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Evaluation of Chitosan as a Natural Disintegrant in the Formulation of Aspirin Orally Disintegrating Tablets

Desy Nawangsari*[1], Hazim Fikri Alfianto[1], Ayu Pujianti[1], Nur Rahmawati[1], & Deva Krisna Kadarani[2]

[1]*Pharmacy Study Program, Faculty of Health, Universitas Harapan Bangsa, Purwokerto, Indonesia*
[2]*Department Chemical Engineering, Faculty Science and Technology, University of Manchester, Manchester, United Kingdom*

ABSTRACT: Aspirin is an antiplatelet that is used for the therapy and prevention of stroke, many strokes occur in elderly people. Orally Disintegrating Tablet (ODT) can be dissolved quickly making it easier for geriatric patients to swallow. This study aims to determine the effect of variation in the concentration of chitosan as a disintegrating agent on the physical properties of ODT aspirin. Aspirin ODT tablets were produced by direct compression in 3 formulas with variations of chitosan of 3.5%, 7% and 14%. The results showed that a chitosan concentration of 3.5% yielded optimal tablet properties: disintegration time of 23.66 seconds, friability of 0.41%, and dissolution of 96.81%. Statistically significant differences ($p < 0.05$) were observed among the formulations in terms of in hardness ($p = 0.027$), friability ($p = 0.010$) and disintegration time ($p = 0.000$). The disintegration mechanism of chitosan involves swelling, wicking, and strain recovery. At lower concentrations, chitosan promotes rapid water uptake and particle expansion, facilitating fast breakdown of the tablet matrix. In contrast, higher chitosan levels may induce gel formation that hinders water penetration, thus delaying disintegration. In conclusion, chitosan at a concentration of 3.5% effectively functions as a natural disintegrant in aspirin ODTs, offering rapid disintegration and high dissolution, which is suitable for geriatric patients with swallowing difficulties.

Keywords: **aspirin; chitosan; disintegration time; orally disintegrating tablets; natural disintegrant; elderly patients.**

Introduction

Acetyl salicylic acid is commonly called as aspirin and chemically classified as Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) together with other organic acids including ibuprofen. It has molecular formula of $CH_3COOC_6H_4COOH$ with molecular weight is 180.16 g/mol according to pubchem.ncbi.nlm.nih.gov compound summary of aspirin. The mechanism action of aspirin related to irreversible acetylation of cyclooxygenase-1 (COX-1) and -2 (COX-2) by aspirin that inhibited prostaglandin synthesis, which imply to decrease pain, fever, and inflammation. In plateleter, other metabolism pathway of aspirin Carried out irreversibly acetylates COX-1 on serine 530 to prevent arachidonic acid from reaching active site of COX-1, that inhibits prostaglandin formation in thromboxane A_2 and also inhibit platelet aggregation. Clinical studies of aspirin also shows that low dose of aspirin (81-100 mg daily) can used to prevent myocardial infarction and stroke in ischemic heart or cerebrovascular disease [1,2]. Age is one of the risk factors for stroke that doubles every 10 years after the age of 55 years, about 75% of all stroke events occur in people aged ≥ 65 years [3].

Orally disintegrating tablets (ODTs) dosage form in patient is highly increased demands in pharmaceutical industry due to several advantages, particularly for improve drug bioavailability and immediately release drug properties benefiting drug administration with swallowing challenges, children, and for quick onset of action. Difficulty in swallow is termed as dysphagia, that is a common occurrence in stroke or also called Post Stroke Dysphagia (PSD), as many as 50% of acute stroke patients experience dysphagia [4].

As Food and Drug Administration (FDA) has determined that ODT as a solid dosage form containing medicinal substance that disintegrate rapidly, within seconds when placed on tongue. On the other hand, European Pharmacopoeia (Ph. Eur) has identified ODT as uncoated tablets intended to be in mouth where they disperse rapidly before

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***Corresponding Author:** Desy Nawangsari
1Pharmacy Study Program, Faculty of Health, Universitas Harapan Bangsa, Purwokerto, Indonesia, 53182 | Email: desynawangsari@uhb.ac.id

being swallowed and as tablets that should disintegrate in 3 minutes. For drug delivery system (DDS), ODT as a delivery system can rapidly disintegrate in mouth upon contact with saliva though without additional water. ODT also introduces a short onset of action related to, after drug administration, it continously undergoes pre-gastric mucosa absorption within seconds [5]. The pre-gastric absorption anticipates early stage of hepatic metabolism that improves the bioavailability of drug [6].

