Coumarin-Resveratrol-Inspired Hybrids as Monoamine Oxidase B Inhibitors: 3-Phenylcoumarin versus trans-6-Styrylcoumarin

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Abstract

Monoamine oxidases (MAOs) are attractive targets in drug design. The inhibition of one of the isoforms (A or B) is responsible for modulating the levels of different neurotransmitters in the central nervous system, as well as the production of reactive oxygen species. Molecules that act selectively on one of the MAO isoforms have been studied deeply, and coumarin has been described as a promising scaffold. In the current manuscript we describe a comparative study between 3-phenylcoumarin (endo coumarin-resveratrol-inspired hybrid) and trans-6-styrylcoumarin (exo coumarin-resveratrol-inspired hybrid). Crystallographic structures of both compounds were obtained and analyzed. 3D-QSAR models, in particular CoMFA and CoMSIA, docking simulations and molecular dynamics simulations have been performed to support and better understand the interaction of these molecules with both MAO isoforms. Both molecules proved to inhibit MAO-B, with trans-6-styrylcoumarin being 107 times more active than 3-phenylcoumarin, and 267 times more active than trans-resveratrol.

Author keywords

3-phenylcoumarin; 3D-QSAR models; Molecular docking; Molecular dynamics; Monoamine oxidase B inhibitors; Trans-6-styrylcoumarin; Trans-resveratrol