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FORMULATION AND EVALUATION OF PARACETAMOL TABLET TO ASSESS THE BINDING PROPERTY OF SWEET LEMON PEEL PECTIN

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ABSTRACT

The aim of present work was to extract pectin from dried as well as wet sweet lemon fruit peels to assess its binding property in tablets using paracetamol as a model drug. Firstly sweet lemon peel or its powder was subjected to simple water heating extraction method and pectin was isolated using ethanol as precipitating agent. Then after four batches were formulated using pectin in different proportions. Precompression and post compression studies were perform for each formulation. The results obtained for all precompression and post compression parameter were found within acceptable range of pharmacopoeias. On the basis of peel pectin can act as a excellent binder in dosage forms. Since it is of natural origin and sweet lemon peel available at low cost it may prove to be better binder over commercially used synthetic binders.

KEYWORDS: Binding property, Sweet lemon peel pectin, Simple hot water based extraction.

INTRODUCTION

In indian subcontiment the sweet lime (Citrus limettarisso), is commonly known as "Mosambi". It is best cultivated in India, China, southern Japan, Vietnam, Malaysia, Indonesia and Thailand and is native to Asia and. This fruit is eaten fresh or squeezed to make juice, it is rich source of vitamin C and replenish energy.[1,2]

Pectin mainly comprise of the partial methyl esters of polygalacturonic acid and their sodium, potassium, calcium, and ammonium salts. By the extraction in an aquous medium of approval plant material these salts are obtained. It is odourless or has slightly characteristic odour and occurs as a white to light brown powderor granular and.[3]

In the food, pharmaceutical and biotechnological industry pectin have more applicable. It comprise of non-sugar contituents, essentially meethonol, acetic acid, phenolic acid and occasionally amide groups.[4]

Commertial pectin are almost exclusively derived from citrus peel or apple pimac at prsent, both of which are by products of juice manufacturing units. 10-15% of pectin in Apple pomac contain on a dry matter basis. 20-30% of pectin contain by Citrus peel which is relatively higher compared to that of apples.[5] blood cholesterol levels reduced by consumption of pectin. Pectine is degrade in the large intestine and colon by microorganisms and liberate short-chain fatty acids that have positive effect on health.[6,7,8]

In an attempt to verify the use the use of pectin as polymer in dosage forms this research work was initiated. The scope of present work is to establish orange peel pectin as a binding agent against the commertially used one's like starch. For this purpose, paracetamol which is analgesic and antipyretic was selected as a model drug.

Botanical classification of Sweet lemon

Kingdom	:-	Plantae
Division	:-	Magnoliophyta
Class	:-	Dicotyledons
Sub class	:-	Sapindales
Order	:-	Rosidae
Family	:-	Rutaceae
Sub family	:-	Aurantoideae
Sub genera	:-	Papeda

Fig 1- Sweet lemon & its peel.

Synonyms

Citrus limetta is frequently known as sweet lime, sweet lemon and sweet limetta.and is called by different names in different parts of the world.

Geographical distribution

Mosambi fruit is also known as sweet lime. It is best cultivated in India, China, south Japan, Vietnam, Malaysia, Indonesia and Thailand and is native plant of Asia.

MATERIALS AND METHODS

Materials

Paracetamol (Acetaminophen) was taken as the drug. Lactose was used as diluent.The polyvinyl pyrrolidone (PVP), corn starch paste and gelatine solution (acacia mucilage) were the investigated binder materials. Magnesium stearate was used as lubricant. The corn starch is used as disintegrant and talk were used as glident. All these materials used were analytical grade.

Apparatus

Micro pipette, Electronic Balance, Heater, No.12 (710mm) and 60 meshes, Oven, Dissolution test station, Disintegration Test System, Tablet Hardness Tester, Friabulator, and UV/VIS spectrophotometer.[9]

