بسم الله الرحمن الرحيم

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تم رفع هذه الرسالة بواسطة / مني مغربي أحمد

بقسم التوثيق الإلكتروني بمركز الشبكات وتكنولوجيا المعلومات دون أدنى مسئولية عن محتوى هذه الرسالة.

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Faculty of Specific Education

Home Economics Department

(Food and Nutrition Sciences)

The potential protective role of pomegranate molasses against biochemical changes induced by doxorubicin in male rats

A thesis submitted in partial fulfillment of the requirements for the degree of Doctor in Philosophy Specific Education

In

Home Economics

(Food and Nutrition Sciences)

Presented by

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2022

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Declaration

I hereby declare that no part of this dissertation has been submitted to Alexandria University or to any other University in Egypt or abroad as part of the requirements to obtain another degree. Furthermore, Alexandria University code of ethics and rules of academic integrity have been followed.

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Hoda Abdelrahman Yossef Shallan

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ACP	acid phosphatase
ALP	alkaline phosphatase
ALT	alanine aminotransferase
AST	aspartate aminotransferase
BW	Body weight
BWG	body weight gain
CAS	carotid artery stenosis
CAT	Catalase
CIMT	carotid intima–media thickness
CP	Cisplatin
CVD	Cardiovascular disease
Cyt c	cytochrome C
DOX	Doxorubicin
DZA	Diazinon
ECG	electrocardiographic
FBW	final body weight
$Fe2^{+}$	Ferrous
$Fe3^{+}$	Ferric ion
FN	urine fibronectin
GAG	glycosaminoglycan
GGT	gamma-glutamyl transferase
GPX	Glutathione Peroxidase
GSH	Reduced Glutathione
H_2O_2	Hydrogen Peroxide
HDL-c	high- density lipoprotein-cholesterol
HF	heart failure
IBW	initial body weight

LDH	Lactate Dehydrogenase
LDL-c	low-density lipoprotein-cholesterol
LPL	lipoprotein lipase
MDA	Malondialdehyde
NADPH	Nicotinamide adenine dinucleotide phosphate hydrogen
NAG	N-acetyl-D-glucosaminidase
NCD	noncommunicable disease
NO	Nitric Oxide
$O^{\cdot -2}$	Superoxide Anions
OH	Hydroxyl
PARP	Poly (ADP-ribose) polymerase
PCC	protein carbonyl content
PFE	pomegranate fruit extract
PJ	Pomegranate juice
PM	Pomegranate molasses
PON1	paraoxonase 1
PPARc	Peroxisome proliferator activated receptor gamma
PUFAs	Polyunsaturated fatty acids
QT interval	Electrocardiography
ROS	reactive oxygen species
SOD	Super oxide dismutase
TAC	Total antioxidant capacity
TAC	Total Antioxidant Capacity
TAG	triacylglycerol
TBARS	Thiobarbituric acid reactive substances
TL	Total lipids
Top II	topoisomerase II
VLDL-c	very low-density lipoprotein-cholesterol

Abstract

Doxorubicin (DOX) is one of the most common and widely used chemotherapeutic agents for a variety of cancers. Doxorubicin has been shown to generate oxidative stress, which leads to hepatotoxicity and cardiotoxicity. Pomegranate molasses (PM) is a nutrient-dense substance. It contains four times the antioxidant content of pomegranate juice. Zinc, iron, calcium, and phosphorous are all abundant in it. The current study's goal is to see how doxorubicin affects the liver and heart in male rats, as well as how pomegranate molasses can help alleviate these side effects.

20 Male rats were randomly divided into four groups namely the control group, the pomegranate molasses group, the doxorubicin group, and the combination group.

Dox was given as a single injection into the peritoneum, while PM was given orally once daily for two weeks.

The body weight, as well as the weight of the liver and the heart, were not impacted in rats administered pomegranate molasses during the trial. NO and TBARS levels in plasma, liver, and heart were significantly lower in rats given pomegranate molasses alone. However, there was an increase in TAC, SOD, CAT, and GSH in plasma, liver, and heart. The activity of AST, ALT, and AlP enzymes in the plasma was significantly reduced, whereas the activity of AST, ALT, AlP, ACP, and GGT enzymes in the liver was significantly increased. It also resulted in a considerable drop in the concentration of all lipid profiles in plasma, with the exception of HDL-c, which increased.

On the other hand, rats given doxorubicin exhibited a drop in heart weight, but a considerable rise in gained weight and liver weight. Doxorubicin increased NO and TBARS levels in plasma, liver, and heart while it decreased TAC, SOD, CAT, and GSH levels in plasma, liver, and heart. Dox treatment increased the activity of AST, ALT, and AlP in plasma, but it decreased the activity of AST, ALT, AlP, ACP, and GGT in the liver. In comparison to the control group, doxorubicin treatment resulted in a considerable increase in plasma lipid levels, except the level of HDL-c which decreased.

The use of pomegranate molasses and doxorubicin in combination minimised organ damage and improved results.

While the pomegranate molasses group's liver and heart tissues exhibited a normal fibromuscular structure, the doxorubicin group's liver and heart tissues indicated several abnormalities at the cellular level