

A Comprehensive Study on Fast Dispersible and Slow-Releasing Characteristic of Orange Peel Pectin in Relation to Established Synthetic Polymer

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ABSTRACT

Introduction: In the present work, the method to extract, isolate, and characterize orange peel pectin using soxhlation, and thereafter, the use of this polymer-polymer in the formulation of fast dispersible and slow-releasing tablet has been studied. Thereafter, the evaluation and comparison of fast dispersible/slow-releasing tablets using orange peel pectin versus prepared using sodium starch glycolate (SSG) were carried out. **Materials and Methods:** In the present investigation, extraction methodology was employed for isolation of pectin from orange peels. Four different batches with each polymer were prepared with varying concentration of superdisintegrant and bulking agent using diclofenac sodium as model drug. Diclofenac sodium stands as easily available, cheap, and good candidate to demonstrate disintegrant property. The formulation involved wet granulation method for the preparation of tablets of each batch. The tablets were evaluated for hardness, friability, thickness, wetting time, deaggregation time, and *in vitro* release characteristic data.

Results: It was observed that parameters for batch O2* were comparable with that of synthetic superdisintegrant. This batch gave around 92.12% drug release in period of 90 min. The study showed that orange peel pectin could be a potential candidate for formulation of orodispersible dosage forms in competence to SSG, which is established superdisintegrant.

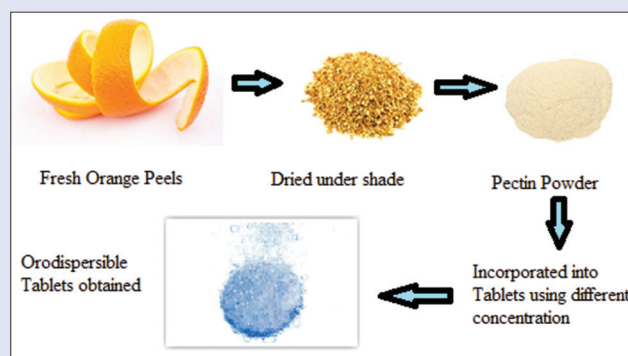
Conclusion: The results led to the conclusion that the use of natural polymers in formulation of pharmaceutical dosage form can be put into practice on industrial scale meeting the similar requirements as done by synthetic polymers.

Key words: Fast dispersible, novel drug delivery system, sodium starch glycolate, soxhlation, superdisintegrant

SUMMARY

- The present work aims to demonstrate and establish the use of naturally derived polymer, i.e., orange peel pectin as a superdisintegrant. The extraction

methodology has been discussed followed by comparative analysis with a synthetic polymer.



Abbreviations used: O1–O2: Batches Containing Orange peel pectin, S1–S2: Batches containing SSG, SSG: Sodium starch glycolate, NDDS: Novel drug delivery system.

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INTRODUCTION

Fast dispersible/slow-releasing drug delivery systems are rapidly gaining acceptance as an important novel drug delivery technology. By various cited works over the past few years, tablet disintegration has received considerable attention as an essential step in obtaining fast drug release.^[1-3] Dispersible tablets are intended to dissolve or disintegrate rapidly in the mouth for which various natural and synthetic disintegrants, are included in the formulations as also reported in literature.^[4] Pectins of natural origin are preferred over semi-synthetic and synthetic substances because they are comparatively cheaper, abundantly available, nonirritating, and nontoxic in nature. The extraction of pectin at laboratory scale makes the whole process cheaper and affordable in comparison to synthetic polymeric systems. The advantage of fast dissolving and slow-releasing tablets as a new type of solid dosage form has been widely recognized since the term “oro-dispersible tablet” appears in the European Pharmacopoeia (Suppl. 4.1, IV Ed.), which

defines it as “uncovered tablet for buccal cavity, where it disperses before ingestion.”^[5] Interestingly, these tablets display a fast and spontaneous deaggregation in the mouth, soon after the contact with saliva, though they can be handled or extracted from the package without alteration. In this case, active moiety can rapidly dissolve in the saliva and so absorbed through buccal mucosa. To fulfil this requirement, pectin is used as polymer which is highly soluble in water so release of drug can

