Swelling Behavior and Drug Release of Interpenetrating Network Composed of PVA and Chitosan

Fathel S. Matty
Zainab M. MohiALDeen
Dept. of Chemistry/College of Education for Pure Science (Ibn-AL Haitham)/University of Baghdad
zainabmohy.zm@gmail.com
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Abstract

PVA and chitosan biodegradable, non-toxic, biocompatible polymers convenient for use in drug release.

In this study polyvinyl alcohol (PVA) and chitosan (CS) hydrogels crosslinked with glutaraldehyde (GA) with different ratio morphology and structure characterization interpenetrating polymer network (IPN). They were investigated by Fourier transmission infrared spectroscopy (FTIR), scanning electron microscope (SEM), UV-Visible spectrophotometer, swelling of hydrogel and drug release were studied by changing crosslinking ratio and PH.

Keywords: swelling, poly vinyl alcohol, chitosan, interpenetrating network, hydrogels, mebeverine hydrochloride.

Introduction

Hydrogel is a hydrophilic polymer network that can swell and also retain large amounts of water with its porous structure in the result of this, the area of hydrogel research has expanded in the last years, so they performed well for different biomedical applications [1].

Recent advances application of hydrogels intended to achieve the fabrication of artificial organs, in specific drugs delivery and in a precise way to make wear contact lenses [2].

Hydrogels become swollen because they have the ability to absorb water, about 10-20 times of its specific weight [3]. The presence of hydrophilic groups such as (–COOH, -OH, -$CONH_2$, -CONH, -SO_3H) …etc. in polymers hydrogel structure gives hydrogels affinity to absorb large amount of water [4].

The space inside the hydrogels network that is available to accommodate water can be made use to determine the capacity of hydrogel swelling [5].

The water that polymer hydrogels absorbed is dependent on numerous factors like network parameters, hydrogels structure (porous or poreless), nature of solution, and drying techniques [6].

Chemical crosslinking is the best method to generate remaining unchanged hydrogel networks by synthesizing covalent bonding between different polymer chains [7].

Hydrogels based on chitosan and polyvinyl alcohol have many pharmaceutical and biomedical applications in drug delivery system. Many efforts and large studies were made to synthesize the CS/PVA hydrogels and their controlled drug delivery system was extensively studied by research workers [8].

In this study, hydrogel films were prepared by crosslinking of PVA\Chitosan blended by Glutaraldehyde with varying amounts. The FTIR, SEM, Swelling and Mebeverine hydrochloride as drug delivery properties of these films were investigated.

Experimental

Materials

PVAsamples was purchased from Aldrich Co. (with 98%, M.wt=7200. Chitosan from HIMEDIA Purity 99% Mn =5000. Glutaraldehyde from CDH purity 99%, Hydrochloric acid from CDH Purity 35-38%, and Sodium acetate from CDH Purity 99%.

Synthesis of IPN Chitosan\PVA Hyrdogel with GA

The hydrogel films were prepared by solvent casting method, the formation of chitosan-PVA interpenetrating pH-sensitive hydrogel is due to the reaction between amino groups of chitosan, the PVA polymer and aldehyde groups of the glutaraldehyde as a crosslinker. Different weights of PVA shown in tables (1.1) were dissolved in hot ionized water at (80 °C).

This solution was mixed in a (50 ml) beaker at room temperature, with (2% glacial acetic acid) and five different percentages of glutaraldehyde (see table (1.1)) were incorporated as crosslinking material. The reaction mixture was stirred magnetically for 30 mints, and then the cross linked polymer was formed. The reaction mixture was transferred into glass rectangular container that used for casting a IPN polymer shape with dimension 17 ×8 × 0.5 cm^3 height made, left at room temperature for 3 days, for dryness, and then a thin film was formed. This was dried at 40 °C for 3 h by using thermal oven [9].

Drug (MVH) release in the IPN Hydrogel

Different weights of PVA as shown in tables (1.2) were dissolved in hot ionized water at (80 °C), this solution was mixed in (50 ml) beaker after cooling to room temperature, chitosan with (2% glacial acetic acid), and add (0.14 wt\wt%) of (MVH) as drug five different

percentages of glutaraldehyde like the tables (1) and (2) were incorporated as crosslinking material. The reaction mixture was stirred magnetically for 30 mints, and then the cross linked polymer was formed. The reaction mixture was transferred into glass rectangular container that used for casting a IPN polymer shape with dimension 17 ×8 × 0.5 cm^3 height made, left at room temperature for 3 days, for dryness, and then a thin film was formed. This was dried at 40 °C for 3 h by using thermal oven, then left in water bath (37°C) and calculate the drug release in UV-Visible spectrophotometer each 10 min [9].

