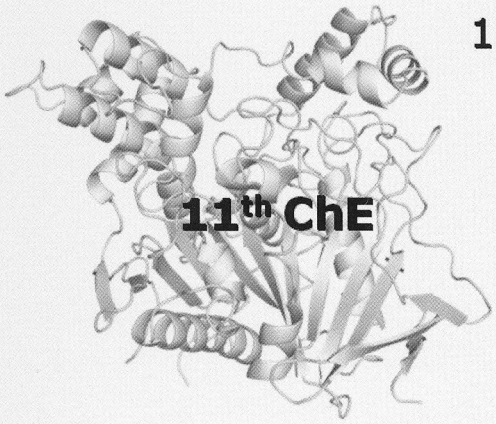

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Book of Abstracts

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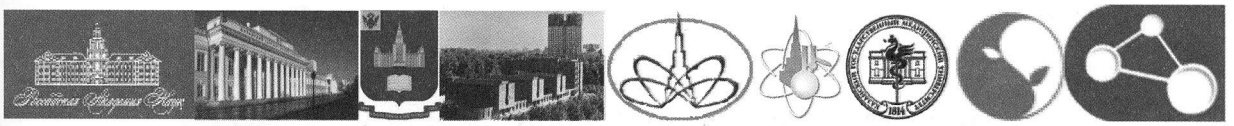

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TISSUE-SPECIFIC INHIBITORS OF ACETYLCHOLINESTERASE FOR TREATMENT OF MYASTHENIA GRAVIS

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Acetylcholinesterase (AChE) inhibitors are widely used in medical practice for symptomatic treatment for Myasthenia Gravis (MG) and Alzheimer disease. However, virtually all anti-AChE agents possess various side effects mostly as a result of lack of selectivity among various organs and tissues. Anti-AChE drugs suppress the cholinesterase activity both in organs requiring pharmacological correction and those organs where correction is not necessary. Application of traditional AChE inhibitors is always associated with side effects mostly caused by hyperactivation of cholinoreceptors of vegetative nerve systems (mainly smooth muscles and myocardium), such as diarrhea, excessive salivation, nausea, vomiting, pain in the stomach, bradycardia, arrhythmia, enhancement of bronchial secretion, hypotension etc. The drawbacks could be overcome by using inhibitors capable of inactivating AChE selectively in definite organs (skeletal muscles in case of MG) in doses ineffective with respect to smooth muscles and myocardium. Quite recently the evidences of the possibility of "skeletal muscle-specific" AChE inhibition have appeared when a new set of promising compounds, the alkylammonium derivatives of 6-methyluracil (ADEMs), have been synthesized and identified as inhibitors of AChE. We have shown that the synapses of locomotor muscles are more sensitive to the action of ADEMs as compared to synapses of smooth muscles or myocardium. These observations indicate that ADEMs can be perspective AChE inhibitors for treatment of MG lacking the majority of side effects on smooth muscles and myocardium.

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