

FTIK-P10 OD FORMULACIJE DO PACIJENTA:**IZAZOVI U RAZVOJU KLINIČKI PRIMENJIVIH LIPIDNIH NANOČESTICA**O. Milić, M. Zurković, S. Savić, M. Savić, B. Stanojević*Univerzitet u Beogradu – Farmaceutski fakultet, Beograd, Srbija*

Lipidne nanočestice (engl. *Lipid Nanoparticles* – LNPs) jedna su od retkih nanotehnoloških platformi koje su uspešno prešle put od laboratorije do pacijenta, o čemu svedoči njihova primena u mRNA vakcinama protiv COVID-19 i u lečenju naslednih bolesti jetre. Cilj ovog rada bio je da se, kroz pregled i kritičku analizu novije literature (period 2020–2026), sagleda nesklad između fizičko-hemijskih i računarskih pokazatelja koji se rutinski koriste za procenu LNP formulacija i bioloških ishoda koji određuju njihovu terapijsku efikasnost. Analizirana je literatura iz šest oblasti razvoja LNP: proizvodnje mikrofluidnim postupkom, liofilizacije, transdermalne isporuke mikroigla, optimizacije formulacija primenom mašinskog učenja, izlaska iz endozoma (engl. *endosomal escape*) i formiranja proteinske korone. Analiza je pokazala da proizvodni procesi koji se pokazuju kao pouzdani na laboratorijskom/pilot nivou neretko gube reproduktivnost pri prenosu na proizvodni/industrijski nivo, dok modeli za računarsku optimizaciju zavise od podataka opterećenih potrebom za uspešnim formulacijama. Efikasnost izlaska iz endozoma izrazito je niska – prema objavljenim podacima svega 1–2% internalizovane siRNA dospeva u citosol, a nijedna poređena formulacija nije prešla 10% efikasnosti napuštanja endozoma, uprkos razlikama u fizičko-hemijskim svojstvima. Za karakterizaciju proteinske korone, od koje zavisi biodistribucija LNP, gotovo isključivo se koristi plazma zdravih ispitanika, iako se ciljna populacija pacijenata razlikuje prema patofiziološkom stanju, što značajno utiče na distribuciju nanočestica u organizmu. Na osnovu sprovedene analize zaključuje se da dalji napredak u razvoju LNP ne zavisi isključivo od novih tehnologija, već od sistematskog preispitivanja neproverenih pretpostavki i uvođenja funkcionalne, biološki relevantne validacije kao standarda u proceni LNP formulacija.

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FTIK-P10 FROM FORMULATION TO PATIENT:**CHALLENGES IN THE DEVELOPMENT OF CLINICALLY APPLICABLE LIPID NANOPARTICLES**O. Milić, M. Zurković, S. Savić, M. Savić, B. Stanojević*University of Belgrade – Faculty of Pharmacy, Belgrade, Serbia*

Lipid nanoparticles (LNPs) are among the few nanotechnology platforms that have successfully transitioned from the laboratory to the clinic, as demonstrated by their use in mRNA vaccines against COVID-19 and in treatments for hereditary liver diseases. This review aimed to critically examine the literature from 2020–2026 to assess the discrepancy between the physicochemical and computational parameters routinely used to evaluate LNP formulations and the biological outcomes that ultimately determine their therapeutic efficacy. The analysis covered six key areas of LNP development: microfluidic production, lyophilization, transdermal microneedle delivery, formulation optimization via machine learning, endosomal escape, and protein corona formation. The findings indicate that manufacturing processes that are reliable at the laboratory or pilot scale frequently lose reproducibility when translated to production or industrial scale, while computational optimization models depend on datasets that are inherently biased toward successful formulations. Endosomal escape efficiency remains strikingly low – according to published data, only 1–2% of internalized siRNA reaches the cytosol, and none of the compared formulations exceeded 10% escape efficiency, despite differences in their physicochemical properties. The protein corona, which governs LNP biodistribution, is almost exclusively characterized using plasma from healthy volunteers, even though the target patient population differs in pathophysiological status – a factor that substantially influences nanoparticle distribution *in vivo*. Based on this analysis, further progress in LNP development appears to depend not only on novel technologies, but more critically on the systematic re-evaluation of unverified assumptions and the establishment of functional, biologically relevant validation as a standard for assessing LNP formulations.

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