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Review article

Protein encapsulation by electrospinning and electrospraying

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ABSTRACT

Given the increasing interest in the use of peptide- and protein-based agents in therapeutic strategies, it is fundamental to develop delivery systems capable of preserving the biological activity of these molecules upon administration, and which can provide tuneable release profiles. Electrohydrodynamic (EHD) techniques, encompassing electrospinning and electrospraying, allow the generation of fibres and particles with high surface area-to-volume ratios, versatile architectures, and highly controllable release profiles. This review is focused on exploring the potential of different EHD methods (including blend, emulsion, and co−/multi-axial electrospinning and electrospraying) for the development of peptide and protein delivery systems. An overview of the principles of each technique is first presented, followed by a survey of the literature on the encapsulation of enzymes, growth factors, antibodies, hormones, and vaccine antigens using EHD approaches. The possibility for localised delivery using stimuli-responsive systems is also explored. Finally, the advantages and challenges with each EHD method are summarised, and the necessary steps for clinical translation and scaled-up production of electrospun and electrosprayed protein delivery systems are discussed.

1. Introduction

Peptides and proteins are arguably the most multifunctional biomolecules in the body, participating as catalysts in biochemical reactions, driving inflammatory responses, modulating cell proliferation and differentiation, and regulating metabolic and signalling pathways [1]. A very wide range of pathological conditions, including genetic, metabolic, inflammatory, and oncological diseases, arise from abnormalities related to endogenous protein function. Consequently, interest in peptides and proteins as therapeutic biological agents has dramatically increased over the past few decades. In 1982, recombinant insulin was approved by the United States (US) Food and Drug Administration (FDA) and became the first recombinant protein-based therapeutic agent to be introduced to the market [1–3]; since then, more than 60 FDA-approved protein drugs have been commercialised, and a great number more are currently under evaluation in preclinical and clinical trials [4].

Therapeutic protein-based agents offer several advantages over traditional small molecule drugs. Owing to their larger size and multiple sites of interaction, they act on the intended target with a very high specificity, potentially decreasing the adverse side effects that are inevitably associated with small molecules [1,5]. Further, proteins usually carry out physiological functions that are too complex to be fully reproduced by any other compound [1]. As an example, transforming growth factor β (TGF-β) is a cytokine involved in a multitude of biological responses, including wound healing, inflammation, adult stem

Abbreviation list: ALP, Alkaline phosphatase; BMP, Bone morphogenetic protein; bFGF, Basic fibroblast growth factor; BSA, Bovine serum albumin; CAM, Chorioallantoic membrane; CD, Circular dichroism; CTGF, Connective tissue growth factor; DSDP, Dual-source dual-power; EC, Endothelial cell; ECM, Extracellular matrix; EGF, Epidermal growth factor; ELISA, Enzyme-linked immunosorbent assay; FDA, United States Food and Drug Administration; FITC, Fluorescein isothiocyanate; GAG, Glycosaminoglycan; GDNF, Glial cell line-derived neurotrophic factor; GI, Gastrointestinal; HRP, Horseradish peroxidase; IGF-1, Insulin-like growth factor; IFN-γ, Interferon-γ; LbL, Layer-by-layer; LSCM, Laser scanning confocal microscopy; MSC, Mesenchymal stem cell; NGF, Nerve growth factor; OVA, Ovalbumin; PDGF, Platelet-derived growth factor; SDS-PAGE, Sodium dodecyl sulphate-polyacrylamide gel electrophoresis; SMC, Smooth muscle cell; TE, Tissue engineering; TGF-β, Transforming growth factor β; TNF-α, Tumour necrosis factor α; tPA, Tissue plasminogen activator; VEGF, Vascular endothelial growth factor.

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