Republic of Iraq
Ministry of High Education and Scientific Research
Al-Qadisiya University
College of Pharmacy

Synthesis, Characterization, and Drug Release Study of Chemically Crosslinked pH-Sensitive Poly(acrylamide-Carboxymethyl cellulose)Hydrogels

A Research

Submitted to the college of pharmacy Al-Qadisiya University in partial Fulfillment of Requirements of B.Sc. Degree of Science in pharmaceutical

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بسم الله الرحمن الرحيم

(ن وَالْقَلَمِ وَمَا يَسْطُرُونَ 1 ۝ مَا أَنْتَ بِنِعْمَةِ رَبِّكَ بِمَجْنُونٍ 2 ۝ وَإِنَّ
لَكَ لَأَجْرًا غَيْرَ مَمْنُونٍ 3 ۝ وَإِنَّكَ لَعَلَى خُلُقٍ عَظِيمٍ 4 ۝ فَسَتُبْصِرُ
وَيُبْصِرُونَ 5 ۝ بِأَيِّيكُمُ الْمَفْتُونُ 6 ۝ إِنَّ رَبَّكَ هُوَ أَعْلَمُ بِمَنْ ضَلَّ
عَنْ سَبِيلِهِ وَهُوَ أَعْلَمُ بِالْمُهْتَدِينَ 7 ۝)

صدق الله العلي العظيم

سورة القلم الآية (1-7)

Dedication

To Al-Imam Al Mahdy

To my mother , my father

And All my family

To all the people who are

Sit in my heart.

Acknowledgments

Special thanks for the supervisor of my research Dr. (Nadhir Dhaman) and all who help me in my research

Abstract

This study is concerned with a significant of application chemistry in the field of physical and medical pharmacy. It deals with adsorption and desorption systems of drug (metformin hydrochloride) on surfaces poly(Acrylamide - Carboxymethyl cellulose) hydrogel at variable conditions of pH. The polymeric hydrogels was used as adsorbent for release metformin hydrochloride from aqueous solution. Adsorption experments were carried-out by using UV visible spectrophotometer. Hydrogel of poly (AAm-CMC) were prepared by free radical polymerization. The chemical structures of polymer hydrogels were analyzed by Fourier Transform Infrared spectrophotometer (FTIR).

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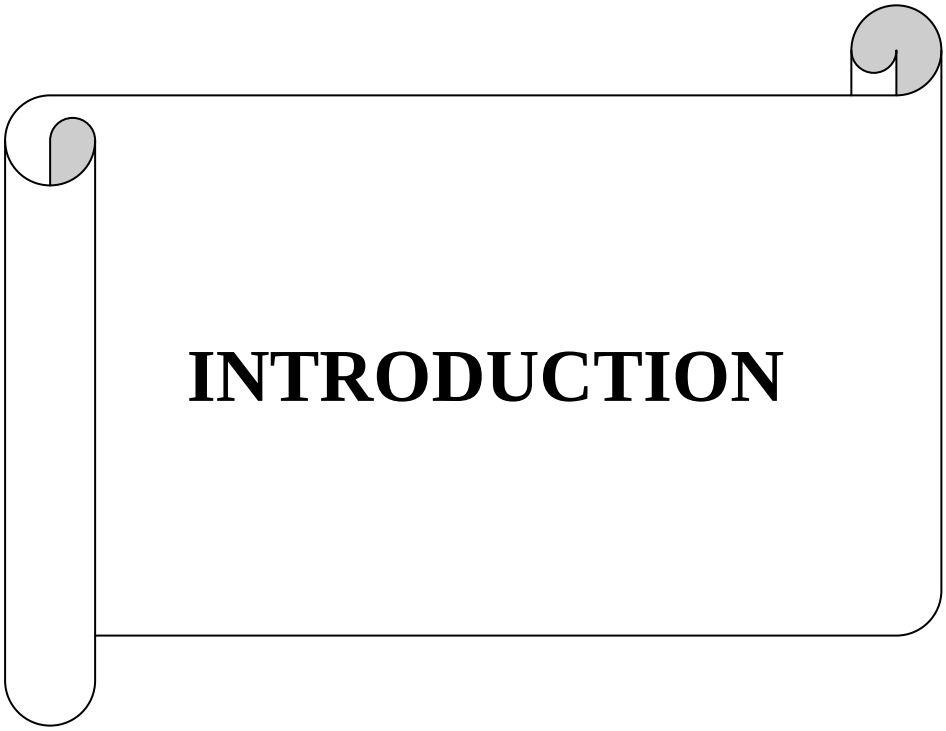


INTRODUCTION

CHAPTER ONE

INTRODUCTION

1.1General Introduction

The high water content and soft consistency, which are similar to natural tissue, give hydrogel great potential for biomedical and pharmaceutical applications. The high water content of it conduces to their biocompatibility. It cross linked structures composed of hydrophilic copolymer. They are capable to imbibing large amounts of water molecules or biological fluids in their pores of the network but are insoluble in aqueous media. Hydrogels studied for many applications in tissue regeneration, drug delivery, and in biological seeing for number of reasons [(1)]:

1-Hydrogel have highly tunable mechanical properties, for example elasticity can be tailored by modifying cross -link densities.

2-By using a range of well-established chemistries biological molecules can incorporated covalently into hydrogel structures.

3-Hydrogels can be designed to change properties (e.g. swelling/collapse or solution to gel transitions)in response to externally applied triggers, such as temperature, ionic strength, solvent polarity, electric magnetic field, light, or small(bio)molecules.

4-Hydrogels provide inert surfaces that prevent nonspecific adsorption of protein, a properties known as anti-fouling.

5-It provide suitable semi wet, three-dimensional environments for molecular-level biological interactions.

1.2 Hydrogels

Hydrogel have been used extensively in the development of the smart drug delivery system. A hydrogel is a cross-linked polymer network of flexible hydrophilic that are able to absorb solute molecules and water. Solute can diffuse through the hydrogel structure due to higher water content and porous structure network. After immersion in water, hydrogel 'hydrophilic polymer chains are insoluble in the aqueous phase because they are connected one to other by cross-links. As polymeric networks, both gel and hydrogel might be similar chemically ,but they are physically distinct. Their characteristic water-insoluble behavior is attributed to the presence of chemical or physical cross-links, which provide physical integrity and network structure[(2)].Fig(1.1) show the different behavior in an aqueous environment of both gel and hydrogel, showing different behaviors in an aqueous environment. Solid circles represent covalent cross-links and hollow circles represent virtual cross-links formed by entanglements [(3)].

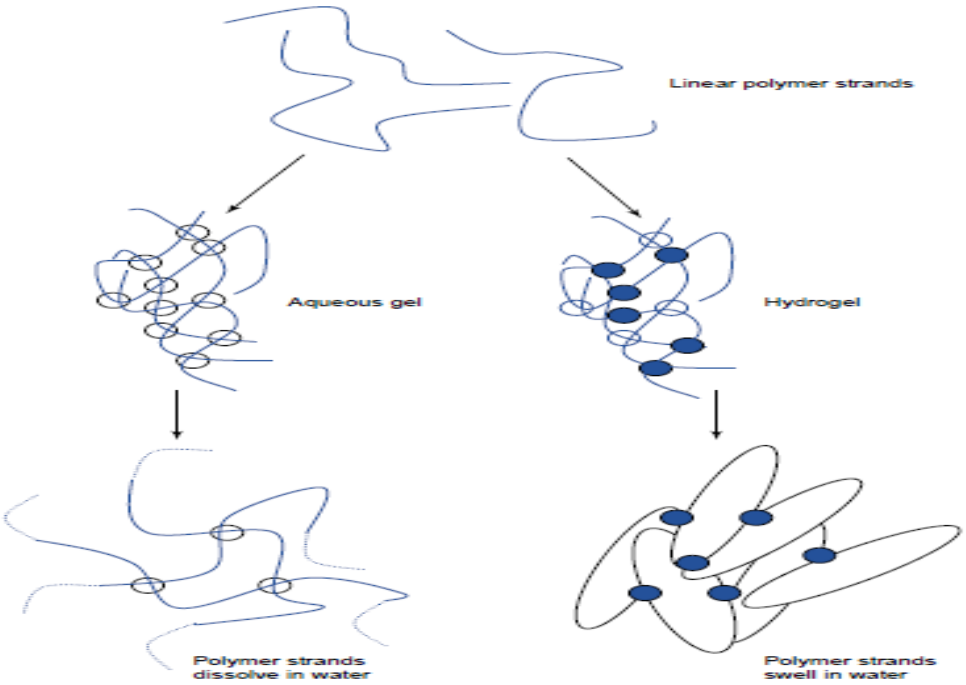


Fig (1.1)polymer strands forming a gel and a hydrogel

1.3 Classification of hydrogels

Hydrogels have been classified according to their physical properties, source, nature of swelling, method of preparation, and ionic charge as explained below:

