Preparation and characterisation of acrylate-based microparticles, of varying compositions and sizes, for photosensitiser incorporation

J. V. Moore, C. P. McCoy, N. J. Irwin, L. Carson, G. P. Andrews,
School of Pharmacy, Queen's University Belfast, Northern Ireland, BT9 7BL, UK

Introduction: Photosensitisers (PSs) are agents that generate reactive oxygen species (ROS), in the presence of oxygen, when illuminated with low intensity light from the visible region of the electromagnetic spectrum [1]. Photodynamic antimicrobial chemotherapy (PACT) exploits the cytotoxic nature of these ROS to destroy a range of microorganisms, thus an array of potential applications for this therapy have been investigated; from treating infections to the production of materials with inherent antimicrobial properties. The majority of PACT studies to date suggest the need for intracellular PS uptake by the target microorganism to elicit a cidal action upon light activation. However, previous work carried out in our group has successfully demonstrated the permanent localisation of PSs to hydrogel surfaces for antimicrobial applications, such as the development of a novel photoactive intraocular lens biomaterial. The mechanism of action of these photoactive materials relies on diffusion of the generated singlet oxygen from their surface to cause photo-oxidative damage to microbial cells in the immediate vicinity [2-5]. For such materials the available surface area could influence the quantity of PS incorporation, thus potentially limiting its microbicidal activity. Here we report the production and characterisation of acrylate-based microparticles, of varying compositions and sizes, which provide large surface areas for PS attachment.

Methods: Polymer monoliths with different compositions and charges were synthesised: p(HEMA), p(MMA), p(HEMA-co-MMA), p(HEMA-co-DEAEMA), and p(HEMA-co-MAA). Mixtures of the required monomers, an ethyleneglycol-dimethacrylate crosslinker, and a thermal initiator were injected into moulds and polymerised via free radical polymerisation. An oscillatory ball mill (Retsch MM200) was used to mechanically break up the polymer films to produce particles within the micron size range. Milling parameters were kept constant except for duration, which ranged from 1-12 minutes depending on the material's physical hardness. The particles produced were separated using sieves with a range of pore sizes: 45, 63, 90, 180, 250, and 355 μm. A Keyence optical digital microscope was used to analyse the particle size distribution and quality for each sample. A concentrated cationic PS solution was used to load the p(HEMA-co-MAA) particles of various sizes. PS uptake was confirmed qualitatively by Fourier Transform Infrared (FTIR) spectroscopy and quantified using a UV-Vis spectroscopy method.

Results: The five different polymer compositions were chosen to produce polymeric microparticles with varing chemical and physical properties to allow incorporation of a variety of PS types. Following analysis of particle quality and size distribution of the milled samples, a 4 minute milling duration was considered optimum for the three brittle, non-MMA containing polymers. The physically hard, MMA-containing particles had an overall improved quality, however considerably less of the particles produced fell into the 0-90 μm size range despite the extended milling periods (up to 12 minutes). The p(HEMA-co-MAA) microparticles were taken forward for preliminary PS incorporation studies. Similar to the method used in previous work to localise PSs to hydrogel surfaces, a cationic PS was electrostatically bound to the carboxylate groups of the MAA-containing particles [2-4]. Initial work showed successful uptake of the PS by the particles. FTIR spectroscopy confirmed non-covalent PS incorporation to the polymer microparticles. UV-Vis spectroscopy was used to quantify PS uptake, with an increase in uptake observed with a rise in particle surface area: 4.48 ± 0.15 %w/w for the largest particles compared to 6.33 ± 0.06 %w/w for the smallest.

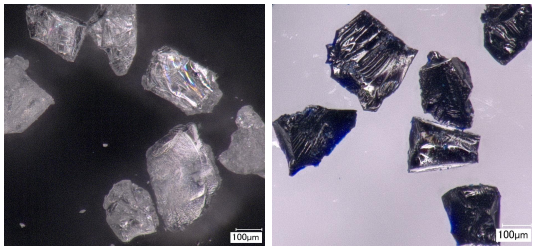

Figure 1: p(HEMA-co-MAA) particles within the 181-250 μm size range before (left) and after (right) PS loading.

Conclusion: A ball milling technique was successfully employed to produce acrylate-based microparticles of controlled size. Initial analysis of PS uptake by the p(HEMA-co-MAA) microparticles suggest the potential for these particles, along with the other candidate particles, to provide large surface areas for PS incorporation and subsequent photocatalytic generation of ROS for antimicrobial applications. Future work will be conducted to assess the antimicrobial efficacy of different PS/polymer microparticle combinations against a broad range of microorganisms.

Abbreviations used: 2-hydroxyethyl methacrylate (HEMA); methacrylic acid (MAA); 2-diethylaminoethyl methacrylate (DEAEMA); methyl methacrylate (MMA)

[1] Hamblin MR. Photochem Photobiol Sci. 2004;3:436–450 [2] Brady C. J Phys Chem B. 2007;111: 527–534 [3] Parsons C. Biomaterials. 2009;30:597–602 [4] McCoy CP. Biomaterials. 2012;33:7952-7958 [5] Craig RA. Expert opinion on drug delivery. 2015;12:85-101