

Olive Tree: A Source of Functional Bioactive Components

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Abstract: The olive tree (*Olea europaea* L.) is an iconic symbol of the Mediterranean region since ancient times and products derived from its fruit and leaves have been used both as a food and as traditional medicine. Phytochemical studies have demonstrated olive oil, olives and processed olives as a rich source of phenolic compounds which are the most important components of the polar fraction of olive fruit, oil leaves and bark, owing to their health properties as natural antioxidants. The role of high content of antioxidative compounds is related to human health. Olive oil provides protection against heart disease by controlling low density lipoprotein (LDL) while raising high density lipoprotein (HDL) cholesterol levels. Compounds such as hydroxytyrosol and oleuropein are antioxidants that demonstrate some health effects in the prevention of certain diseases and ageing. The major phenolics include hydroxytyrosol, tyrosol, and oleuropein which are believed to be responsible for a number of biological activities.

This paper summarizes current knowledge on the physiological effects of phenolics present in different parts of olive tree, on human health. Studies (human, animal and in vitro) have shown that olive oil phenolics have positive effects on certain physiological parameters, such as plasma lipoproteins, oxidative damage, inflammatory markers, platelet and cellular function, and antimicrobial activity. Apparently, regular consumption of virgin olive oil containing phenolic compounds manifests in health benefits.

Keywords: olive, phenolic compounds, health benefits, human diet.

I. Introduction

The Olive (*Olea europaea* L.) tree belongs to the family Oleaceae and is native to tropical and warm temperate regions of the world. According to an estimate of Food and Agriculture Organization (FAO), in 2009, 9.9 million hectares (ha) were planted with olive trees with production of oil about 2.9 million tonnes worldwide. Olive oil has been used as a nutritious food, drug and as cosmetics for centuries by the Mediterranean people. During last few decades' olive has been a subject of much scientific interest for approving its multiple biological, therapeutic and functional food applications.

Numerous epidemiological and clinical studies acknowledged olive oil as a source of food and medicine. The most important functional properties of olive oil are antioxidant, anti-microbial, anti-inflammatory and anti-cancer as evident from a variety of studies. These biological activities and individual taste are due to the presence of unique bio-active compounds in the olives, namely phenolics (e.g., oleuropein, hydroxytyrosol, verbascoside and derivatives), tocopherols and carotenoids, amongst others [23].

1.1. Phenolic Constituents Present in Olive

Olive contains multiple minor components such as polyphenols [34]. Several parameters affect olive phenolic contents and these include genotype, pedoclimatic conditions, agronomic techniques (e.g. irrigation, fertilization), and the developmental stage of the drupe [8, 14, 16, 46, 47, 48]. Flavonoids, including flavonols and anthocyanins and tannins are important classes of phenolic compounds since they have many biological functions. Phenolic compounds, present in olive and olive oil have anti-oxidant, anti-atherogenic, anti-diabetic and anti-cancerogenic properties [63, 59].

2. Valuable Constituents in Different Parts of Olive

A variety of valuable and functional components are present in different parts of olive tree as described below:

2.1. Fruit

Olive fruit contains both lipophilic and hydrophilic phenolics. Among the lipophilic phenols the most important are cresols while the major hydrophilic phenols include phenolic acids, phenolic alcohols, flavonoids and secoiridoids [23]. Flavonoids are abundantly present in fruit tissues at the early stages of growth and development. Accumulation of polyphenols in fruit tissue at the early stages of development of olive and many other fruits has been a common biosynthetic pathway [18]. The distribution and structure of the chemical constituents of olive fruit is complex and dependent on parameters including variety, cultivation practices, geographical origin, and the level of maturation.