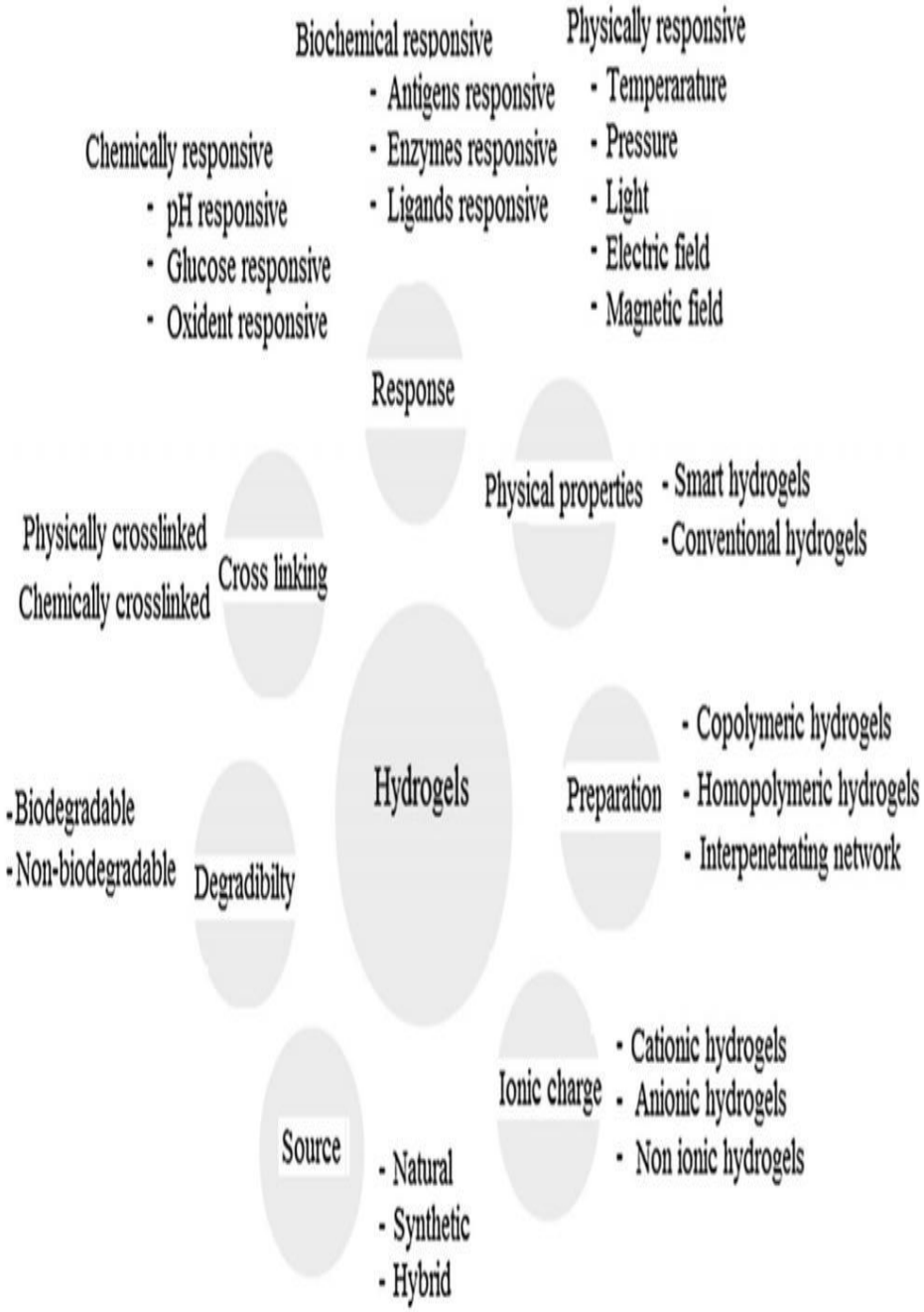


Fig (1.2) Classification of hydrogel based on their different properties.

1.4 Stimuli responsive hydrogel

Hydrogels can exhibit reversible and yet discontinuous volume phase change in response to various stimuli, not only because their unique properties but also of their potential for technological and biomedical applications. In response to different stimuli hydrogels can exhibit dramatic change in their swelling behavior[3].Various environmental conditions that have been explored for modulating drug delivery are represented in figure (1.3)

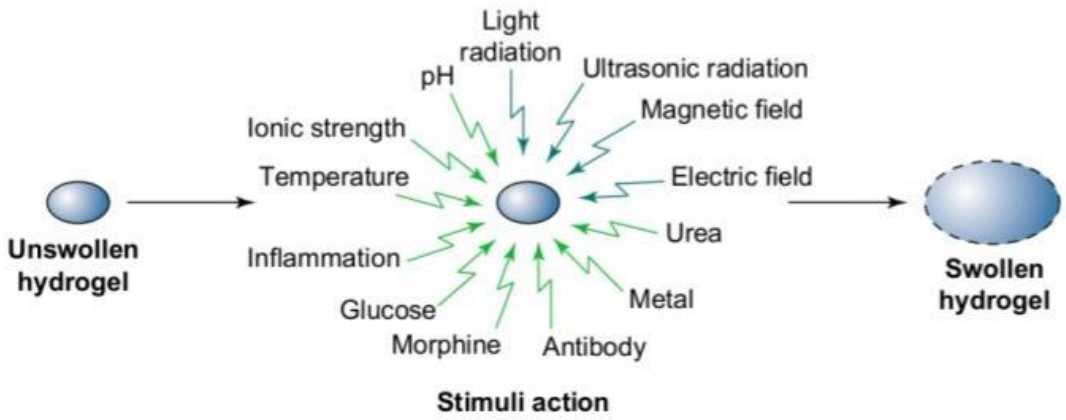


Fig (1.3) Stimuli responsive swelling of hydrogels

The response mechanisms to these stimuli are based on the chemical structure of the polymer network (e.g. Functionality of polymer chain, side groups, branches and cross-links).For example the network that contain weak basic or acidic pendent groups(ionic hydrogels),depending on pH of solution and ionic strength this functional group undergo ionization as result of swelling mechanism. Examples of some commonly studied environment-responsive hydrogels include poly(acrylic acid),polyacryl amide(PAAm),poly(N-isopropyl acryl amide)(PNIPAAm), poly(N,N-'diethyl amino ethyl methacrylate)(PDEAEM).Owing to shrinkage properties or swelling, It have been extensively studied and used as smart materials for

various biomedical applications such as biomaterials, drug delivery devices, and biosciences. [4]

1.4.1 pH-Responsive hydrogel

The difference in pH at several body sites such as vagina, bloods vessels, and gastrointestinal tract, provide suitable base for pH responsive drug release. In addition, local pH changes in response to specific substrates can be generated and used for modulating drug release. The pH responsive drug delivery systems have been targeted for oral controlled drug delivery, taste masking of bitter drug and intravascular drug release during elevated blood pH in certain cardiovascular defects.

1.4.1.1. Polymer structure

For preparation of pH, sensitive hydrogels polyelectrolytes are usually suited. In response to change in environmental pH, ionic pendant groups of polymeric backbones release or accept protons. Most common examples of pH responsive hydrogels are poly (acrylic acid) (PAA), poly (diethyl amino ethyl methacrylate) (PDEAEMA), and poly (dimethyl amino ethyl methacrylate) (PDMAEMA).

