

**METABOLIC STUDY ON SOME AGENTS
AFFECTING OBESITY INDUCED IN
EXPERIMENTAL RATS**

Thesis

**Submitted for fulfilment of Master Degree in
Pharmaceutical Sciences (Biochemistry)**

By

Maha Abdo Ali Ahmad

B.Sc. of Pharmacy (2001)

Supervisors

Prof. Dr. Mohamed M. El Seweidy

Professor of Biochemistry Department

Faculty of Pharmacy

Zagazig University

Dr. Fatmah Rizk Abdullah

Professor of Biochemistry

Faculty of Pharmacy

Zagazig University

Faculty of Pharmacy

Zagazig University

2008

بسم الله الرحمن الرحيم
“ قالوا سبحانك لا علم لنا إلا ما علمتنا
إنك أنت العليم الحكيم ”

صدق الله العظيم

(سورة البقرة – الآية 32)

*Dedicated to all whom have
Supported me
And Contributed
To the birth of this
Work*

*My Husband, Children, Mother,
Sisters,*

And

*Memory of my Father
Nevertheless My Mentor Professor*

LIST OF ABBREVIATION

According to order in the text

WHO	World Health Organization
TNF – α	Tumour necrosis factor – alpha
LPL	Lipo protein lipase
GLUT	Glucose transporter expression
IGF – 1	Insulin like growth factor - one
ob	Obese gene
EIn	Energy intake
EOUT	Energy expenditure
BMD	Bone mineral density
DEXA	Dual Energy X-ray Absorptiometry
BMI	Body mass index
BED	Binge eating disorder
GH	Growth hormone
ECG	Electro cardiogram
KDa	Kilo Dalton
ICAM-1	Intercellular cell adhesion molecules - one
VCAM-1	Vascular cell adhesion molecule – one
E- selectin	Endothelial – selectin type of cell adhesion molecule
ALT	Alanine aminotransferase
β -AR	Beta adrenergic receptor
T2D	Type two diabetes
P450	Cytochrom P450 (liver enzyme)
LV	Left ventricle
aMSH	Alpha melanocyte-stimulating hormone
UCP1	Uncoupling Protein one
ACC1	Acetyl-CoA Carboxylase one

POMC	ProOpioMelanoCortin
ACP1	Acid Phosphatase one
MC4Rs	MelanoCortin four Receptor
AGRP	AGouti-Related Protein
cAMP	Cyclic adenosine monophosphate
K cal	Kilo calorie
TG	Triacylglycerol
GABA	Gamma amino butyric acid
NPY	Neuropeptide Y (a potent feeding stimulant secreted by cells in the gut and in the hypothalamus)
IL – 6	Interleukin- six
IL - 1	Interleukin-one
IGFBP-3	Insulin- binding protein three
IGFBP	Insulin- binding protein from one to six
ADMA	Asymmetric dimethylarginine
AMPK	AMP-activated protein kinase
eNOS	Endothelial nitric oxide synthase
PKB	Protein kinase beta
NO	Nitric oxide
LDL	Low-density lipoprotein
NAFLD	Non-alcoholic fatty liver disease
NASH	Non-alcoholic steato hepatitis
ORAC	Oxygen radical absorbance capacity
TE	Trolox equivalents
LEP	Leptin gene symbol
NF – α β	Nuclear factor alpha & beta
ROS	Reactive oxygen species
CRP	C – reactive protein
mRNAs	Messenger Ribonucleic acids

