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## Review Article

Novel positioning of *Olea europaea* L. (Olive) from farm to pharma indexed in pharmacopeiaAfreen Usmani<sup>1</sup>, Rania I.M. Almoselhy<sup>2\*</sup><sup>1</sup>MESCO Institute of Pharmacy, Uttar Pradesh, India<sup>2</sup>Oils and Fats Research Department - Food Technology Research Institute - Agricultural Research Center, Giza, Egypt

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## ABSTRACT

The current study explores the transformative journey of *Olea europaea* L. (Olive) from its traditional role in random traditional medicine to its current positioning in pharmacopeia as a pharmaceutical preparation with defined dosage and indications. The comprehensive examination covers botanical and chemical profiles, traditional uses, pharmacological activities, extraction techniques, quality control, regulatory status, clinical studies, and future directions. Various analytical methods, including spectroscopic and chromatographic approaches, are discussed for quality evaluation and detection of adulteration. Additionally, the regulatory landscape, particularly within the European Union, is outlined, emphasizing the importance of accurate labeling and geographical origin disclosure. The regulatory status of *Olea europaea* L. varies across regions, ranging from restrictions due to safety concerns to inclusion in pharmacopeias as traditional herbal medicine or pharmaceutical preparations. A pivotal development highlighted is the incorporation of Olive into Egyptian pharmacopeia, signifying a significant shift towards evidence-based therapy and reinforcing its acceptance in mainstream healthcare.

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## 1. Introduction

The olive tree is an evergreen since it is a member of the Oleaceae family. Though it may also adapt to moderate climates at other latitudes, this plant is characteristic of the Mediterranean flora. *Olea europaea* L. comprises numerous subspecies; however, the distinction between the wild varieties (*Olea europaea* Var. *sylvestris* (Mill.) *lehr*), which are distinguished by small fruits with minimal oil content, and the cultivated variety (*Olea europaea* Var. *europaea* L.), which yields edible fruits with characteristics that differ significantly based on the cultivar, the soil, and the climate conditions in which the plant has grown, is particularly significant from an economic standpoint.<sup>1</sup>

Olive trees are grown on over 4 million hectares, mostly in the Mediterranean regions of the European Union (EU) including traditional, intense, and ultra-intensive groves with yearly consumption of about 500,000 tons by each of Italy and Spain as the EU's major olive oil users, with Greece having the highest consumption of olive oil per person (12 kg) annually. EU regions produce olives that stand out for their unique qualities and characteristics when compared to olives from other regions of the world. Since 2013, the EU has accounted for 67% of global olive oil production and 53% of global oil consumption. Italy is a major contributor to the production of premium oil, which is further distinguished based on the source region. Particularly, oils from the northern region of Italy are linked to more fruity aromas and a fairly distinct taste, whilst oils from the southern region are more likely to have a richer and stronger character.<sup>2</sup>

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Olive is well-documented in various civilizations throughout the world.<sup>3</sup>

1. **Ancient Times:** Olives and olive oil, the world's first vegetable oil, are revered and found in ancient texts. One of the Old Testament olive tree traditions tells of a pigeon that returned to Noah's Ark carrying a piece of the tree's branch, signaling the end of the flood and the olive branch's subsequent reputation as a symbol of peace.
2. **Ancient Egypt:** Olive happened not just at sacred writings but also in daily life, the administration, and athletics inside a society. Egyptians spent a great deal on olive. Tutankhamun, the pharaoh, was adorned with an olive branch-woven crown of justice.
3. **Ancient Greek:** Because olive trees were revered in ancient Greek mythology, only virgin girls and boys who took an oath to refrain from touching someone of the other sex were permitted to gather olives. We know that in the past, athletes who won races at the Olympic Games were awarded olives as a crown.
4. **Roman Civilization:** According to Roman mythology, Ramos and Ramulus were born beneath an olive tree, and it was from this olive branch that ambassadors arrived in a nation bearing the hope of peace. In Roman customs, olive oil was used for weddings and funerals. The deceased was blessed by sprinkling olive oil on his face, which was thought to cleanse him of his sins. Romans advocated planting olive trees because they are revered as holy in many aspects of life.
5. **Islamic Medicine:** *Olea europaea* L. has been extensively used in traditional Islamic medicine for various therapeutic purposes. Olives and olive oil are mentioned in Quran and in the Hadith (sayings of Prophet Muhammad) to take oil of olive and massage with it – it is a blessed tree.
6. **Contemporary Research:** Besides being used for healthy life style in Mediterranean countries, in recent years, there has been a growing interest in the scientific community to study the bioactive components responsible for the potential health benefits of oils and leaves of *Olea europaea* L. Research work has focused on their antioxidant, anti-inflammatory, and antimicrobial properties, as well as their potential role in the management of various chronic diseases as cardiovascular disease (CVD).

