TABLE 2

THE EFFECT OF ACETYLSALICYLIC ACID* ON THE HYPOPROTHROMBINEMIA INDUCED IN THE RAT BY FEEDING 2.5 MG DICUMAROL†

Dose of acetylsalicylic acid (mg)	Prothrombin time (sec) of 12.5% plasma		No. of rats
	Acetylsalicylic acid given 12 hr after anticoagulant	Acetylsalicylic acid given with anticoagulant	
None	116 (86–152)	116 (86–152)	365
10	109 (70–150)	113 (100–125)	12
100	87 (60–160)	101 (98–105)	14
200	88 (78–129)	78 (51– 97)	12
300	89 (78–113)	66 (60– 80)	12

* Given by stomach tube in a suspension with 2% gum tragacanth.

† In the standard procedure of this laboratory (3), blood samples are removed 24 hr following the administration of the anticoagulant.

to explain vitamin K-salicylate antagonism. The *in vivo* detoxication of salicylates is known to produce a variety of degradation and conjugation products (*10*), a mechanism which conceivably could lead to the accumulation of an agent acting as an inhibitor of coumarin hypoprothrombinemia. Similarly, the evolution of a metabolically derived inhibitor would explain the relative difficulty in inducing hypoprothrombinemia with salicylates. It may be suggested that salicylate detoxication results in a derivative which closely resembles the as yet unknown metabolic derivative(s) of 3,3′-methylenebis(4-hydroxycoumarin) causative of hypoprothrombinemia and as a biological antagonist produces inhibition of hypoprothrombinemia. That the salicylate factor can accumulate in sufficient quantity preceding the administration of the anticoagulant may explain why an inhibition results, whereas a superimposed hypoprothrombinemia develops from administration of salicylates *after* the anticoagulant.

That salicylates can be given to rats *after* coumarin anticoagulant hypoprothrombinemia has been established and still reduce its extent militates against the possibility that salicylates may inhibit Dicumarol absorption, and points up the difference in susceptibility of dogs and rats to the hypoprothrombinemia induced by salicylic acid (*1, 2*). The testing of individual metabolic derivatives of the salicylate molecule in animals given Dicumarol has yet to be done and may prove helpful in elucidating the pathway of coumarin anticoagulants.

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Effects of Soils and Sunlight on Dilute Concentrations of Sodium Pentachlorophenate[1]

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In field trials to determine the effects of potential molluscacides on the snail intermediate hosts of *Schistosoma mansoni,* the human blood fluke in Brazil, variable results were occasionally obtained with a given chemical. The probability of soil being one of the factors that influence the efficacy of molluscacides was indicated by observations that the mortality of snails was usually lower in test plots having a muddy bottom. These observations were further supported by tests showing that concentrations of the pentachlorophenate group of molluscacides decreased most rapidly in test plots having a thick underlying layer of soft mud. With the tests developed by Haskins (*1*), microgram quantities of the molluscacides, copper and sodium pentachlorophenates, were easily determined. Unfortunately, analytical methods for determining other molluscacides in high dilutions were not available.

To exclude other factors that may inactivate molluscacides under field conditions, experiments to determine the effect of various soils on sodium pentachlorophenate were carried on in the laboratory. For the tests, different types of water-saturated soil, taken from waters inhabited by planorbid snails, were packed into 1000-ml beakers at the proportions indicated in Table 1. Each beaker was then filled with a solution having a pH of 7.2 and containing 10 ppm sodium pentachlorophenate. Dried mud was used in Expts. 5 and 6, and in the latter it was mixed with the solution until an opaque suspension was formed. A 10-ppm solution of sodium pentachlorophenate served as a control (No. 9). The room temperature during the period of observation ranged from 27° to 33° C.

The laboratory findings corroborate the field observations in that various earthy materials in some way reduced the concentrations of sodium pentachlorophenate. The greater the depth of the mud in proportion to the depth of the water (Expts. 1–4), the more rapid the decrease. Although the mud used in these experiments came from the same place, similar results were obtained with soils from other sites. In preparation of Expt. 5 the water became cloudy with a suspension of mud, which apparently caused the very rapid diminution in concentration of the chemical. Deliberate stirring of the soil suspension (No. 6) resulted in a reduction to 5 ppm in 1 hr, with only a trace of chemical present 4 hr after treatment. In Expts. 7 and 8 the sandy loam and sand with smaller quantities of

[1] From studies conducted at the Instituto Aggeu Magalhães by the Laboratory of Tropical Diseases of the National Institutes of Health, USPHS, under the sponsorship of the Pan American Sanitary Bureau in cooperation with the Divisão de Organisação Sanitaria do Departamento Nacional de Saude of Brazil.

