MINISTRY OF HIGHER EDUCATION AND SCIENTIFIC RESEARCH

UNIVERSITY OF BABYLON

COLLEGE OF PHARMACY

Graduation project

Bio-hydrogel material as a carrier drug systems

Prepared by

Zahraa Salem Shinawa

Mariam Alaa Mohammed

Mays Ghalib Juma

Supervised by

Dr. Nour Hadi Issa

2022_2023

Introduction

Hydrogels are hydrophilic, three-dimensional and cross-linked networks, able to absorb large amounts of water but, due to the formation of cross-link network present in hydrogel structure, are not soluble in an aqueous environment . Hydrogels have been produced from many synthetic and natural polymers . High water absorption capacity and biocompatibility make hydrogels an ideal candidate to be used in biomedical felds such as controlled drug delivery, tissue engineering, wound dressing, sanitary pads, dental materials and cell therapy, as well as in agriculture, ophthalmic application, moisture, and sensor . Nanocomposite hydrogels are defned as cross-linked, three-dimensional, swollen networks which possess nanoparticles. This network was formed by both covalent and non-covalent bonds using chemical and physical interactions. The existence of nanoparticles in hydrogel gives unique physicochemical properties to them including mechanical, optical and thermal. These unique properties led them to be used in electronics, optics, sensors, catalyst, separation devices as well as drug delivery and many others .

Since PVA is inert and stable, it is generally considered as a safe and biocompatible material . OH groups on PVA chains can be reacted by various organic and inorganic materials . PVA can be cross-linked by diferent physical and chemical methods to obtain a hydrogel.

dimethyl sulfoxide (DMSO) is a clear odorless liquid that can form a hydrogel with PVA . Due to their biocompatibility, harmlessness, transparency, non-toxicity and non-carcinogenic, PVA hydrogels have attracted much attention. Hence, they are suitable for pharmaceutical and biomaterial applications such as contact lenses, lining for the artifcial heart, wound dressing, drug delivery and artifcial cartilage for orthopedic surgery .

Metal oxide nanoparticles are used in most scientifc and industrial applications. Oxides of transition metals are an important class of semiconductors. Among oxide of transition metals, (ZnO , Sio2 , Tio2), have a different application such as catalytic agent, solar energy transformation, gas sensing materials and electronics . ZnO NPs have become one of the most popular metal oxide nanoparticles in biological applications due to their excellent biocompatibility, economic, and low toxicity. ZnO NPs have emerged a promising potential in biomedicine, especially in the fields of anticancer and antibacterial fields, which are involved with their potent ability to trigger excess reactive oxygen species (ROS) production, release zinc ions, and induce cell apoptosis. In addition, zinc is well known to keep the structural integrity of insulin. TiO2 with a high photocatalytic activity and antibacterial properties for use as a self- cleaning transparent coatings for windows in outdoors applications. TiO2 nanoparticles was assessed quantitatively against two types of bacteria, (Pseudomonas aeruginosa), and (Staphylococcus aurous).

Drug delivery system (DDS) is described as prolonged controlled drug release systems. DDS is designed to change the pharmacokinetics and biodistribution of their associated drugs and their function as a drug reservoir or both. Various biomaterials have been investigated to control drug release. Among them, hydrogels are suitable for drug delivery because of easy diffusion of the drug into the hydrogel and little interaction with the drug .

Experimental

Materials

PVA was obtained from Aldrich with a molecular weight of 125,000, and dimethyl sulfoxide (DMSO) , NaOH, metal oxide nanoparticles (ZnO , TiO_2, SiO_2) , HCl, d-glucose, urea, $CaCl_2$ and $MgSO_4$ were purchased from Merck (Darmstadt, Germany). During this process, deionized water was used.

Preparation of PVA hydrogel

PVA hydrogel was prepared by the following procedure: Five milliliters of DMSO crosslinker was added to pre-dissolved 10 g of PVA in 100 mL of 3% w/v NaOH solution, drop by drop by syringe until a homogenous mixture was obtained.

Afterward, the prepared mixture was placed in a warm water bath at 80 °C for 90 min.

The obtained insoluble hydrogel was washed successively by water in order to remove residual NaOH and DMSO in cross-linked PVA. Then, it was dried in an oven at 50 °C for 24 hr .

