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Preparation and Characterization of Amoxicillin Loaded Bismuth Oxide as Drug Delivery System for Biomedical Applications

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INORGANIC mesoporous nanomaterials are highly suitable for adsorbing and loading bioactive medicinal substances due to their unique chemical and physical properties. Recently, bismuth oxide nanoparticles have gained attention for their large surface area and biocompatibility, positioning them as promising carriers for drug delivery. In this study, amoxicillin antibiotic was loaded into mesoporous nanomaterials (Bi_2O_3) prepared specifically for local antibiotic delivery systems. The efficient drug-loading abilities of these nanoparticles make them highly desirable for targeted drug delivery systems. To evaluate their effectiveness in drug loading, release, and bone regeneration, we created mesoporous nanoparticles (MBiNs) using the polymer sacrificial technique in this study. Although the preparation method had minimal impact on their physicochemical properties, the nanoparticles exhibited unique microstructural features. Additional research is required to gain a comprehensive understanding of these nanoparticles and uncover their potential applications in medicine. The Bi_2O_3 mesoporous nanomaterials were characterized using XRD, FTIR, and TEM techniques. These prepared nanomaterials show significant potential for application in drug delivery systems for bone regeneration and in enhancing the properties of other medical products.

Keywords: Bismuth oxide, drug delivery, bone regeneration, amoxicillin antibiotic.

Introduction

There has been a growing focus on human health concerns, leading pharmaceutical companies and the scientific community to commit to enhancing their knowledge and implementing new medications and processes. Although there are already many established treatments, there is a pressing demand for innovative technologies that can facilitate the healing of damaged tissues additionally, the development of new antimicrobial drugs that can effectively address the increasing problem of antibiotic resistance has become of utmost importance. [1].

In recent times, there has been a notable increase in the utilization of artificial nanoparticles (NPs) across various sectors, such as electronics, biological applications, and the pharmaceutical industry. Bismuth nanoparticles (Bi-NPs) have particularly garnered attention in biomedical applications due to their favorable attributes of low toxicity and environmentally friendly nature. [2]. Moreover, the cost-effectiveness and abundant availability of Bismuth (Bi) make it an attractive option for large-scale applications [3]. Bi chalcogenide nanostructures possess inherent electrical and optical properties that render them suitable for a wide range of biomedical uses [4]. The antibacterial effects of metal-based nanoparticles (NPs) are influenced by various factors, including the generation of reactive oxygen species (ROS), release of cations from the NPs, depletion of ATP, impairment of membranes, malfunctioning of proteins, and interference with nutrient assimilation [5, 6]. However, the preparation conditions for the aforementioned nanoparticles (Bi_2O_3) have not been standardized or extensively studied. Therefore, this study aimed to design mesoporous nanomaterials using a uniform method and investigate the behavior of each nanoparticle in drug delivery profiles. Specifically, mesoporous MBiNs nanomaterials

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were synthesized, analyzed, and their physicochemical and morphological properties were examined and correlated with their potential

Materials and method

High-quality starting materials were acquired from Sigma Aldrich and other multinational chemistry companies. Specifically, these included polyacrylamide (C_3H_5NO)n (its Purity 99%) with an average molecular weight of 150,000 g/mol (CAS Number: 9003-05-8) and bismuth oxychloride (BiOCl) (its Purity 99%) .

Preparation method of Bismuth oxide

The MBiNs were developed based on previous research with some modifications [2]. Initially, 400 ml of distilled water and 1 g of polyacrylamide were mixed using a magnetic stirrer at 80 °C. Separately, the oxide precursors were completely dissolved in 1200 ml of the appropriate medium (either distilled water or ethanol) using a magnetic stirrer, according to the molar weights of bismuth chloride. The bismuth oxide solutions were then mixed with the polymer solution while being continuously stirred. These mixtures were left to dry overnight at 100°C in an oven dryer. To determine the morphology of the produced nanoparticles, the dried powders were calcined at 600°C.

Characterizations

Samples were characterized by X-ray diffraction (XRD) model Bruker axs, D8 ADVANCE, HR-TEM. Specifications of utilized TEM (JEOL, Japan, JEM2100, Electron Microscope, and HR-TEM), a Fourier Transformer Infrared spectrophotometer (FT-IR) (model FT/IR-6100 type A), and A UV spectrophotometer.

