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Development and *in vitro/in vivo* evaluation of tamarind seed gum-based oral disintegrating tablets after fabrication by freeze drying

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ABSTRACT

To overcome swallowing problems, particularly among the aging population, oral disintegrating tablets (ODTs) have been developed to disintegrate instantly in saliva. Here we developed novel diclofenac sodium ODTs by freeze drying and evaluated their efficacy using *in vitro* and *in vivo* tests. A sugar alcohol, mannitol, sorbitol, or xylitol, was used as the excipient and tamarind (*Tamarindus indica*) seed gum (crude or modified forms) was used as a binder in the freeze-dried tablets. Tablets with appropriate portions of the sugar alcohol (30–60 mg) and gum (50–100 mg) showed a good appearance. However, those containing mannitol had better appearance and integrity and were easier to remove from molds than those containing sorbitol or xylitol. The tablet properties thickness, diameter, and weigh variation were controlled to monitor tablet quality. The ODT formulation containing diclofenac sodium, polyethylene glycol (PEG) 4000, modified tamarind seed gum, and mannitol showed the shortest disintegration time (less than 2 min) in phosphate buffer (pH 6.8). Moreover, this formulation achieved 100% drug release in less than 6 min. These data warant the application of freeze drying using gum as a binder for the fabrication of ODTs containing heat-sensitive active pharmaceutical ingredients.

1. Introduction

Oral administration is the most natural, simple, convenient, and safe mode of drug administration. Accordingly, approximately 90% of all medications are oral formulations and they constitute more than half of the drugs sold in markets [1]. However, conventional oral dosage forms have poor patient compliance due to difficulty in swallowing, particularly by geriatric and pediatric patients. To overcome these concerns, oral disintegrating tablets (ODTs), also known as orodispersible and rapidly disintegrating tablets, have been developed as solid dosage forms that disintegrate rapidly in the mouth due to the action of saliva [2]. ODTs disintegrate instantly, and their rapid dissolution or dispersion in saliva leads to rapid drug release in the mouth [3]. Furthermore, the dosage form of ODTs has improved patient acceptance and compliance and may offer better biopharmaceutical properties and efficacy and increased bioavailability compared with conventional oral dosage forms [4].

Several techniques are available for the manufacture of ODTs, including freeze drying, molding, sublimation, spray drying, and direct compression [5]. Among these, freeze drying offers a more rapid disintegration due to the porous structure of the resulting tablets. Freeze drying involves the freezing, primary drying, and secondary drying stages, and Ghaidhani and co-workers showed that it protects oxidizable substances in vacuum [6]. Moreover, the ensuing dehydration under aseptic conditions reduces the risk of contamination and allows preservation for longer periods with sustained sterility. This technique is also particularly suitable for thermolabile substances because it does not involve high temperatures that can cause thermal degradation. Freeze drying also leads to minimal changes in material properties because microbial growth and enzyme activities are abolished at low temperatures.

Mannitol is a common sugar-based excipient for ODTs that are formulated using freeze drying, and the chemical structures of mannitol, sorbitol, and xylitol are rich in hydroxyl groups, leading to better solubility and enhanced drug bioavailability. In this study, we compared these sugar excipients as diluents and disintegrants in ODT formulations and assessed the resulting tablet appearances, dissolutions, and drug release times.

Tamarind (*Tamarindus indica*) seed gum is a high molecular weight, neutral branched polysaccharide comprising a cellulose-like backbone that carries xylose and galactoxylose substances. This seed gum is insoluble in organic solvents but disperses with gentle heating to form a

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highly viscous mucilaginous gel solution with a broad pH tolerance and adhesive qualities [7]. Furthermore, tamarind seed gum is a non-toxic and non-irritant substance with hemostatic activities. Modified tamarind seed gum or carboxymethylxyloglucan is a derivative of xyloglucan that is formed by carboxymethylation using aqueous NaOH and monochloroacetic acid. The resulting substitution of hydroxyl groups with carboxymethyl groups enhances its solubility [8]. In line with the previous study reporting buccal delivery of drugs using mucoadhesive polymers such as polysaccharides [7], tamarind seed gum (crude or modified) was used as a binder during the preparation of tablet formulation by direct compression showing good mechanical properties and maintenance of tablet integrity [9].

In this study, the ODTs prepared from differing alcohol sugar using freeze drying were developed. The selected model drug was diclofenac sodium, a non-steroidal anti-inflammatory drug diclofenac sodium. In particular, we assessed the general appearance, weight variations, physicochemical properties, and moisture content and determined the disintegration and dissolution times *in vitro*. Subsequently, disintegration times were recorded in the oral cavity, and taste and mouth feel properties were assessed in human subjects. Besides developing a diclofenac ODT formulation, we predicted the freeze drying parameters and excipient compositions of ODTs to be used for the development of drugs in future.

2. Material and methods

2.1. Materials

Tamarind was obtained from Uthaitanee province, Thailand. Diclofenac sodium was supplied by Amoli Organics Ltd. (Mumbai, India). Mannitol (F-Melt type M) Lot No. 507002 was obtained from Fuji Chemical Industry Co., Ltd. (Toyama, Japan). Sorbitol and xylitol were purchased from Merck, and all other chemicals were of standard pharmaceutical grade.

