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Research Article

The Effect of Oleoropine on the Expression of the DNA of Methyl transferase (DNMT) in the Pancreatic Cancer

Amirhossein Alimohammadian[1*] and Negin Maleki[2]

[1]Department of Medical Laboratory, Ardabil Branch, Islamic Azad University, Ardabil, Iran; [2]Member of the Brilliant Talent of Young and Elite People Youth Club of Ardabil Islamic Azad University, Iran

Abstract

Malignancy is referred to today as a reason for mortality in cutting edge and immature nations. Numerous examinations point to the constructive outcome of olives as an unsaturated lipid against malignancy, which is additionally part of the Mediterranean eating routine. The phenolic mixes of olive oil, which have numerous restorative properties, incorporate mitigating hostile to an oxidant, against atherogenic against disease, against ischemic, lipid, antimicrobial and hostile to viral properties. Oleuropein comprises of hydroxytyrosol (3,4′-dihydroxyphenylethanol), elenolic corrosive, and glucose. The Memeli assortment of olive tree leaves was picked haphazardly from a similar tree developed in Zanjan (Iran). Oleuropein is a phenolic secoiridoid glycoside and a standout amongst the most plenteous bioactive segments contained in Olea europaea, which is known to balance a few oncogenic flagging pathways. Through the research, it is concluded oleuropein may have an anti-metabolic impact on malignancy, and the impact of anti-metastatic on the system of TIMP expansion and concealment of MMP quality articulation has been appeared to have a huge impact on keeping the disease in a steady state and keeping the defilement of close-by cells. There is solid proof from cell models which shows that olive polyphenols, and explicitly the blend found in olive leaf, can balance and cooperate with atomic pathways and in doing as such may restrain the movement and improvement of malignant growth.

Keywords: Pancreatic cancer; DNMT-Oleoropin-CA19-9

Introduction

Cancer is known today as a cause of mortality in advanced and underdeveloped countries. Many studies point to the positive effect of olives as an unsaturated lipid against cancer, which is also part of the Mediterranean diet. The phenolic compounds of olive oil, which have many medicinal properties, include anti-inflammatory anti-oxidant, anti-atherogenic anti-cancer, anti-ischemic, lipid, antimicrobial and antiviral properties [1]. Phenolic compounds range of phenols in olive oil provides some of its health benefits. The total phenolic content reported is in the range of 196-600 mg/kg. Although the reported levels of phenolic components in olive oil vary greatly, a conclusive and consistent conclusion is that virgin olive oil has a greater phenolic content than virgin olive oil. He and colleagues showed that the difference in the levels of specific phenols and the total amount of phenols in the oil is shown. The accumulation of phenols depends on a number of factors including environmental conditions, olive production methods, and storage conditions. Olive oil can be divided into three groups: simple phenols, saccharides, and lignans, all of which prevent auto-oxidation. The main phenols are hydroxy triazole, trisole, lupine and lithosporoid. Hydroxytriazole and Triazole are simple phenols. Valoropine is sucrose [2]. Simple hydroxy triazole and thrysalen phenols are from hydrolysis of agglutinin conjugates of erythropoietin and lysteroy saccharides. The hydrolysis of polypropene that occurs during the storage of olive oil. Leads to the formation of triazole, hydroxy triazole and ethanol [3].

***Corresponding author:** Department of Medical Laboratory, Ardabil branch, Islamic Azad University, Ardabil Iran, Tel: 9613316400; E-mail: amalimohammadian@gmail.com

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Hydroxytriazole, also found in olive oil, decomposes into the brain as an exudate due to dystonia and is an endogenous neurotransmitter. The amount of phenolic fruit of the olive grows when it grows, after six months the major phenols are glucocytes lygstroids and olivine [2]. When the olive grows perfectly, these components are liberated with glucosidase free glucosidase enzyme glucosidase. Unlike glucosides, free sucrose can be identified in olive oil. Because they are able to pass through oil barriers, these components break down into the oil. Black Olive Extract (from the outer layer of black olives) has a higher accumulation and accumulation of phenolic components and has a higher antioxidant capacity than green olive extract [2].

The catechol group is able to stabilize free radicals by forming the molecules of hydrogen atoms. Of the three main phenols is the olive oil, the hydroxy triazole and the olipine catechol, and the monosubstituted thiazole monophenol, it has been argued that all the phenols in the olive oil are important only for the catechol In studies of laboratory animals, the oleuropein properties of cancer have been shown that the work of phenolic compounds of olive oil inhibits the stages of cancer progression, which accomplishes this important function by controlling the oxidative stress entailed in the DNA of antimicrobial, pro-apoptotic. The cytosine methylation in the CpG islets in the promoturgeon region is an important mechanism in regulating the expression of genes, and this arrangement can play a role in the developmental and evolutionary stages and, by binding to TLR9, produces IL12, and produces IFN gamma that results in stimulation cytotoxicity of NK cells, or after evolution, can be a factor in silencing the expression of genes, especially in some cancer cells. Although studies of specific methylation characteristics of the gene showed that there is a DNA correction in the order of genes [3]. They did not prove that methylation of the gene is the main cause of its stopping. To examine this question, we had to consider tissue culture cells as a sample system. These cells are quite similar to their own specimens in the opposite view, which is similar in many genes to methylation, as seen in the main tissues and this information in culture. Hence, these cells should have a mechanism to carry out a specific methylation characteristic from generation to generation and this has been proven by the transfer of DNA to the tissue culture cells. When DNA is introduced into its methylation form, it retains its unchanged properties permanently [4]. On the other hand, it changes in vitro methylated structures, indicating that fibroblasts do not have di-methylation and neuro-methylation activity and can clearly maintain the induced property. In-vivo, methyl methacrylates are found almost in the CpG sediment, and when it's revealed, it's improved in every cytosine. And it forms only methyl groups in these areas. It is possible that the symmetry of the CpG paired nucleotide atom will remain as a substitute for methylation. In-vivo, each section actually grows on both sides of the DNA of the DNA. Are rapidly replicated, although the mixed strata remain unchanged and restorations are carried out by an enzyme that is very specific for the hemitimatized residues [5]. Hence, any CpG that does not change from the first after bloating also stays that way, while CpG is methylated by the methyl group in the DNA of the first DNA and is recovering again. Transmission of the DNA gene DNA can be used to evaluate the effect of methylation on the gene's form. When glycoprotein B or Y genes are transmitted in vitro and are sent to fibroblasts, it is clearly shown that DNA replication indirectly indicates that endogenous globin genes in similar cells are also due to Their changes are inactive, the effect of methylation, in this case, seems to report a broader activity, while all of the altered genes have been digested when they are changed, and at the same time, a similar phenomenon can be observed in several tissue cultures. This effect is also limited to the *in-vitro* metylide screen. Both the X and Hprt genes and the improved muscle detection gene in T1/2 cells shown in by researcher laser which are inactive in infiltration and the same operation is performed smoothly in the endogenous viral sequence [6].

Material and Methods

Oleuropein consists of hydroxytyrosol (3,4′-dihydroxyphenylethanol), elenolic acid, and glucose. The Memeli variety of olive tree leaves was picked randomly from the same tree grown in Zanjan (Iran). The optimal conditions were obtained as follows: ethanol concentration 75% (v/v), extraction temperature 50°C, ultrasonic power 600 W, extraction time 3 min, liquid to solid ratio 30:1 (ml/g), and extraction pressure 25 kPa. Under these optimal conditions, the oleuropein extraction was 7.08 ± 0.05%. A total yield of oleuropein of 7.67 ± 0.02% was obtained after three extractions using URPE. The extraction efficiency reached 92.3% after one extraction [7]. Phenols of olives are also responsible for the resistance of olive oil to oxidative rancidity. Additionally, compared with the other extraction techniques, i.e, Conventional Solvent Extraction (CSE) under atmospheric pressure, Reduced-Pressure Boiling Extraction (RBE) and ultrasound-assisted extraction the oleuropein yield and extraction time by URPE was the highest and shortest, respectively. URPE could break the olive leaf cell effectively. The results indicated that URPE was an extremely useful and important extraction method for natural products. The developed method was tested on two herbal formulations. The oleuropein was successfully identified using HPLC to characterize elution time in comparison to an authentic standard. HPLC was then used in purification and fractions were lyophilized. Isolated oleuropein was greater than 94% in comparison to the authentic standard. The role of oleuropein in expressing some genes is of concern to many researchers. In the Pancreatic cancer cells, the most important marker for the methylation of the promoter is the CA19-9 gene. In this study, different concentrations of nano-oleuropein on the expression of the gene expression in DNMT were investigated using Real-Time PCR. MTT solution is obtained at a concentration of 5 mg/ml (W/V) by dissolving in PBS, and then sterilizing with a 0.2-micron filter and storing at 4°C. For the passage of cancer cells, after preparing the hood and all the necessary materials for the passage, transfer the cell containing the cell from the incubator to the sub-hood and slowly discard the cellular environment and use the PBS solution to wash the cells. Deplete dead cells and anti-trypsin compounds from the cell's environment [8]. Then slowly pour 600 µl of trypsin and slowly transfer to the cells, and by tilting and flask, the trypsin is allowed to pass to all points containing the cell. Then, place the

flask in an incubator for 3 minutes until trypsin is broken down by protein degradation The adhesive causes the cells to separate from the flask floor, after which the flask is removed from the incubator and, by insertion of gentle blows into the flask, causes the cells to be separated from each other and their single-cellularization. The cells were then examined under a microscope and assured of the cell's single cellularity [9]. After this step, the cells quickly added to the medium with 10% FBS to neutralize trypsin and not damage the cells themselves. After adding the medium, pipetting the cells multiple times and thoroughly washing the flask wall until all the cells are collected, then centrifuging the cells at about 1000 rpm for 5 minutes and then removing the outer environment of the cell. Poured into a flask with a ratio of 1/3 (or we can freeze 3 to 4 million flasks, of which about 1/3 of the cells are about two creatinine) and the medium containing the serum is added and cultivated. To increase the precision of work Cells can be counted and the number or proportion of cells transferred to each flask. Measuring cellular life by MTT In this method, salt (MTT), which is soluble in water and yellow, is used by the mitochondrial dehydrogenation of the living cells to become water-insoluble Purmazan color. The amount of purple produced is proportional to the number of live cells [10].

The process of work is as follows: In a 96-well plate, 8,000 cells were cultured for MDA-MB-231 and 20,000 cells for each McF-7 with 200 µl complete media (DMEM medium plus 10%) in each well. After 24 hours, the environment of the cells was replaced and 200 µl of DMEM medium plus 10% FBS was added to each well with different concentrations of alkaloid extract (1 g/ml, 10 g/ml, 20 g/ml, 30 g/ml, 40 g/ml, 50 g/ml, 60 g/ml, 80 g/ml of 100 µ) and then the plate was wrapped in foil for 24 hours in an incubator at 37°C, 5% CO2 and 95% Hg. After 24 hours, empty the environment in each well, and again add to each well 180 µl of the environment without FBS plus 20 µl of MTT (5 MTT in PBS 1 ml with pH=7.2), and for 60 minutes stylish. You should cover the plate thoroughly with foil, after 60 minutes, transfer the plate to the incubator and leave it for 5 hours under these conditions. At this stage, after 5 hours of incubation of the cells, the inside of the well was empty and added to each well of DMSO 200 µl, and stylized for 10 minutes, until the formazan of the metabolic product of MTT in DMSO was completely dissolved. Sample OD read at 540 nm. Using SPSS software for statistical analysis of MTT data, a significant difference was found between the groups (concentration) in terms of OD at the probability level of less than 1% of the LSR test. The preference of concentrations in terms of OD was investigated by the Duncan test. And the regression equation was used to determine the linearity of the graph and the 2R ratio. Considering that the regression equation can also be used to predict OD.

Results

We find that DNMT1 expression is elevated in pancreatic tumors. Oleuropein increased BAX and simultaneously suppressed Bcl-2 in oleuropein-treated ER-negative pancreatic cancer cells as in Figure 1. The results showed that the relative expression of DNMT1 gene was significantly reduced by the action of 31 ppm nano-oleuropein in the pancreatic cancer cell line, shown in Figure 2. Current research has shown that oleuropein acts as an anticancer agent by several major mechanisms. In any case, oleuropein is a new type of anti-cancer compound that targets many stages in cancer progression. As an antioxidant, it may protect cells against genetic damage. As an anti-angiogenic agent, it can prevent tumor progression. Ultimately, by inhibiting cancer cells directly, it can lead to a tumor. The unique combination of these properties in a single molecule should promote oleuropein from a food ingredient to an active cancer drug that is suitable for human studies.