2.2. Oil

Olive oil differs from other edible oils not only in its fatty acid composition, but also in the presence of minor bioactive compounds because it is consumed unrefined. All of the types of olive oil contain essentially the same fatty acids, but not the same concentrations of minor components such as triterpene acids and alcohols, α -tocopherol, squalene, phenolic acids, lignans, and polyphenols. Major phenolic compounds in olive oil are generally classified as simple phenols (e.g., hydroxytyrosol, tyrosol, vanillic acid); secoiridoids (e.g., oleuropein glucoside), dialdehydic forms of oleuropein; and polyphenols and flavonols [37; 49].

2.3. Leaves

Olive leaves have been widely used in traditional remedies for viral infections, yeast infections, and to fight colds and flu in European and Mediterranean countries. They have been used in the human diet as extracts, herbal teas, and powder and contain several potentially bioactive compounds that may have antioxidant, antihypertensive, antiatherogenic, anti-inflammatory, hypo-glycemic, and hypocholesterolemic properties [53]. It reduces LDL, or bad cholesterol, increases blood flow by relaxing the arteries and lowers blood pressure [27, 4]. The major active components in olive leaf are known to be oleuropein and other compound such as hydroxytyrosol, tyrosol, vanillin, luteolin, p-coumaric acid, caffeic acid, vanillic acid, rutin, diosmetin, diosmetin-7-glucoside, apigenin-7-glucoside and luteolin-7-glucoside [41]. Recently, the demand for whole olive leaf and olive leaf extract has increased for use in foodstuff, functional food materials and food additives [60].

2.4. Bark or Wood

A variety of antioxidants have been isolated and identified in the ethylacetate extract of olive wood. Besides having antioxidative activities, it has been reported that oleuropein and (+)-cycloolivil possess anti-platelet aggregation properties, and these compounds can also inhibit protein tyrosine phosphorylation, as well as prevent thrombotic complications associated with platelet hyperaggregability [26]. A new secoiridoid compound, oleuropein-3'-methylether, together with six known secoiridoids, 7'S-hydroxyoleuropein, jaspolyanoside, ligustroside 3'-O- β -D-glucoside, jaspolyoside, isojaspolyoside A and oleuropein 3'-O- β -D-glucoside, were recently isolated from olive wood [38].

3. Bioactivity of Phenolic Constituents

Olive oil contains polyphenols which have a significantly greater antioxidative effect than those contained in other vegetable oils. Although most vegetable oils (sunflower, soy, rape seed) contain similar amounts of unsaturated fatty acids with attributable health benefits, they are nevertheless ineffective in fighting certain basic factors associated with chronic diseases [35], consequently, the daily intake of recommended doses of olive oil results in a considerable protective effect against colon and breast cancer, as well as skin cancer and pre-mature aging of the skin [57, 58]. The source of olive oil health effects are the biophenols and squalenes (oleocanthal, tyrosol, hydroxytyrosol, oleuropein) it contains. They provide an exceptional antioxidative activity, removing harmful compounds from the body [20].

3.1. Anti-Oxidative

It is well known that the oxidative stress produced by free radicals is responsible for the development of several diseases such as atherosclerosis, different kinds of cancer, inflammatory diseases and Parkinson's disease. The high correlation found between total phenols content determined colorimetrically and free radical scavenging activity supports the antioxidant effect of these compounds [12].

The antioxidative property of olive oil contributes to many of its health benefits. Oleuropein and its hydrolysis product hydroxytyrosol are the most potent antioxidants. The antioxidant activity of olive oil *in vitro* has been well documented and linked to such benefits as chemoprotection, anti-inflammatory action, and prevention of atherosclerotic plaque formation. Care is needed when extrapolating *in vitro* data to *in vivo* models because it cannot be assumed that the effects seen when cells are exposed directly to olive oil extracts will be seen when olive oil is consumed in the diet. It has been estimated that 55-66 percent of olive oil phenols are

absorbed after ingestion, the majority in the small intestine. 53 phenols are believed to act in the blood vessels to prevent LDL oxidation [61].

