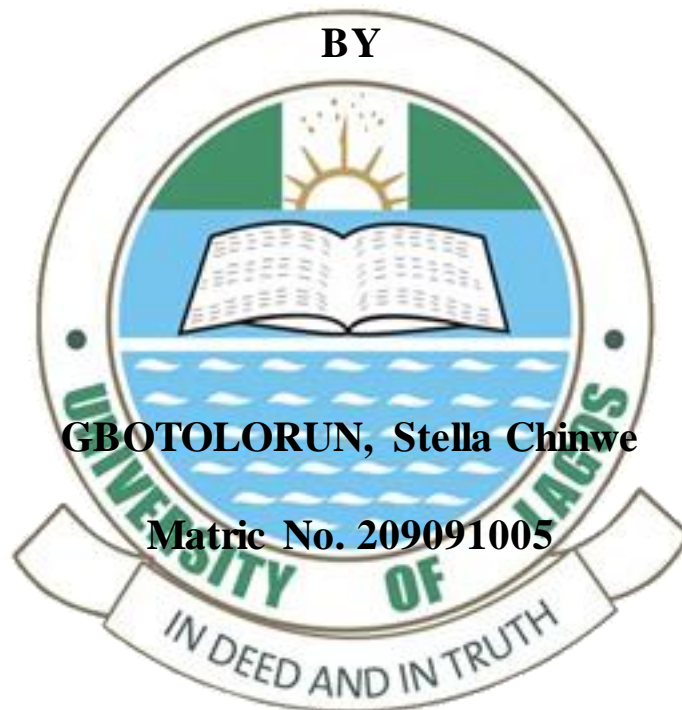


**HISTOMORPHOLOGICAL STUDIES OF THE EFFECTS
OF AMODIAQUINE ON THE OVARY IN SPRAGUE-
DAWLEY RATS**

BY



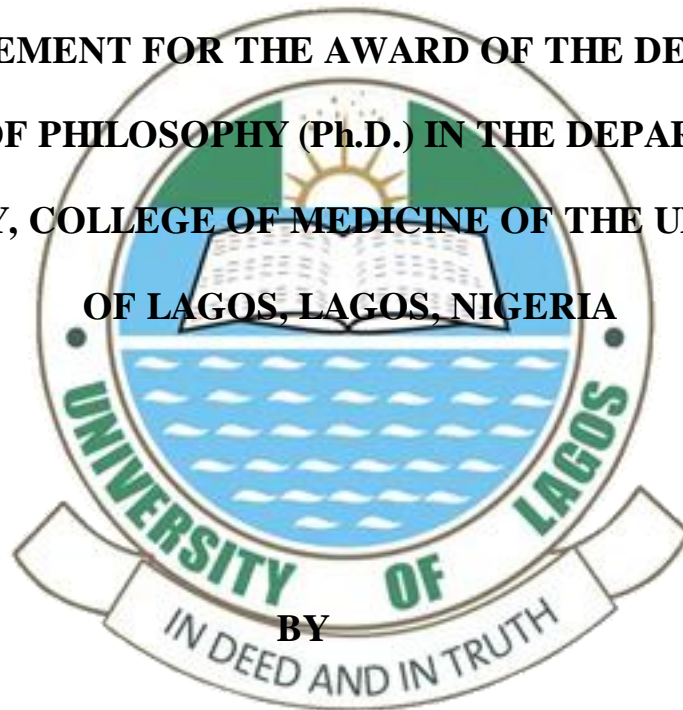
GBOTOLORUN, Stella Chinwe

Matric No. 209091005

SEPTEMBER, 2010

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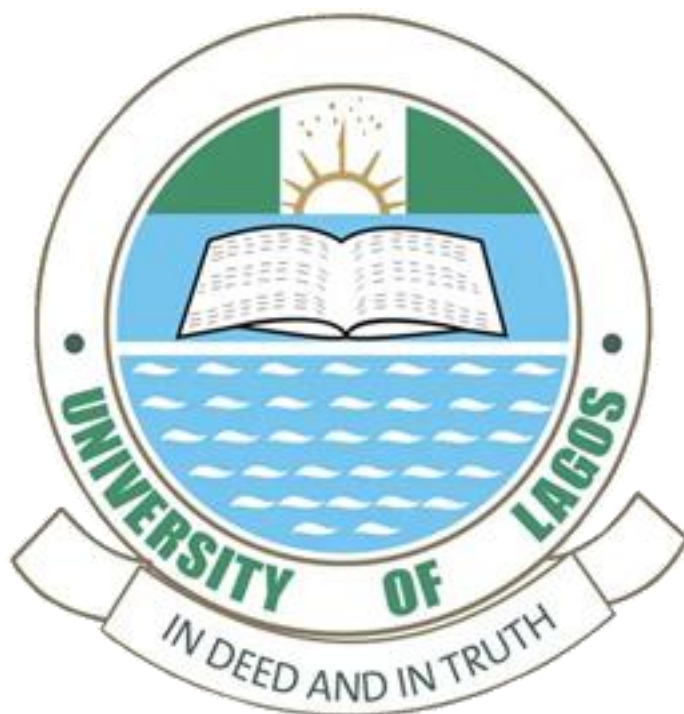
**THESIS SUBMITTED TO THE SCHOOL OF POSTGRADUATE
STUDIES, UNIVERSITY OF LAGOS, IN FULFILMENT OF THE
REQUIREMENT FOR THE AWARD OF THE DEGREE OF
DOCTOR OF PHILOSOPHY (Ph.D.) IN THE DEPARTMENT OF
ANATOMY, COLLEGE OF MEDICINE OF THE UNIVERSITY
OF LAGOS, LAGOS, NIGERIA**



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B.Sc. Anatomy (Portharcourt, 1998), M.Sc. Anatomy (Lagos, 2002)

SEPTEMBER, 2010



DECLARATION

We hereby declare that the thesis titled “HISTOMORPHOLOGICAL STUDIES OF THE EFFECTS OF AMODIAQUINE ON THE OVARY IN SPRAGUE-DAWLEY RATS” is a record of original research work carried out by GBOTOLORUN, Stella Chinwe in the Department of Anatomy, College of Medicine of the University Of Lagos, Nigeria.

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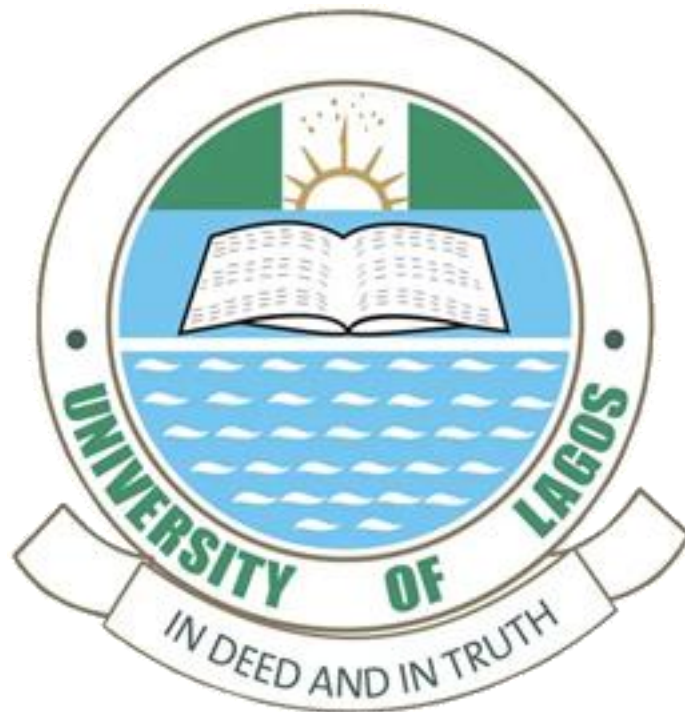
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SIGNATURE

DATE

DEDICATION

This work is dedicated to my darling husband Olalekan, and my lovely children, Ayooluwa and Anuoluwapo who have made my life more meaningful and purposeful. God bless you all.



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What will it profit a man if he gains the whole world and loses his soul? That is the biggest question everyone must ask himself/herself one day and I want to thank God Almighty that he has helped me answer this question truthfully and also to make the right choice. I want to also thank God for life and inspiration because “in Him I live and move and have my being”.

