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Metal Oxide Nanocarriers for Smarter Anti-Inflammatory Therapy: Diclofenac Delivery Reinvented

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Abstract

This work is concerned with the development and in vitro evaluation of magnesium oxide (MgO), copper oxide (CuO), and silver oxide (Ag_2O) nanoparticles as potential nanocarriers of the anti-inflammatory drug Diclofenac Potassium. The nanoparticles were prepared by controlled chemical precipitation and exhibited nanosized particle diameter, regular morphology, and stable zeta potential. FTIR analysis clearly confirmed successful drug loading, evidenced by a characteristic shift in the carboxylate bands, and $\Delta\nu$ values within 135–150 cm^{-1}, confirming bridging or bidentate coordination of Diclofenac to the metaloxide surfaces. Drug-loading studies presented high encapsulation efficiency for all formulations, while release analysis showed sustained drugrelease profiles, with Ag_2O–DP exhibiting the slowest and most controlled release. In-vitro assays such as trypsin inhibition and serum protein protection studies showed enhanced biological activity of the drug-loaded nanoparticles compared to the free drug, wherein Ag_2O–DP consistently presented the highest antiinflammatory potential. Overall, these results suggest that metal oxide nanoparticles provide strong drug–nanoparticle interactions, structural stability, and improved therapeutic performance. Among the three formulations tested, Ag_2O–DP was identified as the most promising, followed by CuO–DP and MgO–DP, and therefore this work points out the possible use of metal oxide nanocarriers in controlled anti-inflammatory drug-delivery applications.

Keywords: Metal oxide nanoparticles; Diclofenac Potassium; Bridging coordination; Drug loading; Controlled release; Trypsin inhibition; Serum protein protection; Nanomedicine; Antiinflammatory delivery system.

Introduction

Inflammation is a complex, defense biological response elicited after injury, infection, or tissue damage and is implicated centrally in several chronic diseases such as arthritis, cardiovascular disorders, and autoimmune diseases. The prime treatment for inflammatory disorders involves nonsteroidal anti-inflammatory drugs due to their inhibitory action against the cyclooxygenases COX-1/COX-2. However, long-term NSAID treatment leads to gastrointestinal, renal, and hepatic toxicities, thus limiting the therapeutic window and application in long-term treatments [1]. Among the common NSAIDs prescribed is Diclofenac Potassium, which acts quickly but is characterized by very short half-lives and poor targeting to tissues with systemic side effects, a problem that can be minimized using nanocarriers capable of controlled release [2].

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So far, nanotechnology-based drug delivery systems have the potential to improve the pharmacokinetic profile, reduce toxicity, enhance solubility, and provide sustained release for small-molecule drugs such as NSAIDs [3]. Several nanocarriers, including polymeric nanoparticles, liposomes, lipid nanocarriers, and inorganic nanoparticles, have been applied to control drug release profiles, enhancing their therapeutic efficacy. In the case of diclofenac, nanosuspensions and nanoparticulate carriers showed enhanced dissolution and antiin flammatory performance in preclinical studies [4]. This will be a development rationale for embedding Diclofenac Potassium into nanoparticles with improved pharmacological behavior. Among these, Ag_2O, CuO, and MgO nanoparticles have attracted considerable interest in biomedical applications owing to their intrinsic properties of antimicrobial, anti-inflammatory, and antioxidant activities. Silver nanoparticles exhibited suppression of major proinflammatory cytokines such as TNF-α and IL-1β, demonstrating excellent anti-inflammatory potential in cell and animal models [5]. Copper-based nanomaterials also exhibit remarkable anti-inflammatory and antioxidant properties contributing to the alleviation of oxidative stress and cytokine release [6]. MgO nanoparticles additionally confer excellent biocompatibility with immunomodulatory advantages concerning the regulation of macrophage phenotypes and enhanced wound-healing responses [7].

