The Defensive Role of Alkaloids in Insects and Plants

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Introduction

The term alkaloid (= alkali-like) is applied in a rather loose sense to denote naturally occurring organic compounds containing nitrogen (mostly in ring structures) and thus displaying basicity. According to their biosynthesis, the majority of these compounds can be regarded as derivatives of certain amino acids, viz. lysine, ornithine, phenylalanine, tryptophane and tyrosine, while terpenoid, steroid and other precursors are incorporated into their carbon skeletons. Many phytoalkaloids (about 3000 different ones are known so far) occur dissolved as cations in plant sap, and on evaporation of the former, they react with available organic acids to form salts which subsequently are deposited in vacuoles rather than in the protoplasm. Moreover, they tend to accumulate in the peripheral parts (bark, leaves, fruit) which can be shed. The alkaloids may thus be regarded as excretory products or so-called secondary substances which are offshoots from the primary metabolic pathways.

Most of the alkaloids exert in various animals a more or less specific action upon different regions of their nervous system[1]. The cholinomimetic alkaloids may be subdivided into compounds which act preferentially on postsynaptic neurone receptors, the neuromuscular junction as well as the receptors of secretory glands. Other alkaloids act primarily by blocking the acetylcholine receptors and influence autonomic effector cells rather than ganglion cells (e.g. tropane alkaloids). Inhibitors of cholinesterase cause accumulation of acetylcholine and therefore continuous stimulation of cholinergic receptors (e.g. physostigmine). The sympathomimetic compounds are either releasers of noradrenaline (e.g. tyramine, ephedrine, *Rauwolfia* alkaloids), inhibitors of its readsorption (e.g. cocaine) or act as adrenergic blocking agents (yohimbine, ergot alkaloids). Colchicine and the *Vinca* alkaloids are known to inhibit the incorporation of uridine into RNA. The *Veratrum* alkaloids cause repetitive discharges of nerve cells, apparently by delaying repolarization (possibly by action on lipid components and an ATPase in the cell membrane).

Chemical defense of terrestrial plants

Relatively few protective interactions of plants involve physical force (e.g. thorns, blades, adhesives) only; many plant species utilize certain compounds among a multitude of secondary substances, pertaining to the acetogenins, alkaloids, phenylpropanes, steroids, terpenoids and other groups, to deter predators[2,3] as well as to control competitive organisms in their surrounding[4,5].

It has been known for some time that *Veratrum* and *Tobacco* alkaloids are rather toxic for a variety of organisms[6] and, in fact, since ancient times man has taken advantage of such pesticidal properties to protect his cultured plants from insect attack[7,8]. Moreover, several modern pesticides aimed against sucking insect and mite species are based on alkaloid structure, i.e. they comprise pyrazole, pyrrol, pyrimidine, benzimidazole, phtalimide or quinoxaline moieties[9].

Several alkaloids have marked pathological effects on insects including their endosymbionts[10] manifested by retardation of growth, development[6] and reproduc-

Table I. Phagorepellent alkaloids for some phytophagous insect species

Compound	Structure[a]	Plant source	Deterred species	Family	References
Tomatine	**1**	Tomato	*Leptinotarsa decemlineata*[b]	*Chrysomelidae*	18, 19, 23
Demissine	**2**	*Solanum demissum*	dto	dto	
Capsaicine	**3**	Red pepper	dto	dto	24
Nicotine	**4**	Tobacco	dto	dto	
Solanine	**5**	Potato	*Pieris brassicae*[b]		
Quinine	**6**	Cinchona bark	dto	*Pieridae*	22
Gramine	**7**	Graminae, Aceraceae	*Schistocerca gregaria*[c]	Acrididae	25
Caffeine	**8**	Tea, coffee, cola	*Dysdercus fulvoniger*[c]		26
			Dysdercus koenigii[c]		
			Dysdercus völkeri[c]	Pyrrhocoridae	
			Spilostethus pandurus	Lygaeidae	
Conessine	**9**	*Apocynaceae*	*Dysdercus fulvoniger*[c]	Pyrrhocoridae	
			Dysdercus koenigii[c]		
			Dysdercus völkeri[c]		

[a] See figure. [b] = Larvae. [c] = Adults.

tion[11] as well as paralysis and mortality[12] according to the dosage received. For example, nicotine poisoning in insects reveals tremors and convulsions (hyperactivity), subsequently paralysis, which is usually followed by rapid mortality. There is good evidence that the toxic effects of nicotine and related alkaloids (with structural resemblance to acetylcholine and a highly basic nitrogen) are due to direct combination of those alkaloids with the acetylcholine receptor, a membrane-bound site that binds acetylcholine and mediates the transmission of neuron impulses[13].

