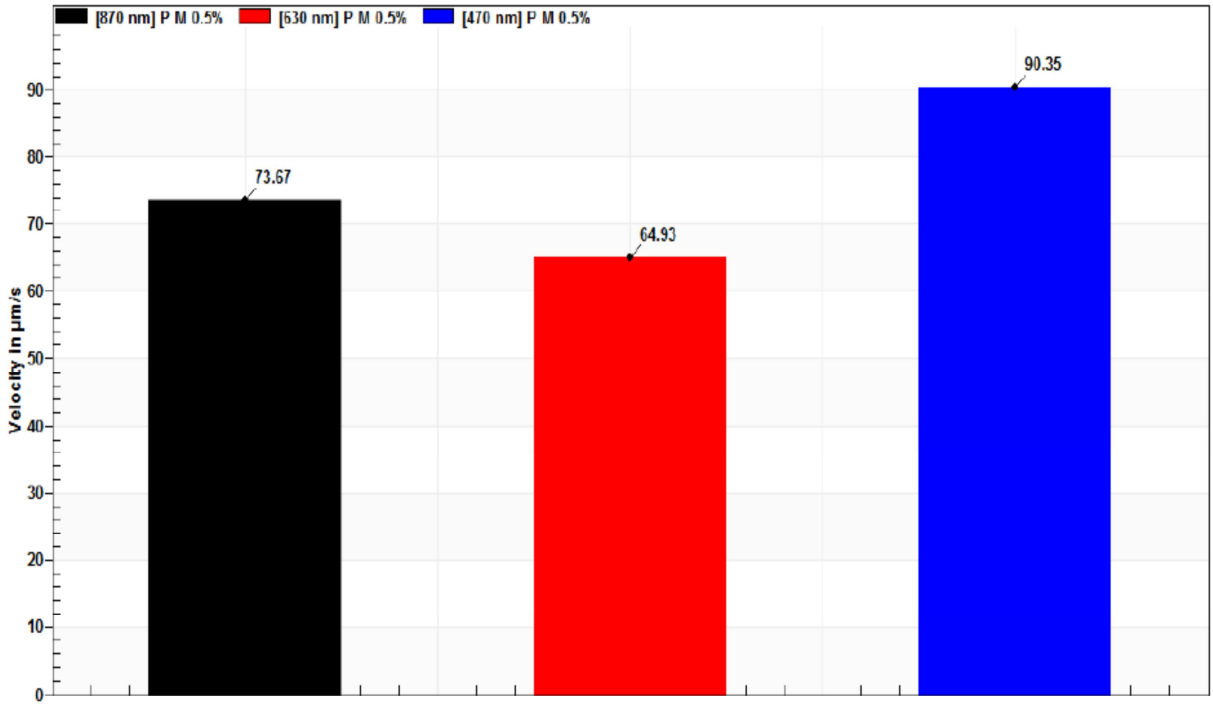




Results:

Sample Name	Time in s	Extinction Ratio 470 nm/870 nm	Mean in %	StdDev in %
P M 0.5%	8,939	1.825	1.642	0.1879

Figure 4. Extinction profiles for paracetamol suspension containing 0.5% of POM as suspending agent measured at 30º tilt and 60 ºC temperature: Front tracking – sedimentation velocity



Results:

Sample Name	Start in s	End in s	Value at End in µm	Mean RCA in g	Velocity in µm/s	StdDev in µm/s
[870 nm] P M 0.5%	506.9	526.9	14,342	-x-	73.67	11.99
[630 nm] P M 0.5%	546.7	696.7	35,568	-x-	64.93	16.18
[470 nm] P M 0.5%	626.8	656.8	15,123	-x-	90.35	17.92

Sample Name	Intercept in µm	StdDev in µm	Corr. coeff.	Mean in µm	StdDev in µm
[870 nm] P M 0.5%	-24,403	-x-	0.9894	13,701	708.6
[630 nm] P M 0.5%	-10,596	-x-	0.9143	29,096	4,624
[470 nm] P M 0.5%	-43,653	-x-	0.8064	14,540	1,040

Determination of resuspendability of suspension samples

Resuspendability is the ability to resuspend the settled particles with a minimum amount of shaking after a suspension has sedimented on standing for some time.

Procedure

The resuspendability of the suspensions was evaluated qualitatively. The suspensions were allowed to sediment in stoppered glass jars for 1 month. The test was performed on samples in triplicate by shaking the sedimented suspensions manually at 180° movement, after sedimentation was completed [18]. Based on the numbers of shaking required to disperse the sediment uniformly into a suspension, the formulations were evaluated. Cake formation was

also evaluated qualitatively. Formulations requiring more than 10 shakings were considered positive for cake formation.

