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Formulation and evaluation of fast disintegrating tablets of domperidone using chitosan-glycine conjugates as superdisintegrant

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ABSTRACT

Purpose: The present research was envisaged to employ chitosan-glycine conjugates as superdisintegrant for developing fast disintegrating tablets of domperidone. **Materials and Methods:** Chitosan-glycine conjugates were prepared by physical mixing and microwave-assisted technique. Micromeritic study, Fourier transform infrared, scanning electron microscopy, and X-ray diffraction methods were employed for characterizing the powdered conjugates. The formulated FDTs were evaluated for wetting time, water absorption ratio, disintegration time, *in vitro* drug release, and other tablet parametric tests. **Results and Discussion:** The effective pore radius of unadulterated chitosan was found to be 18.45±1.27 μm whereas the chitosan-glycine conjugates prepared by physical technique and microwave technique showed effective pore radius in the range of 21.26±0.96–24.22±2.35 μm and 27.14±3.02–31.55± 2.81 μm, respectively. Conjugates prepared by both the techniques were found to have great powder flow properties. Intermolecular bridging between chitosan and glycine was held responsible for the increased swelling potential and tablet superdisintegrant property of the conjugates. The results of wetting time, water absorption ratio, and disintegration time were found to extend from 33±1.14 to 78±1.13 s, 40±0.11 to 86±0.04 %, and 21±3 to 85±3 s, respectively. **Conclusion:** Conjugates of chitosan with glycine have significant tablet superdisintegrant potential and can be used for developing fast disintegrating formulations.

Keywords: Chitosan, glycine-chitosan conjugates, tablet superdisintegrant

INTRODUCTION

Tablets are the principal dosage form among the existing oral drug formulations due to their easy supply chain, long-term stability, and least manufacturing expenses. However, there are certain drawbacks associated with the conventional tablet dosage form: (1) Poor dose flexibility, which raises significant safety issues in some cases of pediatrics and geriatrics, and (2) need of water for its administration.[1] Fast disintegrating tablets (FDTs) have become an increasingly common sector in the pharmaceutical industry in the past 10 years. FDTs are solid unit dosage forms which disintegrate in few seconds for releasing the drug for desired therapeutic action.[2] They provide convenient administration to patients who cannot gulp down medications such as pediatrics, geriatrics, dementia sufferers, or psychiatric patients.[3] They are also beneficial in case of travel sickness, abrupt allergic attacks, or coughing where quick onset of action is essential. The danger of choking or stifling caused during the intake of conventional oral dosage formulations is also avoided, thus providing improved safety.[4] "Fast disintegrating," "fast dissolve," "quick dissolve," "rapid melt," "quick melt," "mouth dissolving," "orally disintegrating," "orodispersible," "melt in mouth," etc., are the terms that represent this drug delivery system.[5]

Disintegration and dissolution of the tablet should occur at a faster rate to ensure instant bioavailability of the drug. Disintegrants are the agents usually incorporated in the tablet formulation which help in breaking the physical forces within the compressed tablet and thereby promote disintegration when exposed to a fluid environment.[6] Recently, superdisintegrants are being explored due to their enhanced disintegration efficiency at the lower concentrations when compared to disintegrants.[7] Superdisintegrants such as croscarmellose

sodium, crospovidone, and sodium starch glycolate have been widely employed as standard superdisintegrants in various tablet formulations.[8]

Chitosan is frequently used as a disintegrant in tablet formulations. However, to use chitosan as tablet superdisintegrant, various modifications of the biopolymers are reported in the literature. El-Barghouthi and Eftaiha developed a new excipient by coprecipitation of chitosan and silica. The intimate physical mixing of chitosan and silica led to the formation of a hydrophilic and highly absorbent material, which resulted in enhanced water uptake, improved powder flow and compaction properties along with superior disintegration performance.[9] In another study, Goel *et al.* formulated FDTs of Ondansetron hydrochloride containing novel superdisintegrant (chitosan-alginate (1:1) interpolymer complex and chitin). Chitin (10% w/w), glycine (40% w/w), and CTN-ALG (3% w/w) were found to exhibit superdisintegrant action when used in combination. It is also presumed that by conjugating the disintegrant (chitosan) with an amino acid moiety (glycine), the disintegration time can be reduced and hence suggested the idea of novel biocompatible superdisintegrant.[10] Rashid *et al.* developed chitin-metal silicates as binding superdisintegrants as they possess both binding and disintegration properties.[11] Singh *et al.* employed starch glycine conjugates for developing FDTs of domperidone.[12]

In the present study, chitosan-glycine conjugates were synthesized and utilized in the development of FDTs of domperidone. It is an antagonist of the dopamine receptors and is widely preferred for treating abdominal problems such as bloating, vomiting, feeling of fullness, and nausea. It increases the contraction and motility in the stomach which promotes the emptying rate of the stomach and thereby provides relief from nausea.[13] The conjugates were prepared by microwave and physical methods and were characterized by scanning electron microscopy (SEM), X-ray diffraction (XRD), and Fourier transform infrared (FTIR) techniques. Micromeritic studies were performed to evaluate the flow properties of the conjugates. The formulated FDTs were evaluated for various parametric tests of tablets.

MATERIALS AND METHODS

Materials

Domperidone was received as a gift sample from Ankur Drugs and Pharmaceuticals (Baddi, Himachal Pradesh, India). Chitosan was purchased from Sigma-Aldrich, USA, and glycine was purchased from Merck, Mumbai. Marketed Domperidone DT: Vomistop by Cipla Pharmaceuticals Ltd., Baddi, India (Batch No.B260703) was procured from a retail pharmacy in Mohali, Punjab.

