



Investigation of Binding Efficacy of Pectin Isolated from *Solanum betaceum Cav* using Tableting Technology

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Abstract

Pectin's are widely used in food industry and Pharmaceutical industry. It is also a natural part of the human diet. The current research work deals with the isolation and preliminary characterization of pectin from tree tomato (*Solanum betaceum Cav*) and further to evaluate its binding property with starch and Poly Vinyl Pyrollidone (PVP). The pectin was subjected to phytochemical and physicochemical characterization and its suitability to use as binding agent. FT-IR spectroscopy, DSC studies were performed for drug, *Solanum betaceum Cav* pectin (SBP) powder and the tablets were prepared with isolated pectin and other binders. Paracetamol tablets were prepared by wet granulation method containing mannitol and microcrystalline cellulose as diluents, using 4%, 8% and 12 %w/w of SBP, starch and PVP as binding agents in the tablet formulation. Precompressional properties of granules and tablets such as Carr's index, Hausner's ratio and angle of repose and quality control tests like weight variation, thickness, friability, hardness and disintegration time were determine and found satisfactory. The *in vitro* release studies shows that release rate of drug is decreased with increase in the SBP percentage in the formulation. *Solanum betaceum Cav* pectin powder showed good binding. The binding efficiency of *Solanum betaceum Cav* pectin was comparable with binding character of starch 12% and PVP 8%. The pectin isolated from *Solanum betaceum Cav* can be used as binder in the formulation of tablets.

Keywords: *Solanum betaceum Cav* pectin, Fruit pectin, Tree tomato, Tamarillo pectin, Natural binder, Natural excipients.

Introduction

Polymeric substances may be defined as those substances derived from natural sources by biosynthesis or chemical synthesis of biological matter. They are termed as natural pectins or biopolymers [1, 2]. In pharmaceutical field, biopolymers have been established as promising carriers of drug molecules or part of drug delivery system due to their capability of biodegradation when exposed to a living system.

Many topical and oral pharmaceutical systems now employing these natural pectins. Naturally occurring pectin is located in the middle lamella, primary and secondary cell wall of plant tissue [3]. The pectins are believed to be composed of atleast seventeen types of monosaccharides. The sugar moieties determine the various physicochemical properties of the polymer. Pectin is principally extracted from citrus peels and

apple pomace under mild acidic conditions [4]. In plant cells, pectin consists most of the complex set of pectins particularly abundant in the nonwoody parts of nearly all terrestrial plants. The amount, structure and chemical composition varies between plant [5]. Pectin can be used in Pharmaceutical and food industries as a stabilizing agent, gelling agent, emulsifier and thickener. The present research deals with exploring a pectin from tree tomato which is an edible fruit rich in nutritional qualities, a good source of antioxidant compounds, calcium, phosphorus, potassium and iron, sugars, organic acids, pectins and flavonoids [6].

Tamarillo commonly known as tree tomato is a subtropical non-climatic fruit with red skin and flesh yields throughout the year. Scientifically it is called as *Solanum betaceum Cav* available in India.

The pectin content of the fruit was found to be rich before ripening of the fruit. so the study focus on evaluation of pectin isolated from *Solanum betaceum Cav* for its binding efficiency as a pharmaceutical aid in tablet technology [7].

Materials

The fruit were collected from Ooty and was identified as *Solanum betaceum Cav* and a specimen is deposited in Botanical Survey of India, Coimbatore. All other chemicals and reagents used for the study were of analytical grade purchased from Sigma Aldrich chemicals Pvt. Ltd., Chennai.

Methods

Extraction of Pectin

The collected fruits were cut into small pieces and dried. The dried pieces were soaked in distilled water and are homogenized in water with a homogenizer for 2 hours. Then the homogenized solution was kept 1 hour for complete release of pectin into water. The solution was squeezed and filtered through double layered muslin bag.

Isolation of Pectin

The filtrate was collected and precipitated with three times its volume of acetone. The obtained precipitate was further washed three times with acetone to isolate the precipitate which was kept undisturbed to sediment. The light brown color sediment was separated and dried under vacuum for 60 hours. Finally, the isolated pectin was powdered, passed through sieve number 80 and stored in desiccators for use in subsequent tests. The yield was found to be 6.4 g pectin/500g of fruits [8].

Characterization of Pectin

The isolate was characterized for its Physiochemical properties like organoleptic characters, solubility, pH, loss on drying, ash value, swelling index, viscosity, XRD,

bulkiness, flow characters with standard procedures. Phytochemical evaluation for the presence of various phytoconstituents was also performed [9].

Formulation of tablets

Preformulation studies

Drug – Excipient Compatibility studies:

Physical mixture of drug and pectin were filled in the prewashed, dried plastic container and sealed. The sealed container was stored at $37^{\circ}\text{C} \pm 0.5^{\circ}\text{C}$ for 28 days in stability chamber. At the end of 28 days plastic container were removed from stability chamber and subjected for drug-excipient compatibility studies. The study was carried out by thermal and FTIR analysis.

Thermal analysis

Thermal properties of melting point of *Solanum betaceum Cav* pectin and drug and physical mixture of pectin and drug powder 1:1 ratio was characterized by using DSC, (SDT Q600 V20.9 Build 20). The powdered materials were sealed in aluminium pan and heated from $10.00^{\circ}\text{C}/\text{min}$ to $400.00^{\circ}\text{C}/\text{min}$. The decomposed melting temperature was measured and observed.

FTIR analysis

Pure drug sample, isolated pectin powder of *Solanum betaceum Cav* and the physical mixture of drug with excipient in the ratio 1:1 were subjected to IR spectral studies using FTIR spectrophotometer. A physical mixture of drug and isolated pectin was mixed with desirable quantity of potassium bromide. 100 mg of this mixture was compressed to form a transparent pellet using hydraulic press at 15 tons pressure. It was scanned from $4000\text{-}400\text{ cm}^{-1}$ in a FTIR – 8400 Shimadzu, JAPAN. The individual spectra of the drug and pectin were analyzed [10].

Preparation of paracetamol tablets

Table 1: Composition of Paracetamol tablets using *Solanum betaceum Cav* pectin, Starch and PVP as Binding Agents

Formula	B1 (4%)	B2 (6%)	B3 (8%)	B4 (4%)	B5 (6%)	B6 (8%)	B7 (4%)	B8 (6%)	B9 (8%)
Ingredients									
Paracetamol	250	250	250	250	250	250	250	250	250
Mannitol	80.8	76.8	72.8	80.8	76.8	72.8	80.8	76.8	72.8

Microcrystalline Cellulose	40	36	32	40	36	32	40	36	32
<i>Solanum betaceum Cav</i> pectin (Binder)	16	24	32	-	-	-	-	-	-
Starch (Binder)	-	-	-	16	24	32	-	-	-
Polyvinyl pyrrolidone (Binder)	-	-	-	-	-	-	16	24	32
Sodium methylparaben	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8
Sodium propyl paraben	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4
Demineralized water	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
Talc	8	8	8	8	8	8	8	8	8
Magnesium Stearate	4	4	4	4	4	4	4	4	4
Total weight	400	400	400	400	400	400	400	400	400

All the above ingredients quantities are mg/tablet.

Different batches of granules from B1 to B9 were prepared using pectin isolated from *Solanum betaceum Cav*, starch and PVP as binder by wet granulation technique. All the ingredients were weighed separately and passed through sieve number 60. Then the materials were placed in a transparent plastic container and blended for 5 minutes. After mixing, the binder solution prepared with demineralized water was added to the blend and kneaded to prepare the granules.

The granules were prepared by wet granulation method by passing through sieve number 36. The obtained granules were dried at 30°C in hot air oven and then collected in a container. Talc and magnesium stearate were added and mixed well. The granules were subjected to precompressional evaluation and compressed into tablets [11].

Precompressional Evaluation of Granules

The flow property of the granules were assessed by determination of bulk density, tapped density, Hausner ratio, Carr's index and angle of repose as per the standard procedure and formula.

Compression of Tablets

The granules of batches B1 to B9 were compressed into an average weight of 400mg per tablet using rotary punch tablet compression machine (Cadmach

Machineries) fitted with a concave punch and die set.

