# THE INTERACTION OF STEROIDAL HORMONES WITH MUCUS GLYCOPROTEINS

G.P.Martin,C.Marriott and I.W.Kellaway,Pharmaceutics Research Unit,Department of Pharmacy, University of Nottingham, Nottingham, NG7 2RD

It is known that progestogens induce thick cervical mucus whereas under the influence of oestrogens a more copious and mobile mucus is secreted. The activity of the cervix is mediated through the changes in the physical properties of cervical mucus which occur during the normal menstrual cycle. The transport of sperm is facilitated by the thin mid-cycle mucus and prevented at other times by mucus of increased viscosity and elasticity. Such hostile mucus acts as a 'natural' contraceptive and can be produced by synthetic progestogens administered either orally or locally. However, no study has been made of the interaction of either progestogens or oestrogens with mucus glycoproteins although Westphal (1964) has shown that $\alpha_1$-acid glycoprotein has a strong affinity for progesterone and Kesseru and others (1975) have shown that the addition of progesterone to cervical mucus in vitro suppresses and arrests sperm penetration. This study investigates the interaction of progesterone and ethinyloestradiol with mucus glycoprotein sols and gels.

The effect of both steroids on the physical properties of the mucus gel has been investigated by the use of non destuctive creep compliance testing (Martin and others, 1978). Freeze dried mucus powder was reconstituted to a total solids content of 2.5% w/v using either a saturated solution of the steroid or a water control. Progesterone induced a thickening of the mucus gel since a 25% increase in both elasticity and viscosity occurred. However, no significant difference (P=0.99) was apparent between the ethinyloestradiol treated samples and the water controls.

The solubility of progesterone in the presence of aqueous solutions of glycoprotein was determined after equilibration for 24 hours at 37°C. A linear increase in solubility was observed from 0.045mMl$^{-1}$ in water to 0.083mMl$^{-1}$ in 5% w/v of glycoprotein. Since glycoprotein molecules are unlikely to form micellar aggregates then it is concluded that the increase in solubility is due to an interaction between the steroid and the glycoprotein.

This interaction was further examined in dilute solution by U-tube viscometry. The intrinsic viscosity, $[\eta]$, was determined for the glycoprotein using water, phosphate buffer, or Tris/HCl buffer (pH 7 ). When water was used as the solvent irreproducible flow times were obtained, almost certainly attributable to heterogeneous aggregates. Although the flow times were reproducible in Tris buffer considerable scatter was observed in the values of the specific viscosity, $\eta_{sp}$. Incomplete hydration was considered to be the cause of these effects and the problem was obviated when isotonic phosphate buffer was used. Plots of $\eta_{sp}/c$ produced linear relationships up to 0.8 mg ml$^{-1}$ after which a curve was produced due to molecular association. Progesterone caused an increase in $[\eta]$ which indicates an increase in the dissymmetry of the glycoprotein molecule. Ethinyloestradiol produced a smaller increase in $[\eta]$ although both steroids reduced the value of the Huggins constant, k'. These effects were confirmed by measurement of turbidity at 550nm when a decrease occurred with both steroids although progesterone was the most effective.

Westphal,U.(1964). J.Am.Oil Chem.Soc., 41, 481-490.
Kesseru,E.,Camacho-Ortega,P.& others (1975). Fertil. Steril., 26, 57-61.
Martin,G.P., Marriott,C.& Kellaway,I.W.(1978). Gut, 19, 103-107.