## 2. Plant Profile of *Olea europaea* L.<sup>4-7</sup>

1. **Botanical Name:** *Olea europaea* Linn.
2. **Family:** Oleaceae
3. **Syns :** *Olea sativa*; *Olea pallida* Salisb.
4. **English:** Olive
5. **Spanish:** Olivo; Aceituno

## 6. Arabic: Zaytun

### 3. Distribution<sup>7</sup>

*Olea europaea* L. is endemic to Africa, the Middle East, and S. Central China. It is mostly found in the subtropical biome and grows as a shrub or tree. It has social and environmental applications, is used as fuel and food, and is utilized as a medication and animal feed.

#### 3.1. Native to

Afghanistan, Albania, Algeria, Angola, Baleares, Botswana, Burundi, Canary Is., Cape Provinces, China South-Central, Cyprus, Djibouti, East Aegean Is., Eritrea, Ethiopia, Free State, Greece, Iran, Italy, Kenya, Kriti, KwaZulu-Natal, Lesotho, Libya, Madeira, Malawi, Mauritius, Morocco, Mozambique, Namibia, Nepal, Niger, Northern Provinces, Oman, Pakistan, Palestine, Portugal, Rwanda, Réunion, Sardegna, Saudi Arabia, Sicilia, Somalia, Spain, Sudan, Swaziland, Tanzania, Tunisia, Turkey, Turkey-in-Europe, Uganda, West Himalaya, Yemen, Yugoslavia, Zambia, Zaire, Zimbabwe

#### 3.2. Introduced into

Argentina Northeast, Ascension, Bermuda, China Southeast, Corse, Egypt, France, Hainan, Hawaii, India, Iraq, Jawa, Korea, Krym, Lebanon-Syria, Marianas, Mexico Southwest, New Zealand North, Norfolk Is., St.Helena, Taiwan, Tibet, Tubuai Is.

### 4. Phytochemical Composition of *Olea europaea* L.<sup>8-12</sup>

The nutritional and organoleptic qualities of extra virgin olive oil (EVOO), which is regarded as the best olive oil, are highly valued. Furthermore, its use is becoming more and more common outside of the Mediterranean region, where it serves as the primary dietary source of fat. Triglycerides (TAG) of about 98% that make up EVOO are 80% monounsaturated fatty acids (MUFA), which include oleic acid (C18:1). These MUFAs are what give EVOO its physicochemical characteristics. Certain chemicals, like triterpenic acids and phenolic compounds, which are known to have health advantages, are present in the remaining unsaponifiable fraction (1-2%). The fatty acid (FA) profile and antioxidant and anti-inflammatory phenolic component richness of extra virgin olive oil (EVOO) are linked to a number of health advantages, such as the prevention of diabetes, cancer, heart disease, and neurodegeneration. While all extra virgin olive oil (EVOO) is made using the same basic technique, there are differences in its composition and sensory attributes depending on a number of factors, including the kind and ripeness of the olives, the processing technology employed, and the storage conditions. Nevertheless, in order to fall under

the EVOO category (as opposed to virgin or olive oil), a few requirements must be met: Free fatty acidity should not exceed 0.8%, production should only use mechanical methods, and the oil should have fruity qualities and no sensory flaws. Indicators of quality and authenticity, such as a low peroxide and UV spectrophotometric values ( $K_{270} < 0.22$ ,  $\Delta K \leq 0.01$ ), should also be present in EVOO.

#### 4.1. Categories of olive oil<sup>2</sup>

The properties of the olive oil must adhere to the limitations set forth by EU regulations for that category in order for it to be marketed under that name. Ensuring that this is the case is the duty of the operators and the EU member states.

##### 4.1.1. Eight different categories of olive oils and olive-pomace oils exist

1. Extra-virgin olive oil,
2. Virgin olive oil,
3. Virgin lampante olive oil,
4. Refined olive oil,
5. Olive oil composed of refined olive oil and virgin olive oils,
6. Olive pomace oil,
7. Crude olive-pomace oil,
8. Refined olive pomace oil.

