RESEARCH ARTICLE

Preparation of Bentonite Clay/TiO_2 Nanocomposites Surface as Drug Carrier: *In-vitro* Release Study of Chloramphenicol Drug

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ABSTRACT

The delivery of pharmaceuticals via nanocomposites has become a fascinating area of study in recent years, with applications in the development of tools and the treatment of infections and cancer. The porous properties of titanium dioxide and clay nanocomposites play a key role in the targeted delivery system. So, the large surface area and porous volume have more interest in the delivery of drugs and their loading. In this study, bentonite clay and titanium dioxide (TiO_2) nanocomposites were synthesized by a hydrothermal method to guide infections and drugs. The composites of nanocomposites were used by the adsorption technique as loading drugs and studied for their ability to deliver drugs. It was confirmed that titanium oxide was added to the bentonite clay through the EDX and XRD. Sharp diffraction values were observed by the X-ray spectrum for clay and titanium oxide and less intensity for the superimposed (TiO_2/bentonite), While it was found that EDX spreads the titanium and other ions. The thermal stability of the composite (TiO_2/bentonite) was increased after adding titanium dioxide nanoparticles. The removal rate of chloramphenicol was higher in the base media, reaching 98% for both bentonite and TiO_2/bentonite. An examination of the release rate of the drug was carried out by bentonite clay and TiO_2/bentonite in the stomach and blood media, and the percentage of release was 26.6 and 5% in pH 1.2 and 7.5 for bentonite and 54.6 and 23.6% in pH 1.2 and 7.5, respectively, for TiO_2/bentonite.

Keywords: Nanocomposite, TiO_2, Clay, Adsorption, Drug delivery, Chloramphenicol drug.

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INTRODUCTION

Natural and inorganic clay known as bentonite contains a variety of minerals, including quartz, zeolite, beidellite, and montmorillonite. Bentonite has been a top choice for creating controlled drug delivery systems because it interacts with drug molecules aggressively and delays their subsequent release. Bentonite's most important component is the lamellar sheet structure of montmorillonite, which contains exchangeable cations between the layer.[1] The bentonite clay acquires a net negative charge as a result of the substitution of cations (such as Si^{4+}, Al^{3+}, and Mg^{2+}) between the nano clay sheets.[2] The existence of MMT sheets accounts for the physical characteristics of bentonite, such as its high swelling and adsorption capability. Researchers are very interested in (MMT) because of its abundance, affordability, nontoxicity, and environmental friendliness.[3] Numerous research studies have demonstrated how adding bentonite as a filler ingredient enhances the mechanical and thermal properties of the resulting polymer nanocomposite systems.[4]

The main elements that make TiO_2/clay nanocomposites extremely active are their high porosity, high surface area, and the existence of highly active sites. Compared to TiO_2 that is commercially available TiO_2/clay nanocomposites tend to load and release various chemical molecules and medications more actively. The exchangeable cations also correct the charge imbalance and lead to the intercalation of TiO_2 NPs. On the surface of the bentonite, they include the ions calcium (Ca), sodium (Na), and potassium (K).[7] Due to this distinctive property of Bent, various cationic inorganic materials can be effectively intercalated to the adsorbent surface and interlayers to produce an active nanocomposite.[5]

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Drug delivery (DD) based on controlled release technology was first studied in the 1970. These devices are made to: (i) maintain the drug's therapeutic action in the plasma, (ii) extend and control the drug's release time in the body; (iii) regulate the drug's location *in-vivo* at a particular target tissue or organ and (iv) should be mechanically durable, able to hold a high drug dosage, biodegradable, and non-toxic. So, modern drug delivery techniques include a variety of carrier matrices, including polymers, nanoparticles, liposomes, dendrimers, and porous materials like mesoporous materials and bentonite nanocomposites.[6-8]

Per the description above, our goal was to create bentonite clay with titanium dioxide (TiO_2) added as reinforcement. The use of bentonite/TiO_2 composites as drug delivery systems in novel methods has been the subject of research. Spectroscopy (UV-vis), electron dispersive spectroscopy (EDX), thermogravimetric (TGA), and field emission scanning electron microscopy (FESEM) were used to analyze the physicochemical characteristics of the produced composites. The release of chloramphenicol from bentonite composite and bentonite/TiO_2 composite matrices was evaluated using the *in-vitro* drug diffusion study.

