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herba polonica
International journal edited by the Institute of Natural Fibres and Medicinal Plants
National Research Institute
Vol. 67 No. 2 2021

Received: 2020-10-23
Accepted: 2021-04-16
Available online: 2021-06-30

DOI: 10.2478/hepo-2021-0008

REVIEW PAPER

Phytochemistry and biological activities of *Opuntia* seed oils: *Opuntia dillenii* (Ker Gawl.) Haw. and *Opuntia ficus-indica* (L.) Mill. A review

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Summary

Opuntia species belong to semi-arid and arid regions of Mexico and the United States. *O. ficus-indica* and *O. dillenii* are commonly used in alternative medicine to treat various diseases. Up to date, several scientific works have been carried out on the different parts of these plants. However, over the last few years, studies have been focusing on the oil obtained from the fruit seeds of these species. For this reason, this study aims to draw the attention of researchers toward the phytochemical and the pharmacological effects of these two *Opuntia* oils, which would help set up other scientific projects that promote these products. Phytochemical studies have shown that these oils are rich in biologically active molecules, such as unsaturated fatty acids and phytosterols (mainly linoleic acid and β-sitosterol), as well as vitamin E, which is represented only by the γ-tocopherol. Besides, these oils are rich in polyphenols that protect them from photo-oxidation. Moreover, several studies have shown their antioxidant, anti-diabetic, antibacterial, antifungal, anti-inflammatory, hepatoprotective, and gastroprotective activities, as well as their hypolipidemic properties. The beneficial effects of these oils include also their ability to block the weight loss, and what makes them more interesting is their safety, according to the literature.

Key words: ***Opuntia ficus-indica, Opuntia dillenii, seed oil, phytochemistry, biological effect***

Słowa kluczowe: ***Opuntia ficus-indica, Opuntia dillenii, olej z nasion, fitochemia, działanie biologiczne***

INTRODUCTION

Opuntia is a plant species belonging to the *Cactaceae* family. It is native to semi-arid and arid regions of Mexico and the southern United States [1]. This genus was introduced to Europe and North Africa in the 16th century [2], and it is currently found everywhere in the world. Moreover, among the *Cactaceae* family, *O. dillenii* and *O. ficus-indica* are the most frequently used species in the traditional medicine of many countries to treat several pathologies [3-6]. However, little interest has been given to the use of the fruit seeds because the body is unable to digest them and therefore to benefit from their constitutions. Several scientific studies have been interested in studying the different vegetative parts (pulp, seed, peel, and cladode) of these two species to assess or confirm their beneficial biological effects on various diseases [7, 8]. Over the last few years, researchers have been interested in studying the seed oils of these two *Opuntia* species and have found that they are rich in very active molecules [9, 10]. Other studies have shown several biological effects of these oils.

The bibliographic research was focused on the phytochemical and biological studies of *O. ficus-indica* and *O. dillenii* seed oils. The phytochemical profile of these two *Opuntia* oils has shown an abundance of unsaturated fatty acids, sterols, tocopherols and polyphenols. Moreover, their biological potentials cover the antioxidant, antidiabetic, anti-inflammatory, antibacterial, antifungal, hypolipidemic, hepatoprotective and gastroprotective properties, as well as the inhibition of weight loss.

This review provides a detailed overview of the seed oils obtained from *O. dillenii* and *O. ficus-indica* and covers phytochemical, pharmacological and toxicological studies.

METHODOLOGY

In this article, a comprehensive literature search has been conducted to provide a thorough overview of the seed oils of *O. ficus-indica* and *O. dillenii*. Our literature search was done using Google Scholar search engine and via PubMed, Scopus, Science Direct databases, using the following keywords: "*O. ficus-indica*", "*O. dillenii*", "seed oil", "phytochemistry" and "biological effect". Reference lists of the papers that were retrieved were also examined to identify further papers. This bibliographic search was focused on all the articles published in 4 years (2018–2021).

PHYTOCHEMISTRY OF *OPUNTIA* OILS

The seeds of *Opuntia* arouse a lot of interest over the last few years. Their constituents were characterized in multiple studies and their nutritional values were evaluated. Besides, studies were focused on the oil contained in the seeds of *Opuntia* of which the yield is variable despite the geographical and climatic proximity between countries. In general, there are several techniques for extracting the high added value products present in plants. These techniques can be conventional (used for a long time) or new (developed recently) [11]. The vegetable oil from *Opuntia* seeds is mainly obtained by solvent extraction. Other methods, like cold pressing and supercritical carbon dioxide extraction, are used less frequently. The yield is generally low and varies from one extraction technique to another. The difference in the oil content of cactus seeds from different locations can be explained by the variability in geographic, climatic and environmental conditions. Other reasons, such as analytical conditions, may also affect this content [12]. The seed oil yield of *Opuntia* (7 to 15%) is much lower than those reported for other well-known seed oils such as argan kernels (50%), unroasted argan (28.49%), sesame seed (54%), black seed (34%), sunflower (44%), soybean (19%) and olives (20%) [13-16]. Moreover, the seed oil yield of these two *Opuntia* species (*O. ficus-indica* and *O. dillenii*) is high when compared to others, such as the *Xoconostle* seeds oil from Mexico (2.45 and 3.52%) [17]. These oils belong to the category of "polyunsaturated" fatty acids like the majority of vegetable oils. According to all the studies carried out on the chemical composition of these oils, they are composed of a high amount of fatty acids, in particular polyunsaturated fatty acids, mainly linoleic acid and oleic acid. The latter ones have the property to reduce the risk of developing inflammatory, autoimmune and cardiovascular diseases. These oils are also rich in unsaponifiable compounds, in general β-sitosterol (which is the base of the active ingredients and that can be found in medicinal plants) [18] and γ-tocopherol (an antioxidant nutrient that plays an important role in neutralizing free radicals generated by the normal cell activity and by various stressors). Tocopherols are antioxidant molecules that prevent the initiation of lipid peroxidation. They have also shown the ability to neutralize lipid peroxide radicals [19]. Among all these phytochemical studies, there are the ones that were interested in the quantification and identification of the polyphenols of *O. dillenii* seed oil. It was confirmed that these molecules exhibit antioxidant, anti-cancer, anti-inflammatory and antiviral activities. These activities are attributed to the ability of these compounds to reduce free radicals, but also to their affinity for a wide variety of proteins, including certain enzymes (angiotensin II, β-glucuronidase, UDP-glucuronosyltransferase, catechol-O-methyl transferase, sulfotransferases) and receptors (estrogenic receptors) [20]. Also, the used technique of extraction influences the quantity and quality of the extracted polyphenols [11]. In a study realized on *O. dillenii* oil, they showed that the technique used to extract the oil from the seeds of this plant influences the yield, the diversity of phenolic compounds and the biological activity of this oil. The oil extracted with SC-CO_2 was highly enriched with polyphenols than the one extracted with hexane. The polyphenol profiles showed that the SC-CO_2 process extracts more compounds (45 compounds) than hexane (11 compounds). In addition, the antioxidant and antimicrobial activities of SC-CO_2 extract was higher [10].

