



STUDIES ON THE PROPERTIES OF CHITOSAN-STARCH BEADS AND THEIR APPLICATION AS DRUG RELEASE MATERIALS

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ABSTRACT

In this work, chitosan and blends of chitosan-starch beads were prepared and crosslinked with glutaraldehyde (pentane-1,5-dial). The blends were prepared with 1:1, 2:1 and 3:1 chitosan-starch ratios. Metformin hydrochloride (N,N-dimethylimidodicarbonimidic diamide hydrochloride), a type 2 diabetes drug, was incorporated into them. The materials were subjected to swellability tests and the effects of time and pH were established. Fourier Transformed Infrared Spectrophotometric (FTIR) analysis was also carried out on the materials and their potentials as drug release systems studied. The results obtained from the FTIR studies showed that the uncrosslinked chitosan-starch bead showed O-H stretching band at 3424cm^{-1} and N-H band at 1640cm^{-1} . The chitosan-starch bead also showed a band at 597cm^{-1} corresponding to C-Cl band, due to the presence of metformin hydrochloride in the bead and its O-H stretching band was very strong and broad due to the numerous -OH groups in starch and chitosan. The results of swelling studies showed that the percent swellability of the polymer matrices increased in both the crosslinked and uncrosslinked beads as the amount of starch in them increased. The uncrosslinked chitosan beads had maximum swelling of 83.74%, while its crosslinked analogue had 47.93% in acidic medium (pH 2.06) within the range of test period of 60 minutes. The amount of drug released by the 1:1, 2:1 and 3:1 crosslinked chitosan-starch beads (13.90, 13.60, and 12.30mg/L, respectively) was much lower than that of their uncrosslinked analogues (22.50, 20.90, and 16.60mg/L, respectively) after 120 minutes, suggesting that the release of drug is delayed by crosslinking. This suggests that the crosslinked chitosan-starch beads can be used for regulating release of drugs in solid dosages such as beads or tablets.

Keywords: chitosan, chitosan-starch beads, drug release, metformin hydrochloride, swelling

INTRODUCTION

Polymers are macromolecules composed of repeating structural units of monomers connected by covalent chemical bonds. There are many types of polymers and they exist in two broad areas which are natural and synthetic polymers. Natural polymers such as proteins, collagen, silk, keratin, carbohydrates, starch, glycogen, chitosan are widely used materials for conventional applications and even as drug delivery systems. These materials are widely used because they are chemically inert, nontoxic, less expensive, biodegradable, eco-friendly and readily available (Bansal *et al.*, 2011).

Among the naturally occurring polymers, chitosan, starch and their derivatives have been studied by many researchers (Ostrawska-Czubenko *et al.*, 2011). Chitosan is a linear polysaccharide composed of randomly distributed β -(1-4)-linked D-glucosamine (deacetylated unit) and N-acetyl-D-glucosamine (acetylated unit). Chitosan has also been defined as the deacetylated derivative of chitin which is a water insoluble polymer. (N-acetyl-D-glucosamine) are found in nature and present in insect exoskeletons, crabs, shrimps, lobsters, and fungal cell walls. It is a natural, biodegradable, biocompatible, bioadhesive polymer, and is gaining attention in the pharmaceutical field for a wide range of drug delivery (Bhumkar and Pokharkar, 2006).

The wide varieties of applications of chitosan are due not only to its excellent biocompatibility, biodegradability, and economic efficiency, but also due to distinct chemical structures with high percentage of primary amino groups (-NH₂) for easy binding to bio-molecules such as DNAs and proteins (Park *et al.*, 2007).

Blending of chitosan with other polymers such as starch and crosslinking them are both convenient and effective methods of improving the physical and chemical properties of chitosan for practical applications. Crosslinking of chitosan can be achieved by reacting chitosan with epichlorohydrin or ethyleneglycol diglycidyl ether (Ngah *et al.*, 2002), sodium tripolyphosphate (Bhumkar and Pokharkar, 2006), or glutaraldehyde (Ostrawka-Czubenko *et al.*, 2011; Sudha *et al.*, 2012; Kumari and Rani, 2011; Rohindra *et al.*, 2004). Immunization studies carried out on rats using glutaraldehyde-crosslinked chitosan showed promising tolerance by living tissues of the rat muscles (Rohindra *et al.*, 2004), making it a preferred crosslinking agent.

Starch is one of the ubiquitous natural polymers for use as a biopolymer because it is a versatile biodegradable polymer, with immense potential and low price for use in non-food industries (Sudha *et al.*, 2012).

In view of this, starch has been receiving growing attention since the 1970s. Maize starch and its major components, amylose and amylopectin, are biopolymers which are attractive raw materials for use as components in packaging materials (Sudha *et al.*, 2012). They have been used to produce biodegradable materials to partially or entirely replace plastic polymer films because of their low cost and renewability, as well as their possessing good mechanical properties. However, compared to common synthetic polymers, the biodegradable products based on starch, unfortunately, still revealed many disadvantages which are mainly attributed to the highly hydrophilic character of starch polymer (Sudha *et al.*, 2012).

