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Original Article

EVALUATION OF CALLINECTES CHITOSAN AS A SUPERDISINTEGRANT IN METRONIDAZOLE TABLET

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ABSTRACT

Objective: The objective of this study is to evaluate callinectes chitosan as a superdisintegrant in tablet formulation; superdisintegrants are incorporated into tablets at concentrations below 5% of tablet weight to effect prompt break-up of tablets after administration.

Methods: Chitosan was extracted from shells of *Callinectes gladiator*. The polymer was characterized and then used as a disintegrant (in comparison with Ac-Di-Sol® and corn starch) at concentrations of 2, 4 and 8% for the formulation of metronidazole tablets. The micromeritic properties of granules; and mechanical and release properties of the tablets were studied.

Results: A yield of 36.7% chitosan having degree of deacetylation of 62.7% was obtained from the crab shell. Fourier Transform Infrared absorption bands at 1495 and 3240 cm^{-1} typical of N-H bending and stretching respectively; and endothermic peak of 159 °C typical of melting of chitosan were obtained. No adverse interaction between the chitosan and metronidazole was observed. The disintegration times of tablets containing 2, 4 and 8% chitosan were 12.2, 10.4 and 9.3 min respectively.

Conclusion: Callinectes chitosan is suitable for use as a superdisintegrant in tablets. It appears to be superior to corn starch as disintegrant although less effective compared to Ac-Di-Sol®. However, the relative cheapness and ready availability of chitosan would make it to be preferred to Ac-Di-Sol®.

Keywords: *Callinectes gladiator*, Chitosan, Metronidazole, Superdisintegrant

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INTRODUCTION

A disintegrant is an essential component of all immediate-release tablets. The function is to ensure prompt break-up of tablets after oral administration to enable drug release [1]. Disintegration time of no longer than 15 min is required for all immediate-release tablets. Starch is normally incorporated at concentrations of 5–15% to function as a tablet disintegrant. Conversely, certain substances called superdisintegrants can be used at concentrations below 5% to achieve acceptable tablet disintegration; or used at normal concentrations of 5–15% to achieve disintegration within 1 min. Examples of such substances are: sodium starch glycolate and croscarmellose sodium [2]. An ideal disintegrant should have poor solubility, poor gel formation, good hydration capacity, good flow properties and no tendency to form complexes with drugs.

Chitosan has been described as a versatile hydrophilic polymer of great importance in drug delivery. It is a deacetylated product of chitin which is a major component of the shells of crustaceans such as shrimps and crabs [3]. Chitosan has limited solubility, high biodegradability and it is non-toxic [4]. These properties are desirable of a good disintegrant.

Croscarmellose sodium is cross-linked sodium carboxymethyl cellulose while sodium starch glycolate is sodium salt of cross-linked and etherified potato starch [2]. Therefore, chitin and chitosan are chemically related to croscarmellose. Chitosan, compared to chitin, has a better effect on tablet disintegration. Moisture sorption and water uptake were found to be the major mechanisms of disintegration for chitosan while dissolution was related to its swelling [5]. Use of disintegrants in equal proportions for intra-and extra-granular incorporation is better than 100% intra-granular or 100% extra-granular incorporation [5].

Crabs are neglected component of the aquatic system despite their great diversity, wide distribution and great food value [6]. They form a substantial proportion of the diet of coastal towns of Nigeria, Benin, Togo, Ivory Coast and Ghana [7, 8]. Callinectes is a genus of crabs containing sixteen species. The swimming crab, *Callinectes gladiator benedict* is a decapod crustacean which is abundantly available in the coastal areas of Akwa Ibom State, Nigeria [9, 10]. Earlier work has shown that Callinectes chitosan incorporated as permeation enhancer at concentrations of 1-5% had a positive influence on the disintegration of ciprofloxacin tablet [10].

Metronidazole is a poorly compressible anti-protozoal [11]. It can thus be formulated using a strong binder as acacia gum so that the effectiveness of chitosan as a disintegrant can be appropriately investigated. The stronger the binder, the more effective must be the disintegrating agent for the tablet to release the incorporated drug [12]. Utilization of chitosan as a superdisintegrant would not only provide a means of disposing seafood waste but will dispel the rigour of converting starch and cellulose to the corresponding superdisintegrants. This work was aimed at evaluating callinectes chitosan as a superdisintegrant in metronidazole tablet.

MATERIALS AND METHODS

Materials

Materials used were: corn starch (BDH Chemicals, England), Ac-Di-Sol® (Signet Chemical Corporation, India), metronidazole powder (Sigma Aldrich, Germany), magnesium stearate, talc and acacia gum (BDH Chemicals, England).

