

Extraction, Characterization, and Evaluation of Chia Seed Mucilage as a Natural Superdisintegrant in Donepezil Hydrochloride Fast-Dissolving Films

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Abstract: Natural gums and mucilage have attracted considerable interest as multifunctional pharmaceutical excipients owing to their biocompatibility, biodegradability, and cost-effectiveness. The present study investigated the potential of *Salvia hispanica* (chia) seed mucilage as a natural superdisintegrant in the development of oral disintegrating films (ODFs) of Donepezil hydrochloride, an acetylcholinesterase inhibitor indicated for the management of Alzheimer's disease. Chia seed mucilage was isolated and characterized for its physicochemical properties. Donepezil hydrochloride-loaded ODFs (F1–F6) were prepared by the solvent casting method using different concentrations of chia seed mucilage. The formulations were evaluated for appearance, weight variation, thickness, folding endurance, surface pH, moisture loss, drug content, in vitro disintegration time, and in vitro dissolution. Drug–excipient compatibility was assessed by FTIR, while surface morphology was examined using scanning electron microscopy (SEM). The optimized formulation was subjected to accelerated stability studies as per ICH guidelines ($40 \pm 2^\circ\text{C}/75 \pm 5\% \text{ RH}$) for 2 months. FTIR analysis confirmed the absence of significant drug–excipient interactions, while SEM revealed a rough, plate-like, and flaky surface morphology. All formulations complied with acceptable pharmacopeial limits for physicochemical characteristics, with drug content ranging from 94.2–99.2%. Film thickness varied between 50.33 and 60.41 μm , and moisture loss ranged from 2.08–3.96%. Disintegration time increased with increasing mucilage concentration and ranged from 42.1 to 59.5 s. Among all formulations, F3 demonstrated the shortest disintegration time ($42.1 \pm 1.14 \text{ s}$) and the highest cumulative drug release (99.72% within 6 min). Accelerated stability studies showed no significant changes in the physicochemical properties, drug content, disintegration time, or dissolution profile of the optimized formulation. Chia seed mucilage proved to be a promising natural superdisintegrant for the formulation of Donepezil hydrochloride oral disintegrating films. The optimized formulation (F3) exhibited rapid disintegration, excellent drug release, and satisfactory stability, highlighting its potential as an effective immediate-release oral drug delivery system for improved patient compliance.

Keywords: Oral disintegrating film; *Salvia hispanica*; Chia seed mucilage; Natural superdisintegrant; Solvent casting; Alzheimer's disease.

Introduction

Since the 1970s, oral fast disintegrating drug delivery systems (OFDDS) have gained significant attention because they rapidly dissolve in the oral cavity, providing a faster onset of action than conventional tablets and capsules¹. These systems improve patient compliance, particularly for paediatric, geriatric, and dysphagic

patients who experience difficulty swallowing solid dosage forms². Oral disintegrating films (ODFs) are thin, flexible dosage forms that rapidly dissolve in the oral cavity without water, enabling quick drug release and improved bioavailability. They enhance patient compliance, especially in paediatric, geriatric, and dysphagic patients, while effective taste masking is essential to ensure palatability and patient acceptance³.

From a commercial perspective oral film drug delivery technology offers an opportunity to extend revenue lifecycles for pharmaceutical companies whose drug patent is expiring and will soon be vulnerable to generic competition⁴. Although oral disintegrating films offer several advantages, they have limitations such as low drug-loading capacity, challenges in achieving uniform dose distribution, and high hygroscopicity. Therefore, appropriate moisture-resistant packaging and comprehensive stability studies are essential to ensure product quality, safety, and efficacy throughout its shelf life⁵. Thin films were developed to overcome the swallowing difficulties associated with conventional tablets and capsules. Oral disintegrating films (ODFs) rapidly dissolve in saliva, enabling fast drug release, improved bioavailability, and enhanced patient compliance. They can also be formulated for oral, sublingual, buccal, or ophthalmic drug delivery depending on the therapeutic application⁶. The oral mucosa is the protective mucous membrane lining the oral cavity, serving as a barrier against mechanical injury, microorganisms, and harmful substances. It is classified into three regions: masticatory mucosa (25%), specialized mucosa (15%), and lining mucosa (60%), which together cover approximately 200 cm² of surface area. The oral cavity comprises the buccal, sublingual, gingival, and palatal regions, all of which can serve as potential sites for drug absorption⁷. The tongue is a muscular organ covered by a mucous membrane that forms the floor of the oral cavity. It contains intrinsic muscles, which alter the tongue's shape for speech and swallowing, and extrinsic muscles, which facilitate movements such as forward, backward, and side-to-side motion⁸. The oral mucosa is permeable to certain drugs, enabling rapid absorption and therapeutic action. Drug permeability is influenced by factors such as mucosal thickness, degree of keratinization, and lipid content, collectively known as the oral mucosal barrier. Among the different regions, drug permeability is highest in the sublingual mucosa, followed by the buccal mucosa, and is lowest in the palatal mucosa⁹. Owing to its excellent mucilage-forming ability and functional properties, chia is widely used in pharmaceutical, nutraceutical, and functional food applications, where its mucilage serves as a promising natural polymer¹⁹⁻²¹. Chia seed mucilage possesses excellent water-holding, viscosity, emulsifying, and film-forming properties, making it a promising natural polymer for pharmaceutical and food applications. It is widely used as a stabilizer, binder, suspending agent, and functional coating material, with significant potential in the development of edible films and drug delivery systems.²³

Material and Methods

The formulation was prepared using Donepezil as the active pharmaceutical ingredient, obtained as a gift sample from IPCA Laboratories Ltd., Silvassa. Hydroxypropyl methylcellulose (HPMC), polyethylene glycol 400 (PEG 400), mannitol, and citric acid were procured from Research Lab Fine Chem Industries, Mumbai, while glycerol was obtained from Chemdyes Corporation, Gujarat. Chia seeds were purchased from the local market in Pune and used as the natural polymer source.

Standardization of API

The sample of donepezil was examined for its physical appearance and color and it reported. Melting point of donepezil can be done by using (Thiele tube Laboratory glassware) conventional method designed to contain and heat an oil bath, care is taken to maintain uniform heating. Solubility of drug was measured in distilled water. 3 ml of distilled water was taken in each glass vials of 5 ml capacity. The small amount of drug was added with some increase in proportion, stirring until saturation level is exists²⁴.