2.2. ODT preparation by freeze drying

As shown in Table 1, ODTs were prepared using diclofenac sodium, PEG 4000, tamarind seed gum (crude or modified), and a sugar alcohol (mannitol, xylitol, or sorbitol). These components were weighed accurately, mixed in distilled water, and then dispersed using a magnetic stirrer to adjust the diclofenac sodium dose to 25 mg per 3 mL. Subsequently, 3-mL aliquots of the suspension were poured into the mold to produce a tablet containing 25 mg of diclofenac sodium. Tablets were then frozen at −41 °C and freeze dried overnight at a shelf temperature of −101 °C and a pressure of 0.5 Pa using a freeze dryer (FreeZone 4.5 L Labconco, Czech Republic).

2.3. General appearance

General appearances of tablets, including their shape, size, consistency, and surface texture, are important parameters for patient acceptance. Therefore, diameters and thicknesses of ten tablets from each formulation were examined using a digital Vernier caliper (Mitutoyo, Japan). Other physical appearances were optically observed.

2.4. wt variations

To test for weight uniformity, ten tablets from each formulation were weighed collectively and individually and average weights were calculated. Finally, individual tablet weights were compared with average weights to ascertain that they were within permissible limits as follows [10]:

$$\%\ Weight\ Variation = \frac{Average\ weight - Individual\ weight}{Average\ weight} \times 100 \quad (1)$$

2.5. wt change

Ten tablets from each formulation were weighed collectively and individually and weight changes were calculated using the following equation:

$$\%\ Weight\ change = \frac{Ideal\ weight - Actual\ weight}{Ideal\ weight} \times 100 \quad (2)$$

2.6. Moisture content

Moisture contents were determined using the loss on drying method. In this experiment, three tablets from each formulation were placed in the sample pan collectively and individually, and initial weights of ODTs were recorded. The balance lid was then closed for the drying process, and weights of ODTs were recorded and moisture contents of the initial samples were calculated using the following equation:

$$\%\ Moisture\ content = \frac{Weight\ of\ water}{Initial\ weight\ of\ ODT} \quad (3)$$

2.7. Fourier transform infrared (FTIR) spectroscopy

To investigate the effects of the freeze drying process on the drug–polymer interactions, diclofenac sodium, gum, sugar alcohol (mannitol, xylitol, or sorbitol), and their freeze drying mixture at ratio of 5:10:8 (diclofenac sodium: gum: sugar alcohol) were pulverized and blended with KBr and then compressed. The pellets were then analyzed using an FTIR spectrophotometer (model Magna-IR system 750, Nicolet Biomedical Inc., USA).

2.8. Differential scanning calorimetry (DSC)

The DSC thermograms of diclofenac sodium, gum, sugar alcohol (mannitol, xylitol, or sorbitol) and their freeze drying mixture at ratio of 5:10:8 (diclofenac sodium: gum: sugar alcohol) were measured using a differential scanning calorimeter (model Sapphire, PerkinElmer, USA) with indium as a standard. Each sample (2–3 mg) was weighed into a solid aluminum pan. The temperature was increased from 20 °C to 300 °C at 10 °C/min under nitrogen.

2.9. Powder X-ray diffraction (PXRD)

The powder X-ray diffraction patterns of the diclofenac sodium, gum, sugar alcohol (mannitol, xylitol, or sorbitol) and their freeze drying mixture at ratio of 5:10:8 (diclofenac sodium: gum: sugar alcohol) were obtained using a powder X-ray diffractometer (model D8, Bruker, Germany) under the following conditions: graphite monochromatized Cu Kα radiation, voltage = 45 kV, electric current = 40 mA, slit: DS1°, SS1°, RS 0.15 nm, and scanning ratio 2θ = 5°/min.

2.10. In vitro disintegration times

Three tablets were randomly selected from each formulation and placed individually in beakers containing 50 mL of phosphate buffer (pH 6.8). Disintegration times were then recorded at 37 °C ± 2 °C [5].

2.11. In vitro drug release profile

Dissolution times were examined using a USP Type II Apparatus (Paddle type) at 75 rpm. In this experiment, tablets were placed in 900 ml of phosphate buffer (pH 6.8) at 37 °C ± 0.5 °C, and the resulting dissolution medium was sampled in 5-mL aliquots after 1, 2, 4, 6, 8, 10, 15, 30, 60, and 120 min. Dissolved drug contents were then

Table 1
Formulations of diclofenac sodium ODT were fabricated using freeze drying.

Formulation code	Diclofenac Sodium (mg)	PEG 4000 (mg)	Tamarind seed gum (mg)		Sugar alcohol (mg)		
			Crude	Modified	Mannitol	Sorbitol	Xylitol
F1	25	8	10	-	20	-	-
F2	25	8	10	-	30	-	-
F3	25	8	10	-	40	-	-
F4	25	8	20	-	40	-	-
F5	25	8	30	-	40	-	-
F6	25	8	40	-	40	-	-
F7	25	8	50	-	40	-	-
$F7_m$	25	8	-	50	40	-	-
$F7_s$	25	8	50	-	-	40	-
$F7_{sm}$	25	8	-	50	-	40	-
$F7_x$	25	8	50	-	-	-	40
$F7_{xm}$	25	8	-	50	-	-	40
F8	25	8	60	-	40	-	-
$F8_m$	25	8	-	60	40	-	-
$F8_s$	25	8	60	-	-	40	-
$F8_{sm}$	25	8	-	60	-	40	-
$F8_x$	25	8	60	-	-	-	40
$F8_{xm}$	25	8	-	60	-	-	40
F9	25	8	70	-	40	-	-
$F9_m$	25	8	-	70	40	-	-
$F9_s$	25	8	70	-	-	40	-
$F9_{sm}$	25	8	-	70	-	40	-
$F9_x$	25	8	70	-	-	-	40
$F9_{xm}$	25	8	-	70	-	-	40

No subscript: mannitol with crude tamarind seed gum.
s: sorbitol with crude tamarind seed gum.
x: xylitol with crude tamarind seed gum.
m: mannitol with modified tamarind seed gum.
sm: sorbitol with modified tamarind seed gum.
xm: xylitol with modified tamarind seed gum.

determined using a UV/Vis-spectrophotometer (U-2900, Hitachi, Japan) at a wavelength of 275.5 nm.