Collection of crab shells and extraction of chitosan

Shells of *Callinectes gladiator* were obtained from Oron, Akwa Ibom State, Nigeria. Chitosan was derived from the shells by employing the three stages of deproteination, demineralization and deacetylation using the methods described by Olorunsola *et al.* [10].

Determination of degree of deacetylation

The degree of deacetylation was determined using potentiometric acid-base titration method described by Borriand and Rinardo [13] with

modification. Homogenous solution of chitosan was prepared in 0.4 M HCl and titrated against 0.1 M NaOH solution at room temperature. The endpoints were detected by inflection of pH values. The two inflections were noted (the first one corresponded to HCl neutralization and the second to neutralization of ammonium ions of chitosan). The degree of deacetylation (%DD) was calculated using equations 1 and 2.

$$\%DD = 100 - \%DA \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (1)$$

$$\%DA = \frac{\text{Difference in pH inflection}}{\text{Initial pH value}} X 100\ \% \quad \ldots\ldots \quad (2)$$

where DA is degree of acetylation.

Granulation

Nine batches of metronidazole tablets based on tablet formula in table 1 were prepared by wet granulation (tablet weight being 400 mg and batch size being 100 tablets). The disintegrant properties of chitosan extracted from the shells of *Callinectes gladiator* was evaluated in comparison with corn starch and Ac-Di-Sol® (croscarmellose sodium). The disintegrants were incorporated in equal portions as intra and extragranular disintegrants.

Table 1: Tablet formula

Ingredient	Batches								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Metronidazole (%)	50	50	50	50	50	50	50	50	50
Lactose (%)	43	41	37	43	41	37	43	41	37
Acacia gum (%)	3	3	3	3	3	3	3	3	3
Chitosan (%)	2	4	8	-	-	-	-	-	-
Corn starch (%)	-	-	-	2	4	8	-	-	-
Ac-Di-Sol® (%)	-	-	-	-	-	-	2	4	8
Talc (%)	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Mg stearate (%)	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5

F1=formulation containing 2% chitosan, F2=formulation containing 4% chitosan, F3=formulation containing 8% chitosan, F4=formulation containing 2% corn starch, F5=formulation containing 4% corn starch, F6=formulation containing 8% corn starch, F7=formulation containing 2% Ac-Di-Sol®, F8=formulation containing 4% Ac-Di-Sol®, F9=formulation containing 8% Ac-Di-Sol®

The weighed quantities of metronidazole, lactose and intragranular disintegrant were dry-mixed for 5 min and then moistened with solution of acacia gum. The wet mass was screened through a 2.0 mm mesh and dried in a hot air oven (Gallenkamp, Germany) at 60 °C for 1 h. The dried granules were screened again through a 1.0 mm mesh.

Compatibility studies

Fourier transform infrared (FTIR) spectroscopy

Samples of metronidazole, chitosan, lactose, acacia gum and dried granules of F2 were prepared separately in a potassium bromide disk in a hydrostatic press at 6-8 tons pressure. The FTIR spectrum of each sample was recorded at scanning range of 350 to 4,000 cm-1 using a spectrophotometer (model 8400S, Shimadzu Corporation, Kyoto-Japan).

Differential scanning calorimetry (DSC)

DSC analysis was carried out on samples of metronidazole, chitosan, lactose, acacia gum and dried granules of F2. Analysis of each sample, placed in an Al 40 µl crucible was carried out using a STAR^e SW 12.10 DSC machine (Mettler-Toledo, GmbH Germany). The scanning was carried out over a temperature range of 50–350 °C.

Physicochemical characterization of granules

Scanning electron microscopy (SEM)

Surface morphology of the granules of F3, F6 and F9 were observed using an EVO/MAIO scanning electron microscope (Carl Zeiss, Germany). Each sample was placed on the sample holder and vacuum was created using the vacuum pump. The electron gun equipped with a variable pressure aperture was aligned to finely focus the electron beam on the sample; and different magnifications (x100, x200, x500, and x1000) were employed to examine the sample. The magnification that produced the best resolution was selected and the image was taken.

Determination of densities

A 13 g sample was placed in a 50 ml measuring cylinder and the bulk volume taken. The system was tapped 100 times after which the volume was retaken. The bulk density (BD) and tapped density (TD) were calculated as the ratio of mass to the corresponding volume [11].