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be easily achieved. It has already been demonstrated that freeze drying, sublimation, molding, or direct compression are general techniques which can be used to prepare this type of tablets. This is supported by the previous researches.^[6] Scientists have reported the use of Diclofenac sodium as model drug.^[7] Diclofenac is a nonsteroidal anti-inflammatory drug taken to reduce inflammation and acts as an analgesic reducing pain in conditions such as arthritis or acute injury. It can also be used to reduce menstrual pain, dysmenorrhea. Diclofenac is available as a generic drug in a number of formulations, and it is over the counter use is approved in some countries for minor aches and pains and fever associated with common infections.

Orodispersible tablets make a good market due to their quick onset of action as compared to conventional dosage forms. The aim of the present work is to find out whether equally effective natural polymers such as pectins derived from fruit waste could be envisaged as competent disintegrating polymer.

MATERIALS AND METHODS

Orange peel was obtained from a juice shop of Lucknow. Diclofenac sodium was obtained as a gift sample from Alkem Laboratories, Baddi, Himachal Pradesh. The materials used include cellulose microcrystalline (fine powder), talc, and magnesium stearate (Rankem Limited, New Delhi).

Isolation of pectin

Dried orange peel powder was used for extraction. The extraction was carried out using Soxhlet apparatus. Weighed quantity of powder was taken. The water to be used for extraction was acidified using 0.5N citric acid and pH was maintained around 2. The content in the round bottom flask contained acidified water and was heated continuously at 75°C for around 7–8 h after the start of first siphon cycle. The proportion of powder to solvent was taken in ratio 1:8. After the heating period was over the mixture was passed through two-fold muslin cloth and was cooled to room temperature. A volume of 400 ml of ethyl alcohol was added to the solution with continuous stirring for 15 min. The mixture was kept for 2 h without stirring. Pectin was precipitated and filtered through four layered muslin cloth. The precipitate was washed 2–3 times by 600 ml of ethyl alcohol, to further remove any impurity remaining. Finally, precipitate was subjected to drying at 35°C–40°C in hot air oven, sieved (no. 80), and stored in desiccator until use.

Preparation of tablets

The formula for the evaluation of disintegrating property of extracted pectin was designed as per Table 1. The preparation of tablets was carried out into two different steps as follows:

Granulation

Weighed quantity of diclofenac sodium, orange peel pectin, microcrystalline cellulose, talc, and magnesium stearate was added according to formula of four batches individually. According to the formula all the ingredients were mixed with the help of mortar and pestle, with distilled water being used to form a wet mass. The wet mass was passed through sieve no. 20 to prepare granules. Granules of all

batches were dried at 45°C for 5 h and stored in air dried packets for further evaluation study.

Compression

Defined amount of granules was used to prepare tablets all batches. Powder was compressed using a single punch tableting machine (Cadmach Machinery Co. Pvt. Ltd., India) equipped with 8 mm punch at 0.4 ton pressure.

Technological parameters

All prepared matrix tablets were evaluated for weight variation as per USP XXIV monograph.^[8] Twenty tablets of each batch were used to evaluate weight variation among tablets, and standard deviation was calculated. To assess the friability parameters, tablets of all batches were used to evaluate friability as per USP XXIV monograph. Friability testing was done by Roche friabilator (Model: PX/FTA-902) with triplicate readings. One of the major parameters into consideration was hardness of the tablets. It was determined for all batches using Electrolab digital force gauze Hardness tester. The test was carried out in triplicate for all batches as per USP XXIV monograph for uncoated tablets. Thickness was measured by Verniers caliper as per USP XXIV monograph. The readings were carried out in triplicate and average value was noted.

Wetting and deaggregation time

Tablets of all batches were placed in petri dish (10 cm in diameter) containing 10 ml water at room temperature. The wetting time is that necessary for the complete wetting of the tablet. This test was carried out in triplicate.

