

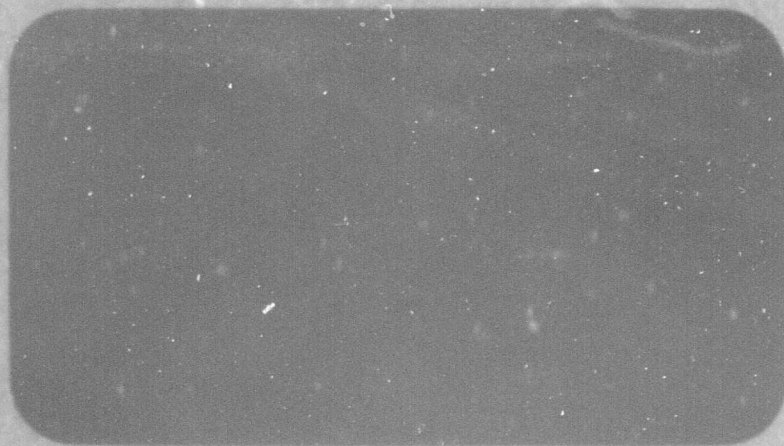
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✓ Report No. IITRI-C222-10
(Quarterly Progress Report)

DEVELOPMENT OF AN ORALLY EFFECTIVE
INSECT REPELLENT

Headquarters
U.S. Army Medical Research and
Development Command
Office of the Surgeon General
Washington, 25, D. C.

Report No. IITRI-C222-10
(Quarterly Progress Report)

Headquarters
U.S. Army Medical Research and Development Command
Office of the Surgeon General
Washington 25, D.C.

Attention: Major Lee Roy J. Jones

DEVELOPMENT OF AN ORALLY EFFECTIVE INSECT REPELLENT

IITRI Project No. C222
Contract No. DA-49-193-MD-2281

August 1 to October 31, 1964

I. INTRODUCTION

The object of this program is the development of an insect repellent which is effective when administered internally.

During the period covered by this report, unexpected deaths occurred in our mosquito colony and resulted in considerable loss of time. We now have available to us the consulting services of Dr. K. S. Rai, Assistant Professor of Biology and Associate Director of Mosquito Genetic Program at the University of Notre Dame. The procedures for raising mosquitoes and maintaining the colony have been thoroughly reviewed by Dr. Rai, and the revisions suggested have been incorporated in our procedures. We hope to obtain good colonies soon and to resume active investigation.

Studies have been initiated on chemically induced feeding behavior of mosquitos through an animal membrane. Owen¹ reported

¹Owen, W. B., J. Insect. Physiol. 9, 73, 1963.

that adenosine triphosphate induced feeding response in mosquitoes. We confirmed the Owen's findings in our in vitro test system. In addition, several other compounds were tested.

The minimum effective repellent concentration of several compounds was determined in vivo.

II. PROCEDURES

The procedures for in vivo tests, i.e., application of the test compound on mouse skin, and in vitro tests, i.e., homogenization of the test compound in blood and feeding of it by mosquitoes through an artificial membrane, have been described in our previous reports.

To test chemically induced insect feeding, the in vitro procedure was modified. The test compound was dissolved in 0.15 M sodium chloride solution instead of in blood. Outdated citrated human blood was used for comparison.

III. RESULTS

Table 1 gives the data on in vitro feeding of mosquitoes on various compounds. Of the compounds tested, only ATP induced significant feeding. Concentrations of 10^{-3} M and 10^{-4} M were the most effective. In each experiment the feeding was compared with the feeding induced by blood. It is interesting that heating of the ATP solution had little effect on its ability to induce feeding

Table 1

**EFFECT OF CHEMICAL COMPOUNDS ON FEEDING RESPONSE
OF MOSQUITOES THROUGH ARTIFICIAL MEMBRANE**

<u>Agent</u>	<u>Concentration, molar</u>	<u>Feeding, % of Blood^a</u>	
		<u>Number Engorged</u>	<u>Solution Ingested</u>
Adenosine-r- triphosphate	10 ⁻²	4	6
		29	8
	10 ⁻³	48	28
	10 ⁻³	52	36
	10 ⁻³	77	95
	10 ⁻³	98	108
	10 ⁻⁴	136	129
	10 ⁻⁴	121	119
	10 ⁻⁴	49	53
	10 ⁻⁴	28	50
	10 ⁻⁵	19	27
	10 ⁻⁵	20	26
	10 ⁻⁶	2	1
	10 ⁻⁶	11	14
	10 ⁻⁷	2	13
	10 ⁻⁷	0	1
Adenosine-5- triphosphate, heated to boiling and cooled	10 ⁻³	55	35
	10 ⁻³	77	46
	10 ⁻⁴	99	100
	10 ⁻⁴	86	75
Adenosine-5-monophosphate	10 ⁻³	17	14
	10 ⁻³	11	8
	10 ⁻⁴	6	4
Adenine	10 ⁻³	0	0
	10 ⁻³	0	0
	10 ⁻⁴	0	0
Guanine	10 ⁻³	0	0
	10 ⁻³	0	0
	10 ⁻⁴	0	0
Uridine	10 ⁻³	0	0
	10 ⁻³	0	0
	10 ⁻⁴	0	0

Table 1 (cont.)

