

**STUDY OF THE TOXICOGENOMIC EFFECT OF
COMMON FOOD ADDITIVES USING SOME
YEAST STRAINS**

By

SHIMAA EL-SAYED RASHAD EL-SAYED

B.Sc.Agric. Sci. (Biotechnology), Cairo University, 2004

M.Sc.Agric.Sci.(Genetics), Ain Shamus University, 2012

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This thesis for Ph.D. degree has been approved by:

Dr. Mohammed Rizk Abu El-Magd El-Ghannam

Associate Prof. of Anatomy and Embryology, Faculty of Veterinary
Medicine, Kafrelsheikh University.

Dr. Nermin Mahmoud Abdel-Gawad

Prof. of Genetics, Faculty of Agriculture, Ain Shams University.

Dr. Eman Mahmoud Fahmy

Prof. Emeritus of Genetics, Faculty of Agriculture, Ain Shams
University.

Dr. Fatthy Mohammed Abdel-Tawab

Prof. Emeritus of Molecular Genetics, Faculty of Agriculture, Ain
Shams University.

Date of Examination:

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SHIMAA EL-SAYED RASHAD EL-SAYED

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Under the supervision of:

Dr. Fatthy Mohammed Abdel-Tawab

Prof. Emeritus of Genetics, Department of Genetics, Faculty of
Agriculture, Ain Shams University (principal supervisor).

Dr. Eman Mahmoud Fahmy

Prof. Emeritus of Genetics, Department of Genetics, Faculty of
Agriculture, Ain Shams University.

Dr. Ashraf Gamil Attallah

Researcher Prof. of Genetics, Department of Microbial Genetics,
National Research Center

ABSTRACT

Shimaa El-Sayed Rashad El-Sayed: Study of the toxicogenomic effect of common food additives using some yeast strains. Unpublished PhD. Thesis, Department of Genetics, Faculty of Agriculture, Ain Shams University, 2019.

A comet assay was performed to assess DNA damage in yeast deletion strains after treatment by the recommended concentrations of the food additives. yeast knockout haploid strains (YKO) strains exhibited a significant DNA damage ($P < 0.05$) which was observed by an increase in tail length, tail DNA% and tail moment as compared to the normal control strains. The results showed that food additives monosodium glutamate (MSG), sodium benzoate (SB) and saffron induced profound cytotoxicity in cancer cells, i.e., human lung cancer (A549), human breast cancer (MCF7), human colon cancer (Caco-2), respectively. In addition, those food additives generated cytotoxic activities on normal lung cell lines (Wi38), respectively. Flow cytometric analysis demonstrated that treatment of human hepatocellular carcinoma cells (Caco-2) cells with food additives increased G2/M phase cell cycle arrest. The quantitative real time-PCR was used to measure the mRNA levels of *p53*, *Bax*, and *Bcl-2* genes. The data showed that food additives changed transcriptional levels of these related genes. The mRNA expression of *p53* and *Bax* were up-regulated, but, the transcription of *Bcl2* was significantly down-regulated compared to the control in Coca-3 cells. Protein-protein interaction maps provided a valuable framework for a better understanding of the functional organization of the proteome. To detect interacting pairs of human proteins (*RAD51*, *RECQL*, *MLH1* and *IGF2BP2*) systematically, a protein matrix of human was screened by automated yeast knockout proteins (*RAD51*, *SGS1*, *MLH1* and *IMP2*) interaction. The results revealed that food additives stimulated cytotoxicity by decreased cell viability in cancer and normal cell lines. Cell cycle blocking at the G2/M phase was evident. Moreover, induction of apoptosis via increased *p53*

and *Bax* mRNA expression levels accompanied with reduced *Bcl2* gene expression which are correlated with apoptosis pathway was observed. Thus, the use of MSG, SB and Saffron could result in negative health biohazards to human beings. This calls for strict control of the threshold levels that should be permitted for the industrial products containing food additives as it could reflect biosafety hazards to human and environment.

Keywords: Yeast knockout, Comet assay, Cell lines, Flow cytometry, Real time-PCR, Neutral red assay.

