ISSN: 0975 -8542

Journal of Global Pharma Technology

Available Online at: www.jgpt.co.in

RESEARCH ARTICLE

Synthesis & Characterization of Chitosan Schiff Base Hydrogel for Controlled Drug Release

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Abstract

Chitosan-schiff base with three different ratios of para-Dimethyl aminobenzaldehyde& chitosan Schiff base hydrogels have been prepared for controlled drug release study. The synthesized chitosan Schiff base and chitosan Schiff base hydrogel were characterized by FT-IR, UV-Visible, SEM, analysis. Swelling properties of the hydrogel were investigated at three different media pH (2, 7, 10). The swelling degree varied with the pH, amount of crosslinking agent glutaraldehyde and with the amount of para-Dimethylaminobenzaldehyde for the hydrogels. All hydrogels were used for controlled drug release system. Aspirin was used as model drug, in three different buffer solution (2, 7, 10) as release media. The rate of release of drugs in the pH2 is more than that of pH7 and pH10 in the polymer hydrogels.

Keywords: *Chitosan, Chitosan Schiff base, Hydrogel, Controlled drug release.*

Introduction

Hydrogels are three-dimensional network of the cross-linked polymer swollen in water or biological fluids. These polymers are smart enough to respond to the changes of environmental stimuli (pH, ionic strength, temp, electric field, enzymes etc.) and they are swelling and shrink accordingly. They are rubbery and soft in the swelling state, like the living tissue having excellent biocompatibility. Since these biomaterials are widely used in many different fields of pharmaceutical and biomedical engineering [1]. Controlled drug delivery is system that delivers drug at a predetermined time, locally or systemically.

This includes the maintenance levels of drug within a desired level, the need for less administrations, optimum drug use and increased compliance of patient. The drug delivery system should be biocompatible, mechanically strong, inert, comfortable for the patient, achieving high drug loading, safe from accidental release, simply administer and remove, fabricate easily and sterilizable [2].Chitosan, is the main product of deacetylation of chitin, a cationic polymer combined by ß-1-4 glucosidic linkage.

Chitosan have excellent properties; low toxicity, biodegradability, biocompatibility and bioactivity [3].For its excellent properties chitosan have received interest in many fields including antimicrobials, biomedical materials, cosmetics, food additives and agricultural material. For these properties, chitosan has been used in pharmaceutical and biomedical branches as a matrix of micro particulate and crosslinked polymer hydrogel for controlled drug release [4-6]. Schiff base containing imine groups can be prepared from the condensation reaction between active carbonyl groups and amino groups. They have better physiological activities and applications in antibacterial, antiphlogistic and antiviral domains [7].

Experimental

Materials

Chitosan derived from shrimp-shell chitin with 95% degree of deacetylation was obtained from HUISUN PHARMA and all reagents and solvents were obtained from Sigma-Aldrich, HIMEDIA, CDH, BDH, and Solvochem.

Synthesis of Graft Polymer (Chitosan Schiff base) [8]

Chitosan was dissolved in a mixed solution of ethanol with glacial acetic acid and stirred for 30 min at room temperature. Then three different ratios of the aldehyde Para-Dimethylaminobenzaldehyde (pDMAB) were added to the mixture to prepare three different ratios from graft polymer as described in the table 1-1. The mixture was magnetically stirred and heated at 60°C for 24 h. After cooling, the crude product was washed with ethanol. The product was dried at room temperature for 24h. The synthetic route of chitosan Schiff base is shown in Figure 1-1.