Preparation of nanocomposite hydrogel

PVA/(TiO_2 , SiO_2 , ZnO) nanocomposite hydrogels were prepared by the following method: 0.5 g

of dried hydrogel was immersed into the different concentration of (TiO_2 , SiO_2 , ZnO) (0.05 , 0.1 ,0.15 and 0.2 M) for 48 h. Afterward,(Ti , Si , Zn) ions loaded

hydrogels were taken out and washed with distilled water to remove unreacted (Ti , Si , Zn) ions from the surface of hydrogels. The washed hydrogels were immersed in NaOH solution (100 mL of 0.2 M) for 24 h. After the oxidation of the (Ti , Si , Zn) ions bound, hydrogels containing (Ti , Si , Zn) nanoparticles were washed with distilled water and dried in an oven at 50 °C for 24 h.

ZnO concentration	**Weight of ZnO**	**Weight of PVA before immersion**	**Weight of PVA after immersion**
0.05 M	0.4 g	2.11 g	2.53 g
0.1 M	0.8 g	1.19 g	1.3 g
0.15	1.2 g	1.82 g	1.93 g

SiO2 concentration	**Weight of SiO2**	**Weight of PVA before immersion**	**Weight of PVA after immersion**
0.005 M	0.03 g	2.51 g	
0.01 M	0.06 g	2.5 g	
0.015 M	0.09 g	2.16 g	2.33 g

TiO2 concentration	**Weight of TiO2**	**Weight of PVA before immersion**	**Weight of PVA after immersion**
0.005 M	0.11 g	2.6 g	
0.01 M	0.07 g	2.51 g	
0.015 M	0.03 g	2.27 g	2.47 g

Swelling measurement

The equilibrium swelling (ES) of hydrogels was determined in distilled water and various physiological solutions; Distilled water , PVA/TiO2 , urea , CaCl2 . 0.2 g of PVA/(ZnO , TiO2 , SiO2) nanocomposite hydrogels were immersed in 50 mL of prepared solution at room temperature for 48 h to reach maximum swelling capacity.

Mechanical test	Pure hydrogel	PVA/TiO2	Swelling in distilled	Swelling in urea	Swelling in CaCl2
Tensile strength MPa	1.48	3.76	4.61	4.39	4.86
Tear resistance	1.24	2.89	3.17	4.15	4.13
Compression	6.31	14.41	8.97	9.3	8.91
Hardness shore A	53	37.79	39.12	38	37.5
Young modulus	1.83	1.142	0.97	0.98	1.11
Elongation	320	338	354	379	381
Resilience %	18.3	33.2	21.6	19.63	18.98

Investigation of drug delivery

Ibuprofen was used as a drug model in this work. The loading of PVA/(ZnO,TiO2,SiO2) nanocomposite hydrogels by Ibuprofen was carried out as follows: 0.2 g of prepared dry hydrogels were added to 20 mL of Ibuprofen solution (50 ppm in distilled water) under stirring at room temperature for 72 h. Excess free Ibuprofen was removed by filtration and washing. The amount of loaded drug in hydrogels was calculated by UV–Vis spectroscopy at 275 nm using Equation :

$$\text{Drug loading}\ (\%) = \frac{\text{amount of drug in hydrogel}}{\text{amount of dry hydrogel}} \times 100.$$

as show in the table :

Drug concentration	Amount of drug loaded (ibuprofen) %	Amount of drug loaded (flagyl) %
0.3	0.8	0.83
0.35	0.83	0.88
0.4	0.89	0.89
0.45	0.93	0.91
0.5	0.96	0.95

Results and discussion

Formation of polyvinyl alcohol hydrogel

To synthesize PVA hydrogel, DMSO was used as a crosslinker. Each DMSO molecule reacted with two hydroxyl groups on the PVA chain. Two hydroxyl groups of PVA chain reacted with an DMSO molecule to produce one hydroxyl group [35].

In situ formation of (ZnO , TiO2 , SiO2) nanoparticles

PVA reacts to different inorganic or organic substances via OH groups attached to its macromolecular chain [15]. Most of the metal ions such as Si^{4+} , Ti^{4+} and Zn^{2+} can form stable complexes with electron-rich compounds containing O, N and S elements, such as an amine (NH2), hydroxyl (OH) and thiol (SH) groups [37]. The produced (Si^{4+} , Ti^{4+} and Zn^{2+}) ions were bounded to hydroxyl groups via metal complexation, and by adding hydrogel to NaOH solution, (Si^{4+} , Ti^{4+} and Zn^{2+}) ions were converted to zinc oxide , silicon dioxide ,titanium dioxide nanoparticles .