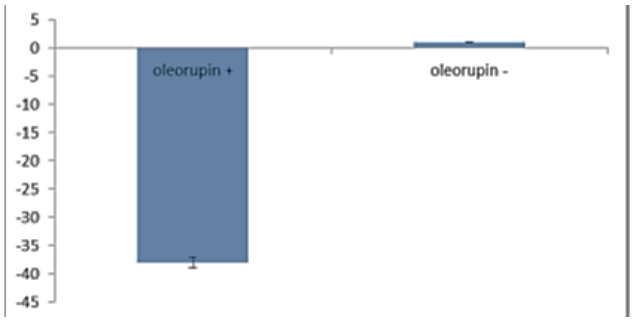

Figure 1: Test of DNMT1 gene expression in pancreatic cancer cell line on the chart.

P_{value}	DF	T	Standard Deviation	Average	Group	Variable
0/0001	58	99/144	5/3	-51/38	+Oleoropine	MT3
			3/0	1	_ Oleoropine	

Figure 2: Mean and T results of the expression of the methyl transferase 3 gene expression in the pancreatic cancer cell line.

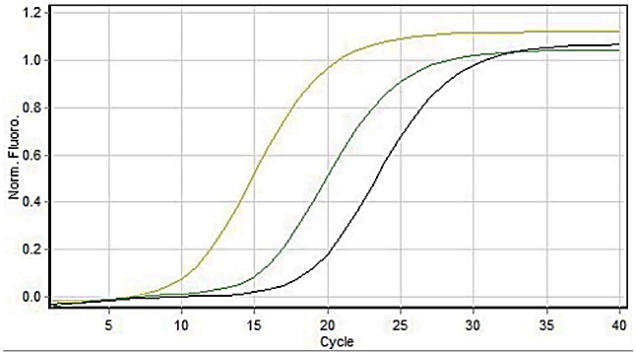

Figure 3: Relative component of methyltransferase gene 3.

The graphical results show the relative expression of methyltransferase 3 genes using e-ΔΔCT compared to the beta-actin control gene in the logarithmic phase in the graphs above shows in Figure 3.

Discussion and Conclusion

To combat cancer, medical science has relied on superior toxicity. Many therapeutic approaches do not differentiate between healthy cells and cancer cells, leading to toxicity and unwanted side effects. In recent years, many efforts have focused

on identifying and testing anticoagulants such as cancer treatment. Recent advances suggest that powerful survival mechanisms are released under hypocycline conditions in cancerous cells demonstrated by Blagosklonny. This may explain the limited success of many anti-angiogenesis therapies. In which surviving patients experience more tumor after the initial treatment of invasive growth. These arguments can be better understood in the context of the microscope of the tumor. In the tumor containing less than 300 cells, there is at least genetic variation. At this stage, the tumor is more vulnerable to drugs, because all cells are equally susceptible to the clonal nature of the tumor. At this time, curative treatments will be more effective in preventing further tumor growth. Unfortunately, existing technologies are still not capable of detecting 300 types of cancer cells, and patients are untreated when tumors become vascular, the number of cells increases exponentially and the genetic diversity of the tumor cells becomes wider. At this point in time, the current technology can detect tumors, and cancer treatment begins. If the antidote treatment method is given when the tumor is highly vasoconstrictor, the selected process occurs in the tumor and leads to the growth of oxygen-deficient cells that can survive and multiply in this new environment. Due to the fact that oloropine is rapidly targeting cancer cells before targeting its tumor vessel, the selected process may not be conducted by oxygen deficiency. Oleuropein is a phenolic secoiridoid glycoside and one of the most abundant bioactive components contained in Olea europaea, which is known to modulate several oncogenic signaling pathways. There is strong evidence from cell models which demonstrates that olive polyphenols, and specifically the combination found in olive leaf, are able to modulate and interact with molecular pathways and in doing so may inhibit the progression and development of cancer. It was shown that Oleuropein induces breast cancer cell proliferation and cell death [10] and also stated that the combination of Oleuropein by blocking the G1 phase to S in the front of the cell division, which is approximately the same effect of chemotherapy drugs used with lesser harm. It was stated that oleuropein may have an antimetabolic effect on cancer, and the effect of antimetastatic on the mechanism of TIMP augmentation and suppression of MMP gene expression has been shown to have a significant effect on keeping cancer in a stable state And preventing the contamination of nearby cells [11]. Obviously, by reducing the expression of the MT gene, methylation can be reduced, and the expression of exonenced genes may be re-performed.

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