Fatty acids

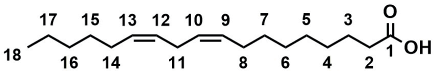
The chemical composition study of the seed oils obtained from *O. ficus-indica* and *O. dillenii* has shown that these two oils belong to "polyunsaturated" oils [21]. Linoleic acid remains the predominant fatty acid in these seed oils, despite the origin of the plant (Morocco, Algeria, Tunisia, Turkey, Germany, Mexico and China), followed by palmitic acid and oleic acid [9, 14, 22-28]. The chemical composition of these *Opuntia* oils is similar to those of other *Opuntia* species like *O. elatior* [29]. In general, this major fatty acid is high in *O. dillenii* oil in comparison with *O. ficus-indica* oil. Moreover, *O. ficus-indica* seed oil from the region of Ain el Rahma in Algeria contains the greatest linoleic acid content in comparison with other regions [9]. However, the absence of oleic acid has been noticed in *O. dillenii* seed oils from Morocco and China [9, 30]. Also, other fatty acids were determined in small amounts in these oils: palmitic, myristic, stearic, palmitoleic, elaidic, vaccenic, arachidic, linoleic, oleic, linolenic, behenic, cetoleic, and lignoceric (fig. 1) [31]. The difference in the quality and quantity of fatty acids in *O. dillenii* and *O. ficus-indica* oils is generally linked to the climate and the geographical area that these two plants come from [32]. Moreover, the fatty acid composition of cactus grown in different places is significantly different. It is well known that this composition is strongly influenced by the climatic factors and the type of soil in which they have grown [33]. Likewise, genetic factors may be involved as well. In a study performed in Morocco, *O. dillenii* oil (80.38) is richer in polyunsaturated fatty acids than *O. ficus-indica* oil (69.83) [9]. These results are in agreement with those published by Tlili *et al.* [31] where they found that *O. ficus-indica* oil contains 56.6% of linoleic acid, 20.19% of oleic acid, 12.24% of palmitic acid and 3.69% of stearic acid. On the contrary, Yuan-Gang *et al.* [30] reported that linolenic acid represents the main constituent of fatty acids (66.56%) in the oil of total lipids *O. dillenii*, followed by palmitic acid (19.78%), stearic acid (9.01%) and linoleic acid (2.65%). The difference observed could be due to the degree of maturity of the fruit. Indeed, these authors suggested that there was an increase in the content of saturated fatty acids towards the end of the fruit ripening.

Sterols

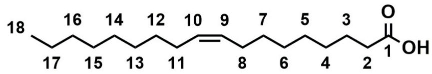
All the phytochemical studies that have been performed on *Opuntia* seed oils to determine their phytosterols composition have shown that only seed oils from Morocco, Tunisia, and Germany are rich in sterols, with β-sitosterol being the most dominant. *O. ficus-indica* seed oil is the richest in sterol content, in comparison to oils from other *Opuntia* species [9, 14, 24, 28, 34]. Indeed, this phytosterol is also found in other vegetable oils, such as soybean, sunflower and olive oils [16, 35]. Concerning the sterol diversity, seed oils from Morocco (Sidi Ifni) and Tunisia (Zelféne, Sbeïtla and Kairouan) are the richest in sterol types (campesterol, Δ5-avenasterol, stigmasterol, Δ7-avenasterol, Δ7-stigmasterol and cholesterol) (fig. 2) [14, 24].

Vitamin E

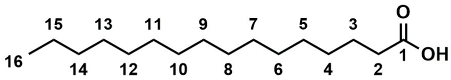
The high content of total tocopherols is the specificity of cactus seed oils [12, 16, 28]. On the one hand, studies have shown that *O. ficus-indica* oil is very rich in tocopherols, and γ-tocopherol is the most dominant in this oil [9, 12, 28, 34, 36, 37]. On the other hand, these constituents were absent or present in small quantities in *O. dillenii* seed oil. Oils from the regions of Berlin (Germany) and Sidi Ifni (Morocco) have the highest γ-tocopherol content in comparison with *Opuntia* seed oils from other regions in Morocco (Oujda) and Tunisia [9, 27]. Also, seed oils from these two countries are characterized by the presence of other tocopherol types, generally α-tocopherol, β-tocopherol, β-carotene and vitamin K_1 (fig. 3) [14, 28].



