JOURNAL OF NATURAL REMEDIES
DOI: 10.18311/jnr/2024/43884

RESEARCH ARTICLE

Formulation and *In Vitro* Evaluation of Aceclofenac Orally Disintegrating Tablets using the Natural Superdisintegrants

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Abstract

Background: Oral disintegrating tablets are engineered to dissolve in saliva extremely quickly, typically within a matter of seconds. **Aim:** The aim of the research was to develop and assess aceclofenac Oral Disintegrating Tablets (ODT) through wet granulation, employing natural super disintegrants in different concentrations. **Methods:** The chitosan was isolated from the prawn shell using different concentrations of formulated trails, including F1, F2, F3, F4, and F5. Aceclofenac orally disintegrating tablets were prepared and characterized for various parameters including hardness, friability, weight uniformity, drug content, disintegration time, and *in vitro* dissolution studies. **Results:** Among the formulations, F5 exhibited superior performance in terms of rapid disintegration with 29 sec and the highest percentage of drug release with 98.91% compared to the others. **Conclusion**: Increasing the concentration of isolated chitosan from prawn shell results in an increased dissolution profile and a decrease in disintegration time.

Keywords: Aceclofenac, Chitosan, ODT, Super Disintegrants, Wet Granulation

1. Introduction

Administering drugs through solid oral distribution is the most convenient and rapid method. Compared to other oral dosage forms, these dosage forms have a number of benefits. Oral disintegrating tablets are uncoated tablets intended for homogeneous dispersion in water prior to administration[1]. Dysphagia disrupts people of any gender, notably ordinary citizens, elderly institutionalised individuals, and those in sustained care homes. According to a study-Quantity, surface, shape, and flavour of pills are the most typical allegations concerning trouble in swallowing tablets. Geriatric, paediatric, and travelling individuals who might lack quick accessibility to water requires easy-to-swallow dose forms[2-4]. Aceclofenac is a type of medication that reduces inflammation and tenderness associated with disorders such as gout, rheumatoid arthritis, and ankylosing spondylitis[5]. Aceclofenac works by inhibiting COX-2, which in turn reduces the production of a number of inflammatory mediators from the Arachidonic Acid (AA) pathway, such as prostaglandin E2 (PGE2), IL-1, and TNF[5].

2. Materials and Methods

Aceclofenac was acquired from Karpagam Pharma LLB, Coimbatore. Lactose, polyvinyl pyrrolidone, hydroxypropyl methyl cellulose, sucrose, vanillin flavour, magnesium stearate, talcum powder, and isopropyl alcohol were received from Karpagam Laboratories as gift samples. Prawn shells collected from the local fish market in Coimbatore. The chemicals are all of scientific grade, with purity percentages ranging from 96.60 to 99.90 %.

2.1 Preparation of Aceclofenac Oral Disintegrating Tablets

Aceclofenac oral disintegrating tablets were developed using the wet granulation technique. Materials such as aceclofenac, hydroxypropyl methyl cellulose, lactose,

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Article Received on: 06.05.2024 Revised on: 09.08.2024 Accepted on: 12.08.2024

saccharin, polyvinylpyrrolidone, and vanillin were separately passed through a 40# sieve and thoroughly mixed. Starch was added to Isopropyl Alcohol (IPA) and added to the above blend to make cohesive mass. The cohesive mass was sieved through a 40# sieve and subsequently dried in a hot air oven at 60–70 °C for one hour. Talc and magnesium stearate were sieved 20# separately and added to the above blend, mixed and compressed using 16 station tablet compression machine. The composition of various Aceclofenac oral disintegrating tablets is depicted in Table 1[6].

2.2 Extraction of Chitosan from Prawn Shell

The crab shells were thoroughly cleaned with distilled water to get rid of contaminants. After drying in a hot air oven at 80°C for an hour, the cleaned shells were crushed using a mortar and pestle. To ensure uniform particle size for ease of use, the particles were sieved to a finer size using a 2.0mm mesh sieve. For further study, the processed shell sample was kept in a clear glass bottle. Deproteinization, demineralization, and deacetylation are three processes that are used to make chitosan from powdered prawn shells.

