INTERACTION OF THYMOQUINONE with ALPHA 7 NICOTINIC ACETYLCHOLINE RECEPTOR IN LPS-INDUCED NEUROINFLAMMATORY MODEL.

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Alzheimer's disease (AD) is neurodegenerative disorder resulting from loss of cholinergic neurons in brain especially acetylcholine. It has been reported that α7 nicotinic acetylcholine receptors (α7 nAchRs) play an important role in cognitive function and can be target therapy for treating cognitive deficits. α7 nAchR agonists cause memory enhancement through phosphorylation of cAMP response element binding protein (CREB). Thymoquinone (TQ) was recently considered as acetylcholine esterase inhibitor and increased α7 nAchR expression in brain. However, the effect of TQ as α7 agonist has not been investigated. Our aim was to investigate the mechanism of action of TQ on α7 nAchR.

Neuroinflammatory AD rat model was developed by injecting LPS i.p (0.8 mg/kg) once. A specific α7 agonist and α7 positive allosteric modulator were used. Rats were injected with TQ (10 mg/kg) i.p for 5 consecutive days with or without α7 positive allosteric and another qroup with α7 agonist + α7 positive allosteric modulator. After one week, rat brains were subjected to immunohistochemical studies. Molecular docking studies were done in which TQ was docked on chimeric acetylcholine binding protein.

Results indicate significant decrease in amyloid plaques with significant increase in p-CREB expression in TQ treated groups especially the group treated with TQ and allosteric modulator. Docking results show hydrophobic interactions of TQ similar to ligand interactions in complex with the receptors. This indicates the possible direct agonistic effect of TQ on α7 nAchR and its role in modulating cognitive defects. TQ can be promising therapeutic module for treatment of AD.