Evaluation of Tablets

The compressed tablets were evaluated for its quality controls test such as weight uniformity, thickness, hardness, friability, drug content, disintegration time and invitro dissolution. The tests were performed as per the procedure in the monograph. All the batches were evaluated and compared for its quality control tests [12].

Weight variation

Twenty tablets of each batch were used to evaluate weight variation among the batch and mean and standard deviation was calculated.

Friability

Friability testing was done by Roche friabilator with readings in triplicate. Twenty tablets from each batch were determined for friability.

Hardness

Hardness of all batches was determined using Monsanto hardness tester. The test was carried out in triplicate for all batches as per the monograph for uncoated tablets.

Thickness

The thickness was determined using vernier caliper and the results were expressed as mean values of 10 determinations, with standard deviations.

Drug content

The tablets were powdered, quantity equivalent to 150 mg of Paracetamol in tablet powder was accurately weighted and dissolved in 50 ml of 0.1 M sodium hydroxide, diluted with 100 ml of water, shaken for 15 minutes and added sufficient water to produce 200.0 ml and mixed well and filtered. Further 10.0 ml of the filtrate was diluted to 100.0ml with water. Subsequently to 10.0 ml of the resulting solution, 10 ml of 0.1 M sodium hydroxide was added and diluted to 100.0 ml with water and mixed well. Finally analyzed at 257nm using UV visible spectrophotometer (Shimadzu UV-2450, Japan).

In vitro dissolution studies

In vitro drug release studies of all the formulations were carried out using USP type- II tablet dissolution test apparatus as per IP. At first 900 ml of dissolution medium of phosphate buffer pH 5.8 was placed in basket container with temperature maintained at $37\pm 2^\circ\text{C}$. Then the tablet was introduced into the basket container and paddle was rotated at 50 rpm up to 30 minutes. 2 ml Sample solution was withdrawn at 5, 10, 15, 20, 25, and 30 minutes time intervals from the basket container and again 2 ml of fresh dissolution medium was replaced into the basket container to maintain constant volume.

The obtained sample solution was filtered by Whatman filter paper and diluted with 100 ml of phosphate buffer pH 5.8 and mixed well. The absorbance of the resulting solution was measured at 243 nm using UV -Visible

spectrophotometer and calculated the percentage drug release of paracetamol.

Statistical Factors

Similarity index and dissimilarity index between the different batches of tablets using starch and PVP as binder was compared with pectin from *Solanum betaceum Cav* as binder to demonstrate the dissolution similarity [13].

Results and Discussion

Characterization of isolated Pectin Powder

The isolated pectin from the pectin was studied for its phytochemical and physicochemical of properties of *Solanum betaceum Cav* and the results were observed and presented in Table 2 and 3. The identification tests of pectin gave positive test for carbohydrate, pectin in Molisch's and ruthenium tests respectively and the iodine test gave negative test for starch, thus pectin was confirmed. The powder was light green in nature with mucilaginous taste and no characteristic odor.

Extracted and purified pectin was evaluated for viscosity and pH. The pH of the pectin was found to be 6.1, showing that it may be less irritating on gastrointestinal tract and hence was suitable for uncoated tablets and the viscosity of 1% w/v solution was found to be 1.12 cps. The flow properties of pectin powder were determined by Carr's index, Hausner's ratio and angle of repose was found to be >23 , >1.25 , and $36^\circ - 40^\circ$ indicated passable flow properties.

Table 2: Phytochemical characterization of isolated pectin from *Solanum betaceum Cav*

S. No	Parameters	Observed	Results
1.	Molisch's test	Violet green colour present at junction of two layers	Carbohydrate present
2.	Ruthenium test	Pink colour developed	Pectin present
3.	Iodine test	No colour present in solution	Pectin Present

Table 3: Physicochemical characterization of isolated pectin from *Solanum betaceum Cav*

Parameters	Observed
Organoleptic properties	Light green colour, amorphous nature, Pectinnous, odourless.
Solubility	Soluble water and swell to form gel and practically insoluble in acetone, ethanol, chloroform and other organic solvents.
Loss on drying (%)	10.2%
Swelling index	55.1%
Bulk density	$0.48\pm 0.51 \text{ g/cm}^3$
Tapped density	$0.53\pm 0.056 \text{ g/cm}^3$
Carr's index	9.4 ± 0.851
Hausner's ratio	1.1 ± 0.046
Angle of repose ($^\circ$)	$23.0\pm 1.26^\circ$

pH (1%w/v)	6.1
Total Ash (%)	1.24%
Water-soluble ash (%)	2.7%
Acid insoluble ash (%)	0.15%
Viscosity (1% w/v solution)	1.12 cps

Preformulation Studies

Drug- Excipient Compatibility Studies

Thermal Analysis

Differential Scanning Colorimetry (DSC)

The figure 1, 2 and 3 shows the DSC spectra of paracetamol, polymer and 1:1 ratio of paracetamol and polymer. In DSC spectra of paracetamol is observed a sharp endotherm melting point. The DSC Spectra of the natural plant polymer shows a broad endotherm. In DSC thermal gram of 1:1 ratio (paracetamol: polymer) observed both sharp endotherm of Paracetamol and broad endotherm of plant polymer without any

shift. This concludes that paracetamol and *Solanum betaceum Cav* are compatible for the formulation.

FTIR spectrum in Figure 4, 5, and 6 and the interpretation data of spectral comparison in table 4 indicated that there was no shift in the spectrum, which confirms the compatibility of drug and excipients used for the formulations.

The surface morphology of pectin powder was observed by XRD (X-ray diffraction method). The results were shown in Figure 7. By the spectra obtained by XRD, the powdered *Solanum betaceum Cav* shows the presence of numerous halos with weak peaks which indicate amorphous nature of the material.

