XLVIII Reunión Anual de la Sociedad Argentina de Biofísica

Libro de Resúmenes

SAB
XLVIII

27 al 29 de noviembre de 2019
Universidad Nacional de San Luis

XLVIII Reunión Anual de la Sociedad Argentina de Biofísica / compilado por Sebastián Andujar ...
[et al.]. - 1a ed . - Buenos Aires : SAB - Sociedad Argentina de Biofísica, 2019.
Libro digital, PDF

Archivo Digital: descarga
ISBN 978-987-27591-7-9

1. Biofísica. 2. Investigación. I. Andujar, Sebastián, comp.
CDD 570

Diagramación y Edición

M. Soledad Celej, Juan Pablo Acierno

Diseño de Tapa y Logo

Comité Organizador

Asistencia Técnica Web

Juan Pablo Acierno

Conformational and electronic intricacies of dopamine interacting with the D2 Dopamine Receptor. A comprehensive theoretical study

Goicoechea Moro L[a], Tosso R[a], Parravicini O[a], **Zarycz MNC**[a], Angelina E[b], Vettorazzi M[a], Andujar S[a], Enriz R[a]

a - Facultad de Química Bioquímica y Farmacia, Universidad Nacional de San Luis, Chacabuco 915, 5700 San Luis, Argentina. IMIBIO-SL (CONICET), Chacabuco 915, 5700 San Luis, Argentina

b - Laboratorio de Estructura Molecular y Propiedades, Área de Química Física, Departamento de Química, Facultad de Ciencias Exactas y Naturales y Agrimensura, Universidad Nacional del Nordeste. Av. Libertad 5470, Corrientes (3400), Argentina

Understanding of the biological behavior of different L-R complexes requires determining the conformational and electronic aspects of both the small ligand as well as the binding site of its receptor. Here we report the conformational and electronic behavior of dopamine (DO) interacting at the active site of the D2 dopamine receptor (D2DR). The selection of this molecular target is due to two main reasons: it is a molecular target of great importance for medicinal chemistry and very useful structural information has been recently reported due to the D2DR has been crystallized. Different computational techniques have been used in combination in this study. In this way, docking calculations, molecular dynamics simulations and quantum mechanical calculations have been performed. Moreover, the different molecular interactions of the complexes were evaluated in detail using two techniques: QTAIM (Quantum Theory of Atoms in Molecules) and NMR nuclear magnetic shielding constants calculations.

Our study goes much further than any previously done, since for the first time we have been able to obtain and report the complete conformational potential energy surface (PES) for DO in its binding pocket. Analysis of the complete PES is the most comprehensive way to understand the conformational behavior of a ligand such as DO, which possesses two rotatable bonds, since it is possible to locate all critical points on the surface and even see its different conformational inter-conversion paths.

Our study indicates that seven different conformations of DO are the most relevant. From these seven ones, two are those that could be considered as the biologically relevant conformations of DO. On the other hand, the most important molecular interactions that stabilize these molecular complexes are those with Asp80, Val81, Cys84, Thr85, Ser159, Ser160, Ser163, Phe164 and Tyr403.

Acknowldegments

The authors thank Universidad Nacional de San Luis (UNSL-Argentina) and Consejo Nacional de Investigaciones Cientifícas y Técnicas (CONICET-Argentina) for financial support.