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Preparation and characterization of cellulose/poly (N-vinyl-2-pyrrolidone hydrogels

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Abstract

Cellulose powder / poly (N-vinyl-2-pyrrolidone) (CP/PVP) and carboxymethylcellulose / poly (N-vinyl-2-pyrrolidone) (CMC/PVP) hydrogels were synthesized at different reaction conditions using ammonium persulphate as initiator. The optimum reaction conditions to prepare such gels are PVP molecular weight (40000 Dalton), PVP concentration (60%), APS/polymers weight ratio (100%), reaction time (45 min), reaction temperature (90 °C), as well as CP/PVP or CMC/PVP weight ratio (30 %). The prepared matrices were characterized via FTIR as well as scan electron microscope analysis. The release profiles of sodium diclofenac form the CP/PVP and CMC/PVP gels at pH 7 were studied. Release studies showed burst release for both matrices at first 30 min followed by sustained behavior. Matrices PVP/CMC showed highest release of DS due to repulsive forces between polymer chains.

Keyword: cellulose; PVP; CMC, sodium diclofenac.

1. Introduction

Recently, polymer blends drive the scientists for intensive academic research to respond to the growing need for new functional polymeric materials to meet the particular needs, improve processingability, reduce cost, and wide the industrial applications. By polymer blends, new polymeric materials having unique properties can be obtained, without synthesis, via combining of the individual polymers characteristics [1-6].

Curing of burns, wounds, and ulcers commonly needs dermal therapeutics that can be achieved via drug delivery systems to transport the active molecules, like drugs, proteins, peptides, and interferons to the target site using hydrogel materials. The hydrogels have merits of the mechanical support, topography, as well as biochemical properties which make them functionally a proper choice as biomedical materials [7]. Hydrogels are natural or synthetic polymeric ssubstances crosslinked by physical and/or chemical means to absorb and retain water for a long period of time [8,9]. Hydrogels are used mainly in wound healing, wound dressing, cartilage, and bone regeneration, in addition to their role as carriers to deliver drugs inside the human body through the topical administration [10,11]. The dressings keep the tissue hydrated as well as absorb the moisture from the wound exudates, and thus provide cellular regeneration [12].

Cellulose is the most abundant biomolecule in nature. It consists of anhydro-glucose units attached together with 1,4-β-glucosidic bonds besides intermolecular hydrogen bonds. To widen the cellulose applications, it is commonly modified via esterification or etherfication of its hydroxyl groups. The most widely cellulose derivatives are cellulose ethers, like methylcellulose, hydroxypropyl methylcellulose, ethyl cellulose, hydroxyethylcellulose, as well as sodium

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carboxymethyl cellulose. Cellulose has the merits of hydrophilicity, renewability, biocompatibility, biodegradability, and nontoxicity. Conseuqetly, cellulose-based hydrogels beside other biopolymer-based hydrogels have also the aforementioned favorable properties [13-17].

The most widely cellulose derivatives are cellulose ethers, like methylcellulose, hydroxypropyl methylcellulose, ethyl cellulose, hydroxyethyl cellulose, as well as sodium carboxymethyl cellulose. Cellulose has the merits of hydrophilicity, renewability, biocompatibility, biodegradability, and nontoxicity. Consequently, cellulose-based hydrogels beside other biopolymer-based hydrogels have also the aforementioned favorable properties [18-22].

Poly (N-vinyl-2-pyrrolidone) (PVP) is a synthetic, nontoxic, hydrophilic, and biocompatible polymer which renders it to be used in many pharmaceutical and biomedical applications including films, tablets, and hydrogels [23-25]. PVP is commonly used as a drug carrier for sustainable drug release [26]. Upon treating of PVP aqueous solutions with persulfate anions, chain scission and/or cross-linking of PVP have been observed, depending on the persulfate concentration. In addition, oxidative degradation and ring opening lactam ring may be also occurred [27, 28].

Towards biodegrability, the present work aims to invistigate factors affecting preparation of cellulose/PVP gel, using persulfate anions as initiator, for carrying and releasing of sodium diclophinac.

2. Experimental

2.1. Materials

Poly (N-vinyl-2-pyrrolidone) **(**PVP) of molecular weight 40000 Dalton from Sigma Aldrich, was used. Cellulose powder (CP), supplied by Sigma Aldrich, was used. Carboxyl methyl cellulose (CMC), supplied by Sigma Aldrich, was used. Sodium diclofenac (SD), Sigma Aldrich, was used. Ammonium persulfate (APS) and ammonium hydroxide were laboratory grade chemicals.

