

of the myometrium to oxytocin rather than to an increase in the amounts of oxytocin released into the blood. Since the hypothalamus is functionally connected with both neurohypophysis and adenohypophysis it is tempting to speculate that the relay we have demonstrated between uterus and hypothalamus may be concerned not only with the release of oxytocin but also with effecting increased myometrial sensitivity to it, factors which together underly the mechanism of normal parturition.

This work was done while one of us (E. P. L.) held an M.R.C. clinical research training fellowship.

Financial support was granted to G. W. T. by the Leeds Regional Hospital Board and Bradford A fellowship grant.

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## PHARMACOLOGY

### Isolation and Identification of the 20 $\beta$ -Hydroxy Derivatives of 6 $\beta$ -Hydroxycortisol and 6 $\beta$ -Hydroxycortisone in Liquor Amnii

THE presence of C-6 oxygenated steroids in neonatal urine was first reported by Ulstrom *et al.*<sup>1</sup> It has been demonstrated<sup>2,3</sup> that placental tissue incubated under standard conditions, is able to oxygenate at the C-6 position, while the work of Frantz *et al.*<sup>4</sup> has indicated that during pregnancy the urinary concentrations of the polar steroid 6 $\beta$ -hydroxycortisol is elevated above the normal non-pregnant state. It appeared likely, therefore, that similar polar steroids might be present in liquor amnii.

In a previous communication<sup>5</sup>, the isolation and identification of 6 $\beta$ ,11 $\beta$ ,17 $\alpha$ ,21-tetrahydroxy-pregn-4-ene-3-20-dione (6 $\beta$ -hydroxycortisol) in liquor amnii were reported. At this time the presence of three additional polar steroids was recognized. Two of these compounds have now been identified as 6 $\beta$ ,17 $\alpha$ ,20 $\beta$ ,21-tetrahydroxy-pregn-4-ene-3,11-dione (compound 3) and 6 $\beta$ ,11 $\beta$ ,17 $\alpha$ ,20 $\beta$ ,21-pentahydroxy-pregn-4-ene-3-one (compound 4).

Liquor amnii, obtained at the time of labour, was extracted with ethyl acetate, using the methods previously described<sup>5</sup>. The purified extract was chromatographed in a modified *BuC* system<sup>6</sup> and the chromatogram treated with a 2 : 1 solution of 10 per cent aqueous sodium hydroxide in 50 per cent methanol and 0.02 per cent blue tetrazolium. It was dried in an oven at 60° C for 10 min. When the chromatogram was viewed under ultra-violet light, using a minus blue 4 gelatine filter (Ilford), three brilliant fluorescent zones were observed. The least polar of these has been previously identified as 6 $\beta$ -hydroxycortisol

Table 1. PROPERTIES OF THE 20 $\beta$ -HYDROXY DERIVATIVES OF 6 $\beta$ -HYDROXYCORTISOL AND 6 $\beta$ -HYDROXYCORTISONE

	Compound 20 $\beta$ -6 $\beta$ -OHF		Compound 20 $\beta$ -6 $\beta$ -OHE	
	Isolated	Ref.	Isolated	Ref.
1 Ultra-violet absorption in ethanol	238 m $\mu$	238 m $\mu$	238 m $\mu$	238 m $\mu$
2 Reaction with blue tetrazolium	Neg.	Neg.	Neg.	Neg.
3 Mobility in chromatographic system Mod. <i>BuC</i> (ref. 6)	0.01	0.01	0.03	0.03
4 Mobility after the oxidation of the product from Reaction 3 with sodium bismuthate				
<i>B</i> /50 syst. (ref. 9)	0.24	0.24	0.32	0.32
<i>LB</i> 21/80 (ref. 9)	0.01	0.01	0.03	0.03
5 Mobility after acetylation of the product from Reaction 4				
<i>LT</i> /2185 (ref. 9)	0.15	0.15	0.31	0.31
6 Mobility after further oxidation of the product from Reaction 5 using chromic acid				
<i>LT</i> /2185 (ref. 9)	0.31	0.31	0.31	0.31
7 Mobility after reduction of the product from Reaction 4 using <i>Zn/HAc</i> (ref. 9)				
<i>LT</i> /2185 (ref. 9)	0.24	0.24	0.38	0.38

(compound 1) (ref. 5). Quantities of the other two zones (compounds 3 and 4) were collected from subsequent chromatograms, and were carried through a series of chemical and enzymatic steps. Identification of these 20 $\beta$ -hydroxy derivatives of 6 $\beta$ -hydroxycortisol and 6 $\beta$ -hydroxycortisone was based on the properties as listed in Table 1. The products from each procedure were compared chromatographically with reference steroids. In each case an agreement of *R<sub>F</sub>* values was found.

The configuration of the side-chain was elucidated using the enzyme 20 $\beta$ -hydroxysteroid dehydrogenase<sup>7</sup>, and by an examination of the chromatographic properties of the steroids. The reference steroids for this comparison were obtained by treating 6 $\beta$ -hydroxycortisol and 6 $\beta$ -hydroxycortisone with sodium borohydride at 0° C (ref. 8).

This work was carried out during the tenure of a research grant to one of us (M. L.) from the Medical Research Council of Ireland.

20 $\beta$ ,6 $\beta$ -hydroxycortisol was kindly supplied by Prof. W. Klyne and Dr. C. B. Thornton from the Steroid Reference Collection, Westfield College, London.

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### Formation of Tetrahydropapaveroline from Dopamine *in vitro*

In 1938, Holtz *et al.*<sup>1</sup> reported that dopamine, which is pressor in the cat, was converted to a depressor substance after incubation with monoamine oxidase (MAO), for example, extracts of guinea pig kidneys. These authors suggested that the depressor agent might be dihydroxyphenyl acetic aldehyde, the primary deamination product of dopamine, since the addition of semicarbazide prevented the formation of the depressor substance.