The Carr's index (CI) and Hausner's ratio (HR) were also calculated using equations 3 and 4.

$$CI = \frac{TD - BD}{TD} X \ 100\ \% \quad \ldots\ldots\ldots \quad (3)$$

$$HR = \frac{TD}{BD} \quad \ldots\ldots\ldots\ldots \quad (4)$$

The true density (D_t) of the granules were determined by the specific gravity bottle method. A clean 25 ml specific gravity bottle was filled with xylene and the weight of the bottle with xylene was determined. Some of the xylene was poured out and 1g of sample was transferred into the bottle. More xylene was added until the bottle was filled. The excess fluid was wiped off. The weight of the bottle and its content was taken. The true density was calculated using equation 5.

$$Dt = \frac{w}{a + w - b} X \ SG \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (5)$$

where w is the weight of granules, a is weight of bottle+xylene; b is weight of bottle+xylene+granules and SG is the specific gravity of xylene.

Compression

The required quantities of the extragranular disintegrant, talc and magnesium stearate were weighed and gently blended with the dried granules. The granules were compressed at a pressure of 15 KN using a single punch tableting machine (Erweka, Germany).

Tablet evaluation

Compact density

The diameter and thickness of three tablets per batch were determined using digital caliper (Z 540-1, USA) while the masses were determined using Mettler analytical balance. The compact density, CD, was calculated using equations 6.

$$CD = m/\pi r^2 t \quad \ldots\ldots\ldots\ldots\ldots\ldots (6)$$

where m = mass, r = radius and t = thickness of tablet.

Crushing strength

The crushing strength of five tablets from each batch was determined using Mosanto hardness tester (Laboratory Tree Co., India). The load applied to cause crushing was recorded and the mean crushing strength was calculated [10].

Friability

Ten tablets were dedusted, weighed together and then subjected to abrasion test using Roche frabilator (Erweka, Germany) operated at 25 rpm for 4 min. The tablets were dedusted properly again and then reweighed collectively. The difference in weight was determined and the friability value was calculated as ratio of change in weight to original weight expressed in percentage [10].

Tablet porosity

The tablet porosity Φ was determined using equation 7.

$$\Phi = 1 - \frac{CD}{Dt} \quad \text{..... (7)}$$

where CD = compact (tablet) density and D_t = true density of granules.

Disintegration time

Six tablets from each batch were subjected to disintegration test in a freshly prepared 0.1 N HCl at 37 °C using USP disintegration apparatus (Erweka, Germany). The disintegration times were taken and the mean disintegration time was calculated [14].

***In vitro* drug release**

A tablet was placed in the dry basket of the U. S. P. dissolution apparatus containing 900 ml of 0.1 N HCl thermostatically maintained at 37±0.5 °C. The apparatus was set to a rotational speed of 100 rpm for 1 h. A 10 ml sample was taken at 5, 10, 20, 30, 45 and 60 min with subsequent replacement with equal volume of the dissolution medium. Each withdrawn sample was filtered and the absorbance was taken at 277 nm using UV spectrophotometer (Jenway, England). Cumulative percent drug released was calculated and plotted against time [11].

Statistical analysis

Data were expressed as mean±standard error of mean. Statistical analysis was done using one-way analysis of variance followed by Turkey-Kramer multiple comparison test using GraphPad Instat-3 software. Significance of difference was set at *p-values* less than 0.05.

RESULTS

The percentage yield of chitosan from the *Callinectes gladiator* shell was 36.7% and the degree of deacetylation was 62.7%.

The FTIR spectra of individual ingredients and that of dried granules of F2 are shown in fig. 1. The spectrum of callinectes chitosan was characterized by ten peaks and two bands. The two bands were of high intensity and located at positions 1495 and 3240 cm^{-1}. All the major peaks in the spectrum of metronidazole were retained in the spectrum of F2. The intensity of peaks between 2200 and 3000 cm-1 in the spectrum of metronidazole were reduced in the spectrum of F2. Also, some of the peaks in the spectrum of individual ingredients were superimposed in the spectrum of F2.

The DSC thermograms are shown in fig. 2. The thermogram of metronidazole showed an endothermic peak at 159 °C and an exothermic peak at 280 °C. The thermogram of chitosan showed two endothermic peaks at 129 and 179 °C while the thermograms of lactose showed three endothermic peaks at 148, 218 and 232 °C. The thermograms of acacia gum showed a wide endothermic transition having a peak at 80 °C followed by a wide exothermic transition having a peak at 300 °C. The thermogram of F2 was characterized by two endothermic peaks at 148 and 159 °C followed by two exothermic peaks at 205 and 240 °C.

The surface morphology of F3, F6 and F9 are shown in fig. 3. The granules of F3 and F6 appeared singly and were oval to spherical in shape with rough edges while those of F9 appeared in clusters, were of diverse shapes and with rough edges.

