INVESTIGATION OF ALBUMIN ADSORPTION ON DK-I-56-1 NANOCRYSTALS BY DYNAMIC LIGHT SCATTERING

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After parenteral administration, nanoparticles interact with different proteins, forming a shell called corona, which further influence nanoparticles' biodistribution. Protein adsorption is affected by particle size and shape, but also by molecular interactions of chemical groups from the particle surface and amino-acid residues of the proteins. In human plasma, albumin is the most abundant protein so it is frequently used for the investigation of protein-nanoparticle interactions (1). In this study we investigated the attachment of bovine serum albumin (BSA) to recently developed nanocrystals (2) of DK-I-56-1 (7-methoxy-2-(4-methoxy-d3-phenyl)-2,5-dihydro-3H-pyrazolo[4,3-c]quinolin-3-one), stabilized by polysorbate 80 (NS2) or the combination of polysorbate 80 and poloxamer 407 (NS4). Nanocrystal dispersion was incubated in medium containing 0.1% or 1% BSA in phosphate buffer saline (pH 7,4) at 37 °C for 1 h. Particle size analysis was conducted by dynamic light scattering in 10 min interval, at 37 °C on Zetasizer ZS90 (Malvern Instruments Ltd., Worcestershire, UK). It was shown that albumin adsorption was influenced by the nanocrystal formulation and albumin concentration, but not incubation time. In a medium with 0.1% BSA, no particle size difference was noticed in either formulation. However, in case of NS2, after the addition of 1% albumin, particle size and particle size distribution increased, which indicated albumin binding. On the other hand, in formulation NS4, with higher albumin concentration two peaks were visible, one from the free albumin, and one from nanocrystal particles. Therefore, it could be concluded that the affinity of albumin was influenced mainly by the interaction with the nanocrystal stabilizers.

References

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ISPITIVANJE ADSORBOVANJA ALBUMINA NA NANOKRISTALE DK-I-56-1 METODOM DINAMIČKOG RASIPANJA SVETLOSTI

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Nakon parenteralne primene, nanočestice stupaju u interakciju sa različitim proteinima i dolazi do formiranja omotača poznatog kao *corona*, što dalje utiče na njihovu biodistribuciju. Adsorbovanje proteina zavisi od veličine i oblika čestica, ali i od molekulskih interakcija hemijskih grupa na površini nanočestica i aminokiselinskih ostataka proteina. U humanoj plazmi od proteina je u najvećem procentu prisutan albumin, pa se u istraživanjima on najviše koristi za ispitivanje interakcija između nanočestica i proteina (1). U ovoj studiji ispitivano je vezivanje goveđeg serum albumina (BSA) za nedavno razvijane nanokristale (2) DK-I-56-1 (7-metoksi-2-(4-metoksi-d3-fenil)-2,5-dihidro-3H-pirazolo-[4,3-c]hinolin-3-on) stabilizovane polisorbatom 80 (NS2) ili kombinacijom polisorbata 80 i poloksamera 407 (NS4). Disperzija nanokristala inkubirana je u medijumu sa 0,1% ili 1% BSA u fosfatnom puferu (pH 7,4) na 37 °C tokom 1 h. Analiza veličine čestica sprovedena je metodom dinamičkog rasipanja svetlosti u intervalima od 10 min, na 37 °C, na uređaju Zetasizer ZS90 (Malvern Instruments Ltd., Worcestershire, UK). Pokazano je da adsorbovanje albumina zavisi od sastava formulacije nanokristala i koncentracije albumina, ali ne i od vremena inkubiranja. U medijumu sa 0,1% albumina, nisu uočene razlike u veličini čestica formulacija NS2 ni NS4. Međutim, u slučaju NS2, nakon dodatka 1% albumina, došlo je do povećanja veličine čestica i distribucije veličine čestica, što ukazuje na vezivanje proteina. Sa druge strane, kod formulacije NS4 pri višoj koncentraciji albumina mogla su se uočiti dva pika, od kojih jedan potiče od slobodnog albumina, a drugi od nanokristalne čestice. Stoga, može se zaključiti da je afinitet albumina pre svega zavisio od interakcije sa stabilizatorima nanokristala.

Literatura

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