

Some Observations on the Toxicology of Natural Products

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Are Poisonous Plants Really Only Dangerous to Humans?

Certainly, poisonous plants affect our collective imagination, general public and even experts. Some plants are definitely toxic and dangerous: the hemlock, the plant from which we get the curare, strychnine, is an example of toxicity but a lot more can be given. However, other plants are considered completely edible, such as potatoes, tomatoes, eggplants, and others are considered partially edible such as elderberry, robinia pseudo-acacia, because only a specific part of them is edible.

Toxic plants, of course, must not be swallowed or accidentally eaten. However, they are very useful to man, especially from the pharmaceutical point of view. In fact, it should be noted that a toxic plant contains active ingredients highly poisonous chemical, which can be profitably used to prepare drugs which sometimes are lifesaving. An example of that is *Taxus baccata* L., *Taxus brevifolia* Nutt. and other species of the genus *Taxus*, all plants that nurserymen commonly call the "tree of death" because of its well-known high toxicity. Despite such toxicity, from the beginning of the 1990s, taxol has been obtained from them and it has been successfully used in the treatment of some cancers affecting the uterus and ovaries

Several are the examples that can be made in this respect: the plant *Digitalis purpurea* L. and related species used in the treatment of heart failure; some species of the family Solanaceae used in the preparation of the drug Buscopan; *Papaver somniferum* L. better known as opium poppy, that produces morphine, papaverine, codeine, thebaine, and many other compounds, and the list can be much longer.

It is only our knowledge, our desire and curiosity to know, to be informed that allow us to avoid serious troubles for our health and that of young people, who have the duty to pass on our knowledge.

Why do Plants in Particular Produce a Wide Range of Toxic Substances?

Generally speaking we tend to remember toxic substances which are produced by plants much more than those produced by animals. The most widely accepted interpretation at international level is that plants are anchored to the ground with their roots, and consequently cannot escape from attacks by predators. Their production of toxic chemicals is a form of defense in order to deter animals from eating them.

These chemicals, which have a range of toxicity from high to low, are called "secondary metabolites", because when the first Authors began to study these molecules, they did not seem to be essential to the life of the plant. Such view has changed over the years and nowadays such substances are considered important for the plants that produce them. In fact, it is because of the presence of these metabolites that in the majority of cases animals after having tasted a toxic plant do not return to feed on them. This is not the case for insects that have a detoxification metabolism different from that of mammals.

Plants then produce thousands of chemicals, different from species to species, and which serve to ward off predators (e.g. the nematode worms are predators of the land that attack the roots of plants) or even

to attract pollinating insects. Among the effects of the presence of these toxic chemicals is the incompatibility with a few other plant species. For example, it has been noted that under and all around the shaft of the walnut *Juglans regia* it is difficult to grow other plants because this tree produces juglone in its leaves, stems and roots a chemical compound, that prevents and slows down the growth of other plants, which eventually germinate near it. Juglone is known as an allelopathic substance, namely that chemically influences the presence of other plants in the surrounding environment. However, there are some (few) plants that can live close to walnut-trees and that obviously are not affected in their growth.

Allelopathy can be defined as the production of toxic chemicals by a species to impede the growth of another species (it is also called chemistry competition). Many terrestrial plants release allelopathic substances that inhibit the germination or growth of plants of other species around them: e.g. pines, sage releasing volatile terpenes and Australian eucalyptus essential oils

Sometimes, the presence of some organisms which can be seen as parasites can also have a positive effect on the plant because they induce a defense to other types of parasites by the plant itself. Allelopathic substances may be used by man as natural herbicides. The products of secondary metabolism are basically chemical intermediates with which plants communicate with the environment that surrounds them, including animals, with the aim of finding the most suitable conditions in order to live.

The animal world does not present such a wide range of chemically diverse natural substances and toxic. Exceptions to that are the animals that live anchored to the seabed, such as sponges, Madre pores, and corals. These marine animals do not have the possibility to move and therefore (it seems) they defend themselves chemically, by producing toxic chemicals (compounds that have cytotoxic activity, antimalarial, antibiotic, anticancer and others in them) to deter predators. Overall, at least 10% of marine organisms produce cytotoxic substances which have strong antimicrobial properties and / or antivirals.

Currently, despite the increasing introduction of synthetic drugs, approximately 45% of single-molecule therapeutic agents listed in the pharmacopoeias, are of natural origin or derive directly from natural molecules. The chemical diversity that characterizes natural molecules makes the exploration of their biological characteristics, not only a major source of new compounds that could be used for the creation of new drugs, but also a useful tool for the discovery of novel mechanisms of action.

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