EXTRACTION OF PECTIN

METHOD 1

In 0.01N HCl the fresh and dried lemon peels were digested separately for a period of 1.5 hours at temperature 80-90°C. Firstly 80g of peel was taken and added with 200 ml 0.01N HCl. The mixture was then heated maintaining the temperatiure at 80-90°C. The heated solution was cooled after 1.5 hours and then it was filtered through cloth and pressed the cloth to recover the extract from the solution. The Whattman No 3 filter paper was used for the further filtered extract by using funnel. To keep the total solution volume of 200 ml make up solvent upto the mark. Then 80 g peel was added to the 200 ml of solution it and then the same steps were repeated for five times to get a viscous solution of the extract. The 400g peel and 452 ml solvent were used to obtaine such solution. 0.01NHCl solution added nn order to keep filtrate volume constant, in each cycle. By adding absolute ethanol 95% of purity the pectin was precipitate in isopropanol and methanol in a ratio of 1:2 separately in different separating funnel to analysis the effect of precipitating agent. The precipitated pectin was separated after 2 hours and then filtered it. The precipitate of pectine was dried at 40°C in a vacuum oven.[10]

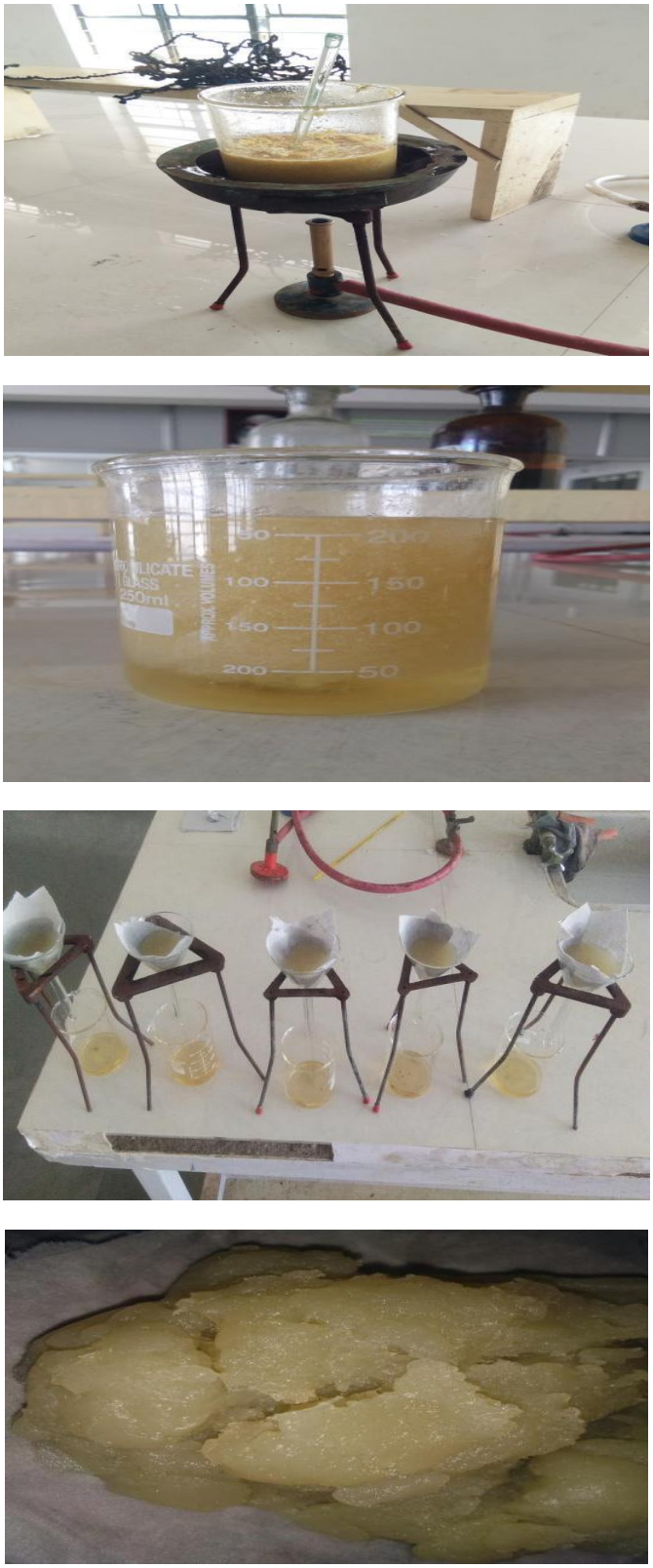

Fig.: Method of Extraction.

METHOD 2

The 100 gram dried peels were transferred separately into a beaker (1000mL) which contain 500mL of water and 2.5mL of HCL was added to give a pH of 2.2. Then each of the peel was boiled for 45 min separately. Thereafter, from the extracts the peels were removed by filtering through a filter paper. Then the cake was washed with 250mL boiled water and the combined filter allowed to cool at 25°C to minimize heat degradation of the pectin.

