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Synthesis of chitosan based hydrogel nanocomposite for controlled release of cisplatin drug

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Key words: Superabsorbent nanocomposite, cisplatin, drug delivery, chitosan based hydrogel.

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Abstract

In this work, hydrogel nanocomposite was synthesized and studied targeted drug delivery by this hydrogel nanocomposite in pHs 1 to 6 and 7.4. The chitosan based hydrogel nanocomposite was synthesized via bonded acetaldehyde monomer on chitosan in presence MMT- Na^+nanoclay. The superabsorbent nanocomposite structure was confirmed by FT-IR spectroscopy, SEM and XRD tests. The swelling behavior of superabsorbent nanocomposite examined in solutions with pH values 1 to 12. Then, cisplatin drug loaded in hydrogel nanocomposit and the amount of release drug was investigated in buffer solution with pH=7.4 via UV/Vis spectrophotometer.

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Introduction

In recent years, more studies have been done on synthesis and swelling behavior of hydrogels via free radical polymerization and cross linking in the presence of an initiator and a cross linking agent. superabsorbent hydrogels have more applications in the field of hygienic products (Chen JF. *et al.* 2004), agriculture (Hosseinzadeh H. *et al.*,2004), drug delivery systems , food additives, pharmaceuticals, and Biosensor (Li ZZ. *et al.* 2004). In compare of pure hydrogels, for improve of mechanical, thermal, swelling and deswelling properties is used from various fillers such as clay (Wu JH. *et al.* 2000) and nanoclays. hydrogel nanocomposite was synthesized by grafting acrylic acid on the organophilic montmorillonite with high thermal stability and swelling ratio (Weian Z. *et al.* 2005). Recently , more studies reported about synthesis and using chitosan based hydorgel nanocomposite such as Heating effect on swelling and rheological behavior on Chitosan modified MMT-poly (AMPS) nanocomposite hydrogel (Kabiri K. *et al.*2010) and a novel polyacrylamide nanocomposite hydrogel reinforced with natural chitosan nanofibers (Zhou C. *et al.* 2011). In the treatment of solid tumours the platinum-based chemotherapeutic drug cisplatin is highly effective. Study on Cisplatin drug delivery done using different method such as gold-coated iron oxide nanoparticles for enhanced tumour targeting with external magnetic fields(Wagstaff AJ.2012)Polymer--cisplatin conjugate nanoparticles for acid-responsive drug delivery(Aryal S. *et al.* 2010).In this study, a pH-sensitive hydrogels nanocomposite was synthesized based on chitosan and monomer by in the presence of acetaldehyde and nano clay montmorillonite. The drug release behavior of hydrogel nanocomposites is carried out in an acidic medium.

Material and methods

Chitosan (M_{av}= 22,742) and acetaldehyde% 99.9 of were purchased from Merck and nanoclay-type Na^+montmorillonite (Na-MMT) from Southern Clay (USA) were used and the cisplatin drug was purchased from Sobhan company. FTIR model Bommem MB and UV-visible model Perkin-Elmer CT 068598 USA, M-XL 30 Philips model SEM instrument. X-ray diffraction data corresponding to (XRD) was measured by Philips xpert 3600 was used.

Synthesis of Nano composite hydrogel

20 ml of distilled water containing 2% acetic acid in beaker equipped with a mechanical stirrer at a constant temperature bath has been spilled, the amount of chitosan (1.0 g) is added to the reactor and at constant temperature for 10 minutes with constant speed mechanical stirrer 300rpm also incorporate a fully resolved. After the dissolution of chitosan, a certain amount of montmorillonite MMT (0.01 g) is added. Then a certain amount of acetaldehyde monomer (0.3 mmol) is added. After stirring the reaction for 10 minutes at the same temperature, the reaction has been completed and temperature was hod, gel is formed. With squeeze the gel in 200 ml of ethanol production that put the gel after 2 h ethanol to remove. The hydrogel nanocomposite was completely dried in the oven (50 ^oC, 2 days).

