blowing steadily through the tube. An observer seated outside the circle will hear the periodic rise and fall of pitch accompanying the approach and recession of the whistle. For this experiment a medium pitch is preferable to a high, since the *ratio* of pitches for approach and recession, $n_1/n_2 = V + v/V - v$, is independent of the "rest pitch" of the whistle, whereas the ear is more sensitive to variation of pitch at 2,500 vib./sec. than at 5,000.

Using whistles of smaller diameter than those described here, the author has pursued the beat-note phenomenon to the upper limit of audibility, where the beat-note disappears as soon as either whistle exceeds the audible range of the ear—in this case above 22,000 vib./sec.

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AUTOMATIC HYPODERMIC INJECTOR

SELF-ADMINISTRATION of medicine by the hypodermic method has become very common in recent years. Ever since Dr. Banting, of Toronto, in 1922, isolated the hormone insulin from the islands of Langerhans in the pancreas, the injection of this substance before each meal has become the recognized treatment of diabetes. The hormones of other internal secretory glands are being isolated, and promise to become control medication in various deficiency diseases. Being of organic chemical composition, hormones are digested when taken by mouth, and must be injected subcutaneously to give their systemic effect. Patients who suffer from a hormone deficiency must have the substitute injections so frequently, usually several times a day, that it becomes impractical to have them administered by a doctor or a nurse, and necessitates the patients giving themselves the injections. Besides hormones, other substances that must be injected frequently over a prolonged period of time, such as hay fever vaccine, for example, are best administered by the patients themselves.

Hypodermic self-injection, however, has the drawback that ordinarily it is painful. And to inflict pain upon oneself is against the deep-rooted instinct of self-preservation. The fear of pain causes a hesitancy on the part of the patient when he is about to push in the needle. Hence the procedure becomes slower and more awkward than it need be. Slower penetration results in more distortion of the skin, more stretching and tearing of the sensitive nerve endings, and consequently more pain.

Due to this drawback many diabetic patients are denying themselves the health-preserving and life-saving benefits that insulin would give them. Diabetes is markedly on the increase, involving over a half million people in this country alone, and has climbed into tenth place in the list of death causes. In order to encourage diabetics to use insulin, an automatic injector has been perfected, which eliminates pain by the extreme rapidity with which the needle is plunged into the tissues, and which substitutes an automatic thrust for the fearful manual push.

The automatic injector consists of a compression spring, within a metal casing which fits around the upper end of an ordinary insulin syringe. The calibrated lower end of the syringe is left uncovered so that the dose of medication may be properly measured. The spring is released by means of a trigger. An adjustable foot-rest at the bottom assures the correct depth and angle of needle insertion, and makes it practically impossible to break off the needle in the tissues. The syringe as well as the needle are separately removable for sterilization purposes. The injector is easily operated by laymen, is very durable, and last but not least is reasonable in price.

It is hoped that this little device will save many a timid person from an early grave, and will dislodge diabetes from the upper part of the list of death causes.

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SPECIAL ARTICLES

THE ERGOT ALKALOIDS

A RECENT preliminary report[1] has been made of the isolation of proline (as the double gold salt of its methyl ester) after hydrolysis of ergotinine in methyl alcoholic hydrochloric acid solution and also from among the products of the reductive cleavage of this alkaloid with sodium in butyl alcohol. Among the products of the latter we have also obtained several other bases, one of which was interpreted as a substituted piperazine, $C_{14}H_{20}N_2$, resulting possibly from the reduction of the mixed anhydride of proline and phenylalanine and another base, a phenylpropanolamine, possibly a phenylalanine product. These interpretations have been more recently substantiated by the isolation of phenylalanine itself from the products of the alkaline hydrolysis of ergotinine. Thus ergotinine and therefore ergotoxine are built up of the four constituents, lysergic acid (as its amide, ergine) isobutyryl formic acid, proline and phenylalanine. The accepted formula for ergotinine, $C_{35}H_{39}O_5N_5$, is consistent with the conjugation of these components (in peptide linkage) with the loss of three moles of water.

We have more recently made a preliminary study of ergotamine (obtained from the ergotamine tartrate of the Sandoz Chemical Works) by the same methods.

[1] W. A. Jacobs and L. C. Craig, *Jour. Am. Chem. Soc.*, 57: 383, 1935; *Jour. Biol. Chem.*, 108: 595, 1935.