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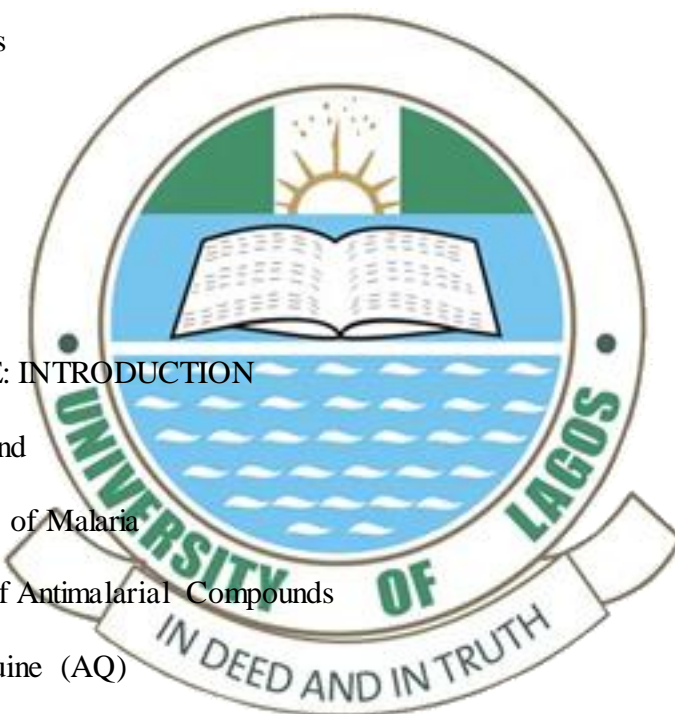
I also wish to express my sincere appreciation to Drs Duru, Ibeabuchi and Olabiya for their judgemental and critical contributions towards this study. To my other colleagues, Drs Aiyegbusi, Kusemiju and Yama, Mrs Dosumu, Ini-Okoko, Bakare, I say thank you.

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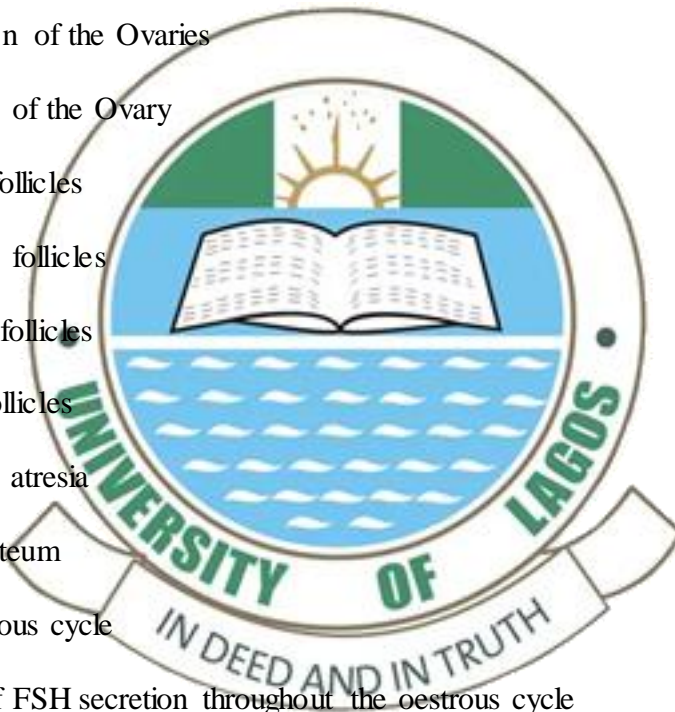
I express my sincere appreciation to Professor Banjo and Dr Anunobi of the department of Morbid Anatomy. To my parents Mr J.C Ndife and Mr and Mrs Gbotolorun, thank you for your support and encouragement. To my Daddy, I say thank you for believing in me.

