Review

Overview of the therapeutic and or pharmaceutical effects of olive mill waste water on the gastroduodenal mucosa injuries

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Abstract

Introduction: The purpose of this study is to review the literature supporting the use of olive mill waste water (OMW) in the management of gastroduodenal *mucosa* lesions and or ulcer.
Methods: Current benchmark data is collected from the DSA for the running year. The survey process is inspired by using various databases to summarise credible research in the *in-vivo* and *in-vitro* literature through the systematic use of electronic databases and resources such as Google scholar, Springer link, Science Direct and PubMed. To provide a full and wide scope of relevant evidence, the inclusion criteria for this review were set to filter out studies that assessed the relationship between OMW and gastroduodenal mucosa lesions and or ulcer.
Results: A variety of literature was reviewed in order to obtain as much information as possible, and a total of 43 studies were selected for inclusion in this overview. This paper focuses on the relationship between OMW and healing effects of gastroduodenal ulcer. It would be useful to scrutinize the data resulting from the study of the physiological and metabolic effects. The meta-analysis has shown that polyphenols from *Olea europaea*, and therefore those from their OMW, have numerous biological activities, both in terms of primary and secondary prevention, in particular gastroprotective and anti-ulcer activity. Previous research has suspected that OMW polyphenols may have both anti-inflammatory and antioxidant properties, which may help to protect the stomach lining from damage and reduce the risk of developing ulcers. They may also help by suppressing the proliferation of *Helicobacter pylori*, widely diagnosed in clinical development of gastric wound ulcer.
Conclusion: According to diverse studies, OMW compounds have shown potential healling activity. Its anti-inflammatory, antioxidant and antibacterial properties may help to protect the stomach mucosa and reduce the risk of developing lesions of the gastroduodenal mucosa. However, further research is needed to fully clarify their mechanisms of their potential health benefits.

Key Words: Olive production and derivates - Olive mill waste water - Gastroduodenal mucosa lesions - *Helicobacter pylori* - Bioactive compounds - Healing Effect.

Introduction

The olive-growing sector occupies a major place in Algeria. According to the estimations from the FAO (2017), Algeria remains a modest producer of olive oil, ranking 10th among the top ten olive oil-producing countries in the Mediterranean (FAO, 2017). Algeria's total olive-growing area has increased during recent years, and it has reached 500.000 hectares in 2021, with a production of 80.000 tonnes of olive oil. Olive-growing in Algeria is characterized in particular by its varietal diversity and the large number of oil mills, which exceeds 1.600. The Tlemcen region alone has 31 oil mills (DSA, 2025). Industrial olive by-products contain a range of bioactive molecules that are a worrying source of environmental pollution. In terms of value, these bioactive components also include health-protective effects, closely linked to those found in the fruit *Olea europaea*. Over the last few decade, numerous studies have described in detail their antioxidant, anti-inflammatory, immunomodulatory, analgesic, antimicrobial, antihypertensive, anticancer and antihyperglycaemic effects, antioxidant, anti-inflammatory, immunomodulatory, antimicrobial, antihypertensive, anticancer and antihyperglycaemic

activities, antihypertensive, anticancer and antihyperglycaemic (Foti et al., 2021). Therefore, the growing interest in natural bioactive properties represents a new exciting opportunity for oil mills. The aim of this study is to overview the published literatures supporting the use of oil mill wastewater (OMW) in the management of gastroduodenal mucosal lesions and/or ulcers. Statistical data relating to the rate of production of these by-products being provided by the Tlemcen DSA (2025).

A priori, gastroduodenal ulcer encompasses ulcers of the esophagus, stomach and duodenum (Costa et al., 2024). for decades, it has been considered one of the main clinical issues with high mortality and morbidity rates. Many factors have been reported to be involved in the pathophysiology of ulcer development such as the chronic *Helicobacter pylori* (*H. pylori*) infection which is a Gram-negative bacterium that infects about half of the world's population and about 80% of the population in developing countries, it colonizes the gastric mucosa and triggers pathologic conditions, and the use of Nonsteroidal Anti-inflammatory Drugs (NSAIDs), which naturally include the Acetylsalicylic acid (ASA) for a long period of time, stress, cigarette smoking, nutritional deficiencies…etc, are the most common etiological antecedents. This disease results from gastrointestinal mucosal damage caused from an imbalance of aggressive gastric luminal agents and defensive mucosal factors (Waldum, 2024). Referring to the symptoms associated with peptic ulcer, it is characterized by the painful formation of sores in the mucosa of the stomach, esophagus or/and duodenum. Although the symptoms may appear as swelling, eructation, nausea and vomiting, loss of appetite, weight loss, bloody vomit and black faeces caused by bleeding in the stomach, heartburn or throbbing, they often occur a few hours after a meal or during the night, but disappear when food or water is consumed (Misal, 2024). Diagnosis of infection has two inseparable components: bacterial identification proper and identification of the endoscopic and histological lesions induced by the bacteria. A distinction is usually made between non-invasive tests (serology, urea-13C breath test, search for *H. pylori* antigen in stools), invasive tests (endoscopic biopsies of the gastric mucosa for anatomopathological purposes), and bacteriological tests (*H. pylori* cultures or PCR), (Lamarque et al., 2012). According to Singh et al., (2024), peptic ulcer disease can be treated with curative agents used to heal the ulcer and may be prevented through cytoprotective or gastroprotective mechanisms. Some medicinal plants and by-products resulting from the agri-food industry such as liquid oleic co-products also called olive mill waste water (OMW) have exhibited prophylactic and/or curative antiulcer activities via multitarget actions, due to their phenolic compounds profile, so therefore creating a research opportunity for drug discovery for the treatment of ulcers. Polyphenols in *Olea europaea* and their derivatives are highly varied and can be divided into seven basic groups: phenolic alcohols, benzoic derivatives, cinnamic derivatives, flavonoids, isochromans, lignans and secoiridoids. The various constituents of these groups in turn enclose "O-glucosides", in whose case one or more hydroxyl groups are linked to one or more carbohydrates, mainly including glucose and, in small proportions, rhamnose and disaccharides (Gouvinhas et al., 2017). The aim of this work is to shed light on the huge polluting volume of this waste and to investigate, in terms of recovery, the curative effect of OMW on the gastroduodenal mucosa lesions.