Only extra-virgin olive oil, virgin olive oil, olive oil made of refined olive oil and virgin olive oil, and olive pomace oil are available for direct retail purchase. Not all categories can be sold to consumers. The classifications, traits, and production of olive oil are further described in a factsheet created by the European Commission.

##### 4.2. The different categories of olive oils are graded according to quality parameters, relating to:

1. Physico-chemical characteristics, such as the acidity level, peroxide index, fatty acid content and sterols composition;
2. Organoleptic (sensory) characteristics, such as the fruitiness and the absence of organoleptic defects.

##### 4.3. Virgin olive oils

1. Extra virgin olive oil is the category with the highest quality. From an organoleptic point of view, it has no defects and is fruity. Its acidity level must not exceed 0.8%.
2. Virgin olive oil may have some sensory defects but at very low level. Its acidity must not exceed 2%.
3. Lampante olive oil is a lower quality virgin olive oil with an acidity of more than 2%, with no fruity characteristics and substantial sensory defects. Lampante olive oil is not intended to be marketed at retail stage. It is refined or used for industrial purposes.

#### 4.4. Other categories of olive oil

The following categories of olive oils are not virgin olive oils

1. Refined olive oil is the product obtained after the refining of a defective virgin olive oil (lampante olive oil for instance). It is not intended to be marketed at retail stage. It has a degree of acidity up to 0.3%.
2. Olive oil composed of refined olive oil and virgin olive oils is an oil resulting from the blending of refined olive oil with extra virgin and/or virgin olive oils. It has a degree of acidity up to 1%.
3. Crude olive-pomace oil: the olive-pomace is the residual paste obtained after the oil is extracted from the olives. The oil obtained from that paste is called crude olive-pomace oil.
4. Refined olive-pomace oil: crude olive-pomace oil can be refined and blended with virgin olive oils. The result of that blend is called refined olive-pomace oil. Its degree of acidity can be up to 1%.

### 5. Extraction and Formulation Techniques of *Olea europaea* L.<sup>13–15</sup>

#### 5.1. Extraction techniques<sup>13</sup>

1. **Traditional Extraction Methods** : The traditional method for extra virgin olive oil (EVOO) mechanical cold-press extraction involve three main processes: crushing, malaxation, and centrifugation. Firstly, the olive fruits are washed thoroughly and then crushed by hammer mill and the paste is pumped to a malaxer where it is warmed and mixed until the oil begins to separate. The resulting paste is pumped to a centrifuge where the solids are separated from the liquids and the vegetable water and oil are further separated in a final centrifugal process.
2. **Modern Extraction Approaches** : Current scientific study in the field of olive oil extraction has concentrated on enhancing quality, with special attention to maximizing extraction efficiency and shortening process length. Lately, research has been carried out to enhance the conventional malaxation method and get favorable outcomes for oil output and consumption. Emerging technologies such as microwave (MW), pulsed electric field (PEF), and ultrasound (US) have been incorporated into the traditional virgin olive oil extraction process in order to achieve these goals.

It is significant to say that *Olea europaea* L. oil is characterized by premier quality and safety, as it does not require additional refining, bleaching, and deodorizing (RBD)<sup>16</sup> as many vegetable and seed oils, which are possibly accompanied with risky contaminants.<sup>17</sup>

## 5.2. Formulation strategies<sup>14</sup>

1. **Encapsulation Techniques :** Harvesting and pruning olive (*Olea europaea* L.) trees produce a significant amount of biomass in the form of leaves and branches, which are regarded as byproducts or agro-industrial waste. The olive leaf is a biomass-rich plant that also includes a number of phenolic compounds, secoiridoids, and flavonoids that offer many health benefits, including antioxidant, antibacterial, antiviral, anti-inflammatory, and anti-carcinogenic properties. Olive leaf extracts provide promise for novel uses in the cosmetic, pharmacological, and food sectors. Encapsulation techniques can successfully address the shortcomings in preservation, stability, bioactivity, and bioavailability, all of which are critical to the effectiveness of these drugs. Using the Solution Enhanced Dispersion by Supercritical Fluids (SEDS) method, it was possible to successfully encapsulate olive leaf extracts. This method maximizes the therapeutic efficiency of the bioactive ingredients.
2. **Combination Formulations:**<sup>15</sup> To increase the therapeutic effects of olive leaf extract (OLE), combining them with other natural substances or pharmaceutical agents has been investigated. The potential of synergistic combinations to treat a range of health issues, such as oxidative stress, microbial infections, and inflammation, has been investigated. Using a Ucerin basis, a topical cream containing 2% OLE was created. After melting the urea at 65 to 70 °C and cooling it to 40 °C, other formulation ingredients were added. 10% propylene glycol, 2% OLE, and 0.1% ascorbic acid were present in the formulation. The early onset of effects of 2% OLE cream on herpes simplex virus (HSV-1) and its clinical efficacy are both confirmed by this investigation, establishing its clinical relevance. OLE may therefore be especially important for patients for whom the current standard treatment is either not available or not tolerated as an active pharmacological component of topical therapies for the treatment of HSV-1.