The protective effects of olive against the chronic and degenerative diseases are attributed to the biophenol components, particularly, hydroxytyrosol rather than to the unsaturated fatty acids content of the olive oil. Other potential mechanisms include inhibition of platelet aggregation, the anti-atherogenic activity, inhibition of the changes of DNA, reduction of free radical production in the faecal matrix and increase in the ratio between the reduced and oxidized forms of glutathione [3].

3.2. Cardiovascular

Phenolic compounds have a protective effect against cardiovascular diseases [19] by protecting against LDL oxidation that is a crucial step in the progress of atherogenic processes [51]. In comparison to saturated fatty acids, olive oil reduces LDL cholesterol, and compared with carbohydrates, it maintains or even increases the levels of HDL cholesterol. In addition, it improves the major risk factors for cardiovascular disease, such as the lipoprotein profile, blood pressure, glucose metabolism and antithrombotic profile. It is relatively resistant to oxidation and contains a large amount of antioxidants relative to its polyunsaturated fat content. Some polyphenol constituents of virgin olive oil (hydroxytyrosol and oleuropein) are potent scavengers of superoxide radicals and inhibit LDL oxidation [52]. In addition, consumption of virgin olive oil (VOO) with high phenolic content significantly increases HDL [49], considered as protective factor against cardiovascular diseases. The high content of mono-unsaturated fatty acids makes olive oil able to reduce the rate of cardiovascular disorders and some tumours thanks also to the abundant presence of antioxidant agents, such as tocopherols, tocotrienols.

3.3. Anti-Diabetic

Olive oil is considered as the pillar of the Mediterranean diet. Some of these effects are attributed beside the monounsaturated fatty acids (MUFA) to the minor components of VOO. Moreover, MUFA-rich diet prevents central fat redistribution and the postprandial decrease in peripheral adiponectin gene expression and insulin resistance induced by a carbohydrate-rich diet in insulin-resistant subjects [28, 7], (up to 6%–9% of dry matter in the leaves comprises of Oleuropein), that possesses a wide range of pharmacologic and health-promoting properties. It has been associated with improved glucose metabolism [31]. The hypo-glycemic and antioxidant effects of oleuropein have also been reported in alloxan-diabetic rabbits [25].

3.4. Anti-Inflammatory/Anti-Cancer

Oleocanthal another functional component found in olive oil may have potential as a therapeutic agent in the inhibition of carcinoma progression and supports substantial evidence that populations residing in the Mediterranean region have a reduced incidence of prostate, breast, lung and gastrointestinal cancer [9]. It is important to note that while there is strong evidence that oleocanthal is an effective anti-inflammatory agent and demonstrates pharmacological characteristics in vitro, recent evidence demonstrates that oleocanthal may exert therapeutic properties against the pathogenesis of c-Met kinase induced malignancies. Elnagar and colleagues [1] have reported that oleocanthal possesses anti-proliferative effects in human breast and prostate cancer lines. Also Khanal and colleagues [44] recently showed that oleocanthal has an anti-proliferative effect and prevents tumour induced cell transformation in mouse epidermal JB6 Cl41 cells. The mechanism of action in which oleocanthal achieved this was via the inhibition of extracellular signal-regulated kinases 1/2 and p90RSK phosphorylation [51].

Table-1. Bioactive Components Present in Different Parts of Olive and Olive By-Products

Compound name	Plant part/by product	Bioactivity	References
Chlorogenic acid	fruit	anti-oxidant, anti-inflammatory, anti-diabetic, anti-mutagenic/ anti-carcinogenic properties	[24]
Vanillic acid	fruit, virgin olive oil, olive oil cake, leaf	anti-bacterial	[54]
Syringic acid	fruit, virgin olive oil	anti-microbial activities	[5]
Gallic acid	fruit, virgin olive oil	anti-microbial activities	[54]
<i>p</i> -hydroxybenzoic acid	fruit, virgin olive oil	antioxidant, anti-mutagenic	[32]
Caffeic acid	fruit, virgin olive oil, leaf, olive oil cake	anti-oxidant activity, anticancer, antimicrobial activities	[5, 42, 54, 62]
Ferulic acid	fruit, virgin olive oil	anti-bacterial, anti-cancer	[54, 62]
Sinapic acid	fruit	anti-oxidant activity	[10]
Protocatechuic acid	fruit	anti-oxidant activity, anti-bacterial	[43, 54]
<i>p</i> -coumaric acid	fruit, virgin olive oil, olive oil cake, leaf	anti-microbial activities	[5, 54]
<i>o</i> -coumaric acid	fruit, virgin olive oil	anti-bacterial	[54]
Cinnamic acid	fruit, virgin olive oil	free radical scavenging properties, anti-microbial activity	[39]

