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SHORT COMMUNICATION

Anxiogenic-like effects of *Uncaria tomentosa* (Willd.) DC. aqueous extract in an elevated plus maze test in mice: a preliminary study

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The purpose of this study was to examine the effect of orally administered *Uncaria tomentosa* aqueous extracts (UTE) (Willd. ex Roem. & Schult.) DC. (Rubiaceae) during 7, 15, 30 and 90 days of treatment on the expression of anxiety, as expressed in the elevated plus maze test in male Albino Swiss mice. UTE revealed an anxiogenic effect in relation to the control group at 15 and 30 days, but it was reversed after 90 days of administration, without affecting the locomotor activity or any deleterious effects on the overall performance of the animal, either for its ambulation, or clinical status, and body weight and organ weight/body weight from liver, lung and kidney were unaffected. These biphasic effects are usually indicative of heterogeneity in sites of action due to the presence of many alkaloids (speciophylline, uncarine F and uncarine E) and flavanols (catechin and epigallocatechin) identified and isolated from UTE.

Keywords: *Uncaria tomentosa*; plus maze; rodent; anxiety test; behavioural

1. Introduction

Anxiety disorders are currently the most predominant psychiatric diseases in the USA and in the Europe, affecting between 10% and 30% of the general population and represent a serious and ever-increasing spending for these countries (Rice & Miller 1998; Wittchen et al. 2001). The elevated plus maze (EPM) test is a sensitive test, and in the animal models, the EPM is one of the most popular animal tests used for research on the behavioural pharmacology of anxiety and neurobiological anxiety mechanisms (Treit et al. 1993). Anxiolytic agents increase, whereas anxiogenic compounds decrease the percentage of time spent on open arms (Lister 1987).

Very few studies have examined the long-term consequences of *Uncaria tomentosa* aqueous extracts (UTE) administration in laboratory animals; and moreover, there are no reports about the effects of UTE on anxiety-like behaviour in mice. Nevertheless, other authors describe that *Uncaria rhynchophylla* (Miq.) Havil has an anxiolytic-like effect mediated by the stimulation of 5-HT_{1A} receptors, one specie very close to *U. tomentosa* which apparently has the same complex and specialised opening mechanism (Shi et al. 2003; Jung et al. 2006).

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The aim of this study was to evaluate the action of the UTE for 7, 15, 30 and 90 days in a model of anxiety in mice. In this work, it was demonstrated that the administration of UTE in murine on different days was able to induce temporary anxiogenic effects, without modifying the clinical status or locomotion.

2. Results and discussion

The medical plants have been used as medicament based simply on a traditional folk use that has been perpetuated along numerous generations in anxiety disorders (Rex et al. 2002; Carlini 2003; Jorm et al. 2004; Newman & Cragg 2007; Cryan & Sweeney 2011). In accordance with Santa María et al. (1997) and Roque et al. (2009), the administration of extracts on different days did not induce overt clinical signs and any symptoms of intoxication or abnormalities in tissues in mice and no difference in water consumption was noted for control versus treatment groups during all experiments (mL/kg/h; $n = 8$; 5.59 ± 0.27 vs 5.58 ± 0.41, respectively, or in initial and final weights, respectively (g, *n*:6). Control: 34.09 ± 0.92, 33.65 ± 1.42; UTE-7: 32.96 ± 085, 32.75 ± 1.04; UTE-15: 34.17 ± 0.92, 33.50 ± 1.21; UTE-30: 34.36 ± 1.03, 35.33 ± 1.27; UTE-90: 34.88 ± 0.88, 33.6 ± 0.69; or in effects of oral administration of UTE on relative organ weights (*n*:6; organ weight/body weight) × 100). Kidney, control: 0.51 ± 0.02, UTE-7: 0.43 ± 0.03, UTE-15: 0.45 ± 0.03, UTE-30: 0.41 ± 0.03, UTE-90: 0.46 ± 0.02. Lung, control: 0.38 ± 0.02, UTE-7: 0.32 ± 0.03, UTE-15: 0.44 ± 0.02, UTE-30: 0.40 ± 0.01, UTE-90: 0.38 ± 0.01. Liver, control: 1.95 ± 0.16, UTE-7: 1.79 ± 0.12, UTE-15: 1.98 ± 0.13, UTE-30: 2.01 ± 0.18, UTE-90: 2.01 ± 0.09.

In this experimental design, the animal is forced to drink a decoction (which might not be liked by the animal) because it has no other liquid to drink. This itself might cause which anxiety seen on days 15 and 30, but when we compare the amount of water drunk with the intake of UTE in all experiments, no difference was found, thereby demonstrating that the aqueous extract does not produce any stress effect *per se* in the range of concentration tested. The oral administration of UTE for 15 or 30 days in mice exposed to the EPM significantly decreased the percentage of time spent in open arms and also the percentage of open arm entries compared with the control ($p \leq 0.05$, Table S1, Supplementary information). However, treatment for 7 or 90 days with UTE had no significant effect. Different levels of expression of the percentage of time spent in open arms and the percentage of open arm entries were equal to all controls at different times. These data indicate that UTE exerted anxiogenic effects on 15 and 30 days post oral administration, which was reversed after 90 days without change in the locomotor activity during the experimental elapsed time.

The purpose of our work was not to identify the compounds of this plant, because the chemical composition of this aqueous extract has been described by several authors. *U. tomentosa* has been shown to have many different chemical components, including alkaloids (more than 17 different alkaloids), flavonoids, quinovic acid glycosides, tannins, sterols, procyanidins and polyhydroxylated triterpenes (de Matta et al. 1976; Ganzera et al. 2001; Muhammad et al. 2001; Kitajima et al. 2004; Montoro et al. 2004). Cat's claw (*Uncaria tomentosa*) has many constituents and could be responsible for its central nervous system (CNS) actions (Wagner et al. 1985; Senatore et al. 1989) and a phytochemical analysis of UTE revealed that CNS effects have been attributed to the components such as plant phenolics, flavonoids, phenylpropanoids, triterpenes, quinovic acid and glycosides. The effect of total alkaloids was shown to be partly due to major constituents such as pteropodine, isopteropodine, mitraphylline, isomitraphylline, speciophyline and uncarine, which could have effects on the CNS (Aquino et al. 1991). Also in accordance with other authors, our experiments confirmed that the water extract of UTE acts on the CNS (Mohamed et al. 2000; Jurgensen et al. 2005).

3. Conclusion

In conclusion, our data presented here demonstrated that UTE have a transient anxiogenic effect (as demonstrated by the plus maze test). Additional studies to refute or confirm the effects of UTE are necessary to investigate the possible mechanisms involved.

Supplementary material

Supplementary material relating to this article is available online, alongside Table S1.

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