Evaluate the effect of zinc oxide nanoparticles using black seed hydroalcoholic extract on histopathological changes and BAX, Bcl-2 and Caspase-3 expressions in cisplatin-induced testicular damage in male mice

## Abstract

**Background** : Today, infertility is one of the major problems of most countries in the world, including Iran, which has affected many people. One of the main causes of male infertility is destruction of sperm-producing germ lines by a process called apoptosis, which leads to a decrease in the number of sperm.

**Aim:** Investigating the effect of zinc oxide nanoparticles synthesized using black seed hydroalcoholic extract on histopathological changes and BAX, Bcl-2 and Caspase-3 expression in testicular tissue damage cisplatin induced in male mice

Materials and Methods: In this study, In this study, 30 adult male mice with an approximate weight of 25-30 grams and an approximate age of 2 months were used. Mices were divided into five groups of six, including 1) Control group (received normal saline), 2) Cisplatin group (received normal saline + a single dose of cisplatin 7.5 mg/kg on the 5th day of the study), 3) Cisplatin group + black seed extract (received black seed extract at a dose of 200 mg/kg + a single dose of cisplatin 7.5 mg/kg on day 5 of the study), 4) Cisplatin group + zinc oxide nanoparticles synthesized using black seed extract (received zinc oxide nanoparticles synthesized using black seed extract at a dose of 200 mg/kg + a single dose of cisplatin 7.5 mg/kg on the 5th day of study), 5) Cisplatin group + zinc oxide nanoparticle (received zinc oxide nanoparticles at a dose of 25 mg/kg + a single dose of cisplatin 7.5 mg/kg on the 5th day of the study). Zinc oxide nanoparticles synthesized using black seed extract by green synthesis method. The synthesized nanoparticles were characterized using BET and TGA studies. Histopathological changes were evaluated using hematoxylen-eosin staining. The expression of BAX, Bcl-2 and Caspase-3 genes were investigated by real-time PCR method.

**Results:** The findings of the study for the first time showed that the treatment with zinc oxide nanoparticles synthesized using black seed extract significantly reduces the cisplatin induced index of tissue damage, improves the Johnson score and the height of the germinal epithelium (P<0.05). In addition, treatment with zinc oxide nanoparticles synthesized using black seed decreased the BAX and Caspase-3 expressions and increased the Bcl-2 expression.

**Conclusion**: Our study results for the first time showed that the use of zinc oxide nanoparticles synthesized using black seed extract had more protective effects compared to black seed extract or zinc oxide nanoparticle, only, in preventing testis histopathological changes and it prevent from germ cell apoptosis, as well as, infertility caused by decreased sperm production. Therefore, it seems that zinc oxide nanoparticles synthesized using black seed extract can be one of the excellent options to prevent infertility in the future.

Keywords: Infertility, ZnO NPs, Black seed, Mice, Apoptosis, Cisplatin