<u>Agent</u>	<u>Concentration, molar</u>	<u>Feeding, % of Blood^a</u>	
		<u>Number Engorged</u>	<u>Solution Ingested</u>
Uricil	10 ⁻³	0	0
	10 ⁻³	0	0
	10 ⁻⁴	0	0
Thiamine hydrochloride	10 ⁻³	0	0
	10 ⁻³	0	0
	10 ⁻⁴	2	0
Riboflavin phosphate	10 ⁻³	0	0
	10 ⁻³	0	0
	10 ⁻⁴	0	0
Acetylcholine	10 ⁻² to 10 ⁻⁷	0	0
Carbachol	10 ⁻²	2	9
	10 ⁻³	0	5
	10 ⁻⁴	0	1
	10 ⁻⁵	2	1
	10 ⁻⁶	0	1
	10 ⁻⁷	2	2
Succinylcholine chloride	10 ⁻² to 10 ⁻⁷	0	0

^aEach experiment consisted of exposing 50 mosquitoes to the solution. Between 4 to 15 experiments were conducted with blood to provide controls.

Table 2

EFFECT OF CHEMICAL COMPOUNDS ON FEEDING RESPONSE OF MOSQUITOES
ON MOUSE SKIN OR THROUGH ARTIFICIAL MEMBRANE

<u>Compound</u>	<u>Mode of Feeding</u>	<u>Conc., mg/ml</u>	<u>Feeding, % of Untreated</u> <u>Number Engorged</u>	<u>Blood Ingested</u>
Pentylentetrazole	Membrane	1.0	74	20
			42	11
		0.1	58	50
			59	41
	Skin	1.0	72	64
			72	71
		0.1	88	84
			60	47
Phenobarbital sodium	Membrane	1.0	46	13
			43	15
		0.1	37	20
			67	39
	Skin	1.0	67	49
			75	53
		0.1	61	37
			58	45
Strychnine sulfate	Membrane	1.0	0	0
			0	0
		0.1	42	47
			10	13
	Skin	1.0	29	19
			61	52
		0.1	20	15
			13	11
Caffeine hydrobromide	Membrane	1.0	29	7
			68	13
		0.1	85	49
			62	47
	Skin	1.0	36	35
			95	80
		0.1	103	64
			78	84

Table 2 (cont.)

<u>Compound</u>	<u>Mode of Feeding</u>	<u>Conc., mg/ml</u>	<u>Feeding, % of Untreated</u> <u>Number Engorged</u>	<u>Blood Ingested</u>	
Dimethylsulfoxide	Membrane	1.0	89	78	
			67	52	
	Skin	0.1	88	121	
			80	116	
		1.0	33	36	
			48	59	
Glutethimide	Skin	0.1	11	6	
			9	2	
		1.0	6	6	
			21	20	
		0.1	67	46	
			57	48	
Vanillic acid diethylamide	Membrane	0.01	71	51	
			87	64	
		1.0	2	2	
			0	0	
			0	0	
			0	0	
Vanillic acid diethylamide	Membrane	0.1	9	8	
			3	2	
		Skin	1.0	0	0
				17	21
	0.1		57	51	
			11	8	
	0.01		34	24	
			31	16	
	Skin	0.001	43	44	
			93	73	
		97	87		

on hungry mosquitoes.

These experiments will be continued with a view toward defining chemical structures which induce feeding in the mosquitoes. The information obtained from these experiments may provide a basis for designing chemical compounds which antagonize the effects of chemicals which induce feeding behavior.

Table 2 shows the effectiveness of several compounds on in vitro and in vivo mosquito feeding. Of the compounds tested, strychnine and the diethylamide of vanillic acid showed promising results. These compounds will be investigated further, and the effectiveness of other potential repellents will be determined.

IV. RECORDS

Robert Fosler and Richard Markwart contributed to the progress of this investigation. The data are recorded in Logbooks C14373 and C14999.

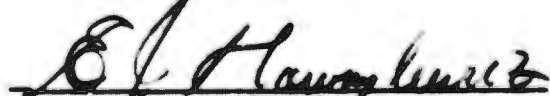
Respectfully submitted,

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