Determination of swelling degree

Swelling degrees of the samples were gravimetrically determined by tea-bag method. The tea-bag was made of nylon screen. A tea-bag containing 0.1 g of sample was entirely immersed in distilled water. It was taken out of the water at regular time intervals, wiped superficially with a filter paper, weighed, and replaced in the same water to ensure a state of equilibrium swelling. Swelling degree was calculated from the following equation:

$S\ (g/g) = ((Ws-Wd)/Wd)$

Where Ws and Wd are the weights of swollen and dry sample, respectively (Zhang W.A *et al*, 2005).

The pH sensitivity of nanocomposite hydrogels

To evaluate the sensitivity of the synthesized nanocomposite hydrogel to pH environment, the inflation rate was measured buffer with a pH of 1 to 12 (Wu JH. *et al.*, 2000).

Drug loading in hydrogel nanocomposite

10 mg of the drug cisplatin in 50 ml distilled water solution and a solution to the drug concentration in

100 ppm was prepared. Then, 0.5 gr of hydrogel nanocomposite was synthesized to add into drug solution and hydrogel nanocomposite for days at a constant temperature had to put his medication to be absorbed by the hydrogel nanocomposite. Then, the samples were filtered when we smooth the hydrogel nanocomposite with some distilled water to wash the drug attached to the surface of the gel samples should be washed thoroughly. Volume of the solution on the filter size and quantity 3.5 ml of it to obtain the total amount of drug loaded on there and absorb it much we are making. hydrogel nanocomposite loaded by vacuum oven drying at 40 °C and we sift classified by certain mesh (mesh 40 to 60, 250 to 350 μm) from the loaded hydrogel nanocomposite for drug delivery of its to select (Mahkam M. 2004).

Concentration method

The wavelength of the UV absorption of the drug in be used to measure concentrations of is used UV-visible spectroscopy method (figures 1 and 2). This standard curve was prepared for the use of these curves; the absorption of light into the volume concentration in easily is done (Salonen J. 2005).

Controlled release of drug

In this set of experiments, a certain amount (0.2) g of the hydrogel nanocomposite put into beaker, buffer solution with the pH and temperature of the water bath is 37°C. Then, in constant temperature mixture was stirred. Gradually and the influence of the buffer solution into the swollen hydrogel nanocomposite and hydrogel nanocomposite loaded drug is released over time and increases the drug concentration in the buffer solution. for measuring of drug concentration in the buffer solution during its release, for two hours, samples taken from the system (each 3.5 mL) and we measured the absorption rate. the concentration of the drug release from the low Bear Lambr (A = LKCε) further diluted with buffer, absorbance measure lies (Slowing II. *et al.* 2008).

Results and discussion

Mechanism of hydrogel synthesis

The proposed mechanism for the synthesis of hydrogel in the form of (Li Z.2004) is given. When acetaldehyde monomer is added to the medium, to coupled electron-amino groups of chitosan monomer with carbonyl group the carbonyl group of connective and a pair of electrons on the oxygen of the carbonyl group can move and chitosan nitrogen deficiency. The next step is a proton transfer from nitrogen to oxygen and water lost and C = N group was formed. The N amine accepts a proton from the amino group of chitosan on other electron pair is ready to accept the environment (Song SW. 2005).

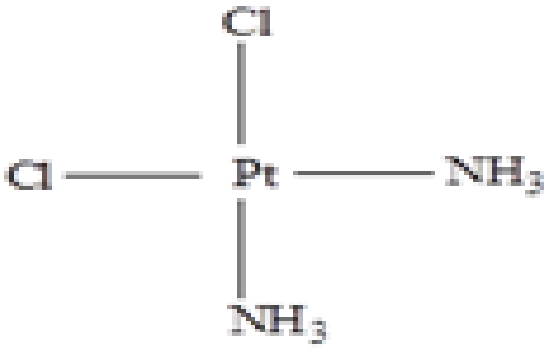

Fig. 1. Structure of cisplatin.