Although hampered by a very limited amount of material, suggestive results have been secured. In addition to lysergic acid and ammonia,[2] phenylalanine has been obtained from it. Less success, however, was experienced in our attempts to obtain proline as the gold salt of its ester from the alkaline hydrolysis of ergotamine or after its reductive cleavage with sodium in butyl alcohol. However, in the latter case we have isolated in addition to α- and β-dihydrolysergol the picrate of the piperazine, $C_{14}H_{20}N_2$, corresponding with that obtained from ergotinine. There can be little doubt, therefore, that proline is also a constituent of ergotamine. This conclusion was supported by the strong pyrrol test given by the mixed amino-acid fraction obtained from the alkaloid after alkaline hydrolysis.

In another respect, however, we have noted a striking difference between ergotinine and ergotamine. By no method have we succeeded in detecting either isobutyryl formic acid as such, or its reduction product α-hydroxyisovaleric acid, as products of the cleavage of ergotamine.

Since the accepted formula for ergotamine is $C_{33}H_{35}O_5N_5$, which differs therefore from that of ergotinine by C_2H_4, the possibility was considered by us that in ergotamine and therefore also ergotaminine pyruvic acid occurs in place of the isobutyryl formic acid of ergotinine and ergotoxine. Our experience has given support to this suggestion. If ergotamine is heated a short while with dilute alcoholic alkali, the resulting solution gives a red color with nitroprusside similar to that given by pyruvic acid and which changes after addition of ammonium chloride through purple to blue. This reaction is not given by ergotinine under the same conditions. In addition, it has been possible to obtain in very small yield a phenylhydrazone from the acid fraction of the cleavage products of ergotamine, which gave the same melting point (189–190°) as the phenylhydrazone of pyruvic acid. A mixture of the two showed no depression.

On pyrolysis of ergotamine and under conditions which with ergotinine gave isobutyryl formamide without difficulty, none of the latter substance was obtained from ergotamine. Other crystalline substances, however, were found in the sublimate which are now under investigation.

It is suggested that while ergotinine and ergotoxine are derivatives of lysergic acid, isobutyryl formic acid, proline and phenylalanine, in ergotamine and therefore ergotaminine isobutyryl formic acid is replaced by pyruvic acid.

Lysergic acid has probably a biogenetic relationship to tryptophane and isobutyryl formic and pyruvic acids to valine (hydroxyvaline?) and alanine (serine?), respectively.

We are attempting to confirm these findings by further investigations.

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[2] This is in agreement with the isolation of ergine from this alkaloid by Smith and Timmis (*Jour. Chem. Soc.*, 1932: 1543).

ASCORBIC ACID (VITAMIN C) AND PHOTOGRAPHIC DEVELOPING ACTION

UNTIL recently, knowledge of the chemistry of vitamin C was limited to assumptions drawn from the behavior of antiscorbutic concentrates. The experiments of the early investigators were reviewed by McCollum and Simmonds[1] in 1929 and by Sherman and Smith[2] in 1931. The evidence indicated that vitamin C was a reducing substance which was highly susceptible to oxidation in alkaline solution but comparatively stable in acid and which gave some of the reactions of polyphenols.

These properties so strongly reminded me of the photographic developing agents that, in 1931, I prepared an antiscorbutic concentrate from decitrated lemon juice, made it alkaline and tested it for developing action. It produced faint blackening on light-struck photographic emulsion. Thus encouraged, I reversed the procedure, testing numerous developing agents for antiscorbutic action. Needless to say, this attempted short cut to the identification of vitamin C was unsuccessful; still the developing action of the lemon juice concentrate remained to be explained. Following the recent isolation and synthesis of vitamin C (*l*-ascorbic acid),[3] I have employed the commercial product in a resumption of the photographic experiments.

Ascorbic acid, dissolved in water with sodium sulphite (preservative) and sodium carbonate (accelerator) in the usual proportions of a developing solution, is a rapid developer which produces a black image and considerable fog. It is unusually sensitive to bromide (restrainer). As little as 20 mgm of potassium bromide per liter of solution markedly restrains fog, considerably slows development, requires longer exposure and changes the color of the image from black to brown. The developing action is illustrated by experiments with Formula 1, prepared by dissolving the chemicals in the order indicated. This solution, in a stoppered bottle, remains usable for about a week.

[1] E. V. McCollum and N. Simmonds, "The Newer Knowledge of Nutrition," 4th ed., New York, Macmillan, 1929.

[2] H. C. Sherman and S. L. Smith, "The Vitamins," 2nd ed., New York, Chemical Catalog Company, 1931.

[3] L. J. Harris, *Ann. Rev. Biochem.*, 3: 264, 1934.