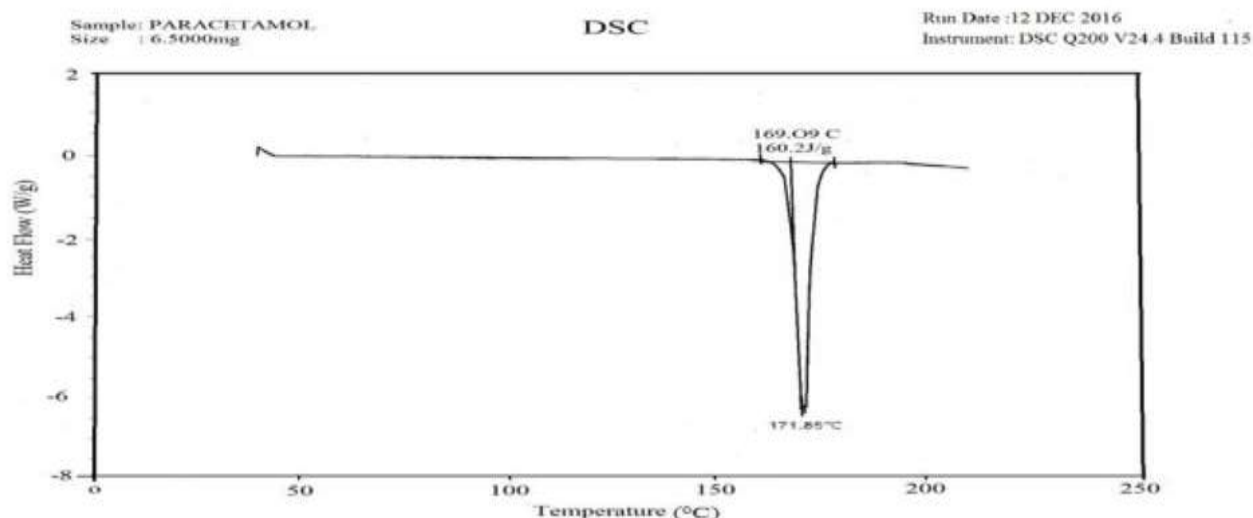


Figure 1: DSC of paracetamol

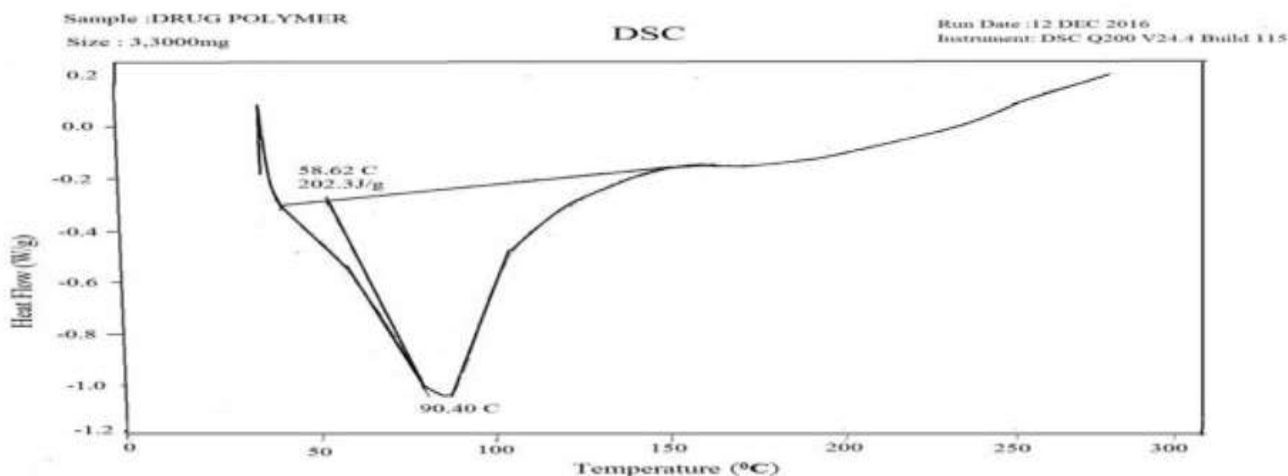


Figure 2: DSC of *Solanum betaceum Cav*

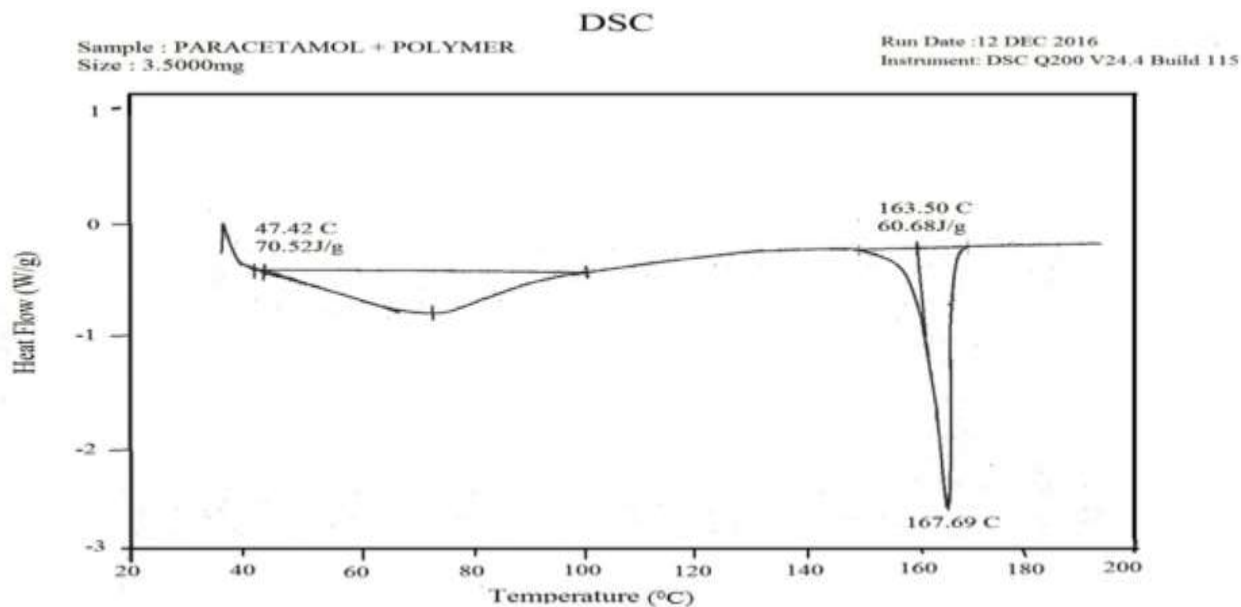


Figure: 3: DSC of paracetamol + *Solanum betaceum Cav*

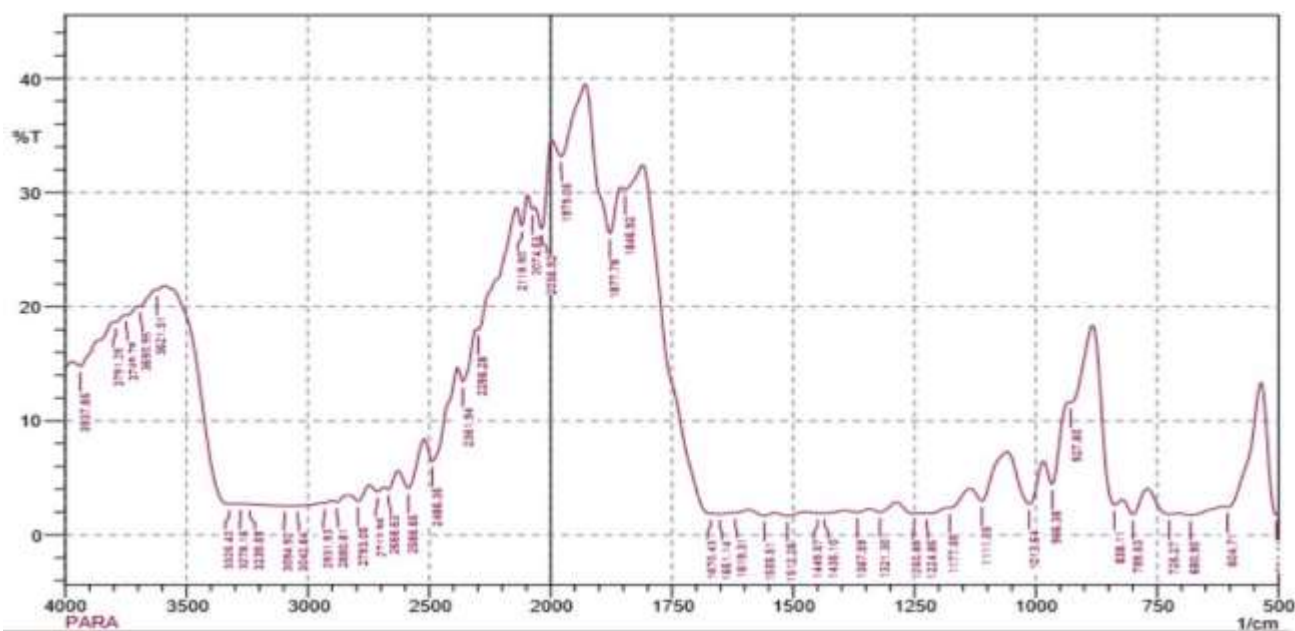


Figure: 4: FTIR analysis of *Solanum betaceum Cav*

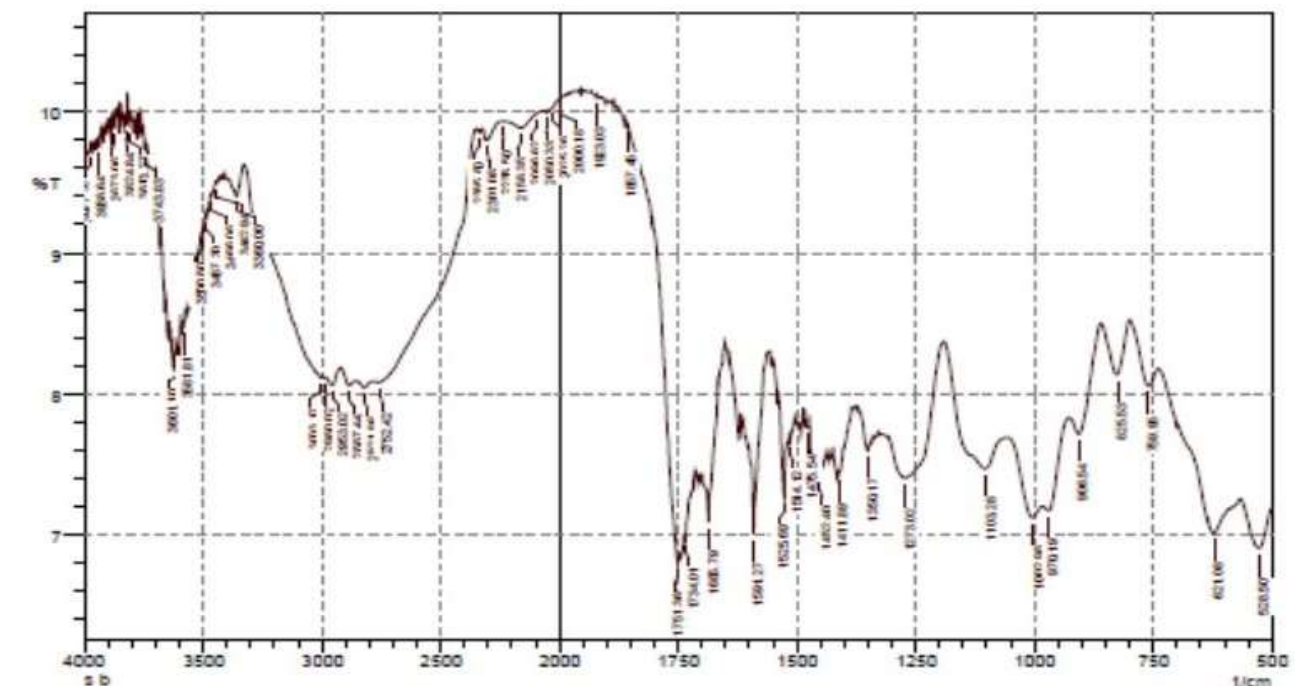


Figure: 5: FTIR analysis of paracetamol

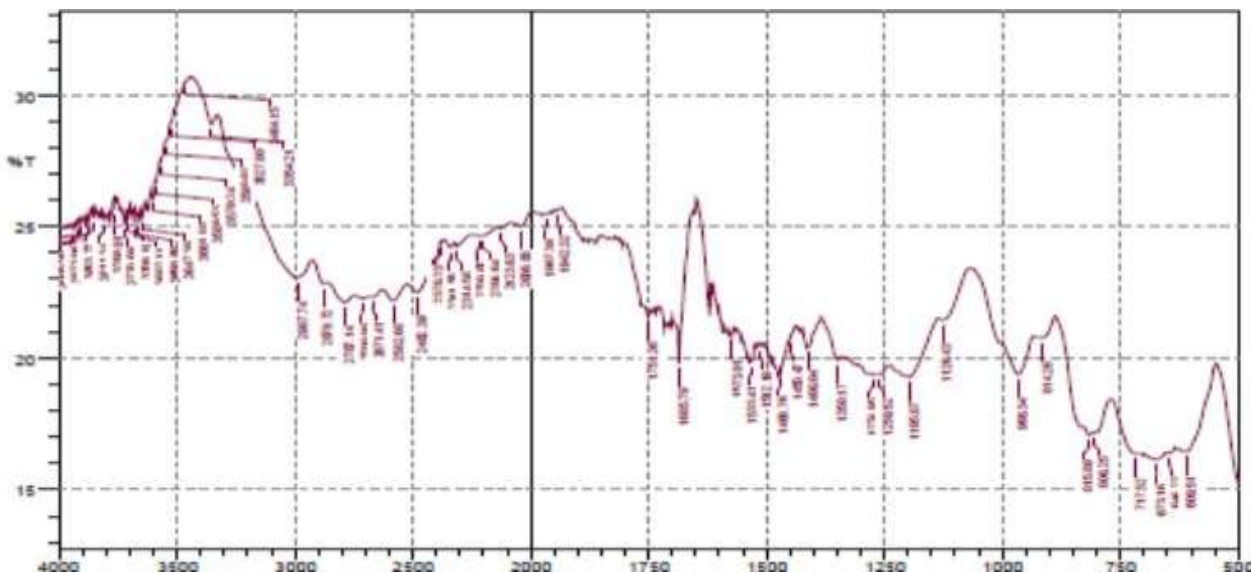


Figure 6: FTIR of *Solanum betaceum Cav* & paracetamol