2.12. In vivo study

In vivo evaluations of disintegration time, mouth feel, and taste of ODT samples were performed by 3 healthy men and 3 healthy women who were aged between 20 and 25 years. The volunteers were informed of the protocol and purpose of the study and provided informed consent for participation. The study was performed in accordance with the regulations of the Declaration of Helsinki [11].

2.12.1. Tablet disintegration in oral cavities

Volunteers were asked to rinse their oral cavities with water prior to the test and were then instructed to place a small amount of diclofenac sodium powder on their tongues for 5–10 s. The material was then immediately spat out, and volunteers were asked to rinse their oral cavities again before tasting ODTs. Single tablets were then placed on the tongue. The time was noted as soon as the tablet touched the tongue. Subsequently, volunteers were instructed to move their tongues gently to press their upper jaw. The maximum duration of these tests was 3 min. The endpoint of disintegration was recorded as the time at which no solid traces of the tablet were present on the tongue [11].

2.12.2. Taste and mouthfeel sensory evaluations

Volunteer opinions of taste were rated using the following score values: 0, good; 1, better than diclofenac sodium; 2, slightly better than diclofenac sodium; 3, similar to diclofenac sodium; 4, worse than diclofenac sodium; and for mouthfeel and 0, No roughness; 1, slight roughness; 2, moderate roughness; and 3, high roughness.

2.13. Stability tests

Stability tests were performed to determine the effects of temperature and relative humidity (RH) on ideal formulations in zip lock plastic bags under accelerated storage conditions of 40 °C/75% RH. Physical evaluations and *in vitro* drug release assessments were performed after 30 days [12].

2.14. Statistical analysis

Analysis of variance and Levene's test for homogeneity of variance were performed using SPSS version 10.0 for Windows (SPSS Inc., USA). *Post-hoc* testing ($P < 0.05$) of multiple comparisons was performed using Scheffé or Games-Howell tests for differences that were identified as significant using Levene's test.

3. Results and discussion

3.1. Preliminary studies of ODTs

In preliminary studies, we varied the amounts of tamarind seed gum (crude or modified) and mannitol and determined optimal portions of excipients in terms of stability of the resulting ODTs. Subsequently, F7–F9 and $F7_m$–$F9_m$ were selected for their physical stability and tolerable disintegration times of less than 3.30 min. The selected ODTs were then reformulated by replacing mannitol with sorbitol and xylitol, as shown in Table 1.

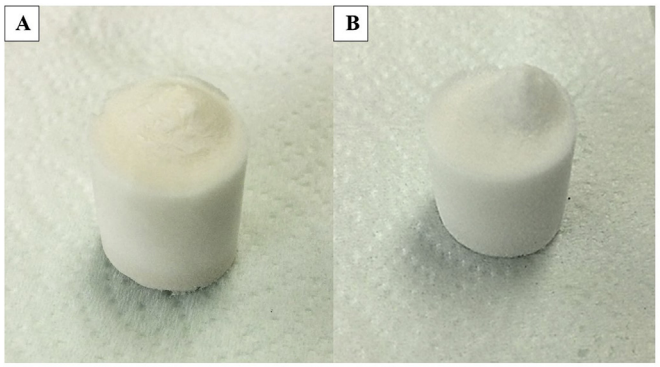

Fig. 1. ODTs with crude (A) and modified (B) tamarind seed gum.

3.2. Physical evaluation of ODTs

In evaluations of general appearance, colors of ODTs were affected by the type of tamarind seed gum used. In Fig. 1, we show that ODTs containing crude tamarind seed gum are beige, whereas those containing modified tamarind seed gum are white, probably owing to the removal of the high polysaccharide and protein contents of crude tamarind seed gum during the carboxymethylation process [13]. Tablet diameters were 11–14 mm with a relative standard deviation of less than 1%. However, thicknesses varied widely between 7 and 14 mm, with a relative standard deviation of less than 3% (Fig. 2). In addition, tablet thicknesses were affected by the types of sugar excipients used because freeze dried tablets that were formulated using sorbitol and xylitol tended to stick to the mold and were difficult to remove. However, percent weight variations were between 1.4% and 7.2% and were considered within acceptable limits [14].

Tablet weight changes varied between 3.5% and 26.8% and were not related to portions of tamarind seed gum. However, types of sugar-based excipients and tamarind seed gums influenced tablet weight changes (Fig. 3). In particular, although weight changes of tablets containing mannitol were not affected by the type of tamarind seed gum, those containing sorbitol or xylitol and modified tamarind seed gum exhibited much higher weight changes than the corresponding tablets containing crude tamarind seed gum. These data may reflect the hygroscopicity of sugar-based excipients. In particular, sorbitol and xylitol have high sensitivity to moisture, and their combination with modified tamarind seed gum, which also has a high ability to absorb moisture, is highly hygroscopic [15], leading to adherence of tablets to the molds and influences on weight changes.

The effects of varying types and amounts of tamarind seed gum and sugar-based excipients on tablet moisture contents are illustrated in Figs. 4 and 5, respectively. Higher amounts of tamarind seed gum resulted in higher tablet moisture contents, and ODTs containing mannitol and modified tamarind seed gum showed the highest moisture contents.

