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Comparative assessment of a novel neuroprotectant against citicoline in a thrombus-induced cerebral ischemia mouse model

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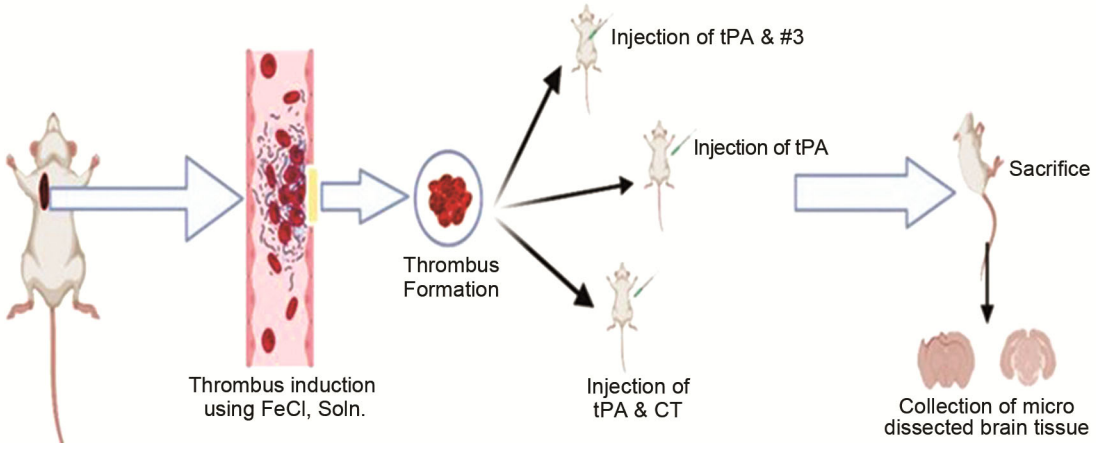
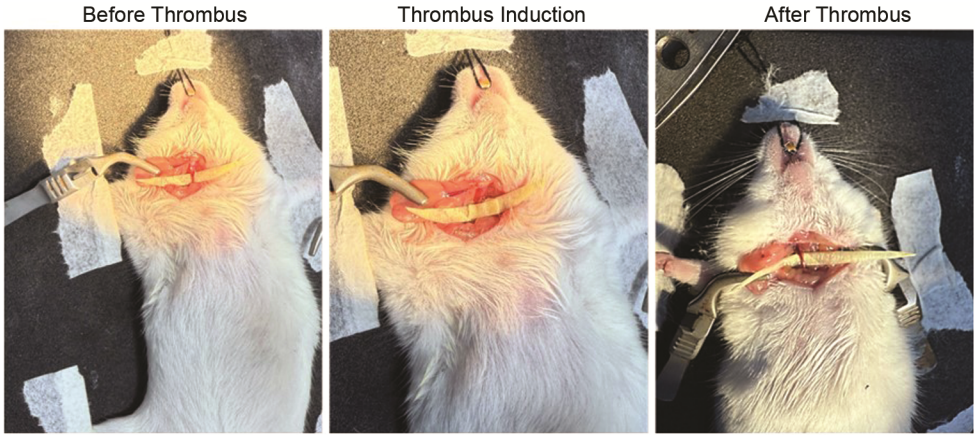
Stroke is one of the leading causes of mortality and morbidity worldwide. Among the two major forms of stroke (ischemic and hemorrhagic), ischemic stroke is the most prevalent and occurs when cerebral or cervical blood vessels are occluded. Ischemic occlusion can result from the formation of a thrombus within the cerebral or cervical vasculature (thrombosis), the migration of an embolus from a distant site, such as the heart, to the brain (embolism), or severe arterial stenosis in or leading to the brain. Despite substantial advancements in medical science over the past two decades, there remains a paucity of neuroprotective agents available for stroke management. Citicoline is an FDA-approved agent that has demonstrated promising efficacy in treating ischemic stroke. It functions as a neuroprotectant in ischemic stroke patients, facilitating their recovery. A novel spiro tricyclic compound [IM-1725-RS-109] or compound #3 has already exhibited significant anti-inflammatory, neurogenic, and neuritogenic properties in a preclinical BCCAo stroke model in mice. We compared our novel compound with citicoline in a thrombus-induced ischemic stroke model and found that our compound demonstrated superior anti-inflammatory and neurogenic effects. Behavioral assessments revealed that treated animals showed greater restoration of locomotor activity and motor coordination post-stroke than citicoline-treated animals. Hence, we propose that our novel spirotricyclic compound has the potential to emerge as a therapeutic agent for ischemic stroke in the near future.

Keywords: Neurodegeneration, Oxidative stress, Motor deficits, Reperfusion Injury, Anti-inflammatory, Neurogenesis



Supplementary Figure 1 — The figure shows a graphical demonstration of the experimental design.



Supplementary Figure 2 — The Figure Induction of thrombus using $FeCl_3$solution-soaked strips.

Table 1: List of Primers used for qRT-PCR studies:

RPL32:	F.W. ATCAGGCACCAGTCAGACCGATR.V. GTTGCTCCCATAACCGATGTTGG	
NeuroD1:	F.W. CCTTGCTACTCCAAGACCCAGAR.V. TTGCAGAGCGTCTGTACGAAGG	
Dcx :	F.W.CTGACTCAGGTAACGACCAAGAC	R.V. TTCCAGGGCTTGTGGGTGTA
IL-6:	F.W. TACCACTTCACAAGTCGGAGGC	R.V. CTGCAAGTGCATCATCGTTGTTC
IL-1β	F.W. AAAGTGCGCTTCAGCATGTC	R.V. ACCCGCTGATCTCCTTGAGTA