Table (1) experience 1

No. of sample	CS (wt\wt)	PVA (wt\wt)	GA (v\v)
1.	1.84%	0.14%	0.22%
2.	1.84%	0.14%	0.44%
3.	1.84%	0.14%	0.66%
4.	1.84%	0.14%	0.88%
5.	1.84%	0.14%	1.1%

Table (2) experience 2

No. ofsample	CS (wt\wt)	PVA (wt\wt)	GA (V\V)	MVH (wt\wt)
1.	1.84%	0.14%	0.22%	0.14%
2.	1.84%	0.14%	0.44%	0.14%
3.	1.84%	0.14%	0.66%	0.14%
4.	1.84%	0.14%	0.88%	0.14%
5.	1.84%	0.14%	1.1%	0.14%

Swelling

The swelling ratio determined (Rs) was determined by dried hydrogel pieces, by treating the hydrogel 0.1 g in 100 ml of a range of pH (1.2, 4.7,6.8) and was permitted to soak for 60 min at 37 °C. The hydrogel samples were collected by filtration after 10 min. The (Rs) is calculated from equation (1):

$$\mathbf{Rs\%} = \frac{\mathbf{ws-wd}}{\mathbf{wd}} \mathbf{\ x\ 100}\ldots\ldots\ldots\mathbf{(1)}$$

Ws=The weight of swollen IPN polymer.
Wd=The weight of dry IPN polymer.

Calibration Curve of mebeverine hydrochloride

UV-Vis spectroscopy of mebeverine hydrochloride was obtained using 1 cm width quartz curette. The λ max that related to the maximum absorbance of mebeverine hydrochloride was observed at 221nm [10].

In order to estimate the drug concentration during the drug release studies calibration curve for mebeverine hydrochloride was construed from the absorbance data.

Results and Discussion

In our study, IPN hydrogels was synthesized which consisted of PVA, chitosan, glutaraldehyde as crosslinker as shown in figures (1) and (2) below. The reactions between amino groups of chitosan, the PVA polymer and the aldehyde groups of glutaraldehyde as crosslinker [11,12], with different amounts. The FTIR, SEM, Swelling and Mebeverine hydrochloride as drug delivery properties of these films were characterized.

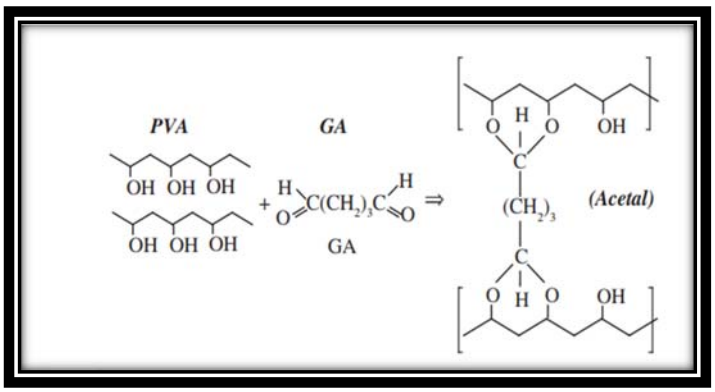

Figure (1): Crosslinking reaction between PVA and glutaraldehyde.

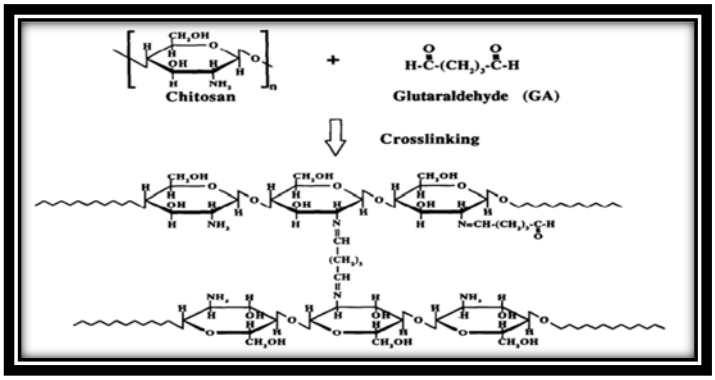

Figure (2): Crosslinking reaction between chitosan and glutaraldehyde.

