Purified Secretin and Pancreozymin

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For a number of years we have been engaged in work on the purification of the gastrointestinal hormones gastrin, secretin, pancreozymin and cholecystokinin. The impetus to this was given by repeated requests from clinical workers for these substances, the pharmaceutical houses being unable to provide them. From the classical work of Hammarsten, Ågren and Lagerlöf in Sweden and of Ivy and coworkers in the USA it is well known that secretin can be used for diagnostic purposes. The pancreozymin of Harper and Raper would, if available in purified form, evidently be a valuable supplement to secretin.

It proved possible to prepare a non-toxic secretin with an activity of 1 000 cat units per mg. This activity, assayed in the cat, was checked clinically [1]. The activity was surprisingly high in view of the fact that the crystalline secretin picrolonates reported in the literature, and claimed to represent the pure secretin [2] had an activity of 250 c.u. per mg.

Further work showed that the preparations assaying 1 000 c.u. per mg were still very crude. It was in fact possible to prepare secretin with an activity of 25 000 c.u. per mg [3]. The method for preparing this very active material is not yet worked out in detail and the yield of the material is poor. Preparations with an activity of 10 000 c.u. per mg can, however, be obtained routinely and have also been tested clinically.

We have applied isoelectric separations and fractionation with organic solvents as well as ion-exchange. In the latter the use of non-cross-linked naturally occurring acids and bases has been preferred instead of the various commercially available resins. The acids used have been polygalacturonic, polymannuronic and stearic, the bases stearylamine and deacetylated chitin.

For the purification of pancreozymin similar methods have been applied. We have prepared material which can be used clinically. A definite increase in output of pancreatic enzymes as well as a contraction of the gall bladder can be observed after the injection of 1 mg of this substance in an adult person.

By means of these purified hormones we have been able to confirm the view expressed by Pavlov long ago, that there are two mechanisms regulating the external pancreatic secretion, one controlling the secretion of water and bicarbonate and the other the secretion of enzymes.

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2. Greengard, H. in Pincus, G. and Thimann, K. V. *The Hormones*, Acad. Press. Ltd, New York 1948, Vol. I, p. 203.
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Quasi-racemic Compounds between Optically Active Positional Isomers of Methyl-substituted Octadecanoic Acids

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A pair of optical antipodes often crystallise together to form a racemic compound consisting of equal amounts of the two components. If one of the antipodes is subjected to a small change in the molecular structure it may still form a compound with the unaltered antipode. Such compounds have been called quasi-racemic by Fredga [1], who has made extensive use of them for the determination of the steric configuration of optically active molecules.

It has now been found that such a quasi-racemic compound is formed between (+)-9-D-methyloctadecanoic acid and (+)-10-L-methyloctadecanoic acid. The antipodes of both 9- and 10-methyloctadecanoic acid melt at 12.5—12.9°. 9-D,L-Methyl-octadecanoic acid melts at 38.7—39.2° whereas the racemic compound between the antipodes of 10-methyloctadecanoic acid is dimorphous with melting-points of 20.9—21.6° and 25.8—26.1° respectively [2]. An equimolecular mixture of (+)-9-D-methyloctadecanoic acid and (+)-10-L-methyloctadecanoic acid (antipode of tuberculostearic acid) melts at 18.6—18.7°. The corresponding mixture of (+)-9-D-methyloctadecanoic acid and (—)-10-D-methyloctadecanoic acid melts at about 5°.

Details will be published later.

1. Fredga, A. *The Svedberg 1884 30/8 1944*, Uppsala 1944, p. 261.
2. Ställberg-Stenhagen, S. *Arkiv Kemi, Mineral. Geol.* **26 A** (1948) No. 12 and unpublished data.