

tension. Losee and Van Slyke⁶ interpreted the lowered plasma bicarbonate found by themselves, and lowered alveolar carbon dioxide found by others as indicating increased acid production during pregnancy. Marrack and Boone stress the effect of hyperpnea, also investigated by Hasselbalch and Gammeltoft. Bock⁷ has recently found some evidence for the acid overproduction theory.

Evidence for increased acid production on the one hand, and evidence for a slightly more alkaline reaction of the blood on the other seem rather paradoxical. If increased acid production alone were responsible for the lowered bicarbonate, one would expect lowering of bicarbonate to run slightly ahead of lowering of carbon dioxide tension, pH remaining to the lower part of the normal range. If, on the other hand, bicarbonate were lowered indirectly, through lowering of carbon dioxide (hyperpnea), the reverse changes would be expected. The increased irritability of the respiratory center during pregnancy, found by Hasselbalch, would connect the two factors.

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Physiological action of carnosine.

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The material used in this work was produced by Drs. Louis Baumann and Thorsten Ingwaldsen. The natural carnosine was prepared by them from extracts of horse muscle, and the synthetic was produced by them in their work on the synthesis of carnosine from histidine and β -Alanine. For the method of preparation and the evidence for the chemical purity of the carnosine reference is made to the article by Baumann and Ingwaldsen.¹

⁶ Losee, J. R., and Van Slyke, D. D., *Am. J. M. Sc.*, 1917, cliii, 94.

⁷ Bock, A., *Klin. therap. Wchnschr.*, 1924, iii, 2294.

¹ Baumann, L., and Ingwaldsen, T., *J. Biol. Chem.*, 1918, xxxv, 263.

The action of the natural and synthetic substance was found to be identical in all experiments. When tried separately neither the histidine nor alanine used by Baumann and Ingwaldsen in their synthesis of carnosine gave the physiological action produced by carnosine. Complete hydrolysis under conditions which do not destroy the action of other known substances having a similar action, such as histamine, did destroy the effectiveness of the carnosine. It therefore appears certain that the physiological actions described are due to the peculiarity of the dipeptid, carnosine, and not to any impurities.

Subcutaneous injection of 2 gm. in 11 K. dog caused vomiting, diarrhea and the general symptoms of severe toxic shock. Intravenous injection of 10 mg. in 1½ K. cat under ether anesthesia, gave same result as to intestinal activity and carotid blood pressure fell from a normal of 124 mm. to 94 mm. and on a second injection of 16 mg. it fell from a normal of 109 mm. to 85 mm. or a drop of from 24 to 28 mm. The general systemic effect of the carnosine was similar to if not identical with that produced by histamine, but required larger quantities to be effective. Since our experiments upon intact animals, Goldschmidt² has attempted to show that the action of carnosine upon the circulatory system is entirely limited to the splanchnic area.

Upon the isolated rabbit intestine and also upon strips of guinea pig uterus, carnosine produced a marked increase in the tonal and rhythmical contractions when such strips were immersed in Tyroid's or Ringer's solution containing carnosine in amounts sufficient to give 1-2000 dilution. Its action upon these strips is again qualitatively and quantitatively similar to histamine in dilutions of 1 to 100,000. Koinaroff³ has also shown that carnosine is a powerful stimulant to motor activity of intestines. Further experiments with carnosine to determine definitely the point of action in its effect upon blood pressure and upon involuntary muscle are in progress.

² Goldschmidt, E., *Arch. f. d. ges. Physiol.*, 1924, cccii, 435.

³ Koinaroff, S. A., *Chem. Zentralbl.*, 1922, 636.