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| **Fabrication of PLGA Particles Loaded with Polymyxin B Sulphate using Coaxial Electrospraying** |
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| **Background:** Polymyxin B (PMB), a cyclic lipopeptide, is an FDA approved antibiotic that is selective against Gram negative bacteria{Iudin, 2020 #12}. It has become a last-line treatment due to its serious adverse side effects, such as nephrotoxicity and neurotoxicity, which are dose-dependent. However, there has been a revival of interest in PMB due to it being one of the few antibiotics effective against several multidrug-resistant Gram-negative bacteria such as *Pseudomonas aeruginosa*. The development of a controlled release subcutaneous formulation that can maintain the concentration of PMB within the target area under the concentration-time curve (AUC) values of 50–100 mgh/L could reduce the drug’s toxicity compared to intravenous administration. Hence, the aim of this study was to develop and characterise controlled release poly (lactic-co-glycolic acid) (PLGA) particles loaded with PMB sulphate using coaxial electrospraying (CES).  |
| **Methods:** To achieve a stable CES process that produces spherical particles, extensive optimisation of operational and solution parameters was required. Formulation development included exploring several organic solvents (2,2,2-trifluoroethanol, dichloromethane and chloroform), different molecular weights (MW), and various concentrations of PLGA 50:50 for the shell solution as well as the incorporation of polyethylene glycol (PEG) within the core peptide solution. Scanning electron microscopy (SEM) was used to characterise the size and morphology of the particles. |
| **Results:** The CES process was the most stable with 2,2,2-trifluoroethanol as the solvent for the shell solution. The use of dichloromethane and chloroform resulted in solidification within the Taylor cone which destabilised the CES process. The MW and concentration of the PLGA in organic solvent had a large influence on the morphology of the particles. High MW PLGA and high concentrations resulted in the presence of fibres. While low MW PLGA resulted in an unstable ES process. SEM analysis revealed medium MW PLGA within the concentration range of 6-8% (w/v, in 2,2,2-trifluoroethanol) to produce particles rather than fibres. The presence of PEG in the core peptide solution positively affected the morphology resulting in more spherical particles at 5% (w/v). The polydispersity of the PLGA particles was affected by both operational parameters (e.g., the flow rate of the ES solutions and the spinneret-to-collector distance) and the ES solution parameters (e.g., the PLGA concentration of the shell solution and presence of PEG in core peptide solution). |
| **Conclusions:** A stable CES process was achieved and PLGA particles loaded with PMB were successfully produced. However, further optimisation is needed to eliminate the presence of flat and concaved particles as well as further improve the polydispersity of the ES particles. Future work includes determining the particles release profile and antibacterial testing.  |