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Letter to the Editor

Potential problems with aqueous steroid solutions

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We have recently studied aspects of the absorption and enterohepatic circulation of various steroids, e.g. norethisterone (Back et al 1980), ethinyloestradiol (Back et al 1978) and oestrone sulphate (Back et al 1981). The concentration of steroid in most of the studies was 10 μg ml^{-1} in phosphate buffered −0·9% NaCl (saline) —ethanol (9:1, v/v). Other workers have used similar (Schedl & Clifton 1961; Pelzmann 1973) or greater (Meli et al 1968; James et al 1980) steroid concentrations in absorption studies. We would now like to draw attention to a problem we have encountered with oestrone in phosphate-buffered saline (PBS)—ethanol.

According to the Merck Index the aqueous solubility of oestrone is about 30 μg ml^{-1}, and we commenced a program of absorption studies using a 10 μg ml^{-1} solution of [^{3}H]oestrone in PBS–ethanol (9:1, v/v). However, we observed a considerable loss of drug from solution irrespective of the container in which the solution was held (polypropylene vials, polycarbonate tubes, polyallomer tubes, glass tubes). The same was not true for five other steroids examined under the same conditions (oestradiol, ethinyloestradiol, testosterone, progesterone and 1-norgestrel) or for oestrone at a concentration of 2 μg ml^{-1} (in PBS–ethanol, 9:1) or less. The particular problem with oestrone is clearly associated with its solubility in PBS as can be seen on reference to Table 1. When the ratio of ethanol is increased the percentage of oestrone lost from solution is decreased.

It needs to be stressed that oestrone, 10 μg ml^{-1} in PBS–ethanol, 9:1, v/v passes the test which most experimentalists would use, i.e. it appears to be in solution. The data however, show that it does not remain in solution and there is 'sticking' to the wall of the container. The partition coefficients of oestrone, oestradiol, progesterone and testosterone are similar (Higuchi et al 1980) and therefore the present finding is not directly related to lipophilicity.

There have been several reports on the adsorption of highly lipophilic drugs (including steroids) to soft plastics (Westphal 1955; Levin et al 1965; Minder et al 1970; Krieglstein et al 1972; Bruning et al 1981), and a warning given that this phenomenon can constitute a serious source of error (Minder et al 1970). The present finding has highlighted the need for care when aqueous steroid solutions are used and that each steroid should be thoroughly tested not only for adsorption (which will normally only be seen with extremely low concentrations) but also for solubility phenomena with higher concentrations.

Table 1. Effect of varying the ratio of PBS–ethanol on the loss of oestrone (10 μg ml^{-1}) from solution kept in polypropylene vials

PBS–ethanol	Percentage 'loss'
9:1	42·0 ± 2·1
7:1	33·1 ± 3·3
4:1	2·9 ± 1·0
1:1	1·1 ± 0·5
0:1	0·6 ± 0·3

Solutions of [^{3}H]oestrone were incubated for 1 h. Results are mean ± s.d. of 4 experiments.

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