TABLE OF CONTENTS

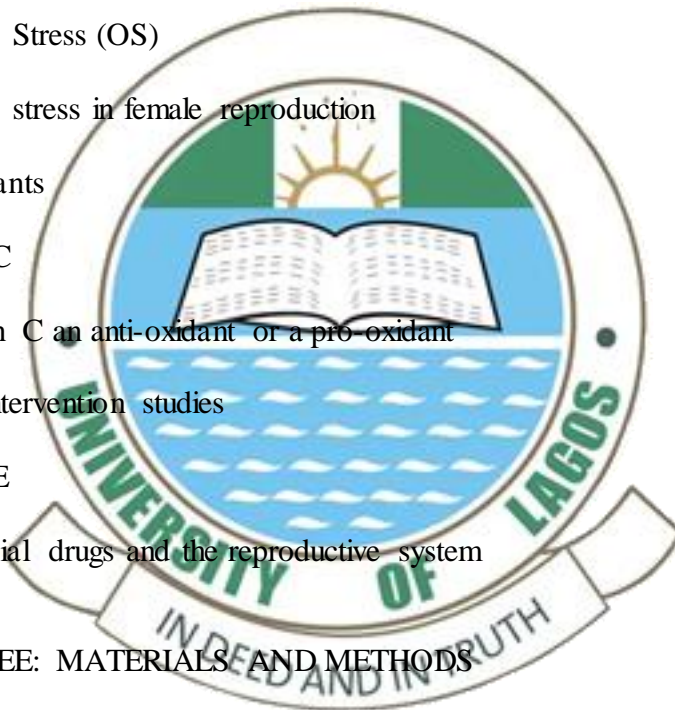
CONTENTS	PAGE
Cover page	i
Title page	ii
Certification	iii
Declaration	iv
Dedication	v
Acknowledgement	vi
Table of Contents	vii
List of Tables	xii
List of Plates	xiv
Abstract	xvii
CHAPTER ONE: INTRODUCTION	1
1.1 Background	1
1.1.1 Incidence of Malaria	1
1.1.2 History of Antimalarial Compounds	2
1.1.3 Amodiaquine (AQ)	3
1.1.4 Chemical Structure of Amodiaquine	4
1.1.5 Uses of Amodiaquine	5
1.2 Statement of the Problem	5
1.3 Overall Objective of the Study	7
1.4 Specific objectives of the Study	7
1.5 Significance of the Study	7
1.6 Operational Definitions of Terms	8



CHAPTER TWO: LITERATURE REVIEW	9
2.1 Metabolism of amodiaquine	9
2.2 Toxicity data on amodiaquine	11
2.3 Amodiaquine and pregnancy	14
2.4.0 The ovary	16
2.4.1 Gross anatomy of the Ovary	17
2.4.2 Arterial supply of the Ovaries	18
2.4.3 Venous and lymphatic drainage of the Ovaries	18
2.4.4 Innervation of the Ovaries	18
2.5.0 Histology of the Ovary	19
2.5.1 Ovarian follicles	20
2.5.2 Primordial follicles	20
2.5.3 Growing follicles	21
2.5.4 Mature follicles	22
2.5.5 Follicular atresia	23
2.5.6 Corpus luteum	23
2.6 The oestrous cycle	24
2.7 Pattern of FSH secretion throughout the oestrous cycle	26
2.8 Pattern of LH secretion throughout the oestrous cycle	26
2.9 Pattern of PRL secretion throughout the oestrous cycle	27
2.10 Folliculogenesis	28
2.10.1 Early folliculogenesis in humans	30
2.10.2 Early folliculogenesis in rodents	32
2.11 Follicle-stimulating hormone receptors and oocytes	33
2.12 Dominant selection of oocyte	36

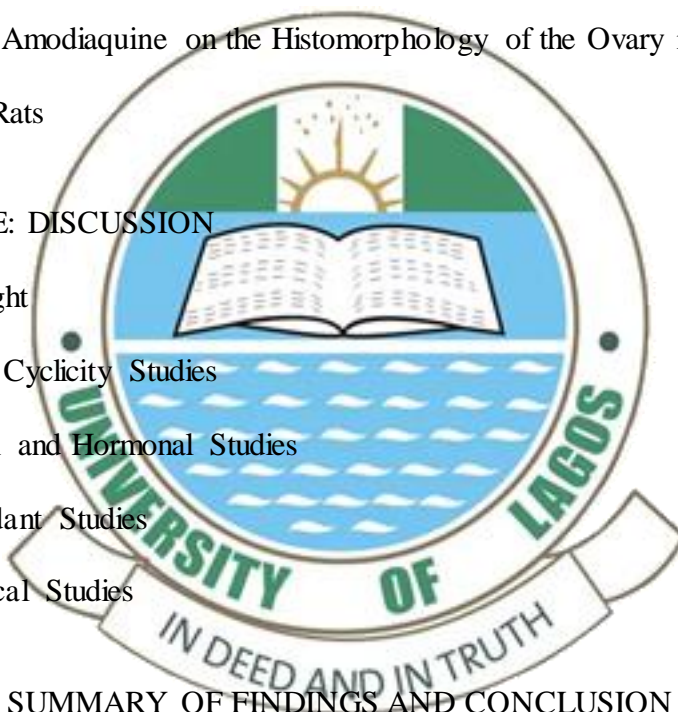


2.13	Oocyte recruitment	39
2.14	Role of oocyte in primary follicular growth	41
2.15	Preantral follicle growth and differentiation	44
2.16	Gonadotropin regulation of preantral follicles	47
2.17	FSH rescue of antral follicles	49
2.18	Cyclic changes of the ovarian surface epithelium (OSE) in the rat	51
2.19	Oocyte programmed cell death	55
2.20	Gonadotropin surge-attenuating factor	58
2.21	Oxidative Stress (OS)	59
2.21.1	Oxidative stress in female reproduction	62
2.22	Anti-oxidants	65
2.23	Vitamin C	67
2.23.1	Is Vitamin C an anti-oxidant or a pro-oxidant	69
2.23.2	Human intervention studies	70
2.24	Vitamin E	76
2.25	Antimalarial drugs and the reproductive system	80
CHAPTER THREE: MATERIALS AND METHODS		87
3.1	Experimental animals	87
3.2	Experimental protocols	87
3.3	Pilot study	87
3.3.1	A study of the effect of amodiaquine on the histology of the ovary	87
3.3.2	A study of the effect of amodiaquine on ovulation	87
3.4	Main study	88



3.4.1	Experiment 1: Determination of the effects of chronic administration of amodiaquine for 28 days on the oestrous cycle and on the morphology of the ovary	88
3.4.2	Experiment 2: Determination of the effect of amodiaquine on ovulation	89
3.4.3	Experiment 3: Determination of the effect of AQ on enzymatic antioxidant status in the Ovary and co-administration with Vitamin C and Vitamin E	90
3.4.4	Experiment 4: Determination of the effect of AQ on reproductive hormone	91
3.5	Amodiaquine administration	92
3.6	Vitamin C administration	92
3.7	Vitamin E administration	93
3.8	Determination of oestrous cycle	93
3.9	Determination of ovulation	94
3.10	Tissue processing for light microscopy	94
3.11	Determination of superoxide dismutase	94
3.12	Determination of catalase	95
3.13	Determination of reproductive hormones	95
3.13.1	Determination of FSH	95
3.13.2	Determination of LH	96
3.13.3	Determination of PRL	96
3.14	Statistical analysis	97
CHAPTER FOUR: RESULTS		98
4.1	Effect of Amodiaquine on Body Weight of Sprague-Dawley Rats	98
4.2	Effect of Amodiaquine on Oestrous Cycle	98
4.3	Effect of Amodiaquine on Ovulation	99