To overcome the disadvantageous properties of chitosan or starch, the polymer blending technique, which represents a more versatile approach for the development of new materials, is often used. This is because the properties of blends can be varied over a wide range. Relative to a single-component polymeric material, a blend enjoys several degrees of freedom that allow tailoring of the material to meet the requirements suitable for effective drug delivery and even adsorption process (Sudha *et al.*, 2012). Blending of chitosan with starch results in the formation of edible coating with good film forming and mechanical properties (Srisuk and Srikulkit, 2008).

Blended biopolymers can be crosslinked to enhance their properties and broaden their applications. However, the addition of these chemical substances (crosslinking materials) can be limited due to their toxicity (Kumari and Rani, 2011).

The release of drugs from chitosan-based solid dosage depends upon the morphology, size, density, and extent of crosslinking of the particulate system, physico-chemical properties of drug as well as the polymer characteristics such as whether the polymer is hydrophilic or hydrophobic, has gel formation potentials, swelling capacity, muco-adhesive or bioadhesive properties and also depends on the presence of other excipients present in the dosage form (Bansal *et al.*, 2011). Since chitosan does not cause any biological hazard and is inexpensive, it is suitable for use in the preparation of solid dosage forms of commercial drugs (Dutta *et al.*, 2004).

Chitosan and its derivatives in the form of beads have been reported to have effective delivery of some drugs such as insulin, gentamicin sulphate, diclofenac, clarithromycin, cimetidine, famotidine, bovine serum albumin, clozapin, ovalbumin, doxorubicin, metformin hydrochloride, ofloxacin, 5-fluorouracil (Bansal *et al.*, 2011; Kumari and Rani, 2011).

In this study, chitosan-starch beads containing different chitosan-starch ratios, and their crosslinks have been prepared with the incorporation of metformin hydrochloride as a model drug and their swellability and drug release abilities examined. Metformin hydrochloride (N,N-dimethylimidodicarbonimidic diamide hydrochloride) is the first line of drug for the treatment of type 2 diabetes, particularly in overweight and obese people.

MATERIALS AND METHODS

Glutaraldehyde (pentane-1,5-dial), (25%) was supplied by Qualikems (India), while metformin hydrochloride was supplied by Ecomed Pharmaceuticals (Nigeria) as Synformin, sodium hydroxide, acetic acid, sodium hypochlorite, and concentrated hydrochloric acid were of analytical grades from BDH.

Preparation of chitosan from snail shells (Hossein *et al.*, 2008)

African giant land snail shells (*Archachatina marginata*) were collected from a local market in Mbaitoli Local Government Area of Imo State, Nigeria, washed, sun-dried for two weeks and pulverized. The ground shells were later sieved with a mesh sieve (425 μ m).

The production of chitosan from the ground shells was achieved by the reported methods of Hossein *et al.*, 2008.

A typical process involved the following stages:

(i) **deproteinization** (ii) **decalcification** (iii) **decolouration** and (iv) **deacetylation**.

Deproteinization: The sieved snail shell powder (250.0g) was treated with 3.0L of 1.2M NaOH solution for two and half hours at 75^oC, with stirring at intervals. After the heating process, the solution was allowed to cool, then, the excess NaOH solution was removed by decantation, followed by washing the powder with deionized water to neutral pH, filtration, and air-drying of the residue (Hossein *et al.*, 2008).

Decalcification: The recovered sample from the deproteinization process (226.8g) was placed into 2.72L of 0.7M HCl solution for 20 minutes. The excess HCl solution was removed by decantation, followed by washing of the sample to neutral pH with deionized water, filtration and air-drying (Hossein *et al.*, 2008).

Decolourization: The sample obtained from the decalcification process (125.4g) was dispersed in 1.5L of 0.3% (v/v) solution of NaOCl (containing 12.5% available chlorine). The mixture was allowed to stand for 1 hour and the excess NaOCl removed by decantation, followed by washing to neutral pH with deionized water and air drying to obtain chitin (95.7g) (Hossein *et al.*, 2008).

Deacetylation of Chitin: The chitin (95.7g) was treated with 1.4L of 50% NaOH solution (i.e. 12.5M) for 20 minutes at about 120^oC. The solution was allowed to cool, then, the excess NaOH solution was removed by decantation, followed by washing of the sample to neutral pH, filtration with a sintered glass (No. 3) and air drying to obtain chitosan (27.8g) (Hossein *et al.*, 2008).

Preparation of uncrosslinked and crosslinked chitosan-starch beads as drug release systems.

Uncrosslinked Beads: Chitosan (1.0g) and metformin hydrochloride (0.5g) were mixed together and introduced into 20.0cm³ of 5.0% aqueous acetic acid to dissolve.

Three other portions of 1.0g chitosan and 0.5g of metformin hydrochloride were also prepared followed by the addition of 0.33g, 0.5g and 1.0g starch, respectively, and also placed in same concentration of acetic acid to dissolve. This gives 3:1, 2:1 and 1:1 chitosan-starch ratios, respectively.

The solutions were each stirred for 4 hours to ensure proper homogenization. Each of the solutions were sucked into a 5.0cm³ syringe and carefully extruded into a 100.0cm³ solution of 0.5M NaOH to coagulate the solutions and form the beads.

The beads were left in the NaOH solution for 20 minutes with stirring and were thereafter carefully recovered and repeatedly washed with de-ionized water to a neutral pH and air-dried (Kumari and Rani, 2011; Ngah *et al.*, 2002).

