Journal of
Clinical and Pharmaceutical Research
RESEARCH OPEN ACCESS

Formulation and Characterization of Copper Oxide Solid Lipid Micro-Particles

Slesha Kumar Kosuru[1]*, Ch. Hemalatha[1], K. Venkat[1], K. Jahnavi Sravanthi[1], V. Kondala Rao[1], M.V.K Tejaswini[1], Santhosh Kumar Gandham[2]

[1]Department of Pharmaceutical Analysis & Quality Assurance, Lydia College of Pharmacy, Ravulapalem, Andhra Pradesh, India.

[2]Department of Pharmacology, Lydia College of Pharmacy, Ravulapalem, Andhra Pradesh, India.

ARTICLE INFO

Article History:
Received: 04.05.2025
Revised: 19.06.2025
Accepted: 17.07.2025

Keywords:
Copper Oxide; Scanning Electron Microscopy; Solid Lipid Micro-Particles; Zeta Potential

Corresponding Author:
Mr. Slesha Kumar Kosuru M.Pharm.,
Assistant Professor,
Department of Pharmaceutical Analysis & Quality Assurance,
Lydia College of Pharmacy,
Ravulapalem, Andhra Pradesh, India.
Email: sleshakumar555@gmail.com

ABSTRACT

Aim: The main aim of this study is to evaluate the morphology, particle size, zeta potential and anti-microbial activity of the formulated micro-particles to establish their potential application.

Methods: CuO-SLMs were synthesized using the micro-emulsion-based method by incorporating stearylamine and Tween 80. Characterization was done by SEM analysis and antimicrobial activity was evaluated using pour plate and streaking methods.

Results: SEM confirmed spherical micro-particles with smooth surfaces and a size range of 2 µm, showing good water dispersibility. The CuO-SLMs demonstrated superior antimicrobial activity against both Gram-positive and Gram-negative bacteria compared to standard antibiotic Ciprofloxacin.

Conclusion: This study effectively formulated CuO-MPs utilising the micro-emulsion-based approach. The synthesised micro-particles demonstrated superior spherical shape, a smooth surface and a restricted size distribution within the micrometre scale. The zeta potential study verified the colloidal stability of the formulation, demonstrating little aggregation and effective dispersion in aqueous conditions. Moreover, the CuO-SLMs exhibited substantial antibacterial efficacy against the evaluated bacterial strains, surpassing the conventional antibiotic Ciprofloxacin.

Introduction

Novel drug delivery systems (NDDS) has a major role to play in achieving better therapeutic efficacy, minimizing side effects and improving patient compliance [1]. Low solubility, limited bioavailability, fast metabolism and non-specific distribution of the drug are some common limitations when it comes to conventional approaches for drug delivery. Submicron liposomes are considered to be a potential solution to this problem by delivering the drug in a controlled manner at its site of action [2,3]. Higher dissolution of the drug, controlled release patterns, biocompatibility and utilizations of both lipophilic as well as hydrophilic drugs are some exclusive advantages of Solid Lipid Micro particles (SLMs) [4].

In an aqueous system, the colloidal carriers composed of surfactant-coated solid lipid allow the controlled drug delivery and increase the therapeutic efficiency [5-7]. Due to their ability to generate reactive oxygen species causing the oxidative stress in microbial cells, Copper Oxide Micro Particles (Cuo-MPs) have antibacterial, antifungal and anticancer properties. At increased doses aggregation, reduced bioavailability and possible cyto-toxicity are the significant limitations due to the direct administration of Cuo-MPs. By augmenting their dispersibilty, stability and controlled release, we can strengthen the therapeutic efficacy and decrease the toxicity by integrating the Cuo-MPs into SLMs that can mitigate these limitations [8,9]. The main aim of this study is to evaluate the morphology, particle size, zeta potential and anti-microbial activity of the formulated micro-particles to establish their potential application.

Materials & Methods:

Materials: Stearyl amine, cationic lipid, stabiliser (HiMedia), Tween 80: Non-ionic surfactant (Loba Chemie), CuO-MPs and Distilled Water.

