



**Studying In vivo and In vitro Bioavailability of Ferrous Sulfate  
and Folic Acid Using of Microemulsions as Colloidal Carriers**

**By**

**SEDEEQ MUSTAFA AL-DOORI**

**Supervisor**

**Dr. JAMAL ALYOUSSEF AL-KRAD**

**This thesis was submitted in partial fulfillment of the  
requirement for the Master's degree in the pharmaceutical  
sciences**

**Faculty of Pharmacy**

**Isra University**

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

يَرْفَعِ اللَّهُ الَّذِينَ آمَنُوا مِنْكُمْ وَالَّذِينَ

أُوتُوا الْعِلْمَ دَرَجَاتٍ وَاللَّهُ بِمَا

تَعْمَلُونَ خَبِيرٌ

صدق الله العظيم

المجادلة ١١

# *Committee Decision*

**Thesis (Studying In vivo and In vitro Bioavailability of Ferrous Sulfate and Folic Acid Using of Microemulsions as Colloidal Carriers)**

**Was successfully and approved on -----**

**Examination committee**

**signature**

**Dr. Jamal AL-krad (Supervisor)**

\_\_\_\_\_

**Assist. Prof. of pharmaceutical technology and biopharmacy**

**Dr. Ahmed A. Talhoni (examiner)**

\_\_\_\_\_

**Assist. Prof. of pharmacology**

**Dr. Hatim AL-khatib (examiner)**

\_\_\_\_\_

**Associate Prof. of industrial pharmacy and pharmaceuticals**

# ***Authorization Statement***

**I, Sedeeq Mustafa Al-Doori, authorize Isra University to supply hard and electronic copies of my thesis to libraries, establishment, or bodies and institutions concerned with research and scientific studies upon request, according to the university regulations.**

**Name : Sedeeq Mustafa Al-Doori**

**Date : 5/6/2018**

**Signature :**

# *Dedication*

*To the last final prophets and messengers of almighty Allah our master, leader and teacher Muhammad bin Abdullah (peace and blessing be upon him).*

*To the memory of my father who always encouraged me to seek knowledge.*

*My precious diamond and the light of my life, to my dear mother who became both a father and a mother to me. thanks to her prayers asking almighty God helping me to reach this level of education.*

*To my brothers and sisters, who created the motives inside me to continue my study and give me the power in this life.*

*To everyone who helps, teach me and take my hand to the right path in seeking knowledge.*

*Sedeeq M. Al-Doori*

*2018*

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***Sedeeq M. Al-Doori***

***2018***

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## *List of Abbreviations*

<b>Abbreviation</b>	<b>Meaning</b>
%	Percentage
°C	Degree Celsius
FA	Folic Acid
FeSO <sub>4</sub> 7H <sub>2</sub> O	Ferrous Sulfate Heptahydrate
BV	Blood Volume
cm <sup>2</sup>	Square centimeter
HPLC	High performance liquid chromatography
Eq	Equation
GIT	Gastrointestinal tract
Gr	Gram
Hr	Hour
L	Litter
μL	Microliter
Mg	Milligram
micg	Microgram
Min	Minute
m <sup>2</sup>	Square meter
Mwt	Molecular weight



Nm	Nanometer
Mm	Millimeter
pH	Negative logarithm of hydrogen ion concentration
RDA	Required Daily Amount
DMSO	Dimethyl sulfoxide
MEs	Microemulsions
O/W	Oil in Water
W/O	Water in Oil
SC	Subcutaneous
IPM	Isopropyl Myristate
Da	Dalton
TDDS	Transdermal Drug Delivery System
WBC <sub>s</sub>	White Blood Cells
RBC <sub>s</sub>	Red Blood Cells
HCL	Hydrochloric Acid
NaOH	Sodium Hydroxide
PO	Oral rout
IV	Intravenous route
IM	Intramuscular route
UV	Ultraviolet
CNS	Central Nerves System

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**Abstract**

The recent advance in drug delivery systems aims to enhance the safety and efficacy of treatment during the formulation of dosage form to be appropriate for the treatment and to achieve the best compliance and acceptance of the patient. One of these formulations is microemulsion. Microemulsions are potent drug delivery systems for transdermal application.

Ferrous sulfate and folic acid are usually used in treatment of anemia especially among women. However, the oral application of ferrous sulfate is associated with low bioavailability, gastrointestinal problems (constipation, flatulence, nausea, unpleasant taste, stomach pain) and food interaction.

The purpose of this study is to evaluation of in vitro and in vivo transdermal bioavailability of ferrous sulfate and folic acid in new developed microemulsions by my college to overcome many problems related with oral dosage form.

Four formulas of  $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$  microemulsions were tested in vitro using franz diffusion cell and in vivo.

Also, eight formulas of FA were selected to calculate the flux through the skin using franz diffusion cells and the penetrated amount quantified using HPLC.

S1 ( $\text{FeSO}_4$  19.2mg) showed the best flux about ( $0.01303 \text{ mg/cm}^2 \cdot \text{h}$ ). Furthermore, in the treated induced anemic rats by applying 0.5 ml of microemulsion over the skin for 28 days show weight and hematocrit (%) improvement and the improvement was proportional to the concentration.

Moreover the formula F3 3.17mg 4S:2T of folic acid microemulsion showed the best flux of ( $0.01147 \text{ mg/cm}^2 \cdot \text{h}$ ).

The developed systems showed good transdermal which candidate them be a good carrier for transdermal application of folic acid and ferrous sulfate.