Preparation of Chitosan-glycine Conjugates

Novel conjugates of chitosan and glycine were prepared in the ratio of 1:1, 1:5, and 1:10 with the help of physical method and microwave method. In physical method, powders of chitosan and glycine were mixed by tumbling method for duration of 15 min to ensure proper mixing of the two powders. In microwave method, the conjugates were prepared by physically mixing chitosan and glycine for 15 min by tumbling method followed by subjecting the physical mixture of powders to microwave treatment (three cycles of 2-min heating and 1-min cooling) at 600 W microwave power. The conjugates prepared by the two methods were then collected, passed through mesh no. 35 sieve (pore size 595 μm) and placed in a desiccator until next usage.

Characterization of the Chitosan-glycine Conjugates

The prepared chitosan-glycine conjugates were tested for several pre-compression parameters including bulk density, tapped density, angle of repose, Carr's compressibility index (CI), Hausner's ratio, loss on drying (LOD), swelling index, effective pore radius, and pH. Post-compression testing was performed with the help of techniques such as FTIR, XRD, and SEM.

Micromeritic studies

Poured density (D_p), tapped density (D_t) angle of repose (θ), Carr's CI, and Hausner's ratio were calculated by the given equations:

$$D_p = M/V_p$$

Where M is the mass of the powder and V_p is the poured volume of the powder.

$$D_t = M/V_t$$

Where M is the mass of the powder and Vt is the volume of the powder obtained after 100 taps.

$$\theta = \tan^{-1}(h/r)$$

Where θ is the angle of repose, "h" is the height of the powder pile, and "r" is the radius of the powder pile.

$$CI = [(D_t - D_p)/D_t] \times 100$$

Where D_t refers to tapped density of the powder and D_p refers to the poured density of the powder.

$$\text{Hausner's ratio} = D_t/D_p$$

Where D_t refers to the tapped density and D_p refers to the poured density.

LOD

The presence of solvents or moisture in the sample is detected with the help of LOD method. The samples were initially weighed and then heated over 100 ± 5°C for around 2 h. Next, they were cooled, re-weighed and kept in a desiccator. The percentage loss was determined by the formula given below.

$$\%\ LOD = [(W_1 - W_2)/W_1] \times 100$$

Swelling index

For a small-scale batch, the swelling index was measured with the help of a graduated cylinder. An adequate volume of water was poured into 1 g of powder sample for producing a uniform dispersion of 100 ml. The volume of the powder sample in the beginning as well as the volume of the powder after swelling

(24 h time period) was measured. The following equation determines the swelling index.

$$\text{Swelling index} = [(V_2 - V_1)/V_1] \times 100$$

Where V_1 and V_2 indicate the volume of powder sample before and subsequent to hydration, respectively.

Effective pore radius ($R_{eff.p}$)

$R_{eff.P}$ of powder blend was determined by completely filling a 2 ml micropipette tip with powder blend and then weighing it (W_i). Then the solvent n-hexane was added in a dropwise manner on the bed top till the time it reached the bottom of the tip. Then reweighing of the tip was done (W_f) and value of the effective pore radius is given by the following formula:

$$R_{eff.P} = (W_f - W_i)/2\pi\gamma$$

pH

One gram of the prepared chitosan-glycine conjugates was added to 100 ml of distilled water and pH of the dispersion was calculated using digital pH meter at 37 ± 2°C. Triplicate results were recorded.

Attenuated total reflectance - FTIR spectroscopy (ATR-FTIR)

ATR FTIR spectrometer (Alpha, Bruker, Japan) was utilized for the IR analysis of the respective samples. The evaluation of samples was done in the wavelength range of 4000 cm^{-1}–400 cm^{-1}.

X-ray powder diffraction

The diffractograms of different samples were obtained using the X-pert pro (USA) which is configured in Bragg–Brentano geometry. The equipment consists of a copper anode in glass tubing and a graphite monochromator. The operating conditions were set at 40 mA and 40 kV. The samples having size smaller than 250 μm were mounted on a glass slide arbitrarily. The signals reflected at an angle of 2θ were scanned at a rate of 0.21°/s and registered from 0° to 60°C.

SEM

The samples taken for surface study were examined using scanning electron micrographs which were taken using Hitachi 4300 SE/N SEM at an accelerating potential of 10 kV. The sample investigation was done by placing the sample on the silver plate of the specimen stage in a vacuum evaporator.

Formulation of FDTs

Direct compression technique was followed for formulating FDTs of domperidone. All the formulations were prepared using 10 mg dose of the active pharmaceutical ingredient and Avicel 102 as the diluent. The powder blend was then sieved using mesh # 60. Talc and magnesium stearate were incorporated with additional 5 min mixing. The final powder mixture was converted to tablets with the help of multi punching machine (AK Industries, Nakodar, Punjab, India) having 6.75 mm biconcave round die-punches. Adjustment of compression was done so as to obtain suitable hardness for fast disintegrating tablets as specified in the pharmacopeia (3–5 kg/cm^2). Different FDT formulations batches prepared chitosan-glycine conjugates as superdisintegrant are depicted in Table 1.

Evaluation of the Formulated FDTs

The prepared tablets were assessed for diverse parameters such as diameter, thickness, hardness, content uniformity, and friability.