In aqueous media of appropriate pH and ionic strength the pendant groups ionize and develop fixed charges on the polymer network, generating electrostatic repulsive forces responsible of pH dependent swelling and deswelling of the hydrogel, there by controlling drug release .Significant change in mesh size of polymeric networks occur as result of small pH changes. Pendant groups of anionic hydrogels ,such as carboxyl, are ionized in media which are a pH above pKa of the ionizable species, leading to swelling of the hydrogels because of a large osmotic force by the presence of ions. Anionic hydrogels dissolve more at high pH. Conversely, in case of cationic hydrogels, pendant groups, such as amines, are ionized at pH below

pKa of the ionizable species. Thus at low pH environment, ionization increases, causing increasing in dissolving and swelling .as expanded in figure (1.4).Apart from synthetic polymers, natural polymer such as chitosan, cellulose and their derivatives have also shown pH responsive swelling behavior under appropriate conditions of pH. [3]

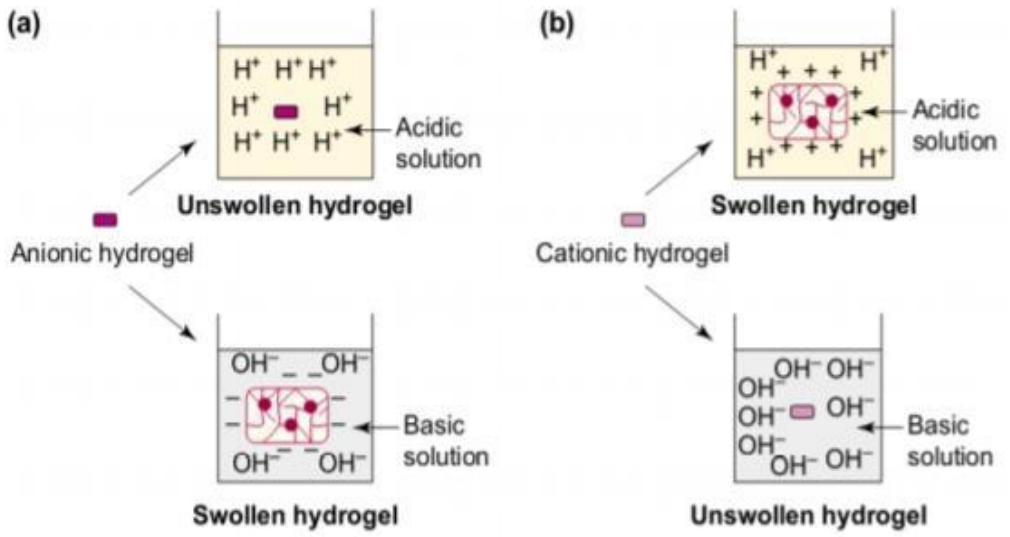
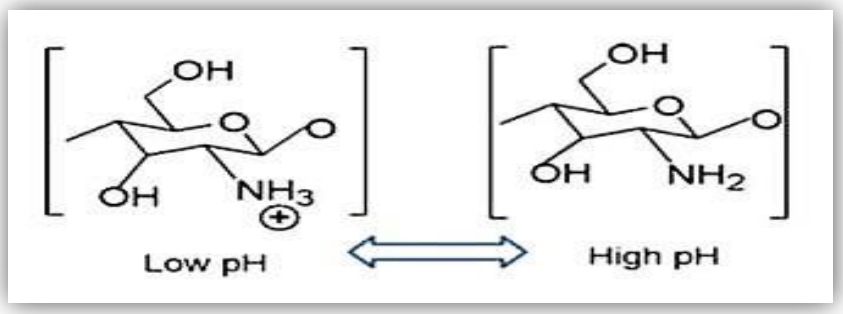


Fig (1.4) The pH responsive swelling of (a) anionic and (b) cationic hydrogels

For example amine groups of chitosan are protonated to form R-NH_3^+ conferring polycationic behavior in aqueous acidic solution (pH<6.5), while chitosan amines.[5] figure (1.5).



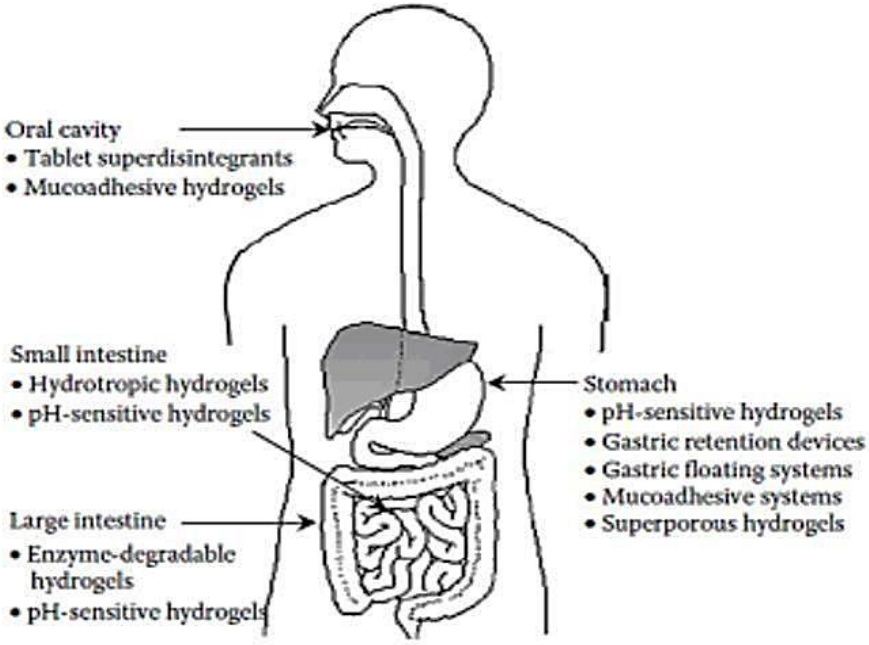
Fig(1.5) The schematic illustration of pH dependent ionization of chitosan

1.4.1.2 Properties of pH responsive hydrogels

Depending on the pH of the environment hydrogels made of cross-linked polyelectrolyte show large variations in swelling properties .Like the basic or acidic groups of monoacids or monobases ,pendant acidic or basic groups on polyelectrolytes undergo ionization .Due to electrostatic effects exerted by other ionized groups ,ionization of polyelectrolytes is more difficult. Maleic anhydride ,2-hydroxyethyl methacrylate and methyl acryl ate are neutral comonomers that can adjust the swelling and responsiveness of polyelectrolyte hydrogels .Different comonomers provide different hydrophobicity to the polymer chain ,leading to different pH- responsive behavior. [6]

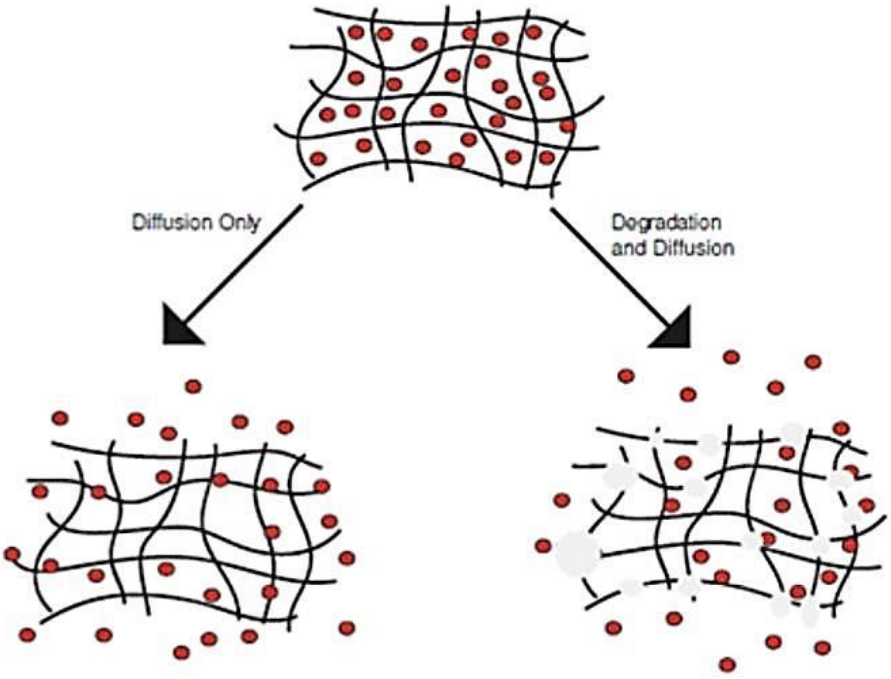
1.5 Drug Delivery Systems

The major issue for researchers has always been treatment of diseases. The protein ,peptides and other materials have been identified as "drug" which can be used to treat physiological life processes, pain ,discomfort. Increasing understandings of cellular biology at the molecular level and breakthroughs in proteomics have led to the concept of gene delivery.Following administration(oral, intravenous) drug must reach site of action in specific amount and in specific manner. Different type of hydrogels can be used for drug delivery to specific parts of GIT ranging from oral cavity to the colon[7,8].,as shown in figure(1.6).