Differential scanning calorimetry

DSC study was done on the physical states of pure medication, pure carrier, pure physical mixes, and EXTs.

Under a nitrogen atmosphere, the temperature range used ranged from 30 to 250°C at a heating rate of 20°C/min. To maintain the inert atmosphere at the experiment's target rate of 40 ml/min, nitrogen gas might be purged during the process. The few samples are moved and heated in an aluminium pan with crimps²⁵.

Determination standard curve of donepezil

Donepezil, accurately weighed at 10.0 mg, was diluted in a volumetric flask of methanol to produce a stock solution containing 100 ug/ml. Using methanol, a range of solutions of 5, 10, 15, 20, 25 and 20 g/ml were prepared from this stock solution²⁶. As a blank solution, methanol was used to scan all of the solutions between 200 and 400 nm.

FT-IR Studies of Drug

The infrared spectrums of Donepezil drug were recorded using IR- spectrophotometer (Bruker) ²⁷. The spectrum was scanned over a frequency range of 4000-400cm⁻¹ with a resolution 4cm⁻¹.

Extraction and characterization of chia seed mucilage

The required quantity of chia seeds was accurately weighed using a Shimadzu AUX220 analytical balance and hydrated in distilled water at a 1:40 ratio at 25°C. The dispersion was stirred on a magnetic stirrer (Remi 1MLH) for 2 h to ensure complete hydration and mucilage extraction. The resulting viscous dispersion was centrifuged at 6000 rpm for 50 min using a laboratory centrifuge, producing three distinct layers. The upper seed layer and excess water containing soluble carbohydrates were carefully removed, and the mucilage gel was collected using a spatula. The extracted mucilage was dried in a hot air oven (Dolphins) at 50°C, ground into a fine powder, passed through sieve No. 80, and stored in a desiccator at room temperature until further use²⁸.

The isolated mucilage was subjected for various organoleptic evaluations such as color, Oduor, shape, taste and special features like touch and texture. pH of 1% w/v solution of the extracted mucilage was determined using a digital pH meter. The powdered sample of extracted mucilage was transferred into a capillary tube and byusing melting point apparatus melting point was determined²⁹.

Percent yield

Based on the quantity of chia seeds used for mucilage extraction and the quantity of dried mucilage obtained, the % yield was determined. The formula listed below was used to determine the percentage yield²⁹.

% yield=	Weight of dried mucilage obtained	×100
	Weight of seeds taken for extraction of mucilage	

Swelling index

Using the approach described, the swelling index of mucilage was calculated. A 50 mL measuring cylinder was carefully filled with 1g of mucilage powder after being precisely weighed. The volume was diluted with water to make 50ml. The cylinder was set aside and shaken gently for one hour at intervals of ten minutes³⁰. After that, the cylinder was left in a quiet area for 24 hours. After 24 hours, the mucilage's volume was measured. The following equation was used to determine the swelling index (SI).

Swelling Index (SI)=	Initial volume of powder in measuring cylinder	×100
	Final volume of powder in measuring cylinder	

Solubility test

The extracted mucilage of chia seed was subjected for solubility test in different solvents as per British Pharmacopoeia specifications.

FTIR Study

The infrared spectrums of chia seed mucilage were recorded using IR- spectrophotometer (Bruker) ²⁷. The spectrum was scanned over a frequency range of 4000-400cm⁻¹ with a resolution 4cm⁻¹[28].

Drug-Excipients compatibility study

The compatibility of drug and excipients under experimental condition is important prerequisite before formulation. Fourier Transform Infrared Spectroscopy was used to determine the purity of the drug sample and interaction of the drug with the polymers. Infrared spectra of drug and polymers, alone and in physical mixture were taken. Then it was investigated for possible interaction between polymer and drug and compared with the standard IR spectra of the pure drug³¹.

Preparation of oral disintegrating film:

Donepezil oral disintegrating films (ODFs) were prepared by the solvent casting method using varying concentrations of chia seed mucilage as a natural super-disintegrant, as shown in Table 1. Hydroxypropyl methylcellulose (HPMC) and dried chia mucilage were separately dispersed in 5 mL of distilled water and allowed to hydrate overnight to ensure complete swelling. Subsequently, glycerol and citric acid were incorporated into formulations F1, F2, and F3, whereas polyethylene glycol 400 (PEG 400) and citric acid were added to formulations F4, F5, and F6 as plasticizers³².

The hydrated chia mucilage dispersion was gradually added to the HPMC solution, which was maintained at 60°C, and the mixture was homogenized at 2000 rpm for 30 min to obtain a uniform polymeric solution. Donepezil hydrochloride, mannitol, and pineapple flavour were separately dissolved in distilled water and then incorporated into the polymeric mixture under continuous stirring. The resulting casting solution was stirred for an additional 1 h to ensure uniform drug distribution and then allowed to stand at room temperature to eliminate entrapped air bubbles.

The final homogeneous solution was cast onto a Petri plate (9.6 cm diameter) and dried in a hot air oven at 40°C for 6 h. After complete drying, the films were carefully peeled from the casting surface and visually inspected for defects such as cracks or air pockets. The dried films were cut into uniform dimensions of 2 cm × 2 cm, corresponding to the required dose, and stored in a desiccator until further evaluation. Finally, the films were individually wrapped in aluminium foil and stored in airtight glass containers to protect them from moisture and maintain their mechanical integrity and elasticity.

Table 1. Composition of Oral Disintegrating Film of Donepezil

S.N.	Ingredients	F1	F2	F3	F4	F5	F6
1	Donepezil HCL (mg)	90	90	90	90	90	90
2	HPMC (mg)	400	400	400	400	400	400
3	Salvia hispanica mucilage (mg)	9	18	27	9	18	27
4	Glycerol (g)	0.3	0.3	0.3	-	-	-
5	PEG 400(g)	-	-	-	0.3	0.3	0.3
6	Mannitol (mg)	9	9	9	9	9	9

7	Citric acid(mg)	5	5	5	5	5	5
8	Flavour(ml)	0.2	0.2	0.2	0.2	0.2	0.2
9	Colour(ml)	0.3	0.3	0.3	0.3	0.3	0.3
10	D.W. (up to20 ml)	20	20	20	20	20	20

The oral disintegrating film (ODF) of donepezil was formulated to deliver a dose of 5 mg per individual film. The casting solution was poured into a Petri plate with a radius of 4.8 cm, providing a total casting area of 72.34 cm². Each individual film was cut into a 4 cm² unit. Based on the total casting area, approximately 18 films ($72.34/4 = 18.05$) were obtained from one Petri plate. Therefore, the total amount of donepezil incorporated into the casting solution was 90 mg (18×5 mg), ensuring that each 4 cm² film contained 5 mg of donepezil.

