

Computer chemistry of non-peptide oxytocin agonists.Taizou Hayano¹, Shiroh Kishioka²¹*Div.neuro-psychiat.Nokamikousei -Hp.* , ²*Dept.Pharmacol.Med-coll.WakayamaMed-Univ.*

Oxytocin is a 9-amino acid peptide that is neurosecreted from the paraventricular nucleus of the hypothalamus and the supraoptic nucleus and enters the blood from the posterior lobe of the pituitary gland. Peripheral effects are smooth muscle contraction and lactation. One kind of oxytocin receptor is Gq of 7-transmembrane G protein. There are three types of Vasopressin, V1, V2, and V3, V1 and V3 are G protein phosphorylated inositol / Ca systems, and V2 is a cAMP system.

Oxytocin nasal spray administration reduces runaway, sting, fear and anxiety. A therapeutic effect on Autistic Spectrum Disorder can be expected. This is why non-peptide compounds of oxytocin are expected. There are commercially available non-peptide oxytocin drugs. We used known data of D.M. Ashworth et al. An analysis by computational chemistry was attempted using the data of the structure-activity relationship report published by them.

The method optimizes the chemical structure of the compound with MOPAC6 in Winmostar and calculates the molecular structure and physicochemical indices. The number of compounds in the paper is 27, but EC50 is measured for 19 from No.9 to No.27. Multivariate analysis, when the dependent variable is EC50 and the independent variable is a physicochemical index in multiple regression analysis (decrease-increase method), the probability $p = 0.0182$ * is significant.

$$EC50 = -25.4 * (\text{all E}) + 9234.8 * (\text{ionization E}) - 1473.5 * (\text{field number}) - 94437.1$$

Multiple correlation coefficient $R = 0.6912$

In the molecular image, the frontier electrons of highly active molecules gather in a diazepine ring, and the UV spectrum absorption band is on the shorter wavelength side of 180 nm. In the low activity molecule, the frontier electrons were dispersed in the side chain, and the UV spectrum was shifted to the longer wavelength side of 190 nm. Other calculations method were also interesting results.