FABRICATION OF TEMPERATURE AND pH SENSITIVE BIOPOLYMER/CLAY BIOCOMPOSITE AS DRUG CARRIER FOR RANITIDINE – HCl

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ABSTRACT

The scientific studies on drug delivery systems that transport drugs to the targeted tissues, at a certain rate and desired time intervals, have gained popularity. The main goal of the drug delivery and release systems is to maintain the drug level in the blood plasma by balancing the amount of active ingredient. In this study, pH and temperature sensitive drug carriers were prepared using chitosan as a biopolymer and clay as a natural material. The characterization of the prepared materials was performed for structural analysis by FT-IR and for morphological analysis by SEM instruments. The swelling properties of the prepared materials were investigated. In this work, Ranitidine-HCl was used as a model drug. The prepared drug carriers were first loaded with Ranitidine-HCl and release properties of the materials were investigated at two different temperatures (25ºC, 37ºC) and various pH medium. The data obtained from the experiments indicated that the maximum release of Ranitidine–HCl from the prepared sample was observed at pH=7,6 buffer solution at both temperatures by comparing buffer solutions. It has been shown that the materials prepared in this study are suitable carriers for the Ranitidine-HCl drug active ingredient.

Keywords: Drug carrier, controlled release, clay, Ranitidine-HCl, drug release kinetics.

INTRODUCTION

The use of polymers in drug delivery systems has gained importance in scientific studies. However. Due to the problems such as inability of the adaptation to the body, disintegration problem after finishing its

function etc. scientists have turned to polymers produced from biological raw materials in their scientific research (Valderruten,Valverde, Zuluaga, & Ruiz-Durántez, 2014). Therefore, biopolymers are considered as the most promising materials for the purpose of using in tissue engineering processes (Biswal, 2021).

Many studies on drug delivery have been carried out to date, but these studies have not yet completed their development process and are still a potential source of hope that can be the answer to future expectations in the field of medicine (Fu et al., 2021; Jeong, & Gutowska, 2002). The primary aim of these studies on controlled drug release systems is to minimize the dose of the drug, to prolong the use of the drug, to prevent the patient from harmful and side-effects of the drug and to increase the quality of life. Controlled drug release systems have gained importance in every field of medicine (especially oncology, endocrinology and cardiology) in a short time (Rodrigues Filho et al., 2011). Zhao and Li prepared the drug carriers in their work using biodegradable microcapsules produced from biopolymers. They have achieved successful results in controlled release systems in reducing the systemic side effects and increasing the efficiency of the drug with biodegradable microcapsules (Zhao, & Li, 2008). Rafati and co-workers prepared the drug carriers based on poly(ethylene glycol) (PEG) and silica (SiO_2) controlled release of enroflaxacin which was shown as drug-PEG-SiO_2 (Rafati, Ebadi, Bavafa, & Nowroozi, 2018). Liu et al. have studied pH-sensitive amphiphilic hydrogel with interpenetrating polymer networks (IPN structure). They showed that the release of N-acetyl-5-methoxytryptamine (melatonine, MEL) from IPN was sensitive to chance in pH (Liu et al., 2006). Kamoun and his co-workers worked on poly(vinyl alcohol/sodium alginate cross-linked membranes for wound dressing process. They characterized prepared materials and bio-evaluated their system (Kamoun, Kenawy, Tamer, El-Meligy, & Mohy Eldin, 2015).

Recent advances in the drug loading and delivery systems require more effective drug carriers which are stimuli-responsive drug release. Organic and inorganic hybrid materials as biopolymers and clay minerals produced with excess of new properties. Such polymers with sensor feature that can respond to external stimuli are called stimulus-sensitive polymers or smart polymers. Advanced drug delivery applications need sophisticated drug carriers to respond to environmental or biological stimuli (LeBaron, Wang, & Pinnavaia, 1999). pH-sensitive systems contain functional groups that ionize and respond to pH changes in the environment. Acidic and basic functional groups in their structure ionize and form an electrical charge as positive or negative charge. These electrostatic forces repel each other, and as a result, liquid enters the cross-linked structure, and the polymer swells.

In this work, pH and temperature sensitive drug loading and release materials from biopolymers and natural material such as clay, were prepared. The swelling properties of the prepared materials in buffer solutions at different pHs were observed.

MATERIAL AND METHODS OF WORK

Materials

Chitosan was purchased from Sigma Aldrich, Acrylic acid (AA) was obtained from Prochema; Bentonite clay was obtained from Anatolia, Turkey. Acetic acid, KPS and HNO_3 were supplied from Merck. Ranitine-HCl drug active agent ($C_{13}H_{23}ClN_4O_3S$) was from a drug company and the structure is given in Figure 1.

Figure 1. Chemical structure of Ranitidine HCl.

Preparation of drug carrier (Chitosan/PAA/Clay)

Chitosan (1 g) was dissolved in 60 ml acetic acid solution (1%v) at 65 ºC. The polymer initiator (KPS 1%) and Acrylic acid (4.5 g) were added to the mixture and stirred for 1 hour. After adding the crosslinker, the modified clay (0.2 g) was added to the homogenous solution and was poured into a Teflon petri dish and dried until it reached constant weight.

