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Preparation and characterization of chitosan-based hydrogel for drug delivery of 5-Fluro uracile

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Abstract

In this paper, we reported the synthesis and behavior of chitosan based hydrogel and controlled drug delivery by hydrogel in different pH. The chitosan based hydrogel was synthesized via bonding of acetaldehyde monomer on chitosan .the mechanism of hydrogel formation confirmed by FT-IR, SEM, and XRD. The hydrogel absorbtion rate was studied in pH 1-12. Loading of 5-Fluro uracile drug, loaded rate and drug delivery percent have been done in buffer solutions of pH 1 to 12.

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Introduction

Hydrogels are superabsorbent polymers that can absorb and retain extremely large amounts of a liquid relative to their own mass(Hoffman, A. S. 2002).There are biomaterials that consist of a water-swollen network of crosslinked polymer chains (Kabiri, K. 2003). Hydrogels can be synthesized from chains of natural polymers such as collagen or alginate or from synthetic polymers such as poly(vinyl alcohol) (PVA) or polyacrylic acid (Anseth KS, and *et al* 1996).various hydrogels was studied in application based on structure such as thermal sensitive(Jian H.,2006) pH-sensetive (Richter A. and *et al*, 2008), magnetic (Giani G. and *et al*, 2012) and *et al*. Hydrogel system is applicable to the sustained drug release in different medium for specific structure (Kabiri, K. 2003). In the traditional delivery system there are not control time, drug release rate and delivery location (Bhattarai , 2010). then, drug concentration in blood was different and it maybe causes less effective and more side effects.drug delivery system with controlled release will be able to determine the time and location of drug release (Bhattarai N. , 2010) .Some drugs have an optimum concentration range that in this point efficiency maximum was obtained. In this area, concentrations are toxic or have not therapeutic effects (Vashist A. and *et al*, 2014). In addition, success for remedy of difficult diseases such as cancer should need to drug release in targeted media (Kumaresh S. 2001). For obtained to this purpose, the studies were done control of pharmacokinetics, Pharmacodynamics, nonspecific toxicity, immunogenetics and efficiency of drugs is carried out(Peppas, N. A.,1986) pH-sensitive hydrogels are known as novel controlled drug delivery system that when chitosan based hydrogel was synthesized with pH-sensitive for characterization of drug delivery in variey pH(Sunil A.2004).

Material and methods

Chitosan (Mw=22742) was purchased from Fluka company. Acetaldehyde (50%wt) from Merck company and acetic acid was supplied by mojallali company.5-flurouracil was purchased from sobhan company.

Preparation of hydrogel

0.1 gr chitosan was dispersant in 20 ml distillated water contain 2% acetic acid

0.2 and allowed to dissolved for 15 min under stirring in 100 ml flask.

0.3 then, 0.3ml acetaldehyde was added to this solution. After 15 min, cross- linking gel completely formed. For dehydaration, gel added to 200 ml ethanol for 2 h.then, hydrogel was dried in oven(50).

pH sensitivity characterization of hydrogel

pH-sensetive was studied by swelling rate of hydrogel in different buffer solutions(pH=1-12).for this purpose, after preparation of different buffer solutions, 0.1 gr hydrogel was added to buffer solution in 200 ml beaker and measure swelling rate.

Drug loading in hydrogel

Drug solution with 0.320mole concentration was prepared by 10.0 ml 5-flurouracil drug in 50.0 ml distillated water. Then, to other beaker containing 0.5 gr hydrogel in 100 ml distillated water, was added drug solution and hold in constant temperature for some day until absorbed by hydrogel. After filtration, hydrogel was washed with distillated water.the hydrogel was dried in oven (40).total loaded drug was measured via UV-Visible in filtration solution.

Concentration measurement

Concentration measurement was done by UV-Visible spectroscopy. Standard curve was prepared and by it sample concentration was determined.

Controlled release of drug test

2.0 gr of the hydrogel into beaker containing 80 ml buffer solution with the pH on the water bath (37^{o}C) and stirring.with influence of the buffer solution into the hydrogel and swelling , loaded drug is released to time and increases the drug concentration in the buffer solution. Measuring of drug concentration was done in the buffer solution during its release. After increase of time, with absorbent rate measurement (UV-Visible) in every time could determine drug concentration in buffer solutions, This is done to measurement of the release of the drug in different

pH .