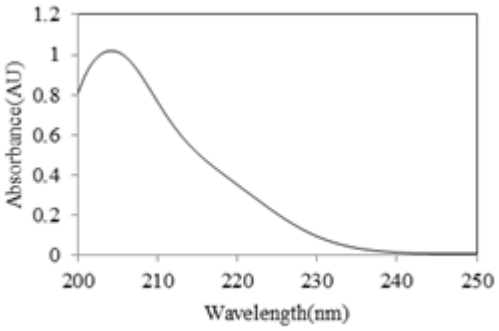

Fig. 2. UV-visible spectroscopy.

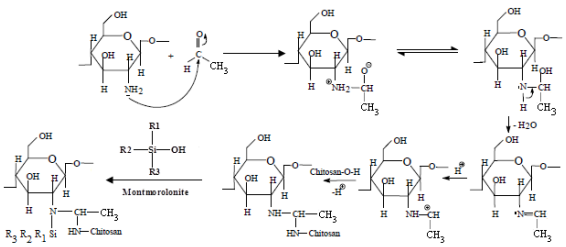

Fig. 3. Mechanism of hydrogel preparation.

Spectral properties of Nano composite hydrogel

The spectrum of chitosan (figure 4a), hydroxyl groups of chitosan shown as peak in 3430.1 cm^{-1} area

.corresponding to figure 4a, 1660.4 cm^{-1} is for the carbonyl group. hydrogel nanocomposite spectrum was shown 984cm^{-1} peak corresponding to the Si-N bond and 452cm^{-1}bending vibration peak is related to the Si-N bond.

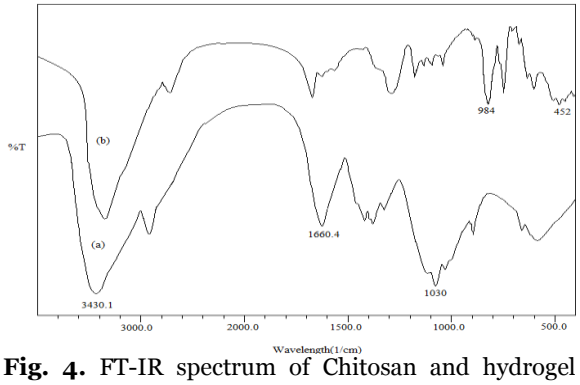

Fig. 4. FT-IR spectrum of Chitosan and hydrogel nanocomposite.

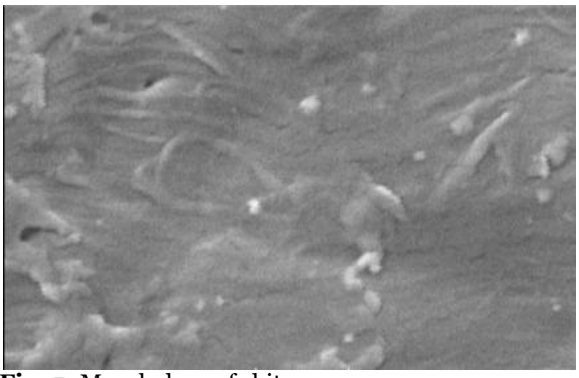

Fig. 5. Morphology of chitosan.

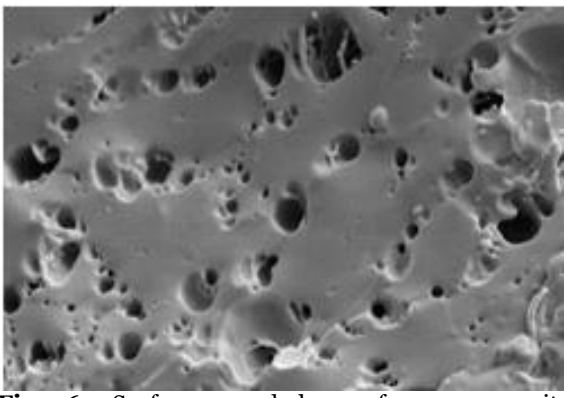

Fig. 6. Surface morphology of nanocomposite hydrogel.

Morphology of the synthesized nanocomposite hydrogel

Consideration of Surface morphology in SEM images (Figure 5, 6)), hydrogels has not any pores and hydogel nanocomposite have pores on surface.

