stimulated cyclic AMP in the liver (*14*). However, this does not occur under the conditions of our experiments, and the result is not entirely unexpected since glucagon is more effective in increasing cyclic AMP than insulin is in reducing it (*8*).

Since the glucose effect occurs without changes in cyclic AMP concentrations, it can be concluded that insulin does not mediate glucose repression, at least by affecting the concentration of the cyclic nucleotide. Furthermore, experiments on intact and diabetic adrenalectomized rats (*15*) do not support a primary role for insulin in hepatic glucose repression.

The addition of glucose to cultures of *Escherichia coli* resulted in a tenfold decrease in intracellular cyclic AMP (*5*). If the mechanism of the hepatic "glucose effect" is similar to that in catabolic repression in bacteria, similar changes in cyclic nucleotide might be expected. Our results indicate that glucose administration does not affect the concentrations in liver of cyclic AMP induced by glucagon, and thus glucose repression in mammalian liver is probably not associated with the decrease in cyclic nucleotide seen in bacterial systems. In view of our results at least two explanations can be offered in regard to the mechanism of glucose repression in mammalian liver. The effect of glucose may be entirely unrelated to the mode of action of cyclic AMP during the induction of enzyme synthesis. As was indicated earlier, glucose is able to repress the corticosteroid induction of tryptophan pyrrolase and tyrosine aminotransferase (*4, 5*). Alternatively, glucose may act indirectly by interferring with the mechanism by which cyclic nucleotides induce enzyme synthesis. This latter explanation is compatible with the finding that N^6,O^2-dibutyryl cyclic AMP reverses the glucose repression of serine dehydratase (*6*). Neither of these two alternative mechanisms necessitates changes in the concentration of cyclic AMP after the administration of glucose. Whether both mechanisms may in one way or another be applicable or whether other mechanisms could also be functioning remains to be determined.

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26 May 1971

Diethylamide of Thujic Acid: A Potent Repellent of Aedes aegypti

Abstract. *A series of novel, representatively substituted amides of thujic acid were prepared and screened for insect repellent and attractant potential. In repellency tests the* N,N-*diethylamide was the most potent compound, surpassing the activity of the standard repellents dimethyl phthalate and fencholic acid. In contrast, the* N-*monoethylamide displayed attractant activity.*

Compounds presently in use as insect repellents and, particularly, as agents preventing attacks of blood-feeding and disease-transmitting insects upon man and animals cover a range of specific applications. However, in certain applications the properties or activities of these compounds, or both, are not always ideal (*1*). We here report tests on a novel type of compound, namely, the amides **II** of thujic acid **I** (see Fig. 1 and Table 1); the *N,N*-diethylamide **IId** in particular has shown interesting insect repellent activity against *Aedes aegypti, Periplaneta americana* (American cockroach), and *Blatella germanica* (German cockroach).

Table 1. Substituent R^1 and R^2 groups in amide **II** (see Fig. 1).

Amide II	R^1	R^2
a	CH_3	H
b	CH_3	CH_3
c	C_2H_5	H
d	C_2H_5	C_2H_5
e	n-C_4H_9	H
f	n-C_4H_9	n-C_4H_9
g	C_6H_{11}*	H
h	CH_2–C_6H_5	H
i	o-C_6H_4–OCH_3	H
j	p-C_6H_4–Cl	H
k	C_3H_2NS†	H
ℓ	$(CH_2)_5$	

* Cyclohexyl. † Thiazolyl.

The wood of the western red cedar (*Thuja plicata* Donn) is renowned for its resistance against attack by various insect species. However, little is known about the activity of specific wood components (*2*). In our studies on cedar extractives we explored the insect-controlling potential of thujic acid and its derivatives with emphasis on its amides. In addition to other evidence, we particularly noted the structural similarity between the commonly used insect repellent *N,N*-diethyl-*m*-toluamide **III** and the projected amide structures, for example, **IId**. Inspection of molecular models revealed that in **II** and **III** the distances between the ring-positioned CH_3 groups and the nitrogen atoms of the amide groups are almost identical, about 5 Å, owing to the troughlike conformation of thujic acid (*3*). (In **II** we obviously measured the distance to the CH_3 group which is situated above the plane of the heptatriene ring.)

We prepared a series of amides of thujic acid **IIa** through **IIℓ** by conventional reactions of either its methyl ester or its chloride (*4*) with the appropriate amine in water or in an organic solvent, for example, benzene. The amides of thujic acid with lower molecular weights are distillable oils; the amides with higher molecular weights

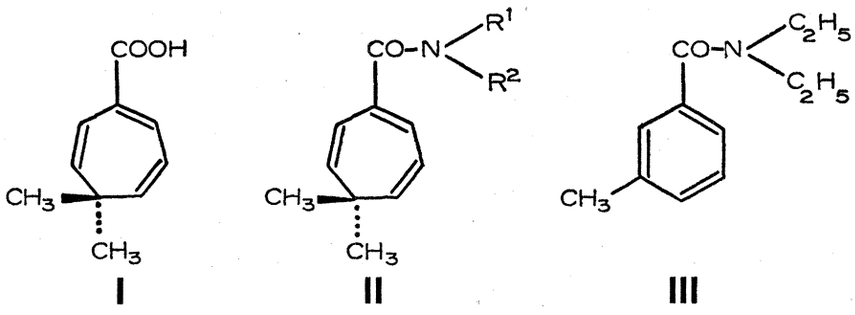

Fig. 1. Structures of thujic acid **I**, the amides of thujic acid **II**, and *N,N*-diethyl-*m*-toluamide **III**. Substituent R^1 and R^2 groups for **II** are identified in Table 1.

are crystalline solids. Elemental analysis, gas-liquid chromatography, and infrared spectroscopy confirmed the identity and purity of the compounds prepared and submitted for testing. Only the amide and the anilide of thujic acid have been prepared previously. Neither of these compounds showed any type of biological activity (*5*).

