



The government has the clear responsibility to weigh the importance of large-scale experiments to the advance of knowledge or to national security against the possibility of adverse and destructive effects. The scientific community must assist the government in arriving at rational judgments and in interpreting the issues to the public (18).

The necessary support must be provided to conduct adequate studies of the biological effects of a sea-level canal. Modern science can identify significant processes, quantify the relations of many oceanographic complexities, and resolve them in predictable patterns.

I believe that a control commission for environmental manipulation should be established and that this commission should be given broad powers of approving, disapproving, or modifying all major alterations of the marine or terrestrial environments in the United States, or any place where United States government or private contractors might be active. This commission should be multidisciplinary, independent of any single government agency, bureau, university, or private

research institution, and it should have adequate funding to support its own investigations (19). Such a commission should be in operation before a sea-level canal is built, and its decisions should be made with the benefit of comprehensive biological investigations.

#### References and Notes

1. D. A. Arosemena, *Documentary Diplomatic History of The Panama Canal* (Imprenta Nacional, Panama, R.P., 1961).
2. Atlantic-Pacific Interoceanic Canal Study Commission, *A Plan For Study of Engineering Feasibility of Alternate Sea-Level Canal Routes Connecting the Atlantic and Pacific Oceans* (Atlantic-Pacific Interoceanic Canal Study Commission, Washington, D.C., 1965), 61 pp.
3. S. F. Hildebrand, *Sci. Mon.* **44**, 242 (1937); *Zoologica* **24**, 15 (1939).
4. R. W. Rubinfoff and I. Rubinfoff, *Nature* **217**, 476 (1968).
5. A. Ben-Tuvia, *Copeia* **1966**, 254 (1966).
6. C. S. Elton, *The Ecology of Invasions by Animals and Plants* (Methuen, London, 1958), p. 15.
7. U.S. Fish and Wildlife Service, personal communication.
8. D. Pimental, *Science* **159**, 1432 (1968).
9. W. P. Woodring, *Proc. Amer. Phil. Soc.* **110**, 425 (1966).
10. J. J. Lloyd, in *Backbone of the Americas* (American Association of Petroleum Geologists, Tulsa, Okla., 1962), p. 88.
11. A. Günther, *Trans. Zool. Soc. London* **6**, 377 (1869); C. H. Gilbert and E. C. Starks, *Mem. Calif. Acad. Sci.* **4**, 1-304 (1904); S. Ekman, *Zoogeography of the Sea* (Sidgwick and Jackson, London, 1953), pp. 30-55.

12. W. S. Wooster, *Amer. Mus. Natur. Hist. Bull.* **118**, 119 (1959); M. B. Schaefer, Y. M. M. Bishop, G. V. Howard, *Bull. Inter-Amer. Trop. Tuna Comm.* **3**, 79 (1958); E. D. Forsbergh, *ibid.* **7**, 1 (1963); T. J. Smayda, *ibid.*, p. 191.
13. E. Mayr, *Animal Species and Evolution* (Harvard Univ. Press, Cambridge, Mass., 1963), 797 pp.; I. Rubinfoff, *Natur. Hist.* **74**, 69 (1965).
14. M. J. D. White, *Science* **159**, 1065 (1968).
15. I. Rubinfoff and R. W. Rubinfoff, in preparation.
16. C. O'D. Iselin, personal communication.
17. It is commonly believed that population fluctuations in tropical species are minimum, but this certainly is not true of reptiles (O. Sexton, in press); mammals and birds (M. Moynihan, personal communication); at least some groups of insects (R. Dressler, personal communication); and it is my impression that the fluctuations in marine fishes are at least as great as in land animals. It is important to recognize that population studies should begin at least 10 to 20 years before a canal is completed if normal long-term population fluctuations are to be mapped. Without this data a canal may be "blamed" for sudden reduction or disappearance of species which might just coincidentally be at a density nadir.
18. *New York Times* (23 October 1963), p. 24.
19. For a recent discussion of federal activities in environmental control, see *Environmental Quality*, Hearings before the House Subcommittee on Science Research and Development, Jan.-Mar., 1968, Emilio Q. Daddario, chairman (U.S. Government Printing Office, Washington, D.C., 1968).
20. Based in part on research supported by NSF grant GB-3450 and grants from the Smithsonian Research Foundation. I thank W. Aron, S. Galler, P. Glynn, E. Mayr, R. Menzies, M. Moynihan, R. Rubinfoff, N. Smith, R. Topp for criticizing the manuscript.

## Heart Poisons in the Monarch Butterfly

Some aposematic butterflies obtain protection from cardenolides present in their food plants.

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It was noted nearly a hundred years ago that butterflies of the subfamily Danainae were unpalatable to the majority of insectivorous birds (1), and this observation has frequently been confirmed (2-6), both in nature and in the laboratory. Some species, however, can apparently eat these butterflies with impunity. Swynnerton (7), who was the first to record vomiting in captive birds following the ingestion of *Danaus chrysippus* (L.) and *Amauris echeria lobengula* Sharpe, believed that *Crateropus* spp. (babblers) preferred

this type of food (and other distasteful species such as blister beetles, *Mylabris* spp.); he also found that *Lophoceros melanoleucus* (Licht.) suffered little or no ill effects from eating danaids. One of us observed that *Kittacincla malabarica* (Gm.) ate *D. plexippus* without hesitation (8, 9) despite the fact that it usually regurgitated the insect immediately and then re-swallowed it. When very hungry, many species of birds (2) will eat one or even two specimens of danaids, and shrikes (*Lanius*) have been seen im-

paling them on thorns in their food stores.