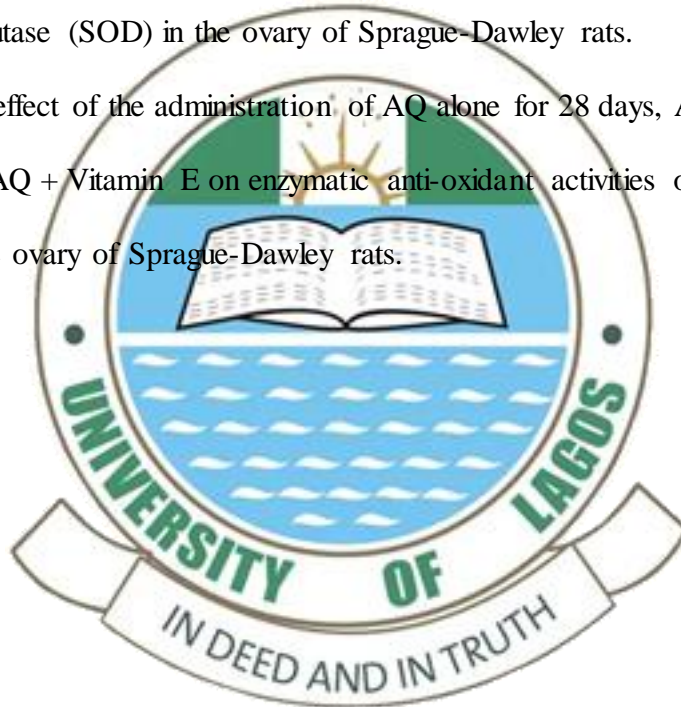
4.4	Effect of Amodiaquine on Serum Concentration of Prolactin	105
4.5	Effect of Amodiaquine on Serum Concentration of Follicle-Stimulating Hormone	105
4.6	Effect of Amodiaquine on Serum Concentration of Luteinizing Hormone	106
4.7	Effect of Amodiaquine on Superoxide Dismutase Activity in the Ovary of Sprague-Dawley Rats	112
4.8	Effect of Amodiaquine on Catalase Activity in the Ovary of Sprague-Dawley Rats	112
4.9	Effect of Amodiaquine on the Histomorphology of the Ovary in Sprague-Dawley Rats	116
CHAPTER FIVE: DISCUSSION		145
5.1	Bodyweight	145
5.2	Oestrous Cyclicity Studies	145
5.3	Ovulation and Hormonal Studies	147
5.4	Anti-Oxidant Studies	150
5.5	Histological Studies	152
CHAPTER SIX: SUMMARY OF FINDINGS AND CONCLUSION		155
6.1	Summary of Findings	155
6.2	Contributions to Knowledge	155
6.3	Conclusions	156
	Reference	157



LIST OF TABLES

Table 1: The effect of oral administration of AQ alone for 28 days, AQ + Vitamin C and AQ + Vitamin E on bodyweight of Sprague-Dawley rats	100
Table 2: The effect of intraperitoneal administration of AQ alone for 28 days, AQ + Vitamin C and AQ + Vitamin E on bodyweight of Sprague-Dawley rats.	101
Table 3: The effect of the administration of AQ alone for 28 days, AQ + Vit C and AQ + Vit E on the length of the oestrous cycle in Sprague-Dawley rats.	102
Table 4: The effect of the oral administration of AQ alone for 28 days, AQ + Vitamin C and AQ + Vitamin E on the mean number of days spent in the phases of the oestrus cycle in Sprague-Dawley rats.	103
Table 5: The effect of the intraperitoneal administration of AQ alone for 28 days, AQ + Vitamin C and AQ + Vitamin E on the mean number of days spent in the phases of the oestrus cycle in Sprague-Dawley rats.	104
Table 6: The effect of the oral administration of AQ alone, AQ + Vitamin C and AQ + Vitamin E on the number of ova shed (Mean \pm SD) in the oviduct in the morning of estrus in Sprague-Dawley rats	107
Table 7: The effect of the intraperitoneal administration of AQ alone, AQ + Vitamin C and AQ + Vitamin E on the number of ova shed (Mean \pm SD) in the oviduct in the morning of estrus in Sprague-Dawley rats	108
Table 8: The effect of the oral and intraperitoneal administration of AQ alone, AQ + Vitamin C and AQ + Vitamin E on the concentration of Prolactin (PRL) at 6 p.m. on proestrus in Sprague-Dawley rats.	109

Table 9: The effect of the oral and intraperitoneal administration of AQ alone, AQ + Vitamin C and AQ + Vitamin E on the concentration of Follicle-stimulating hormone (FSH) at 6 p.m. on proestrus in Sprague-Dawley rats.	110
Table 10: The effect of the oral and intraperitoneal administration of AQ alone, AQ + Vitamin C and AQ + Vitamin E on the concentration of Luteinizing hormone (LH) at 6 p.m. on proestrus in Sprague-Dawley rats.	111
Table 11: The effect of the administration of AQ alone for 28 days, AQ + Vitamin C and AQ + Vitamin E on enzymatic anti-oxidant activities of superoxide dismutase (SOD) in the ovary of Sprague-Dawley rats.	114
Table 12: The effect of the administration of AQ alone for 28 days, AQ + Vitamin C and AQ + Vitamin E on enzymatic anti-oxidant activities of catalase (CAT) in the ovary of Sprague-Dawley rats.	115