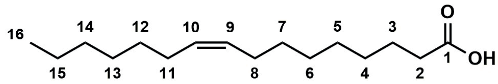
Linoleic acid



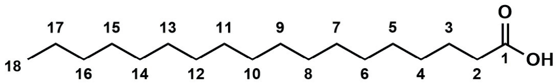
Oleic acid



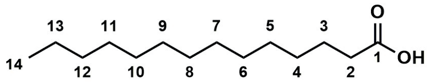
Palmitic acid



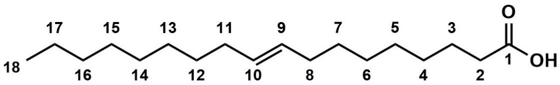
Palmitoleic acid



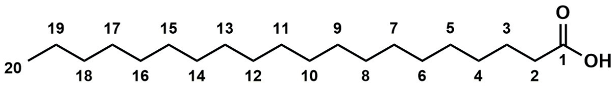
Stearic acid



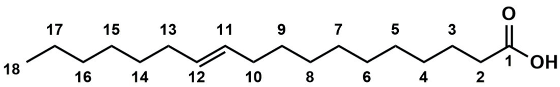
Myristic acid



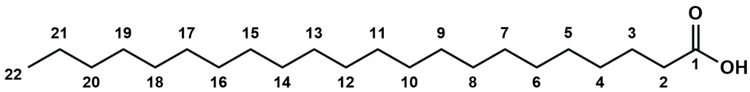
Elaidic acid



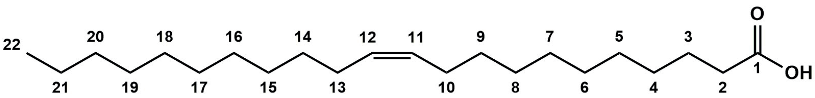
Arachidic acid



Vaccenic acid

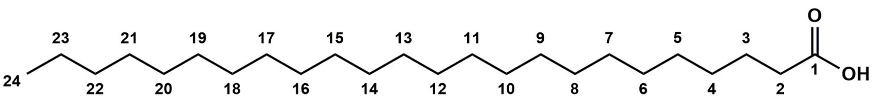


Behenic acid

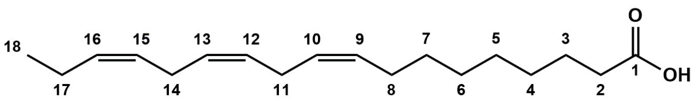


Cetoleic acid

(Z)-docos-11-enoic acid



Lignoceric acid



Linolenic acid

Figure 1.

Structural formulas of fatty acids present in *Opuntia* oil

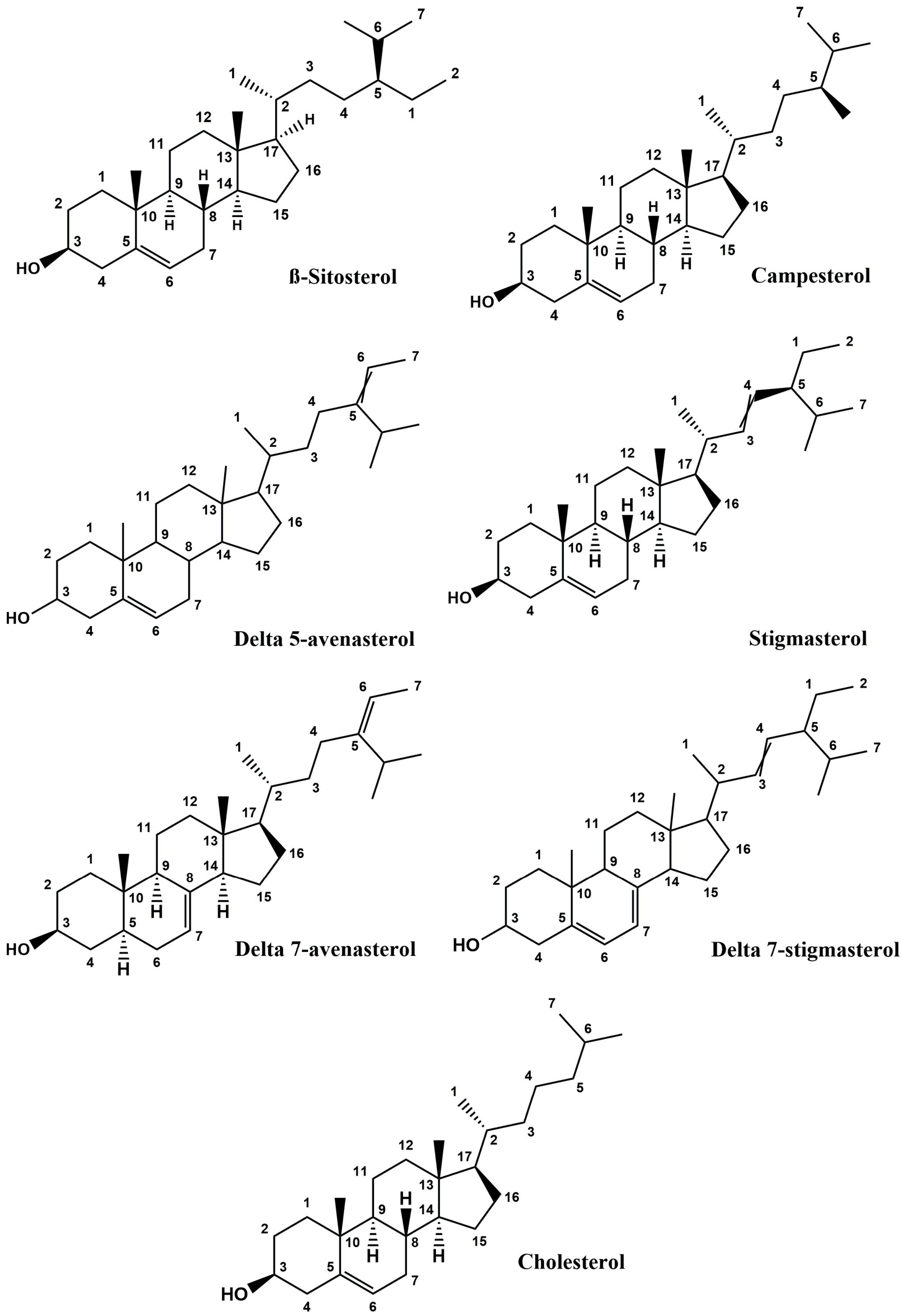
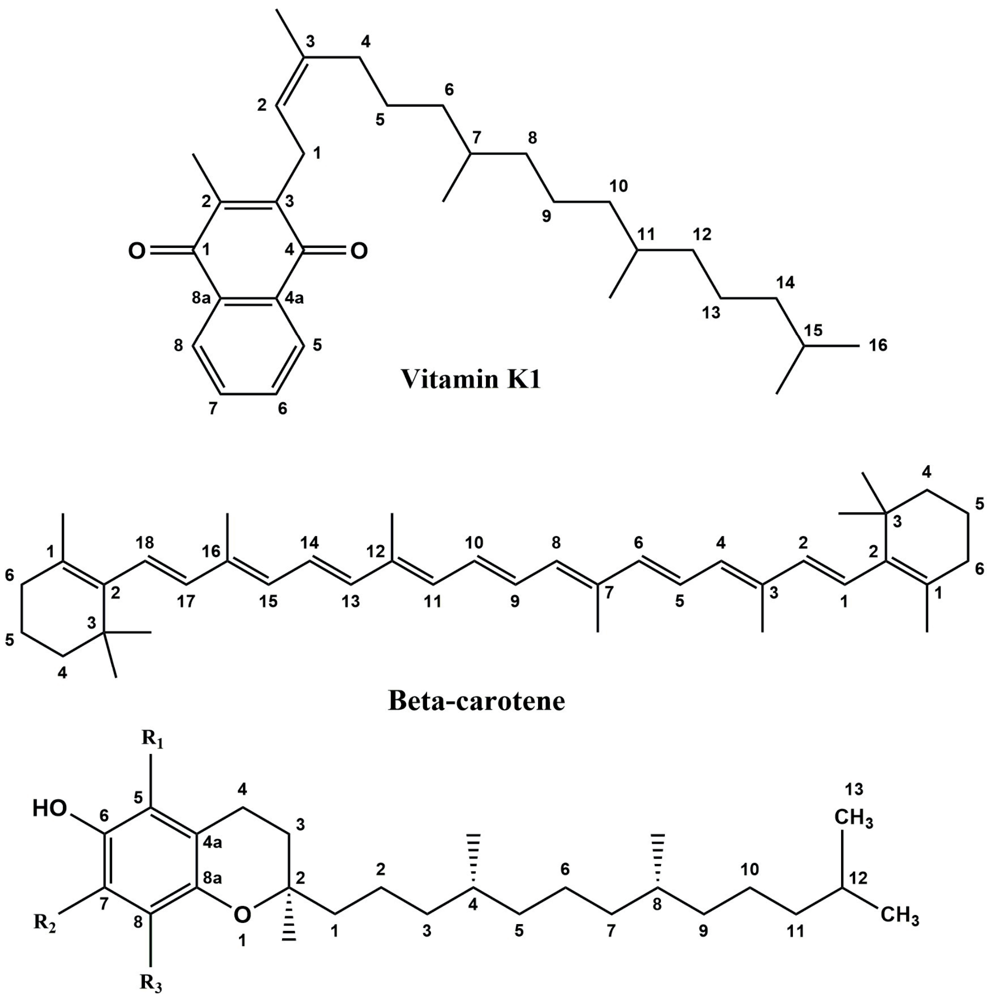


