

Polymeric Nanoparticles and Nanofibers for Local Delivery of Poorly Soluble Drugs

Aiman Abu Ammar¹

¹Department of Pharmaceutical Engineering, Azrieli College of Engineering
Jerusalem, Israel
aimanab@jce.ac.il

Extended Abstract

Poor aqueous solubility of drugs is becoming an increasingly pronounced challenge in the formulation and development of drug delivery systems. Issues associated with poor solubility can lead to low bioavailability resulting in suboptimal drug delivery [1]. Moreover, poorly water-soluble drugs need to be formulated in co-solvents or surfactant solutions to enhance their solubility, but many of these solutions are responsible for the severe side effects [2]. The introduction of nanotechnology in the field of drug delivery has enabled the development of new approaches for the treatment of several diseases, to improve efficiency and safety of drugs, by controlling the drug-release rate and place [3]. Poly(lactic-co-glycolic) acid (PLGA) is the FDA-approved copolymer that attracts considerable interest as a base material for biomedical and pharmaceutical applications, due to its biocompatibility and biodegradability [4]. Nanoprecipitation method is a one-step process, generally used to incorporate hydrophobic drugs in the polymer matrix to obtain nanoparticles. Moreover, electrospinning technique is a versatile approach for encapsulating therapeutic agents in nanofibers. Nano-sized dosage forms possess large surface area to volume ratio that alters the chemical, physical, and biological properties of the dosage form, and consequently improves the drug pharmacokinetics and pharmacodynamics. Furthermore, such nanodrug delivery systems provide sustained drug release for a prolonged time [5].

In this talk, the development of PLGA nanoparticles and nanofibers for local delivery of poorly soluble model drugs amphotericin B (AMB) and mometasone furoate (MF) will be presented.

Cutaneous leishmaniasis (CL) is an infectious disease caused by the protozoan *Leishmania* and characterized by localized skin lesions at the site of infection. The available therapies of CL are constrained by treatment period, route of administration, inadequate efficacy, toxicity, and cost. AMB is a macrolide polyene antibiotic, it has potent antifungal and antileishmanial activity, however, poor water solubility at physiological pH and high toxicity limit its therapeutic efficiency and clinical use. Currently, the AMB formulations used in clinical practice for CL treatment are intravenously administered. Therefore, the objective of this study was to design a PLGA-based nanodelivery system loaded with AMB, for controlled release of the drug, enabling single intralesional AMB injection and extended antileishmanial activity against *Leishmania major* which causes CL. The mean diameter of AMB NPs was about 90 nm with polydispersity index (PDI) of 0.2, and the ζ potential value was approximately -27 mV. AMB release from AMB NPs exhibited a biphasic pattern over a period of 7 days. Moreover, *in vitro* cytotoxic effect and antileishmanial activity were evaluated and proved the crucial role of AMB encapsulation in enhancing parasite inhibition for prolonged time period. Finally, the efficacy of AMB NPs and AMB deoxycholate after single intralesional injection was evaluated using *L. major*-infected mice. AMB NPs elicited a greater lesion-reducing effect as compared to other groups [6].

Intubation-related morbidity is a common secondary complication to airway mucosal damage due to the use of an endotracheal tube (ETT), which produces local pressure on the trachea and larynx. The common clinical approach to manage airway mucosal damage is systemic administration of steroids prior to extubation. Herein, ETTs were coated by electrospun PLGA fibers loaded with MF to facilitate local treatment, improve drug efficiency, and avoid systemic steroid related side effects. The novel delivery system was fully characterized, by means of drug loading, morphology, and mechanical stability of fiber mats. Moreover, *in vitro* release study demonstrated controlled release of MF over 14 days. The MF-coated ETTs proved effective in reducing laryngeal mucosal thickness and submucosal gland edema using an *in vivo* rat model [7].

Taken together, in a view of a translational approach, PLGA nanoparticles and nanofibers for local delivery of poorly soluble drugs would be a good choice.

References

- [1] A. Bhakay, et al., "Bioavailability Enhancement of Poorly Water-Soluble Drugs via Nanocomposites: Formulation–Processing Aspects and Challenges," *Pharmaceutics*, vol. 10, no 3, pp. 86, 2018.
- [2] A. Abu Ammar, et al., "A Lipophilic Pt (IV) Oxaliplatin Derivative Enhances Antitumor Activity," *J. Med. Chem.*, vol. 59, no. 19, pp. 9035-9046, 2016.
- [3] J. K. Patra, et al., "Nano based drug delivery systems: recent developments and future prospects," *J. Nanobiotechnology*, vol. 16, no. 1, pp. 71, 2018.
- [4] D. N. Kapoor, et al., "PLGA: a unique polymer for drug delivery," *Ther Deliv.*, vol. 6, no. 1, pp. 41-58, 2015.
- [5] F. Din, et al., "Effective use of nanocarriers as drug delivery systems for the treatment of selected tumors," *Int J Nanomedicine*, vol. 12, pp. 7291-7309, 2017.
- [6] A. Abu Ammar, et al., "Amphotericin B-loaded nanoparticles for local treatment of cutaneous leishmaniasis," *Drug Deliv Transl Res.*, vol. 9, no. 1, pp. 76-84, 2019.
- [7] A. Abu Ammar, et al., "Local delivery of mometasone furoate from an eluting endotracheal tube," *J. Control. Release*, vol. 272, pp. 54-61, 2018.