Phagorepellents in food-plant selection

A number of alkaloids function as phagorepellents for certain insect species and may be phagostimulants for others[14–16]. In fact, the distribution of steroid alkaloids in the *Solanaceae* has a decisive influence on host plant selection by larvae and adults of the potato beetle. Tomatine, in a concentration approximating to that found in tomato plants (about 0.12 m*M* per 1000 g fresh leaves[17]), limits food consumption of the larvae and prevents their growth at higher levels[18]. Incorporation of either demissine or tomatine to potato leaves resulting in a alkaloid content of 0.1 to 0.5% renders them unpalatable to the larvae[19], whereas a similar concentration of solanine in potato certainly does not repell them from the leaves[18]. Adult *Leptinotarsa decemlineata* normally feed in presence of levels up to 0.6% of solanine and chaconine, which both occur in potato plants at a ratio of 1:1. However, when potato leaves were infused with solutions of either tomatine or demissine to yield an alkaloid concentration of 0.3%, potato beetles refused to feed on this substrate. Under those conditions, the threshold level of phagorepellence was about 0.1% tomatine or demissine, whilst the alkaloid receptor of the taste hairs of potato beetles (located on the 5th tarsal segment) can be stimulated by 0.01% tomatine or 0.15% solanine, respectively[20]. The higher tolerance for tomatine during feeding could be ascribed to the modifying effect of other stimuli present in the plant sap. The fact that the alkaloid receptor is approximately 10 times less sensitive to solanine than to tomatine reflects the adaptation of potato beetles to their main host plant.

Food intake of the Cotton leafworm *Prodenia litura* is diminished by addition of isoboldine (an alkaloid from *Cocculus trilobus*) to its host-plant, whereas ingestion by *Calpe excavata*, normally feeding on *Cocculus*, is not affected by this alkaloid[21]. Dietary presence of quinine sulfate or chloride at $4 \times 10^{-7}\ M$ or $1.5 \times 10^{-6}\ M$, respectively, reduces larval food consumption in *Pieris brassicae* by approximately 75%[22]. Additional examples of alkaloid phagorepellents are given in Table I and in the Figure. On the other hand, adult aphids (*Acythosiphon spartii*) were observed to change their feeding sites on broom (*Sarothamnus scoparius*) according to the movement of sparteine between various parts of the host-plant and this alkaloid was subsequently shown to act as a phagostimulant stabilizing the aphid population in the most favorable situation[27].

Table II. Alkaloids stimulating a phagorepellent receptor in the medial sensillum styloconicum of lepidopterous larvae (after Schoonhoven[15])

Alkaloid	Structure[a]	Bombyx mori	Pieris brassicae	Lymantria dispar
Quinine	**6**	+[b]	+	+
Strychnine	**10**	+	+	+
Brucine	**11**	+	+	
Nicotine	**4**	+	+	
Berberine	**12**	+	+	
Pilocarpine	**13**	+	+	
Atropine	**14**		+	
Scopolamine	**15**	+	+	
Morphine	**16**		+	
Conessine	**9**	+	+	+
Sparteine	**17**		+	
Tomatine	**1**		+	
Caffeine	**8**	+	—[b]	+

[a] See Figure. [b] +, stimulation; —, inhibition.

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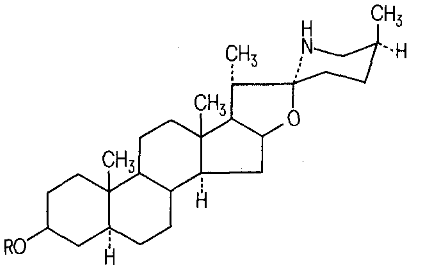
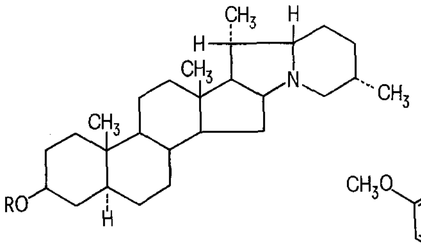
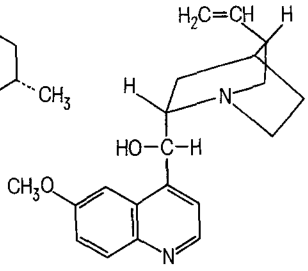
It has been postulated that the gradual development of secondary plant substances in the course of evolution was somehow related with insect speciation, and that insects were compelled to adapt to an environment of continuously increasing chemical complexity[2]. Accordingly, the appearance of fatal poisons in the plant world has necessitated the development of a delicate sensory system with the capacity of qualitative and quantitative discrimination[15].

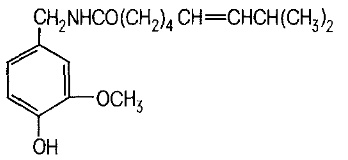
Sensory recognition of alkaloids

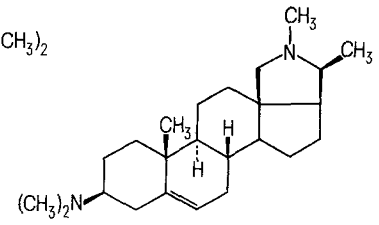
Let us now consider the mode of action of phagorepellent alkaloids. The gustatory receptors, mainly found on the maxillae and maxillary palpi of many insect larvae, most probably make the final assay of food before it is ingested or rejected. Alkaloids may act on the receptor neurons by means of suppressing the activity of various gustatory receptors responding

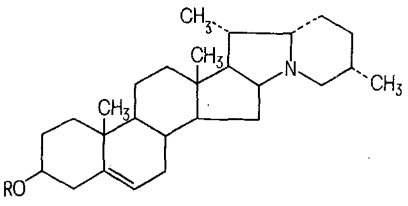

R = ß-Lycotetraose
Tomatine (**1**)

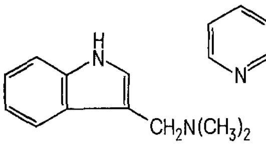

R = ß-Lycotetraose
Demissine (**2**)

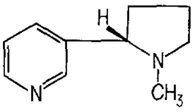

Quinine (**6**)

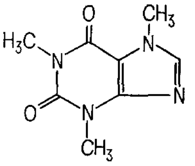

Capsaicine (**3**)

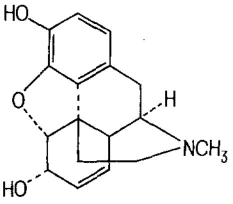

Conessine (**9**)

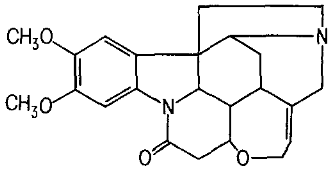

R = ß-Solatriose
Solanine (**5**)

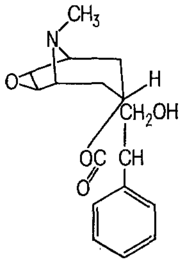

Gramine (**7**)

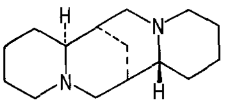

Nicotine (**4**)

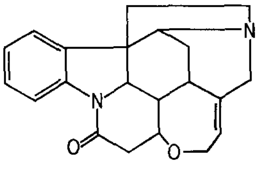

Caffeine (**8**)

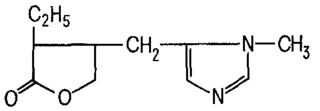

Morphine (**16**)

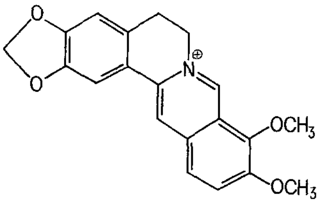

Brucine (**11**)

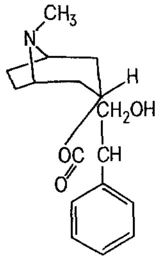

Scopolamine (**15**)


Sparteine (**17**)


Strychnine (**10**)


Pilocarpine (**13**)


Berberine (**12**)