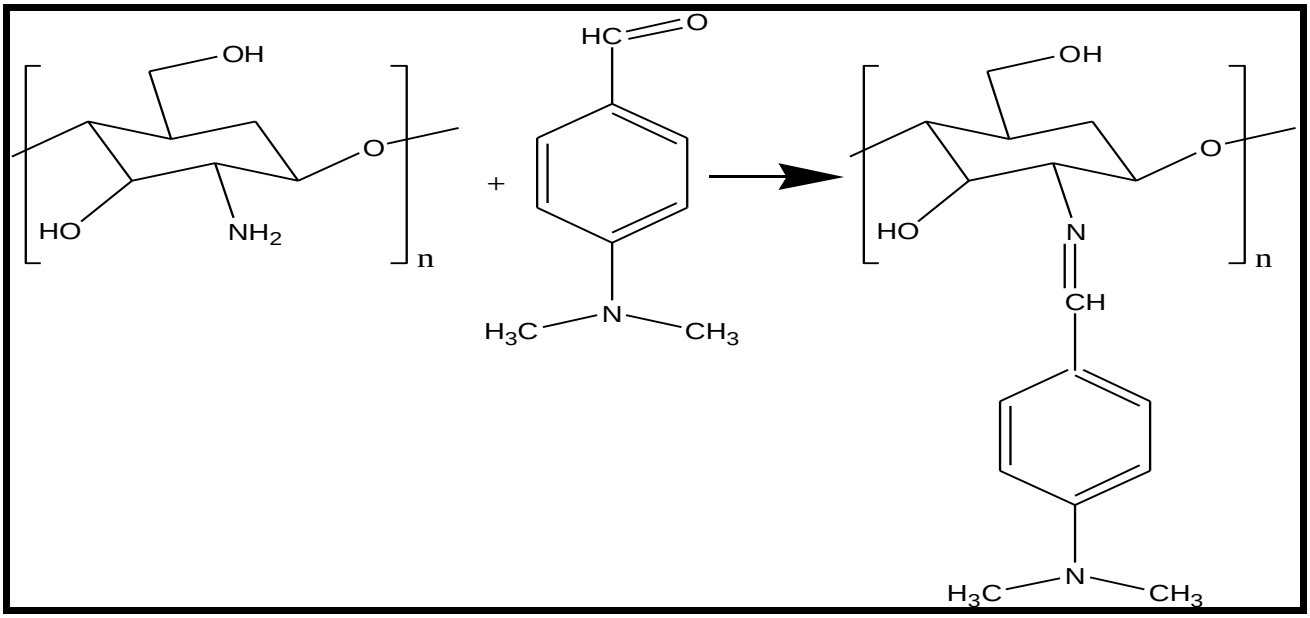

Figure 1-1: The synthetic route of chitosan-based Schiff base

Preparation of Cross linking Chitosan-pDMAB with glutaraldehyde

The polymer hydrogels were prepared by mixing different ratios from 1%*Ch-pDMAB* (A) solution, 25% glutaraldehyde is shown in the Table 1-2. After mixing, the product was poured into 24 wells plate and the hydrogel was formed within 30 min. The hydrogel was dried overnight at room temperature. The same method was obtained to prepare hydrogels for B and C compounds with different ratios of glutaraldehyde as shown in the Table1-2.

Table 1-1: The prepared samples from graft polymers

NO.	Polymer	Chitosan (gm)	DMAB (gm)
A	chitosan	5	3.5
B	chitosan	5	5
C	chitosan	5	6.5
NO.		*Ch-pDMAB* (A) 1% (ml)	GA25% (ml)
A1		50	0.15
A2		50	0.2
A3		50	0.25
NO.		*Ch-pDMAB* (A) 1% (ml)	GA25% (ml)
B1		50	0.15
B2		50	0.2
B3		50	0.25
NO.		*Ch-pDMAB* (A) 1% (ml)	GA25% (ml)
C1		50	0.15
C2		50	0.2
C3		50	0.25

Table 1-2: Synthesis derivatives A1 to A3, B1 to B3, and C1 to C3 hydrogels

NO.	Polymer	Chitosan (gm)	DMAB (gm)
A	chitosan	5	3.5
B	chitosan	5	5
C	chitosan	5	6.5

Instruments

FTIR spectrophotometers of Shimadzu Company as KBr disc in the wavelength range of (4000-400) cm-1 were recorded using IR prestige-21. The electronic spectra were measured in the range of 200- 1100 nm for 10^{-3}Mby using Distilled water by using UV-Visible spectrophotometer type shimadzu UV-160A using quartz cell of (1.0 cm) length. The surface morphology is analyzed using scanning electron microscope (SEM), model (AIS2300C). The fracture surface was observed at different magnifications, all samples were coated with gold.

Swelling Studies

The degrees of swelling and swelling behavior of the hydrogels were studied in different pH (2, 7, 10) media. The degree of swelling (DS) was determined using the equation:

% DS = (W2 - W1) / W1 x 100 (1)

In equation (1) W1 and W2 are the weight of dry hydrogel and the wet hydrogel, respectively [9].

Drug Loading

To study the drug loading property of the hydrogels, Aspirin (As) has been used as a model drug. The drug concentration was determined spectrophotometrically at (276 nm).

Results and Discussion

FTIR Studies

The FT-IR spectrum of chitosan para-Dimethylaminobenzaldehyde Schiff base *(Ch-pDMAB)* was represented in Figure (1-2). It showed a new absorption band at 1639.49 cm^{-1} attributed to vibration of C=N of imine group for the three different ratios of the aromatic aldehyde (A, B, C), and absorption bands at 1593.20, 1597.06, 1597.06 cm^{-1} respectively for the three different ratios of the aromatic aldehyde (A, B, C) attributed to the C=C stretching in the aromatic ring of the aldehyde. FT-IR spectrum for the crosslinked *(Ch-pDMAB)*by different ratios of glutaraldehyde.

