2-METHYL AND 2-METHYLENE ANALOGS OF 1α-HYDROXY-19-NORVITAMIN D₃: SYNTHESIS, BIOLOGICAL ACTIVITIES AND DOCKING TO THE LIGAND BINDING DOMAIN OF RAT VITAMIN D RECEPTOR

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Introduction
The discovery of the mitogenic activity of vitamin D₃, 1,25-dihydroxyvitamin D₃ (1,25(OH)₂D₃), the active form of vitamin D₃, has contributed to the understanding of the role of vitamin D in many physiological processes. The actions of vitamin D₃ are mediated by the vitamin D receptor (VDR), a member of the nuclear receptor superfamily. Recent studies have suggested that vitamin D₃ can affect the immune system and play a role in immunomodulation.

Docking
Receptor binding simulations (100 000 iterations each) were performed by FlexX software from Veristat. Interactions around the single bond of the ligand were allowed during docking. The top 10 of the calculated interactions were presented for each compound.

Biology
1. Measurement of Binding to the Peripheral Intestinal Vitamin D Receptor: The presented results (Figure 5) indicate that a binding ability of synthesized 2-methylene analogs, 2,4- and 4- times lower than that of 19-norvitamin D₃ compounds of high biological activity: Synthesis and biological evaluation of 2-hydroxymethyl, 2-methyl and 2-methylene analogues, J. Med. Chem. 41 (1998) 4662-4674.

References