Crosslinked beads: Some of the beads were crosslinked by soaking them in 0.1% glutaraldehyde solution for 24 hours. The crosslinked beads were then recovered, washed repeatedly with de-ionized water to neutral pH, filtered and air-dried. The crosslink density (extent of crosslinking) was also determined (Rohindra *et al.*, 2004).

Characterization of the chitosan and chitosan-starch beads.

FTIR Spectral Analysis:

Infrared transmission spectra of the uncrosslinked chitosan-starch beads were studied using Perkin-Elmer Fourier Transformed Infrared Spectrophotometer (model 2000) (FTIR) in KBr discs from 4000 to 400cm⁻¹ (Pavia *et al.*, 2001).

Swellability studies

The swelling ability of the uncrosslinked and crosslinked chitosan and chitosan-starch beads were measured by determining the extent of water uptake, using the methods of Rohindra *et al.*, 2004, the percent water uptake being based on the relationship:

$$\% \text{water uptake} = \frac{W_s - W_d}{W_d} \times 100,$$

where W_d and W_s are the dry and swollen weights of the materials, respectively. The effect of time on water uptake was carried out by determining

%water uptake of test material at time intervals of 10,20,30,40,50, and 60 minutes, at fixed pH.

Drug release studies

The drug release experiments were carried out at 31°C in acidic medium (0.1M HCl; pH 2.06). Beads containing the drug (metformin hydrochloride) were placed in the release medium (60cm³ of 0.1M HCl) and after 10 minutes intervals, portions of 5cm³ of the mixture were withdrawn from the beaker for the drug assessment. The withdrawn samples were assessed spectrophotometrically to determine the amount of drug released at 320nm where they had maximum absorbance, using a UV-Visible Spectrophotometer (JENWAY 6320D) (Kumari and Rani, 2011).

RESULTS AND DISCUSSION

Figure 1 shows the spectra of the uncrosslinked chitosan-starch beads. The small sharp but weak band at 3754cm⁻¹ is attributed to O-H stretching, which shows enhanced hydrogen bonding of the -OH groups. The broad band at 3424cm⁻¹ is the O-H stretching of both starch and chitosan, overlapping the N-H stretching vibration of secondary amines in the same region. This band is strong because of the numerous -OH groups in starch and chitosan. The bands at 2929cm⁻¹ and 2857cm⁻¹ represent -CH₂ aliphatic groups. The band at 1740cm⁻¹ corresponds to C=O stretching of amide, which may be an evidence of an incomplete deacetylation of the acetyl group in chitin. The doublet at 1640cm⁻¹ and 1557cm⁻¹ is attributed to N-H bending, which overlaps the C=N stretching band in the same region. The strong, broad band at 1411cm⁻¹ is the C-H bending of alkyl groups. The bands at 1140cm⁻¹ and 1031cm⁻¹ correspond to -C-O-C- glycosidic linkage in the ring. The broad band at 666cm⁻¹ is attributed to N-H bending of primary amines. The band at 597cm⁻¹ of medium intensity corresponds to the band for C-Cl, pointing to the incorporated metformin hydrochloride (Pavia *et al.*, 2001).

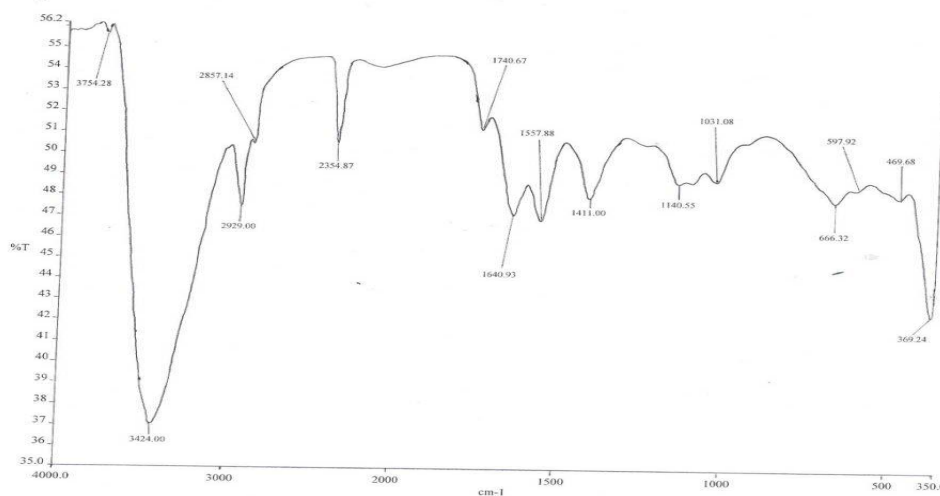


Figure 1: FTIR spectra of undisclosed chitosan – starch beads

The results of the studies on percent water uptake (swellability) of the chitosan and chitosan-starch beads with time (minutes) in acidic medium (pH 2.06) are presented in Figures 2 and 3 (see also Tables 1 and 2).