The extracted pectin was precipitated by adding 200mL 95% ethanol to 100mL of the extracted pectin was precipitated with thorough stirring. Then left for 30 min to allow the pectin float on the surface. Then the gelatinous pectin flocculants was then skimmed off. By washing in 200mL ethanol the extracted pectin was purified and then to remove the residual HCl and universal salt pressed on a nylon cloth. Then the resulting pectin was weighed and shredded into small pieces and was air dried (McGready 1996). Finally, by using a pestle and mortar and weighed using a digital weighing balance the dried pectin was further reduced into smaller pieces. Percentage yield of pectin from initial wet peels was then determined on both wet and dry weight basis.[11]

CHARACTERIZATION OF PECTIN

The dried pectin obtained from the peels of sweet lime was subjected to the following qualitative and quantitative test to characterize them.[12]

Qualitative tests

Colour- Done by visual observation;

Solubility of dry pectin in cold and hot water- The pectin samples (0.25%) were separatel placed in a conical flask with 10 ml of 95% ethanol added followed by 50 ml distilled water. Then the mixture was shaken vigorously to form a suspension which was then heated at 85-95°C for 15 min.

Solubility of pectin solution in cold and hot alkali- 1 ml of sodium hydroxide and 0.1 N NaOH was added to 5ml of pectin solution and then heated at 85- 90°C for 15 min;

Table 1: Qualitative test observation.

Parameters	Sweet lime pectin
Colour	Brown
Solubility in cold water	Dissolve vigorously after slightly shaking
Solubility in hot water	The mixture dissolves
Solubility of pectin solution in cold water	Suspension forms yellow precipitate
Solubility of pectin suspension in hot alkali	Suspension dissolve

Preparation of Tablets

Table 2: Preparation of Paracetamol tablets.[13] (About 20 tablets were prepared for each formulation).

Ingredients	Formulation 1	Formulation 2	Formulation 3	Formulation 4
Paracetamol	5gm	5 gm	5 gm	5 gm
Binder	0.2 gm	0.4 gm	0.6 gm	0.8 gm
PVP	0.6 gm	0.6 gm	0.6 gm	0.6 gm
Lactose	2.12 gm	1.92 gm	1.72 gm	1.52 gm
talc	0.08 gm	0.08 gm	0.08gm	0.08 gm

Preparation of tablets

Direct Compression Method

The term “direct compression” is defined as the process by which tablets are compressed directly from powder mixture of exipient and suitable excipients.[14]

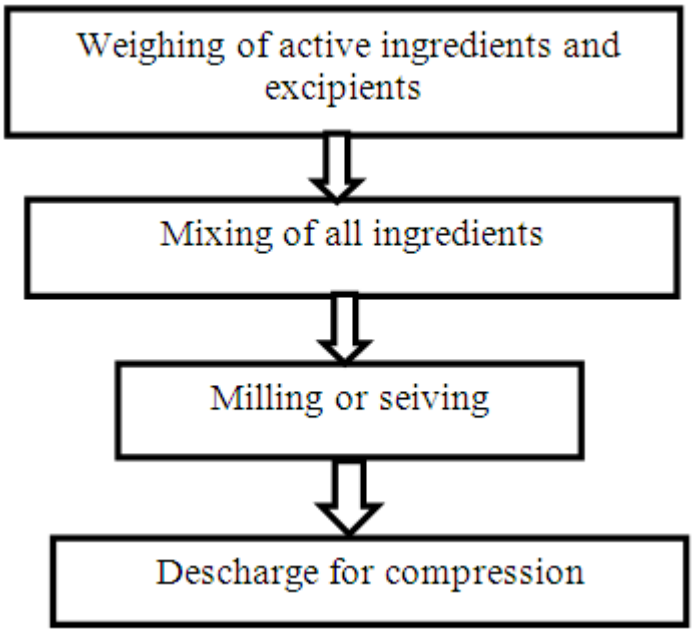

Fig 3: Direct Compression Method.

Merits of direct compression method

As compared to other Direct compression method is more efficient and economical process, because it involves only dry blending and compaction of exipient and necessary excipients.

Economical process is the most important advantage of direct compression method. Reduced processing time, reduced labor costs, fewer manufacturing steps, and less number of equipments are required, less process validation, reduced consumption of power.

Elimination of heat and moisture, thus increasing the stability and the suitability of the process for thermolabile and moisture sensitive API's.