The deaggregation test was performed according to the methods described in European Pharmacopoeia IVth edition. The deaggregation time is the time required for a tablet to turn into small fragments, when immersed in water at room temperature, without stirring.

Drug content

In accordance with the cited works,^[9] tablets were powdered, and 50 mg equivalent weight of Diclofenac sodium in tablet powder was accurately weighed and transferred into a 100 ml volumetric flask. Initially, 10 ml of phosphate buffer (pH6.6) was added and shaken for 10 min then, the volume was made up to 100 ml with buffer. Subsequently, the solution in volumetric flask was filtered, and 1 ml of the filtrate was diluted and analyzed at 276 nm using ultraviolet (UV)-visible spectrophotometer (Shimadzu UV-2450, Japan). The drug content of the each sample was estimated from their standard curve was prepared.

In vitro dissolution study

The dissolution test was performed at 37°C using the paddle method at 100 rpm with 900 ml phosphate buffer (pH 6.6) as a dissolution medium. For this digital tablet, dissolution test apparatus (Lab India Disso 2000, India) was used. At predetermined intervals, 5 ml of the medium was sampled and filtered. The filtrate was analyzed by UV/visible variable wavelength spectrophotometer at 276 nm.

RESULTS

Among physical parameters, hardness of the tablets ranged from 16.7 ± 0.02 (O4) to 29.20 ± 0.02 (O1) in case of orange peel pectin as disintegrant and between 19.90 ± 0.02 (S3) and 26.30 ± 0.03 (S1). The hardest tablet was found for batch O1 in case of orange peel pectin as disintegrant. The weight variation, friability, and thickness values of all the fabricated tablets, in reference to average values for each parameter, were found within the official limits for both the disintegrants. As the concentration of natural polymer increased,

Table 1: Formula for different batches using two different polymers

Formulation/ ingredients	Drug (mg)	Disintegrant* (mg)	MCC (mg)	Talc (mg)	Magnesium stearate (mg)
Batch 1	50	5	135	6	4
Batch 2	50	10	130	6	4
Batch 3	50	15	125	6	4
Batch 4	50	20	120	6	4

*Orange peel pectin/sodium starch glycolate. MCC: Microcrystalline cellulose

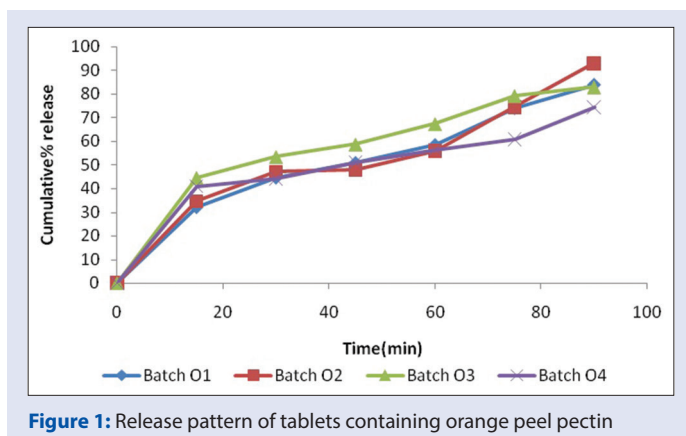
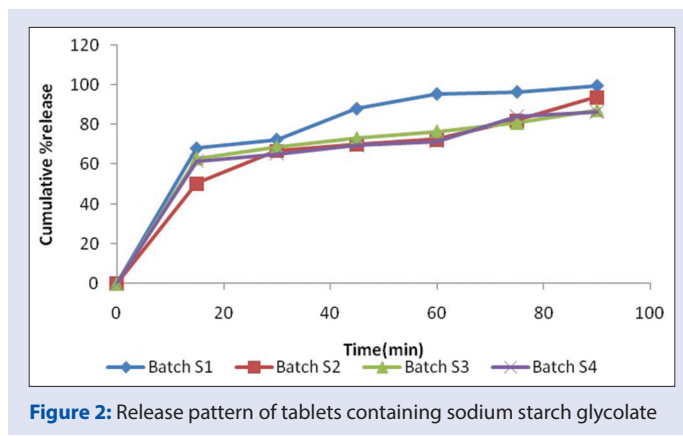