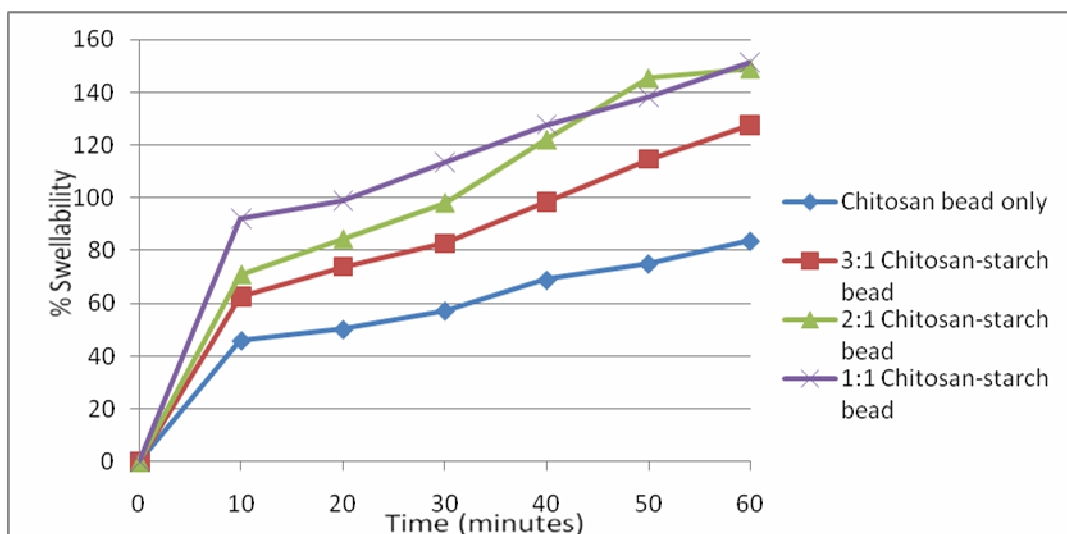


Figure 2: Plot of % swellability against time (minutes) for uncrosslinked chitosan and chitosan-starch beads in acidic medium (pH 2.06).

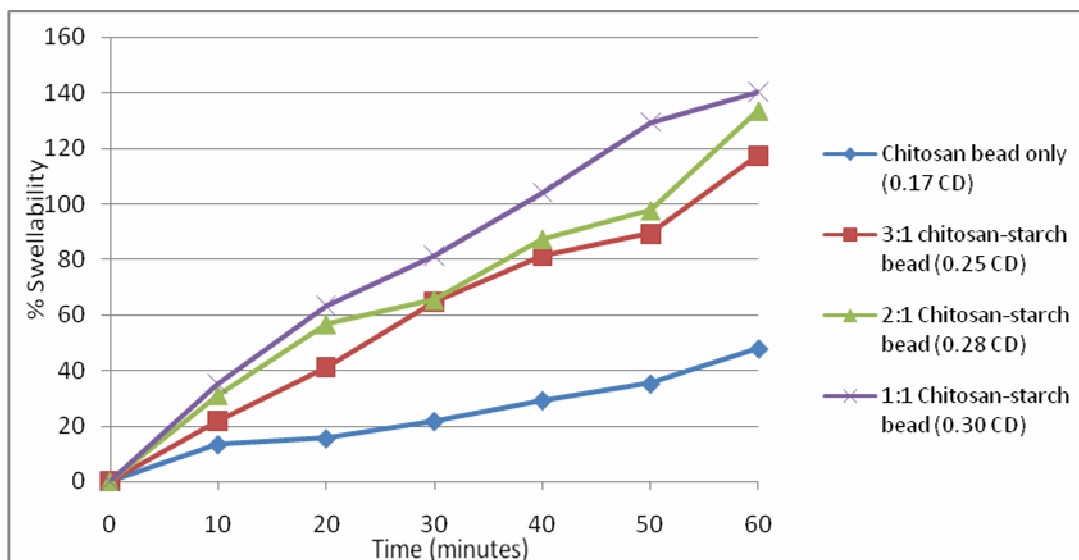


Figure 3: Plot of % swellability against time (minutes) for glutaraldehyde-crosslinked chitosan and chitosan-starch beads in acidic medium (pH 2.06).

The percent swellability of the uncrosslinked and crosslinked chitosan and chitosan-starch beads increased as time and amount of starch increases in acidic medium. The increase in swellability followed the order chitosan-starch beads (1:1) > (2:1) > (3:1) > beads with only chitosan. This can be explained based on the fact that, increase in starch composition increased the hydrophilicity of the beads due to the reinforcement with -OH groups from chitosan. The synergistic effect of -OH groups (from starch and chitosan) and -NH groups (from chitosan) may have created enhanced binding sites for water molecules. However, the uncrosslinked chitosan and chitosan-starch beads showed higher percent swellability in acidic medium than their crosslinked counterparts. This is because, crosslinking occurs via

the amino groups of chitosan and this is aided by the lone pair of electrons on the nitrogen atoms of the amino groups as shown in Figure 4, reducing the binding sites of the blend for water and therefore affecting swellability.

The results represented in Fig. 2 for the dependence of percent swellability on time for the uncrosslinked chitosan and chitosan-starch beads in acidic medium show that the rate of water uptake (swelling rate) of the uncrosslinked chitosan and chitosan beads is rapid in the first 10 minutes and then becomes almost steady up to 60 minutes, while that for the crosslinked chitosan and chitosan-starch beads represented in Fig. 3 exhibited an almost steady swelling rate from 0 to 60 minutes.

In general, the swellability of chitosan is affected by three factors:

1. Presence of hydroxyl (-OH) groups in the chitosan chain, which enhance their hydrophilicity.
2. Presence of amino (-NH₂) groups in the chitosan chain, which gets protonated in water, mostly in acidic medium.
3. Flexibility of the chitosan polymeric matrix, which can allow for easy penetration of solution (Mourya *et al.*, 2010).

The mechanism for the reaction between the amino groups of chitosan and the carbonyl groups of the crosslinking agent, glutaraldehyde as summarized by Ostrawka-Czubenko *et al.*, 2011, which confirms that the amino groups (-NH₂) of chitosan are the crosslinking sites, is shown in Fig. 4.

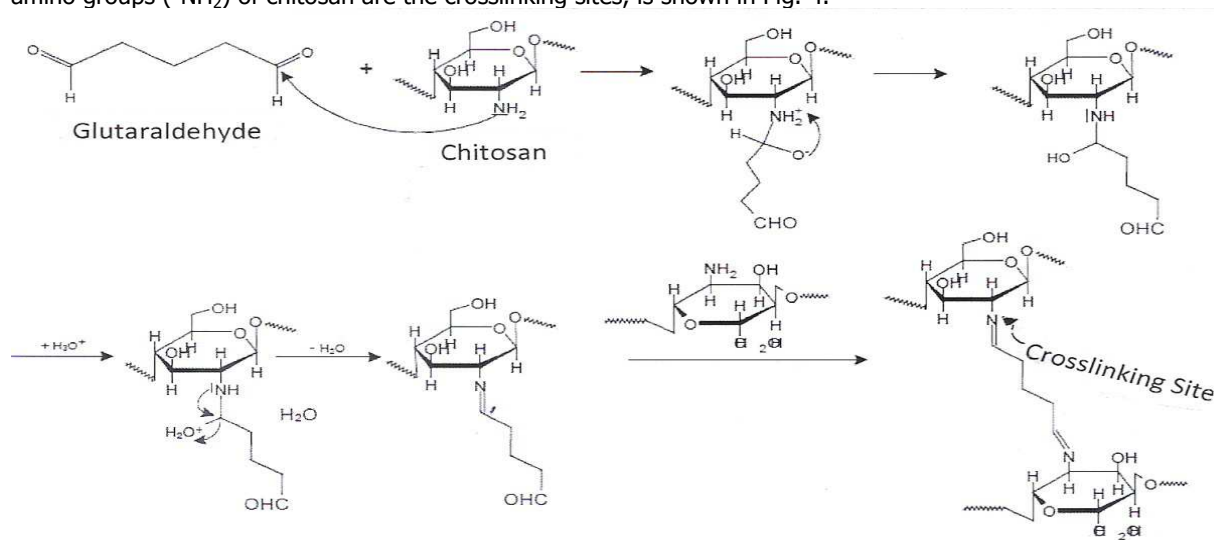


Figure 4: Reaction mechanism for the reaction between the amino group of chitosan and carbonyl groups of glutaraldehyde.

The results of the studies on percent swellability of the chitosan and chitosan-starch beads with time (minutes) in basic medium (pH 8.03) are presented in Figures 5 and 6 (see also Tables 3 and 4). The results presented in Figs 5 and 6 show that in basic medium (pH 8.03), the percent swellability of both uncrosslinked and crosslinked chitosan and chitosan-starch beads were lower than in the acidic medium. In basic medium (pH 8.03), the swelling that occurred can be said to be mainly driven by solvent diffusion because it is considered that chain penetration by solvent due to protonation of amino groups is absent (Kumari *et al.*, 2011). The lower percent swellability of these beads in basic medium may be attributed to the absence of protonation of the amino groups of the chitosan moiety which would

have led to faster intra-hydrogen-bond dissociation (breakage of self association of chitosan and starch) and efficient solvent diffusion (Kumari *et al.*, 2011).

The results represented in Fig. 5 for the dependence of percent swellability on time for the uncrosslinked chitosan and chitosan-starch beads in basic medium show that the rate of increase in percent swellability of the uncrosslinked chitosan and chitosan beads is rapid in the first ten minutes and then becomes almost steady up to 60 minutes, whereas the result represented in Figure 6 for the crosslinked beads show that, the rate of increase in percent swellability of the crosslinked chitosan and chitosan-starch beads was almost steady all through the swelling time of 0 to 60 minutes.