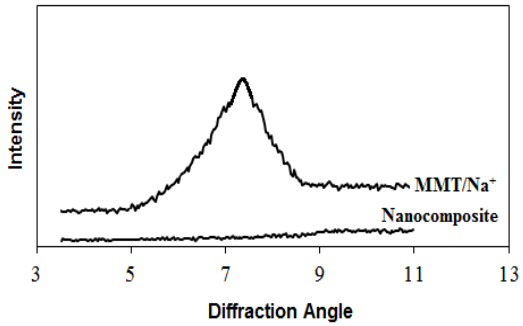

Fig. 7. XRD analyses of nanoclay and hydrogel/clay nanocomposites.

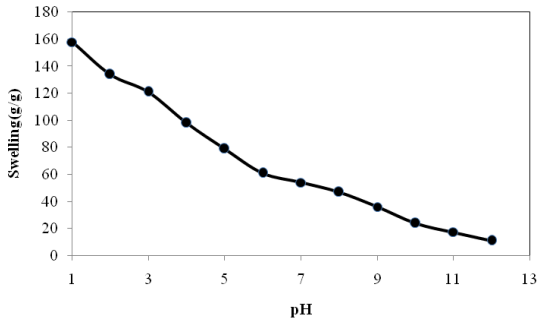

Fig. 8. Swelling behaviors of hydrogel nanocomposite.

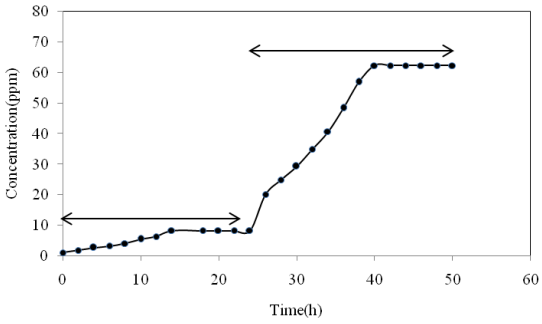

Fig. 9. Drug release at pH 1 and 7.4.

Results of X-ray diffraction spectra

In Figure 7, XRD analyses of nanoclay and hydrogel/clay nanocomposites are compared. Further phase analysis of the clay was not quantified. Corresponding intergallery distances between the clay layers were calculated by the Bragg equation:

$2d \sin \theta = n\lambda$

X-ray diffraction curves of nanocomposite shown completly removal of the peak and still nanoclay rational distribution of hydrogels nanocomposite and uniform shape. The distance between layers of the hydrogels nanocomposite shown the van der Waals

forces between the layers of montmorillonite and hydrogels structure is formed (Chen JF. *et al.*2004).

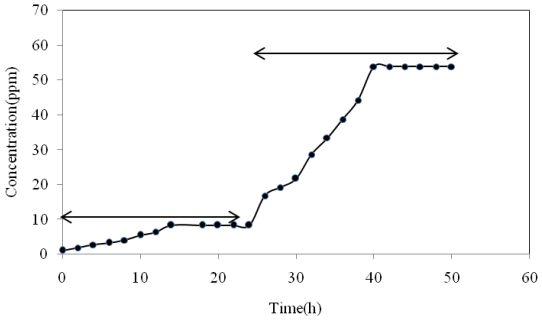

Fig. 10. Drug release at pH 2 and 7.4.

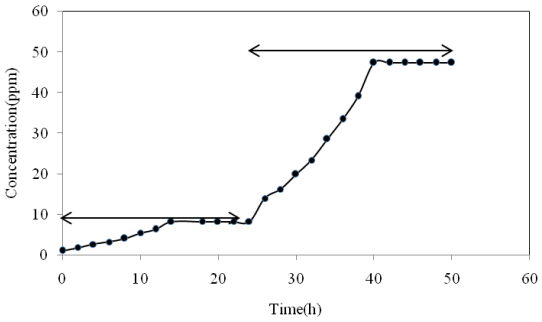

Fig. 11. Drug release at pH 3 and 7.4.

