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Abstract

Synthesis, Molecular Docking Analysis, ADMET and Drug Likeness Prediction of a Benzenesulfonamide Derivative Analogue of SLC-0111 †

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Abstract: Carbonic anhydrases are metalloenzymes that regulate the interconversion of CO_2 and H_2CO_3, a reaction involved in many physiological processes. A disfunction of these enzymes is known to induce many diseases such as glaucoma, epilepsy and cancer. As a result, there is a need to design new target molecules with inhibitory effects on carbonic anhydrases (CAs). The most well-known compounds that inhibit CAs are sulfonamide-containing molecules, including valdecoxib, acetazolamide and the antitumor agent recently introduced to phase II clinical trials: the SLC-0111. With an intention to obtain a new potential drug candidate, an analogue of the SLC-0111 compound was designed and synthesized using sulfanilamide, chlorosulfonyl isocyanate and aniline. IR (infrared), NMR (nuclear magnetic resonance) spectroscopy and EA (elemental analysis) were used in the characterization of the structure. In order to explore the potentiality of our newly synthesized product to inhibit Cas, a docking simulation was performed on the binding pockets of both carbonic anhydrase II complexed with valdecoxib (pdb: 2AW1) and carbonic anhydrase IX complexed with SLC-0111 (pdb: 5JN3). The new derivative revealed an interesting stability inside the cavities of CA II and CA IX with docking scores of −9.782 and −7.466, respectively, and showed an efficient binding affinity in both cases through the formation of metal coordination with Zn and a hydrogen bond with the Thr199, which is known to be essential for the inhibition. Other significant extra interactions were also observed with other residues in isoform II. Further, the pharmacokinetics properties and drug likeness were predicted using in silico tools: SwissADME and MolSoft online servers.

Keywords: molecular docking; carbonic anhydrase; benzenesulfonamide; SLC-0111; ADMET

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