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**Design, preparation and evaluation of Glipizide solid lipid
nanoparticles for improving its oral bioavailability**

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**This thesis was submitted in partial fulfillment of the requirements for the
master's degree of pharmaceutical Sciences**


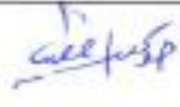
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اسأل الله ان يجعلكم عوضي بالدنيا

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شقيقي وصديقي لازلت اري فيه حنان وعطف ابي

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اسأل الله ان يجمعني بكم علي خير

..

هولاء هم رفقاء عمري وشركاء كفاحي

اهدي لهم نجاحي

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LIST of ABBREVIATIONS or SYMBOLS

Abbreviation	Whole name
AUC	Area under the curve
BCS	Biopharmaceutical classification system
C _{max}	Maximum concentration
Conc.	Concentration
D.I.	De ionized
dl	Deciliter
% DC	Percent drug content
DLLST	Dynamic laser light scattering technique
DMF	dimethylformamide
% DL	Percent drug loading
E	Rates of change in blood glucose level with time
% E E	Percent Entrapment Efficiency
Glip.	Glipizide
GTT	Glucose tolerance testing
HLB	Hydrophilic-lipophilic balance
HSH	High shear homogenization
HPLC	High performance liquid chromatography
HPMC	Hydroxypropyl Methylcellulose
hrs.	Hours
IU	International Unit
K	Rate constant
K ₁₀	Elimination rate constant (K ₁₀)
LC-MS-MS	Liquid Chromatography Mass Spectrometry
LOD	limit of detection
LOQ	limit of quantitation
μg	Microgram
μl	Microliter
M.P.	Melting Point
mV	Millivolt
ng	Nanogram
PCS	photon correlation spectroscopy
PDI	Polydispersity index
PRBA	Percentage relative bioavailability
PS	particle size
PTA	Phosphotungistic acid
% PY	Percentage production yield
r	correlation coefficient
Rpm	Round per minute
SD	Standard deviation
SLNs	Solid Lipid Nanoparticles
SLN 7	Formula no. 7
STZ	Streptozotocin
t _{1/2}	Half-life
t ₅₀	Time taken to release 50% of Glip. (Hours)

t ₉₀	Time taken to release 90% of Glip. (Hours)
TEM	Transmission Electron Microscope
t max	Time of maximum concentration
®	Trade Mark
USP	United states pharmacopeia
UV	Ultra violet
ZP	Zeta potential (ξ)

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Design, preparation and evaluation of Glipizide solid lipid nanoparticles for improving its oral bioavailability

By

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Supervisor

Dr. Jamal Alyoussef Alkarrad

ABSTRACT

The main aim of the present thesis is to develop Glipizide solid lipid nanoparticles (Glip-SLNs) for improving its bioavailability, therapeutic efficacy and increasing duration of action. Eight different formulae of Glip.-SLNs were produced by HSH and sonication technique. Solubility study was performed on different lipids including Beeswax, Compritol® 888 ATO, Precirol® ATO 5 and stearic acid to identify appropriate lipids for formulation of Glip.-SLNs. Particle size, PDI, zeta potential, %DC, %EE, %DL, %PY and in-vitro release parameters (t₅₀ and t₉₀) were taken as responses to detect the optimized formula. The results indicated solubility of Glip. in Compritol® 888 ATO and Precirol® ATO 5 which have low Hydrophilic-lipophilic balance (HLB). A valid HPLC method for analysis of Glip- SLNs showed the retention time of Glip. was 4.1 min. and the method was linear over a range of 1-20 µg/ml. Formula (SLN7) which composed of precirol as lipid base, span 60 as lipid surfactant, lutrol F 127 as aqueous surfactant and methocel E5 (1%) as viscosity increasing agent was the optimized formula. Particle size, PDI, ZP, % DC, % EE, % DL, % PY, t₅₀ and t₉₀ for optimized formula were 217 nm,

0.307, -13.80 mV, 99.29 %, 93.45%, 60.32%, 95.82%, 17.68 hrs. and 31.75 hrs. respectively.

On comparing oral bioavailability of Glip- SLNs (SLN7) with marketed product (Minidiab[®] 5 mg tablet) as tested by the rate of change in blood glucose level (E) in wistar rats after single oral dose, the bioavailability of (SLN7) has 2.50 folds increase than marketed product. Results of Liquid Chromatography Mass Spectrometry (LC-MS) for analysis of SN7 and marketed product in plasma of wistar rats showed percentage relative bioavailability (PRBA) of Glip. - SLNs (SLN 7) in comparison to marketed product (Minidiab[®] 5 mg tablet) was 413.00 %.