Insects, Poisons, and Medicine: the Other One Percent[1]

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We have been aware for the last decade or so that the world's population is steadily increasing and that Mankind may be forced to overcome the world's protein crisis by relying on less conservative sources of protein, such as insects. Fortunately, a small percentage (about 1%) of the insects known can cause severe reactions or death if consumed. These poisonous insects in many cases are truly deadly to man since they contain toxic chemicals stored in their bodies for purposes of protecting themselves or their species from natural enemies. To eat one of these insects is to be truly poisoned! These toxic chemicals may be synthesized by the insects themselves, or may be taken in with the food that they eat and simply sequestered within the body for future use. The possibility of eating an insect in our normal diet, much less a poisonous one, is minimized by the Federal Food, Drug, and Cosmetic Act, which calls for the food industry to practice minimum standards of sanitation. Nevertheless, it is nearly impossible to eliminate insects as contaminants in our food. One finds aphids in the lettuce and spinach one purchases at the market, and in the salads we eat at home or in restaurants; the small black or brown specks in flour or bakery products may be fragments of the Mediterranean flour moth, flour beetle, rice or granary weevil; and there may be maggots in fruit juices, larvae in catsup, beetles in spices. In fact, it has been estimated that every 248 grams (8 oz.) of raisins may contain up to 10 *Drosophila* adults or 35 maggots. A can of coffee may contain at least 3 insects. Every one hundred grams of broccoli or spinach may average 30-50 aphids, thrips, and mites. Hops, an essential ingredient in beer, may have up to 25,000 aphids per one hundred grams, and so on! The incredible job of totally eliminating insects from our diet is nearly impossible, a fact recognized by the Federal Food and Drug Administration, which sets limits as to the number or percentage of insects, their parts, eggs, or secretions, that is allowable in specified foods.

The chance of eating a poisonous insect is less probable in places other than the Western world where eating insects is commonplace. A vast quantity and variety of insects are eaten as a delicacy and food staple by many peoples, whose experience has given them the ability to distinguish between poisonous and safely-edible insects.

Insects that are considered poisonous have evolved these toxic substances in order to blunt the attacks from an incredible variety of animals as well as microorganisms. Often these poisons are extremely toxic. The common wood ant, *Formica rufus,* stores formic acid, HCOOH, a universally poisonous substance, in its venom glands at a concentration ranging from 50 to 70% (a quantity which

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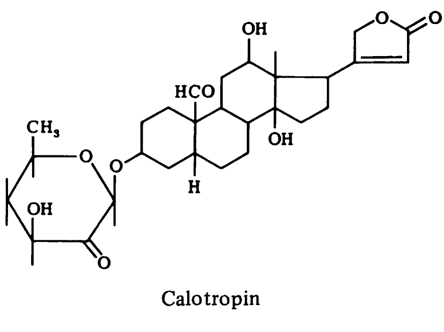
may amount to 20% of the whole body weight of the insect) without injury to itself. Another example is the hydrogen cyanide (HCN) secreting burnet moth species belonging to the genus *Zygaena* whose resistance to cyanide poisoning makes the moths virtually immune to the traditional killing jars of entomologists! The zygaenid moths release HCN after tissue injury and at least part of the cyanide is detoxified by the enzyme rhodanese, converting HCN to non-toxic thiocyanate ion. Millipedes of the genus *Julus* and the common blue butterfly,

$$\mathrm{HCN} \xrightarrow{\text{rhodanese}} \mathrm{HSCN}\ \text{(thiocyanate)}$$

Polyommatus icarus, both can generate HCN if disturbed, and likewise detoxify this compound with the enzyme rhodanese. However, this protective enzyme is not found in the burnet moths, the larvae of which feed on laurel leaves containing large amounts of cyanide. Is it possible that the burnet moth larvae have midgut cells that are impermeable to this poison? Or is the poison detoxified by conjugation with another molecule and easily eliminated via the excretory system? Or is there another detoxifying enzyme besides rhodanese operating in the burnet moths? These questions remain unanswered. The assassin bug, *Platymeris rhadamanthus,* contains a salivary venom which can be ejected at a vertebrate predator. The hydrolytic enzymes in the venom – trypsin, hyaluronidase, and a phospholipase, collectively cause extreme pain and edema if mucuous membranes are attacked.

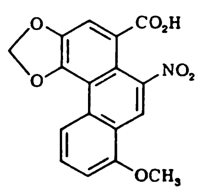
An interesting phenomenon is how predators survive eating poisonous insects. It is known that larvae of the monarch butterfly, *Danaus plexippus,* feed on plants belonging to the milkweed family, Asclepidaceae, which contains toxic compounds, among which are the cardenolides or cardiac glycosides, such as calotropin or its isomer, calactin. The cardenolides are potent heart stimulants and cause severe vomiting in vertebrates. Many birds attempt to swallow the monarchs, but without success. Blue jays vomit within 10-15 minutes after swallowing monarchs, the poison acting on the smooth muscles of the stomach, leading to contraction and regurgitation of the food. Blue jays have been known



Calotropin

to starve to death rather than eat a monarch after having previously experienced eating one earlier. However, some bird species can actually survive on a regular diet of poisonous insects. The quail can consume large numbers of monarchs containing enough poison to kill fifty people, without effect. It has been estimated that the poison in the hemolymph of just two monarchs is sufficient to kill a starling. It is not known whether protective enzymes are present in the quail. The arctiid moth, *Arctia caja,* sequester cardenolides when reared on *Digitalis* and pyrrolizidine alkaloids from *Senecio.* The larvae, if fed on both these plants, can sequester both compounds despite the chemical dissimilarities between the two pointing to a common physiological base underlying the sequestration process. Lygaeids are interesting in that they sequester polar cardenolides in their dorsal-lateral spaces, while non-polar cardenolides are found in their hemolymph. More commonly, vertebrate predators would encounter the non-polar and more emetic cardenolides after biting into the bug.

Larvae of certain swallowtail species of the genus *Papilio* sequester various kinds of aristocholic acid derived from plants belonging to the family Aristolochiaceae. Adults may contain up to 100 mg of this acid, which belongs to the nitrophenanthrene family of compounds known for their bitterness and toxic properties.

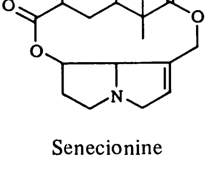


Aristolochic acid-I

Primitive and ancient man made use of poisonous insects and their poisonous by-products. Toxic or "heady" honey was well-known in ancient times. Alan Landsburg, in his book entitled *The Insects Are Coming,* writes that Xenophon, a Greek, chronicled the war between the Greeks and Persians in a book *Expedition Of Cyrus.* Xenophon narrates how the Greek army was stalled in its advance to the city of Colchis by heady honey. An excerpt from that book: "Having passed the summit, the Greeks encamped in a number of villages containing an abundance of provisions. As to other things there, there was nothing at which they were surprised; but the number of beehives was extraordinary and all the soldiers that ate the combs lost their senses, vomited, and were affected with purging, and none of them were able to stand upright; and such as had eaten only a little, were like men intoxicated; and such as had eaten much were like men at the point of death. They lay upon the ground in great numbers, as if there were a great defeat. The next 3-4 days, they recovered." The Greeks, having learned from this bad experience, used this knowledge to their advantage against the Romans in a military technique akin to an ancient version of chemical warfare. A Greek general placed poisonous honey along the mountain passes and routes to be taken by the Roman general Pompey. Pompey's soldiers ate the bait, became intoxicated, were attacked and defeated. Reports of "heady" honey come from past colonial America, northern Japan, provinces of old Russia, South America, and in the United States (New Jersey). In all cases, the poisonousness of the honey is derived from toxic chemicals in the nectar of flowers collected by the bees. Honey produced from many varieties of heather, azalea, wolfbane, andromeda, laurel, jasmine, rhododendron, and other plants have been found to be poisonous. It has been estimated that 31 grams (1 oz.) of "heady" honey can kill a guinea pig, 454 grams (1 lb.) a human adult if consumed.

Primitive peoples throughout the ages have used the venoms of insects as well as spiders in their hunting or warfare in order to slow down, sicken, or kill their adversary or prey. Landsburg in his book, *The Insects Are Coming,* cites anthropologist Elizabeth Thomas describing in her book, *The Harmless People,* how bushmen of the African Kalahari Desert use poisonous beetle pupae to bring down antelope. An excerpt from her book: "The yellow pupae, the bushmen say, are males with sacs of poison only under their front legs. To get the poison, bushmen pull off a leg and squeeze out a single drop, discarding the rest of the body. The orange pupae are said to be females, with poison throughout the entire body. To get poison from these pupae, the bushmen tap the grub all over to mash the insides; then pull off the head and squeeze the insides out, like toothpaste from a tube." The poison is then mixed with a sticky binding material which comes from tree bark. "They chew the bark thoroughly and spit the mash into a little mortar made from the knee bone of an antelope, a nice little cup into which the bushmen have squeezed the milky juice of sanseviera plants, got by wringing the heavy, thick leaves. This juice has an irritating effect when it is dissolved in a wound and causes the antelope to rub and scratch its wounded spot against a tree, which stimulates circulation in the area resulting in carrying the poison quickly through the body, hastening death. The paste in the mortar is throughly mixed, then smeared with a straw on the foreshaft of arrows, never on the head: For if the sharp wedges of the head were poisoned, any child might accidently nick himself and die." Although the prey is antelope, the potency of the poison should not be underestimated. Thomas further writes: "The technology of hunting is the most complex in Kung culture, and the most involved aspect of that technology is their amazing poison. Without it, the little unfeathered arrows, driven by a light bow, would be useless against big game. With the poison, a Kung hunter could bring down an elephant." This arrow poison is a toxic saponin compound, similar to a glycoside, which is extracted from a beetle, *Diamphidia locusta.*