2.2. Methods

2.2.1. Preparation of CP/PVP and CMC/PVP hydrogels

The CP/PVP and CMC/PVP hydrogels were synthesized in 150 ml polypropylene beaker by addition of different weights of CP or CMC powder to PVP aqueous solution of specific concentration with continuous stirring followed by raising the reaction medium temperatureto a certain temperature in agitated water bath. After that, a freshly prepared ammonium persulfatesolution of a specific concentration was added to the reaction medium and the reaction was then left for a period of time. After the reaction completion, the reaction contents were neutralized with ammonia solution, washed with distilled water and finally dried at 50 ^{O}C.

2.3. Drug loading

The CP/PVP and CMC/PVP hydrogels were loaded with SD as follows: 0.3 g of either of The CP/PVP or CMC/PVP hydrogels was added to 100 ml of 0.3% of SD aqueous solution at pH7 in a 250 mL stoppered glass bottle. The bottle was then shaken at 150 rpm for 3h, centrifuged and then the concentration of SD in the filtrate was assessed colorimetically at the wave length of the maximum absorption of the drug (285 nm) using UV- 2101PC SHIMADZU spectrophotometer. The amount of the SD entrapped in the aforementioned matrices was determined as a result of the difference between the remained amount of SD in the filtrate and the added SD [24-27].

2.4. In vitro drug releasing

The SD release profiles from The CP/PVP or CMC/PVP hydrogels was achieved at 37 ^{O}C for 5 h by adjusting the releasing medium pH at 7, where every 30 min 2 ml of the solution was withdrawn and spectrophotometrically assessed [29-32].

2.5. Testing and analysis

- The degree of swelling was assessed by impregnating a specific dry weight of the prepared hydrogels in distilled water at 37 ^{O}C for 24 h, followed by

removing, wiping gently with a filter paper and weighing [29-33]:

Degree of swelling (%) = (Wh−Wd)/Wd X 100, where Wh and Wd are the matrix hydrated weight and the matrix dry weight respectively.

- Gel fraction percentage was assessed as an indication for the degree of firmness of the prepared gels structures [29-32]. The gel fraction was calculated according to the following equation: Gel fraction (%)= (Wa/Wi) X100, where Wi is the initial weight of the hydrogel and Wa is the constant weight of the hydrated that gel after leaving it to swell in distilled water at 37 ^{O}C for 24 h.
- Infra Red (IR) spectroscopy was carried out using FT/IR-4700 FTIR Spectrometer from JASCO.
- Scanning electron microscope (SEM) images of the CS/PVP and CG/PVP matrices were obtained using SEM Model Quanta 250 FEG (Field Emission Gun) attached with EDX Unit (Energy Dispersive X-Ray Analysis), with accelerating voltage 30 kV, magnification 14× up to 1,000,000 and resolution for Gun, FEI company, Netherlands.

3. Results and discussion

3.1. Tentative mechanism of CP/PVP gel formation

It was reported before [23, 24] that treating of PVP aqueous solutions with persulfate anions, leads to a formation of crosslinked PVP matrix in addition to PVP oxidative species as well as opened lactam rings. Introducing of CP into the aforementioned reaction medium gives rise to a reaction product containing a mixture of crossilinked PVP, PVP grafted CP, and ungrafted CP (intact and oxidized), all in a state of entanglement [29-33]. In a same procedure, CMC was replaced with CP in the aforementioned reaction medium giving rise to a formation of CMC/PVPmatrix. The formation mechanism of either the CP/CPVP or CMC/CPVP networks is given below[32,33]:

$$PVP + \dot{R} \longrightarrow \underset{\text{(PVP macroradicals)}}{PVP^{\bullet}} + RH \quad \text{..... (1)}$$

where $\dot{R}$ represents $SO_4^{\bullet}$ and $^{\bullet}OH$ free radicals

$$PVP^{\bullet} + PVP^{\bullet} \longrightarrow \underset{\text{(Crosslinked PVP)}}{PVP - PVP} \quad \text{..... (2)}$$

$$CP + \dot{R} \longrightarrow \underset{\text{(CP macroradicals)}}{CP^{\bullet}} \quad \text{..... (3)}$$

$$PVP^{\bullet} + CP^{\bullet} \longrightarrow \underset{\text{(CP grafted PVP)}}{PVP - CP} \quad \text{..... (4)}$$

$$CMC + \dot{R} \longrightarrow \underset{\text{(CMC macroradicals)}}{CMC^{\bullet}} \quad \text{..... (5)}$$

$$PVP^{\bullet} + CMC^{\bullet} \longrightarrow \underset{\text{(CMC grafte PVP)}}{PVP - CMC} \quad \text{..... (6)}$$

