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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 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. Morphology and internal structure of electrosprayed particles were characterized with scanning electron microscopy (SEM) and transmission electron microscopy (TEM), respectively. An antimicrobial test using Pseudomonas aeruginosa (NCTC 12903) was used to confirm whether the electrosprayed peptide retained its pharmacological effect. |
| **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 at 5% (w/v) positively affected the morphology resulting in more spherical particles and lower polydispersity. However, further increase in PEG concentration to 10% (w/v) had a disadvantageous effect, leading to the presence of fibres. The flow rate of the ES solutions impacted both the morphology and polydispersity of the electrosprayed particles. TEM analysis indicated that a core-shell structure was not achieved using CES. However, these PMB-loaded particles were found to possess antimicrobial activity against Pseudomonas aeruginosa. This may suggest that electrospraying had little or no effect on peptide structure as the pharmacological effect was retained. |
| **Conclusions:** A stable CES process was achieved and PLGA particles loaded with PMB were successfully produced. Further optimisation is needed to eliminate the presence of flat and concaved particles as well as reduce the polydispersity of the ES particles. Future work includes determining the encapsulation efficiency, the long-term release profile of these electrosprayed particles and defining their internal structure. |