Formulation of Diclofenac Potassium with metal-oxide nanoparticles forms a multi-modal therapeutic platform wherein both the drug and metallic matrix contribute to anti-inflammatory action. The release of metal ions can decrease oxidative stress, inhibit inflammatory mediators, and provide local antimicrobial activity, hence complementing NSAID pharmacodynamics [8]. More interestingly, metal-oxide nanocarriers can substantially modify the drug-release kinetic profile due to the introduction of physicochemical interactions such as hydrogen bonding, electrostatic attraction, and interfacial adsorption that slow desorption and hence provide sustained delivery at the target site [9]. Interaction with proteins and enzymes in biological systems forms one of the important mechanistic components in the action of nanoparticle therapeutics. Metal-oxide nanoparticles are known to bind serum proteins and modulate the activity of proteases, a phenomenon pertinent to inflammation where enzymes like trypsin and matrix metalloproteinases contribute toward tissue breakdown. There are indeed reports that metallic nanoparticles may inhibit proteolytic activity via direct surface interactions, thus offering a secondary protective mechanism for tissues under oxidative or inflammatory stress [10]. Integration of silver, copper, and magnesium oxides with Diclofenac Potassium, having their unique biological properties, offers a new strategy toward the development of nextgeneration anti-inflammatory therapeutics. These hybrid nanoparticles may (a) enhance the stability of drugs, (b) prolong the release, (c) facilitate anti-inflammatory action through a dual mechanism, and (d) reduce systemic toxicity. The present study, therefore, attempts to synthesize and characterize Diclofenac Potassium-loaded MgO, CuO, and Ag_2O nanoparticles and assess their inhibitory potential through trypsin inhibition and serum protein protection assays.

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Materials and Methods Materials

Magnesium nitrate hexahydrate ($Mg(NO_3)_2 \cdot 6H_2O$), copper sulfate pentahydrate ($CuSO_4 \cdot 5H_2O$), silver nitrate ($AgNO_3$), sodium hydroxide (NaOH), Diclofenac Potassium (DP), trypsin enzyme, casein substrate, bovine serum albumin (BSA), and phosphate-buffered saline (PBS, pH 7.4) were purchased in analytical grade. All reagents were used without further purification. Distilled water was used for all preparations.

Synthesis of Metal Oxide Nanoparticles Synthesis of Magnesium Oxide (MgO) Nanoparticles

A 0.1 M solution of $Mg(NO_3)_2 \cdot 6H_2O$ was prepared and stirred continuously. A 0.2 M NaOH solution was added dropwise until the pH reached 12, leading to the formation of magnesium hydroxide.

Reaction 1 – Precipitation of Magnesium Hydroxide:

$Mg(NO_3)_2 + 2NaOH \rightarrow Mg(OH)_2\downarrow + 2NaNO_3$

The precipitate was washed, dried at 80 °C, and calcined at 450 °C for 3 hours to obtain MgO nanoparticles.

Reaction 2 – Thermal Conversion to Magnesium Oxide:

$Mg(OH)_2 \rightarrow MgO + H_2O$ Synthesis of Copper Oxide (CuO) Nanoparticles

$CuSO_4 \cdot 5H_2O$ (0.1 M) was dissolved in distilled water and heated to 60 °C. NaOH (0.2 M) was added slowly to form a blue precipitate of copper hydroxide. **Reaction 3 – Formation of Copper Hydroxide:**

$CuSO_4 + 2NaOH \rightarrow Cu(OH)_2\downarrow + Na_2SO_4$

The precipitate was stirred for 2 hours and heated at 120 °C to convert it into CuO nanoparticles.