2.3 Deproteinization of the Prawn Shells

The prawn shells were deproteinized by soaking 5 g of them in 1.25M NaOH for 3 hours at ambient temperature. Afterward, the blends were allowed to settle. Decantation was used to remove extra NaOH before washing with deionized water to bring the pH level back to normal. By using whatman filter paper no. 4, filtration was carried out. To obtain a deproteinized material, the residue was oven-dried for 45 min at 80°C.

Table 1. Formulation of aceclofenac oro dispersible tablets

Ingre dients(mg)	F1	F2	F3	F4	F5
Aceclofenac	100	100	100	100	100
Chitosan	0	0.9	1.8	2.7	3.6
Lactose	101.6	100.7	99.8	98.9	98
HPMC	50	50	50	50	50
PVP	0.4	0.4	0.4	0.4	0.4
Starch	30	30	30	30	30
Sucrose	10	10	10	10	10
Vanilla flavour	2	2	2	2	2
Talc	3	3	3	3	3
Magnesium stearate	3	3	3	3	3
IPA	qs	qs	qs	qs	qs
Total	300mg	300mg	300mg	300mg	300mg

2.4 Demineralization of Prawn Shells

To demineralize the deproteinized prawn shells, 3 g of the material was soaked in 1.25 M HCl in a 250 cm^3 conical flask for 5 hours at 80°C as per the method. The resulting product heated up after it was allowed enough time to escape heat and adjust. By decanting surplus of HCl, with the help of deionized water to clean, the pH is brought to a neutral state. Subsequently, to make chitin, the residue was filtered via Whatman filter paper no. 4 and dried for 45 min over 80°C in the oven.

2.5 Deacetylation of Chitin

1 g of the developed chitin was treated with 0.5 M NaOH for 2 hours at 100°C to deacetylate it, resulting in the production of chitosan. The blend was heated and allowed to escape heat and adjust. Decantation was carried out to remove extra NaOH, and the pH was then balanced by cleaning with deionized water. Upon filtration, the resulting product was dehydrated for 45 min over 80°C in the oven to produce chitosan[7].

2.6 Pre-formulation Studies

Bulk density, tapped density, angle of repose, compressibility index, and Hausner's ratio were evaluated for the granules of each formulation[8,9].

2.6.1 Bulk Density

By pouring the contents into a cylinder with graduated levels, their bulk density was found out. Both the total volume (Vt) and the powder mass (M) were estimated.

2.6.2 Tapped Density

Using density apparatus, a previously identified quantity of blends were set in a cylinder and tapped 100 times. The powdered mass (M) and the minimal amount that the cylinder could carry (Vt) were also assessed.

2.6.3 Hausner's Ratio

The powder flow is indirectly measured by Hausner's ratio, which indicates good flow characteristics when it

is between 1.17 and 1.20. Granules in all formulations were found to have a Hausner's ratio between 1.17 and 1.20.

2.6.4 Compressibility Index

The Carr's index examines of how easily substance can made to flow. Granules in all formulations were found to have a compressibility index between 14 and 17.

2.6.5 Angle of Repose

The angle of repose was calculated using the funnel technique, where the mixture was poured through a vertically adjustable funnel until achieving the desired cone height (h).The heap's radius (r) was measured; indicated are ideal flow parameters then the angle of repose can be found within 35°C.

2.7 Evaluation of Aceclofenac ODTs

2.7.1 Weight Variation

Twenty tablets were randomly selected from each batch, and their individual weights were measured. The tablets' weight variance was then calculated by comparing each tablet's weight to the batch's average weight[10].

2.7.2 Friability

The roche friabilator was used to assess tablet friability at 25 rpm for 4 minutes. Twenty tablets were weighed both before and after the test to determine their friability[11].

