Letters

"Thinking Claws"

In an article which appeared in *Science* [**127**, 521 (1958)], "Blocking by picrotoxin of peripheral inhibition in crayfish," by Van der Kloot, Robbins, and Cooke, the opening paragraph states: "In vertebrates, inhibition takes place within the central nervous system. But a crayfish 'thinks in its claws' "; this is followed by reference (*1*), which reads: "C. A. G. Wiersma, in *Recent Advances in Invertebrate Physiology* (Univ. of Oregon Press, 1957); P. Hoffman, *Z. Biol.* **63**, 411 (1914); **64**, 247 (1914)."

Any reader not familiar with the facts must be under the impression that either Hoffman or I is the author of this sentence. Since there is hardly any statement with which I disagree more strongly than the one quoted, I want to take this opportunity to point out that it does not occur in any of the papers referred to. It seems to have originated in Prosser's *Comparative Animal Physiology* (Saunders, Philadelphia, 1950), where, on page 597, the statement "A crab 'thinks in its claws' " appears as far as I know for the first time in literature, notwithstanding the quotes. As this is a type of slogan which apparently leaves a lasting impression in many minds, but is completely false in content, I hope this note will contribute to its everlasting suppression.

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We are sorry that Wiersma dislikes the phrase, because his studies on crustacean muscle are so important. Our reference was misleading; the disputed phrase in fact was quoted from C. A. G. Wiersma, *Symposia on Quantitative Biology* **17**, 157 (1952). As it does not appear in quotation marks, we mistakenly assumed that Wiersma was its author. I agree that—if taken literally—the "slogan" is untrue and is the stuff of poetry rather than of science. On the other hand, the phrase is more than fiction; it is a creative account of the integration of nerve impulses which goes on at a crustacean muscle. And the literature of science would be poorer if robbed of the factitious. Who would want to bury the obvious untruth, "Life has an itch to live" [C. S. Sherrington, *Man on his Nature* (Cambridge, 1951), p. 170], or never speak again of "the wisdom of the body" (W. B. Cannon), when these phrases, like the one in question, express fundamental biological ideas in an exhilarating fashion?

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Cholinesterase Inhibitors

The 7 Nov. 1958 issue of *Science* [**128**, 1136 (1958)] carried a challenging article by W. H. Orgell *et al.*, entitled "Inhibition of human plasma cholinesterase in vitro by extracts of solanaceous plants."

The authors of this article have unquestionably demonstrated the existence of a cholinesterase inhibitor in extracts of solanaceous plants. Nevertheless, in my opinion, the quite plausible possibility that steroidal amine glucosides were present was rather lightly dismissed. The possibly unintentional neglect to acknowledge this distinct possibility might lead to a rather fallacious impression on the part of the casual reader, and therefore I wish to contribute a few thoughts of general interest.

The rather simple and crude preparation of plant extracts described in the article does by no means remove solanine (or solanidine in its numerous forms) from the substrate, nor from suspicion. Furthermore, the inhibition pattern for various parts of the potato plant or tuber coincides remarkably with that of solanine distribution. I do not propose to claim that solanine, in spite of its pronounced physiological and hemolytic action, is associated or directly responsible for cholinesterase inhibition. This is more probably due to the presence of free alkaloid solanidine, the product of enzymatic or acid solanine hydrolysis. Solanine alone has been resolved into alpha, beta, and gamma fractions, the latter presumably an artifact of the extraction procedure (*1*). Apparently the alkaloid solanidine has a wider occurrence than was assumed heretofore, since it is also the building block of three forms of chaconine in potato leaves. The possible presence of these steroidal amines in potato-plant extracts must not be overlooked, particularly in view of our

(Continued on page 68)

Letters

(Continued from page 66)

limited knowledge of their physical and chemical nature. In this respect it is noteworthy that potato tubers with high levels of solanine are considered toxic and dangerous for human consumption.

I attribute the toxic effects of such tubers to the presence of free solanidine in tuber tissues (*2*). In other words, the remarkable structural similarity to cholesterol is indicative of a relatively easy diffusion of solanidine into the blood stream, while the absorption of solanine appears to be blocked in the digestive tract (*3*). Thus, one is not far from the thought that the toxic effects may be linked, at least in part, with a direct action of solanidine upon the cholinesterase system.

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We are in general agreement with Zitnak's suggestions regarding cholinesterase inhibition by the steroidal alkaloid glycosides and feel that his hypothesis for the physiological action of these substances merits investigation. To support the possibility that solanine, chaconine, and related glycoalkaloids are chiefly responsible for the inhibition of plasma cholinesterase by potato extracts, we would like to call attention to the report of Pokrovsky (*1*), who determined that solanine and solanidine were powerful inhibitors of horse serum cholinesterase, the aglycone solanidine being approximately twice as inhibitory as solanine in his tests. Pokrovsky also found that solanine was approximately 25 times more inhibitory (on the basis of I_{50} values estimated from graphical data) to nonspecific (horse serum) cholinesterase than to specific (rabbit brain) cholinesterase. This corresponds to our own results on comparing the action of potato-leaf extract against nonspecific (human plasma) and specific (human red cell) cholinesterase and perhaps has some bearing on the genetic differences between human beings in the response of their serum cholinesterase to Nupercaine and the inhibitor from potato extracts, as reported by Harris (*2*). We have confirmed Pokrovsky's observations with our own preparations of crystalline alkaloid from Irish Cobbler tuber sprouts, and also have noted the correspondence between the distribution of solanine (*3*) and inhibitor in the potato plant. We might point out that Pokrovsky has also suggested that the symptoms of solanine poisoning might reflect the cholinesterase inhibitory properties of solanine.

However, we would like to emphasize that there may be cholinesterase-inhibitory substances present in extracts of solanaceous plants other than the steroidal amine glycosides and their derivatives. As a specific example, we have found that aqueous extracts of the common garden petunia are a very potent source of cholinesterase inhibitor (I_{50} = 6 mg of fresh leaf tissue against 5 ml of human plasma), yet no precipitate forms on alkalinization to *p*H 10, as would be expected if solanine or related substances were present (*4*), and the extracts do not give the usual color reactions for the steroidal amine glycosides. Our method of extraction was developed specifically for rapid routine assay of the total cholinesterase inhibitory potency of large numbers of plant-tissue samples, and our extracts certainly contain the steroidal amine glycosides as well as other inhibitory substances.

An interesting question arises in regard to the "function" of these potent natural enzyme inhibitors in higher plants. Fraenkel (*5*) suggests that alkaloids and other secondary plant substances may have arisen in evolutionary response to selection pressure exerted by insects and other parasites and predators. We are currently studying the possibility that natural enzyme inhibitors represent a protective mechanism against the extracellular digestive enzymes secreted by many insects and plant pathogens.

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