Evaluation of Films

The film sample was evaluated for its colour, odour, appearance, weight variation, thickness and folding endurance. By cutting the film and calculating the weight of each individual film, the weight variation of a film is calculated in triplicate. It is crucial to confirm thickness uniformity because it directly correlates with the film's dose accuracy. A calibrated Trimos V+ height gauge is used to measure a film's thickness before the mean average is computed. The average is computed using three readings from each of the batch. The film's folding endurance was tested by folding a single piece of film repeatedly until it broke. The quantity of folds that the film could withstand at the same location without breaking determined the folding endurance. Six films were evaluated³³.

Drug content

A random sample of films was used to test the homogeneity of film content. The Donepezil films were held in phosphate buffer 6.8 pH and allowed 24 hours of stirring time. The solution was filtered, diluted, and the drug content was determined using a UV spectrophotometer to measure absorbance at 313 nm in comparison to phosphate buffer pH 6.8 solutions as a blank. The concentration of donepezil in µg/ml was then determined using a regression equation³⁴.

Percentage drug content = Practical drug content / Theoretical drug content X 100

Surface pH study

In order to look at potential adverse effects in vivo, the surface pH of oral films is measured. We made an effort to maintain the pH as close to neutral as we could because an acidic or alkaline pH may irritate mucosa. A composite glass electrode is used for this. By allowing the film to come into contact with 10 ml of phosphate buffer pH 6.8 in a Petri dish for some time at room temperature, the film is given the chance to swell. By placing the electrode on the film surface and allowing it to equilibrate for 1 minute, the pH is measured³⁵.

Moisture loss

Percent moisture loss is a parameter that determines the hygroscopicity of a film. Usually, this parameter is determined by first finding the initial weight of the film, afterward, putting this film in a desiccator for three days. Desiccator contains calcium carbonate. After three days, strips are taken out and weighed again. Moisture loss is determined by applying the following formula³⁶.

Percentage moisture loss = initial weight - final weight / initial weight × 100

In-vitro disintegration test

When oral film comes into contact with saliva or water, it begins to break down at the disintegration time. Disintegration time was investigated using a USP (United States Pharmacopoeia) disintegration device. For calculating the disintegration period of films with very quick disintegration, there are no clear criteria available. When a film is placed on 2 mL of distilled water in a petri dish, the amount of time it takes for the film to dissolve entirely is measured³⁷.

In-vitro Dissolution study

For any formulation drug release from the dosage form is the important parameter to be measured. Drug release of oral disintegrating film of donepezil was evaluated by *in vitro* dissolution test apparatus³⁸. Mostly the test was performed using basket apparatus at 50 rpm and 300 ml of phosphate buffer pH 6.8. The temperature was maintained at 37±0.5°C. The film was placed in basket. Aliquots of 5 ml were withdrawn at predetermined time intervals of 1, 2, 3, 4, 5 and 6 minutes and the volume was replaced with fresh dissolution medium. Above 5 ml samples were filtered through Whatman filter paper and analyzed for Donepezil after appropriate dilution by measuring the absorbance at 313 nm.

Scanning electron microscopy (SEM)

Scanning electron microscopy (SEM) was used to examine the morphology of the oral strip at a specific magnification. The distinction between the upper and lower sides of the films was discussed in the study. Additionally, it aids in determining API distribution³⁹.

FT-IR of formulated film

The IR spectrum of formulated oral film of F3 is recorded using FTIR by ATR method. The spectrum was scanned over a frequency range of 4000-400 cm⁻¹.

Stability studies

To evaluate the stability of the drug formulation, stability experiments were conducted in accordance with ICH. A package made of aluminium and plastic was laminated and used to seal the optimized F3 formulation. The samples were kept at 40 °C and 75% RH for two months. At the conclusion of the investigation, the formulation's physical properties, weight variation, thickness, folding endurance, drug content, and drug release characteristics were examined⁴⁰.

Result and Discussion

Standardization of API

Determination of standard curve of donepezil hydrochloride

These solutions were scanned in spectrum mode between 200-400 nm. The absorbance of resulting solutions was measured at 313 nm and calibration curve was plotted. Linearity range was found to be 5-25 µg/ml for donepezil at 313 nm (Fig. 1). The correlation coefficient was found to be 0.9994, which shows good linearity between above range. The slope was found to be 0.0366 and intercept was found to be 0.017.

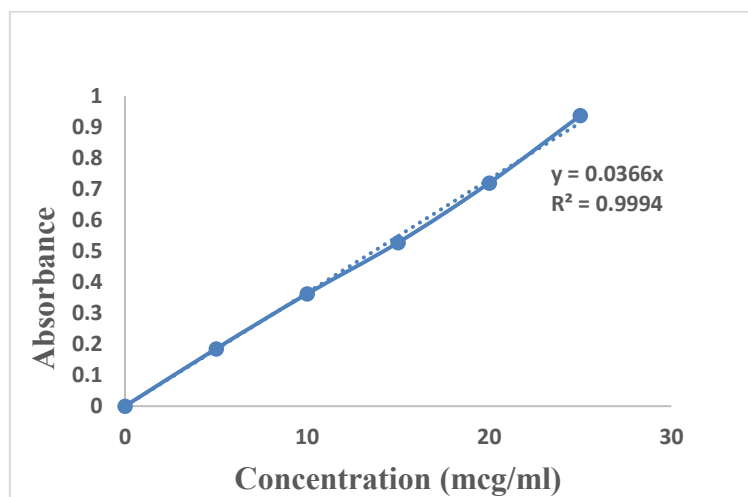


Figure 1. Calibration curve of donepezil hydrochloride.

Physicochemical parameter

The drug was obtained as a white to off-white, odorless powder with a characteristic bitter taste. It exhibited a melting point of 231°C, indicating good thermal stability. Solubility studies revealed that the drug was freely soluble in water and methanol, facilitating its suitability for formulation development and analytical studies, while it was insoluble in dimethyl sulfoxide (DMSO). These physicochemical characteristics are consistent with the reported properties of the pure drug and confirm its identity and suitability for further pharmaceutical formulation (Table 2).