Materiel and methods

Current data proxy: The collection of statistical data at the agricultural services (DSA, 2025) makes it possible to highlight this typical polluting by-product in terms of a possible biological recovery.

Literature Search strategy: The literature search was reported out using a series of databases covering review articles from PubMed, Scopus and Web of Science, Sciencedirect and Google Scholar. The search strategy used the following keywords:

- OMW - Olives byproducts pubmed - Olive polyphenols pubmed - Hydroxytyrosol - from *Olea europaea,* alcaloids, secoiridoides, iridoids, etc.
- Biological activities of olive byproducts - Anti-inflammatory activities of olive - Anti-inflammatory activities of olive by products - Polyphenols and gastroduodenal injuries healing

Inclusion criteria: The main inclusion criteria were as follows:

In vitro and *In vivo* studies - Top-ranked studies -Most recent studies -Studies in English language -Studies on the phytotherapeutic aspect of OMW -Article reviews - Original papers - Retrospective and observational studies.

Results and Discussion

Olive and oil production and rate of generated OMW

Concretely, the olive industry generates two types of by-products, one liquid, represented by vegetation water or OMW, and the other solid, represented by pomace. Olives contain around 20% oil, 30% pomace and 50% OMW. The latter results from the water contained in the fruit (olives) and the manufacturing water added during the crushing process (Aggoun et al., 2016).

The main statistical sources for the rate of production of olives, oils and OMW are provided by the Tlemcen DSA (2025). The oleic cultivated area and oil olive production in the wilaya of Tlemcen (N-west of Algeria) evolved from 13698 to 16470 ha between 2015 and 2025. The olive yield fluctuated between 379184 and 773040 qx with an average value of 643492.40 ± 123357.57qx. That of olive oil varied from 29775 to 79884 hl with an average value of 51270.50 ± 15253.49 hl. The rate of OMW ranged from 757449 to 1481077 hl with an average value of 1203763.20 ± 277071.91 hl in the same period (Fig 1-2). Olive products are obtained by several techniques, those used in the wilaya of Tlemcen are:

- Traditional technique (Press system), which follows a discontinuous process, and in this case encompasses the semi-traditional production technique.
- Modern technique, which is similar to the previous technique in the initial stage.
- The modern technique generates more co-products and therefore a pomace value ranging from 35 to 50kg per 100kg of olives and a OMW value ranging from 80 to 125L per 100kg of olives, (DSA, 2025).

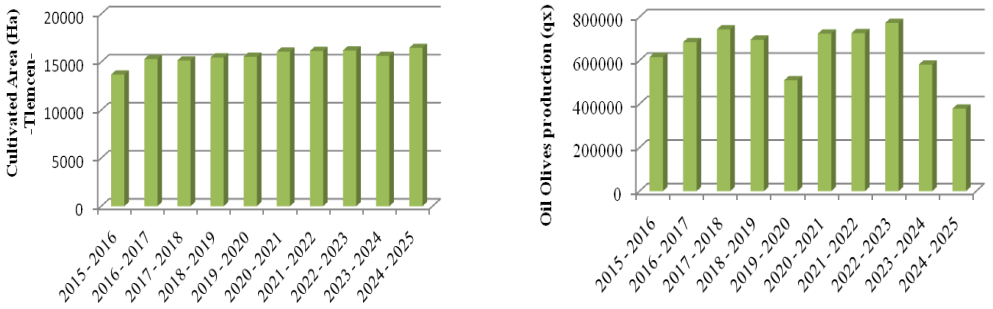

Fig 1. Olive cultivated area and olive production in the Wilaya of Tlemcen (N-west of Algeria) during ten years (2015 – 2025), (DSA, 2025)