3.2. Factors affecting of the CP/PVP gel formation

3.2.1. APS/polymers weight ratio

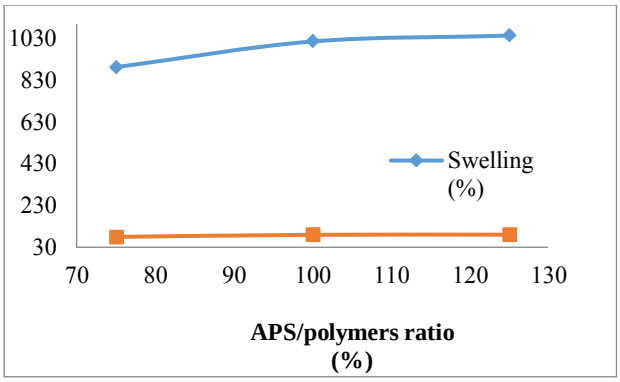


Figure 1: Effect of APS/polymers weight ratio on percent swelling and gel fraction of CP/PVP gel.

PVP MW, 40,000; [polymers], 60%; CP/PVP weight ratio, 30%; reaction temp., 90 ^{O}C; reaction time, 45 min. Swelling properties was assessed at pH 5 and 25 ^{O}C.

Figure 1 clarifies the effect of APS/polymers weight ratio on swellability and gel fraction of the formed CP/PVP matrix. It is clear that, increasing of APS concentration in the reaction medium from 70 to 100%, based on polymer weight, leads to a progressive enhancement in gel fraction as well as swellability of the formed gel which could be related to increasing of the free radicals and macroradicals amount which brings about PVP crosslinking as well as CP grafting with PVP reactions [29-33]. Beyond the ratio of 100%, within the range

studied, a marginal variation in extents of both nominated properties was observed reflecting the faster rate of termination that exceeds the initiation rate [34-38].

3.2.2. Polymersconcentration

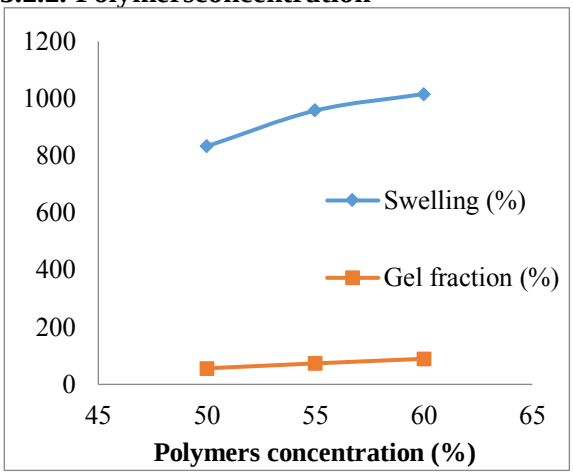


Figure 2: Effect of polymers concentration on percent swelling and gel fraction of CP/PVP gel.

PVP MW, 40,000; APS/polymers weight ratio, 100%, CP/PVP weight ratio, 30%;reaction temp., 90 ^{O}C; reaction time, 45 min. Swelling properties was assessed at pH 5 and 25 ^{O}C.

Figure 2 shows the effect of PVP solution concentration on the CP/PVP matrix percent swelling and gel fraction properties. Obviously, the foregoing properties extents of the formed gel increase gradually by increasing the PVP concentration to 60% which could be associated with the availability of that polymers molecules in vicinity of each other that in turn enhances molecular collisions of reactants and thereby the gel formation.

The higher increase in PVP concentration practically is difficult due to incomplete solubility of PVP as well as the liquid amount is insufficient for complete wetting of CP [34-38].

