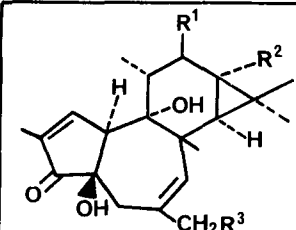


PRO-INFLAMMATORY AND TUMOUR PROMOTING PHORBOL AND 12-DEOXYPHORBOL ESTER-INDUCED CHANGES IN RABBIT SKIN MICROVASCULATURE

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Tigliane esters induce an inflammatory response in mammalian skin. The erythema and oedema which develops would suggest a typical inflammatory reaction characterised by hyperaemia and plasma exudation (Evans and Schmidt 1980). We have therefore examined the effects of seven compounds of this series in rabbit skin *in vivo*. The hair was clipped from the backs of male rabbits and 2 ml of Evans blue dye (2.5% w/v) containing ^{131}I -human serum albumen (15 $\mu\text{Ci}/\text{kg}$) was injected into the marginal ear vein. Brietal (1% w/v) was administered via the same cannula as an anaesthetic. Test solutions of esters (1 $\mu\text{g}/\text{ml}$ of 1% acetone in saline) containing ^{133}Xe (100 $\mu\text{Ci}/\text{ml}$) were injected intradermally (0.1 ml) in random block order according to a fixed site pattern. After 20 min animals were killed, the skin removed and the sites cut out by means of a steel punch. Samples were counted for radioactivity using an automatic γ -counter. Skin ^{131}I counts were expressed as volumes of blood plasma and flow changes were calculated as percentage changes of ^{133}Xe washout over that in control sites (Williams 1979).

	R ¹	R ²	R ³	% Blood flow change
		Tetradecanoate	Acetate	OH
	OH	OH	OH	not significant
	H	Phenylacetate	OH	-50±5
	H	"	Acetate	-35±5
	H	Angelate	OH	-43±6
	H	"	Acetate	-20±4

12-Deoxyphorbol-phenylacetate, 12-deoxyphorbol-angelate and their C-20 acetates induced vasoconstriction in rabbit skin in doses of 100 ng per site. Tetradecanoylphorbolacetate (TPA) was less active whilst phorbol the parent alcohol had no significant effects. The ability of tigliane esters to contract rather than dilate rabbit blood vessels was confirmed *in vitro*, in that each of the active compounds produced prolonged contraction of superfused rabbit aorta in doses of from 1 to 5 μg . Surprisingly also, these esters had no significant effects upon plasma exudation in rabbit skin. When repeated using 100 ng PGE_1 together with 100 ng of esters, plasma exudations of up to 40 μl per site were recorded. It has been shown (Williams 1976) that E series PG's produce a potentiation of exudation responses of histamine and bradykinin, whilst having little effect upon exudation alone. It is possible that the inflammatory reaction induced by tigliane esters is an indirect effect due to the release of mediators, rather than a direct pharmacological action on skin microvasculature.

Evans, F.J., Schmidt, R.J. (1980) *Planta Med.* 38: 289-316
 Williams, T.J. (1976) *Br. J. Pharmacol.* 56: 341-343
 Williams, T.J. (1979) *Ibid.* 65: 517-524