In Vitro Evaluation of Drug Loading and Release.

The bismuth oxide nanomaterial (100 mg) was immersed in 50 ml of ethanol containing 200 mg of amoxicillin powder, resulting in a concentration of 2 mg/ml. To ensure uniform drug loading within the porous structures of the MBiNs, the mixture was placed in a shaker incubator at 200 rpm for 18 hours. Finally, the powder was dried at 37°C.

Amox release profiles were determined by submersing the drug-loaded nanoparticles in PBS at pH 7.4 and 37°C. To begin, the drug-loaded samples were put in 50 ml of PBS. At defined intervals, 3 ml of the solution was taken and replaced with 3 ml of a new PBS. The obtained solutions were maintained in the freezer for future measurements. A UV spectrophotometer with a 275 nm wavelength was used to quantify the amount of Amox released into the solution

[7]which requires effective treatment methods. This study compares the reaction kinetics, degradation pathways, and antibacterial activity of AMX in the UV/H2O2 and UV/persulfate (S2O82−, PS. A previously defined standard curve was used to calculate the medication concentrations. In addition, the measured release data in the PBS from each nanomaterial were compared to mathematical models of zero order, diffusion and Korsmeyer Peppas models.

Results and discussion

TEM analysis

Figure 1 illustrates the transmission electron microscopy (TEM) image of the synthesized mesoporous Bi2O3 nanomaterial, providing insights into its shape, size, distribution, and morphology. TEM analysis of the MBiNs sample revealed the presence of semi-round nanoparticles with diameters ranging from 9.79 to 13.70 nm. The image also displayed distinct lattice fringes indicating interplanar spacing at the nanoscale, consistent with the mesoporous structure of Bi2O3 [8]. The TEM analysis confirmed the crystalline nature of the nanostructures in the sample.

XRD analysis

Figure 2 displays the X-ray diffraction (XRD) patterns of the mesoporous Bi2O3 nanomaterials, both unloaded and loaded with Amox. In the XRD analysis of Bi2O3 (free of the drug), observed peaks indicate the crystalline nature of Bi2O3 nanoparticles. These peaks correspond to the monoclinic crystal phase of Bi2O3 (COD: No-96-152-6459) at specific 2θ values, namely 15°, 28.56°, 34.35°, 42.52°, 46.50°, and 58.58° [9]. On the other hand, the XRD pattern of Bi2O3 loaded with the drug (Bi2O3/Amox) reveals the crystalline structure of Bi2O3, along with characteristic peaks of amoxicillin trihydrate at 2θ values of 12.11, 14.73, 17.57, 18.43, 25.48, and 27.38. These amoxicillin peaks appear with low intensity due to the small amount of drug loading [10].

FTIR analysis

Figure 3 depicts the Fourier-transform infrared (FT-IR) spectrum of the synthesized mesoporous Bi_2O_3 nanomaterials, both unloaded and loaded with Amox. In the FT-IR analysis of the bismuth oxide nanoparticle absorption bands corresponding to various functional groups were observed. The O–H stretching vibrations were detected at

3421 $cm^{-1.}$ The peak at 1400 cm^{-1} is attributed to C-O vibrations, which may be derived from atmospheric exposure. The presence of the metal-oxygen (Bi-O) bond is indicated by the peak at the range of 435~505 $cm^{-1.}$ Additionally, absorption bands at 600 cm^{-1} signify the stretching mode of Bi-O, while the peak at 3429 cm^{-1} represents the stretching vibration of O-H. Bands at 2900 cm^{-1}, 2800 $cm^{-1.}$ 1113 cm-1, and 1046 cm^{-1} are associated with the vibrations of the CH2 aliphatic group and C-O bonds originating from the beta vulgaris precursor [11]. The FTIR analysis of the mesoporous nanoparticles loaded with the drug (Amox) revealed the presence of characteristic peaks of amoxicillin trihydrate. However, these peaks appeared with low intensity due to the small amount of drug loading or maximum inclusion within the pores of the nanoparticles [10-12]. The infrared spectrum of the amoxicillin trihydrate sample exhibited bands ranging from 3525 to 557 cm^{-1}. According to Min et al. [13], two small bands at 3525 and 3461 cm^{-1} correspond to the presence of crystallization water (-OH stretch) and amide (-NH stretching), respectively. This is followed by bands at 3178 and 3039 cm^{-1}, which are characteristic of phenol (-OH stretching) and aromatic (-CH stretching) groups, respectively. Prominent and distinct bands between 1800 and 1650 cm^{-1} (1776 and 1687 cm^{-1}) indicate the presence of carbonyl (-C=O) in the beta-lactam ring and amide groups. The asymmetric stretching of carboxylate groups is responsible for the band at 1581 cm^{-1}. Bands at 1484 and 1120 cm^{-1} are assigned to the N-C lengths of primary amine and O-C, respectively, as described by Zha et al. [14]. Several bands between 1150 and 950 cm^{-1} indicated the characteristic in-plane CH bending vibrations typical of aromatic compounds. There is no additional literature information available about the other bands. Both XRD and FTIR findings confirm that Amox can be effectively and safely incorporated into the nanoparticles' structure without affecting the physicochemical properties of both the carrier and the drug.

