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# Polyphenols benefits of olive leaf (*Olea europaea* L) to human health

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## Abstract

**Introduction:** The phenolic compounds present in olive leaves (*Olea europaea* L.) confer benefits to the human health.

**Objectives:** To review the scientific literature about the benefits of the polyphenols of olive leaves to human health.

**Method:** Literature review in the LILACS-BIREME, SciELO and MEDLINE databases for publications in English, Portuguese and Spanish with the descriptors “*Olea europaea*”, “olive leaves”, “olive leaf”, “olive leaves extracts”, “olive leaf extracts”, “phenolic compounds”, “polyphenols”, “oleuropein”, “chemical composition”, and “health”. There were identified 92 articles, but only 38 related to the objectives of the study and 9 articles cited in the works were included due to their relevance.

**Results and discussion:** The phenolic compounds present in olive leaves, especially the oleuropein, are associated to antioxidant, antihypertensive, hypoglycemic, hypocholesterolemic and cardioprotective activity. Furthermore, studies associate the oleuropein to an anti-inflammatory effect in trauma of the bone marrow and as a support in the treatment of obesity.

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Key words: *Olea europaea*. Olive leaves. Phenolic compounds. Oleuropein. Health.

## BENEFICIOS POLIFENOLES HOJA DE OLIVO (OLEA EUROPAEA L) PARA LA SALUD HUMANA

## Resumen

**Introducción:** Los compuestos fenólicos presentes en las hojas del olivo (*olea europaea* L.) conferir beneficios para la salud humana.

**Objetivos:** Revisar la literatura científica sobre los beneficios de los polifenoles de hojas de olivo para la salud humana.

**Método:** Revisión de la literatura en las bases de datos lilacs-bireme, scielo y medline para publicaciones en inglés, portugués y español con los descriptores “*olea europaea*”, “*hojas de olivo*”, “*hoja de olivo*”, “*hojas de olivo extractos*”, “*los extractos de hoja de olivo*”, “*compuestos fenólicos*”, “*polifenoles*”, “*oleuropeína*”, “*composición química*”, y “*salud*”. Se identificaron 92 artículos, pero sólo 38 en relación con los objetivos del estudio y 9 artículos citados en las obras se incluyeron debido a su relevancia.

**Resultados y discusión:** Los compuestos fenólicos presentes en las hojas del olivo, especialmente la oleuropeína, se asocian a antioxidante, antihipertensivo, hipoglucemiante, actividad hipocolesterolémico y cardioprotector. además, los estudios asocian la oleuropeína a un efecto anti-inflamatorio en trauma de la médula ósea y como soporte en el tratamiento de la obesidad.

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Palabras clave: *Olea europaea*. Hojas de olivo. Compuestos fenólicos. Oleuropeína. Salud.

## Abbreviations

AGEs: Advanced glycation end products.  
AI: Atherosclerotic index.

ALT: Alanine aminotransferase.  
AMI: Acute myocardial infarction.  
AST: Aspartate aminotransferase.  
CAT: Catalase.  
CK: Creatin kinase.  
CK-MB: Creatin kinase-MB.  
COX-2: Cyclooxygenase-2.  
CP: Crude protein.  
CPK: Creatine phosphokinase.  
CPK-MB: Creatine phosphokinase-MB.  
TC: Total cholesterol.  
CTE: Catechin equivalent.  
DBP: Diastolic blood pressure.  
DM2: Type 2 diabetes mellitus.