Wetting time

A culture dish was filled with 6 ml solution of Eosin (water-soluble dye) and twice-folded tissue paper (10.75 mm × 12 mm) was kept in it. The tablet was kept on the top of the tissue paper. Wetting time was recorded as the time which the tablets took to absorb the solution till its top surface.

Water absorption ratio

The water absorption ratio was determined by a method similar to the wetting time technique. The tablet was weighed before as well as after complete wetting took place. The following formula was used for calculating the water absorption ratio, denoted by R.

$$R = [(W_b - W_a)/W_b] \times 100$$

Where W_a and W_b refer to the weight of the tablet before and subsequent to absorption of water, respectively.

Porosity

Porosity determines the empty spaces present in a substance. It is the ratio of the volume of pores over the total volume and its value lies in the range of 0 and 1. The porosity of the tablets was determined using the given formula:

$$\varepsilon = (1 - M/\rho_{true} \times V)$$

Table 1: Composition of the different fast dissolving tablet formulations batches

Code	Domperidone (mg)	Chitosan-glycine conjugate		Avicel 102 (mg)	Magnesium Stearate (mg)	Talc (mg)	Total weight (mg)
		Physical mixture (mg)	microwave Mixture (mg)				
F1	10	5 (1:1)	-	83	1	1	100
F2	10	-	5 (1:1)	83	1	1	100
F3	10	5 (1:5)	-	83	1	1	100
F4	10	-	5 (1:5)	83	1	1	100
F5	10	5 (1:10)	-	83	1	1	100
F6	10	-	5 (1:10)	83	1	1	100

Where M is the weight of the tablet, V is the volume of the tablet, and ρ_{true} is the true density of the blend.

The true density of the powder mixture was determined with the help of true density meter (Smart Pycno 30).

Disintegration time

The disintegration test for the formulated batches of FDTs was conducted with the help of USP disintegration apparatus (EI Product, Panchkula, India). The disintegration medium used for this purpose was 900 ml of 0.1N HCl.

In vitro dissolution studies and similarity factor (f2)

The *in vitro* dissolution was investigated with the help of the USP dissolution apparatus II (Lab India, DS 8000). The rotation per minute for the paddles was set at 50 and the dissolution medium used for the study was 900 ml of 0.1 N HCL (pH 1.2) at 37±0.5°C. Sampling of the test was done by drawing, out of 5 ml samples after particular time periods and filtering them using Whatman filter paper. The samples were then appropriately diluted and analyzed with the help of ultraviolet-visible spectrophotometer (Systronics 2202) at λ_{max} 284 nm. Drug concentration for different samples was calculated and expressed in the form of cumulative percent drug release. The similarity factor (f2) is considered to be the logarithmic transformation of the sum-squared error of differences between the test (T_j) and reference (R_j) products over all time points. It is considered as a useful way to compare the dissolution rates if there are more than three or four dissolution time points. The given formula is used to calculate the similarity factor:

$$f(2) = 50 \times \log\left\{\left[1 + \left(\frac{1}{n}\right)\sum_{j=1}^{n} W_j \left|R_j - \right|2\right] - 0.5 \times 100\right\}$$

Where Wj is an optional weight factor.

In the range of 0–100, if the f2 value is 100 then both the test and reference samples are identical whereas it tends to be 0 if they are non-identical. The f2 values should be nearer to 100, to depict similar dissolution profile.

RESULTS AND DISCUSSION

Pre-compression Evaluation

The micrometrics studies for the respective conjugates were investigated and the results are compiled in Table 2. The studies mainly included exploring the bulk density, tapped density, Carr's CI, Hausner's ratio, angle of repose, LOD, effective pore radius swelling behavior, and pH. Angle of repose of pure chitosan was 43.25 ± 4.52. Angle of repose of chitosan-glycine conjugates synthesized by physical and microwave method was observed to be ranging between 35.22 ± 3.81–37.15 ± 2.95 and 29.67 ± 2.82–31.20 ± 1.82, respectively. Carr's index of chitosan-glycine conjugates synthesized by physical and microwave method fell in the range of 15.78 ± 0.88–26.82 ± 1.75 and 12.5 ± 0.99–21.21 ± 0.76, respectively, which showed that the prepared formulations had acceptable to good flow properties in comparison to glycine (34.28). Hausner's ratio of the conjugates synthesized by physical and microwave method extended from 1.19 ± 0.124 to 1.37 ± 0.10 and 1.14 ± 0.05 to 1.27 ± 0.15, respectively.

The novel conjugates of chitosan-glycine prepared with the help of physical method and microwave assistance were studied for the swelling index which was found to be ranging from 31.71 ± 3.75 to 38.10 ± 3.30 and 45.93 ± 4.71 to 55.22 ± 4.56, respectively. The swelling index of pure chitosan was 25.50 ± 2.30. The swelling index of chitosan-glycine conjugates was found to be higher than pure chitosan and probably intermolecular bridging between chitosan and glycine along with the availability of more hydrophilic groups could be held responsible for the increase in swelling property of the conjugates. The physically prepared and microwave assisted conjugates had effective pore radius of 21.30 ± 0.96–24.22 ± 2.25 mm and 27.14 ± 3.02–31.55 ± 2.81 mm, respectively.

