Volume 107, Issue 8, August 2018, Pages 2136-2143

Bioadhesive Chitosan-Coated Cationic Nanoliposomes With Improved Insulin Encapsulation and Prolonged Oral Hypoglycemic Effect in Diabetic Mice

Shalaby, T.I.[a], El-Refaie, W.M.[b]

[a] Department of Medical Biophysics, Medical Research Institute, Alexandria University, Egypt

[b] Department of Pharmaceutics, Faculty of Pharmacy and Drug Manufacturing, Pharos University in Alexandria, Egypt

Abstract:

Oral administration of insulin is hampered by the lack of carriers that can efficiently achieve high encapsulation, avoid gastric degradation, overcome mucosal barriers, and prolong the hypoglycemic effect. Chitosan (CS)-coated insulin-loaded cationic liposomes have been developed and optimized for improved oral delivery. Liposomes were prepared cationic to improve insulin encapsulation. CS was selected as a mucoadhesive coat to prolong the system's residence and absorption. The performance of CS-coated liposomes compared with uncoated liposomes was examined in vitro, ex vivo, and in vivo in streptozotocin-induced diabetic mice. Free uncoated liposomes showed high positive zeta potential of +58.8 ± 2.2 mV that reduced (+29.9 ± 1.4 mV) after insulin encapsulation, confirming the obtained high entrapment efficiency of 87.5 ± 0.6%. CS-coated liposomes showed nanosize of 439.0 ± 12.3 nm and zeta potential of +60.5 ± 1.9 mV. In vitro insulin release was limited to 18.9 ± 0.35% in simulated gastric fluid, whereas in simulated intestinal fluid, 73.33 ± 0.68% was released after 48 h from CS-coated liposomes. Ex vivo intestinal mucoadhesion showed increased tissue residence of CS-coated liposomes compared with uncoated liposomes. A striking reduction in the glucose level was observed 1 h after oral administration of CS-coated liposomes and maintained up to 8 h ($p < 0.01$ vs. insulin solution or uncoated liposomes) within the normal value 129.29 ± 3.15 mg/dL. In conclusion, CS-coated insulin-loaded cationic liposomes improved loading efficiency with promising prolonged pharmacological effect.

Reference: