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Antimicrobial activity of olive oil against microbial infections

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Abstract: Olive oil and olive extracts have been used in folk medicine since ancient times. Romans and Greeks employed olive extracts to treat many diseases and an extract of boiled olive leaves was administered as a drink to malaria patients during the 19th century. Hence, the Mediterranean countries have cultivated the olive tree (*Olea europaea* L.) to produce olive oil, table olives and olive leaf extracts for centuries. At present, both olive oil and table olives are important components of the Mediterranean diet and are largely consumed throughout the world. In addition, there are many enterprises that commercialize olive leaf extracts to treat a myriad of diseases, many of them caused by microorganisms. Recently, the importance of preventive medicine has been gradually recognized in the field of orthopaedic surgery with a concept that peak bone mass should be increased in childhood as much as possible for the prevention of osteoporosis (Ohtani *et al.*, 2009). The aim of the current study is to explore the antimicrobial activity of olive oil against microbial infections. To achieve the aim of research, the researcher applied the exploratory approach where dozens of relevant studies were reviewed and explored in order to collect the results needed to enrich the discussion within the current study. The results of study indicated the efficiency of antimicrobial activity of olive oil against microbial infections.

Keywords: olive oil, antibiotic, bacteria, diseases.

فعالية زيت الزيتون كمضاد حيوي

منيرة صالح مشبب ال حلاص القحطاني
كلية العلوم || جامعة الملك سعود || الرياض || المملكة العربية السعودية
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الملخص: تعد شجرة الزيتون من الأشجار المباركة التي ورد ذكرها في القرآن، وتتوطن هذه الشجرة في مناطق متعددة حول العالم من أهمها منطقة حوض البحر الأبيض المتوسط وأجزاء من آسيا الصغرى. والزيت المستخرج من هذه الفاكهة عن طريق العصر يعرف بزيت الزيتون. إن زيت الزيتون معروف عند العرب بضوئه الصافي، قال تعالى: (يَكَادُ زَيْتُهَا يُضِيءُ وَلَوْ لَمْ تَمْسَسْهُ نَارٌ) سورة النور، آية 35. وهو عبارة عن مادة دهنية غير مشبعة(Triglyceride) ويحتوي على مكونات نشطة كثيرة تشمل حمض الأوليك، المركبات الفينولية، والسكوالين، والتي توجد غالبا في العصرة الأولى من زيت الزيتون البكر. إن زيت الزيتون باختلاف مصادره يستخدم لعلاج العديد من الامراض مُلطِّف، ملين، مدر للصفراء، مفتت للحصى، مفيد لمرضى السكر، لعلاج الروماتيزم، التهاب الأعصاب. إن زيت الزيتون قد تجلى نشاطه كمضادات للميكروبات ضد عدة أنواع من البكتيريا المتسببة في الالتهابات المعوية والتنفسية. وعلى الرغم من أنه قد أجريت غالبية الأبحاث على هذا الزيت، فقد وجدت دراسة حديثة على زيت الزيتون البكر تثبت أنه يعمل ضد بكتيريا *Helicobacter pylori* (السبب الرئيسي لقرحة المعدة وسرطان المعدة)، حيث أظهرت بعض الأنواع المقاومة، للمضادات الحيوية المستخدمة عادة للقضاء على العدوى علاج القرحة، استجابتها لزيت الزيتون، الأمر الذي يدعو لإجراء المزيد من البحوث على مركبات أخرى لعلاج مثل هذه العدوى. لأنه قد تم تحديد وجود مركبات فينولية ذات خصائص مضادة للبكتيريا. وعليه كان هدف هذه الدراسة إلقاء الضوء على الدراسات التي توضح النشاط المضاد لزيوت الزيتون ضد الأنواع الميكروبية المسببة للأمراض الميكروبية وما لهذا الموضوع على الجانب الصحي

والبيئي. وللتعرف على قدرة زيت الزيتون ومركباته على الوقاية من العدوى الميكروبية، التبع الباحث المنهاج الاستكشافي حيث قام بالاطلاع على العديد من الدراسات السابقة ذات الصلة ومن ثم استنتاج الدور الفعال لمركبات زيت الزيتون في الوقاية من البكتيريا.

الكلمات المفتاحية: زيت الزيتون، مضاد حيوي، بكتيريا، أمراض.

Introduction

The olive tree, *Olea europaea*, is native to the Mediterranean basin and parts of Asia Minor. References to the olive tree date back to Biblical and Roman times and to Greek mythology. The fruit and compression extracted oil have a wide range of therapeutic and culinary applications and belongs the *O. europaea* to kingdom green plants, division magnoliophyta (flowering plants), family oleaceae (Gilani *et al.*, 2005).

Among edible vegetable oils, olive oil is one of the few consumed unrefined, which means that as well as its triglyceride composition it possesses other minor bioactive components such as sterols, vitamins, escualene, polyphenols, and others. The consumption of olive oil has recently been considered healthy by the U.S. Food and Drug Administration on the basis of its high content in monounsaturated fatty acids (oleic acid), although numerous researchers and studies have indicated that the minor components may also contribute to the beneficial effects of olive oil to human health, in particular the phenolic compounds (Visioli and Galli, 2002).

Olive oil is obtained from the fruits -technically named drupes- of *O. europea*, a tree that is best grown between the 3 and the 45 parallel. Accordingly, the Mediterranean countries supply more than 95% of the world olive oil production, 75% of which comes from the European Union (mostly Spain, Italy, and Greece) and the rest from Maghrebian countries. Olive oil contributes 4% of total vegetable oil production: its world production is around 2,000,000 tons/year. Due to the increasing popularity of the Mediterranean diet, in which olive oil is the major fat component, its production is now expanding to non-traditional producers such as The United States, Canada, Australia, South America, and Japan. Depending on its chemical properties and its degree of acidity, olive oil is classified into different grades (Garcia *et al.,* 2003), that also serve as guidelines for the consumer in the choice of the preferred kind of oil.

Consumption of olive oil is increasing in non-Mediterranean areas such as The United States (olive oil imports exceed 100,000 metric tons/year), Canada, former Soviet Union, Australia, and Japan, due to the growing interest in the Mediterranean diet and its healthful properties (Newmark, 1997).

Olive oil also constitutes a major component of the “Mediterranean diet”. The chief active components of olive oil include oleic acid phenol constituents, and squalene. The main phenolics include hydroxytyrosol tyrosol, and oleuropein, which occur in highest levels in virgin olive oil and have demonstrated antioxidant activity (Gardner and Kraemer, 1995).

It has to be said that there are three types of olive oil: (i) virgin olive oil, obtained directly from fresh fruits; (ii) olive oil, a mixture of virgin olive oil and refined olive oil; and (iii) pomace olive oil, a mixture of virgin olive oil and refined pomace oil. All of them have the same content of total fatty acids but not phenolic compounds, which are higher in virgin olive oil followed by olive oil and pomace olive oil. The type of olive variety also determines the phenolic composition of the virgin olive oil (Garcia *et al.,* 2003).

The content of minor components of an olive oil varies, depending on the cultivar, climat ripeness of the olives at harvesting, and the processing system for the type of olive oil: virgin, common (ordinary), or pomace (Gimeno *et al.,* 2002).

Olive oil is approximately 72 percent oleic acid, a monoun- saturated fatty acid (Newmark, 1997). Olive oil is unique with respect to the high oleic acid content because the majority of seed oils are composed primarily of polyunsaturated fatty acids, including the essential omega-6 fatty acid, linoleic acid. Compared to polyunsaturated fatty acids, oleic acid is monounsaturated, meaning it has one double bond, making it much less susceptible to oxidation and contributing to the antioxidant action, high stability, and long shelf life of olive oil (Owen *et al.*, 2000).

