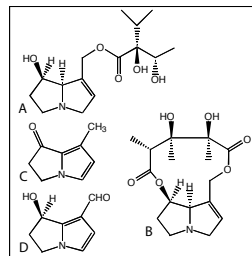


# Pharmacophagy in Lepidoptera

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which contain pyrrolizidine alkaloids (PAs). With their proboscides they apply a fluid onto the dry plant material to extract PAs for uptake as solution. The same behaviour can be elicited by pure PAs, showing that the target compounds also represent the source of the luring stimulatory cues and that there are no other chemicals involved in eliciting this response; long-range attraction is mediated by volatile breakdown products of the non-volatile PAs.



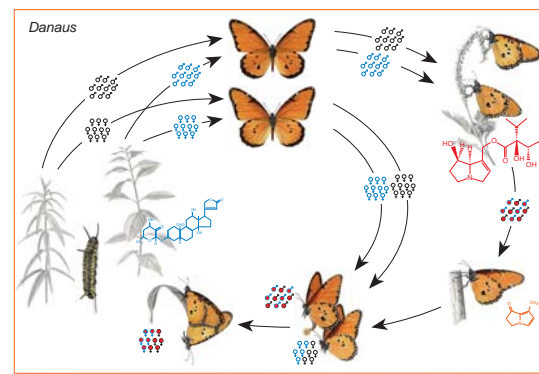
Molecular structures of PAs (A lycopsamine; B monocrotaline) and dihydropyrrolizines used as male pheromones (C danaidone; D hydroxy-danaidone).

direct connection between intraspecific sexual communication and chemical defence. The energy-consuming, non-nutritional relationship to 'supplementary host plants' although they are not required to maintain life can therefore increase the insects' fitness in two ways: PAs serve to expand survival prospects and the chances of reproductive success.

The above statements are generalized and quite superficial – a more detailed look reveals much greater complexity. Diversity occurs in almost every aspect studied: taxonomic, morphological, chemical, behavioural, ecological; and whether related to proximate or to ultimate aspects. Apart from the special way of gathering PAs, storage of PAs for defence appears to be the only common denominator of all the taxa involved.

## Taxonomic and functional diversity

- PA-pharmacophagous insects are found in a variety of terrestrial habitats, predominantly in tropical ecosystems.
- Insect species concerned belong to unrelated taxa, indicating that PA-pharmacophagy has evolved independently several times. Often only the males are pharmacophagous, but there are others of which only females or both sexes exhibit this trait.
- PAs serve as precursors for the biosynthesis of male pheromones in some butterflies and moths, but not all PA-pharmacophagous species possessing androconial organs utilize PAs in this respect.
- PA-derived pheromones are employed in different courtship strategies; chemically identical compounds can have quite diverse meanings in different taxa.
- The pheromone-releasing structures are morphologically diverse, too. They can be pneumatically or hydraulically expandable brush-like organs in the abdomen, or hair tufts on the wings or legs.



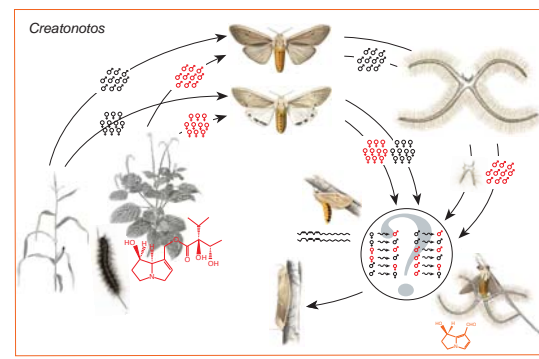
Schematic representation of the relation between *Danaus chrysippus* and secondary plant metabolites. The caterpillars obtain cardiac glycosides from some primary hosts. Adult males pharmacophagously gather PAs from secondary hosts; only then (and after establishing contacts between abdominal and alar androconial glands) males can produce danaidone and have a chance with females. During copulation males transfer PAs as nuptial gifts to females.

## Diversity in specificity

- Pyrrolizidine alkaloids are a large group of chemicals with diverse structures, in nature usually occurring as *N*-oxides. PAs utilized by insects represent only a fraction of the compounds which chemists call PAs. The most relevant PA-sources for insects include plants of the genera *Heliotropium* and *Tournefortia* (Boraginaceae), *Crotalaria* (Fabaceae), and *Senecio* and *Eupatorium* (Asteraceae). PAs of these plants are mixtures of mono- or di- or cyclic esters, mostly made up by the necine alcohols retronecine and heliotridine.
- PA-pharmacophagous insects exhibit more or less wide specificity in their behavioural response to sources of PAs; some species discriminate between a given set of PAs or between plants containing these chemicals, others don't.
- There is diversity also in the specificity of PA-storage, i.e., there is often selective storage of certain PAs out of the mixture present in the plants visited. In addition, several species chemically modify in part some of the ingested plant PAs.
- There is specificity in conversion into pheromones. So far, 10 PA-derived pheromone components are known, but one only, hydroxydanaidone, is widespread, occurring in numerous unrelated species.

## Variation

- Leaving qualitative aspects of PA-chemistry aside, considerable quantitative variation at different levels is a major basic character intimately linked with pharmacophagy.
- Inter-specific variation is to be expected in a polyphyletic phenomenon, due to different biologies and different degrees of adaptation of the taxa concerned.
- Intra-specific variation is simply a result of the sex-bias in PA-pharmacophagy.
- Individual variation in acquisition of different amounts of chemicals results necessarily from the active search for and ingestion of certain substances, the sources of which vary in availability in the environment as well as in their content of PAs; also, the insects' ability to find and process the compounds is variable.
- There is also temporal intra-individual variation with respect to defensive chemicals and to pheromones. Species transferring PAs via spermatophores exhibit a sudden loss in males and a sudden gain in females – perhaps followed by 'recharging' in males with new visits to PA-sources; females lose PAs when laying eggs and receive new loads by additional matings. Respectively, pheromones are produced, disseminated during courtship – and, at least in some species, perhaps synthesized again.



