Vitamin D analogous – structure and charge density analysis. Maura Malinska¹, Andrzej Kutner², Krzysztof Wozniak³, ¹Faculty of Chemistry, University of Warsaw, Poland, ²Pharmaceutical Research Institute, Warsaw, Poland
E-mail: mmalinska@chem.uw.edu.pl

The biological actions of the hormonally active form of vitamin D₃, 1,25-dihydroxyvitamin or calcitriol and its synthetic analogs are mediated by the nuclear vitamin receptor VDR [1], which is also involved in cell proliferation, differentiation, and immunomodulation. For example, activated T and B lymphocytes, prostate, breast, and colon cancer cells exhibit increased level of VDR protein when compared with their normal counterparts. This activation or disease-specific up-regulation of VDR protein provides an opportunity to treat these conditions with VDR ligands. Calcipotriol, Calcitriol and Alfacalcidol are examples of vitamin D analogs that have undergone clinical trials with positive outcome [2,3]. Conformational analysis and multipole model based on Hansen-Coppens formalism [4] obtained from theoretical structure factors. This approach revealed differences between the above analogous. The conformation of the cyclohexane A-ring is especially important as it does participate in protein binding. This ring exist in the two chair conformations, called α-form and β-form, in which hydroxyl at C₃ is in equatorial and axial positions, respectively. Studies of the vitamin D receptor (VDR) ligand binding domain, indicated strong hydrogen bonds between C1-OH and C3-OH hydroxyls and aminoacid residues Thr415 and Tyr401, respectively [5]. The charge density analysis shows that the change in side chain exert an influence on the whole molecule. Study of hydrated and anhydrous crystal structures and obtained multipole model demonstrate conformational and charge density distribution differences in molecules with α and β-forms of A-ring.

E-mail: magdalena.woiniska@student.uw.edu.pl

Popular force fields usually employ point charges. Supplanting atomic charges with higher electrostatic moments leads to more accurate charge distribution models. New generation force fields based on multipole models require high level of transferability of atomic multipole moments. The aim of this work was to analyze the level of charge density for understanding of chemical properties.