Data concerning the health benefits of oleic acid are conflicting. It has been reported that oleic acid plays a role in cancer prevention. Whether this is a secondary effect of the fatty acid on oil stability (preventing oxidative stress) or a direct anticancer effect remains debatable (Visioli *et al.,* 2002). Preference for the latter theory is based on the fact that, although oleic acid is found in high concentration in olive oil (Menendez *et al.,* 2005), it is also found in relatively high levels in foodstuffs that form a major part of Western diets in non-Mediterranean countries (Visioli *et al.*, 2004). For example, beef and poultry contain 30 to 45 percent oleic acid, while oils such as palm, peanut, soybean, and sunflower contain 25 to 49 percent oleic acid (Newmark, 1997). These countries do not have the low incidence of CHD and cancer typical of the Mediterranean countries. This fact could be due to the comparatively low levels of oleic acid and concomitant high levels of other fatty acids. Several in vitro and in vivo studies have examined the effect of oleic acid on cancer. Llor and Pons conducted in vitro experiments on the effect of olive oil or isolated oleic acid on colorectal neoplasia. They concluded olive oil induces apoptosis and cell differentiation and down-regulates the expression of cyclooxygenase-2 (COX-2) and Bcl-2. COX-2 is believed to play an important role in colorectal cancer development, while Bcl-2 is an intracellular protein that inhibits apoptosis. Oleic acid alone exhibited cell-line specific apoptotic induction, since HT-29 cells were affected but not Caco-2 cells. Oleic acid had no effect on the down-regulation of COX-2 and Bcl-2. Olive oil was found to have no effect on cell proliferation. The researchers concluded oleic acid plays a minor role, if any; in colorectal chemoprotection and that other components of olive oil are involved in this protective process (Llor *et al.*, 2003).

In vitro studies conducted by Menendez *et al.*, examined the effect of oleic acid on breast cancer cell lines (Menendez *et al.*, 2005). The study results are encouraging and support the theory that oleic acid is important in chemoprotection. The researchers reported oleic acid down-regulates the over-expression of Her-2/neu, an oncogene over-expressed in approximately 20-percent of breast carcinomas. The gene, also know as erb-B2, encodes for the p185Her-2/neu oncoprotein, a transmembrane tyrosine kinase orphan receptor that, under normal cellular conditions, is highly regulated because it controls many cell functions, such as differentiation, proliferation, and apoptosis. Deregulation of p185Her-2/neu greatly increases the risk of cancer development. In addition to oleic acid alone, the authors also looked at the effect of oleic acid when compared to and given simultaneously with the anticancer drug trastuzumab. Trastuzumab is a human monoclonal antibody that targets p185Her-2/neu. Menendez *et al.*, found oleic acid acts synergistically with trastuzumab to enhance its action when used against cell cultures that over-express the Her-2/neu oncogene (Menendez *et al.*, 2005). Following these results, Menendez *et al.*, sought to identify the mechanism of action for the down-regulation of the Her-2/ ne oncogene by oleic acid (Menendez *et al.*, 2006). The research focused on polyomavirus enhancer activator 3 (PEA3), a protein that represses the expression of Her-2/neu. They found oleic acid up-regulates PEA3. Low levels of PEA3 are found in cells over-expressing Her-2/neu; whereas, high levels of PEA3 are associated with low p185Her-2/ neu expression (Menendez *et al.*, 2006). Since these data are from in vitro cell lines, the authors warn the results cannot be extrapolated to prove exogenous consumption of oleic acid downregulates Her-2/neu expression via up-regulation of PEA3 in vivo.

A range of phenols in olive oil provides some of its health benefits. The total phenolic content has been reported to be in the range of 196-500 mg/kg (Owen *et al.*, 2000). Although the reported levels of phenolic compounds in olive oil vary widely, one consistent conclusion is that extra virgin olive oil has a higher phenolic content than refined virgin olive oil (Owen *et al.*, 2000; Tuck and Hayball, 2002). Owen *et al.* showed this difference was reflected in the levels of individual phenols as well as the total quantity of phenols in the oil (Owen *et al.*, 2000). The concentration of phenols depends on a number of factors, including environmental growth conditions, method of oil production, and storage conditions (Visioli *et al.*, 2002).

Olive oil phenols can be divided into three categories: simple phenols, secoiridoids, and lignans, all of which inhibit auto-oxidation. Major phenols include hydroxytyrosol, tyrosol, oleuropein (Perona *et al.*, 2006) and ligstroside (Owen *et al.*, 2000).

Hydroxytyrosol and tyrosol are simple phenols and oleuropein is a secoiridoid. The simple phenols hydroxytyrosol and tyrosol are formed from the hydrolysis of the secoiridoid aglycones of oleuropein and ligstroside. Hydrolysis of oleuropein, which occurs during olive oil storage (Romero *et al.*, 2007), results in the formation of hydroxytyrosol, tyrosol, and ethanol (Martinez *et al.*, 2001). As well as being present in olive oil, hydroxytyrosol is endogenous to the brain as a catabolite of neurotransmitter breakdown (Visioli *et al.*, 2002).

The phenolic content of the olive fruit changes as it grows and develops. After six months of growth, the major phenols are the glucosides of ligstroside and oleuropein (Owen *et al.*, 2000). As the olive matures these compounds are deglycosylated by glucosidase enzymes to free secoiridoids (Owen *et al.*, 2000). Unlike the glucosides, free secoiridoids can be detected in olive oil. Because the free secoiridoids are able to cross the oil/water barrier, these compounds partition into the oil (Owen *et al.*, 2000). Black olive pericarp extract (from the outer layer of the black olive) has a higher concentration of phenolic compounds and a higher antioxidant capacity than green olive pericarp extract (Owen *et al.*, 2004).

It has been known for many years that compounds with a catechol group exhibit antioxidant activity (Visioli *et al.*, 2002). The catechol group is able to stabilize free radicals through the formation of intramolecular hydrogen bonds. Of the three main phenols in olive oil, hydroxytyrosol and oleuropein are catechols and tyrosol is a mono-phenol. It has been suggested that, of all the phenols present in olive oil, only the catechols are important (Visioli *et al.*, 2002).

Hydroxytyrosol and oleuropein scavenge free radicals and inhibit low density lipoprotein (LDL) oxidation (Visioli *et al.*, 2002; Owen *et al.*, 2000). These two phenols show dose-dependent activity and are considered potent antioxidants, demonstrating activity in the micro-molar range. Both are more potent at scavenging free radicals than the endogenous antioxidant vitamin E and the exogenous antioxidants dimethyl sulfoxide (DMSO) and butylated hydroxytoluene (BHT) (Visioli *et al.*, 2002; Owen *et al.*, 2000). These two catechols have been shown to scavenge a variety of endogenous and exogenous free radicals and oxidants, including those generated by hydrogen peroxide (Owen *et al.*, 2000), hypochlorous acid, and xanthine/ xanthine oxidase (Visioli *et al.*, 2002). Higher concentrations of tyrosol are needed to exert an antioxidant effect.

Using hydroxyl radical scavenging as a measure of antioxidant capacity, Owen *et al.*, concluded olive oil has a higher antioxidant capacity than seed oils and extra virgin olive oil is more potent than refined virgin olive oil (Owen *et al.*, 2000) due to its higher concentration of antioxidants. Similar results were obtained when xanthine oxidase (Owen *et al.*, 2000) and hypochlorous acid (Visioli *et al.*, 2002) were used. Olive oil phenols are capable of scavenging free radicals produced in the fecal matrix, which is thought to explain the epidemiological data suggesting a colonic chemoprotective effect of olive oil (Owen *et al.*, 2000).

One mechanism associated with the anticancer effects of hydroxytyrosol and oleuropein is prevention of DNA damage, which can prevent mutagenesis and carcinogenesis (Visioli *et al.*, 2002). Hydroxytyrosol, however, has biological activity beyond its antioxidant capacity, as it can affect a range of enzymes, including cyclooxygenase and NADH oxidase (Visioli *et al.*, 2002), and reduce platelet aggregation (Visioli *et al.*, 2002; Fabiani *et al.*, 2002).

Recently a secoiridoid derivative, oleocanthal – the dialdehydic form of deacetoxy-ligstroside aglycone – was identified. This compound, having an extreme irritant effect on the throat, has demonstrated inhibition of cyclooxygenase enzymes and anti-inflammatory activity (Beauchamp *et al.*, 2005).

Squalene, ubiquitous in nature, is a triterpene hydrocarbon and a major intermediate in the biosynthesis of cholesterol. Although found in both plants and animals, it is found in vastly different amounts (Newmark, 1997). While olive oil is composed of approximately 0.7 percent squalene (Newmark, 1997); other foods and oils typically have squalene levels in the range of 0.002-0.03 percent. Only a slight difference is observed between the level of squalene in extra virgin and refined virgin olive oils (extra virgin having higher levels) (Owen *et al.*, 2000).

Although squalene is widely distributed throughout the body, the majority is transported to the skin (Newmark, 1997). Sebum has high levels (12%); whereas, adipose tissue has much lower levels (0.001-0.04%) (Newmark, 1997).

