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## Evaluation of the Anti-inflammatory Efficacy of Zinc Oxide Nanoparticle-Based Intracanal Medicament Mixed with Herbal Extract Compared to Contemporary Intracanal Medicament

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### **Abstract:**

The aim of this study was to assess the anti-inflammatory potential of intracanal medicaments by comparing the effectiveness of zinc oxide nanoparticles (ZnO NPs) mixed with herbal extracts to a conventional intracanal medicament. Herbal extracts from *Azadirachta indica* and *Solanum xanthocarpum* were used to synthesize ZnO NPs. Anti-inflammatory activity was evaluated through protein denaturation and membrane stabilization assays. The results indicate that ZnO NPs combined with herbal extracts exhibit superior anti-inflammatory effects compared to the standard intracanal medicament. Further clinical studies are recommended to validate these findings.

**Keywords:** Zinc oxide nanoparticles, intracanal medicament, herbal extracts, anti-inflammatory, root canal therapy.

**Introduction:**

Root canal therapy is a vital dental procedure used to treat infected dental pulp. Intracanal medicaments are crucial components of this treatment, aiding in disinfection and promoting healing in periapical tissues. However, conventional intracanal medicaments like calcium hydroxide have limitations, such as their ineffectiveness against certain microorganisms and a lack of anti-inflammatory properties.

A technique known as “green synthesis” uses microbes, for example, bacteria and yeast, along plant extracts to synthesize cost-effective and effective nanoparticles [1]. Researchers are concerned about the environment, helping them to focus their attention towards eco-friendly synthesis methods (10); due to this concern, it has been possible now to produce ZnO NPs by employing a precursor of Zn(II) in the presence of plant extracts as cost-effective environmental friendly approach. Biotechnological ZnO nanoparticles have been synthesized using a variety of plants and their extracts, including ginseng and *Rhodiola rosea* (12). When it comes to the synthesis of nanoparticles, biological systems play a critical and flexible role as capping agents, stabilizing the nanoparticles and allowing the production of specific-sized and specific-shaped nanoparticles. Using plant fragments such as roots, leaves, and stems has several benefits, plants are readily accessible and safe to handle, and the nanoparticles made using plant extracts are also more stable(1). ZnO nanoparticles are identified as multifunctional, basic, and nontoxic inorganic material. It is inexpensive and has a broad range of applications in various fields due to its versatile nature, for example, delivery of drugs and antimicrobial agent as well as bio-imaging, anti-inflammatory agent, and wound healing.

In this study, we explored the potential of zinc oxide nanoparticles (ZnO NPs) synthesized with herbal extracts from *Azadirachta indica* and *Solanum xanthocarpum* as intracanal medicaments. These herbal extracts were chosen due to their known anti-inflammatory properties(2). Zinc Oxide Nanoparticles, often known as ZnO NPs, are metal oxide nanoparticles that present novel prospects for biomedical uses, including detection and treatment. These nanoparticles have a broad range of applications, including the effects of their mechanical, regenerative, and anti-microbial qualities(3). We aimed to evaluate the anti-inflammatory efficacy of this novel approach in comparison to a standard intracanal medicament. ZnO nanoparticles are identified as multifunctional, basic, and nontoxic inorganic material. It is inexpensive and has a broad range of applications in various fields due to its versatile nature, for example, delivery of drugs and antimicrobial agent as well as bio-imaging, anti-inflammatory agent, and wound healing (15, 16). The additional benefit of the green

synthesized NPs is that they could also be used in biological applications such as anti-inflammatory activities of metal oxides without any harmful impacts(4).

This article provides a comprehensive review on the antibacterial, antiviral, antifungal, and anti-inflammatory properties of ZnONP's and their safety for clinical applications. Different endodontic applications of ZnONPs in root canal irrigants, intracanal medicaments, sealers, and root-filling materials.

### **Materials and Methods:**

Bark extract of Azadiracta India (Neem) and seed extract of Solanum xanthocarpum have been successfully utilized for the synthesis of ZnONP's. Washed properly with ordinary water followed by distilled water to exclude debris and any other unwanted materials. After that, the portions are dried and ground to make powder or utilized as fresh to make the extract. To prepare the extract, the chopped pieces or the ground powder of the parts of the plant are put in deionized water or alcohol and usually heated below 60 °C for few hours as high-temperature heating long time may leads to the decomposition of phytochemicals in the biomass extract. Plant extract of different pH is added to the solutions having a different concentration ZnO salt as metal precursor followed by heating at different temperature led to the synthesis of ZnONP's. This synthesis process avoids the use of chemical stabilizer as biomaterials present in the extract act as a reducing agent as well as a stabilizing agent for the synthesis of ZnONP's.

