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Liposome Loaded Polysaccharide Based Hydrogels: Promising Delayed Release Biomaterials

Authors : J. Desbrieres, M. Popa, C. Peptu, S. Bacaita

Abstract : Because of their favorable properties (non-toxicity, biodegradability, mucoadhesivity etc.), polysaccharides were studied as biomaterials and as pharmaceutical excipients in drug formulations. These formulations may be produced in a wide variety of forms including hydrogels, hydrogel based particles (or capsules), films etc. In these formulations, the polysaccharide based materials are able to provide local delivery of loaded therapeutic agents but their delivery can be rapid and not easily time-controllable due to, particularly, the burst effect. This leads to a loss in drug efficiency and lifetime. To overcome the consequences of burst effect, systems involving liposomes incorporated into polysaccharide hydrogels may appear as a promising material in tissue engineering, regenerative medicine and drug loading systems. Liposomes are spherical self-closed structures, composed of curved lipid bilayers, which enclose part of the surrounding solvent into their structure. The simplicity of production, their biocompatibility, the size and similar composition of cells, the possibility of size adjustment for specific applications, the ability of hydrophilic or/and hydrophobic drug loading make them a revolutionary tool in nanomedicine and biomedical domain. Drug delivery systems were developed as hydrogels containing chitosan or carboxymethylcellulose (CMC) as polysaccharides and gelatin (GEL) as polypeptide, and phosphatidylcholine or phosphatidylcholine/cholesterol liposomes able to accurately control this delivery, without any burst effect. Hydrogels based on CMC were covalently crosslinked using glutaraldehyde, whereas chitosan based hydrogels were double crosslinked (ionically using sodium tripolyphosphate or sodium sulphate and covalently using glutaraldehyde). It has been proven that the liposome integrity is highly protected during the crosslinking procedure for the formation of the film network. Calcein was used as model active matter for delivery experiments. Multi-Lamellar vesicles (MLV) and Small Uni-Lamellar Vesicles (SUV) were prepared and compared. The liposomes are well distributed throughout the whole area of the film, and the vesicle distribution is equivalent (for both types of liposomes evaluated) on the film surface as well as deeper (100 microns) in the film matrix. An obvious decrease of the burst effect was observed in presence of liposomes as well as a uniform increase of calcein release that continues even at large time scales. Liposomes act as an extra barrier for calcein release. Systems containing MLVs release higher amounts of calcein compared to systems containing SUVs, although these liposomes are more stable in the matrix and diffuse with difficulty. This difference comes from the higher quantity of calcein present within the MLV in relation with their size. Modeling of release kinetics curves was performed and the release of hydrophilic drugs may be described by a multi-scale mechanism characterized by four distinct phases, each of them being characterized by a different kinetics model (Higuchi equation, Korsmeyer-Peppas model etc.). Knowledge of such models will be a very interesting tool for designing new formulations for tissue engineering, regenerative medicine and drug delivery systems.

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