Instrumental Evaluation

ATR-FTIR analysis

The interaction between chitosan and glycine was studied with the help of ATR-FTIR spectrophotometer. The FTIR spectra of samples are depicted in Figures 1 and 2. Figure 3a shows the

Table 2: Micromeritic and physicochemical evaluation of powder chitosan-glycine conjugates

S.No.	Parameter	Observation						
		Chitosan	Chitosan-glycine conjugate					
			Physical mixture			Microwave mixture		
			1:1	1:5	1:10	1:1	1:5	1:10
1	Bulk density (g/cm^3)	0.48±0.11	0.31±0.07	0.32±0.06	0.30±0.09	0.28±0.05	0.26±0.05	0.27±0.08
2	Tapped density (g/cm^3)	0.67±0.15	0.40±0.09	0.38±0.07	0.41±0.09	0.32±0.08	0.33±0.10	0.31±0.05
3	Carr's index (%)	28.35±1.54	22.50±1.17	15.78±0.88	26.82±1.75	12.5±0.99	21.21±0.76	12.90±0.85
4	Hausner ratio	1.40±0.22	1.29±0.16	1.19±0.124	1.37±0.10	1.14±0.05	1.27±0.15	1.15±0.11
5	Angle of repose (°)	43.25±4.52	36.69±3.04	37.15±2.95	35.22±3.81	29.67±2.82	31.20±1.82	30.11±3.05
6	Swelling index (%)	25.50±2.20	31.71±3.75	33.64±2.43	38.10±3.30	45.93±4.71	52.57±4.90	55.22±4.56
7	pH	9.1	8.6	9.1	8.8	8.4	9.0	8.4
8	LOD (%)	10.11±0.09	8.45±0.12	9.5±0.11	9.2±0.16	8.16±0.22	9.6±0.20	10.7±0.16
9	Effective pore radius (μm)	18.56±1.43	21.30±0.96	25.41±2.32	24.22±2.25	27.14±3.02	28.11±1.53	31.55±2.81

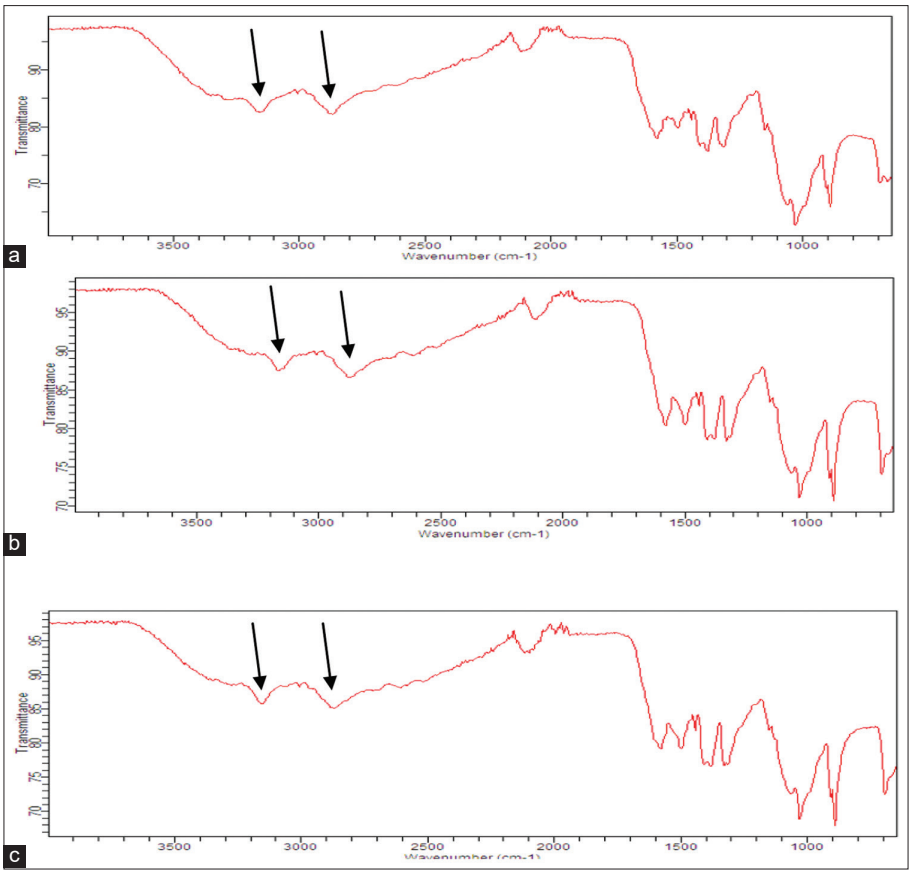

Figure 1: Fourier transform infrared spectra of chitosan-glycine conjugates developed by microwave technique in the ratio (a) 1:10, (b) 1:5, (c) 1:1