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DXR: Doxorubicin.  
 EPCs: Endothelial progenitor cells.  
 GAE: Gallic acid equivalent.  
 GSSG: Oxidized glutathione.  
 HDL-c: High-density lipoprotein cholesterol.  
 HF: Heart failure.  
 HO-1: Heme oxygenase-1.  
 IL-1 $\beta$ : Interleukin-1 $\beta$ .  
 IL-6: Interleukin-6.  
 iNOS: Inducible nitric oxide synthase.  
 LDH: Lactate dehydrogenase.  
 LDL-c: Low-density lipoprotein cholesterol.  
 MDA: Erythrocyte malondialdehyde.  
 NA: Nicotinamide.  
 NO: Nitric oxide.  
 Nrf2: Erythroid 2-related factor.  
 PARP: Peroxisome proliferatoractivated receptor.  
 PARP $\gamma$ : Peroxisome proliferatoractivated receptor.  
 SBP: Systolic blood pressure.  
 SOD: Superoxide dismutase.  
 STZ: Streptozotocin.  
 TBARS: Thiobarbituric acid-reactive substance.  
 TEAC: Trolox under defined conditions.  
 TG: Triglycerides.  
 TNF $\alpha$ : Tumor necrosis factor- $\alpha$ .

## Introduction

The olive tree (*Olea europaea* L.) is cultivated in many parts of the world, but the Mediterranean region is the main area of agricultural production, it represents approximately 98% of the growing around the world<sup>1</sup>. Apart from the Mediterranean region, the olive tree is cultivated on a large scale in the Arabian Peninsula, India and Asia<sup>2</sup>.

The main product extracted from the olive tree is the olive oil, of a global production of 11 million tons per year<sup>3</sup>. The olive oil is one of the bases of the Mediterranean Diet, widely studied for its antioxidant benefit<sup>4</sup>, particularly given to the large number of phenolic compounds present in the olive tree<sup>5</sup>. However, the olive leaves also contain phenolic compounds; the oleuropein, hydroxytyrosol, verbascoside, apigenin-7-glucoside and luteolin-7-glucoside are the most abundant already identified in olive leaf extracts<sup>6</sup>. The term “olive leaves” refers to a mixture of leaves and branches from both the pruning of olive trees and the harvesting and cleaning of olives<sup>7</sup>.

The large number of phenolic compounds present in olive leaves aroused the interest of researchers around the world and the studies with animals and humans have reported beneficial health effects such as the capacity of antioxidant<sup>6</sup>, anti-hypertensive<sup>8</sup>, hypoglycemic<sup>9</sup>, hypocholesterolemic<sup>10</sup>, cardioprotective<sup>11</sup>, anti-inflammatory<sup>12</sup> and as coadjuvant in the treatment of obesity<sup>13</sup>. This study aims to review the scientific literature about the benefits of polyphenols of olive leaves to human health.

## Method

This work is a literature review. There were consulted the LILACS-BIREME, SCIELO and MEDLINE databases. Scientific papers published in English, Portuguese and Spanish between the period of 2000 and 2014 about olive leaves and the benefits to human health were selected. The “*Olea europaea*”, “olive leaves”, “olive leaf”, “olive leaves extracts”, “olive leaf extracts”, “phenolic compounds”, “polyphenols”, “oleuropein”, “chemical composition” and “health” descriptors have been used to search in the database. Ninety-two articles were identified, but only 38 were related to the objectives of this study. The first analysis of the articles was conducted by the title and then by the abstract. Besides these, 9 references that have been cited in the articles were included in the articles that were found due to its relevance to the study.

## Results and discussion

### *Chemical characteristics and bioavailability of olive leaves*

The chemical composition of olive leaves varies according to origin, proportion of branches present in the extract, storage conditions, weather conditions, moisture content and degree of soil contamination<sup>14,15</sup>. The nutritional composition of the extract from olive leaves is strongly influenced by processing (drying and extraction)<sup>16</sup>. One study showed that the dehydration by lyophilization, air drying and oven drying reduced the nutritional value of the extract<sup>14</sup> and that the greatest loss of nutritive value was in the chopped samples before processing<sup>15</sup>.

An in vitro study has shown that the dehydration process has no significant influence on the bioavailability, but the composition of the extract modifies meaningfully the digestion process because the oleuropein and verbascoside are quite resistant to gastric digestion but is largely degraded in the intestinal phase. In the study, the luteolin-7-O-glucoside was the most stable phenolic compound in the in vitro simulation of the digestion process<sup>17</sup>.