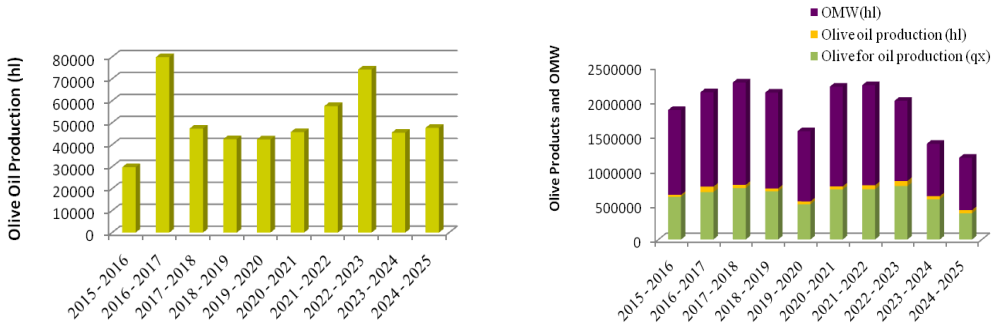

Fig 2. Oil production and OMW levels (DSA, 2025)

Characteristics of OMW

Composition of OMW

The main components of OMW are sumerrized in Table 1. The main components of OMW consist of dry residue, organic matter, lipids, polyphenols, suggar, organic acids and total nitrogen, (Zbakha and El Abbassi, 2012).

Organic fraction of OMW

The organic matter in OMW, with concentrations ranging between 16.7 and 81.6 g/l, comprises:

- An insoluble fraction made up mainly of olive pulp, representing suspended and colloidal matter.
- A soluble fraction found in the aqueous phase and containing lipids, sugars, organic acids, pectins and phenolic compounds, including vitamins and sometimes traces of pesticides (Zbakha and El Abbassi, 2012).

Table 1 : Chemical composition of OMW (Zbakha and El Abbassi, 2012)

Composition	Content
Ph	4.7 - 5.7
Dry residue (g/L)	11.5 – 102
Organic matter (g/L)	16.5- 81.6
Lipids (g/L)	1.64 - 9.8
Suggar	1.3 - 8.79
organic acids	0.78 – 1
Polyphenols (g/L)	0.002 - 11.5
Total Nitrogen	0.06 - 0.95

Phenolic fractions of OMW

Phenolic compounds can be grouped into three different classes, differentiated by :

- The degree of complexity of the basic skeleton (from a simple C6 to highly polymerized forms).
- The degree of modification of this skeleton (degree of oxidation, hydroxylation, methylation).
- The possible linkages of these basic molecules with other molecules such as carbohydrates, lipids, proteins, or with other secondary metabolites that may or may not be phenolic compounds (Attard and Lia, 2024).

The phenolic profile of OMW differs from that of the fruit. Whereas olives are very rich in glucosed secoiridoids; OMW have a high concentration of secoiridoid derivatives such as hydroxytyrosol, tyrosol and Hy-EDA. OMW are very rich in phenolic acids, which explains their acidic character. Variety, extraction system (type of pressing, time and temperature of mixing), addition of hot water and sodium chloride (NaCl) during olive crushing are the factors that affect the phenolic yield of olive oil and OMW (Bernini et al.,2024).

Vitamins

Vitamins are a group of complex organic substances vital and crucial for the body's proper functioning. They are present in small quantities in natural foods and food products. They are classified into two main categories:

- Fat-soluble vitamins, such as A, D, E and K
- Water-soluble B-class vitamins (B1, B2, B3, B6, B9 and B12...) and vitamin C (ascorbic acid).
- Several vitamins have been identified in OMW, the most frequent being group D and B vitamins and vitamin PP, with an average concentration of 124 mg/kg of margines (Albini et al., 2024; Bartkowiak-Wieczorek and Madry, 2024).

Treatment of gastroduodenal lesions and/or ulcers

Actually, many synthetic antiulcer drugs are used in the clinic, such as antacids, histamine H2 receptor antagonists proton pump inhibitors (PPI), nonsteroidal anti-Inflammatory drugs (NSAIDs) and antibiotics (Table 2).

