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Prediction of Henry's Law Constant of Benzimidazole derivatives Using Quantum Chemical calculation

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ABSTRACT

*The benzimidazole nucleus is an important heterocyclic ring, and interest in the chemistry,synthesis and microbiology of this pharmacophore continues to be fuelled by its antifungal [1],antitubercular [2], antioxidant [3, 4], and antiallergic [5, 6] properties. In this study Henry's law constants at T = 293.2K are calculated for some Benzimidazole and derivatives drugs in water by Hartree Fock methods at (HF/6-31+G**) level of theory using the Poisson-Boltzmann solvation model.*

Keyword: Benzimidazole and derivatives Drug, Hartree Fock,Henry law, Free energy.

INTRODUCTION

Henry's law, chemical law stating that the amount of a gas that dissolves in a liquid is proportional to the partial pressure of the gas over the liquid, provided no chemical reaction takes place between the liquid and the gas. It is named after William Henry (1774-1836), the English chemist who first reported the relationship.[7] From an environmental point of view, an important partition coefficient is the Henry's law constant (K) which can be calculated straightforwardly from the free energies of solvation in water.[8]

$$K(\rho, T) = RT\,\rho \exp\left(\frac{\Delta G\ sol}{RT}\right)$$

Where ρ is the density of the pure solvent, which is equal to that of the solvation in the limit of infinite dilution.

According to the above discussion, the caculation of log P of Benzimidazole and derivatives Drug are important. The benzimidazole nucleus, which is a useful structure for further molecular exploration and for the development of new pharmaceutical compounds, has been studied intensively. Some benzimidazoles have also found applications as pre- or post-harvest fungicides for control of a wide range of fungi affecting field crops, stored fruit and vegetables. Other reports have revealed that these molecules are also present in a variety of antiparasitic [9, 10,11] and herbicidal agents. Albendazole, fenbendazole and their sulphoxide derivatives are methylcarbamate benzimidazoles with a broad spectrum anthelmintic activity, widely used in human and veterinary medicine [12,13]. In recent years, benzimidazole derivatives have been attracted particular interest due to their antiviral activity against HCV (Hepatitis C virus) [14,15]. In this article, We have selected twelve Benzimidazole derivatives and performed based on the theoretical molecular descriptors calculated by the GAUSSIAN software and selected.[16,17]

Computational Method

The geometry of the molecules used here was fully optimized by Hartree Fock (HF) calculations with the (6-31+G**) basis set in the Gaussian 03 package. The Gibbs solvation free energies of drugs in water were calculated based on HF method for Benzimidazole derivatives.

RESULTS AND DISCUSSION

The results are presented in Table 1. HF /6-31+G** method estimated more negative solvation free energies. Henry's law constant was calculated from equation (1) by using of free energy solvation. Comparison of ΔG_{cav} with surface area shows that the ΔG_{cav} is often high for large-structure drugs and low for small drugs. However, the surface area is calculated in gas phase, but the ΔG_{cav} is calculated in solution. Therefore, the interaction between solute and solvent sometimes results in the lower ΔG_{cav} for small drugs.The calculated values are given in Table 2. The polarizability of a molecule is a measure of the degree to which the electron density distribution of the molecule can be distorted by an applied electric field. The attractive part of the Van der Waals interaction is a good measure of the polarizability.

Table 1.the solvation Gibbs free energy in water and Henry,s costant based on HF/6-31+G**

compound	ΔGsol(water)/HF	K(ρ,T)/HF
Albendazole	-11.43	2.4669×10^{-6}
Mebendazole	-14.41	1.6127×10^{-8}
fenbendazole	-11.24	3.3997×10^{-6}
Benzimidazole	-10.47	1.2471×10^{-5}
Thiabendazole	-15.02	5.7595×10^{-9}
flubendazole	-17.37	1.0905×10^{-10}
5,6- dimethylbenzimidazole	-9.39	7.7207×10^{-5}
Oxfendazole	-14.39	1.6681×10^{-8}
Oxibendazole	-12.73	2.7488×10^{-7}
compund1	-12.35	5.2206×10^{-7}
compund2	-11.48	2.2673×10^{-6}
compund3	-11.68	1.6176×10^{-6}

Table2. The free energy of cavity formation (kcal/mol) in water for drugs

compound	ΔGcav
Albendazole	33.8
Mebendazole	35.82
fenbendazole	36.15
Benzimidazole	15.83
Thiabendazole	24.11
flubendazole	36.89
5,6- dimethylbenzimidazole	19.93
Oxfendazole	37.15
Oxibendazole	32.04
compund1	33.67
compund2	36.27
compund3	35.92

Table 3 . The structure and electronic parameters of drugs from HF/6-31+G method**

compound	polarizability
Albendazole	28.732
Mebendazole	32.352
fenbendazole	32.887
Benzimidazole	14.45
Thiabendazole	22.923
flubendazole	31.173
5,6- dimethylbenzimidazole	18.12
Oxfendazole	25.825
Oxibendazole	31
compund1	31.084
compund2	33.012
compund3	32.919

The polarizability of a molecule can also enhance solubility in water. Dipole-dipole interaction is visualized most easily and results from attraction of opposite partial charges of molecular and groups. This Van der Waals force is likely to be relevant to inhalational anesthetic binding, because most of these molecules have a permanent dipole moment. Induced dipole-dipole interactions result from the distortion of an atom's electron density distribution (polarization) in the presence of a strong dipole moment (such as in a protein cavity lined by polar residues). Highly polarizable molecules are expected to be strongly attracted to other molecules.Polarizability is a function of atomic mass. The calculated values are given in Table 3.

CONCLUSION

In this study, we have applied ab initio method for calculation of some properties and the free energy solvation in solvent. The first calculations began with the geometry optimization of drugs by using of HF method . Then, solvation free energy of drugs in the water and other properties were calculated based on HF method. Factor such as polarizability, is related to the interaction between solute and solvent.

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