2.7.3 Thickness of Tablet

The thickness of three tablets from each batch was measured using a Vernier caliper (Mitutoyo Corporation, Japan). The mean and SD values were calculated[12].

2.7.4 Hardness[13]

Tablet breaking strength was assessed using a Monsanto hardness tester. It was calculated in kg/cm^2, and the tablet was rotated until it shattered. The acceptable hardness limits for tablets should be between 4-6 kg/cm^2.

2.7.5 Drug Content

From each batch, one tablet was ground into a fine powder using a mortar and pestle. 5mg of Aceclofenac are taken from the crushed tablet and diluted in 20 ml of ethanol. The solution was filtered to extract 0.1 ml, which was subsequently diluted in 10 ml of ethanol. The absorbance of the resulting solution was then analyzed using a UV spectrometer (UV Lab India) with a spectrophotometric method at 276 nm[14].

2.7.6 In vitro Disintegration Test

According to USP, a disintegration time test was performed. Six tablets of every formulation were randomly taken and placed in a disintegration device with 900 ml of purified water. The temperature of the disintegration tester was regulated at 37 ± 2°C. Disintegration Time (DT) refers to the duration required for tablets to entirely dissolve, parting no detectable residue inside the apparatus[15].

2.7.7 In vitro Dissolution Test

USP dissolution apparatus Type-II (paddle) at 50 RPM was used as part of an *in vitro* dissolution investigation. Phosphate buffer was used to uphold the temperature at 37°C (pH 5.8) as the dissolving media. A fresh phosphate buffer was added in instead of the sample after each 5 ml of dissolving medium was removed from the intestine at intervals of 5, 10, 15, 20, 25, and 30 minutes. By employing a UV spectrophotometer and measuring absorbance at 203 nm, the samples were utilised to estimate the amount of drug content that was contained in them[16].

3. Results and Discussion

Aceclofenac oral dispersible tablets were developed in this latest study using the wet granulation process. Natural super disintegrants were used in varying amounts to create formulations in order to study how varied concentrations affected how quickly medications released. The physical evaluation of the prepared mixed powder using a few parameters revealed that it was suitable for compression into tablets.

3.1 Evaluation of the Extracted Chitosan

3.1.1 Fourier Transform Infrared Spectroscopy (FTIR) Analysis of Chitosan

As shown in Figures 1 and 2, Chitosan's FTIR spectra revealed absorption peaks at 3254.64, 2872.88,

1617.72, 1551.40, 1375.52, 1306.89, 1259.53, 1202.46, 1153.01, 112.61, 1067.59, 1007.26, 951.09, 894.64, and 525.47 cm^{-1}. The N-H and O-H bending vibrations peaks that overlap are responsible for the absorption peak at 3254.64 cm^{1}. The absorbance maxima at 2872.88 cm^{-1}, 1617.72 cm^{-1}, and 1551.40 cm^{-1} correspond to the C-H stretching of the polymeric link, the N-H in-plane bend, and the O-H deformation in-plane, respectively. The distinct absorption peaks at 1007.26 and 894.64 cm^{-1} are emerges via C-O stretching of O-H groups as a result of deformation. The peak recorded at 525.47 cm^{-1} is attributed to N-H amines.

3.1.2 X-Ray Diffraction (XRD) Analysis of Chitosan Extraction

Figure 3 displays the XRD pattern of the produced chitosan, exhibiting two prominent peaks at 2θ = 9.1 and 19.800, indicative of its semi-crystalline nature. A high degree of crystallinity in the chitosan structure is indicated by the presence of crystals I and II. Its structural regularity, polarity, hydrogen link content, and ability to pack polymer chains are all possible causes of the polymer's high crystallinity development. Other minerals found as parts of the prawn shells can be explained by the existence of additional peaks in the diffractogram of chitosan.