Table 2 : Current Synthetic antiulcer drugs

Molecule	Mode of action and period of treatment	References
H2-antihistamines	H2-antihistamines reduce the amounts of acid produced by the stomach	*Yadav et al., (2024)*
Pantoprazole	Proton Pump Inhibitor	*Vadakutt & Doshi (2024)*
Polaprezinc (zinc L-carnosine complex)	Inhibits the activity of the transcription FNF-*kappa* B and decreases the expression of many inflammatory cytokines - Promotes the expression of PDGF-B, VEGF, NGF, and various heat shock proteins (HSPs).	*Wang et al., (2024)*
Omeprazol	Prevents stress induced gastric ulcer by direct inhibition of Matrix metalloproteinases -Inhibit gastric acid production in the stomach.	*Singh et al., (2024)*
L'amoxicillin /clarithromycin / Metronidazole	Reduce the infection by *Helicobacter pylori*	*Misal et al., (2024)*

Biological and bioactives properties of OMW

The keyword search strategy was overly wide-ranging, so it was necessary to select those that were most relevant to the objective of our study. The search of electronic databases revealed the publication of several reviews and original papers in the scientific literature, studying and illustrating the biological activities of the bioactive compounds present in *Olea europaea and its by-products*, such as anti-inflammatory, antioxidant, antimicrobial and preventive activity against gastroduodenal mucosal lesions. Searches were identified by targeting the key words cited above, using meta-analyses and systematic reviews. Published papers were broken down by number, year of publication and journal (ScienceDirect and PubMed) (Fig 3). The outcomes of a meta-analysis of research on olive by-products, in particular OMWs, could be expected to provide further useful indications on the potential health benefits and pharmacological characteristics of these by-products and help direct future research and clinical application (Table 3).

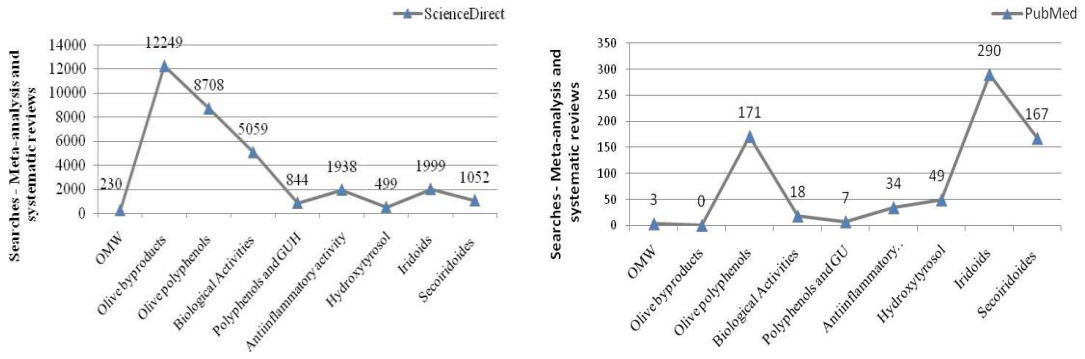

Fig 3. Identification of searches using meta-analysis and systematic reviews via web-based platforms

The bioactive compounds found in OMW, in particularly esters, hydroxytyrosol, tyrosol, verbascoside and oleuropein have a various beneficial rôles that can be linked to the biological and biotechnological research field (Harun et al., 2025; Zoubdane et al., 2024; Khalil et al., 2024),

The target objective of this study was to explore the potential application of OMW as a natural compound to minimise disorders linked to oxidative stress generated in lesions of the gastroduodenal mucosa and/or peptic ulcer. The latter is presented as a round or oval lesion in the mucosa of the stomach or duodenum that has been

corroded by gastric acidity and digestive juices. It can be caused by infection with *H. pylori* or by the use of drugs, such as aspirin or other non-steroidal anti-inflammatory drugs (NSAIDs), which weaken the mucosa of the stomach or duodenum. The *H. pylori* is a Gram-negative spiral-shaped microorganism adapted to an acidic environment. The predisposing infection of the body leads to gastric atrophy and a decrease in acid production, probably due to an increase in the local production of interleukin-1-*beta,* predominantly body involvement

Table 3: Biological effects of the major phenolic components of OMW

Olive phenolic compounds	Health	References
Hydroxytyrosol	Anti-inflammatory activity	Harun et al., (2025)
	Anticancer activity	Calahorra et al., (2024)
	Antioxydant activity	Gonçalves et al., (2024b)
	Antineurodegenerative effects	Reyes-Corral et al., (2024)
	Antifungal and antibacterial activities	Al-Rimawi et al., (2024)
	Protecting effect of the skin	Chen et al., (2024a)
	Antidiabetic effects	Harun et al., (2025)
	Gastroprotective activity	Bartkowiak-Wieczorek & Madry (2024)
	Thrombolytic and haemolytic activities	Giurranna et al., (2024)
Oleuropeine	Antioxydant activity	Khalil et al., (2024)
	Anticancer activity	Yılmaz & Zdemir (2024)
	Anti-diabetic effects,ability to inhibit the enzymes α-glucosidase and α-amylase	Mohamed et al., (2024)
	Neuroprotective effects	Gonçalves et al., (2024a)
	Anti-inflammatory and Immunosuppressive effects and anti-aging activity	Chen et al., (2024b) Laveriano-Santos, et al., (2024)
	Antifungal effects and antimicrobial activities	Al-Rimawi et al., (2024)
	Antiviral activity: Hepatitis B virus, Herpes simplex virus, Human immunodeficiency virus	Ali & Salama (2024)
	Gastroprotective effects	Abdellah et al., (2024)
Tyrosol	Antioxidant and anti-inflammatory effects	Zoubdane et al., (2024)
	Cytopretective activity and prevention from obesity	Salucci et al., (2024)
	Antifungal effect and antibacterial activities	Moghadam et al., (2024)
	Attenuates hepatic steatosis and fibrosis	Gabbia et al., (2024)
	Protecting effect of the hypertension	Dabravolski et al., (2024)
	Neuroprotective effects	Naseroleslami et al., (2024)
Verbascoside	Antifungal effect and antibacterial activities	Li et al., (2024)
	Anticancer effects	Yücer et al., (2024)
	Neuroprotectives effects	Mao et al., (2024)
	Antioxidant activity	Deng et al., (2024)
	Antiinflamatory Activity	Pongkitwitoon et al., (2024)