Slater (10) in 1887 suggested that gaily colored caterpillars were protected by the poisonous substances they obtained from the plants they feed on. Our observations suggest that this surmise is correct in the case of *Danaus*. Slater's choice of examples was somewhat unfortunate as he included in his list species which, although brightly colored, are essentially cryptic in habit. He thus bracketed the larvae of *Danaus* and of the oleander hawkmoth [*Deilephila nerii* (L.)].

Haase (11) was also of the opinion that warningly colored species (that is, aposematic species) obtained their deterrent qualities directly from the foliage consumed by their larvae. Poulton (12), with more insight, agreed that this might well be the case for those groups which specialize in feeding on one group of toxic plants, all closely related (examples are the dan-

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Table 1. Yield of crude extracts and intensity of the tetranitrodiphenyl reaction for cardenolides.

Kind of Extract	Yield (in mg) from 730 males	Yield (in mg) from 810 females	Intensity of tetranitrodiphenyl reaction
Petroleum ether	3200	6200	—
Ether	7380	6260	++
Chloroform	710	175	++
Chloroform-ethanol	1440	830	+

aids, feeding on Asclepiadaceae, and the pharmacophagus papilios, feeding on *Aristolochia*) but not for all aposematic species. [It should be noted that several species—for example, *Streblus asper* Lour (13)—of Moraceae, a family not infrequently used as alternative food plants by danaids, contain a milky latex and are occasionally rich in cardenolides (14).] It is now known that various arctiids are unpalatable or poisonous irrespective of the plants on which they feed (15), and that zygæonids (*Zygaena* and *Procris*) release hydrocyanic acid from their bodies when they are crushed, whether or not their food plants are cyanogenic (16). It is to be expected that the Acraeinae, which are generally acknowledged to be among the more highly unpalatable groups of butterflies so far tested, and which feed on a wide variety of plants, secrete poisonous or repellent substances quite independently of any toxins which may occur in some of their food plants.

Trimen (17) as long ago as 1887, with great perspicacity, wrote: "Apart

from the unpalatable nature which renders it distasteful to insect eaters there can be no doubt that the wide prevalence of [*Danaus*] *chrysippus* is largely due to the circumstances that the larvae affect chiefly, if not solely, Asclepiad plants, which very few if any herbivorous mammals will feed on." He was thus the first to appreciate that the Danainae obtain varied advantages and protection at all stages of their life cycle from their association with asclepiad plants. This is a fact of primary importance, since it is now believed by many that, in the long run, population size is regulated not by predators and parasites but by food limitation (18), and that the competition which leads to the evolution and stabilization of warning coloration of the imagines (adult butterflies) is intraspecific. A further factor contributing to the success of the butterflies that lay eggs and feed on *Asclepias* could be the bactericidal qualities of the latex of the plant (19). Such qualities have also been reported for the hemolymph of *Oncopeltus fasciatus* Dallas, the large milkweed bug (20), which feeds on the seeds of asclepiad plants, but no such activity could be demonstrated in the blood of the larvae of *Danaus plexippus* or of the arctiid moth *Euchaetias egle* Drury, or the milkweed beetle [*Tetraopes tetraophthalmus* (Furst.)].

In the experiments described below it has been shown that *Danaus plexippus* contains heart poisons (21), mainly calactin and calotropin, in its body tissues and that *D. chrysippus* is also rich in cardiac glycosides (22).

## Experimental Material

Monarch butterflies were reared in captivity for pharmacological and chemical study. Eggs of specimens caught near Trinidad, West Indies, were hatched and fed on one of their natural food plants, *Asclepias curassavica* L., by Lincoln Brower. Living pupae (which eclosed later) were sent by air-mail to London for pharmacological and preliminary chemical investigation. Subsequently a larger number of adult butterflies (730 males and 810 females) originating from stock caught in south-central Florida and reared (also by Lincoln Brower) on *A. curassavica* grown from seed collected in Trinidad were sent by airfreight to Basel. These were killed, by freezing, within 27 hours of emergence and were kept in a deepfreeze at  $-20^{\circ}\text{C}$  for periods of not more than 6 months and not less than 24 hours. For transport, the butterflies were put in ten polyethylene bottles, each containing 140 milliliters of 95-percent ethanol, kept at  $5^{\circ}$  to  $10^{\circ}\text{C}$ ; they were mailed to Basel on 16 November 1965. They arrived in Basel on 18 November and were kept at  $-15^{\circ}\text{C}$  until extracts were prepared, on 25 November in the case of the females and 1 December in the case of the males.

