Cairo University

Faculty of Veterinary Medicine

Comparative Pharmacodynamic/Pharmacokinetic Studies on Tetracycline Hydrochloride and Its Loaded Nano-emulsion Formula

Thesis submitted by

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Abstract

Tetracycline Hcl loaded nanoemulsion (TC-NE) was prepared, characterized and stability was assessed. MDS from 32.33±3.81 to 101.5±9.86 nm.; size has 3 S/CoS ratios were 1:1, 1:2 and 2:1. PDI value (0.11± 0.01: 0.41± 0.07). ZP values (-25.45±3.43 to -33.47±2.11 mV.) TEM showed spherical globules with uniform droplet size.

Pharmacokinetics and pharmacodynamics of TC-Hcl powder and TC-NE were studied in rabbits following a single iv and oral dose (50 mg/kg b.wt). TC-NE had higher distribution volume V2 and slowly cleared Cl2 than TC- Hcl. Significant longer half-life for TC-NE than for TC-Hcl powder with calculated C_{max}, achieved at prolonged calculated tmax in TC-NE than in TC-Hcl oral treated rabbits, respectively. A Significant higher AUC0-inf. (20.377 ± 1.4841 µg/ml.h and 11.056 ± 0.5835 µg/ml.h) at prolonged MRT (3.926 ± 0.4712 h. and 2.771 ± 0.2932 h.) and higher bioavailability in TC-NE than TC-Hcl, respectively. Some changes in histopathology, liver and kidneys function were observed with the two formulas. No difference in antibacterial and MIC between TC-NE than TC-Hcl.

Conclusion: The nanoemulsion formulation improves both pharmacokinetis and pharmacodynamics and not affect the antibacterial efficacy as compared with TC-Hcl formula. This formulation can be useful for reduce the used dose to obtain the same serum concentration, reduce tissue effect and save cost of medication. Further studies are needed for clinical evaluation of the TC-Hcl formula.

Dedication

I wish to introduce my deep gratitude and utmost thanks to:

My parents

and

Special thanks to

my wife

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List of Abbreviations

TC-Hcl	Tetracycline hydrochloride powder
TC-NE	Tetracycline hydrochloride loaded nanemulsion.
MIC	Minimal inhibitory concentration.
$t.0.5_{ka}$	Absorption half-life time.
$t.0.5_{\beta}$	Elimination half-life time.
Cl_2	Clearance rate from the peripheral compartment.
C_{max}	Maximum blood concentration in blood after oral administration.
T_{max}	Time at which maximum blood concentration in blood after oral administration is reached.
$AUC_{0\text{-}inf}$	Area under time concentration curve from zero time to infinity.
MRT	Time of drug persistence in the body.
F	Bioavailability.
C^0	Plasma concentration at zero time of administration.
K_{10}	Distribution constant in the central compartment.
K_{12}	Distribution constant from the central compartment to peripheral compartment .
K_{21}	Distribution constant from the peripheral compartment to central compartment .
V_{dss}	Volume of distribution at steady state.
PK	Pharmacokinetics
PD	Pharmacodynamics
HPLC	High performance liquid chromatography
TC	Tetracycline
TCs	Tetracyclines
S/CoS	Surfactant/Cosurfuctant
MC	Microbiological assay

Chapter (1)

Introduction