APPLICATION OF 3D PRINTING PHOTOPOLYMERIZATION TECHNIQUE IN THE FABRICATION OF TWO-LAYERED TABLETS

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In recent years, introduction of modern technologies, such as 3D printing, has opened a new chapter and caused a paradigm shift from manufacturing of large-scale to small batches of medicines tailored accordingly to the specific needs of patients (1). The aim of this study was to formulate and fabricate two-layered tablets using digital light processing (DLP) technique, which utilizes light irradiation to create solid objects from photoreactive liquid resin in a layer-by-layer manner. Hydrochlorothiazide (HHT, 5%,w/w) and warfarin sodium (VRN, 5%,w/w) were selected as model drugs, commonly used together in the treatment of cardiovascular diseases. 3D printing process was initiated with 0.10% of photoinitiator, at a constant ratio of poly(ethylene glycol)diacrylate and poly(ethylene glycol) 400, 1:1, with the addition of water (10%,w/w). 3D tablets, with each of the active substances in a separate layer, 8.00 mm in diameter and 1.50 mm thick, as well as combined two-layered tablets with HHT and VRN in individual layers, were successfully printed with Wanhao D8 printer. Dissolution test results showed immediate, but incomplete release of VRN (81.47 ± 1.47%, after 45 min) from individual layers, while the release of HHT was prolonged and complete (98.17 ± 3.11%, after 8 h). Significantly slower and incomplete release of VRN and HHT from combined tablets was observed. The absence of interactions and the presence of a layered structure were confirmed. DLP technique has a potential to provide fast fabrication of combined tablets, while further optimization of formulation factors is necessary in order to achieve complete drug release.

References

1. Wang J, Zhang Y, Aghda NH, Pillai AR, Thakkar R, Nokhodchi A, et al. Emerging 3D printing technologies for drug delivery devices: Current status and future perspective. Adv Drug Deliv Rev. 2021;174:294–316.

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PRIMENA FOTOPOLIMERIZACIONE TEHNIKE 3D ŠTAMPE LEKOVA U IZRADI DVOSLOJNIH TABLETA

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Poslednjih godina, uvođenjem savremenih tehnologija, poput 3D štampe, otvorilo se novo poglavlje u načinu proizvodnje lekova i uslovilo razvoj fundamentalnih promena, pri čemu serijska proizvodnja velikih šarži pretenduje da bude zamenjena malim serijama lekova prilagođenih specifičnim potrebama pacijenata (1). Cilj ovog istraživanja bio je da se formulišu i izrade dvoslojne tablete primenom tehnike digitalne obrade svetlosti (DLP) koja omogućava dobijanje objekata mehanizmom nanošenja materijala "sloj po sloj" iz tečne fotopolimerizacione smole pod uticajem svetlosti. Hidrohlortiazid (HHT, 5%, m/m) i varfarin-natrijum (VRN, 5%, m/m) odabrani su kao model lekovite supstance, koje se obično primenjuju zajedno u lečenju kardiovaskularnih bolesti. Proces 3D štampanja sproveden je u prisustvu 0,10% fotoinicijatora, pri konstantnom masenom odnosu poli(etilen glikol)diakrilata i poli(etilen glikola) 400, 1:1, uz dodatak 10% vode. 3D tablete, sa svakom od aktivnih supstanci u posebnom sloju, prečnika 8,00 mm i debljine 1,50 mm, kao i kombinovane dvoslojne tablete sa HHT i VRN u pojedinačnim slojevima, uspešno su odštampane u *Wanhao* D8 štampaču. Prilikom ispitivanja brzine rastvaranja lekovite supstance iz pojedinačnih slojeva, došlo je do trenutnog (81,47 ± 1,47% nakon 45 min), ali nepotpunog oslobađanja VRN, dok je HHT u potpunosti oslobođen, prateći kinetiku produženog oslobađanja (98,17 ± 3,11%, nakon 8 h). Zapaženo je znatno sporije i nepotpuno oslobađanje VRN i HHT iz kombinovanih dvoslojnih tableta, nakon 8 h. Potvrđeno je odsustvo interakcija i prisustvo slojevite strukture. DLP tehnika ima potencijal da obezbedi brzu izradu kombinovanih tableta, pri čemu je neophodna dalja optimizacija formulacionih faktora u cilju postizanja potpunog oslobađanja lekovite supstance.

Literatura

1. Wang J, Zhang Y, Aghda NH, Pillai AR, Thakkar R, Nokhodchi A, et al. Emerging 3D printing technologies for drug delivery devices: Current status and future perspective. Adv Drug Deliv Rev. 2021;174:294–316.

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