

**THE INFLEUENCE OF GARLIC AS
AN ANTICARCINOGENIC AGENT
ON APOPTOTIC POTENTIAL
DURING ORAL CARCINOGENESIS
IN ALBINO RATS**

Thesis

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*To my great parents
&
my whole precious
family*

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i-LIST OF ABBREVIATIONS

WORDS	ABBREVIATIONS
Dimethylbenz[a]anthracene	DMBA
Organosulfur compounds	OSCs
diallyl sulfide	DAS
diallyl disulfide	DAD
diallyl trisulfide	DAT
S-allyl cysteine	SAC
S-allyl mercaptocysteine	SAMC
glutathione-S-transferase	GST
N-methyl-N-nitrosourea	MNU
N-methyl-N-nitro-N-nitroso-guanidine	MNUG
nuclear factor kappa B	NF-kB
reactive oxygen species	ROS
N-methyl-N-benzylntrosamine	MBN
glutathion peroxidase	GPx
Deoxyribonucleic acid	DNA
Reduced glutathione	GSH

WORDS	ABBREVIATIONS
Tissue transglutaminase	tTG
mitochondrial membrane potential	MMP
Tumor necrosis factor- α	TNF- α
cyclin-dependent kinases	CdKs
Cystein proteases-caspases	CASP
death receptor-mediated pathway	Fas receptor

ii-List of Figures

<i>Figure Number</i>	<i>Figure Caption</i>	<i>Pages</i>
Figure (1)	A diagrammatic presentation of the multistage process of carcinogenesis.	3
Figure (2)	A diagram illustrating the action of both wild and mutant P53 gene.	6
Figure (3)	Chemical reactions in processed Allium vegetables & generation of organosulfur compounds	12
Figure (4)	Chemical structure of widely studied natural organosulfur compounds.	12
Figure (5)	Diagrammatic presentation of normal cell cycle progression	15
Figure (6)	A summary of the chemopreventive effect of dietary garlic	20
Figure (7)	A figure illustrating the final phase of apoptosis. Notice the apoptotic bodies formation that are phagocytosed by macrophages.	22
Figure (8)	a diagram illustrating the role of the tumor suppressor gene p53 in apoptosis.	24
Figure (9)	A diagram presenting one of the suggested apoptotic mechanisms of garlic.	29

ii-List of Figures

<i>Figure Number</i>	<i>Figure Caption</i>	<i>Pages</i>
Figure (10)	A copy of display seen on the screen of the image analyzer masking areas of Bax expression in epithelium by a blue binary colour to measure the area % of Bax expression.	39
Figure (11)	A copy of display seen on the screen of the image analyzer showing conversion into gray color (A), masking it by a blue color (B) to measure the optical density of Bax expression.	39
Figure (12)	A photomicrograph of the palatal area of an animal of group 1 at the end of the experiment	40
Figure (13)	A photomicrograph of the palatal area of an animal of group 2 at the end of the experiment.	40
Figure (14-63)	Histopathology of the specimens of the experimental groups	42-76
Figure (64)	Bar chart illustrating the difference in area % of the nuclear p53 expression in the normal control and the different experimental groups.	80
Figure (65)	Bar chart illustrating the difference in optical density of the nuclear p53 expression in the normal control and the different experimental groups.	80
Figure (66)	Bar chart illustrating the difference in area %	

	of the cytoplasmic Bax expression in the normal control (Gr 1) and the different experimental groups	83
Figure (67)	Bar chart illustrating the difference in optical density of the cytoplasmic Bax expression in the normal control and the different experimental groups.	83

iii-List of Tables

<i>Table Number</i>	<i>Table Title</i>	<i>Pages</i>
Table (1)	The Control and experimental animals	34
Table (2)	The difference in area % of p53 expression among the different groups and it's statistical significance using T-test.	78
Table (3)	The optical density of the nuclear p53 expression among the different groups and it's statistical significance using T- test	79
Table (4)	The difference in area % of Bax expression among the different groups and it's statistical significance using T-test.	81
Table (5)	The optical density of the cytoplasmic Bax expression and it's statistical significance among The different groups using T- test.	82
Table (6)	The area % and optical density of nuclear p53 and cytoplasmic Bax expression among the different experimental groups and its statistical significance using ANOVA test.	84

Contents

<i>chapter</i>	<i>pages</i>
List of abbreviation	<i>i</i>
List of Figures	<i>ii</i>
List of tables	<i>iii</i>
Introduction and review of literature	1
Oral cancer	1
Induction of cancer	4
Chemoprevention	8
Garlic	10
Active ingredients of garlic	11
Medicinal effect of garlic	13
Chemopreventive effect of garlic	13
Apoptosis	20
Phases of apoptosis	21
Pathways of apoptosis	25
Role of garlic in apoptosis induction	26
Aim of the study	31
Materials and methods	32
Results	40
Discussion	83
Conclusion	95
Summary	96
References	99
Arabic summary	

Oral cancer

Carcinoma of the oral cavity is a devastating illness that might result from life style, nutritional and environmental insults with severe impact on the function as well as cosmetic appearance of the affected individuals (*Notani, 2000*). It was found that environmental factors play a major role in the etiology of more than 80% of human malignancies that account for 7 millions deaths per year worldwide (*Thilly, 2003*).

Among many risk factors, tobacco and alcohol are the major causes of oral carcinogenesis being involved in more than 75% of oral cancer in USA, France and Italy (*Ning, et al., 2002*).

Carcinogenesis is a multistage process consisting of three major steps: initiation, promotion and progression. In the initiation stage, the normal cell is subjected to DNA damage, either due to environmental factors including chemicals, radiation and viruses or due to genetic affection (*Kusama et al., 1996, Park et al., 2002 and Magonetti et al., 2006*).

The pervious factors induce mutation in the genome of the somatic cells with activation of growth-promoting oncogenes, inactivation of cancer suppressor genes or alterations of genes that regulate apoptosis. The expression of altered gene products leads to clonal expansion of the transformed somatic cells (promotion) and then with additional mutations (progression), a malignant neoplasm is established (fig. 1) (*Kumar et al., 2003 and Sarkar, 2004*)

Stem cell biology research provided new insights in the cancer pathogenesis and the possible involvement of stem cells in head and neck tumors, considering cancer as a stem-cell disorder (*Bianchini et al., 2008*).

Since carcinogenesis is considered a multistep process, in which accumulation of genetic alterations are required to transform a normal cell into a cancer cell (*Braakhuis et al., 2005*), only long time residents of the mucosa, most likely the stem cells have the ability to accumulate the genetic hits that will result in cancer development (*Owens and Watt, 2003 and Lee & Herlyn, 2007*).

Accordingly, when the stem cell acquires one or more genetic alterations, it will form a patch in the mucosal epithelium with genetically altered daughter cells (*Gollins, 2001 and pardal et al., 2005*). As a result of this process, cancer stem cell escapes the normal control mechanisms and gains growth advantages where the patch starts to expand and areas of the normal epithelium will be replaced by cell populations that become more genetically aberrant forming a malignant clone that progress into carcinoma (*Forastiere et al., 2001 and Costea et al., 2006*).