Figure (1-3) shows that after cross-linking reaction shift occurs to the(N–H and O–H stretching vibration) bands when compared with the samples of *(Ch-pDMAB)* (A, B, C), This may due to the decrease in the number ofNH_2 and O-H groups, new band at 1705.07, 1712.79, 1712.79cm^{-1} referred to the C=O group of the unreacted glutaraldehyde of crosslinked *Ch-pDMAB* (A,B,C) respectively , 1639.49, 1635.64, 1639.49 cm^{-1}due to C=N of cross linked *(Ch-pDMAB)* (A,B,C) respectively [10,11].

Scanning electron microscope studies (SEM)

SEM micrographs were used to study the changes in the surface morphology for the prepared polymer hydrogels. Figures (1-4) to (1-9) illustrates the surface morphology of samples(A,B,C) the pure *(Ch-pDMAB)*Schiff base, from the SEM photos we can notice an increase in the pore average size comparing to the pore size in the hydrogels crosslinked with glutaraldehyde. The changes in surface morphology are due to the new bonds in the polymer hydrogels that created by adding glutaraldehyde as crosslinking agent to the polymer.

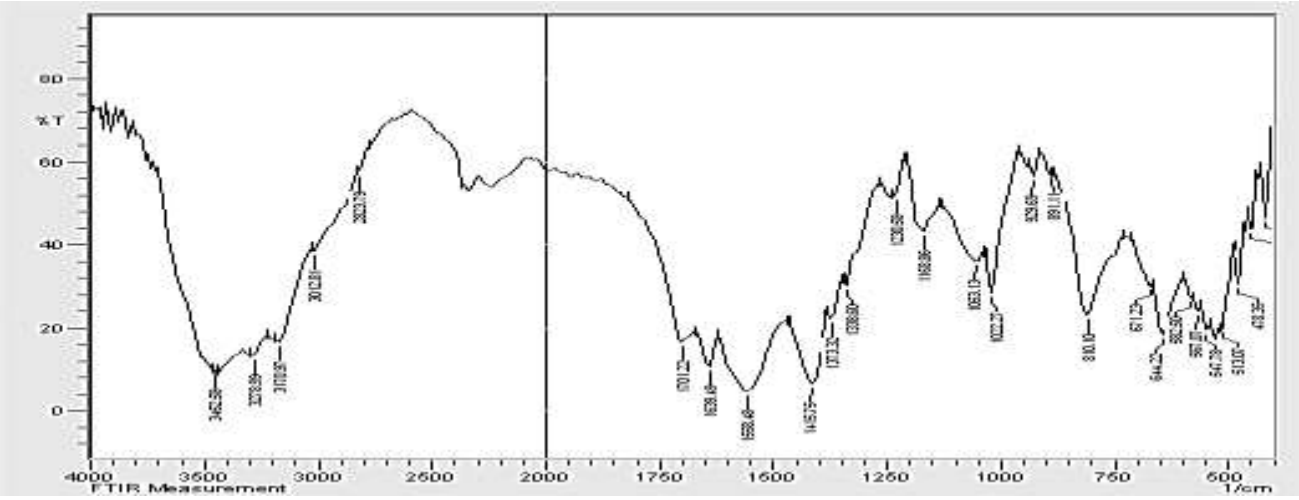

Figure1-2: FT-IR spectrum of chitosan Schiff base (A)

