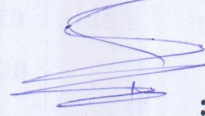


نموذج التفويض

أنا الحمزة حوشي خلف، أفوض جامعة الإسراء بتزويد نسخ من رسالتي للمكتبات أو المؤسسات أو الهيئات أو الأشخاص عند طلبهم حسب التعليمات النافذة في الجامعة.



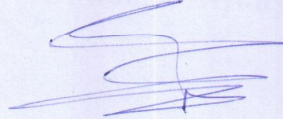
التوقيع :

2020/06/15 التاريخ :

Authorization Form

I **Alhamza Hoshi Khalaf**, authorize Al Isra University to supply copies of my Thesis to Libraries or establishments or Individuals on request, according to Isra University regulations.

Signature:



Date: 2020/06/15



**Preparing Sustained Release Alogliptin Tablets Using
Bentonite by Granulation**

By

Alhamza Hoshi Khalaf

Supervisor

Dr Jamal Alyoussef Alkrad

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

Faculty of Pharmacy

Isra University

June , 2020

COMMITTEE DECISION


This Thesis (Preparing Sustained Release Alogliptin Tablets Using Bentonite by Granulation) was successfully Defended and Approved on

Examinations Committee

Signature

Dr. Jamal Alyoussef Alkrad (Supervisor)

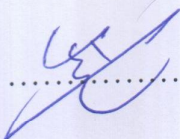
Associated Professor of Pharmaceutical
Technology and Biopharmacy
Isra University



.....

Dr. Ahmed Aljaberi (External examiner)

Associated Professor of Pharmaceutical
Technology and Biopharmacy
Applied Science Private University

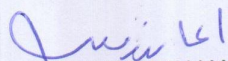


.....

Dr. Eman Darweesh Misbah ALZamily

(Internal examiner)

Assistant Professor of Pharmaceutics and Drug
Delivery
Isra University



.....

Dedication

To the last final prophet and messenger 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.

Acknowledgments

First of all praise be to Allah, Most Gracious, Most Merciful, for his unlimited support and favors.

I would like to express my thanks to **Dr. Jamal Alyoussef Alkrad**, my supervisor and head of the Department of Pharmaceutics, for his wise advices, patience and encouragement throughout all stages of my study.

I am so thankful to College of Pharmacy, University of Isra for offering the opportunity to continue my graduate study.

I would like also to express my grateful thanks to **my family**, for their patience, help, support and love.

Finally, I would like to extend my thanks to all others who helped me to finish this work.

Alhamza

Table of Contents

Subject	Page
Committee Decision.....	ii
Dedication.....	iii
Acknowledgement.....	iv
Table of Contents.....	v
List of Tables.....	vi
List of figures	viii
List of Abbreviations.....	ix
Abstract.....	xi
Chapter One	
Introduction	
1. Introduction.....	2
1.1 Alogliptin.....	2
1.2 Modified release drug delivery systems	3
1.2.1 Drug release by Diffusion.....	4
1.2.2 Release of drug by dissolution.....	5
1.2.3Release of drugs by osmotic pumping	7
1.2.4Release of drugs from pH dependent formulations.....	8
1.2.5 Release of drugs from pH dependent formulations.....	8
1.2.6 Release of drug by altering the density of formulations.....	8
1.3 Hydroxypropyl methylcellulose (HPMC).....	8
1.4 Bentonite and previous studies.....	9
1.5 Objectives.....	10
1.6 Aims of the Study.....	10
1.7 Research Questions.....	10
1.8 Hypothesis.....	10

Chapter Two	
Methodology	
2. Materials and instruments	12
2.1 Materials	12
2.2 Methods and instruments	12
2.2.1 Granulation and tableting	13
2.2.3 Differential scanning calorimeter (DSC) measurements.....	13
2.2.3 Fourier transform infrared spectroscopy (FTIR) Measurements	13
2.2.4 X-ray diffraction (XRD) characterization	13
2.2.5 Flow ability measurement.....	14
2.2.6 Measuring of the friability.....	14
2.2.7 Hardness measurement	14
2.2.8 Dissolution Profile	14
2.2.9 High pressure liquid chromatogram (HPLC) assay.....	14
2.2.10 Statistical evaluation.....	15
Chapter Three	
Results	
3. Results.....	17
3.1 Flow ability of granules	17
3.2 Hardness and friability of the tablets	17
3.3 FTIR-measurements	18
3.4 DSC measurements	20
3.5 HPLC-method	21
3.6 Dissolution rate of aloglpitin from the tablets	22
Chapter Four	
Discussion	
4. Discussion.....	26
5.Conclusion.....	28
References.....	29