MATERIALS AND METHODS

Calcium-Bentonite used in this study was obtained from Iraq; Titanium dioxide (TiO_2), hydrogen peroxide (H_2O_2), and chloramphenicol drugs were purchased from Sigma-Aldrich, Germany.

Preparation of Acid-activated Bentonite Clay

Before drug delivery, the bentonite clay was purified by removing organic impurities using H_2O_2 solution. Bentonite Clay was obtained from the geological survey in Iraq. In a flask, a 20 g sample of bentonite clay was soaked in 0.1 N HCl acid in 100 mL of water for 24 hours at 25°C. The acid-activated sample was washed thoroughly several times with distilled water until the pH reached 7 and dried at 65°C in an oven. The bentonite was purified, crushed in mill, and sieved to achieve a particle size of 100/150 mesh.

Preparation of Clay/TiO_2 Composite

A composite (clay decorated with TiO_2) was prepared using a hydrothermal method. In 5 g of TiO_2 in 20 mL of distilled water and 2 g clay in 20 mL of distilled water were mixed, then 100 mL diluted to with distilled water and mixed for 30 minutes to get the required solution. The resulting mixes were autoclaved for 24 hours at 160°C. The produced white-brown precipitate was filtered, rinsed with distilled water, and dried for 24 hours at 80°C to obtain a fine powder. Then it was irradiated using ultrasound for 10 minutes. The radiation of the ultrasound process would increase the capacity for adsorption by aggregation and dispersion of particles.[9]

Characterization Methods

The characterizations of clay and clay/TiO_2 composites were behavior using several methods using several methods, such as Scanning electron microscopy (SEM), EDX, X-ray diffraction (XRD), TGA, DTA, and UV-visible Spectrophotometer. The a surface analysis was done in (MIRA3, Tescn, Czech Republic, and Iran) FE-SEM at 15.0 kV. The particle sizes were investigated by X-ray diffraction (XRD) on the XRD-6000, Shimadzu, Japan, using the X-ray source Cu/Kα1 at a wavelength of 0.15040 nm. The analysis was carried out at an angle of 2°, ranging from 5 to 80°. Thermal stability was monitored using Perkin Elmer (USA) (TGA 4000). All spectral analyses were done by the UV-1800 UV-visible (Shimadzu, Japan)

Protocol of Drug Delivery

The drug release of nanocomposites was examined between pH 1.2 and 7.4 and physiological temperature of 37°C in environments similar to gastric juice and blood to replicate the body's biological state. The amount of chloramphenicol in the buffer solution was measured using UV-vis absorbance (UV-1800, Shimadzu, Instrument Japan). Our earlier investigations used a similar method to prepare these buffer solutions.[10]

RESULTS AND DISCUSSION

FE-SEM- EDX Analysis

The results of the FE-SEM analysis of the surface morphology of bentonite, bentonite/TiO_2, and clay/TiO_2 loading drug in diameter of about 2 to 5 μm are shown in Figure 1. This Figure illustrates the various surface morphologies that bentonite exhibits in bentonite-TiO_2 composites.[11,12] The surface morphology of bentonite frequently resembles an aflake-like structure with a smooth surface in some of the particles, despite the addition of TiO_2 particles to create a bentonite-TiO2 composite (smaller TiO_2 grains on the outer face of bentonite), while clay/TiO_2 loading drug. The shape gave a smoother and softer surface due to the good distribution of particles. This shows that the clay/TiO_2 particles had a favorable surface for loading the drug's chloramphenicol.[13-15] The composite's considerable titanium content is revealed by the EDX spectrum as shown in Figure 2.

