PEG derivatives, a new platform technology for pharmaceutical research in drug delivery

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ABSTRACT
Methoxy polyethylene glycol (mPEG) with high molecular weight which has been used as a coating agent in drug delivery systems leads to more therapeutic efficacy. This supports the hypothesis that coating the drugs with higher molecular weight of PEG derivatives. The coating agent, methoxy polyethylene glycol propionaldehyde 20KDa (mPEG-ALD 20KDa), is a new platform technology for pharmaceutical research in drug delivery.

Keywords: Drug delivery system, mPEG-ALD, PEG derivatives, hypothesis

INTRODUCTION
Methoxy polyethylene glycol (mPEG) is a synthetic polymer with wide applications in pharmaceutical industry. PEGylation, the covalent binding of polyethylene glycol to a molecule such as protein or liposome, has a key role to improve drug delivery systems. Different molecular weights of the chemical compounds were used as a coating agent in drug delivery systems such as ploy lactic-co-glycolic acid (PLGA) and crown ether [1-3]. Conjugation of PEG derivatives to peptide, liposome and nanoparticles has been developed recently. However, PEG-coated molecules are useful
strategies to overcome the limitations and increase circulation time and also prevent removal of the drugs by liver and spleen. This supports the hypothesis that coating the drugs with higher molecular weight of PEG derivatives. To explore this hypothesis, a literature review was carried out to provide information relating to PEG derivatives which PEG molecules covalently attached to drugs. Distearoylphosphatidylethanolamine (DSPE-PEG), methoxy polyethylene glycol propionaldehyde 20KDa (mPEG-ALD) and polyethylene glycol puerarin (PEG-PUE) are new PEG with higher molecular weight that have not been widely used in pharmaceutical industry. It is important to try clinical studies of PEG-coated drugs. For example, mPEG-ALD is a coating agent which was characterized by reverse phase high performance liquid chromatography (RP-HPLC), atmospheric pressure chemical ionization mass spectrometry (APCI-MS) and nuclear magnetic resonance spectroscopy (H-NMR) [2]. Structural analysis of the mPEG-ALD identified many degradation aldehyde products such as formaldehyde. However, monitoring aldehydes in the PEG derivatives is essential to control quality of the products. Many compounds such as PLGA and DSPE-PEG were used extensively for drug delivery [3], but some compounds for example, mPEG-ALD 20KDa rarely was used in pharmaceutical industry [4]. The coating agent, mPEG-ALD 20KDa, is a new platform technology for pharmaceutical research in drug delivery.

The new generation of liposome coated with polyethylene glycol leads to obtain stable liposome using different methods [5]. The film method (FM) is the simplest method to obtain stable PEG-coated liposome. The circulation time of drug was prolonged by attaching PEG derivatives to the drug [6]. PEGylated liposomes have been used as pharmaceutical carriers in drug delivery systems. The structure characterization, in vitro and in vivo assay of PEGylated liposomes with low molecular weight of PEG molecules have been studied extensively, but PEGylated liposomes with high molecular weight of PEG molecules (mPEG-ALD 20KDa) have been evaluated rarely. Nevertheless, more studies are required to optimize the formulation of PEG-coated liposomes with high molecular weight of PEG. Optimum conditions of the prepared liposomes depend on the composition of mixture of final formulation and the time of evaporation [5].

One of the most important PEG derivatives is mPEG-ALD 20KDa which was synthesized according to the Williamson reaction by mPEG propionaldehyde acetal formation in acidic environment [7]. The chemical analysis of synthesized mPEG-ALD 20KDa were confirmed by FTIR and H-NMR spectroscopy [4,7]. The
related lipid formulation was phosphatidylcoline:cholesterol: mPEG-ALD 20KDa in 65:30:5 mole ratio. Molecular dynamics (MD) simulations using different pakages such as NAMD, GROMACS, SIESTA have been used to investigate self-assembly mechanism of phospholipid molecules and PEGylation mechanism [8,9]. All of these mechanisms are evaluated using different pakages and simulated the surface of the drug delivery systems. The results reveal that the drug encapsulated inside liposomes and nanocarriers is weakly or strongly bounded.

REFERENCES