Drug release

The loading efficiencies of Amox within the fabricated mesoporous nanoparticles were 98.15 for MBiNs, samples. A UV spectrophotometer set at =275nm was used to measure the amount of drug released into the PBS buffer solution. Figure 4 depicts the cumulative drug release (%CDR) patterns of amoxicillin released from prepared mesoporous (MBiNs, sample) suspensions. According to the release profile, the release profiles of Bi_2O_3, sample show protracted burst release, of 15 % to 20 within 60h, and it was linear up to 100h for the sample. About 30 % of the drug was released from mesoporous Bi_2O_3 sample within approximately 700 h [15, 16].

Furthermore, the release kinetics of amoxicillin from the nanomaterials were analyzed by fitting them to various mathematical models, as detailed in Table 1. From the table, it is evident that the release kinetics from MBiNs were best described by the Korsmeyer-Peppas model, indicated by the highest R^2 values (0.865). This suggests that amoxicillin was released from these fabricated nanomaterials primarily through the processes of hydration and nanomaterial degradation.

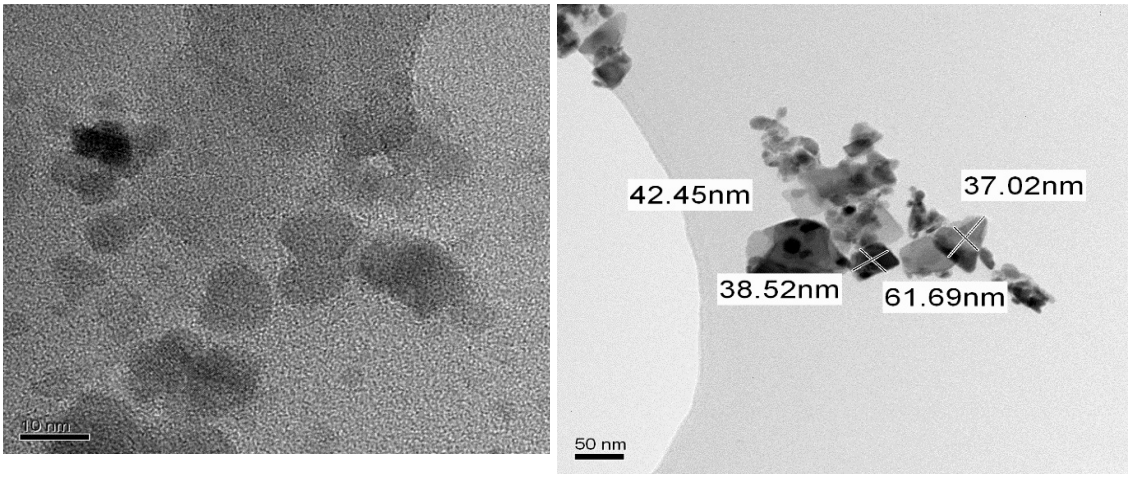

Fig.1. TEM images of MBiNs before drug loading.

