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Monoacylglycerol lipase inhibitor, JZL-184, like aspirin, has neuroprotective effects in the mice middle cerebral artery occlusion model of stroke

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Background and Objective: Investigators are searching to find new therapeutic strategies to reduce stroke secondary injury. JZL-184 (JZL) is an inhibitory factor for the production of arachidonic acid (AA). Thus, it suppresses of AA metabolites which are the cause of inflammation and tissue edema. Therefore, JZL may be considered for suppression of stroke secondary injury in mice middle cerebral artery occlusion (MCAO) model. Additionally, Aspirin is a known anti-inflammatory factor which is used to reduce pro-inflammatory secondary injury. The aim of this study was to determine the effects of JZL on the reduction of stroke secondary injury and to compare them with Aspirin effects.

Material and methods: MCAO model has been induced and accordingly 83 male MCAO induced mice have been introduced to the study. The animals were divided into seven groups including intact, controls, vehicle, Aspirin, JZL 4, 8 and 16 mg/kg administrated groups. Brain edema and infarction, behavioral functions and brain levels of IL-10, TNF-α and matrix metalloproteinase-9 (MMP9) have been examined in the evaluated groups.

Results: The results revealed that JZL reduced brain edema, infarction, brain levels of TNF- $\alpha$  and MMP9 and also increased brain levels of IL-10 as well as improved behavioral functions in all three concentrations. The therapeutic effects of JZL were observed as well as Aspirin.

Conclusion: Based on the results, it seems that JZL can be considered as a good candidate for inhibition of stroke secondary injury in the case of delayed treatment.

Keywords: Stroke, MCAO, JZL-184, Aspirin, Monoacylglycerol lipase