Aiming for increasing rapid disintegration time of aspirin, this study refers to some tablet formulas involve disintegrant agent to break the tablet matrix into fragments when in contact with saliva. Natural and synthetic disintegrant agent can be used in the drug formulation, however, natural substances is more sustainable in aspect of availability, cost, and biodegradability. One of the natural disintegrant agent refers to chitosan. It has a chemical structure of a linear binary heteropolysaccharide formed of beta-1,4-linked glucosamine, which has variability of *N*-deacetylation from chitin derived from crab, shrimp shells, mushroom cell walls. It has been used for drug delivery system study of meloxicam to improve solubility and therapeutic dose using different technological characteristics, that found out chitosan is appropriate biopolymer to moderate disintegration process in ODT [6]. Other studies of evaluation the combined chitosan and microcrystalline cellulose as direct compression excipients also suggested that chitosan promotes flowability of powder mix and rapid disintegration of tablet at low concentration and enables extended release at high concentration [7].

This research evaluates the underexplored potential of chitosan as a natural disintegrant in the formulation of aspirin tablets for enhancing drug's disintegration time. Main feature on this investigation is to examine physical properties of ODT aspirin to identify of which optimal concentration of chitosan presenting in the aspirin's formulations that support our main objectives. The conceptual framework of the disintegration mechanism of modified aspirin ODT (orodispersible tablet) with chitosan as a natural disintegrant is shown in Figure 1. Conventional tablet formulations without chitosan undergo slower disintegration, but formulations with chitosan can accelerate disintegration due to its properties as a natural disintegrant. To determine how quickly the tablet disintegrates in the oral cavity, a disintegration time evaluation was conducted. Therefore, it is expected that the addition of chitosan will enhance the disintegration efficiency of aspirin ODT tablets.

As structure of granules plays primary role in production procedures and final formulation, parameters such as particle morphology, size, shape, and mechanical properties are essential in selection of formulation ingredients [8]. It also has further implication to uniformity, dissolution rate, bioavailability and stability. However, this study been limited a few aspect on formulation and evaluation starting from tablet manufacturing process, pre compression evaluation, and physical assessment for the parameters of taste, color, odor, uniformity, hardness, and disintegration time according to the minimum criteria of drug's acceptance. In addition, different technological applied during manufacturing process may compomise the formula quality, but this study only focus on the direct felting method. This preliminary study may require further additional comprehensive physicochemical and stability study to manage bioavailability, efficacy, and safety aspects.

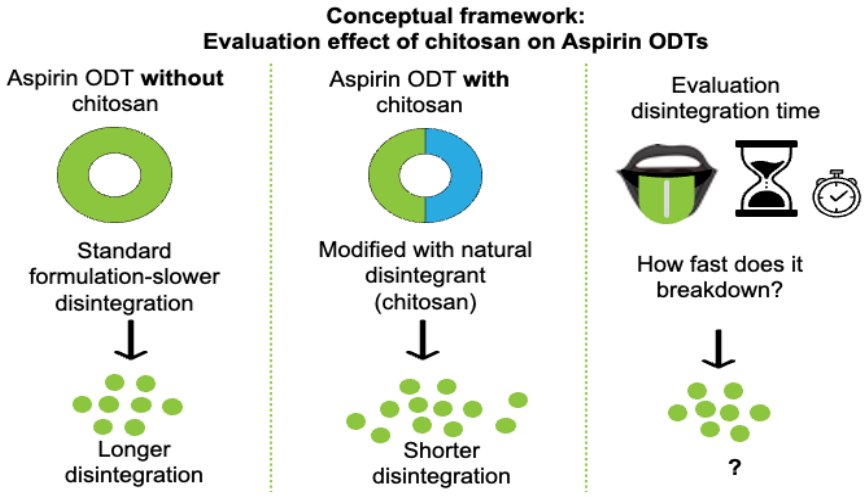

Figure 1. Schematic representation of chitosan-mediated tablet disintegration mechanisms.

