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Formulation and evaluation of ibuprofen tablets using orange peel pectin as binding agent

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ABSTRACT

The aim of present study was to extract pectin from dried orange fruit peels and assess its binding property in tablets using ibuprofen as a model drug. Extraction of pectin was carried out by microwave assisted extraction technique and pectin was isolated using acetone as a precipitating agent. Three different batches of tablets were formulated using pectin in different proportions (10, 20, 30 mg) and to compare the binding property of pectin, a reference batch was also formulated using starch as a binding agent instead of isolated pectin. Pre-compression and post-compression evaluation studies were performed for all formulations and found to be within the range as prescribed in the pharmacopoeias. Friability and disintegrating time of formulation F3 (30 mg of pectin) showed better results when compared to other formulations. In vitro dissolution studies revealed that formulation F3 containing 30 mg of pectin showed 82 % drug release which was almost similar to that of the reference batch F4 (85 %) containing same amount of starch as a binding agent. In vitro drug release kinetics of all the four batches followed korsmeyer-peppas model. In view of better friability, hardness, disintegration time and drug release properties of the pectin formulation, orange peel pectin can serve as an excellent binder in tablet dosage form.

Key Words: Binding property, Microwave assisted extraction technique, Orange peel pectin and Release kinetics.

INTRODUCTION

Pharmaceutical excipients plays a major role in drug formulations from processing aids that increase lubricity, enhance flowability, and improve compressibility and compatibility to agents that impart a scientific functional property to the final product[1]. Pectin is a structural heteropolysaccharide contained in the primary cell walls of terrestrial plants. Apple, quince, plume, gooseberry, oranges, cherries and grapes contain pectin. It is essential component in the initial growth and in the ripening process and has been found to be useful in area of drug delivery[2]. Pectin mainly consists of partial methyl esters of polygalacturonic acid and their sodium, potassium, calcium and ammonium salts. Pectin occurs as a white to light brown powder

or granular, and is odorless or has slightly characteristic odor[3]. The synthetic polymers used as excipients have many disadvantages such as high cost, toxicity, non-biodegradability and environmental pollution caused during their synthesis. Natural polymer like pectin is easy to isolate and purify, it is non-toxic and biocompatible. Pectins have been used in food industry but recently they are being explored for their other pharmaceutical applications such as binding, thickening, suspending properties. For this study, ibuprofen a non-steroidal anti-inflammatory drug was selected as a model drug, which is a propionic acid derivative used in the treatment of rheumatoid arthritis and osteoarthritis[4].

MATERIALS AND METHODS

All the chemicals and reagents used were of high quality analytical grade.

Extraction of pectin

Extraction of pectin from dried orange fruit peel was carried out by microwave assisted extraction technique[5]. 25 g of dried orange peel was cut into small pieces and soaked in 200 ml of distilled water for 2 h in a 1000 ml beaker. Its pH was adjusted to 4.5 by using 10 % tartaric acid solution and subjected to microwave irradiation at 160 W for 10 min. It was then filtered while hot; filtrate was cooled and poured into a beaker containing 600 ml of acetone to precipitate out pectin. The precipitated pectin was then separated by vacuum filtration and washed with acetone to make the pectin free from acidic ions. Pectin thus obtained was completely dried at 37º Cin a hot air oven. The dried pectin was then powdered and passed through sieve no # 60 and weighed. To confirm its identity, the pectin was subjected to various chemical tests. The process was repeated several times to extract more pectin.

Drug excipient interaction

FTIR spectra of pure drug, polymer (pectin), physical mixture of drug and polymer were obtained in KBr pellets at moderate scanning speed between 4000-400 cm^{-1} using a Shimadzu FTIR 1601 PC.

Preparation of tablets

Tablets were prepared by using wet granulation technique. The formula for single tablet per batch required to prepare 600 mg of ibuprofen tablets is given in Table1. Required quantity of drug, binder, disintegrant and diluents were grinded and passed through sieve no # 40 separately and then mixed uniformly by using water as granulating agent to get a wet dough mass which was screened through sieve no # 16 to obtain coarse granules and dried at 45 ºC for 1 h.

Table 1: Formula used to prepare tablet of Ibuprofen

S. No	Ingredients	Formulations			
		F1(mg)	F2(mg)	F3(mg)	F4(mg) (Ref)
1	Ibuprofen	400	400	400	400
2	Polyvinyl pyrollidone	30	30	30	30
3	Pectin	10	20	30	-
4	Starch	-	-	-	20
4	Di calcium phosphate	153	143	133	143
5	Talc	5	5	5	5
6	Magnesium stearate	2	2	2	2

Weight of each tablet = 600 mg

The dried granules were then passed through sieve no # 20 to obtain uniform sized granules. Required quantities of glidant and lubricant was added to the granules and mixed uniformly. The resultant granules were compressed into tablets by using single punch rotary compression machine. To compare the binding property of pectin, controlled tablets were prepared using starch as binding agent instead of isolated pectin[6].40 tablets were prepared for each batch and stored in an air tight container for further studies.