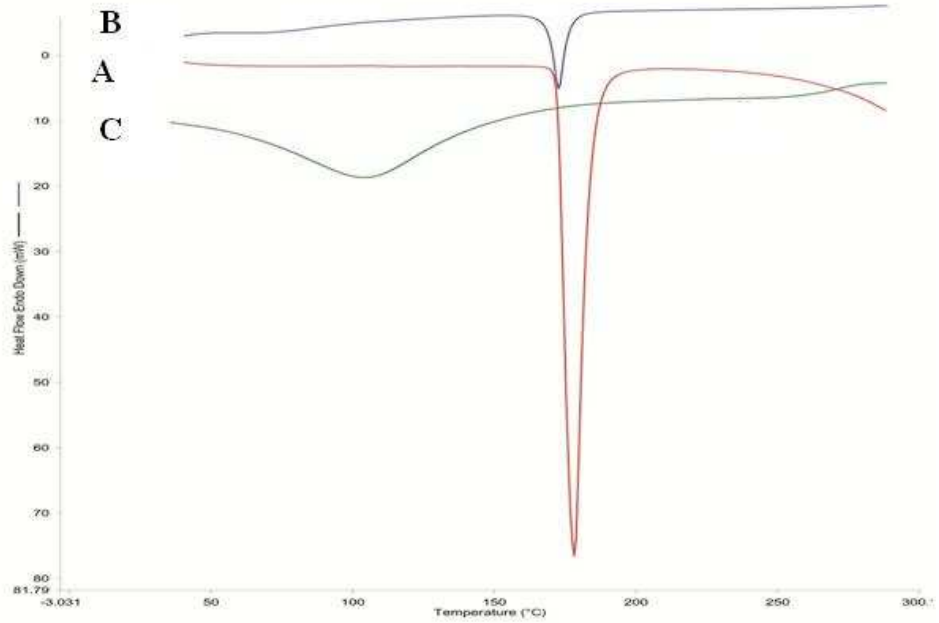
RESULTS AND DISCUSSION

Compatibility studies

DSC Studies

Result of DSC study shown in **Figure 5** describes thermal behaviour of paracetamol with POM. DSC thermograms of paracetamol and the suspending agent POM and their physical mixtures were studied on the samples stored at 25±2 °C. The characteristic peak pattern indicated that paracetamol had undergone thermal transition at 178.16 °C (melting endotherm of paracetamol), and PO mucilage at 104.15 °C. The peak of pure paracetamol and pure suspending agent was retained in the physical mixture during the study period at the storage condition. In the physical mixtures of paracetamol with the suspending agent, the thermal transition occurring at 178.16 °C was not affected as shown in Figure 5, indicating compatibility. There were no significant changes in the peak shape and peak positions suggesting no significant interactions between the drug and the suspending agent POM.

Figure 5: DSC thermograms of (A) Paracetamol, (B) Mixture of Paracetamol and Mucilage (POM) and (C) Mucilage

