

## **IN VITRO RELEASE OF METFORMIN HYDROCHLORIDE FROM TOPICAL VEHICLES FOR DERMAL DRUG DELIVERY**

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An important role in a number of skin pathologies (e.g. melanoma) of metformin hydrochloride (MET), a commonly used drug for antidiabetic therapy, is recently reported. Due to large dose, low efficiency and systemic side effects, MET oral administration is not considered as appropriate for therapy of such diseases. To achieve the best treatment of skin disorders, drug penetration into deeper skin layers represents an important scientific interest (1). Since drug release is a prerequisite for drug skin absorption and its therapeutic efficacy (2), *in vitro* release study was performed as to select appropriate topical formulations for MET dermal delivery. Two creams (amphiphilic and hydrophilic) and two hydrogels with 30% (w/w) MET and two microemulsions of MET (5%, w/w) were used as vehicles for topical application of MET. The *in vitro* drug release tests were performed using Franz diffusion cells. The obtained results suggested that MET release was strongly influenced by physicochemical properties and structure of the investigated vehicles. MET detected in the receptor chamber was the highest for hydrogels compared to the other formulations. MET release from both creams was limited and reached up to 8.54 mg/cm<sup>2</sup> after 8h. Microemulsions containing a six-fold lower drug concentration released up to 5.37 mg/cm<sup>2</sup> of MET, however, a greater proportion of MET reached the receptor phase from microemulsions than from creams. The results of the current study indicated a better *in vitro* performance of MET hydrogels and microemulsions and they could be developed further through adequate *ex vivo* and *in vivo* studies.

### **References**

1. Mousa IA, Hammady TM, Gad S, Zaitone SA, El-Sherbiny M, Sayed OM. Formulation and Characterization of Metformin-Loaded Ethosomes for Topical Application to Experimentally Induced Skin Cancer in Mice. *Pharmaceuticals*. 2022;15(6).
2. Shah VP, Yacobi A, Radulescu FS, Miron DS, Lane ME. A Science Based Approach to Topical Drug Classification System (TCS). *Int J Pharm*. 2015;491(1-2):21-5.

### **Acknowledgements**

This research is a part of the Project 19.032/961-149/19 financially supported by the Ministry for Scientific-Technological Development, Higher Education and Information Society, Republic of Srpska.

## **IN VITRO OSLOBAĐANJE METFORMIN-HIDROHLORIDA IZ VEHIKULUMA ZA DERMALNU ISPORUKU LIJEKA**

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Metformin-hidrohlorid (MET), uobičajeno korišćen lijek u terapiji dijabetesa, našao je primjenu u terapiji različitih patologija kože (npr. melanoma). Zbog visoke doze, male efikasnosti i sistemskih neželjenih efekata, oralna primjena MET nije adekvatna u terapiji ovakvih oboljenja. Da bi se postigao optimalan efekat u terapiji kožnih bolesti, potrebna je penetracija lijeka u dublje slojeve kože, za šta postoji veliko naučno interesovanje (1). S obzirom da je oslobađanje lijeka iz nosača preduslov za njegovu apsorpciju preko kože i efikasnost (2), sprovedena je *in vitro* studija kako bi se utvrdile pogodne formulacije za dermalnu isporuku MET. Dva krema (amfilni i hidrofilni) i dva hidrogela sa 30% (m/m) MET, te dvije mikroemulzije sa 5% (m/m) lijeka, su korišćeni kao nosači za lokalnu primjenu MET. *In vitro* ispitivanje oslobađanja lijeka je izvedeno primjenom *Franz*-ovih difuzionih ćelija. Dobijeni rezultati ukazuju da su na oslobađanje MET iz formulacija značajno uticale fizičko-hemijske osobine i struktura nosača. Količina MET u receptorskoj komori bila je najviša u slučaju primjene hidrogelova u poređenju sa drugim formulacijama. Količina oslobođenog MET iz kremova je bila ograničena i dostigla je 8,54 mg/cm<sup>2</sup> poslije 8h ispitivanja. Mikroemulzije koje su sadržavale šest puta nižu koncentraciju lijeka su oslobodile do 5,37 mg/cm<sup>2</sup> MET, međutim, u odnosu na primijenjenu količinu lijeka, veći udio MET je prešao iz mikroemulzija u receptorsku fazu nego iz kremova. Rezultati sprovedene studije ukazuju na bolje *in vitro* performanse MET hidrogelova i mikroemulzija i oni mogu dalje da se istražuju kroz odgovarajuće *ex vivo* i *in vivo* studije.

### **Reference**

1. Mousa IA, Hammady TM, Gad S, Zaitone SA, El-Sherbiny M, Sayed OM. Formulation and Characterization of Metformin-Loaded Ethosomes for Topical Application to Experimentally Induced Skin Cancer in Mice. *Pharmaceuticals*. 2022;15(6).
2. Shah VP, Yacobi A, Radulescu FS, Miron DS, Lane ME. A Science Based Approach to Topical Drug Classification System (TCS). *Int J Pharm*. 2015;491(1-2):21-5.

### **Zahvalnica**

Ovo istraživanje je urađeno u okviru projekta 19.032/961-149/19 finansiranog od strane Ministarstva za naučnotehnoški razvoj, visoko obrazovanje i informacione tehnologije Republike Srpske.