NATURAL PRODUCTS EFFECT OF TREATMENTS ON GENE TARGETING METABOLISM ON BREAST CANCER

Salwa E. Mohamed¹, Midaa N. Ashry², Khalil Halfawy³, Wael H.Roshdy⁴, and Wael S. Abdel-Mageed⁵
¹ Molecular Cell Biology & Molecular Biology Department, Genetic Engineering and Biotechnology Research Institute (GEBRI), University of Sadat City, Egypt.
² Medical Laboratories Department, Faculty of Applied Medical Sciences, October 6 University, Egypt.
³ Molecular Genetics and Molecular Biology Department, Genetic Engineering and Biotechnology Research Institute, Sadat City University, Egypt.
⁴ Central Public Health Laboratories, Ministry of Health and Population, Cairo, Egypt.
⁵ Genetics Department, Faculty of Agriculture, Beni-Suif University, Egypt.

ABSTRACT
Breast cancer is among the most common malignant tumors. It is the second leading cause of cancer deaths among women. While mutation in the BRCA1 and BRCA2 genes confer risk of developing breast cancer, Insulin-like growth factors (IGFs) IGF-1 and IGF-2 are associated with the development and progression of breast cancer. Curcumin is a polyphenol natural product isolated from the rhizome of Curcuma longa. For centuries, curcumin has been used in medicinal preparations and as a food colorant. In recent years, Curcumin, has been reported to have anticancer and chemoprevention effects on breast cancer. Particularly, curcumin has been recognized as an effective anticancer agent that regulates multiple intracellular signaling pathways. This study is designed to investigate the effect of curcumin on gene targeting metabolism on breast cancer.

To achieve this aim we conducted the study on MCF-7 cell lines, and evaluate the cytotoxicity of different concentration of curcumin by MTT assay, RNA extracted from MCF-7 cell lines by Qiagen method and reverse transcriptase to cDNA finally quantification of the expression of genes (IGF-1, IGF-2 and BRCA1) by Real time PCR (RT-PCR).

The results showed that different concentration of curcumin make inactivation for genes related to breast cancer (IGF1, IGF2 and BRCA1) and can stop the breast cancer pathway.
Conclusively, breast cancer is among the most common malignant tumors. It is the second leading cause of cancer mortality among women in the world. Curcumin, an active derivative from turmeric, has been investigated to have anticancer and chemoprevention effects on breast cancer. In this study, different concentrations of curcumin influence the expression of gene targeting metabolism on breast cancer and make inactivation to it which may lead to stopping the breast cancer pathway. Our data demonstrated that curcumin could be used as the treatment of breast cancer.

Keywords: Breast cancer, IGFs genes, BRCA genes, Curcumin.

INTRODUCTION

Cancer is not just one disease, but a large group of almost 100 diseases. It has become one of the top causes of morbidity and mortality, with approximately 19.3 a million new cases and about 10.0 a million deaths in 2018, based on the Global Cancer (GLOBOCAN 2020) (Sung et al., 2021). In other words, cancer is responsible for nearly one of the six deaths, leading to its recognition as one of the world’s most prominent “killers” (Stewart et al., 2016). In addition to that, the global cancer burden is expected to be 28.4 million cases in 2040, a 47% rise from 2020, with a larger increase in transitioning (64% to 95%) versus transitioned (32% to 56%) countries due to demographic changes, although this may be further exacerbated by increasing risk factors associated with globalization and a growing economy (Sung et al., 2021).

As the leading malignancy in females, Breast cancer is the most commonly diagnosed cancer among women worldwide (Ferlay et al., 2015). There are several recognized risk factors for breast cancer development including hormonal, reproductive, and menstrual history, age, lack of exercise, alcohol, radiation, benign breast disease, and obesity. Nevertheless, the key factor to breast cancer development is the early onset of disease (Yang et al., 2011). Risk factors for breast cancer include early menarche, late menopause, nulliparity, contraceptive use, hormonal replacement therapy, above-average body mass index, exposure to environmental pollutants, smoking, use of alcohol, and family history (Lambrechts et al., 2011).