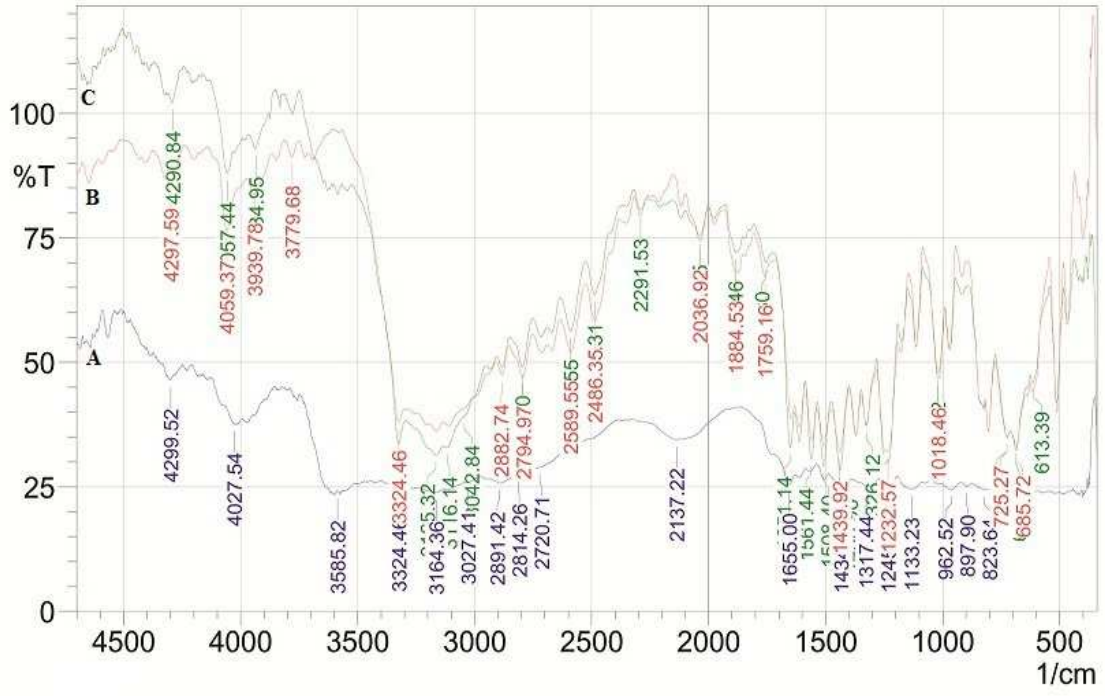


FT-IR Studies

Compatibility of paracetamol with suspending agent POM was studied using FT-IR spectroscopy. Interactions in the sample are derived or deduced by FT-IR studies from changes in the characteristic peaks. However, some broadening of peaks due to hydrogen bonding was expected while using the excipients from natural origin and also due to moisture without indicating any significant interaction. If all the characteristic peaks are retained and there is no significant change in the peak position, compatibility can be expected.

The samples were stored at 25± 2 °C and were scanned in the region of 4000 $cm^{-1}$and 400 cm^{-1}. The FT-IR spectrum obtained for paracetamol showed various prominent and characteristic peaks. The characteristic broad and strong peak around 3500cm^{-1} indicates the presence of O-H stretching, the presence of peak at 1651cm^{-1} indicates C=O stretching for amide group. The spike at 3563 cm^{-1} indicates the presence of N-H stretching. The peak at 2900 cm^{-1} indicates the presence of C-H stretching. The peak around 3100 cm^{-1} indicates the presence of aromatic C-H stretching. The presence of characteristic spikes for O-H stretching, C=O stretching, N-H stretching, C-H stretching and no new bands or shift in characteristic peaks appeared in the physical mixtures of paracetamol with the suspending agent POM as shown in Figure 6 indicate no significant interaction between the drug and the selected suspending agent.

Figure 6: IR spectra of (A) Paracetamol, (B) Mixture of Paracetamol with Mucilage (POM) and (C) Mucilage (POM)



Determination of physical stability of suspensions

Determination of instability index and sedimentation velocity of suspensions

Separation analyser LUMiReader® PSA 453 was employed for stability determinations. LUM 10 mm, PC, synthetic sample cells were used for separation studies. Measurements were carried out at 0˚ tilt and 30 °C, 30˚ tilt and 30 °C and 30˚ tilt and 60 °C for the suspension samples. Tilting the sample from its normal upright position allows an increase in the separation rate at gravity without any additional external forces. The inclined position of the sample tube due to a tilt of 30˚ resulted in accelerated sedimentation velocity compared to the upright position of the tube at 0˚ tilt as evident from the results shown in Table 2 and Table 3. A sample volume of 2 ml was used in the determinations. Measurements at 30˚ tilt resulted in accelerated measurements.

Table 2: LUMIReader stability data for paracetamol suspensions at 0 tilt & 30 ˚C, 30 tilt & 30˚C and 30 tilt & 60˚C

Conc.	Instability index at suspending agent concentration of			Front tracking Sedimentation velocity (µm/s) at suspending agent concentration of			Extinction ratio (470 nm/870 nm) at suspending agent concentration of		
	0˚ tilt-30 ˚C	**30˚ tilt-30 ˚C**	**30˚ tilt-60 ˚C**	**0˚ tilt-30 ˚C**	**30˚ tilt-30 ˚C**	**30˚ tilt-60 ˚C**	**0˚ tilt-30 ˚C**	**30˚ tilt-30 ˚C**	**30˚ tilt-60 ˚C**
0.25	0.1005	0.1532	0.3165	0.001	0.154	1.909	1.115	1.125	1.238
0.5	0.1224	0.1434	0.5291	-x-	-x-	73.67	1.118	1.119	1.825
0.75	0.1254	0.1545	0.4549	-x-	-x-	13.4	1.145	1.168	1.484
1.0	0.1420	0.158	0.3285	-x-	-x-	2.28	1.20	1.250	1.762

The extinction profiles were recorded at three wavelengths i.e., 470 nm (blue), 630 nm (red) and 870 nm (NIR) with the help of the software SEPView® installed in the instrument. The profiles were automatically saved in the instrument. The extinction profiles of 870 nm (near infrared) wavelength were taken into account for determination of sedimentation stability in the present work as the near infrared light region is sensitive for measurement of data of coarse particles. Blue light (470 nm) is sensitive for nano range particles.