## 6. Pharmacological Properties Of *Olea europaea* L.

Studies have indicated that *Olea europaea* L. (Figures 1, 2) may be useful in treating a range of illnesses, including cancers, heart problems, digestive issues, liver problems, asthma, depression, headaches, migraines, analgesics, rheumatoid arthritis, infertility, wound healing, neurological, and nephrological conditions. Its antibacterial, antifungal, immunomodulatory, anti-inflammatory, and antioxidant qualities have also been shown in studies. Studies on *Olea europaea* L. have demonstrated that it is a viable natural therapy for COVID-19, as it has been shown to improve immune function and viral clearance. *Olea*

*europaea* L. has also been studied for its ability to manage diabetes; studies have shown that it has hypoglycemic activity and lowers blood glucose levels. Additionally, olive has been shown to be effective against a variety of viruses as an antiviral. Overall, *Olea europaea* L. exhibits potential for a wide range of medical uses.

## 7. Clinical studies and Efficacy of *Olea europaea* L

Table 1 summarizes the Pharmacological activities of *Olea europaea* L. with respective mechanisms of action.

## 8. Quality Control and Standardization<sup>1</sup>

### 8.1. Authentication techniques for *Olea europaea* L

One of the most crucial objectives for scientists working in the agri-food industry is the certification of food quality in the context of the global market. International agencies have produced precise rules on quality standards for oils since consumers, producers, and distributors are very interested in determining the authenticity and traceability of food products. Extra virgin olive oils (EVOOs) and vegetable oils (VOs) are extensively utilized in the chemical, pharmaceutical, cosmetic, and culinary industries. Since extra virgin olive oil (EVOO) is thought to be crucial to a Mediterranean diet, a great deal of research has been done on it to determine its origin and find evidence of adulteration and fraud. Numerous analytical methods, including as mid-infrared resonance (MIR), near-infrared resonance (NIR), and <sup>1</sup>H and <sup>13</sup>C nuclear magnetic resonance imaging (NMR) imaging, have been employed to evaluate the quality and look into oil adulteration. Other spectroscopic methods, like ultraviolet spectrometry, Fourier transform infrared (FTIR) spectroscopy,<sup>48–50</sup> fluorescence spectroscopy, Raman spectroscopy, and fluorescence spectroscopy, have a lot of potential for characterizing various olive oil samples from the perspective of organic substances and, consequently, detecting their adulteration. To find out what trace elements are in oils, researchers frequently utilize inductive coupled plasma optical emission spectroscopy (ICP-OES), inductive coupled plasma mass spectrometry (ICP-MS), and graphite furnace atomic absorption spectrometry (GF-AAS). To find EVOOs adulterated with organic components, GC and HPLC were often used in conjunction with MS. The use of volatile-species distribution as a fingerprint to evaluate non-degradation, traceability, and authentication based on head-space sampling and GC has been documented in a number of papers. The majority of these methods are costly and/or complicated, thus it would be ideal to have a quicker, easier, and less expensive process. Voltammetry satisfies these conditions and could be a good substitute for other methods when identifying adulteration in olive oil. Researchers proposed that correlations may be formed between the olive cultivar and/or their place of origin and



