Effect of *Hypericum caprifoliatum* Cham. & Schltdt. (Guttiferae) in the predictive model of depression associated with forced swimming test: chronic variable stress.

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**Introduction:** The genus *Hypericum* has been widely studied, and our group has demonstrated that South Brazilian native species have antidepressant-like (Daudt, Phytotherapy Research, v.14, p. 344,2000) and antinociceptive (Viana, Fundam. Clin. Pharmacol. v.20, p. 507, 2006) activities in rodents. *Hypericum caprifoliatum* showed promising results in the forced swimming test (FST) (Viana, Fundam. Clin. Pharmacol. v.20, p. 507, 2006). Chronic stress has been proposed as a depression model in animals; it induces an increase of immobility time in the FST (Tagliari, Neurochem. Res v. 36, p.487, 2010). The aim of this study was to evaluate the antidepressant-like effect of an *H. caprifoliatum* n-hexane extract (HCP) in rats submitted to the chronic variable stress model followed by FST.

**Experimental part:** The extraction of the dried plant material was carried out with n-hexane (plant/solvent 1:4 w/v) by maceration for 24 or 48 hours, followed by filtration and evaporation of the solvent under reduced pressure at 45°C. Wistar male rats (250 g) were stressed daily during 40 days. Different stressors were applied at different times of the day without following a specific sequence, making the test unpredictable. Only one stressor was used each day. At day 41, 24h after the last session of chronic stress, animals were exposed to the FST during 15 minutes (pre-test). Immediately, the treatment was started (180 mg/kg/day for 5 days: 2 daily doses of 90 mg/kg, p.o.). At day 46, the animals were exposed to the FST for 5 minutes (test). The immobility time was registered at the pre-test and test. The protocols were approved by UFRGS Research Ethical Committee (project number 22091).

**Results / Discussion:** The stressed group (453.7±189.0, n=15) showed higher immobility time in the pre-test compared to the control group (275.5±142.64, n=18) (p<0.01, Student t-test) demonstrating that it induced a depressive-like behavior. HCP reduced the immobility only in the stressed groups (98.7±20.6, n=8) compared to vehicle-treated stressed animals (184.1±65.2, n=7) (p <0.01, Two way RM ANOVA) unlike what happened with the group not stressed. We can presume that the HCP effect is more pronounced in the context of a model of depression where the disease is already installed.

**Conclusion:** *H. caprifoliatum* presents antidepressant-like effect in an animal model of depression, which is supposed to have more construct validity than FST. This reinforces the notion that *H. caprifoliatum* should be useful to develop new antidepressant drugs.

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