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Anthelmintic Properties of Certain Alkyl Cresols.*

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In a study of anthelmintics being carried out in this laboratory, it has been shown that certain resorcinols have marked anthelmintic properties,[1] hexylresorcinol having the most intense action of the normal alkyl resorcinols. Both hexylresorcinol and heptylresorcinol have been given in ascaris, hookworm, and trichuris infestations, hexylresorcinol being found to have the greatest efficiency.[2] The latter has now been given by us to over 2,000 cases controlled by the Stoll egg counting method, without any indication of toxic effects, and with an average efficiency of approximately 90% in ascaris, 85% in hookworm disease, and 55% in trichuriasis.[1, 3] The lower resorcinols were found to be less active *in vitro,* resorcinol itself having relatively very little action. It was first shown by Johnson and Lane that the antiseptic action of resorcinol could be increased by the introduction of alkyl groups and that this antiseptic action increased with the length of the straight alkyl chain up through butyl resorcinol.[4] Leonard then showed that the antiseptic action of these alkyl resorcinols reached a peak with hexylresorcinol and that this member of the series had the least toxicity.[5] This idea of introducing alkyl groups into substances with known antiseptic action was recently taken up by Coulthard, Marshall and Pyman, who showed the variation of phenol coefficients in homologous series of phenols.[6] As with the resorcinols a similar increase in the phenol coefficient with an increase in molecular weight of the alkyl chain, the maximum being found in 5-n-amyl-o-cresol, was demonstrated.

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[1] Lamson, P. D., Caldwell, E. L., Brown, H. W., and Ward, C. B., *Am. J. Hyg.*, 1931, **13**, 568.

[2] Lamson, P. D., Caldwell, E. L., Brown, H. W., and Ward, C. B., *Am. J. Hyg.*, in press.

[3] Lamson, P. D., Brown, H. W., Robbins, B. H., and Ward, C. B., *Am. J. Hyg.*, 1931, **8**, 803.

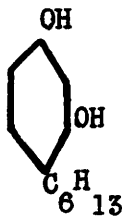
[4] Johnson, T. B., and Lane, F. W., *J. Am. Chem. Soc.*, 1921, **43**, 348.

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

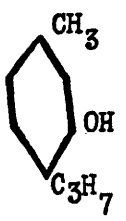
[6] Coulthard, C. E., Marshall, J., and Pyman, F. L., *J. Chem. Soc.*, 1930, 280.

The fact that thymol, a very effective anthelmintic which is 4-iso-propyl-m-cresol is infinitely more effective on ascaris than simple m-cresol suggested to us that straight chain cresols might be made with still greater anthelmintic properties.

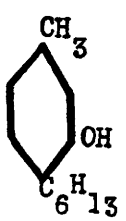
As we could not obtain these compounds we have as yet been unable to make a comparison of the anthelmintic properties of all of them. However hexyl and heptyl m-cresols were chosen for investi-



Hexylresorcinol



4-iso-propyl m-cresol (Thymol)



4-n-hexyl m-cresol

gation, synthesized in this laboratory, and compared with the hexyl- and heptyl-resorcinols already studied by us. These substances were found to be very active on ascaris *in vitro* although slightly less so than hexylresorcinol and effectively removed ascaris from dogs. This is of interest in showing an increase in anthelmintic properties with the increase in length of the alkyl chain, as compared with the relatively ineffective phenol or m-cresol. The introduction of the methyl group into phenol is well known to reduce its toxicity and it might be expected that these higher cresols would show a still less toxic action. Our experiments with 4-n-hexyl-m-cresol in rats and dogs confirm this view, and a paper by Broom[7] which has just appeared, since this note was sent to press, shows the 4-n-amyl-m-cresol to have a toxicity less than that of hexylresorcinol in animals, and this substance has been taken in therapeutic amounts by man without any indication of intoxication.[8] Because of certain properties of 4-n-hexyl-m-cresol, namely its being a liquid, and causing less local irritation than hexylresorcinol, further experiments in both animal and man are being carried out in order to determine its possible value as a human anthelmintic.

[7] Broom, W. A., *Brit. J. Exp. Path.*, 1931, **12**, 327.

[8] Coulthard, C. E., *Brit. J. Exp. Path.*, 1931, **12**, 331.