**Figure 1:** *Olea europaea* L. - Olive fruits, Extra virgin olive oil (EVOO), Olive grove, Olive leaves (OL)



**Figure 2:** Experimental design of *Olea europaea* l. from farm to pharma

**Table 1:** Pharmacological activities of *Olea europaea* L. and their respective mechanisms of action

Pharmacological Activities	Mechanism of Action	References
Anticancer	Induction of apoptosis in cancer cells -Suppression of tumor cell proliferation -Inhibition of angiogenesis - A potent anti-tumoral protection against human gastric cancer cells. - Regulation of cell processes such as cell migration, cell cycle arrest, mitochondrial-mediated apoptosis, and JAK/STAT signaling pathway inhibition.	18–25
Cardiovascular diseases (CVD)	Regulation of lipid profile - Hypolipidemic - Inhibition of arterial hypertension	21,26–35
Gastroprotective	Modulation of gut microbiota - Act as Prebiotic compounds	21
Hepatoprotective	Attenuating oxidative stress in the liver - Restoring liver function - Exerts beneficial effects on non-alcoholic fatty liver disease by relieving fat accumulation, oxidative stress, and mitochondrial dysfunction mediated by the activation of mitophagy via the AMPK/PINK1 pathway	21
Respiratory health	Bronchodilatory effects - Reduction of airway inflammation - Viable natural therapy for COVID-19, as it has been shown to improve immune function and viral clearance.	21
Antidepressant	Regulation of neurotransmitter levels - Modulation of neuroendocrine factors	21
Analgesic and antipyretic	Inhibition of pain mediators - Modulation of pain signaling pathways	21
Anti-arthritic	Reduction of joint inflammation - Modulation of immune responses in arthritis	21
Reproductive health	Regulation of reproductive hormone levels - Enhancement of fertility parameters	21
Wound healing	Promotion of cell proliferation and migration - Stimulation of collagen synthesis	36
Neuroprotective	Inhibition of Alzheimer. - Reduced risk of neural disordersAntioxidant protection against neurotoxic insults - Modulation of neuroinflammation and cognitive dysfunction by regulating the PI3K/Akt/mTOR signalling pathway.	21
Nephroprotective	Reduction of oxidative stress in the kidneys. - Preservation of renal function. - Improving renal damage and endothelial dysfunction.	21
Antimicrobial	Disruption of microbial cell membranes Inhibition of microbial growth	21,33,35,37
Antifungal	Disruption of fungal cell membranes Inhibition of fungal growth	33,35
Immunomodulatory	Immune-stimulating activity	21
Anti-inflammatory	Inhibition of inflammation, oxidative stress, coagulation, platelet aggregation, fibrinolysis, and endothelial dysfunction. • Regulation of the production of nitric oxide and inflammatory cytokines.	21,29,37–41
Antioxidant	Scavenging reactive oxygen species Enhancing endogenous antioxidant enzymes Reduce oxidative stress. Inhibit the signalling pathway of PI3K/AKT/mTOR-HIF-1 $\alpha$ which is caused by hypoxia.	21,37,39,41–43
Antiviral	Inhibition of viral replication Stimulation of immune responses	15,33,35,42,44
Anti-diabetic	Improving insulin sensitivity Modulating glucose metabolism	21,32,34
Anti-allergic	Modulation of histamine release Inhibition of allergic inflammatory mediators Reducing the allergic symptoms scores	45
Bone health	Enhancement of bone mineral density Promotion of osteoblast activity	46
Diuretic	Enhanced renal excretion of water and electrolytes Modulation of kidney function	43
Hypotensive	Regulation of the hypertension, LDL lag time and blood lipid profile. Increase vasodilatory nitric oxide (NO) and reduce vasoconstrictor markers.	21,43,47
Ocular diseases	Inhibition of glaucoma • Inhibition of diabetic retinopathy	21
Women Health	Inhibition of preeclampsia Inhibition of Hypertensive disorders of pregnancy (HDP) Protective against gestational diabetes and gestational weight gain. Prevent breast ulcers, Nipple irritation, and nipple sore.	21,36

the electrochemical response of a modified screen-printed electrode.

### 8.2. Regulatory guidelines and standardization

The production, distribution, and regulation of oils have all been addressed by the European Union (EU). Oil packing and labeling guidelines are outlined in EU Regulation No. 1019/02, and the Commission Implementing Regulation EU No. 1335/13 (2013) mandates that the label must state the oil's geographic origin. The package or label of olive oil shall bear information about the region from which it is gathered, as mandated by EU Regulation No. 29/12 (European Commission Implementing Regulation, 2012). The document also specifies that basic terms like "blend of olive oils of EU origin," "blend of olive oils not of EU origin," or "blend of olive oils of EU origin and not of EU origin" should be mentioned on the labeling of the oils' origin in order to provide more clarity.

