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Effect of Some Environmental Toxicants on Oxidative Stress Related Genes in Rats

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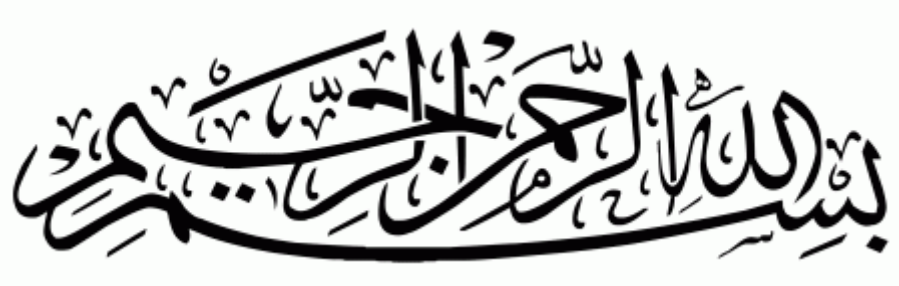
Abstract: Dietary components have recently received rapidly expanding attention for their potential to halt or reverse the development of many oxidative stress-mediated diseases after exposure to environmental toxicants. 7, 12 Dimethyl Benz(a)anthracene (DMBA) is one of the most common environmental pollutants. The aim of the present study was to evaluate the chemopreventive effects of Broccoli as nutritional components against DMBA intoxication in rats. A daily dose of Aqueous and methanolic broccoli extracts (1ml/Rat,150mg/kg) respectively were given to 50 days old female rats for 26 successive weeks after carcinogen intoxication with a single dose of (20mg/ml) of DMBA. DMBA intoxication resulted in redox imbalance (decreased GSH level and increased MDA level), and increased DNA damage fragmentation in liver, kidney and brain and bcl2 gene in kidney and brain. Besides, it affected the level of expression of GST gene in liver, kidney and brain tissue but not affected cfos gene level of expression. The aqueous and methanolic broccoli extract supplements ameliorated the adverse effects induced by DMBA intoxication by increasing the level of GSH and decreasing the MDA level with concomitant lowering in DNA fragmentation, decreased expression of GST and bcl2 in liver and brain, respectively as well as up-regulated GST and bcl2 expression in kidney. Broccoli as dietary components had a strong chemoprotective effect against oxidative stress, DNA damage and genotoxicity induced by DMBA intoxication in rats.

Keywords: DMBA; oxidative stress; DNA Fragmentation; gene expression; genotoxicity; Broccoli.



Dedication

To

My Father

My Mother

My Husband

My Brothers

and My Sons

for Their Love and Great Support

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LIST OF ABBREVIATIONS

Abbreviation	Scientific name
8-OHdG	: 8-oxo-2′-deoxyguanosine.
AD	: Alzheimer's disease.
AhR	: aryl hydrocarbon receptor.
ALS	: amyotrophic lateral sclerosis.
AP-1	: activator protein.
APAF-1	: Apoptotic protease activating factor -1.
As	: arsenic.
B(a)p	: benzo(a)pyrene.
BAK	: Bcl-2 homologous antagonist/killer.
BAX	: Bcl-2-associated X protein.
BCL2	: B-cell lymphoma 2.
BER	: base excision repair.
Bp	: Base pair.
BRAF	: is a human gene that encodes a protein called B-Raf. also referred to as proto-oncogene.
BSE	: Broccoli sprout extract.
cAMP	: Cyclic adenosine monophosphate.
CAT	: catalase.
Cd	: Cadmium.
CD36 mRNA	: cluster of differentiation 36 mRNA.
cDNA	: complementary DNA.
c-fos	: proto-oncogene.
C-Jun	: protein that in humans is encoded by the JUN gene. c-Jun, in combination with c-Fos, forms the AP-1 early response transcription factor.
Co	: cobalt.
COX **COPD**	: cyclooxygenases. : Chronic obstructive pulmonary disease.
CpG island	: regions of the genome that contain a large number of CpG dinucleotide repeats.
Cr	: chromium.
CREB	: cAMP response element-binding protein.
Cu	: Copper.
CVDs	: Cardiovascular diseases.
CYP	: cytochromes P450.
CYP1A1	: cytochrome p450 1A1.

CYP1B1	: cytochrome p450 1B1.
CYP3A4	: cytochrome p450 3A4.
DDW	: Deionized Distilled Water.
DISC	: death-inducing signaling complex.
DMBA	: 7,12 Dimethyl Benz (a) anthracene.
DNA	: Deoxyribonucleic acid.
dNTP	: Deoxynucleotide triphosphate.
DPA	: Diphenylamine.
DPPH	: 2,2′-diphenyl-1-picrylhydrazyl radical.
dT	: deoxythymidines.
DTNB	: Dithio-bis-2-nitrobenzoic acid.
EDTA	: Ethylene diamine tetra acetic acid.
ER	: Erucin.
ERK	: extracellular signal-regulated kinase.
Fe	: Iron.
Fe^{3+}	: ferric ions.
GDP	: guanosine diphosphate.
GEFs	: guanine–nucleotide exchange factors.
GPx	: glutathione peroxidase.
GSH	: reduced glutathione.
GST	: glutathione- s- transferase.
GTP	: Guanosine-5'-triphosphate.
GTPases	: guanosine triphosphate hydrolase enzymes.
H&E	: hematoxylin and eosin.
H2O2	: hydrogen peroxide.
Hg	: mercury.
HOCl	: hypochlorous acid.
IL-1b	: Interleukin -1 beta.
ITCs	: isothiocyanates.
LDL	: Low density lipoproteins.
LOX	: lipoxygenases.
MAPEG	: membrane-associated proteins involved in eicosanoid and glutathione metabolism.
MAPK	: mitogen-activated protein kinase.
MAPKKK	: mitogen-activated protein kinase kinase kinase.
MDA	: malondialdehyde.
NaCl	: Sodium chloride.
NADPH	: Nicotinamide adenine dinucleotide phosphate.

NF- κβ	: Nuclear factor κβ P65.
NF-kappa B	: nuclear factor kappa-light-chain-enhancer of activated B cells.
NOS	: nitric oxide synthase.
NTC	: non template control.
O2	: singlet oxygen.
O-2	: Superoxide radicals.
OH	: hydroxyl radicals.
ONOO-	: peroxynitrite.
ORAC	: The Oxygen Radical Absorbance Capacity.
p450s	: Cytochromes p450.
PAHs	: polyaromatic hydrocarbons.
Pb	: lead.
qRT-PCR	: Quantitative Reverse Transcription Polymerase Chain Reaction.
RAS	: Rat sarcoma virus protein.
RBCs	: Red Blood Cells.
RNA	: Ribonucleic acid.
ROS	: reactive oxygen species.
RTK	: receptor tyrosine kinase.
RT-PCR	: Reverse Transcriptase Polymerase Chain Reaction.
SDS	: Sodium dodecyl sulfate.
SN	: supernatant.
SOD	: superoxide dismutase.
SRF	: serum response factor.
TAE	: Tris acetate EDTA.
TBA	: Thiobarbituric acid.
TCA	: Trichloroacetic acid.
TCF	: The ternary complex factor.
TE	: Tris EDTA.
TGF-beta	: Transforming growth factor beta.
TNF	: tumor necrosis factor.
TNF-alpha	: Tumor necrosis factor -alpha.
TP53	: tumor protein p53.
US EPA	: U.S. Environmental Protection Agency.