Table 2. The physicochemical characteristics of Donepezil

Property	Observation
Color	A white to off-white powder
Odour	Odorless
Solubility	Freely soluble in water and methanol
Taste	Bitter
Melting point	231°C
Solubility	Freely soluble in water and methanol. Insoluble in DMSO

Differential scanning calorimetry

The DSC thermogram of Donepezil exhibited a sharp endothermic peak corresponding to its melting event, confirming its crystalline nature. The thermogram showed an onset temperature of 225.87°C, a peak melting temperature of 231–232°C, and an endset temperature of 232.83°C. The observed melting point closely agrees with the reported melting range of Donepezil, indicating the purity and identity of the drug (Fig. 2). The sharp and well-defined endothermic peak suggests a highly crystalline material with no evidence of thermal degradation or impurities within the studied temperature range. These findings confirm the thermal stability of Donepezil and its suitability for further formulation development.

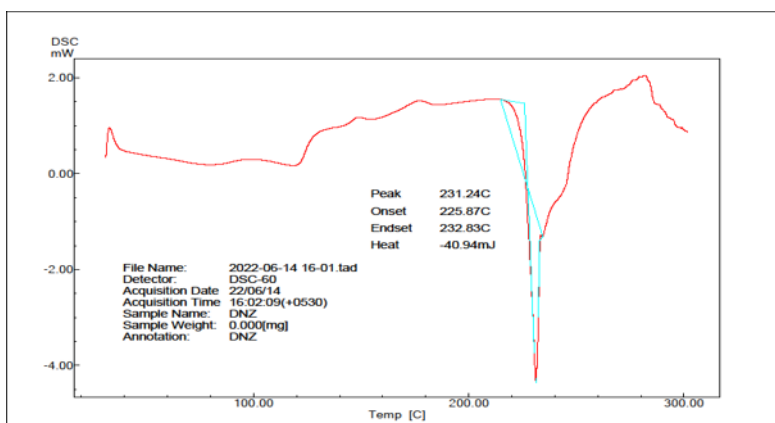


Figure 2. The DSC thermogram of donepezil hydrochloride.

FT-IR Studies of Drug

The infrared spectrums of Donepezil drug were recorded and the intense absorption at 1680 cm^{-1} is characteristic of the indanone ketone ($\text{C}=\text{O}$) and is one of the indicative peaks confirming Donepezil (Fig.3). Aromatic C–H stretching vibrations were observed at 3070 and 3003 cm^{-1} , while aliphatic C–H stretching bands appeared at 2932 – 2853 cm^{-1} . The aromatic skeletal C=C stretching vibrations were detected at 1643 , 1592 , and 1499 cm^{-1} . Strong bands in the 1261 – 1034 cm^{-1} region were assigned to C–O–C stretching vibrations of the methoxy ether groups. The absorption near 1036 cm^{-1} corresponded to C–N stretching of the piperidine ring. Broad absorptions between 3404 and 2553 cm^{-1} were attributed to hydrogen-bonded interactions associated with the protonated tertiary amine in the hydrochloride salt.

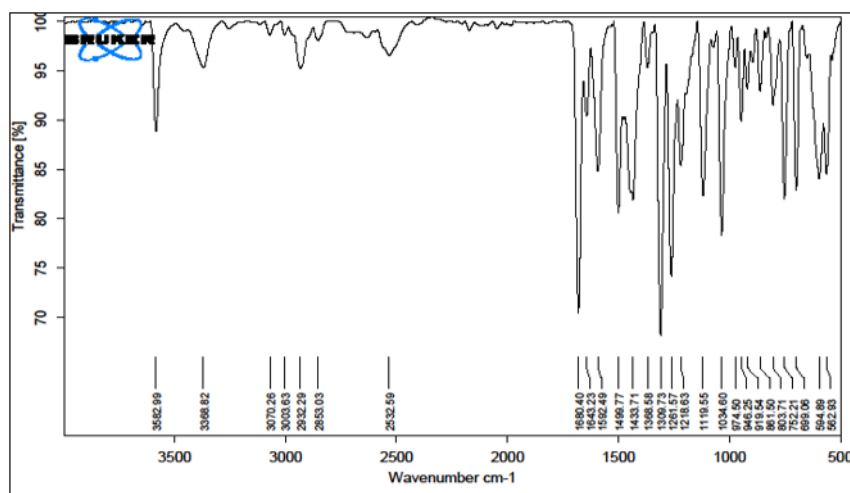


Figure 3. FTIR spectra of donepezil hydrochloride.

These characteristic absorption bands confirm the structural integrity and identity of Donepezil hydrochloride.

Characterization of chia seed mucilage

Physicochemical Properties

The isolated mucilage was subjected for physicochemical evaluations and result was depicted in table 3. The extracted mucilage was obtained as a greyish-white, odourless, flaky material with a mucilaginous taste. It readily formed a viscous solution in water, confirming its hydrophilic nature. The mucilage exhibited a near-

neutral pH (6.4), a swelling index of 9, viscosity of 416 cps (1% solution), 8% yield, and a melting point of 231°C, indicating good swelling ability and thermal stability. Preliminary phytochemical evaluation showed positive results for carbohydrates (Molisch's test), glycosides, mucilage (Ruthenium red test), and reducing sugars (Fehling's test), while tests for tannins, proteins, and alkaloids were negative. These findings confirm that the extracted material is a polysaccharide-rich natural mucilage with suitable physicochemical properties for potential application as a pharmaceutical excipient.

Table 3. Physicochemical evaluation of *Salvia hispanica* mucilage.