Characterization of PVA and chitosan IPN by FTIR

Figures (3) and (4) and (5) show the FITR spectra of chitosan, PVA, chitosan-PVA IPN, the spectrum of pure chitosan figure (3) shows a strong absorption band in the range (3410-3117) cm-¹ correspond to combined peaks of OH, intermolecular hydrogen bonding and N-H stretching band. The (C-H) stretching vibration of the polymer beak bone in manifested through strong peak of 2920 – 2878 cm-¹ [13].

The bands at 1639 cm-¹ and 1601 cm-¹ were due to c=o stretching of secondary band caused by partial de acetylation of chitin and N-H bending of the primary amino group (NH2) respectively [14].

Absorption band at 1096 cm-¹ was assigned to the stretching band of C-O-C Bridge.

FTIR spectrum of pure PVA sample figure (4) shows the (C-H) board alkyl baud in the range (2943-2855 cm^{-1}), -OH stretching (3383 – 3422 cm^{-1}) "intermolecular and intramalecular hydrogen bounding" due to high hydrophilic forces occur among PVA chains the baud at (1096 cm^{-1}) was assigned to the (C-O) stretching bound. This bound has been used an assessment tool of PVA structure because it in a semi – crystalline synthetic may form some domains depending on several process parameters [11].

FTIR spectrum of PVA\chitosan (IPN) figure (5) shows a strong band at 1095.57 cm^{1} of (C-O-C) group, due to the crosslinking of PVA with glutaraldehyde. Chemical crosslinking of chitosan with glutaraldehyde can be caused by the Schiff base formation as shown by the 1616 cm^{-1} band associated with the C=N group [15].

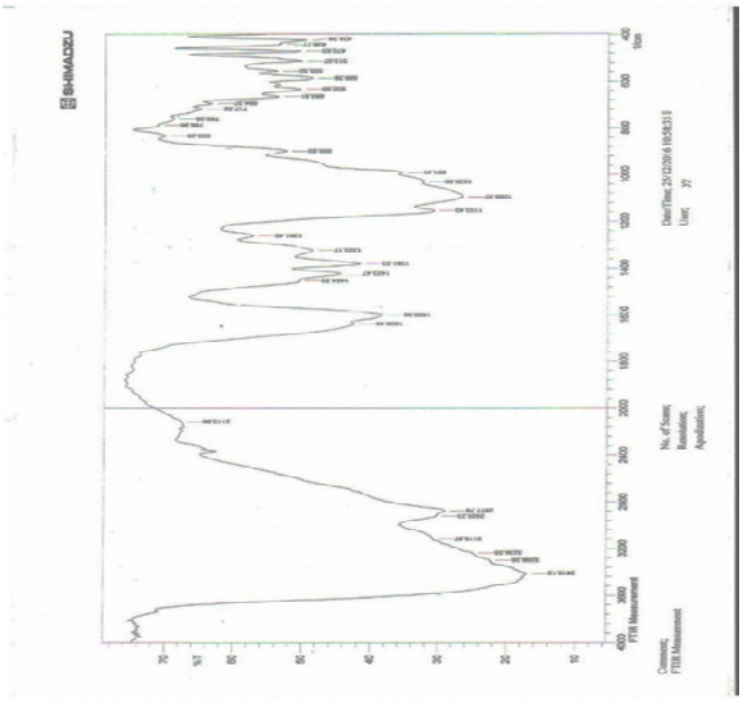

Figure (3): FTIR spectrum of pure chitosan.

