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Research Article

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Iron-oxide Nanoparticles Modified by Copper-Organic Framework as Carrier for Naproxen Drug Delivery

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ABSTRACT

In this research, a method was presented for synthesizing magnetic nanoparticles and modifying them with a new group of porous nanomaterials. Initially, Iron oxide nanoparticles were prepared by co-precipitation method which modified by (3-aminopropyl) trimethoxysilane in toluene, followed by stabilization by the Cu-Benzen 1,3-dicarboxylic acid (BDC) metal-organic. The product examined for structural properties using infrared Fourier spectroscopy (FT-IR), powder X-ray diffraction (PXRD), thermal gravimetric analysis (TGA), elemental analysis (EA), vibrational sampling magnetometer (VSM), and field-emission scanning electron microscopy. The operational parameters like pH, absorption time, and the adsorbent capacity determined the naproxen content in human urine which successfully extracted and determined by HPLC. Moreover, the adsorption process examined by three isotherms models of Langmuir, Freundlich, and Temkin. It was found that each gram of the synthesized adsorbent was able to adsorb 1.5 mg of naproxen. The average particle size of the synthesized adsorbent reported to be 20-50 nm. The loading capacity and the release kinetics in simulated gastric showed that both of these parameters were affected by the surface properties of the mesoporous silica material. Approximately 50% of naproxen was released in the simulated gastric fluid at pH=5 less than 5 minutes. Results of the absorption process of naproxen by Fe_3O_4/Cu (BDC) were congruent with the results of Higuchi model, one of the drug release theories from a degradable surface.

Keywords: Magnetic nanoparticles; Copper-organic framework; Naproxen; Drug delivery

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INTRODUCTION

Naproxen is used to relieve pain from various conditions such as headaches, muscle aches, tendonitis, dental pain, and menstrual cramps. It also reduces pain, swelling, and joint stiffness caused by arthritis, bursitis, and gout attacks. This medication is known as a nonsteroidal anti-inflammatory drug (NSAID). It works by blocking the body's production of certain natural substances that cause inflammation. The structure and preparation of chemical structures used in medicinal consumption are only part of the battle against diseases. Maintaining the drug concentration in blood and other bodily fluids in suitable values and time are among the crucial issues in controlled drug release systems. Indeed, in order to maintain the concentration of drug in plasma within desirable levels,

sometimes it is needed to use the medication several times a day. This, in turn, causes the drug not to have the desired effect and even bring about further side effects [1]. The first controlled drug release systems were produced in the early 1970s. Since then, such systems have been attracting a great deal of attention [2,3]. One of the vital features in drug release systems is predictable rate independent of the releasing environment. Maintaining the drug concentration levels within the desired limit, requiring direct usage of drug, and greater compliance in the patient, as well as diminished sided effects, are the advantages of controlled-release drug delivery systems [4,5]. The kinetics of drug release is of significance in the technological development of drug release in the body, which depends on various factors including heat, pH, relative humidity, enzyme, and physicochemical properties of their carriers [6,7]. Target full transfer of drug with the aims of prolonging the drug presence time, decreasing toxicity, and enhancing the drug half-life has led to significant improvements in pharmacologic treatments. This is thanks to pharmacokinetic changes in the drug in nano-based drug delivery systems [8]. Among the advantages of magnetic nanoparticles for medical applications are the size, remote controllability, and resonance reaction to field variations [9]. One of the imperative reasons that have given biomedical uses to magnetic nanoparticles is their biocompatibility. In many *in vivo* and *in-vitro* investigations, these particles have shown little toxicity. Coated nanoparticles enjoy less toxicity not only due to presence of biocompatible coating but also because of fewer attachment sites for proteins, ions, and other components [10]. When compared with heavy metal-based nanoparticles, magnetic nanoparticles have less toxicity, and even in some cases, they are regarded as nontoxic. The nanoparticles that have part of the body's physiological iron, their iron oxide content is metabolized and stored by Ferritin-transferrin and Hemosiderin protein [11].

Three-dimensional coordination polymers which have permanent pores and are known as Metal-Organic Frameworks (MOFs) are more of interest. This is because it is possible to incorporate many molecules in their networks for various applications. Selection of metal ions or secondary structural units not only can result in topological diversity, but also the pores present in walls can be programmed for various uses [12,13]. Regular porous networks which bring about accurate control of drug loading and reduction of kinetic effects, the high volume of pores for trapping of drug, high surface area which develops a high potential for drug adsorption, and functionalizing active surface using functional groups for loading and releasing drug, are among the most important uses of MOFs in drug releasing systems [14,15].