Eggs of *Danaus chrysippus* (L.) were obtained from two pairs caught, while copulating, in a garden near Bulawayo, Rhodesia; after hatching, the caterpillars were reared at Ashton, Peterborough, on plants of *Asclepias curassavica* L. grown at the Royal Botanic Gardens, Kew, and in Milton, Peterborough. The imagines were stored in a freezer at  $-10^{\circ}\text{C}$  until they were tested, 24 months later. *Zenillia adamsoni* Thompson, a tachinid parasite, was bred from the pupae of *D. plexippus* from Trinidad.

## Pharmacological and

### Preliminary Chemical Study

Details of this investigation have already been published (21). Neither pupae nor butterflies contained significant amounts of toxins capable of causing rapid contraction of the guinea pig ileum—toxins such as acetylcholine, histamine, or 5-hydroxytryptamine, which are often present in poisonous insects (15). On the other hand, both pupae and adults were found to contain a toxin which closely resembled the cardiac glycosides of digitalis in

Table 2. Cardenolides isolated from the monarch butterflies (combined values for 1540 butterflies).

Compound*	Sample number	Amount (mg)		$R_F^{\dagger}$	$R_{\text{calotropin}}$
		Crude	Crystals (melting points, in degrees Celsius, in parentheses)		
Calotropagenin	TR 1362	32	1.8 (225°–228°)	0.12	0.43
Calotoxin	TR 1347	23	1.5 (219°–223°)	.16	.57
Unknown 2		13		.21	.75
Unknown 3		10		.25	.90
Calotropin	TR 1363	25	1 (218°–225°)	.28	1.00
			4 (205°–220°)	.28	1.00
Unknown 4		2.2		.45	1.60
Calactin	TR 1364	48	18 (242°–245°)	.50	1.78
Unknown 1 (= U1 Santavy ‡ = TR 1342 from <i>Poekilocerus</i> )§	TR 1375	1.5		.73	2.61
Unknown 5		3.5		.78	2.78
Uzarigenin (= TR 1361 from <i>Poekilocerus</i> )§	TR 1374	2.5		.83	2.96

\* Identification was made by paper chromatography and thin-layer chromatography in appropriate systems (24); identification of the crystalline components was further based on melting point, on mixed melting point, on rotation, and in part on mass spectra. † As determined by paper chromatography for the system tetrahydrofuran and benzene (1 part each) on Whatman No. 1 filter paper impregnated with 34-percent formamide. ‡ Cardenolide of unknown structure isolated from the leaves of *Asclepias curassavica* (38). § See (24).

pharmacological properties, absorption of ultraviolet radiations, and color reaction with 3,5-dinitrobenzoic acid and potassium hydroxyde (21, 23). Paper chromatography showed that the toxin contained three main compounds, which were called "plexippins A, B, and C"; these have subsequently (24) been identified as calactin, calotropin, and calotropagenin, as discussed below. It is known, and we have confirmed, that the lethal dose of either calactin or calotropin for a cat is about 0.11 milligram per kilogram (24, footnote 18; 25).

By using the assay method of the United States Pharmacopoeia to measure the concentration of digitalis-like substances by determining their lethal effect in cats, it was found that the monarch butterflies and pupae each contained an amount of toxin equivalent to approximately 0.2 milligram of calactin (about 1.8 times the lethal dose for a cat). A similar estimate of the content of digitalis-like compounds was obtained by means of spectrophotometric measurements (26) on dichloromethane extractable toxin. An aqueous extract of *Danaus chrysippus* was tested for its action on the frog heart, by methods described elsewhere (21). It was found to have digitalis-like activity of the same order as that found for the monarch, corresponding to a calactin content of 100 to 200 micrograms per gram (22). Forty pupae of *Zenillia adamsoni* Thompson were also tested and found to have digitalis-like activity similar to that of *D. chrysippus* but, in this case, perhaps due to the presence of compounds more polar than calactin, since preliminary experiments showed that the active material could not be extracted from aqueous solution into dichloromethane.

### Chemical Investigation

The techniques used were similar to those used in studies of the grasshopper [*Poekilocerus bufonius* (Klug)] (24, 27), but the investigation proved more difficult since the monarch butterfly lacks a poison gland, from which the toxic principles are more easily collected. In the monarch, the poisons are present in the hemolymph and are distributed throughout the whole body (21), and the entire insect was therefore used in obtaining extracts for analysis. It should be noted that the imago feeds only on the nonpoisonous nectar, and that, consequently, its di-

Table 3. Nontoxic by-products obtained in crystalline form (see text).

Compound	Sample number	Amount (mg)	
		Crude	Crystals (melting points, in degrees Celsius, in parentheses)
Orange pigment*	TR 1352	185	4 (170°-175°)
Fatty acids mixture †	TR 1325, 1326, 1327	1800	210 (50°-51°, 55°-57°, 64°-65°)
Cholesterol ‡	TR 1358		772 (144°-145°)
Sterol mixture §	TR 1357		382 (125°-142°)
Insoluble pigment	TR 1365		4000 (High, with decomposition)

\* Isolated from ether extract. The same pigment was isolated from leaves of *Asclepias curassavica* and also from *Gonolobus rostratus* (Vahl) Roemer et Schultes, a plant, native to Trinidad, of the family Asclepiadaceae. † Mixtures of different composition; according to the mass spectral analysis, mainly stearic, palmitic, and two higher homologs of  $M^+$ :  $m/e = 312$  and  $340$  ( $M^+$  = mass of the molecular ion;  $m/e =$  mass/charge). ‡ Nearly pure, as determined by gas chromatography. § A mixture of cholesterol, campesterol and  $\beta$ -sitosterol and perhaps stereoisomers, as determined by gas chromatography. || The pigment was insoluble in chloroform; it was isolated from the aqueous phase after extraction with chloroform and ethanol. It was soluble in dilute mineral acid and precipitated after neutralization.

gestive tract does not contain any poisonous material.

In analyses made in Basel, 730 male butterflies (total weight, 493.7 grams) and 810 female butterflies (total weight, 494.2 grams) were used. Solvent extraction was performed in a  $CO_2$  atmosphere on batches containing 150 insects of one sex. Each batch was homogenized with 200 milliliters of 80-percent aqueous methanol warmed to 60°C, and the homogenate was filtered by suction. The residue was extracted seven times, in the manner described, and the final residue was discarded. All extracts were united with the first alcohol extract, and this clear yellow solution was shaken three times with 500 milliliters of petroleum ether. The petroleum ether extracts were then "back-extracted" three times with 50 milliliters of 80-percent methanol.

The aqueous methanol phase from each batch of insects was concentrated in a vacuum at 55°C to a volume of approximately 100 milliliters; the resulting aqueous suspension was shaken three times with 200 milliliters of ether, four times with 200 milliliters of chloroform, and eight times with 120 milliliters of a mixture (3 parts to 2 parts) of chloroform and ethanol. The extracts were washed by a counter-current procedure, each successively with 20 milliliters of water, 20 milliliters of 2N sodium carbonate solution, and 20 milliliters of water. The washed extracts were dried over anhydrous  $Na_2SO_4$ , and the remaining solvent was evaporated in a vacuum. Table 1 shows the yield of crude extracts and the intensity of the tetranitrodiphenyl reaction (28) for cardenolides.

Paper chromatography showed that the chloroform-ethanol extract did not contain calactin, calotropin, and calotropagenin but contained only highly

polar cardenolides; these may include autoxidation products, but they were not further investigated.

Ether and chloroform extracts were chromatographed on a silica-gel column with a slow gradient from a mixture of benzene and ether to a mixture (1 part each) of chloroform, methanol, and ethyl acetate; paper chromatography and thin-layer chromatography were used as controls. Fractions containing mixtures were rechromatographed according to Duncan's method (29); 600 parts of silica gel were used for each part of cardenolide mixture and cyclohexane-ethyl acetate was used as the solvent. For analysis of the final fractions the solvent was changed to pure ethyl acetate. The remaining mixtures were separated by preparative paper chromatography (30) (1 part each of tetrahydrofuran and benzene on Whatman paper No. 1 impregnated with 34-percent formamide).

This procedure yielded ten cardenolides from the monarch extracts. The four main compounds were obtained as pure or nearly pure crystals. The other six, which were present in very small amounts and were obtained as amorphous concentrates, each showing only one spot in appropriate systems when analyzed by paper chromatography and thin-layer chromatography (24), may have contained unknown impurities noncardenolide in nature. Five of the ten cardenolides were identified as known compounds—namely, calotropagenin, calotoxin, calotropin, calactin, and uzarigenin. Of these, calactin and calotropin were identical with plexippin A and plexippin B, respectively; plexippin C corresponded to a mixture of calotropagenin and calotoxin, which show similar properties in some paper-chromatography systems. Table 2 gives the yields of pure and crude cardeno-

lides. The values shown for crude cardenolides are approximations. The yields differed to some extent for male and female butterflies, but the differences were within the limits of experimental error (31) and were probably not significant. We therefore give the combined figures for all 1540 butterflies. Apart from cardenolides, some nontoxic compounds (tetranitrodiphenyl reaction negative) were isolated; these are given in Table 3. These results show that calotropagenin, calotoxin, calotropin, and calactin are the main cardenolides present in the monarch but that uzarigenin and five other, unidentified cardenolides were also present, all in smaller amounts. Fifty eggs (total weight, 8 milligrams) were also analyzed and found to contain appreciable amounts of cardenolides. Paper chromatography and thin-layer chromatography showed calactin, calotropin, calotropagenin, and calotoxin to be present (total amount, about

0.012 milligram, or approximately 0.15 percent).

The amounts of components found for the monarch extracts through these methods of isolation (0.1 milligram of total crude cardenolides still containing inactive impurities and genins of low biological activity) are much smaller than the amounts (equivalent to 0.2 milligram of pure calactin) estimated, by pharmacological methods, for freshly killed monarchs. This is mainly due to the unfavorable effects of storage in alcohol. All cardenolides containing an aldehyde group (32), including the calotropis compounds (33), deteriorate quite rapidly in solution, mainly by autoxidation. It should be noted, however, that the original stock of the two samples of butterflies (the sample studied when the butterflies were freshly killed and the sample studied after storage in alcohol) came from different localities, the one from Trinidad and the other from Florida.