Preparation of CuO-SLMs: By using the micro emulsion based technique, CuO-SLMs were prepared [10]. About, 200 mg of stearylamine was weighed accurately and transfer it into a clean beaker. About 0.5 mL of Tween 80 was added to the beaker and stirred

gently until the components dispersed. At this stage, incomplete homogenization may leave some fine particles. Incorporated 100 mg of copper oxide into the mixture and continued the stirring to achieve uniform dispersion of the drug within the lipid–surfactant matrix. Gradually, distilled water (up to 50 mL) was added and maintained continuous stirring. Beaker was placed on a magnetic stirrer and continued the stirring process until a homogeneous mixture of stearylamine, Tween 80 and copper oxide in the aqueous phase was obtained.

However, due to the inherent solid nature of stearyl amine, some fine particles remained unsolved and dissipated continuously. The calculated volume of distilled water was added gradually to the beaker of stearyl amine and Tween 80 solution. The water was slowly added while stirring constantly to make sure that all the parts mixed together evenly. After that, the whole mixture was put on a magnetic stirrer and stirred for a longer time to make a homogeneous micro-emulsion. This was a necessary step to achieve even distribution of CuO-MPs in lipid matrix.

For further treatment, refinement of the micro particle size and to achieve better uniformity, the prepared dispersion was optionally subjected to sonication using either a probe or bath sonicator. Applying these procedures enabled the reduced particles to a micro size, stabilised the final formulation and improved uniformity in texture. The CuO-SLM dispersion was carefully controlled and kept at room temperature ready for testing and characterisation which included morphology, zeta potential and antibacterial activity analysis.

Characterisation of CuO-SLMs: We characterised the physicochemical properties, stability and bio-activity of our CuO-SLM by using various methods.

Scanning Electron Microscopy: Scanning electron microscopy was used to investigate the surface and morphology of CuO-SLM. This technique allowed us to determine size distribution, surface smoothness and morphology of the microparticles from the high quality images.

Zeta Potential Analysis: Zeta potential measurement was used for analysis of surface charge and stability of the micro-particles. From this, the strength of the electrostatic attraction between adjacent positively charge particles was estimated and this could indicate the stability of the physical properties of the various components of the colloidal system.

Antimicrobial Activity: CuO-SLM inactivation efficacy against different bacterial species was evaluated by the pour plate and streaking techniques. Zone of inhibition of CuO-SLM was compared to that of standard antibiotic Ciprofloxacin [11-17].

Results

In this study, microemulsion method has been employed to confirm the size, shape and stability of CuO-SLM and its antibacterial efficiency.

Particle Size: Scanning electronic microscopy of the CuO-SLM particles was found to be spherical with flats shaped bent surfaces and particle size was observed to be 2µm.

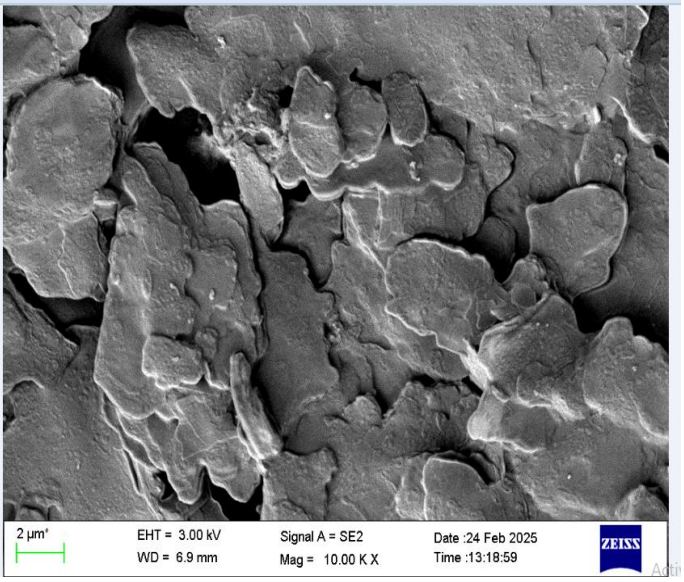

Figure1: CuO-MPs particle size (2µm)

Zeta potential: Zeta potential measurements in this study showed that the microparticle was well-dispersed in the aqueous phase with minimal aggregation, suggesting that the formulation had good colloidal stability.