S. No	Properties evaluated	Observations
1	Colour	Greyish white
2	Taste	Mucilaginous
3	Odour	Odourless
4	Appearance	Flaky appearance
5	Solubility	Forms viscous solution in water
6	pH (By Digital pH meter)	6.4*
7	Swelling Index	9*
8	% yield	8 %
9	Melting point	231°C
10	Viscosity (1% solution)	416 cps*
11	Test for Carbohydrates (Molisch's test)	+ve
12	Test for Tannins (Ferric chloride test)	-ve
13	Test for proteins (Ninhydrin test)	-ve
14	Test for alkaloids (Wagner's test)	-ve
15	Test for glycosides	+ve
16	Test for mucilage (Ruthenium red test)	+ve
17	Test for reducing sugar (Fehling's test)	+ve

FTIR Study

A broad absorption band observed around 3400–3300 cm^{-1} is attributed to the O–H stretching vibration of hydroxyl groups, confirming the presence of extensive hydrogen bonding typical of carbohydrate polymers. The absorption peaks at 2920–2850 cm^{-1} correspond to the C–H stretching vibrations of aliphatic –CH and –CH₂

groups. A weak band around $1740\text{--}1650\text{ cm}^{-1}$ may be assigned to $\text{C}=\text{O}$ stretching of ester/carboxyl groups or to the H-O-H bending vibration of absorbed moisture, indicating the hydrophilic nature of the mucilage. The peaks observed in the region of $1600\text{--}1400\text{ cm}^{-1}$ are associated with asymmetric and symmetric stretching vibrations of carboxylate ($-\text{COO}^-$) groups and CH_2 bending, suggesting the presence of uronic acid residues commonly found in plant mucilages. Strong absorption bands between 1200 and 1000 cm^{-1} , particularly around $1150\text{--}1030\text{ cm}^{-1}$, are characteristic of C-O-C glycosidic linkages and C-O stretching vibrations of polysaccharides, confirming the carbohydrate backbone of the extracted mucilage. The bands observed below 900 cm^{-1} are attributed to C-H out-of-plane bending and vibrations related to the glycosidic ring structure (Fig. 3).

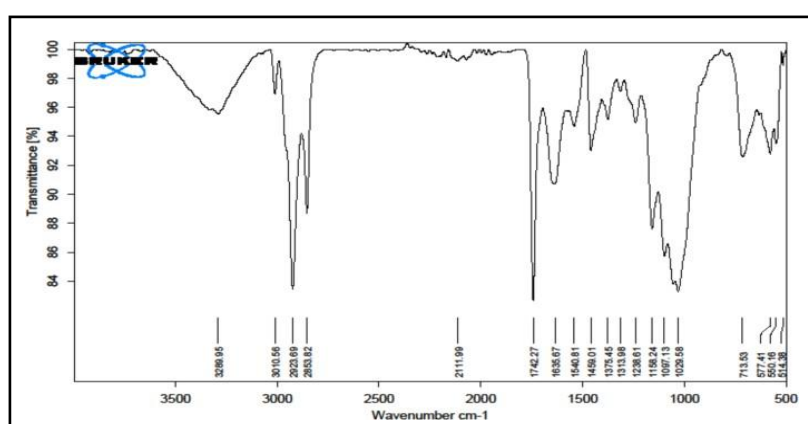


Figure 3. FTIR spectra of chia seed mucilage.

Overall, the FTIR spectrum confirms that the extracted material is a polysaccharide-rich natural mucilage containing abundant hydroxyl, aliphatic, carboxyl, and glycosidic functional groups. The absence of additional prominent peaks corresponding to synthetic or foreign functional groups indicates that the extraction process preserved the native chemical structure of the mucilage without significant chemical modification, supporting its suitability as a natural pharmaceutical excipient for formulation development.

Drug-Excipients compatibility study

The FTIR spectrum of the drug-polymer physical mixture exhibited the characteristic absorption bands of both Donepezil and the natural polymer without any significant shift, disappearance, or appearance of new peaks (Fig. 4). The broad absorption band at $3583\text{--}3370\text{ cm}^{-1}$ corresponds to O-H stretching vibrations of the hydroxyl groups present in the mucilage. The peaks at 3070 cm^{-1} and $2924\text{--}2865\text{ cm}^{-1}$ are attributed to aromatic and aliphatic C-H stretching vibrations, respectively. A prominent absorption band at 1680 cm^{-1} is assigned to C=O stretching, while the peaks at $1649\text{--}1438\text{ cm}^{-1}$ correspond to C=C stretching of aromatic rings and CH_2 bending vibrations. The strong bands observed in the region of $1367\text{--}1024\text{ cm}^{-1}$ are characteristic of C-N , C-O , and C-O-C stretching vibrations, indicating the presence of ether and glycosidic linkages. The peaks below 1000 cm^{-1} ($948\text{--}562\text{ cm}^{-1}$) are attributed to aromatic C-H bending and ring deformation vibrations.

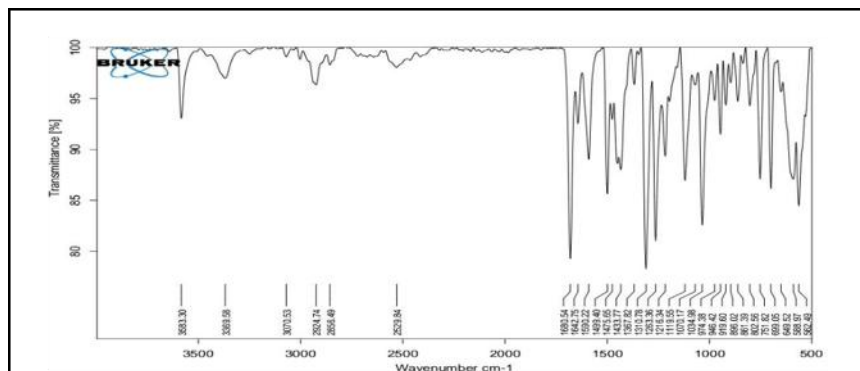


Figure 4. IR spectra of physical mixture of Natural Polymer + Donepezil

The retention of all the characteristic functional group peaks of Donepezil and the natural mucilage without any significant spectral changes indicates the absence of chemical interaction or incompatibility between the drug and the polymer. Thus, the FTIR study confirms that the extracted natural mucilage is compatible with Donepezil, supporting its suitability as a natural excipient for the development of oral disintegrating films.

Preparation and evaluation of oral disintegrating film

The oral disintegrating film (ODF) of donepezil was formulated to deliver a dose of 5 mg per individual film. The film showed transparent appearance (Fig. 5).