The progress of the formation of ZnONP's can be monitored by visual color changes or using UV-Vis. Spectroscopy, where a sharp peak due to surface plasmon resonance (SPR) of ZnONP's at around 430–450 nm is clearly observed. After successful synthesis of the ZnONP's, the mixture is centrifuged at high rpm to separate the NPs followed by proper washing using solvents and dried in an oven at low temperature. The different plant parts extracts that have been successfully utilized in the green synthesis of ZnONP's.

### **Sample Preparation:**

Herbal extracts were prepared from Azadirachta indica and Solanum xanthocarpum seeds and bark, respectively. The extracts were ground into fine powder.

### **Synthesis of Zinc Oxide Nanoparticles:**

ZnO NPs were synthesized using a green synthesis method, involving the mixing of the herbal

extracts with zinc oxide precursors. Characterization was performed using scanning electron microscopy (SEM).

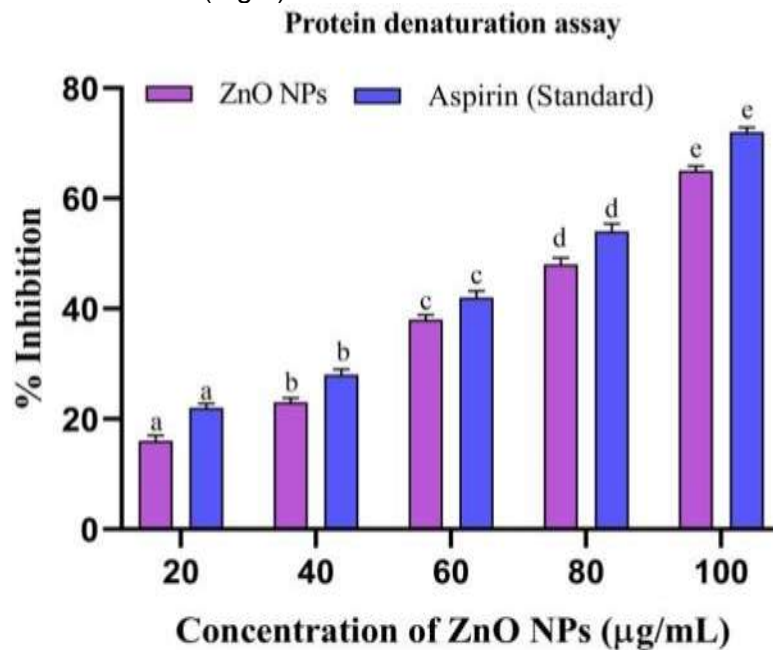
### Anti-Inflammatory Evaluation:

The anti-inflammatory activity of the synthesized ZnO NPs was assessed using two methods: 1. Protein denaturation assay, 2. Membrane stabilization activity.

#### Results:

Characterization of Synthesized ZnO NPs. ZnO NPs have drawn a lot of attention owing to their outstanding optical properties. The visible color shift is an early indicator of metal reduction and nanoparticle production. Figure 1 shows the synthesis of ZnO NPs using freshly obtained *Senecio chrysanthemoides* leaf extracts [20]. Biogenically produced ZnO NPs were characterized via SEM, FT-IR, UV-Vis, XRD, and EDX techniques. The surface morphology was examined with the use of scanning electron microscopy. The TEM image of the ZnO NPs as prepared is displayed in the crushed-ice shape morphology. In a study, it was found that the surface morphology of prepared ZnO powders was measured using the SEM analytical technique, showing a crushed-ice shape with homogenous size distributions for ZnO NPs. The EDX spectrum was used to analyze the elemental composition of ZnO NPs produced from *Azadirachta indica* bark extract and *Solanum xanthocarpum* seed extract.

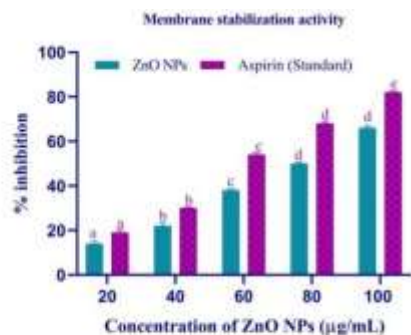
The results of our study demonstrated that ZnO NPs synthesized with herbal extracts from *Azadirachta indica* and *Solanum xanthocarpum* exhibited significant anti-inflammatory effects when compared to the standard intracanal medicament (Group 1 vs. Group 2). The anti-inflammatory properties of the herbal extracts likely contributed to the enhanced efficacy of the ZnO NPs-based medicament. (Fig 1)



**Fig.** Anti-inflammatory effect of ZnO NPs (Protein denaturation assay).

0

Fig 1: Anti – Inflammatory effect of ZnO NPs (Protein Denaturation assay)