Reaction 4 – Dehydration to Copper Oxide:

$Cu(OH)_2 \rightarrow CuO + H_2O$ Synthesis of Silver Oxide (Ag_2O) Nanoparticles

A 0.05 M $AgNO_3$ solution was prepared, and NaOH (0.1 M) was added dropwise until a brownish precipitate of Ag_2O formed. **Reaction 5 – Formation of Silver Oxide:**

$2AgNO_3 + 2NaOH \rightarrow Ag_2O\downarrow + 2NaNO_3 + H_2O$ Preparation of Diclofenac Potassium–Loaded Nanoparticles

Each nanoparticle batch (100 mg) was dispersed in 25 mL of Diclofenac Potassium solution (1 mg/mL) and stirred for 24 hours. Diclofenac Potassium undergoes ionic dissociation as: **Reaction 6 – Ionization of Diclofenac Potassium:**

$DP\text{–}K \rightarrow DP^- + K^+$

The negatively charged diclofenac (DP^-) binds to positively charged metal ion sites on MgO, CuO, and Ag_2O nanoparticle surfaces.

Reaction 7 – Drug–Nanoparticle Complex Formation:

$M^{2+} + DP^- \rightarrow M(DP)^+$

(where M = Mg^{2+}, Cu^{2+}, Ag^+ surface site)

The drug-loaded nanoparticles were centrifuged, washed, and dried at 40 °C.

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Encapsulation efficiency:

EE% = ((Wi - Wf) / Wi) × 100

Characterization of Nanoparticles

FTIR, UV–Vis spectroscopy, XRD, DLS-based particle size, and zeta potential analysis were performed to determine structural and physicochemical properties.

In-Vitro Drug Release Study

Drug-loaded nanoparticles (10 mg) were placed in PBS (pH 7.4) at 37 °C using a dialysis membrane. Samples were collected from 0–72 hours and analyzed at 276 nm.

Trypsin Inhibition Assay

Trypsin (1 mg/mL) was incubated with nanoparticle samples at 37 °C. Casein substrate was added, and hydrolysis was monitored at 280 nm.

% Inhibition = (1 - As/Ac) × 100

Serum Protein Protection Assay

BSA (1% w/v) was exposed to oxidative stress using H_2O_2. Nanoparticle-treated samples were evaluated at 660 nm to determine prevention of protein denaturation.

Results

MgO, CuO, and Ag_2O nanoparticles were successfully synthesized by controlled alkaline precipitation, followed by dehydration or calcination steps. Each of these formulations presented nanoparticles that were clearly different in visual and physical characteristics, with MgO appearing as a fine white powder, CuO forming as a dark brown material, and Ag_2O appearing as a grey-black powder. These were also the expected profiles for metal oxide formation. The synthesis was highly reproducible from batch to batch, with overall yields ranging between 82–90%, which confirmed efficiency in the method of preparation. All nanoparticles were then drug-loaded with Diclofenac Potassium after synthesis, resulting in stable drug-bound nanomaterials suitable for further testing.

TABLE 1. Physical Characteristics and Yield of Synthesized Nanoparticles

Nanoparticle Type	Physical Appearance	Yield (%)
MgO	Fine white powder	80–88%
CuO	Dark brown powder	82–89%
Ag_2O	Grey–black powder	85–92%

Table 1 summarizes the physical characteristics of the synthesized metal oxide nanoparticles. MgO appeared as a fine white powder, while CuO and Ag_2O exhibited darker tones consistent with their known oxide forms. The yields for all nanoparticles ranged between 80–92%, indicating efficient synthesis and minimal loss during washing and drying steps.

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FTIR analysis

FTIR analysis confirmed that Diclofenac Potassium was successfully loaded onto all three nanoparticles (MgO–DP, CuO–DP, Ag_2O–DP). The broad peaks around 3200–3100 cm^{-1} correspond to O–H groups on the nanoparticle surfaces, while peaks in the 3030–2800 cm^{-1} region indicate the presence of Diclofenac aromatic C–H bonds.

The most important observation was the shift in the carboxylate bands: the asymmetric COO^- stretch appeared around 1550–1580 cm^{-1}, and the symmetric stretch near 1400–1410 cm^{-1}. The difference between these peaks ($\Delta\nu$) for all formulations fell in the range of 135–150 cm^{-1}, which is typical for bridging or bidentate coordination. This means the carboxylate group of Diclofenac binds to two metal atoms on the nanoparticle surface, forming a stable drug–nanoparticle complex.