Fig(1.6) Various hydrogels and hydrogel formulations that can be used in different segments of the GIT for drug delivery

Hydrogels mechanical properties ,drug loading and controlled drug release capability give it suitability for pharmaceutical applications. Drug loaded hydrogels ay act as reservoirs that release the drug, either in sustained way or immediately ,by mechanisms such as erosion or diffusion. Hydrogels can also be used for site specific drug delivery in which it act as targeting agents ,using two main methods: (a)systems that modify their structure ,swelling ,eroding, in response to changes in the characteristics of the physiological medium(smart hydrogels)and(b)devices in which the drug is covalently bonded to the polymer by a labile covalent bond that can broken at specific biological conditions[(10)].



Fig(1.7) Mechanisms of drug release

1.6 Literature Review

Nizam El-Din et. al. prepared hydrogels based on gamma radiation of aqueous solutions composed essentially of acrylamide monomer(AAm)and different ratios(5-20%) of carboxymethyl cellulose(CMC).They use methylene blue indicator as drug model, the results showed that the gel fraction of AAm/CMC hydrogels deceases greatly with increasing the contents of CMC in the initial feeding solution. The kinetic study showed that the swelling of all hydrogels tended to reach the equilibrium state after 5 hr. However, the swelling of AAm/CMC hydrogels was greater than the hydrogels based on pure AAm. On the other hand ,it was found that the swelling of all hydrogels changed within temperature range of 30-40°C and within pH range of 4-8.It was found that the percentage of release from the hydrogels increase with time to reach 80% after 3hr at pH of 2 compared to 100% at pH of 8.

Zendehedel et. al. studied the preparation of novel semi-interpenetrating hydrogels composed of poly(acrylamide-co-acrylic acid) and polyvinyl alcohol and the adsorption of the hydrogels for methylene blue removal from aqueous solution .Linear poly(vinyl alcohol) increased the strength of the gels by forming semi interpenetrating polymer network(sIPN) best molar ratio for the final hydrogels were determined as 1.5 for acrylamide, 2 for acrylic acid,0.0002 of polyvinyl alcohol and 0.05 for bisacryl amide.

The composites could be used as good membranes for removal of cationic dyes from aqueous solution while they did not release harmful materials in to water in addition no desorption occur even after a few months.

Wang, et. al. studied pH sensitive konjacglocomannan/Sodium alginate(KGM/SA)and KGM/SA/graphene oxide(KGMA/SA/GO)hydrogels ,GO binding effector the drug used is 5FU,the result of this study is that GO good drug binding effector for controlling the release rate of the drug and(KGM/GO-3)hydrogels could be suitable polymer carrier for the site specific drug delivery in the intestine.

Baner jee et. al. develop (IPN) hydrogel microsphere for oral controlled release application .Hydrogels microspheres of sodium carboxymethyl cellulose and polyvinyl alcohol hydrogel were prepared by oil/water emulsion, Study of NaCMC/PVA hydrogels for oral controlled release delivery of NSAID, Diclofenac Sodium. They found that %of drug loading ,extent of cross-linking, density and NaCMC content influence release of drug.

1.7 Metformin Hydrochloride:

Metformin HCL marketed under the trade name glucophage is the first line medication for the treatment of DM type 2,Particularly over weight .It is also used to treat polycystic ovarian syndrome(PCOS).Pharmacologists suggest that metformin prevent cardiovascular and cancer complications of DM and is not associated with weight gain. It is taken by mouth.

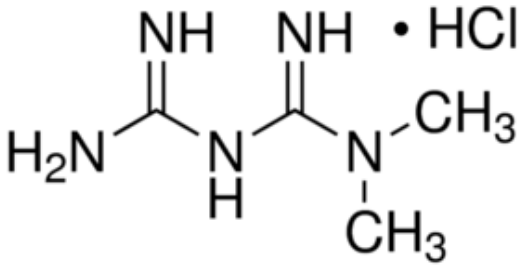
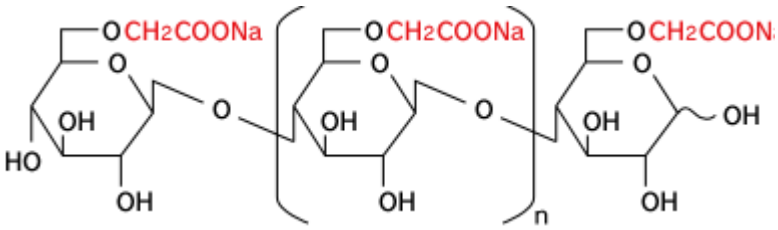


Figure (1.8) Structure of metformin hydrochloride

1.8 Carboxy methyl cellulose

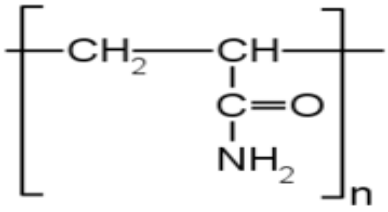
CMC is anionic polyelectrolyte which has good water solubility resulting from CH2OOH group in its skeleton. It also has unique characteristics such as transparency, high viscosity، hydrophilicity, nontoxicity, biodegrade ability, film forming ability and biocompatibility .Hydrogel that are synthesized by cross linking CMC have high absorptivity and posses dynamic viscoelasticities and excellent physical properties .



Fig(1.9) Structure of CMC

1.9 Polyacryl amide(PAAm)

Poly acryl amide(PAAm) is neutral hydrogel that are more suitable for drug delivery systems (DDS) as they are biocompatible and not very reactive .PAAm gel is chemically inert and nontoxic. It have been used in many in vivo and in vitro studies to deliver various drugs.



Fig(1-10) Structure of Polyacryl amide(PAAm)

Aim of the work

The aim of the work is summarized in following points:

1.Synthesis of crosslinked poly(Acrylamide –Carboxy methyl cellulose).

2.Explore feasibility utilizing polymeric hydrogels as adsorbent for drug .

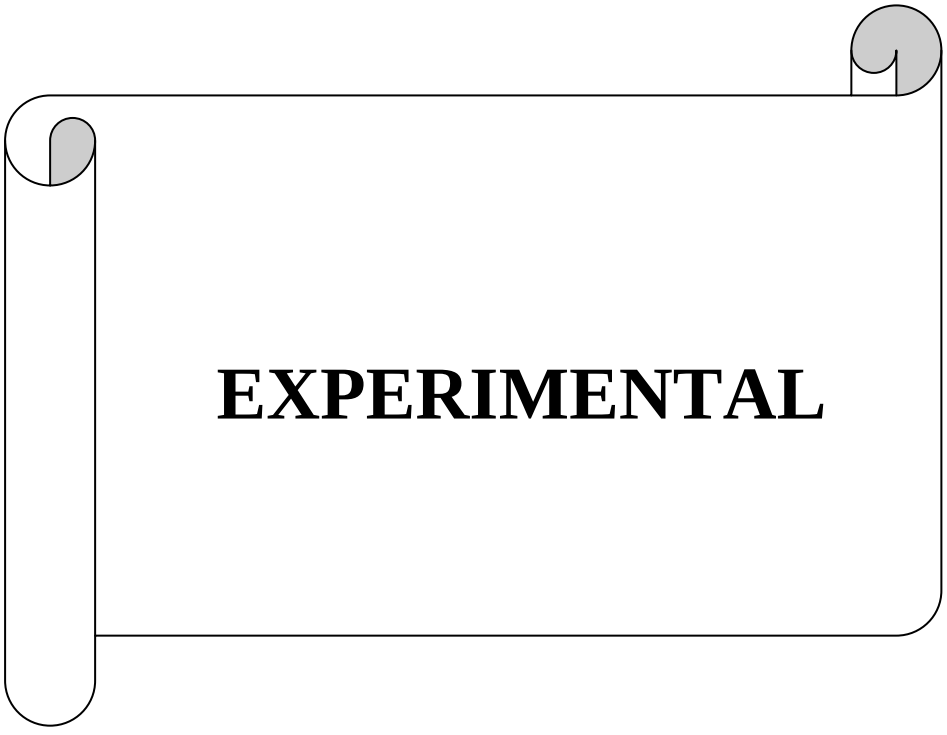
3.Characterization of the synthesized Polymeric hydrogels and adsorption studies by FTIR and UV-Vis spectrophotometer.

4.Study the surface polymeric hydrogels capacity on adsorption of drug model.

5.The effect of pH on the release of the drug from the surface of the polymeric hydrogels.

6-Study the release of the drug from the surface of the polymeric hydrogels(desorption)

CHAPTER TWO



EXPERIMENTAL

EXPERMENTAL

[2-1] Chemicals

Table [2-1] shows the used chemicals in experimental part.