predisposes to gastric ulcer and gastric adenocarcinoma (Lamarque, 2012). The pathogenesis of gastroduodenal injuries induced by non-steroidal anti-inflammatory drugs is mainly due to a reduction in blood flow to the mucosa, as a result of the inhibition of vasodilatory prostaglandins produced by cyclooxygenase. The subsequent step is the adhesion of leukocytes to the endothelium, which may depend on cyclooxygenase-2. Endothelial

lesions exacerbate the fall in mucosal blood flow and promote the inflammatory process in the gastric mucosa. The inflammatory mechanism is amplified by TNFα expression in polymorphonuclear cells induced by non-steroidal anti-inflammatory drugs. A relatively few days after the start of treatment, epithelial growth and increased mucosal blood flow, which depend in part on the expression of cyclooxygenase-2 and nitric oxide, counteract the damaging process. Specific inhibitors of inducible cyclooxygenase-2 lowered gastrointestinal toxicity, which may be linked in part to the protective effect of cyclooxygenase-2 on the gastrointestinal mucosa during inflammation or epithelial remodelling. Selective inhibitors may be worsening inflammatory bowel disease. Non-steroidal inflammatory drugs, but possibly not selective inhibitors, increase the mucosal damage associated with *H. pylori*-induced gastritis (Lamarque, 2012).

Olea europae, member of *Oleaceae* family from Mediterranean countries and its derivates (such OMW) is caracterised by bioactive compounds which have a high capacity to scavenge free radicals and decrease reactive oxygen species (ROS), as well as inhibiting inflammation via several pathways, and having anti-apoptotic and cytoprotective effects (Malik et al., 2024). A large number of scientific publications have identified the fundamental characteristics between OMW components (lipids, leaves, dry residue, organic matter, pulp, etc) and gastric injuries. OMW generated as by-products from the olive industry, contains a diverse range of organic compounds such as polyphenols and other substances that can be very deleterious to the environment. Bartkowiak-Wieczorek & Madry (2024) in their study hightlighted the potential of extra virgin olive oil polyphenols namely hydroxytyrosol and tyrosol ; also found in OMW ; in promoting tissue repair and regeneration, suggesting potential applications in wound healing processes such as cell adhesion, chemotaxis, and phagocytosis. Moreover, the research conducted by Abdellah et al., (2024) demobstrated that olive leaves extracts stimulated gastric mucus content by 169 % and increased the curative index by 55 %, compared with untreated gastric ulcer rats. The results obtained by Harun et al., (2025) revealed that polyphenols such hydroxytyrosol had significant anti-inflammatory effects (Table 3). Similar results are underlined by Pongkitwitoon et al., (2024), Chen et al., (2024b) and Laveriano-Santos et al., (2024). The antibacterial activities of OMW were hightlighted by Al-Rimawi et al., (2024), Moghadam et al., (2024) and Li et al., (2024) who showed significant impact on many bacteria strains ; targeting the *H.pylori* species in research would be an interesting prospect to investigate.

Despite its great impact for pollution, OMW is a rich source of natural phenolic compounds that can be extracted. These natural phenolic compounds can be used in the pharmaceutical and food biotechnologies (Soares et al., 2024; Bernini et al., 2024). Several systematic reviews of the literature, including various studies on the pathogenesis of damage to the gastroduodenal mucosa disease, have shown that oxidative stress was the main cause of these diseases. Therfore, the suppression of oxidative stress by antioxidants such as phenolic compounds, which are found in apreciable amount in olive products, as well as in their OMW, would be a likely way of treating this pathology. Overall, these recent studies suggest that polyphenols from OMW may have positive effects on mucosal gastroduodenal injuries, including reducing ulcer size, increasing the thickness of the stomach mucosa, reducing oxidative stress and inflammation, and inhibiting the growth of *Helicobacter pylori* (Harun et al., 2025, Wang et al., 2024, Abdellah et al., 2024).

