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PHYSICOCHEMICAL PROPERTY OF DRUG MOLECULES WITH RESPECT TO DRUG ACTIONS

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ABSTRACT

The physicochemical properties of molecules play vital role towards the specific behavior of compounds. The drug molecules exhibit unique features by virtue of their physicochemical properties. Drug's physical and chemical attributes are referred to as its physicochemical properties. Physicochemical characteristics affect pharmacodynamic and pharmacokinetic behavior of drugs. Physicochemical characteristics affect interactions of drug with biological receptor and this interaction is responsible for pharmacological action of drug molecule. Partition coefficient, ionization, surface activity, solubility, chelation, hydrogen bonding, isosterism and partition coefficient, etc. are major physicochemical properties which affect biological behavior of drug. The researcher in current scenario is putting great effort for altering biological activity of drug by modifying their physicochemical characteristics. The toxicity of drug can also be reduced by altering their inherent features. Considering these all aspect present article exploring physicochemical property of drug molecules and their effects on drug action.

Key-Words: ***Drug, Physicochemical, Partition coefficient, Ionization, Solubility***

Introduction

Drug action is the outcome of drug molecules interacting with either healthy or unhealthy physiological processes. In this regards the spatial configuration of the drug molecules in the solution determines their physical characteristics. They have a certain chemical make-up that affects the receptors in biological or chemical ways. Medicines typically interact with receptors and produce certain biological responses. The interaction of drug with receptors (proteins, enzymes and cell lipids, etc.) depends upon the physical and chemical qualities of drug molecules, thus it is stated that the physical and chemical features of drug are greatly related with their therapeutic effect [1-4]. The common physicochemical property of drugs is depicted in **Figure 1**.

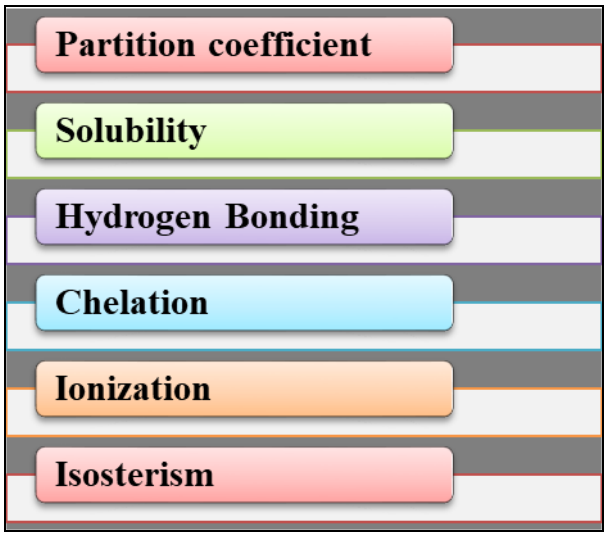

Figure 1: Physicochemical Properties of Drug Molecules

Partition Coefficient

It is the ratio of a compound's concentration in two separate mediums that are immiscible in equilibrium. This factor decides how medications move through the cell's lipid membranes from the location of application to the site of action. The drug's structure and any functional groups which may be hydrophilic or lipophilic attached to it dictate the coefficient.

The ability of a medicine to dissolve liquid phase is referred to as lipophilicity. Drugs that are very water-soluble cannot enter lipid-rich organs like the brain and other neural tissue, while drugs that are particularly lipophilic will remain at the point of initial loss, such as adipose tissue, and won't be able to move quickly from this location to the target, one of the many physiochemical variables that affects how medications are transported, distributed, and reach their targets is the partition coefficient. The drug concentration equilibrium constant for a two-phase molecule is the partition coefficient. It is challenging to measure partition coefficients in live systems; 1-octanol is commonly employed as the lipid phase and a pH 7.4 phosphate buffer as the aqueous phase for *in-vitro* experimental purpose. It is common to use the partition coefficient as a metric of lipophilicity [4-7].

Solubility

The solubility of a solute at a particular temperature is the quantity of

solute that dissolves in a solvent at equilibrium. Temperature, pressure and pH affect solubility of drug molecules. The concept of solubility is used to generate a dosage of medications, thus solubility is considered as crucial factor in drug development process. The drug interaction is conceivable when the drug is in the solution phase prior to its absorption.

The biochemical reactions depend on the dissolution of small molecules or the dispersion of macromolecular fragments in an aqueous phase because water makes up a substantial component of all biological structures. Non-aqueous lipid structures, including organelle and plasma membranes, make up the majority of a cell and can dissolve both polar and non-polar hydrophobic compounds. One key physical characteristic that all physiologically and pharmacologically significant small molecules share is that they are all soluble since only in solution can they bind to cellular and sub-cellular structures that contain drug receptors, leading to pharmacological action. All organic compounds' atoms and molecules are connected by a variety of bonds and these forces play a significant role in solubility of drug in biological system.