Particle size uniformity.

Prime particle dissolution.

Each primary drug particle is liberated in case of directly compressed tablets after disintegration.

The chances of batch-to-batch variation are negligible, because the unit operations required for manufacturing processes is fewer.

Chemical stability problems for API and excipient would be avoided.

Provides stability against the effect of aging which affects the dissolution rates.

Evaluation Test

Weight variation test

The purpose of this test is to verify the uniformity of each batch which ultimately reflects the drug content uniformity in all the formulation batches. The test was performed as per the official procedure, 20 tablets were randomly selected and weighed individually and also average weight was calculated. The difference between average and individual weight was calculated, further %weight variation was calculated and compare with the USP limits.[15]

Fig 4: Weighing machine.

Friability test

Usually this test is performed to check possible wear and tear loss in tablet during the transportation and this is closely related to tablet hardness. Usually it is performed in the Roche Friabilator. The 10 tablets were selected randomly and their initial weight (W1) was recorded and after that these weighed 10 tablets were placed in the friabilator and for four minutes at 25 rpm speed and 100

revolutions, the friabilator was operated. The tablets were weighed again (W2) and the percent loss. The official permissible limit for friability is 1%.[15]

Fig. 5: Friability test apparatus.

Hardness test

Five tablets containing each sample were subjected for hardness tester and the crushing strength of the tablet was measured. The average hardness of the tablets was calculated and standard deviation was determined.

Fig. 6:- Monsantto hardness tester.

Disintegration test

Fig.7: Disintegration test apparatus.

Six tablets containing each sample were placed in disintegration apparatus, where the volume of disintegration medium was 900 ml of water maintained at 37±1°C. To break each tablet into small particles and pass through the mesh, the time taken was recorded and average time was calculated.

Dissolution test

A potassium phosphate buffer (pH 5.8) was prepared and the temperature was maintained at 37±1 oc throughout the experiment for all samples following the USP procedure. Then Samples were withdrawn after 5, 10, 15, 20, 30, 45 and 60 minutes and an equivalent amount of fresh buffer solution were immediately introduced as replacement. The samples were filtered and suitably diluted with 0.1 sodium hydroxide solutions and then assayed for the drug content by measuring the absorbance at 257 nm using UV-1800 spectrophotometer. Phosphate buffer was used as a blank and necessary correction was made for dilution when calculating for drug content. In addition, Dissolution profile of three brands was done using USP II apparatus with 50 rpm, 900ml of phosphate buffer and temperature of 37±1^{o}C.

Assay

For determination of the content of studied samples Standard preparation USP, HPLC method was used The Standard USP Acetaminophen was dissolved in a mobile phase [water: methanol (3:1 v/v)]

Assay preparation: 20 tablets were weighed for each sampl and a quantity of powder equivalent to 0.1g was transferred to 200 ml of volumetric flask. Then the 100 ml of mobile phase was added to the volumetric flask, the solution was then mechanically shaked for 10 minutes. By using mobile phase the resulting solution was diluted to volume, water: methanol (3:1). 5 ml of aliquot was transferred to 250 ml of volumetric flask and diluted to volume with mobile phase. After that solution was filtered.

Chromatographic Conditions: The chromatographic conditions for the HPLC analysis were Reverse phase HPLC using C-18 Column. Flow rate was set up at 1.5ml/min; Mobile phase: Water: Methanol (3:1); Injection volume 10 L and UV- Detector, 243nm.

RESULT

Weight variation test

Results obtained are given in Table 2. According to the ingredients composition in Table 1, According to the Table 2, it is clear that the all tablet samples complies from with the standard as the individual weight does not deviate from the mean (average value) more than permitted in terms of percentage. The difference in average weights is due to the type and the concentration of binders. PVP agglomerates the fine powder upon addition of alcohol as in the procedure and the tackiness aid to hold the individual granules together. So this strengthens the intergranular forces between granules as well as intragranular forces in each granule, resulting an increase in average weight. Average weights obtained for binders namely lactose and talc, were less than the expected weight.

Table 3: Effects of binder on weight of Tablets.