Conclusion

This study is intended to offer guidance for the development of new therapeutic agents for the potential role in the treatment of mucosal gastroduodenal injuries and /or *H. pylori* infection. Many studies have been undertaken on olive by-products demonstrating the beneficial effects of their phenolic compounds on diseases, but to date, there are still no studies showing the effect of crude or purified OMW extracts on mucosal gastroduodenal damage. OMW itself contains many bioactive compounds which have already been shown to have health effect, but the relationship between OMW and mucosal gastroduodenal lesions is not yet fully understood. The management of *H. pylori* infection should be based on the assessment of antibiotic sensitivity. This review highlights promotive avenues for future research related to OMW and therapeutic interventions in the management of *H. pylori*-associated gastric lesions. Further research is needed to better explain the mechanisms behind these effects and to determine the optimal treatment, as well as to develop safe and effective remedies for this common gastrointestinal disorder.

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Conflict of interest

There is no conflict of interest to be declared.

Bibliographical references

- Abdellah F, Silarbi T, Zouidi F, Hamden K (2024). Effects of Olea oleaster leaf extract and purified oleuropein on ethanol-induced gastric ulcer in male Wistar rats. Iranian Journal of Basic Medical Sciences *27*(8) : 996. https://doi: 10.22038/IJBMS.2024.76135.16474
- Aggoun M, Arhab R, Cornu A, Portelli J, Barkat M, Graulet B (2016). Olive mill wastewater microconstituents composition according to olive variety and extraction process. Food chemistry 209 : 72-80. https://doi.org/10.1016/j.foodchem.2016.04.034
- Albini A, Calabrone L, Albini F, Corradino P, Cristoni S, Noonan DM (2024). A nutraceutical supplement derived from olive oil byproducts exhibits potential cancer preventive properties in preclinical studies and increases vitamin D levels. Cancer Research 84(6_Supplement) : 7298-7298. https://doi.org/10.1158/1538-7445.AM2024-7298
- Ali SI, Salama A (2024). Natural Immunomodulatory Agents as a Complementary Therapy for Poxviruses. Poxviruses : 337-354. https://doi.org/10.1007/978-3-031-57165-7_22
- Al-Rimawi F, Sbeih M, Amayreh M, Rahhal B, Mudalal S (2024). Evaluation of the antibacterial and antifungal properties of oleuropein, olea Europea leaf extract, and thymus vulgaris oil. BMC Complementary Medicine and Therapies 24(1) : 297. https://doi.org/10.1186/s12906-024-04596-x
- Attard K, Lia F (2024). The Antioxidant and Bioactive Potential of Olive Mill Waste. IntechOpen. https://doi: 10.5772/intechopen.1004127
- Bartkowiak-Wieczorek J, Madry E (2024). Natural Products and Health. Nutrients 16 : 415. https://doi.org/10.3390/ nu16030415
- Bernini R, Campo M, Cassiani C, Fochetti A, Ieri F, Lombardi, et al., (2024). Polyphenol-Rich Extracts from Agroindustrial Waste and Byproducts: Results and Perspectives According to the Green Chemistry and Circular Economy. J. Agric. Food Chem 72 (23) : 12871–12895. https://doi.org/10.1021/acs.jafc.4c00945
- Calahorra J, Blaya-Cánovas JL, Castellini-Pérez O, Aparicio-Puerta E, Cives-Losada C, Marin JJ, et al., (2024). Unlocking the effective alliance of β-lapachone and hydroxytyrosol against triple-negative breast cancer cells. Biomedicine & Pharmacotherapy 174 : 116439. https://doi.org/10.1016/j.biopha.2024.116439
- Chen S, Cai T, Lu J, Le J, Zhang J, Yao Q, Chen L (2024a). Hydroxytyrosol promotes random skin flap survival by activating SIRT1-mediated enhancement of autophagy. Journal of Functional Foods 121 : 106443. https://doi.org/10.1016/j.jff.2024.106443
- Chen Y, Zheng Y, Wen X, Huang J, Song Y, Cui Y, Xie X (2024b). Anti-inflammatory effects of Olive (olea europaea L.) fruit extract in LPS-stimulated RAW264. 7 cells via MAPK and NF-κB signal pathways. Molecular Biology Reports 51(1) : 774. https://doi: 10.18632/aging.100691
- Costa LCMC, Carvalho MG, Pereira ACGC, Neto RGT, Figueiredo LCA, Barros-Pinheiro M (2024). Diagnostic Methods for *Helicobacter pylori*. Med Princ Pract 33:173-184. https:// 10.1159/000538349
- Dabravolski SA, Pleshko EM, Sukhorukov VN, Glanz VY, Sobenin IA, Orekhov AN (2024). Use of Olives-derived Phytochemicals for Prevention and Treatment of Atherosclerosis: An Update. Current Topics in Medicinal Chemistry 24(25): 2173-2190. https://doi.org/10.2174/0115680266314560240806101445
- Deng Y, Zhou J, Wang B, Xu X, Huang T, Xu Z, Zhao C (2024). Optimization of Different Extraction Methods for Phenolic Compound Verbascoside from Chinese Olea europaea Leaves Using Deep Eutectic Solvents: Impact on Antioxidant and Anticancer Activities. Molecules 29(17) : 4219. https://doi.org/10.3390/molecules29174219
- DSA (2025). Tlemcen Agricultural Services Department. Wilaya of Tlemcen-Algeria.
- FAO (2017). Food And Agriculture Organization. https://www.fao.org/countryprofiles.

