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The investigation of synaptic monoamine uptake in rat brain synaptosomes

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Background: Monoamine uptake inhibitors represent a drug class with paramount importance in the treatment of depression and other CNS disorders. For screening new inhibitor candidates *in vitro* methods are to be used instead of animals. Synaptosomes are more physiologic than cell lines and allow the analysis of interactions of various transporter systems.

Aims: We aimed at developing a synaptosome model appropriate for assessing synaptic monoamine transport.

Methods: The effect of reuptake inhibitors and other drugs on monoamine transport was examined using synaptosomes isolated from rat brain. 4-(4-(Dimethylamino)styryl)-N-methylpyridinium (ASP⁺), a selective, fluorescent substrate of monoamine carriers

was used to monitor monoamine uptake by measuring its intracellular accumulation by fluorescence detection.

Results: ASP⁺ was found to accumulate into the synaptosomes on a concentration-dependent and saturable manner. Optimal ASP⁺ concentration was chosen from the linear part of the curve. The method was validated by known monoamine-reuptake inhibitors that concentration-dependently inhibited ASP⁺ uptake according to their selectivity demonstrating the applicability of the model. The method was used assaying uptake inhibitory effect of tolperisone and other CMRs. These results can support the potential analgesic effect of tolperisone in neuropathic pain.

Conclusions: A fast and high throughput method for studying monoamine transport in synaptosomes was optimized and validated by established uptake inhibitors. The method can be used to study the effect of potential inhibitors.

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Conflict of interest

The authors declare no conflicts of interest.

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