Results and discussion

Mechanism of hydrogel synthesis, spectral properties of hydrogels

the proposed mechanism for the synthesis of hydrogel such as in figure **1**.in step1,cationic polymerization condition was obtained via dissolving of chitosan in acidic medium. Amino group of chitosan monomer attracted to carbonyl group. Then, the N=C group was obtained that preparation in reaction to other chitosan.

Table 1. Graph of the swelling rate in pH (buffer solutions).

pH	1	2	3	4	5	6	7	8	9	10	11	12
ES(g/g)	112	102.5	96	84	69	54.8	48	34	22.8	15.6	10.9	6

Table 2. Drug release data in various pH.

pH	1	2	3	4	5	6	7	8	9
concentrate(ppm)	726.5	629	531.5	518.5	313.5	302.5	279	257.5	204
Percent release	84.97	73.56	62.16	60.64	36.66	35.38	32.63	30.11	23.86

In order to confirm the chemical structure, in the FT-IR spectrum of chitosan, 3429 cm^{-1} corresponding to hydroxyl groups that represent. 1656 Cm^{-1} to the carbonyl group of chitosan can be confirmed (Figure 2). FT-IR spectra of chitosan-based hydrogels showed. The hydrogel is synthesized by the reaction of between the amino groups of chitosan and carbonyl group. N-H, aliphatics C-H and C-N were presented in figure 3.

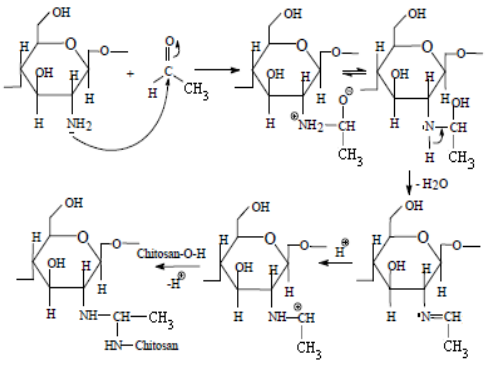

Fig. 1. Proposed mechanism for the synthesis of hydrogel.

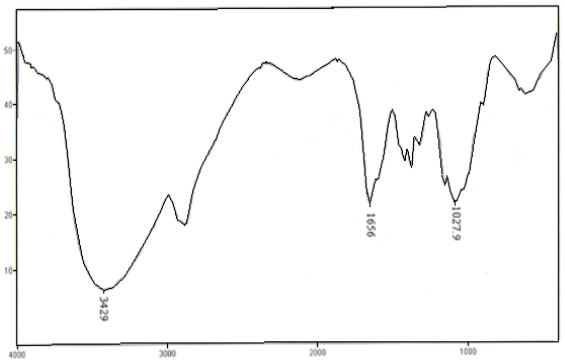

Fig. 2. FT-IR spectra of chitosan.

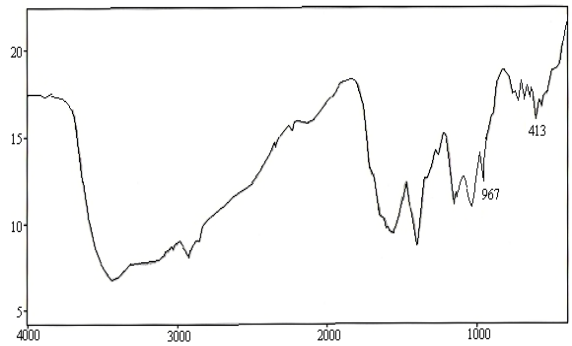

Fig. 3. FT-IR spectra of hydrogel.

Surface morphologhy of hydrogel

Figure 4 SEM photograph was shown chitsan along has not any porous in microscopy structure but Polymeric network in chitosan based hydrogel was created various porous in structure (figure5). With loading of drug in hydrogel, all of porous was replaced (figure 6).

Characterization of pH sensitive in hydrogel

Study of pH-sensetive in hydrogel was done based on swelling rate in various pH.swelling rate maximum was obtained in pH=1.swelling rate is dependence to medium pH. High concentration of ions was increased swelling rate because of repulsion of ions in hydrogel.

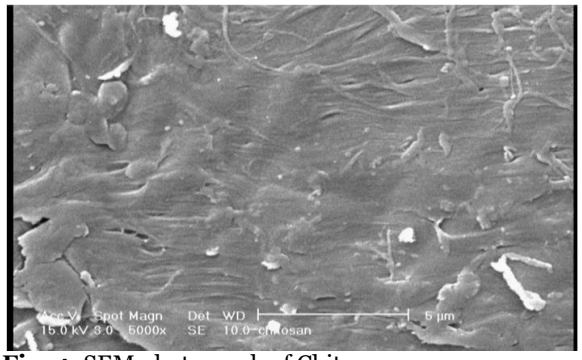

Fig. 4. SEM photograph of Chitosan.