Table 4: Interpretation of *Solanum betaceum Cav* & paracetamol

S. no	Observed peaks	Range (cm ⁻¹)	Characteristic group
1	806.25	860-680(s)	Aromatic C-H bending
2	1688.79	1690-1630(s)	Amide C=H stretch
3	3660.89	3700-3500(s)	Amide N=H stretch
4	3354.21	3550-3200(broad ,s)	Phenol O-H stretch
5	1685.75	1750-1680(s)	Ketone C=O stretch

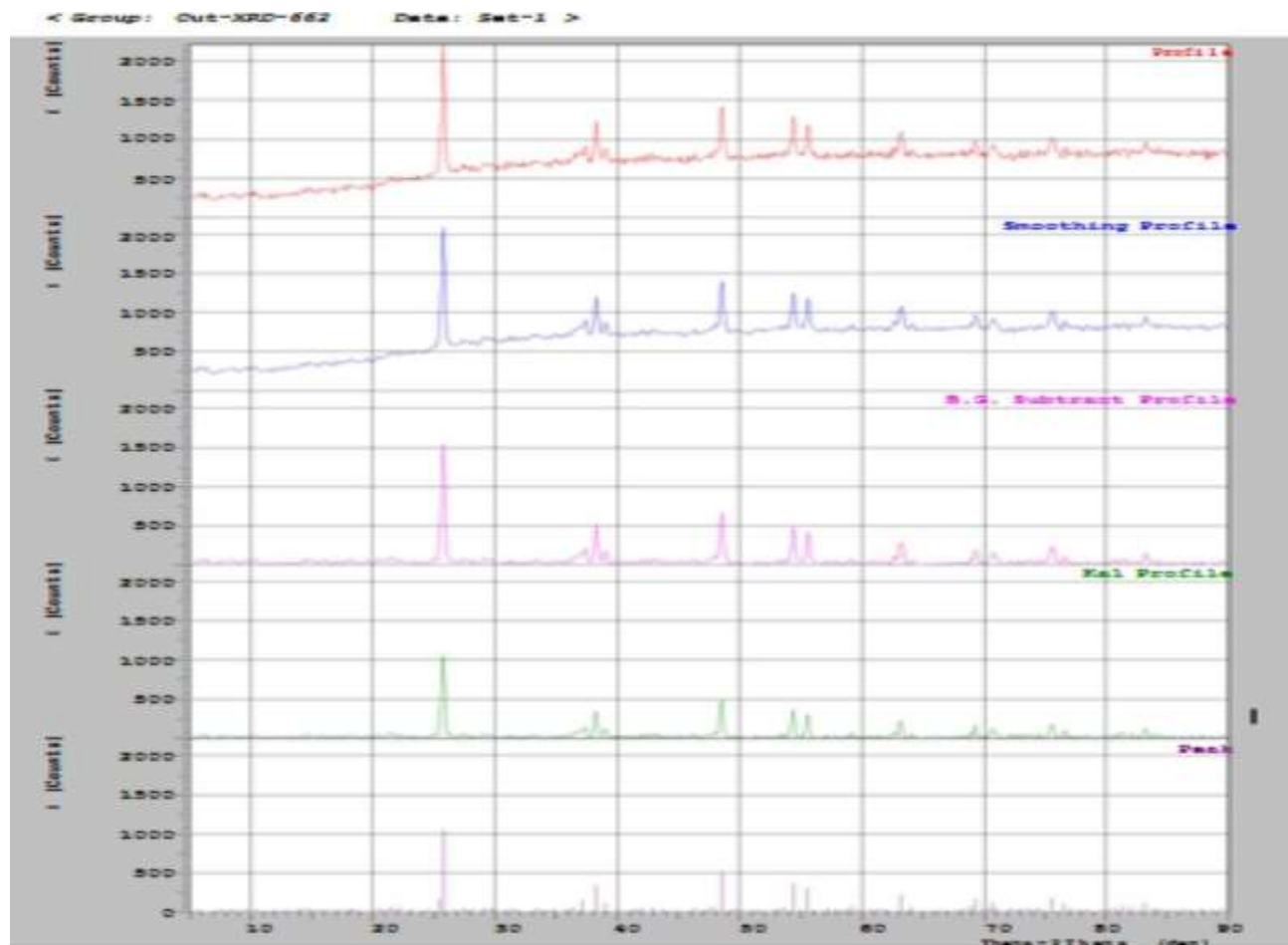


Figure 7: XRD analysis of *Solanum betaceum Cav Pectin*

Precompressional Evaluation

The flow properties of prepared granules of different batches were determined and the results are presented in Table 5.

