NON-PARENTERAL DELIVERY OF TETANUS TOXOID VACCINE USING LIPOSOMES

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We are attempting to optimise the delivery of antigens for mucosal and systemic immunisation using non-parenteral routes to produce a comparable or more efficient response than the conventional subcutaneous (S.C.) method. The stimulation of antibody production is influenced by the route and schedule of administration, the vaccine preparation and the adjuvant used (Karen et al 1985). The present study involves the production of tetanus toxoid - specific serum antibodies in guinea pigs vaccinated, via the oral and nasal routes, with the tetanus vaccine formulated in DSPC (Distearoyl Lecithin) liposomes. Tetanus toxoid is a very high molecular weight protein. It has already been shown that liposomes can act as immunological adjuvants for various antigens (Davis et al 1986). Encapsulation efficiency (70% ± 1.8) and release characteristics of the tetanus toxoid from liposomes were studied using Lowry protein assay and HPLC techniques.

Pigmented guinea pigs (n=5 per group) were immunised via oral and nasal routes. A vaccine dose of 60 µg tetanus toxoid was given nasally and orally on weeks 1, 2 and 4 in phosphate buffered saline (PBS) or in liposomes. In addition, 6 µg of tetanus toxoid in PBS was given via the normal parenteral route of delivery (intramuscular, i.m) on weeks 1 and 4 for control.

Serum samples were collected from the guinea pigs at intervals during the immunisation. Antibody responses to the tetanus toxoid were monitored by a microplate ELISA method. Results showed that tetanus toxoid given orally or nasally in PBS or entrapped in DSPC liposomes will result in a specific IgG response. Although by week 6, antibody titres for nasal route and i.m. delivery were comparable by week 20, all the formulations delivered using the mucosal routes appeared to be identical and much higher than pre-vaccination values (Table 1). Oral liposomal delivery produced an increase in titres. The liposomes on the whole did not appear to have an adjuvant effect on the immune response to tetanus toxoid. High titres using the i.m. route were sustained during the experimental period.

Table 1 Geometric mean (log_2) ELISA titre of serum IgG Antibody

Route	Formulation	Pre-bleed	Week 3	Week 6	Week 20
i.m.	PBS	6.6 (±0.18)	7.0 (±0.19)	11.7 (±0.99)	11.4 (±1.48)
oral	PBS	7.3 (±0.55)	7.3 (±0.55)	8.5 (±2.06)	9.0 (±0.83)
oral	Liposomes	6.4 (±0.18)	6.4 (±0.13)	10.0 (±0.83)	9.7 (±2.2)
nasal	PBS	6.1 (±0.61)	6.2 (±0.42)	11.4 (±1.5)	9.7 (±1.21)
nasal	liposomes	6.9 (±0.27)	6.8 (±0.27)	10.5 (±0.72)	9.6 (±0.56)
Control		6.3 (±0.13)	6.3 (±0.40)	6.6(±0.16)	6.4 (±0.21)

In conclusion, oral and nasal delivery of the tetanus vaccine appears to show promise and worthy of further investigation.

Davis, D.A. et al (1986/87) Immunology Letters.14: 341-348
Karen, D.F. et al (1985) Infect. Immun. 47: 123-128