A METHOD FOR THE COVALENT ATTACHMENT OF MONOCLONAL ANTIBODIES TO NANOPARTICLES

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Polyalkylcyanoacrylate nanoparticles coated with monoclonal antibody (anti-osteogenic sarcoma) are able to interact specifically with target tumour cells in vitro (Illum et al, 1983). However, the intravenous administration of these immuno-nanoparticles to mice bearing human tumour xenografts resulted mainly in deposition of the particles in the liver with no significant tumour uptake (Illum et al, 1984). This lack of in vivo specificity was primarily considered to be due to displacement of antibody by serum proteins. However, it should be possible to overcome such displacement by attaching the antibody covalently to the nanoparticles. This communication describes the feasibility of linking antibodies and other amines to nanoparticles via dextran molecules used as stabilisers in nanoparticle formation and present at the particle surface (Douglas et al, 1985).

Nanoparticles were formed by the aqueous dispersion polymerisation of butyl 2-cyanoacrylate in the presence of dextran 70 (Douglas et al, 1985). After isolation, by centrifugation, the nanoparticles were suspended (10mg/ml) in 0.4% sodium periodate solution to oxidise the surface dextran. A simple amine, aniline, was used as a model compound for covalent coupling to the aldehyde groups introduced by the periodate oxidation. The uptake of aniline from solution in McIlvaines buffer by oxidised and non-oxidised nanoparticles was determined spectrophotometrically. Figure 1 shows that the uptake was greatly enhanced for nanoparticles treated with periodate in the pH range of 3-7 compared to non-treated particles. The optimum pH for coupling was found to be 4 for aniline. Adsorption isotherms were constructed at pH4 and a maximum uptake of ~ 5 x 10^{-4} mole aniline per gram nanoparticles was found for covalently linked aniline. This corresponds to approximately 25% of the total theoretical capacity for covalent binding via imine formation. Furthermore, the release rate of aniline into buffer solution was reduced markedly for covalently linked aniline. These initial studies demonstrate the potential of covalently coupling amino compounds to the nanoparticle surface. Theoretically application of this technique to the linking of antibodies should overcome the problem of antibody displacement. Covalent coupling may also be useful for increasing the payload of nanoparticles for basic cytotoxics and for decreasing the release rate of these compounds.

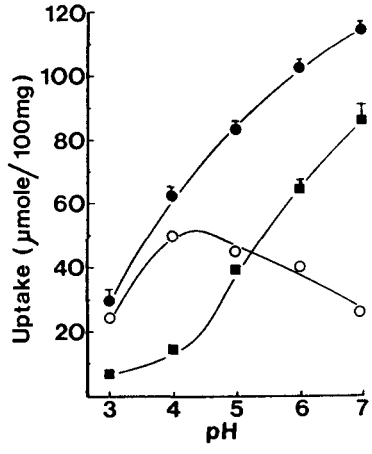

Figure 1. Uptake of aniline onto nanoparticles (■) and periodate treated nanoparticles (●) as a function of pH. Subtraction of the two curves gives the uptake due to covalent linking (○). (n=3, bar = standard deviation).

Douglas, S.J., et al (1985), J. Colloid Interface Sci., 103:154-163

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