Investigation of the Impact of Ionic Liquids on Acyclovir Derivative Solubility through Computational Analysis

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Nucleosides are synthetic drugs used as antiviral or anticancer agents. Acyclovir is one of the most common nucleoside analogs which are used as an antiviral drug in the treatment of chickenpox, Simplex Virus Infections, and Shingles. Despite being a potential medical candidate in Human simplex viral infection (HSV), acyclovir like other nucleosides is faced with poor solubility in water and organic solvents hindering its bioavailability and membrane permeation. With this significance, ionic liquids have emerged as ideal candidates in synthetic processes of nucleoside-based drugs. ILs have been observed to be a promising solvent to be used compared to organic solvents with the capability of improving the solubility of nucleosides. To accomplish this task the solvation mechanism was identified.

We performed a molecular dynamics simulation of an acyclovir derivative in water and seven ionic liquids to gain insight into the solvation mechanism. By examining the contribution of van der Waals and columbic interactions, we derived solvation free energy to quantify the solvation mechanism. Furthermore, structural analysis was carried out to identify all possible interactions that could affect the drug's solubility.

According to the findings, ionic liquid has more negative solvation free energy toward acyclovir derivative. Additionally, 1-methyl-3-butylimidazolium acetate performed better in boosting the solubility of acyclovir derivative as compared to other Ionic Liquids employed. This means that acyclovir derivatives are more readily soluble in ionic liquid than in water. Furthermore, A connection matrix also reveals that the acyclovir derivative H2 and H7 have a high tendency to form strong hydrogen bonds with the oxygen and fluorine atoms found in the anionic parts of Ionic Liquids. On the other hand, minimal hydrogen bonds were observed during the interaction of other atoms contained in acyclovir derivative with the Ionic liquid atoms.

Generally, from the results one can say that utilizing Ionic Liquid during the manufacturing process of these drugs can improves the solubility of acyclovir derivatives. This information can be utilized as a foundation for further investigations in order to improve nucleoside solubility

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