Structure Activity Relationship: Who is she?

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It is known for more than a century that the biological activity of a substance is a function of its chemical composition and constitution. Certainly, there exists a way to predict biological activity from the molecular structure of a chemical substance. The prediction of toxicity from structure activity relationship models is already being used both by regulatory agencies and by industry - to develop new compounds. The goal of the article is to introduce, to pre-university and university students, the concept of structure activity relationship analysis.

The Structure-Activity Relationship (SAR) is a means by which the biological activity of a chemical substance on living beings or the physico-chemical effects of a chemical substance on the environment can be related to its molecular structure. The existence of relationship may be assessed by considering a series of chemical substances, making systematic changes to them and observing the effect upon desired biological activities.

To understand the relationship between chemical structure and biological activity is important because it can speed up the process of drug design and can also help to find better drugs. The traditional approach was to synthesize a series of new chemical substances and to experimentally evaluate all of them. This approach to determine SAR is expensive and time consuming. It is possible to use the already existing experimental information and develop models that are in the form of equations. They help to rapidly predict the fate or biological activity from chemical structure and once developed they are inexpensive to use.

This way, the SAR analysis allow to eliminate chemical substances that will never make it to market for environmental or human health reasons, and to quickly identify less toxic, more rapidly degradable substances. By careful SAR analysis, it is possible

to eliminate problematic chemical substances before time and money are heavily spent on research, development and large scale production. Already, the prediction of toxicity thorough structure activity relationship models is being used both by industry to develop new compounds, and also by regulatory agencies.

There are many tools and approaches that can be used to generate SAR. Which one the scientist uses just depends on whether they are predicting a chemical property like solubility in water or a biological activity like toxicity to animals and plants or even humans. The basic steps for developing SAR are shown in figure 1.

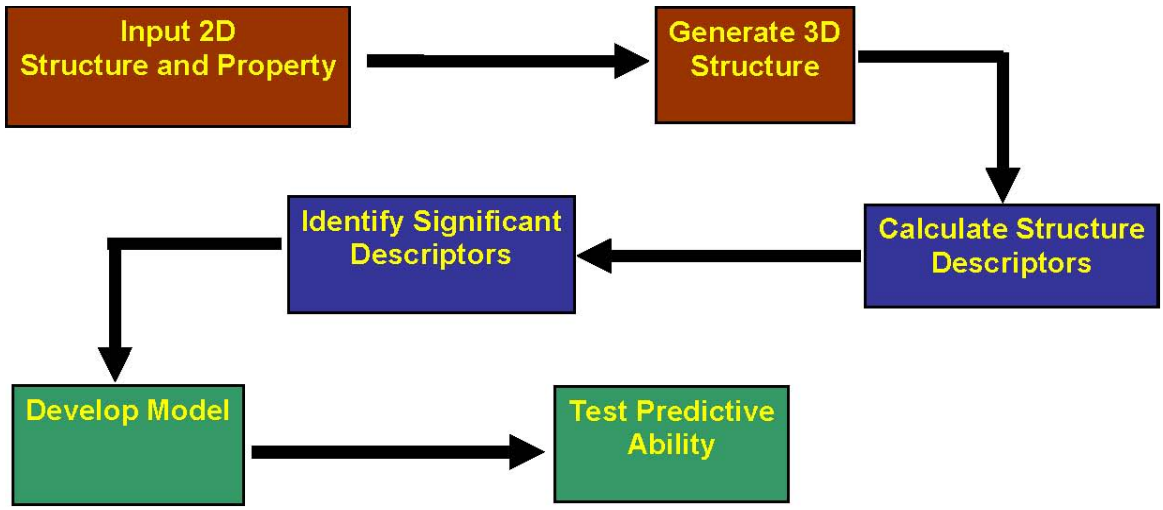

Figure 1. Basic steps in predicting structure activity relationships.

One can understand a lot about how a chemical substance is going to behave from its structure. For example, small chemical substances containing from one to four carbon atoms are gases at room temperature (methane CH_4, ethane C_2H_6, propane C_3H_8, butane C_4H_{10}). As more carbons are added, the substance becomes a liquid (hexane, a liquid, has six carbon atoms, C_6H_{14}) and finally a solid (octadecane, a solid, $C_{18}H_{38}$). If we add one oxygen atom to methane (CH_4), the chemical substance formed is a liquid we know as methanol (CH_3OH). As we add chlorine atoms, nitrogen atoms or any other atom, we can predict the activity these additions will have on the chemical substance's behavior. This behavior is not limited to predicting whether the chemical substance is a solid, liquid or gas, but includes predicting how toxic or biodegradable

the substance will be.

This kind of information is useful for scientists to predict and understand basic properties, such as desired biological activity, toxicity and biodegradability, before any data are generated from experiments in the laboratory. From the activity, toxicity and biodegradability information, the scientists are able to estimate exposure and risk to living beings and the environment. Drug discovery often involves the use of SAR to identify chemical structures that could have desired activities on specific targets and have low toxicity.

The field of SAR analysis is multidisciplinary. Computational chemistry essentially combines mathematics and chemistry, and deals with finding relationships called Structure Activity Relationships. However, it helps if one understands biology too.

Sources of information:

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