Evaluation of antinociceptive activity of the essential oil of *Stevia elatior* Kunt

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Stevia elatior Kunth is a plant from Asteraceae family that grows in Central America and Mexico and in northern South America (1).The aim of this study was to evaluate the antinociceptive activity of the essential oil (EO) from *Stevia elatior* Kunt. Aerial parts of *S. elatior* were collected in September/2014, in San José Chacayá, Sololá, Guatemala. EO was obtained by hydrodistillation using a Clevenger-type apparatus for 2 h. Swiss *Webster* mice (20-25g, n=6) were orally pretreated with 10, 30 or 100 µL/kg doses and evaluated in formalin- or capsaicin-induced licking response and hot plate test. One hour after treatment mice received intraplantar injection (20 µL) of formalin (2.5%) or capsaicin (5.2 nmol/paw). The time (in seconds, sec) that animal spent licking the injected paw was counted with a stopwatch during the first 5 minutes (1st phase) and between 15 and 30 min (2nd phase) or during 5 min, after formalin or capsaicin injection, respectively. In hot plate test, animals were placed on a plate (Insight Equipment, Brazil) set at 55±1°C. At 30 min intervals between 30 and 180 min, after oral administration of EO or vehicle the reaction time was recorded when the animals licked their fore- and hind-paws and jumped. Baseline was considered the mean reaction time obtained at 60 and 30 min before administration of the compounds or vehicle, and was defined as the normal reaction of the animal to the temperature. Antinociception was calculated by the area under the curve (AUC) of responses between 30 and 180 min after drug administration. EO significantly reduced 1st and 2nd phases of formalin-induced licking, 1st phase: vehicle-treated group = 42.4 ± 7.7 sec *versus* 23 ± 10.4* sec (45.7%); 18.1 ± 3.6* sec (57.3%) and 16.2 ± 7.1* sec (61.9%) to 10, 30 and 100 µL/kg, respectively; and 2nd phase: vehicle-treated group = 224.7 ± 25.7 sec *versus* 195.5 ± 16.6 (12.1%); 127.7 ± 31.3* sec (43.2%) and 77.6 ± 26.3* sec (65.5%) to 10, 30 and 100 µL/kg, respectively. Higher doses of EO also reduced capsaicin-induced licking: vehicle-treated group = 57.8 ± 7.8 sec *versus* 41.6 ± 9.9 sec (28%); 25 ± 10.2* sec (56.8%) and 18.1 ± 6.2* sec (68.7%). EO also demonstrated significant effect at the hot plate model. Doses of EO significantly increased the AUC values when compared with vehicle-treated group. Vehicle-treated group = 986.5 ± 193.1; 10 µL/kg = 1,725.5 ± 370 (74.9% increase); 30 µL/kg = 1,229.5 ± 152.2 (24.6% increase); 100 µL/kg = 1,868.5 ± 339.1 (89.4% increase). Our results are the first evidence that EO from *S. elatior* Kunt produce peripheral and central antinociceptive effects. The mechanism of antinociception and antinociceptive pathways involved in *S. elatior* effect are under investigation.

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