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## Analysis and biochemical characterization of degradation products of anti-Alzheimer's drugs

In this PhD research, the stability of three anti-Alzheimer's drugs tacrine, (-) huperzine A and galantamine was investigated. Alzheimer's disease is an incurable neurodegenerative disease that worldwide affects more than 25 million, mostly elderly, people. Research is directed at improving the quality of life for Alzheimer's patients by generating more potent drugs with fewer side effects. An integral part in the drug development process is stability analysis, which is important to avoid a loss of potency or even the formation of harmful degradation products. Therefore, degradation products have to be characterized both chemically and biologically.

For tacrine, a huge number of degradation products was found under oxidative conditions. (-) Huperzine A under irradiation formed a new photoisomer. Galantamine also showed degradation under irradiation, as well as under oxidative and acidic conditions. The structures of formed degradation products were elucidated with techniques such as mass spectrometry and nuclear magnetic resonance spectroscopy. Furthermore, their inhibitory activity against the target enzyme Acetylcholinesterase (AChE) was evaluated. AChE catalyzes the degradation of acetylcholine, an important neurotransmitter. Drugs that inhibit AChE result in increasing the level of acetylcholine which may be advantageous for Alzheimer's patients. Several of the (oxidative) degradation products of tacrine and galantamine showed activity against AChE, whereas the photoisomer of (-) huperzine A did not.