Gallic acid	fruit	antioxidant, anti-apoptotic effects	[40]
Hydroxycinnamic acid Derivative verbascoside	fruit	anti-microbial activity	[55]
Oleuropein	fruit, olive oil cake	inhibitors of platelet aggregation, breast cancer, anti-oxidant activity, anti-microbial activities	[2, 5, 11, 13, 17, 30, 43]
Hydroxytyrosol	fruit, virgin olive oil, leaf, olive oil cake	anti-mutagenic/anti-carcinogenic, inhibit platelet aggregation, increased bone formation, anti-proliferative, anti-oxidant activity, breast cancer, anti-microbial activities	[5, 6, 21, 43]
<i>p</i> -hydroxyphenylethanol (tyrosol)	fruit, leaf, olive oil cake	increased bone formation, anti-bacterial, anti-microbial activities	[5, 13, 43, 54]
Luteolin, Luteolin 7- <i>o</i> -glucoside	fruit, virgin olive oil, leaf	anti-inflammatory, inhibitors of platelet aggregation, atherosclerosis and restenosis	[2, 56]
Apigenin, Apigenin 7- <i>o</i> -glucoside	fruit, virgin olive oil, leaf	anti-mutagenic/anti-carcinogenic anti-bacterial, anti-oxidant activity, alzheimer's, liver diseases	[33, 45, 50]
Anthocyanins	fruit	lower cardiovascular risk	[15]
Cyanidin 3- <i>o</i> -glucoside	fruit	anti-oxidant activity, anti-carcinogenic, vasoprotective, anti-inflammatory, anti-obesity, anti-diabetes effects	[22]
Cyanidin 3- <i>o</i> -rutinoside	fruit	anti-oxidant activity, anti-carcinogenic, vasoprotective, anti-inflammatory, anti-obesity, anti-diabetes effects	[22]
Oleanolic acid	fruit skin	anti-proliferative activity	[36]
Maslinic acids	fruit skin	anti-proliferative activity	[36]
Lignans	virgin olive oil	anti-cancer activity, anti-tumoral	[55]

4. Conclusion

The standardization of olives and olive oil dietary intakes, based on the known chemical composition, will help to provide sound clinical basis for assessment of potential anti-atherosclerotic, anti-hypertensive, anticancer, anti-platelet aggregation and immune modulatory functionalities of olive bioactives and thus development of olive-based functional foods and nutraceuticals.

