

# Theoretical study of dopamine. Application of the HSAB principle to the study of drug-receptor interactions

Aliste, Marcela P.

We present a theoretical conformational study of neutral and N- protonated form of dopamine in which we relate its pharmacological activity to the chemical hardness. We have found that the neutral form presents small fluctuations in the energy and the chemical hardness with the conformational variables, whereas the N-protonated form shows significant changes in both properties. An important result is that the Principle of Maximum Hardness is satisfied. The trans coplanar rotamers are postulated as the pharmacophoric conformation(s) because these rotamers show minimal chemical hardness. In addition, we have calculated the hardness of a model of the anionic binding site of the dopamine receptor, which is formed by a formate ion and two benzenes. We have compared the hardness calculated for this model with the hardness of the isolated formate anion, and found that the hardness of the base in the binding site is lower than that of the isolated formate group. Also, it is found that the hard