ent terminals evoked by NMDA and similar excitants are caused indirectly via the release of another substance, possibly potassium into extracellular space.

Supported by the Medical Research Council.

Reference

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Clinically-used dyes are inhibitors of prostaglandin E_2 inactivation in rat isolated lung

Y.S. BAKHLE

Department of Pharmacology, Institute of Basic Medical Sciences, Royal College of Surgeons of England, Lincoln's Inn Fields, London WC2A 3PN

Indicator dyes such as bromcresol green and thymol blue prevent the inactivation of prostaglandin $F_{2\alpha}$ (Bito & Baroody, 1974) and prostaglandin E_2 (Bakhle, Jancar & Whittle, 1978) in rat isolated lungs. Other dye molecules are used in clinical practice for a variety of purposes and we have therefore studied the effect of some clinically used dye molecules on the pulmonary inactivation of prostaglandin E_2.

The inactivation of prostaglandin E_2 on a single passage through rat isolated lungs perfused with Krebs solution (8 ml/min) was measured by bioassay on the hamster stomach strip (Bakhle *et al.*, 1978). In each experiment the inactivation of prostaglandin E_2 was measured before, and 20 min after infusing the dye under investigation through the pulmonary circulation. The effect, if any, of the dye was rapidly attained (within 15 min) and remained constant for as long as the dye was infused. After the dye infusion was stopped, the inactivation tended to return towards the original level but recovery from dye treatment was not systematically studied. The results summarised in the Table show that all the dyes inhibited prostaglandin E_2 inactivation, the least potent being methylene blue.

The effect of the dyes can also be demonstrated by injecting the dye during an infusion of prostaglandin E_2. For instance, a constant infusion of prostaglandin E_2 (2 or 20 ng/ml) through the pulmonary circulation produced no contraction of the assay tissue superfused with lung effluent. However, an injection of sulphobromophthalein (0.25 μmole; 210 μg) through the lung caused a contraction equivalent to about 10 or 100 ng prostaglandin E_2 respectively. Injection of this dose of sulphobromophthalein directly to the tissue was without effect.

The results show that these dyes, and perhaps others in clinical use, interfere with at least one physiological process and suggest that the assumption that they are pharmacologically inert may no longer be valid.

References

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Table 1 Inhibition of pulmonary inactivation of prostaglandin E_2 by dyes

Concentration required (μM) to produce 20% inhibition				
Indocyanine green	*Sulphobromophthalein*	*Phenol red*	*Evans blue*	*Methylene blue*
(775)	(838)	(354)	(961)	(356)
<0.4	2.5	9	7	90

These values have been taken from dose–effect studies using at least two doses of dye and at least 8 separate experiments. The number in brackets is the MW of the dye.