3.2.3. Reaction time

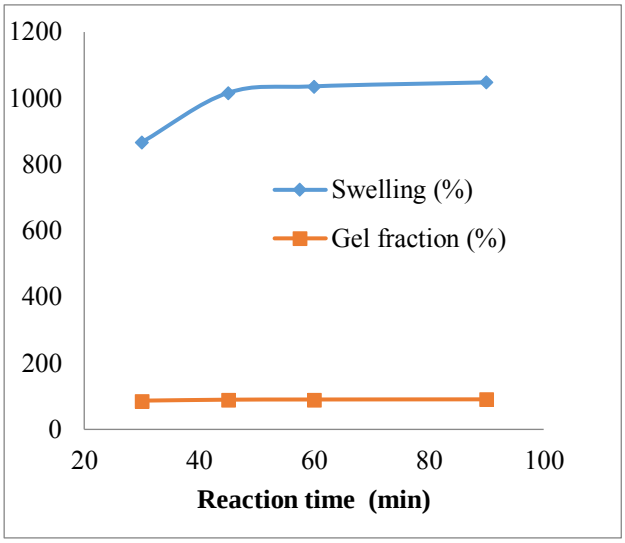


Figure 3: Effect of reaction time on percent swelling and gel fraction of CP/PVP gel.

PVP MW, 40,000; APS/polymers weight ratio, 100%; polymers conc., 60%; CP/PVP weight ratio, 30%; reaction temp., 90^{O}C. Swelling properties was assessed at pH 5 and 25 ^{O}C.

Figure 3 shows extents of the swelling and gel fraction properties of CP/PVP gel as a function of the reaction time. Obviously, both the percent swelling and gel fraction of the CP/PVP gel exhibits ascending trend during the first 45 min which could be explained by the presence of both polymers and initiator at higher concentrations offering the opportunity to form a tighter gel after 45 min.

The longer time than 45 min, within the range studied, has practically no impact on extent of the foregoing properties which could be attributed to the depletion in the reactants molecules as well as increasing of the reaction medium viscosity that indeed hinders further reactions [34-38].

3.2.4. Reaction temperature

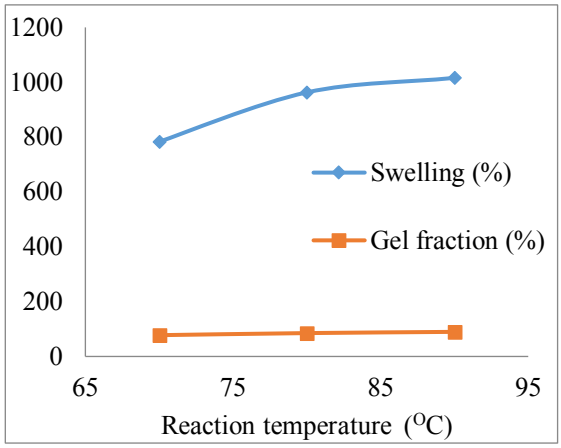


Figure 4: Effect of reaction temperature on percent swelling and gel fraction of CP/PVP gel.

PVP MW, 40,000; APS/polymers weight ratio, 100%, polymers conc., 60%; CP/PVP weight ratio, 30%; reaction time, 45 min. Swelling properties was assessed at pH 5 and 25 ^{O}C.

Figure 4 reveals the effect of reaction temperature (70 – 90 ^{O}C) on swelling as well as gel fraction properties of the CP/PVP gel. The results shows that extents of the aforementioned properties were significantly promoted by the progresive increasing of the reaction temperature, within the range studied, which can be interpreted in terms of the faster rate of $(NH_4)_2S_2O_8$ decomposition into free radical species as well as increasing of the reactants molecules mobility which would certainly enhance the PVP crosslinking reaction effeciency [34-38].

3.2.5. CP/PVP ratio

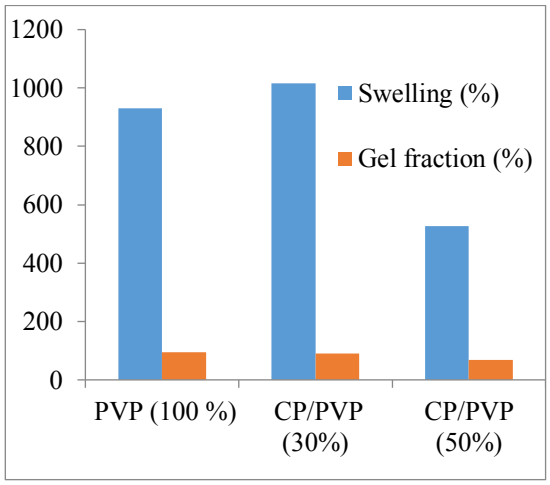


Figure 5: Effect of CP/PVP weight ratio on percent swelling and gel fraction of CP/PVP gel.

