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#### INTERACTION OF SOME POLYOXOTUNSTATES WITH ACETYLCHOLINESTERASE

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Polyoxometalates (POMs) are polyanionic oligomeric aggregates of transition metal ions, such as tungsten, molybdenum, vanadium, etc. held together by oxygen bridges, with a high density of negative charge. They are relatively stable, some even highly stable in aqueous solutions at biological pH values. In addition to applications in catalysis, separations, analysis, and as electrondense imaging agents, some of these complexes have been shown to exhibit biological activity *in vitro* as well as *in vivo* ranging from anti-cancer, antibiotic, and antiviral to antidiabetic effects. Recent investigations reported some polyoxotungstates as reversible inhibitors of acetylcholinesterase (AChE), making them potential anti-Alzheimer's drugs.

AChE is a serine hydrolase mainly found at neuromuscular junctions and cholinergic brain synapses. Its principal biological role is the termination of impulse transmission at cholinergic synapses. Reversible inhibitors of AChE mostly have therapeutic applications, while toxic effects are associated with irreversible AChE activity modulators. Reversible inhibitors play an important role in the pharmacological manipulation of the enzyme activity, and have been applied in the diagnostic and/or treatment of various diseases such as: myasthenia gravis, AD, postoperative ileus, bladder distention, glaucoma, as well as antidote to anticholinergic overdose.

The effect of four new synthesized polyoxotungstates soluble in water on AChE activity was studied. AChE is purified from electric eel and commercially available. The enzyme was treated in vitro with polyoxotungstates in the concentration range from  $1\times 10^{-7}$  to  $1\times 10^{-3}$  mol/L at  $37^{\circ}C$  for 15 minutes, and the incubation time was 12 min. The obtained dependence remaining enzyme activity vs. the inhibitor concentration fitted the sigmoidal function.  $IC_{50}values$ , indicating the enzyme sensitivity toward the inhibitor and the inhibitory capacity of the analyzed compounds, were determined from the inhibition sigmoidal curves.  $Na_{10}[H_2W_{12}O_{42}]\times 27H_2O$  did not markedly reduce AChE activity at the highest investigated concentration (1 mmol/L).  $K_7[SiV_3W_9O_{40}]\times 10H_2O$  exhibited a weak inhibitory potential, causing 50% decrease in the enzyme activity at  $5\times 10^{-4}$  mol/L. However, AChE sensitivity in the presence of  $K_7[Ti_2PW_{10}O_{40}]$  was several hundred times higher, reaching  $IC_{50}$  at  $1.15\times 10^{-6}$  mol/L. Furthermore,  $(NH_4)_{14}[NaP_5W_{30}O_{110}]\times 31H_2O$  demonstrated the strongest capacity to inhibit AChE. In the presence of its low concentration of  $2\times 10^{-8}$  mol/L, the enzyme activity was noticeably reduced related to the control value (obtained without inhibitor), while 50% decrease in AChE activity was achieved at  $3.8\times 10^{-7}$  mol/L.



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