Aspirin or acetyl salicylic acid is an NSAID that also has an effect as an antiplatelet [9]. This active ingredient is used in both primary prevention and secondary prevention of ischemic stroke [10]. Age is one of the risk factors for stroke that doubles every 10 years after the age of 55 years, about 75% of all stroke events occur in people aged ≥ 65 years in globally [3].

Many geriatric patients are unwilling to accept/ consume tablets for fear of choking or fear of difficulty swallowing (dysphagia) [11]. Dysphagia is a common occurrence in stroke or also called Post Stroke Dysphagia (PSD), as many as 50% of acute stroke patients experience dysphagia [4]. Orally Disintegrating Tablet (ODT) can be a solution because it provides convenience for patients who have difficulty swallowing such as geriatrics, stroke patients and children [12].

Orally Disintegrating Tablets (ODT) or orodispersible tablets are non-coated tablets with use placed in the mouth and will dissolve quickly before swallowing [13]. ODT has the advantage of fast onset, high absorption and also improves patient compliance [14,15]. Disintegrants are materials that cause the disintegration of tablets when in contact with water [16]. Chitosan is a disintegrant that can be used in ODT formulations and has a fast and good disintegration action [7].

Based on what has been mentioned, researchers are interested in conducting research and making ODT aspirin with variations of chitosan as a disintegrant to study its effect on the physical quality of ODT aspirin and determine the optimal concentration of chitosan as a disintegrant.

Methods

Materials

The materials used in this study were aspirin (Merck, Germany), chitosan (Merck, Germany), Avicel PH 102 (Merck, Germany), magnesium stearate (Merck, Germany), mannitol (Merck, Germany), and sorbitol (Merck, Germany), all materials were of pharmaceutical grade.

Tablet Manufacturing

Tablets were prepared in 3 (three) different formulas by direct compression. Preparation of pre compression by mixing until homogeneous aspirin (active substance), chitosan (crusher), avicel PH 102 (binder), mannitol and sorbitol (filler) for ± 15 minutes, before mixing the material is sieved using mesh 12. After that, magnesium stearate that has been sieved with mesh 40 (lubricant) is added for 2 minutes. Each formula was molded as many as 300 tablets.

Initially, the powdered components aspirin (active pharmaceutical ingredient), chitosan (disintegrant), Avicel PH 102 (binder), mannitol, and sorbitol (fillers) were individually passed through a mesh no. 12 sieve to ensure uniform particle size. These ingredients were then blended together in a dry mixing process for approximately 15 minutes to achieve a homogeneous powder mixture. Following this, magnesium stearate, previously sieved through mesh no. 40, was added as a lubricant and mixed gently for an additional 2 minutes to avoid over-lubrication. Each formulation was compressed into tablets using a tablet press, producing a batch size of 300 tablets per formula showed in Figure 2.

The composition of ODT aspirin tablet formulas with varying concentrations of chitosan as a natural disintegrant is shown in Figure 2. The three formulas compared are F1 (3.5% chitosan), F2 (7%), and F3 (14%). The gradual increase in chitosan concentration in F1, F2, and F3 aims to evaluate its effect on tablet disintegration time.

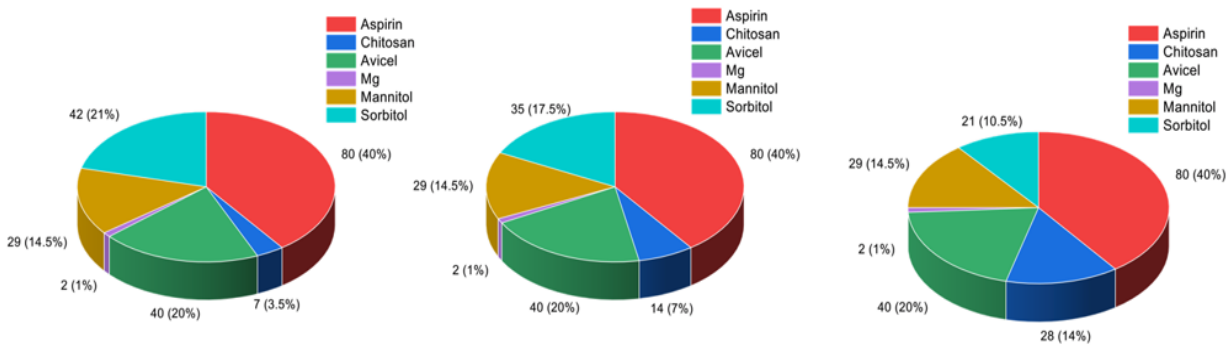

Figure 2. Composition of aspirin ODT formulations with varying chitosan concentration (see: dark blue part) (Formula F1 (3.5%), F2 (7%), and F3 (14%).