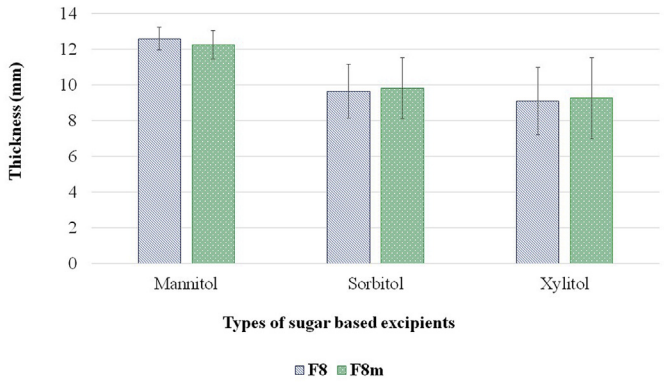

Fig. 2. Effects of types of sugar-based excipients and types of tamarind seed gum on tablet thickness.

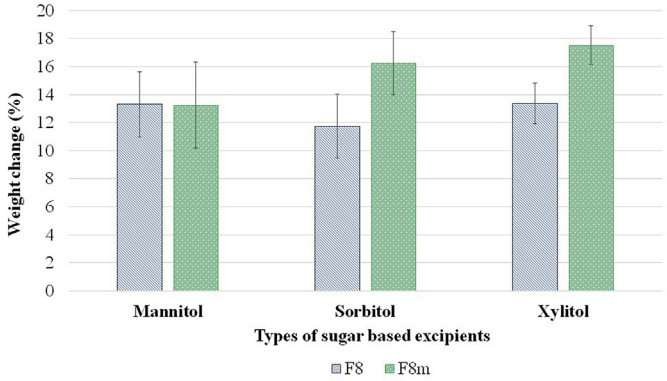

Fig. 3. Effects of sugar types and tamarind seed gum carboxymethylation on weight changes of tablets.

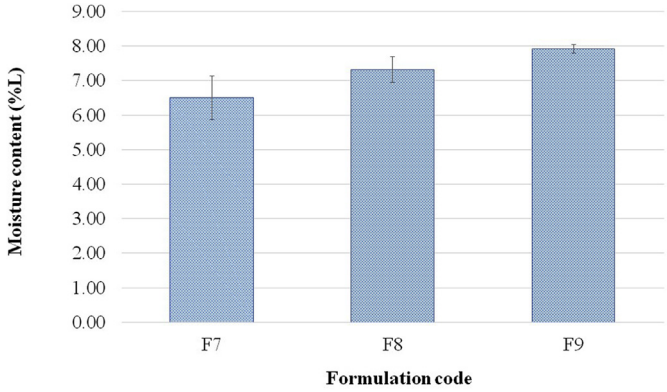

Fig. 4. Effects of tamarind seed gum contents on moisture levels in tablets.

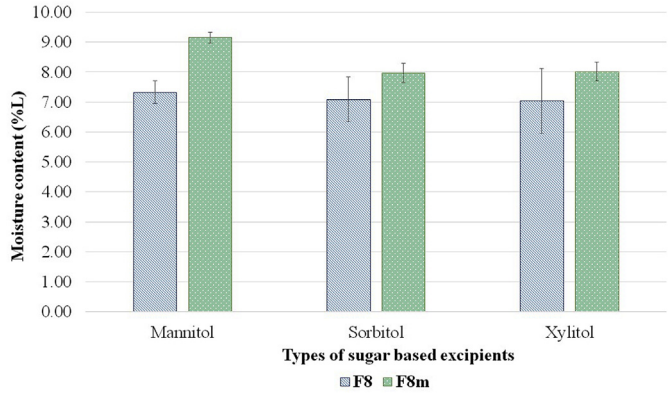

Fig. 5. Effects of sugar types and tamarind seed gum carboxymethylation on moisture contents of tablets.

3.3. Fourier transform infrared (FTIR) spectroscopy

The FITR spectra of diclofenac sodium, gum, sugar alcohol (mannitol, xylitol, or sorbitol) and their freeze drying mixture at ratio of 5:10:8 (diclofenac sodium: gum: sugar alcohol) are presented in Fig. 6. Diclofenac sodium showed characteristic absorption bands associated with C=O stretching of carboxylate anion at 1540 and 1403 cm^{-1} and N–H stretching of secondary amine at 3445 cm^{-1}. After dissolved in water, mixed with other excipients and dried by freeze drying, peak of the drug shifted to around 1650 cm^{-1} referring to C=O stretching of