The results shown in Table 2 indicated that the instability index was lowest (0.1005) with suspension formulation containing 0.25 % of POM at 0 tilt and 30 C; instability index was 0.5291with suspensions with 0.5 % at 30 tilt and 60 ˚C. The detailed values of instability index, sedimentation velocity (front tracking) and extinction ratio (470 nm/870 nm) are given under Table 2. Instability index generally ranges between 0 to 1 and the higher this value, more unstable the suspension is. Therefore, Instability index is a very useful tool for comparison of different suspending agents and selection of suitable suspending agents during suspension formulation development. Basing

on the results of instability index it is presumed that 0.25 % of POM is suitable as suspending agent for preparation of stable suspensions of paracetamol.

Determination of resuspendability of suspension samples

Resuspendability is the ability to resuspend settled particles with a minimum amount of shaking after a suspension has sedimented on standing for some time. The suspension should redisperse with minimum effort on shaking for ease of administration. It is an important prerequisite for a good and stable suspension. Results of resuspendability are given under **Table 3.**

Results shown in **Table 3** indicate that the formulations containing 0.25% POM were easily resuspendable when used as suspending agents as they required less number of shakings for obtaining uniform dispersion.

Table 3: Results of resuspendability evaluation on paracetamol suspensions (n=3)

Sample	Suspending agent	% of suspending agent	Number of shakings required to get a uniform dispersion (average of 3 findings)	Caking
F1	POM	0.25	1.33	No
F2	POM	0.50	2.66	No
F3	POM3	0.75	2.33	No
F4	POM	1.00	3.33	No

Considering the results of instability index, sedimentation velocity and resuspendability of the suspensions it can be further inferred that 0.25 % of POM can be considered suitable as suspending agent for preparation of stable suspensions of paracetamol.

Quantitative evaluation of resuspendability of the suspension by using LUMIReader

The optimized sample was checked for proper resuspendability by studying the separation kinetics with the help of the LUMIReader. The sample cell containing the suspension stored for 1 month was shaken 2 times manually at 180^{o} movement and the extinction profiles were obtained using the same SOP followed for the fresh sample. A comparison was made between the profiles obtained for the fresh sample and the sample stored for 1 month. The results are given in **Table 4.**

Table 4. Quantitative evaluation of resuspendability of paracetamol suspension

Sample	Instability index		Sedimentation velocity (μm/s)		Extinction ratio (470 nm/870 nm)	
	Fresh sample	Stored sample	Fresh sample	Stored sample	Fresh sample	Stored sample
F1	0.1005	0.1005	0.001	0.001	1.115	1.125

Sedimentation velocity was minimum with 0.25% POM as observed from front tracking analysis of the formulations. Formulations containing 0.5% POM resulted in sedimentation velocitiy of 73.67 μm/s at 30 tilt and 60 ˚C. Extinction ratio (470 nm/870 nm) for formulation containing 0.25% POM was found to be lowest (1.115). The above results suggest that the difference in extinctions at 470 nm and 870 nm is small for the formulation F1 resulting in lowest extinction ratio for the formulations compared indicating minimum changes in particle sizes in these suspensions.

Considering all the parameters like instability index, sedimentation velocity, cake formation, changes in particle size of the suspended particles, the suspension formulation F1 containing PO mucilage at 0.25% concentration was chosen as the stable suspension. FTIR and DSC studies showed that the mucilage was compatible with paracetamol.

CONCLUSION

Considering the study results obtained from separation analysis of suspensions employing LUMiReader®, it can be derived that the suspension formulations can be easily compared by the parameter “Instability index” as this parameter takes into account of all the properties of the suspension like sedimentation velocity, clarifying velocity, particle size distribution changes etc. The instability index ranges between 0 to 1 and, higher this value, more unstable the suspension is. Therefore, Instability index is a very useful and important tool for comparison of different suspending agents and selection of suitable suspending agents in suspension formulation development. POM at a concentration of 0.25% can be used in the formulation of paracetamol suspension. The mucilage is a natural suspending agent that can be used as an effective alternative for traditional suspending agents.

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