

Effect of Prontosil and Prontylin on Metabolism of Bacteria.

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Donagk discovered¹ that certain sulfonamide compounds are good therapeutic agents against certain bacterial infections, a discovery confirmed by a number of investigators; but the mechanism of this action has not yet been explained.

The bactericidal properties of the reduced sulfonamide compounds, as shown by the inhibition of bacterial growth in cultures, have been reported (Fourneau and coworkers,² Colebrook, Buttle, and O'Meara,³ Long and Bliss⁴). Since the oxidized forms (Prontosil, Prontosil soluble) were found devoid of bactericidal properties, it has been assumed that these drugs become active by their reduction in the animal body (Bliss and Long⁵).

The effect of Prontosil (4-sulfonamide, 2,4'-diamino azobenzol) and of Prontylin* (*p*-amino benzene sulfonamide) on the metabolism of hemolytic streptococci, *B. coli*, *B. Friedlander*, and gonococci was studied in an endeavor to clarify the mechanism of their chemotherapeutic properties. The experiments were performed at 38° with the usual Warburg-Barcroft respiration apparatus. The bacteria were washed in 0.9% NaCl and suspended in the same salt solution, which was buffered to pH 6.87 by addition of phosphates. The concentration of the drugs was 0.01 M per liter; that of metabolites, 0.008 M per liter. Each experiment was done in quadruplicate, the maximum error being 5%. Prontosil had no effect on the metabolism of these bacteria. Prontylin had a slight inhibiting effect on the oxidation of glucose by hemolytic streptococci, and on the oxidation of glucose and lactate by *B. Friedlander* (Table I).

Prontosil, which is irreversibly reduced by Na₂S₂O₄, has an apparent reduction potential of +0.100 volt ±0.01 at pH 6.93. As

¹ Donagk, G., *Angew. Chem.*, 1935, **48**, 657; *Deutsch. Med. Woch.*, 1935, **61**, 256; *Klin. Woch.*, 1936, **15**, 1585.

² Fourneau, E., Trefouel, J., Nitti, F., and Bovet, D., *Compt. rend. Soc. Biol.*, 1936, **122**, 652.

³ Colebrook, L., Buttle, G. A. H., and O'Meara, R. A. Q., *Lancet*, 1936, **2**, 1323.

⁴ Long, P. H., and Bliss, E. A., *J. Am. Med. Assn.*, 1937, **108**, 32.

⁵ Bliss, E. A., and Long, P. H., *Bull. Johns Hopkins Hosp.*, 1937, **60**, 149.

* Prontosil and Prontylin were kindly supplied to us by the Winthrop Chemical Co.

TABLE I.
Effect of Prontosil and Prontylin on Metabolism of Bacteria.

Bacteria	Metabolite	O ₂ consumption—cmm. per hour			Inhibition, %
		Control	Prontosil	Prontylin	
Hemolytic streptococcus	Glucose	127.3	125.1	117.3	None 7.9
<i>B. coli</i>	''	655.1	673.2	642.1	None ''
''	Pyruvate	713.4	752.4	732.6	'' ''
Gonococci	Glucose	579.5	597.7	609.5	'' ''
''	Pyruvate	667.5	650.0	602.0	'' 9.8
<i>B. Friedlander</i>	Glucose	106.2		93.3	12.1
	Lactate	141.4		108.4	23.3

there exist in the animal body a number of oxidation-reduction systems of more negative potential, Prontosil might be easily reduced in the body. *In vitro*, however, Prontosil is not reduced by glutathione at pH 7.31 (temp., 25°).

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Assay of Progesterone by a New Method.

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Heretofore all the methods used for the assay of progesterone are based upon morphological changes in the uterine mucosa. Usually immature or mature rabbits have been employed. Suitable sensitization of the uterus has been obtained either by the injection of an oestrus-producing hormone (oestrone) or by using rabbits in spontaneous heat. The present communication, however, deals with preliminary experiments on a "physiological" method of assaying progesterone, *i. e.*, by determining the dose necessary to cause contraction of the non-pregnant cat's uterus in response to sympathetic stimulation.

Ovulation and corpus-luteum formation in the cat, as in the rabbit, take place after copulation but not spontaneously so that the ovaries of isolated non-pregnant adult cats do not contain corpora lutea. A further peculiarity of the cat's uterus is the change in its response to hypogastric stimulation or epinephrine as a result of