EuroSciCon

8th Edition of International Conference on

Chemistry Education and Research

August 27-28, 2018
Zurich, Switzerland

Cheong Siew Lee et al., J Org Inorg Chem 2018, Volume 4
DOI: 10.21767/2472-1123-C5-014

RATIONAL DESIGN OF NEW LIGANDS AS HUMAN ADENOSINE RECEPTOR ANTAGONISTS: TRANSITION FROM TRICYCLIC TO BICYCLIC SCAFFOLD-BASED DERIVATIVES

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There are four known subtypes of human adenosine receptors, classified as A1, A2A, A2B and A3 adenosine receptors. They regulate a large array of physiological and pathological functions in the human body. Ligands targeting these adenosine receptor subtypes have been reported to possess therapeutic potential in various diseases. Of note, antagonists of the adenosine receptor subtypes have been shown to be pharmacologically beneficial in modulating Alzheimer's disease, Parkinson's disease, inflammatory disorders and cancer. Over the past decades, medicinal chemists have strived to synthesize and characterize new derivatives as human adenosine receptor antagonists with biological activities of interest. In particular, our research group has been working on the rational design, structural optimization and characterization of new compounds acting as potent human A3 and A2A adenosine receptor antagonists. These compounds have displayed good binding affinities ranging from nanomolar to low micromolar. In this paper, structural modification of new derivatives based on tricyclic scaffold template, and subsequent transition to the design of new compounds with bicyclic scaffold will be discussed in details. In addition, molecular modeling studies, such as molecular docking and quantitative structure-activity relationship analysis performed in tandem to rationalize the binding affinity profiles obtained from the pharmacological studies will also be elaborated. In brief, the integration of medicinal chemistry, pharmacology and computational approaches employed has led to the identification of potent and selective human adenosine receptors antagonists.

Biography

Dr Cheong Siew Lee has obtained her degree in Pharmacy and PhD in Medicinal Chemistry from the National University of Singapore, Singapore. She has then undergone her postdoctoral training at the Institut für Pharmakologie, Universität Würzburg, Germany. Currently, she works as a lecturer at the Department of Pharmaceutical Chemistry, International Medical University, Malaysia. Her research interests revolve mainly around structural optimization of new ligands targeting adenosine receptors and dopamine receptors as well as application of computational approaches and pharmacological characterization in the drug design and discovery. Her research work has been published in various top international peer-reviewed journals and book chapters.

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