TABLE 1

CHANGES IN THE CONCENTRATION OF SODIUM PENTACHLOROPHENATE IN LABORATORY EXPERIMENTS WITH VARIOUS TYPES AND AMOUNTS OF SOIL

Time after applying chemical	(No. of expt.) 1	2	3	4	5	6	7	8	9
	(Proportional volumes of solution and soil) Sol. 3 Mud 1	Sol. 1 Mud 1	Sol. 1 Mud 3	Sol. 1 Mud 7	Sol. 1 Dry Mud 1	Sol. 3 Mixed Mud 1	Sol. 1 Loam 3	Sol. 1 Sand 3	Sol. —
	(Concentration in ppm)								
4 hr	10	10	10	10 –	10 –	T*†	10	10	10
21 "	10	10	10 –	5	1	0	10	10	10
29 "	10 –	10 –	5 +	5 –	1	0	10	10 –	10
2 days	10 –	5	5 –	2 –	T	0	10	10 –	10
3 "	10 –	5	2 +	1	T	0	10 –	10 –	10
4 "	5 +	5 –	2 –	T	0	0	5 +	10 –	10
5 "	5	5 –	1	T	0	0	5 –	10 –	10
7 "	5	2 –	T	T	0	0	T	10 –	10
11 "	5 –	2 –	T	0	0	0	T	10 –	10
17 "	2 –	1	0	0	0	0	T	0	10
21 "	2 –	T	0	0	0	0	T	0	10
30 "	1	T	0	0	0	0	0	0	10

* T = Trace of chemical.
† Reduced to 5 ppm in 1 hr.

organic matter and clays had a much less pronounced effect on the concentration of sodium pentachlorophenate. Other conditions being equal, an increased residual effect could be expected after application of chemicals in waters having sandy beds. During a 72-day period all chemical determinations of the control, Expt. 9, were consistently 10 ppm.

Facilities were not available to determine the manner in which silt and clays reduced the concentration of the salts of pentachlorophenol in solution. Presumably the principal process is adsorption of the chemical by the fine particles of soil, but possibly it could be due to actual inorganic or organic chemical combinations, or a coalition of these factors.

To determine the effects of sunlight on dilute solutions of sodium pentachlorophenate, laboratory preparations identical to those in Table 1 were exposed to about 8 hr of direct sunlight at temperatures not over 38° C. The concentration of the chemical in all the experiments was reduced from the original 10 ppm to 0 or 1 ppm after 8 hr exposure. It may be noteworthy that even a clear aqueous solution containing 10 ppm of sodium pentachlorophenate tested 1 ppm after the same period of exposure. The results were similar when the experiments were repeated. It was also found that following 8 hr of exposure to sunlight these preparations were only 0–20% effective against *Australorbis glabratus* within a 24-hr period.

Under field conditions mud and sunlight may be important factors in reducing the efficacy of some molluscacides. The effects of mud can be minimized by applying the chemicals when the waters are clear and by exercising care not to disturb the mud during the period of treatment. Proper allowance should be made when chemicals must be applied in muddy waters. Indications are that sunlight is a major factor in reducing the concentration of some chemicals in very shallow open waters but not in deep waters. In the field, sunlight appears to be less of a factor than mud in reducing the concentration of chemicals because most of the waters are shaded by rooted and floating vegetation and often by high banks.

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Nonfixation of Carbon Dioxide into Organic Acids in Blood[1]

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Although there is evidence in the literature for the existence of the physiologically important organic acids of the Krebs cycle in blood, data on their physiologic origin or role in this fluid are far from complete. Doubtless the lack of methods of isolation for these acids has contributed to the enigma. The extent to which tissue acids are diffusible into blood, and the scope of the function of the cycle in blood as compared to some other tissue such as liver, have not been considered. One approach to these problems was recognized when labeled organic acids were chromatographically isolated from tissues of mice injected in-

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