References

- [1]. A. Elnagar, P. Sylvester and K. El Sayed. *Planta Medica*. 77:1013-1019 (2011).
- [2]. A. M. Dell, O. Maschi, G. V. Galli, R. Fagnani, E. Dal Cero, D. Caruso and E. Bosisio. *Br. J. Nutr.* 99, 945–951 (2008).
- [3]. A. Machowetz, H. E. Poulsen, S. Gruendel, A. Weimann, M. Fitó, J. Marrugat, R. D. L. Torre, J. T. Salonen, K. Nyssönen, and J. Mursu. *FASEB J.* 21:45–52 (2007).
- [4]. A. N. Sudjana, C. D'Orazio, V. Ryan, N. Rasool, J. Ng, N. Islam, T. V. Riley and K. A. Hammer. *Int. J. Antimicrob. Agents*, 33(5): 461-463 (2009).
- [5]. A. P. Pereira, I. C. Ferreira, F. Marcelino, P. Valentão, P. B. Andrade, R. Seabra, L. Estevinho, A. Bento and J. A. Pereira. *Molecules*. 12(5):1153-1162 (2007).
- [6]. A. Petroni, M. Blasevich, M. Salami, N. Papini, G. Montedoro and C. Galli. *Thromb. Res.* 78, 151–160. (1995).
- [7]. A. R. Al Jamal and A. Ibrahim. *Int J Diabetes & Metab.* 19:19-22 (2011).
- [8]. B. Aganchich, H. Tah, S. Wahbi, C. Elmodaffar, R. Serraj. *Plant Biosyst* 141: 252–264 (2007).
- [9]. B. L. Dixon, A. F. Subar, U. Peters, J. L. Weissfeld, R. S. Bresalier and A. Risch. *J. Nutri.* 137:2443-2450 (2007).
- [10]. C. Angela, C. Nunzia, L. Vito, M. Fiorenza, P. Sandra, P. Maria, T. Nunzia and L. Vincenzo. *J. Agric. Food Chem.* 58 (15): 8585–8590 (2010).
- [11]. C. Manna, S. D'Angelo, V. Migliardi, E. Loffredi, O. Mazzoni, P. Morrica, P. Galletti and V. Zappia. *J. Agric. Food Chem.* 50:6521–6526 (2002).
- [12]. C. S. Sánchez, A. M. T. González, García-Parrilla, M. C. Granados, J. J. Q. de la. H. L. G. Serrena and M. C. L. Martinez. *Chim. Acta.* 593, 103-107. <http://dox.doi:10.1016/j.aca.2007.04.037> PMID:17531830
- [13]. C. Sara, L. Lisa, and K. Russell. *Int. J. Mol. Sci.* 11, 458-479 (2010).
- [14]. C. Sgromo, C. Colao, L. Reale, F. Orlandi, E. Rugini, and F. Fornaciari. *Plant Biosyst* 144: 733–739 (2010).
- [15]. C. W. Taylor. *Anthocyanins in Cardiovascular Disease*. American Society for Nutrition. *Adv. Nutr.* 2: 1–7(2011).
- [16]. E. Assab, P. Rampino, G. Mita, and C. Perrotta. *Plant Biosyst.* 145: 419–425 (2011).
- [17]. E. Speroni, M. C. Guerra, A. Minghetti, N. Crespi-Perellino, P. Pasini, F. Piazza and A. Roda. *Phytotherapy Res.* 12:98–100 (1998).
- [18]. F. Alagna, N. D'Agostino, L. Torchia, M. Servili, R. Rao and M. Pietrella. *Comparative 454 pyrosequencing of transcripts from olive genotypes during fruit development*. *BMC Genomics.* 10:399 (2009).
- [19]. F. Galvano, L. L. Fauci, G. Graziani, R. Ferracane, R. Masella, C. D. Giacomo, A. Scacco, M. D'Archivio, L. Vanella and G. Galvano. *Monti Iblei.* 10(4): 650-656 (2007).
- [20]. F. Ivan, Situm, M., Bulat, V., Harsapin, M., Fistonic, N. and Verbanac. *Medicinski Glasnik.* 9(1): 1-9 (2012).
- [21]. G. Corona, M. Deiana, A. Incani, D. Vauzour, M. A. Dessi and J. P. E. Spencer. *Mol. Nutr. Food Res.* 53, 897–903 (2009).
- [22]. G. Fabio, L. F. Luca, V. Paola, F. Vincenzo, V. Luca and F. Ann Ist Super Sanità, 43(4): 382-393 (2007).