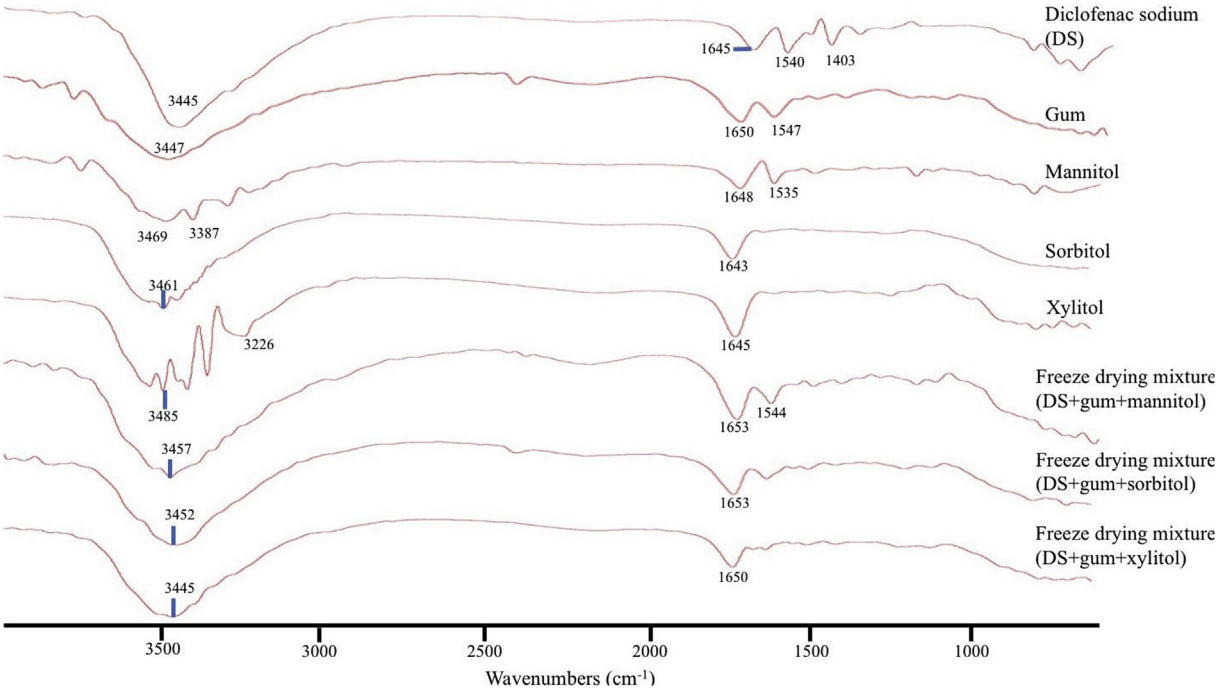

Fig. 6. FTIR spectra of diclofenac sodium, gum, mannitol, xylitol, sorbitol and their freeze drying mixture (diclofenac sodium: gum: sugar alcohol).

carboxylic acid which altered from salt form to acid form as previously reported [16]. Modified gum showed characteristic absorption bands associated with the stretching vibration of –OH in the 3500 - 3300 cm^{-1} region, –CH in the 3000 - 2800 cm^{-1} region, and at 3370 cm^{-1} to 3340 cm^{-1}, due to OH stretching of some OH groups in carboxymethylation moiety. A peak around 1421 and 1395 cm^{-1} for the modified gum were concerned with the symmetrical stretching vibration of carboxylate ions [9]. The freeze drying mixtures of all formulation still present characteristic peak of the starting materials (gum and alcohol sugars) except the active ingredient which altered to acid form.

3.4. Differential scanning calorimetry (DSC)

Fig. 7 shows DSC curves, which provided the thermal behavior of the starting materials and the freeze dried product from different alcohol sugar. The pure diclofenac sodium showed a characteristic endothermic peak around 64.48 °C and 100.30 °C. Then degradation peak of diclofenac sodium was observed at 227.54 °C. The gum DSC thermogram did not present any sharp peaks indicating its amorphous structure. The sharp endothermic peaks of mannitol, sorbitol, and xylitol were found at 168.79 °C, 100.80 °C, and 95.93 °C, respectively. These refer to crystallinity and purity of the alcohol sugars. For the freeze-dried products, all of the mixtures show small endothermic peaks around 143.62 °C–163.21 °C. This might be due to crystallinity structure change of the alcohol sugars. Moreover, the DSC curves of mixtures present a tremble pattern from 230 °C which is the degradation peak of diclofenac sodium.

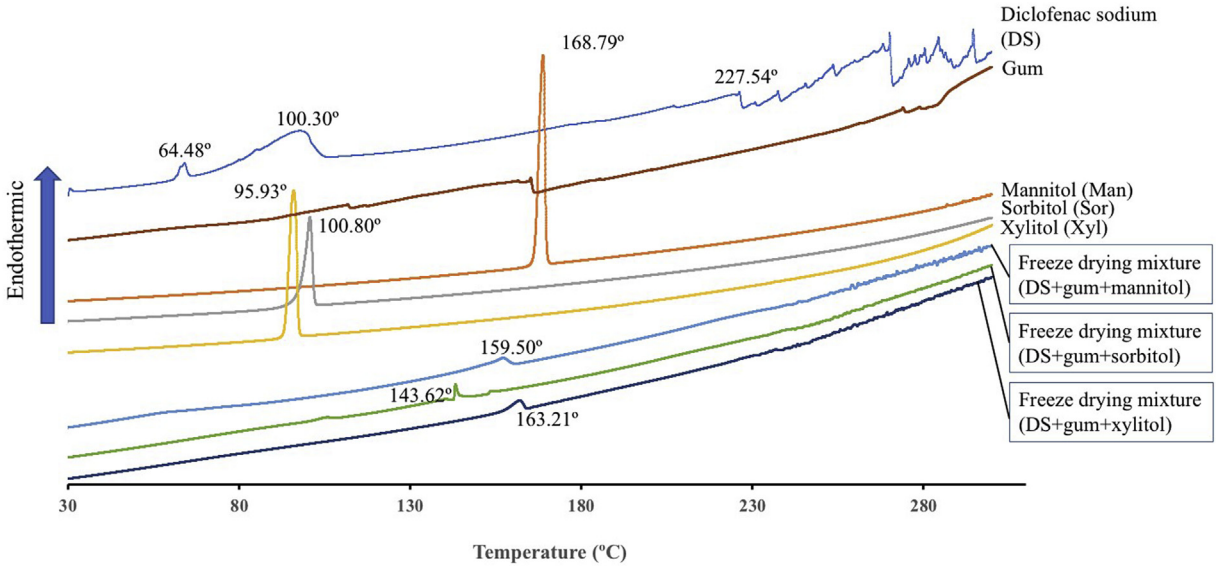

Fig. 7. DSC thermograms of diclofenac sodium, gum, mannitol, xylitol, sorbitol and their freeze drying mixture (diclofenac sodium: gum: sugar alcohol).

