Anti-allergy properties of PRD-92-Ea [5,5-Dimethyl-11-oxo 5H, 11H-(2) benzopyrano (4,3-g) (1) benzopyran-9-carboxylic acid ethanolamine]

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PRD-92-Ea inhibits the PCA reaction in the rat when given by oral or intravenous routes (Stewart, Devlin & Freter, 1974). However, PRD-92-Ea has also been reported to antagonize *in vitro* 5-HT, bradykinin, SRS-A and histamine (Possanza, Bauen & Stewart, 1975). Therefore, the anti-allergy profile of this drug has been further investigated in the guinea-pig and rat using an isotopic method for measuring increased vascular permeability (Morley, Wolstencroft & Dumonde, 1973).

Guinea-pigs and rats received an intravenous injection of 1–2 μCi of [^{125}I]-HSA in 2% Evans Blue Dye. Inflammatory responses were elicited at 12 sites of flank skin by local injection of irritant (eg 48/80) or antigen (egg albumin in the rat and BGG in the guinea-pig) into passively sensitized sites. Drugs were given intravenously, orally or locally. The use of local administration of both antigen and drug permits dose response curves to anti-allergy drugs to be adequately defined with small numbers of animals.

In the guinea-pig PRD-92-Ea caused little inhibition of IgG mediated PCA reactions whereas in the rat reaginic PCA reactions were strongly inhibited by local ($ED_{50} = 0.35$ μg/site) or systemic ($ED_{50} = 0.5$ mg/kg) administration. However, responses to 48/80 (1 μg/site) and peptide 401 (1 μg/site) were partially antagonized (up to 50%) in both species by local injection of PRD-92-Ea. Inflammatory responses in the guinea-pig to local administration of histamine (1 μg/site), 5-HT (60 μg/site) or bradykinin (0.5 μg/site) were not inhibited by local PRD-92-Ea up to a concentration of 2 mg/site. Similarly in the rat, comparable responses to these mediators were not antagonized by local injection of PRD-92-Ea up to 0.5 mg/site. Systemic injection of PRD-92-Ea (75 mg/kg) into guinea-pigs was found to reduce PCA, Arthus, 48/80, histamine and bradykinin reactions but such concentrations greatly exceeded the systemic doses which effectively inhibit rat PCA responses; $ED_{50} = 0.5$ mg/kg (El-Azab & Stewart, 1977).

These properties of PRD-92-Ea are consistent with this drug acting *in vivo* specifically as an anti-allergy agent rather than as an antagonist of putative mediator responses.

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Effects of D-penicillamine and levamisole on delayed hypersensitivity reactions in the rat and mouse

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D-penicillamine and levamisole are antirheumatic drugs with a late onset of action and differ from conventional non-steroidal anti-inflammatory agents in showing no anti-inflammatory effects in animal models (Huskisson, Dieppe, Scott, Trapnell, Balme & Willoughby, 1976). Their mode of action in rheumatoid arthritis is unknown but levamisole has been reported to stimulate both humoral and cell mediated immunity (Renoux & Renoux, 1972; Tripodi, Parkes & Brugmans, 1973). It has been suggested that D-penicillamine may possess similar immunostimulatory properties (Dieppe, Willoughby, Huskisson & Arrigoni-Martelli, 1976).

The effects of daily oral administration of 25 mg/kg D-penicillamine and 5 mg/kg levamisole upon delayed hypersensitivity reactions to *Bacillus pertussis* in the rat, and sheep red blood cells in the mouse were examined. Rats were implanted with sponges soaked in *B. pertussis* (Ford-Hutchinson, Smith, Elliott, Bolam, Walker, Lobo, Badcock, Colledge & Billimoria, 1975) having been sensitized twelve days