The content of crude protein (CP) varies between 9.5 and 12.9%<sup>15</sup>; they are rich in amino acids such as arginine, leucine, proline, glycine, valine and alanine and poor in cysteine, methionine and lysine<sup>18</sup>. The greatest proportion of hemicellulose fibers are arabinosa type, whereas the branches have predominantly mannose<sup>19</sup>.

### *Polyphenols of olive leaves*

The Mediterranean diet is known for its health benefits, especially given to the large amount of polyphenols present in fruits, vegetables, oilseeds and olive

oil<sup>6</sup>. The extra virgin olive oil is produced from the fruit of the olive tree, botanically known as *Olea europaea* L, rich in polyphenols and known for its antioxidant capacity<sup>20</sup>. However, the olive leaves contain higher amount of polyphenols than olive oil. For example, the amount of oleuropein, which is the most abundant phenolic compound ranges from 0.005% and 0.12% in olive oil while in olive leaves it ranges between 1 and 14%<sup>4</sup>.

Phenolic compounds are secondary products to the metabolism of vegetables. In the case of the olive tree, the olive polyphenols are a consequence of the reactivity to pathogen attack and the response to insect injuries<sup>4</sup>.

There are five groups of identified phenolic compounds in olive tree: oleuropeosides (*oleuropein* and *verbascoside*); flavones (*luteolin-7-glucoside*, *apigenin-7-glucoside*, *diosmetin-7-glucoside*, *luteolin* and *diosmetin*); flavonols (*rutin*); flavan-3-ols (*catechin*) and substituted phenols (*tyrosol*, *hydroxytyrosol*, *vanillin*, *vanillic acid* and *caffeic acid*). The *oleuropein* is the most abundant phenolic compound in olive leaves, followed by *hydroxytyrosol*, *luteolin-7-glucosides*, *apigenin-7-glucosides* and *verbascoside*. The *hydroxytyrosol* is the precursor of the *oleuropein*, while the *verbascoside* is a conjugated glucoside of *hydroxytyrosol* and *caffeic acid*<sup>6</sup>.

The total content of flavonoids and polyphenols of olive leaves was determined as 2.058 mg GAE (gallic acid equivalent) per 100 g and 858 mg CTE (catechin equivalent) per 100 g, values similar to a red grape<sup>21</sup>.

#### Antioxidant activity of olive leaves

Reactive species of oxygen and nitrogen are produced constantly in the human body. They are essential for many cellular mechanisms such as energy production, chemical signaling and immune function and its production is controlled by enzymes such as superoxide dismutase (SOD), glutathione peroxidase and catalase (CAT), however, when there is an excess in the production of these reactive species there can occur an oxidative damage at cellular level. This cell damage is related to the increased risk of chronic diseases such as cardiovascular disease and cancer<sup>22</sup>. However, it is believed that the antioxidants may prevent or minimize oxidative damage and, consequently, reduce the risk of chronic diseases<sup>6</sup>.

Table I shows the phenolic compounds from olive leaves identified by Benavente-Garcia and collaborators in comparison to Trolox under defined conditions (TEAC). The flavonol rhamnoglucoside *rutin* (TEAC 2.75mM), flavan-3-ol *catechin* (TEAC 2.28mM) and flavone *luteolin* (TEAC 2.25mM) are the compounds with highest capacity for scavenging the ABTS•+ radical cation<sup>6</sup>.

The antioxidant activity of *oleuropein* is related to the *hydroxytyrosol* moiety in its structure. Compared

**Table I**  
Antioxidant activity of phenolic compounds  
from olive leaves

Phenolic compound	TEAC (mmol/L)
Olive leaf extract	1.58 ± 0.06
Rutin	2.75 ± 0.05
Catechin	2.28 ± 0.04
Luteolin	2.25 ± 0.11
Hydroxytyrosol	1.57 ± 0.12
Diosmetin	1.42 ± 0.07
Caffeic acid	1.37 ± 0.08
Verbascoside	1.02 ± 0.07
Oleuropein	0.88 ± 0.09
Luteolin-7-glucoside	0.71 ± 0.04
Vanillic acid	0.67 ± 0.09
Diosmetin-7-glucoside	0.64 ± 0.09
Apigenin-7-glucoside	0.42 ± 0.03
Tyrosol	0.35 ± 0.05
Vanillin	0.13 ± 0.01