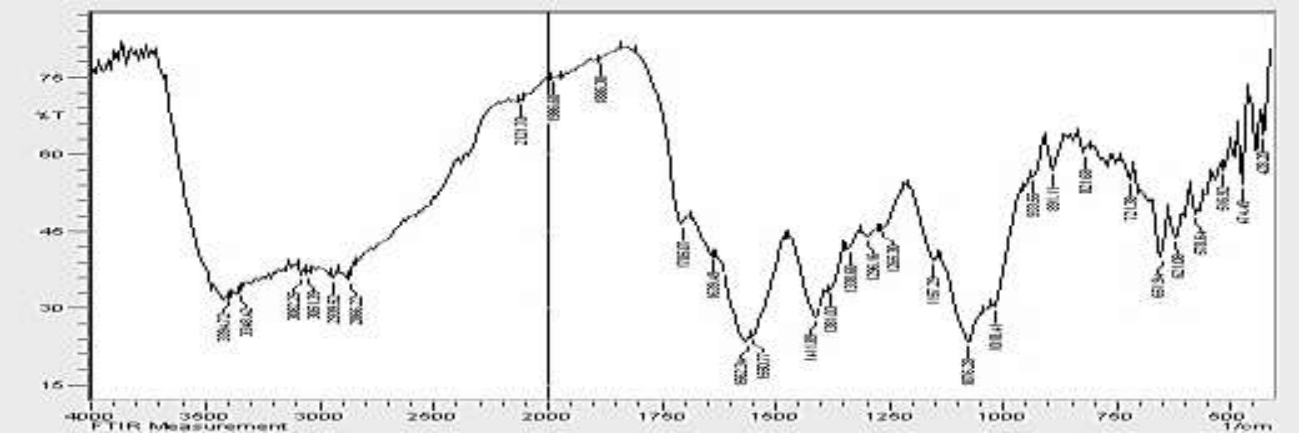

Figure 1-3: FT-IR spectrum of hydrogel A1

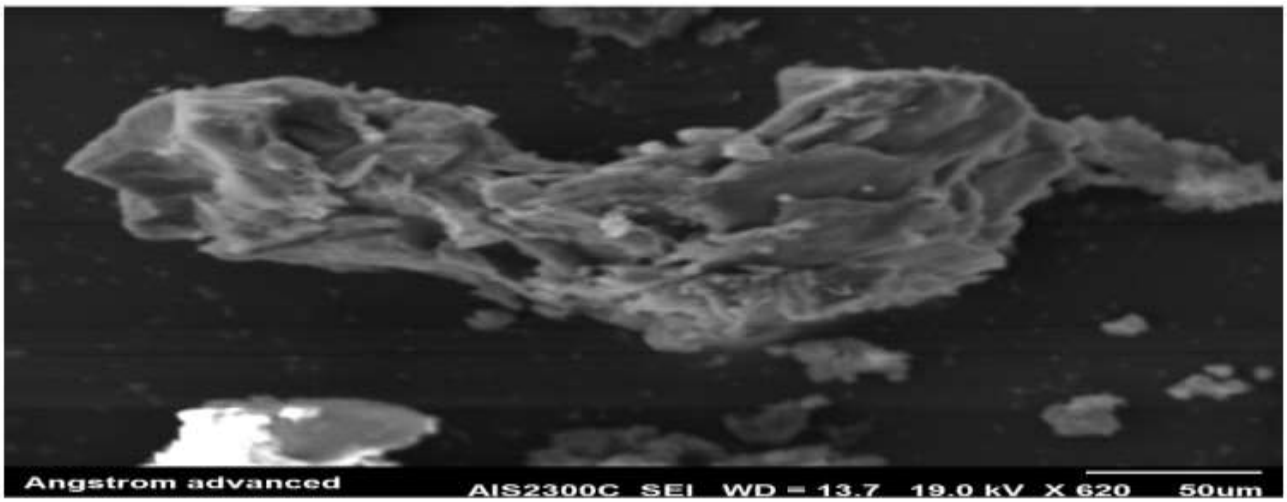

Figure 1-4: SEM images of chitosan Schiff base A

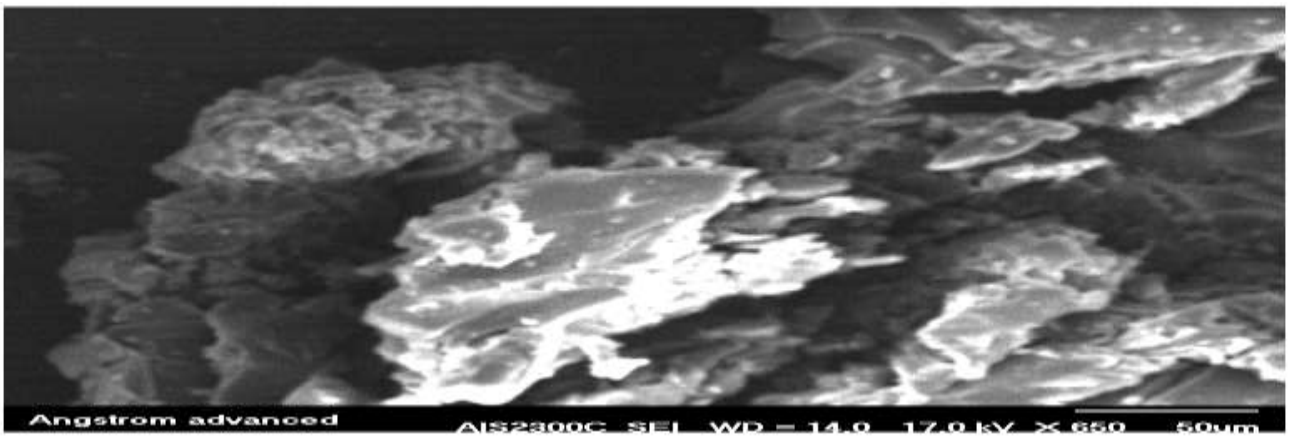

Figure 1-5: SEM images of hydrogel A1

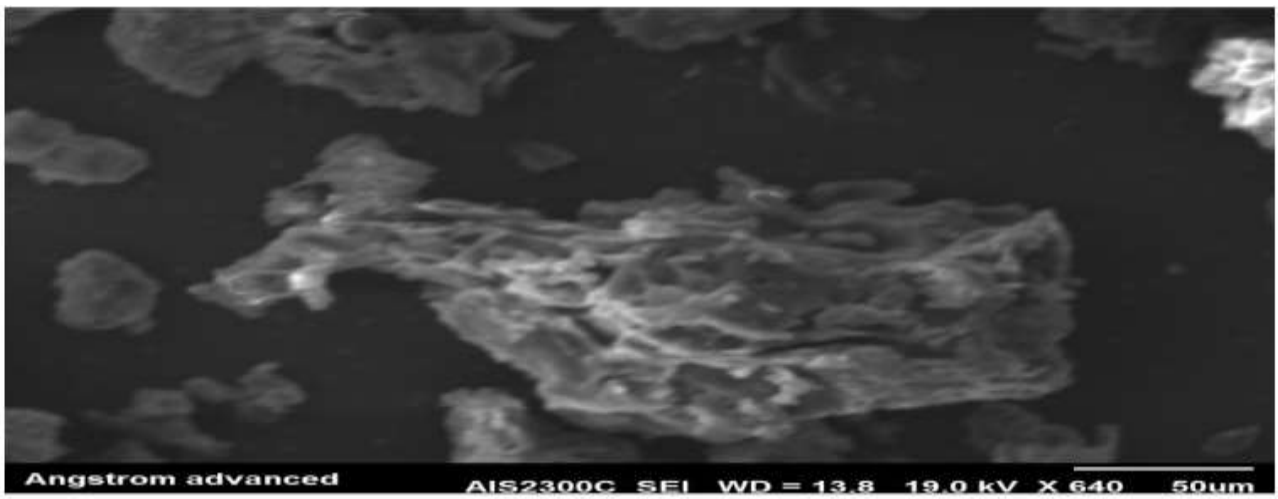

Figure 1-6: SEM images of chitosan Schiff base B

