Daniel, of G. D. Searle and Company, for supplies of oxandrolone.

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BIOLOGY

Possible New Approach to the Chemical Control of Plant Feeding Insects

THE chemical control of insects has been hampered by the widespread development of strains which are resistant to insecticides[1]. Resistance mechanisms often involve detoxication processes[2], and many detoxication mechanisms in resistant strains have two features in common. First, they are not peculiar to the resistant insects. Susceptible strains often degrade the insecticide by similar metabolic pathways, but much less extensively, and the biochemical novelty which confers resistance is thus often quantitative rather than qualitative. Moreover, comparable detoxication pathways establish the natural tolerance of species which lack resistant strains[2,3]. Second, resistance involving detoxication can usually be overcome or reduced if the insecticide is applied with a non-toxic dose of synergist[2]. The synergists appear to inhibit enzymes involved in detoxication. The best known are methylenedioxyphenyl compounds such as piperonyl butoxide and sesamex which reduce the resistance of insects to DDT[2,4,5], pyrethrins[6], organophosphates[5], carbamates[7] and dieldrin[8], and the tolerance of susceptible strains to these and other insecticides, including several derived from plants, as discussed in refs. 9 and 10.

Whereas resistance to man made insecticides has evolved in a few decades, relationships between insects and plants have evolved since long before the evolution of man himself. Plants have evolved minor constituents which have been called secondary plant substances and include glucosides, alkaloids, etc., which are often specific to particular plant taxons. The function of many of these compounds is unknown, but Fraenkel considered that the host-specificity of plant-feeding insects was based on their presence or absence[11]. This interpretation may not always be applicable[12]; nevertheless, it is obvious that a successful pest must be able to tolerate any substance present in its host plant. Some secondary plant substances are highly active pharmacological substances, or are mammalicidal. Some—for example, pyrethrum and nicotine—are insecticidal[13], and it has been suggested that others —for example, cyanogenic glucosides[14], alkaloids[15] and mustard oils[16]—protect plants from the attack of insects or other pathogens.

Although investigations of plant–host relationships have involved studies of the repellency, attractiveness or toxicity of secondary plant substances, little seems to be known about the mechanisms by which potentially toxic substances in the normal host plant are tolerated. Of seven species of insect feeding on tobacco plants, however, three are known to detoxify nicotine[17].

It seems probable that some other plant feeding insects tolerate poisonous substances in their plant hosts because they have evolved detoxification mechanisms. If so, it should be possible to interfere with these mechanisms by the application of a synergist. Such compounds would represent a new type of chemical control agent which need not be toxic because they would act by enhancing the effectiveness of naturally occurring plant protectant substances. They would be unlikely to affect predatory and pollinating insects and would probably be most useful in plants containing potentially toxic substances chiefly in those parts not eaten by man—for example, solanin in the leaves of potato plants. Such compounds might also be effective against other plant pathogens such as fungi.

In view of the long period during which the interrelationships between plants and insects have evolved, it is possible that some secondary plant substances have evolved as synergists to enhance the action of other naturally occurring protective substances. In this respect, it is of interest that the synergistic properties of the methylenedioxyphenyl compounds were discovered when sesamin was found to be the active principle responsible for the synergism of pyrethrins by sesame oil[9]. More than three hundred compounds containing the methylenedioxyphenyl group, including alkaloids, flavones, benzophenones and lignan compounds, are known to occur naturally in plants[18], and several besides sesamin have been shown to synergize insecticides[19–21].

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Nature's Time-scale: Degenerative Disease in Man

MCCORMICK[1] recently formulated the following hypothesis: "All naturally occurring phenomena proceed according to exponential functions of time and each process in Nature conforms to its own unique time-scale". He finds that the empirical equation

$$Y = \exp(-kt^{-c}) \qquad (1)$$

describes a variety of different processes and that the values of the constants k and c are characteristic of the particular process. Fremlin[2] points out that for any natural phenomenon the value of t must be subjected to an arbitrary cut-off at some finite value and that this kind of law is usually restricted to processes which occur under controlled conditions. In replying to Fremlin's[2] objection that equation (1) is incapable of describing periodic phenomena, McCormick[3] concedes that in such situations a series of exponential growth and decay functions are needed, each valid within certain limits of t.

The age distribution of disease in man is of considerable interest in the context of this discussion. Clinicians have