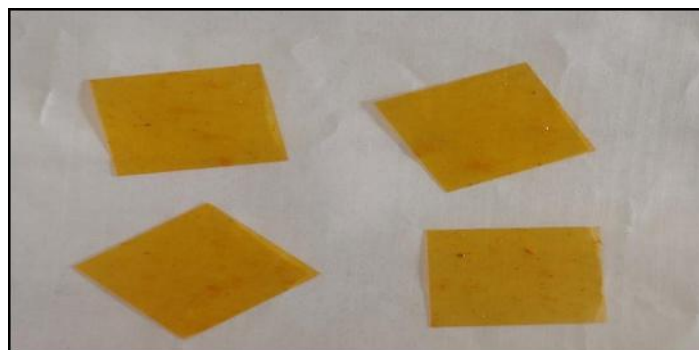


Figure 5. Oral disintegrating films

Weight Variation of Oral Disintegrating Films

The weight of film increases as the concentration of chia mucilage increases. The weight variation study demonstrated that all oral disintegrating films exhibited uniform weight with acceptable standard deviations, indicating consistency in the solvent casting process (Table 4). The film weight increased progressively from 25.77 ± 2.68 mg (F1) to 38.04 ± 1.31 mg (F6), corresponding to the increase in polymer concentration. The observed increase in film weight confirmed the successful incorporation of higher amounts of film-forming polymers and excipients without affecting the uniformity of the formulations. Overall, all formulations showed satisfactory weight uniformity, suggesting reproducible film preparation and consistent drug distribution.

Table 4. Weight Variation of Oral Disintegrating Films

Formulation code	Weight of films(mg)
F1	25.77 ± 2.68

F2	27.82± 1.52
F3	30.41± 2.83
F4	32.75± 0.92
F5	35.84± 1.36
F6	38.04± 1.31

All values are expressed as mean ±SD, n=6

Thickness of film

The thickness of all formulation was measured with Trimos height gauge. Around 90% of wet film thickness was lost during drying. Three random films of F1 to F6 selected and measured. Select three films randomly. The results of F1-F6 are given in Table 5. For the prepared film a good uniformity of thickness was observed.

The thickness of the oral disintegrating films ranged from $50.33 \pm 2.51 \mu\text{m}$ to $60.41 \pm 2.95 \mu\text{m}$, indicating good uniformity among all formulations. Formulation F1 exhibited the lowest thickness, whereas F6 showed the highest thickness. The slight increase in film thickness with increasing polymer concentration may be attributed to the greater solid content in the casting solution. The low standard deviation values indicated uniform film casting and reproducible formulation preparation.

Table 5. Thickness of oral films

Formulation code	Thickness(mm)
F1	50.33±2.51
F2	54.66±3.86
F3	55.37±1.24
F4	52.66±3.51
F5	55.83±3.49
F6	60.41±2.95

All values are expressed as mean ±SD, n=3

Folding Endurance.

The folding endurance test was performed and all the prepared ODFs have an acceptable folding endurance. In folding endurance test no films developed any visible cracks or breaks, thus showing good folding endurance. F3 has higher folding endurance when compared with other ODFs. As concentration of chia mucilage increases F4, F5 and F6 show brittle film. The mean value of six reading was calculated and the result given in Table 6.

Table 6. Folding endurance of films

Formulation code	Folding endurance
F1	33.66± 1.63

F2	39.16± 1.28
F3	54.51± 1.85
F4	41.83± 1.47
F5	40.65± 1.96
F6	30.36± 1.75

All values are expressed as mean ±SD, n=6

The folding endurance values ranged from 30.36 ± 1.75 to 54.51 ± 1.85 (mean ± SD, $n = 6$). Among all formulations, F3 exhibited the highest folding endurance (54.51 ± 1.85), indicating superior flexibility and resistance to repeated folding without breaking. In contrast, F6 showed the lowest folding endurance (30.36 ± 1.75). Overall, the results demonstrated that all formulations possessed adequate mechanical strength for handling, with F3 exhibiting the most favorable mechanical properties.

In-vitro disintegration study

The in vitro disintegration study demonstrated that all oral disintegrating films disintegrated rapidly, with disintegration times ranging from 42.1 ± 1.14 to 59.5 ± 1.25 seconds (mean ± SD, $n = 3$). Among all formulations, F3 exhibited the shortest disintegration time (42.1 ± 1.14 s), indicating the fastest film disintegration, whereas F6 showed the longest disintegration time (59.5 ± 1.25 s). The rapid disintegration observed in F3 may be attributed to its optimized polymer composition, which facilitated quicker hydration and film breakdown. Overall, all formulations complied with the characteristics of fast disintegrating oral films, with F3 demonstrating the most desirable disintegration performance. The results indicate that the disintegration time increases as the concentration of mucilage increased. This can be due to the fact that as the concentration of mucilage increases, it causes an increase in the apparent viscosity. Further, the intermolecular motion of the particles gets restricted and leads to the formation of an interfacial film which slows down the disintegration time. The result given in Table 7.

Table 7. *In -vitro* disintegration time

Formulation code	Disintegration time (sec)
F1	53.4± 1.67
F2	54.3± 2.16
F3	42.1± 1.14
F4	50.2± 2.31
F5	55.5± 1.23
F6	59.5± 1.25

All values are expressed as mean ±SD, n=3

Surface pH of the films

If Surface pH is acidic or alkaline pH of administered dosage forms can irritate the oral mucosa. The measured surface pH was found to be close to neutral in all the formulations and range of oral pH i.e., 6.8 +1; which means that they have less potential to irritate the oral mucosa and therefore they should be fairly comfortable.

Surface pH result given in Table 8.

Table 8. Surface pH of oral films

Formulation code	Surface pH
F1	6.52± 0.06
F2	6.49± 0.05
F3	6.81± 0.19
F4	6.41± 0.09
F5	6.53± 0.17
F6	6.42± 0.08

All values are expressed as mean ±SD, n=3

Drug Content of Oral Disintegrating Films

The drug content of all oral disintegrating film formulations was found to be within the acceptable pharmacopoeial limits, ranging from $94.2 \pm 0.12\%$ to $99.2 \pm 0.03\%$ (mean ± SD, $n = 3$), indicating uniform drug distribution throughout the films (Table 9). Among the formulations, F3 exhibited the highest drug content ($99.2 \pm 0.03\%$), while F1 showed the lowest ($94.2 \pm 0.12\%$). The low standard deviation values confirmed the reproducibility of the solvent casting process and uniformity of drug incorporation. Overall, all formulations complied with the USP acceptance criteria for content uniformity, demonstrating satisfactory drug loading and formulation consistency.

