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Nano-mixed micelles: An approach to enhance the oral bioavailability of BCS class III drug

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Purpose: The main purpose for this study was to investigate the ability of mixed micelles formulation (MMs) made of phosphatidylcholine (PPC) and BS (sodium cholate) loaded with cefotaxime sodium (CEF) and 3α,7α-dihydroxy-12-keto-5β-cholanate (MKC) complex to enhance the oral bioavailability of CEF in rats.

Methods: Thin-film hydration method was used to prepare CEF loaded MMs using different BS concentrations. MMs were characterized and the oral bioavailability of CEF in MMs formulation was assessed and the pharmacokinetic (PK) of CEF-loaded MMs in comparison with CEF-BS complex and CEF aqueous solution were evaluated using 24 male Wistar rats. Blood samples were collected for up to 24h and CEF analyzed using a validated HPLC assay.

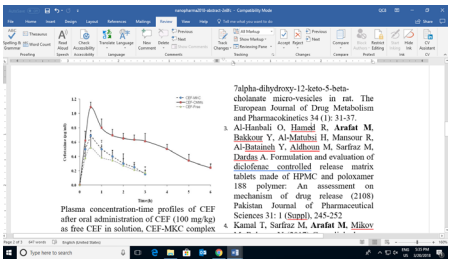

Figure: Plasma concentration-time profiles of CEF after oral administration of CEF (100mg/kg) as free CEF in solution, CEF-MKC complex and CEF-loaded mixed micelles given to rats (data are mean±S.D., n=6).

Results: PK data showed that the oral bioavailability of CEF in MMs was found to be (4.21%) higher compared to the CEF in aqueous solution (1.30%). Cmax of CEF in MMs formulation was higher (1.06±0.1µg/ml) compared to CEF-MKC complex (0.59±0.1µg/ml) and CEF in aqueous solution (0.52±0.1µg/ml). Similarly, the mean values for AUC0-t of CEF in MMs formulation was higher (3.75±0.8h .µg/ml) compared to CEF-MKC complex (1.52±0.2h.µg/ml) and CEF in aqueous solution (1.03±0.4h.µg/ml, respectively).

Conclusions: The mixed micelles formulation composed of PPC and BS was able to increase the intestinal epithelial cell efflux of drug and eventually enhance the oral bioavailability of BCS class III drug CEF up to 4-fold.

Recent Publications

1. Arafat M, Kirchhoefer C, Mikov M, Sarfraz M and Löbenberg M (2017) Nanosized liposomes containing bile salt: a vesicular nanocarrier for enhancing oral bioavailability of BCS class III drug. journal of pharmacy and pharmaceutical sciences. 20: 305-318.

2. Golocorbin-Kon S, Mikov M, Arafat M, Lepojevic Z, Mikov I, Sahman-Zaimovic M and Tomic Z (2009) Cefotaxime pharmacokinetics after oral application in the form of 3alpha, 7alpha-dihydroxy-12-keto-5-beta-cholanate micro-vesicles in rat. The European Journal of Drug Metabolism and Pharmacokinetics. 34 (1): 31-37.

3. Al-Hanbali O, Hamed R, Arafat M, Bakkour Y, Al-Matubsi H, Mansour R, Al-Bataineh Y, Aldhoun M, Sarfraz M and Dardas A (2018) Formulation and evaluation of diclofenac-controlled release matrix tablets made of HPMC and poloxamer 188 polymer: An assessment on mechanism of drug release (2108) Pakistan Journal of Pharmaceutical Sciences. 31 (1): 245-252.

4. Kamal T, Sarfraz M, Arafat M, Mikov M and Rahman N (2017) Cross-linked guar gum and sodium borate-based microspheres as colon-targeted anticancer drug delivery systems for 5-fluorouracil Pakistan Journal of Pharmaceutical Sciences 30 (6): 2329-2336.

5. Arafat M, Golocorbin-Kon S and Mikov M (2015) The Measurement of Cefotaxime Sodium in Rat Plasma After Oral Administration: A Sensitive HPLC-UV Method. International Journal of Pharmacy and Pharmaceutical Sciences. 7 (4): 343-346.

Biography

Mosab Arafat is a licensed Pharmacist who graduated with Doctoral Degree (PhD) in Nanomedicines from School of Pharmacy, University of Otago, New Zealand. His research work interests involved the application of nanotechnology on oral drug delivery system to develop and characterize a nanoformulation of a protein like drug molecules such as insulin for oral administration. He has developed, improved and formulated a novel oral nanoformulation of the broad-spectrum antibiotic, cephalosporin. He has succeeded to increase its oral bioavailability up to 20 times. He has lately moved to UAE and currently he is an Assistant Professor at the College of Pharmacy, Al Ain University of Science and Technology. He is also working very closely with pharmaceutical industries and providing consultancies, is a Formulation and Development Team Leader at PharmaTechno, Sydney, Australia.

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