Schematic representation of the relation between *Cretonotos transiens* and PAs. The caterpillars are polyphagous and utilize a wide spectrum of primary hosts. In males PAs are being stored. In males PAs determine the size of the androconial organs (coremata) and serve as precursors for the pheromone hydroxy-danaidone. Courtship behaviour remains an enigma, probably multiple mate-finding strategies exist which might depend on the PA status of the individual.

Relationships between insects and plants are by no means restricted to the nutritional dimension. Plant secondary metabolites not only play a major role in host specificity by mediating host recognition and host localization, but many insects also sequester them as defensive compounds for chemical protection against antagonists. If secondary chemicals are utilized by specialists, they alone usually do not modify insect behaviour, and their ingestion usually occurs incidentally, in the course of feeding – although physiological adaptations are required to avoid noxious effects for the specialist itself.

In contrast, the special kind of relationship between insects and plants called 'pharmacophagy' is non-nutritional and exclusively mediated by and directed towards plant secondary compounds. Here, a brief characterization of pharmacophagy and its diverse facets (behavioural, chemical, physiological, ecological and taxonomic) is provided to demonstrate the challenge of comparative studies for gaining insight into, e.g., mechanisms of insect-plant relationships, chemoreceptor specificities, chemical defence and chemically mediated mate-choice, all in an evolutionary perspective.

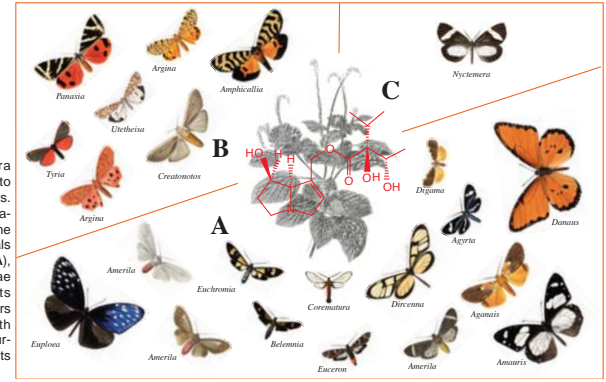
## Pharmacophagy

Insects are called pharmacophagous if they search for certain secondary substances directly, take them up and utilize them for a specific and fitness-increasing purpose other than primary metabolism or merely host recognition.

Pharmacophagy in adult Lepidoptera usually involves plants taxonomically unrelated to the nutritional host plant(s) of a given species, i.e. it reflects an insect-plant relationship separate from those plants which provide nutrients for larvae or adults. For example, adults of numerous Danainae, Ithomiinae, Arctiinae, and Ctenuchinae are attracted to dry parts of plants

PAs are generally repellent to non-adapted animals and serve as protective devices for the plants that produce them. By sequestration and storage of PAs many, if not all, PA-pharmacophagous taxa gain protection from predators, and this is reflected by the aposematic coloration and lifestyle of many of the species in question. In addition, males of several lepidopterans use PAs as precursors for the biosynthesis of major sex pheromone components required for the acceptance of a courting male by a female. Such sexual communication can also relate to chemical defence: with his spermatophore a male can transfer large amounts of PAs as a nuptial gift to the female, which then gains protection for herself and also protects her offspring by incorporating PAs into her eggs. In some species it is likely that the strength of the male pheromone stimulus permits a female to assess the amount of PAs she can expect to receive during copulation. Thus there can be a

Some Lepidoptera having a relation to PA-containing plants. All have an aposematic coloration; of some only adult individuals visit dry PA-plants (A), of others the larvae feed on PA-Plants (B), and for yet others PA-plants are both larval hosts and sources of PAs for adults (C).



Caterpillar of *Cretonotos transiens* consuming a glass-fibre disc impregnated with PAs

## Conclusions and prospects

In summary, PA-pharmacophagy is a multifaceted syndrome, and there are no prime examples which illustrate the entire range of adaptive features. To date, we only understand in some detail a few aspects in a limited number of species, and we cannot generalize much, or make any specific predictions. This situation will probably remain, even if many more cases are

studied in some depth. However, basic mechanisms have been discovered and techniques for detailed investigations on different aspects are available. Thus there is good reason to assume that, from comparative approaches to PA-pharmacophagy, we can gain deeper insights into ecological factors governing evolution of chemical defences and chemical communication. Because pharmacophagy is not related to primary metabolic processes and ordinary host plants, qualitative as well as quantitative manipulations of defensive potency and/or pheromonal outfit are possible without any artificial disturbance of the insects. For example, relevant experimental approaches to female mate-choice and mimicry are possible; quantitative biochemical studies on storage and conversion can be undertaken; because of the uniformity of both stimuli and behavioural responses, comparative electrophysiological studies of PA-insects can provide basic data on the evolution of (olfactory / gustatory) chemoreceptor specificity; etc.

PA-pharmacophagy is not restricted to adult Lepidoptera. The larvae of several taxa are known to sequester PAs (cf. *Cretonotos*, above); some incidentally, others pharmacophagously. In both cases the use of PAs for pheromone biosynthesis and/or for defence can be demonstrated. PA-pharmacophagy also occurs in other orders of insects (Orthoptera, Coleoptera, Diptera) in a similarly complex phenomenology, and more and more cases of pharmacophagy to other secondary products are being recognized. Considering the entire spectrum of cases of (PA-)pharmacophagy reveals complex systems, well-suited to assist our understanding of diversity in an evolutionary context.