

### Letters to the Editor

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#### Hexuronic Acid as the Antiscorbutic Factor

A CHARACTERISTIC property of Prof. Szent-Györgyi's hexuronic acid is its behaviour towards iodine. Two atoms of iodine are taken up in aqueous solution (neutral or acid) with formation of two molecules of hydrogen iodide. We find that this is due to oxidation at a double bond. The intervention of water is essential and the product, which is not a di-iodide, can be reduced to hexuronic acid. Regeneration of hexuronic acid occurs only when the aqueous solution of the oxidation product is reduced, for example, by evaporation in the presence of hydrogen iodide.

The biological activity of the acid is probably due to this double function of oxidation and reduction which, unique among purely carbon compounds, is reminiscent of the behaviour of glutathione. The product obtained by the action of neutral iodine on the acid undergoes further oxidation by sodium hypiodite. One atomic proportion of oxygen is absorbed, two new carboxylic acid groups are formed and oxalic acid (1 mol.) is produced quantitatively. Acid permanganate introduces one atom of oxygen into hexuronic acid with extreme readiness and thereafter oxidation proceeds more slowly with elimination of carbon dioxide until three atoms of oxygen have been absorbed. This leads to the formation of a trihydroxy butyric acid (possibly *d*-threonic) which has been isolated as the optically active crystalline amide  $\text{CH}_2\text{OMe}\cdot\text{CHOMe}\cdot\text{CHOMe}\cdot\text{CONH}_2$ . When heated with hydrochloric acid hexuronic acid gives furfural in quantitative yield. These observations suggest that hexuronic acid (which, from analysis of its salts we have proved to be a monobasic acid  $\text{C}_6\text{H}_8\text{O}_6\cdot\text{COOH}$  and not a lactone of an acid  $\text{C}_6\text{H}_8\text{O}_6\cdot\text{COOH}$ ) has the structure  $\text{COOH}\cdot\text{CO}\cdot\text{CO}\cdot\text{CH}_2\cdot\text{CHOH}\cdot\text{CH}_2\cdot\text{OH}$ .

The following observations which we have made are consistent with this view. Hexuronic acid forms a di-phenyl-hydrazone  $\text{C}_6\text{H}_8\text{O}_4\text{:}(\text{N}\cdot\text{NHPh})_2$ , also a hydrated di-*p*-bromo-phenylhydrazone, and reacts slowly at 15° with *o*-toluylene diamine giving a well-defined condensation product. The sodium or calcium salt of hexuronic acid gives an intense violet colour with ferric chloride but with the free acid the coloration is fleeting. The sodium salt gives with sodium nitroprusside a deep blue colour, changing to green and then red. The acid and its salts show an intense absorption band with head at about 265  $\mu$ .

Hexuronic acid contains one carboxyl and three potential hydroxyl groups (alcoholic or enolic) and gives a triacetate and a trimethyl ether which both reduce neutral permanganate. When heated at about 175° the acid loses carbon dioxide without darkening or melting (when heated rapidly the pure acid melts at 192°). Whilst the acid has  $[\alpha]_{\text{D}}^{25} + 24^\circ$  in water the sodium salt has a much higher rotation, +105° in neutral solution, +135° in *N*/10 alkali, (keto-enol transformation). Hexuronic acid appears to be incapable of forming a lactone and its solutions do not display

mutarotation. The slow change ( $[\alpha]_{\text{D}}^{25} + 24^\circ + 31^\circ$ ) which occurs with aqueous solutions in glass vessels is due to partial neutralisation of the acid by alkali dissolved from the glass. Alkaline solutions of the acid are stable in the absence of oxygen.

These observations indicate the presence of an optically active diketo-acid containing a  $-\text{CH}_2-$  group. These groups must be united in such a way that the stringent requirements of the crystallographic and X-ray data are satisfied. It is essential, for example, that the carbon and oxygen atoms (with one exception) should lie in a plane and that the length and breadth of the molecule should be 8.8 and 6.1 Å, respectively. A critical survey of various possibilities from the chemical, optical and X-ray data has led us to the conclusion that the properties of hexuronic acid are best accounted for by the above structure. This can react also in the enolic modification,  $\text{CO}_2\text{H}\cdot\text{CO}\cdot\text{C}(\text{OH})=\text{CH}\cdot\text{CHOH}\cdot\text{CH}_2\cdot\text{OH}$ .

We have examined (with R. W. Herbert) the absorption spectrum of de-citrated lemon juice and have estimated that the hexuronic acid content corresponds with the recorded evaluation of the antiscorbutic activity of isolated hexuronic acid.

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#### A Peculiar Visual Experience

WHILE I was engaged in flashlight colour photography, using large charges of magnesium and the ordinary touch-paper method of ignition, the fuse on one occasion apparently failed to act, but, just as I was about to replace it, the flash took place. My head was less than a foot above the explosion point, and the flame must have reached my face, as my eyebrows and hair were singed, and my spectacles were completely coated with a dense, firmly adherent film of magnesium oxide.

My subsequent visual sensations were as follows: for an indeterminate period, which, after making generous allowance for subjective impressions, I would estimate at about twenty seconds, there was a complete 'black-out'. After this period (during which I removed my glasses and rubbed my eyes) I observed the filament of a 100 watt gas-filled lamp, about three feet distant and screened by a thin orange silk shade, which appeared as a bright red line. In about twenty seconds more (this and subsequent times were taken with a watch) I could distinguish general details of the furniture of the room, which was fairly well lighted, in red monochrome. The colour changed from deep maroon to light claret in about fifteen seconds, and then to an orange shade in about ten seconds more, but a prominent red object retained its normal shade. Then the background and white objects changed suddenly—too quickly for the time to be observed—to a green, at first olive, afterwards brightening to emerald. This stage lasted nearly twenty seconds, and it was noted that the red and orange objects appeared in their natural colours. The green shade then faded away rapidly, and the whites, after a slight intermediate yellow tinge, appeared for the first time. The total illumination appeared to