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Opinion

The Essential of the Solubility for Drug Action

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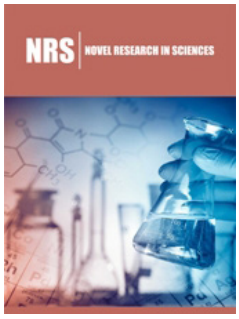

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Opinion

Solubility is one of the most important properties in drug discovery and it can affect many research areas regarding biological activity, in vivo efficacy, toxicity testing, pharmacokinetics, and formulation [1]. The solubility of a compound is based on its structural and conditions of solution such as hydrogen bonding, lipophilicity, molecular volume, ionizability, etc [2]. Neutral organic compounds tend to be hydrophobic; that is, they are less soluble in water than in organic solvents with the exception of organic compounds that contain ionizable groups as well as low molecular weight alcohols, amines, and carboxylic acids where hydrogen bonding occurs [3].

Solubility can occasionally provide an unpredictably beneficial amount of information. Compounds with 4 carbons or less will easily dissolve in water, whereas compounds with 8 carbons or more will be insoluble. Likewise, compounds containing 5 to 7 carbons may or may not dissolve, called partial solubility. If your compound dissolves in water, you will also want to check the pH of the solution. Amines will typically be basic, and carboxylic acids will typically be acidic. Most other compounds will be neutral.

There are two main types of solubility: natural solubility and chemical solubility. In the natural solubility, there is no chemical reaction between the solvent and solute molecules, and each keeps its natural and chemical properties, and can be separated from each other. In the chemical solubility, there is an interface between the solute molecules, i.e., the organic compound with the solvent molecules. Both solute and solvent cannot be separated or recovered thereafter [4].

The concept of functional groups is fundamental in organic chemistry, both in order to identify structures and for predicting properties. Functional groups can have critical influence on the chemical and physical properties of organic compounds. Molecules are classified on the basis of their functional groups. Alcohols, for example, all have the subunit C-O-H. All alcohols tend to be slightly hydrophilic, usually form esters, and usually can be converted to the corresponding halides. Most functional groups feature heteroatoms (atoms other than C and H). Organic compounds are classified according to functional groups, alcohols, carboxylic acids, amines, etc [3]. Drugs are classified accordingly to the chemical moiety or functional group. They may be further subclassified as hydrocarbons, halogenated compounds, alcohols, carboxylic acids, phenols, nitro compounds, amides, amines, sulphonamides, sulphones, stilbenes, thioureas, ureides, etc [5].

Each functional group has a solubility effect to evaluate the overall pharmacodynamic and pharmacokinetic properties of any given drug molecule [6]. The addition of a single functional group to a given molecule will affect the overall solubility of that molecule. Furthermore, the positioning of these functional groups plays an important role in their anticancer activities. For example, the addition of a methyl group to a drug molecule can greatly alter the drug's

pharmacological properties [7]. A catalyst has been developed that enables this 'magic methyl effect' to be rapidly explored for drug discovery. Addition of a metabolically susceptible N-methyl group can also sometimes be advantageous in reducing polarity [8,9]. Also, the addition of aromatic heterocycles will have a lesser effect on increasing the lipophilicity than carbon-containing aromatics but will increase PSA and this might begin to reduce oral absorption and/or cell penetration [10]. Addition of hydrogen atom with a methyl group in carbamate can result in profound potency enhancement [11,12]. Indole core is also entitled as "Privileged Scaffolds" which bind to multiple receptors with high affinity, and it is useful for the target-based design and development of anticancer agents [13].

The drugs for antitumor are derived from compounds that are produced by bacteria, which are actually the source of many of the antibiotics we use today. In nature, these bacteria use the antibiotics that they produce to inhibit or kill other bacteria in their environment. In the human body, antitumor antibiotics target cancer cells. Antitumor antibiotics treat cancer by affecting the genetic material within cancerous cell. This prevents cancer cells from growing and spreading. Numerous promising drug candidates including antitumor drugs suffer greatly from insufficient aqueous solubility, and as a result, incomplete absorption and low bioactivity hinder their application in clinical cases. About 40% of drugs developed in the past and about 90% of the drugs in development are poorly soluble drugs [14].

There are many compounds that are identified to have higher activity during early screening but that have lower aqueous solubility. These compounds are mainly selected by high-throughput and receptor-based in vitro screening techniques [15]. In the screening process, some lipophilicity is frequently required for a drug to pass through the cell membrane to reach the receptor site and a lipophilic group is often required for the drug to have an affinity with the receptor. Awkwardly, compounds with high lipophilicity usually have low water solubility. Low water solubility is often an obstacle for the further development of a compound because poorly water soluble drugs usually need high doses in order to reach therapeutic plasma concentrations after oral administration. So as to overcome this problem, a solubilization technique is typically used. The most commonly used techniques are pH adjustment, cosolvent, micellization, complexation, and pH adjustment combined with one of these methods [15]. Thus, it should be recognized that aqueous and lipid solubility is essential for drug action.

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