The main cause of breast cancer is related with a personal or family history of the disease and inherited genetic mutations in the breast cancer susceptibility genes BRCA1 and BRCA2. BRCA1 and BRCA2 are two of the most important breast cancer susceptibility genes (Tinelli et al., 2010). The
BRCA genes play a critical role in cell damage repair and induce cell death to those cells if the damage is beyond rescue. BRCA mutation leads to abnormal breast tissue proliferation and increases breast cancer risk (Downs and Wang, 2015).

Insulin-like growth factors (IGFs) are associated with the development and progression of breast cancer. IGF-1 and IGF-2 transmit their signals through two paralogous receptor proteins located in the plasma membrane: the type 1 IGF receptor and the insulin receptor (IGF receptors). High circulating IGF-1 concentrations and low blood IGF binding protein concentrations are risk factors for several types of cancer including breast cancer (Schernhammer et al., 2005 and Renehan et al., 2006). Some studies indicate that IGF-2 activates ER-a and ER-b and modulates their translocation to the nucleus, membrane organelles and the mitochondria (Richardson et al., 2011). The IGFs and IGF-IR function to promote proliferation inhibit death and stimulate transformation in breast cancer cells. Besides their mitogenic ability, IGFs also mediates several other responses. IGFs protect breast cancer cells from apoptosis and promote survival (Rubin and Baserga, 1995). IGFs provide radioprotection and resistance of breast cancer cells to chemotherapeutic agents (Gooch et al., 1999).

No single treatment for cancer seems possible. Patients are often given a combination of therapies and palliative care, such as surgery, radiation, immunotherapy, chemotherapy, or gene therapy, depending on the type and stage of cancer and the patient’s health status, age, and personal characteristics (Gupta et al., 2013a).

Curcumin is the main active ingredient in the rhizome of turmeric (Curcuma longa). Curcumin has a variety of therapeutic properties including antioxidant, analgesic, anti-inflammatory, antiseptic activity, and anti-carcinogenic activity (Perrone et al., 2015). Curcumin is generally recognized as safe by the FDA. Curcumin was known to be safe for human consumption up to 12g/day during clinical trials without recording any side effects (Gupta et al., 2013b). However, some studies indicated that high concentrations of curcumin affected directly on the genetic material in the nucleus as well mitochondrial DNA in cancer cell lines (Cao et al., 2006). To overcome the drawbacks of bioavailability and rapid metabolism of curcumin, efforts were achieved to develop novel synthetic curcumin formulations (Toden and Goel, 2017).

Curcumin is a hydrophobic polyphenol derived from turmeric, a traditional Indian spice. Curcumin has been used as an ethnic drug for the treatment of diverse diseases. Particularly, curcumin has been recognized as an effective anticancer agent that regulates multiple intracellular signaling
pathways (Singletary et al., 1996). Curcumin is known as a yellow pigment that is extracted from Curcuma longa (Mirzaei et al., 2017). Multiple lines of evidence indicated that curcumin and its analogs show a range of pharmacological properties such as anti-cancer, anti-inflammatory, and antioxidant (Mirzaei et al., 2017). Among of these properties, anti-cancer effects of curcumin are known as one of the important effects of it. It has been shown that curcumin could exert their anti-cancer properties via inhibition of angiogenesis, cell proliferation, metastasis, and invasion (Zhou et al., 2017). Moreover, curcumin could induce apoptosis in cancer cell line, regulation of cell cycle, and increase of chemotherapy sensitivity (Zhou et al., 2017). Several mechanisms have been proposed to account for the action of curcumin in breast cancer cells. Several reports have described the anticarcinogenic activity of curcumin in a variety of breast cancer cell lines. One study established that the antiproliferative effect of curcumin in human breast cancer cell lines, including hormone-dependent, hormone-independent, and multidrug-resistant cells, was time- and dose-dependent, and correlated with curcumin's inhibition of the ornithine decarboxylase activity (Aggarwal et al., 2006). The focus of this short review is to describe effect of curcumin in the regulation of gene expression in breast cancer. Therefore, this study aimed to evaluate the molecular effect of curcumin on gene targeting energy metabolism of breast cancer.