Table2: FTIR Results for Drug-Loaded Nanoparticles (MgO–DP, CuO–DP, Ag_2O–DP)

Formulation	Key FTIR Peaks (cm^{-1})	Assignment	Interpretation
MgO–DP	3190–3157	O–H surface stretching	Presence of surface hydroxyls, hydration layer
	3090–2995	Aromatic C–H / N–H	Confirms Diclofenac aromatic groups
	1552	ν_asym(COO^-)	Carboxylate bound to Mg surface
	1408	ν_sym(COO^-)	Carboxylate coordination band
	$\Delta\nu \approx 144$	—	Bridging/bidentate binding
	598–423	Mg–O	Confirms MgO core structure
CuO–DP	3176–3116	O–H stretching	Adsorbed water + surface hydroxyls
	2998–2754	Aromatic C–H	Drug presence
	1591–1586	ν_asym(COO^-)	Carboxylate–Cu interaction
	1453–1425	ν_sym(COO^-)	Carboxylate coordination
	$\Delta\nu \approx 135$–160	—	Bridging/bidentate binding
	600–450	Cu–O	Confirms CuO lattice vibration

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Ag_2O–DP	3180–3100	O–H stretching	Surface hydroxyl groups
	3037–2731	Aromatic C–H	Drug functional groups
	1554–1520	ν_asym(COO^-)	Carboxylate–Ag binding
	1409–1403	ν_sym(COO^-)	Carboxylate coordination
	Δν ≈ 148–150	—	Bridging/bidentate binding
	600–500	Ag–O	Confirms Ag_2O nanoparticle formation

TABLE 3. Particle Size, PDI, and Zeta Potential of Drug-Loaded Nanoparticles

Formulation	Particle Size (nm)	PDI Range	Zeta Potential (mV)
MgO–DP	90–110	0.28–0.34	–19 to –23
CuO–DP	105–125	0.24–0.30	–21 to –25
Ag_2O–DP	70–85	0.20–0.25	–25 to –30

Table 3 displays the hydrodynamic particle size, polydispersity indices, and surface charge of drug-loaded nanoparticles. All formulations maintained nanoscale dimensions with **PDI values < 0.35**, indicating satisfactory uniformity. The negative zeta potential values reflect good colloidal stability, with Ag_2O–DP showing the highest stability due to its slightly more negative charge.

TABLE 4. UV–Visible Spectroscopy Results

Formulation	λmax of DP (nm)	λmax After Loading (nm)	Observed Shift
MgO–DP	276–278	281–285	+4 to +7 nm
CuO–DP	272–275	278–283	+5 to +8 nm
Ag_2O–DP	270–273	277–281	+6 to +10 nm

Table 4 outlines the UV–Vis spectral changes before and after drug loading. All formulations showed a bathochromic shift, confirming interaction between Diclofenac Potassium and nanoparticle surfaces. Ag_2O–DP exhibited the greatest shift, likely due to stronger surface binding and stabilization of the drug's electronic environment.

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TABLE 5. XRD Profile Summary of Synthesized Nanoparticles

Nanoparticle	Crystal Phase	Major Peaks (2θ, °)	Notes
MgO	Cubic	36–38, 42–44, 62–65	High crystallinity with sharp peaks
CuO	Monoclinic	32–35, 35–39, 48–52	Consistent with monoclinic CuO pattern
Ag_2O	Cubic	26–29, 31–34, 54–57	Matches standard Ag_2O JCPDS data

Table 5 summarizes the XRD-confirmed crystalline phases of the nanoparticles. The observed peaks correspond to standard JCPDS reference patterns for MgO, CuO, and Ag_2O, indicating successful synthesis and phase purity. No additional peaks were detected, confirming the absence of residual precursors.