Figure 2.

Structural formulas of phytosterols present in *Opuntia* oil



Compound	R1	R2	R3
α-Tocopherol	CH_3	CH_3	CH_3
β-Tocopherol	CH_3	H	CH_3
γ- Tocopherol	H	CH_3	CH_3

Figure 3.

Structural formulas of tocopherols present in *Opuntia* oil

Polyphenols

Koubaa *et al.* reported that *Opuntia* seed oil from the region of Sfax (Tunisia), extracted using SC-CO_2, was richer in polyphenols (172.2±11.9 *μ*g GAE/g oil) than the oil extracted with hexane (76.0±6.9 *μ*g GAE/g oil). The SC-CO_2 technique led to the extraction of more polyphenols (45 compounds) than hexane (11 compounds). In general, the abundant polyphenol molecules in this oil are catechol, cinnamic acid, 3-phenylpropionic acid, syringic acid, psoralen, sinapaldehyde, 3'-O-methylcatechin, (+)-gallocatechin, 4'-O-methyl-(-)-epicatechin-3'-O-glucuronide, bisdemethoxycurcumin and viscutin 1 (fig. 4) [10]. In another study, it was shown that *O. ficus-indica* seed oil consists of a total phenolic content of 551.0±0.3 mg GAE/L [38]. A study carried out by Khémiri *et al.* on *O. ficus-indica* seed oil from Tunisia indicated that this oil has a carotenoid content of 10.520 mg/kg oil, total chlorophyll content of 4.57 mg/kg oil, a flavonoid content of 3.1 mg QE/g oil and total phenolic content of 26.5 mg GAE/g oil [39]. Also, a study conducted on *O. dillenii* from Morocco showed that it is rich in polyphenols (518.18±14.36 mg GAE/kg oil) [40].

Volatile compounds

A study conducted by Karabagias *et al.* on *O. ficus-indica* seed oil showed that this oil is made up of 221 volatile compounds. These compounds could be grouped into alcohol (9.13%), acids (2.70%), esters (2.82%), aldehydes (62.72%), ketones (4.38%), hydrocarbons (5.06%) and other compounds (12.71%). The most dominant volatile compounds are aldehydes, and among them, pentanal, 2-propenal, hexanal, heptanal, 2-hexenal, octanal, 2-octenal, 2-heptenal, and trans-4,5-epoxy-(E)-2-decenal, nonanal 2,4-decadienal (E recorded the highest proportions) [38]. Also, Zito *et al.* reported that *O. ficus-indica* seed oil obtained from Sanguigna cultivar grown in Sicily, contains mainly hydrocarbons (38.5%), fatty acids and derivatives (31.9%), and terpenes (12.4%), while the seed oil obtained from Surfarina cultivar grown in the same region contains higher contents of fatty acids and derivatives (68.9%), followed by terpenes (10.9%) [41].

BIOLOGICAL PROPERTIES OF *OPUNTIA* SEED OIL

In last few years, researchers have been interested in *Opuntia* oils. Moreover, the oil from *O. ficus-indica* seeds has been more studied than the one from *O. dillenii* seeds (fig. 5).