MATERIALS & METHODS

1. Chemicals

Dulbecco’s modified Eagle's medium (DMEM), fetal bovine serum (FBS), Trypsin-EDTA (1x) and antibiotic solution (penicillin and streptomycin), and phosphate-buffered saline (PBS), 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazoliumbromide (MTT), propidium iodide and dimethyl sulfoxid (DMSO). All chemicals were obtained from Central Public Health Laboratories in Egypt (CPHL). Primers were obtained from (Applied Biosystems), RNA extraction kit obtained from (Qiagen, Hilden, Germany) and PCR kit HERA SYBER GREEN/ROX RT-qPCR obtained from (Applied Biosystems, Foster City, California, USA). All work was done in the Central Public Health Laboratories in Egypt (CPHL).

2. Preparation of Curcumin

Curcuma longa (Turmeric) root were selected based on their ethnomedical importance. Healthy disease-free roots were purchased from local market in Egypt. The plant materials were dried and pulverized. A weight of 40
mg of well air-dried powder of Curcuma longa roots was infused in aqueous solution (100ml) until complete exhaustion. The infusion was filtered through four-layered muslin cloth. Total concentration of obtained extract was 40 mg/L that was stored at 4°C till further use.

3. Cell line and cell culture

Human breast cancer cell line, MCF7, was obtained from central public health laboratories in Egypt (CPHL). The cells were cultivated in T75 tissue culture flasks in low glucose Dulbecco’s modified Eagle's medium (DMEM) supplemented with 10% fetal bovine serum, 100 μg/mL penicillin, 100 μg/mL streptomycin, 2 mM/L-glutamine and incubated in a 95% humidified incubator containing 5% CO2 at 37°C. Now cells ready for treatment with curcumin.

4. Cytotoxicity

To evaluate the cell viability and cell cytotoxicity was assessed using the 3-(4, 5-dimethylthiazol -2-yl)-2, 5-diphenyltetrazolium bromide (MTT) assay (Mossman, 1983). Briefly, cells were seeded in 96-well plates in DMEM supplemented with 10% fetal bovine serum, and 1% antibiotic antimycotic mixture. After 24 h of cell preparation, the growth medium was aspirated from each well and the cells washed with 1X phosphate buffered saline (PBS). Different concentrations of curcumin were two fold serially diluted in DMEM then added to cultured cells in 96-well plate in triplicate and incubated for 24 h post treatment to determine the cytotoxic concentration 50 (CC50). The medium was then removed and the monolayer of cells washed with 1X PBS three times before adding MTT solution (20 μL/well of 5 mg/ml stock solution) and incubated at 37 °C for 4 h till formulation of formazan crystals. Crystals were dissolved using a volume of 200 μL of of acidified isopropanol and the absorbance measured at λmax 540 nm using an ELISA microplate reader. Finally, the percentage of cytotoxicity compared to the untreated cells was determined. The CC50 of curcumin was determined from a linear exponential equation:

\[
\% \text{ Cytotoxicity} = \frac{(\text{Absorbance of cell without treatment} - \text{Absorbance of cell with treatment})}{\text{Absorbance of cell without treatment}} \times 100
\]