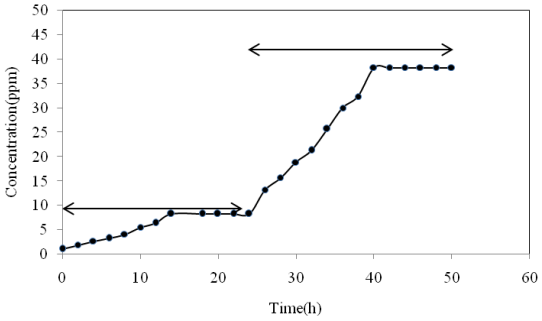

Fig. 12. Drug release at pH 4 and 7.4.

pH response characteristics

To investigate the swelling behavior at various pH levels, the hydrogel nanocomposite samples were swollen in several buffer solutions of pH 1 to 12 at room temperature. Figure 8 shown the swelling behaviors of hydrogel nanocomposite with dependent to pH. The hydrogel nanocomposite shown a lower specific solution content at basic pH as compared with acidic pH. Since high concentration of charged ionic groups in the hydrogel increases swelling due to osmosis and charge repulsion. Thus, swelling decreases when the degree of ionization of hydrogel decreases. At pH 2–4, unreacted amino groups of chitosan ionized in an acid, the ammonium ion. The ammonium ion would be attached to the hydrogels by ionic bonds. Therefore, the weight of the hydrogels increased in acidic buffer. At high pH (pH 7–10), pH sensitive behavior is typical of ionic hydrogels. Therefore, on the basis of observations, it can be said that only greater number of unreacted amino groups are not necessary criteria for highest total water content; degree of crosslinking is also an essential parameter for highest total water content at different pH levels (Bardajee GR. *et al.* 2011).

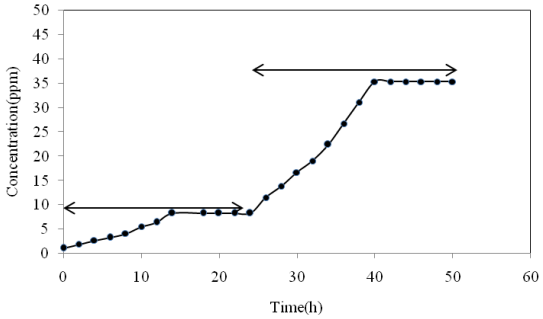

Fig. 13. Drug release at pH 5 and 7.4.

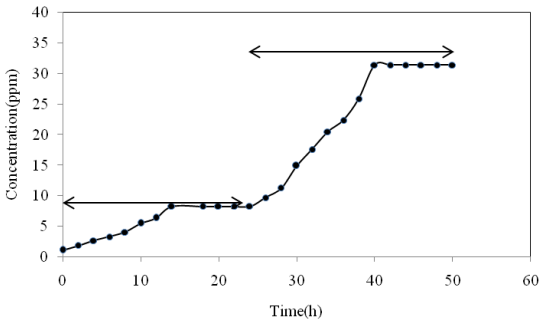

Fig. 14. Drug release at pH 6 and 7.4.

Release of drug from the hydrogel nanocomposite

Figures 9 to 14, UV spectrum drug release of cisplatin are observed. The rate of drug release from the hydrogel nanocomposite in water is directly related to the rate of inflation. The amount of loaded drug hydrogel nanocomposite increases, because the inflation rate is great in hydrogels nanocomposite when this drug is water .The rate of drug release was calculated from the relationship.

Conclusions

Hydrogel nanocomposite based on chitosan was prepared by from polymerization of acetaldehyde in

the presence of montmorillonite. Surface morphology of chitosan and hydrogels nanocomposite are indicated it. The hydrogel nanocomposite with different water absorption at different pH showed that water absorption rate in acidic medium is higher. Increase the infiltration rate into the hydrogel nanocomposite network increase of drug release rate.