NO	Compound	Company	M.wt	Purity %
1	acrylamide	HI media	71.08	99.0
2	N,N-Methylene bis acrylamide	Sigma Aldrich	154.17	99.9
3	Potassium per sulfate	Fluka	270.32	98.0
4	N,N,ŃŃ-tetra methyl ethylene diamine	LLC	116.24	99.0
5	Carboxyl methyl cellulose	Pancreas	262.19	99
6	Hydrochloric acid	BDH	36.46	37
7	Distilled water	Iraq localProduct	18.02	_

[2-2] drug used

NO	Drug	Company	M.wt	Purity %
1	Metformin hydrochloride	HI media	129.1636	99.0

[2-3] Instrumental

Table [2-3] shows used of equipment in experimental part

No	Instrument	Model	Company	Source	Work place
1	UV-Visible Spectrophotometer double Beam	UV-1800	Shimadzu	Japan	University of Al Qadisiyah
2	Shaking Incubator	LSI-3016A	Labtech	Korea	University of Al Qadisiyah
3	Oven	LDO- 080N	Labtech	Korea	University of Al Qadisiyah
4	pHE-meter	pH-3110	WTW	Germany	University of Al Qadisiyah
5	Centrifuge,6000 rpm	EBA 20	Hettich	Germany	University of Al Qadisiyah
6	Hot- Plate with Magnetic Stirrer	LMS-1003	Latch	Korea	University of Al Qadisiyah
7	Vortex Mixer	LVM-202	Labtech	Korea	University of Al Qadisiyah
8	Electronic balance	L420 B	Sartorius	Germany	University of Al Qadisiyah
9	Water Bath	K- WBBL	K&k	Korea	University of Al Qadisiyah
10	Distilled- water	CO-LTD	Labtech	Korea	University of Al Qadisiyah

[2-4] Methodology

2-4-1 preparation of hydrogel

2g of Acrylamide (AAM) was dissolved in10ml of distilled water and then added to 20g of carboxymethyl cellulose (CMC) then solution was added into in a three necked 250ml round bottom flask . which equipped with a stirring apparatus and a reflux condenser. when mixture heated at 60C°inside digital water bath then added MBA(prepared 0.12g in 2 ml of distilled water). to aqueous solution. then added KPS (prepared 0.04 ml in 2ml of distilled water) to solution as initiator, and finally add 1.25ml TEMED as drop was added onto solution .polymerization process occur after 60min. the reaction was stopped after 2 hour, the prepared cross linked poly(AAm-CMC) hydrogel was poured Petri dish and soaked with distilled water for one day to remove any possible residual monomers and dried in oven at 80°C for 5 hour, to form crosslinked poly(AAm-CMC) hydrogel with constant weight.

2-4-2 Preparation of calibration curve

Wavelength of maximum absorbency (λmax) was recorded for model drug metformin dissolved in aqueous media and found 235nm. Figure(2-1)

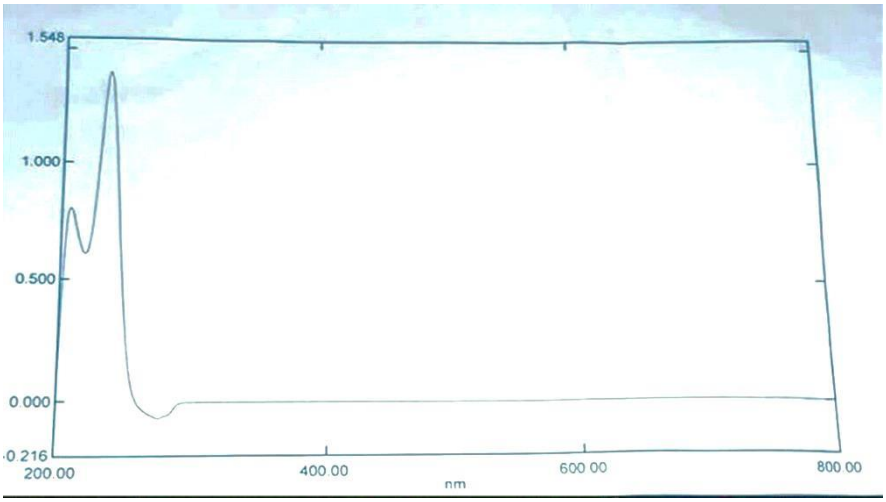


Figure [2-1] : UV Spectrum of metformin

2-4-3 preparation of stock solution

The solution were prepared from 500 ppm was prepared by dissolving 0.5g of metformin in 1000ml of distilled water. solution of different concentration were prepared by serial dilution at wavelength maximum and plotted against concentration values, Figure(2-2)

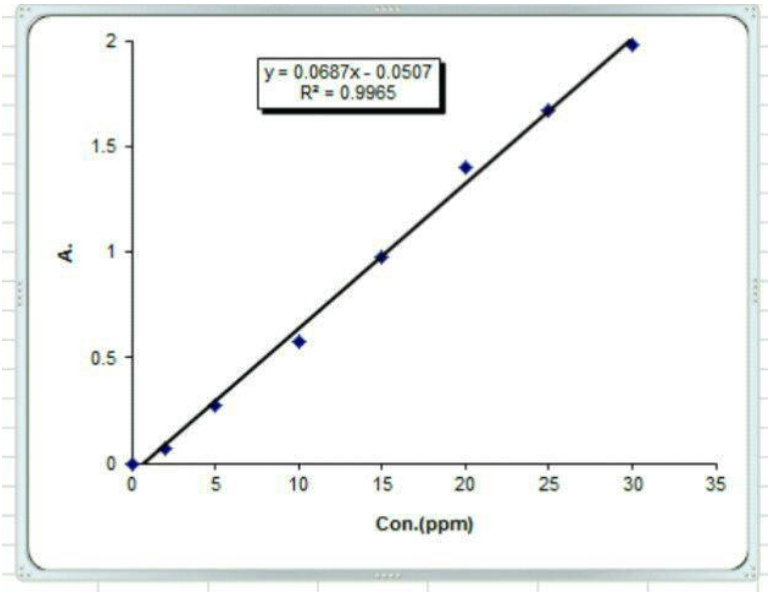


Figure (2-2) Calibration curve for data of metformin (absorbance in 1cm) at 235nm

2-4-4 Effect of Particles Size of Adsorbent

The surfaces were then ground and sieved by using a different mesh sieve (75 ,125,250) µm, where used fixed concentration of drug 25ppm and shaken with 0.1 g of adsorbent at 37^{o}C. for two hours after the separation by centrifuge and then measured the absorbance of each sample and determine the appropriate particle size of the adsorption process.

2-4-5 Determine Weight of Adsorbent

A series of weights (0.01-0.15)g from poly(AAm-CMC)hydrogel and added 10 ml of the drug solution (25 ppm) and put in the shaker for two hours after the separation by centrifuge and then measured the absorbance of each sample and determine the appropriate weight of the adsorption process.

2-4-6 Equilibrium Time of Adsorption System

The equilibrium time of the adsorbent drug on the surface hydrogels when all the conditions of the temperature and the pH function were constant with the change of the time factor, Prepare solution of drug with concentration 25ppm , Determine the kinetics of adsorption the drug on the surface of hydrogel by taking 10 ml of the drug solution and adding 0.1 g of hydrogel and placed in the shaker at 37 ° C and different time (1-300)min, the separation by centrifuge and then measured the absorbance of each sample and determine the appropriate of time optimum in the adsorption process.

2-4-7 Study of swelling Ratio of prepared polymer:

Studied swelling ratio for polymer prepared from through put it 0.1 g of hydrogel in different acidic medias (pH= 1.2 , pH= 7.2) through different times accomplish drew polymer from solution and put it on filter paper to remove high liquid then calculated ratio Swelling according to equation:

$$\text{Swelling Ratio} = \frac{w_s - w_d}{w_d} * 100$$

2-4-8 Determination of gel fraction

Samples of the prepared hydrogels were accurately weighed (W_0) and then extracted with distilled water and then dried in a vacuum oven at 80 ^{0}C to a constant dry weight (W_1). The gel fraction is calculated according to the following equation:

$$\text{Gel fraction}\,(\%) = (W_1/W_0) \times 100$$

2-4-9 Loading of drug

Powdered samples (1 g), with average particle sizes 75-mesh μg, were accurately weighted and immersed in a drug solution 100 ppm at 37.0°C for 24 h. The swollen hydrogels loaded with drug were placed in a vacuum oven and dried under vacuum at 37°C.