The modification process of bentonite was performed by HNO_3 (2 %). For this purpose, 10 g bentonite was mixed with 200 ml HNO_3 (2 %) solution for 2 hours. This solution was first filtered and washed with distilled water. The filtrated bentonite was then dried in an oven at 80 °C for 24 h.

The characterization of the prepared sample

The characterization studies of the prepared materials were performed by using FT-IR and SEM instruments. FTIR spectroscopy was conducted using Thermo Nicolet IS-10 instrument and the Spectrum was recorded in the wavelength region of 4000 to 400 cm^{-1}. The morphology of the sample was studied by SEM ((ZEISS EVO LS10). The samples were first coated with gold.

The swelling behavior of the sample was compared in different media as pH=2,0; pH=7,6 buffer solutions and in distilled water (pH=6,5).

Drug release studies of the Ranitidine-HCl delivered samples were examined at two different temperatures and different pH solutions.

RESULTS AND DISCUSSION

The aim of this research was to develop a controlled delivery system containing Ranitidine-HCl the release of the drug was performed at different pH and temperatures. The characterization of the sample was studied. Fig. 2 represents FTIR results of clay and Chitosan/PAA/Clay.

FT-IR spectrum of the (KTS-g-PAA)/Clay sample showed that the H-O-H absorption band due to vibration in the clay observed around 1633cm^{-1} was overlapped with the -NH peak seen 1640 in KTS-g-PAA. The -COOH stress peak in the sample can be observed at 1714cm^{-1}. The peaks in clay observed between the 1000-792cm^{-1} range showed the -OH bending vibrations and Si-O peaks in the tetrahedral and octahedral structure of the clay. These peaks can also be seen in the sample as slightly shifted to the left (Figure 2).

The morphological structure of the prepared sample was examined by SEM (Figure 3).

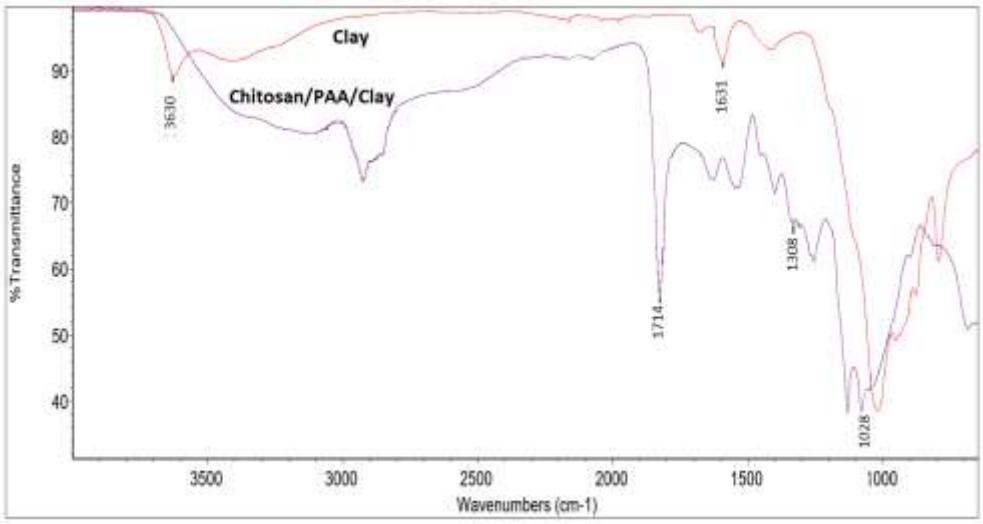

Figure 2. compares Chitosan/PAA/clay prepared material with clay.

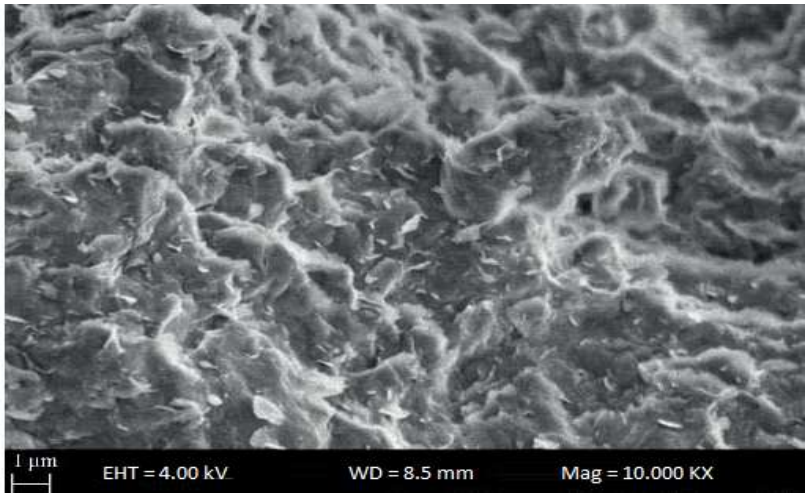

Figure 3. SEM migrograph of Chitosan/PAA/clay.

