



Effect of Saponin Encapsulated by Ferritin Nanoparticles on Fetal Lung Development in Female Mice with *Streptococcus pneumoniae*

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Abstract

BACKGROUND: The effect of nanoherbal substances in the treatment of infectious diseases before mating or during pregnancy must be evaluated. Saponin has adverse effects on a pregnant mother and her fetal through complex mechanisms.

OBJECTIVES: This study aims to investigate the toxic effects of saponin encapsulated by ferritin nanoparticles (Nanosaponin) on fetal lung development in female mice with *Streptococcus pneumoniae*.

METHODS: Extraction of crude saponin from licorice roots was done by the powder heating and using 20 % ethanol and diethyl ether. Then, n-butanol and 5 % sodium chloride solution were added to the aqueous layer. The mice were divided into five groups of 10 including control, pneumonia, pneumonia treated with ferritin, pneumonia treated with saponin, and pneumonia treated with nanosaponin. Then, two groups of untreated pregnant pneumonia and pregnant pneumonia treated with nanosaponin were separated. In this study, tumor necrosis factor alpha (IFN- γ), heparin-binding epidermal growth factor-like growth factor (HB-EGF), Methyl-CpG binding domain 2 (MBD-2), and kruppel like factor 2 (KLF-2) genes were evaluated in the maternal lungs, and TNF- α level was evaluated using ELISA method in the fetal lungs. Maternal tissue, uterus tissue, and fetal lung were examined by hematoxylin and eosin staining, and maternal body tissue was examined by trichromason staining and Oxidative stress parameters were investigated.

RESULTS: Nano saponin decreased the expression of IFN- γ ($P < 0.05$) ($P < 0.01$), MBD-2 ($P < 0.05$) and HB-EGF genes, KLF-2 protein level and TNF- α levels in fetal lung. The thickness of uterine myometrium and blood flow of endometrium increased the number of live embryos and the rate of successful pregnancy. In addition, Nano saponin effectively improved the oxidative stress response in the fetus without any harmful effect on the mother's liver tissue.

CONCLUSIONS: The nanosaponin has no toxic effects on the study organs of the mother and fetus. It has therapeutic effects on the fetal lung development process after the infection of mother with *Streptococcus pneumoniae*.

Keywords: Fetus, Ferritin nanoparticles, Lung, Saponin, *Streptococcus pneumoniae*

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Figure Legends and Table Captions

Table 1. The primer sequence used in Real-time PCR.

Figure 1. Morphology of nanosaponin using the scanning electron microscope.

Figure 2. Fertilization by a fertile sperm using Giemsa staining technique. A) Control group; B) Pneumonia group treated with nanosaponin.

Figure 3. Protein levels of KLF-2 and GAPDH using Western blot assay.

Figure 4. Histopathology images of liver tissue in (A) control group and (B) pneumonia group treated with nanosaponin.

Figure 5. Light microscope images of uterine tissue (H&E staining) in fetuses born from (A) control group and (B) pneumonia group treated with nanosaponin.

Figure 6. Microscopic images of fetal lung tissue (H&E staining) in fetuses born from (A) Control group and (B) pneumonia group treated with nanosaponin.