The solubility can be increased by following approaches:

- ✓ Use of co-solvents
- ✓ Use of surfactants
- ✓ Structural alterations
- ✓ Facilitating the formation of complexes

Hydrogen Bonding

Hydrogen bond; is a type of electrostatic attraction, which may exist due to the difference in electronegativity. Atoms with different electronegativities, such as oxygen and hydrogen, nitrogen and hydrogen, fluorine and hydrogen can form hydrogen bonds.

Two forms of hydrogen bonding are possible; intermolecular (in between two molecules) and intramolecular (with in a molecule). In order to analyze the physicochemical qualities, viscosity, surface tensions, acid strength, boiling point, drug-receptor interactions and melting point the hydrogen bonding play important role. Hydrogen bond contributed greatly towards the solubility and higher range of boiling or melting point of some compounds, these all phenomena mainly observed in case of intermolecular hydrogen bonding. Contrary to this intra-molecular hydrogen bonding sometimes leads lower range of boiling point and less solubility in water [6-8].

Chelation (Complexation)

Complex molecules fail to permeate lipid membranes, which reduces the drug's ability to exert its intended pharmacological effects. Complexation slows diffusion because it decreases absorption rate. Tetracycline, for instance, forms a complex with calcium in milk that slows the drug's rate of diffusion.

Ionization:

It is the process through which an atom or molecule acquires negative or positive charges by receiving or losing electrons and undergoing chemical modifications. This depends on the drug's pH and pKa value. The physicochemical feature of a drug's solubility, which aids in drug-receptor interaction, is greatly influenced by ionization.

The non-ionized form enables the drug to cross cell membranes, whereas the ionized form gives the drug strong water solubility, which is required for efficient drug-receptor binding interactions. As a result, for better pharmacodynamic and pharmacokinetic qualities, an appropriate combination of ionized and non-ionized forms is needed.

Dissociation Constant

The dissociation constant measures how likely it is for a bigger complex to dissociate into smaller parts. This value aids in understanding and estimating the drug molecule's chemical behavior. This is employed to ascertain the deprotonation of atoms and molecules as well as the binding of proteins to ligands. These variables control the physicochemical characteristics of medicines.

Redox potential

Redox, commonly referred to as the oxidation-reduction potential, is a quantitative term that expresses a compound's ability to gain or lose electrons. One of the most significant physicochemical characteristics, particularly in the context of vitamin preparations where it governs the drug's activity.

Stereochemistry

This area of chemistry is concerned with how atoms and molecules are arranged in space and how that arrangement affects a compound's physicochemical qualities. The physicochemical action of the medicine can be affected by the isomeric molecules and any changes to their structure.

In psychiatric medications, stereochemistry plays a key role in the development of the pharmaceuticals. These medications employ enantiomers as a result, one enantiomer may be more successful from a biological standpoint, whilst another concentrates on the therapeutic effects or pharmacokinetics, i.e.; (S)-methyldopa causes hypersensitivity, whereas (R)-methyldopa has no effect.

Isosterism and Bioisosterism:

Isosteres are substances with precisely possess the same numbers of atoms and molecules; for instance, N_2 and CO, N_2O and CO_2, etc.

Bioisosterism is a physicochemical feature, and biological isosteres are isosteres that reflect the same kinds of biological activity. Size, pKa value, solubility, conformation, hydrogen bond formation, reactivity, hydrophobicity and stability, etc. are all regulated by bioisosterism. The concept of bioisosterism can be utilized to improve drug's stability, side effects and pharmacokinetics.

Surface Activity

The surface tension controls how quickly a medicine is absorbed. Surfactants with lower concentrations lower surface tension, which speeds up the rate at which medications are absorbed. This depends on the surfactant's chemical composition, impact on biological membranes, concentration, and ability to form micelles. Hence, the drug's physicochemical properties are affected.

Protein Binding

Protein binding is the process by which a protein binds to a non-specific or non-functional location without causing any biological activity to occur. Albumin is a blood protein that frequently takes role in

protein binding and affects availability of drug for site specific biological action [7-9].

Conclusion

Drug's physicochemical properties are influenced by a number of variables, including pH, pressure and temperature, etc. These variables affects partition coefficients, pKa values, dissociation constants and others properties of the medication. The physicochemical characteristics of drug molecules, such as boiling point, viscosity, surface activity, partition coefficient, ionization, hydrogen bonding, chelation, and isosterism, have a significant impact on pharmacokinetic and pharmacodynamic behavior of drug molecule. Weak forces, including ionic bonds, hydrogen bonds, Van der Waals forces, and dipole-dipole forces, determine how drug molecules interact with extracellular substances in the body and control their physicochemical characteristics. In light of the fact that the drug's physicochemical characteristics are crucial to both its kinetic and therapeutic activity.

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