Due to squalene's structure, it is more likely to scavenge singlet oxygen species than hydroxyl radicals (Newmark, 1997). Exposure to high levels of ultraviolet radiation causes the formation of carcinogenic singlet oxygen species within the skin, where a high concentration of squalene may provide a chemoprotective effect (Newmark, 1997). Squalene, found in high amounts in the Mediterranean diet, is believed to be responsible for the lower incidence of skin cancer seen in epidemiological studies of populations consuming this diet.

Animal studies have shown topical squalene has an inhibitory action on chemically-induced skin carcinomas (Newmark, 1997). Squalene added to the diet of rats resulted in an 80 percent increase in serum squalene levels and inhibition of the hepatic enzyme HMG-CoA reductase (Newmark, 1997). The enzyme inhibition may be due to squalene or its metabolites. HMG-CoA reductase, the rate-limiting enzyme in the biosynthesis of cholesterol, results in decreased production of cholesterol and the intermediates formed during its biosynthesis. These intermediates are commonly needed to activate oncogenes (Newmark, 1997). One important intermediate is the compound farnesyl pyrophosphate (FPP), which is involved in the prenylation of several oncoproteins. Because other dietary substances that cause a reduction in FPP levels cause a reduction in tumor growth, squalene is hypothesized to work in the same manner (Newmark, 1997). Following acute administration of squalene, the rate of cholesterol synthesis increased 9-24 hours post-administration (Relas *et al.*, 2000).

Antioxidants are believed to be responsible for a number of olive oil's biological activities. Oleic acid, a monounsaturated fatty acid, has shown activity in cancer prevention, while squalene has also been identified as having anticancer effects. Olive oil consumption has benefit for colon and breast cancer prevention. The oil has been widely studied for its effects on coronary heart disease (CHD), specifically for its ability to reduce blood pressure and low density lipoprotein (LDL) cholesterol (Emily *et al.*, 2007).

Antimicrobial activity of hydroxytyrosol, tyrosol, and oleuropein has been demonstrated against several strains of bacteria implicated in intestinal and respiratory infections. Although the majority of research has been conducted on the oil, consumption of whole olives might also confer health benefits (Emily *et al.*, 2007).

Literature Review

Treatment of bacterial infections

The treatment of bacterial infections is based primarily on the use of antibiotics, including widespread prescription and/or sometimes inappropriate for these antibacterial agents can result in the selection of multiresistant bacterial strains from which the importance of directing research towards medicinal plants as a source of new molecules with antibacterial activity to limit the emergence of the phenomenon of multidrug resistance (Larousse, 2001; Haddouchi et al., 2008). The presence of an antibiotic may kill most of the bacteria in an environment but the resistant survivors can eventually re-establish themselves and pass their resistance genes on to their offspring and, often, to other species of bacteria. Both medical and veterinary uses of antibiotics have resulted in the appearance of resistant strains of bacteria. Resistant bacteria which are human pathogens may cause disease that are difficult to treat; even if the resistant bacteria are not human pathogens, they may still be dangerous because they can transfer their antibiotic resistance genes to other bacteria that are pathogenic (Barton, 1998; Khachatourians, 1998).

Plant materials as therapeutic remedies

Even today, plant materials play a major role in primary health care as therapeutic remedies in many countries (Czygan, 1993; Ody, 1993). Plants still continue to be an important source of drugs for majority of the world population (Holzl, 1993; Maisenbacher et al., 1995). In the present time, drug resistance in microbes is a very serious problem. Hence, plant origin herbal medicines are considered as safe alternatives of synthetic drugs. There are varied methods of medicines like Aurveda, Homeopathy and Unani, which utilize plant materials for drug production. Currently, Aurveda considered as a vital system of medicine and governed the worldwide recognition and having non-toxic substances. However, newly discovered non-antibiotic substances such as certain essential oils (Sonboli et al., 2006) and their constituent chemicals (Chavan et al., 2006) have shown good fighting potential against drug resistant pathogens (Cowan, 1999; Ahmad and Beg, 2001). Essential oils are aromatic oily liquids, which are obtained from various plant parts such as flowers, buds, seeds, leaves, twigs, bark, woods, fruits and roots by steam distillation. Scientifically these oils have been proved highly potent antimicrobial agents in comparison to antibiotics. These plant essential oils are rich source of scents and used in food preservation and aromatherapy. These possess multiple antimicrobial for exampl, antibacterial (Ozcan et al., 2006), antifungal (Cafarchia et al., 2002), anticancer, antiviral and antioxidant properties (Salehi et al., 2005; Vardar-Unlu et al., 2003), against viruses, bacteria and fungi (Kalemba and Kunicka, 2003).

The World Health Organization estimates that approximately 80% of the people rely on traditional medicine for their primary health care. Most of these therapies are based on the use of plant extracts or their active components (Craig, 1999).

Oil and its biological activities

Mention here, for example, not to limit the use of vegetable oils in the treatment and as anti-microbial:

Anise (Pimpinella anisum) oil, which is an aromatic plant, was used for its stimulating effects on digestion and its antiparasitic (Cabuk et al., 2003), antibacterial (Singh et al., 2002; Tabanca et al., 2003), antifungal (Soliman and Badeaa, 2002), antipyretic (Afifi et al., 1994) and laxative (Chicouri and Chicouri, 2000) properties.

Clove bud (Syzigium caryophyllatum) oil has biological activities, such as antibacterial, antifungal, insecticidal and antioxidant properties, and are used traditionally as flavouring agent and antimicrobial material in food (Lee and Shibamoto, 2001; Huang et al., 2002; Velluti et al., 2003). The high levels of eugenol contained in clove essential oil responsible for strong antimicrobial activity. When its essential oil extracts killed many Grampositive and Gram negative organisms including some fungi. The antimicrobial activity of clove is attributable to eugenol, oleic acids and lipids found in its essential oils. While clove extracts were found to inhibit the growth of Pseudomonas aeruginosa, Candida albicans, Staphylococcus aureus, Salmonella choleraesuis, Klebsiella pneumoniae, (Cosentino et al., 1999; Hammer et al., 1999) found the aqueous extracts of clove to possess no antimicrobial activity against Pseudomonas aeruginosa, Staphylococcus aureus or Escherichia coli but possessed some activity against Shigella flexneri.

This phenolic compound can denature proteins and reacts with cell membrane phospholipids changing their permeability (Briozzo, 1989; Deans and Ritchie, 1987). Syzygium species have been reported to possess antibacterial (Shafi et al., 2002) and anti-inflammatory activity (Muruganadan et al., 2001). (Boulos, 1993) reported that the buds of clove were used in folk medicine as diuretic, odontalgic, stomachic, tonicardiac, aromatic condiment properties and condiment with carminative and stimulant activity Several compounds from S. aromaticum (namely 5, 7-dihydroxy-2-methylchromone-8-C-β-D-glucopyranoside, biflorin, kaempferol, rhamnocitrin, myricetin, gallic acid, ellagic acid and oleanolic acid) have been found to possess growth inhibitory activity against oral pathogens (Cai, 1996).

The antimicrobial activity of coconut (Cocos nucifera) oil has been reported earlier by (Obi et al., 2005). Coconut oil has been confirmed to possess antimicrobial, antiviral and antiprotozoal activities (Isaacs and Thormar, 1991; Thormar, 1996; Enig, 2003). Phytochemical studies indicated that lauric acid which is its major fatty acid component was highly responsible for the activities of the oil (Peat, 2003).

Topical application of gum (Eucalyptus sp.) oil is effective against methicillin resistant Staphylococcus aureus infection (Sherry et al., 2001). Moreover, the antibacterial action of oil of Eucalyptus on local application is also reported (Kumar, 1988; Ahmad and Beg, 2001). Eucalyptol (1, 8-cineole) is the active ingredient of the Eucalyptus oil (Bruneton, 1995).

The anti-microbial activity of juniper (Juniperus communis) oil is mentioned in all of them. The antimicrobial properties of some plant-derived essential oils have been known for many years (Morris et al., 1979; Deans and Ritchie, 1987; Janssen et al., 1987; Newall et al., 1996), but they were confirmed in some recent publications (Nelson, 1997) reported in vitro activity of juniper oil against methicillin-resistant Staphylococcus aureus and vancomycin-resistant Enterococcus faecium.