TEAC: Trolox equivalent antioxidant capacity. Adapted Benavente-García et al. (2000).

with the *hydroxytyrosol*, the ability of scavenging the radical cation ABTS•+ is lower because of the molecular weight of the *oleuropein*. The study suggests that the olive phenolics compounds exhibit a synergistic behavior in the capacity of elimination of free radical when mixed in the form of extract, superior to the antioxidant capacity of the vitamin C and E<sup>6</sup>.

#### Benefits of polyphenols of olive leaves to human health

The polyphenols of olive leaves have numerous beneficial effects to human health, such as antioxidant capacity<sup>6</sup>, anti-hypertensive<sup>8</sup>, hypoglycemic<sup>9</sup>, hypocholesterolemic<sup>10</sup>, cardioprotective<sup>11</sup>, anti-inflammatory<sup>12</sup> and as a coadjuvant in the treatment of obesity<sup>13</sup>.

#### Antihypertensive effects of polyphenols of the olive leaf

The antihypertensive action of olive leaf extract has been shown in several studies. A study with 40 monozygotic prehypertensive twins that evaluated the effects of the daily dose of 500mg and 1000mg of olive leaf extract on systolic blood pressure (SBP) and diastolic blood pressure (DBP) for 8 weeks showed

a significant reduction in SBP and DBP of the group who received a 1000 mg daily dose. The group that received 500 mg decreased its SBP and DBP, however, it was not meaningful<sup>23</sup>. A study of Susalit and collaborators evaluated the effect of olive leaf extract on the SBP and DBP in individuals with stage 1 hypertension. The study showed that a dose of 500mg twice a day, for a total daily dose of 1000 mg, was able to reduce both systolic and diastolic pressure. The antihypertensive activity of olive leaf extracts was compared to the captopril medicament in a dose of 12.5 - 25mg, twice a day<sup>8</sup>. Another study that used animal models with diabetes mellitus type 2 (DM2) and renal hypertension induced by streptozotocin (STZ), nicotinamide (NA) and placement of solid plexiglass clips on left renal arteries showed a reduction in SBP due to the antioxidant activity of olive leaf extract, induced by the release of nitric oxide (NO) and sympatholytic activity<sup>24</sup>. Another study corroborated the findings showing that the oleuropein confers cardiovascular protection in animal models with DM2 and renal hypertension concomitantly, particularly when the extract has been used at a dose of 60 mg/kg per day<sup>11</sup>. The mechanisms responsible for the anti-hypertensive effect of the oleuropein are not well determined, however, some studies attribute this effect to the inhibition of angiotensin converting enzyme, a calcium channel-blocking activity and restoration of endothelial function<sup>26</sup>, the vasodilation<sup>27</sup> and radicalscavenging activity<sup>10</sup>.

#### Hypocholesterolemic effects of the polyphenol of olive leaf

The phenolic compound of olive leaves and olive oil in the Mediterranean diet is associated to a reduced incidence of cardiovascular diseases, as antioxidants minimize the deleterious effects of free radicals in the body. It is believed that the process may involve phospholipase C activation and arachidonic acid metabolism, and it is thought to reduce hydrogen peroxide<sup>28</sup>.

