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CONCLUSION
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The ester of LCA and ascorbic acid abbreviated as FED was synthesized and purified. The intermediates and FED were adequately characterized by FTIR, NMR and mass spectrometry. FED was found to be adequately stable in physiological conditions. It was found to be safe both in acute toxicity and sub-chronic toxicity tests. It showed relatively less plasma protein binding. Oral bioavailability of LCA was enhanced and was found to be about 69% from FED administration. The brain availability of LCA was also higher, following oral intake of FED. It also enhanced the elimination half-life of LCA by 2 hrs. The enhanced pharmacokinetic parameters were also reflected in the pharmacodynamics of LCA. Upon oral administration of FED, it stimulated CNS and improved motor co-ordination in animals. It also enhanced spatial memory which suggested its capacity for cholinergic modulation. This was further evident from its ability to lower acetylcholinesterase activity in brain. It further exhibited potential for protection against chemical and stress induced neurotoxicity. It showed adequate protection against haloperidol induced catatonia and pilocarpine induced seizure. It further showed protection against kainic acid induced neurotoxicity. In forced swimming stress model, it exhibited significant protection of various tissues including liver, kidney, heart and brain. Most of these models have reactive oxygen species as the major contributing factor for the neurotoxicity. In stress induced model, FED pre-treatment showed good in vivo antioxidant action, based on the findings that, it maintained superoxide dismutase activity in brain. It also lowered lipid peroxidation in brain which further supported its in vivo antioxidant action.

Ang-II induced inflammation and stress are common to hypertension and neurodegeneration. LCA and losartan with their established antihypertensive action due to blockade of AT1 activation are ideal candidates for application against neurodegeneration. Their poor oral bioavailability coupled with poor brain permeability are the major hurdles in their repurposing against CNS disorder. In this perspective, FED can be considered as an alternative. With better oral bioavailability and brain availability it can ensure adequate level of LCA to effectively block AT1 mediated inflammation and related CNS disorder.
More direct and clinical evidences are necessary to establish its utility. Nonetheless, this work has provided enough proof of concept, which can be taken forward for application against CNS disorder. Considering the central role of AT1 activation in inflammation, further work in this direction may be useful in repurposing LCA against other inflammatory disorders.