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Reference

Aryal S, Hu CMJ, Zhang L. 2010. Polymer--cisplatin conjugate nanoparticles for acid-responsive drug delivery. ACS Nano **4,** 251-8. http://dx.doi.org/10.1021/nn9014032

Bardajee GR, Pourjavadi A, Ghavami S, Soleyman R, Jafarpour F. 2011. UV-prepared salep-based nanoporous hydrogel for controlled release of tetracycline hydrochloride in colon. Journal of Photochemistry and Photobiology B: Biology **102,** 232-40. http://dx.doi.org/10.1016/j.jphotobiol.2010.12.008

Chen JF, Ding HM, Wang JX, Shao L. 2004.Preparation and characterization of porous hollow silica nanoparticles for drug delivery application. Biomaterials **25,** 723–72. http://dx.doi.org/10.1016/S0142-9612(03)00566-0

Hosseinzadeh H, Pourjavadi A, Zohuriaan-Mehr MJ. 2004. Modified Carrageenans 2. Synthesis of a novel smart superabsorbent hydrogel with low salt sensitivity. Journal of Biomaterial Science Polymer Edition **15,** 1499-1511.

Kabiri K, Mirzadeh H, Zohuriaan-Mehr JM. 2010.Chitosan modified MMT-poly(AMPS) nanocomposite hydrogel: Heating effect on swelling and rheological behavior.Journal of Applied Polymer Science **116,** 2548–2556. http://dx.doi.org/10.1002/app.31727

Li ZZ, Wen LX, Shao L, Chen JF. 2004.Fabrication of porous hollow silica nanoparticles and their application in drug release control. Journal of Controlled Release **98,** 245–254. http://dx.doi.org/10.1016/j.jconrel.2004.04.019

Mahkam M, Allahverdipoor M. 2004. Controlled release of biomolecules from pH-sensitive network polymers prepared by radiation polymerization.Drug Targeting **12,** 151–156. http://dx.doi.org/10.1080/10611860410001688009

Sadeghi M, Hosseinzadeh H. *2008*. Synthesis of Starch–Poly(Sodium Acrylate-co-Acrylamide) Superabsorbent Hydrogel with Salt and pH-Responsiveness Properties as a Drug Delivery System. Journal of Bioactive and Compatible. Polymers **381,** 23. http://dx.doi.org/10.1177/0883911508093504

Salonen J, Laitinen L, Kaukonen AM, Tuura J, Björkqvist M, Heikkilä T, Vähä-Heikkilä K, Hirvonen J, Lehto VP. 2005. Mesoporous silicon microparticles for oral drug delivery: loading and release of five model drugs.Journal of Control Release **108,** 362-74. http://dx.doi.org/10.1016/j.jconrel.2005.08.017

Slowing II, Vivero-Escoto JL, Wu CW, Lin VS. 2008. Mesoporous silica nanoparticles as controlled release drug delivery and gene transfection carriers**.**Advanced Drug Delivery Reveiw **60,** 1278-88. http://dx.doi.org/10.1016/j.addr.2008.03.012

Song SW, Hidajat K, Kawi S. 2005.Functionalized SBA-15 materials as carriers for controlled drug delivery: influence of surface properties on matrix-drug interactions. Langmuir **21,** 9568-75. http://dx.doi.org/10.1021/la051167e

Wagstaff AJ, Brown SD, Holden MR, Craig GE, Plumb JA, Brown RE, Schreiter N, Chrzanowski W, Wheate NJ. 2012. Cisplatin

drug delivery using gold-coated iron oxide nanoparticles for enhanced tumour targeting with external magnetic fields. Inorganica Chimica Acta **393**, 328–333.
http://dx.doi.org/10.1016/j.ica.2012.05.012

Wu JH, Lin JM, Zhou M, Wei CR. *2000.*Synthesis and properties of starch-graft-polyacrylamide/clay superabsorbent composite. Macromolecular Rapid Communications **21,** 1032.
http://dx.doi.org/10.1002/1521-3927(20001001)21:1

Weian Z, Wei L, Yue'e F. 2005. Synthesis and properties of a novel hydrogel nanocomposites. Material Letters **59,** 287.
http://dx.doi.org/10.1016/j.matlet.2005.04.033

Zhou C, Wu Q. 2011. A novel polyacrylamide nanocomposite hydrogel reinforced with natural chitosan nanofibers. Colloids Surface B Biointerfaces **84,** 155-62.
http://dx.doi.org/10.1016/j.colsurfb.2010.12.030