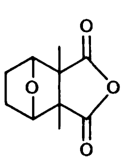
Many poisons in insects may have evolved expecially against vertebrate predators. For example, the cinnabar moth, *Callimorpha jacobaeae,* contains poisonous senecio alkaloids and histamines potent only against vertebrates. A great



Senecionine

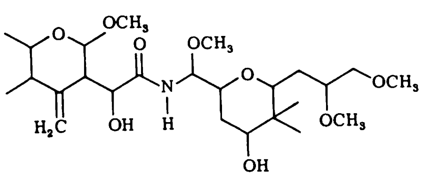
many other poisons elaborated by insects are designed to kill other insects. An interesting case involves the hymenopterous venoms, especially those in solitary wasps of the family Pompilidae. These wasps sting their prey and inject a poison composed of a polypeptide compound with kinin-like properties, i.e., vasoactive peptides, as well as hydrolyzing enzymes such as hyaluronidase and phospholipase A, and histamines. The injected prey remains paralyzed for months, but the heart is apparently not affected, continuing to beat. The braconid parasites belonging to the genus *Habrobracon,* will paralyze its prey on which its own larvae will develop. The prey will exhibit paralysis, which will remain until it dies, while the muscles of the heart and gut continue to function. In this way, the prey is kept preserved for the young for months.

Several of these insect poisons have been, and are now being used in the area of medicine. Recent experiments with yellow honey ants belonging to the genus *Myrmecocystus* have shown that several chemicals isolated from this insect are potent hallucinogens already well-known to various Indian tribes in California. Perhaps the most famous or infamous insect product is Spanish fly, which is neither Spanish in origin nor a fly. Spanish flies are actually derived from blister beetles belonging to the family Meloidae. Spanish fly has been used for a long time as wart removers, to induce blisters, to restore hair, and as an aphrodisiac. In fact, it is the venom which the beetle stores in its body, known as cantharidin, that is the active principle of Spanish fly. The venom is used nowadays in the



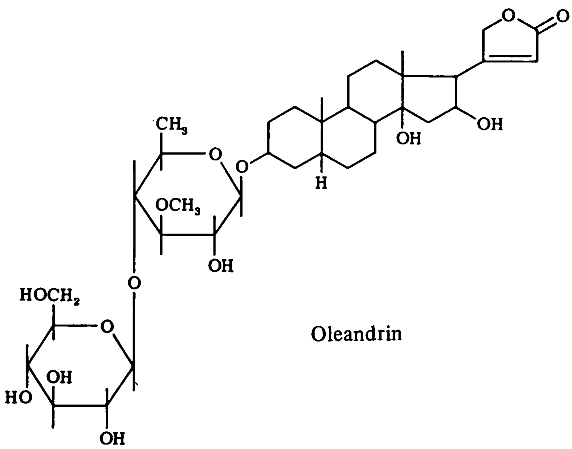
Cantharidin

treatment of a few urogenital disorders. Spanish fly was once considered the essential ingredient in love potions, acting as an irritant to the sexual organs if ingested. The attempt of drugged individuals to scratch, rub, and soothe the irritation has been interpreted as attempts to relieve sexual tensions. Roman gladiators used large doses of the powdered beetle to keep their orgies going and took hot baths to sweat out the toxins. A poison, called pederin, a secretion of a staphylinid beetle of the genus *Paederus,* has been found to inhibit the growth of certain cancers. Bee venom tablets, with the active ingredient being



Pederin

the protein mellitin, are swallowed for rheumatism and high blood pressure. Heart poisons, such as those cardiac glycosides found in the monarch butterfly and the oleander hawk moth, *Deilephila nerii,* are being used to control cardiac problems. The main steroid found in the oleander leaves is oleandrin, which is sequestered by ctenuchid larvae, along with several other related compounds, including stropeside, which show cardiac glycoside activity.



Oleandrin

Indeed, many claims have been made concerning the medicinal value of a multitude of products from a great many insect species which, in many cases, have their origins as folk medicines and as cures among the more primitive peoples. These products are often scoffed at by modern medical practitioners. However, there may be a legitimate basis for many of these claims, which only careful scientific scrutiny can uncover.

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