

**PROTECTIVE EFFECT OF VERNONIA AMYGDALINA ON 1, 2-
DIMETHYLHYDRAZINE-INDUCED TOXICITY IN RATS**

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CERTIFICATION

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We, the undersigned attest and declare that the thesis of **Augustine Osasemeaga OKPIABHELE** titled, “The Protective Effects of *Vernonia amygdalina* on 1, 2 Dimethylhydrazine Induced Toxicity in Rats” has successfully passed the anti-plagiarism test and does not violate any copyright regulations.

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DEDICATION

I dedicate this thesis to God Almighty for His continuous blessings, guidance, protection and good health. Also, to my dear parents, Sir and Lady V. A. U. Okpiabhele KSJI and my siblings, relatives and colleagues.

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LIST OF ABBREVIATIONS

%GSH	–	Concentration of Reduced Glutathione
AC	–	Atherogenic coefficient
AIP	–	Atherogenic index of plasmas
ALP	–	Alkaline Phosphatase
ALT	–	Alanine Aminotransferase
ANOVA	–	Analysis of variance
AOM	–	Azoxymethane (AOM)
AP	–	Acute pancreatitis
AST	–	Aspartate Aminotransferase
BUN	–	Blood Urea Nitrogen
CK	–	Creatine Kinase
Cl ⁻	–	Chloride ion
CRR	–	Cardiac risk ratio
CT	–	Computed Tomography
CVD	–	Cardiovascular Disease
DMH	–	1, 2- Dimethyl hydrazine
DNA	–	Deoxyribonucleic Acid
EDTA	–	Ethylenediaminetetraacetic acid
ERCP	–	Endoscopic Retrograde Cholangiopancreatography
GFR	–	Glomerular Filtration Rate
GIT	–	Gastrointestinal
GPx	–	Glutathione Peroxidase

GR	–	Glutathione reductase
GRAN	–	Granulocytes
GSH	–	Glutathione
HB	–	Haemoglobin
HCO ₃ ⁻	–	Bicarbonate ion
HDL-C	–	High Density Lipoprotein Cholesterol
K ⁺	–	Potassium ion
LDH	–	Lactate dehydrogenase
LDL	–	Low Density Lipoprotein
LDL-C	–	Low Density Lipoprotein Cholesterol
LYM	–	Lymphocytes
MAM	–	Methylazoxymethanol
MCH	–	Mean Corpuscular Haemoglobin
MCHC	–	Mean Corpuscular Haemoglobin Concentration
MCV	–	Mean Corpuscular Volume
MDA	–	Malondialdehyde
MPV	–	Mean Platelet Volume
Na ⁺	–	Sodium ion
NO	–	Nitric oxide
PCT	–	Platelet count
PCV	–	Packed cell volume
PDW	–	Platelet Distribution Width
P-LCR	–	Platelet Large Cell Ratio

PLT	– Platelet
RBC	– Red blood cell
RDW-CV	– Red Cell Distribution Width - Coefficient of Variation
RDW-SD	– Red Cell Distribution Width Standard Deviation
RNA	– Ribonucleic Acid
ROS	– Reactive Oxygen Species
SEM	– Standard Error Mean
SOD	– Superoxide Dismutase
TAG	– Triacylglycerol
TP	– Total Protein
UBTH	– University of Benin Teaching Hospital
VA	– <i>Vernonia amygdalina</i>
VLDL	– Very Low-Density Lipoprotein
WBC	– White blood cell
WHO	– World Health Organization

ABSTRACT

Vernonia amygdalina (bitter leaf) has been reported to possess different biological effects which is why it is perceived as a wonder herb by locals. 1, 2-Dimethylhydrazine (DMH), a potent carcinogen is renowned for its toxicity. The aim of the present study was to investigate the protective effect of *Vernonia amygdalina* (VA) on DMH-induced toxicity in rats.

Forty (40) male Wistar albino rats weighing 150 – 200 g were randomly assigned to eight (8) groups (5 rats per group): control, DMH, silymarin, VA only, pretreatment [200 mg/kg body weight (bwt)], pretreatment (400 mg/kg bwt), post-treatment (200 mg/kg bwt), and post-treatment (400 mg/kg bwt) groups. With the exception of control and VA only groups, the rats were exposed to DMH before or after treatment with VA via intraperitoneal route at a single dose of 40 mg/kg bwt. Rats in the silymarin group were treated with the standard hepato-/cardio-protective drug, silymarin (100 mg/kg bwt). The treatment lasted for 21 days. At the end of the treatment period the rats were euthanized and blood/tissue samples collected for biochemical analyses. Oxidative stress markers were measured in rat organs (liver, kidney, heart, pancreas and colon). Portions of excised organs were subjected to histopathological examination.

The results showed that exposure of adult male Wistar albino rats to DMH resulted in significant increases ($p < 0.05$) in the relative organ weights, total protein (TP), activities/levels of liver, kidney and cardiac function parameters, lipid peroxidation index [malondialdehyde (MDA)], lipid profile [total cholesterol (TC), triacylglycerol (TG), very-low density lipoprotein cholesterol (VLDL-C), low-density lipoprotein cholesterol (LDL-C)], and cardiovascular disease risk factors [atherogenic index of plasma (AIP), atherogenic coefficient (AC) and cardiac risk ratio (CRR)], but it reduced the activities/levels of antioxidant enzymes/molecules ($p < 0.05$). However, treatment of the rats with ethanol extract of *V. amygdalina* leaves significantly reduced the activities/levels of the

indices of liver, kidney and cardiac function, MDA, TP, TC, TG, VLDL-C, LDL-C and cardiovascular disease risk factors, while enhancing the activities/levels of antioxidant enzymes/molecules ($p < 0.05$). The plant extract also significantly ameliorated the structural alterations/distortions caused by DMH to rat organs ($p < 0.05$). These results indicate that ethanol extract of the medicinal plant leaves can effectively ameliorate DMH-induced systemic toxicity in Wistar rats.