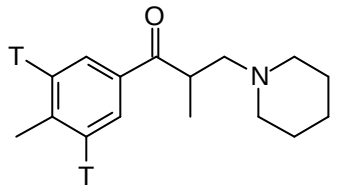
Abstract

Tolperison - old drug or new lead-structure

The main topic of this work was specified by investigations about the mode of action and pharmacology of Tolperisone. This substance is presently the most prescribed drug for treating abnormally increased muscle tone. The exact mode of action and the location of its pharmacological site is still unknown. Indications suggest channel-blocking properties both in central and in peripheral regions.

To investigate these properties of Tolperisone the nicotinic actylcholine receptor was used as a model. For the exact analysis of the ligand-receptor interactions photoaffinitylabeling experiments were used. At first a radioactive derivative of Tolperison (**1**) was synthesized to localize the drug after the labeling experiment in the protein-mixture. A radioactive derivative of Tolperisone with high specific activity was synthesized whose absorption at a wavelength of about 270 nm was used for the photoaffinityexperiment. The results of the photolabeling-experiments suggest the already supposed channel-blocking activity.



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For the use of Tolperison at a less powerful wavelength several synthetic strategies towards Tolperisone-derivates carrying a photolabile group could be demonstrated. The synthesis of Azido-tolperison was shown to be most efficient.

Besides the organic methods quantitative structure activity relationships were used to compare Tolperisone and other muscle relaxants. For this purposes the structures of different muscle relaxants were correlated with their biological activity. As biological activities data from pharmacological tests in the literature were used. The resulting models were used to estimate the potency of new drugs as well to find Tolperisone-related structures by the means of database mining and detect new lead structures for improved muscle relaxants.