The candidate compounds were screened and evaluated at the Entomology Research Division, U.S. Department of Agriculture, Beltsville, Maryland (*6*), and at the Insect Pathology Research Institute, Department of Fisheries and Forestry, Sault Sainte Marie, Ontario (*7*). Brief reference is made here to part of the results obtained at the former institution.

In repellency tests carried out with *Aedes aegypti*, individuals exposed their arms covered with cotton stockings, treated with 3.3 g of the screened compound per square foot (0.093 m^2) of stocking, for 1 minute at intervals of from 1 to 7 days in cages containing mosquitoes. The measure of the repellency was given by the number of days with lasting protection until five mosquito bites occurred in a 1-minute period. Under these conditions the diethylamide **IId** was effective for 50 days, whereas the standard repellent dimethyl phthalate is effective for 11 to 22 days. The exceptionally active compound 2-butyl-2-ethyl-1,3-propanediol is effective for 196 days (*8*).

Repellency screening with American and German cockroaches was carried out with two cardboard boxes, one treated with 1 ml of a 1 percent acetone solution of the tested compound and the other a blank. Each of the boxes had a volume of 82 ml. Ten male and ten female insects were given the choice of entering either box. The duration of the experiment was 1 week. Six times each day at regular intervals the number of insects in each box was counted. After each count the insects were shaken out, and the positions of the boxes were reversed. The measure of repellency was given by the percentage of insects in the treated and untreated box, respectively. Fencholic acid, a standard repellent, was tested concurrently with the candidate repellent. In these tests the *N,N*-diethylamide **IId** was at least 35 percent more active than fencholic acid.

The evidence presented here seems to suggest that a prerequisite for repellent activity in this class of compounds appears to be dialkyl substitution on the amide nitrogen. The *N,N*-dimethylamide **IIb** exhibited repellent activity against mosquitoes for 1 day but failed to repel cockroaches. The *N,N*-dibutylamide **IIf** had about 25 percent of the effectiveness of fencholic acid in repelling *Blatella germanica* but was inactive against *Aedes aegypti*. The aromatic, heterocyclic, and carbocyclic amides **IIg** through **II**ℓ were inactive, as were the *N*-monoalkylamides **IIa**, **IIc**, and **IIe**. Both the *N*-monoethylamide **IIc** and the *N*-monocyclohexylamide **IIg** showed a distinct degree of attractancy toward *Aedes aegypti*. Unfortunately, the extreme difference in volatility between **IIc** as well as **IIg** and the standard attractant L(+)lactic acid does not allow for a more quantitative comparison.

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4. The chloride of thujic acid was prepared by the *N,N*-dimethylformamide-catalyzed reaction of the acid with thionyl chloride at room temperature. The 50 mole percent excess of $SOCl_2$ used in the reaction was subsequently distilled off, and the crude chloride was used directly. Thujic acid is known to isomerize under acidic conditions of *p*-isopropylbenzoic acid. In a set of control experiments we ruled out the occurrence of this rearrangement under our experimental conditions.
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7. We appreciate the cooperation of Dr. J. Weatherston.
8. Our work was originally initiated on the basis of an analogy between amide **III** and the projected amides **II**. However, the results presented here relate to standard compounds that are more specific repellents for insect species used for the screening tests described.
9. Work was partly supported by the National Research Council of Canada. We acknowledge permission to publish this report given by MacMillan Bloedel Research, Ltd.
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1 June 1971

Binding of DDT to Lecithin

Abstract. *An interaction between DDT and lecithin is indicated by the reciprocal effects of each compound on the proton magnetic resonance spectrum of the other. The phosphoryl choline moiety of the lecithin and the benzylic proton of the DDT seem to be involved. The most pronounced response in the proton magnetic resonance spectrum of the lecithin produced by increasing concentrations of DDT was a change in the chemical shift of the resonance peak due to the protons of the choline methyl groups. Increasing concentrations of lecithin produced changes in the chemical shift of the resonance peaks of the benzylic proton and adjacent ring protons of the DDT. Equilibrium constant of 0.597 ± 0.015 molal^{-1} was obtained for this interaction.*

The toxicity of DDT [1,1,1-trichloro-2,2-bis(*p*-chlorophenyl)ethane] is generally attributed to its effect on the central nervous system where it produces an excitatory effect on axons. In an effort to define the molecular basis of the response, Matsumura and O'Brien have demonstrated that DDT will bind to components of cockroach nerve (*1*). Using spectral and fluorescence data these workers have postulated the formation of a charge-transfer complex. This hypothesis is open to criticism because comparable spectral changes can