junctival smears examination, in which a differentiation between epithelial and reticulo-endothelial cells becomes particularly difficult if based, as commonly performed, solely upon morphological criteria. It cannot be excluded, however, that the macrophages present in the sub-epithelial layers of the conjunctiva, as normal constituents or evoked by the phlogistic process, can play a role in the infectious process as well as in the mechanism of immunity.

Riassunto. L'infezione di culture in vitro di macrofagi di topo con due diversi ceppi di agente del tracoma, determina la comparsa di tipiche inclusioni intracitoplasmatiche, e, in seguito, di lisi cellulare. Lo sviluppo delle inclusioni è stato studiato a tempi diversi dall'infezione. Sulla base dell'osservazione morfologica, si suppone che l'agente del tracoma possa moltiplicarsi in tali culture cellulari, determinando un secondo ciclo di infezione.

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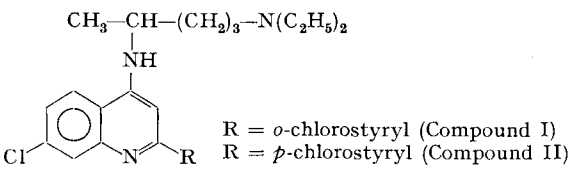
Antiviral Activity of some Derivatives of 2-Styrylquinoline

Various styrylquinolines have been shown to possess antimicrobial activity against nemathelminthes[1], protozoa[2,3], fungi[3], and bacteria[3]. In addition, inhibition of tumors has been reported from time to time[4-6]. These studies and the recent finding that chloroquine inhibited replication of a DNA bacteriophage[7] have encouraged us to investigate the antiviral activity of this broad group of compounds. Two 4-diethylaminoalkylamino derivatives of 7-chloro-2-styrylquinoline[3] (I, II) were studied in our standard virus-assay systems and found to possess significant activity against Semliki Forest Virus (SFV).



R = *o*-chlorostyryl (Compound I)
R = *p*-chlorostyryl (Compound II)

In vivo activity of 2 styrylquinolines against Semliki Forest Virus

Experiment No.	Compound	Drug dose (mg/mouse at stated times)	Treatment regimen[a]	Challenge dose of Virus (LD_{50}/mouse)[b]	Antiviral activity (% S/T)[c]
I	1	2.5	A	2.0	50
		0.25			0
		0.025			0
	–	–	–	–	–
	2	2.5	A	2.0	50
		0.25			0
		0.025			0
	control	–	–	2.0	0
II	1	1.0	B	2.5	100
	2	1.0	B		70
	control	–	–	2.5	10
III	1	1.0	C	3.5	30
	control	–	–	3.5	0
IV	1	1.0	D	16	54
	control	–	–	16	0

[a] Animals were treated by s.c. injection: (A) 2 h before, and then 24 and 48 h after infection; (B) 24 and 4 h before, and at 4, 24 and 72 h after infection; (C) at 30 min; 24, 48 and 72 h after infection; (D) same protocol as B except that last dose was given 48 h after infection. [b] Route of infection was i.p.; LD_{50} = lethal dose, 50% endpoint. [c] Per cent surviving animals 2 weeks after challenge.

The drugs were solubilized in distilled water and injected s.c. using multiple dosage schedules as summarized in the Table. At non-toxic concentrations, both compounds protected significant numbers of mice from the lethal effects of SFV infection especially when treatment regimens included prechallenge drug doses. When compound I was incubated in vitro with approximately 3.5 LD_{50} (mouse) of SFV prior to injection into mice by the i.p. route, more than 85% of the test animals survived. 2 weeks after challenge, survivors from all experiments appeared to be healthy and free from the signs of paralysis so characteristic of SFV infection in this species. The small skin lesion, which occurred at the site of injection, was grossly resolved at this time.

Since SFV is a neurotropic virus, but at the same time is an uncommon natural human or animal pathogen, it would be of interest to see whether these or other styrylquinolines would act against human neurotropic viruses. Preliminary data from this laboratory suggest that compound I and II may have marginal activity against influenza virus (type A, PR_8) in mice, but not in eggs. Neither compound appears to possess significant activity against vaccinia virus in eggs or in rabbits.

The mode of antiviral action of these 2 styrylquinolines remains to be elucidated.

Zusammenfassung. In Mäuseversuchen wurde gezeigt, dass gewisse Styrylquinoline in vivo eine Wirkung gegen Semliki-Forest-Virus haben.

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