X-ray Diffraction Analysis

By XRD patterns were obtained to investigate the structures and composites of a. bentonite, b. TiO_2 and bentonite/TiO_2. The pattern of a. bentonite contains characteristic peaks at = 19.8, 24.1, 2, and 35.1, that can be indexed to (100), (200), (011), and (110) reflections, respectively, of the rhombohedral crystal structure of bentonite.[16] While the pattern of b. TiO_2 contains characteristic peaks at peaks 36.54 and 54.9 which are assigned to (101) and (211) planes, respectively[16] while in Figure 3 c Peak reduction is brought on by bentonite addition, which distorts the TiO_2 lattice and bentonite can obscure the growth of TiO_2,[17] and the peak corresponding to 26.4 in bentonite shifts to 26.3 (110) so With support of bentonite and titanium, the characteristic montmorillonite peak shafted to right and disappered some peaks.[18]

Thermo gravimetric analysis (TGA)

In Figure 4, shows TGA analysis results of clay, TiO_2, and clay/TiO_2, for TiO_2, a weight loss of 0.2–0.4 mg was observed

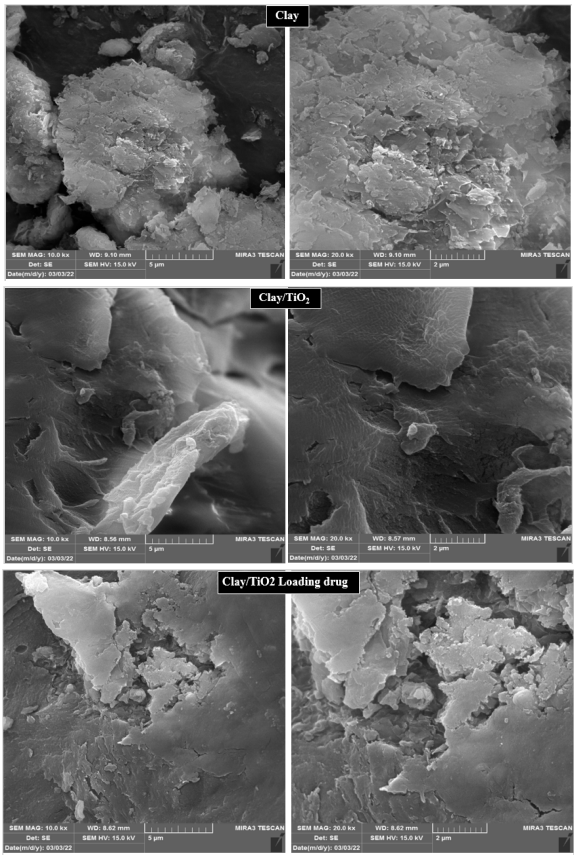

Figure 1: FE-SEM micrographs of Clay, clay-TiO_2, and clay/TiO_2 loading drug at different magnification powers (5 and 2 µm)