Evaluation of granules

The prepared granules were evaluated for all pre-compression parameters like bulk density, tapped density, bulkiness, hausner's ratio, compressibility index and angle of repose. The evaluation was carried out using the methods prescribed in pharmacopoeias[7],[8],[9].

Evaluation of compressed tablets

Weight Variation:

Randomly selected 20 tablets were weighed individually and together in single pan balance. The average weight was noted and standard deviation was calculated. The tablet passes the test if not more than two tablets fall outside the percentage limit[10]. Weight variation test for tablets of all the batches were carried out as per IP (the weight variation limit is ± 5 %).

Friability[11]**:**

Friability test was carried out by Roche friabilator with readings in triplicate. Preweighed 10 tablets were allowed for 100 revolutions in 4 min and were dedusted. The percentage weight loss was calculated by reweighing the tablets. The percentage friability was then calculated by:

$$F = \frac{W\,[initial] - W\,[final]}{W\,[initial]} \times 100$$

Hardness[12]**:**

The Monsanto hardness tester was used to determine the tablet hardness. The tablet was held between affixed and moving jaw. Scale was adjusted to zero; load was gradually increased until the tablet fractured. The value of the load at that point gives a measure of the hardness of the tablet which was expressed in kg/cm^2.

Thickness:

The thickness of prepared tablets was determined using vernier caliper and the results were expressed as mean values of 10 determination.

Drug Content:

Ten tablets were weighed and powdered and 400 mg equivalent weight of ibuprofen was accurately weighed and transferred into a 100 ml volumetric flask. It was dissolved and made up the volume with phosphate buffer pH 7.4. Subsequently the solution in volumetric flask was filtered and suitable dilutions were made and analyzed at 223 nm using UV-Visible spectrophotometer (Shimadzu UV-1601). The drug content of each sample was estimated from standard curve of ibuprofen using phosphate buffer pH 7.4.

Disintegration test:

The USP device to test disintegration was six glass tubes that are 3 long, open at the top and held against 10 screen at the bottom end of the basket rack assembly. One tablet is placed in each tube and basket rack is positioned in 1 liter beaker of distilled water at 37± 2ºC, such that the tablets remain below the surface of the liquid on their upward movement and descend not closer than

2.5 cm from the bottom of the beaker. Suspend the assembly in the beaker containing water and operate the apparatus for 15 min. remove the assembly from the liquid. The tablets pass the test if all of them have disintegrated.

***In Vitro* Drug Release Studies:**

In vitro drug release was studied using Electrolab Dissolution Apparatus (8 basket) taking 900 ml phosphate buffer pH 7.4 as a dissolution medium maintained at 37 ± 1 ºC for 5 h at 50 rpm. 2ml of sample was withdrawn and diluted to 50 ml with phosphate buffer pH 7.4. Samples were analyzed spectrophotometrically at 223 nm and the percentage drug release was calculated[11].

RESULTS AND DISCUSSION

Pectin was extracted by microwave assisted extraction technique and 740 mg of pectin was obtained from 25 g of dried orange fruit peel. Microwave assisted extraction methods require shorter time and less solvents with higher extraction rate and better products of lower costs. The drug-excipient interaction study was carried out by FTIR spectroscopy revealed that there was no interaction between the drug and orange peel derived pectin as there was no significant shift in the principle peaks of ibuprofen, shown in Fig.1.