- [23]. G. Rahele, A., Farooq M. A., Khalid, G. Anwarul-Hassan, and S. Nazamid. *Int. J. Mol. Sci.*, 13:3291-3340 (2012). doi:10.3390/ijms13033291.
- [24]. H. A. Eun, W. K. Dae, J. S. Min, W. K. Soon, N. K. Young, K. Duk-Soo, S. L. Soon, K. Joon, P. Jinseu, S. E. Won, S. H. Hyun, and Y. C. Soo. *Exp Neurobiol.* 20(4):169-175 (2011).
- [25]. H. Jemai, A. El Feki and S. Sayadi. *J. Agric. Food Chem.* 57:8798–8804 (2009).
- [26]. H. Zbidi, S. Salido, J. Altarejos, M. Pérez-Bonilla, A. Bartegi and J. A. Rosado. *Blood Cell Mol. Dis.*, 42:279–285 (2009).
- [27]. I. Singh, M. Mok, A. M. Christensen, A. H. Turner and J. A. Hawley. *Nutr. Metab. Cardiovasc. Dis.*, 18(2): 127-132 (2008).
- [28]. J. A. Paniagua, S. A., Gallego de la, I. Romero, A. Vidal-Puig, J. M. Latre, E. Sanchez, P. Perez-Martinez, J. Lopez-Miranda, and F. Perez-Jimenez. *Diabetes Care.* 30:1717-1723 (2007).
- [29]. J. Fernandez-Bolanos, G. Rodriguez, R. Rodriguez, A. Heredia, R. Guillen and A. Jimenez. *J. Agric. Food Chem.* 50:6804–6811 (2002).
- [30]. J. Han, T. P. N. Talorete, P. Yamada and H. Isoda. *Cytotechnology.* 59:45–53 (2009).
- [31]. J. Wainstein, G. Tali, B. Mona, B. D. Yosefa, D. Eran, K. Zohar, and M. Zecharia. *J Med Food*, 15(7):1–6 (2012).
- [32]. K. Shahriar and J. M. Robin. *Molecules* 15:7985-8005 (2010).
- [33]. L. Rui, Z. Bin, W. Dong-En, Y. Tianyu, P. Long, T. Qin, M.A. Saeed, L. Jian-Jun and W. Jinyi. 17(12), 14748-14764 (2012).
- [34]. M. J. Lopez, F. Perez-Jimenez, E. Ros, R. De Caterina, L. Badimon, and M. I. Covas. *Nutr. Metabol. Cardiovasc. Dis.* 20:284e94 (2008).
- [35]. M. J. Parnham and D. Verbanac. Mild plant and dietary immunomodulators. In: Nijkamp F.P., Parnham M.J. (Ed.). *Principles of Immunopharmacology*. 3rd revised and extended edition. Basel: Springer AG: 451-72 (2011).
- [36]. M. Juan, J. Planas, V. Ruiz-Gutierrez, H. Daniel and U. Wenzel. *Br. J. Nutr.* 100, 36–43 (2008).
- [37]. M. Palumbo, and L. J. Harris. UC Regents, Davis Campus, UC Davis Olive Center. 2011. www.olivecenter.ucdavis.edu
- [38]. M. Pérez-Bonilla, S. Salido, A. V. B. Teris, P. D. Waard, P.J. Linares-Palomino, A. Sánchez, J. Altarejos. *Food Chem.* 124, 36–41 (2011)
- [39]. M. Sova. *Mini Rev Med Chem.* 12(8):749-67(2012).
- [40]. Ö. Erol-Dayi, N. Arda, G. Erdem. *Eur J Nutr.* 51(8): 955-60 (2012).
- [41]. O. H. Lee, B. Y. Lee, J. Lee, H. B. Lee, J. Y. Son, C. S. Park, K. Shetty and Y. C. Kim. *Bioresour Technol.* 100(23): 6107-6113 (2009).
- [42]. O. Vieira, J. Laranjinha, V. Madeira and L. Almeida. *Biochemical Pharmacology* 55:333–340 (1998).
