

## BIO-TRANSFORMATION OF [23-<sup>14</sup>C] DIGITOXIN IN DIGITALIS THAPSI L.

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Although knowledge of the biosynthetic pathway of the cardenolide nucleus is now complete (Tschesche 1971, 1972; Aberhard et al 1973) the course of subsequent transformation into the complex range of cardiac glycosides in Digitalis is not fully understood.

Previously reported investigations of the biotransformation of cardenolides have been carried out with enzyme preparations (Franz & Meier 1969), cell tissue cultures (Furuya et al 1970; Reinhard 1975), and leaf discs (Weiler 1979). Plants of Digitalis purpurea have been found to convert (G-<sup>3</sup>H-digitoxin into glycosides of the A, B and E series (Mekkawi 1978). The present investigation reports the incorporation of [23-<sup>14</sup>C]-digitoxin.

Digitalis thapsi L. first year plants converted injected [23-<sup>14</sup>C]-digitoxin to cardenolides of the A series (acetyl digitoxin, desacetyl lanatoside A, lanatoside A and digitoxigenin), B series (desacetyl lanatoside B, gitoxin, gitoxigenin and strosposide) and the E series (verodoxin and gitaloxin). Glucosylation of digitoxin occurred at a faster rate than any other transformation, in addition acetylation, 16-8 formylation and interchange of sugar moiety occurred.

These findings (Fig. 1) confirm the fluctuations in the proportions of A and B series cardenolides determined by colorimetric assay using the methods described in the European Pharmacopoeia (Fig.2).

Fig.1. Proportion of radioactive cardenolides at weekly intervals after injection of [23-<sup>14</sup>C]-digitoxin.

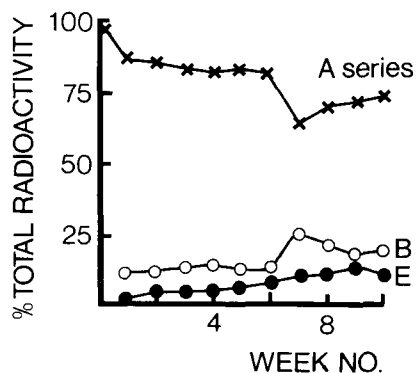
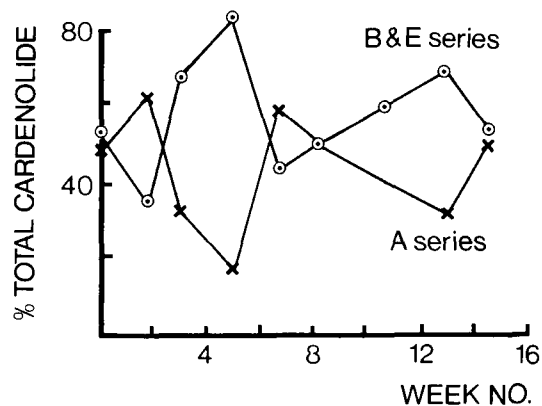


Fig.2. Proportion of cardenolides measured by chemical assay over a period of 15 weeks.



- Aberhard, D.J., Lloyd-Jones, J.G. and Caspi, E. (1973) *Phytochemistry* 12:1065.  
 European Pharmacopoeia, Vol.III (1976) Maisonneuve S.A.  
 Franz, G. and Meier, H. (1969) *Planta Med.* 4:396  
 Furuya, T., Hirotsu, M. and Shinohara, T. (1970) *Chem.Pharm.Bull.* 18: 1080  
 Mekkawi, A.G. (1978) Ph.D. Thesis, University of Bradford  
 Tschesche, R. (1971) *Planta Med. Supp:* 34  
 Tschesche, R. (1972) *Proc.Roy.Soc. (London):* 180:187  
 Weiler, E.W. (1979) *Planta Med.* 35: 162