TABLE 6. Drug Loading and Encapsulation Efficiency

Formulation	Drug Loading (%)	Encapsulation Efficiency (EE%)
MgO–DP	12–18%	68–75%
CuO–DP	15–20%	75–83%
Ag_2O–DP	18–24%	85–92%

Table 6 demonstrates the drug-loading behavior of each nanoparticle type. All nanoparticles successfully incorporated Diclofenac Potassium, with Ag_2O–DP showing the highest efficiency (85–92%), suggesting strong drug–surface interactions and higher affinity for the carboxylate functional group.

TABLE 7. In-vitro Drug Release Profile (0–72 h)

Formulation	Initial Burst Release (0–2 h)	Sustained Release (2–72 h)	Final Cumulative Release (%)
MgO–DP	18–28%	Gradual	60–70%
CuO–DP	20–32%	Moderate	70–78%
Ag_2O–DP	15–25%	Slow, extended	78–85%

Table 7 presents the drug-release behavior of the formulations. All nanoparticles exhibited a characteristic initial burst release followed by a prolonged sustained-release phase. Ag_2O–DP demonstrated the most extended release profile, consistent with its higher encapsulation efficiency and stronger drug binding.

TABLE 8. Trypsin Inhibition Activity

Formulation	Trypsin Inhibition (%)
MgO–DP	58–65%
CuO–DP	68–75%

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Ag_2O–DP	80–88%

Table 8 reports the inhibitory effects of the nanoparticles on trypsin activity. All drug-loaded nanoparticles reduced enzymatic activity, but the highest inhibition was observed in Ag_2O–DP, indicating superior anti-inflammatory potential.

TABLE 9. Serum Protein Protection Activity

Formulation	Serum Protein Protection (%)
MgO–DP	75–82%
CuO–DP	80–86%
Ag_2O–DP	87–93%

Table 9 showcases the ability of nanoparticles to protect serum proteins from oxidative damage. Ag_2O–DP again displayed the strongest protective effect, suggesting that this formulation is most effective in preventing protein denaturation during inflammatory stress.

Discussion

The high surface area, tuneable chemistry, and intrinsic biological activities of MONPs render them a versatile platform in drug delivery. In this work, MgO, CuO, and Ag_2O nanoparticles were synthesized, functionalized, and assessed as carriers of the model drug Diclofenac Potassium. Successful synthesis, high encapsulation efficiency, and significant in-vitro antiinflammatory performances point toward great potential for these nanoparticles in theranostics. These results are in agreement with several previously published studies and review articles showing the appropriateness of metal oxides in biomedical systems due to their physicochemical stability and functional versatility (11, 12.)

Synthesis and Physical Properties

All the nanoparticles demonstrated specific appearances where MgO was white, CuO was dark/brownish, while Ag_2O was grey-black. Their yields were between 80 – 92%, which indicated high precipitation with very minimal loss during washing and calcination processes. High yield synthesis of MONPs is crucial, particularly in ensuring reproducibility and scalability, especially when intended for biomedical applications. These findings are in line with previous studies where metal oxide nanoparticles synthesized through wet chemical methods exhibited stable yields and morphological reliability (11)

Of interest, metal oxides are valued for their stability and compatibility with surface functionalization. This allows for conjugation or the adsorption of drugs without altering core structural properties, a critical characteristic in drug delivery systems (12). In this context, the synthesized nanoparticles provided an optimal scaffold for Diclofenac Potassium loading.

FTIR analysis confirmed successful loading of Diclofenac onto MgO, CuO, and Ag_2O nanoparticles through characteristic shifts in the carboxylate region. The appearance of $\nu_{asym}(COO^-)$ around 1550–1580 cm^{-1} and $\nu_{sym}(COO^-)$ near 1400 cm^{-1}, along with $\Delta\nu$

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values of 135–150 cm^{-1}, indicates bridging/bidentate coordination, where the drug's carboxylate group binds simultaneously to two metal atoms on the nanoparticle surface. This mode of binding suggests a strong and stable interaction, supporting sustained drug retention. Additionally, metal–oxygen bands below 600 cm^{-1} confirmed the structural integrity of MgO, CuO, and Ag_2O cores after drug incorporation. Together, these findings demonstrate effective functionalization of the nanoparticles and strong drug–nanoparticle interactions favorable for controlled release applications.

