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Effect of Hexylresorcinol upon Ascaris and Hookworm Eggs.*

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Ascaris eggs from canine, porcine and human sources are noted for their resistance to many chemicals. Cram[1] in a summary of various workers' experiments shows that acids, alkalies and alcohols as well as many bactericidal agents do not prevent normal development of ascaris eggs. Of the active substances reported by Cram are carbolic acid which in 5% solution kills the pig ascarid egg in 10 hours, and cresol which in 3% solution kills them in 5 hours. The most active substance is probably "hyperactive" iodine which has been shown by Chandler[2] to kill ascarid eggs within 10 minutes.

Hexylresorcinol, a substance related to phenol, has been shown by Lamson, Brown, Ward, Robbins[3, 4] to be a very effective anthelmintic against both the dog and human ascarid. The purpose of this paper is to bring attention to the great activity of hexylresorcinol upon ascaris eggs (*Ascaris suum*).

Method of testing drug action upon eggs. Eggs were obtained by dissecting out the anterior 2 inches of adult ascaris uteri which were cut into short sections, placed in water and well shaken, to prevent large adherent egg masses. The hookworm eggs were obtained by macerating dog stools in saturated saline and looping off the upper layer containing the eggs which were washed in tap water. In both cases the eggs were placed in the solution to be tested and at intervals a sample was removed and the eggs washed several times, placed in flasks of tap water at room temperature, and examined from time to time to note their death or development to the embryonated stage. Controls in tap water were run with each experiment. The differentiation of live from dead eggs is sometimes difficult; the best criterion is their development when placed in a favorable medium. Occasionally large egg masses persisted despite vigorous

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1 Cram, E. B., *J. Agr. Res.*, 1924, **27**, 167.

2 Chandler, W. C., *Quart. Bull. Mich. Agr. Coll.*, 1924, Feb. 1.

3 Lamson, P. D., Brown, H. W., and Ward, C. B., *North Am. Veterinarian*, 1931, January.

4 Lamson, P. D., Brown, H. W., Robbins, B. H., and Ward, C. B., *Am. J. Hyg.*, 1931, **13**, 803.

TABLE I.
The Effect of Resorcinol and Hexylresorcinol Solutions upon the Eggs of *Ascaris suum*.
Eggs with outer albuminous coat intact.

Time in solution	1% Hexyl-resorcinol suspension	0.1% Hexyl-resorcinol	0.05%* Hexyl-resorcinol	1% Hexyl-resorcinol 1% KOH	S. T.-37	1% resorcinol
15 min.	All dead within 5 minutes	Embryo-nated Active	Embryo-nated Active	Embryo-nated Active	Embryo-nated Active	Embryo-nated Active
30 "		Few dead	"	"	"	"
1 hr.		Maj. dead	"	"	"	"
2 "		" "	"	"	"	"
5 "		All dead	"	"	"	"
15 "		" "	"	"	"	"
27 "		" "	Few dead	"	"	"
48 "		" "	" "	"	"	"
100 "		" "	Many dead	"	"	"
196 "		" "	Maj. dead	"	"	"
386 "		" "	All dead	"	"	"

0.01% hexylresorcinol—eggs all embryonated and active.

shakings. The solutions were often unable to penetrate these masses and as a result only the peripheral eggs were killed while those in the center of the mass developed normally.

The effect of resorcinol upon ascaris eggs. The rapidity with which the different solutions kill the ascaris eggs is shown in Table I. In a 1% hexylresorcinol suspension the eggs were all killed within 5 minutes. Immediately after this immersion they appeared cleared, the cytoplasm changing from the usual deep brown to a very light yellow.

Hexylresorcinol is soluble in tap water, which is approximately neutral, to an extent of about 0.05%; ascaris eggs left as long as 15 hours in solutions of this strength developed normally to the embryonated stage. However, after 27 hours in this solution a number of the eggs were killed and the number of dead eggs increased until after 386 hours (16 days) in this solution all of the eggs were dead.

Since hexylresorcinol is more soluble in alkaline solution, in making up the 0.1% solutions, 0.2% sodium bicarbonate was added. The majority of the eggs in this solution were killed in from one to 2 hours and were all killed in 5 hours. A small percent of the eggs were killed in 30 to 45 minutes. Eggs develop normally in a 0.01% hexylresorcinol solution.

The effect of hexylresorcinol upon ascaris eggs is considerably decreased when the hexylresorcinol is dissolved in an efficient solvent. Thus a 0.1% solution of hexylresorcinol in 30% glycerine

(S.T.-37 of Sharp and Dohme) permitted normal development of the eggs. This same effect of solubility is further shown by the fact that a 1% hexylresorcinol solution made possible by the addition of 1% potassium hydroxide, did not prevent the normal development of the eggs. The increased solubility of the hexylresorcinol seems to prevent its being taken up by the ascaris eggs. This inability of the eggs to remove hexylresorcinol from solution is similar to that reported by Lamson, Ward, Brown (unpublished data) who show that the adult worm likewise is very slowly acted upon by hexylresorcinol when in solution in olive oil and glycerine in which it is quite soluble. On the other hand dilute aqueous suspensions and solutions kill them very rapidly.

TABLE II.
The Effect of Hexylresorcinol Solutions Upon the Eggs of *Ascaris suum*.
Eggs with outer albuminous coat removed.

Time in solution	0.1% Hexyl-resorcinol	0.05% Hexyl-resorcinol	S. T.-37	30% Glycerine	1% KOH
15 min.	All dead	Embryonated Active	Embryonated Active	Embryonated Active	Embryonated Active
1 hr.	" "	"	"	"	"
5 "	" "	"	"	"	"
15 "	" "	"	"	"	"
27 "	" "	Few dead	Maj'y dead	"	"
48 "	" "	Many dead	All dead	"	"
100 "	" "	All dead	" "	"	"
196 "	" "	" "	" "	"	"
386 "	" "	" "	" "	"	"

Ascaris eggs, the outside albumin coating of which had been removed by 1% potassium hydroxide, were killed more rapidly by the hexylresorcinol solutions than were the eggs with albumin coating intact (Table II). Those in the 0.1% hexylresorcinol solution were all killed within 15 minutes while those in the 0.05% solution and S.T.-37 were all killed within 100 and 48 hours respectively. The greater rapidity with which hexylresorcinol kills the ascaris eggs the albumin shell of which has been removed indicates that this layer aids materially in the resistance of ascaris eggs against chemicals. The hexylresorcinol is a protein precipitant and probably precipitates the albuminous layer to some extent, for ascaris eggs left in the hexylresorcinol solutions develop a changed albuminous outer coating as shown by the fact that it becomes much more compact and that a 1% KOH solution will no longer remove it in 48 hours, while with eggs not treated with hexylresorcinol this removal is a matter of a few minutes.

The action of resorcinol solution upon ascaris eggs is very different from that of hexylresorcinol. Resorcinol solutions of 0.1% and 1% permit normal development of the eggs, while those in a 5% solution did not develop past the one cell stage. This lack of action may be due to the great solubility of resorcinol in water. The difference in action on ascaris eggs of resorcinol and hexylresorcinol is in accord with the work of Leonard[5] who showed that the bactericidal action of resorcinol is increased by the addition of an alkyl chain and reaches its maximum activity with a 6 carbon straight chain group (n-hexylresorcinol).

Effect of hexylresorcinol upon hookworm eggs and larvae (Ancylostoma caninum).

Hookworm eggs are killed within 24 hours by a 0.05% solution of hexylresorcinol. Hookworm eggs contained in fluid feces to which was added 25 cc. of 0.05% hexylresorcinol, or 25 cc. S.T.-37 solution, all failed to develop and after 8 days were distinctly degenerated with their cytoplasm in a single dark mass. Controls to which 25 cc. of tap water had been added showed eggs in all stages of development as well as active rhabditiform and filariform larvae.

Some of the early filariform hookworm larvae placed in .05% hexylresorcinol and in S.T.-37 lost their activity within 5 minutes and were all dead in 10 minutes. Larvae in a 30% glycerine solution were likewise killed (possibly an osmotic effect) so it is not likely that the hexylresorcinol of the S.T.-37 was the only factor in their death.†

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Interrelation Between Secretion and Incretion.

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All attempts of different investigators to find out the interrelation between the external and internal secretion of the pancreatic gland have not been successful because the methods used, evaluation of

[5] Leonard, V., *J. Am. Med. Assn.*, 1924, **83**, 2005.

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