It was observed that the flow ability ranges were decreased when binder concentration was increased. When compared with starch and PVP granules, the flow property of

granules slightly differs. The Carr's index, Hausner's ratio and Angle of repose values of the granules made from the pectin was found

to be <23, <1.25 and 25° - 30° respectively. Hence all the granules exhibited excellent flow properties.

Table 5: Determination of precompressional parameters

Binders	SBP			STARCH			PVP		
	B1	B2	B3	B4	F5	B6	B7	B8	B9
Formulations code	(4%)	(6%)	(8%)	(4%)	(6%)	(8%)	(4%)	(6%)	(8%)
Parameters	(4%)	(6%)	(8%)	(4%)	(6%)	(8%)	(4%)	(6%)	(8%)
Bulk density (g/ml)	0.315 ±0.00	0.319 ±0.00	0.326 ±0.00	0.434 ±0.00	0.442 ±0.00	0.446 ±0.00	0.438 ±0.00	0.446 ±0.00	0.442 ±0.00
Tapped density (g/ml)	0.356 ±0.00	0.357 ±0.00	0.359 ±0.00	0.526 ±0.00	0.500 ±0.00	0.490 ±0.00	0.505 ±0.00	0.490 ±0.00	0.480 ±0.00
Carr's index (%)	14.4 ±0.00	10.6 ±0.00	9.1 ±0.01	17.5 ±0.01	11.6 ±0.00	9.0 ±0.03	13.3 ±0.04	9.0 ±0.03	7.9 ±0.00
Hausner's ratio	1.13 ±0.00	1.11 ±0.00	1.2 ±0.01	1.21 ±0.00	1.13 ±0.00	1.10 ±0.01	1.15 ±0.00	1.10 ±0.01	1.10 ±0.02
Angle of repose (°)	23.3°	24.1°	26.3°	29.7°	26.4°	25.9°	29.9°	28.4°	27.8°

SB = *Solanum betaceum* Cav, PVP = Polyvinylpyrrolidone

Evaluation of tablets

The different batches (B1 to B9) of tablets were prepared using isolated pectin(SBP) as binding agent at three different percentages. For comparison, starch and PVP were used as binding agents. The prepared tablets were evaluated and the results of their weight variation, hardness, thickness, diameter, friability, disintegration time and assay were presented in Table 6. All the batches of tablets exhibited a good uniformity in content. The hardness of the tablets increased with increase in percentage of

binding agent. The tablets prepared with 8% of pectin showed more hardness when compared to tablets prepared using 4% and 6%. The friability values were decreased with increase in binder concentration. The overall friability values were within the specified limits. The disintegration time of tablets were found to be increased with increase in binder concentration from 4% to 8%. This behavior can be attributed to the swelling properties of the pectin. But the overall disintegration time values were within IP limits.

Table 6: Evaluation of tablets

Binders	SBP			STARCH			PVP		
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Formulations code	(4%)	(6%)	(8%)	(4%)	(6%)	(8%)	(4%)	(6%)	(8%)
Parameters	(4%)	(6%)	(8%)	(4%)	(6%)	(8%)	(4%)	(6%)	(8%)
Weight variation (mg)	400.1	400.0	401.4	400.0	401.1	400.2	401.0	401.2	400.1
Hardness (kg/cm ²)	4.5	5.5	6.5	4.0	4.5	5.0	4.5	5.0	6.5
Thickness (mm)	4.8	4.8	5.0	4.8	5.0	4.8	4.9	5.0	4.8
Diameter (mm)	10.14	10.14	10.12	10.14	10.12	10.14	10.14	10.14	10.14
Friability (% w/w)	0.3	0.6	0.4	0.3	0.7	0.4	0.7	0.5	0.5
Disintegration time	9min 5sec	17min 8sec	23min /28sec	1min/ 48sec	3min/ 52sec	5min/ 22sec	1min/ 54sec	5min/ 49sec	13min/ 36sec
Assay (%)	99.7	99.6	98.9	100.1	98.8	99.8	98.7	100.2	99.9

In vitro Dissolution Studies of Tablets

In vitro dissolution profile of tablets was

shown in Figure 8, Table 7. This study showed that the drug release from the tablets prepared using the pectin with 4% and 6%

concentrations were found to be more than 80% and 90% was found to be less than 80% in 30 minutes. The drug release was found to be increased with decrease in the concentration of pectin. From the graph, the drug release of B1 and B2 batches showed a sharp increase, whereas B3 showed less drug release compared to other standard batches. The friability and disintegration time of all the formulations were found to be within IP limits. The drug releases of B1& B2 formulations were within IP standard but not B3 formulation as the release was slow as

the binder concentration was increased. The formulations B1 to B3 compared with B4 to B9 showed similar release profile at various concentration. The percentage profile release of at 30 mins of B1, B4 and B7 were found to be 92.8, 92.8 and 92.4, for B2, B5 and B8 were 85.6, 85.9 and 72.4 percentage. In vitro release for B3, B6, and B9 were 71.5, 74.8 and 63.3 percentage. The result indicates that the release was decreased with increase in binder concentration. The drug release percentage of the pectin (SBP) was comparable with starch and PVP.

Table 7: In vitro drug release of tablets using isolated pectin and standard binders

Binders	SB			STARCH			PVP		
	Formulations code								
Dissolution time (min)	B1 (4%)	B2 (6%)	B3 (8%)	B4 (4%)	B5 (6%)	B6 (8%)	B7 (4%)	B8 (6%)	B9 (8%)
5	25.7	18.9	7.4	32.7	27.3	21.2	31.7	27.4	20.3
10	39.5	31.4	15.9	44.2	36.8	31.9	44.8	30.4	27.0
15	56.4	42.8	29.8	56.2	44.7	44.7	51.3	43.0	39.6
20	69.6	54.3	41.6	70.3	60.8	52.8	69.4	50.8	46.9
25	79.3	68.4	59.1	81.4	73.6	63.6	76.7	65.2	55.1
30	92.8	85.6	71.5	92.8	85.9	74.8	92.4	72.4	63.3