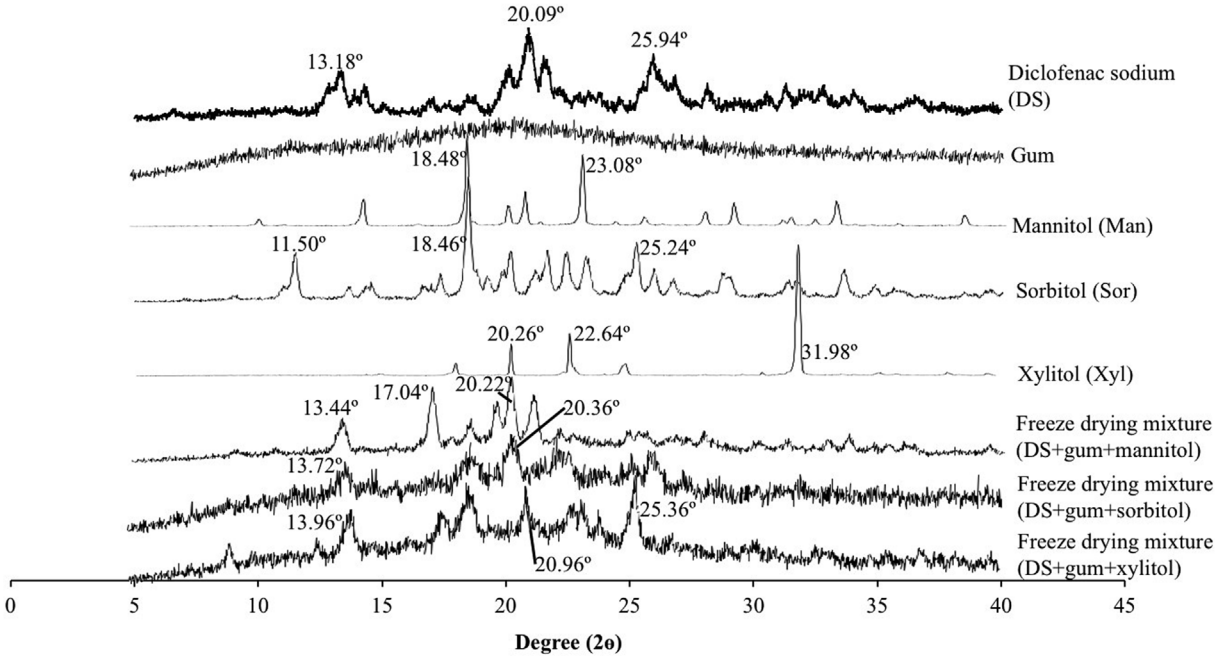

Fig. 8. PXRD patterns of diclofenac sodium, gum, mannitol, xylitol, sorbitol and their freeze drying mixture (diclofenac sodium: gum: sugar alcohol).

3.5. Powder X-ray diffraction (PXRD)

PXRD was used to determine the effect of freeze drying process on the crystallinity of the lyophilized product as depicted in Fig. 8. Diclofenac sodium showed important PXRD peak at 13.18°, 20.09°, and 25.94° [17] indicating its crystallinity structure while a typical halo PXRD pattern was observed in gum. Mannitol, sorbitol, and xylitol exhibited their characteristic sharp peaks referring to their crystallinity structure. The PXRD of freeze drying mixture displayed vital peaks of diclofenac sodium but broader. This reveals less crystallinity of the drug in the freeze dried product [18].

3.6. In vitro disintegration times

Disintegration times of diclofenac sodium ODTs containing crude and modified tamarind seed gum (Fig. 9) increased with tamarind seed gum contents, probably owing to the formation of a gel layer around the tablet that hindered water penetration [8]. However, the tablets

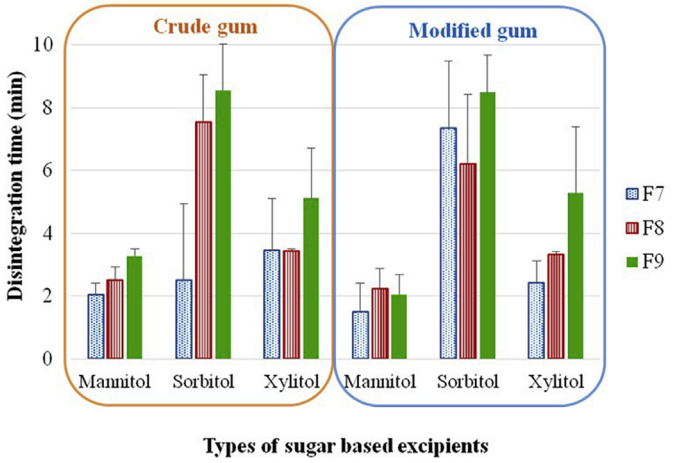

Fig. 9. *In vitro* disintegration time of diclofenac sodium ODT formulated using crude and
modified tamarind seed gums.

$F9_m$ and $F7_{sm}$ demonstrated an immediate change in trend, showing disintegration times shorter than those of $F8_m$ and longer than those of $F8_m$ and $F9_m$. In further analyses, types of tamarind seed gum failed to affect disintegration times significantly, whereas those of sugars influenced disintegration times, with mannitol, xylitol, and sorbitol showing the shortest to longest disintegration times in this order.