Table 1: Zeta Potential and Electrophoretic Mobility Results

Peak No.	Zeta Potential (mV)	Electrophoretic Mobility ($cm^2/V \cdot s$)
1	-20.3	-0.000157
Mean	-20.3 mV	-0.000157 $cm^2/V \cdot s$

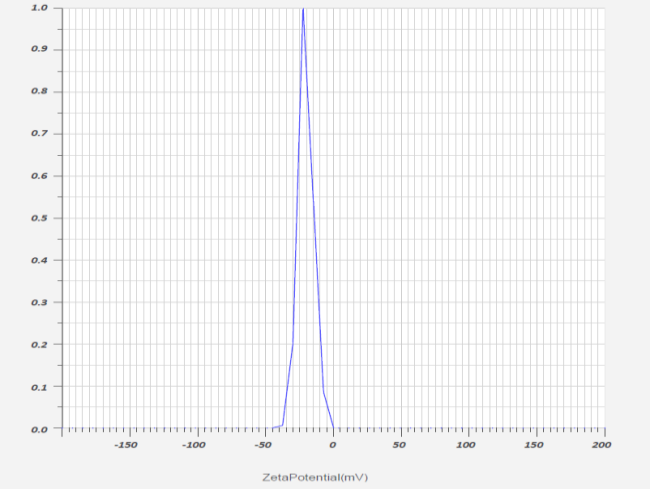

Figure 2: Zeta Potential mean (mV) - 20.3 m

Antimicrobial activity: Antimicrobial screening demonstrated a notable antimicrobial activity against tested bacterial strains. The inhibition zone created by the CuO-SLM was higher than that of the reference drug Ciprofloxacin, which confirmed the potent antibacterial performance of micro-particles. This higher activity could be attributed to the small particle size and the antibacterial inhibitory effect of CuO.

Figure 3: Zone of inhibition for test and control

Table 2: Antimicrobial Activity of CuO-SLM **compared with ciprofloxacin**

Bacterial species	Gram stain	CuO Micro particles (MIC, µg/ml)	Zone of inhibition (µm)	Ciprofloxa-cin (MIC, µg/ml)	Zone of inhibition (µm)
Staphylo-coccus aureus (ATCC 25923)	Gram-Positive	10	28	10	32
E- coli (ATCC 25922)	Gram-Negative	10	25	10	31

Discussion

Microemulsion method-prepared of CuO-SLM was quite homogeneous and stable. The method proved to be effective in producing micro-particles, with homogenous spherical morphology and smooth surface confirmed by SEM examination. The SEM images showed a particle size of 2 µm. The improved antibacterial activity for the CuO-SLM over regular Ciprofloxacin can be attributed to numerous factors. The reduced particle size increases the surface area to volume ratio leading to increased contact with microbial cells. In addition, CuO-MPs have been known to generate the reactive oxygen species (ROS) including superoxide and hydrogen peroxide that can damage the microbial cellular membrane, proteins, and DNA. The natural property of CuO and micro scale size significantly boosted the antibacterial performance yielded in this work. CuO antibacterial activity and its stability in dispersion, as found by zeta potential study, suggest the low amount of particle aggregation, leading to long shelf life coupled with consistent performance. The well-controlled particle size and good dispersion stability associated with these micro-particles has prompted us to consider their application in drug delivery systems and cosmetic products for which stability, bioavailability and safety are critical features [18–20].

Conclusion

In this work, CuO-MPs were prepared successfully through micro-emulsion-mediated method. The formed micro-particles exhibited well spherical shape, smooth surface and limited size distribution in the micrometre scale. Zeta-potential measurement confirmed the colloidal stability of the formulation with low aggregation and excellent dispersion in water. Additionally, the CuO-SLMs showed impressive antibacterial activity against all tested bacteria in comparison with that of common antibiotic ciprofloxacin. The enhanced activity may be attributed to the small particle size and antibacterial performance of CuO, especially for its ability to release reactive oxygen species (ROS). Considering the favorable physiochemical properties and biological activity, it implies that the CuO-SLMs are particularly promising for drug delivery applications, especially in sustained release system, targeted delivery and improved therapeutic effect.

Abbreviations

SLMs – Solid Lipid Micro-particles
CuO-MPs – Copper Oxide Micro Particles
SEM – Scanning Electron Microscopy
ROS – Reactive Oxygen Species.

Acknowledgements

The author acknowledges to Lydia College of Pharmacy for providing the necessary facilities to carry out this research.

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