SAVREMENE TENDENCIJE U RAZVOJU NOSAČA LEKOVITIH SUPSTANCI

Marija Primorac, Ljiljana Đorđević, Dragana Vasiljević

Institut za farmaceutsku tehnologiju i kozmetologiju,
Farmaceutski fakultet, Beograd

Savremeni nosači lekovitih supstanci mogu značajno poboljšati kvalitet, bezbednost i efikasnost leka. Koloidni nosači (nanočestice, submikronske/mikroemulzije, micele, liposomi, dendrimeri) imaju značajan potencijal u formulaciji novijih farmaceutskih oblika i nalaze se u velikom broju komercijalnih preparata.

Cilj rada je upoznavanje sa osobinama i mogućnostima primene nanočestica, polimernih micela i dendrimera, kao nosača lekovitih supstanci, u dizajniranju i razvoju novih lekova.

Sprovedena su brojna istraživanja u cilju razvoja i unapređenja nanočestica kao nosača lekovitih supstanci i dijagnostičkih sredstava. Neki od značajnih rezultata u okviru ovih istraživanja odnose se na: povećanje selektivnosti isporuke leka uz minimiziranje sporednih efekata, prevazilaženje bioloških barijera, povećanje biološke raspoloživosti, unapređenje kontrolisanog/produženog oslobađanja leka i komplijanse, a ulažu se i ozbiljni napori za povećanje preciznosti ciljne isporuke leka na intraćelijskom nivou. Na ovaj način otvara se mogućnost da se lekovi-kandidati, koji su ranije odbačeni zbog neprihvatljivog toksikološkog profila, ili nemogućnosti da budu primenjeni u konvencionalnim farmaceutskim oblicima zbog male biološke raspoloživosti ili nestabilnosti, reformulišu kao nanočestični sistemi.

S druge strane, bitan aspekt nanomedicine je i razvoj novih efikasnih dijagnostičkih i skrining tehnika tako da nanočesticni sistemi sve vise dobijaju na značaju u oblasti molekularne dijagnostike. Čestice nanometarskih dimenzija, upotrebljene kao markeri, povećavaju osetljivost, brzinu i fleksibilnost bioloških testova merenjem prisustva ili aktivnosti odabrane supstance.

Polimerne micele kao nanonosači lekovitih supstanci i gena intenzivno se istražuju poslednjih nekoliko godina. Struktura i fizičko-hemijske osobine amfifilnih blok kopolimera, koji formiraju polimerne micele, utiču na važne osobine ovih nosača kao što su: veličina čestica, stabilnost, kapacitet inkapsulacije i kinetika oslobađanja lekovite supstance. Rezultati dosadašnjih pretkliničkih i kliničkih ispitivanja micelarnih formulacija antikancerskih lekova (paklitaksel, doksorubicin) opravdavaju dalja istraživanja.

Dendrimeri su sintetski monodisperzni makromolekuli koji se dobijaju odgovarajućim "arhitektonskim" dizajniranjem jezgra, višestrukih bočnih (račvastih) molekula i površinskih molekula. Precizna simetrična arhitektura dendrimera, tačno definisana veličina (2-10 nm), oblik, dužina/gustina račvastih jedinica i funkcionalnost površine, čini ove nanonosače pogodnim za inkapsulaciju/vezivanje/adsorpciju lekovitih supstanci i gena. Brojna istraživanja rezultovala su razvojem prvog preparata zasnovanog na tehnologiji dendrimera (VivaGel™) koji se nalazi u fazi kliničkih ispitivanja.

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AZVOJU NOSAČA
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Dragana Vasiljević

i kozmetologiju,
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NOVEL TRENDS IN THE DEVELOPMENT OF DRUG CARRIERS

Marija Primorac, Ljiljana Đorđević, Dragana Vasiljević

Department of Pharmaceutical Technology and Cosmetology,
Faculty of Pharmacy, Belgrade

Novel drug carrier systems may significantly enhance quality, safety and efficacy of drugs. Colloidal drug carriers such as nanoparticles, submicron emulsions/microemulsions, micelles as well as liposomes, show great potential in formulation of novel dosage forms, and are present in a great number of commercial products.

The aim of this paper is to introduce to properties of nanoparticles, polimeric micelles and dendrimers as drug delivery carriers in design and development of new drugs.

Extensive investigation has been carried out to develop and improve nanoparticles as carriers of drugs and imaging agents. Some important results of these investigations are: increasing a precision of delivery while minimizing side effects, overcoming biological barriers, enhancing bioavailability, improving controlled/sustained release of drugs and patient compliance, enabling more precise targeting to the level of direct intracelular delivery.

Nanotechnology is opening new therapeutic opportunities for agents that cannot be used effectively as conventional drug formulations due to poor bioavailability or drug instability. Drug candidates that failed previously because of unacceptable toxicity profiles or inability to administer them in conventional forms, may be reformulated as nanopartculate delivery systems.

On the other hand, main aspect of nanomedicine is the development of novel and more effective diagnostic and screening techniques, so nanoparticulate systems are important in the field of molecular diagnostics. Nanoscale particles, used as labels, increase the sensitivity, speed and flexibility of biological tests measuring the presence or activity of selected substance.

Polymeric micelles have been intensively studied in recent years as nanocarrier system for drug and gene delivery. Critical features of the polymeric micelles as drug carriers, including particle size, stability, and loading capacity and release kinetics of drugs, can be modulated by the structures and physicochemical properties of the constituent amphiphilic block copolimers. Until now, several micellar formulations of antitumor drugs (paclitaxel, doxorubicin) have been studied in preclinical and clinical trials, and their utility has been demonstrated.

Dendrimers are synthetic macromolecules with symmetrical architecture consisting of central core, branched units and surface molecules. The high level of control possible over the architectural design of dendrimers, their size (2-10 nm), shape, branching length/density, and their surface functionality, clearly distinguishes these structures as unique and optimum carriers for drug molecules and gene transfection. The bioactive agents may be encapsulated into the interior of the dendrimers or chemically attached/physically adsorbed onto the dendrimer surface. As a result of numerous investigations, the first therapeutic product based on dendrimer technology, VivaGel™, has been developed, and is currently undergoing clinical trials.