2-4-10 Determination of loading efficiency

The amount of drug content entrapped in the hydrogels was determined by an indirect method. After the gel preparation, the washings were collected, filtered with a 0·45 μm Millipore filter and tested at λmax 235 nm using UV/VIS spectrophotometer (UV- 8500, Shimadzu, Kyoto, Japan).

The drugs entrapped exhibited the same λmax as the free drug. This clearly indicates that the drugs entrapped have not undergone any possible chemical reaction during the matrix formation. The difference between the amount of drug initially employed and the drug content in the washings is taken as an indication of the amount of drug entrapped:

$$\text{Drug entrapment (\%)} = \frac{\text{Mass of drug present in hydrogel}}{\text{Theoretical mass of DS}} \times 100$$

The drug release percent was calculated twice using the following equation:

$$\text{Released drug (\%)} = \frac{R_t}{L} \times 100,$$

where L and R_t represent the initial amount of drug loaded and the final amount of drug released at time t.

CHAPTER THREE

RESULTS & DISCUSSION

3-1 -Preparation of hydrogel

There are sequence of processes for preparation poly(AAm-CMC) hydrogel include added acrylamide to carboxyl methyl cellulose then solution was added into in a three necked 250ml round bottom flask. then added MBA and KBS initiator as drop last added TEMDA as accelerator for reaction (figure 3-1) explain the chemical reaction for preparation :

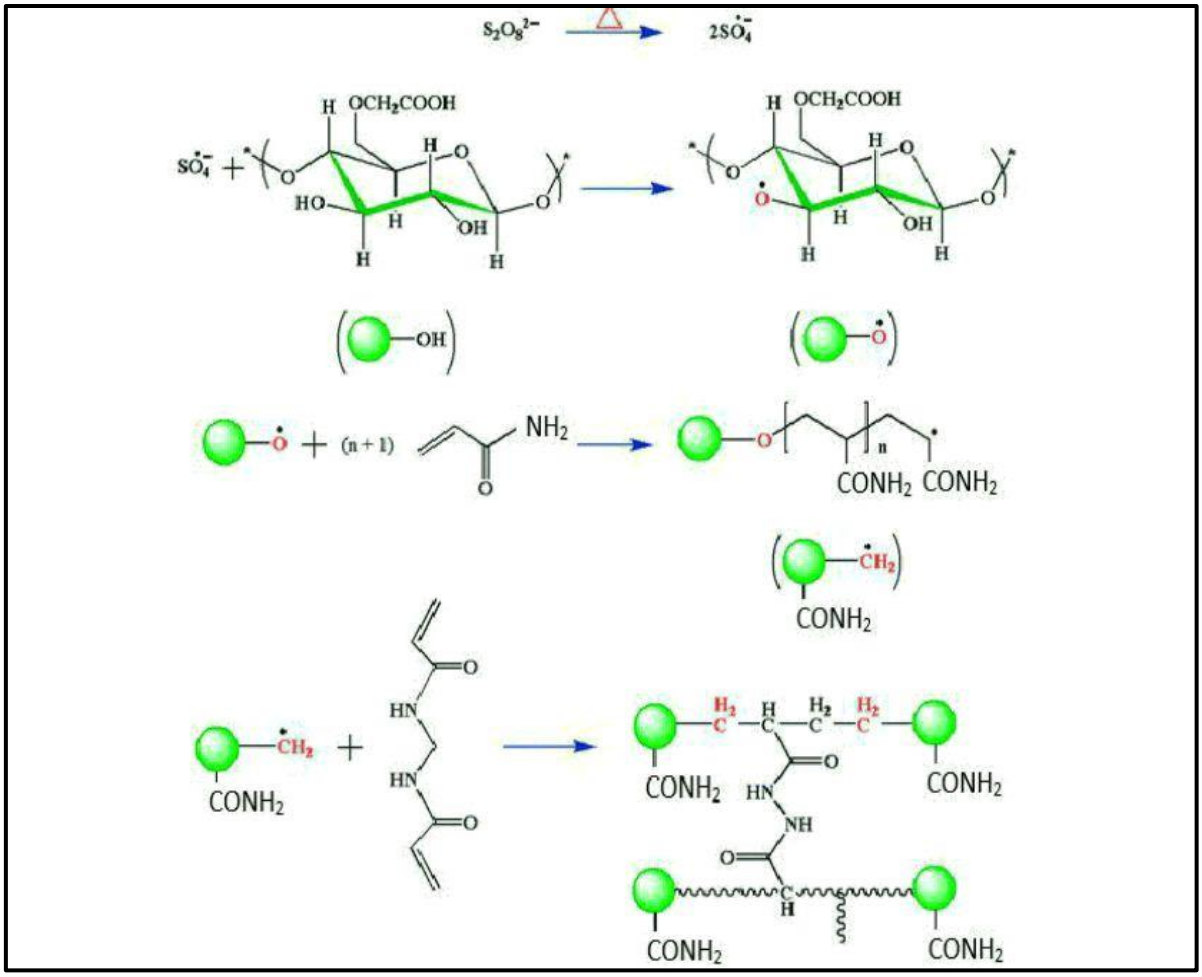
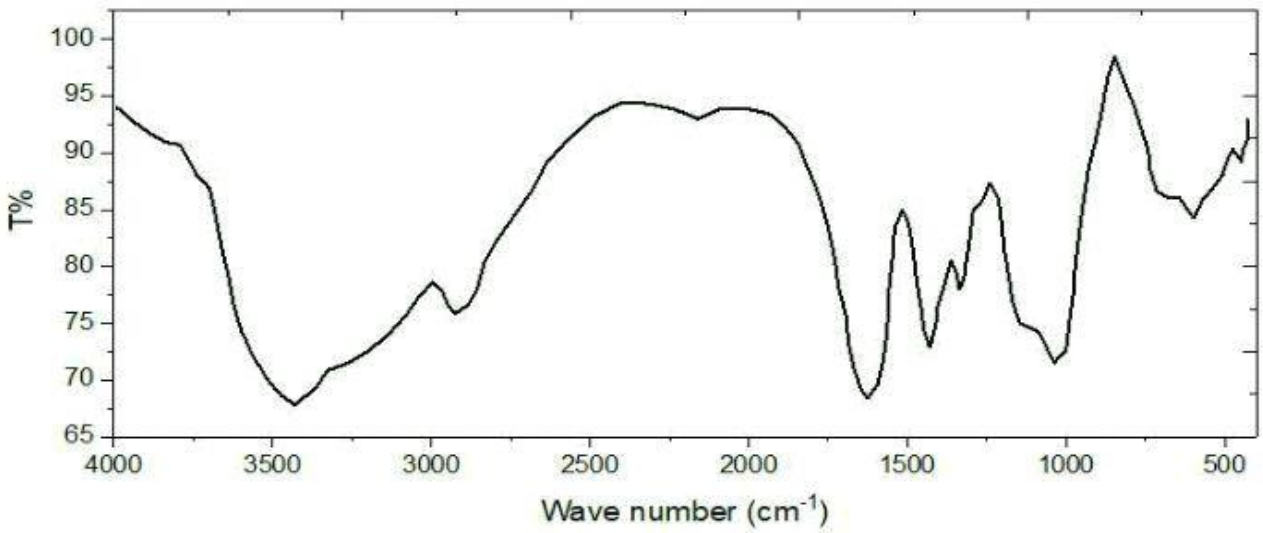


Figure (3-1) Steps preparation of hydrogel

3-2 -FT IR Measurements

The FTIR spectroscopy of the chemical structures of synthesized hydrogels. the spectra of CMC, poly(AAm-CMC) samples respectively. The FT-IR spectrum of pure CMC presents the broad absorption band at 3445cm^{-1} indicating the stretching frequency of the –OH groups. The bands at 2932 and 1065cm^{-1} represent the stretching vibration of C–H and C–O bonds, respectively.



(3-2) FT-IR spectrum of poly(AAm-CMC)

In the FT-IR spectrum of poly(AAm-CMC) the presence of amide groups is confirmed by appeared bands at 3209 and 1611cm^{-1} correspondent to the stretching and bending of N–H in amide groups.

The characteristic functional groups of the CMC and AAm units. In the FTIR spectra of poly(AAm-CMC) hydrogel, the emergence of peaks at 3345 and 3185 cm^{-1}, correspond to the N-H stretching, the peaks at 2981 and 2927 cm^{-1} refer to the C-H stretching vibration. The peaks at 1646(C=O) and 1600 (-NH bending) cm^{-1}indicate amide I and amide II groups of the poly(AAm-CMC) hydrogel, respectively.