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CONTENTS

	Pages
LIST OF TABLES.....	IX
LIST OF FIGURES.....	XI
LIST OF ABBREVIATIONS.....	XV
I.INTRODUCTION.....	1
II.REVIEW OF LITERATURE	6
1. Toxicogenomics	6
1.1. Toxicogenomics and Yeast.....	7
1.2. Toxicogenomics and Yeast Knockouts strains.....	8
2. Yeast and Cancer	9
2.1. <i>S. cerevisiae</i> and Cancer	9
2.2. Genes related with cancer in <i>S. cerevisiae</i> which are homologous with human genes	10
2.2.1. Inner Membrane Protease 2 (IMP2) as human cancer genes	10
2.2.2. MLH1 with human genes	12
2.2.3. Slow Growth Suppressor 1 (SGS1) with human genes ..	13
2.2.4. RAD51 with human genes.....	13
3. Food Additives and genotoxicity:.....	14
3.1. Saffron	15
3.2. Mono Sodium Glutamate	16
3.3. Sodium Benzoate	18
4. Cell Lines	20
4.1. Cell Lines and cancer	20
4.2. Estimation of viability of cell by Neutral red uptake (NRU) assay	22
5. Comet Assay and Genotoxicity	22
6. Flow Cytometry	24
7. Estimation of expression of cancer genes with real-time PCR	25
7.1. Real-time PCR	25

II

8.	Protein-protein interaction	28
8.1.	Genetic interaction	28
8.1.1.	Prediction of Gene interaction	30
8.2.	Prediction of Protein-protein interaction	31
8.2.1.	Protein-protein interaction in yeast	33
8.2.2.	Protein-protein interaction in Human	34
III.	MATERIALS AND METHODS	37
1.	Materials	37
1.1	. Yeast <i>Saccharomyces cerevisiae</i> (Haploid Strain).....	37
1.2.	Human cell lines and cultures	37
1.3.	Food additives	38
2.	Methods	38
2-1.	Media of Yeast Strains	38
2-1-1	Solid Medium.....	38
2-1-2	Liquid Medium	38
2.2.	Measurement method of Yeast Comet Assay (YCA)	39
2.2.1.	Preparation of glycerol stocks of yeast	40
2.2.2.	Generation of Comet Assay	40
2.2.3.	Preparation of solutions and buffers	42
2.2.3.1.	Phosphate buffer saline (PBS)	42
2.2.3.2.	Lysis buffer: Ingredients per 1000 mL	42
2.2.3.3.	Electrophoresis Buffer (300 mM NaOH / 1 mM EDTA)	42
2.2.3.4.	Neutralization Buffer	43
2.2.3.5.	Staining Solution	43
2.3.	Cancer Cell Line	44
2.3.1.	Neutral red uptake assay for the estimation of cell viability/ cytotoxicity protocol	45
2.4.	Cell cycle by propidium iodide using Flow Cytometry (Applied Bio-system, US).....	47
2.4.1.	Preparing sample for Flow cytometry:.....	47
2.5.	Molecular investigation	49

III

2.5.1. RNA extraction.....	49
2.5.2. cDNA synthesis	51
2.5.3. RNA extraction.....	52
2.5.3.1. Quantification of RNA using Nanodrop.....	52
2.5.4. Real time PCR.....	53
2.5.4.1. Primers preparation.....	53
2.6. Bioinformatics.....	55
2.6.1. Selection of knockout yeast strains.....	55
2.6.2. Selection of yeast haploid strains lacking genes which are homologous with human cancer genes.....	56
2.6.3. Prediction of protein-protein interaction.....	56
2.7. Statistical analysis.....	56
IV. RESULTS AND DISCUSSION	57
1. In Silico Selection of yeast haploid strains lacking genes which are homologous with some human cancer genes.	57
1.1. Prediction of protein-protein interaction for yeast (Networking).	74
2. Yeast comet assay (YCA)	76
1.2. DNA fragmentation by comet assay	76
1.2.1. Genotoxic effect to yeast strains of different food additives by comet assay.	77
1.2.1.1 Toxicity to (YKO) strains tested with Saffron by Comet Assay.	77
1.2.1.2. Toxicity to (YKO) strains tested with MSG by Comet Assay.	79
1.2.1.3. Toxicity to (YKO) strains tested with SB by Comet Assay.	81
3. Cell Line analysis	83
3.1.Effect of saffron on the viability percentages of the four cell lines (Caco-3, MCF7, A549 and Wi38) by neutral red uptaking assay (NRU).	83
3.2. The effect of MSG on the viability of cell lines	86