Neem (Azadirachta indica) oil suppresses several species of pathogenic bacteria such as Staphylococcus aureus and Staphylococcus typhosa, all strains of Mycobacterium tuberculosis (Chaurasia and Jain, 1978; Rao et al., 1986). The growth of Salmonella paratyphi and Vibrio cholerae was inhibited (Rao, 2005). Efficacy of NIM-76, a spermicidal fraction from neem oil was investigated for its antimicrobial action against certain bacteria, fungi and poliovirus as compared to whole neem oil. This shows that NIM-76 has a potent broad spectrum antimicrobial activity (SaiRam, 2000). Available antimicrobial agents can control the infection but they are expensive and rapid emergence of anti-microbial resistance. Neem may be used for its easy availability and significant effect against bacteria. The neem tree is still regarded as 'village dispensary' (Tuhin et al., 2007).

Sesame (Sesamum indicum) oil has the antibacterial activity against Streptococcus mutans, Lactobacillus acidophilus and total bacteria. Therefore, oil-pulling could be useful for maintaining oral hygiene (Durai et al., 2008).

Tea tree (Melaleuca alternifolia) oil has been shown to have many beneficial medicinal uses as an antiseptic, antifungal and antibacterial agent (Carson and Riley, 1995). Antimicrobial action of tea tree oil on five common bacteria Bacillus subtilis, Escherichia coli, Micrococcus roseus, Sarcina luteus, and Serratia marcescens component to have antimicrobial activity in tea tree oil is attributed to terpinen-4-ol. If our experiment shows tea tree oil's effectiveness as an antimicrobial agent, it would be suitable in many cleaning products and without adverse health or environmental effects. Tea tree oil has been shown to inhibit cellular respiration in E. coli, and by disrupting the permeability barrier of microbial membranes the oil causes the cells to die (Cox et al., 199; De Prijck et al., 2008) indicated death of Escherichia coli, Proteus mirabilis, Staphylococcus aureus and Pseudomonas aeruginosa after exposure to a mixture of tea tree oil and jojoba oil.

In recent decades, researchers have published over 2000 scientific works (Le francois et al., 2006) on the therapeutic potential of garlic (Allium sativum), one of the most used plants in traditional medicine and the wider cited in the literature for its medicinal properties. The essential oil of Allium sativum extract is best known primarily for its antibacterial activity which is attributed to particular compounds that contain sulfides (Amagase et al., 2000).

In order to enhance the aromatic plant Allium sativum in our country we considered important to study in the context of this work the chemical composition of essential oil of this plant and its antibacterial activity compared to different strains of Pseudomonas aeruginosa; a bacterium that often causes problems for its intrinsic resistance to several antibacterial agents and its capacity to acquire resistance during antibiotic therapy (Sihem Khadri1 et al., 2010).

Anti-microbial activity of the volatile oil of seeds of Nigella sativa was done against a wide range of pathogenic microorganism (Nazma Ara1 et al., 2005).

Historically, the products of O. europaea have been used as aphrodisiacs, emollients, laxatives, nutritives, sedatives, and tonics. Specific conditions traditionally treated include colic, alopecia, paralysis, rheumatic pain, sciatica, and hypertension (Gilani et al., 2005). The olive can be consumed whole as either the fully ripe black fruit or as the unripe green fruit. Olive oil, the major source of dietary fat in the countries where olives are grown (Wahrburg et al., 2002; Visioli et al., 2002), constitutes part the commonly referred to "Mediterranean diet" of countries that surround the Mediterranean Sea and tend to have a low incidence of chronic degenerative disease (Harwood and Yaqoob, 2002). Although there are dietary variations among Mediterranean countries, a common feature is the high consumption of olive oil, either uncooked or as the primary cooking fat (Harwood and Yaqoob, 2002). Half the total fat consumed in the Mediterranean diet comes from cooking with olive oil, with deep fat frying being the most common method used (Harwood and Yaqoob, 2002).

In the latter part of the 20th century, Keys et al. conducted the Seven Countries Study, which revealed the Mediterranean diet is linked to a reduced incidence of degenerative diseases, particularly coronary heart disease (CHD) and cancers of the breast, skin, and colon (Keys et al., 1986; Owen et al., 2004). This study inspired much research into the Mediterranean diet. In addition to olive oil, the Mediterranean diet is rich in healthful fiber, fish, fruits, and vegetables (Owen et al., 2004). Since olive oil is the major energy source in the Mediterranean diet, recent research has focused on the contribution it makes to reported health benefits of the diet. Compared to diets of other countries, the Mediterranean diet has a relatively high fat content; however, as the diet is associated with a low incidence of cancer and CHD, despite the high fat intake, it has been suggested the type of fat is more important than the total amount consumed (Owen et al., 2004).

To manufacture olive oil, olives are crushed to create a pomace, which is then homogenized before being pressed to produce oil. The first oil extracted is the high quality extra virgin olive oil – produced using centrifugation and water only. The pomace can then be processed again to yield the lower quality refined virgin olive oil. Further extraction with organic solvents can be undertaken to produce low quality refined husk oil (Owen et al., 2000). Olive oil is believed to exert its biological benefits mainly via constituent antioxidants. Although the composition of olive oil is complex, the major groups of compounds thought to contribute to its observed health benefits include oleic acid, phenolics, and squalene, all of which have been found to inhibit oxidative stress (Owen et al., 2000). Around 80% or more of the olive oil phenolic compounds are lost in the refination process, thus, their content is higher in virgin olive oil (around 230 mg/kg, common range 130-350 mg/kg) than in other olive oils (Owen et al., 2000).

Antioxidants in olives protect them from oxidation by the high temperatures and ultraviolet radiation of the Mediterranean climate (Visioli et al., 2002). The physical methods used to produce olive oil preserve many of its antioxidant compounds. This is not seen with other vegetable and seed oils, which tend to be more refined. Factors affecting the environmental conditions of growing olives alter the constituents of the oil, including its antioxidant properties (Visioli et al., 2002).

The role of Extra Virgin Olive Oil

The regular consumption of extra virgin olive oil is believed to protect against a variety of pathological processes, including the development of cancer, in particular colon cancer (Hashim et al., 2005). Its ability to inhibit colon cancer development has been demonstrated in cultured large intestinal cancer cells (Llor et al., 2003), in animals (Bartoli et al., 2000) and in humans (Owen et al., 2000). Its ability to inhibit colorectal neoplastic processes (Owen et al., 2000) are thought to be mediated, in part, by phenolic compounds present in olive oil, such as hydroxytyrosol (HT) (Guichard et al., 2006), lignans (Sung et al., 1998) and secoiridoids (Li et al., 1999). In fact, treatment of human colon adenocarcinoma cells with olive oil phenolics inhibits initiation, promotion and metastasis of the colon carcinogenesis process (Gill et al., 2008). Although extra virgin olive oil is rich in a variety of phenolic compounds, HT has been the subject of most investigations, primarily because it is the most bioavailable. However, the biological properties of any olive oil polyphenol will depend on the extent to which it is absorbed or metabolized in the gastrointestinal tract. Previously, we have shown that whilst HT levels are relatively low in olive oil, they may increase following the gastric hydrolysis and colonic fermentation of secoiridoids present in olive oil (Corona et al., 2006), resulting in colonic concentrations in the high lM. For these reasons, HT is likely to be a major candidate for the biological activity exerted by olive oil polyphenols on adenocarcinoma cells in vivo (Corona et al., 2006). Indeed, the anticancer properties of HT have previously been demonstrated in HL60 leukaemia cells (Della Ragione et al., 2000; Fabiani et al., 2002), melanoma cells (D'Angelo et al., 2005) and colon cancer cell lines (Guichard et al., 2006; Fabiani et al., 2002). The cellular mechanisms by which olive oil polyphenols exert anticancer effects is thought to be linked to their ability to interact with the mitogen activated protein kinase (MAPK) pathway and cyclooxygenase-2 expression (COX- 2). The overexpression of COX-2 in colorectal cancer cells has a strong association with colorectal neoplasias via thepromotion of cell survival, cell growth, migration, invasion and angiogenesis (Chell et al., 2006). The MAPKs, extracellular signalregulated kinases (ERK), c-Jun N-terminal kinase (JNK) and p38 are viewed as attractive candidates for anticancer therapies, based on their central role in regulating COX-2, cell cycle progression and thus the growth of cells from a broad spectrum of human cancers (Sebolt-Leopold and Herrera, 2004). Recently, we reported that an olive oil phenolic extract, containing only 6.3% of free HT, exerted a strong inhibitory effect on the growth of colon adenocarcinoma cells through the inhibition of p38/cAMP response element-binding (CREB) signalling, a decrease in COX-2 expression and the stimulation of a G2/M phase cell cycle block (Corona et al., 2007).