SCD – 1	Stearoyl - CoA desaturase -one
WAT	White adipose tissue
IPAT	Inter peritoneal adipose tissue
NEFA	Non- esterified fatty acid
LDL	Low density lipoprotein
HDL	Height density lipoprotein
Apo A	Apolipoprotein A
Apo B	Apolipoprotein B
PGF	Pomegranate flower extract
PJ	Pomegranate Juice
NF- KB	Nuclear factor kappa B
HAE	Hydro alcoholic extract
TC	Total cholesterol
HDL – C	High density lipoprotein cholesterol
ASCVD	Atherosclerotic cardiovascular disease
LDL – C	Low density lipoprotein cholesterol
VHM	Ventromedial hypothalamus
CNS	Central nervous system
GLUT- 4	Glucose transporter four
EGCG	Epigallocatechingallate
SREBP-1	Sterol-regulated element binding protein one
HUVECs	Human umbilical vein endothelial cells
AUC	Area under curve
EGC	Epigallocatechin
EC	Epi catechin
NA-cAMP	Nicotinamide Adenine cyclic adenosine monophosphate
IL – 8	Interleukin-eight
LPS	Lipopolysaccharide
mTOR	Mediated signaling pathways in the tumor

	cells
EA	Ellagic acid
CAS	Carotid artery stenosis
IMT	Intimal-Medial Thickness
COX-2	Cyclooxygenase - two
PW	Pomegranate wine
RW	Red wine
NAC	N-acetyl cysteine
M – 1	Mixture one
M – 2	Mixture two

LIST OF TABLES

	Page
Table 1: Effect of oral administration of green tea extract (10 mg / kg), curcuminoids (500 mg / kg), pomegranate juice (500 mg / kg), chitosan powder (3000 mg / total body weight) daily either individually or in combination forms on serum TClevel (mg / dl) of obese rats after 3 and 5 weeks.	4-2
Table2: Effect of oral administration of green tea extract (10 mg / kg), curcuminoids (500 mg / kg), pomegranate juice (500 mg / kg), chitosan powder (3000 mg / total body weight) daily either individually or in combination forms on serum TG level (mg / dl) of obese rats after 3 and 5 weeks.	4-5
Table 3: Effect of oral administration of green tea extract (10 mg / kg), curcuminoids (500 mg / kg), pomegranate juice (500 mg / kg), chitosan powder (3000 mg / total body weight) daily either individually or in combination forms on serum HDLc	4-8

level (mg / dl) of obese rats after 3 and 5 weeks.

Table 4: Effect of oral administration of green tea extract (10 mg / kg), curcuminoids (500 mg / kg), pomegranate juice (500 mg / kg), chitosan powder (3000 mg / total body weight) daily either individually or in combination forms on serum TC / HDLc ratio of obese rats after 3 and 5 weeks. 4-11

Table 5: Effect of oral administration of green tea extract (10 mg / kg), curcuminoids (500 mg / kg), pomegranate juice (500 mg / kg), chitosan powder (3000 mg/ total body weight) daily either individually or in combination forms on serum TNF - α level (ng / ml) of obese rats after 3 and 5 weeks. 4-14

Table 6: Effect of oral administration of green tea extract (10 mg / kg), curcuminoids (500 mg / kg), pomegranate juice (500 mg / kg), chitosan powder (3000 mg / total body weight) daily either individually or in combination forms on serum leptin level (ng / ml) of obese rats after 3 and 5 weeks. 4-17

- Table 7:** Effect of oral administration of green tea extract (10 mg / kg), curcuminoids (500 mg / kg), pomegranate juice (500 mg / kg), chitosan powder (3000 mg / total body weight) daily either individually or in combination forms on serum IGF – I level (ng / ml) of obese rats after 3 and 5 weeks.
- Table 8:** Effect of oral administration of green tea extract (10 mg / kg), curcuminoids (500 mg / kg), pomegranate juice (500 mg / kg), chitosan powder (3000 mg / total body weight) daily either individually or in combination forms on triacylglycerol content adipose tissue extract (mg /dl) of obese rats after 3 and 5 weeks. 4-23
- Table 9:** Effect of oral administration of green tea extract (10 mg / kg), curcuminoids (500 mg / kg), pomegranate juice (500 mg / kg), chitosan powder (3000 mg / total body weight) daily either individually or in combination forms on body weight in rats after 3 and 5 weeks. 4-26
- Table 10:** Effect of oral administration of total green tea extract (10 mg/ kg / day), curcuminoids (500 mg / kg for alcoholic extract / day), pomegranate juice (500 mg / kg / day), chitosan powder (3000 mg / to total body weight / day) either 4-29

individually or in combined forms on waist circumference in rats for 3 and 5 weeks.