## 9. Regulatory Status and Inclusion in Pharmacopeia of *Olea europaea* L

### 9.1. Regulatory status of *Olea europaea* L.

*Olea europaea* L. has differing regulatory statuses in various nations and areas. Some nations have restricted its usage because of worries about its safety and effectiveness, while others have placed it in their pharmacopeia as a traditional medicine. Its regulatory status has been further complicated by the absence of standard rules for the production, processing, and quality control of products derived from *Olea europaea* L. Some places classify it as a nutritional supplement, while other places include it in the category of traditional herbal medicine.

### 9.2. Inclusion in pharmacopeia<sup>5,51–56</sup>

The Egyptian Drug Authority (EDA) issued the Egyptian Herbal Monograph on 01.06.2023, which signals a dramatic change in the status of olives. No longer limited to their traditional use as therapeutic plants, olives now hold a major place in the pharmacopeia as approved pharmaceutical preparations. This change is a significant advancement since Olive is now recognized as a medication that can be purchased from pharmacies, confirming its position in conventional medical procedures and recognizing its medicinal value.

Furthermore, Olive's pharmacopeia entry highlights the increasing acceptance of its safety and effectiveness, which is supported by strict standardization and scientific examination. Olive's conversion to a pharmaceutical product signifies a move away from its prior status as a medication only found in traditional treatment and toward evidence-based therapy. This paradigm change highlights the necessity of adhering to pharmacological norms,

standardizing dosages, and developing clear administration protocols in order to guarantee the efficacy and consistency of the olive products that are sold in pharmacies.

Moreover, the incorporation of Olive into the pharmacopeia signifies the increasing recognition and support of its therapeutic qualities by the mainstream medical community. This inclusion strengthens olive's standing as a recognized and reliable therapeutic agent while also improving accessibility for patients and boosting healthcare professionals' confidence in providing olive-based medications.

In conclusion, there has been a notable progress in the fusion of conventional and contemporary healthcare systems with Olive's move from historical use in traditional medicine to its current position in the pharmacopeia as a pharmaceutical preparation sold in pharmacies. This shift is evidence of the increasing acceptance of traditional herbal medicines in modern healthcare procedures, as well as the transformational potential of scientific validation.

## 10. Challenges and Opportunities

Significant obstacles to the standardization of products based on *Olea europaea* L. include adulteration, variations in the amount of active compounds, and a dearth of reliable clinical evidence. Establishing established procedures for extraction, cultivation, and quality evaluation is essential to guaranteeing the security and effectiveness of formulations containing *Olea europaea* L. Establishing thorough standards for the use of *Olea europaea* L. in healthcare practices requires cooperation between regulatory agencies, research institutes, and practitioners of herbal medicine.

## 11. Safety and Side Effects of *Olea europaea* L

For millennia, people have utilized *Olea europaea* L. in traditional medicine. Although its possible health advantages have been the subject of numerous research, it is important to take into account any potential risks as well as safety concerns when using it.

### 11.1. Safety profile

Because of its possible health advantages, *Olea europaea* L. is widely regarded as safe to eat and has been used as a culinary and medicinal herb. *Olea europaea* L. has a long history of usage in traditional medicine and an excellent safety profile with no notable known toxicity or side effects.

### 11.2. Adverse reactions

Although it has a generally good safety profile, some people could have negative responses or side effects. Frequently reported adverse effects linked to *Olea europaea* L. eating, include

### 11.3. Allergic Reactions

Rarely, adverse reactions have been documented to *Olea europaea* L. topical application or ingestion, including skin rashes, itching, and breathing difficulties. When utilizing *Olea europaea* L., people who are known to be allergic to plants in the Oleaceae family should use caution.

#### 11.3.1. Gastrointestinal disturbances

Some people may get moderate gastrointestinal symptoms, like nausea, vomiting, or upset stomach, especially if they take concentrated or larger doses of *Olea europaea* L. These effects are usually moderate and temporary, though.

#### 11.3.2. Drug Interactions

It is crucial to take into account any possible drug interactions between *Olea europaea* L. and specific prescriptions. Because *Olea europaea* L. has the ability to impact drug transporters and metabolic enzymes, it may interact with several drugs. Before adding *Olea europaea* L. to a pharmaceutical regimen, people taking drugs should speak with a healthcare provider to avoid any potential interactions or negative effects.

#### 11.3.3. Pregnancy and Lactation

There isn't much information about the safety of *Olea europaea* L. during pregnancy and lactation. *Olea europaea* L. should not be used by pregnant or lactating women as a precaution since there is insufficient information available to support its safety during these times.