Among the compounds mentioned, only the structure of uzarigenin (Fig. 1) is known (34). Crout *et al.* (35) have suggested the formula of Fig. 2 for calotropagenin, of Fig. 3 for calotropin, and of Fig. 4 for calotoxin, but these formulas are still hypothetical. Calactin is an isomer of calotropin (Fig. 3), probably a stereoisomer having the same general formula (Fig. 3) but a different configuration at C-3<sup>1</sup> (24).

Calactin, calotropin, and calotoxin, together with related compounds, are the main cardenolides of the latex as well as of the leaves of *Calotropis procera* (24, 36). Uzarigenin is also present in this material in small quantities (37). Santavy *et al.* (38) found that *Asclepias curassavica* leaves from Trinidad contained exactly the same compounds. This finding differs from the results of Tschesche *et al.* (39) for *A. curassavica* from Brazil.

sects, steroid biosynthesis either does not occur or is exceedingly rare (41). The fact that the cardioactive toxin of the monarch butterfly is of the cardenolide type therefore supports the suggestion that it is derived from the food plant and stored either unchanged or with only minor metabolic transformation.

It has now been demonstrated that several species of grasshoppers [*Poeciloceris bufonius* (Klug), *P. pictus* (Fab.), *Phymateus viridipes* Stål, and *P. bacatus* (Stål)] which also feed on asclepiad plants accumulate cardiac glycosides in their body tissues (24). Although in both *Danaus* and *P. bufonius* the main cardenolides stored are calactin and calotropin, the butterfly is somewhat less selective than the grasshopper. It is interesting to note that these aposematic insects, which belong to different orders and have different distributions and habits, have nevertheless selected the same two compounds as the major component of their defense mechanisms. Furthermore the cardenolides seem to provide effective protection against the majority of vertebrate

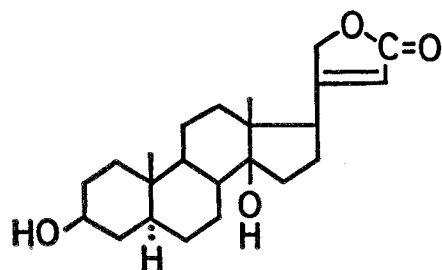


Fig. 1. Structure of uzarigenin.

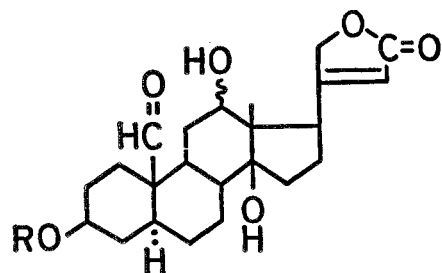


Fig. 2. Structure (hypothetical) of calotropagenin. R=H.

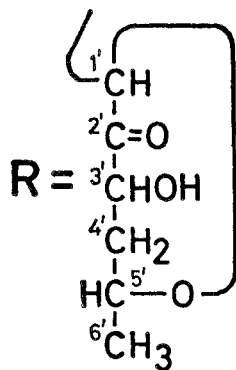


Fig. 3. Part R of structure (hypothetical) of calotropin and its isomer calactin.

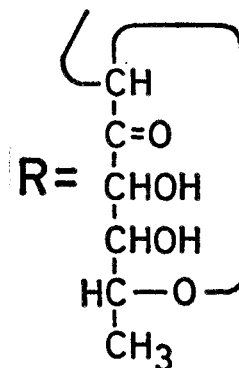


Fig. 4. Part R of structure (hypothetical) of calotoxin.

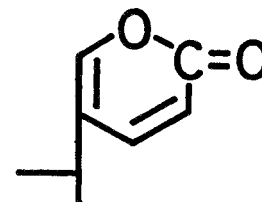


Fig. 5. The pentadienolide side chain of the toad poisons.

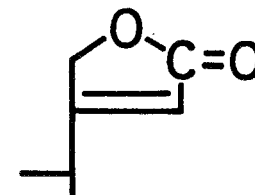


Fig. 6. The butenolide ring of cardenolides.

## Discussion

The only digitalis-like toxins previously known to occur in the animal kingdom are the toad poisons. These possess the pharmacological properties of digitalis and are very similar to it in chemical structure but have a pentadienolide side chain (Fig. 5) instead of the butenolide ring (Fig. 6) of cardenolides. The toad poisons and digitalis can easily be distinguished by differences in ultraviolet absorption. Toads can synthesize the heart poisons which they contain (40), but, in in-

predators (6, 27, 42). Apart from the exceptions noted by Swynnerton (2), the known bird predators of *Danaus* are relatively few (43). Captive monkeys also reject these butterflies (44). Mice, however, are said to "wreak havoc" among the hibernating hordes of *Danaus* (45), and it was found that laboratory white mice, house mice (*Mus musculus* L.), and long-tailed field mice [*Apodemus sylvaticus* (L.)] all ate the monarch with avidity. Furthermore, they ate the monarch's food plant without apparently suffering any after-effects. Field mice also raided the greenhouse at Ashton, Peterborough, where the *D. chrysippus* were reared and destroyed 50 percent of our stock of half-grown larvae. It is well known that mice are relatively insensitive to cardiac glycosides (46). There are also scattered records in the literature of lizards, including geckos (47, 48), occasionally consuming danaiids. As for invertebrate predators, there are records (3, 4) of certain large red dragonflies and large wasps in Africa attacking *D. chrysippus*, and this butterfly is not infrequently found in the webs of certain spiders (43). Mantids have also been reported as predators (48), although in captivity (3) they eat *Danaus* with some reluctance. Ants are said to consume the bodies of *Danaus* (43), and extracts of these butterflies mixed with cream were acceptable to the ant *Solonopsis molesta* (Say) (49). It is possible, however, that the species of plant on which the monarch feeds determines the degree of acceptability of this butterfly to ant predators. Like many aposematic lepidoptera, danaiids are heavily parasitized by tachinids (Diptera) (50), although Urquhart states (43) that, in the northern part of their breeding range, parasitism by flies was found to be under 2 percent. It is interesting to note that an extract of 40 pupae of *Zenillia adamsoni* Thompson showed a digitalis-like activity (51), since the pupae of tachinids and of hymenopterans parasitizing *Zygaena* were found to contain no hydrocyanic acid (16). A virus (52) has recently been reported as a major cause of the fluctuations in numbers known to occur in North American populations of *D. plexippus*.

Apart from its toxic properties, calactin has a bitter and very persistent taste. It is not surprising, therefore, to find that many captive birds rejected *Danaus* initially on the strength of the taste alone (2, 9). However, others, such as the blue jay [*Cyano-*

*citta cristata bromia* (Oberholser)] (6) and the British jay [*Garrulus glandarius* (L)] (9), learn to avoid *Danaus*, and other insects containing calactin, only after a disagreeable experience following ingestion.

The assumptions of the older naturalists, based on the study of wild birds and on extensive experiments with captive predators, are supported by our observations. Both *Danaus plexippus* and *D. chrysippus* possess, apart from a powerful smell and taste, "unpleasantness of a more fundamental character" (3). Swynnerton (2, 7) and Marshall (3) rightly deduced that this quality was "indigestibility" (noxious properties) (53), a quality which has destined these butterflies to serve as models for a variety of less well protected species, in both the Old World and the New.

Trimen (17), furthermore, realized that the association of the butterfly with a food plant avoided by large herbivores was of primary importance in the protection of the early stages of the life cycle. Thus, a group of butterflies has been evolved which is immune to the toxic effect of certain of the secondary plant substances (54) produced by the Asclepiadaceae, and at least two species of *Danaus* are capable of incorporating and subsequently storing these products at all stages of their life histories, and of using them for their own protection.

### Summary

Heart poisons (cardenolides) are present in the body tissues of *Danaus plexippus* and *D. chrysippus*, butterflies that feed on *Asclepias curassavica* L. (fam. Asclepiadaceae) and related plants. These cardenolides, principally calactin and calotropin, render the insects indigestible and distasteful to the large majority of vertebrate predators, but one of the major protections these butterflies enjoy lies in the fact that their food plants are generally avoided by herbivores.

### References and Notes

1. J. Newton, quoted in A. G. Butler, *Nature* 3, 165 (1870); R. Meldola, *Proc. Entomol. Soc. London* 1877, 12 (1877).
2. C. F. M. Swynnerton, *J. Linnean Soc. (Zool.)* 33, 203 (1919).
3. G. A. K. Marshall, *Trans. Entomol. Soc. London* 1902, 287 (1902).
4. H. Eltringham, *African Mimetic Butterflies* (Oxford Univ. Press, Oxford, 1910).
5. F. M. Jones, *Trans. Entomol. Soc. London* 80, 345 (1932); ———, *Trans. Roy. Entomol. Soc. London* 82, 443 (1934); J. V. Brower, *Evolution* 12, 32 (1958).
6. L. P. Brower and J. V. Brower, *Zoologica* 49, 137 (1964).

7. C. F. M. Swynnerton, *J. South African Ornithological Union* 11, 32 (1915).
8. C. Lane, *Entomol. Mon. Mag.* 93, 172 (1957).
9. M. Rothschild, personal observations.
10. J. W. Slater, *Trans. Entomol. Soc. London* 1877, 205 (1877).
11. E. Haase, *Researches on Mimicry on the Basis of a Natural Classification of the Papilionidae*, pt. 2, *Researches on Mimicry* (Nägele, Stuttgart, 1896).
12. E. B. Poulton, *Proc. Entomol. Soc. London* 1916, 65 (1916).
13. G. H. E. Hopkins, *Insects of Samoa* (British Museum of Natural History, London, 1935), vol. 3, pp. 1-64; M. J. Manski, *Quaderni Nat.* 16, 68 (1960); D. G. Sevastopulo, "Food Plants of the East African Lepidoptera," in preparation.
14. C. Justen, W. Wehrli, T. Reichstein, *Helv. Chim. Acta* 45, 2285 (1962).
15. J. F. D. Frazer and M. Rothschild, in *Proc. Int. Congr. Entomol. 11th, Vienna, 1959* (1960), p. 249.
16. D. A. Jones, J. Parsons, M. Rothschild, *Nature* 193, 52 (1962).
17. R. Trimen, *South African Butterflies* (London, 1887), vol. 1, pp. 34, 54.
18. C. L. Remington, in *Proc. Int. Congr. Zool. 16th, Washington, 1962* (1963), p. 145.
19. E. H. Salkeld, *Can. J. Zool.* 38, 449 (1960).
20. H. Frings, E. Goldberg, J. C. Arentzen, *Science* 108, 689 (1948).
21. J. A. Parsons, *J. Physiol. London* 178, 290 (1965).
22. ———, R. J. Summers, M. Rothschild, personal observations.
23. D. L. Kedde, *Pharmaceutisch Weekblad Nederland* 82, 741 (1947).
24. T. Reichstein, M. Rothschild, L. Brower, L. Fishelson, J. A. Parsons, J. von Euw, *Naturw. Rundschau* 20, 499 (1967).
25. K. K. Chen, C. I. Bliss, E. B. Robbins, *J. Pharmacol. Exp. Therap.* 74, 223 (1942).
26. The band with  $\lambda_{\text{max}}^{\text{ETOH}} = 217$  millimeter (ETOH refers to ethanol used as solvent) and molecular extinction coefficient  $\epsilon = 16,500$  is typical for all cardenolides; see L. F. Fieser and M. Fieser, *Steroids* (Reinhold, New York, 1959).
27. J. von Euw, L. Fishelson, J. A. Parsons, T. Reichstein, M. Rothschild, *Nature* 214, 35 (1967).
28. R. Mauli, C. Tamm, T. Reichstein, *Helv. Chim. Acta* 40, 284 (1957).
29. G. R. Duncan, *J. Chromatog.* 8, 37 (1962).
30. E. von Arx and R. Neher, *Helv. Chim. Acta* 39, 1664 (1956).
31. The method used was adapted mainly for qualitative identification and isolation of the compounds, rather than for estimation of the exact amounts present.
32. A. von Wartburg, J. Binkert, E. Angliker, *Helv. Chim. Acta* 45, 2139 (1962); J. Binkert, E. Angliker, A. von Wartburg, *ibid.*, p. 2122; A. von Wartburg, *ibid.*, 46, 591 (1963).
33. G. Hesse, W. Geiger, G. Lettenbauer, *Ann. Chem.* 625, 167 (1959).
34. S. Rangaswami and T. Reichstein, *Helv. Chim. Acta* 32, 939 (1949).
35. D. H. G. Crout, R. F. Curtis, C. H. Hassall, T. L. Jones, *Tetrahedron Letters* 1963, 63 (1963); D. H. G. Crout, C. H. Hassall, T. L. Jones, *J. Chem. Soc.* 1964, 2187 (1964).
36. G. Hesse, L. J. Henser, F. Hütz, F. Reicheneder, *Ann. Chem.* 566, 130 (1950).
37. A. Brüscheiler, thesis, University of Basel.
38. F. Santavy, J. von Euw, T. Reichstein, in preparation.
39. R. Tschesche, D. Forstmann, V. K. M. Rao, *Chem. Ber.* 91, 1204 (1958); R. Tschesche, G. Snatzke, G. Grimmer, *Naturwissenschaften* 46, 263 (1959).
40. M. D. Siperstein, A. W. Murray, E. Titus, *Arch. Biochem. Biophys.* 67, 154 (1957).
41. R. B. Clayton, A. M. Edwards, K. Bloch, *Nature* 195, 1125 (1962); R. B. Clayton, *J. Lipid. Res.* 5, 3 (1964).
42. M. Rothschild, *Proc. Roy. Entomol. Soc. London Ser. C* 31, 32 (1966).
43. F. A. Urquhart, *The Monarch Butterfly* (Univ. of Toronto Press, Toronto, 1960), pp. 70, 207-211.
44. G. D. Hale Carpenter, *Trans. Entomol. Soc. London* 1921, 1 (1921).
45. A. H. Clark, *Smithsonian Inst. Ann. Rep.* 926, 421 (1927).
46. M. Krogh, *Acta Med. Scand. Suppl.* 26, 512 (1928).
47. G. H. Gurney, *Entomologist* 61, 1 (1928); ———, *ibid.*, p. 33; T. B. Fletcher, *Proc. Entomol. Soc. London* 4, 105 (1929); F. Finn,

- J. Asiatic Soc. Bengal* **65**, 42 (1896); N. Manders, *Proc. Zool. Soc.* **1911**, 696 (1911).  
 48. K. A. C. Doig, *Proc. Entomol. Soc. London* **5**, 5 (1930).  
 49. F. M. Jones, *Proc. Roy. Entomol. Soc. London Ser. A* **12**, 74 (1937).  
 50. J. W. Yerbury, *J. Bombay Nat. Hist. Soc.* **7**, 207 (1892); J. Brewer and G. M. Thomas, *J. Lepidoptera Soc.* **20**, 235 (1966); W. R. Thompson, *Catalogue of the Parasites and Predators of Insect Pests* (Imperial Agricultural Bureau, Institute of Entomology, Parasite Service, Belleville, Ontario, Canada, 1945), pt. 6.