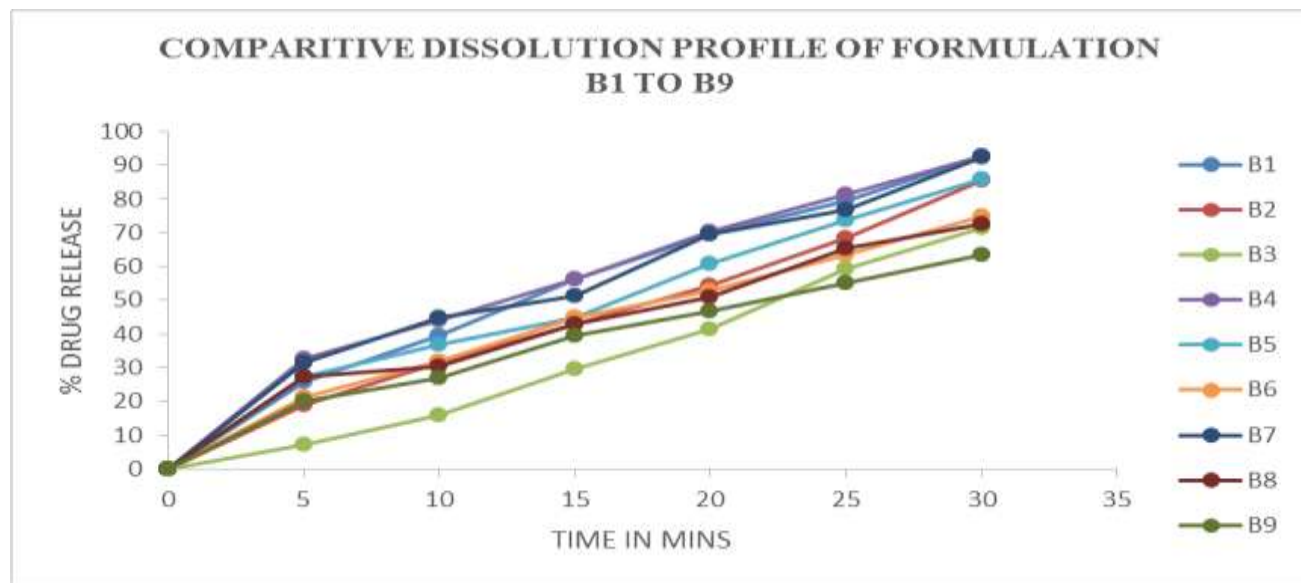


Figure: 8 Comparative dissolution profiles for formulation (B1 to B9)

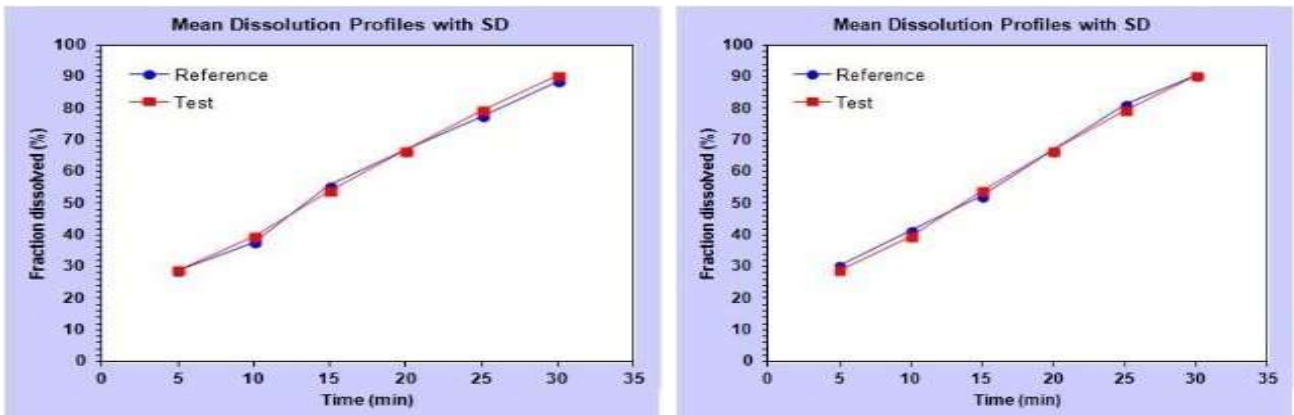
Statistical factor

Statistical factor of *in vitro* dissolution profile comparison of with isolated pectin starch and PVP as binding agents were studied using DD solver software for difference factor (f1), similarity factor (f2), and Rescigno index (ξ)

values. Those are presented in Table 8 and the graphs were showed in Figure 9 to 14. It shows that the comparison of mean (R) reference and mean (T) test values of difference factor (f1) were below 15, similarity factor (f2) were above 50 and Rescigno index were almost 0.

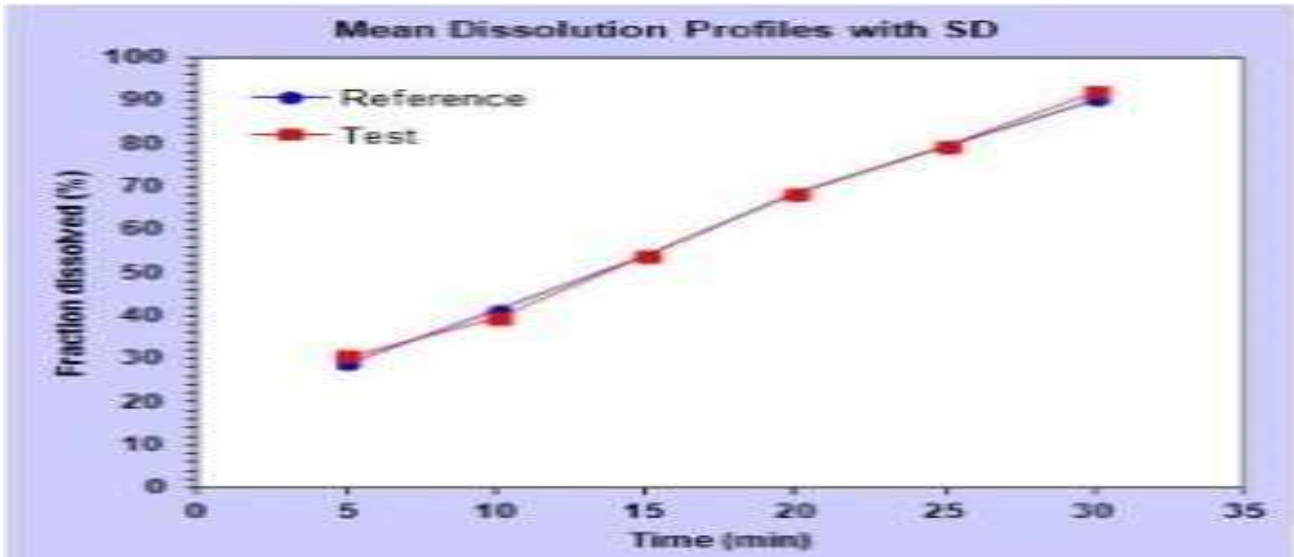
Table 8: Statistical factors

Difference factor (f1)	2.00	1.49	1.99	1.94	1.03	0.99
Similarity factor (f2)	87.71	89.75	87.51	87.51	92.04	92.04
Rescigno index (ξ)	0.0099	0.0070	0.0114	0.0098	0.0059	0.0057



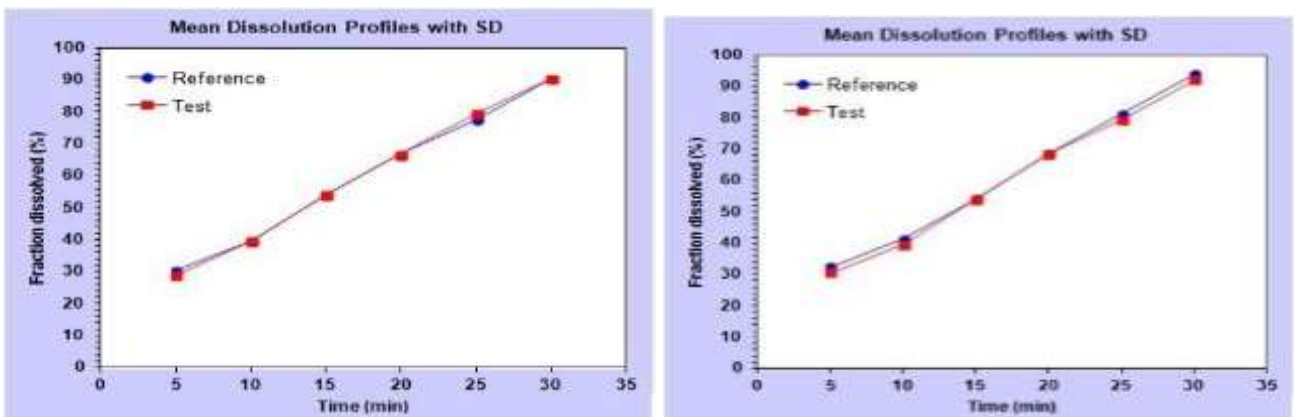
A

B



C

Figure: 09: Difference factor of SB compared with STARCH a) B1Vs B4; b) B2 Vs B5; c) B3 Vs B6