The peaks at 1450, 1407 and 1321 cm^{-1} are assigned to the scissoring of CH_2, symmetrical stretching of COO and the twisting of CH2units of the hydrogels. The peak at 1118 cm^{-1} is an important (CH O-CH) unit of poly(AAm-CMC)

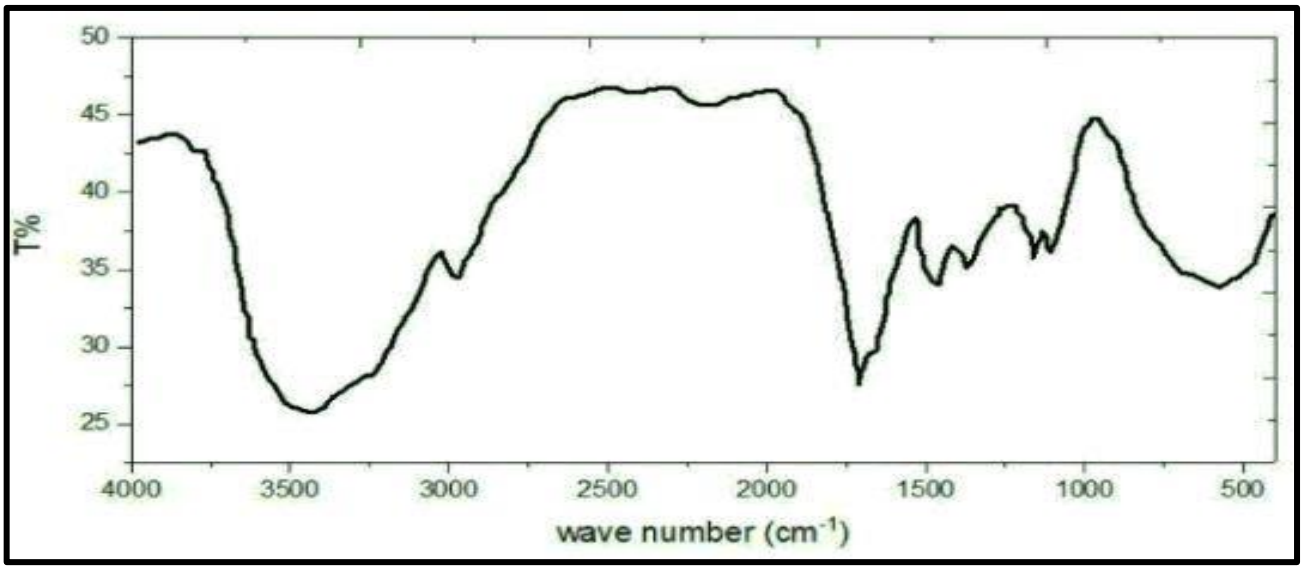


Figure (3-3) FT-IR spectrum of poly(AAm-CMC)

3-3- Effect Particles size of adsorbent

The effect of the size of surface mines was studied for its important in the process of adsorption . A constant concentration was used for the drug (25mg/L) and weight (0.1g) of surface mines. showed the results figure (3-4) the amount of material adsorbed was higher in the case mines that have size 75µm

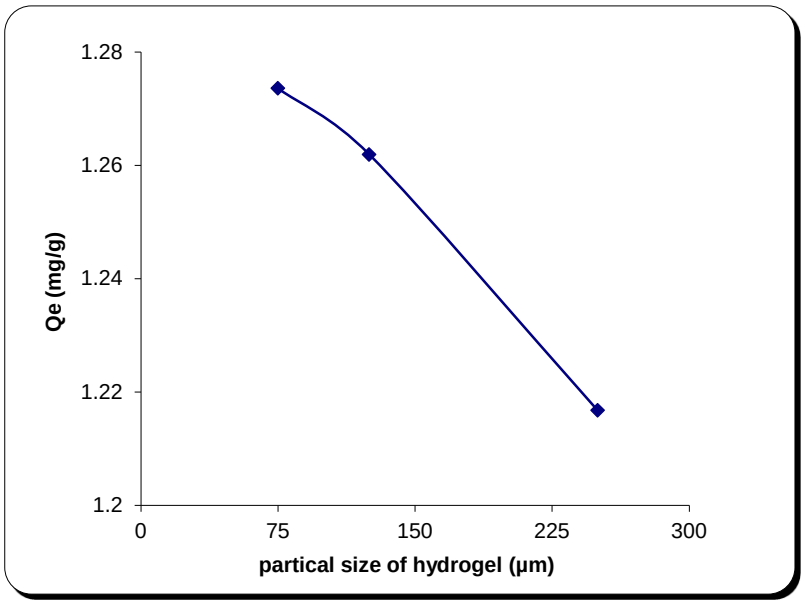


Figure (3-4) effect the particle size of surface on amount of material adsorbed at 35°C

3-4- Effect of surface weight

Adsorption study for metformin Hydrochloride done by using poly(AAm-CMC) hydrogel at constant concentration(25 mg/L) at different weight of poly(AAm-CMC) hydrogel at 37^0C temperature. Study results shown figure(3-4). The explained results in figure(3-5) show that the amount of therapeutic agent being adsorbed increased as the weight of adsorbing agent is increased. Any increase in adsorbing agent weight mean an increase in the number of active sites of polymer capable of therapeutic agent adsorption. This high activity of adsorbing agent permit it to adsorb large quantity of metformin that percent in solution until reach a limited value , that is amount of adsorbing agent in saturation state, not effected by any additional polymer weight , That mean Solution become in complete equilibrium state(11).

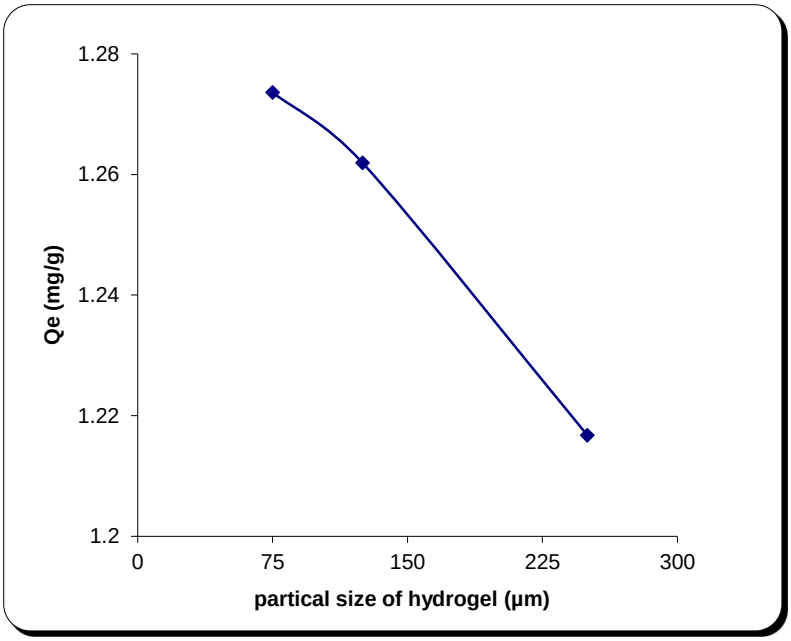


Figure (3-5) Effect of surface weight

3-5-Equilibrium time

Equilibrium time for hydrogel drug being adsorbed have been studded on adsorbing surface at different times (1-300 min) at 37^0C know most appropriate time for adsorption process, by adding (0.1gm) from polymer to 10 ml of 120 ppm solution of metformin hydrochloride. It has been shown that adsorption capacity increased with time until reach constant value at 120 min[(12)] .as shown in figure(3-6).