It was seen the homogeneous and smooth structure of the prepared sample. No clustering was found in the structure of the sample.

Fig. 4 shows the comparable studies of the swelling behavior of the Chitosan/PAA/clay sample.

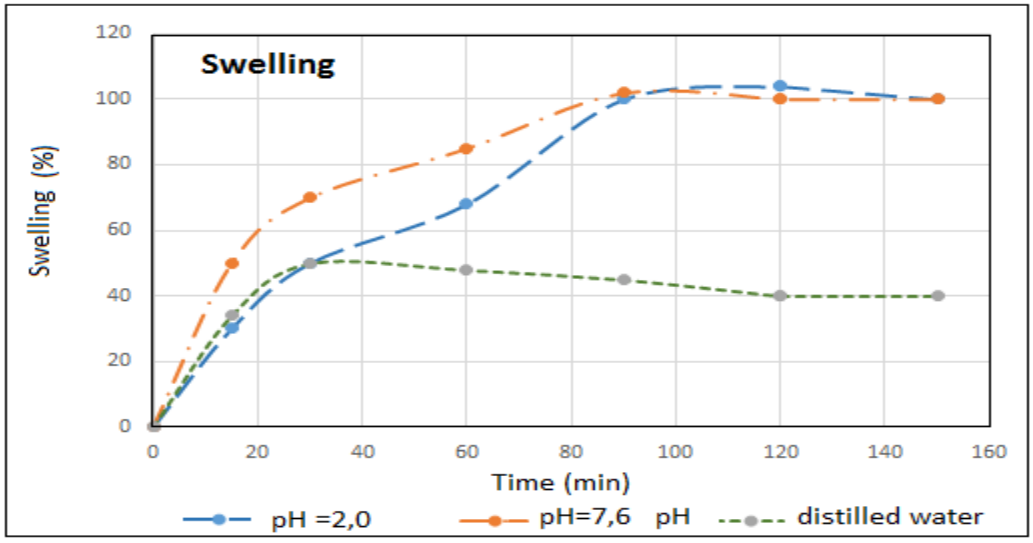

Figure 4. The swelling of Chitosan/PAA/clay at different media.

The highest swelling value was initially observed in pH:7.6 buffer solution. But maximum swelling was 100% for the both buffer solutions.

Figure 5. shows the release percentage of the drug at pH 2.0 and 7.6 buffer solutions and the distilled water.

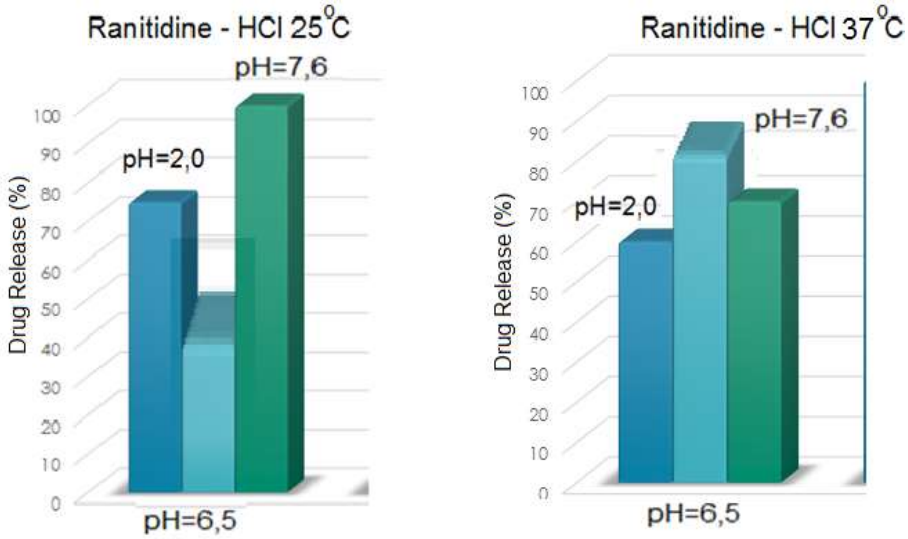

Figure 5. The release percentage of Ranitidine HCl at different pH solutions and 2 different temperatures.

The releasing of Ranitine- HCl from the prepared material is sensitive to temperature and pH as seen in Fig.5. By comparing the buffer solutions, the maximum release of the drug was observed in pH=7.6 at both temperatures (25ºC and 37ºC). The time reaching to the equilibrium (in pH=2.0 buffer solution) of the release process was 240 min. But for the buffer solution at pH=7.6 the equilibrium time was found 150 min which is shorter than the acidic medium.

CONCLUSIONS

In this work, biocomposite intended for drug delivery systems was prepared from chitosan, acetic acid and modified bentonite clay. FTIR spectra showed incorporation of clay into chitosan clay. SEM micrographs showed no clustering. Swelling studies showed good swelling properties for the both buffer solutions (pH = 7.2 and pH = 2). The drug release kinetics of Ranitine- HCl from the prepared material showed that this material is sensitive to temperature and pH. All results confirmed that the prepared material is suitable as drug carrier for the Ranitidine-HCl as active substance.

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