PVP MW, 40,000; APS/polymers weight ratio, 100%, polymers conc., 60%; reaction temp., 90 ^{O}C; reaction time, 45 min. Swelling properties was assessed at pH 5 and 25 ^{O}C.

The effect of CP/PVP ratio on swellability as well as gel fraction of the formed CP/PVP network is illustrated in Figure 5. It is clearly seen that incorporation of CP in the reaction medium with a ratio of 30%, based on weight of PVP, significantly enhances swellability but decreases gel fraction of the formed gel reflecting the higher CP swelling properties, with respect to the crosslinked PVP, as well as the decreasing in effeciency of the PVP crosslinking reaction. Higher ratios than 30 and up to 50%, brings about a worthy decreasing in extents of the foregoing properties suggesting the reduction in molecular collisions of PVP thereby decreasing the opportunities to be crosslinked [34-38]

3.2.6. Substrate type

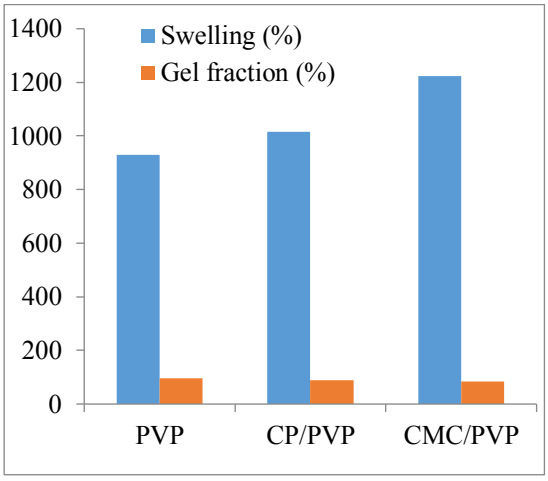


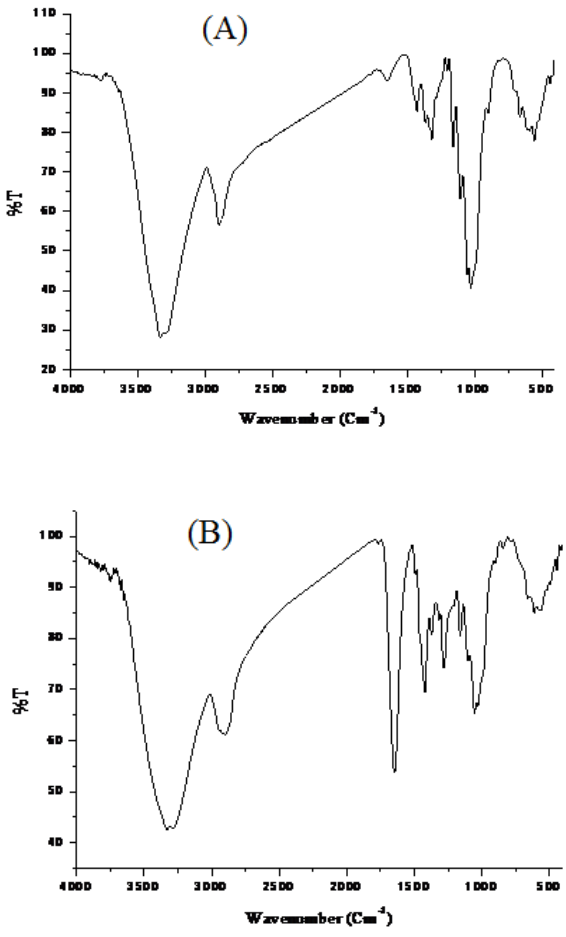
Figure 6: Effect of substrate type on percent swelling and gel fraction of the formed gels.