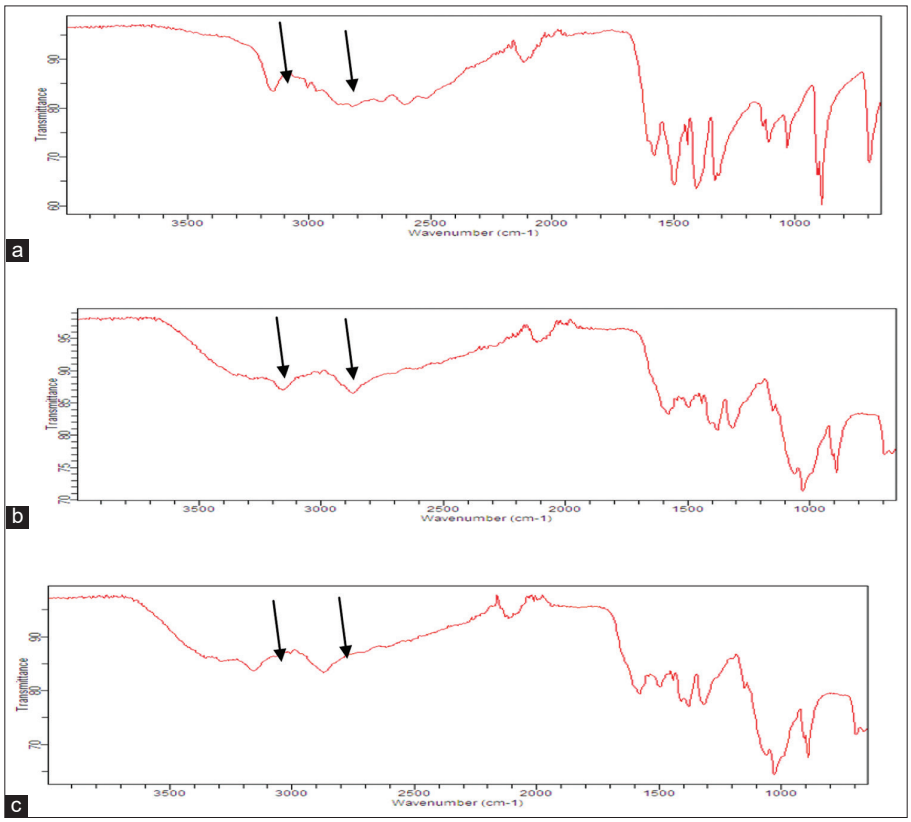

Figure 2: Fourier transform infrared spectra of chitosan-glycine conjugates developed by physical technique in the ratio (a) 1:10, (b) 1:5, (c) 1:1

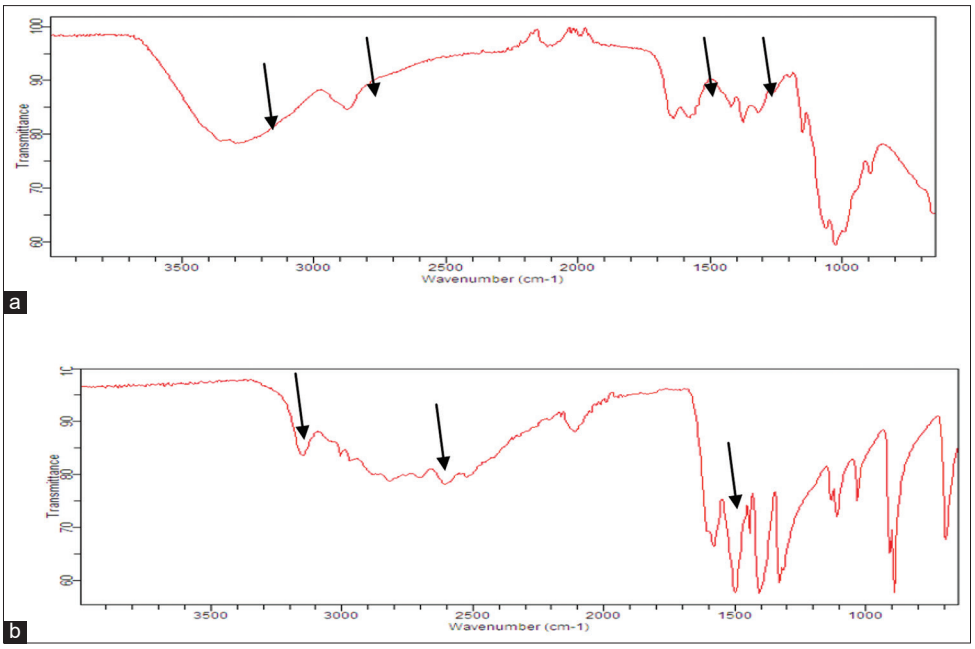

Figure 3: Fourier transform infrared spectra of (a) chitosan, (b) glycine

FTIR spectra of pure chitosan. A peak at 2865 cm^{-1} represents C-H stretching and 3380 cm^{-1} represents N-H stretching. The characteristic peak of amide I, II, and III in chitosan is evident at 1657, 1553, and 1310 cm^{-1}, respectively. CH_3 symmetrical deformation peak is found at 1450 cm^{-1} whereas a peak at 1040 cm^{-1} represents C-O stretching vibrations. The saccharide structure of chitosan is represented by a peak at 800 cm^{-1}. The FTIR spectral peaks of glycine are shown in Figure 3b. Symmetrical and asymmetrical NH_2 stretching is shown by the peaks at 3465 cm^{-1} and 3252 cm^{-1}, respectively. The peaks at 3424 cm^{-1}, 2980 cm^{-1}, and 2079 cm^{-1} represent OH stretching, CH stretching, and C=O stretching, respectively. NH bending is shown at 1610 cm^{-1} and OH bending is shown at 1412 cm^{-1}. The peaks at 1320 cm^{-1} and 1040 cm^{-1} represent CH_2 deformation and C-C stretching, respectively.

Chemical modification can be done on the amine and two hydroxyl groups present in each glucosamine unit of chitosan. These group acts as reactive sites for interaction with the glycine moiety. The reduction in intensity an appearance of characteristic strong band at around 3190 cm^{-1} and 2885 cm^{-1} in the FTIR spectra of the chitosan-glycine conjugates correspond to the vibrations of OH group, extended vibrations of NH group, and inter-hydrogen bonding. A reduction in intensity of C=O stretching vibrations of glycine indicates the involvement of COO^- in hydrogen bonding with the reactive groups of chitosan. Intermolecular bridging in the chitosan-glycine conjugates is responsible for the increased swelling potential and hence lead to an increase in the disintegration of the conjugates.

