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Patterns of binding of aluminum-containing adjuvants to *Haemophilus influenzae* Type B and *Meningococcal* group C conjugate vaccines and components

Robert B D Otto
Makerere University, Uganda

The basis of *Haemophilus influenzae* type b (Hib) and *Neisseria meningitides* serogroup C (MenC) glycoconjugates binding to aluminum-containing adjuvants was studied. By measuring the amount of polysaccharide and protein in the non-adsorbed supernatant, the adjuvant, aluminum phosphate, AlPO4, was found to be less efficient than aluminum hydroxide, Al(OH)3 at binding to the conjugates, at concentrations relevant to licensed vaccine formulations and when equimolar. At neutral pH, binding of TT conjugates to AlPO4 was facilitated through the carrier protein, with only weak binding of AlPO4 to CRM_{197} being observed. There was slightly higher binding of either adjuvant to tetanus toxoid conjugates, than to CRM_{197}–conjugates. This was verified in AlPO4 formulations containing DTwPeHib, where the adsorption of TT-conjugated Hib was higher than CRM197–conjugated Hib. At neutral pH, the anionic Hib and MenC polysaccharides did not appreciably bind to AlPO4, but did bind to Al(OH)3, due to electrostatic interactions. Phosphate ions reduced the binding of the conjugates to the adjuvants. These patterns of adjuvant adsorption can form the basis for future formulation studies with individual and combination vaccines containing saccharide-protein conjugates.

r.bdotto@yahoo.com

Solvent exchange-induced *in situ* forming gel comprising eudragit RS-antimicrobial drugs

Thawatchai Phaechamud, Jongjan Mahadlek and Tiraniti Chuenbarn
Silpakorn University, Thailand

Eudragit RS (ERS), a quaternary polyacrylate positively charged polymer, exhibits a very low permeability and swells in aqueous media independently of pH without dissolving. Owing to its high solubility in N-methyl pyrrolidone (NMP) it was interesting to apply as polymer matrix for solvent-exchanged *in situ* forming gel which this drug delivery system was in sol form and transforming into solid-like after injection and exposure to the aqueous fluid of the body. The aim of this research was to study the parameters affecting the gel properties, drug release and antimicrobial activities of the *in situ* forming gels prepared from Eudragit RS dissolved in NMP to deliver the antimicrobial agents (doxycycline hyclate, metronidazole and benzyl peroxide) for periodontitis treatment. The solvent exchange between NMP and an external aqueous simulated gingival crevicular fluid stimulated the dissolved Eudragit RS transforming into the opaque rigid gel. Doxycycline hyclate, metronidazole and benzyl peroxide loaded-ERS systems exhibited Newtonian flow which their syringeabilities were acceptable. The higher-loaded Eudragit RS promoted the more prolongation of drug release because of the retardation of water diffusion into the precipitated matrix. Antimicrobial activities against *Staphylococcus aureus, Escherichia coli, Candida albicans, Streptococcus mutans and Porphyrommonas gingivalis* depended on type of drugs and test microorganisms. Doxycycline hyclate loaded-Eudragit RS systems showed these activities greater than the others however all of them could inhibit the all test microorganisms. Thus the solvent exchange-induced *in situ* forming gels comprising Eudragit RS-antimicrobial drugs exhibited potential use as localized delivery systems for periodontitis treatment.

thawatchaienator@gmail.com