respectively. Acid hydrolysis of these mixtures liberated hexosamines, fucose, and galactose together with small amounts of glucose and mannose. This suggests that most of the polysaccharide in these tissues was of the blood-group substance type. The glucose probably originated from the glycogen[9] which constituted 0·35 per cent of the duodenal ulcer tissue and 0·30 and 0·29 per cent respectively of the stomach carcinomas (all yields calculated on the dried fat-extracted tissue). Ionophoretic analysis of the crude polysaccharide mixtures revealed the presence of small amounts of acidic polysaccharides staining with toluidine blue[10] accompanied by much larger amounts of neutral polysaccharides.

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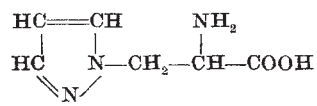
α-Amino-β-(pyrazolyl-N) Propionic Acid : a New Amino-Acid from *Citrullus vulgaris* (Water Melon)

During recent years, several new amino- and imino-acids have been characterized as components of the non-protein nitrogen fraction of plant materials. Another example has now been found in seeds of *Citrullus vulgaris* (water melon, var. Tom Watson). The structure of this new amino-acid (hereafter termed β*PA*) is as follows :



α-Amino-β-(pyrazolyl-N) propionic acid
or β-(pyrazolyl-N) alanine

This amino-acid is unique in that it is the first example of a natural product which contains a pyrazole ring. Furthermore, in contrast to the other heterocyclic ring-containing amino-acids, histidine and tryptophan, the side-chain of β*PA* is attached to the pyrazole ring through a carbon to nitrogen bond.

The presence of the amino-acid was detected by two-dimensional paper chromatography (water-saturated phenol : butanol/acetic acid/water) in a 70 per cent (v/v) ethanol extract of ground seeds. It occupied a position very similar to that of proline on two-dimensional chromatograms. The compound reacted with ninhydrin to give a normal bluish-purple spot. With Ehrlich's reagent (*p*-dimethylaminobenzaldehyde) it gave a yellow-coloured spot, and it formed a copper complex with copper acetylacetonate, so indicating the presence of an α-amino group.

By ion exchange chromatography ('Zeokarb 215' and 'Dowex 50'–0·25 *N* ammonia displacement), 3 gm. of β*PA* was isolated from 10 lb. of water melon seeds. The amino-acid was crystallized twice from distilled water (solubility approximately 4 gm./100 ml.), and yielded a white solid with an elemental analysis of C, 46·7 ; H, 5·7 ; N, 27·1 ; O (by difference), 20·4. The calculated values for β*PA* are C, 46·4 ; H, 5·8 ; N, 27·0 ; O, 20·8.

Therefore, the isolated material had an empirical formula of $C_6H_9N_3O_2$, and was isomeric with histidine. This formula provides too few hydrogen atoms for the more normal saturated open-chain amino-acid structure. The compound was found to be stable to strong mineral acid (6 *N* hydrochloric acid at 100° for 24 hr.) and alkali (5 *N* barium hydroxide at 100° for 24 hr.). Treatment of the isolate with 55 per cent (w/w) hydriodic acid at 120° for 24 hr. degraded it, and alanine was identified as the only ninhydrin-reactive product by comparison with an authentic sample of the amino-acid on paper chromatograms developed in water-saturated phenol, butanol/acetic acid/water mixture, butanol saturated with 2 *N* ammonia, and ethyl acetate/pyridine/water (organic phase of 2 : 1 : 2 parts by volume mixture). The fission of an alanine moiety in this way not only indicated its presence in the structure of the isolate but also suggested that the alanine residue was attached to the remainder of the molecule through a C—N linkage (the corresponding C—C linkage found in histidine is stable to hydrogen iodide reduction).

The remaining atoms of the formula are most simply accommodated by assuming the presence of an imidazole or pyrazole ring system. It would appear that Shinano and Kaya[1] have isolated a smaller quantity of the same substance from the press-juice of water melon ; both isolates had the same elemental analysis and m.p. (decomp.) in the range 236–238° C. The Japanese workers suggested that their isolate was α-amino-β-(imidazolyl-N) propionic acid, although no definite proof for the presence of the imidazole residue was given. Our evidence provides no support for the idea of an imidazole ring. The isolate failed to give the Pauli test, and did not possess a *pK* in the *p*H range 6–7, normally a feature of imidazole derivatives. Pyrazole derivatives have an analogous *pK* in the *p*H range 2–3 ; the titration curve of the isolate showed a weak point of inflexion in this range. Nuclear magnetic resonance spectra[2] performed on the isolate and various N-substituted imidazole and pyrazole derivatives proved almost certainly that the isolate contained the pyrazole ring system. The fine structure of the spectrum of the isolate also indicated an unsubstituted α-amino group in the alanine residue and the presence of a —CH_2— group and an N—C linkage. These requirements are all met by the above structure for β*PA*.

Crude, small-scale preparations of β*PA* and β-(imidazolyl-N) alanine (β*IA*) have been made. The silver salts of pyrazole and imidazole respectively were refluxed in methanol with the methyl ester of β-chloroalanine hydrochloride (prepared by the method of Fischer and Raske[3]). After removal of the methanol and hydrolysis with 6 *N* hydrochloric acid, the reaction mixtures contained three amino-acids. Serine and a trace of a compound, probably alanine, accompanied either β*PA* or β*IA*. The synthetic β*PA* was inseparable from the isolated material on paper chromatograms, whereas β*IA* was easily resolved from the isolate. β*IA* had an R_F very similar to that of histidine in water-saturated phenol; in butanol/acetic acid/water mixture it moved slightly more slowly than histidine. The yields obtained in these preparations were low, but it is hoped that a future large-scale preparation of β*PA* may provide sufficient crystalline material for comparisons to be made with the natural substance using other accepted physico-chemical techniques.

We wish to thank the Ferry-Morse Seed Co. (California) for supplying the seed, Dr. I. L. Finar for advice on the syntheses, and Drs. J. H. Ridd and R. F. M. White for their help with the nuclear magnetic resonance spectra.

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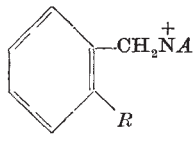
ANIMAL PHYSIOLOGY

New Antiadrenergic Compounds

We have found that the benzyl quaternary ammonium compounds (I, patents pending) have a novel and highly specific blocking action on the peripheral sympathetic nervous system, which resembles that following section of adrenergic nerves and differs from that produced by adrenolytics, ganglion-blocking agents and reserpine.



(I)

Compounds of the above type were screened by examining their efficacy in relaxing the nictitating membrane when injected subcutaneously in the cat. Activity was highest in the quaternary compounds (I; R = H) and the *ortho*-substituted analogues (I; R = *Me*, F, Cl, Br, I, and NO_2). Activity was also very sharply influenced by the cationic head, high activity being encountered in the compounds I with $NA = NMe_2Et$, $NMe_2(CH_2)_2OH$, $EtN(CH_2)_4$, $HO(CH_2)_2N(CH_2)_4$. Lower homologues such as I with $NA = NMe_3$, R = Br were inactive and higher homologues showed much reduced activities. There was no mydriasis or other overt effect in cats injected with any of these compounds, except one (I; $NA = NMe_2Et$, R = H) which caused marked parasympathomimetic effects.

One of the most active compounds, 373*C*57 (I; $NA = NMe_2Et$, R = Br), was examined in detail, as its bromide, and the findings indicating its mode of action are summarized as follows.

After subcutaneous injection of 5–10 mgm./kgm. of 373*C*57 in the unanæsthetized cat, the nictitating membrane gradually relaxed, becoming fully exposed in 4–6 hr., and retracted only after approximately 24 hr. Similarly, in cats under chloralose anæsthesia, 373*C*57 gradually inhibited the effect of indirect stimulation of the nictitating membrane irrespective of whether the stimuli were applied to the pre- or post-ganglionic nerve; the block was most marked when the stimulation was continuous. This inhibitory effect was accompanied by a gradual and prolonged fall in blood pressure often preceded, when the drug was given intravenously, by a small temporary rise. The response of the heart to stimulation of the cardio-accelerans nerve was blocked, and the pressor effects of intravenous injections of adrenaline and noradrenaline were increased.

373*C*57 blocked the response to stimulation of the adrenergic nerve in various isolated preparations. Thus it prevented the vasoconstriction caused by stimulating the greater auricular nerve in the perfused rabbit ear, the relaxation of the rabbit ileum during stimulation of the visceral efferents, and the contraction of the rabbit uterus elicited through the hypogastric nerve. The effects of adrenaline and noradrenaline on these preparations were enhanced after giving 373*C*57.

In the cat, the pressor effects of intravenous dimethylphenylpiperazinium iodide and splanchnic nerve stimulation which are mediated by the adrenal medulla were greater after giving 373*C*57, whereas the hypertension caused by the ganglion-stimulating action of dimethylphenylpiperazinium iodide in the adrenalectomized animal was blocked. This shows that the antiadrenergic action of 373*C*57 is not accompanied by an interference with the adrenal mechanism, such as occurs with the ganglion-blocking drugs or reserpine.

Some of the properties of 373*C*57 resemble those of the 2 : 6-xylylether of choline bromide, *TM*10[1,2], but unlike this compound, 373*C*57 does not cause parasympathomimetic effects or deplete the pressor amine content of the rat adrenal. The latter finding, if it applied also to the adrenergic nerve, would indicate that it is unlikely that 373*C*57 acts either by depleting the local stores of catechol amines or by inhibiting the biogenesis of noradrenaline in adrenergic nerves, as was postulated[3] might be the mode of action of *TM*10. 373*C*57 caused no overt behavioural changes in animals, and this together with the absence of depletion of the catechol amine content of the adrenal medulla of rats is in contrast with the actions of reserpine.

Together with our colleagues, Drs. A. McCoubrey and W. G. Duncombe, we have studied the distribution in tissues of 373*C*57 labelled with carbon-14 in one of its methyl groups. Following subcutaneous injection in cats, much higher concentrations of radioactivity were found in adrenergic nerves, sympathetic ganglia and tissues with a rich adrenergic innervation, than in other tissues. The concentration of 373*C*57 indicated to be present in adrenergic nerves, when applied topically, blocked the physiological responses to stimulation of the pre- and post-ganglionic cervical