EFFECT OF SOME VITAMINS ON THE EXPERIMENTAL ANIMALS SUFFERING FROM CHRONIC DISEASES

By

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B. Sc. Agric. Sci. (Agric. Biochemistry), Fac. Agric., Ain Shams Univ., 2000
M. Sc. Agric. Sci. (Agric. Biochemistry), Fac. Agric., Cairo Univ., 2008

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APPROVAL SHEET

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ABSTRACT

The present study was carried out to study the inhibitory effect of vitamins E, K_3, C and their mixtures on breast cancer induced by N-methyl-N-nitrosourea (MNU) in female Sprague-Dawley rats. The results showed that the serum progesterone hormone, hemoglobin levels and RBCs count were significantly higher ($p<0.05$) in the negative control group than in the breast cancer group. The injection with vitamins E, K_3, C and their mixtures especially, intraperitoneally injected with vitamins (K_3+C) mixture and vitamins (E+K_3+C) mixture caused significantly increased in serum progesterone hormone, hemoglobin levels and RBCs count compared with breast cancer group. Breast cancer group produced a significant ($P < 0.05$) increase in CEA, estrogen hormone, WBCs count and ALP activity compared with negative control group. It was noticed that upon rats injection with vitamin E, vitamins (E+C) mixture, vitamin K and vitamin C caused a marked reduce in CEA, estrogen hormone, WBCs count and ALP activity especially, rats were intraperitoneally injected with vitamins (K_3+C) mixture and vitamins (E+K_3+C) mixture delayed abnormal rising of serum CEA, estrogen hormone, WBCs and ALP activity compared with breast cancer control. There was significant increase in calcium, phosphate, femoral length, breaking force, femoral wet weight, bone volume and bone density in treated group with vitamins E, K_3, C and their mixtures than in breast cancer group. The increase levels of these parameters with time and the decrease in CEA, estrogen, WBCs and ALP activity showed that they could be of importance in monitoring cancer treatment and disease progress in a resource-poor setting. Histopathological analysis was carried out to confirm the efficacy of vitamins E, K_3, C and their mixtures in the inhibition of breast cancer induction in female Sprague-Dawley rats. These findings suggest that the injection with vitamins E, K_3, C and their mixtures significantly reduced the incidence and growth of MNU-induced mammary tumors, therefore has strong potential as a useful therapeutic regimen for inhibiting breast cancer development.

Key words: Vitamin E, Vitamin K_3, Vitamin C, Breast cancer, Bone density.

DEDICATION

I dedicate this work to my parents, my brother Samer, my sister Rasha, for their prayers, love, concern and pride in my work were always a major source of strength to me and their support made an everlasting impression on my life and for courage to complete this project successfully. Special and great thanks to my wife and my kids, Jana, Samer and Yehia, for their continuous encouragement, patience and great help throughout the conduction of this work.

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LIST OF ABBREVIATIONS

$(NH_4)_2C_2O_4$	ammonium oxalate
µM	micromolar
$1,25(OH)_2D$	calcitriol
4T1	murine mammary cancer
A	absorbance
AA	acetic acid
ACI	august Copenhagen Irish
ACP	acid phosphatase
AIF-siRNA	apoptosis-inducing factor- Small interfering ribonucleic acid
ALP	alkaline phosphatase
ANF	naphthoflavone
ANOVA	analysis of Variance
APC	activated protein C
ATP	adenosine-triphosphate
BCS	breast cancer survivors
BMD	bone mineral density
BMI	body mass index
BMMs	bone marrow-derived monocyte/macrophage cells
BMP	bone morphogenetic protein
cDNA	complementary deoxyribonucleic acid
CEA	carcinoembryonic antigen
COX	cyclooxygenase
CRP	C-reactive protein
DEA	diethanolamine
DMBA	7,12-Dimethylbenz(a)anthracene
DMSO	dimethyl sulfoxide
DNA	deoxyribonucleic acid
DNase	deoxyribonuclease
E2	17β-estradiol
EIA	enzyme immunoassay
EPO	evening primrose oil
ER	estrogen receptor
ERK	extracellular signal-regulated kinase
ERT	estrogen replacement therapy
GC	glucocorticoid

GLa	γ-carboxyglutamic acid
GSH	glutathione
H&E	hematoxylin and eosin stain
H_2O_2	hydrogen peroxide
Hap	hydroxyapatite
Hb	hemoglobin
HCl	hydrochloric acid
$HClO_4$	perchloric acid concentrate
HER2/neu	human epidermal growth factor receptor-2/neu
HMG-CoA	3-hydroxy-3-methyl-glutaryl-CoA
HNO_3	Nitric acid
HRP	horseradish peroxidase
i.p	Intraperitoneal
i.v.	intravenous
IC50	half maximal inhibitory concentration
IgE	immunoglobulin E
IL-6	interleukin-6
IU	international Unit
IVC	intravenous vitamin C
$KMnO_4$	Potassium permanganate
LLC	Lewis lung carcinoma
LPS	lipopolysaccharide
LSD	least significant difference
MAPK/ErK	mitogen-activated protein kinase/extracellular regulated kinase
MCSF	macrophage colony stimulating factor
MEN	menadione
mmol	millimole
MMP	metalloproteinase
MMTV-PyMT	mouse mammary tumor virus- polyoma virus middle T antigen
MNU	N-methyl-N-nitrosourea
mRNA	messenger ribonucleic acid
N	normality
NF-κB	nuclear factor-Kappa B
NH_4OH	Ammonium hydroxide
nm23-H1	nonmetastatic protein 23 homolog 1
NS	nutrient supplement
ODS	Osteogenic disorder shionogi

OPG	Osteoprotegerin
OS	oxidative stress
PAI	plasminogen activator inhibitor
PCNA	Proliferating cell nuclear antigen
PCR	polymerase chain reaction
Pg	picogram
PTH	parathyroid hormone
PyMT	polyoma virus middle T antigen
QoL	quality of life
RA	retinoic acid
RANK	receptor activator of nuclear factor kappa-B
RANKL	receptor activator of nuclear factor kappa-B ligand
RBCs	red blood cells
RNS	reactive nitrogen species
ROS	reactive oxygen species
rpm	revolutions per minute
SD	standard deviation
siRNA	small interfering ribonucleic acid
SOD	superoxide dismutase
TBARS	thiobarbituric acid-reactive substance
TEA	tocopheryloxyacetic acid
TGFß	transforming growth factor ß
Th2	T-helper cell
THP1	human monocytic cell line
TIMP-1	tissue inhibitor of metalloproteinase-1
TMB	tetramethylbenzidine
TNF	tumor necrosis factor
TOS	tocopheryl succinate
uPA	urokinase plasminogen activator
UV	ultraviolet
VACSERA	holding company of biological sera and vaccines
Vis	visible
WACS	women’s antioxidant cardiovascular study
WBCs	white blood cells

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