A RADIO-TRACER STUDY ON THE CATABOLISM OF LINAMARIN

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ABSTRACT

Manioc (cassava) contains a cyanogenic glucoside linamarin, 2 (β - D - glucopyranosyloxy) isobutyronitrile. Linamarin is suspected to be toxic directly, in addition to being a precursor of free cyanide found in this plant material. Manioc has been associated with acute toxicity as well as chronic toxicity; the latter being associated with thiocyanate which is a product of detoxification of cyanide. However, the direct role of linamarin is not clear. Linamarin was synthesised using ^{14}C labelled KCN as starting material. Using this material acetone cyanohydrin was first prepared and then reacted with acetobromoglucose (synthesized from glucose) to yield linamarin tetra-acetate. The tetra-acetate was hydrolysed to produce linamarin which contained a ^{14}C label in its cyanide moiety.

The linamarin was fed to rats and the appearance of radioactivity in the hepatic portal blood, peripheral blood, urine and faeces was monitored. The faeces did not contain significant activity, showing that all the label was absorbed into the blood stream. Radioactivity was detected 6 h after feeding, in the hepatic portal blood and attained a maximum in the peripheral blood on the third day. Only a small

percentage of the isotope appeared in the urine during the course of the week, while no radioactivity was detected in the respiratory CO_2. The smaller amount of radioactivity detected in the urine reached a maximum in 2 days.

Both hepatic portal blood and peripheral blood showed the presence of one major metabolite, which proved not to be linamarin. Radiochromatogram scans also showed the presence of another metabolite in small quantities. On comparing the major metabolite with the $Ba(OH)_2$ hydrolysate of linamarin, it was found that they had identical R_f values and similar IR spectra. This metabolite also had a glucose moiety, and much of the radioactive C appeared to be in a carboxylate group. It therefore appeared that the metabolite was identical to the $Ba(OH)_2$ hydrolysate of linamarin, which is the glucoside of α - hydroxy iso-butyric acid. Urine also contained a similar metabolite. In addition, urine also appeared to have some linamarin.

On the basis of this study it appears, linamarin is fully absorbed by the gut before or after hydrolysis of the C-N bond, to produce the glucoside of α - hydroxy iso-butyric acid. This compound is successively detected in the hepatic portal blood, peripheral blood,

and urine. There is an anomaly, where the radioactivity in urine peaks before the peak in the peripheral blood is reached. It appears probable that this is due to at least some of the radioactivity in urine being linamarin. Another interesting point is that the radioactivity is to a great extent not excreted. From this the inference is drawn that the α-hydroxy isobutyric acid skeleton is used for other metabolic pathways.