Antioxidant effect

In vitro studies

Ramirez-Moreno *et al.* in Mexico evaluated the antioxidant activity of *O. ficus-indica* seed oil extracted by three different solvents (ethyl acetate, ethanol and hexane), and showed that these oils have a significant scavenging activity against the 2,2-diphenyl-1-picrylhydrazyl radical (DPPH). The oil extracted with ethyl acetate had the highest antioxidant activity (274 μmol TE/20 mg of extract), followed by ethanol (247 μmol TE/20 mg of extract), and hexane which had the lowest values. These results showed that the type of solvent employed for the extraction could influence the antioxidant effect of these oils [25]. This activity was observed in another study in Mexico, in which a different extraction method was used: the ultrasound. The results of the antioxidant activity showed an IC_{50} of 289 μmol TE/100 g and 66.25 mg AAE/100 g for DPPH and 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) ($ABTS^+$), respectively [42]. Besides, the antioxidant property of the Moroccan *O. ficus-indica* seed oil (from Oujda) was studied employing a DPPH test. The data showed that the antioxidant property of this oil (IC_{50}=19.79±0.023 μl/ml) was greater than that of the ascorbic acid used as a reference (IC_{50}=16.56±0.019 μg/ml). Also, the antioxidant potencial of the seed oil was shown to be concentration-dependent [14]. Ali *et al.* evaluated the Moroccan *O. ficus-indica* seed oil and showed that it displays a strong antioxidant property *via* an IC_{50} value of 0.96 mg/ml. Therefore, the overall productivity of this oil for DPPH scavenging is 90 min [(86.20±0.13%), 6 mg/ml], and it was smaller than that of ascorbic acid [(97.12±0.57%), 1.6 mg/ml]. Besides, the antioxidant potential of this oil rose in proportion to its amount in the solution [43]. In another work, the antioxidant activity of two fractions of *O. ficus-indica* seed oil from Tunisia (glyceride and unsaponifiable) extracted by cold pressure, was tested by three methods: DPPH, ABTS, and β-carotene bleaching. The scavenging effect on the DPPH radical of the unsaponifiable and glyceridic fractions of *O. ficus-indica* seed oil was significantly different (IC_{50}=11.5 and 13.5 mg/ml, respectively). Besides, the antioxidant activity of the glyceridic and unsaponifiable fractions of *O. ficus-indica* seed oil on the ABTS radical were also substantially different (IC_{50}=25.4 and 15 mg/ml, respectively). Results displayed that *O. ficus-indica* oil fractions prevent the bleaching of β-carotene at various degrees. On the contrary to the findings of the ABTS test, the unsaponifiable fraction seems to be more effective against the β-carotene bleaching. Therefore, the unsaponifiable fraction showed a greater capacity (IC_{50}=5 mg/ml) in scavenging ABTS than the glyceridic fraction (IC_{50}=17.5 mg/ml) [44]. In another study, the antioxidant activity of the *O. ficus-indica* seed oil from Tunisia was evaluated, using the β-carotene bleaching and DPPH radical scavenging tests. The results demonstrated a significant antioxidant property of this seed oil, which is superior to the ascorbic acid and butylated hydroxytoluene (BHT) used as references [22]. Also, in another work, the seed oil from *O. ficus-indica* showed a high antioxidant activity *in vitro* (84.00±0.01%) [38]. The red and yellow *O. ficus-indica* seed oils obtained using Soxhlet as an extraction

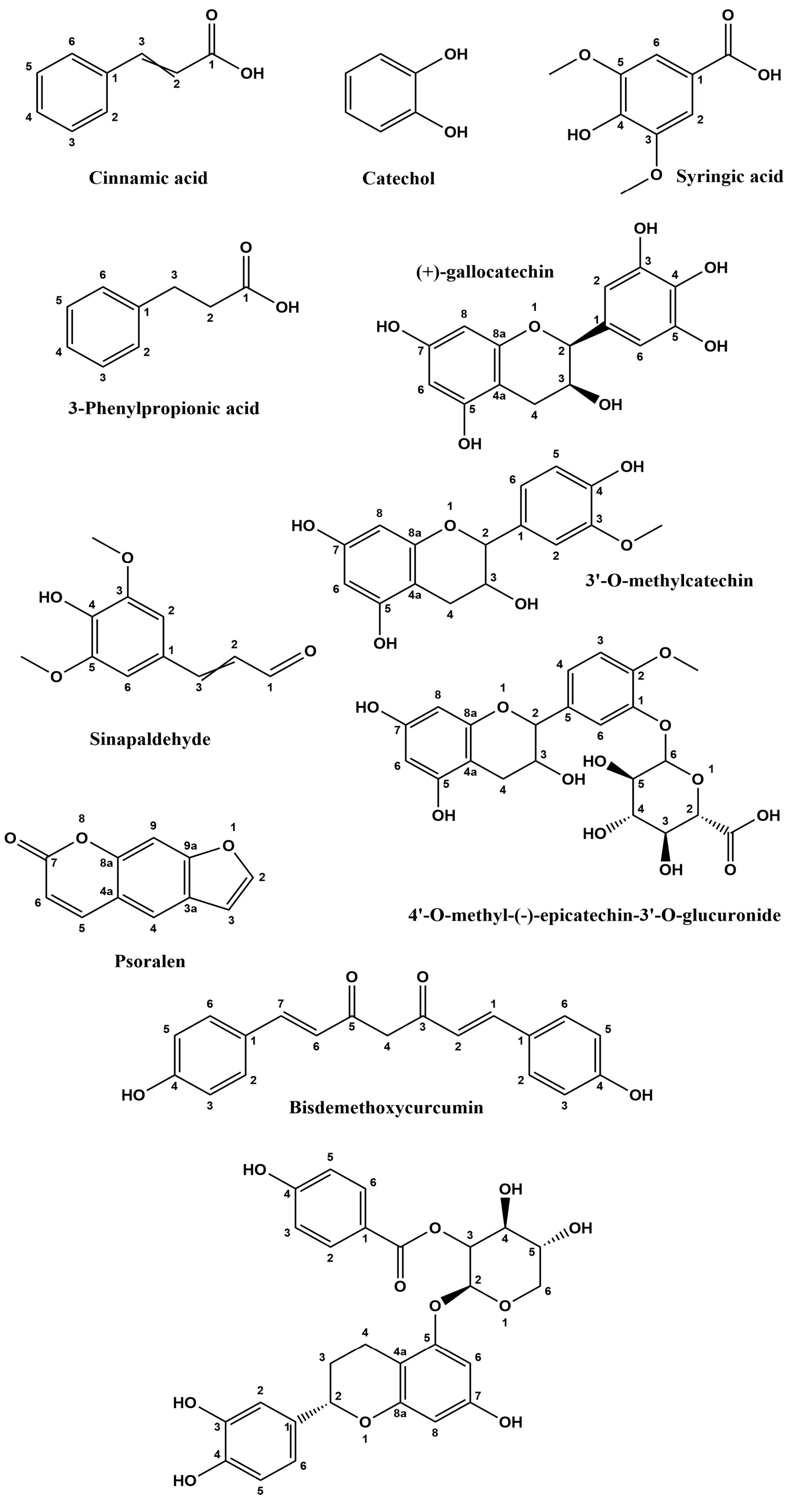


Figure 4.