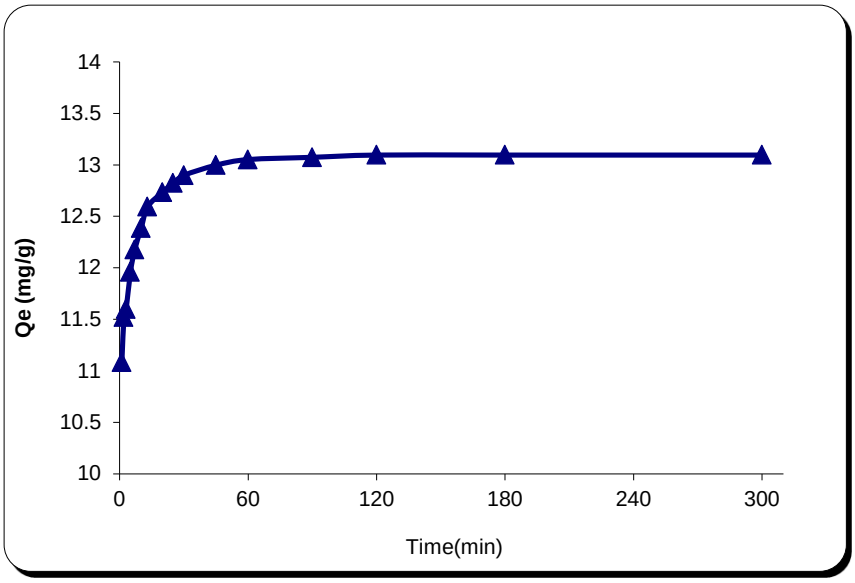


Figure (3-6) Equilibrium time

3-6- Swelling studies

Swelling studies of poly (AAM-CMC) were carried-out at pH. (1.2, and 7.4) and at time (6h) and temperature (37^0C) (Fig. 3-7). Maximum swelling was observed at pH 7.4 whereas, a lesser swelling ratio was observed in acidic as well as in alkaline medium. This could be due to the fact that at 7.4 pH water molecules undergo hydrogen bonding, thereby giving rise to a cage-like structure allowing the accommodation of more and more water molecules for the swelling of candidate polymer. However, amide group of Polyacryl amide upon acid and base hydrolysis got converted into carboxylate ion (COO^-) and resulted in the COO^- ion repulsion with the COO^- ions present on the backbone molecules. In case of acidic medium, COO^- ion repulsion is screened by H^+ ions which did not allowed the network to expand and resulted in decreased swelling ratio . Further increase in acidic character

resulted in increased concentration of H^+ ions and increased screening effect and decreased COO^- ion repulsion and hence a decreased swelling ratio. [13]

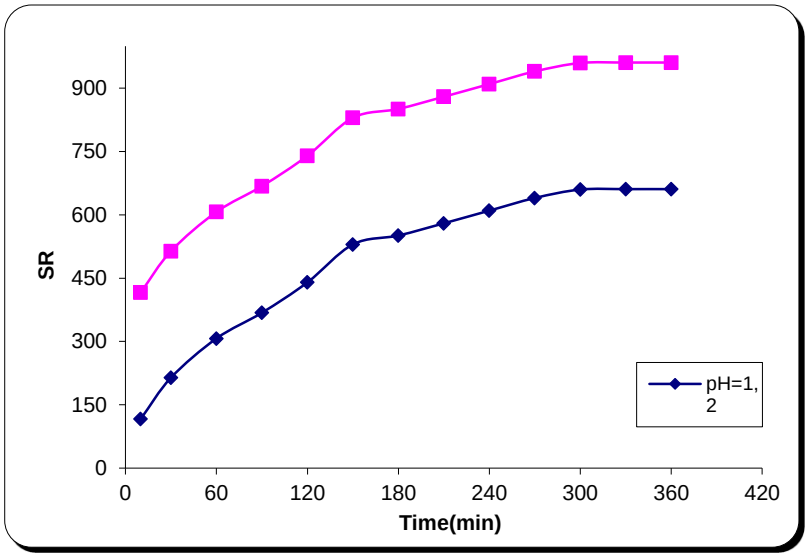


Figure (3-7) Swelling Ratio

3-7- In-Vitro Drug Release

The drug release was studied in both simulated gastric fluid (pH 1.2) and simulated intestinal fluid (pH 7.4) and the profiles are depicted in Fig. (3-8) The release of drug in pH 1.2 solution was slower compared to that in pH 7.4 buffer solution this was due to a higher swelling of hydrogel in alkaline pH condition.

The release of adsorbed drug occurs after water penetrates the polymeric networks and this is followed by diffusion along the aqueous pathways. Thus, drug release is related to the swelling characters of hydrogels. In order to determine the release of metformin hydrochloride, a standard curve representing the absorbance at λmax of 235nm.

The percentage release of metformin hydrochloride was carried out as a function of time at different pH values by 0.2g of AM/CMC hydrogels and is

shown in Fig.(3-8) It can be seen that the percentage release from the hydrogel increases with time to reach 20% after4h at pH of 1.2 compared to 80% at pH of 7.2. This suggests that the drug release properties of poly(AM-CMC) hydrogels are not exactly pH sensitive. This is because the release of metformin hydrochloride from these hydrogels is close. However, at high pH value, the swelling is higher than that at pH1.2, i.e. the pore size at pH7.2 is much higher than that at pH1.2 leading to the highest swelling of the networks and resulting in more drug release. [14 , 15]

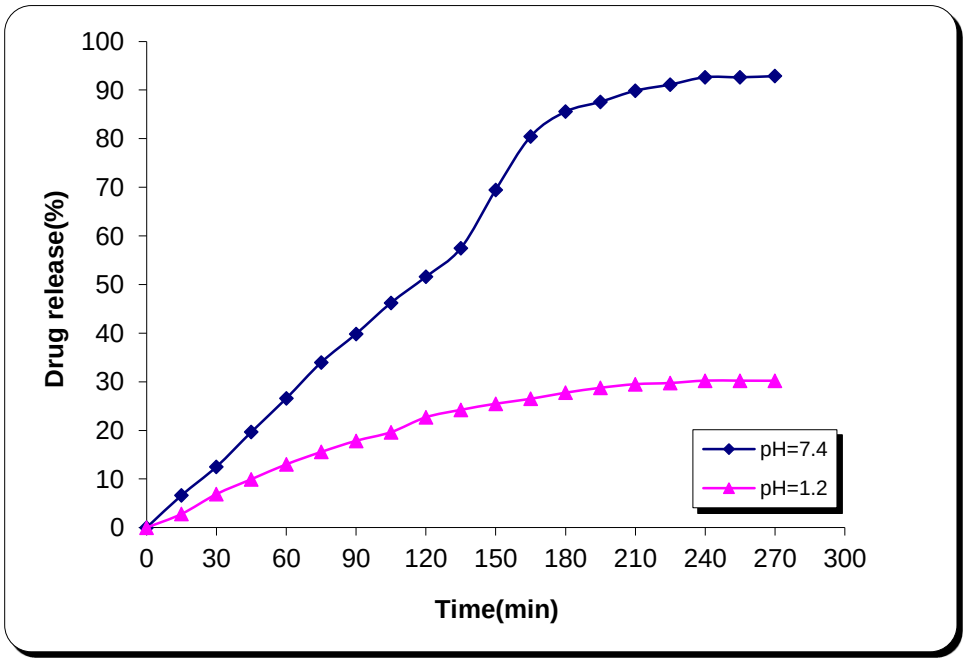


Figure (3-8) Drug Release

Conclusions

On the basis of the experimental results of this investigation, the following conclusions can be drawn:

1- Hydrogel can be used as an adsorbent for the removal of Metformin Hydrochloride from solution.

2- Hydrogels are higher swelling ratio in basic media than acidic media.

3- Equilibrium time of metformin is reached at 180 min.

4- The percentage removal of drug was dependent on pH solution because the hydrogels are sensitive for pH .

5- Particles size are effected on adsorption process, because the increase the surface are of hydrogels.

6- Amount of adsorbed drug increased in typical intestine content at pH 7.4.

7- The drug is higher release at pH 7.4 than pH 1.2 .

الخلاصـــــة

تركزت الدراسة في هذا البحث الذي يهتم بتطبيقات كيمياء السطح وفي مجال الصيدلة الفيزيائية والطبية، حيث تناول البحث أنظمة امتزاز - ابتزاز (Metformin) على سطح الهلام المائي بولي (AAm-CMC)المتشابك عند ظروف مختلفة من الدالة الحامضية ودرجة حرارة.استخدم سطح الهلام المائي كمادة مازة لدواء (Metformin) من محلوله المائي. حيث تم دراسة تجارب الامتزاز باستخدام التقنية الطيفية للأشعة فوق البنفسجية . تم تحضير السطح باستخدام طريقة البلمرة بالجذور الحرة .حيث تم تحديد التركيب الكيميائي للهلام المائي المتشابك باستخدام طيف الأشعة تحت الحمراء (FTIR).

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جمهورية العراق
وزارة التعليم العالي والبحث العلمي
جامعة القادسية – كلية الصيدلة

تحضير ودراسة خواص تحرر الدواء من الهلام المائي المتشابك الحساسة بالدالة الحامضة بولي (اكريل امايد – كربوكسي مثيل سليلوز)

بحث

مقدم الى كلية الصيدلة جامعة القادسية وهو جزء من متطلبات نيل درجة البكالوريوس في علم الصيدلة

بـــواسطة

محمد حمزة

لمياء حمزة

المشرف

أ.م.د ناظر ضمان

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