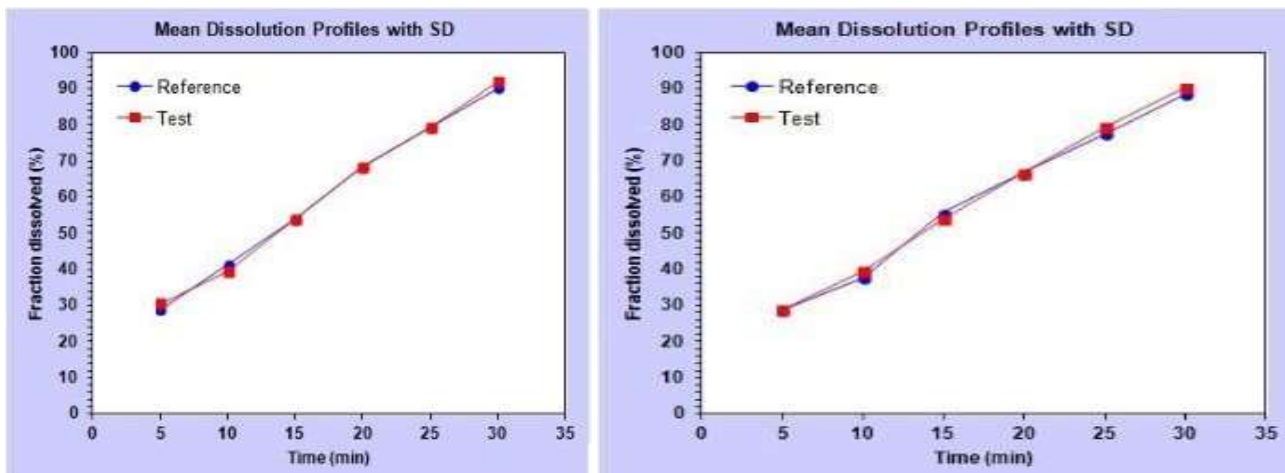
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E



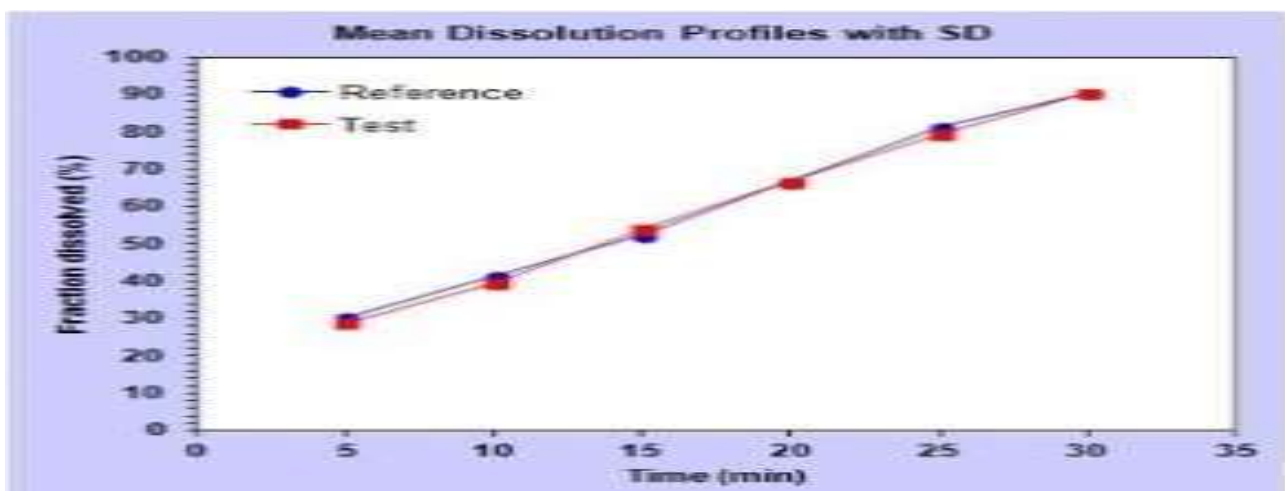
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Figure: 10: Difference factor of SB compared with PVP d) B1Vs B7; e) B2 Vs B8; f) B3 Vs B9



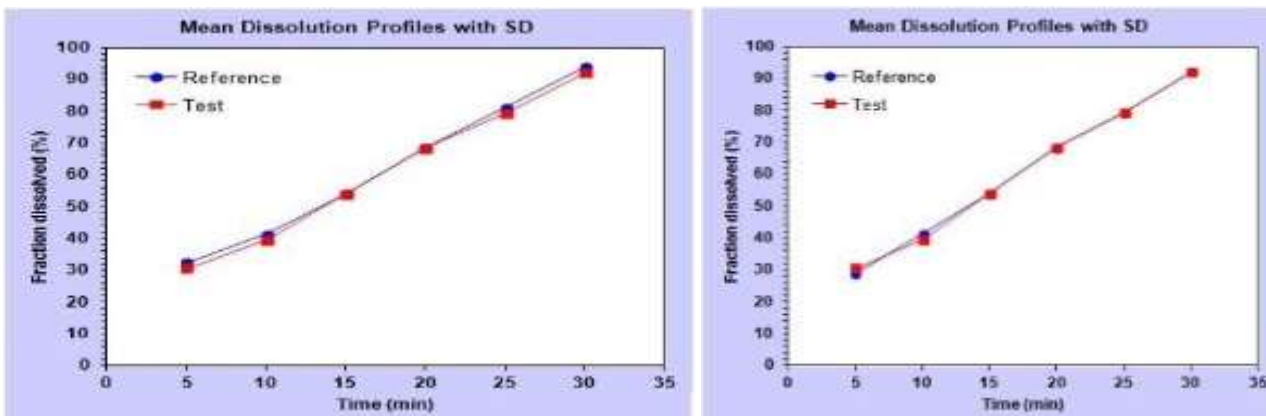
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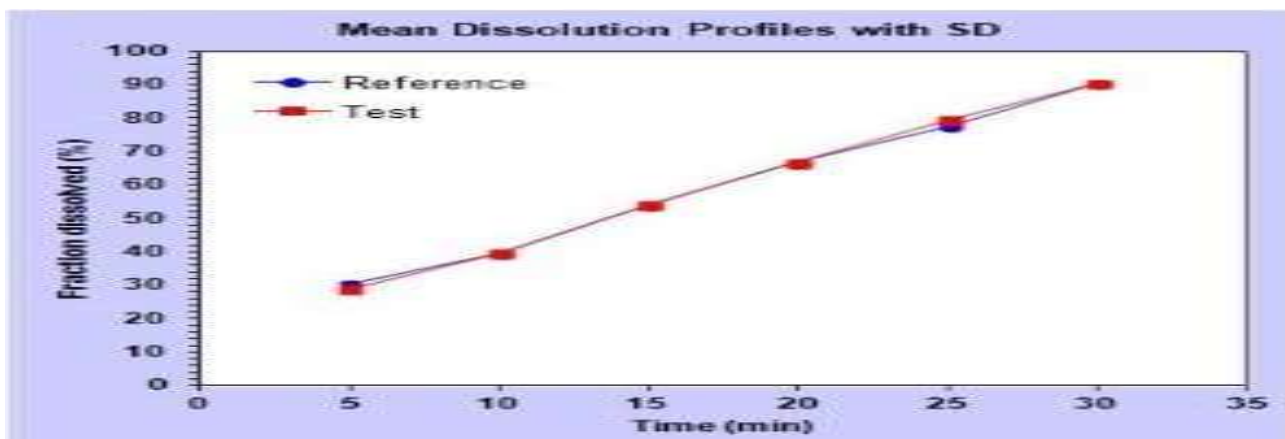
I

Figure 11: Similarity factor of SB compared with STARCH g) B1Vs B4; h) B2 Vs B5; i) B3 Vs B6



J

K



L

Figure 12: Similarity factor of SB compared with PVP j) B1Vs B7; k) B2 Vs B8; l) B3 Vs B9