Table 9. Drug content of oral films

Formulation code	Drug content (%)
F1	94.2± 0.12
F2	96.3± 0.04
F3	99.2± 0.03
F4	97.5± 0.08
F5	97.7± 0.31
F6	95.2± 0.07

All values are expressed as mean ±SD, n=3

Percentage Moisture Loss of Oral Disintegrating Films

The % moisture loss of the formulations ranged from 2.08% to 3.96%. Among all formulations, F3 exhibited the lowest moisture loss (2.08%), indicating better moisture retention and enhanced film stability, whereas F4 showed the highest moisture loss (3.96%), followed closely by F6 (3.93%). The results suggest that all formulations possessed acceptable moisture loss values, reflecting good physical stability during storage, with F3 demonstrating the most favorable moisture retention characteristics (Table 10).

Table 10. % Moisture loss of oral film

Formulation code	% Moisture loss
F1	3.22
F2	3.24
F3	2.08
F4	3.96
F5	3.17
F6	3.93

In-vitro Dissolution study

In vitro dissolution test:

The cumulative percentage drug release profiles of formulations F1–F6 are presented in Table 11. All formulations exhibited a rapid increase in drug release with increasing dissolution time, achieving more than 94% cumulative drug release within 6 minutes. During the initial stages (1–3 min), formulations showed differences in release profiles, which can be attributed to variations in the type and concentration of the natural Superdisintegrant and plasticizer used in the formulations. Formulation F6 exhibited the highest initial drug release at 3 minutes (49.49%), followed by F5 (43.59%) and F4 (36.18%), indicating faster hydration and disintegration during the early phase. At 4 minutes, F5 demonstrated the highest cumulative drug release (66.50%), whereas F2, F4, and F6 exhibited drug release values of 57.23%, 55.39%, and 61.97%, respectively. By the end of the dissolution study (6 min), all formulations released nearly the entire drug content, with cumulative drug release ranging from 94.28% to 99.72%. Among the formulations, F3 exhibited the highest cumulative drug release (99.72%), followed by F2 (96.31%), F6 (96.25%), F4 (95.10%), F5 (95.48%), and F1 (94.28%).

Table 11. In vitro dissolution studies of oral film

Time (min)	%Cumulative drug release					
	F1	F2	F3	F4	F5	F6
1	8.93	5.01	4.90	7.26	6.84	5.42
2	14.72	15.92	16.34	10.72	28.74	25.86
3	29.21	30.45	31.06	36.18	43.59	49.49
4	45.06	57.23	49.04	55.39	66.50	61.97
5	78.49	70.29	73.56	74.51	71.41	72.06
6	94.28	96.31	99.72	95.10	95.48	96.25

The enhanced dissolution observed with formulation F3 may be attributed to its optimized polymer composition and rapid film disintegration, which facilitated faster drug diffusion into the dissolution medium. Overall, the

results confirmed that all oral films provided rapid drug release, demonstrating their suitability for immediate-release oral drug delivery applications.

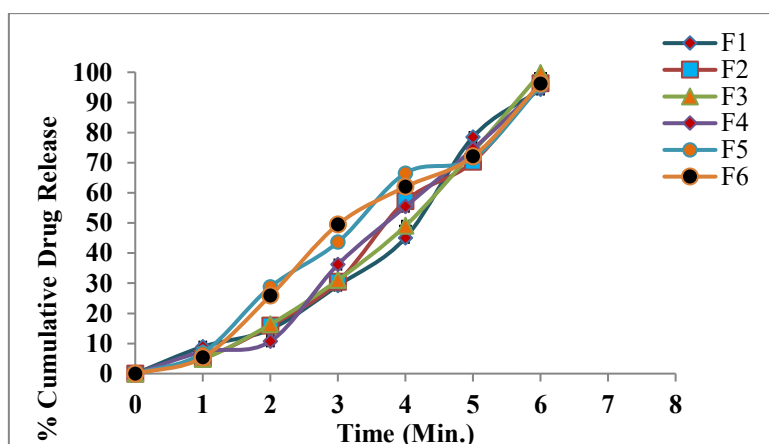


Figure 6. The cumulative percentage drug release profiles of formulations F1–F6

It is explained as the quantity of drug substance that goes into the solution per unit time under standardized conditions of liquid /solid interface, solvent concentration and temperature. In such drug delivery system, drug is supposed to be released rapidly to get immediately absorbed in blood circulation for faster onset of action. The USP Type II apparatus (basket). The results indicate F3 shows largest dissolution. That the drug release decreases as the concentration of mucilage increased.

Scanning Electron Microscopy

The SEM micrograph revealed a relatively rough and irregular surface with the presence of plate-like and flaky structures distributed throughout the film (Fig. 7). These structures may be attributed to the polymer matrix and the incorporated natural mucilage. No large cracks or surface defects were observed, indicating good film integrity and uniform formulation. The measured particle dimensions ranged from approximately 1.3 to 3.4 μm , demonstrating a homogeneous distribution of the film components. The morphological characteristics suggest that the optimized formulation possessed a stable surface architecture, which could facilitate rapid hydration and disintegration, thereby contributing to efficient drug release.

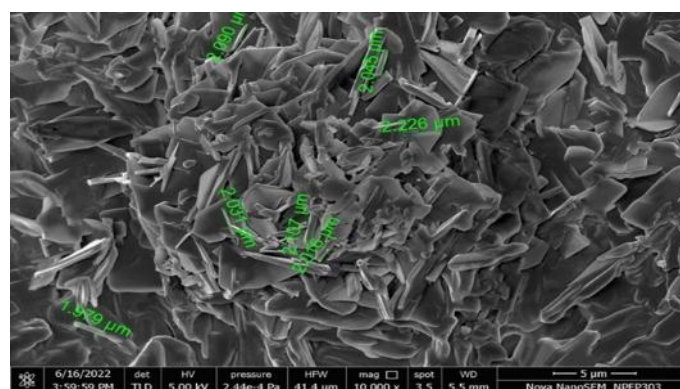


Figure 7. The surface morphology of the optimized oral disintegrating film (SEM).

