Potential Antidepressant-like Activity of Novel Isoquinoline Derivatives, Compounds of Low Toxicity in Mice

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Introduction: Depression is a serious disorder in today’s society characterized by expression and regulation of mood and emotions, accompanied with abnormalities of limbic system structures. It is an illness that has a lifetime prevalence approaching 15–25% associated with significant morbidity and mortality. In view of the above considerations, the aim of this study was to evaluate antidepressant-like and toxicological properties of 7-fluoro-N,3-diphenylisoquinolin-1-amine (1a) and 3N-(4-chlorophenyl)-7-fluoro-3-phenylisoquinolin-1-amine (1b). Material and Methods: To investigate the antidepressant-like behavior, mice were submitted to the forced swimming test (FST). The locomotor activity was carried out in the activity chamber. The animals were treated with 10 mg kg$^{-1}$ intragastrically (i.g.) with 1a or 1b compound or canola oil (vehicle) 30, 45 and 60 min before test. Twenty four hours after treatment the animals were killed by cervical dislocation and the liver, kidney and brain were quickly removed for biochemical assays, δ-aminolevulinate dehydratase (δ-ALA-D) and Na$^+$, K$^+$-ATPase activities. Results and discussion: A single dose of 1a and 1b, independent of treatment time, had antidepressant-like profiles of action, which was demonstrated by the reduction in the immobility time recorded in the mouse FST. The FST is therapeutically useful for screening antidepressant drugs and is very well accepted as a reliable indicator of this kind of pharmacological activity. A single dose of 1a and 1b did not alter the behavioral performance of animals in the activity chamber. The locomotor performance of animals is essential for the FST to avoid false positive results. Compounds 1a and 1b did not show acute toxicity evaluated by δ-ALA-D and Na$^+$, K$^+$-ATPase activities, two enzymes sensitive to oxidizing agents. Conclusion: Compounds 1a and 1b showed antidepressant-like activity and low toxicity in mice. These are promising novel isoquinoline compounds that could be useful for treatment of depression.

Palavra chave: Isoquinoline, Antidepressant-like, Toxicology

Patrocínio: FAPERGS, CNPq and CAPES