5. Real-time polymerase chain reaction with SYBR green:

Total RNA was extracted from cells using RNeasy Mini Kit (Qiagen) extraction kit according to the manufacturer’s protocol (Qiagen, Hilden, Germany). Subsequently, Five hundred nanograms of the purified RNA were used to synthesize the complementary DNA(cDNA) with Reverse
Transcriptase according to the manufacturer’s protocol (HERA SYBR® green RT-qPCR kit). The quantitative real-time PCR (qRT-PCR) according to the manufacturer’s protocol (HERA SYBR green RT-qPCR kit). Reaction mixture (20 μl) comprises the following: 2.0 μl of RNA template, 1.0 μl of RT Enzyme Mix, 1.0 μl HERA RT-qPCR Master Mix (Thermo Scientific) and 1.0 μl of each primer (100 μM forward and reverse primers) until 20 μl Nuclease free water. Reactions were run in triplicate on Applied Biosystems 7500 real-time PCR system (Applied Biosystems, Foster City, California, USA). The cycling conditions were as follows: Stage 1 (Reverse Transcription) 15 min at 50 °C, Stage 2 (Enz. Activation) 5 min at 95 °C, Stage 3.1 (Denaturation) 10s at 95 °C, Stage 3.2 (Annealing/Extention) 30s at 60 °C, DNA were amplified by 50 cycles of PCR. The primer sequences were as follows: for IGF1 forward primer, (5′-CTTGGACTTGTGACCAAATGG -3′), IGF1 reverse primer, (5′- GTTCGTGCCAATTACATTCA -3′); IGF2 forward primer, (5′- TCCTGGACGTACTGTCGTA -3′), IGF2 reverse primer, (5′- CCTCCATTGGCTTACTGGG -3′); BRACA1 Forward primer, (5′- GGACGTGTCAITAGITCTTTGG -3′), BRACA1 reverse primer, (5′- TTGCAATGAGATACTCATAGGAA -3′) and for β actin, forward (5′- CACCATTGGCAATGAGCGGTTC -3) and reverse (5′- AGGTCTTTGGCGATGTCCACGT -3). (NM_001101). Ct values were normalized to the values of the control β-actin house-keeping transcripts and log fold change was calculated according to the equation of 2^\Delta\Delta ct (Rao et al., 2013).

6. Statistical evaluation

Statistical analysis: Results are expressed as mean ± S.E and values of P>0.05 were not considered significantly different, whereas values of P<0.05 and P<0.01 were considered significant and highly significant respectively. The one-way ANOVA test was used for statistical analysis, followed by Bonferroni’s Multiple Comparison test. (Roa et al., 1985). A value of P< 0.05 was considered as statistically significant. For all statistical tools; the threshold of significance was fixed at the 0.05 level.

RESULTS AND DISCUSSION

Curcumin has been found to suppress carcinogenesis of the breast and other organs. Using curcumin as a therapeutic and preventive agent in breast cancer is perplexed by its diverse biological activity, much of which remains inexplicable (Wang et al., 2016). Breast cancer is considered the most common
cancer for women worldwide and it is now the second leading cause of cancer-related deaths among females in the world. Since breast cancer is highly resistant to chemotherapy, alternative anticancer strategies have been developed. In particular, many studies have demonstrated that curcumin, a derivative of turmeric, can be used as natural agent in treatment of some types of cancer by playing anti-proliferative and antioxidant effects (Bimonte et al., 2015).

1. Cytotoxicity of curcumin extract on MCF-7 cell line:
   The cytotoxicity of the curcumin extract was evaluated in MCF-7 cell line using MTT assay. The curcumin was almost not toxic for studied cells up to a dose of 64µg/µl (Fig.1). The toxic effect of tested extract was dose-dependent. The result showed that the cytotoxic concentration 50 (CC50) value of curcumin was 64µg/µl. Therefore, for further studies we selected the safe concentrations of 25 µg/µl and 50 µg/µl for subsequent cellular signal studies.

![Figure 1](image)

**Figure 1:** The cytotoxicity Effect of the curcumin on the viability of MCF-7 cell lines treated and measured by MTT assay. **TC50=64 µg/µl.**

2. Molecular evaluation for gene expression by real time PCR:
   These findings revealed the effects of the different concentration of curcumin (25-50 µg/µl) on the different genes like (IGF-1-IGF-2 and BRCA-1) in breast cancer on MCF-7 cell line. which the figures show the log fold change of gene and the different duration time (0 h, 8h, 16h, 24h, 32h, 40h, 48h, 56h, 64h and 72h), the figures expressed the significant and non-significant, the comparison between each hour to the first 8hour and comparison between each gene and the different concentration of curcumin (25-50 µg/µl).This molecular evaluation for gene expression was measured by Real Time PCR.
Table 1: Effect of concentration of curcumin (25-50 µg/µl) on IGF-1 gene