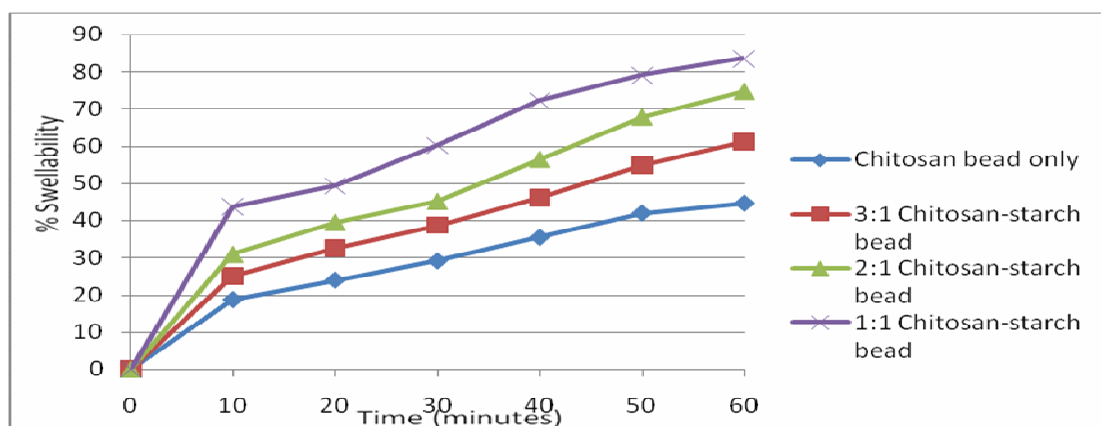


Figure 5: Plot of % swellability against time (minutes) for uncrosslinked chitosan and chitosan-starch beads in basic medium (pH 8.03).

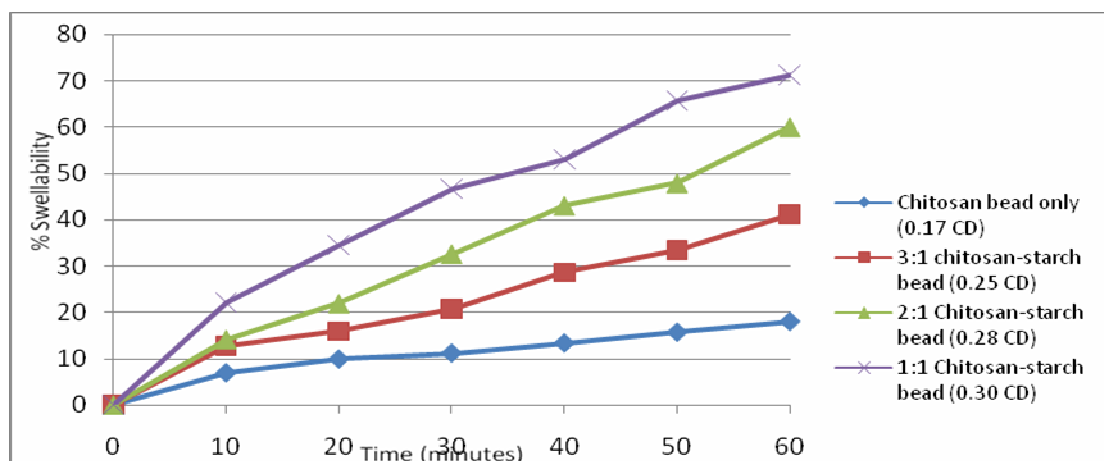


Figure 6: Plot of % swellability against time (minutes) for glutaraldehyde crosslinked chitosan and chitosan-starch beads in basic medium (pH 8.03).

Figure 7 shows the appearance of the chitosan-starch beads used in the drug release studies. The drug release studies in acidic medium (0.1M HCl; pH 2.06) is important because the target site of activity of the drug used in this study (metformin hydrochloride) is in

the human stomach which regularly secretes HCl, making the physiological environment of the stomach to be acidic with a pH range of between 1.0 to 4.5 (Raymond, 1991). The stomach usually maintains a pH range that may not be too far from pH 2.



Figure 7: The chitosan beads.

The results of the drug release studies carried out on the uncrosslinked and crosslinked chitosan and chitosan-starch beads in acidic medium (0.1M HCl; pH 2.06) are shown in Figures 8 and 9 (see also Tables 5 and 6). The uncrosslinked and crosslinked chitosan and chitosan-starch beads showed an increase in the amount of drug released as the time increased as seen in Figs 8 and 9. This increase can also be linked to the amount of starch present in the beads because an increase in the amount of starch increases the number of -OH groups in the beads, hence increasing hydrophilicity of the beads. This increase in hydrophilicity leads to an increase in the rate at which solvent can penetrate the chitosan-starch bead matrices, causing the beads to swell and release drugs. The results represented in Figs 8 and 9 also show that both uncrosslinked and crosslinked chitosan and chitosan-starch beads showed rapid release of drug in the first 10 minutes of the study and exhibited an almost steady release of drug afterwards. This is because, the mechanism of drug release for materials is that the materials usually

swell slowly and their matrices collapse progressively before the release of the drugs in them (Kumari *et al.*, 2011). Comparing the results represented in Figure 8 with those in figure 9 showed that a higher amount of drug was released by the uncrosslinked chitosan and chitosan-starch beads than their crosslinked counterparts. This is obtained by comparing the amount of drug released by the uncrosslinked and crosslinked beads in the first 10 minutes of the study. For example, uncrosslinked chitosan bead released 8.40mg/L of drug in the first 10 minutes, while the crosslinked chitosan bead released 5.00mg/L of drug. Uncrosslinked 3:1 chitosan-starch bead released 9.50mg/L of drug, while the crosslinked 3:1 chitosan-starch beads released 7.30mg/L of drug in the first 10 minutes. This shows that there is delayed release of drug by the crosslinked chitosan and chitosan-starch beads. This may be because of the compactness of the crosslinked analogue of the beads, leading to less penetration of solvent into their polymer matrix (Kumari *et al.*, 2011).

