FORMULATION OF IBUPROFEN-MODIFIED RELEASE HYDROPHILIC AND LIPID MATRIX TABLETS USING CO-PROCESSED EXCIPIENTS

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Formulation of modified-release ibuprofen tablets presents a challenge due to its high dose, limited compressibility and compactibility. The potential for preparing ibuprofen modified release matrix tablets, by direct compression procedure using co-processed excipients (1, 2), was evaluated. Co-processed excipients of hydrophilic and lipid properties were used. Commercially available co-processed excipient based on hydroxypropylmethylcellulose and lactose (RetaLac®), as well as co-processed excipient made in-house, using lipid matrix forming agent based on glyceryl palmitostearate (Precirol®) and lactose were used. The influence of co-processed excipient type, ibuprofen ammount in tablets (25% and 50%) and the compression load (100 and 500 kg) on the mechanical properties of the hydrophilic or lipid matrix tablets was evaluated. Also, ibuprofen release rate was investigated in a rotating paddle apparatus with medium change (0.1M HCl and phosphate buffer pH 6.8). The tensile strength of formulations was in the range of 0.5-2 MPa. The compression load and the co-processed excipient type showed a significant effect on tensile strength. Ibuprofen was released in a sustained manner from all formulations, with the amount released after 8 hours varying from 35 to 80%, depending on the matrix forming material type. The release of ibuprofen from lipid matrix tablets was slower compared to hydrophilic tablets, with neither the compression load nor the ibuprofen content showing a significant effect. Zero-order kinetics was achieved from both types of matrix tablets. Based on the obtained results, it can be concluded that co-processed excipients enable direct compression of ibuprofen modified release hydrophilic and lipid matrix tablets.

References

1. Ćirin-Varađan, S., Đuriš, J., Mirković, M., Ivanović, M., Parojčić, J., Aleksić, I., 2022. Comparative evaluation of mechanical properties of lactose-based excipients co-processed with lipophilic glycerides as meltable binders. *J Drug Deliv Sci Tech*, 67: 102981.
2. Rebouh, S., Lefnaoui, S., Bouhedda, M., Yahoum, M.M., Hanini, S., 2019. Neuro-fuzzy modeling of ibuprofen-sustained release from tablets based on different cellulose derivatives. *Drug Deliv Transl Res*, 9(1): 162-177.

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FORMULACIJA HIDROFILNIH I LIPIDNIH MATRIKS TABLETA SA MODIFIKOVANIM OSLOBAĐANJEM IBUPROFENA PRIMENOM KOPROCESOVANIH EKSCIPIJENASA

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Formulacija tableta sa modifikovanim oslobađanjem ibuprofena predstavlja izazov zbog visoke doze lekovite supstance ograničene kompresibilnosti i kompaktibilnosti. U ovom radu procenjena je mogućnost izrade matriks tableta sa modifikovanim oslobađanjem ibuprofena postupkom direktne kompresije uz primenu koprocesovanih ekscipijenasa (1, 2). Upotrebljeni su koprocesovani ekscipijensi hidrofilnih i lipidnih karakteristika. Korišćeni su komercijalno dostupan koprocesovani ekscipijens na bazi hidroksipropilmetilceluloze i laktoze (*RetaLac*®), kao i koprocesovani ekscipijens izrađen u laboratorijskim uslovima, kao lipidno matriks formirajuće sredstvo na bazi glicerilpalmitostearata (*Precirol*®) i laktoze. Praćen je uticaj vrste koprocesovanog ekscipijensa, udela ibuprofena u tabletama (25%, odnosno 50%) i opterećenja pri kompresiji (100, odnosno 500 kg) na mehaničke karakteristike izrađenih hidrofilnih, odnosno lipidnih matriks tableta. Takođe, ispitivana je brzina oslobađanja ibuprofena iz pripremljenih matriks tableta u aparaturi sa rotirajućim lopaticama uz izmenu medijuma (0,1M HCl i fosfatni pufer pH 6,8). Zatezna čvrstoća ispitivanih formulacija je bila u opsegu ~ 0.5-2 MPa. Opterećenje pri kompresiji i tip koprocesovanog ekscipijensa su pokazali značajan uticaj na zateznu čvrstoću. Ibuprofen se iz svih formulacija oslobađao usporeno, pri čemu je količina oslobođena nakon 8 sati ispitivanja varirala od 35 do 80%, u zavisnosti od prirode matriks formirajućeg materijala. Oslobađanje ibuprofena iz lipidnih matriks tableta je bilo sporije u poređenju sa hidrofilnim tabletama, pri čemu ni opterećenje pri kompresiji ni udeo ibuprofena nisu pokazali značajan uticaj. Iz oba tipa matriks tableta postignuto je oslobađanje ibuprofena kinetikom nultog reda. Na osnovu dobijenih rezultata može se zaključiti da koprocesovani ekscipijensi omogućavaju izradu hidrofilnih i lipidnih matriks tableta sa modifikovanim oslobađanjem ibuprofena postupkom direktne kompresije.

Literatura

1. Ćirin-Varađan, S., Đuriš, J., Mirković, M., Ivanović, M., Parojčić, J., Aleksić, I., 2022. Comparative evaluation of mechanical properties of lactose-based excipients co-processed with lipophilic glycerides as meltable binders. *J Drug Deliv Sci Tech*, 67: 102981.
2. Rebouh, S., Lefnaoui, S., Bouhedda, M., Yahoum, M.M., Hanini, S., 2019. Neuro-fuzzy modeling of ibuprofen-sustained release from tablets based on different cellulose derivatives. *Drug Deliv Transl Res*, 9(1): 162-177.

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