Pre compression evaluation

Evaluation of pre compression includes flowability test, angle of repose, Carr's index and Hausner ratio tests [17]. Flowability test was using a granule flow tester by weighing 50 grams of pre compression, then placed on the test equipment in a closed state. The cover was opened and the granule flow time was recorded. The height and diameter of the test results were then measured for the determination of the angle of repose. Carr's index and Hausner ratio were determined using tapped density. It started with weighing the pre compression and then placed it on a measuring cup with a volume of 100 mL after which it was stopped 40 times.

Evaluation of Orally Disintegrating Tablets (ODT) Aspirin

Physical properties

Organoleptic Evaluation

Criteria of drug acceptance are including fundamental physical properties of taste, color, shape, and odor according to standard pharmacopeia (USP and EU). This set of acceptability criteria is a major influential factor on many patients to comply to drug administration which is a crucial aspect contribute to formulation development stage [20,21]. A drug has its most beneficial when it can be accepted and consumed correctly by the patient [22]. In this preliminary study, organoleptic test of aspirin tablet formulation has been Carried out to assess those criterias mentioned above.

Weight and Size Uniformity Test

The tablet weight was measured using an analytical balance (Mettler Toledo, USA). The weight uniformity test was Carried out by weighing 20 tablets one by one and calculating the average tablet weight. No more than 2 tablets should deviate from the average weight in column A and none should deviate from the average weight in column B [23]. The uniformity test was Carried out by measuring the diameter and thickness of the tablet using a caliper. Tablets are said to meet size uniformity if the diameter of the tablet is not more than 3 times and not less than 4/3 of the tablet thickness [23].

The right combination of taste, color and odor in a pharmaceutical products contributes to drug acceptance. A drug has its most beneficial when it can be accepted and consumed correctly by the patient [22]. Organoleptic test was conducted by looking at the shape, color,taste, and odor of the tablets.

Hardness and Friability Test

Hardness test was conducted using a hardness tester. 10 tablets were taken and then placed in an upright position on the tool. The distance between the anvil and the spring bolt is adjusted so that the tablet is crushed and then the lever is rotated until the tablet breaks. A force of about 4kg is considered to meet the minimum requirement for hardness [22]. The friability test was conducted using a friability tester (Bonnin, Germany). The friability test was conducted with 20 tablets cleaned of dust and weighed then placed in the friability tester then run with 25 rpm for 100 revolutions. The tablets were then again cleaned of dust and weighed. Tablets are declared to meet the requirements if the friability value is not more than 1% [22].

Disintegration Time

Disintegration time was measured using a disintegration tester (Biobase, China). Disintegration time testing was Carried out by two methods, namely using a disintegrator tester and saliva simulation. As many as 6 tablets were taken, then put into the basket on the disintegrator tester. The tube was raised and lowered regularly with water media at a temperature between 37 ºC ± 2ºC and the tablet disintegration time was recorded, the tablet was said to be qualified if it disintegrated in no more than 1 minute [24,25]. A Petri dish with a diameter of 10 cm was filled with 30 ml of saliva simulation liquid at 37 ºC and then the tablet was placed in the middle, the tablet was said to be qualified if it disintegrated in no more than 3 minutes [13,26].

Dissolution Test

The dissolution test was performed using a dissolution tester (Biobase, China), and absorbance measurements were carried out with a UV-Visible spectrophotometer (Biobase BK-D590, China) at a wavelength of 227 nm. The initial step of the dissolution test Carried out was the preparation of a series solution and determination of the maximum wavelength. Serial solutions were made in concentrations of 6, 8, 10, 12, and 14 ppm. ODT aspirin dissolution test was conducted with a dissolution tester with a type 1 (basket) device with 50 rpm for 30 minutes. The dissolution medium was 500 ml of 0.05 M acetate dapar prepared by mixing 2.99 g sodium acetate trihydrate and 1.66 ml glacial acetic acid P with water up to 1000 ml with pH 4.50 ± 0.05. The test was Carried out for 30 minutes and samples were taken at 5, 10, 15 and 30 minutes with a volume of 5 ml. Each sampling, the medium volume was replaced with a new medium solution with the same volume. Samples were measured

for absorbance with a spectrophotometer at the maximum wavelength [24].

