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Solid drug nanoparticles as oral and long acting parenteral drug delivery for infectious diseases

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Nanomedicine has focused heavily considerably on acute disease over several decades; however, there is considerable clinical need for new interventions for infectious disease prevention and therapy that allows patients to manage currently life-long conditions. Oral dosing is the only widely patient-acceptable administration format for chronic disease as daily, or more frequent, injections are not well tolerated. For prevention of disease and long term therapy, adherence to dosing regimens is critical to either maintain control or maintain protection over long periods. Here, we have generated a new approach to Solid Drug Nanoparticle (SDN) formation and rapid candidate therapy identification that allows 1000's of nanoparticle options to be generated and accelerated through a series of pharmacological tests to establish potential benefits. Two case studies will be presented, namely a candidate for reduced oral dose HIV therapy and a prophylactic antimalarial injection that provides long-term protection to infection.

Methodology & Theoretical Orientation: Solid drug nanoparticle candidates were generated using an accelerated Emulsion-Templated Freeze Drying (ETFD) screening approach in both cases of HIV and malaria nanomedicine production. "Hits" were selected based on their chemical performance and progressed to a series of pharmacological studies that characterized a number of relevant factors. "Leads" were selected based on their pharmacological potential and, in the case of HIV candidate nanomedicines, translated from ETFD screen manufacture to cGMP production using Emulsion Spray Drying (EFD). Powdered products from EFD were hand filled into capsules for human healthy volunteer evaluation.

Findings: Oral dosing of two HIV antiretroviral SDNs has shown the potential for a 50% reduction of the dose of drug within daily regimens containing efavirenz or lopinavir. In the case of antimalarial prophylaxis, an intramuscular depot injection of SDNs has been shown to produce a minimum of 28 day protection in a mouse model, offering possible long-term protection in future human studies.

Conclusion & Significance: Combined and systematic solid drug nanoparticle screening by both materials chemistry and pharmacology allows rapid identification of new nanomedicine candidates for diverse diseases with the potential for rapid translation to clinic.

Biography

Steve Rannard is a materials chemist at the University of Liverpool (UoL) where he holds a personal Chair in the Department of Chemistry. He is the academic lead for Nanomedicine within the Materials Innovation Factory and Director of the Radiomaterials Laboratory. Steve spent 16 years in industry (Cookson, Courtaulds, Unilever) and has co-founded three start-up companies (IOTA NanoSolutions Ltd, Hydra Polymers Ltd and Tandem Nano Ltd). Since returning to academia in 2007 his collaborative grant income from funders including MRC (UK), EPSRC (UK), NIH (US), USAID, CRUK, CHAI, and BSAC (UK) and industry has exceeded £16m and his current research focuses materials science onto unmet medical/clinical needs to target new patient benefits using scalable polymer nanoparticle synthesis, solid drug nanoparticle formulation and nanoemulsion platforms.

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