The beneficial effects of polyphenols of the olive leaf on the lipid profile such as decrease of total cholesterol (TC), low-density lipoprotein cholesterol (LDL-c) and triglycerides (TG) have been reported. In this study, the difference between the treatment group and the control group was not significant for the TG, although the serum level decreased 23.2% in the group that received 1000 mg of olive leaf extract per day<sup>8</sup>. This reduction was slightly lower than the fenofibrate, a potent anti-triglyceride agent<sup>29</sup>. In a study mentioned previously, with 40 monozygotic prehypertensive twins, there was a significant reduction in LDL-c<sup>23</sup>. A study with mice fed with a diet rich in cholesterol showed that oral administration of olive leaf extract, acid extract hydrolyzate and enzymatic hydrolyzate extract reduced the blood levels of TC, TG, LDL-c. In addition, the mice that received the phenolic extracts had their levels of high-den-

sity lipoprotein cholesterol (HDL-c) reestablished. ( $p < 0.05$ ). The study suggests hypocholesterolemic effect of the phenolic compounds in the olive leaf extracts. The study also calculated the atherosclerotic index (AI), defined as the ratio of LDL-c and HDL-c, which was significantly lower in the groups that were administered phenolic compounds present in the olive leaf extracts ( $p < 0.05$ ) and showed that there was a significant reduction in the hepatic activity of CAT and SOD in mice fed with a cholesterol-rich diet compared with the control group. However, the levels were restored in the presence of phenolic compounds present in the olive leaf extracts ( $p < 0.05$ )<sup>30</sup>. A similar study with hypercholesterolemic rabbits showed that administration of 10 or 20 mg / kg of *oleuropein* for 6 weeks decreased the TC and the TG ( $p < 0.05$ )<sup>31</sup>. In relation to the effects of polyphenols of the olive leaf in hypocholesterolemic associated with hyperglycemia, a study that assessed the effects of the administration of extracts of oleuropein and hydroxytyrosol in diabetic mice at concentrations of 16 and 8 mg/kg of body weight showed significantly lower concentrations of TC in diabetic rats that received *oleuropein* and hydroxytyrosol compared with the control group. The administration of extracts rich in phenolic compounds was able to restore the lipid profile, especially in the groups that received oleuropein and hydroxytyrosol in a concentration of 16 mg/kg of body weight, showing that oleuropein and hydroxytyrosol olive leaf extract can correct significantly the hypercholesterolemia coupled with hyperglycemia<sup>10</sup>.

#### Cardioprotective effects of polyphenols of olive leaf

In addition to the antihypertensive and hypocholesterolemic effect described in the scientific literature, the polyphenols of olive leaf have other cardioprotective effects. A study that evaluated the effects of oleuropein on myocardial injury showed that the administration of 20 mg/kg of body weight prior the induction of ischemia in rats resulted in decreased release of creatine kinase (CK), which is an important marker of gravity of the cardiac injury and of oxidized glutathione (GSSG), which is a sensitive marker of heart's exposure to oxidative stress. To assess the specific molecular oxidative alterations the study also measured the concentration of thiobarbituric acid-reactive substance (TBARS), which seems to increase considerably in the cardiac muscle after the ischemia, indicating a severe oxidative change in the membrane of phospholipids. The study found no significant increase in TBARS in the mice that received oleuropein compared to the control group, suggesting cardioprotective effect<sup>32</sup>. Janahmadi and collaborators, in a study that evaluated the cardiovascular protection of oleuropein in mice, showed that pre-treatment with *oleuropein* provides protection



for acute myocardial infarction (AMI), preventing the development of heart failure (HF) secondary to AMI. The improvement of the cardiac function may be due to the reduction of the infarction size and the cardiac injury, including improvement in the serum levels of creatin kinase-MB (CK-MB), troponin I and lactate dehydrogenase (LDH)<sup>33</sup>. Another study showed that the administration of *oleuropein* at 10 or 20mg/kg for 6 weeks or of 20 mg/kg for 3 weeks reduced the infarct size compared with the control group ( $p=0.001$ )<sup>31</sup>.

