DEMONSTRATIONS

D.1

The assessment of systemically and topically administered anti-inflammatory drugs using u.v. erythema production in the rat

A.J. LEWIS

Scientific Development Group, Organon Laboratories Limited, Newhouse, Lanarkshire ML1 5SH

The delaying action of u.v. induced erythema by non-steroidal but not steroidal anti-inflammatory agents has been demonstrated using the guinea-pig (Winder, Wax, Burr, Been & Rosière, 1958). This anti-erythemic activity correlates well with the anti-inflammatory action of non-steroidal agents. The present study describes a similar model in the rat which is susceptible to both non-steroidal and steroidal anti-inflammatory drugs (AID). Moreover, topical administration of both types of drug is also capable of suppressing the erythematous response.

Male Wistar rats (80-100 g) were shaved and depilated by Veet-O cream. Twenty-four hours later the rats were exposed to u.v. radiation provided by a Hanovia Model 10 Quartz Lamp fitted with a Kodak 18A glass filter transmitting light above 290 nm wavelength. Erythema, assessed subjectively by two observers, was visible 1 h after u.v. exposure for 90 seconds. The maximal response occurred by 4 h in areas exposed for 90 s and longer and was replaced by scab formation by 48 hours.

Drugs were administered subcutaneously or orally in 5% mulgofen 1 h prior to u.v. exposure. Erythema was then assessed at 2, 4 and 24 h after irradiation. For topical administration the drugs were dissolved in ethanol and administered to rats after u.v. exposure. This was achieved by the application of the drug solution (0.2 ml) into a small cylindrical reservoir which surrounded the irradiated skin. Control irradiated animals received an equal volume of ethanol. These areas were immediately covered with Sleek plastic adhesive to prevent drug ingestion and the erythema was assessed 4 h later after removal of this dressing.

Drug treatments were randomized for all routes of administration and the assessors were unaware of the treatment of individual groups.

Both steroidal and non-steroidal AID administered subcutaneously and orally, respectively, delayed the erythema in a dose-related fashion. However, systemically administered steroidal AID suppressed the erythema by less than 50% at doses capable of inhibiting kaolin-induced paw oedemas by greater than 50%. Oral ID_{50} values (mg/kg in parenthesis) have been obtained for several non-steroidal AID including aspirin (148), ibuprofen (22), indomethacin (1.3) and phenylbutazone (17).

The topically administered drugs also produced dose-related suppression of the erythema and ID_{50} values are described in Table 1. A new non-halogenated steroidal agent, Org 6216 (11β-hydroxy-16α,17α,21-trimethyl-pregna-1,4-diene-3,20-dione), possessed very potent topical activity, similar to that shown by indomethacin.

In conclusion, a simple model is described that may be useful for the systemic and topical screening of compounds of potential use as anti-inflammatory drugs.

Table 1 Anti-erythema effects of topically administered AID

Drug	*ID_{50}(mg/rat)*
Org 6216	1.0
Indomethacin	1.3
Dexamethasone	4.8
Phenylbutazone	5.6
Betamethasone-17-valerate	7.8
Hydrocortisone	9.0
Aspirin	9.2
Flufenamic acid	10.9

Drugs administered in 0.2 ml ethanol immediately after u.v. exposure (90 s). Erythema was assessed 4 h after irradiation.

Reference

WINDER, C.V., WAX, J., BURR, V., BEEN, M. & ROSIÈRE, C.E. (1958). A study of pharmacological influences on ultraviolet erythema in guinea pigs. *Arch. int. Pharmacodyn.*, **116**, 261-292.