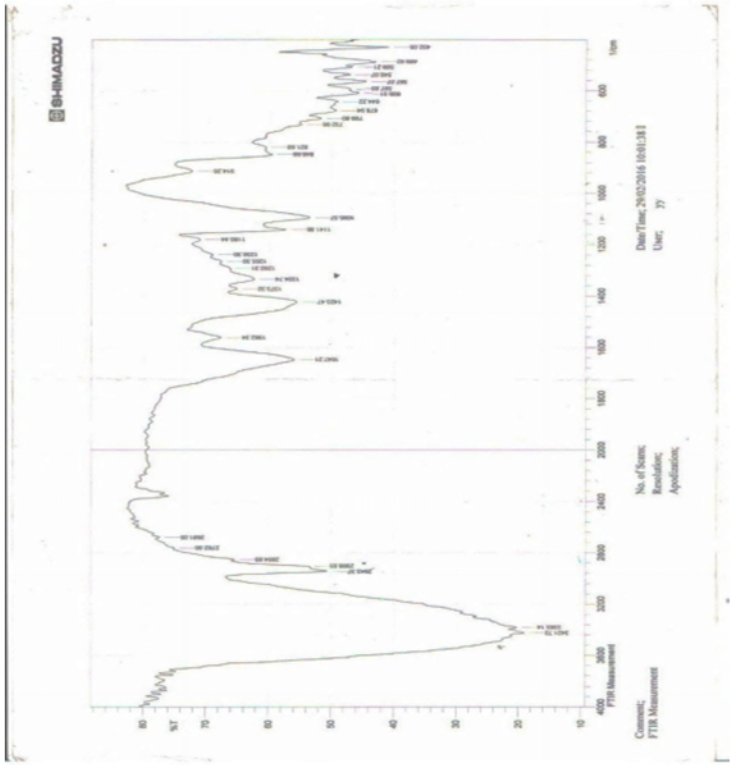

Figure (4): FTIR spectrum of pure PVA.

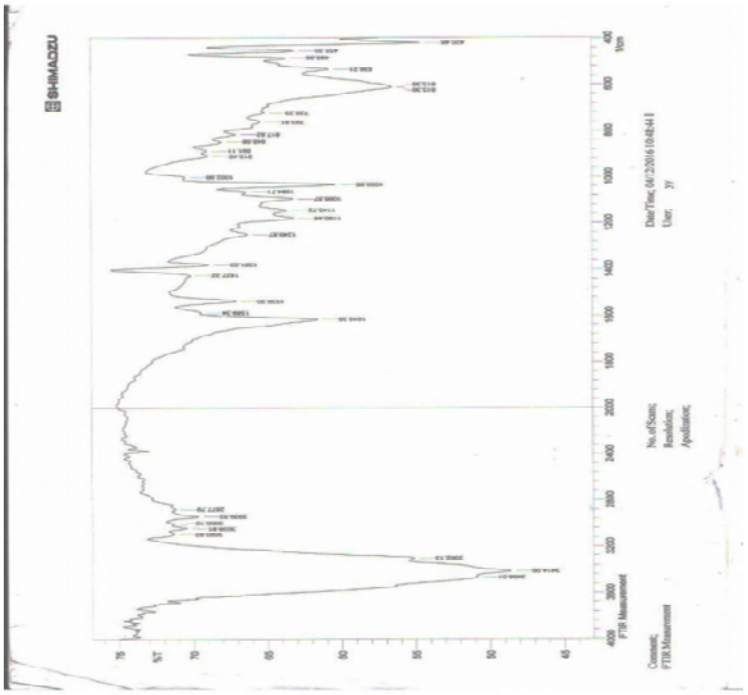

Figure (5): FTIR spectrum of chitosan – PVA IPN

Crosslinking ratio influence on the swelling IPN hydrogel

Crosslinking of hydrogel polymer is the method for reducing the molecular size of the polymer hydrogel for drug diffusion and drug release may be achieved by decrease in the value of swelling of hydrogel [16].

The swelling ratio of all samples in buffer solution of pH (1.2, 4.7 and 6.8) have shown an increase with time.

The behavior of swelling using various content of GA (0.22%, 0.44%, 0.66%, 0.88% and 1.1% v\v %) and with constant ratio of chitosan and PVA hydrogel within time indicated that the swelling ability of the hydrogel decreased with the increase of GA amount in hydrogel [17].

The swelling ratio attributed to ionizable functional groups. The concentration of GA had influence on the swelling ratio of hydrogel. The increase of crosslinking agent effect polymer network and which reduces the size of pores upon hydrogel formation [18].

pH influence on swelling IPN hydrogel

Figures (6-8) show pH sensitive characterize of IPN hydrogel.All hydrogels samples reached at equilibrium after (60) min, and the swelling test was performed under various pH values (1.2, 4.7 and 6.8).