Figure 1: Release pattern of tablets containing orange peel pectin

Figure 2: Release pattern of tablets containing sodium starch glycolate

Table 2: Physical parameters of tablets formulated with orange peel pectin

Parameters	Batch O1	Batch O2	Batch O3	Batch O4
Weight variation (mg)	201.3±0.92	199.8±0.53	199.6±0.84	200.8±0.09
Friability (%)	0.08±0.01	0.08±0.05	0.10±0.04	0.13±0.03
Hardness (n)	29.20±0.02	21.0±0.02	20.10±0.03	16.7±0.02
Thickness (mm)	2.73±0.03	2.69±0.02	2.70±0.02	2.70±0.02
Wetting time (s)	110	150	160	180
Deaggregation time (s)	112	160	165	190
Drug content (mg)	46.81	43.78	28.75	31.76
Disintegration (min)	18.02	22.81	28.63	30.74

Table 3: Physical parameters of tablets formulated with sodium starch glycolate

Parameters	Batch S1	Batch S2	Batch S3	Batch S4
Weight variation (mg)	200.6±0.92	201.3±0.08	200.1±0.09	199.8±0.10
Friability (%)	0.06±0.02	0.05±0.08	0.05±0.05	0.15±0.06
Hardness (n)	26.30±0.03	22.80±0.02	19.90±0.02	18.50±0.03
Thickness (mm)	2.52±0.0114	2.53±0.03	2.50±0.02	2.51±0.0114
Wetting time (s)	109	95	100	90
Deaggregation time (s)	111	97	103	94
Drug content (mg)	40.78	46.81	37.78	31.75
Disintegration (min)	6.71	8.63	9.52	11.00

swelling index also increased. The drug content in all the batches of two formulations was quite uniform. The comparative data have been tabulated in Tables 2 and 3.

Deaggregation time for batches with orange peel pectin ranged from 112 to 190 s. whereas in case of sodium starch glycolate (SSG) as superdisintegrant, it ranged from 97 to 111 s. *In vitro* dissolution study when carried out at pH 6.6 reveals that batch O₂ gives best release of 92.12% in 90 min study in comparison to batch S1 with cumulative percentage release of 99.47%. The comparative release graphs of orange peel pectin and SSG among their various batches are indicative of the release pattern [Figures 1 and 2].

It was also found that batch O₂, which consisted of 10 mg of orange peel pectin as disintegrant exhibited a fast dispersible and slow-releasing effect as compared to other batches. It released 92.12% drug with disintegration time of 22.81 min. Except batch S1, all the batches of SSG gave lesser release than formulations prepared with orange peel pectin.

DISCUSSION

Relative study of physical parameters of tablets of each batch of orange peel pectin reveals that the tablets compressed using SSG as disintegrant were quite harder thus can be easily handled. The

direct relationship was observed between swelling index and gum concentration for orange peel pectin when used as disintegrant. It was noticed that when orange peel pectin was used as disintegrant, swelling index increased which may be probably due to water absorption capacity of the polymer. Equivalent ranges of deaggregation time show also illustrates that water uptake capacity of orange peel pectin are significant. Water uptake capacity is attributed to faster uptake of water due to the porous structure formed thus facilitating the disintegrant to bring faster disintegration. The *in vitro* release study illustrates that batch O₂ shows lesser release than S1 but, it can be concluded on the basis of all posttableting parameters that naturally obtained Orange peel pectin (OPP) stands as a good candidate to act as disintegrant, and it is possible to design promising fast dispersible/slow-releasing tablet using this polymer.^[9-19]

CONCLUSION

Overall, the results suggest that fast dispersible/slow-releasing tablets can suitably be formulated and comparative study of various parameters clearly states the fact that the naturally obtained orange peel pectin can be used as a good candidate to act as disintegrant though not as stronger as synthetic SSG and it is possible to design promising fast dispersible/slow-releasing diclofenac sodium tablet.

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Conflicts of interest

There are no conflicts of interest.

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