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Optimization and Evaluation of a Potential Immunomodulator-loaded Nanoparticulate Nasal Vaccine

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Objective. Development and characterization of a biodegradable nanoparticulate nasal vaccine formulation using NALT-associated receptor ligand (NARL) for induction of enhanced immune responses against a model protein antigen (MPA).

Methods. Chitosan-dextran sulphate (CS-DS) nanoparticles were prepared using an ionic gelation/coacervation technique. The optimized nanoparticle formulation was loaded with NARL and MPA and this delivery system was evaluated for *in-vitro* (particle size, zeta potential, electron microscopy, entrapment efficiency, release profile and stability) and *in-vivo* (uptake of nanaoparticles in nasal epithelia) parameters using various techniques including photon correlation spectroscopy, ELISA, SDS-PAGE and confocal microscopy. Further *in-vivo* studies to compare and evaluate immune responses induced by developed formulation are in progress.

Results. CS-DS blank nanoparticles of size and zeta potential in the range of 150 to 400nm and -40 to +60mV respectively, were obtained by this simple method of preparation. An optimized blank CS-DS nanoparticle formulation with particle size 288.4±7.8 nm, zeta potential +31.8±1.6 mV and isoelectric pH 8.9 was used to load MPA or NARL or MPA and NARL. The release study of loaded nanoparticles revealed that only small proportion of NARL or/and MPA (< 25%) get released in initial 6hours. A preliminary *in-vivo* study indicated that NARL-loaded nanoparticles were taken up specifically by nasal associated lymphoid tissue (NALT) in mouse nasal mucosa.

Discussion. The ratio of CS to DS, order of mixing and pH of nanoparticle suspension were identified as important formulation factors governing size and zeta potential of nanoparticles, which in turn affect stability and entrapment efficiency of the formulation. The uptake of nanoparticles by NALT indicates that particulate nature of the formulation and incorporation of NARL may enhance the uptake through NALT cells. The study indicated the potential relevance of NARL as a novel immunomodulator for nasal particulate delivery systems.

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A randomised trial of kunzea oil in comparison with amorolfine nail lacquer for the treatment of toenail onychomycosis

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Introduction: Onychomycosis is a fungal infection of the nail plate or nail bed. It is caused by dermatophytes, other moulds or yeasts. Kunzea oil is listed as a medicine by the Therapeutic Goods Administration in Australia for topical application. It has potent *in vitro* inhibitory action against various dermatophytes and yeast spp. The objective of this study was to compare the effectiveness and tolerability of kunzea oil with amorolfine nail lacquer, in the management of toenail onychomycosis.

Methods: Subjects with toenail onychomycosis affecting at least one great toe were recruited through the Royal Hobart Hospital Podiatry Department. A nail clipping and scraping of the nail bed was taken for mycological examination and only those patients with confirmed dermatophyte onychomycosis and at least 20% involvement of the nail were eligible for the trial. Outcome measures included measures of affected area, healthy toenail area, severity of nail thickening and mycological examination. The study period was 40 weeks.

Results: Ninety-three subjects with culture-confirmed onychomycosis were divided into two groups: test group (n= 32) received topical treatment with kunzea oil, while control group (n= 39) applied amorolfine lacquer. At completion of the trial (week 40±2), both trialled medications were comparable (P>0.05) in symptomatic efficacy assessment parameters (diseased toenail area, disease severity scores). In both test (from a mean (± s.d.) value of 2.0 ± 0.99 cm^2 to 1.24 ± 0.83 cm^2) and control (from a mean (± s.d.) value of 1.81 ± 0.86 cm^2 to 1.16 ± 0.57 cm^2) groups, the diseased toenail area was significantly (P<0.001) decreased after 40 weeks of treatment. Additionally, the healthy nail area in the diseased great toenail showed significant growth in both test ([showing a mean (± s.d.) value of 1.35 ± 0.93 cm^2 to 2.03 ± 1.68 cm^2)]; and control ([displaying a mean (± s.d.) value of 1.58 ± cm^2 to 2.29 ± 1.33 cm^2]) groups after completion of the treatment period. In both treatment measures there was no difference (P>0.05) between treatment regimens. However, the mycological cure rate was higher (P<0.05) in the amorolfine group (95%) compared with the kunzea oil group (45%). The incidence of adverse events was rare (2 cases of minor adverse skin reactions found in the test group and none noted in the control group) for both trial medications.

Discussion: In conclusion, kunzea oil shows a promising potential as a cheap, effective and alternative topical modality for the management of onychomycosis.