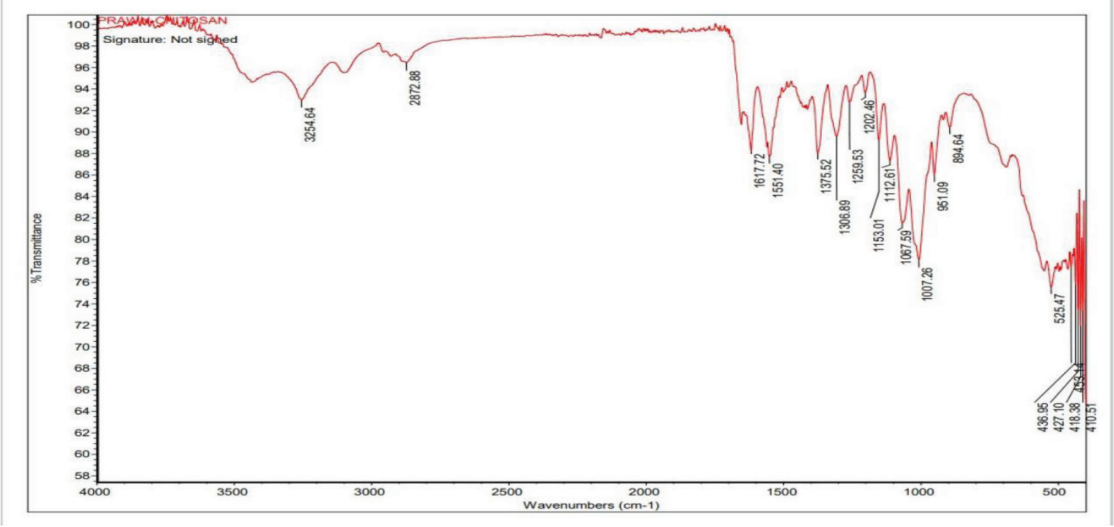

Figure 1. The generated chitosan's FTIR spectrum.

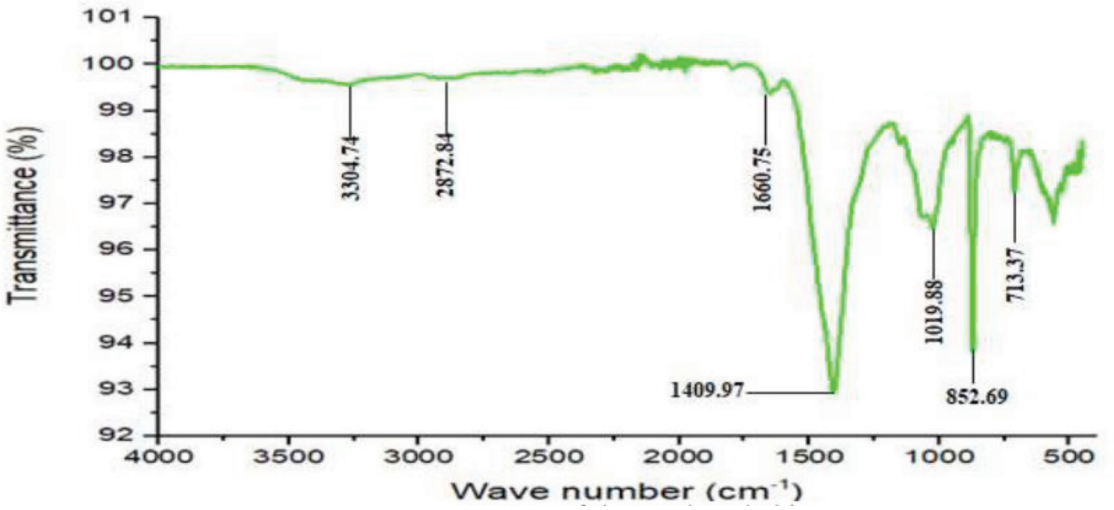

Figure 2. Standard chitosan's FTIR spectrum.

3.2 Precompression Evaluation

Table 2 lists all precompression evaluation studies, encompassing angle of repose, bulk density, tapped density, Hausner's ratio, and Carr's compressibility index. The angle of repose is used to assess the flow characteristics of the powder blend. Powder blends with low angles of repose exhibit superior flow properties compared to those with high angle of repose values. Angle of repose measurements for all formulation blends ranged from 30.17 to 32.08, demonstrating good flow properties.

