CIRCADIAN VARIATION IN SALIVA TRYPTOPHAN CONCENTRATION

Campling, G., Lloyd-Williams, F., Neubauer, H., Redfern, P.H., Pharmacology Group, School of Pharmacy & Pharmacology, University of Bath, Claverton Down, Bath BA2 7AY and Psychiatric Unit, Royal United Hospital, Bath.

There has been considerable interest in recent years in the possibility of using saliva as an alternative to plasma in monitoring drug, metabolite or hormone concentrations. Collection of saliva is generally more acceptable to the patient than venipucture, and there are now many examples demonstrating that concentration in saliva accurately reflects that in plasma. At a previous conference we presented results suggesting that the concentration of tryptophan (TRY) in saliva might be used in this way (Lloyd-Williams et al 1985); we have now extended our studies to investigate TRY concentration in saliva over 24h.

Six healthy volunteers (5M, 1F, age range 21-43, mean 29.5) fasted overnight, collected a mixed, unstimulated saliva sample over a 5 min period at 0600h. Immediately thereafter, a 5 ml blood sample was taken. Further saliva and blood samples were taken at 0900, 1200, 1800, 2100, 2400 and 0300. After sampling at 0900, volunteers were allowed a normal diet with the proviso that meals were taken immediately after sampling. Tryptophan concentrations were measured by HPLC with electrochemical detection (Curzon et al 1981). Saliva samples were treated with 0.2M $HClO_4$ (0.1 ml per 0.9 ml sample) and were passed through 0.4 µm filters before injection onto the column. Free TRY concentration was measured in a 200 µl sample of plasma after ultrafiltration.

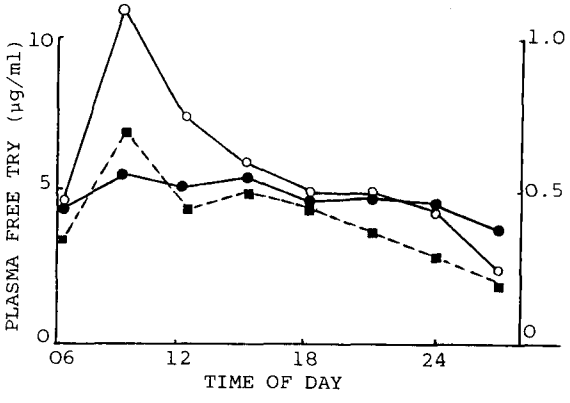

Fig.1 Circadian variation in TRY.
●-plasma free TRY, o-saliva TRY, $\mu g.ml^{-1}$
■-saliva TRY, $\mu g.min^{-1}$

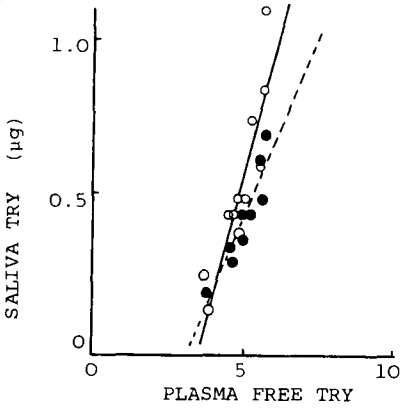

Fig.2 Correlation between plasma free TRY and saliva TRY o-$\mu g.ml^{-1}$, r=0.85; ●-$\mu g.min^{-1}$; r=0.91

Figure 1 shows the variation in saliva and plasma free TRY concentration in a single individual over 24 hr. Figure. 2 shows that the correlation between plasma and saliva values appears slightly better when flow rate is ignored. Although there was considerable inter-individual variation, the pattern of higher levels in the first part of the day, falling to a low point around midnight was consistent; analysis of variance of the pooled saliva data showed a significant [$F(7,40)=7.25, p<0.01$] variation with time. This circadian pattern agrees closely with that reported by Niskanen et al (1976). These results show that estimation of saliva TRY concentration is potentially a useful and more acceptable method of monitoring TRY concentrations in, for example, depressed patients.

Curzon, G. et al (1981) Br. J. Pharmac. 73 555-561.
Lloyd-Williams, F. et al (1984) J. Pharm. Pharmac. 36: 83P.
Niskanen, P. et al (1976) Br. J. Psychiat. 128: 67-73.