<table>
<thead>
<tr>
<th>Concentration of curcumin (25µg/µl) and (50µg/µl) on IGF-1 gene</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hours</td>
</tr>
<tr>
<td>-------</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>8</td>
</tr>
<tr>
<td>16</td>
</tr>
<tr>
<td>24</td>
</tr>
<tr>
<td>32</td>
</tr>
<tr>
<td>40</td>
</tr>
<tr>
<td>48</td>
</tr>
<tr>
<td>56</td>
</tr>
<tr>
<td>64</td>
</tr>
<tr>
<td>72</td>
</tr>
</tbody>
</table>

*Significant at p-value < 0.05
**Highly Significant at p-value < 0.001

Figure 2: Multiple comparisons between the value of different concentrations of Curcumin (25-50 µg/µl) in IGF-1. Data represent the mean ± standard error. The signs (**P < 0.01, *P < 0.05) denote significant differences from control and other treatment groups.

The effect of curcumin concentration (25-50µg/µl) on IGF-1 gene was highly statistically significant changed between (72 and 64 hours) and (8 hours). The
dose response as indicated in (Figure 2 and Table 1) and The effect of curcumin concentration (25µg/µl) on IGF-2 gene was highly statistically significant changed between (72 hours) and (8 hours) and during curcumin concentration (50µg/µl) on IGF-2 gene was highly statistically significant changed between (32,56 and 64 hours) and (8 hours) show in (Figure 3 and Table 2). The effect of curcumin concentration (25µg/µl) on BRCA1 gene was highly statistically significant changed between (24,32 and 40 hours) and (8 hours) and during curcumin concentration (50µg/µl) on BRCA1 gene was highly statistically significant changed between (16,24 and 32 hours) and (8 hours) show in (Figure 4 and Table 3) *in vitro* presence of various concentration of curcumin (25-50 µg/µl) indicated a significant increase of the down regulatin for (IGF-1,IGF-2 and BRCA1) gene. The different concentration of curcumin(25-50µg/µl) and the different duration time (0 h, 8h, 16h, 24h, 32h, 40h, 48h, 56h, 64h and 72h) effect on inactivation of (IGF-1-IGF-2 and BRCA-1) genes.

**Table 2: Effect of concentration of curcumin (25-50µg/µl) on IGF-2 gene**

<table>
<thead>
<tr>
<th>Concentration of curcumin (25µg/µl) and (50µg/µl) on IGF-2 gene</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hours</strong></td>
<td><strong>IGF-2 At (25µg/µl) curcumin</strong></td>
</tr>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td>-0.63 ± 0.23*</td>
</tr>
<tr>
<td>16</td>
<td>-1.05 ± 0.18*</td>
</tr>
<tr>
<td>24</td>
<td>-1.98 ± 1.11*</td>
</tr>
<tr>
<td>32</td>
<td>-1.89 ± 1.02*</td>
</tr>
<tr>
<td>40</td>
<td>-2.49 ± 1.62*</td>
</tr>
<tr>
<td>48</td>
<td>-2.91 ± 2.04*</td>
</tr>
<tr>
<td>56</td>
<td>-3.01 ± 2.14*</td>
</tr>
<tr>
<td>64</td>
<td>-3.1 ± 2.23*</td>
</tr>
<tr>
<td>72</td>
<td>-3.49 ± 2.62**</td>
</tr>
</tbody>
</table>

