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Lipid-polymer hybrid nanoparticles versatile platform for controlled delivery of chemo-therapeutics

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Lipid polymer hybrid nanoparticles (LPHNPs) for the controlled delivery of hydrophilic doxorubicin hydrochloride (DOX.HCl) and lipophilic DOX base have been fabricated by the single step modified nanoprecipitation method. Poly (D, L-lactide-coglycolide) (PLGA), lecithin and 1,2-distearoyl-Sn-glycero-3-phosphoethanolamine-N-[methoxy (polyethylene glycol)-2000 (DSPEPEG 2000) were selected as structural components. The mean particle size was 173–208nm, an encapsulation efficiency of 17.8±1.9 to 43.8±4.4% and 40.3±0.6 to 59. 8±1.4% for DOX.HCl and DOX base, respectively. The drug release profile was in the range 33–57% in 24h and follow the Higuchi model (R2=0.9867–0.9450) and Fickian diffusion (n<0.5). However, the release of DOX base was slower than DOX.HCl. The in vitro cytotoxicity studies and confocal imaging showed safety, good biocompatibility and a higher degree of particle internalization. The higher internalization of DOX base was attributed to higher permeability of lipophilic component and better hydrophobic interaction of particles with cell membranes. Compared to the free DOX, the DOX.HCl and DOX base loaded LPHNPs showed higher antiproliferation effects in MDA-MB231 and PC3 cells. Therefore, LPHNPs have provided a potential drug delivery strategy for safe, controlled delivery of both hydrophilic and lipophilic form of DOX in cancer cells. Lipid–polymer hybrid nanoparticles (LPHNPs) are next-generation core–shell nanostructures, conceptually derived from both liposome and polymeric nanoparticles (NPs), where a polymer core remains enveloped by a lipid layer. Although they have garnered significant interest, they remain not yet widely exploited or ubiquitous. Recently, a fundamental transformation has occurred in the preparation of LPHNPs, characterized by a transition from a two-step to a one-step strategy, involving synchronous self-assembly of polymers and lipids. Owing to its two-in-one structure, this approach is of particular interest as a combinatorial drug delivery platform in oncology. In particular, the outer surface can be decorated in multifarious ways for active targeting of anticancer therapy, delivery of DNA or RNA materials, and use as a diagnostic imaging agent. This review will provide an update on recent key advancements in design, synthesis, and bioactivity evaluation as well as discussion of future clinical possibilities of LPHNPs.

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Nanotechnology is a compelling medicinal platform with the potential to greatly impact the delivery of a plethora of therapeutics, encompassing small molecule therapeutics, genes, RNAs, peptides, and diagnostic imaging agents, as well as holding great promise for improving the therapeutic index and pharmacokinetics of several drugs under systemic settings. In general, these payloads are encapsulated within or covalently grafted on the surface of the nanocarriers, and after being systemically incorporated, their release is monitored by factors such as formulation of the matrix, pH of the microenvironment, and temperature of the surroudings. The inherent potential of nanoparticles (NPs) for therapeutic cargo delivery is primarily attributable to few key parameters, including average nanometric size, homogeneity, surface potential, and drug loading, among others. Surface-coated immuno-inert NPs

can also skillfully bypass the reticuloendothelial system yielding increased bioavailability of encapsulated drugs. The plausible advantages of nanocarriers are summarized as follows: improvement to a drug's overall pharmacokinetic and pharmacodynamic properties without alteration of its molecular structure; enhanced effective tissue targeting, cellular targeting, and molecular targeting; the ability to circumvent many inherent biological impediments; targeted and nontargeted drug delivery to their respective site of action (cytosol, nucleus, etc) and enhanced therapeutic index of the drug; delivery of multiple drugs with differing chemical properties. Polymeric NPs, on the contrary, can be manufactured (via nanoprecipitation or the double emulsion method) by self-assembly of biodegradable amphiphilic block copolymers with varying hydrophobicities and are appropriate for systemic administration. The core–shell structure of polymeric NPs facilitates encapsulation of hydrophobic drugs and sustained drug release and extends circulation time. Their surfaces can also be decorated with ligands for targeted drug delivery. For instance, Genexol-PM is a polymer-based NP formulation of paclitaxel (PCX) and poly (d,l-lactide)-b-polyethylene glycol-methoxy (PLGA-mPEG), which has been approved for metastatic breast cancer therapy in Korea and the European Union. In order to utilize the unique attributes of liposomes and polymeric NPs that led to their initial clinical success, but overcome limitations like structural disintegration, limited circulation time, and content leakage, a new progeny of delivery system has been developed: lipid–polymer hybrid nanoparticles (LPHNPs). The hybrid system can be a sturdy drug delivery rostrum with high encapsulation efficiency, well-defined release kinetics, well-tolerated serum stability, and well-triggered tissue, cellular, and molecular targeting properties. In this article, we will review the emerging innovations of LPHNPs, incorporating new developments in their production strategies and drug delivery applications in cancer therapy. As can be inferred from their name, LPHNPs merge the features of both polymeric NPs and liposomes.

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They consist of three building blocks these are 1) a polymer core encapsulating the drug, 2) a lipid mono-layer surrounding the polymer core, and 3) an outer lipid–PEG layer, a steric stabilizer prolonging systemic circulation of the LPHNPs by evading immune destruction. The middle lipid monolayer behaves like a molecular barricade that mitigates the loss of entrapped drugs over the course of the LPHNP formulation and protects the core from degradation by preventing the diffusion of water into the inner core. The molecular mechanics of fusion between lipid and polymer is still under investigation. It is apparent that distinguished methods of LPHNP manufacturing have different mechanisms of formation. For instance, in single-step methods, the polymer precipitates from the organic solvent when added to aqueous media containing lipids, which subsequently spontaneously self-assemble into a monolayer surrounding the core. PEGylated lipids also self-assemble during this step, wherein a lipid moiety clings onto the surface of the polymer core and the PEG chain extends externally toward the aqueous environment. During the two-step method, a plausible mechanism of LPHNP formation may involve an initial bilayer structure formation and adherence to the core, with subsequent disintegration of the bilayer owing to the hydrophobic interaction between polymer and lipid chains. The hybrid formation is thermodynamically favorable, with respect to hydrophobic, van der Waal, and electrostatic interactions.