Structural formulas of polyphenols present in *Opuntia* oil

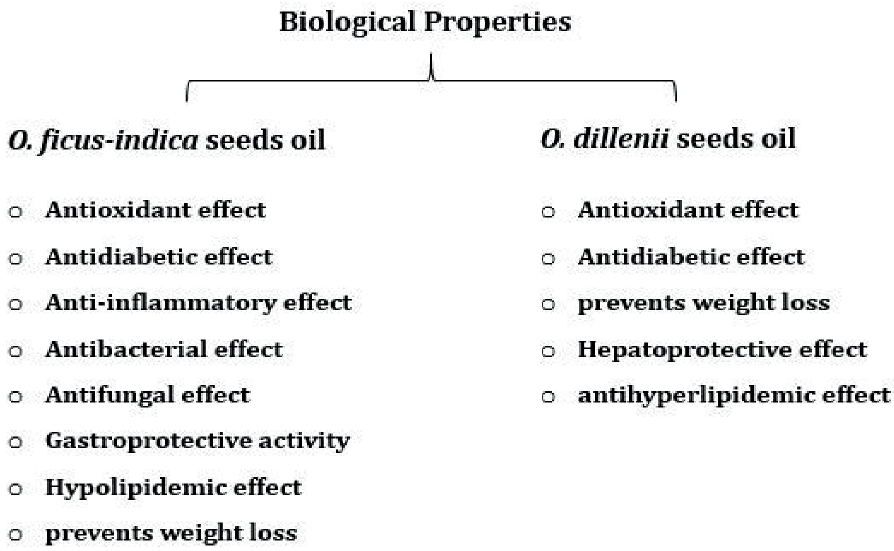


Figure 5.

Biological effects of *O. ficus-indica* and *O. dillenii*

procedure showed an activity that is more promising in the DPPH test with IC_{50} values of 40.9 and 50.2 μg/ml, respectively. The *Opuntia* red seed oil sample also showed a higher ABTS$^{+\bullet}$ radical trapping potential with an IC_{50} value of 48.5 μg/ml, followed by yellow variate oil with an IC_{50} value of 54.3 μg/ml. The analysis of the FRAP test results indicated that the red seed oil sample has a higher ferric reducing ability (65.9 μM Fe (II)/g) while compared to the positive control BHT (63.2 μM Fe (II)/g). Both values were recorded at an oil concentration of 2.5 mg/ml. Also, in the β-carotene bleaching test, the lipid peroxidation protection was demonstrated with IC_{50} values ranging from 67.5 to 97.2 μg/ml and from 60.3 to 78.2 μg/ml, respectively, for the red seed oil and the yellow seed oil at 30 and 60 minutes of incubation [45]. A study carried out by Khémiri *et al.* on the oil of *O. ficus-indica* seeds from Tunisia, indicated that the oil has an important scavenging activity against ABTS and DPPH in comparison with the vitamin C. They registered, respectively, 87.42±0.11 and 88.41±0.59 VCE/g oil [39]. The antioxidant property of *O. dillenii* seed oil was assessed by β-carotene bleaching and DPPH tests. The results demonstrated the significant antioxidant potential of this *Opuntia* seed oil, which is almost comparable to the references (BHT and ascorbic acid). This antioxidant activity was also concentration-dependent [30]. In another work, the antioxidant activity of *O. dillenii* seed oil was assessed employing a DPPH scavenging assay. The data demonstrated that its antioxidant properties (27.210±0.075 μl/ml) are greater than the one of the ascorbic acid (16.560±0.019 μg/ml). Besides, the antioxidant activity of this oil has also been shown to be concentration-dependent [46]. The oil extracted by the SC-CO_2 method or hexane showed a high percentage of inhibition. To test the antioxidant potential of phenolic compounds derived from *O. dillenii* seed oil, the DPPH free radical assay was used. The results obtained demonstrated that the DPPH inhibition increased in proportion to the extract concentration. The IC_{50} values obtained were respectively 3, 5, 9, and 10 μg/ml for ascorbic acid, BHA, hexane-extracted seed oil, and seed oil extracted with SC-CO_2 [47]. Besides, the antioxidant activity of *O. dillenii* seed oil from Iraq was determined. Cactus seed oil showed a strong antioxidant capacity estimated by its ability to reduce oxidation. Besides, the obtained results have shown the powerful trapping activity of cactus oil compared to ascorbic acid. The DPPH reduction activities obtained were respectively 36.5 to 78.1% and 46.5 to 81.3% for the cactus seed oil and ascorbic acid at concentrations of 10, 50, 100, 500, and 1000 μg/ml [48].

Antidiabetic effect

In vitro study

There was a concentration-dependent influence on the carbohydrate hydrolysing enzymes in all of the tested samples. The red *O. ficus-indica* oil showed the highest inhibitory activity with an IC_{50} value lower than that reported for the positive control acarbose (32.7 vs 50.0 μg/ml, respectively). This extract also showed a significant activity against α-glucosidase with an IC_{50} value of 42.4 μg/ml. Besides, the results obtained with the yellow *O. ficus-indica* oil are highly notable, with IC_{50} values of 52.5 and 44.6 μg/ml against α-amylase and α-glucosidase, respectively [29].

In vitro studies

A study conducted in Morocco by Berraaouan *et al.* showed that the oil of *O. ficus-indica* seeds, at an amount of 1 and 2 ml/kg, improves oral glucose tolerance. It significantly reduces the postprandial hyperglycaemia (60 min after glucose loading), with a percentage of 40.33% and 16.01% in healthy rats and streptozotocin-induced diabetic rats, respectively. Also, the seed oil of *O. ficus-indica* significantly decreased the intestinal absorption of glucose with a percentage of 25.42% [49]. In another study, the treatment of mice, injected by an antidiabetogenic agent (alloxan), with the oil of *O. ficus-indica* seed at an amount of 2 ml/kg decreased the incidence of mortality caused by alloxan. Besides, this oil attenuated the increase in blood glucose and decreased bodyweight loss in these mice, in comparison with the mice treated after being injected by this diabetogenic agent. Besides, *O. ficus-indica* seeds oil attenuated the destruction of pancreatic islets induced by alloxan. Indeed, oral administration of this oil in mice injected with alloxan significantly prevented the pancreatic lesions induced by this product. It preserved the diameter and the surface of the islets, as well as the insular number of cells in the normal state while compared to untreated mice [43]. The addition of the *O. ficus-indica* oil to the diet of rats at an amount of 25 g/kg showed a significant hypoglycaemic effect, according to research carried out on *O. ficus-indica* grown in Tunisia. Indeed, a substantial decrease in blood glucose (22%) and a significant improvement in the concentration of glycogen in the liver and muscles was produced by the enrichment of the diet with the oil [50]. Another study conducted by Bouhrim *et al.* showed that the administration of *O. dillenii* seed oil at a dose of 1 and 2 ml/kg for four weeks significantly reduced the hyperglycaemia in diabetic rats. Besides, this oil reduced the urinary glucose levels and increased the hepatic glycogen levels during the treatment period. At the end of this period, an improvement of diabetic symptoms (intake and food, urinary volume) was shown [51]. Moreover, *O. dillenii* seed oil had a major antidiabetogenic effect by minimizing the loss of body weight, the increase in blood sugar levels and the mortality rate in albino mice caused by alloxan [40]. In a study on the mechanisms of action of the antihyperglycaemic effect of *O. dillenii* seeds oil, the results showed that it attenuated significantly the postprandial hyperglycaemia in normal and STZ-diabetic rats. Indeed, *O. dillenii* seed oil significantly decreased the intestinal D-glucose absorption *in situ*. The *ex vivo* test (using chambers) showed that the *O. dillenii* seed oil significantly blocks the SGLT1 (IC_{50} = 60.24 μg/ml). Moreover, *O. dillenii* seed oil induced a significant inhibition of the intestinal α-glucosidase (IC_{50}=278.00±0.01 μg/ml) and the pancreatic α-amylase (IC_{50}=0.81±0.09 mg/ml) *in vitro*. A significant decrease of the postprandial hyperglycaemia was observed in sucrose/starch-loaded normal and STZ-diabetic ODSO-treated rats [52].