3.3. The effect of Sodium Benzoate on the viability percentages of four cell lines.	90
4. Flow Cytometry	93
5. qRT PCR	96
5.1.Effect of Saffron, MSG and SB administration on the relative expression of <i>Bax</i> gene in CaCo-3 cells	96
5.2.Effect of Saffron, MSG and SB administration on the relative expression of <i>P53</i> in CaCo-3 cells	99
5.3. Effect of saffron, MSG and SB administration on the relative expression of <i>Bcl2</i> gene in Caco-3 cells	101
5.4. The role of apoptosis in Saffron induced cytotoxicity related genes such as <i>p53</i> , <i>Bcl-2</i> and <i>Bax</i> in CaCo-3 cells	103
5.5. The role of apoptosis in MSG induced cytotoxicity of some related genes <i>p53</i> , <i>Bcl-2</i> and <i>Bax</i> in CaCo-3 cells	104
5.6. The role of apoptosis in SB induced cytotoxicity related genes such as <i>p53</i> , <i>Bcl-2</i> and <i>Bax</i> in CaCo-3 cells	105
V. SUMMARY	108
VI. REFERENCES	111
ARABIC SUMMEARY	

LIST OF TABLES

Table No.		Page
1	Components of YPD Solid medium	38
2	Components of YPD Liquid medium	39
3	Concentrations and Dissolving of Food additives.	39
4	Components of comet assay	41
5	Forward and reverse primer sequences for and β -actin genes.	53
6	Step One Plus real time thermal cycler reaction mixtures	54
7	PCR program and The thermal cycler condition used during real time PCR	54
8	Selected yeast genes which matched with cancer related human genes.	55
9	Comet assay parameters obtained by image analysis in cells of all groups after treatment with saffron.	77
10	Comet assay parameters obtained by image analysis in cells of all groups after treatment with MSG.	79
11	Comet assay parameters obtained by image analysis in cells of all groups after treatment with SB.	81
12	The effect of saffron on the viability percentages of the four cell lines.	84
13	The effect of MSG on the viability percentages of the four cell lines.	88
14	The effect of SB on the viability percentages of the four cell lines (Caco-3, MCF7, A549 and Wi38).	91
15	Average % of cells in each cell cycle phase in CaCo3 cells	96
16	Changes in relative expression of Baxgene in CaCo-3 cells following treatment by Saffron, MSG and SB compounds.	97

Table No.		Page
17	Effect of Saffron, MSG and SB compounds administration on the relative expression of Bax gene in CaCo3 cells.	97
18	Changes in relative expression of p53 gene in CaCo-3 cells following treatment by Saffron, MSG and SB compounds.	99
19	Effect of MSG, SB and Saffron compounds administration on the relative expression of P53 gene in CaCo3 cells.	101
20	Changes in relative expression of Bcl2 gene in CaCo-3 cells following treatment by MSG, SB and Saffron compounds.	101
21	Effect of Saffron, MSG and SB compounds administration on the relative expression of Bcl2 gene in CaCo ₃ cells.	103

LIST OF FIGURES

Fig. No.		Page
1	The mechanism of development of knock out gene of yeast used to generate the Yeast Deletion Clones.	37
2	Diagram of typical comet showing distribution of DNA in tail and head.	41
3	Gene alignment between human gene <i>IGF2BP2</i> and yeast gene <i>IMP2</i> in Clustal Omega web site ('*' indicate to identical between two aligned, '-' indicate to gaps missing of one) and ('.' indicate to low similar, ':' indicate to more similar used to denote the level of similarity that are not identical) at position.	60
4	Gene alignment between human gene <i>MLH1</i> and yeast gene <i>MLH1</i> in Clustal Omega web site ('*' indicate to identical between two aligned, '-' indicate to gaps missing of one) and ('.' indicate to low similar, ':' indicate to more similar used to denote the level of similarity that are not identical) at position.	63
5	Gene alignment between human gene <i>RAD51</i> and yeast gene <i>RAD51</i> in Clustal Omega web site ('*' indicate to identical between two aligned, '-' indicate to gaps missing of one) and ('.' indicate to low similar, ':' indicate to more similar used to denote the level of similarity that are not identical) at position.	66
6	Gene alignment between human gene <i>RECQL</i> and yeast gene <i>SGS1</i> in Clustal Omega web site ('*' indicate to identical between two aligned, '-' indicate to gaps missing of one) and ('.' indicate to low similar, ':' indicate to more similar used to denote the level of similarity that are not identical) at position.	68