# STUDY THE EFFICACY OF TITANIUM OXIDE ($TIO_2$) NANOPARTICLES AGAINST PROTOSCOLICES OF HYDATID CYSTS

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**ABSTRACT**

Hydatid cyst disease is one of the most common diseases in many places in the world. The infection occurs when human and livestock drinking or eating contaminated water and food with eggs of *Echinococcus granulosus* worm. Surgery is the best solution to eradicate cysts and rapid healing, but it may be accompanied by some risks such as rupture of the cyst and leakage its contents of protoscolices, which leads to the return of infection and spread in the body. Several methods have been used to reduce the risks of surgery, including withdrawal of hydatid fluid and its contents and injection scolicidal substances like ethanol and others. Researchers have recently tested the efficiency of nanoparticles such as selenium, silver, and gold nanoparticles against the protoscolices. The present study aims to test the efficiency of Titanium oxide ($TiO_2$) nanoparticles versus protoscolices of hydatid cyst. Protoscolices were obtained from hydatid cysts in sheeplivers. The $TiO_2$nanoparticles were prepared at concentrations of 250, 500, 1000, 2000, and 4000 µg/ml at different times (15, 30, 60 min.). The results showed the efficacy of all concentrations at all times in the killing of protoscolices compared with control groups.

**Keywords:** Titanium oxide nanoparticles, protoscolices, Scolicidal, hydatidosis

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## INTRODUCTION

Hydatid disease is a zoonosis whose history dates back to antiquity, and despite this fact,it is still a pertinent zoonosis today with massive socioeconomic impact affecting humans worldwide[(1)].*Echinococcus spp.* is the causing factor ofhydatid disease[(2)].The life cycle of this parasite involvesa definitive host (carnivores) sheltering adult worm and an intermediate host (various mammalian) carrying the larva or metacestode (hydatid cyst)[(3)]. Hydatid cysts are large fluid-filled vesicles5-10 cm in diameter, with a thick concentrically laminated cuticle and an internal germinal layer [(4)].The germinal layer is the origin of protoscolices, which are the contagious form to the definitive host, and the source of secondary infectionwhen naturally or experimentally released within mammalian tissues or peritoneal cavity[(5)].The liver and lungs are firstlyinfluenced, but cysts can place in any organ system[(6)].Surgery is the best solution for treating this disease until now, but other methods may play an important role in controlling the disease. Many scolicidal agents were used in conjunction with surgery to prevent the spread of protoscolices and recurrence of infection. Benzimidazole is the onlychemical syntheticlicensed drug for treating the disease.The low effectiveness of this medication has led to adopt alternative treatment techniques such as nanotechnology[(2)].Nanotechnology is a technique based on the use of

systems, devices, materials, and chemicals possessing characteristic properties and functions due to their small size (1-100) nm [7].Titanium dioxide (TiO2) has received great attention from researchers due to its unique properties that have led to its use in a wide range of applications including catalysis, photocatalysis, nano-paint and antibacterial agentsand many other applications[8].

## MATERIALS AND METHODS

**Collection of protoscolices**.

Hydatid cysts samples were obtained from the livers of naturally infected sheep with hydatidosis at the slaughterhouse in Baghdad/Iraq. A 20 ml syringe was used to withdraw the hydatid fluid and its contents of protoscolicesand then put in flasks. The hydatid fluid was left for enough time to allow the protoscolices to precipitate, then collected and suspended with normal saline. The germinal layer of cysts was collected and placed in petri-dish, and after that washed several times to assemble all protoscolices in the same way as before. Smyth & Barrett (9) method was used to calculate the viability of protoscolices.

**Preparation of nanoparticles suspension**

TiO2 NPs (50 nm) were purchased. Nanoparticles suspension was prepared according to the method of Jeng & Swanson (10) with modulation, where 0.4g of TiO2 NPswas weighed and suspended in 100 ml of distilled water and sonicated for 20 minutes before use. Napooni et al. (11) method were adopted to prepare five concentrations for TiO2 NPs (250, 500, 1000, 2000, and 4000) µg/ml with some modifications.

**Solicidal activity of TiO2nanoparticles**

Five concentrations of the TiO2 NPs (250, 500, 1000, 2000, 4000µg/ml) at different exposure times (15, 30, 60) min. were used to evaluate the scolicidal effect of TiO2 NPs against protoscolices of hydatid cysts. Protoscolices suspension (0.5 ml/1000 ps.) wasput in the test tubes, and then 0.5 ml of each concentration of TiO2 NPswere added to every test tube. The mixture (Ps with NPs) incubated at 37°C for 15, 30, and 60 min., and after that, the viability of protoscolices was calculated.

**Statistical analysis**

Statistical package IBM SPSS (version 25) was used to analyze the data. ANOVA and T-tests were used to calculate the differences between experimental groups and control groups ($p<0.05$).

## RESULTS

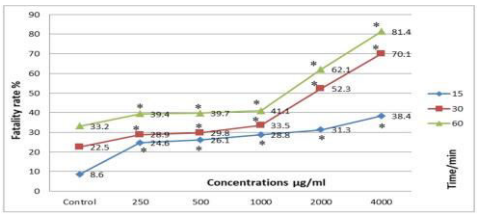


Figure 1: Fatality rate (%) of protoscolices after exposure to TiO2 NPs at various concentrations following various exposure times

* The difference between the experimental groups and control groups is statistical significance ($p<0.05$)

## DISCUSSION

This study was based on previous studies that demonstrated the efficiency of nanoparticles against parasites and other microorganisms. The results of the current study showedthe significant effect of TiO2 atall concentration (250, 500, 1000, 2000, 4000) µg/ml in the killing of protoscolices of hydatid disease after 15, 30, 60 min., when compared with control groups ($p<0.05$).The highest mortality rate was 81.4% at the concentration of4000 µg/ml after 60 min.While Allahvediyev et al. [12] pointed to the importance of both TiO2 and Ag2O NPs in killing drug-resistant bacteria and Leishmania parasites.Yalcinkaya &Lubasova[13] proved the significant effect of TiO2, ZnO, AgNO3, ZrO2, CuO, SnO2 against gram-negative bacteria. Andwhen testing the effect of gold nanoparticles in concentrations of 250, 500, 1000, 2000, 4000 µg/ml against protoscolices of hydatid disease after 5, 10, 20, 30 and 60 min., the highest mortality rate was 76% (4000 µg/ml, 60 min.) (11). Other researcherswere extracted nanoparticles from plants or fungi, such as the study of Rajakumar et al. (14), where they extracted TiO2 NPs from the leaves of *Mangifera indica* L, it was effectiveagainst larvae of some hematophagous parasites.The highest mortality rate has reached 90% and 94% after treatment of the protoscolices with Ag NPs (0.15 mg/ml) and Au NPs (0.3 mg/ml) extracted from *Penicillium aculeatum* after 120 min. respectively (15,16).

## CONCLUSION

In conclusion, this study approved the effectiveness of all TiO2 NPs concentrations in the killing of protoscolices at all given times. However, other studies are necessary, that may include testing the efficiency of TiO2 NPs in vivo, or mixing it with other nanoparticles, plant extracts or drugs.

### ETHICAL CLEARANCE

The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

### CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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