Data Analysis

The data obtained were analyzed using the SPSS 25 program. Normality and homogeneity tests were Carried out to ensure that the data were normally distributed and suitable for the one-way ANOVA test. Significance testing if $p = <0.05$ then it can be said that there is a meaningful difference [27].

Result and Discussion

Tablet Manufacturing Process

The manufacturing process of the orally disintegrating tablets (ODTs) involved several key steps, including blending of active pharmaceutical ingredients (APIs) and excipients, direct compression, and post-compression evaluation. In this study, chitosan was used as a natural disintegrant in the tablet formulation. Chitosan is a natural biopolymer that is easily biodegradable and highly compatible with the human body, posing minimal risk of toxicity and irritation compared to synthetic materials.

Figure 3 illustrates the tablets are white, round, and flat-faced with a cross-scored surface, enabling easy division into smaller doses if needed. The uniformity in shape and size indicates a consistent compression process. No visible signs of capping, lamination, or sticking were observed, suggesting good compatibility among formulation components.

Evaluation of Pre compression

According to this present study, there are 3 (three) different formulations of aspirin ODTs has been fabricated using varies of chitosan's concentration, which are 3.5%, 7.0%, and 14.0%. Some essential drug formulation tests were Carried out including flow rate test to examine equally proportional powder mass in each of tablet. It basically is useful to obtain flow uniformity [19]. This study determined the flowability test of those 3 formulas, which are around 7.53 grams per second as showed up in the Table 1 and can classified as good result refers to reference flow rate should be within 4 to 10 grams per second [12].

Parameter of angle of repose (°) to the flow path has also investigated in this study to understand the internal friction and particle cohesion for illustrating overall flow rate condition [19]. According to the standard specification on angle of repose parameter, this study has a satisfactory result as shown in the Table 1, at around 26 to 27 degree indicating as desirable outcomes related to the standard degree should be within 25 to 30 for the molding mass [19].

Carr's index is defined as the tendency of powder when placed in a limited space to shrink its volume when pressurized or loaded [28]. The Carr's index test results obtained by F1, F2 and F3 are 12.82 ± 0.70%, 13.63 ± 0.69% and 15.44 ± 0.74% respectively. The test results show that the pre compression has a good Carr's index which is in the range of 11-15% [28]. Hausner ratio is a prediction of flow rate based on friction between particles. The Hausner ratio test results obtained by F1, F2 and F3 respectively, are 1.15 ± 0.009, 1.16 ± 0.010 and 1.18 ± 0.011. The test results show that the pre compression has a good Hausner ratio, within the range of 1.12-1.18 [28].

Flow rate test aims to achieve flow uniformity so

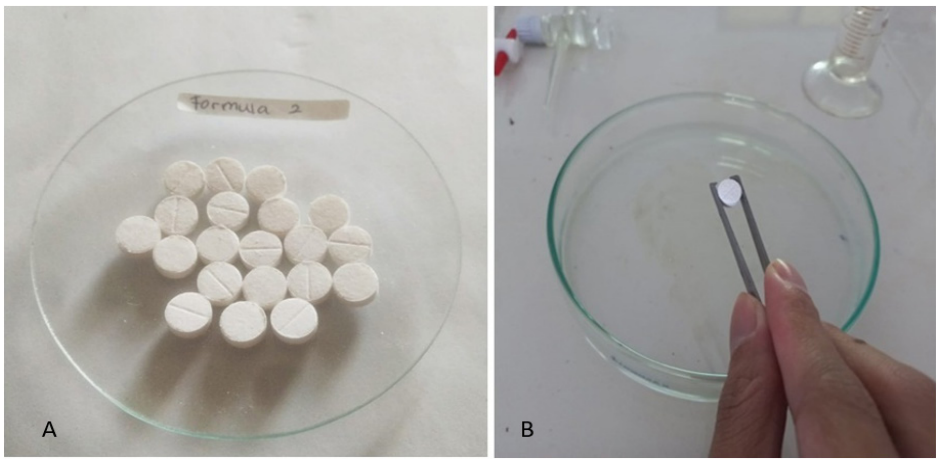

Figure 3. Physical appearance of aspirin ODTs prepared via direct compression in (a) a batch of aspirin ODTs and (b) single tablet of aspirin ODTs.

Table 1. The data collected for flowability test, angle of repose, Carr's index, and Hausner ratio of pre compression formulas.

Parameters	F1 (3.5%)	F2 (7%)	F3 (14%)	*p-value*
Flowability test (gram/s)	7.57 ± 0.23	7.81 ± 0.24	7.91 ± 0.50	0.521
Angle of repose (º)	27.1 ± 0.62	26.96 ± 0.62	26.73 ± 0.47	0.760
Carr's index (%)	12.82 ± 0.70	13.63 ± 0.69	15.44 ± 0.74	0.011*
Hausner ratio	1.15 ± 0.009	1.16 ± 0.010	1.18 ± 0.011	0.011*

*) statistically significant at $p < 0.05$

as to ensure that each tablet has the same or almost the same powder mass [28]. Based on flow rate testing the results for FI, FII and FIII are 7.57 ± 0.23 grams/s, 7.81 ± 0.24 grams/s and 7.91 ± 0.50 grams/s respectively. The test results have a good category in accordance with the literature, namely the flow rate in the good range of 4-10 grams/second [19].

The aim determine angle of repose to the flow path. The angle of repose is a characteristic of internal friction and particle cohesion and can therefore describe the flow rate [28]. The test results of the angle of repose obtained by F1, F2, and F3 are 27.1 ± 0.62º, 26.96 ± 0.62º and 26.73 ± 0.47º, respectively. The test results show that the molding mass has a very good angle of repose in the range of 25-30º [28].

Carr's index is defined as the tendency of powder when placed in a limited space to shrink its volume when pressurized or loaded [28]. The Carr's index test results obtained by F1, F2 and F3 are 12.82 ± 0.70%, 13.63 ± 0.69% and 15.44 ± 0.74% respectively. The test results show that the pre compression has a good Carr's index which is in the range of 11-15% [28]. Hausner ratio is a prediction of flow rate based on friction between particles. The Hausner ratio test results obtained by F1, F2 and F3 respectively, are 1.15 ± 0.009, 1.16 ± 0.010 and 1.18 ± 0.011. The test results show that the pre compression has a good Hausner ratio, within the range of 1.12-1.18 [28].

The results of the one way ANOVA test produced significant differences in the parameters of Carr's index p = 0.011 and Hausner ratio p = 0.011. The results showed that the Carr's index and Hausner ratio worsened as the concentration of chitosan increased. The difference in pre compression evaluation results occurs because chitosan has high porosity. High porosity will cause poor Carr's index and Hausner ratio [28].

Evaluation of ODT Aspirin

Particularly, the most crucial aspect in drug manufacture is maintaining a constant dose per individual. Dose uniformity can be tested with a weight uniformity test [28]. All formulation in this present study demonstrated accepatable weight uniformity as per the USP requirements. Table 2 shows that the mean tablet weights ranged from 205.75 to 205.90 mg with relative standard deviariuons (RSD) below 2% for all batches, and no individual tablets exceeded the permitted deviation limits (±7.5% for 151-300 mg tablets). Statistical analysis revealed no significant differences in tablet weights among these formulations (p-value = 0.988).

Size uniformity revealed that all formulations in this present study exhibited consistent diameter and thickness values, with no statistically significant differences observed across groups (p> 0.005) as shown in Table 3. The measured dimensions met the European Pharmacopoeia requirements for size uniformity, which stipulate that tablet diameter must not exceed three times, nor be less than four thirds, the thickness [23]. This confirms geometric consistency and compressibility control during direct compression [22].

Aspirin ODTs formulas on this study has a significant decrease at the hardness as the chitosan concentration increased, probably due to porosity affecting interparticle

Table 2. Weight uniformity of aspirin ODT formulations.

Formula	Mean weight (mg) ± SD	RSD	n	Criteria met	*p-value*
F1	205.75 ± 3.27	1.59	20	Yes	
F2	205.90 ± 3.11	1.51	20	Yes	0.988
F3	205.80 ± 2.93	1.42	20	Yes	

Table 3. Size uniformity of aspirin ODT formulations.