Tablet no.	Batch 1 % deviation	Batch 2 % deviation	Batch 3 % deviation	Batch 4 % deviation
1	0.39	0.39	0.41	0.39
2	0.39	0.41	0.41	0.41
3	0.38	0.41	0.39	0.41
4	0.39	0.41	0.39	0.38
5	0.39	0.39	0.37	0.39
6	0.41	0.38	0.38	0.39
7	0.41	0.39	0.37	0.38
8	0.40	0.39	0.39	0.41
9	0.37	0.39	0.39	0.41
10	0.39	0.39	0.39	0.39
Average	3.92	3.95	3.89	3.96

Table 4: Effects of binder on Friability.

Batch No.	Before reading	After reading
Batch 1	0.41	0.38
Batch 2	0.39	0.37
Batch 3	0.44	0.39
Batch 4	0.44	0.40

Effect of Binder on Disintegration Time

Disintegration times obtained for four formulations were 13 min, 6 min and 8 min, 10 min respectively, and were compatible with the trend of the values obtained for average weight and hardness. Also they remain below 15 min. So the values are technically and theoretically acceptable. Disintegration time is concerned, binder appear to be good for paracetamol tablet formulation.

Table 5: Effect of Binder on Disintegration Time.

Batch No.	TIME
Batch 1	13 min
Batch 3	8.0 min
Batch 4	10 min

Effects of binder on the tablet hardness

Tablet with talc also gave a fairly high value for hardness test. Hardness of tablets depends on the degree of binding which relies on the amount of the binder and the compression force. Higher hardness in tablet with PVP can be related to its film formation ability and its cohesive strength to make solid bonds between particles. Thus, it was reported that binders with plasto elastic properties undergo deformation under high compression pressure. As a result, binder is forced into the interparticulate spaces resulting more solid bond between granules.[6] This would be the reason to have higher hardness for tablet with binder.

Table 6: Effects of binder on the tablet hardness.

Formulation	Hardness
Batch 1	8
Batch 2	7.5
Batch 3	8.5
Batch 4	8.5

Table 7: Effect of Binder on Dissolution Rate of Tablet

Time (min)	%Release of Drug Content			
	F1	F2	F3	F4
10	0.250	0.215	0.883	0.305
20	0.244	0.202	0.340	0.294
30	0.237	0.194	0.321	0.277
40	0.230	0.183	0.318	0.247
50	0.222	0.165	0.308	0.235
60	0.215	0.118	0.292	0.228

Dissolution studies of paracetamol tablet in Distil Water

Dissolution Test

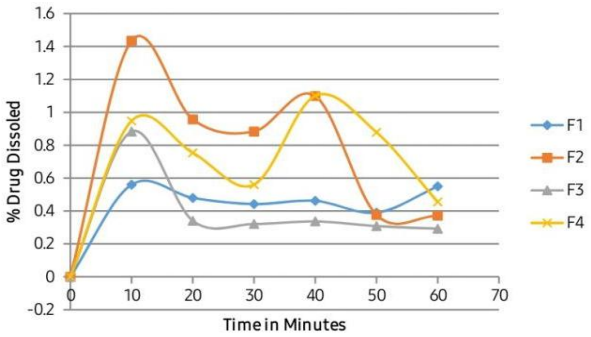

Fig. 8: Calibration curve of paracetamol tablets.

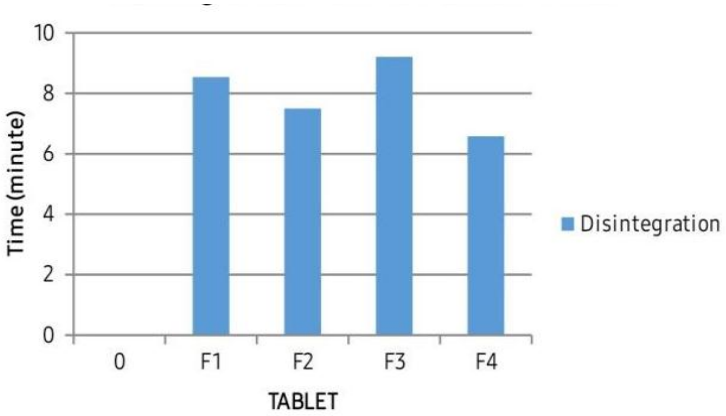

Fig. 9: Disintegration curve of paracetamol tablet.

CONCLUSION

Simple water base heating method is an efficient method for extracting pectin from sweet peel. Also, a major conclusion can be derived on the basis of above experiment that sweet lemon peel pectin which is a polymer of natural origin, has immense potential to replace the commercially existing polymers used as binders in tablet dosage forms.

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