Particle Size, PDI, and Zeta Potential

The particle size analysis disclosed that all the drug-loaded nanoparticulate formulations had a mean particle size in the nanometer range, between 70 and 125 nm, while their respective PDI values were <0.35, indicating good dispersion. Zeta potential values were in the moderately negative range of –19 to –30 mV, supporting the good colloidal stability observed. Such physicochemical characteristics are very crucial because they would have significant impacts on biological events such as cellular uptake, circulation time, and bioavailability. Commonly, NPs within this particle size range avoid rapid renal clearance while skipping uptake by the reticuloendothelial system, hence being ideal for systemic delivery (13).

The negative surface charge of the nanoparticles implies minimal nonspecific interactions with negatively charged serum proteins and cellular membranes. This can lead to lower cytotoxicity and higher stability in vivo. Similar observations have been made in metal oxide nanoparticles loaded with drugs, especially anti-inflammatory agents, where the size and charge profile played a major role in their efficacy and caused minimal cellular stress (13,14).

Drug–Nanoparticle Interactions and Structural Properties UV–Visible Spectroscopy

UV–Vis spectroscopy displayed a uniform bathochromic shift subsequent to drug loading and provided proof of surface interaction between the Diclofenac Potassium and the nanoparticle matrix. The degree of shift was highest in Ag_2O–DP, therefore showing the most binding affinity. Such shifts occur when electronic interactions modify the $\pi \rightarrow \pi^*$ transitions within the drug molecule — a well-documented phenomenon in nanoparticle–drug conjugation (15). These spectral changes reveal that the interaction of Diclofenac molecules with the metal oxide surface is due to electrostatic or coordinative binding rather than nonspecific adsorption.

XRD and Structural Integrity

XRD profiles showed sharp diffraction peaks for the individual standard patterns of the metal oxides: cubic MgO, monoclinic CuO, and cubic Ag_2O. The absence of any extraneous peaks and lattice deformation suggested that drug loading does not disrupt the crystallinity of the nanoparticles. Structural integrity of the nanoparticles is important to retain because a change in the crystal phase can alter surface properties, drug release behavior, and biocompatibility. Previous studies on drug-carrying metal oxide nanocarriers have indicated that drugs mostly attach to their surface without affecting the internal crystal structure, and this maintains mechanical and chemical stability due to the presence of solid rigid cores (16). The results presented herein also follow this trend and confirm that Diclofenac mainly associates with surface functional groups rather than integrating into the lattice.

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Drug Loading Efficiency and Release Profile

Encapsulation efficiencies varied between 68–92%, with the highest loading belonging to Ag_2O–DP due to its larger surface reactivity and enhanced metal–carboxylate affinity. Other differences among MgO, CuO, and Ag_2O can be attributed to their inherent surface chemistries, charge densities, and interaction strengths. Generally, metal-based nanoparticles with high surface energy, such as silver oxide, show superior adsorption capacity for ionizable drugs. The resulting release profiles showed a biphasic pattern with initial burst release followed by sustained release extending to 72 hrs. In fact, biphasic patterns are considered advantageous in anti-inflammatory therapy-an early therapeutic effect by the burst and prolonged maintenance by the sustained fraction. Ag_2O–DP presented the slowest and most controlled release, consistent with its strong binding interactions and higher drug-loading efficiency.

Similar sustained-release behaviors were also reported in various Diclofenac-based polymeric and metallic nanosystems, further validating these results (13,18). This sustained delivery might reduce the frequency of dosing besides minimizing systemic side effects associated with conventional formulations of Diclofenac.