LIST OF PLATES

Plate 1: Micrograph of cross-section of ovary of rat in control group x100	119
Plate 2: Micrograph of cross-section of ovary of rat in control group x400	120
Plate 3: Micrograph of cross-section of ovary of rat in treatment group 6 mg/kg bw AQ oral route for 28 days. x100	121
Plate 4: Micrograph of cross-section of ovary of rat in treatment group 6 mg/kg bw AQ oral route for 28 days. x400	122
Plate 5: Micrograph of cross-section of ovary of rat in treatment group 6 mg/kg bw AQ oral route and co-administration with 0.1 mg/kg bw Vitamin C for 28 days. x100	123
Plate 6: Micrograph of cross-section of ovary of rat in treatment group 6 mg/kg bw AQ oral route and co-administration with 0.1 mg/kg bw Vitamin C for 28 days. x400	124
Plate 7: Micrograph of cross-section of ovary of rat in treatment group 6 mg/kg bw AQ oral route and co-administration with 20 mg/kg bw Vitamin E for 28 days. x100	125
Plate 8: Micrograph of cross-section of ovary of rat in treatment group 6 mg/kg bw AQ oral route and co-administration with 20 mg/kg bw Vitamin E for 28 days. x400	126
Plate 9: Micrograph of cross-section of ovary of rat in treatment group 6 mg/kg bw AQ intraperitoneal route for 28 days. x100	127
Plate 10: Micrograph of cross-section of ovary of rat in treatment group 6 mg/kg bw AQ intraperitoneal route for 28 days. x400	128

Plate 11: Micrograph of cross-section of ovary of rat in treatment group 6 mg/kg bw AQ intraperitoneal route for 28 days and co-administration with 0.1 mg/kg bw Vitamin C. x100	129
Plate 12: Micrograph of cross-section of ovary of rat in treatment group 6 mg/kg bw AQ intraperitoneal route for 28 days and co-administration with 0.1 mg/kg bw Vitamin C. x400	130
Plate 13: Micrograph of cross-section of ovary of rat in treatment group 6 mg/kg bw AQ intraperitoneal route for 28 days and co-administration with 20 mg/kg bw Vitamin E. x100	131
Plate 14: Micrograph of cross-section of ovary of rat in treatment group 6 mg/kg bw AQ intraperitoneal route for 28 days and co-administration with 20 mg/kg bw Vitamin E. x400	132
Plate 15: Micrograph of cross-section of ovary of rat in treatment group 6 mg/kg bw AQ oral route for 28 days. x100	133
Plate 16: Micrograph of cross-section of ovary of rat in treatment group 12 mg/kg bw AQ oral route for 28 days. x400	134
Plate 17: Micrograph of cross-section of ovary of rat in treatment group 12 mg/kg bw of AQ oral route for 28 days and co-administration with 0.1 mg/kg bw of Vitamin C. x100	135
Plate 18: Micrograph of cross-section of ovary of rat in treatment group 12 mg/kg bw of AQ oral route for 28 days and co-administration with 0.1 mg/kg bw of Vitamin C. x400	136
Plate 19: Micrograph of cross-section of ovary of rat in treatment group 12 mg/kg bw of AQ oral route for 28 days and co-administration with 20 mg/kg bw of Vitamin E. x100	137