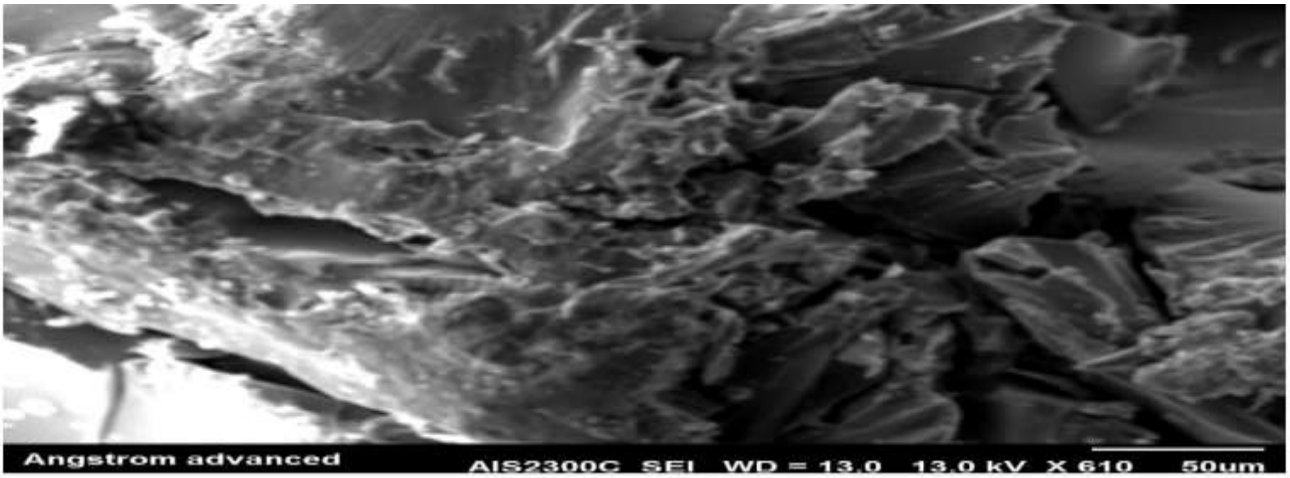

Figure 1-7: SEM images of hydrogel B1

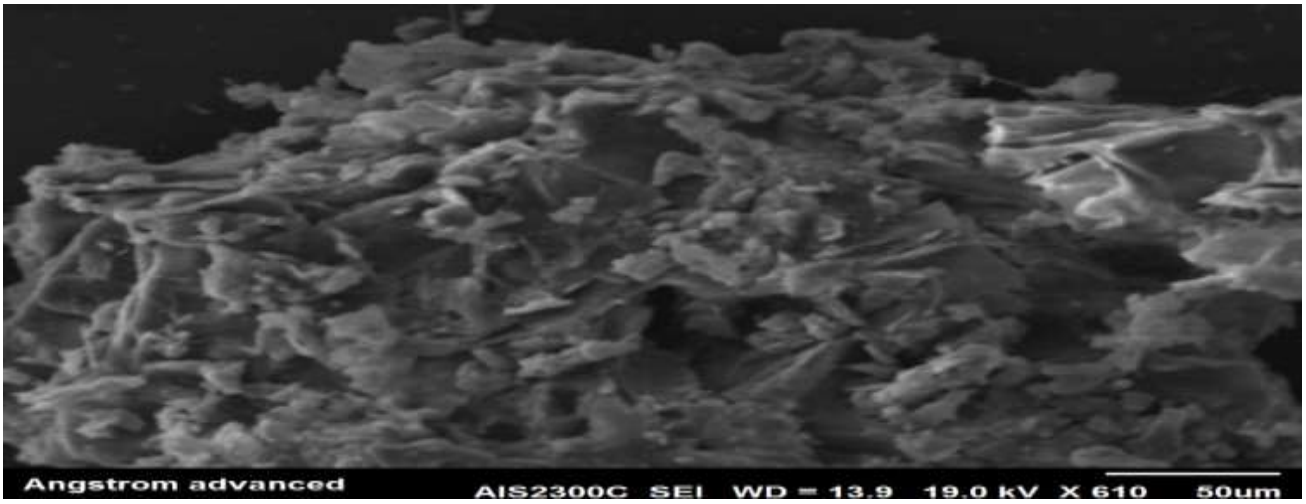

Figure 1-8: SEM images of chitosan Schiff base C

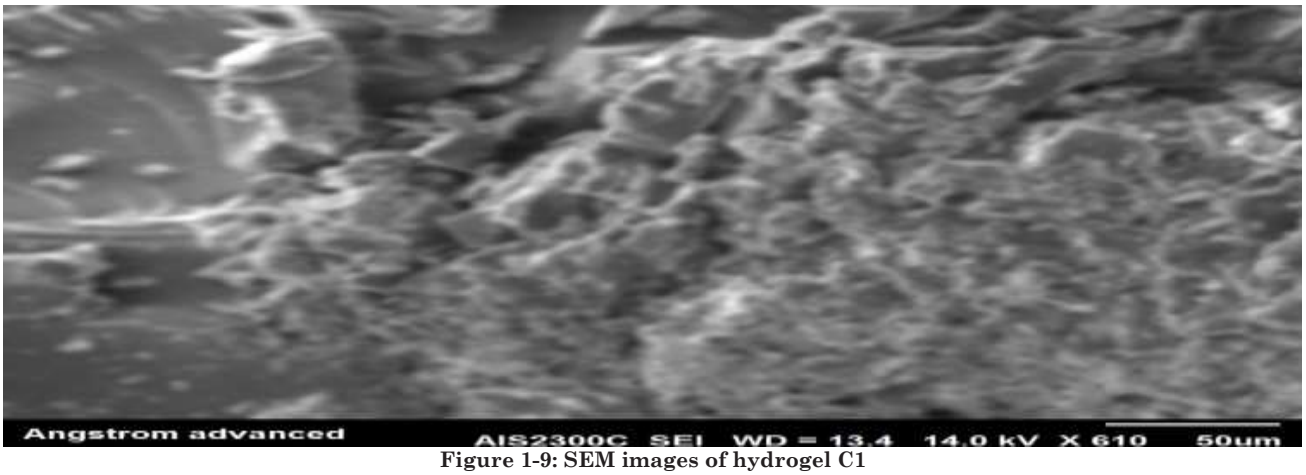

Figure 1-9: SEM images of hydrogel C1

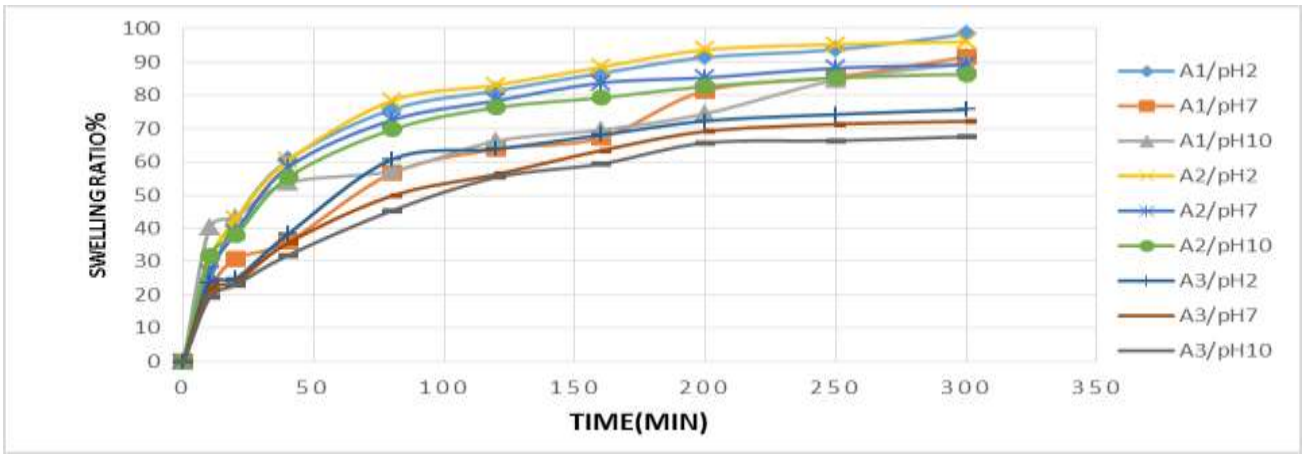

Figure 1-10: the Swelling behavior of the hydrogel A1, A2, A3 in various Ph