All formulation powder blends had bulk densities between 0.28 and 0.30, tapped densities of 0.344 to 0.357, and Carr's index values of 14.53-17.15, indicating acceptable flow properties.

3.3 *In Vitro* Evaluation of Aceclofenac Oral Disintegrating Tablets

Five formulations (F1–F5) in total had been developed, involving a variety of excipients and super disintegrants (Chitosan) in different quantities. ODTs were generated using the wet granulation process. Hardness, weight fluctuation, friability, thickness, content homogeneity, and dissolution were evaluated for the tablets and shown in Table 3. The weight variation of batches F1 to F5 was found to comply with the permissible limits of 300 ± 5 mg. Between 4-6 kg/cm^2 was determined to be the range for tablet hardness. ODTs were found to be 3.47–3.50 mm thick. Friability was found to be under 1%, showing strong resistance to mechanical shear. It was noticed that hardness improved with a decline in the proportion of disintegrants among various formulations.

Formulations with lower concentrations of disintegrants have demonstrated maximum hardness, resulting in reduced friability. The formulations with the lowest hardness and the highest percentage of friability were those that contained large concentrations of disintegrants. Every tablet displays a level of friability

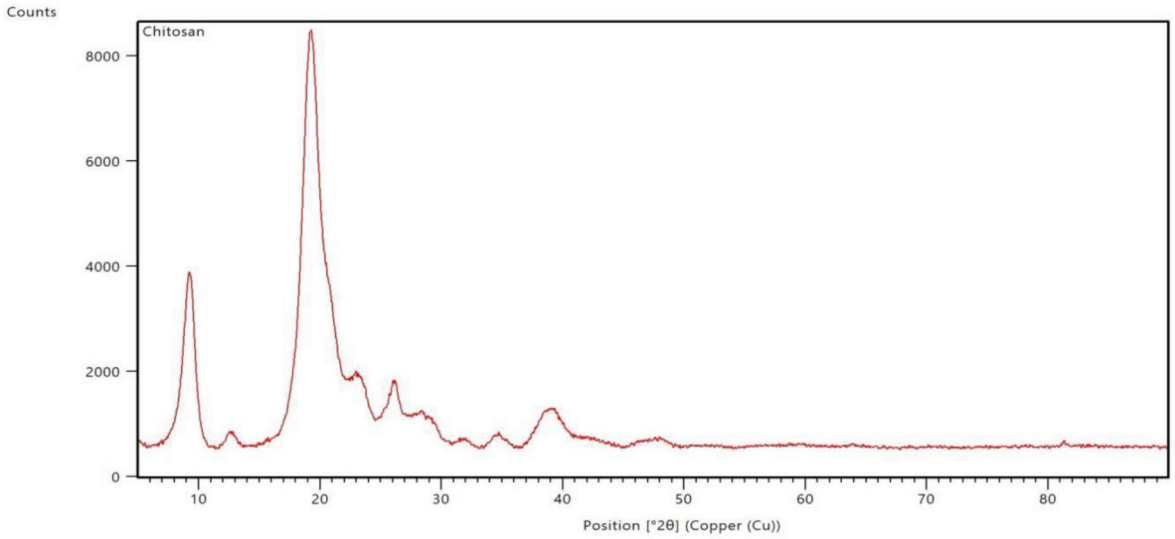

Figure 3. XRD pattern of extracted chitosan.