PVP MW, 40,000; APS/polymers weight ratio, 100%; polymers conc., 60%; substrate/PVP weight ratio, 30%; reaction temp., 90 ^{O}C; reaction time, 45 min. Swelling properties was assessed at pH 5 and 25 ^{O}C.

The effect of inclusion of CP or CMC in PVP crosslinking reaction on swelling and gel fraction properties of the formed gels is clearly shown in Figure 6. It is clear that: i) incorporation of either of CP or CMC in the PVP crosslinking reaction medium results in an upgrading in the formed gels swellability, compared to the crosslinked PVP, ii) swellability of the aforementioned formed gels can be arranged as follows: CMC/PVP > CP/PVP > PVP, and iii) oppositely to percent swelling, the gel fraction of such gels can be arranged as follows: CS/PVP < CG/PVP < PVP. The foregoing arrangements can be attributed to the differences among such polymers with respect to their chemical structure, molecular weight, degree of solubility, mode of interaction, and polarity [39, 40].

3.3. Characterization of the prepared gels

3.3.1. IR analysis



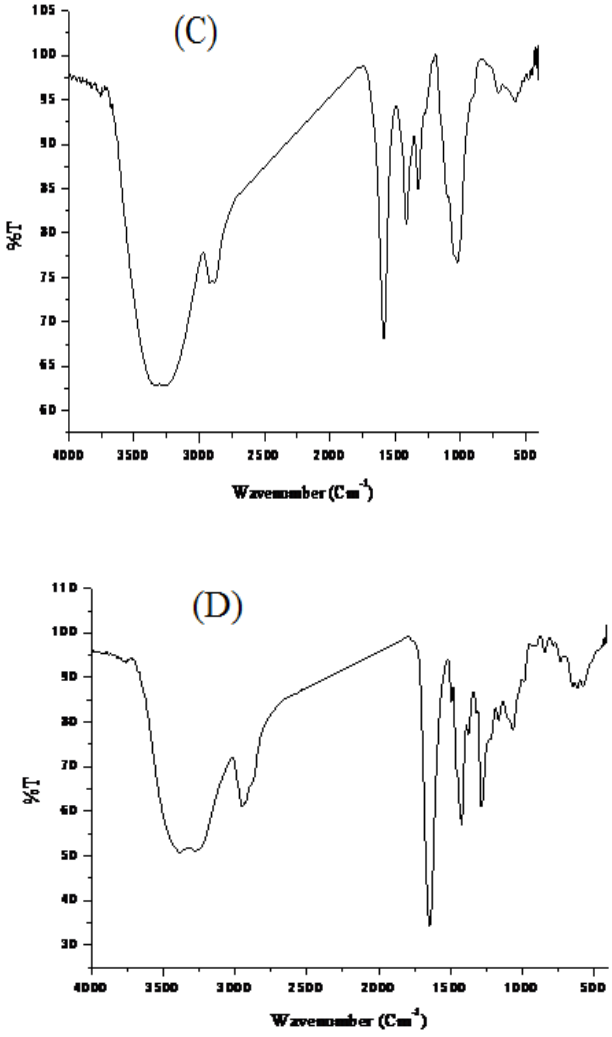


Figure 7: FTIR of (A) CP, (B) CP/PVP gel, (C) CMC, and (D) CMC/PVP gel.

Figure 7 (A) - (D) shows FTIR spectra of CP, CP/PVP, CMC, and CMC/PVP respectively. It is clear that Figure 7 (A) includes peaks at at 3334 cm^{-1} corresponding to –OH stretching of cellulose, a peak at 2900 cm^{-1} corresponding to C-H stretching vibrations, and at 1026 cm^{-1} corresponding to glycosidic linkage [18,19] whereas Figure 7 (B) includes the aforementioned peaks in addition to a strong

peak at 1644 cm^{-1} corresponding to stretching vibration of C=O group of PVP which confirms the formation of the CP/PVP gel matrix. On the other hand, Figure 7 (C) includes peaks at at 3311 cm^{-1} corresponding to –OH stretching of CMC, a peak at 2900 cm^{-1} corresponding to C-H stretching vibrations, a weak peak at 1762 cm^{-1} corresponding to C=O group of carboxylic acid, a peak around 1590 cm^{-1} corresponding to asymmetrical stretching vibrations of COO^- groups, and at 1026 cm^{-1} corresponding to glycosidic linkage whereas Figure 7 (D) includes the same peaks presented in 7 (C) in addition to a strong peak at 1644 cm^{-1} of PVP that overlaps with the asymmetrical stretching vibrations of COO^- groups at 1590 cm^{-1} which confirms the formation of the CMC/PVP gel matrix [18,19,34,35].