Formula	Diameter (cm) ± SD	Thickness (cm) ± SD	*p-value* (Diameter)	*p-value* (Thickness)
FI	0.838 ± 0.01	0.34 ± 0.01	0.838	>0.935
F2	0.839 ± 0.01	0.339 ± 0.01		
F3	0.841 ± 0.01	0.341 ± 0.01		

bonding as chitosan has high porosity referring to weak bond particles and matrix as well as tablet strength [29] [30]. All formulas have good hardness values because the force required is not less than 4kg [22]. A similar trend was observed in friability, represents the strength of tablets against fracture and erosion [31], which remained below the pharmacopeial limit of 1% in all formulations.

For the drug to be available for absorption, the tablet must disintegrate and release the drug for dissolution [22]. Releasing active drug substabce from tablet requires disintegration process tranforming tablet into smaller fragments, which the processing time is a crucial issue [31]. In this study, disintegration time were measured using two methods, which are a disintegrator tester and a simulator saliva model.

Regarding disintegration tester methodology, the results show Table 4 that F1, F2, and F3 has a disintegration time of 23.66 ± 2.51 seconds, 49.66 ± 3.51 seconds and 260.66 ± 5.13 seconds, respectively. F1 and F2 met the ODT disintegration time requirement of no more than 1 minute [25].

Meanwhile, in the simulated saliva disintegration test of F1, F2 and F3 disintegrated in 127.66 ± 6.65 seconds, 167 ± 6.24 seconds and 581.33 ± 8.02 seconds, respectively. As for F1 and F2 met the European Pharmacopeia's standard for ODTs, requiring 3 minutes in the oral cavity [13]. A significant difference in the disintegration times across formulations ($p < 0.001$) was observed. This is attributed to the effect of chitosan concentration at higher levels, chitosan tends to form a gel barrier, limiting water penetration and delaying matrix breakdown [32].

The dissolution test was conducted using a UV-Vis spechtrophotometer at 227 nm, the experimentally determined maximum absorbance wavelength of aspirin. This value aligns closely with literature reports of 232 nm and 237 nm [33,34]. Standard solutions (6, 8, 10, 12 and 14 ppm with reading absorbances of 0.278; 0.345; 0.433; 0.476 and 0.550, respectively) produces a linear calibration curve with the equation of $y = 0.0375 (x) + 0.0789$ with $r = 0.995$.

Figure 4 shows that the dissolution results of the aspirin ODT profile after 30 minutes were 96.81% (F1),

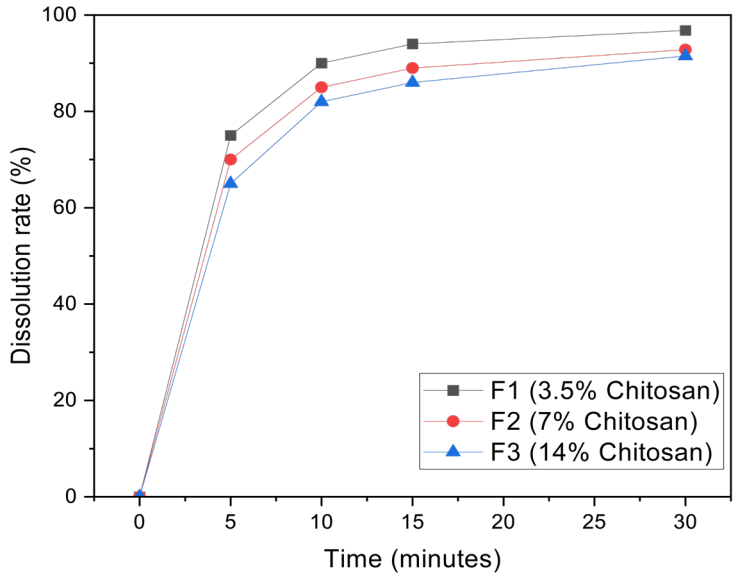

Figure 4. Dissolution profiles of aspirin ODTs (F1, F2, and F3) over 30 minutes in acetate buffer (pH 4.5). F1 (3.5% chitosan) exhibited the most rapid drug release, reaching 96.81% dissolution within 30 minutes.

