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Evaluation of the fluoro alkil losartan-derivative as ^{18}F-labeled radiopharmaceutical candidates for cancer diagnosis: theoretical study

There is sufficient information in vitro and in vivo that indicates that AT1 receptor (part of the blood pressure regulated system Renin-Angiotensin) is overexpressed in malignant tumor. The losartan is one of the most studied antagonist of this receptor, for that reason, this study evaluated the fluoro-alkyl losartan-derivatives (^{18}FAL) as potential candidates of ^{18}F-labeled radiopharmaceuticals for cancer diagnosis. Each derivative is obtained by a SN2 reaction. All calculation are performanced in vacuum as first approximation. The stability of these compounds is studied using the Density Functional Theory with the base 6-31G(2d, 2p). Molecular-Docking (MD) is used to estimate the association with this receptor. The functional M06-2X is the best that describes the featuring of these systems. The vibrational frequencies of the members of family ^{18}FAL structures and the bond dissociation energy (BDE) are also calculated. The most stable derivative is ^{18}FML(n=1), followed by ^{18}FPL(n=3) and ^{18}FEL(n=2) (n=CH_2). Atoms in Molecules topological study is done to characterize the bones and weak intramolecular interactions. All the intramolecular interactions are of the Van der Waals type, the fluoroalkyl chain provides additional stability to the molecule, in addition to generating a phenomenon of folding in this derivatives. MD explains the probability of existence of two conformers, one of them orients the phenyl and tetrazol rings in the same way as the natural ligand within the crystallographic structure of AT1 receptor. The amino acids that most contributes to the stability of the ligand-receptor complex are: Arg-167, Ile-288, Trp-84. ^{18}FML is proposed as the best candidate.

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