Fig.1: IR spectra

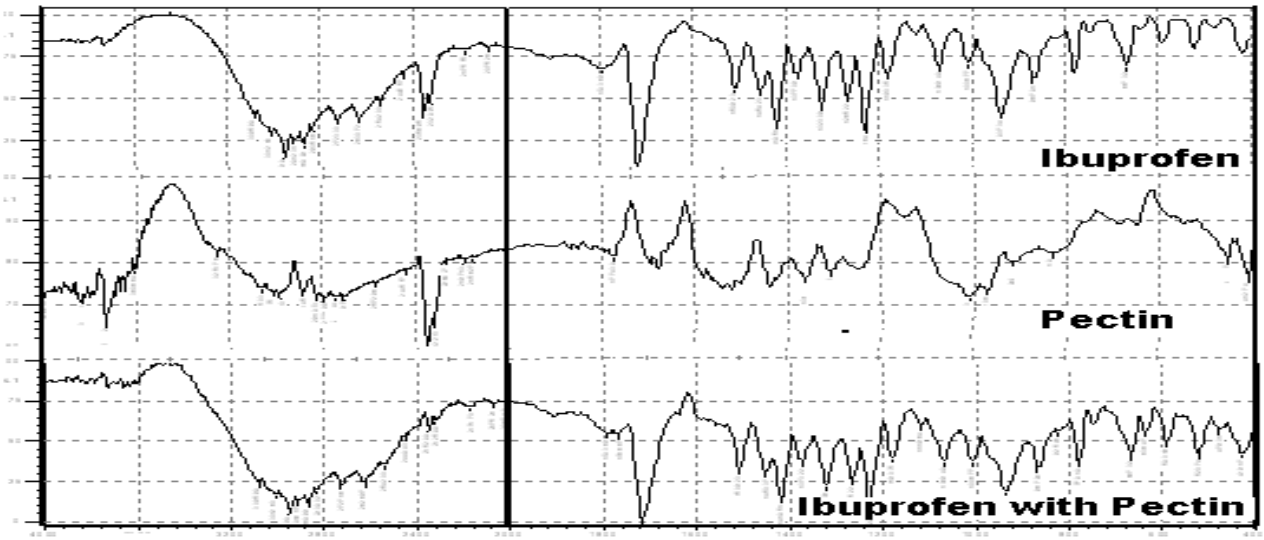


Table 2: Pre-compression properties of granules

S.No	Properties	Formulations			
		F1	F2	F3	F4
1	Weight of the granules(g)	23.6	22.9	23.5	23.2
2	Bulk density(g/cc)	0.3477	0.3447	0.3357	0.3329
3	Tapped density(g/cc)	0.4095	0.395	0.3916	0.3873
4	Bulkiness (cc/g)	2.876	2.9010	2.9788	3.0039
5	Carr's index	15.0915	12.7341	14.2747	14.0459
6	Hausner's ratio	1.1777	1.1459	1.1665	1.1634
7	Angle of repose				
	Without glidant	31º.45'	33º.13'	33º.69'	32º.17'
	With glidant	29º.54'	31º.95'	32º.13'	30º.76'

Granular properties such as bulk density, tapped density, bulkiness, Carr's index, hausner's ratio and angle of repose were studied for all the formulations. The results obtained from these studies of different batches showed not much difference in their values which was shown in Table 2. The values of micromeritic studies ranged within the acceptable limits.

The prepared tablets were evaluated for post compression parameters such as weight variation, hardness, friability, thickness, drug content determination, disintegration and *in vitro* drug release studies as shown in Table 3. The weight variation among all the different batches of tablets ranged between 0.59-0.61 g of which is within the permissible limit (± 5%). Hardness, friability and disintegration time of all the batches showed least variation and found to be within the pharmacopoeial limits.

Table 3: Post-compression evaluation parameters of tablets

S.No	Parameters	Formulations			
		F1	F2	F3	F4
1	Weight variation(g)	0.6035 ± 0.02	0.603 ± 0.02	0.605 ± 0.02	0.599 ± 0.02
2	Friability (%)	0.3972	0.2976	0.1998	0.3006
3	Hardness (kg/cm^2)	5.66	5.73	5.86	5.66
4	Thickness (mm)	3.55	3.46	3.66	3.71
5	Drug content (mg)	390	394	400	394
6	Disintegration time (min)	13	14	14	14
7	*In vitro* percentage drug release	95.34	89.24	82.27	85.56

The *in vitro* drug release studies (Fig.2) was performed for a period of 5 hr using pH 7.4 phosphate buffer and it was observed that F3 showed 82 % drug release which is almost similar to the reference batch F4(85 %) . By using PCP-Disso.V3 software various models such as zero order kinetics, first order kinetics, higuchi and korsmeyer-peppas were applied to determine the kinetics of drug release from the prepared formulations. As per the data obtained from the applied kinetics it can be easily seen that all the formulations showing same release kinetics even in varying the concentration of polymer (pectin). All the four different formulations including the reference batch followed korsmeyer-peppas model and the values of correlation co-efficient for all the formulations were shown in Table 4. Release kinetics of F3 (30 mg of pectin) shown in Fig.3. From the data it can be inferred that pectin at higher concentration (30 mg) has a better binding property than at lower concentration as that of starch. Thus orange peel pectin having an excellent binding capacity, which could be exploited on commercial scale, as possessed all the requisite qualities of a binding agent.