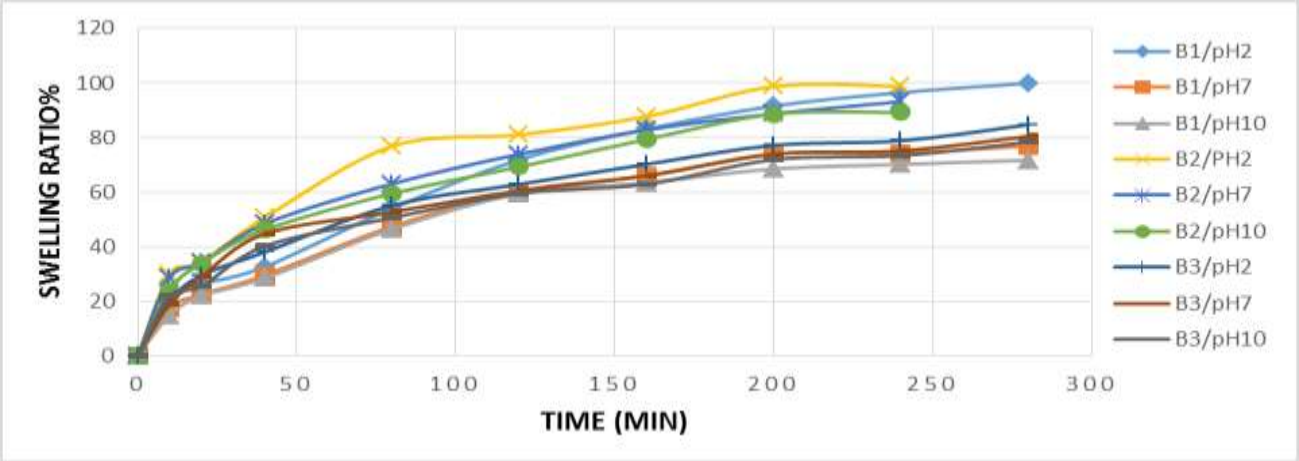

Figure 1-11: the Swelling behavior of the hydrogel B1, B2, B3 in various Ph

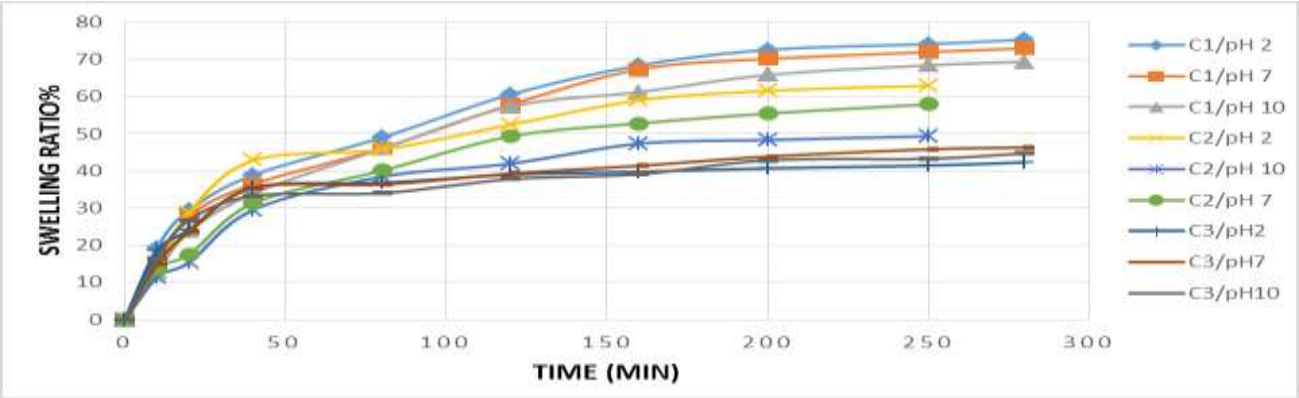

Figure 1-12: The Swelling behavior of the hydrogel C1, C2, C3 in various pH.

Swelling Studies

The swelling degree (Wt %) and the Swelling behavior of the polymer hydrogels were studies in different pH (2, 7, 10). The effects of different pH, different ratio of crosslinking agent and different ratio of grafted polymer on swelling were studied on the polymer hydrogels. The swelling values were higher in the acidic buffer pH2 than in pH7 and in pH10 as shown in figures from (1-10) to (1-12).

