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The Thesis Submitted for the Degree of Master of Science (In the field of Analytical Chemistry)

Molecular Modeling of Some Positron Emission Tomography (PET) Tracers as Imaging Agents

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Abstract

Radiopharmaceuticals are radioactive isotopes containing drugs that have been widely used in molecular imaging techniques. There has been impressive growth in the use of radiopharmaceuticals for the treatment and diagnosis of disease. Despite the wide range of their application, the number of radiopharmaceuticals that have earned approval for regular clinical use is very limited. The increasing cost and development time of new radiopharmaceuticals has driven the search for more efficient strategies for their discovery. Computational modeling techniques cause time and cost savings in radiopharmaceutical design and discovery. Radiolabelled imaging such as positron emission tomography (PET) has been recognized as an important tool in medicinal chemistry. The present study explores three-dimensional quantitative structure-activity relationship analysis of 20 PET imaging agents targeted toward the ghrelin receptor. In order to envisage structurally diverse novel chemicals with better efficacy, CoMFA and CoMSIA model was developed. The developed models showed robustness in terms of statistical parameters. Then the structure-based pharmacophore model used as a query model for screening of 115, 717,173 drug-like molecules from ZINC, PubChem, MolPort, and CHEMBL databases. The molecules obtained were subjected to assessment Lipinski rule of 5. The molecules obtained after filtration was further scrutinized by molecular docking analysis. Eight potential inhibitory molecules have been selected by analyzing the binding interaction. In silico ADMET studies to investigate for compliance with the standard ranges eight hit molecules provided. These eight hit molecules can be utilized for designing novel class ghrelin receptor-PET imaging.

Keyword: Radiopharmaceuticals, positron emission tomography, ghrelin receptor, 3D-QSAR, Molecular docking, Virtual screening