In-Vitro Anti-inflammatory Activities Trypsin Inhibition Assay

Trypsin inhibition becomes a useful indicator of anti-inflammatory activity since excessive proteolytic activity contributes to tissue degradation and inflammatory progression. All drugloaded nanoparticles inhibited the trypsin activity to various extents, with the highest inhibition of 80–88% being caused by Ag_2O–DP. The results reflect both effective drug delivery and a possible intrinsic nanoparticlemediated modulation of protease activity.

Copper- and silver-based nanoparticles have previously demonstrated enzyme-modulating and anti-inflammatory properties, supporting the enhanced inhibition observed here (13,19). The combination of Diclofenac, as a known COX inhibitor, along with metal oxide surfaces synergistically may enhance anti-inflammatory effects beyond what the drug alone has achieved.

Serum Protein Protection Assay

The stability of serum proteins during inflammation is an important factor since oxidative stress commonly causes protein denaturation, which includes functional loss. Results indicated that all formulations reduced protein denaturation under oxidative stress, and once more, the bestperforming was Ag_2O–DP, with 87–93%. **This may result from:**

- Sustained release of Diclofenac for reducing inflammatory oxidative stress.
- Possible antioxidant-like activity of the metal oxide nanoparticles as previously reported in the literature (15,20).
- Surface interactions that stabilize protein structure.

These protein-protective effects indicate therapeutic potential in the prevention of tissue damage associated with inflammation.

Superiority of Ag_2O–DP Formulation

With the aggregation of results from all the various size, stability, drug loading, release kinetics, enzyme inhibition, and protein protection assays preformed, Ag_2O–DP outperformed

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MgO–DP and CuO–DP in every assay. The silver oxide formulations thus appear to offer the most favorable combination of physicochemical and biological attributes. The enhanced performance observed could be because of the bioactive surface chemistry, high surface energy, and strong affinity that silver-based nanomaterials have for organic molecules. However, such advantages have to be weighed against careful toxicity evaluation due to the dose-dependent cytotoxicity of silver nanomaterials.

Limitations and Future Prospects

While the in-vitro results are promising, there are a number of limitations that call for further investigation. Firstly, possible cytotoxicity of CuO and Ag_2O nanoparticles needs to be checked, since both materials exhibited variable biological responses depending on their concentration, particle size, and ion release. Secondly, in-vivo tests have to be conducted in order to understand biodistribution, pharmacokinetics, clearance, and interactions with the immune system. Finally, the optimization of surface functionalization, such as PEGylation or organic capping, should further minimize the toxicity and enhance the stability of the circulation. Based on the strong performance of Ag_2O–DP, future studies need to investigate the in-vivo anti-inflammatory efficacy and safety profile of this material. **Conclusion**

These results from this study confirm that the nanoparticles of MgO, CuO, and Ag_2O are efficient nanocarriers of Diclofenac Potassium with strong binding, structural stability, and enhancement in their biological performance. FTIR analysis confirmed successful drug loading in all the formulations, and it was found that the $\Delta\nu$ values indicated bridging or bidentate coordination-a mode of interaction that strengthens drug attachment and supports sustainedrelease behavior. The IR peaks corresponding to the metal–oxygen lattice remained intact, thereby confirming that drug incorporation did not affect the crystallinity of the nanoparticles.

The drug-loading and release studies showed high encapsulation efficiencies, while Ag_2O–DP showed the most controlled and prolonged release. In addition, the enhanced efficacy of the drug-loaded nanoparticles was further supported through in-vitro biological evaluations, as all the formulations showed improved trypsin inhibition and serum protein protection compared to the free drug. Ag_2O–DP showed superior activity, followed by CuO–DP and MgO–DP, which also exhibited effective results and proved that all three metal oxides offer symptomatic drug-delivery properties. Based on these findings, it is verified that nanoparticles of metal oxides can enhance the performance of conventional anti-inflammatory drugs significantly and may act as potential candidates for advanced systems of drug delivery. These studies need to be extended to in-vivo testing and toxicity assessment to establish their therapeutic potential and clinical utility.

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