

EFFECTS OF BUD EXTRACTS FROM *TILIA TOMENTOSA* MOENCH IN CENTRAL NERVOUS SYSTEM OF MICE: GENDER AND AGE- DEPENDENCY

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Introduction: Bud-derivatives, which are obtained by macerating meristematic fresh tissues of trees and herbaceous plants, represent a relatively new category of botanicals. In particular, in the most countries of the EU, bud-derivatives, named also gemmoderivatives or embryoextracts, are classified as plant food supplements. In a recent paper Allio and colleagues investigated the impact of *Tilia tomentosa* bud extracts (TTBEs) at Gamma-aminobutyric acid (GABA)_Aergic synapses by performing post-synaptic voltage-clamp recordings in hippocampal neurons. Direct application of TTBEs on post-synaptic terminals activated a chloride current in a way consistent with the activation of GABA_A receptors. The involvement of these receptors was confirmed by the observations that either bicuculline and picrotoxin prevented the TTBEs-induced effects.

Materials and methods: Based on these observations, we investigated whether TTBE can modulate the presynaptic release regulating GABA_A receptors located on noradrenergic nerve terminals. Noradrenergic nerve terminals were isolated from the cortex of adult male mice and preloaded with [³H]noradrenaline ([³H]NA) to monitor the release of the endogenous amine. Furthermore, we investigated the effect of “*in vivo*” oral administration of TTBEs on the behavioural performances of both adult (3-6months old) and aged (20-22months old) male and female mice in the hole-board maze and in the light-dark box. In particular, we analysed the behavioural skills related to the spontaneous motor activity, the curiosity and the anxiety of young and old animals administered with the *Tilia* bud derivative. TTBE (1 ÷ 2000 dilution) was dissolved in the drinking water and animals were controlled for the water daily intake and for the gain of weight. Behavioural tests were performed before and at the end of the TTBEs supplementation.

Results: Exposure of synaptosomes to muscimol (10 μM) in superfusion elicited a significant release of the radioactive tracer. TTBEs (1 ÷ 1000), inactive on its own, significantly potentiated the muscimol-evoked releasing activity, consistent with a positive allosteric activity of the bud derivative on the presynaptic release-regulating GABA_A receptors. Interestingly, the behavioural results obtained suggest that the TTBE administration impacts in a gender and an age-dependent manner the curiosity, measured as number of dipping in the hole-board maze and as “time in the light” in the light-dark maze, as well as the spontaneous motor activity.

Conclusion: These findings add new insights on the impact of these bud derivatives in CNS.

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