LIST OF TABLES

Table No.	<i>Table Title</i>	Page
1	Composition of formulated tablets	13
2	The estimated flowability by CAR's index and Hausner ratio	17
3	The hardness and friability of prepared tablets.....	18
4	Some of bands of IR Spectrum aloglpitin and possible related groups.....	19
5	Calculated correlation coefficients for release data.....	24

LIST OF Figures

Table No.	<i>Table figures</i>	Page
1	Structure of alogliptin benzoate.....	2
2	Diffusion of the drug through porous inert membrane.....	5
3	Diffusion of the drug through a matrix.....	6
4	Dissolution from soluble matrix.....	7
5	Chemical structure of hydroxypropyl methylcellulose (HPMC), R = H, -CH ₃ or - (OCH ₂ CHCH ₃)xOH (Deshmukh et al., 2017)	9
6	FTIR-spectra of each of alogliptin, hydroxypropyl methyl cellulose (HPMC), Bentonite and prepared granules of previous components.....	19
7	DSC thermograms of alogliptin, alogliptin and bentonite physical mixture, HPMC and prepared granules of alogliptin with aid of 20% HPMC. Conditions: samples heated from 30 to 210 °C; heating rate:10 °C/min.....	20
8	XRD patterns of bentonite, bentonite- alogliptin granules and bentonite-alogliptin-HPMC mixture (granules with 20% HPMC)	21
9	Chromatogram of alogliptin using HPLC-method	22
10	Calibration curve of AB using HPLC-method.....	22
11	Dissolution profile of alogliptin from 5, 10, 20 and 30% HPMC Bentonite tablet.....	23
12	Gel structure of alogliptin bentonite tablets 20% HPMC after 24 hrs.....	26

List of Abbreviations

Abbreviation	Meaning
%	Percentage
°C	Degree Celsius
HPLC	High performance liquid chromatography
Eq	Equation
GIT	Gastrointestinal tract
g	Gram
hr	Hour
mL	Milliliter
μL	Microliter
Mg	Milligram
μg	Microgram
min	Minute
MWt	Molecular weight
nm	Nanometer
UV	Ultraviolet
HPMC	hydroxypropyl methyl cellulose
DPP-4	dipeptidyl peptidase-4
T2DM	type 2 diabetes mellitus
GLP-1	glucagon-like peptide-1
GRAS	generally recognized as safe
USGS	The United States Geological Survey
AB	Alogliptin benzoate

B	Bentonite
MCC	microcrystalline cellulose
FTIR	Fourier transform infrared spectroscopy
CI	CAR's index
XRD	X-ray diffraction
HR	Hausner Ratio
HPLC	High pressure liquid chromatogram

Preparing Sustained Release Alogliptin Tablets Using Bentonite by Granulation**By****Alhamza Hoshi Khalaf****Supervisor****Dr Jamal Alyoussef Alkrad****ABSTRACT**

This study is designed to evaluate the use of bentonite to develop and optimize sustained release tablets by granulation method. The tablets were prepared using different binders then tested for their pharmacopeal requirements. Also, a HPLC method was developed to assess the release pattern of alogliptin from the tablets. FTIR, DSC and powder-XRD were used to evaluate the compatibility between the drug and bentonite. The results showed that the tablets comply with their compendial requirements and no interaction between the drug and the excipient. Furthermore, the release profile revealed sustained release of alogliptin from the tablets prepared with aid of hydroxypropyl methyl cellulose (HPMC) as a binder. The data fitting showed that diffusion from the tablets followed Fickian model. However, it could be possible to formulate successfully sustained release tablets of alogliptin using bentonite as an excipient. The formulated tablets complied with pharmacopeial requirements. The developed tablets using bentonite by granulation are good candidate for further in vivo evaluation.