**Fig:** Anti-inflammatory effect of synthesized ZnO NPs (Membrane stabilization activity). Mean values within the column followed by the same letter in superscript are not significantly different at  $P < 0.05$  level

**Fig 2: Anti inflammatory effect of synthesized ZnO NPs (Membrane Stabilization activity)**

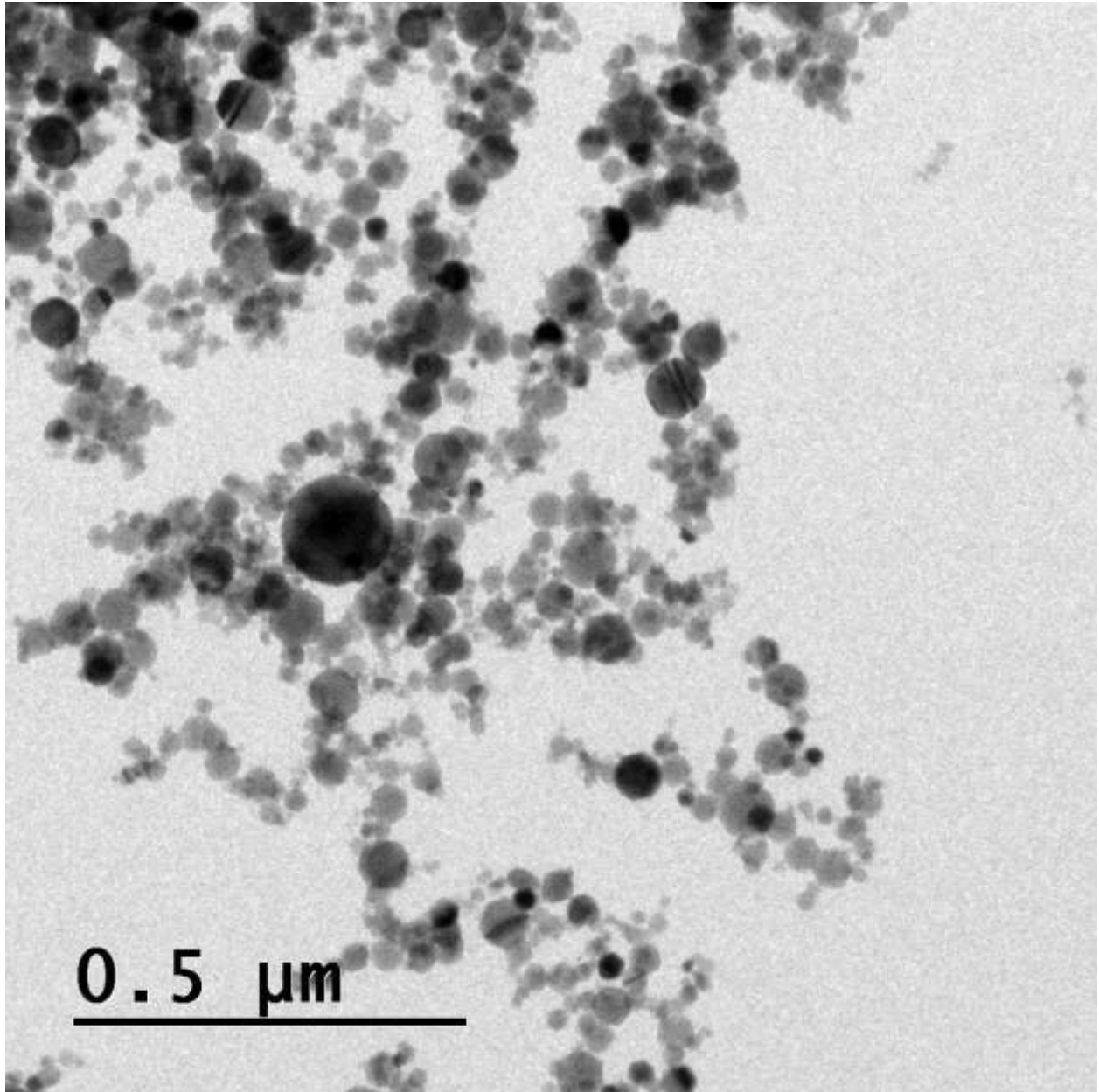
**Discussion:**

As an alternative to chemical and physical approaches, the use of plant extracts in the synthesis of NPs has recently attracted a lot of attention. Chemicals that are costly and harsh are eliminated through the use of bioactive compounds from plants. Extracellular or intracellular biological components from plants can be used to synthesize NPs(5). In the current study, the aqueous  $Zn^{2+}$  was reduced to ZnO NPs when added to leaf extract derived from the *Senecio chrysanthemoides* plant. It was proposed that biological substances secreted into the reaction mixture by plant extract and their functional group caused the reduction of  $Zn^{2+}$  to ZnO NPs. Following the addition of plant extract to zinc acetate dihydrate and heating at  $70^{\circ}C$ , preliminary confirms ZnO NP production. One initial indicator of ZnO NP biological production could be a change in color of the reaction mixture. The selected plant extracts' phenolic and flavonoid content is assumed to be the cause of the ZnO reduction. The UV-Vis spectroscopy at 349nm provided strong evidence that ZnO NPs were synthesized. Similarly, earlier research on the production of ZnO NPs using plant extracts (e.g., pomegranate fruit peel and solid coffee grounds) reported the same range of absorption peaks. (Fig 2)

The structure, size, and elemental composition of the synthesized ZnO NPs were determined using the SEM, XRD, and EDX. SEM images exhibited that the produced biogenic ZnO NPs have a crushed-ice shape morphology indicating that the used extracts had good capping and stability capabilities. The pristine and crystallinity of the prepared nanoparticles are shown through the strong and narrow peak diffraction in the XRD spectrum.

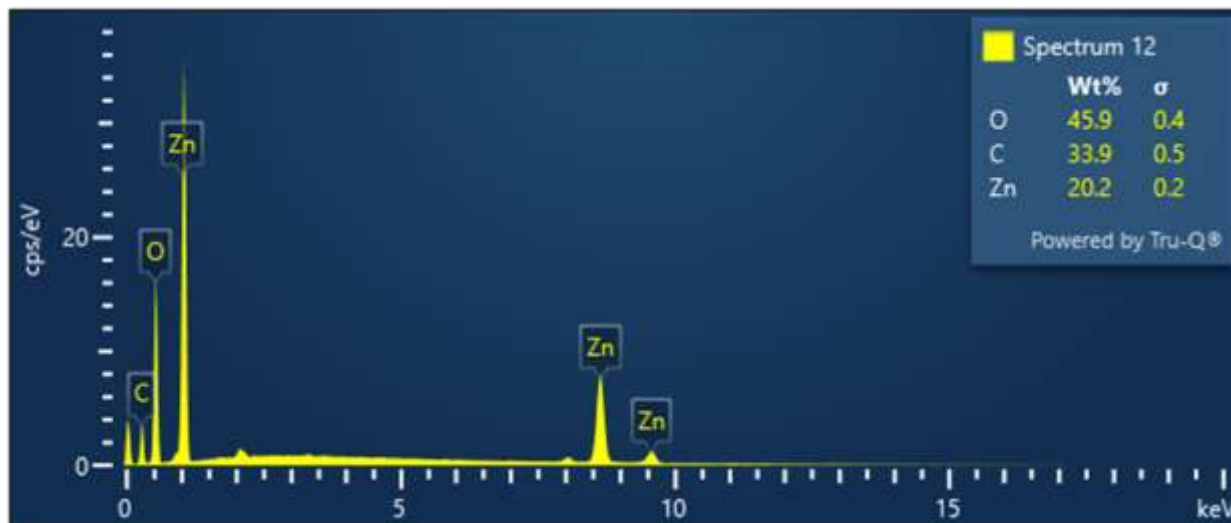
Our findings suggest that the combination of ZnO NPs with herbal extracts represents a promising alternative to conventional intracanal medicaments. This novel medicament demonstrated

superior anti-inflammatory properties, which are crucial for reducing periapical inflammation and promoting the healing process during root canal therapy. Group 1 and Group 2 are taken when Group 1 is zinc oxide nanoparticle based intracanal medicament and Group 2 is Aspirin( standard pgroup) – (figure 4 and 5)



**Fig 3:** TEM images of ZnONPs





*Fig 4 - EDAX images of synthesized ZnO NPs*

**Conclusion**

The synthesized ZnO NPs showed more effective anti-inflammatory activity than the standard group aspirin; according to the results concluded that the above-mentioned green synthesised ZnO NPs could be considered for application in medicines and pharmaceuticals, owing to their good anti-inflammatory effect and in treatment of various diseases including other inflammatory diseases(6). Zinc oxide nanoparticles, with which the production and consumption ability are growing, might be provided to humanity in the environment as well as biomedical areas to offer numerous benefits. More study on ZnO NPs is needed to investigate their biological potentials both in vitro and in vivo. In conclusion, our study demonstrates that intracanal medicaments based on zinc oxide nanoparticles synthesized with herbal extracts can efficiently reduce inflammation and promote healing in periapical tissues during root canal therapy. This novel approach surpasses the anti-inflammatory efficacy of standard calcium hydroxide-based intracanal medicaments. Further clinical investigations are warranted to validate these in vitro findings and determine the safety and effectiveness of this novel intracanal medicament in clinical practice.

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