Table 4: The regression-coefficients and rate constants for release of ibuprofen tablets

Form. Code	Zero order		First order		Higuchi matrix model		PeppasKorsmeyer		Hixon Crowell	
	R	K	R	K	R	K	R	K	R	K
F1	0.9703	18.4414	0.7929	-0.5728	0.8636	33.8320	**0.9745**	9.392	0.8863	-0.1145
F2	0.9963	18.6421	0.9060	-0.4216	0.9219	34.8090	**0.9974**	15.217	0.9552	-0.1015
F3	0.9923	17.2715	0.9419	-0.3324	0.9110	32.1430	**0.9952**	12.851	0.9673	-0.0865
F4	0.9924	17.5589	0.9450	-0.3428	0.9151	32.7376	**0.9945**	13.942	0.9688	-0.0887

Fig.2: *In vitro* dissolution profiles of different formulations

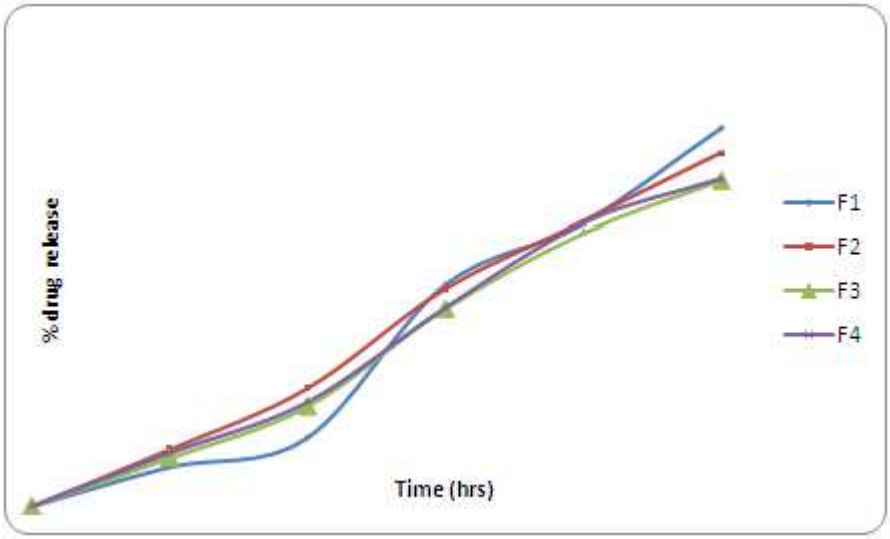
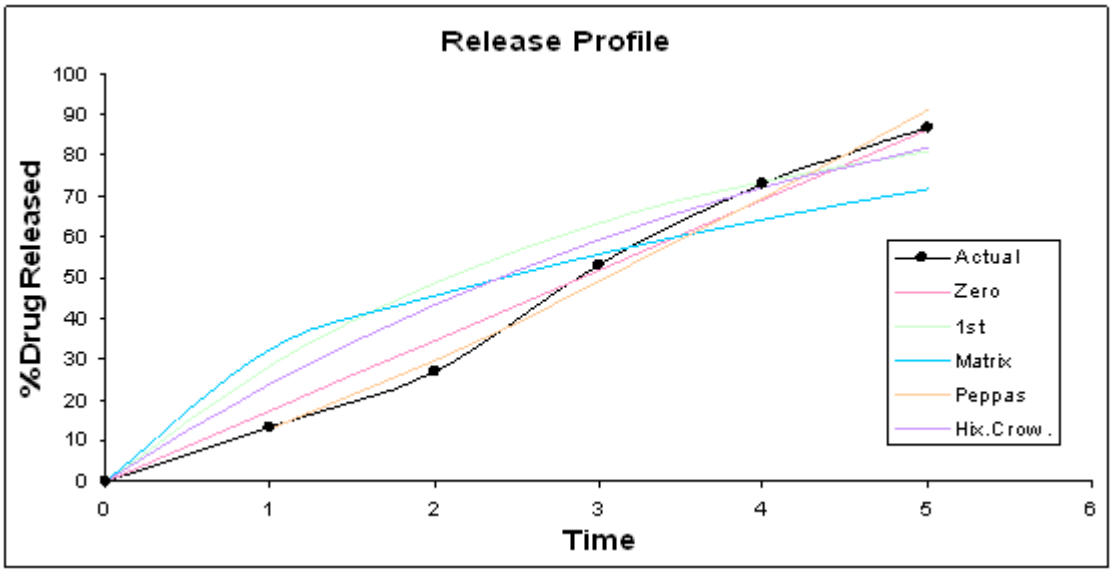


Fig.3: Release kinetics of F3 (30 mg of pectin)



CONCLUSION

Microwave assisted extraction technique is an efficient method for the extraction of pectin from orange peel. As per the results obtained by this study, it can be concluded that orange peel pectin, a natural polymer having an excellent binding property at slightly higher concentration could be employed as a main ingredient in tablet dosage form.

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