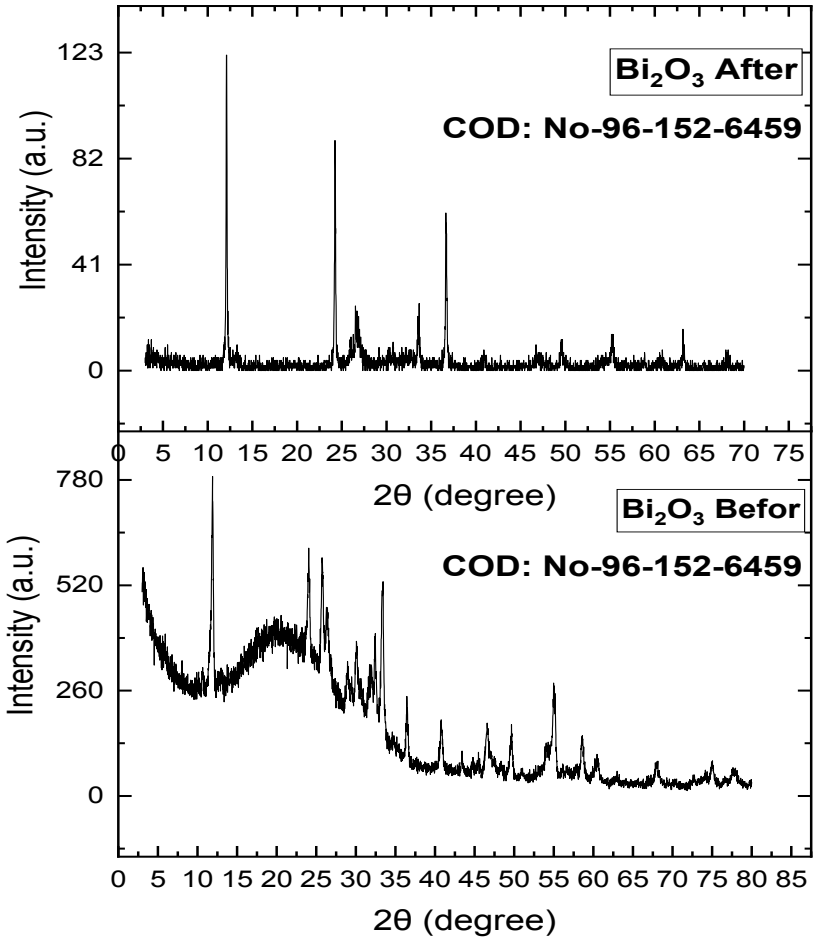

Fig. 2. XRD curves of MBNs before and after drug loading.

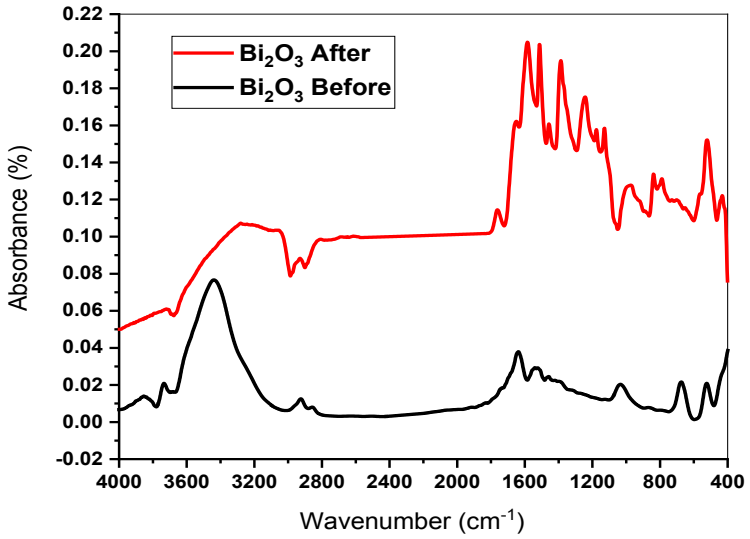

Fig. 3. FTIR measurements of MBNs before and after Amox loading.

