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Pharmacological Characterization of Synthetic Serine Palmitoyltransferase Inhibitors by Biochemical and Cellular Analyses

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Abstract

Human serine palmitoyltransferase (SPT) is a PLP-dependent enzyme residing in the endoplasmic reticulum. It catalyzes the synthesis of 3-ketodihydrosphingosine (3-KDS) from the substrates palmitoyl-CoA and L-serine. It is a rate-limiting enzyme for sphingolipid synthesis in cells. In the present study, we characterized and pharmacologically profiled a series of tetrahydropyrazolopyridine derivatives that potently inhibit human SPT enzymatic activity, including two cell-active derivatives and one

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