ORAL DELIVERY OF VIRAL PROTEIN ANTIGENS USING LIPID CARRIER SYSTEMS

J C Bowen, H O Alpar and M R W Brown, Pharmaceutical Sciences Institute, Aston University, Aston Triangle, Birmingham B4 7ET

Immune responses can be induced by non-parenteral routes. In some cases the orally induced immune responses can be almost identical to those obtained by parenteral immunisation (Thomas & Parrot 1974; Rothberg et al 1967). The stimulation of antibody production is influenced by the route and schedule of administration, the vaccine preparation and the adjuvant used (Karen et al., 1988). Oral vaccine delivery is convenient.

The present study was designed to investigate the production of HSV - specific serum antibodies in guinea pigs vaccinated by the oral route with the Herpes simplex virus (HSV) subunit (glycoprotein) vaccine.

Three groups of guinea pigs (n=8 per group) were orally dosed with 300 μ g of vaccine either as an aqueous preparation, a double emulsion or liposome formulation 5 and 3 weeks before vaginal challenge with HSV 2 virus suspension. Control groups (n=8 per group) of infected and non-infected individuals were also tested in parallel with the dosed animals. The preparation of emulsions and solid (DSPC) liposomes was carried out as described previously (Alpar et al 1989; Kirby & Gregoriadis 1980). A high efficiency of encapsulation of glycoprotein into liposomes was achieved (75% \pm 1.65).

Serum samples were obtained before vaccination prior to virus challenge (day 0) and on day 10 post challenge. The ELISA results showed that the post vaccination HSV - specific IgG antibodies for the oral emulsion have reached slightly higher titres (10.42 \pm 0.91) than that of oral aqueous formulation (9.47 \pm 0.79) without showing any protection. Although antibody titre exhibited by the liposome formulation group (9.75 \pm 0.41) was comparable to that of the emulsion group, the liposome group showed a moderate protection as depicted by a significant reduction in degree of oedema and number of genital lesions (combined measure giving clinical scores) produced after challenge (Table 1). Titres of uninfected controls were not different from the pre-vaccination titres (7.97 \pm 0.63).

Controls		HSV Vaccine Delivered with		
Uninfected	Infected Only	Aqueous Solution	Double Emulsion	DSPC Liposomes
11.3 ± 0.32	27.8 ± 3.11	24.8 ± 1.52	25.6 ± 1.40	12.9 ± 0.73

Table 1 Clinical Scores* day 10 post viral (HSV 2) Challenge

*(Size of Lesion in Relative Units)

Since significant amelioration of the disease cannot be associated with high antibody titres, the protection observed with liposomal delivery is probably due to non-humoral protection (the cellular immune responses).

Thomas, H. C. and Parrot, M. V. (1974) Immunology 27: 631-639 Rothberg, R. M. et al (1967) Immunology 130: 1413-1418 Karen, D. F. et al (1985) Infect. Immun. 47: 123-128 Alpar, H.O. et al (1989) J.Pharm Pharmacol. 41: 137P Kirby, C.J. and Gregoriadis, G. (1980) Biotechnology (Nov) 979-984

146P