FTIR Study of Oral Disintegrating Film

The FTIR spectrum of the optimized Donepezil oral disintegrating film exhibited the characteristic absorption

bands of both the drug and the natural polymer, indicating successful incorporation of the drug into the film matrix. A broad absorption band at 3379.30 cm^{-1} was attributed to O–H stretching vibrations of hydroxyl groups present in the natural mucilage, confirming the hydrophilic nature of the film. The peak at 2927.90 cm^{-1} corresponds to aliphatic C–H stretching vibrations, while the absorption band at 2364.48 cm^{-1} is associated with atmospheric CO_2 . A distinct peak observed at 1604.71 cm^{-1} is assigned to $\text{C}=\text{O}/\text{C}=\text{C}$ stretching vibrations of Donepezil (Fig. 8). The bands at 1459.93 , 1412.90 , and 1369.11 cm^{-1} correspond to CH_2 bending and aromatic ring vibrations. Strong absorption bands in the 1257.62 – 1024.46 cm^{-1} region are attributed to C–N, C–O, and C–O–C stretching vibrations, confirming the presence of glycosidic linkages and ether groups of the polymeric matrix. The peaks below 1000 cm^{-1} (946.01 – 529.31 cm^{-1}) are characteristic of aromatic C–H out-of-plane bending and ring deformation vibrations. The optimized film retained all the characteristic functional group peaks of Donepezil and the natural polymer without any significant shift, disappearance, or formation of new absorption bands. This indicates the absence of chemical interaction or incompatibility between the drug and the excipients during film preparation. Therefore, the FTIR study confirms that the formulation process did not alter the chemical integrity of Donepezil, demonstrating excellent compatibility between the drug and the natural mucilage, which supports the stability and suitability of the optimized oral disintegrating film formulation.

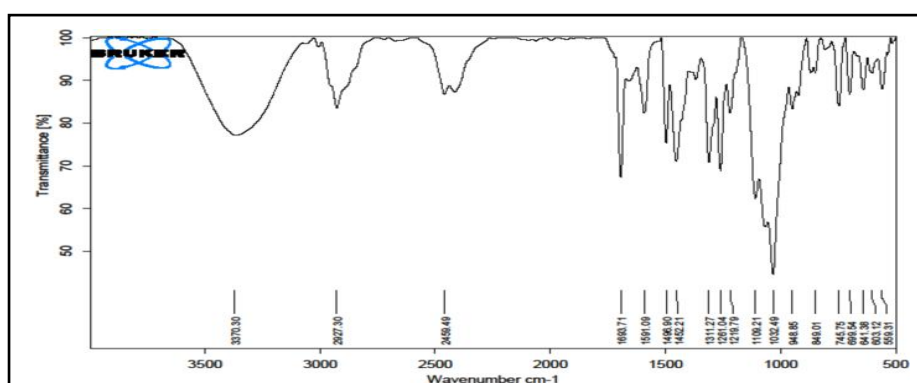


Figure 8. FTIR spectra of formulated film (F3)

Stability Studies (F3)

Optimized F3 formulation was sealed in Aluminium packing laminated with polyethylene. Samples were kept at 40°C and 75% RH for 2 months and the result was depicted in table 12. After 2 months the films were tested. At the end of study period, it was found that there is no significant change in appearance, weight variation, thickness, folding endurance, drug content, *in vitro* disintegration time and percentage drug diffusion study.

Table 12. Stability studies of F3 [Condition ($40^\circ\text{C}/75\%\text{RH}$)]

Parameter	Initial	1 month	2 months
Thickness (mm)	55.37 ± 1.24	55.37 ± 1.24	54.42 ± 0.62
Folding endurance	54.51 ± 1.85	54.51 ± 1.85	54.51 ± 1.80
Weight variation (mg)	30.41 ± 2.83	30.41 ± 2.83	30.41 ± 2.83
Disintegration time (sec)	41	41	42
Drug content (%)	99.2 ± 0.03	99.2 ± 0.03	99.8 ± 0.29

In vitro dissolution (%)	99.72	99.72	99.61
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Conclusion

The pre-formulation and compatibility studies confirmed the suitability of Donepezil hydrochloride and the extracted *Salvia hispanica* (chia seed) mucilage for the development of oral disintegrating films (ODFs). The extracted mucilage was characterized as a greyish-white, odourless, flaky material with a near-neutral pH (6.4), good swelling index (9), viscosity (416 cps), and 8% yield, indicating desirable physicochemical properties for use as a natural superdisintegrant. Preliminary phytochemical analysis confirmed the presence of carbohydrates, mucilage, glycosides, and reducing sugars, while alkaloids, proteins, and tannins were absent, demonstrating the purity and polysaccharide-rich nature of the extracted material. The physicochemical evaluation of Donepezil revealed that it is a white to off-white, odourless, bitter powder with a melting point of 231–232°C and good solubility in water and methanol. Differential Scanning Calorimetry (DSC) showed a sharp endothermic melting peak at 231–232°C, confirming the crystalline nature, purity, and thermal stability of the drug. FTIR analysis of the extracted mucilage confirmed the presence of characteristic hydroxyl, aliphatic, carboxyl, and glycosidic functional groups, consistent with a natural polysaccharide. The FTIR spectra of the drug–polymer physical mixture and the optimized oral disintegrating film retained all the characteristic absorption bands of Donepezil and the natural polymer without significant peak shifts, disappearance, or formation of new peaks. This demonstrated the absence of chemical interaction between the drug and the excipients and confirmed their compatibility.

The measured particle dimensions ranged from approximately 1.3 to 3.4 μm , demonstrating a homogeneous distribution of the film components. The morphological characteristics suggest that the optimized formulation possessed a stable surface architecture, which could facilitate rapid hydration and disintegration, thereby contributing to efficient drug release. All formulations complied with acceptable pharmacopeial limits for physicochemical characteristics, with drug content ranging from 94.2–99.2%. Film thickness varied between 50.33 and 60.41 μm , and moisture loss ranged from 2.08–3.96%. Disintegration time increased with increasing mucilage concentration and ranged from 42.1 to 59.5 s. The dissolution study all formulations released nearly the entire drug content, with cumulative drug release ranging from 94.28% to 99.72%. Among the formulations, F3 exhibited the highest cumulative drug release (99.72%), followed by F2 (96.31%), F6 (96.25%), F4 (95.10%), F5 (95.48%), and F1 (94.28%). Overall, the results confirmed that all oral films provided rapid drug release, demonstrating their suitability for immediate-release oral drug delivery applications. Overall, the pre-formulation, DSC, and FTIR studies established that Donepezil hydrochloride is chemically and thermally stable and is compatible with *Salvia hispanica* mucilage and other formulation excipients. From the stability studies, it was found that there is no significant change in appearance, weight variation, thickness, folding endurance, drug content, *in vitro* disintegration time and percentage drug diffusion study. These findings support the successful utilization of chia seed mucilage as a natural superdisintegrant in the formulation of stable and effective Donepezil oral disintegrating films.

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Conflict of Interest

The authors declare no conflict of interest.

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