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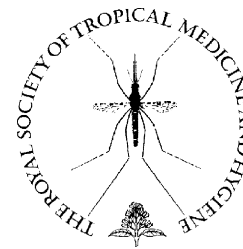
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MINI-REVIEW

Potential impact of nanotechnology on the control of infectious diseases

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Summary Nanotechnology encompasses those technologies used to fabricate materials, including sphere, cubic and needle-like nanoscaled particles (approximately 5–100 nm), and near-nanoscaled devices (up to micrometres). In comparison, mycoplasma are approximately 200 nm in length, and a nanometre is 10^{-9} of a metre. The field of nanotechnology is experiencing rapid growth, with many and diverse potential applications being explored in the biomedical field, including the control of infectious diseases. Nanotechnology not only has the potential to offer improvements to current approaches for immunisation, drug design and delivery, diagnostics and cross-infection control, but is also unexpectedly delivering many new tools and capabilities.

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The potential of nanoparticles to be used as novel adjuvants and the use of nanoemulsions as colloidal vaccine carriers are being explored in the field of immunisation. Calcium nanoparticles have been examined as a vaccine adjuvant to anti-idiotypic antibody against schistosomiasis (Fang et al., 2004). Nanoemulsions, which consist of minute droplets of oil suspended in water and stabilised by detergents, are finding applications for both prevention and treatment of a wide variety of infections. Droplets in nanoemulsions are surface active and react specifically with the outer membrane of infectious organisms. In pre-clinical trials with animals at the University of Michigan, mixtures of the nanoemulsion with either whole virus or protein have been tested as potential vaccines. Such vaccines, which do not require

cold storage and can be administered via the mucosal route, would be particularly suitable for application in developing countries.

Exploitation of the toxic properties of nanoparticulate metals and metal oxides, in particular those that produce reactive oxygen species under UV light, are finding increasing use in antimicrobial formulations and dressings within and outside the hospital environment. Silver and copper and their compounds have been widely studied. In particular, nano silver particles (5–40 nm) have been reported to inactivate most microorganisms, including HIV-1. The high reactivity of titanium dioxide and silicon dioxide is exploited extensively for the bactericidal purposes of these substances in filters and coatings on substrates such as alumina (Han et al., 2005). Significant activity using the latest generation of nanoparticles, and their compound clusters, against fungal and bacterial pathogens, such as methicillin-resistant *Staphylococcus aureus* (MRSA) and *Escherichia coli* has recently been demonstrated at Queen Mary, University

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of London, UK. Research carried out by Retroscreen Virology, Queen Mary and QinetiQ Nanomaterials has also shown the capability to inactivate viruses, including severe acute respiratory syndrome (SARS) and bird flu. For example, specially developed nanoparticle clusters can reduce virus levels by 80–100% through direct contact.

Nanotechnology is finding uses in the rapid diagnosis of infectious diseases, whereby the increased functional surface area per unit volume can be exploited. Biosensors, devices in which a biological sensing element is either intimately connected to or integrated within a transducer, are being developed. Nano-fabricated structures, coated with elements such as gold that have affinity for biomolecules, are incorporated into these biosensors. For example, a rapid method for the detection of urinary tract infection, caused by *E. coli*, has been developed with the application of such an approach (Basu et al., 2004). The detection system, partly based upon ELISA technology, utilises anti-*E. coli* antibody-bound gold nanowire arrays on an anodised porous alumina template. It has also been shown possible to detect minute amounts of target DNA strands with complementary DNA linked to gold nanoparticles (Cao et al., 2002). This particular approach is also finding applications in the detection of single-nucleotide polymorphisms in microarray-based systems. It has even been possible to distinguish antibiotic-resistant bacteria, such as *Staphylococcus aureus*, from non-resistant strains. In addition, biosensors and nucleic acid detection methods are finding applications for the rapid detection of biological warfare agents. In the future, assays based upon the use of magnetic nanoparticles should also offer very sensitive and rapid detection methodologies.

The fundamental properties and bioactivity of drugs and other materials can be changed at the nanometre level. In theory it should be possible to control the characteristics of drugs, including solubility, controlled release and specific site-targeted delivery. A nanotechnological approach to formulate suitable colloidal carriers for the delivery of drugs and genes is currently under investigation by many laboratories. Chitosan-coated nanocapsules as triclosan carriers have been found to be particularly effective in this capacity. This approach may be of use in the delivery of triclosan as an effective antimalarial drug by inhibiting the growth of *Plasmodium falciparum* (Maestrelli et al., 2004). Chitosan can

also effectively bind DNA and protect it from nuclease degradation in vivo. The application of DNA–chitosan nanospheres for gene delivery is currently under investigation.

In theory, certain nanoparticles may be retained within the body for longer than is desirable; thus, the safety profile becomes a matter of overriding significance. Nanomaterials are able to cross biological membranes and gain access to cells, tissues and organs that larger-sized particles normally cannot. Nanomaterials can gain access to the bloodstream following inhalation or ingestion, and some can even penetrate the skin. However, recent studies have shown that a particle's surface chemistry can govern whether it will be suitable for biomedical applications. It remains to be determined how potential toxicity issues will fully impact on the use of nanotechnology in the control of infectious diseases.

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