Table 11: Correlations coefficients between studied parameters after 3 weeks.	4-32
Table 12: Correlations coefficient between studied parameters after 5 weeks.	4-34
Table 13: Correlations coefficient between TNF - α , IGF – I, Leptin, body weight and waist after 3 weeks.	4-36
Table 14: Correlations coefficient between TNF - α , IGF - I, Leptin, triacylglycerol in adipose tissue body weight and waist after 5 weeks.	4-38

LIST OF FIGURES

	Page
Fig(1- a): Effect of oral administration of green tea extract (10 mg / kg), curcuminoids (500 mg / kg), pomegranate juice (500 mg / kg), chitosan powder (3000 mg / total body weight) daily either individually or in combination forms on serum TC level (mg / dl) of obese rats after 3 and 5 weeks.	4-3
Fig (2- a): Effect of oral administration of green tea extract (10 mg / kg), curcuminoids (500 mg / kg), pomegranate juice (500 mg / kg), chitosan powder (3000 mg / total body weight) daily either individually or in combination forms on serum TG level (mg / dl) of obese rats after 3 and 5 weeks.	4-6
Fig (3- a): Effect of oral administration of green tea extract (10 mg / kg), curcuminoids (500 mg / kg), pomegranate juice (500 mg / kg), chitosan powder (3000 mg / total body weight) daily either individually or in combination forms on serum HDLc	4-9

level (mg / dl) of obese rats after 3 and 5 weeks.

- Fig (4- a):** Effect of oral administration of green tea extract (10 mg / kg), curcuminoids (500 mg / kg), pomegranate juice (500 mg / kg), chitosan powder (3000 mg / total body weight) daily either individually or in combination forms on serum TC / HDLc ratio of obese rats after 3 and 5 weeks. 4-12
- Fig (5- a):** Effect of oral administration of green tea extract (10 mg / kg), curcuminoids (500 mg / kg), pomegranate juice (500 mg / kg), chitosan powder (3000 mg/ total body weight) daily either individually or in combination forms on serum TNF - α level (ng / ml) of obese rats after 3 and 5 weeks. 4-15
- Fig(6- a) :** Effect of oral administration of green tea extract (10 mg / kg), curcuminoids (500 mg / kg), pomegranate juice (500 mg / kg), chitosan powder (3000 mg / total body weight) daily either individually or in combination forms on serum leptin level (ng / ml) of obese rats after 3 and 5 weeks. 4-18
- Fig (7- a):** Effect of oral administration of green tea extract (10 mg / kg), curcuminoids (500 mg / kg), pomegranate juice (500 mg / 4-21

kg), chitosan powder (3000 mg / total body weight) daily either individually or in combination forms on serum IGF – I level (ng / ml) of obese rats after 3 and 5 weeks.

Fig (8- a): Effect of oral administration of green tea extract (10 mg / kg), curcuminoids (500 mg / kg), pomegranate juice (500 mg / kg), chitosan powder (3000 mg / total body weight) daily either individually or in combination forms on triacylglycerol content adipose tissue extract (mg /dl) of obese rats after 3 and 5 weeks. 4-24

Fig (9- a): Effect of oral administration of green tea extract (10 mg / kg), curcuminoids (500 mg / kg), pomegranate juice (500 mg / kg), chitosan powder (3000 mg / total body weight) daily either individually or in combination forms on body weight in rats after 3 and 5 weeks. 4-27

Fig (10-a):Effect of oral administration of green tea extract (10 mg/ kg / day), curcuminoids (500 mg / kg for alcoholic extract / day), pomegranate juice (500 mg / kg / day), chitosan powder (3000 mg / to total body weight / day) either individually or in combined forms on waist circumference in rats for 3 and 5 weeks. 4-30