This pH sensitivity are due to the structure of chitosan and chitosan Schiff base where in the acidic medium protonation of the free amino groups may occur leading to dissociation of the hydrogen bonding involving these groups and partial acid hydrolysis of imine bonds of Schiff bases, which frees the chitosan amine groups again for gradual protonation and consequently facilitates the entrance of the swelling fluids into the polymer chains to attain higher values of swelling.

Another factor affect the swelling was aldehyde concentration it was observed that swelling ratio decreased with increasing the concentration of aldehyde and consequently increasing imine bonds in the polymer, the swelling ratio was higher at pH2 and lower at pH10 [9]. The effect of different glutaraldehyde concentration on swelling at pH (2, 7, 10) was studied. It was observed that as the glutaraldehyde content increases the extent of crosslinking increases which will decrease pore volume of the network of polymer hydrogels and decrease the network swelling and lower diffusion of media and decrease water uptake [12].

Controlled Drug Release

For the investigation of drug release behavior in hydrogels, we have determined UV-Visible spectra for Aspirin (As). The maximum absorption wavelength was determined for the drug, (λ max) was measured against the blank at 276 nm for (As). To obtain a calibration curve by Beer`s-Lambert`s low the absorbance was plotted against concentration [13].The specific absorbance is used to calculate the sample concentration, calibration curve of (As) as functions of concentration were plotted.

After attaining maximum swelling, the different drug loads were sampled every1 hr; illustrations (1-13) to (1-15) represent the concentration of drug released with time. In all media pH (2, 7, 10), the release from the

drug loaded samples attained its equilibrium approximately at 15 hrs.

The drug release from all hydrogel was higher in the acidic buffer pH 2 than in PH 7 and pH 10, because the rate of drug release depends on the swelling degree of the hydrogel. The mechanism of release is based on the diffusion through the swollen gels. The hydrogel films attained higher values of swelling equilibrium at pH 2 than pH 7 and pH10. The pH media have great effect on the drug release values than the effect of the gel composition. This may due to the structure of Chitosan Schiff base where its amino groups and imine bonds are the responsible for such pH sensitivity. Also we can notice the effect of the polymer composition on the release behavior that the release was higher at *(Ch-pDMAB)* A than in that for B & C.

References

1. Das N (2013) Preparation methods and properties of hydrogel: a review. Int. J. Pharm. Pharm. Sci., 5(3): 112-117.
2. Bhowmik D, Gopinath H, Kumar BP, Duraivel S, Kumar KS (2012) Controlled release drug delivery systems. The Pharma Innovation, 1: 10.
3. Felt O, Buri P, Gurny R (1998) Chitosan: a unique polysaccharide for drug delivery. Drug development and industrial pharmacy, 24(11): 979-993.
4. Tozaki H, Komoike J, Tada C, Maruyama T, Terabe A, Suzuki T, Muranishi S (1997) Chitosan capsules for colon-specific drug delivery: Improvement of insulin absorption from the rat colon. Journal of pharmaceutical sciences, 86(9), 1016-1021.
5. Paul W, Sharma CP (2000) Chitosan, a drug carrier for the 21^ s^ t century: a review. STP pharma. sciences, 10(1): 5-22.
6. Zhao H R, Wang K, Zhao Y, Pan LQ (2002) Novel sustained-release implants of herb extracts using chitosan. Biomaterials, 23(23): 4459-4462.
7. Sashikala S, Shafi SS (2014) Synthesis and characterization of chitosan Schiff base derivatives. Der. Pharma. Lettre, 6: 90-97.
8. Soliman EA, El-Kousy SM, Abd-Elbary HM, Abou-Zeid AR (2013) Low molecular weight chitosan-based schiff bases: synthesis, characterization and antibacterial activity. American Journal of Food Technology, 8: 1.
9. Gonçalves VL, Laranjeira M, Fávere VT, Pedrosa RC (2005) Effect of crosslinking agents on chitosan microspheres in controlled release of diclofenac sodium. Polímeros, 15(1): 6-12.
10. Soliman EA, El-Kousy SM, Abd-Elbary HM, Abou-Zeid AR (2013) Low molecular weight chitosan-based schiff bases: synthesis, characterization and antibacterial activity. American Journal of Food Technology, 8: 1.
11. Dos Santos JE, Dockal ER, Cavalheiro ET (2005) Synthesis and characterization of Schiff bases from chitosan and salicylaldehyde derivatives. Carbohydrate Polymers, 60(3): 277-282.
12. Hezaveh H, Muhamad II (2012) Effect of natural cross-linker on swelling and structural stability of kappa-carrageenan/hydroxyethyl cellulose pH-sensitive hydrogels. Korean Journal of Chemical Engineering, 1-9.
13. Mirzaei B, E Ramazani SA, A Shafiee M, Danaei M (2013) Studies on glutaraldehyde crosslinked chitosan hydrogel properties for drug delivery systems. International Journal of Polymeric Materials and Polymeric Biomaterials, 62(11): 605-611.