3.3.2. SEM of CP/PVP and CMC/PVP gels

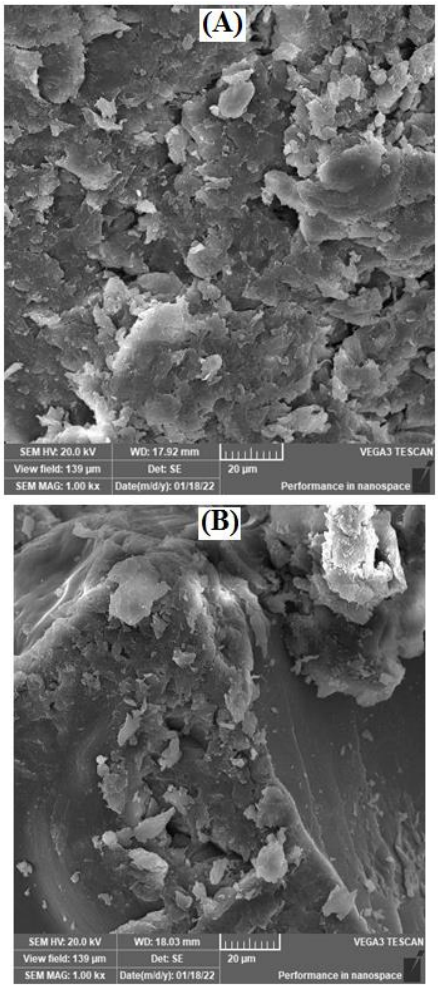


Figure 8: SEM images of (A) CP/PVP and (B) CMC/PVP gels.

The morphology of CP/PVP and CMC/PVP matrices is shown in Figure 8 (A) and (B) respectively. It is obvious that both of that gels have a sponge –like structure containing the crosslinked PVP as well as CP or CMC structures, all in state of entanglement.

3.4. In vitro releasing of sodium diclofenac

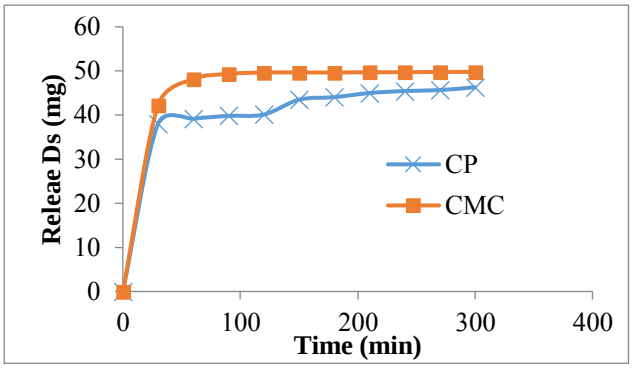


Figure 9: Drug release of sodium Diclofenac at pH 7; (A) CP/PVP and (B) CMC/PVP gels.

The release profiles of sodium diclofenac form the loaded CP/PVP and CMC/PVP gels at pH 7 are represented by Figure 9. It is clearly seen that releasing of sodium diclofenac from CMC/PVP reached a plateau value after about 2.0 hours, whereas the CP/PVP hydrogel continued to release the drug for 5 hours, within the range studied. The matter that can be associated with the differences between such matrices in their amorphousity as well as the ionic interactions between them and the drug molecules. In other words, the repulsive electrostatic interactions between the carboxylic groups of CMC and the drug molecules bearing carboxyl groups and chlorine atoms facilitate releasing of sodium diclofenac from the CMC/PVP gel with a higher extent compared to the CP/PVP gel [43-50].

3.5. Conclusions

- CP/PVP and CMC/PVP gels were prepared at optimal reaction conditions of PVP molecular weight (40000 Dalton), PVP concentration (60%), APS/PVP weight ratio (100%), reaction

time (45 min), reaction temperature (90 ^{O}C), as well as CP/PVP or CMC/PVP weight ratio (25%).

- Such gels were characterized by FTIR as well as scan electron microscope analysis.
- The release profiles of SD form either CP/PVP or CMC/VP hydrogels at pH 7 were investigated.

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