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| Title | **Infection Responsive Delivery of Glycoside Hydrolase and Antibiotic Combination** |
| Keywords (up to 5) | Liquid crystalline, drug delivery, glyceryl monooleate, antimicrobial resistance |
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| Abstract | In light of the looming crisis of antibiotic resistance, novel treatments for highly resistant bacterial infections are trending towards local, co-administration of antibiotics with bio-macromolecules such as enzymes [1]. Highly potent glycoside hydrolases have been developed, such as alginate lyase, to improve the effectiveness of antibiotics against bacterial biofilm infections [2]. With poor stability and the need for local administration of alginate lyase combined with antibiotic gentamicin, nanostructured liquid crystalline gels are a potential protective carrier.  Liquid crystalline gels can be constructed from lipids intercalated with aqueous channels to form mesophases that afford drug delivery [3]. Glyceryl monooleate (GMO) is a lipid commonly used to fabricate liquid crystalline gels, although has a limited application in oral drug delivery due to degradation by pancreatic lipases, resulting in premature drug release, decreasing the benefit of the carrier [4]. Alternatively, for bacterial biofilm infections that require topical treatment, the degradation of gel-structure, resulting in drug release, could be exploited as a response to the bacteria, which secrete lipases as a virulence factor [5]. GMO liquid crystalline gels were therefore investigated for release of alginate lyase and gentamicin in the absence and presence of bacterial lipase, along with the protective ability of the gel compared to solution treatments against *in vitro Pseudomonas aeruginosa* (clinical isolate) biofilms.  Alginate lyase was released to a limited extent (20% over one-week), compared to the rapid release of gentamicin (80% in 48 hours). However, the addition of bacterial lipase substantially increased the release of alginate lyase (three-fold over five-days). Following, the liquid crystalline gel demonstrated equivalent anti-microbial activity of alginate lyase and gentamicin (2.5 log reduction in bacteria) compared to an unformulated solution. GMO liquid crystalline gels are a promising protective carrier, affording infection-responsive delivery of glycoside hydrolase and antibiotics to treat biofilm infections. |
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