Cancer and Olive Oil

There have been many reports on the lower incidence of cancer in animals and humans after consumption of olive oil. A review, by Lipworth *et al*., summarizes the association of olive oil intake with cancer risk in humans (Coni *et al*., 2000). It was concluded in this review that olive oil does not have the cancer-promoting potential of other fat types. However, additional studies will be required to confirm this hypothesis. Numerous studies have shown that these phenols are potent inhibitors of LDL oxidation in vitro (Visioli *et al*., 1995; Visioli and Galli, 1994).The in vivo oxidation of LDL is linked to the formation of atherosclerotic plaques, which are postulated to contribute to the development of coronary heart disease. Olive oil phenols have also been beneficially linked to processes that contribute to the pathogenesis of heart disease and cancer (Manna *et al*., 1997). In particular hydroxytyrosol, one of the major phenolic constituent in olive oil, has been reported to alone reduce the risk of coronary heart disease and atheroscelosis (Grignaffini *et al*., 1994; Salami *et al*., 1995). It has also been postulated that hydroxytyrosol inhibits arachidonic acid lipoxygenase (Petroni *et al*., 1997) or inhibits platelet aggregation (Petroni *et al*., 1995). It is presumed that hydroxytyrosol penetrates in cell membranes and consequently can inhibit the production of leukotriene B4 (LTB4) effectively from endogenous arachidonic acid (Kohyama *et al*., 1997). Oleuropein inhibits androstenedione 6-hydroxylase activity, a CYP3A marker in human liver microsomes (Stupans *et al*., 2000) and oleuropein, but not the structurally similar compounds hydroxytyrosol and secologanin, was found to be a mechanism- based inhibitor of androstenedione 6-hydroxylase activity (Stupans *et al*., 2001).

Psoriasis and atopic dermatitis (AD) represent challenging problems regarding their management and incidence. Atopic dermatitis is the most common inflammatory skin disease in childhood (Schultz-Larsen and Hanifin, 1992), with a 10–15% incidence. Moderate to severe AD can have a profound effect on the quality of life. Treatments include Vaseline, corticosteroids, cetirizine, antibacterial drugs and phototherapy, and there isevidence to support the use of oral cyclosporin, topical steroids, psychological approach an ultraviolet light therapy (Hoare *et al*., 2000). Psoriasis vulgaris (PV) is one of the commonest skin problems seen by general practitioners, affecting 1–2% of the population (Greaves and Weinstein, 1995). Psoriasis is a chronic inflammatory and proliferative disorder of skin that results in a rapid turnover of the skin cells that move rapidly up to the surface in 3–5days. This leads to thickening of the superficial layers. Psoriasis is characterized by red, elevated plaques that are overlaid with thick silvery white scale. Plaque psoriasis is known as chronic stable plaque psoriasis or psoriasis vulgaris. For PV involving less than 20% of body surface area, initial treatment is topical including emollients (paraffin), keratolytics (salicylic acid), coal tar, zinc, retinoids, dithranol, betamethazone and calcipotriene. Adverse effects include skin irritation, salicylate intoxication, unpleasant odor, staining of clothes, thinning of skin, steroid striae, telangiectasia, potential carcinogenic risk and tachyphylaxis with repeated use of steroids. Other treatments such as phototherapy and systemic therapy (methotrexate, cyclosporine, acitretine) are associated with toxicity. Natural remedies seem promising in the management of a wide range of dermatological diseases including PV and AD. Large number of patients with PV reported previous or current use of one or more form of alternative medicine (Fleischer *et al.*, 1996; Jensen, 1990). It was estimated that 35–69% of patients with dermatological diseases used complementary/alternative medicine including herbs, diet, hypnotherapy and natural supplement (Ernst *et al.*, 2000). Intravenous administration of omega oils is safe and effective in the treatment of chronic psoriasis vulqaris (Mayser, 1998). Topical and oral fish oil can be useful in the treatment of psoriasis (Escober, 1992; Bittiner, 1988). Topical application of Aloe vera was found effective in psoriasis (Vogler and Ernst, 1999). Vitamin B12 cream containing avocado oil has potential long-term topical therapy of psoriasis (Stucker *et al.*, 2001). Chamomile preparation proves to be effective in relieving associated signs and symptoms in AD and enhancing granulation and epithelization without deleterious side effect (Ross, 2003). Honey is one of the oldest known medicines. It has been valued highly in the Middle East and was mentioned in the Quran 1400 years ago. It has been used for treatment of respiratory diseases, urinary diseases, gastrointestinal diseases, and skin diseases including ulcers, wounds, eczema, psoriasis and dandruff (Zaghloul *et al.*, 2001). Honey reduces inflammation, edema, and exudation, promotes healing, diminishes scar size, and stimulates tissue regeneration (Molan, 1999; Al-Waili N and Saloom, 1999). Olive oil, beeswax and honey are natural materials that contain favonoids, antioxidants, antibacterial ingredients and effects cytokines production by skin cellswhen applied topically (Tuck and Hayball, 2002; Zanoschi *et al.*, 1991).

Diaper dermatitis is the most common dermatological problem of infancy (Hurwitz, 1981), occurring in 25–65% of children (Jodan *et al.*, 1986), and is caused by the combined irritant effects of wearing a diaper, urine and faeces (Atherton, 2001). Colonisation by *Candida* sp. is significantly more frequent in children with diaper dermatitis than in those with healthy skin, whereas colonisation by *Staphylococcus aureus* does not differ between these two groups (Ferrazzini *et al.*, 2003). Corticosteroids, zinc paste and eosin are well-known topical agents for the treatment of diaper dermatitis. It has been suggested that topical antifungal agents are not indicated for diaper dermatitis; indeed, their safety and effectiveness have not been established in infants (Hoppe, 1997). Olive oil, beeswax and honey are natural products, containing flavonoids, and antioxidant, antibacterial and antifungal compounds that affect the production of cytokines by skin cells when applied topically (Tuck *et al.*, 1993). Previous studies have demonstrated the efficacy of a mixture containing honey, olive oil and beeswax (in a ratio of 1:1:1 v/ v) for the treatment of dermatitis, psoriasis and skin fungal infections (Al-Waili, 2003; Al-Waili, 2004).

Considering the potential hazards of topical corticosteroids, it seems that use of this topical treatment, alone or in combination with other agents, is a possible alternative therapy for diaper dermatitis. This could result in reduced use of prescription drugs and a concomitant reduction in any associated adverse effects (Al-Waili, 2005).

O. europaea preparations have been used widely in folk medicine in European Mediterranean area, Arabia peninsula, India and other tropical and subtropical regions, as diuretic, hypotensive, emollient and for urinary and bladder infections (Samova *et al.*, 2003); they are also employed in the treatment of skin diseases (Elkhalifa, 2002). In a recent open pilot study olive oil mixed with honey and beeswax showed to be effective, after topical application, in the treatment of skin fungal infections; clinical response was obtained in 86% of patients with *Pityriasis versicolor*, 78% of patients with *Tinea cruris* and in 75% of patients with *Tinea corporis* (Al-Waili, 2004).