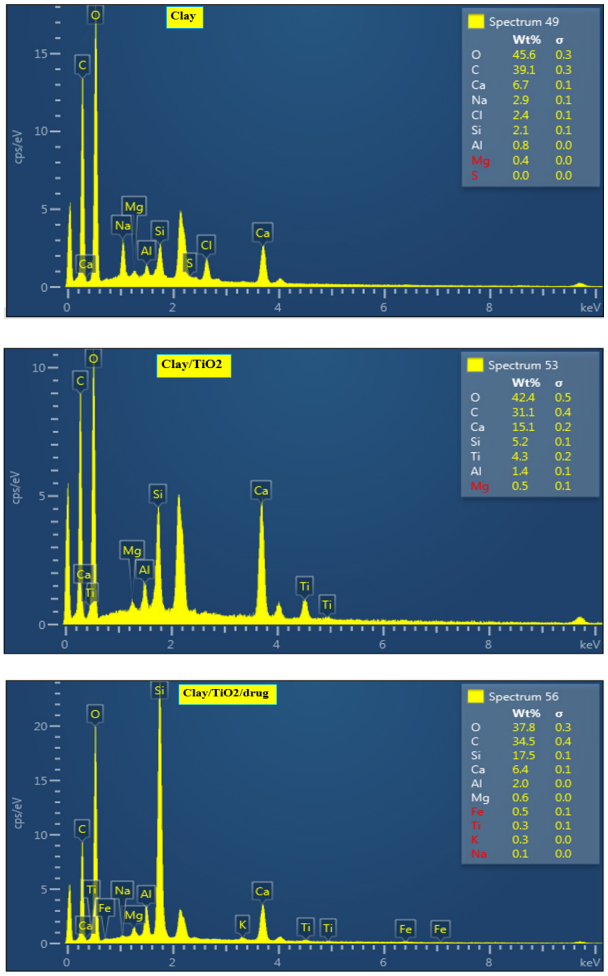

Figure 2: EDX spectra of clay, clay-TiO_2, and clay/TiO_2 loading drug

in range of temperature between 100 to 600°C because of the evaporation of loss of bound water on the nanocomposite. In bentonite clay, a weight loss of 6 mg was observed in range of temperature between 50 to 387°C due to the evaporation of water of crystallization. A slight weight loss (2.8 mg) was observed in range of 390 to 766°C due to the decomposition of bentonite clay.[19] In bentonite clay/TiO_2, there are three stages: the first stage, where the weight loss (0.39 mg) was observed in range between 25 to 200°C due to the evaporation of adsorbed water; the second stage, where the composites lost 2.38 mg in the range of 200 to 380°C because of water of crystallization and the third stage, where the weight loss was 1.98 mg at temperatures 380 to 575°C. Through TGA, it was found that the composite bentonite/TiO_2 is more stable than bentonite clay because of the specificity of the nanomaterial, which led to an increase in the stability of the overlay.[20,21]

Effect Weight and pH on Adsorption

In Figure 5 a, it is shown that the effective weight of the adsorption process is 0.1 g. The removal rate of the drug substance increases with the weight of the adsorbent, and on the other hand, the decrease in the amount of adsorption with the increase in the weight of the adsorbent surface can be attributed to the non-saturation of the adsorption sites of the surface during the adsorption process, in addition to the interactions that occur between the particles (such as the occurrence of agglomeration), which occurs When using high weights on the adsorbent surface. Such interference can lead to a decrease in the surface area of the adsorbent.[22,23] Different pH values (2, 3, 5, 7, 9, and 11) were used to study the pH effect on the adsorption of chloramphenicol drug onto clay and clay/TiO_2. Figure 5(b) depicts the relationship between chloramphenicol removal percentages and the initial pH values of the chloramphenicol solutions. It is clearly seen that the amount of drug removed at pH 2 and 3 is very little. In comparison with clay and clay/TiO_2 nanocomposites, they are excellent adsorbents for drug removal from large pH volumes of aqueous solutions at ranges of 5 to 11. Raising pH was anticipated for drug removal due to an increase in ion species, primarily neutral, that may be absorbed by hydrogen bonding and ion exchange.[24,25]

Drug Delivery

We can select nanocomposite to be used in simulated fluid of blood, it was tested for chloromphenicol release at pH 1.2 and 7.5. As can be seen in Figure 6, it was determined that the release of chloromphenicol from bentonite clay was pH-sensitive. So the medication was released significantly more quickly in pH 1.2 (simulated stomach juice) than it was in neutral settings. In comparison with bentonite/TiO_2, the