A recent study evaluated the capacity of the *oleuropein* to restore the endothelial progenitor cells (EPCs) exposed to angiotensin II. The EPCs are responsible for the neovascularization of ischaemic tissue and may participate in re-endothelization of an injured arterial wall and there is evidence that the angiotensin II impairs the function of the EPCs. EPCs are responsible for neovascularization of tissue and ischaemic may participate in re-endothelization of an arterial wall injured and there is evidence that angiotensin II impairs the function of EPCs. The study showed that the *oleuropein* has protective effect in these cells, not only for its antioxidant capacity, but also because it involves the stimulation of nuclear transcription factor erythroid 2-related factor (Nrf2) and, as a result, increase the expression of heme oxygenase enzyme-1 (HO-1)<sup>34</sup>. The HO-1 enzyme has antioxidant, anti-inflammatory, anti-apoptotic proprieties and it has the ability to re-endothelization of injured arterial wall or neovascularization of ischemic<sup>35</sup>.

The *oleuropein* has also been studied for its protective effect on the administration of certain drugs such as doxorubicin (DXR). The doxorubicin, an anthracycline antibiotic clinically known as adriamycin, is a highly effective antineoplastic drug against many malignant diseases<sup>36,37</sup>, however, the clinical use of DXR is often limited because of its undesirable serious cardiotoxic side effects, probably induced by oxidative stress<sup>38</sup>. An *in vivo* study that evaluated the effect of *oleuropein* in mice treated with DXR showed that the drug increases significantly the release of cardiac enzymes into the systemic circulation ( $p<0.05$ ) and that the concomitant use of *oleuropein* in concentrations of 100 and 200mg/kg of the body weight with DXR reduced the serum levels of creatine phosphokinase (CPK), creatine phosphokinase-MB (CK-MB), LDH, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) ( $p<0.05$ ). Furthermore, the *oleuropein* reduced lipid peroxidation induced by DXR, improving the therapeutic outcome and preventing the cardiotoxic<sup>39</sup>. In another study, the *oleuropein* prevented cardiomyopathy induced by DXR, preserving the contractility of the left ventricular and alleviating the development of inflammatory and degenerative lesions in the myocardium. It also prevented the nitro-oxidative stress, the imbalance in the homeostasis of NO, the expression of pro-apoptotic mediators and the derangement of myocardial metabolism<sup>40</sup>.

## Effects of polyphenols of olive leaf in DM2

The polyphenols of olive leaves, particularly the *oleuropein*, are well known for their hypoglycemic effect; two mechanisms have been suggested to explain this effect: 1) the potential to affect glucose-induced insulin release, and 2) an effect to increase peripheral uptake of glucose<sup>41</sup>. In addition, part of the hypoglycaemic effect is attributed to the antioxidant capacity of *oleuropein*<sup>42</sup>. A study of Jemai and collaborators assessed the effects of the administration of extracts of *oleuropein* and hydroxytyrosol in diabetic mice at concentrations of 16 and 8 mg/kg of body weight. The study showed that the blood glucose levels were significantly lower ( $p<0.05$ ) in diabetic rats after administration of extracts of *oleuropein* and hydroxytyrosol in all concentrations. However, the mice that received *oleuropein* and hydroxytyrosol in a concentration of 16 mg/kg of the body weight showed a hypoglycaemic effect significantly higher than those that received these compounds at a concentration of 8 mg/kg of body weight. The study showed a significant increase in liver glycogen in the groups that received *oleuropein* and hydroxytyrosol extracts compared to the two control groups (normal glucose and diabetic). The mice that received the *oleuropein* at 16mg/kg of body weight showed higher levels of hepatic glycogen concentration ( $p<0.05$ )<sup>10</sup>. A study with diabetic rabbits evaluated the effects of administration of the *oleuropein* extract on the levels of blood glucose. The study used a dose of 20 mg/kg of body weight for a period of 16 weeks and showed a significant effect of the *oleuropein* as hypoglycemic from the 8th week of administration of the extract. The study also revealed that the group treated with *oleuropein* showed a gradual reduction in the levels of erythrocyte malondialdehyde (MDA), which is an oxidative stress marker, significantly from the 10th week of administration compared to the control group. The study suggested the use of *oleuropein* prophylactically in the reduction of complications resulting from oxidative stress in DM2<sup>41</sup>. Another study assessed the capacity of major phenolic components of olive leaf extract (luteolin, hydroxytyrosol, luteolin-4'-O- $\beta$ -D-glucopyranoside, luteolin-7-O- $\beta$ -D-glucopyranoside and *oleuropein*) as inhibitors of the formation of advanced glycation end products (AGEs), showed that luteolin and luteolin-4'-O- $\beta$ -D-glucopyranoside are potent inhibitors of AGEs, i.e., they delay the development of diabetic complications. The *oleuropein* inhibited the formation of AGEs, but it was not significant<sup>9</sup>.

