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Effect of Black Seed (*Nigella sativa*) Ethanol Extract on the Expression of Hypoxia Inducible Factor-1a(HIF-1a) and Endothelial Nitric Oxide Synthase(eNOS) in Placenta of Preeclampsia Mice Model

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Abstract: About 10-15% of direct maternal death is caused by preeclampsia and eclampsia. The first stage pathogenesis of preeclampsia is indicated by an increase in HIF-1α placenta and AT1-AA. The second stage of preeclampsia is indicated by a decrease of eNOS placenta expression. Black seed (Nigella sativa) has thymoquinone and thymol as the active substances has shown potential in the prevention and therapy of preeclampsia. The trial study used 30 pregnant mice (Mus musculus) randomly divided into six groups. Two groups was for control (positive and negative) and other 4 groups were for experimental treatment. Positive control and experiment groups were injected with severe preeclampsia serum in pregnant women. The serum-injected experimental mice group were administered with various doses of N. sativa ethanol extract (500, 1000, 1500, and 2000 mg/kg/day for each group). Mice with a blood pressure of $\geq 140/90$ mmHg and proteinuria of $\geq 10\mu g/day$ served as preeclampsia mice models. Treatment with ethanol extract of N. sativa was performed on days 15 to day 19 of gestation. Data were analyzed to compare the mean of HIF-1α and eNOS, showing a significant effect of ethanol extract of N. sativa in various doses, decreasing the expression of HIF-1α and increasing eNOS in preeclampsia mice models. The optimal dose for both was 1000 mg/kg/day. The results concluded that the N. sativa ethanol extract administration decreased the expression of HIF-1α and increased eNOS expression in the placenta of preeclampsia mice models.

Keywords: eNOS placenta, ethanol extract of *N. sativa*, HIF-1α placenta, preeclampsia.

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