Anti-inflammatory effect

In vivo study

The anti-inflammatory action of the *O. ficus-indica* seed oil has been shown in a study in Morocco. Indeed, the anti-inflammatory activity was evaluated in carrageenan and inflammatory edema of the hind paw induced by experimental trauma in Wistar rats. At a dose of 200 mg/kg, *O. ficus-indica* seed oil significantly inhibited the development of the oedema after 1.5, 3, and 6 hours with a reduction of 72.49%, 63.94% and 92.01%, respectively. Also, the evaluation of the anti-inflammatory activity showed a significant inhibition of the rat paw oedema after 6 h with a reduction of 87.52% and 69.10% at a dose of 200 mg/kg and 300 mg/kg of the *O. ficus-indica* seeds oil, respectively [53].

Antibacterial effect

In vitro study

As far as we know, only two studies have been conducted to evaluate the antibacterial properties of the *O. ficus-indica* seed oil. In the first study, the results showed that the oil extracted with ethanol had a significant antibacterial activity in many bacterial strains and with different inhibition zone diameters. It had a significant antibacterial effect against a wide range of bacteria such as *Escherichia coli* O58:H21 (11.4±0.9 mm), *Staphylococcus aureus* (11.1±1.1 mm), *Listeria monocytogenes* (11.4±0.9 mm) and *Pseudomonas aeruginosa* (15.1±2.0 mm) [25]. In another work, the antibacterial property of the *O. ficus-indica* seed oil was tested against two Gram-negative bacteria and one Gram-positive bacteria. The data of this work showed that this seed oil exhibited an antibacterial activity against *Staphylococcus aureus* and *Escherichia coli*. But, this effect was not noticed against *Pseudomonas aeruginosa* [42]. The disk diffusion approach was used to assess the antimicrobial activity on some selected foodborne pathogens, namely: *Salmonella typhimurium*, *Enterococcus faecalis*, *S. aureus*, *E. coli* and *P. aeruginosa*. Results showed that some *O. ficus-indica* oil fractions inhibit the microorganism growth, depending on the strain sensibility and the fraction nature. The glyceridic fraction did not show an antimicrobial property, whereas the unsaponifiable fraction was active against all the studied pathogens. Therefore, the glyceride-free extract contains interesting bioactive compounds as they can inhibit certain resistant strains especially the Gram-negative ones like *Escherichia coli* [44]. Also, the antibacterial activity of *O. ficus-indica* oil from Tunisia was evaluated against *Enterobacter cloacae.* The results revealed that this oil was able to inhibit this bacterium with an inhibition diameter of 15.5 mm. The positive controls exhibited diameters of 23 mm for Ceftazidime CAZ30 and 10 mm for Colicine CL50. Besides, the results show that the oil tested had a high bactericidal activity of about 1280 AU/ml. The MBC and MIC values of the oil on *Enterobacter cloacae* were 1/128 and 1/64, respectively [54].

Gastroprotective activity

In vitro study

Khémiri *et al.* investigated the therapeutic effect of *O. ficus-indica* cold-pressed seed oil on an ethanol-produced gastric ulcer in rats. The oil was very efficient in the protection of the cytoarchitecture and the gastric mucosa function against the serious damages induced by ethanol intake. It was demonstrated that the pre-treatment with *O. ficus-indica* seed oil can significantly reduce the ulcerated areas with a high ulcer inhibition percentage. Moreover, it was found that the oil could stimulate mucus production, reduce gastric juice volume and may increase pH values. To confirm the gastroprotective efficiency of *O. ficus-indica* oil, a histopathological examination of gastric mucosae biopsies was performed, using hematoxylin and eosin stain. This efficiency was proven against ethanol that leads to the appearance of several symptoms such as inflammation and severe damages like lesions, necrosis, erosions, bleeding and ulcers. Besides, the treatment with *O. ficus-indica* oil reduces, in a dose-dependent manner, the surface of the ulcerated areas produced by ethanol. It also leads to a time gain in the healing process, with a healing rate of 91% on the second day and 99% on the third day. On the fourth day, a complete recovery under the oil treatment was observed. The therapeutic effects of *O. ficus-indica* oil on gastric ulcers could be mediated by its diverse bioactive compounds [39].