Additionally, the unavailability of the amino groups in chitosan as a result of crosslinking, would lead to highly reduced protonation in the medium of study (0.1M HCl; pH 2.06). This would reduce the number of $-NH_2$ groups available for solvent absorption. Furthermore, this delay in the release of drug may be

due to the immobilization of the chains by the crosslinks and the 'trapping' of drugs within the chitosan and chitosan-starch bead matrices, causing the drugs to be more 'tightly' held and hence slowly released in a delayed manner.

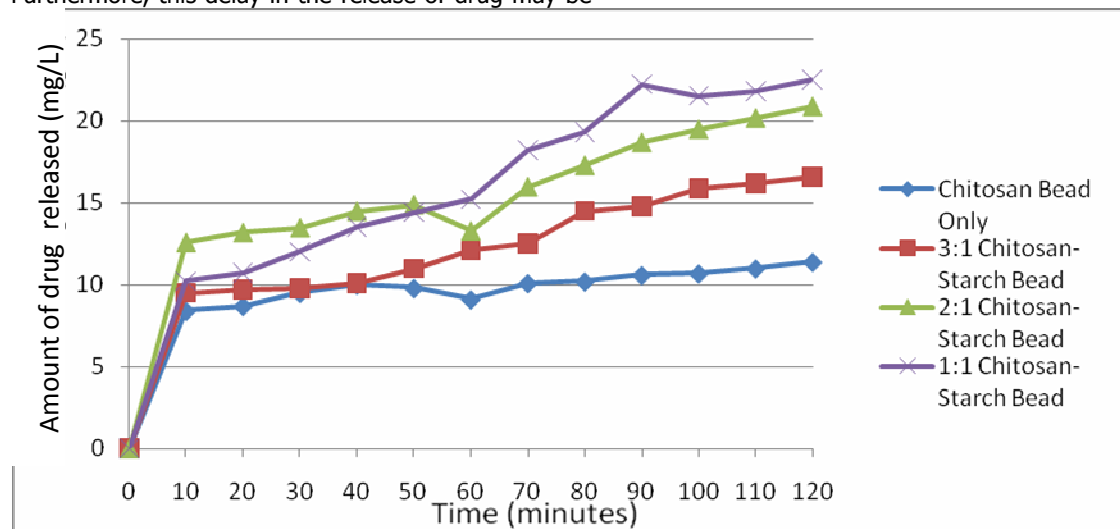


Figure 8: Plot of amount of drug released (mg/L) against time (minutes) for uncrosslinked chitosan and chitosan-starch beads.

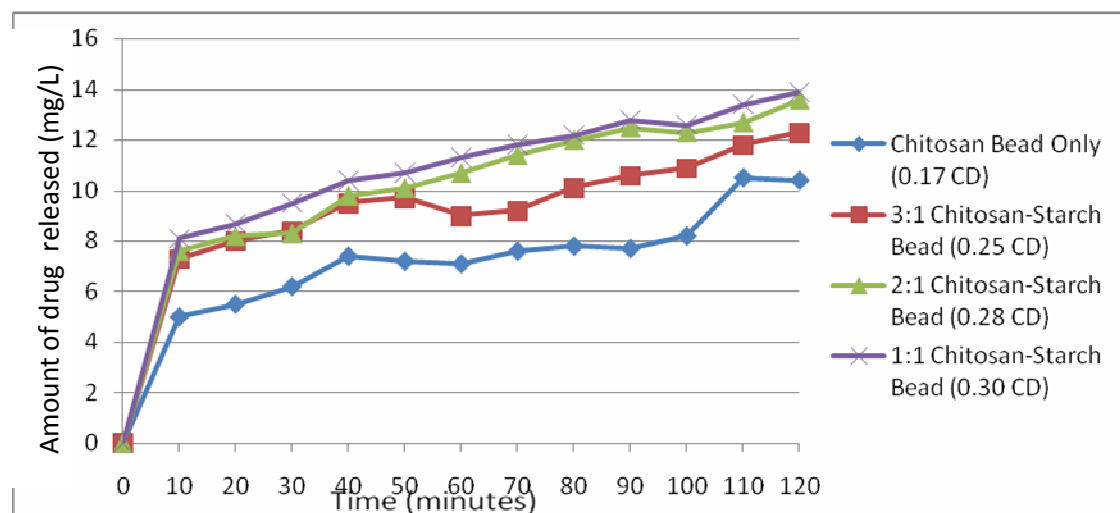


Figure 9: Plot of amount of drug released (mg/L) against time (minutes) for glutaraldehyde crosslinked chitosan and chitosan-starch beads.

CONCLUSION

From the swelling results, it is clear that the rate of swelling of the chitosan-starch beads was dependent on time and pH. Swellability of the materials containing starch increased as the amount of starch blended with the chitosan increases. Crosslinking clearly caused a slower rate of drug-release in chitosan and chitosan-starch beads. This suggests that by skillfully controlling the factors such as extent

of crosslinks, pH and chitosan-starch ratio, the disintegrants (chitosan and chitosan-starch beads) may be applied for regulating the release of certain drugs, where a controlled rate of drug-release from solid dosage is desirable. It is common knowledge that metformin hydrochloride is administered one tablet twice daily, with the aim of gradual release from the table.

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Appendix 1

Table 1: Rate of water uptake (%) for the uncrosslinked chitosan and uncrosslinked chitosan-starch beads in acidic medium (pH 2.06)

BEAD TYPE	% SWELLABILITY					
	10min	20min	30min	40min	50min	60min
Chitosan	46.03	50.27	57.32	69.01	75.14	83.74
chitosan-starch (3:1)	62.64	73.91	82.74	98.52	114.73	127.61
chitosan-starch (2:1)	71.08	84.52	98.21	122.16	145.41	149.03
chitosan-starch (1:1)	92.16	98.87	113.64	127.88	138.23	151.47

Table 2: Effect of crosslinking on rate of water uptake for the crosslinked chitosan and crosslinked chitosan-starch beads in acidic medium (pH 2.06)

BEAD TYPE	CROSSLINK DENSITY	% SWELLABILITY					
		10min	20min	30min	40min	50min	60min
Chitosan	0.17	13.28	15.48	21.72	29.23	35.27	47.93
chitosan-starch (3:1)	0.25	21.72	41.18	64.67	81.23	89.36	117.51
chitosan-starch (2:1)	0.28	31.09	56.69	65.38	87.33	97.71	133.68
chitosan-starch (1:1)	0.30	35.04	63.17	81.31	104.15	129.48	140.42

The results in Tables 1 and 2 are represented in Figures 2 and 3 as plots of % swellability against time (minutes) for uncrosslinked and crosslinked chitosan and chitosan-starch beads respectively.

Appendix 2

Table 3: Rate of water uptake for the uncrosslinked chitosan and uncrosslinked chitosan-starch beads in basic medium (pH 8.03)

BEAD TYPE	% SWELLABILITY					
	10mins	20mins	30mins	40mins	50mins	60mins
Chitosan only	18.68	23.91	29.04	35.38	41.87	44.53
chitosan-starch (3:1)	25.09	32.53	38.77	46.19	54.92	61.28
chitosan-starch (2:1)	30.89	39.52	45.16	56.41	67.82	74.73
chitosan-starch (1:1)	43.70	49.34	60.18	72.25	79.11	83.62

Table 4: Effect of crosslinking on rate of water uptake for the crosslinked chitosan and chitosan beads in basic medium (pH 8.03)

BEAD TYPE	CROSSLINK DENSITY	% SWELLABILITY					
		10mins	20mins	30mins	40mins	50mins	60mins
Chitosan only	0.17	06.97	09.93	11.21	13.39	15.72	18.04
chitosan-starch (3:1)	0.25	12.79	15.91	20.67	28.65	33.42	41.21
chitosan-starch (2:1)	0.28	14.17	21.92	32.65	43.06	47.93	60.09
chitosan-starch (1:1)	0.30	22.17	34.61	46.78	53.11	65.72	71.33

The results in Tables 3 and 4 are represented in Figures 5 and 6 as plots of % swellability against time (minutes) for uncrosslinked and crosslinked chitosan and chitosan-starch beads respectively.

Appendix 3

Table 5: Dependence of the amount of drug released (mg/L) on time (minutes) for the uncrosslinked chitosan and chitosan-starch beads in acidic medium

TIME (mins)	AMOUNT OF DRUG RELEASED (mg/L)			
	Chitosan Bead Only	Chitosan-Starch (3:1) Bead	Chitosan-Starch (2:1) Bead	Chitosan-Starch (1:1) Bead
10	8.40	9.50	12.60	10.20
20	8.70	9.70	13.20	10.70
30	9.50	9.80	13.50	12.00
40	10.00	10.10	14.50	13.50
50	9.80	11.00	14.90	14.40
60	9.10	12.10	13.30	15.20
70	10.10	12.50	16.00	18.20
80	10.20	14.50	20.10	19.30
90	10.60	14.80	17.30	22.20
100	10.70	15.90	18.70	21.50
110	11.00	16.20	19.50	21.80
120	11.40	16.60	20.20	22.50

Table 6: Dependence of the amount of drug released (mg/L) on time (minutes) for the crosslinked chitosan and chitosan-starch beads in acidic medium.

TIME (mins)	AMOUNT OF DRUG RELEASED (mg/L)			
	Chitosan Bead Only	Chitosan-Starch (3:1) Bead	Chitosan-Starch (2:1) Bead	Chitosan-Starch (1:1) Bead
10	5.00	7.30	7.60	8.10
20	5.50	8.00	8.20	8.70
30	6.20	8.40	8.30	9.50
40	7.40	9.50	9.80	10.40
50	7.20	9.70	10.10	10.70
60	7.10	9.00	10.70	11.30
70	7.60	9.20	11.40	11.80
80	7.80	10.10	12.00	12.20
90	7.70	10.60	12.50	12.80
100	8.20	10.90	12.30	12.60
110	10.50	11.80	12.70	13.40
120	10.40	12.30	13.60	13.90

The results in Tables 5 and 6 are represented in Figures 8 and 9 as the amount of drug released (mg/L) against time (minutes) for the uncrosslinked and crosslinked chitosan and chitosan-starch beads respectively.