- Foti P, Romeo FV, Russo N, Pino A, Vaccalluzzo A, Caggia C, Randazzo CL (2021). Olive Mill Wastewater as Renewable Raw Materials to Generate High Added-Value Ingredients for Agro-Food Industries. Appl Sci 11 : 7511. https://doi.org/10.3390/ app11167511
- Gabbia D, Sayaf K, Zanotto I, Colognesi M, Frion-Herrera Y, Carrara M, et al., (2024). Tyrosol attenuates NASH features by reprogramming the hepatic immune milieu. European Journal of Pharmacology 969 : 176453. https://doi.org/10.1016/j.dld.2023.01.130
- Giurranna E, Nencini F, Bettiol A, Borghi S, Argento FR, Emmi G, et al., (2024). Dietary Antioxidants and Natural Compounds in Preventing Thrombosis and Cardiovascular Disease. International Journal of Molecular Sciences 25(21) : 11457. https://doi.org/10.3390/ijms252111457
- Gonçalves M, Aiello A, Rodríguez-Pérez M, Accardi G, Burgos-Ramos E, Silva P (2024a). Olive Oil Components as Novel Antioxidants in Neuroblastoma Treatment: Exploring the Therapeutic Potential of Oleuropein and Hydroxytyrosol. Nutrients 16(6) : 818. https://doi.org/10.3390/nu16060818
- Gonçalves M, Vale N, Silva P (2024b). Neuroprotective Effects of Olive Oil: A Comprehensive Review of Antioxidant Properties. Antioxidants 13(7) : 762. https://doi.org/10.3390/antiox13070762
- Gouvinhas I, Machado N, Sobreira C, Domínguez-Perles R, Gomes S, Rosa E, Barros NA (2017). Critical Review on the Significance of Olive Phytochemicals in Plant Physiology and Human Health. Molecules (Basel, Switzerland 22(11) : 1986. https://doi.org/10.3390/molecules22111986
- Harun N, Adnyana IK, Damayanti S, Kurniati NF (2025). Administration of oleuropein or hydroxytyrosol improves diabetic markers in obese mice. Journal of Pharmacy & Pharmacognosy Research 13(2) : 513-526. https://doi.org/10.3390/antiox8060188
- Khalil AA, Rahman MM, Rauf A, Islam MR, Manna SJ, Khan AA et al., (2024). Oleuropein: Chemistry, extraction techniques and nutraceutical perspectives-An update. Critical Reviews in Food Science and Nutrition 64(27) : 9933-9954. https://doi.org/10.1080/10408398.2023.2218495
- Lamarque D, Burucoa C, Courillon-Mallet A et al., (2012). Révision des recommandations françaises sur la prise en charge de l'infection par *Helicobacter pylori*. Hepato Gastro 19 : 475-502.
- Laveriano-Santos EP, Vallverdú-Queralt A, Bhat R, Tresserra-Rimbau A, Gutiérrez-Alcalde E, Campins-Machado FM et al., (2024). Unlocking the potential of olive residues for functional purposes: update on human intervention trials with health and cosmetic products. Journal of the Science of Food and Agriculture 104(7) : 3816-3822. https://doi.org/10.1002/jsfa.13451
- Li X, Hou Y, Zou H, Wang Y, Xu Y, Wang L et al., (2024). Unraveling the efficacy of verbascoside in thwarting MRSA pathogenicity by targeting sortase A. Applied Microbiology and Biotechnology 108(1) : 1-15. https://doi.org/10.1007/s00253-024-13202-6
- Malik TF, Gnanapandithan K, Singh K (2024). Peptic Ulcer Disease. In: StatPearls. Treasure Island (FL): StatPearls Publishing. PMID: 30521213
- Mao Q, Zhang H, Zhang Z, Lu Y, Pan J, Guo D et al., (2024). Co-decoction of Lilii bulbus and Radix Rehmannia Recens and its key bioactive ingredient verbascoside inhibit neuroinflammation and intestinal permeability associated with chronic stress-induced depression via the gut microbiota-brain axis. Phytomedicine 129 : 155510. https://doi.org/10.1016/j.phymed.2024.155510
- Misal SS, Bhor BV, Chelakara SR (2024). Structural Insights into Potent Anti-ulcer Agents for the Eradication of Helicobacter pylori. Anti-Infective Agents 22(5) : 29-42. https://doi.org/ 10.2174/0122113525296549240402074618
- Moghadam ZSM, Mansour FN, Naseroleslami M, Niri NM (2024). Preparation, characterization, and evaluation of the antimicrobial effects of farnesol-and tyrosol-bearing nanoniosomes on Pseudomonas aeruginosa, Staphylococcus aureus, and Escherichia coli. *Medical* Journal of Tabriz University of Medical Sciences. https://doi.org/:10.34172/mj.2024.024
- Mohamed NA, Hussein MM, Ahmed OM, Al-Jameel SS, Al-Muzafar HM, Amin KA, Abdou HM (2024). Oleuropein ameliorates hyperlipidemia, oxidative stress, inflammatory and liver dysfunction biomarkers, in streptozotocin-induced diabetic rats. J Appl Pharm Sci 14(09): 227–234. http://doi.org/10.7324/JAPS.2024.167994