The increase of pH of solution caused increase in the degree of swelling or amount of water content so at pH (6.8), so the highest swelling and that is mainly attributed to the presence of hydroxyl group in PVA and amino groups in a chitosan, correspondingly. In an environment with low density ionic and the pH is almost neutralizing, the equilibrium is derived to the direction, raising the internal osmotic pressure. When PH is increased from (1.2) to (6.8), an abrupt transition in swelling occurs, with the degree of swelling rising more.

The amount of swelling depended on ratio of GA at (37C°) with different time as shown in figures (3-6) in different pH.

As predictable, the equilibrium degree of the IPN swelling are in reverserelated to GA concentration from (0.22 to 1.1 v\v %), that means when the degree of crosslinking increase, the degree of swelling is decrease. Also when the equilibrium degree is becoming almost natural, so the degree of swelling decreases at all value of pH. The lower degree of swelling is due to the higher network density, which attributed to the network chains became less flexible and reduced the existing free volume pores between the polymer chains [19].

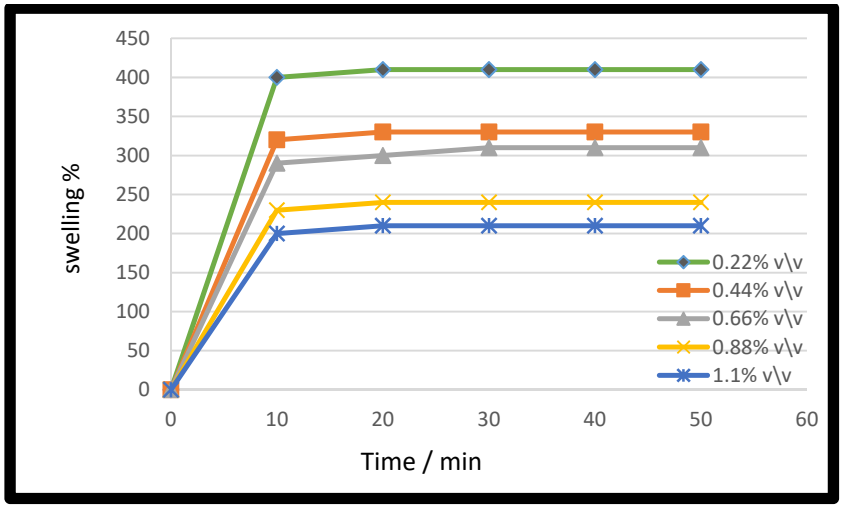

Figure (6): Influence with various ratios of (GA) on swelling for IPN hydrogel in (PH 6.8).

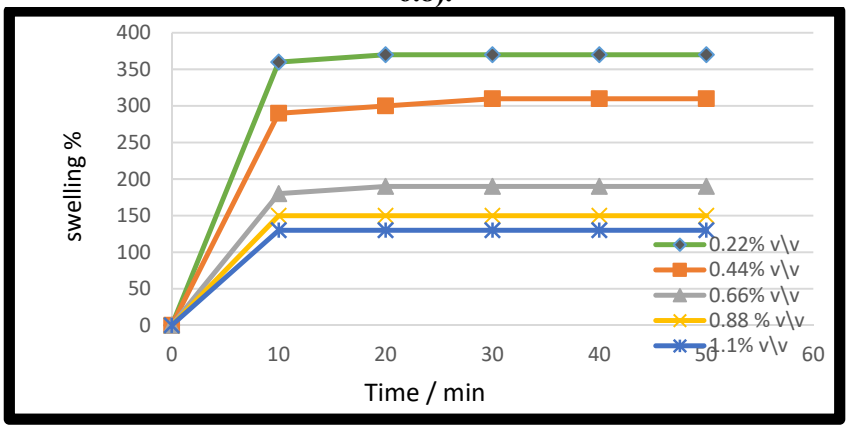

Figure (7): Influence with various ratios of (GA) on swelling for IPN hydrogel in (pH 4.7).

