Clostridium difficile specific bacteriophage microencapsulation within porous Eudragit particles and pH dependent controlled release for colon targeted delivery

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The global threat to human health from antimicrobial resistance in infection causing bacteria has led to renewed interest in the potential of phages as therapeutic agents. In *Clostridium difficile* infections of the colon, targeted delivery of viable phages to the site of infection is important. The punitive environment of the gastrointestinal tract can potentially render free phages inactive prior to reaching the site of infection. Here, we describe the encapsulation and release kinetics *in vitro* of a model *C. difficile* specific *myoviridae* bacteriophage, Phi9CD-KM. The phages were encapsulated in Eudragit® S100 which is a methacrylic acid / methyl methacrylate copolymer; it is insoluble at low pH levels and soluble at the pH of the colon (pH ≥7), making it a suitable encapsulation agent for protecting acid-sensitive phages. Core-shell droplets were produced using a two-phase glass capillary device with counter-current flow focusing (Figure 1). In the absence of encapsulation, phages were rendered inactive within minutes upon exposure to a pH 2 solution mimicking simulated gastric fluid. Release kinetics of the encapsulated phage was studied in different pH solutions. A burst release of phage occurred at pH 7. Slow controlled release over several hours was observed at pH 6.

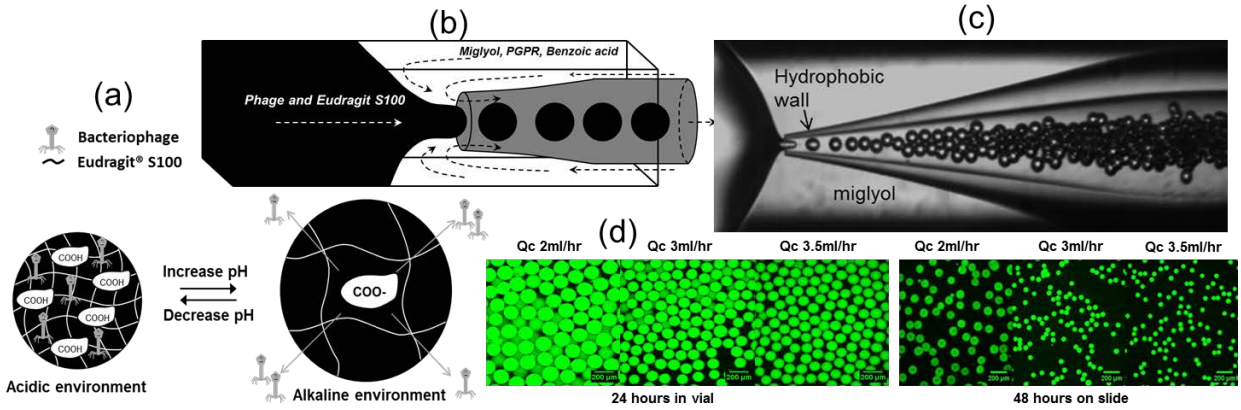

Figure 1. a) Schematic to show the polymer release mechanism; b) schematic of the glass capillary microfluidic device for particle generation; c) screen shot of droplet formation; d) SEM of phage encapsulated particles.