7th Euro-Global Summit on **TOXICOLOGY & Applied Pharmacology**

October 24-26, 2016 Rome, Italy

In vivo and *in vitro* evaluation of the role of NMDAR/NO pathway in neuroprotective effects of lithium

Razieh Mohammad Jafari and Ahmad Reza Dehpour Tehran University of Medical Sciences, Iran

Lithium exerts protective effects against diverse insults *in vitro* and *in vivo*. Neuroprotective effects of lithium were not Deprevented by inclusion of myoinositol nor mimicked by a potent inositol monophosphatase inhibitor, suggesting a mechanism independent of inositol monophosphatase blockade. Recently, increasing evidence has suggested that NMDAR/ nitric oxide (NO) signaling could mediate some lithium-induced responses in the brain and peripheral tissues. However, the probable role of the NMDAR/NO system in the action of lithium has not been fully elucidated. Therefore involvement of NMDA and nitrergic system in anticonvulsant effects of lithium in clonic seizure model induced by pentylenetetrazole in male NMRI mice and in cerebellar granule neurons (CGN) culture is studied. In present study, the NMDAR/NO probable mechanism of lithium evaluated by animal study design including following treatments were done. Injection of a 7-day effective doses of lithium chloride (10, 20, 30, 60 mg/kg, i.p.) before the induction of seizure significantly increased the seizure threshold. The anticonvulsant effect of an effective dose of lithium was prevented by pre-treatment with low and per se non-effective dose of MK-801 (a potent NMDA receptor antagonist) and 7-NI (nNOS inhibitor). 7-NI and MK-801 had no significant effects on seizure threshold. Co-administration of low doses of NMDA antagonists MK-801 and 7-NI with chronic doses of lithium significantly reversed the effect of lithium. Similarity of results with MK-801 alone or 7-NI alone shows that NO releasing is dependent on activation of NMDA receptors and is its downstream pathway. Molecular and cellular studies on CGNs by MTT assay, Griess reaction, Western blotting also have been reported.

mohammadjafari_r@razi.tums.ac.ir