Atropine (**14**)

Structures of some phagorepellent alkaloids (the numbers in parenthesis refer to the numbers given in Tables I and II).

to phagostimulants (as well as nutrients) and/or by stimulation of gustatory receptors which are tuned specifically to feeding inhibitors, the input signal then being interpreted as inhibitory within the central nervous system[22]. Combined anatomical and electrophysiological studies revealed special taste receptors responding to phagorepellent alkaloids in the larvae of several lepidopterous species (Table II). The so-called bitter taste receptors found in the medial sensillum styloconicum of larvae of the silkmoth and the cabbage butterfly, as well as the salicin receptor present in the lateral sensillum styloconicum of *Manduca sexta* larvae respond to an array of alkaloids[15,28]. Interaction between different gustatory stimuli may result in either inhibitory or synergistic responses: stimulation of the bitter taste receptor of silkmoth larvae with sodium chloride increases the reaction of the former to strychnine[29], whilst the responsiveness of the lateral salt receptor of gypsy moth larvae is suppressed by various alkaloids. It follows that the response of the gustatory receptors to alkaloids can be largely modified by a mixture of chemicals as complex as plant sap. Comparing the reaction spectrum of the salicin receptor in the tobacco hornworm (*Manduca sexta*) to various alkaloids suggests that an increase in the number of alkyl side-chains on the heterocyclic ring system leads to an increased phagodeterrent effect in purine derivatives, reaching its maximum in caffeine[15].

Insect defence by alkaloids

TURSCH, BRAEKMAN and DALOZE[30] have shown ample evidence that alkaloids (of diversified structures) are distributed among a restricted number of arthropod species only, whereas this group of compounds is so commonly produced by plant species and particularly by seed plants[31] that the alkaloids represent a taxonomic feature of families[1]. Furthermore, the occurrence of alkaloids seems to be less common in vertebrates than in arthropods. It is conceivable that the alkaloids are a more recent evolutionary supplement to the coactones[32] of arthropods as compared with those of plants.

Most of the arthropod alkaloids known so far have defence or alarm functions, whilst a smaller number of these compounds serve as sexual or trail pheromones[30]. EISNER[33] has classified them among the toxicants with delayed and usually systemic effects (e.g. emetics, vesicants, narcotics), and this classification could as well be applied to the plant alkaloids. It is tempting to speculate that plant feeding insect species have adopted the defensive role of phytoalkaloids for their self-protection against predatory animals and, in addition, utilize suitable metabolites or even sequester the alkaloids from their food plants for the production of such defence compounds. The following are well-known examples for direct incorporation of host-plant alkaloids into insect species. Larvae of the papilionid *Pachlioptera aristolochiae*, which feed exclusively on *Aristolochiaceae*, accumulate aristolochic acid carried through the pupal stage to the adults[34]. The cinabar moth *Callimorpha jacobaeae* and the tiger moth *Arctia caja*, which are unacceptable to a variety of potential predators, contain pyrrolizidine alkaloids, derived from composite food-plants of the genus *Senecio*[35,36]. However, the above moth species are multiply protected and have supplementary defence compounds as well as aposematic colours.

Considering the functional evolution of insect alkaloids, two principal stages may be important. In the first one, the poisons are simply obtained from the food and accumulated in the body tissues (e.g. the lepidopterans *Pachlioptera aristolochiae*, *Callimorpha jacobaeae* and *Arctia caja*[30]). However this defence mechanism is rather imperfect, since an insect has to be tasted or even swallowed, before rejection can occur. Although the predators may learn in the future to avoid such insects, some of the latter would invariably be killed. The same applies to insect species which synthesize their own toxic alkaloids and store them in the haemolymph (e.g. the staphylinid beetle *Paederus fuscipes*[30]). Interestingly enough, the coccinelid beetles, which discharge endogenous coccinelline alkaloids by means of reflex bleeding[30], have a transitory position between the passive defence mechanism mentioned above and an active defence. In the second and most advanced stage, the alkaloids are included in the defensive secretions; none of the insects protected this way needs to be sacrificed (e.g. ants of the genus *Solenopsis* and *Odontomachus*, the staphylinids *Hesperus semirufus*, *Philonthus politus* and the dytiscid beetle *Ilobius fenestratus*[30]).

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