بسم الله الرحمن الرحيم

شبكة المعلومـــــات الجامعية

التوثيق الالكتروني والميكروفيلم

شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

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Effect of Bile Acids on Incidence of Cholesterol Gallstone In Hamsters on Lithogenic Diet.

Thesis
Submitted for fulfillment of Ph. D degree in science
(Biochemistry)

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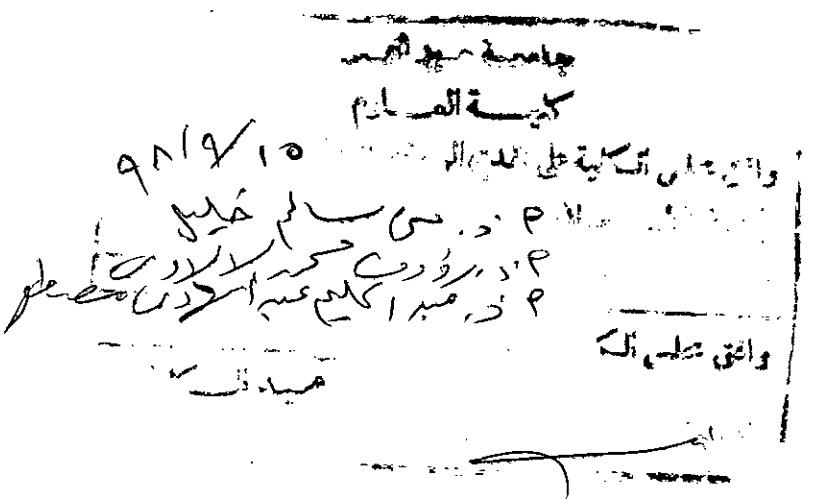

I declare that this thesis has been composed by myself and that the work of which is a record has been done by myself. It has not been submitted for a degree at this or any other university.

Said S. Mousthy

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ABSTRACT

Said Salama Mouslhy

Effect of bile acids on incidence of cholesterol gallstone in hamsters on lithogenic diet

Biochemistry Department, Faculty of Science, Ain Shams University

The effect of bile acids as ursodeoxycholic acid (UDCA) and chenodeoxycholic acid (CDCA) on cholesterol gallstone formation was studied in hamsters. Gallstones were formed in 58% of the animals fed on lithogenic diet for 6 weeks. Supplementation of lithogenic diet with 0.1% UDCA or 0.1% CDCA reduces the formation of gallstones to 25% and 33% respectively. The lithogenic diet caused a significant elevation in serum total cholesterol, LDL-C, HDL-C, liver total cholesterol and a significant decrease in the hydroxymethyglutaryl CoA reductase (HMG CoAR), the rate limiting enzyme in cholesterol synthesis, also biliary total cholesterol was significantly increased as compared with control animals. Addition of 0.1% UDCA or 0.1% CDCA to lithogenic diet tended to lower serum total cholesterol, LDL-C, liver total cholesterol, and inhibition of HMG-CoAR as compared with lithogenic diet ($P<0.001$). The UDCA is more effective than CDCA but the difference is not significant. Histologically, the liver of hamsters fed on lithogenic diet exhibit bile duct proliferation, inflammatory infiltration, accumulation of fat in parenchyma cells. Gallbladder displayed disappearances of trabecula, pyknotic nuclei, flatting of the mucosal cell. Morphologic alterations were ameliorated by supplementation of lithogenic diet with 0.1% UDCA or 0.1% CDCA.

Key words:

Cholesterol gallstone, ursodeoxycholic acid, chenodeoxycholic acid, HMG-CoAR, Hamsters.

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Said S. Moustly

LIST OF ABBREVIATIONS

ACAT	Acyl CoA: cholesterolacyltransferase
A/G	Albumin/Globulin
ALp	Alkaline phosphatase
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
BCG	Bromo cresol green
CA	Cholic acid
CDCA	Chenodeoxycholic acid
CDCA-sul	Chenodeoxycholic acid sulfonate
Conc	Concentration
DCA	Deoxycholic acid
dL	Deciliter
DTNB	Dithionitrobenzoic acid
D.W	Distal water
EDTA	Ethylene diamine tetra-acetic acid
EMD	DL-2-phenyl [6-ethoxybenzothiazolyl-(2)-thio] propionic acid.
Fig	Figure
G	Globulin
g	gram
γ GT	gamma-glutamyl transferase

gp	group
GS	Gallstone
GSF	Gallstone free
HDCA	Hyodeoxycholic acid
HDL-C	High density lipoprotein cholesterol
HMG-CoA	Hydroxymethylglutaryl coenzyme A-reductase
homo-CDCA	homo-chenodeoxycholic acid
homo-UDCA	homo-ursodeoxycholic acid
HPLC	High performance liquid chromatography
Kg	Kilogram
L	Liter
LCA	Lithocholic acid
LD	Lithogenic diet
LDH	Lactate dehydrogenase
LDL-C	Low density lipoprotein cholesterol
M	Molar
MDH	Malate dehydrogenase
MDCA	Murideoxy cholic acid
mg	Miligram
ml	Mililiter
min	Minute

N	Normal
n	Number
$NADP^+$	Nicotinamide adenine dinucleotide phosphate
nm	Nanometer
N.S	Non-significant
P mole	Pico mole
r.p.m	revolution per minute
S.D	Standard deviation
S.E	Standard error
TPN	Total parenteral nutrition
TLC	Thin layer chromatography
TUDCA	Tauro-ursodeoxycholic acid
U	Unit
CDCA	Chenodeoxycholic acid
CDCA-sul	Chenodeoxycholic acid sulfonate
μg	Microgram
μl	Microliter
μmole	Micromole
UV	Ultraviolet
VLDL	Very low density lipoprotein
Vs	Versus