Table 2. Studies on the powder blend's pre-compression

Formulation Code	Bulk Density (gm/cc)	Tapped Density (gm/cc)	Angle of Repose (Degrees)	Carr's Index (%)	Hausner's Ratio
F1	0.294	0.344	30.64±0.85	14.53	1.172
F2	0.303	0.357	31.05±0.37	15.12	1.178
F3	0.285	0.344	32.08±0.45	17.15	1.206
F4	0.294	0.344	30.17±0.29	14.53	1.172
F5	0.303	0.357	32.67±0.21	15.12	1.178

Table 3. *In vitro* evaluation studies of aceclofenac oral disintegrating tablets

Batch No	Weight Variation(mg)	Thickness (mm)	Hardness (Kg/cm2)	Friability (%)	Disintegration Time	Drug Content (%)
F1	300.1±0.0070	3.48±0.04	4.1±0.301	0.45	30 sec	98.66
F2	299.9±0.0353	3.5±0.035	4.0±0.159	0.67	28 sec	99.03
F3	300.08±0.055	3.49±0.01	4.3±0.256	0.44	31 sec	97.96
F4	300.12±0.022	3.48±0.01	4.0±0.159	0.66	28.3 sec	98.36
F5	299.98±0.044	3.47±0.01	4.1±0.301	0.54	29 sec	99.68

Table 4. Percent drug release profile of aceclofenac oral disintegrating tablets

Time (Min)	Percentage Drug Release (%)				
	F1	F2	F3	F4	F5
0	0	0	0	0	0
5	15.09	17.56	20.58	21.37	23.41
10	21.96	25.47	29.38	32.07	34.91
20	29.47	34.43	35.804	40.93	56.35
30	35.82	44.18	47.39	52.45	78.29
40	57.48	70.77	76.52	77.07	89.85
45	71.17	78.73	84.49	98.85	98.91

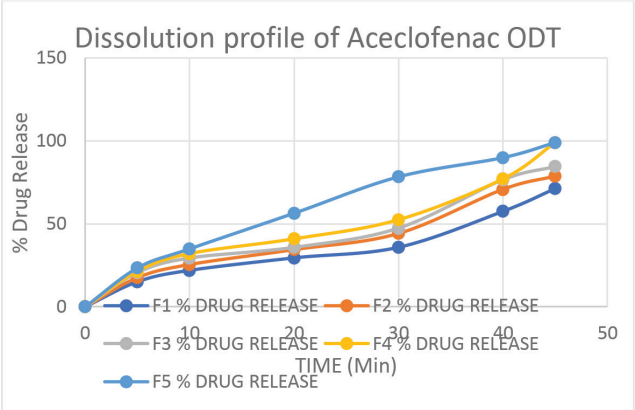

Figure 4. Aceclofenac ODT drug release.

that is within the allowed range (0.44–0.67%). The weight variation test was successful for all formulations, as each tablet showed an average weight change of less than 5%.

3.4 Percent Drug Release Profile of Aceclofenac Oral Disintegrating Tablets

Drug release percentage was measured in 900 ml of pH 5.8 phosphate buffer at 50 rpm and 37°C ± 0.1°C using a type II USP dissolution apparatus and the results were shown in Table 4 and Figure 4.

4. Conclusion

Chitosan is essential for fast disintegration of tablets due to its amide group, which has a high wetting ability. The chitosan isolated from the prawn shell has different concentrations of formulated trails, including F1, F2, F3, F4, and F5. The concentrations are gradually increasing in trails F1 to F5. Chitosan isolated from the prawn shell has no significant incompatibility with FT-IR, XRD, or drug release patterns when used in ODT formulations. It also shows better results in pre- and post-formulation studies. Gradually increasing isolated chitosan in formulated trails shows disintegration times of 30 sec, 28 sec, 31 sec, 28.3 sec, and 29 sec, respectively (F1-F5). The ideal time required for disintegration is also within the standard limit. Different concentrations show the percentage of drug release (71.17%), 78.73%, 84.49%, 98.85%, and 98.91%, respectively (F1-F5) at the end of 45 minutes. This indicates the rapid drug release of the ODT formulation, with maximum medication released within 45 minutes. According to the statistics of the dissolving and disintegration time profiles, super disintegration activity is evident when the concentration of isolated chitosan from prawn shells is gradually increased. An enhanced dissolving profile and a shorter disintegration time are produced by increasing the concentration of isolated chitosan from prawn shell.

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