51. M. Rothschild, T. Reichstein, J. Parsons, R. Aplin, "Poisons in Aposematic Insects," exhibit No. 19, *Conversazione*, The Royal Society, London, 1966.  
 52. F. A. Urquhart, *J. Invertebrate Pathol.* **8**, 492 (1966).  
 53. L. P. Brower, J. V. Brower, J. M. Corvino, *Proc. Nat. Acad. Sci. U.S.A.* **57**, 893 (1967).  
 54. G. Fraenkel, *Proc. Int. Congr. Zool.* **14th**, 1955 (1956), p. 383; P. R. Ehrlich and P. H. Raven, *Evolution* **18**, 586 (1965).  
 55. We thank Dr. Robin Aplin, Professor Lincoln Brower (whose research was supported in part by U.S. National Science Foundation

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## NEWS AND COMMENT

# Desert Research Institute: A Formula for Growth

Reno, Nevada. "Why would anyone want to come to the University of Nevada to do research?" That was the question that meteorologist Wendell A. Mordy posed to university officials back in 1960 when they asked him to head their newly authorized Desert Research Institute (DRI). At the time, Mordy recalls, there seemed to be no very good answer to his question. The university had experienced a severe internal crisis in the 1950's. Although on the rebound, it still enjoyed only a middling reputation. Reno, the self-styled "Biggest Little City in the World," was known more for its gambling halls and divorce mills than for its intellectual climate. Moreover, there was widespread indifference—even hostility—to research among some of the state's political and educational leaders. "I couldn't imagine coming to Nevada," says Mordy. "I thought I would bury myself alive scientifically."

Nevertheless Mordy, an aggressive entrepreneur of science, was intrigued by the opportunity to build an institute from scratch and was encouraged by the likelihood of substantial support from the Nevada-based Max C. Fleischmann Foundation and other sources. He accepted the job, and over the past 8 years, operating on a few simple principles and in a rather freewheeling style, he has guided the DRI to worldwide prominence in certain fields of atmospheric and arid-lands research. The story of his success may prove encouraging for other small institutions that are trying to break into a research world that seems dominated by well-heeled, well-known organizations.

Though the DRI is still too young to have achieved unusual productivity, it is highly regarded by scientists familiar with its work. Walter Orr Roberts, director of the National Center for Atmospheric Research in Boulder, Colo., who is a trustee of the Fleischmann Foundation, told *Science* that Mordy has assembled "just about the strongest cloud physics group in the world today." The institute's prestigious 12-man national advisory board, which is headed by John R. Pierce of Bell Labs and which includes six members of the National Academy of Sciences,\* reported last October that it was "astonished" at the institute's progress. The board congratulated the institute on "a success which could well be described as unparalleled." It judged "all the programs at the Desert Research Institute to be of high excellence," while noting that some had gained "an international reputation."

The principles on which the institute has been built are relatively simple. (i) Don't try to emulate Harvard or Berkeley. Instead, specialize in areas where a small institute can make a unique contribution, either because of outstanding personnel or because of natural advantages in the local environ-

\* Besides Pierce, the advisory board includes Wallace R. Brode, Barnes Engineering Co.; George Clyde, Woodward-Clyde-Sherard & Associates; Fred Eggan, University of Chicago; James E. Faulkner, M.I.T.; George E. Forsythe, Stanford University; Samuel Goudsmit, Brookhaven National Laboratory; Herbert Grier, Edgerton, Germeshausen & Grier; M. King Hubbert, U.S. Geological Survey; Vincent Schaefer, State University of New York at Albany; Per Scholander, Scripps Institute of Oceanography; and Lloyd Smith, Stanford Research Institute. Pierce, Brode, Eggan, Hubbert, Goudsmit, and Scholander are Academy members.

ment. (ii) Go after the very best researchers available and offer them whatever is necessary to attract them. (iii) Give these scientists the best possible working conditions and the greatest possible freedom. ("I don't even know where they are half the time," boasts Mordy.)

Mordy's original plan for the institute envisioned five research programs that seemed appropriate to the desert environment and were not already being carried out by the university. The DRI has successfully initiated four of these programs—in atmospheric physics, desert biology, water resources, and anthropology—but has never been able to find quite the right man to head a program on the economics of desert regions. Meanwhile, programs outside the original plan have been added as unusual opportunities developed. Thus the DRI launched a program of medical research largely because it was able to attract George T. Smith, formerly an associate in pathology at Peter Bent Brigham Hospital and Harvard Medical School, as director. And it has conducted a small program of industrial research to take advantage of funds from local industry. All the programs emphasize studies related to the Nevada environment and there is considerable overlap in research interests—enough, Mordy feels, so that the programs, "knit together in a meaningful way."

Mordy believes three of DRI's laboratories have achieved "international visibility." These are the laboratory of atmospheric physics, the institute's largest component, which was built up by Mordy and is now headed by Patrick Squires, a highly regarded Australian cloud physicist; the laboratory of desert biology, headed by Frits W. Went, eminent Dutch-born plant physiologist; and the Center for Water Resources Research, headed by George B. Maxey, a noted hydrologist and geologist. The institute also claims to have one of the finest cardiac catheteri-