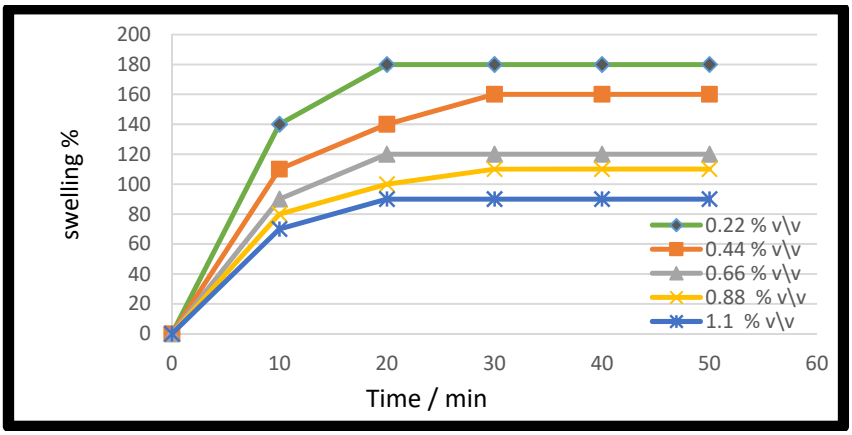

Figure (8): Influence with various ratios of (GA) on swelling for IPN hydrogel in (pH 1.2).

Influence of crosslinking ratio on (MVH) drug release

From figures (9-11), it is seen that a significant decrease in (mebeverine hydrochloride) release rate from PVA\chitosan IPN by increasing the GA% due to the increasing the cross-linking density.

Influence of PH on (MVH) drug release

With a view to examine the influence of PH on the mebeverine hydrochloride from hydrogels, figures (9-11) signalize that when the PH is increase from (pH 1.2 to pH 6.8) a significant increase in the accumulative release is detected for all IPN.

At PH 1.2, the release of drug decreases. This is due to the high acidity that resulted in hydrogen bended and the emigration of drug molecules become low [16]. Thus the (MVH) drug release depends on the PH of the mediaalso on the nature of IPN hydrogel matrix [20]. This suggests that the drugs in the blend can be used to be suitable for the basic environment of the large intestine, colon and rectal mucosa.

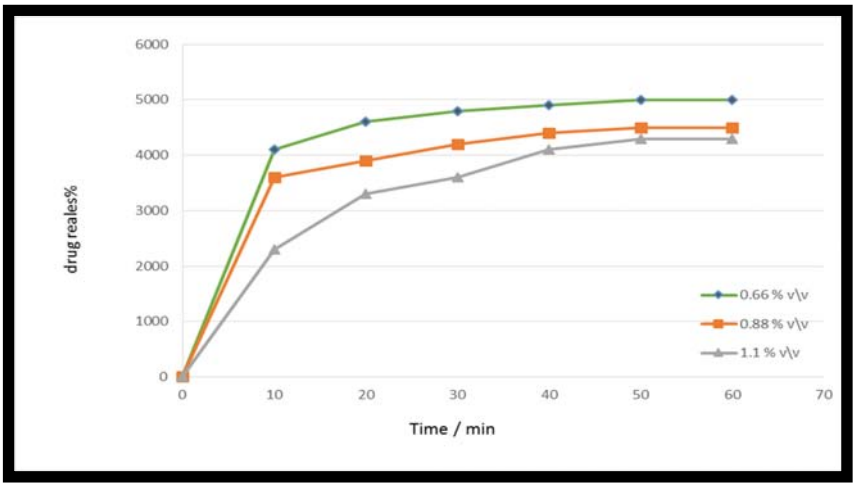

Figure (9): Release (MVH) for IPN hydrogels with different (GA)contentedat(pH6.8).