Table 4. Mechanical properties and disintegration performance of aspirin ODTs.

Test Parameter	F1 (3.5%)	F2 (7%)	F3 (14%)	*p-value*
Hardness (kg)	5.33 ± 0.30	4.53 ± 0.41	4.33 ± 0.30	0.027
Friability (%)	0.41 ± 0.03	0.48 ± 0.05	0.56 ± 0.02	0.010*
Disintegration time (s)	23.66 ± 2.51	49.66 ± 3.51	260.66 ± 5.13	0.000**
Saliva disintegration time (s)	127.66 ± 6.65	16.7 ± 6.24	581.33 ± 8.02	0.000**

*) Statistically significant at $p < 0.05$; **) Highly significant at $p < 0.001$

92.81% (F2), and 91.50% (F3). All formulations met the pharmacopeial requirement of not less than 80% drug release within 30 minutes [24]. Tren data shows decreasing dissolution rate with increasing chitosan concentration was consistent with longer disintegration times. Formulation F1, with 3.5% chitosan, exhibited both the fastest disintegration times and highest dissolution efficiency, confirming its suitability for orodispersible use.

Discussion

The results of this present study demonstrate that the concentration of chitosan significantly affects the physical and functional properties of aspirin ODTs, particularly in relation to disintegration time, hardness, and friability. In comparison of three formulations tested, the tablet containing 3.5% chitosan exhibited superior performance with a rapid disintegration time of 23.66 seconds and dissolution efficiency of 96.81% within 30 minutes.

Tablet disintegration is a crucial phase for drug release and subsequent absorption. The efficiency of this process depends heavily on the nature and concentration of the disintegrant used. At lower concentrations (3.5 %), chitosan promotes rapid water uptake through mechanisms such as swelling, wicking, and strain recovery. Swelling involves omni-directional enlargement of particles, building up pressure that fractures the matrix; wicking refers to capillary-driven water penetration; strain recovery refers to elastic expansion of compressed particles upon wetting—all accelerating disintegration [35].

Strain or shape recovery involves destruction of bonds and release of energy stored in the system upon contact with physiological fluid and heat. Wicking involves penetration of water into the system (leading to destruction of hydrogen bonds and Van der Waals and electrostatic forces) via capillary action [36]. Other disintegration mechanisms are adsorption (heat of wetting) and repulsive forces [37]. These mechanisms promote the breakdown of the tablet matrix into smaller fragments, thereby accelerating disintegration and enhancing dissolution. Conversely, higher concentration of chitosan (14%), appear to induce gel formation upon hydration, which impedes water penetration and delays disintegration. Additionally, increasing chitosan concentration facilitates reduction in tablet hardness and increase in friability—likely due to its high porosity and weakened inter-particle bonding, consistent with previous findings on chitosan excipient interactions [6,35]. This might be attributed to chitosan's high porosity, the inter-particle bonding within the matrix weakens, leading to decreased mechanical strength. This supports the previous findings where excessive chitosan levels compromised tablet integrity due to its low compressibility and high internal porosity [36].

The disintegration test using simulated saliva found out that only 3.5% and 7% chitosan formulations that satisfied the ODT criteria set by regulatory bodies. It means the formulation with 14% chitosan exhibited an excessively long disintegration time, which likely related to formation of a gel barrier that restricted further disintegration.

Overall, these findings support the hypothesis that chitosan has optimal functions as disintegrant at lower concentrations. It shows good disintegration performance and compatibility with direct compression techniques highlight its potential as a sustainable excipient in ODT formulations, especially for patient with swallowing difficulties.

Conclusion

This study demonstrates that the chitosan's concentration significantly influences the physical characteristics and performance of aspirin ODTs. Increasing chitosan concentration led to a reduction in tablet hardness and an increase in friability and disintegration time. The optimal formulation was found at 3.5% chitosan, which resulted in rapid disintegration, high dissolution efficiency (96.81%), and mechanical strength. The findings highlight chitosan's suitability as a natural disintegrant for ODT formulations, especially for swallowing difficulty's patients.

Further research are recommended to evaluate long-term stability, *in vivo* bioavailability, an patient acceptability rate.

Conflict of Interest

The authors have no conflicts of interest regarding this investigation.

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