The same preparation resulted also effective inreducing the symptoms of diaper dermatitis and eradicated *Candida albicans* from 50% of culture positive patients during a 7-day trial (Al-Waili, 2005). Several investigations deal with the ability of *O. europaea* extracts or their pure components to inhibit or delay the growth of microorganisms. An olive leaf water extract was tested against bacteria and fungi: the extract killed almost all bacteria while dermatophytes were inhibited following a 3-day exposure and *Candida albicans* was killed following a 24 h (Markin *et al.*, 2003). Oleuropein and hydroxytyrosol, secoiridoides contained in olive and olive oil, showed antimicrobial activity on ATCC and clinical isolated bacteria responsible for intestinal or respiratory tract infections in man. In particular, oleuropein inhibited the growth of *Salmonella* sp., *Vibrio* sp. and *Staphylococcus aureus* with minimum inhibitory concentration (MIC) between 62.5 and 125 mg/ml for ATCC strains and between 31.25 and 250 mg/ml for clinical isolates. Hydroxytyrosol, derived from oleuropein by enzymatic hydrolysis, showed a more broader spectrum and a higher potency in that inhibited also *Haemophilus influenzae* and *Moraxella catharralis*; its MIC values were between 0.24 and 7.85 mg/ml for ATCC strains and between 0.97 and 31.25 mg/ml for clinical isolates (Bisignano *et al.*, 1999). Furthermore, oleuropein showed activity against several species of *Mycoplasma* (Furneri *et al.*, 2002). Noteworthy is the activity of some aldehydes, volatile flavor components of olive fruit and oil, against different fungal and bacterial strains. Kubo *et al.* (1995) described the antimicrobial activity of long chain saturated and unsaturated aldehydes from olive fruit against a broad spectrum of food-borne microfungal and bacteria strains; among the microorganisms tested, fungi were the most sensitive. This activity is of particular interest since most of plant secondary metabolites show in general more potent activity against Gram-positive bacteria than against fungi. More recently, Bisignano *et al.* (2001) described the activity of some of these compounds against a number of standard bacteria strains that may be causal agents of human infections. The results obtained pointed out that unsaturated aldehydes have a broad antimicrobial spectrum and show similar activity against Gram positive and Gram negative bacteria. It has been hypothesized that these phytochemicals act both on the plasmatic membrane, by perturbating its lipidic fraction, and on intracellular targets (Trombetta *et al.*, 2002; Kubo *et al.*, 2003). Finally, a, b-unsaturated aldehydes for their antimicrobial properties are considered to be involved in the resistance of olive to microbe and insect attack (Kubo and Hanke, 1985).

In patients with postoperative wound infections following caesarean section or hysterectomies, topical honey application causes faster eradication of bacterial infections, reduces antibiotic use and hospital stay, accelerates wound healing, and results in minimal scar formation (Al-Waili and Saloom, 1999). We found that various concentrations of honey in liquid broth (from 30 to 100%, wt/v) inhibited growth of various strains of human pathogenic bacteria and *Candida albicans* (Al-Waili, 2004). In addition, we found that topical application of honey was effective in treating seborrheic dermatitis and dandruff (AL-Waili, 2001). Olive oil inhibits aflatoxin production of both *Aspergillus flavus* and *Aspergillus parasiticus* Comparative antibacterial and antifungal effects of some phenolic compounds (Aziz *et al.*, 1998). The presence of oleuropein, a phenolic compound extracted from olives, delayed the growth of *Staphylococcus aureus* (Tranter *et al.*, 1993). In a mixture with a boric acid and zinc oxide ointment, beeswax was used on patients with chronic eczema and psoriasis with good improvement (Kubota *et al.*, 1983). In addition, beeswax was used as an ointment for skin burn care (Zanoschi *et al.*, 1991).

Olive oil has been reported to favor the mineralization and development of bones (Cicerale *et al.*, 2010). It is a complex compound made of fatty acids, vitamins, volatile components and water soluble components. Olive oil is rich in monounsaturated fatty acids (mainly oleic acid). In addition, it contains adequate amounts of linoleic acid. It contains a group of related natural products with potent antioxidant properties, which are esters of tyrosol and hydroxytyrosol, including oleocanthal and oleuropein as well as vitamin E.

The growing popularity of the Mediterranean diet is due to a large body of epidemiological studies showing how the incidence of certain cancers is the lowest in the Mediterranean basin. It has been suggested that this is largely due to the relatively safe and even protective dietary habits of this area (Simopoulos, 2001; Colomer and Menendez, 2006). Olive oil is an integral ingredient of the traditional Mediterranean diet and several studies attribute many of the healthy advantages of this diet to olive oil's unique characteristics. Indeed, the relationship between the intake of olive oil and cancer risk has become a controversial issue that could have very important repercussions in human health as it may have a potential role in lowering the risk of some human neoplasms (La Vecchia, 2004; Colomer and Menendez, 2006). Thus, different studies have shown that the consumption of olive oil have a potential protective effect towards several malignancies, especially breast cancer (stomach, ovary, colon and endometrium cancer too).

Antioxidants and Olive Oil

Dietary phenolic substances have received much attention due to their biological activity. They have been attributed with positive properties such as having antimutagenic and anticancerogenic effects as well as being antioxidants (Kroll *et al.*, 2003).

In vitro and ex vivo models, olive oil phenolics have shown to have antioxidant properties, higher than that of vitamin E, on lipids and DNA oxidation (Owen *et al.*, 2000; Fito *et al.*, 2000; De la Puerta *et al.*, 1999). They are also able to prevent the endothelial dysfunction by decreasing the expression of cell adhesion molecules (Carluccio *et al.*, 2003), and increasing nitric oxide (NO) production and inducible NO synthesis (Moreno, 2003) by quenching vascular endothelium intracellular free radicals (Massaro *et al.*, 2002). Also, olive oil phenolic compounds inhibited platelet-induced aggregation (Petroni *et al.*, 1995) and have been reported to enhance the mRNA transcription of the antioxidant enzyme glutathione peroxidas (Masella *et al.*, 2004). This last issue, however, seems to be dependent on the tissue in which the gene expression was evaluated (Quiles *et al.*, 2002; Masella *et al.*, 2004). Other potential activities include anti-inflammatory and chemopreventive activity (Beauchamp *et al.*, 2005; Owen *et al.*, 2000). In animal models, olive oil phenolics retained their antioxidant properties in vivo (Visioli *et al.*, 2000; Coni *et al.*, 2000) and delayed the progression of the atherosclerosis (Aviram, 1996). So far, most of the cardio-protective effect of olive oil in the context of the Mediterranean diet has been attributed to its high MUFA content. Recently, the Federal Drug Administration (FDA) of the USA permitted a claim on olive oil labels concerning: "the benefits on the risk of coronary heart disease (CHD) of eating about 2 tablespoons (23 grams) of olive oil daily, due to the monounsaturated fat (MUFA) in olive oil" (Masella *et al.*, 2004). It must be noticed, however، that oleic acid is one of the predominant fatty acids in widely consumed animal foods in Western diets, such as poultry and pork (Linseisen *et al.*, 2002). A direct association of meat intake with the plasma oleic acid concentration was observed in a Swedish female population (Chajes *et al.*, 2001). In this population, oleic acid plasma concentrations were higher than those of females of Granada in Spain, without differences in polyunsaturated (PUFA) levels (Chajes *et al.*, 2001). Thus, perhaps a high oleic acid intake is not the sole primary responsible agent for the healthy properties of olive oil.

In addition to the large body of epidemiological data, experimental evidence that phenolic compounds are uptaken from the diet is accumulating. Experiments with laboratory animals, for example rats or rabbits, have demonstrated a higher resistance to oxidation of LDL obtained from animals fed virgin olive oil, as compared to animals that were only given a triglyceride preparation with an equivalent amount of oleic acid, i.e., triolein (Scaccini *et al.*, 1992) or plain olive oil (Wiseman *et al.*, 1996).

On pathogenic microorganisms the anti-bacterial effect depends of the phenolic compounds and of the strains tested. (Puupponen-Pimia *et al.*, 2005). Simopoulos, Colomer and Menendez reported the anti-microbial properties of pure phenolic compounds and polyphenols of different wines against *Proteus* *mirabilis, Serratia marcescens, Klebsiella pneumoniae, Pseudomonas aeruginosa* and *Staphylococcus aureus* (Simopoulos, 2001; Colomer and Menendez, 2006).

The food contamination by microorganisms has attracted increased attention because it is a problem that has not yet been brought under adequate control despite the preservation techniques available. *Listeria monocytogenes* has been recognized as an emerging foodborne pathogen and has become a major concern to the food-processing industry and to health authorities over the last decades. It is found in soil, water, dairy products, including soft cheeses, and in raw and undercooked meat, poultry, seafood and related produce (Bisignano *et al.*, 1999).

Resistance to anti-microbial agents has become an increasingly important and pressing global problem. So, new classes of anti-microbial drugs are urgently required. In recent years, there has been growing interest in alternative therapies and the therapeutic use of natural products, especially those derived from plants (Rates, 2001). It is generally accepted that phytochemicals are less potent antiinfectives than agents of microbial origin, i.e. antibiotics. However, new classes of anti-microbial drug are urgently required and the phenolic compounds represent a novel set of leads. Future optimization of these compounds through structural alteration may allow the development of a pharmacologically acceptable anti-microbial agent or group of agents (Cushnie and Lamb, 2005).