XRD analysis

The XRD spectra of chitosan, glycine, and chitosan-glycine conjugates prepared by physical mixing and microwave method are shown in Figure 4. The structure of chitosan is characterized by the presence of characteristic peaks at 2θ of 11.30 and 20.82°, which depict the amorphous nature of chitosan. The crystalline nature of the glycine is also well depicted in the XRD spectra. Characteristic peaks of glycine were at 25.26 and 39.01 with 5065.95 and 10489.39 peak areas, respectively. However, chitosan glycine physical mixture exhibited XRD peaks at 18.99 and 29.80 with 1467.90 and 3340.88 peak areas, respectively, and chitosan glycine prepared by microwave methods showed XRD peaks at 23.99 and 29.89 with peak areas of 1690.70 and 5843.09, respectively. The appearance of sharp peaks in case of conjugates clearly indicates that the amorphous nature of chitosan is reduced or in other words, there is an increase in the crystalline nature of chitosan. The reason for this could be attributed to the high level of intermolecular interaction between chitosan and glycine. This leads to an increase in the swelling of the conjugates which further enhances the utilization of chitosan-glycine as tablet superdisintegrant.

SEM analysis

Surface morphological study of pure chitosan and chitosan-glycine conjugates was done by SEM analysis as depicted by Figures 5 and 6, respectively. SEM micrographs of pure chitosan showed the presence of regular, discrete granular structures in the size range of 5–50 mm whereas SEM micrographs of chitosan-glycine conjugates (1:10) developed by microwave technique revealed distortion of the regular structure of chitosan and the presence of surface roughness. The surface roughness could be due to the voids and channels present between the particles which is further accountable for the wicking behavior and superdisintegrant property of chitosan-glycine conjugates.

Post-compression Evaluation

Size, friability, and hardness of the prepared FDTs

Similar conditions were followed while formulating different batches of FDTs so as to prevent variation in the processing

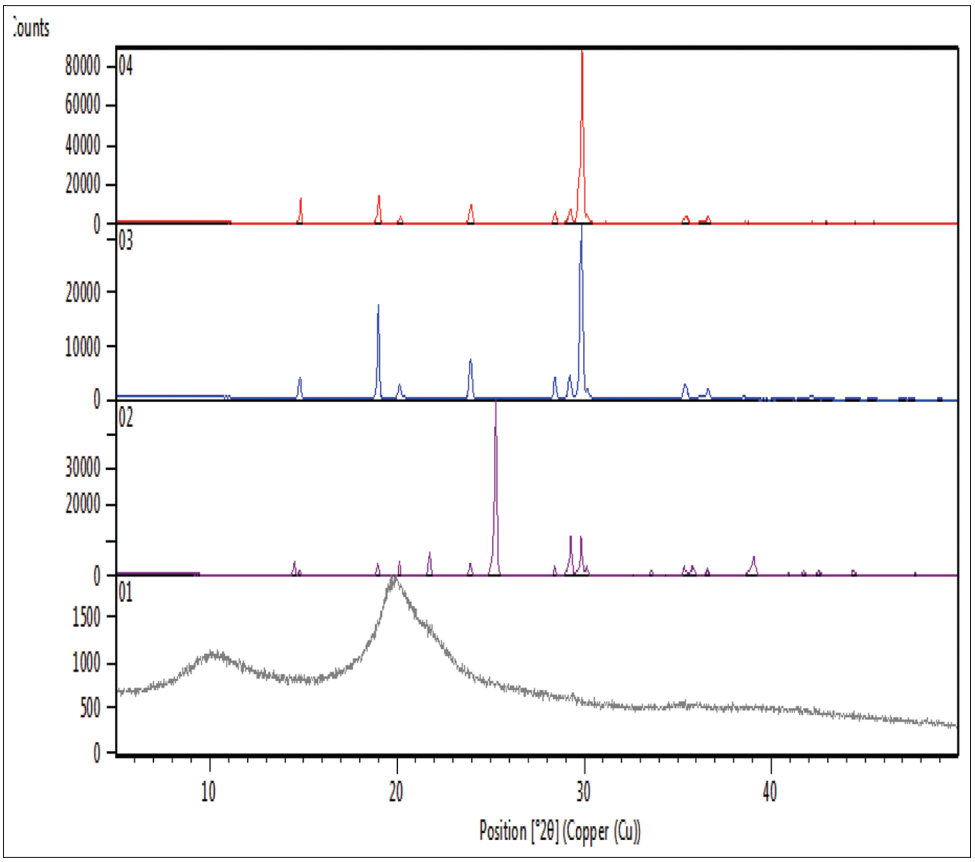

Figure 4: X-ray diffraction spectra of (1) chitosan, (2) glycine, (3) chitosan:glycine (1:10) conjugates prepared by physical mixing, (4) chitosan:glycine (1:10) conjugates prepared by microwave method

