

PUBLICATIONS

PHARMACOLOGICAL AND TECHNOLOGICAL INVESTIGATION OF *Aconitum talassicum* DITERPENE ALKALOIDS TALATIZINE AND ISOTALATIZIDINE

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The acute toxicity and central nervous system (CNS) effects of the diterpene alkaloids talatizine and isotalatizidine, isolated from *Aconitum talassicum*, were investigated. The isolation and purification of diterpene alkaloids are critical technological stages determining the quality, purity, and reproducibility of active pharmaceutical substances, while optimization of extraction and purification processes is essential for obtaining pharmacologically active compounds suitable for further development. Acute toxicity and the general pattern of toxic effects were evaluated in outbred white mice weighing 18–22 g. The median lethal dose (LD₅₀) was determined using the Litchfield–Wilcoxon method. The antiarrhythmic activity of the compounds was assessed using an aconitine-induced arrhythmia model in male rats weighing 170–280 g. Animals were anesthetized with urethane, and each experimental group consisted of five animals. After baseline electrocardiogram (ECG) recording, aconitine (12.5 µg/kg) was administered intravenously via the tail vein. The alkaloids were administered intraperitoneally 1 h before aconitine injection. Cardiac rhythm was monitored using a Schiller VET AT-1 electrocardiograph (Switzerland) in three standard leads before and at 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, and 20 min after aconitine administration. Antiarrhythmic efficacy was evaluated by attenuation of aconitine-induced arrhythmias and restoration of normal ECG rhythm, with an ED₅₀ of 12 mg/kg (i.v.). Conditioned reflex activity was assessed using open-field and maze tests, with hexenal (80 mg/kg), chloral hydrate (310 mg/kg), nicotine (10 mg/kg), arecoline (10 mg/kg), and amphetamine (10 mg/kg) used as pharmacological agents. The test alkaloids were administered intraperitoneally at doses of 2–100 mg/kg, 30 min before administration of the hypnotic or convulsant agents. In our experiments talatizine induced skeletal muscle relaxation and respiratory depression in mice. The LD₅₀ values were 110.2 mg/kg after intravenous administration and 300 mg/kg after intraperitoneal administration. Talatizine exhibited weak CNS activity, reducing locomotor activity and prolonging hexenal-induced sleep at 50–100 mg/kg (i.p.), while showing no significant effect on chloral hydrate-induced sleep. It had no effect on conditioned reflexes at 10–25 mg/kg but suppressed them at 50–100 mg/kg. Isotalatizidine showed LD₅₀ values of 40.1 mg/kg (i.v.) and 170 mg/kg (i.p.) in mice. At sublethal and lethal doses, the compound produced skeletal muscle relaxation, exophthalmos, and respiratory depression. At doses of 20–50 mg/kg (i.p.), isotalatizidine did not significantly affect hexenal- or chloral hydrate-induced sleep, nicotine- or arecoline-induced convulsions, or the stimulant effect of amphetamine (10 mg/kg). In the aconitine-induced arrhythmia model, isotalatizidine did not exhibit antiarrhythmic activity. These pharmacological findings indicate that technological optimization of the isolation and purification process is important for obtaining diterpene alkaloid substances with reproducible biological activity and acceptable quality characteristics for further pharmaceutical development.

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