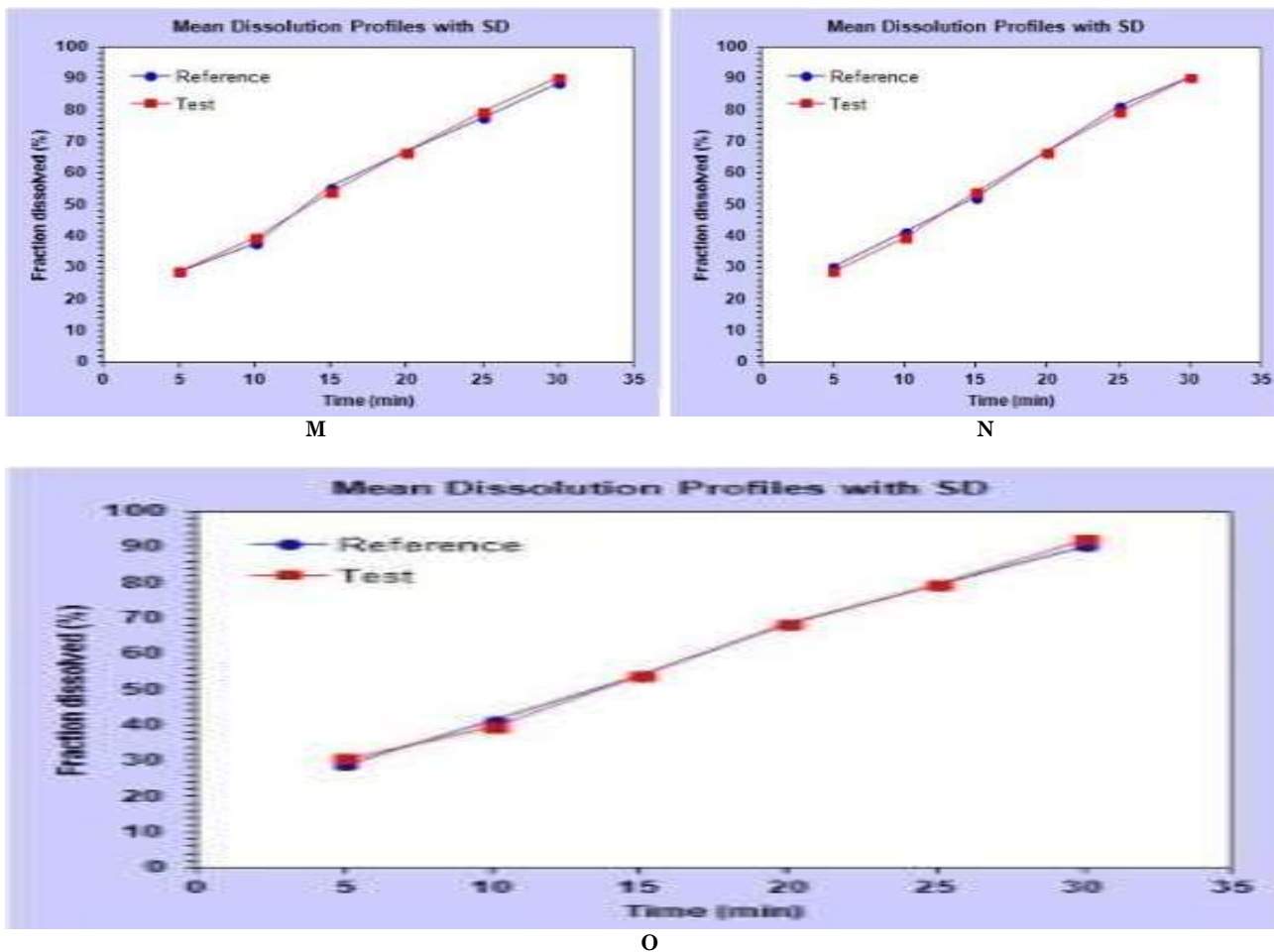


Figure 13: Rescigno index of SB compared with STARCH m) B1Vs B4; o) B2 Vs B5; p) B3 Vs B6

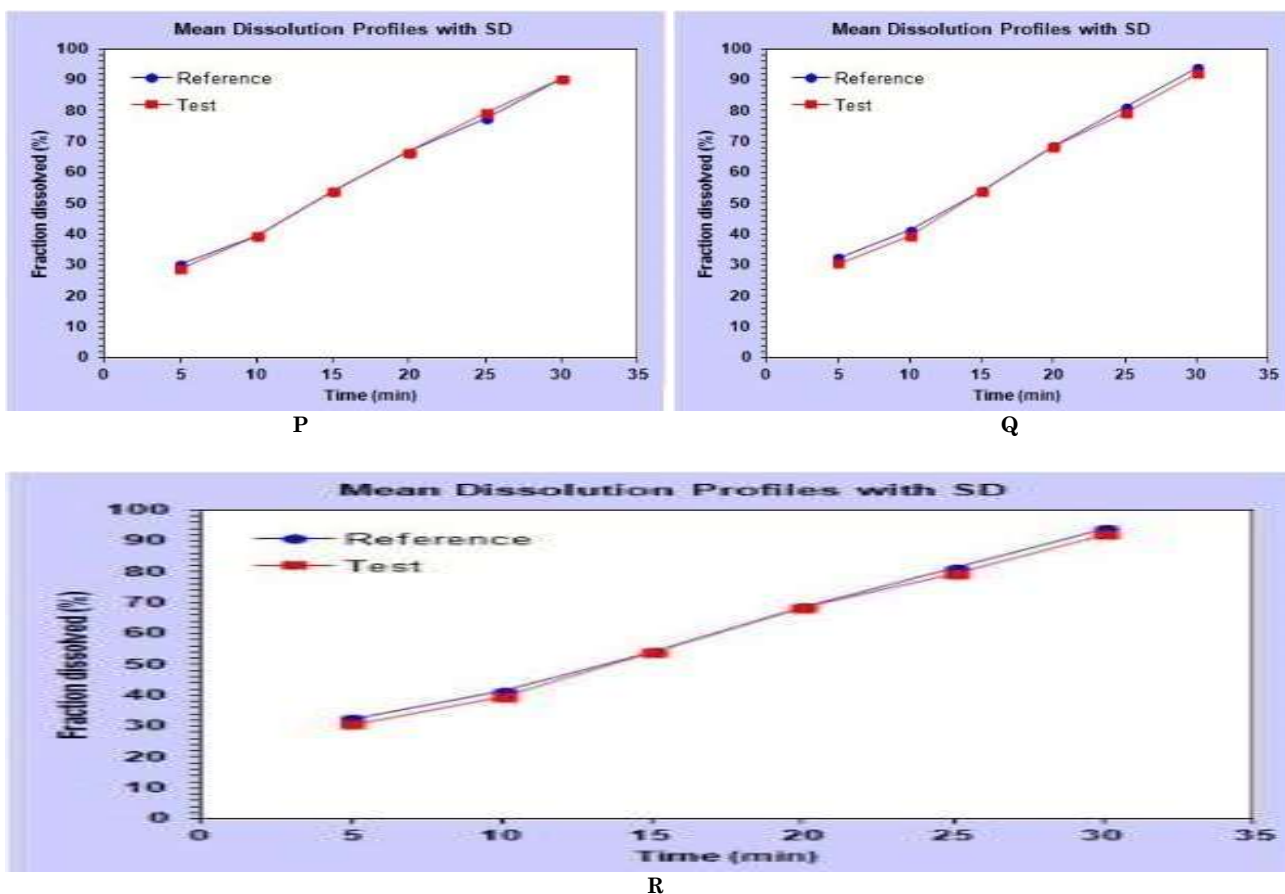


Figure 14: Rescigno index of SB compared with PVP p) B1Vs B7; q) B2 Vs B8; r) B3 Vs B9

Conclusion

On the basis of this research work, pectin

isolated from fruit of *Solanum betaceum Cav* shows excellent binding property when comparison with existing polymers. As pectin

is a natural substance isolated from the edible part using it as a pharmaceutical aid is safe and biocompatible. In future, the polymer characteristics can be studied for sustain release property and it may be used as a novel polymer in drug delivery system.

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