Previously (Hamilton, 1972), dipyridamole was shown to potentiate the vasodilator action to AMP in the splanchnic region of the chloralosed cat. However, in the present experiments, it did not affect the neuronally mediated vasodilatation suggesting that any transmitter involved was unlikely to be of a purinergic nature.

Although in the present work changes of intestinal motility were not recorded, Ross (1973) found that no significant changes of motility occurred concomitant with the vasodilator response. This evidence is supported by the present findings that simultaneous $\alpha$- and $\beta$-adrenoceptor blockade failed to modify the effect. The possibility that adrenaline released from the adrenal medulla mediated this response was excluded by its persistence after propranolol and bilateral adrenal gland injection.

The present findings have confirmed those of Ross (1973) and extended them to exclude certain other transmitters from mediating the vasodilator response that occurs in the splanchnic region of the chloralosed cat in the presence of guanethidine. It remains likely that, as Ross (1973) suggested, stimulation of nerve fibres in the myenteric plexus of the intestinal wall is responsible for the increase in vascular conductance.

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# Effects of psychotropic drugs on prostaglandin biosynthesis *in vitro*

It has recently been shown that various local anaesthetics inhibit prostaglandin biosynthesis (Kunze, Bohn & Vogt, 1974a). Chlorpromazine, a psychotropic drug with local anaesthetic properties (Jarvik, 1970), was one of the most potent inhibitors. Because of these findings we thought it of interest to see, whether inhibition of prostaglandin biosynthesis is a general property of psychotropic drugs. We have studied reserpine, chlorpromazine, diazepam and meprobamate, as representatives of the major and minor tranquillizers. Those were kindly supplied by Ciba-Geigy (Basel, Switzerland), Bayer (Leverkusen, Germany), Hoffmann-La Roche (Basel, Switzerland) and H. Mack (Illertissen, Germany), respectively.

According to a general assumption, prostaglandin biosynthesis occurs in two main steps: a phospholipase A catalysed release of precursor acids, and their conversion into prostaglandins (Kunze & Vogt, 1971). Therefore, the effects of the drugs on endogenous prostaglandin formation were compared with their effects on phospholipase A and prostaglandin synthetase activities. Endogenous prostaglandin formation

Table 1. *Effects of various tranquillizers on endogenous prostaglandin formation in bovine seminal vesicles (BSV) and on the activities of phospholipase A from human plasma (HSP) and prostaglandin synthetase from sheep seminal vesicles (SSV).*

| Drug | IC50 (M) | | |
|---|---|---|---|
| | Prostaglandin biosynthesis (BSV) | Phospholipase A (HSP) | Prostaglandin-synthetase (SSV) |
| Reserpine .. .. | $4{\cdot}8 \times 10^{-6}$ | $7{\cdot}3 \times 10^{-5}$ | $6{\cdot}3 \times 10^{-4}$ |
| Chlorpromazine .. | $3{\cdot}3 \times 10^{-4}$ | $1{\cdot}1 \times 10^{-4}$ | $1{\cdot}8 \times 10^{-4}$ |
| Diazepam .. .. | $2{\cdot}7 \times 10^{-5}$ | $5{\cdot}5 \times 10^{-4}$ | $9{\cdot}8 \times 10^{-4}$ |
| Meprobamate .. .. | $3{\cdot}7 \times 10^{-4}$ | $1{\cdot}8 \times 10^{-4}$ | $2{\cdot}1 \times 10^{-3}$ |

was assayed in homogenates of bovine seminal vesicles (Kunze & others, 1974a), phospholipase A in human seminal plasma (Kunze, Nahas & Wurl, 1974b) and prostaglandin synthetase in partially delipidated microsomes of sheep seminal vesicles (Kunze & others, 1974a), using an incubation mixture with EDTA buffer (125 mM; pH 8·0), 6·25 $\mu$M arachidonic acid and 0·25 mM reduced glutathione.

The results, as summarized in Table 1, indicate inhibition of prostaglandin biosynthesis by all tranquillizers studied. These drugs are more potent inhibitors than local anaesthetics (Kunze & others, 1974a), but are less active than the anti-inflammatory drug indomethacin (Flower, 1974). Meprobamate, the only drug lacking a tertiary amine group, apparently acts mainly through inhibition of phospholipase A. Inhibition by the other psychotropic drugs seems to be unspecific, in that both phospholipase A and prostaglandin synthetase activities are decreased. The concentrations required for inhibition of prostaglandin biosynthesis are fairly high, but these may occur locally *in vivo* in the brain, at least with meprobamate which is clinically administered at relatively high doses of about 400 mg day$^{-1}$ (Physicians' Desk Reference, 1973). In addition, lower concentrations of tranquillizers in the central nervous system could lead to the same degree of inhibition since it is known that bovine seminal vesicles generally require higher drug doses for a given inhibition than do other tissues (Flower, 1974). Whether inhibition of prostaglandin biosynthesis is involved in the basic mechanism of action of tranquillizers, or is a side effect, as postulated for local anaesthetics (Kunze & others, 1974a), has yet to be clarified.

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