*Significant at p-value < 0.05
**Highly Significant at p-value < 0.001
Results means, when we used different concentrations of curcumine (25-50 µg/µl) for different duration time (0 h, 8h, 16h, 24h, 32h, 40h, 48h, 56h, 64h and 72h) on different genes related to breast cancer (IGF-1, IGF-2 and BRCA1), this is lead to down regulation for genes (IGF-1, IGF-2 and BRCA1) and this is the opposite of what supposed during cancer pathway, resulting in inactivation of genes (IGF-1, IGF-2 and BRCA1) and inactivation of genes may lead to stop the pathway of the breast cancer, and the cancer cycle not occur (Table 1 and Fig. 2). At curcumin concentration of (50 µg/µl), significant loss of activation of the gene than at concentration of (25 µg/µl) can be detected during the 0-72 hour’s treatment period. The present experimental IGF-1 was down regulation and inactivation of IGF-1 in the presence of varying concentrations of curcumin (25-50 µg/µl) for different duration time and type of cell lines (MCF-7). These results are in agreement with the study of (Xia et al., 2007 and Choudhuri et al., 2002) he found that in the presence of various concentrations of curcumin for indicated time periods. Curcumin decreased the secretion of IGF-1 with a concomitant increase of IGFBP-3 in a dose-dependent manner. results are also in agreement with the study of (Hosseini et al., 2007).

Figure 3: Multiple comparisons between the value of different concentrations of Curcumin (25-50 µg/µl) in IGF-2. Data represent the mean ± standard error. The signs (**P < 0.01, *P < 0.05) denote significant differences from control and other treatment groups.
al., 2019 and Sachdev and Yee, 2006 ) they proposed that the anti-metastatic effect of curcumin may mediate the downregulation of insulin and insulin-like growth factor-1 receptors, and showed that curcumin significantly decreased insulin and IGF-1 receptors.

The present results found also that IGF-2 gene was higher down regulation in the presence of concentrations of curcumin (50 µg/µl) for different times is significantly higher in that IGF-2 gene in the presence of concentrations of curcumin (25 µg/µl). Results are in agreement with the study of (Tian et al., 2017) he found that curcumin inhibits IGF2 expression in a dose- and time-dependent manner. results of the present study revealed that the curcumin with different concentrations treated different genes on MCF-7 cell lines resulted in significant inhibition of both IGF-1 and IGF-2 (Table 2 and Fig.3).

The present results are in agreement with the study of (Sun et al., 2012 and Lev-Ari et al., 2006) they showed that inhibition of cell survival and induction of apoptosis by curcumin in colorectal adenocarcinoma cell lines is associated with the inhibition of PGE2 synthesis and down-regulation of COX-2.

The present results found also that BRCA1 gene was higher down regulation in the presence of concentrations of curcumin (50 µg/µl) for different time is significantly higher in that in the presence of concentrations of curcumin (25 µg/µl). Our results demonstrate that BRCA1 gene was down regulation in the presence of varying concentrations of curcumin (25-50 µg/µl) for different duration time and gene expression was measured by real time polymers chain reaction (PCR). Results are in agreement with the study of (Rowe et al., 2009). They examined the effect of curcumin on BRCA1 in TNBCs. Total BRCA1 protein expression was induced in MDA468 and HCC1806 cells within 6 h of treatment with 10 μM curcumin (Table 3 and Fig.4).

Conclusively, breast cancer is among the most common malignant tumors. It is the second leading cause of cancer mortality among women in the world. Curcumin, an active derivative from turmeric, has been investigated to have anticancer and chemoprevention effects on breast cancer. In this study different concentrations of curcumin influence the expression of gene targeting metabolism on breast cancer and make inactivation to it which may lead to stopping the breast cancer pathway. The present data demonstrated that curcumin could be used as the treatment of breast cancer.
Table 3: Effect of concentration of curcumin (25-50µg/µl) on BRCA1 gene

