A sensitive method for the assay of 5-hydroxytryptamine

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Commentary by

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Think of any part of the body and you can be sure that the pharmacologist has cut it out, put into an isolated organ bath, or perfused its vessels in order to study the effects of drugs. For bioassay, segments of the gastrointestinal tract or spirally-cut strips of vascular tissue have mainly been used. Such procedures are the backbone not only of bioassay but also of classical pharmacology.

I returned from a two-year postdoc with Arnold Welch at Yale University to become senior lecturer in pharmacology at the Royal College of Surgeons of England, where Bill (later Sir William) Paton was Professor. In surveying the effects of drugs on the isolated stomachs of several laboratory species, I noticed that the white translucent part (as opposed to the thicker, pink, pyloric antrum) of the rat stomach was singularly sensitive to the contractor effects of 5-hydroxytryptamine (5-HT). In the paper I described this part as the fundus, but Brendan Whittle tells me it is the corpus. Happily, the preparation became known as the rat stomach strip (RSS).

I decided to record from the more sensitive longitudinal muscle. The bag was opened down one side, the muscle cut in a zigzag fashion as if making a paper streamer and then pulled out, trimmed and its length recorded on a kymograph with a spring lever. The rat stomach strip was useful, not only for the assay of 5-HT, but also to compare the activities of many analogues of tryptamine (Vane, 1959; Handschumacher & Vane 1967).

At this time, I had not been converted to Gaddum's superfusion technique and so I hung the RSS (which was usually 10-12 cm long) in a 5ml bath with rapid bubbling to ensure good mixing. Because the RSS had no rhythmic tone, a lever giving 16:1 magnification could be used. In order to shorten the time of relaxation in between contractions, the tissue was stretched by an extra weight to a predetermined length during the washing period.

Later, my interests turned to the bioassay of other vasoactive substances and we found that the same tissue, now contracted by a constant concentration of 5HT in the bathing fluid, could be used to assay catecholamines by their relaxant effects (Armitage and Vane, 1964). We also demonstrated the sensitivity of the RSS to prostaglandins and showed the release of a prostaglandin (wrongly identified as PGE_1) from the same tissue (Bennett, Friedman and Vane, 1967).

The rat stomach strip has stood me in good stead over 40 years, contributing to several discoveries, such as the mode of action of aspirin (inhibition of the biosynthesis of prostaglandins) and the discovery of prostacyclin. It is continuing to do so in the William Harvey Research Institute (now 10 years old), where we are studying with renewed intensity the vasoactive hormones released by endothelial cells such as prostacyclin, endothelium-derived relaxing factor (nitric oxide) and endothelin.

References

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