Plate 20: Micrograph of cross-section of ovary of rat in treatment group 12 mg/kg bw of AQ oral route for 28 days and co-administration with 20 mg/kg bw of Vitamin E. x400	138
Plate 21: Micrograph of cross-section of ovary of rat in treatment group 12 mg/kg bw of AQ intraperitoneal route for 28 days. x100	139
Plate 22: Micrograph of cross-section of ovary of rat in treatment group 12 mg/kg bw of AQ intraperitoneal route for 28 days. x400	140
Plate 23: Micrograph of cross-section of ovary of rat in treatment group 12 mg/kg bw of AQ intraperitoneal route for 28 days and co-administration with 0.1 mg/kg bw of Vitamin C. x100	141
Plate 24: Micrograph of cross-section of ovary of rat in treatment group 12 mg/kg bw of AQ intraperitoneal route for 28 days and co-administration with 0.1 mg/kg bw of Vitamin C. x400	142
Plate 25: Micrograph of cross-section of ovary of rat in treatment group 12 mg/kg bw of AQ intraperitoneal route for 28 days and co-administration with 20 mg/kg bw of Vitamin E. x100	143
Plate 26: Micrograph of cross-section of ovary of rat in treatment group 12 mg/kg bw of AQ intraperitoneal route for 28 days and co-administration with 20 mg/kg bw of Vitamin E. x400	144

ABSTRACT

The prevalence of female infertility ranges from 7 to 28% depending on the age of the woman. Although the origin and frequency of infertility vary about 40 to 50% of the aetiology of infertility cases is as a result of female factors. Malaria and the treatment of malaria have being a major challenge for decades. A number of antimalarial drugs have been reported to have anti-fertility actions.

Amodiaquine (AQ) is an anti-malarial drug and belongs to a class of drugs known as the 4-aminoquinolines. It was removed from the essential drug list in 1990 as a result of hepatotoxicity and agranulocytosis that occurred with long-term use. AQ is now making a comeback and is in the spotlight as a partner drug with artemisinin in the World Health Organization (WHO) recommended artemisinin based combination therapies (ACTs). In malaria-endemic regions of the world, self medication with antimalarial drugs is common and it is possible for a person to be treated several times in a year. With the frequency of treatment the risk of adverse events associated with long-term use of AQ may arise.

A number of investigators have carried out studies on the effect of AQ on pregnancy and pregnancy outcomes, however, there remains a dearth of literature on the short-term or long-term effect of AQ on the structure and function of the ovary in the non-pregnant female.

This study was carried out to investigate the histomorphological changes and responses of the ovary of Sprague-Dawley rats to AQ administration. The study was divided into 4 experimental groups. AQ was given at a dose of 6.0 and 12 mg/kg bw via oral and intraperitoneal routes for 28 days. Vitamin C was administered at a dose of 0.1 mg/kg bw 3 days in a week while Vitamin E was given at a dose of 20 mg/kg bw 5 days in a week. In each of the experiments AQ was administered alone, co-administered with

Vitamin C and co-administered with Vitamin E (AQ alone, AQ + Vitamin C and AQ + Vitamin E) according to the treatment protocol. At the end of the experiment all the animals were sacrificed by cervical dislocation.

Oestrus cycle was determined using the vaginal smear method and ovulation was determined at 10:00hr on the day of estrus. The ovary was dissected and processed for histology, assayed for superoxide dismutase and catalase activities and also assayed for reproductive hormones (follicle stimulating hormone (FSH), luteinizing hormone (LH) and prolactin (PRL).

The result of the oestrous cycle showed that AQ prolonged the length of the oestrous cycle and was statistically significant in the group that received 12 mg/kg bw via intraperitoneal route. Co-administration of AQ + Vitamin C increased the cycle length even further and was statistically significant ($p < 0.05$) except in the group that received 6 mg/kg bw intraperitoneal route. The ovulation studies showed that AQ reduced the number of ova that was shed in the morning of estrus and was statistically significant ($p < 0.05$) in the group that received 6.0 and 12 mg/kg bw oral route.

Histology of the ovary showed that AQ increased the number of atretic follicles when compared with the control. There appeared to be more atretic follicles at 12 mg/kg bw than at 6.0 mg/kg bw AQ. AQ caused reduction in the activities of superoxide dismutase and catalase in the ovary and was statistically significant ($p < 0.05$) in the groups that received AQ + Vitamin C.

The expected surge in FSH, LH and PRL between 5 to 7 p.m. on proestrus that is expected for the follicular rupture that occurs at ovulation was experienced in this study. There was no statistically significant difference in the serum concentration of these hormones when compared with the control group. The results obtained in this study shows that AQ is deleterious to the ovary.