Disintegration times of tablets depend on their hygroscopicity and solubility, and high hygroscopicity and solubility lead to longer disintegration times [19]. Although the chemical structures of mannitol and sorbitol are similar, their responses to moisture differ [20]. In particular, sorbitol is more hygroscopic and soluble than mannitol and competes with disintegrants for water, leading to inhibition of disintegration [19].

3.7. In vitro dissolution study

According to the above evaluations, ODTs of the F8 formulations (F8, $F8_m$, $F8_s$, $F8_{sm}$, $F8_x$, and $F8_{xm}$) were selected for *in vitro* dissolution profile assessments because they showed the best physical appearance and had acceptable physical properties. Dissolution profiles of these formulations (Fig. 10) showed that the percentage drug release of all F8

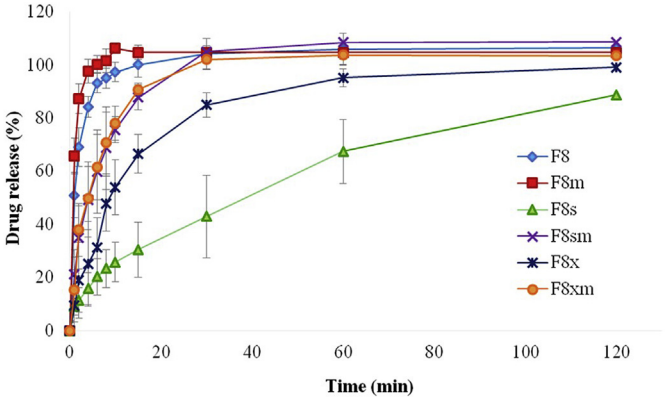

Fig. 10. Dissolution profiles of selected diclofenac sodium ODTs (F8, $F8_m$, $F8_s$, $F8_{sm}$, $F8_x$, and $F8_{xm}$).

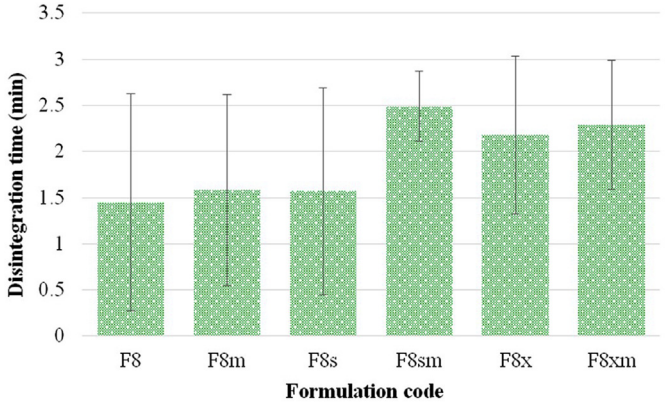

Fig. 11. *In vivo* disintegration time of selected diclofenac sodium ODTs (F8, $F8_m$, $F8_s$, $F8_{sm}$, $F8_x$, and $F8_{xm}$).

formulations was more than 85% in 15 min, except that of $F8_s$ and $F8_x$. $F8_m$ contained modified tamarind seed gum and mannitol and had the best dissolution rate, with 100% drug dissolution in 6 min $F8_m$ contained crude tamarind seed gum and sorbitol and had the least dissolution rate of only 20% in 6 min; it failed to achieve 100% drug release even in 120 min. These results are in agreement with the present disintegration times, again reflecting the retardation of drug release owing to the hygroscopicity of sorbitol and xylitol [19]. Disintegration times influence dissolution rates considerably. Accordingly, rapid disintegration of tablets into small particles with a high total surface area contributes to the high dissolution rate of mannitol ODTs, and increases percent drug release compared with that of tablets that disintegrate slowly. In addition, modified tamarind seed gum enhanced the ODT dissolution rates, and in F8 formulations with sorbitol and xylitol, dissolution rates were much higher in the presence of modified tamarind seed gum than in that of crude tamarind seed gum. Hence, carboxymethylation of starch leads to significant changes in the physicochemical properties of tablets with modified tamarind seed gum, as indicated by their high swelling capacity and water permeability and accelerated drug release [15].

Fig. 13. General appearances of $F8_m$ ODTs after storage in a stability chamber.

3.8. *In vivo study*

The present *in vivo* evaluation of disintegration time, taste, and mouthfeel was performed using the F8 formulations (Fig. 11 and Fig. 12). These data vary among volunteers, likely owing to differing perspectives and the limitations of subjective qualitative methods. Average disintegration times were also much shorter in human mouths than under the present *in vitro* conditions (Figs. 11 and 9) owing to the disintegrating effects of saliva and tongue forces. Moreover, as observed in our *in vitro* studies (Fig. 9), the shortest disintegration time was observed with mannitol-containing tablets, followed by xylitol- and sorbitol-containing tablets (Fig. 11). However, the modification of tamarind seed gum did not lead to enhanced *in vivo* disintegration times. In taste and mouth feel studies (Fig. 12), subjective scores were most favorable for ODTs containing xylitol, followed by those containing sorbitol and mannitol. Most volunteers rated $F8_s$ and $F8_x$ as slightly better than diclofenac sodium; however, overall, the F8 formulations failed to improve the taste of diclofenac sodium. These observations can be explained according to the sweetness of these sugar alcohols relative to sucrose. In particular, xylitol has sweetness similar to sucrose,

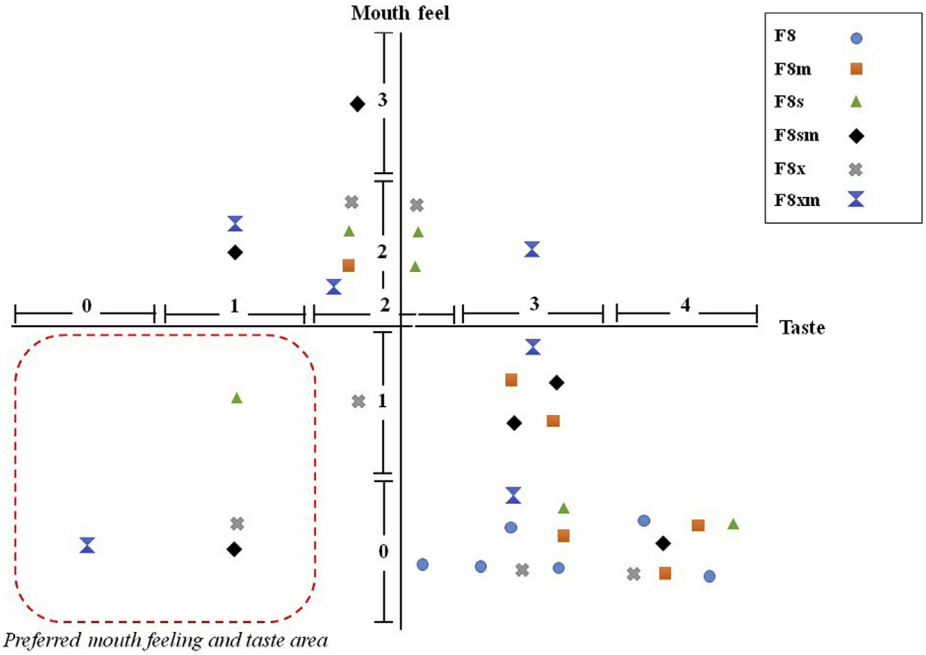

Fig. 12. *In vivo* taste and mouthfeel of selected diclofenac sodium ODTs (F8, $F8_m$, $F8_s$, $F8_{sm}$, $F8_x$, and $F8_{xm}$).

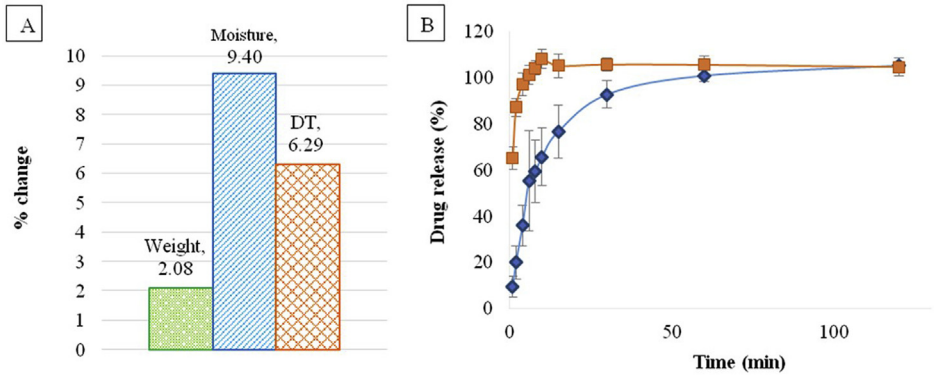

Fig. 14. (A) Changes in weights, moisture contents, and dissolution times; (B) dissolution profiles of selected $F8_m$ ODTs after storage in a stability chamber.

whereas sorbitol and mannitol have about 55% and 50% of the sweetness of sucrose, respectively [21]. Finally, modified gum led to trivial improvement in the taste and mouthfeel of ODTs, and formulations containing mannitol had less roughness than those containing xylitol. Hence, mannitol enhances mouthfeel, and xylitol and sorbitol mask the taste properties. The present data show that $F8_x$ had the most consistently positive taste and mouthfeel scores among the F8 formulations.

3.9. Stability study

Due its physical characteristics, the $F8_m$ formulation was selected for stability tests, and after storage in the stability chamber for almost 1 month, the physical appearances of $F8_m$ tablets did not change with respect to their initial state (Fig. 13). Moreover, as presented in Fig. 14A, tablet weights and moisture contents increased by 2.08% and 9.40%, respectively, over the month in the stability chamber. Corresponding disintegration times and dissolution profiles (Fig. 14A and B) show that zip lock bags offer insufficient protection from environmental moisture, as indicated by the high hygroscopicity of the tablet and gum that retarded tablet disintegration and drug diffusion.

4. Conclusions

The present freeze-drying technique is suitable for the development of ODTs using crude and modified tamarind seed gum as a binder. We identified no significant effect of modified tamarind seed gum on disintegration times. However, the dissolution test showed that modified tamarind seed gum enhances dissolution rates of ODTs. The formulation $F8_m$ was prepared with optimal physical characteristics using carboxymethylated gum and mannitol and had a disintegration time of less than 1.5 min and the best dissolution profile. However, the taste of ODTs containing mannitol requires further improvement to increase patient compliance.

Declaration of competing interest

I am submitting a manuscript for consideration of publication in Journal of Drug Delivery Science and Technology. The manuscript is entitled “Development and *in vitro/in vivo* evaluation of tamarind seed gum-based oral disintegrating tablets after fabrication by freeze drying”. This manuscript has not been published elsewhere and is not under consideration by another journal. I have approved the manuscript and agree with submission to Journal of Drug Delivery Science and Technology. There are no conflicts of interest to declare.

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