DOUBLY ADJUVANTED SNEDDS AS POTENTIAL NANOCARRIERS FOR VACCINES

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ABSTRACT

Self-nanoemulsifying drug delivery systems (SNEDDS) are isotropic mixtures of oil, surfactant and cosurfactant spontaneously forming an o/w nanoemulsion upon mixing with water. The formed nanoemulsion is a thermodynamically stable system with extremely small droplet size (i.e., ≤50 nm). SNEDDS are typically used to enhance the oral bioavailability of poorly water soluble drugs and there already exist marketed formulations of hydrophobic drugs based on SNEDDS technology. Recently, the administration of hydrophilic drugs including therapeutic peptides has been also demonstrated. The present study deals with the development of a novel SNEDDS formulation for vaccine delivery containing two different adjuvants (e.g., squalene and tocopherol-α). Various excipient combinations, and weight ratios of adjuvants, surfactant and cosurfactant for each combination were evaluated with the aid of ternary phase diagrams. The selected formulation was characterized by an average droplet diameter of 28 nm and adjuvant concentrations equal to 250 μg squalene and 100 μg tocopherol-α per 100 μl dose. In order to increase the adjuvants' concentration in the formulation, the effect of the volume of the aqueous phase on the droplet diameter was examined. It was shown that a substantial decrease in the volume of the aqueous phase (e.g., from 99 mL down to 4 mL) resulted in a nanoemulsion with an average droplet diameter of 40 nm and adjuvant concentrations equal to 5000 μg squalene (≥ of squalene concentration in ADAVAX) and 2000 μg tocopherol-α per 100 μl dose. Furthermore, the nanoemuslion was shown to exhibit storage stability at 4^{o}C for more than 3 months. The developed SNEDDS formulation could thus be considered as a promising strategy for the delivery of vaccines.

KEYWORDS: self-nanoemulsifying drug delivery systems, vaccines, adjuvants