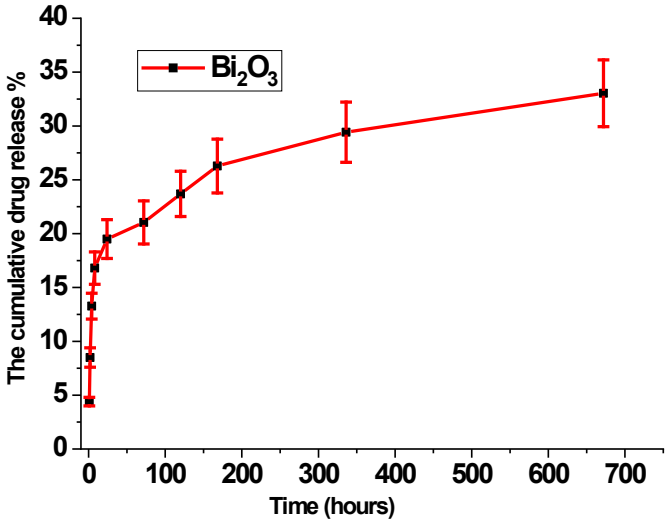

Fig. 4 Amoxicillin release profiles from MBiNs.

TABLE 1 Release kinetics parameters of Amox-loaded bismuth oxide.

Formula code	R^2-value†			Korsmeyer-Peppas model		n	K*	$RE_{0\text{-}720h}$‡ (%)
	Zero-order	Fickian diffusion	Korsmeyer-Peppas model	t_{50}** (hours)	t_{90}*** (hours)			
MBiNs	0.633	0.838	0.865	1044.093	2232.525	0.256	7.169	33.037

n is the diffusion exponent k* is the release rate constant t_{50}** is time required for 50% of the drug to be released t_{90}***is time required for 90% drug release ‡$RE_{0\text{-}672h}$ is the release efficiency of drug from 0 to 672 hours †R^2-value is the value for regression co-efficient.

Conclusions

Patients often require high doses of medication to achieve therapeutic effects due to the lack of specificity and solubility of drug molecules. Pharmaceuticals use various drug carriers to deliver therapeutic substances to specific targets in the body to overcome these challenges. Mesoporous nanomaterials have emerged as a promising solution, allowing for controlled and sustained drug release. These nanoparticles are favored for targeted drug delivery systems because of their effective drug-loading capabilities. In this study, mesoporous nanoparticles (MBiNs) were prepared using the polymer sacrificial method to assess their suitability for drug loading, release, and bone regeneration. The preparation method did not significantly alter their physicochemical properties. The nanoparticles displayed distinct microstructural characteristics. Further investigation is needed to fully understand these nanoparticles and explore their potential medical applications.

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"تحضير وتوصيف أكسيد البزموت المحمل بالأموكسيسيلين كنظام لتوصيل الأدوية للتطبيقات الطبية الحيوية"

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تعتبر المواد النانوية المسامية غير العضوية مناسبة للغاية لامتصاص وتحميل المواد الطبية النشطة بيولوجيًا نظرًا لخصائصها الكيميائية والفيزيائية الفريدة. في الآونة الأخيرة، اكتسبت الجسيمات النانوية لأكسيد البزموت الاهتمام بسبب مساحتها السطحية الكبيرة وتوافقها الحيوي، مما يجعلها حاملات واعدة لتوصيل الأدوية. في هذه الدراسة، تم تحميل المضاد الحيوي الأموكسيسيلين في مواد نانوية متوسطة المسام (Bi_2O_3) تم إعدادها خصيصًا لأنظمة توصيل المضادات الحيوية المحلية. إن القدرات الفعالة لهذه الجسيمات النانوية على تحميل الأدوية تجعلها مرغوبة للغاية لأنظمة توصيل الأدوية المستهدفة. لتقييم فعاليتها في تحميل الدواء وإطلاقه وتجديد العظام، قمنا بإنشاء جسيمات نانوية متوسطة المسام (MBiNs) باستخدام تقنية البوليمر القربانية في هذه الدراسة. على الرغم من أن طريقة التحضير كان لها تأثير ضئيل على خواصها الفيزيائية والكيميائية، إلا أن الجسيمات النانوية أظهرت ميزات بنية مجهرية فريدة من نوعها. هناك حاجة إلى مزيد من البحث للحصول على فهم شامل لهذه الجسيمات النانوية والكشف عن تطبيقاتها المحتملة في الطب. تم تشخيص المواد النانوية متوسطة المسام Bi_2O_3 باستخدام تقنيات XRD، FTIR، وTEM. تظهر هذه المواد النانوية المحضرة إمكانية كبيرة للتطبيق في أنظمة توصيل الأدوية لتجديد العظام وفي تعزيز خصائص المنتجات الطبية الأخرى.