Preparation and Characterization of an Oral Norethindrone Sustained Release/Controlled Release Nanoparticles Formulation Based on Chitosan

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Abstract

Statement of the Problem: Norethindrone has short half-life and low bioavailability. The objective of this research was to prepare an oral Sustained Release/Controlled Release (SR/CR) Liquid Medicated Formulation (LMF) to enhance bioavailability and improve patient compliance. Methodology: Norethindrone was solubilized in HP-ß-CD then complexed with different concentrations of Low Molecular Weight Chitosan (LMWC) (mucoadhesive). PolyElectrolyte Complexes (PECs) were homogenized with oleic acid using different concentrations of tween 80 to form LMFs (nanoemulsions). PECs and LMFs were characterized using DSC, FTIR spectroscopy and SEM images. Particle size, polydispersity index and zeta potential were measured. Dissolution studies were conducted and encapsulation efficiencies were calculated. LMF 2 (optimum formula containing 2.5% w/v LMWC 11 kDa) was administered orally to dogs and mice for pharmacokinetic and adhesion evaluation. Findings: DSC, FTIR spectroscopy and SEM images indicated complex formation. Mean diameters of PECs were 183–425 nm, mean zeta potentials were + 18.6–+ 31 mV, and complexation efficiencies were 18.0–20.6%. Ten to fifteen percent tween 80 was needed to prepare homogenous LMFs. Mean diameter of LMF 2 was 10.5 ± 0.57 nm, mean zeta potential was − 11.07 ± − 0.49 mV, encapsulation efficiency was 95.28 ± 1.75%, and each mL contained 145.5 µ g norethindrone. SEM images showed spherical homogeneous oil droplets. All of these parameters were affected by molecular weight and concentration of chitosan. Norethindrone release from LMFs was controlled (zero order) for 96 h. It was little affected by molecular weight and concentration of chitosan but affected by concentration of tween 80. LMF 2 adhered to GIT for 48 h and enhanced the bioavailability. It showed no cytotoxicity after considering dilution in GIT and was stable for 3 months refrigerated. Conclusion & Significance: an effective SR/CR LMF for norethindrone was prepared.

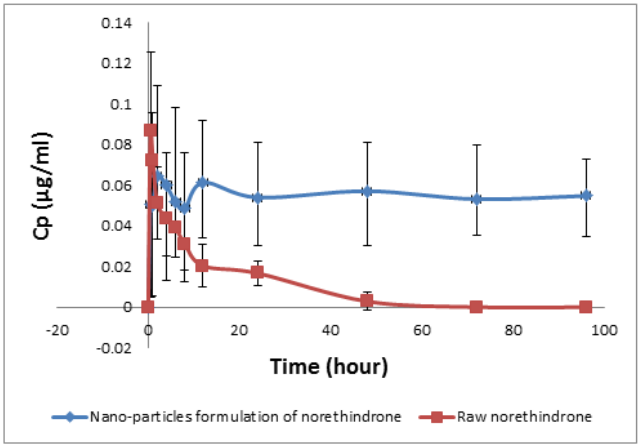


Fig. 1. Average plasma concentration time profile of norethindrone after administration of 10 ml (0.1455 mg/ml) of LMF 2 and norethindrone orally to dogs (n = 6)

Recent Publications (minimum 5)

1. Suhair S. Al-Nimry, Bashar M. Altaani, Razan H. Haddad (2019) RP-HPLC method for determination of norethindrone in dissolution media and application to study release from a controlled release nanoparticulate liquid medicated formulation. J Appl Pharm Sci 9(02):079–086.
2. Bashar M. Altanni, Suhair S. Al-Nimry, Razan H. Haddad , Rana Abu-Dahab (2019) Preparation and Characterization of an Oral Norethindrone Sustained Release/Controlled Release Nanoparticles Formulation Based on Chitosan. AAPS PharmSciTech 7;20(2):54.
3. Suhair Al-Nimry, Khouloud Alkhamis (2018) Effect of Moisture Content of Chitin-Calcium Silicate on Rate of Degradation of Cefotaxime Sodium. AAPS PharmSciTech 19(3):1337-1343.
4. Mai Khanfar, Suhair Al-Nimry (2017) Stabilization and amorphization of lovastatin using different types of silica. AAPS PharmSciTech 18(6):2358-2367.
5. Suhair S. Al-Nimry, Malak A. Jaber (2017) Development and validation of an HPLC-UV method for determination of sertraline hydrochloride and application to study dissolution of tablets. Latin American Journal of Pharmacy 36 (4): 665-72.
6. Suhair Al-Nimry, Khouloud Alkhamis, Kawthar Alzarieni (2017) The effect of specific surface area of chitin-metal silicate coprocessed excipient on the chemical decomposition of cefotaxime sodium. J Pharm Sci 106:570-578.
7. Suhair S. Al-Nimry, Malak A. Jaber (2017) Preparation and Optimization of Sertraline Hydrochloride Tablets with Improved Dissolution through Crystal Modification. AAPS PharmSciTech 18(4):1190-1202.



Biography

Al-Nimry has obtained her Ph. D. in pharmaceutical Technology from Jordan University of Science and Technology in 2005. She has worked at ACDIMA Biocenter as the acting head of bioanalytical unit from 2005-2008. Then she joined the Faculty of pharmacy in Jordan University of Science and Technology as an assistant professor in 2008. She held the position of an assistant dean from 2009-2010. She have been promoted to an Associate professor on 3-01-2017. She has published many articles in the field of enhancing solubility/dissolution rate of poorly soluble drugs, effect of increasing surface area and moisture content on the stability of cefotaxime sodium.

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Notes/Comments: