

# Hypericin Potentates the Effect of Tricyclic Antidepressants on Artificial Lipid Bilayers

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*Hypericum perforatum* extract is used in clinics for treating mild to moderate depression. Co-medication of amitriptyline and *Hypericum* extract decreased plasma levels of the tricyclic antidepressant and his metabolites [1], so a possible interaction of these drugs at the lipid bilayer level is of clinic interest. Black lipid membranes of lecithin were made by the *painted* method and electrical parameters were monitored. The transmembrane conductance was calculated by applying a rectangular pulse of  $\pm 50$  mV and capacitance was recorded by applying a triangular pulse of +20 mV for 1 s, and measuring the induced current. After the application of 10  $\mu$ M tricyclic antidepressant (amitriptyline or imipramine) no significant change of the specific capacitance was detected [2]. Similarly, we monitored the specific conductance until it reaches a steady-state ( $G_m = 36.08 \pm 4.52$  nS/cm<sup>2</sup>), and then the tricyclic antidepressant was applied with no appreciable effect. Hypericin, one of the active compounds of the *Hyperici herba* extract, was purified and her purity was tested by HPLC analysis. Co-application of hypericin (0.18  $\mu$ M) and tricyclic antidepressants (10  $\mu$ M) induces specific patterns of interaction for each antidepressant. Amitriptyline co-applied with hypericin induces a large conductance increase ( $G_m = 39.19 \pm 17.14$  nS/cm<sup>2</sup> for blank experiments and  $G_m = 423.98 \pm 69.68$  nS/cm<sup>2</sup> for amitriptyline). Imipramine co-applied with hypericin results in a lower conductance increase ( $G_m = 124.67 \pm 31.88$  nS/cm<sup>2</sup>). This difference could be explained by a different hydrophobicity and chemical structure. Molecular modelling data (obtained with HYPERCHEM 6) indicates a high hydrophobicity of the hypericin molecule (log P = 7.98) and very low coefficients for amitriptyline (log P = 2.36) and imipramine (log P = 0.23), where P represents the octanol-water partition coefficient.

## References

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- [2] Fisar Z, Krulik R, Beitlova D. *Drug Metabol Drug Interact*. 1991; **9**(3-4):269-81.