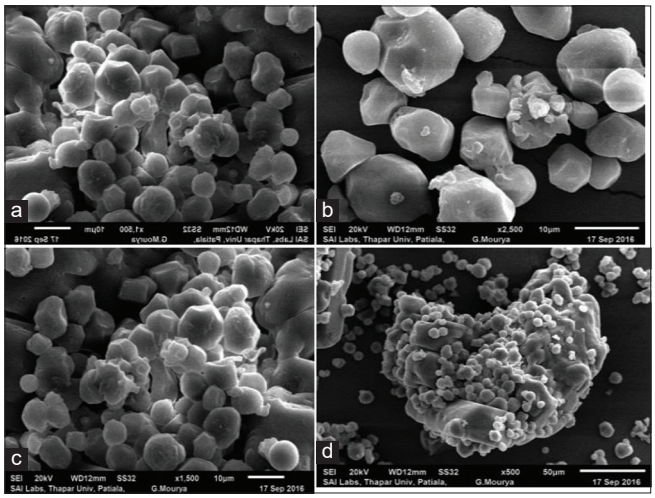

Figure 5: Scanning electron microscopy photomicrograph of pure chitosan at different magnifications (a) ×2500, (b) ×1500, (c) ×1000, (d) ×500

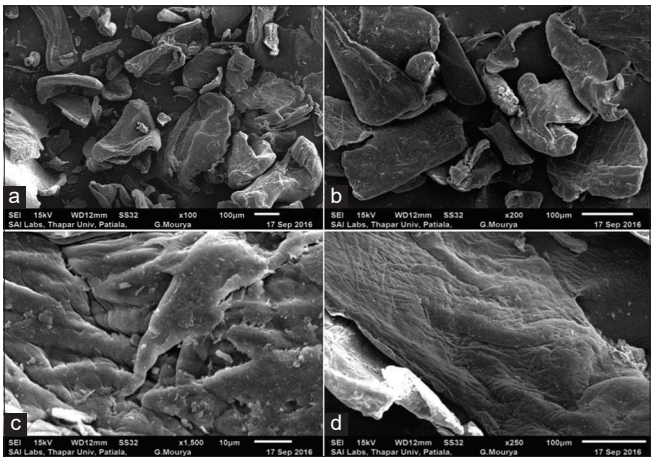

Figure 6: Scanning electron microscopy photomicrographs of chitosan-glycine conjugates developed by microwave technique at different magnification (a) ×500 (b) ×200 (c) ×1500 (d) ×250

parameters. The diameter and thickness of the tablets ranged between 6.73 ± 0.01–6.74 ± 0.05 mm and 3.51 ± 0.04–3.59 ± 0.06 mm, respectively. The results for percentage friability of all the formulations were <1% which indicated good mechanical properties. The hardness of tablets having chitosan-glycine conjugates as superdisintegrant fell in the range of 2.92 ± 0.11–3.86 ± 0.08 kg/cm^2. The drug content of all the six formulations was found to be in the range of 96.50 ± 1.60–99.1 ± 1.088. Table 3 enlists the results for size, friability, hardness, and drug content of the prepared FDTs.

Wetting time, water absorption ratio, disintegration time, and porosity of the prepared FDTs

Wetting time, water absorption ratio, disintegration time, and porosity of the formulated FDTs are presented in Table 4.

Table 3: Results for diameter, thickness, hardness, friability, and drug content of the prepared fast dissolving tablet

Formulation code	Diameter (mm)	Thickness (mm)	Hardness (kg/cm²)	Friability (%)	Drug content (%)
F1	6.74±0.03	3.56±0.03	3.10±0.10	0.90±0.04	98.99±1.11
F2	6.73±0.04	3.51±0.04	3.45±0.07	0.91±0.02	99.10±0.59
F3	6.74±0.05	3.55±0.05	2.92±0.11	0.82±0.05	97.27±0.95
F4	6.73±0.01	3.59±0.06	3.01±0.02	0.92±0.06	96.59±0.88
F5	6.74±0.01	3.51±0.07	3.75±0.11	0.78±0.09	96.50±1.60
F6	6.74±0.02	3.55±0.04	3.86±0.08	0.70±0.05	99.1±1.08

Table 4: Values depicting the wetting time, water absorption ratio, disintegration time, and porosity of the prepared fast dissolving tablet

Formulation code	Wetting time (sec)	Water absorption ratio (%)	Disintegration time (sec)	Porosity (%)
F1	78±1.13	40.11±0.11	85±5	17.51±0.92
F2	69±1.29	52.50±0.11	73±3	19.84±0.85
F3	66±1.11	56.64±0.09	71±2	20.70±1.10
F4	42±1.14	70.28±0.10	50±6	24.15±1.57
F5	33±1.14	78.57±0.04	37±4	28.78±2.62
F6	18±1.67	86.82±0.04	21±3	32.36±2.80

Table 5: Values depicting *in vitro* drug release (after 15 min and 60 min) and the f2 values obtained from the *in vitro* dissolution studies of the prepared fast dissolving tablets

Formulation code	*In vitro* drug release		f2 value
	15 min (%)	60 min (%)	
F1	35.42±4.26	68.20±6.13	37
F2	40.08±3.11	76.52±4.00	41
F3	50.16±5.20	90.05±2.19	65
F4	42.35±2.20	75.00±4.37	42
F5	47.80±5.42	82.71±3.28	53
F6	50.46±3.25	92.22±6.05	74

Wetting time ranged between 33 ± 1.14 and 78 ± 1.13 s for different formulated tablets. Water absorption ratio was observed to lie between 40.11 ± 0.11 and 86.82 ± 0.04%. Disintegration time for the formulated batches of FDTs was found to be ranging between 21 ± 3 and 85 ± 5 s. The rapid breakdown of the tablets could be attributed to the presence of void spaces which resulted in faster penetration of the dissolution media. This led to swelling and wicking, which created hydrodynamic pressure inside the tablets and hence was responsible for the quick and complete disintegration of tablets. The porosity of the FDTs was in the range of 17.51 ± 0.92–32.36 ± 2.80%. The formulations containing the conjugates developed by microwave technique showed better results in comparison with the formulations containing conjugates developed by the physical technique.