In this research, we used Fe_3O_4-Cu (BDC) for delivery of naproxen drug, one of the non-steroidal anti-inflammatory drugs and a potent cyclooxygenase enzyme inhibitor. The purpose of this study was to synthesize nanoparticles and modifying them with metal-organic framework that was studied for adsorbing naproxen in a simulated gastrointestinal medium. The particle composition size and morphology can be easily tuned to optimize the final particle properties

EXPERIMENTAL

Reagent and Instrument

Tetraethyl orthosilicate (TEOS), $FeCl_3.6H_2O$ and $FeCl_2.4H_2O$, and copper acetate were purchased from Merck (Germany). Ammonia aqueous (25 wt.%), and (3-Aminopropyl) trimethoxysilane (APTMS, 99%) were obtained from Sigma Aldrich (Germany). The rest of reagents were as a minimum of analytical grade. Elemental analyses (C, H, N) were determined with ECS400 Costech (Italy), IR spectra were recorded as KBr pellets on Spectrum 100 Fourier transform infrared (FT-IR) from Perkin company (USA). Field-emission scanning electron microscope (FE-SEM) images were recorded on MIRA3LMU from TESCAN Company (Czech Republic). Thermogravimetric analysis (TGA) was used to evaluate thermal stability and was carried out between 20 and 600°C under nitrogen atmosphere using a 209F1-NETZCH Company (Germany). The structure and morphology of Fe_3O_4-Cu (BDC) nanoparticles were identified by powder x-ray diffraction (PXRD) XRD 360 kV, 25 mA, 5 to 80° D5000 SIEMENS

Figure 6: pH impact on the adsorption of Naproxen onto Fe_3O_4/MOF

Figure 7: kinetics of naproxen sorption process on Fe_3O_4/MOF

Isotherm Studies

The following equation has been used to calculate the amount of naproxen at equilibrium q_e (mg g^{-1}) on Fe_3O_4-MOF Cu (BDC):

$$q_e=(C_o-C_e)\ V/W$$

C_0 and Ce (mg L^{-1}) are initial and equilibrium concentrations of the naproxen, V (L) is the solution volume, and W (g) is the mass amount of the Fe_3O_4-MOF, q_{max} is the maximum capacity of adsorbed Naproxen which is equal to the entire monolayer coating the adsorbent surface (mg g^{-1}).

Langmuir isotherm represents homogeneous monolayer adsorption into a mall removing the interactive effects of adsorbed molecules. Its equation is as follows:

$$C_e/q_e=(l/q_{max}K_L)+(C_e/q_{max})$$

K_L is Langmuir constant (L mg^{-1})

R_L is the main concept in Langmuir's equation which expressed by the dimensionless separation factor

$$R_L=l/(l+K_LC_0)$$

R_L can have four values each referring a different state: $R_L=0$, irreversible adsorption; $R_L=1$, linear adsorption; $0<R_L<1$, desirable adsorption; and $R_L>1$, undesirable adsorption (with $R_L=0.71$ indicating desirable adsorption) for naproxen sorption are listed in Table 2.

Freundlich isotherm assume a heterogeneous surface with a non-uniform distribution of adsorption heat on the surface, which is an experimental isotherm. Freundlich predicts that the concentration of material increases on the adsorbent surfaces when the concentration of material grows in the solution. The heterogeneity factor is stated by 1/n and calculated using the following empirical equation:

direction, inflation and the gradation of matrix is negligible, and permeability of the drug is constant [18,19] (Figure 8).

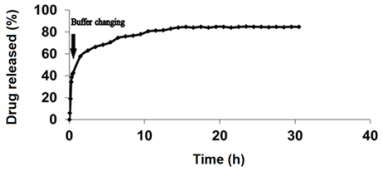

Figure 8: Unloading profile for naproxen in simulated intestinal fluid with pH value of 7.4 and in simulated gastric fluid with pH value of 1.2

CONCLUSION

This study reports high chemical stability and properties efficiency for sorption of Naproxen. In this research, by stabilizing copper metal-organic framework on to iron oxide nanoparticles, the level of adsorption of this compound was maximized and reached the highest possible adsorption, the as-synthesized MOF (Fe_3O_4-Cu (BDC)) offers several sites attached to the adsorbent body. In this way the adsorption capacity has increased significantly. The drug release study perfectly shows the fast release of drug in gastric area and total gently unloading of drug in the intestine area. Finally, the values for method application demonstrates the excellent reproducibility and repeatability parameters of the suggested technique.

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