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Oleuropein and hydroxytyrosol, secoiridoides contained in olive and olive oil, showed antimicrobial activity on ATCC and clinical isolated bacteria responsible for intestinal or respiratory tract infections in man. In particular, oleuropein inhibited the growth of *Salmonella* sp., *Vibrio* sp. and *Staphylococcus aureus* with minimum inhibitory concentration (MIC) between 62.5 and 125 mg/ml for ATCC strains and between 31.25 and 250 mg/ml for clinical isolates. Hydroxytyrosol, derived from oleuropein by enzymatic hydrolysis, showed a broader spectrum and a higher potency in that inhibited also *Haemophilus influenzae* and *Moraxella catharralis*; its MIC values were between 0.24 and 7.85 mg/ml for ATCC strains and between 0.97 and 31.25 mg/ml for clinical isolates (Bisignano *et al.*, 1999). Furthermore, oleuropein showed activity against several species of *Mycoplasma* (Furneri *et al.*, 2002).

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Unsaturated aldehydes for their antimicrobial properties are considered to be involved in the resistance of olive to microbe and insect attack (Kubo and Hanke, 1985).

Furthermore, fatty acids and monoglycerides have been found to have a broad spectrum of microbicidal activity against bacteria and yeasts (Bergsson *et al.*, 2001), and the R,a-unsaturated aldehydes from olives and olive oil flavor have also been demonstrated to possess a noticeable activity against pathogens of the human intestinal and respiratory tracts (Trombetta *et al.*, 2002). In relation to human health, much concern has been focused on phenolic compounds from plants and foods that mayAmong edible modulate microbiota in the intestine by selectively increasing the growth of bifidobacteria and lactobacilli and decreasing that of harmful bacteria such as clostridia (Koo and Cho, 2004; Park *et al.*, 2005). The ingestion of phenolic compounds from olive oil could therefore contribute to a well-balanced microbiota of the human intestine. There is still need for new methods for reducing or eliminating foodborne pathogens, and new biopreservatives from plants or foods (Draughon, 2004) and essential oils (Burt, 2004) are requested. Olive oil may be consumed directly on bread and in fresh salads, but it is also employed in many homemade dishes (mayonnaise, cakes, others), canned tuna (Caponio *et al.*, 2003), salad dressing (Paraskevopoulou *et al.*, 2005), and meat foods (Kayaardi and Gok, 2004), in the preservation of cheese and fish (Tassou *et al.*, 1996), and in cosmetics. Even though olive oil has been used for centuries as a food preservative and in folk medicine, which components of the oil are responsible for this bioactivity remains undiscovered.

Methodology

the researcher applied the exploratory approach where various relevant studies where analyzed and discussed in order to discover the antibacterial activity of the olive oil.

Results and Discussion

Leaves and drupes from the olive tree, Olea europaea , are rich in olive biophenols, such as oleuropein, verbascoside, ligstroside, tyrosol and hydroxytyrosol, which have shown wide antioxidant and antimicrobial properties. In particular, oleuropein (Ole), has exhibited antibacterial activity against a wide variety of Gram-positive and Gram-negative human pathogenetic bacterial strains (Pereira et al., 2007), several fungi, as well as antiviral activity mostly against enveloped virus (Micol et al., 2005).

The molecular mechanism/s underlying the wide biological activity of Ole is not completely understood so far. It is believed that Ole, when digested by intestinal or plant β -glucosidases, yields a glutaraldehyde-like structure which exhibits protein-denaturing properties. These dialdehydic forms seem to exert a more potent bactericidal activity than their respective precursors (Medina et al., 2006). It is also believed that Ole, a medium polarity molecule, can get through cell membranes reaching intracellular targets in a similar way to hydroxytyrosol. Ole partition coefficient has been previously determined in octanol/water and oil/water systems through UV absorbance or HPLC measurements (Paiva-Martins et al., 2003) but it has not been determined in a phospholipid model membrane system yet.

Some authors have previously postulated that Ole may have an internal location in biomembranes (Saija et al., 1995), but others propose a superficial location for Ole in phospolipid bilayers (Paiva-Martins et al., 2003).

Throughout the review of relevant studies, it is clear that the antimicrobial agents existing in the olive oil use different antimicrobial activities in which they may interfere with cell wall synthesis, inhibit protein synthesis, inhibit nucleic acid synthesis or block metabolic pathways to inhibit growth of microorganisms or eliminate them as follow:

Interference with cell wall synthesis: antimicrobial agents can prevent cell wall synthesis, simply by blocking the synthesis of peptidoglycan layer which covers the outer surface of the cytoplasmic membrane.

Interference with protein synthesis: a number of antibacterial agents' act by inhibiting ribosome function. Bacterial ribosomes contain two subunits, the 50S and 30S subunits, binding to these sites cause protein chain termination and inhibit protein synthesis.

Interference with cytoplasmic membrane: this type of antimicrobial agents play role in disruption and destabilization of the cytoplasmic membrane.

Interference with DNA synthesis: a large number of agents interfere with purine and pyrimidine synthesis or with the interconversion or utilization of nucleotides. Other agents act as nucleotide analogs that are incorporated into polynucleotides. Antimicrobial agents may also bind to the enzyme gyrase to block DNA replication.

Besides its decorative properties, as a folk remedy, olive leaf has been used for combating fevers and malaria; also some reports indicated that its extract had a capacity to lower blood pressure in animals, and increase blood flow in the coronary arteries, relieved arrhythmia and prevented intestinal muscle spasms, (Pereira et al., 2007) diarrhea, to treat respiratory and urinary tract infections; also olives, olive oil and olive leaf extracts are some of these foodstuffs with recognized medicinal benefits and food preservation properties dating back to the Egyptian empire (Medina et al., 2007).

There is an uprising interest in antioxidants and bioactive substances from natural sources. The protective effect of diets rich in fruits and vegetables against cardiovascular diseases (McDonald et al.,

2001) and it is also supported by large body epidemiological studies that certain cancers such as breast and colon cancers were the lowest in the Mediterranean Basin where the diets are rich in olives and olive products (Al-Azzawie et al., 2006). These effects have been attributed, in part, to the presence in the Mediterranean diet of antioxidant vitamins, flavanoids and polyphenols that play an important role in disease prevention. In other words, flavonoids and phenolic compounds obtained from olive leaf are known to have diverse biological activities and may also be responsible for the pharmacological actions of olive leaf or, at least synergistically reinforcing those actions.

Even though, there are several groups, remarkable for determination of antioxidant capacity of flavonoids, it is mainly the o-dihydroxy (cathechol) structure which bestows the antioxidant properties to the olive leaf extracts (Benavente-Garcia et al., 2000). However, this is not the only factor that determined the antioxidant capacity of a compound; the stability of formed aroxyl group is another factor that needs to be taken into account. The aroxyl radical species are famous for their extensive electron delocation ability, which is a prerequisite for radical stabilization and generating multiple mesomeric structures. The decay constant of flavonoid aroxyl radicals those

formed during interaction with other radicals show that all most stable aroxyl species contained 3′-4′-catechol B-ring substitution pattern. All other polyphenols form far less stable aroxyl radicals (Benavente-Garcia et al., 2000). The phenolic groups in olive leaf extract, their examples and relative amounts contained within OLE are presented in Table (1). and molecule structure of most commonly encountered ones are given in Figure (1).

Table (1) The phenolic groups in OLE, their examples and relative amounts in OLE (Source: Benavente-Garcia et al., 2000).