In vitro dissolution studies and similarity factor (f2)

The outcome of the *in vitro* dissolution study is depicted in Figures 7 and 8. The formulated FDTs were compared with the marketed formulation of domperidone (Mktd). The *in vitro* drug release after 15 and 60 min from the marketed tablet was 55.65 ± 4.80 and 98.11 ± 3.68%, respectively. *In vitro* drug release from F1, F2, F3, F4, F5, and F6 formulation batches

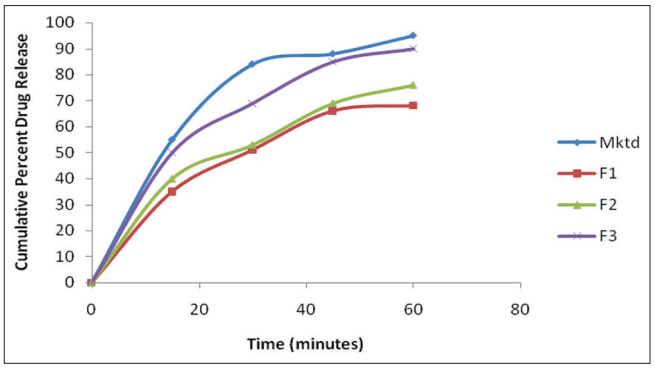

Figure 7: *In vitro* dissolution profiles of marketed domperidone fast dissolving tablet and F1, F2, and F3 formulation batches

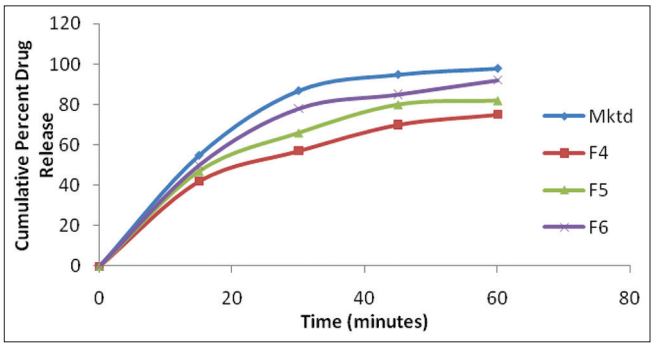

Figure 8: *In vitro* dissolution profiles of marketed domperidone fast dissolving tablet and F4, F5, and F6 formulation batches

was found to be 35.42 ± 4.26%, 40.08 ± 3.11%, 50.16 ± 5.20%, 42.35 ± 2.20%, 47.80 ± 5.42%, and 50.46 ±3.25% for the first 15 min and 68.20 ± 6.13%, 76.52 ± 4.00%, 90.05 ± 2.19%, 75.00 ± 4.37%, 82.71 ± 3.28%, and 92.22 ± 6.05% for 60 min, respectively. The *in vitro* drug release and the f2 value for all the formulation batches are presented in Table 5. The f2 value was found to be ranging between 37 and 74. From

commercial perspective, the superdisintegrant displaying best results in the lowest concentration should be accepted.

CONCLUSION

Chitosan-glycine conjugates formulated with the physical and microwave techniques were utilized as tablet superdisintegrants. Various characterization tests such as angle of repose, bulk density, tapped density, Carr's index, Hausner's ratio, swelling index, and effective pore radius were performed on the powder samples. Conjugates developed by both the techniques showed great powder flowability. ATR-FTIR, XRD, and SEM were utilized to evaluate the conjugates. The effective pore radius of unadulterated chitosan was found to be 18.45 ± 1.27 μm whereas the chitosan-glycine conjugates developed by the physical technique and microwave technique showed effective pore radius in the range of 21.26 ± 0.96–24.22 ± 2.35 μm and 27.14 ± 3.02–31.55 ± 2.81 μm, respectively. FTIR spectra showed intermolecular bridging in chitosan-glycine conjugates to be the major reason for increased swelling potential and subsequent disintegration of the conjugates. XRD results depict that the crystalline structure of conjugates with high degree of intermolecular linkage between chitosan and glycine, improved the swelling rate of the novel conjugates, thereby promoting the usage of chitosan-glycine as a superdisintegrant in tablet formulations. SEM micrographs revealed that interparticulate spaces and channels contributed to the surface roughness and hence potentiated the wicking action as well as the superdisintegrant property of the conjugates. The results of wetting time, water absorption ratio, and disintegration time were found to be in the range of 33 ± 1.14–78 ± 1.13 s, 40 ± 0.11–86 ± 0.04%, and 21 ± 3–85 ± 3 s, respectively. The porosity of tablets ranged between 17.51 ± 0.92 and 32.36 ± 2.80. F6 formulation demonstrated best similarity with the marketed formulation exhibiting f2 value (similarity factor) of 74. Considerable swelling and wicking action of the chitosan-glycine conjugates in the FDTs were found to play a significant role in the superdisintegrants action. Therefore, the chitosan-glycine conjugates can be efficiently utilized as superdisintegrant for developing a faster disintegrating tablet formulation. If these modified biopolymer conjugates could be held economical for large scale manufacturing and their toxicity/regulatory issues are addressed effectively, these could open new opportunities and avenues for companies developing pharmaceutical excipients.

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