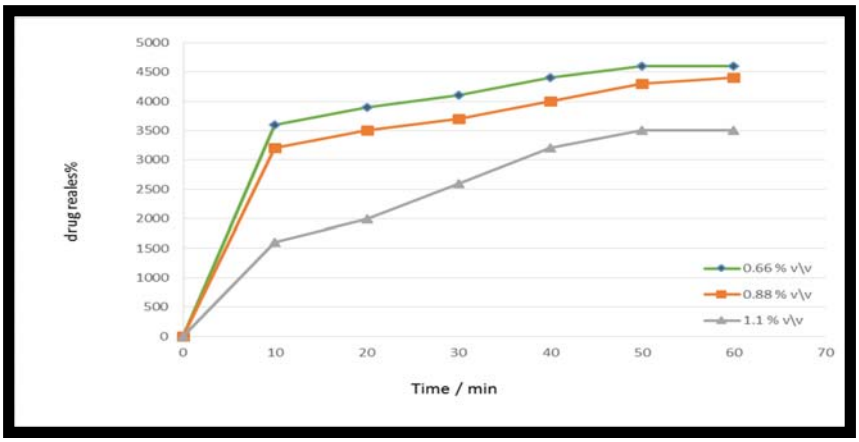

Figure (10): Release (MVH) forIPN hydrogels withdifferent (GA) contentedat(pH 4.7).

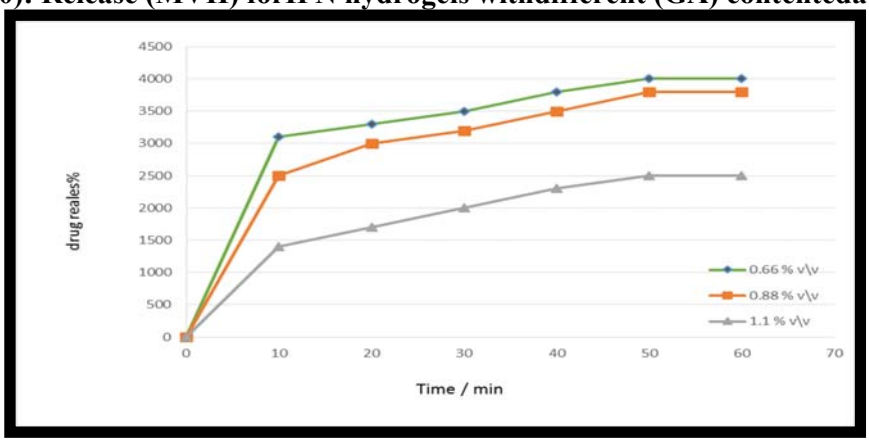

Figure (11): Release (MVH) for IPN hydrogels with different (GA) contented at (pH 1.2).

Scanning Electron Microscope (SEM) Analysis

As shown in figures (12-15), the Scanning Electron Microscope (SEM) of Angstrom advanced, AIS2300, USA IPN hydrogels was clear to naked eye. They show neither separation into two layers, the pore size is reduced. And the surface morphology ofPVA/CS IPN revealednon-porous translucent.

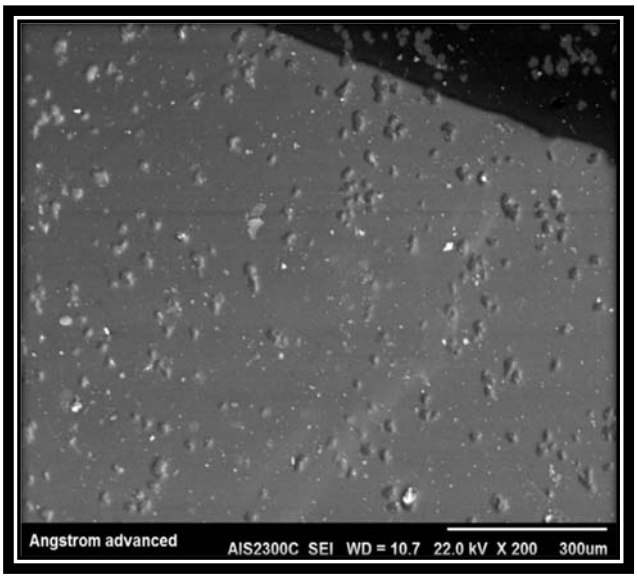

Figure (12): SEM spectrum of chitosan hydrogel.