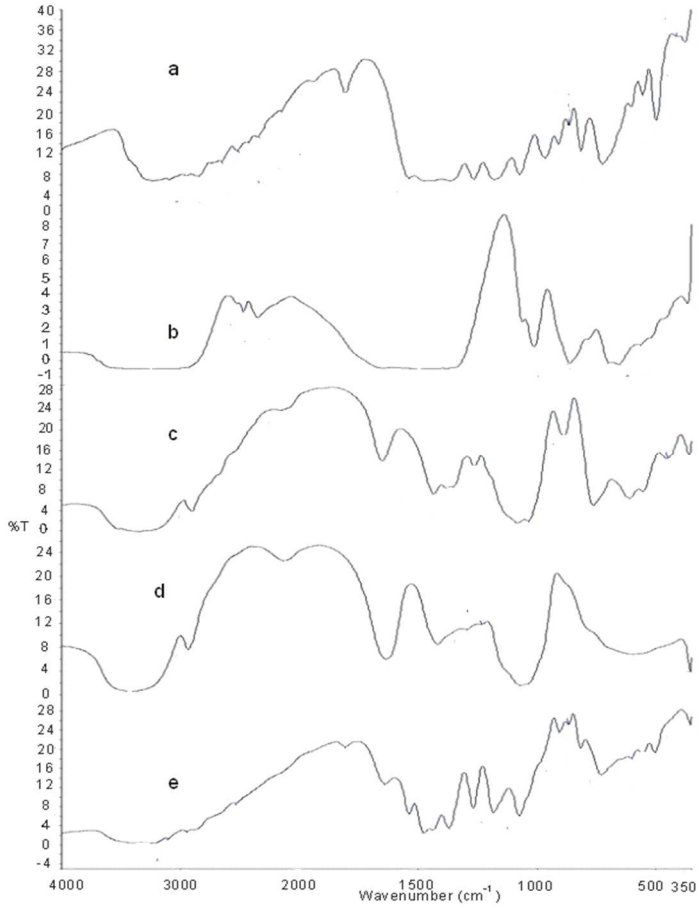


Fig. 1: FTIR spectra of (a) metronidazole (b) chitosan (c) lactose (d) acacia gum and (e) Formulation F2

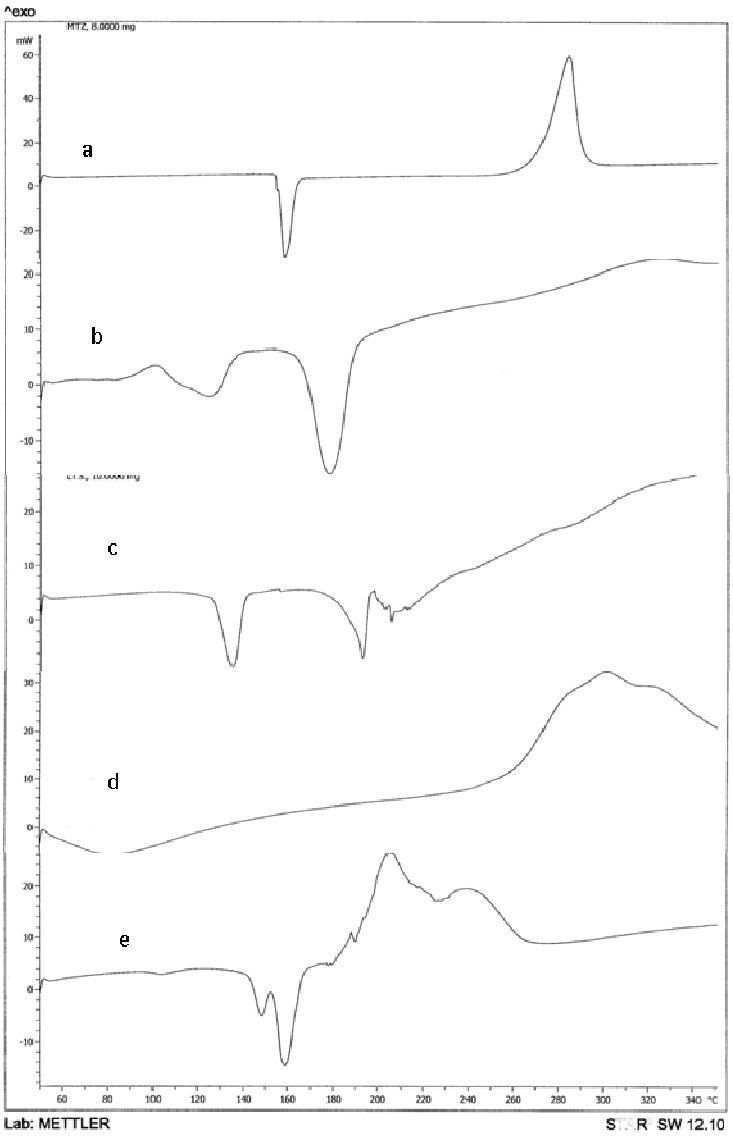
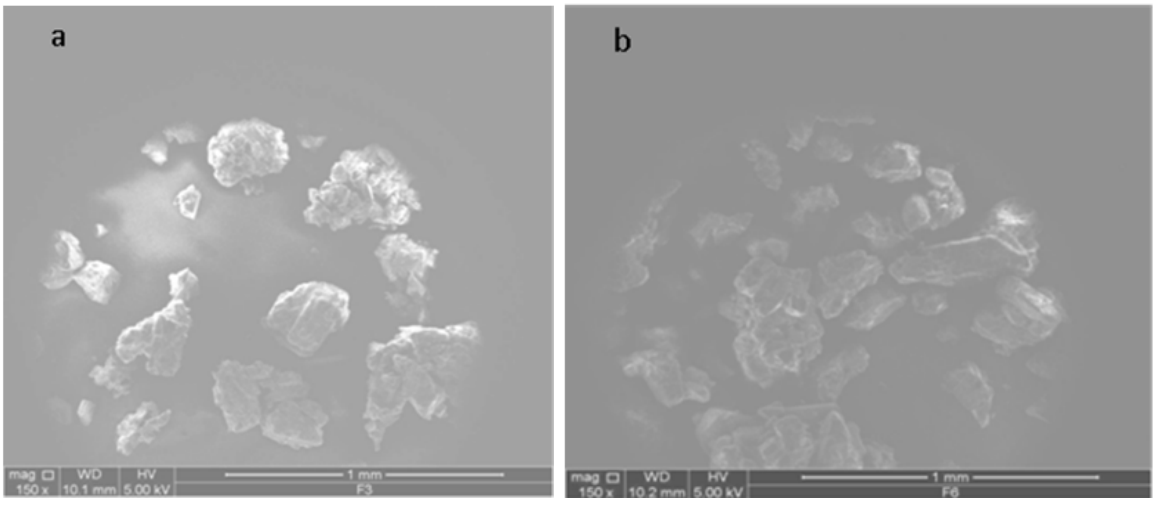


Fig. 2: DSC thermograms of (a) metronidazole (b) chitosan (c) lactose (d) acacia gum and (e) Formulation F2



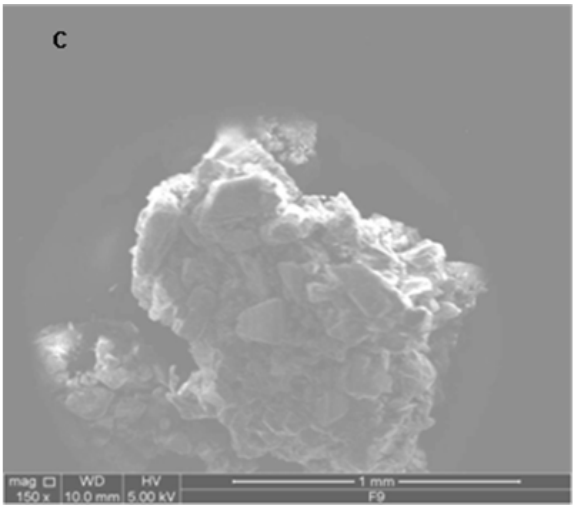


Fig. 3: Scanning electron micrographs of (a) formulation F3 (b) formulation F6 and (c) formulation F9

Table 2: Physical properties of granules

Batch	Bulk density (g/cm^3)	Tapped density (g/cm^3)	True density (g/cm^3)	Carr's index (%)	Hausner's ratio
F1	0.52±0.00	0.70±0.01	1.37±0.00	25.38±2.40	1.36±0.02
F2	0.57±0.02	0.72±0.00	1.36±0.00	20.37±2.32	1.26±0.04
F3	0.60±0.01	0.73±0.01	1.37±0.00	18.11±2.45	1.22±0.04
F4	0.45±0.00	0.56±0.02	1.38±0.00	18.42±2.70	1.23±0.04
F5	0.53±0.01	0.69±0.01	1.37±0.00	23.04±1.30	1.31±0.03
F6	0.50±0.00	0.61±0.01	1.38±0.00	17.98±1.37	1.22±0.02
F7	0.52±0.00	0.64±0.01	1.37±0.00	18.77±1.23	1.23±0.02
F8	0.42±0.00	0.54±0.02	1.38±0.00	23.08±2.95	1.30±0.05
F9	0.44±0.01	0.60±0.01	1.37±0.00	26.09±1.18	1.33±0.02

n=3, data presented as mean±SEM. F1=formulation containing 2% chitosan, F2=formulation containing 4% chitosan, F3=formulation containing 8% chitosan, F4=formulation containing 2% corn starch, F5=formulation containing 4% corn starch, F6=formulation containing 8% corn starch, F7=formulation containing 2% Ac-Di-Sol®, F8=formulation containing 4% Ac-Di-Sol®, F9=formulation containing 8% Ac-Di-Sol®

The physical properties of granules are shown in table 2. The bulk density of the granules was not significantly different. The same observation was made of the tapped density and true density. The Carr's index ranged from 17.98 to 26.09% while the Hausner's ratio ranged from 1.22 to 1.36.

The physical properties of the tablets are shown in table 3. There was no significant difference in the compact density of the tablets. The crushing strength decreased with increase in concentration of chitosan while the value increased with increase in concentration of corn starch and that of Ac-Di-Sol®. Friability was not significantly different for tablets containing chitosan; not significantly different for tablets containing Ac-Di-Sol® but the value decreased significantly with increase in the concentration of corn starch. The porosity of tablets containing chitosan increased with increase in concentration of the disintegrant.

Table 3: Physical properties of tablets

Batch	Compact density (g/cm^3)	Crushing strength (kg)	Friability (%)	Porosity (%)
F1	1.29±0.01	4.45±0.12	0.52±0.03	5.84±0.42
F2	1.29±0.01	4.25±0.11	0.40±0.00	6.28±0.48
F3	1.29±0.01	3.06±0.18	0.39±0.12	6.52±0.42
F4	1.29±0.01	5.83±0.17	0.35±0.07	5.60±0.49
F5	1.30±0.00	6.25±0.15	0.27±0.03	6.04±0.24
F6	1.29±0.01	6.73±0.23	0.19±0.05	5.84±0.42
F7	1.29±0.00	4.40±0.06	0.27±0.07	6.28±0.24
F8	1.30±0.00	5.60±0.06	0.29±0.07	5.80±0.00
F9	1.29±0.00	6.57±0.01	0.29±0.05	5.84±0.00

n=3, data presented as mean±SEM. F1=formulation containing 2% chitosan, F2=formulation containing 4% chitosan, F3=formulation containing 8% chitosan, F4=formulation containing 2% corn starch, F5=formulation containing 4% corn starch, F6=formulation containing 8% corn starch, F7=formulation containing 2% Ac-Di-Sol®, F8=formulation containing 4% Ac-Di-Sol®, F9=formulation containing 8% Ac-Di-Sol®

A plot of disintegration time against formulation type is shown in fig. 4. The disintegration time decreased with increase in concentration of the disintegrants. In term of the type of disintegrant, the disintegration time was in the order Ac-Di-Sol®<chitosan<corn starch. The disintegtation times were all less than 15 min except for formulations F4 and F5.

The dissolution profile of formulations containing 2 and 4% disintegrant concentrations are shown in fig. 5. At 10 min, the cumulative percent drug released was in the order F8>F7>F5>F4>F2>F1. At 60 min, the order was F5>F4> F8>F7>F2>F1.

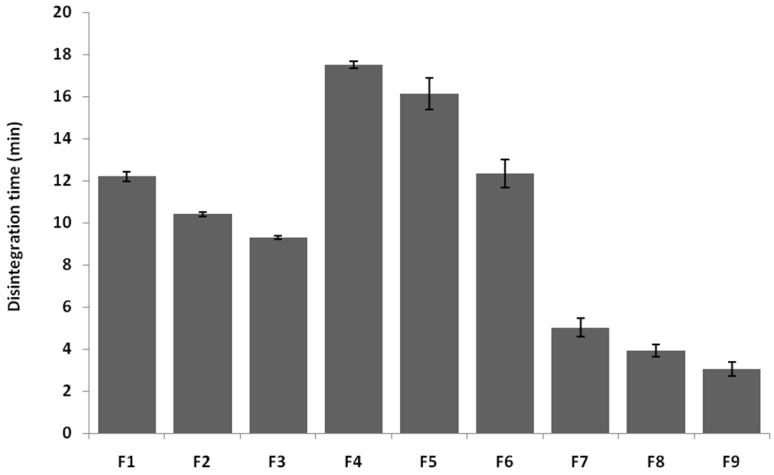


Fig. 4: Graph of disintegration time of different tablet formulations (n=3, data presented as mean±SEM. F1=formulation containing 2% chitosan, F2=formulation containing 4% chitosan, F3=formulation containing 8% chitosan, F4=formulation containing 2% corn starch, F5=formulation containing 4% corn starch, F6=formulation containing 8% corn starch, F7=formulation containing 2% Ac-Di-Sol®, F8=formulation containing 4% Ac-Di-Sol®, F9=formulation containing 8% Ac-Di-Sol®)

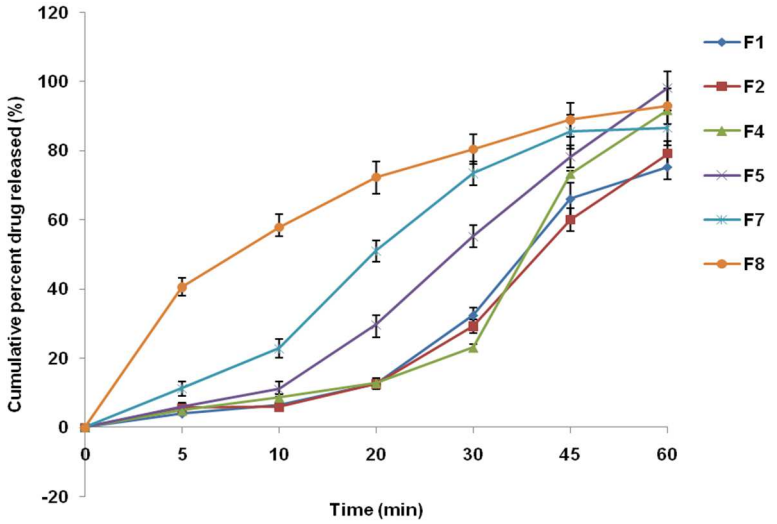


Fig. 5: Dissolution profile of tablets containing 2 and 4 %w/w disintegrant concentration (n=3, data presented as mean±SEM. F1=formulation containing 2% chitosan, F2=formulation containing 4% chitosan, F4=formulation containing 2% corn starch, F5=formulation containing 4% corn starch, F7=formulation containing 2% Ac-Di-Sol®, F8=formulation containing 4% Ac-Di-Sol®)

DISCUSSION

Extraction of chitosan in this study showed a higher yield compared to the work of No and Meyers [15] who reported yields of 13-26% chitosan from crab shells. Variation in yields of chitosan from crab shells has been related to specie of crab used, method of extraction and reaction time [15, 16]. Hence, a relatively high yield of chitosan can be obtained from shells of *Callinectes gladiator*. The Degree of deacetylation shows the number of free amino groups present in chitosan macromolecule [17]. It is an important parameter to be noted as it affects solubility, chemical reactivity and biodegradability. Degree of deacetylation may range from 30 to 95% [18] depending on the available source and procedure. The degree of deacetylation of chitosan extracted in the present work is about average (62.7%). A perfect (100%) degree of deacetylation is very rarely obtained. Puvvada *et al.* [19] concluded that higher DD values are due to higher amount of protein and this affects the chemical, physical and biological properties of chitosan.

The two bands of high intensity at positions 1495 and 3240 cm^{-1} in the spectrum of chitosan can be ascribed to N-H bending and N-H stretching respectively [20]. They suggest effective deacetylation of chitin to form chitosan with prevalence of NH_2 groups [21]. The FTIR spectrum of F2 exhibited the characteristic band of metronidazole. The changes in the intensity of some of the peaks were due to superimposition with the peaks of the spectra of the other ingredients. Hence, the integrity of metronidazole was not adversely affected by the presence of callinectes chitosan.

The first endotherm in the thermogram of callinectes chitosan (fig. 2b) can be ascribed to enthalpy relaxation of the polymer [22] while the second endotherm can be ascribed to the polymer melting [23]. The endothermic and exothermic transitions of metronidazole (fig. 2a) were retained in the thermogram of F2 (fig. 2e). The endothermic transition can be ascribed to melting of the drug [23] while the exothermic transition can be ascribed to degradation [24].

There was no shifting of the endothermic peak from 159 °C. Hence, the melting point of metronidazole was not affected. However, there was a reduction in the exothermic temperature. The other peaks observed in the thermograms of F2 were from the other excipients. The endothermic peak became broadened and shrunk in the thermogram of F2 showing a more amorphous state. The two endothermic peaks of chitosan were superimposed at 148 and 159 °C in the thermogram of F2 [25]. Hence, there was an elevation in enthalpy relaxation temperature and a reduction in the melting point of the chitosan in F2 formulation.

The rough edges of the granules (fig. 3) are indicative of the tendency of the granule to adsorb fluid; and this could promote fluid penetration and hence capillarity. These are desired properties for disintegrant action. They could also enhance the adhesiveness of the granules [26].

A Hausner's ratio of less than 1.25 (or 20% Carr's index) indicates good flow; greater than 1.5 (or 33% Carr's index) indicates poor flow while 1.25 to 1.50 (or 20 to 33% Carr's index) indicates fair flow [27]. Therefore, it can be inferred that granules of F3, F4, F6 and F7 had good flow while the other granules had fair flow. A fair flow can be improved by addition of a glidant [28]. Therefore, talc was added to all the granules at concentration of 1.5 % w/w tablet weight to optimize the granule flow before compression.

The type and concentration of disintegrant had no significant effect on the compact density of the tablets. The decrease in the crushing strength of tablets with increase in the concentration of chitosan was not unexpected. The work of Aucamp and Campus [29] showed that the presence of chitosan in tablet formulation caused a decrease in tablet strength. Hence, care must be taken to use optimal amount of chitosan so that tablet strength will not be compromised. All the tablets passed the test for friability. Friability value of less than 1% is required for a tablet to pass friability test [28]. Friability is a measure of tablet weakness.

There was no significant difference in the tablet porosity. Porosity is very important to disintegration process and its effect depends on the mechanism involved in the disintegration process [30]. For disintegrants that work by capillary action, high porosity is advantageous because water uptake is enhanced for capillarity. For those that work by swelling, high porosity enhances water uptake but reduces the effect of the breaking force because of the void spaces. Hence, optimal porosity must be ensured for this class of disintegrants.

All the tablet formulations containing chitosan and Ac-Di-Sol®passed the test for disintegration time which is maximum of 15 min [28]. A superdisintegrant should be useful at concentrations below 5% [5]. Therefore, callinectes chitosan just like Ac-Di-Sol® is a super-disintegrant. The incorporation of corn starch as disintegrant was only effective above 5%, that is, at 8% showing that it is not a superdisintegrant.

From fig. 4, it is clear that even though chitosan is useful as a superdisintegrant, it is not as effective as Ac-Di-Sol®. The use of chitosan as a superdisintegrant is however economical because it dispels the need for cross-linking required for the production of superdisintegrant from starch and cellulose. Ac-Di-Sol® is cross-linked sodium carboxymethylcellulose while sodium starch glycolate is sodium salt of cross-linked and etherified potato starch [2].

Even though the porosity of the formulations (F1 to F9) is not significantly different, the disintegration time is significantly different. This is because the three polymers bring about disintegration by different mechanisms. For instance, swelling is the major mechanism by which corn starch works as a disintegrant. The absorbed water is transformed into disintegration force [31] which breaks the particle-particle bond in the tablet matrix [32]. In this mechanism, high porosity weakens the breaking force and high amount of such disintegrant is thus required. In contrast, chitosan and AC-Di-Sol® work by capillary action or wicking [33]. High porosity provides the pathway for fluid penetration to displace air bringing about wicking which is the mechanism employed by these disintegrants. Disintegration by wicking is always the first step. There is rapid tablet disintegration even at low concentration of such disintegants [33]. This explains the effectiveness of the callinectes chitosan as a superdisintegrant.

The task of developing rapidly disintegrating tablets (oro-dispersible tablets) can be achieved by using superdisintegrants [34]. Hence, callinectes chitosan can be investigated for this purpose.

Initially (at 5 min), drug release from tablets containing Ac-Di-Sol® was significantly higher than those containing callinectes chitosan and corn starch. Hence, Ac-Di-Sol® is the most suitable for manufacture of oro-dispersible tablets. However, at 60 min, the cumulative percent drug released was not significantly different for all the tablet formulations. There are different mechanisms by which dissolution rate can be enhanced [35]. These include: solid dispersing effect of one polymer on the other, micellar solubilization *et cetera*. These phenomena could influence dissolution such that the cumulative percent drug released eventually became insignificantly different at 60 min.

CONCLUSION

A relatively high yield of chitosan with degree of deacetylation of 62.7% is obtainable from shells of *Callinectes gladiator*. There is no adverse interaction between this polymer and metronidazole. Callinectes chitosan is suitable for use as a super-disintegrant in tablets. Its disintegrant action is inferior to Ac-Di-Sol but superior to corn starch.

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AUTHORS CONTRIBUTION

This work was conceived by the first author who was also responsible for the writing of the manuscript. The three authors were jointly involved in the design of the work and the laboratory work. They all read and approved the manuscript.

CONFLICT OF INTERESTS

There is no conflict of interests associated with this work

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