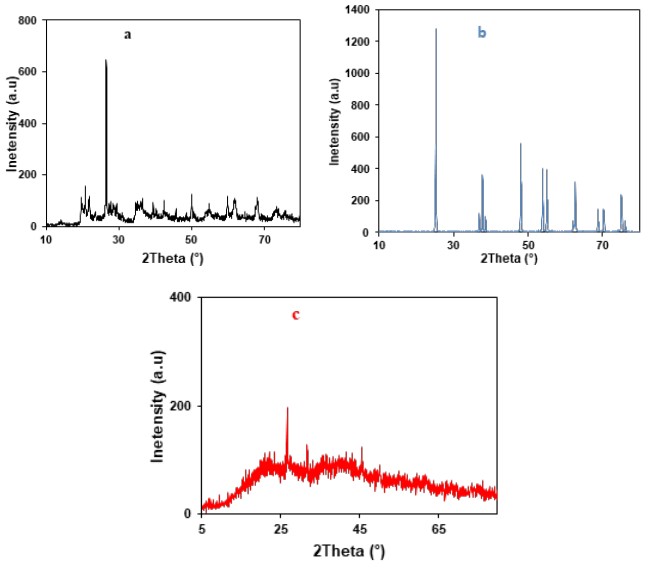

Figure 3: XRD patterns of a. bentonite, b. TiO_2, c. bentonite/TiO_2

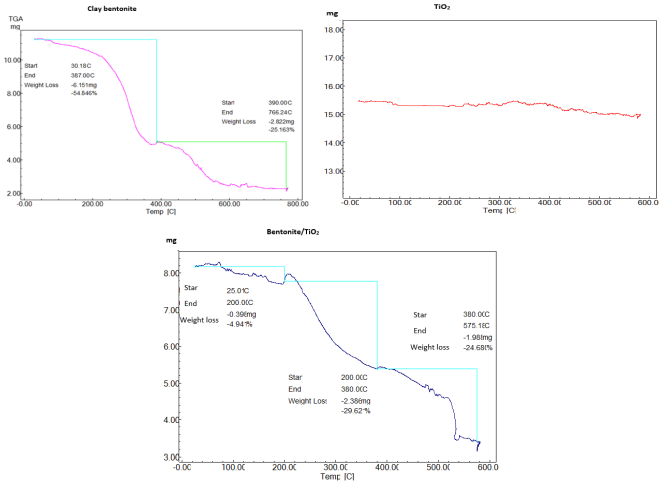

Figure 4: TGA of TiO_2, bentonite and bentonite/TiO_2

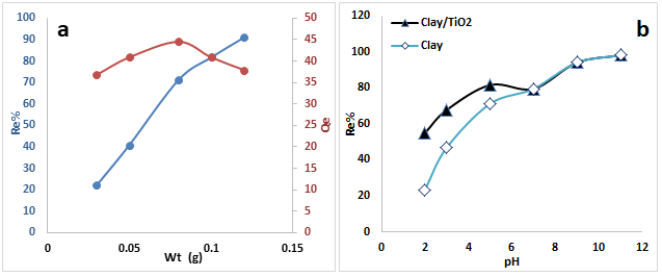

Figure 5: (a) The effect of weight adsorbate on the drug (Co = 50 mg/l, 60 min, pH= 7), (b) effects of pH on chloramphenicol drug adsorption (25ºC, 60 min, 0.1 wt).

release rate at pH 1.2 was lower than in neutral conditions.[1] So, the chloromphenicol release time at different pH levels (high and low) was different on different surfaces. As a result of a quick ion exchange between H+ and the medication, the findings revealed variations in drug release, especially at pH

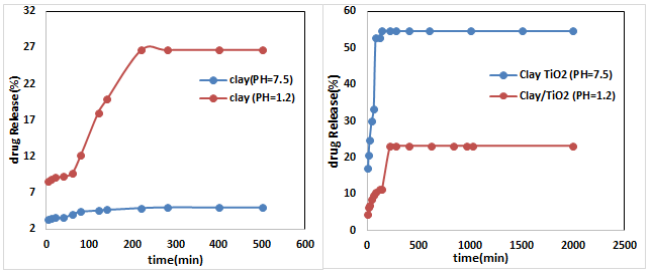

Figure 6: Cumulative Chloramphenicol release (%) at pH 1.2, and 7.5 (at 37ºC and wt = 0.1).

1.2 because the hydrolyzation of titanium dioxide in acidic conditions. Release was continued for 1 and 500 minutes for bentonite and 1 and 2000 minutes for bentonite/TiO2By using this method. This approach is suggested for the use of chloromphenicol orally since it could shield the drug from enzymatic digestion.[26,27]

CONCLUSION

Biocompatible and non-toxic bentonite and TiO_2 nanocomposite were prepared using a new synthesis method by a hydrothermal method in the bentonite matrix that has metallic ions. Incorporation of TiO_2 into the bentonite matrix significantly increased thermal stability, adsorption rate, and drug delivery in acid media. The longest drug release was noted to occur in simulated blood fluid. For bentonite, the release was continued for 1 to 500 minutes and for 1 to 2000 minutes for bentonite/TiO_2. Drug release occurred at a release percent in pH 1.2 (simulated stomach juice) than it did in pH 7.5 and was significantly lower than in neutral circumstances when compared to bentonite/TiO_2. Consequently, different surfaces had variable chloramphenicol release times at high and low pH levels.

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