Group Name	Example Compound	% Amount in OLE
Oleuropeosides	Oleuropein	24.54
	Verbascoside	1.11
Flavones	Luteolin-7-glucoside	1.38
	Apigenin-7-glucoside	1.37
	Diosmetin-7-glucoside	0.54
	Luteolin	0.21
	Diosmetin	0.05
Flavonols	Rutin	0.05
Flavan-3-ols	Catechin	0.04
Substitued Phenols	Tyrosol	0.71
	Hydroxytyrosol	1.46

Group Name	Example Compound	% Amount in OLE
	Vanilin	0.05
	Vannilic acid	0.63
	Caffeic acid	0.34

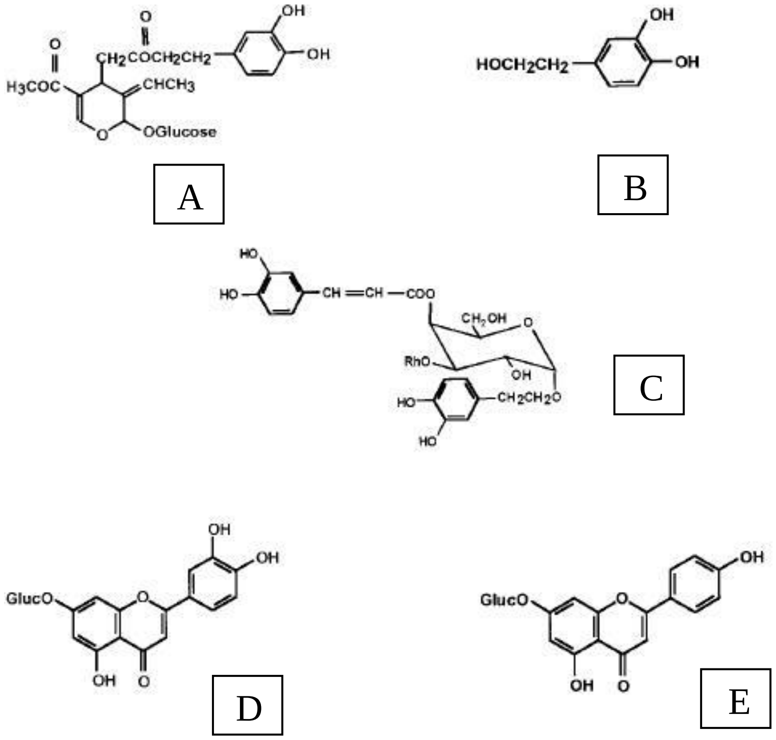


Figure (1) Molecular Structure of Phenolics Richly Obtained from OLE A: Oleuropein, B: Hydroxytyrosol, C: Verbascoside, D: Luteolin-7-glucoside and E: Apigenin-7-glucoside

(Source: Benavente-Garcia et al., 2000).

Low cost phenolic extracts could be obtained from commercially available olive mill waste water (OMWW) to be used as alternatives to synthetic antioxidants as BHA and BHT. Furthermore, hydroxytyrosol derived from OMWW can be used to stabilize edible oils (Fki et al., 2005).

Hayes et al., (2010), reported that, OLE at a concentration of 100 and 200Âµg/g muscle had consistently lower levels of lipid oxidation compared to control in both aerobic and modified atmosphere pack conditions.

Caffeic acid has been identified as one of the most active antioxidants in different in vitro assays in which it has been compared to synthetic antioxidants such as BHT, BHA, Î±-tocopherol or trolox. Medina et al., (2007) found that supplementation of low amounts of caffeic acid in minced horse mackerel muscle showed a high inhibition of rancidity.

Pazos et al., (2007) also reported that, supplementing hydroxytyrosol or grape procyanidins via spraying and glazing significantly decreased the high susceptibility of horse mackerel fillets for lipid oxidations. However, spraying method was more effective probably due to better penetration and accordingly better absorption of polyphenols by fillets. Hydroxytyrosol concentrations ranging from 10 to 100 ppm managed to increase the oxidative stability in bulk fish oil, oil-in-water emulsions and frozen minced fish muscle, however 50 ppm hydroxytyrosol concentration was found to be the most advantageous in delaying lipid oxidation in fish muscle (Pazos et al., 2007).

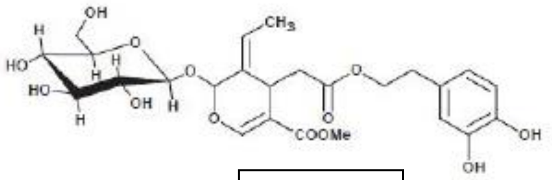
In addition to its antioxidant properties, phenolic compounds within olive leaf extract have shown antimicrobial activities against several microorganisms including; E. coli, Staphylococcus aureus, Klebsiella pneumoniae, Bacillus cereus, Salmonella typhi and Vibrio parahaemolyticu (Markin et al., 2003). Furthermore, OLE affects macrophage function and modulates inflammatory response; those may contribute to activity against infectious agents (Lee-Huang et al., 2003).

Although the individual phenolic compounds in olive leaf extract may show strong in vitro activities, the antioxidant and antimicrobial activities of combined phenolics showed similar or better effects than the individual phenolics (Lee at al. 2010). It had also been previously supported by Pereira et al., (2007) that, extracts may be more beneficial than isolated constituents since a bioactive component can change its properties in the presence of other compounds present in the extract. They also reported the antimicrobial capacity order for several concentrations of OLE as follows; B. cereus ~C. albicans > E. coli> S. aureus> C. neoformans~ K. pneumoniae~ P. aeruginosa> B. subtilis.

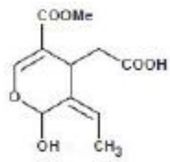
Markin et al., (2003) also reported that water extract of olive leaf with a concentration of 0.6% (w/v) killed E.coli, Ps. aeruginosa, S. aureus and K. pneumonia in 3h exposure. B. subtilis on the other hand was inhibited only when the concentration was increased to 20% (w/v) possibly due to spore forming ability of this species.

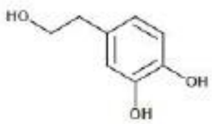
Sudjana et al., (2009), studied antibacterial activity of olive leaf extract with large variety of bacteria. Results indicated that OLE did not present broad-spectrum antibacterial activity, but had appreciable activity on H. pylori and C. jejuni.

The olive oil includes Oleuropein, which is the principal active phenolic compound of olive leaf extract and also that of each and every part of olive tree (Olea auropaea L.). Oleuropein was discovered in 1908 by Bourquelot and Vintilesco (Benavente-Garcia et al., 2000). Oleuropein is a bitter, secoiridoid glycoside that can be found in fruit, bark and leaves of olive tree (Benavente-Garcia et al., 2000). Oleuropein is an ester that consists of elenoic acid and 3,4- Dihydroxyphenylethanol, known as, hydroxytyrosol and elenolic acid, shown in Figure (2).



Oleuropein





Elenolic acid

Hydroxytyrosol

Figure (2) Structure of oleuropein and its components

(Source: Al-Azzawie et al., 2006)

Oleuropein has various pharmacological and health promoting properties including, antiarrythmic, spasmolytic, immÄ±ne-stimulant, cardioprotective (by inhibiting low-density lipoprotein oxidation), hypotensive and anti-inflamatory (responsible for inhibition of 5-lipoxygenase enxyme), hypoglycemic, antiviral (even against HIV), cytostatic (against McCoy cells), molluscicidali endocrinal and an enzyme modulator effects due to its antioxidative properties (Lee-Huang et al., 2003; Al-Azzawie et al., 2006). Even earlier, Fleming et al., (1973), theorized that, green olives had an enzymatic system, activated on brining, that allows hydrolysis of oleuropein into its aglycone which is an antibacterial compound. Oleuropein can easily be transformed into glucose and oleuropein aglycon in presence of β-glucosidase enzyme (Ronalli et al., 2006).

Oleuropein prevents formation of free radicals by its ability to chelating metals such as copper and iron, which catalyze free radical generation reactions such as lipid oxidation. As a protective action oleuropein may also directly neutralize radicals by providing hydroxyl groups (Galli and Visioli, 1999).

Oleuropein and its metabolite hydroxytyrosol both have a catechol group which is required for optimum antioxidant and/or scavenging activity. Both oleuropein and hydroxytyrosol have been reported to be scavengers of superoxide anions and inhibitors of the respiratory burst of neutrophils and hypoclorus acid-derived radicals (Al-Azzawie et al., 2006). They have also been proven to inhibit or delay th growth rate of several human intestinal or respiratory track pathogens such as Heamophilus influenza, Moraxella catarrhalis, Salmonella Typhimurium, Vibrio parahaemplyticus, Staphylococcus aureus, Vibrio cholera and Vibrio alginolyticus mainly due to their protective action provided by their phenolic structures (Pereira et al., 2007).

Conclusion

Olive oil is the main source of fat in Mediterranean diet. The major active components of olive oil include oleic acid, phenolic compounds and squalene which have different benefits such as cancer prevention, antimicrobial and antioxidant activities, and lowering the incidence of skin cancer, respectively. In recent years, the number of studies about the biochemical properties of different varieties of olive oils and their phenolic contents has dramatically increased. In the current study, the researcher highlighted the antimicrobial activity of olive oil against microbial infections through reviewing various of the relevant studies. The results of study indicated the efficiency of antimicrobial activity of olive oil against microbial infections.

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