<table>
<thead>
<tr>
<th>Hours</th>
<th>BRCA1 At (25µg/µl) curcumin</th>
<th>BRCA1 At (50µg/µl) curcumin</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td>-1.5± 0.54*</td>
<td>-1.92± 0.70*</td>
</tr>
<tr>
<td>16</td>
<td>-2.25± 0.20*</td>
<td>-3.01± 0.38**</td>
</tr>
<tr>
<td>24</td>
<td>-2.64± 1.59**</td>
<td>-3.19± 0.56**</td>
</tr>
<tr>
<td>32</td>
<td>-2.88± 0.83**</td>
<td>-3.07± 1.04**</td>
</tr>
<tr>
<td>40</td>
<td>-2.85± 0.80**</td>
<td>-2.67± 0.04*</td>
</tr>
<tr>
<td>48</td>
<td>-2.79± 0.74*</td>
<td>-2.64± 0.01*</td>
</tr>
<tr>
<td>56</td>
<td>-2.64± 0.59*</td>
<td>-2.79± 0.16*</td>
</tr>
<tr>
<td>64</td>
<td>-2.55± 0.50*</td>
<td>-2.76± 0.13*</td>
</tr>
<tr>
<td>72</td>
<td>-2.52± 0.47*</td>
<td>-2.58± 0.04*</td>
</tr>
</tbody>
</table>

*Significant at P-value < 0.05. **Highly Significant at p-value < 0.001.

Figure 4: Multiple comparisons between the value of different concentrations of Curcumin (25-50 µg/µl) in BRCA1. Data represent the mean ± standard error. The signs (**P < 0.01, * P < 0.05) denote significant difference from control and other treatment groups.

REFERENCES


تأثير العلاج بالمنتجات الطبيعية على الجين المستهدفة لعملية الاتباع والطاقة في سرطان الثدي

سلوى السيد محمد 1، ميداء ناصر عشري 2، خليل الحلفاوي 3، وائل رشدي 4، وائل عبد المجيد 5

1 البروجولوجيا الجزيئية للخلايا، قسم البروجولوجيا الجزيئية، معهد أبحاث الهندسة الوراثية والتكنولوجيا الحيوية، جامعة مدينة السادس، مصر.
2 قسم المختبرات الطبية، كلية العلوم الطبية التطبيقية، جامعة 6 أكتوبر، مصر.
3 قسم علم الوراثة الجزيئية والبروجولوجيا الجزيئية، معهد بحوث الهندسة الوراثية والتكنولوجيا الحيوية، جامعة مدينة السادس، مصر.
4 المعامل المركزية للصحة العامة، وزارة الصحة والسكان، القاهرة، مصر.
5 قسم الوراثة، كلية الزراعة، جامعة بني سويف، مصر.

يعد سرطان الثدي من أكثر الأورام الخبيثة شيوعًا وهو ثاني سبب رئيسي لوفيات السرطان بين النساء، في حين أن الظرفات في جينات BRCA1 و BRCA2 تخلق خطر الإصابة بسرطان الثدي. ترتبط عوامل النمو الخبيثة بالأنسولين مع IGF-1 و IGF-2، الكركين هو منتج طبيعي من مادة البوليفينول معزول عن جذور كرمك لونجا. لعدة قرون، تم استخدام الكركين في المستحضرات الطبية وكميلون غذائي في السنوات الأخيرة. تم الإبلاغ عن أن الكركين له تأثيرات مضادة لسرطان الثدي والوقاية الكيميائية على سرطان الثدي. على وجه الخصوص، تم التعرف على الكركين كعامل فعال مضاد للسرطان ينظم مسارات الإشارات المتعددة داخل الخلايا. تم تصميم هذه الدراسة للتحقيق في تأثير الكركين على الجينات المستهدفة الأرض على سرطان الثدي.

لتحقيق هذا الهدف، أجرينا دراسة على خلايا MCF-7، وتشمل البروجولوجيا الخلوية MCF-7، وتقنيات السمية الخلوية (MTT) لتحديد متغيرات الكركين باستخدام مقاييس Qiagen بطريقة Real time PCR (RT-PCR) من خلايا MCF-7 باستخدام Qiagen (BRCA1 و IGF1) و (BRCA2 و IGF2).

النتائج: أظهرت النتائج أن تركيز الكركين المعتدل يؤدي إلى تثبيط الجينات المرتبطة بسرطان الثدي (BRCA1 و IGF1 و BRCA2 و IGF2) ويمكن أن يوقف مسار سرطان الثدي.