

ABSTRACT

Depression is one of the most common neuropsychiatric disorders and is associated with dysfunction of the neuroendocrine system and alterations in specific brain proteins. *Boophone disticha* (*BD*) is an indigenous psychoactive bulb that belongs to the *Amaryllidaceae* family, which is widely used in Southern Africa to treat depression, with scientific evidence of potent antidepressant-like effects. The present study examined the antidepressant effects of *BD* and its mechanisms of action by measuring some behavioural parameters in the elevated plus maze, light dark box, open field forced swimming, brain content of corticosterone, brain derived neurotrophic factor (BDNF), and neuroblast differentiation in the hippocampus of Balb/c mice exposed to the five-day repeated forced swim stress (5dRFSS) and 28 days chronic restraint stress. Male Balb/c mice were subjected to the 5dRFSS and 28 days chronic restraint protocols to induce depressive-like behaviour (decreased swimming, increased floating, decreased open arm entry, decreased time spent in the open arms and decreased head dips in the elevated plus maze test, increased time in dark box in the light dark box test, reduced frequency of rearing and increased time on the sides of the open field in the open field test), and treated with distilled water, fluoxetine and *BD*.

Three weeks *Boophone disticha* treatment (10mg/kg/p.o) significantly attenuated both the 5dRFSS and chronic restraint-induced behavioural abnormalities and the elevated brain tissue corticosterone levels observed in stressed mice. Additionally, 5dRFSS exposure significantly decreased the number of neuroblasts in the hippocampus and BDNF levels in the brain of Balb/c mice, while fluoxetine and *BD* treatment attenuated these changes. In the chronic restraint stressed mice, similar effects of *BD* treatment were observed after 21 days of treatment, however, the levels of corticosterone were not different in control and stressed animals, probably due to habituation to stress. In both 5dRFSS and chronic restraint stress, the antidepressant effects of *BD* were comparable to those of fluoxetine, but unlike fluoxetine, *BD* did not show any anxiogenic effects, suggesting better pharmacological functions. It is important to note that in chronic restraint stress mice, it appeared that animals seemed to have habituated to stressful conditions, demonstrated in part by brain tissue levels of corticosterone that were not elevated in stressed animals treated with distilled water. However, BDNF levels remained significantly low in stressed animals treated with distilled water, suggesting that the effect of chronic stress in this parameter were not reversed when animals habituated.

In conclusion, our study shows that *BD* exerted antidepressant-like effects in both 5dRFSS and chronic restraint stress mice, mediated in part by normalizing brain corticosterone and BDNF levels. Due to some degree of habituation in chronic stress model, caution should be exercised when evaluation effects of treatment in different parameters to evaluate antistress effects of tested agents, particularly levels of corticosterone. Furthermore, the persistent low levels of BDNF suggest that habituation of animals to chronic stress is due to normalising levels of corticosterone but not BDNF. The above occurrence could suggest that recovery from chronic stress without antidepressant treatment could alleviate other behavioural symptoms but not cognitive impairment which is influenced in part by BDNF levels.

Key words: Depression, Antidepressants, Hippocampus, Stress, Behaviour