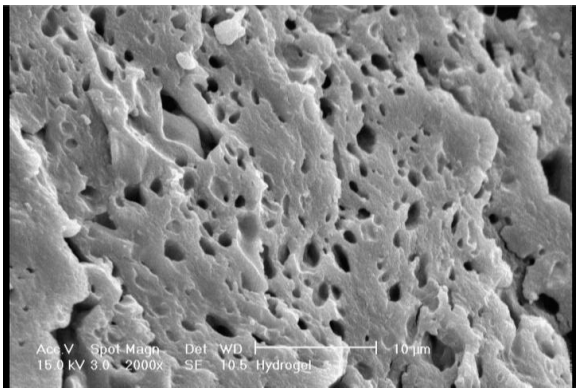

Fig. 5. SEM photograph of chitosan based hydrogel.

Table 1. swelling rate determination in the buffer solutions.

Drug release in the hydrogel

The rate of drug release from the hydrogel network in water is directly related to the rate of inflation**.** The amount of loaded drug in hydrogel was increased. The rate of drug release was calculated from the following relationship. In this equation, L and R_t represent respectively the initial amount of drug loading and drug release at t time is found.The

$$\text{percentage drug release} = \frac{R_t}{L} \times 100$$

Time was need drug release in different pH. The initial concentration of the drug and the concentration of the loaded drug filter are obtained from the following formula:

Concentration of drug loading =concentration below the filter - the initial drug concentration**.** 175mmole=0.145 mmole– 0.320 mmole the initial concentration of the drug was 0.320 mmole, concentration below the filter 0.145mmole, to calculate the amount of drug 0.175mmole, the amount of release drug at pH =1 is 0.149mmole and percentage of drug delivery 85.14% [7-13].

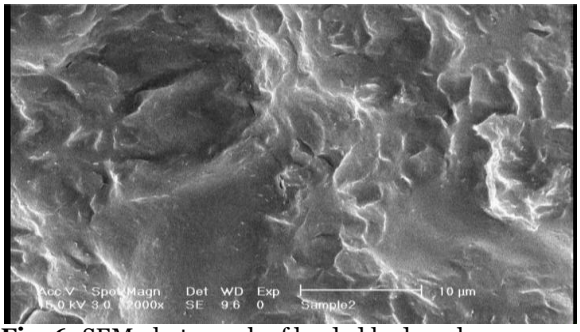

Fig. 6. SEM photogragh of loaded hydrogels.

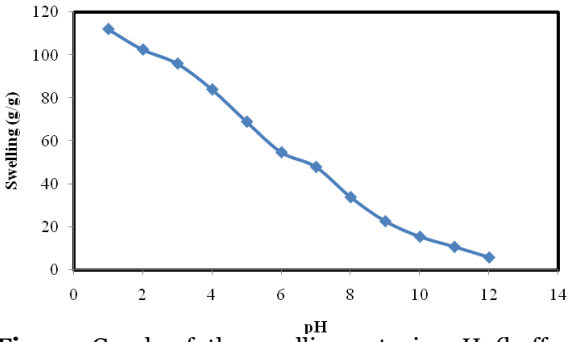

Fig. 7. Graph of the swelling rate in pH (buffer solutions).

Hydrogel swelling behavior is depended on the environment pH that hydrogels was absorbed water and release maximum amount. This hydrogel could use in remedy of cancer cells with targeted drug delivery system. So that drug release at specific sites of the body (acidic pH of cancer cells).

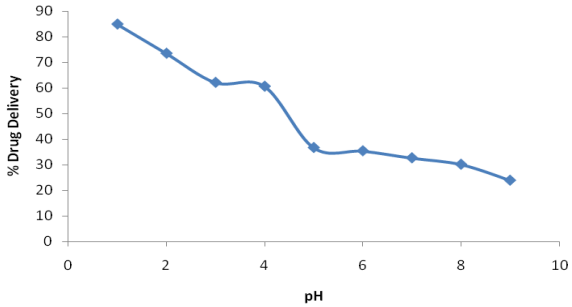

Fig. 8. Graph of drug release at various pHs.

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