- Naseroleslami M, Khakpai F, Jafari-Rastegar N, Hosseininia HS, Mousavi-Niri N (2024). The modulatory effects of tyrosol and nano-tyrosol on anxiety-like behavior and emotional memory in streptozotocin-induced diabetic rats. NeuroReport 35(16) : 1011-1018. http://doi.org/ 10.1097/WNR.0000000000002061
- Pongkitwitoon B, Putalun W, Triwitayakorn K, Kitisripanya T, Kanchanapoom T, Boonsnongcheep P (2024). Anti-inflammatory activity of verbascoside-and isoverbascoside-rich Lamiales medicinal plants. Heliyon 10(1). e23644. https://doi.org/10.1016/j.heliyon.2023.e23644
- Reyes-Corral M, Gil-González L, González-Díaz Á, Tovar-Luzón J, Ayuso MI, Lao-Pérez M et al., (2024). Pretreatment with oleuropein protects the neonatal brain from hypoxia-ischemia by inhibiting apoptosis and neuroinflammation. Journal of Cerebral Blood Flow & Metabolism 0271678X241270237. https://doi.org/10.1177/0271678X2412702
- Salucci S, Burattini S, Versari I, Bavelloni A, Bavelloni F, Curzi D et al., (2024). Morpho-Functional Analyses Demonstrate That Tyrosol Rescues Dexamethasone-Induced Muscle Atrophy. Journal of Functional Morphology and Kinesiology 9(3). https://doi.org/10.3390/jfmk9030124
- Singh K, Kumar R, Singh AP, Malhotra M, Rani R (2024); Peptic Ulcer: A review. Int. J. Med. Phar. Drug Re 8(2) : 38-46. https://creativecommons.org/licenses/by/4.0
- Soares TF, Alves RC, Oliveira MBP (2024). From Olive Oil Production to By-Products: Emergent Technologies to Extract Bioactive Compounds. Food Reviews International : 1-28. https://doi.org/10.1080/87559129.2024.2354331
- Vadakutt J, Doshi GM (2024). Enhancing gastric ulcer management: Novel insights from terazosin-pantoprazole combination therapy. Indian Drugs 61(1) :77. https://doi.org/ 10.53879/id.61.01.14392
- Waldum H. (2024).The Role of The Gastric Juice in the Defence Against Common and Serious Diseases. J Gastro Hepato 10(12): 1-11.
- Wang Q, Tripodi N, Valiukas Z Bell SM, Majid A, De Courten B et al., (2024). The protective role of carnosine against type 2 diabetes-induced cognitive impairment. Food Science & Nutrition 12(6) : 3819-3833. https://doi.org/10.1002/fsn3.4077
- Yadav P, Vengoji R, Jain M, Batra SK, Shonka N (2024). Pathophysiological role of histamine signaling and its implications in glioblastoma. Biochimica et Biophysica Acta (BBA)-Reviews on Cancer 189146. https://doi.org/10.1016/j.bbcan.2024.189146
- Yılmaz G, Zdemir F (2024). Novel Anti-tumor Strategy for Breast Cancer: Synergistic Role of Oleuropein with Paclitaxel Therapeutic in MCF-7 Cells. Anti-Cancer Agents in Medicinal Chemistry-Anti-Cancer Agents) 24(3) : 224-234. https://doi.org/10.2174/0118715206284107231120063630
- Yücer R, Schröder A, Topçu G, Efferth T (2024). Identification of Anti-Inflammatory and Anti-Cancer Compounds Targeting the NF-κB-NLRP3 Inflammasome Pathway from a Phytochemical Library of the Sideritis Genus. Journal of Ethnopharmacology : 119074. https://doi.org/10.1016/j.jep.2024.119074
- Zbakha H, El Abbassi A (2012). Potential use of olive mill wastewater in the preparation of functional beverages: A review. Journal Of Functional Foods (4) : 53 - 65. https://doi.org/10.1016/j.jff.2012.01.002
- Zoubdane N, Abdo RA, Nguyen M, Bentourkia MH, Turcotte EE, Berrougui H et al., (2024). High Tyrosol and Hydroxytyrosol Intake Reduces Arterial Inflammation and Atherosclerotic Lesion Microcalcification in Healthy Older Populations. Antioxidants 13(1) : 130. https://doi.org/10.3390/antiox13010130