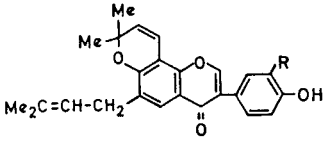
Inhibition of valyl[5] angiotensinamide II by osajin

SIR,—Specific receptors for vasoactive polypeptides have not been demonstrated beyond doubt because of the lack of specific antagonists. Recently, Walaszek & Dyer (1966) offered good but indirect evidence for such receptors.

We now report the antagonism of angiotensinamide II by an isoflavone derivative called osajin (I) isolated from the fruit of *Maclura pomifera* (hedge apples or osage oranges) (Geissman & Hinreiner, 1952) found in the mid-western United States.



I

R = H Osajin
R = OH Pomiferin

Isolated segments of the ileum of guinea-pigs weighing 180–200 g were suspended at 37° in a 10 ml bath of Tyrode solution gassed with oxygen and carbon dioxide. The contractions caused by the various agonists used were recorded on a kymograph. The sensitivity of the preparation to the agonists was first tested, after which osajin was added to the perfusion fluid to give a final concentration of 5 μg/ml. At this point the reactivity to the agonists was reassessed over 2 hr followed by a 2-hr period of recovery. Ten separate experiments were made, five with polypeptides and five with biological amines.

The findings in Fig. 1 demonstrate that osajin antagonised the musculotropic activity of valyl[5] angiotensinamide II but not that of bradykinin or eledoisin. There was no major change in the myotrophic activity of 5-hydroxytryptamine, acetylcholine or histamine.

The mechanism of the antagonist action produced by osajin is not clearly understood. Recently it was reported that valyl[5] angiotensinamide II formed amorphous precipitates with Zn^{++} and Cu^{++} and that perhaps the peptide could

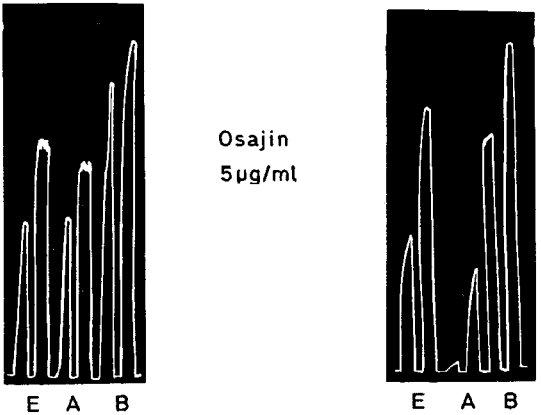


FIG. 1. Influence of osajin on the musculotropic activity of polypeptides. E. Eledoisin, 5 and 10 ng/ml. A. Valyl[5] angiotensinamide II, 10 and 20 ng/ml. B. Bradykinin, 10 and 20 ng/ml.

interact with its receptors in a chelated state (Schwyzer, 1963). The fact that the chelation complex is formed in a 1 to 1 ratio would indicate that the hydroxyl group of the tyrosine residue would be involved. This hydroxyl group has also been found essential for the biological activity of the polypeptide (Bumpus, Khairallah, Arakawa, Page & Smeby, 1961) and also could be involved in the formation of the drug-receptor complex (Walaszek & Dyer, 1966).

The flavonoid compounds have the ability to chelate bivalent metals and it could be possible that osajin irreversibly antagonises the action of valyl[5] angiotensinamide II by complexing a metal which is an integral part of the angiotensin receptor since, like the polypeptide, osajin also contains in its molecular structure a free hydroxyl group.

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Book Review

REMINGTON'S PHARMACEUTICAL SCIENCES, 13th Edition. (RPS XIII.) Pp. xii + 1954 (including Index and over 1000 illustrations). Mack Publishing Company, Easton, Pa., U.S.A., 1965. In Great Britain: John Wiley & Sons, Ltd., London. 212s.

In this new edition of *Remington's Pharmaceutical Sciences* there are 100 chapters, written mostly by separate authors, covering the economic, professional and scientific aspects of pharmacy. The volume is intended both as a text book and as a reference book but as these two functions are clearly separate one wonders what advantage is to be gained by retaining a single mammoth volume. The physical bulk of Remington demands a substantial space on a firm table and this restricts its use as a convenient reference book.

The book is divided into nine parts: Orientation, Physical Pharmacy, Pharmaceutical Manufacturing, Pharmaceutical Chemistry, Pharmaceutical Products, Biological Products, Radiopharmacy, Testing and Analysis, Professional Practice. The layout of material follows the previous editions.

One cannot fail to be impressed by the coverage achieved and the enormous effort involved in the preparation of this book. It is unfortunate however that there is some unnecessary duplication of material particularly in the Physical Pharmacy section. Three different authors have contributed chapters on Surface Activity, Colloidal Dispersion and Emulsification respectively and the same concepts of surface tension are discussed on pages 254 and 284. Gibb's Adsorption theory appears in three different places, pages 257, 273 and 284. On page 286 neither the definition of zeta potential nor Fig. 257 is clear.