- [43]. Olive Oil - Constituents, Quality, Health Properties and Bioconversions. **Boskou Dimitrios**. ISBN 978-953-307-921-9, 510 pages, Publisher: InTech, Chapters published February 01, 2012 under [CC BY 3.0 license](https://creativecommons.org/licenses/by/3.0/) doi: 10.5772/1378.
- [44]. P. Khanal, W. K. Oh, H. J. Yun, G. M. Namgoong, S. G. Ahn and S. M. Kwon. *Carcinogenesis.* 32: 545 (2011).
- [45]. Q. S. Zheng, X. L. Sun, B. Xu, G. Li, & M. Biomed. & Environ. Sci. 18:65-70 (2005).
- [46]. R. D'Andria, A. Lavini, G. Morelli, L. Sebastiani and R. Tognetti. *Plant Biosyst.* 143: 222–231 (2009).
- [47]. R. Tognetti, A. Morales-Sillero, R. D'Andra, J. E. Fernandez, A. Lavini and L. Sebastiani. *Plant Biosyst.* 142:138–148 (2008).
- [48]. Rewald, B., Leuschner, C., Wiesman, Z., Ephrath, J. E. (2011). *Plant Biosyst.*, 145: 12–22.
- [49]. Riachy, M. E., Feliciano P. C., Lorenzo, L., Luis, R. and Mari'a D. L. C. (2011). *Eur. J. Lipid Sci. Technol.*, 113:678–691.
- [50]. S. C. Patil, V. P. Singh, P. S. V. Satyanarayan, N. K. Jain, A. Singh and S. K. Kulkarni. *Pharmacology.* 69:59-67 (2003).
- [51]. S. Cicerale, X. A. Conlan, A. J. Sinclair and R. S. Keast. *Crit. Rev. Food Sci. Nutr.* 49: 218–236 (2009).
- [52]. S. Granados-Principal, J. L. Quiles, C. L. Ramírez-Tortosa, P. Sánchez-Rovira and M. C. Nutr Rev. 68:191–206 (2010).
- [53]. S. N. El and S. Karakaya. *Nutri. Rev.* 67(11):632-8 (2009) doi: 10.1111/j.1753-4887.2009.00248.x.
- [54]. T. Ahmed, N. Naim, R. J. Je, H. H. R. Fares and A. Hassan. Article ID 431021, pp. 9 (2011).
- [55]. T. Elisa, G. Marco, T. Garden, D. M. Danila, G. Santo and L. G. Maurizio. *Nutr Res Rev.* 18, 98–112 (2005).
- [56]. T. J. Kim, J. H. Kim, Y. R. Jin and Y. P. Yun. *Archives of Pharmacal Research*, 29, 67-72. (2006).
- [57]. T. M. Gibson, L. M. Ferrucci, J. A. Tangrea, Schatzkin, A. (2010). *Semin Oncol.* 37:282-96.
- [58]. T. Psaltopoulou, R. L. Kostis, D. Haidopoulos, M. Dimopoulos, D. B. Panagiotakos. *Lipids in Health and Disease.* 10:127 (2011).
- [59]. V. Llorente-Cortes, R. Estruch, M. P. Mena, E. Ros, M. A. M. Gonzalez and M. Fito. *Atherosclerosis* 208: 442–450 (2010).
- [60]. V. M. Fernández-Cabanás, A. Garrido-Varo, M. DelgadoPerteñez and A. Gómez-Cabrera. *Appl. Spectrosc.*, 62(1): 51-58 (2008).
- [61]. W. Emily and L. Brian. *Alternative Medicine Review.* 12: 331-342 (2007).
- [62]. W. Li, N. Li, Y. Tang, B. Li, L. Liu, X. Zhang, H. Fu and J. A. Duan. *Bioorg Med Chem Lett.* 22(19): 6085-8 (2012).
- [63]. Y. Z. H. Y. Hashim, I. R. Rowland, H. Mcglynn, M. Servili, R. Selvaggini and A. Taticchi. *Int. J. Cancer.* 122:495–500 (2008).