Application of QSARs for the design of PET and SPECT imaging agents

Thesis submitted

by

PRIYANKA DE

Doctor of Philosophy (Pharmacy)

Department of Pharmaceutical Technology

Faculty Council of Engineering & Technology

Jadavpur University

Kolkata 700032

2022

Abstract

Positron emission tomography (PET) and single-photon emission computed tomography (SPECT) are non-invasive methodologies which makes use of the dynamic distribution of radiotracer to quantify biological processes. Quantitative structure–activity relationships (QSAR) attempts to develop a correlation between the chemical structures with a well-defined activity. It expresses chemical structures and physiological property in the numerical form and develops a mathematical correlation between them. Furthermore, this relationship can be used to predict the biological response of other existing chemical structures. The proposed work helped in understanding the requisite features essential for binding of PET and SPECT imaging agents to receptors like amyloid beta, tau, adenosine A_{2A}, dopamine (D2), vesicular acetylcholine transporter (VAChT) receptors responsible for neurodegenerative diseases like Alzheimer's and Parkinson's disease. Fragment based 2D-QSAR models were developed against a dataset of nitroimidazole derivatives which helped in understanding fragment features essential for their radiosensitization properties. Furthermore, the chemometric models developed would help in understanding the physicochemical characteristics of newly developed imaging agents even before their synthesis. The results of the present project have generated data that will fill the data gaps and help in development of newer novel compounds/analogues. The simple two-dimensional (2D) descriptors appearing in all the models are easier to compute requiring no conformation analysis or energy minimization process. Thus, this information would help in the future development and synthesis of newer PET and SPECT tracer targeted towards different receptors. Furthermore, new sets of designed PET and SPECT imaging agents with better predicted binding properties are reported against Alzheimer's disease. Further experiments might be conducted in the future on these potential compounds.