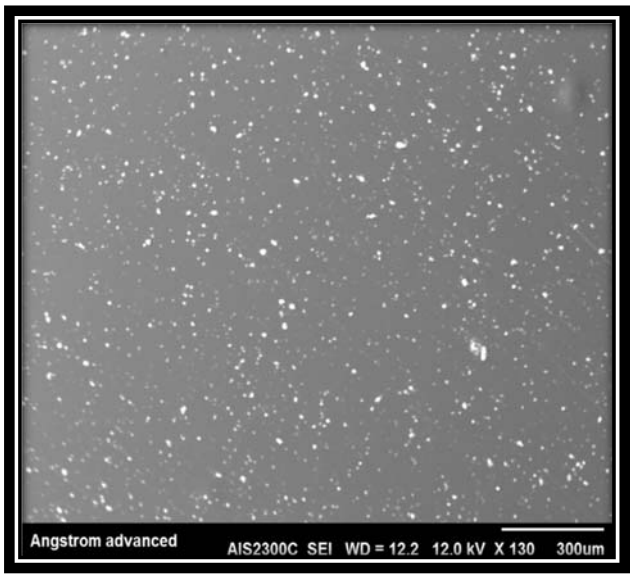

Figure (14): SEM spectrum of PVA and chitosan

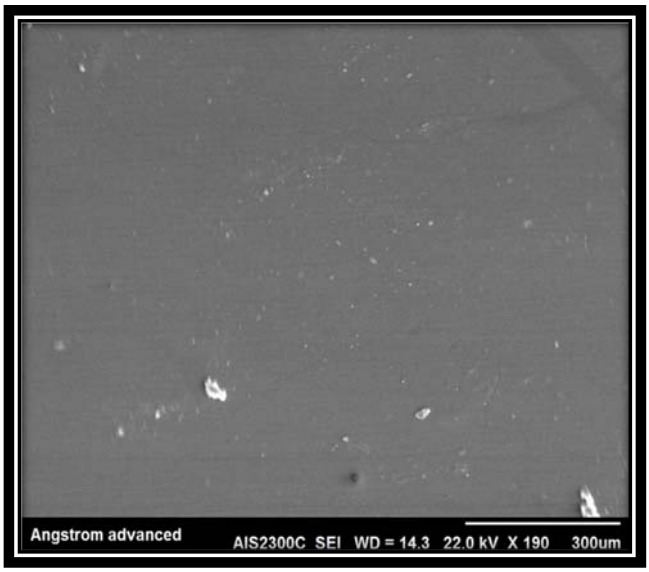

Figure (13): SEM spectrum of PVA hydrogel.

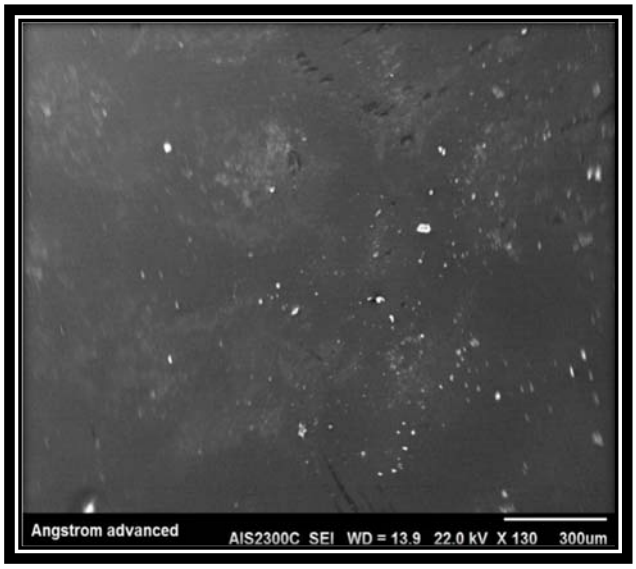

Figure (15): SEM spectrum of PVA and chitosan IPN hydrogel with MVH. IPN hydrogel with (MVH) as drug

Conclusion

1- Modification of PVA and chitosan film by crosslinking with different ratios (0.22%, 0.44%, 0.66%, 0.88% and 1.1% v\v %) GA.
2- FTIR spectroscopy indicates the formation of cross-links hydroxyl groups of PVA and functional group of crosslinking agents chemical crosslinking of chitosan with glutaraldehyde by formation of Schiff base with C=N group. The kind of crosslinking agent and the amount

of crosslinking are very important elements to determining both the drug release and pH – sensitive swelling behavior and.

3- The swelling of PVA/chitosan/GA and hydrogels can be well explained by fiction swelling equilibrium. affected by the density of crosslinking agent, it was found that the maximum swelling ratio was with lowest density of GA.
4- Concerning the type and ratio of crosslinking agent and pH effect on the release up (MVH) for these samples have high release rate drug, it was found that the higher release ratio for the high swelling hydrogel.

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