Antifungal effect

In vitro studies

Ramirez-Moreno *et al.* studied the antifungal potential of *O. ficus-indica* seed oil using two different species of fungi. The oil has significantly inhibited the development of *Saccharomyces cerevisiae* and *Candida albicans* with an inhibition zone diameter of 40.3±4.5 mm and 11.0±1.8 mm, respectively. This property can be attributed to the effect of the polyunsaturated fatty acids present in this oil [25]. Besides, the antifungal activity of *O. ficus-indica* oil from Tunisia was evaluated against three opportunistic cutaneous moulds (*Fusarium*, *Aspergillus* and *Penicillium*), and two yeasts (*Candida sake* and *Candida parapsilosis*). The findings revealed that this oil was capable of inhibiting the growth of pathogenic fungi. The inhibition zone diameter of the genus *Candida* obtained with *O. ficus-indica* oil ranged from 14 to 16.5 mm, respectively, against *C. parapsilosis* and *C. sake*, while 35.5 mm was obtained with Voriconazole and 10 mm was obtained with Amphotericin B. On the one hand, the growth of two of the three tested species of yeast (*C. sake* and *C. parapsilosis*) was inhibited with high MBC and MIC values (1/64 and 1/32 for both sensitive yeasts, respectively). On the other hand, the growth of the three fungal pathogens, *Fusarium*, *Aspergillus* and *Penicillium*, examined with the same MIC and MBC values of ¼ and 1/8, may be decreased by oil [54].

Hypolipidemic effect

In vivo study

According to the research carried out on *O. ficus-indica* from Tunisia, supplementing rats food with the seed oil at an amount of 25 g/kg decreased low-density lipoprotein (LDL) and blood cholesterol, without any remarkable variation in high-density lipoprotein values (HDL) during the treatment [55]. In another work performed by Ennouri *et al.*, dietary supplementation by *O. ficus-indica* seed oil was shown to be effective in reducing the atherogenic risk factors in rats at an amount of 25 g/kg. The addition of this oil in the diet produced a significant lipid-decreasing effect in the treated animals, as compared with the control group receiving a standard diet. Indeed, a very pronounced decrease in total cholesterol and a significant rise in the ratio of HDL cholesterol/total cholesterol were noticed, as compared the treated group to the control. Moreover, the atherogenic index in rats treated with the oil-enriched diet was significantly lower than in the control group [56]. The treatment of diabetic rats for four weeks with oil quantities of 1 and 2 ml/kg significantly reduced the cholesterol and the triglycerides amount [52]. Also, Bouhrim *et al.* showed that the daily intake of the seed oil of *O. dillenii* significantly attunes the increase in the cholesterol, triglycerides, HDL cholesterol/total cholesterol ratio, and the atherogenic index levels in albino mice that were fed with a high-fat diet. Indeed, it did not affect the HDL cholesterol amount [40].

Bodyweight

In vivo study

The supply of *O. ficus-indica* seed oil in mice treated with alloxan significantly inhibited the bodyweight loss induced by this diabetogenic agent compared with mice treated with alloxan alone [49]. In another study, the supplementation of rat food with *Opuntia* seed oil (25 g/kg) during 28 days of treatment induced a linear rise in body weight of rats fed with a high-fat diet, in comparison with the group that has received a standard diet [55]. In a work realized by Bouhrim *et al.*, the *O. dillenii* seed oil was also found to be enhancing the growth performance by decreasing the relative liver index and by increasing body weight gain in rats with CCl_4 hepatotoxicity after 14 days of treatment [56]. Moreover, in another study, the *O. dillenii* seed oil administration with alloxan significantly inhibited the body weight loss in treated groups while compared to the group treated with alloxan only [40].

Hepatoprotective effect

In vivo study

According to a study performed in Morocco, *O. dillenii* seed oil was found to exert a hepatoprotective effect in rats by diminishing alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase activities in plasma, in comparison with rats treated only by CCl_4. Besides, *O. dillenii* seed oil ameliorated the excretory function of the liver, and decreased the total and the direct bilirubin plasma levels. Moreover, *O. dillenii* seed oil also ameliorated the metabolic function of the liver by the restoration of triglycerides, glucose and VLDL-c to normal values, while compared to the CCl_4 control group [52]. Furthermore, the treatment of diabetic rats for four weeks with an *O. dillenii* seed oil in a quantity of 1 and 2 ml/kg protected the hepatotoxicity produced by streptozotocin in diabetic rats by the reduction in ALT and AST [52].

Toxicology and safety of *Opuntia* seed oils

In a study performed by Ali *et al.* to evaluate the toxicity of *O. ficus-indica* oil in mice, it was shown that it is not toxic. Indeed, after intraperitoneal injection or oral administration of the oil at the doses of 1000, 3000, or 5000 μl/kg, no abnormal behavioural or autonomous effects were observed and no mortality happened during the 14 days of the treatment [49]. In another study, a low toxicity of *O. ficus-indica* seed oil was shown. The test showed that the lethal doses (LD_{50}) are 4300 μl/kg and 2720 μl/kg for oral administration and intraperitoneal injection, respectively [57]. From these studies it can be concluded that the *O. ficus-indica* seed oil is not toxic even at high doses [58]. Khémiri *et al.* evaluated the acute toxicity of the *O. ficus-indica* seed oil in adult rats. The results showed that the oil at a dose of 3500 μl/kg and 7000 μl/kg did not exhibit any symptoms of mortality or toxicity in the orally treated animals during the five-day experimental period [39]. The toxicity of *O. dillenii* seed oil was evaluated by Bouhrim *et al.* and the results demonstrated its safety. Indeed, this study showed that this oil does not produce any mortality or signs of toxicity after a single-dose administration in mice. Additionally, the daily intake of the *O. dillenii* seed oil during four weeks does not induce a significant variation in the biochemical parameters and the body weight of rats while compared with the control group. Besides, the cell viability of HepG2 did not change in the presence of *O. dillenii* seed oil [59].

CONCLUSION AND PERSPECTIVES

This review has shown that the seed oils of *O. dillenii* and *O. ficus-indica* have chemical compositions rich in a set of molecules, mostly unsaturated fatty acids, phytosterols, tocopherols and polyphenols. Biologically active molecules allow the studied oil to exert several biological and pharmacological activities (antioxidant, antidiabetic, antibacterial, antifungal, anti-inflammatory, hepatoprotective, hypoglycaemic, hypolipidemic and gastroprotective), and to alleviate the decline of body weight. Moreover, most of the studies focus on *O. ficus-indica*, while *O. dillenii* has drawn the attention of researchers only in the last few years. Besides, the studies that have been carried out on these two species have not indicated a significant difference in their effectiveness. Therefore, more studies should be undertaken in the future to evaluate more biological activities of *O. dillenii* seed oil, and to confirm the uses of these two plants in folk medicine. Until now, all the mentioned biological effects have been carried out on the whole constituents of the oil. A strategy of molecule isolation, identification and testing are necessary.

Ethical approval: The conducted research is not related to either human or animal use.

Conflict of interest: Authors declare no conflict of interest.

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