## 12. Future Directions and Challenges in Harnessing the Potential of *Olea europaea* L

### 12.1. Future directions

#### 12.1.1. Clinical trials and standardization

Thorough clinical trials are essential if *Olea europaea* L. is to reach its full potential. Standardized procedures for dose and delivery must be established in order to assess the medication's safety and effectiveness in a variety of patient demographics.

#### 12.1.2. Mechanistic Understanding

Clarifying the exact molecular processes that underlie the therapeutic actions of *Olea europaea* L. will provide light on the plant's mode of action and facilitate the creation of specialized treatments for particular illnesses.

#### 12.1.3. Formulation development

Investigating novel formulations and delivery methods, such as liposomes, nanoparticles, and nanoemulsions, can increase the stability and bioavailability of bioactive substances, boosting their therapeutic efficacy.

### 12.1.4. Drug interactions and safety profile

In order to include *Olea europaea* L. into conventional medicine and guarantee patient safety, it is imperative to look into possible drug interactions and assess the long-term safety profile of the plant.

### 12.2. Challenges in harnessing the potential of *Olea europaea* L

#### 12.2.1. Diversity in regulatory status

The varying regulatory statuses of *Olea europaea* L. across different nations and regions pose a challenge. Some countries restrict its usage due to safety and efficacy concerns, while others embrace it as traditional medicine or pharmaceutical preparation.

#### 12.2.2. Lack of standardization

The absence of uniform rules for the production, processing, and quality control of *Olea europaea* L. products complicates its integration into mainstream healthcare. Standardization is crucial to ensure consistency in dosage, efficacy, and safety.

#### 12.2.3. Complex authentication and analytical techniques

Authentication techniques, such as mid-infrared resonance (MIR), near-infrared resonance (NIR), and various spectroscopic methods, can be expensive and complex. Developing simpler, cost-effective methods for verifying the authenticity of Olive products is a persistent challenge.

Many analytical methods used for quality evaluation, such as GC, HPLC, and various spectrometric techniques, can be costly and intricate. The need for more accessible, straightforward, and economical processes is essential for widespread adoption.

#### 12.2.4. Geographical variation

Olive cultivars and their places of origin significantly impact the electrochemical response of modified electrodes. Understanding and accounting for this geographical variation present challenges in developing consistent and reliable authentication methods.

#### 12.2.5. Global market dynamics

Adapting to the global market's demand for certified food quality while meeting international standards adds complexity. Striking a balance between traditional practices and contemporary market requirements poses a challenge in harnessing the full potential of *Olea europaea* L.

#### 12.2.6. Educational awareness

Raising awareness among healthcare professionals, consumers, and producers about the evolving role of *Olea europaea* L. from a traditional remedy to a pharmaceutical preparation is essential. Bridging the knowledge gap



ensures informed decisions and acceptance.

#### 12.2.7. Integration into pharmacopeia

The process of integrating *Olea europaea* L. into pharmacopeias faces challenges in establishing clear administration protocols, standardized dosages, and ensuring adherence to pharmacological norms. Overcoming these challenges is crucial for its widespread acceptance and use in pharmacies.

#### 12.2.8. Maintaining therapeutic integrity

Ensuring that the therapeutic integrity of Olive products is maintained during the transition to pharmaceutical preparations is a critical challenge. Balancing standardization without compromising the diverse therapeutic compounds present in *Olea europaea* L. is a delicate task.

### 13. Conclusions

The transition of *Olea europaea* L. into pharmacopeia reflects a paradigm shift, aligning traditional remedies with evidence-based therapies. The meticulous review underscores the importance of adhering to pharmacological norms, standardizing dosages, and establishing clear administration protocols. This inclusion not only enhances Olive's therapeutic standing but also bridges the gap between traditional and modern healthcare systems, showcasing the evolving landscape of herbal medicines in contemporary practices. The newfound recognition and support in mainstream medicine further solidify Olive's position as a reliable therapeutic agent, enhancing accessibility and instilling confidence among healthcare professionals in prescribing Olive.

### 14. Author Contribution

“Conceptualization, A.U. and R.I.M.A.; methodology, A.U. and R.I.M.A.; data curation, A.U. and R.I.M.A.; writing—original draft preparation, A.U. and R.I.M.A.; writing—review and editing, A.U. and R.I.M.A.”

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### 16. Conflict of Interest

None.

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