## Effects of polyphenols of olive leaf in chronic colitis

The effect of *oleuropein* administration in patients with chronic colitis was tested by Giner and collaborators, in a study that evaluated the effects of a diet supplemented with *oleuropein*, equivalent to 500mg/kg of body weight for 56 days in mice with chronic colitis

induced by dextran sulfate sodium. The study showed a reduction in cellular infiltration and consequently in the recruitment of inflammatory cells (macrophage, neutrophil and eosinophil) to the location of the injury. Furthermore, in the group with the diet supplemented with oleuropein decreased the release of inflammatory cytokines such as interleukin-6 (IL-6) and interleukin-1 $\beta$  (IL-1 $\beta$ ). The IL-6 is a pro-inflammatory cytokine that plays an important role in the development of inflammatory intestinal diseases with elevated serum levels of both acute and chronic inflammation. Elevated levels of IL-1 $\beta$  are also correlated with disease activity and associated with active lesions. The study suggests that the oleuropein administration is effective in alleviating symptoms of chronic colitis induced by sodium sulfate<sup>43</sup>.

#### Effects of polyphenols of olive leaf in traumas

The anti-inflammatory effect of oleuropein in spinal cord trauma was tested in mice that were divided in 4 groups, one of them received 20 mg/kg of body weight of oleuropein soon after the spinal cord injury and the other one after 1 hour. The tests were performed 24 hours after the injury. The study showed an attenuation of the levels of tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), IL-1 $\beta$ , nitrotyrosine, inducible nitric oxide synthase (iNOS), cyclooxygenase-2 (COX-2) and peroxisome proliferator-activated receptor (PARP) in the mice that received oleuropein independent of the time of administration. The pro-inflammatory cytokines TNF- $\alpha$  and IL-1 $\beta$  are synthesized immediately after the spinal cord injury worsening the posttraumatic condition by the increase of vascular permeability, recruitment of inflammatory cells and induction of iNOS and COX-2. Thus, the study suggests that oleuropein modulates the inflammatory reactions after spinal cord injury<sup>44</sup>.

#### Effects of polyphenols of olive leaf in obesity

The effect of the *oleuropein* in obesity has also been studied, specifically in substantial modulation of physiological and molecular pathway involved in energy metabolism and adiposity. An *in vitro* study showed that the *oleuropein* reduced the expression of peroxisome proliferator-activated receptor  $\gamma$  (PPAR $\gamma$ ), inhibited adipogenesis and enhanced osteoblastogenesis in stem cells derived from human bone marrow<sup>13</sup>. Another study demonstrated that the *oleuropein* acted on 3T3-L1 cells and reduced preadipocyte differentiation and lipid accumulation and thus regulated the size of fat cells<sup>45</sup>. A study of Svobodova and collaborators showed that the oleuropein has an anti-adipogenic effect through the inhibition and activity and PPAR $\gamma$  which is essential for the formation and function of the adipocytes<sup>46</sup>. The PPAR $\gamma$  is also involved in the regulation of insulin sensitivity. De Bock and collaborators suggested dietary supplementation with polyphenols from olive leaf,

more specifically oleuropein, as a therapeutic strategy for the prevention and treatment of obesity<sup>47</sup>.

## Conclusion

Polyphenols of olive leaf, especially oleuropein, have interesting effects on the human body such as antioxidant capability, antihypertensive, hypoglycemic, hypocholesterolemic, however, many of these effects have been tested in animals and it is necessary to perform studies with human beings to confirm the benefits attributed to polyphenols from olive leaf.

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