CuO Nanoparticles: Synthesis and Biomedical Applications- Antibacterial and Cytotoxic properties

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***Abstract*: This study aims to provide an updated survey of the main synthesis methods of copper oxide (CuO) nanoparticles in order to obtain tailored Nano systems for various biomedical applications. Although not widely investigated as an efficient drug delivery system, CuO nanoparticles have great biological properties including effective antimicrobial action against a wide range of pathogens and also drug resistant bacteria. This review presents the main methods and technological advances in fabrication of nanostructured copper oxides nanoparticles, their antibacterial effects and cytotoxicity.**

***Keywords*: metal oxide nanoparticles, Nanoparticles synthesis, Antibacterial activity, Cytotoxicity**

1. INTRODUCTION

In recent years, nanostructures of transition metal oxides have gained a great attention from material scientists and engineers due to their different properties compared with the corresponding bulk counterparts, which in turn provides promising applications in various fields of technology. Preparation of high quality nanostructures of defined, controllable size and morphology is a critical requirement in order to develop nano devices or other different applications for catalyst, sensing, pharmacy and so on.

CuO, categorized into transition metal oxide group, is a p type, narrow bandgap semiconductor. It has monoclinic structure and many interesting characteristics: super thermal conductivity, photovoltaic properties, high stability, and antimicrobial activity. Due to such exclusive properties, CuO can be used in many technological fields, for example, active catalyst gas sensor, high efficiency thermal conducting material ,magnetic recording media, with very good selectivity, or solar cell applications, high temperature superconductors, catalysis, batteries, gas sensors, solar energy. The nanotechnology development in conjunction with biotechnology has significantly expanded the nanomaterials application in several fields, such as medicine, electronics, wastewater treatment, and water purification, food processing, industrial and household purposes, among others [1-2], or even as an antibacterial agent with low cost and low toxicity[3].

One of the most important parameters in the synthesis of these nanoparticles is the control of particle size, morphology and crystallinity and in order to achieve this goal. Characterization of these nanoparticles can be helpful in modifying and tuning their antibacterial and cytotoxic effects. For instance, it has been established that the antibacterial activity increases with decreasing the particles size. In contrast, the crystallographic orientation appears to have no effect on antibacterial activity, whereas increasing the lattice constants enhances the antibacterial activity. It has also been proposed that different morphologies and crystal growth habits can affect the antibacterial activity [4].

2. OBJECTIVES

The antibacterial activity of metal oxide nanoparticles has received marked global attention as they can be specifically synthesized to exhibit significant toxicity to bacteria. The synthesis approach significantly impacts the properties of such nanoparticles and these properties in turn have a significant impact on their biomedical applications.

Presently, microbial resistance to antibiotics has been reaching a critical level. In exploring various options to address this problem, inorganic nanomaterials, like metal oxide nanoparticles, have emerged as promising candidates since they possess greater durability, lower toxicity and higher stability and selectivity when compared to organic ones. Nanostructured metal oxides have already been extensively studied for their promising use in technology.

Thus, smaller particles are usually the most efficient antibacterial agents. However, this is not the case when decrease in size leads to enhanced aggregation. Also, defects present at the nanoparticles' surface influence strongly antibacterial efficiency. Point defects, such as atoms at edges and in corners give rise to an abrasive surface that may cause the injury of the bacterial cell wall or membrane

Antibacterial activity of metal oxide nanoparticles

Several metal oxides in form of nanoparticles have been reported to exhibit marked antibacterial activity allowing efficient eradication of various bacterial strains. This fact has attracted significant interest of environmental, agricultural and health care industries that are searching for newer and better agents to control or prevent bacterial infections. Although their exact antibacterial mechanism is still under debate, some distinctive mechanisms have been proposed, which include reactive oxygen species (ROS) formation, metal-ion release, particle internalization into bacteria and direct mechanical destruction of bacterial cell wall and/or membrane.

Metal oxide nanoparticles may show bacteriostatic or bactericidal effect. In case of bacteriostatic effect, treated bacteria do not die but stop to reproduce or grow. If treated bacterial cells are removed from the solution containing nanoparticles,

they re-start to grow. This can be easily tested by plating these bacterial cells onto new nanoparticle-free agar. Also, CuO nanoparticles were shown to generate ROS, namely superoxide anions, when adsorbed onto the bacterial cell surfaces or internalized into bacterial cells. Formed ROS induced bactericidal effect in both Gram-positive (S. aureus) and Gram-negative (E. coli) bacteria [5].

The physicochemical characteristics of metal oxide nanoparticles, such as size, crystal structure defects, composition and surface charge, are directly associated with enhanced antibacterial effects. The synthesis and treatment procedures employed can tune these characteristics, and hence produce the desired antibacterial efficacy. For instance, nanoparticles of smaller sizes (<20 nm) can easily penetrate into bacterial cells and may release toxic metal ions upon dissolution [6].

3. METHODOLOGY

Over the last few decades, the synthesis of nanomaterials has been intensively pursued because of their fundamental scientific interest and technological applications. Microwave assisted solvothermal synthesis is a method for preparing a variety of materials such as metals, semiconductors, ceramics and polymers. This process involves the use of solvent under moderate to high pressure and temperature that facilitates the interaction of precursors during synthesis. Copper oxide nanoparticles have been prepared by several methods ranging from thermal reduction, sonochemical method, sol-gel reaction, to gas phase process. Among those, solvothermal process has been shown to be a powerful technique for generating novel materials with interesting properties.

For the preparation of pure CuO nanoparticles, Analytical reagent (AR) grade copper acetate urea, ethylene glycol (as solvent) can use as precursors. Copper acetate and urea can take as solute in the molecular ratio 1:3 and dissolve in 100 ml ethylene glycol individually. The prepared solution is keep in a domestic microwave oven. Microwave irradiation is carried out for about 20 minutes till the solvent is evaporates completely. In the end, the precipitate is wash several times with distilled water and acetone (CH_3COCH_3) to remove the organic impurities. The the sample is anneal for 30 minutes at 100 ^{0}C to improve the ordering.

4. WORK PLAN

The present work is focus on the synthesis and characterization of nanometer-sized pure and doped CuO particles by a simple microwave assisted solvothermal method.

Instrumentation:

Some of the experimental methods of characterization are planned to do in this present work include X-Ray Diffractometry (PXRD), Scanning Electron Microscope analysis (SEM-EDAX), Fourier Transform-Infrared Spectroscopy (FTIR), Optical Analysis (UV-Vis), Electrical studies (AC studies), Thermal studies (TGA/DTA) ,Magnetic studies (VSM), Thin-layer chromatography (TLC)– Agar well diffusion method and Dilution methods

Stabilization and biocompatibility of metal oxide nanoparticles

Notably, metal oxide nanoparticles dissolute partially in water solutions which leads to the modification of their morphology in which formation of new crystallographic phases may take place. Metal oxide nanoparticles of similar size but of different compositions usually show varying cytotoxic effects. The toxicity can also be reduced by doping metal oxide nanoparticles with other metal ions [7].

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Conclusions : Among the oxides of transition metals, CuO nanoparticles are of special interest because, metal oxide nanoparticles are promising candidates for antibacterial applications if the synergic effects of their constituents are effectively harnessed. This is particularly important keeping in mind that the type of the synthesis affects properties like size, shape, morphology, presence and type of stress and defects in the crystal which in turn determines their interaction with bacterial and mammalian cells.

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