Prickly Pear Seed Oil

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The PPSO has been extracted from prickly pear seeds using different extraction techniques, from conventional to advanced, and the PPSO yield varied depending on many factors, including geographic region, harvest period, fruit variety, maturation, extraction method and type of extraction solvent. Based on physicochemical properties of PPSO, it is considered an edible oil and can be used by humans. The chemical characterization of the oil has been reported, and it is sufficiently understood that the PPSO has high nutritive value and can be further studied for its health promotion effects.

Keywords: prickly pear seed oil ; extraction ; chemical characterization ; biological activity

1. Introduction

The growing demand for nutraceuticals and functional foods is paralleled by an increased effort in developing natural products for the prevention or treatment of human diseases. According to several studies, prickly pear seed oil (PPSO) contains high values of important nutrients that make the PPSO an excellent candidate for inclusion in food and healthy products; however, more research is needed to establish new pharmacological possibilities for its further future development and application. Unsaturated fatty acids are the main component of the oil, accounting for up to 80.9%. However, the main unsaturated fatty acids are linoleic and oleic acids [1][2][3].

The PPSO is reported to have several biological activities, including antioxidant in vivo [4] and in vitro [5][6] , antimicrobial [7] [8], antidiabetic [9][1][10][11], lipid-lowering [10], in vitro anticancer [7][11], anti-inflammatory [4][12], anti-ulcer [13] and UV radiation protection of human dermic fibroblasts reducing the cell death [14]. Based on the literature, the oil content in prickly pear seeds is considered low compared to other seeds and the extracted oil is commercialized mainly for cosmetics due to the high price resulting from the time-consuming and laborious process of production [15]. Analysis and physicochemical properties of the PPSO showed that it is edible and suitable for human consumption.

2. Prickly Pear Seed Oil Extraction and Yield

Due to the multiple health benefits of PPSO, an extraction process to preserve the quality of PPSO is of prime importance and thus should receive continuous attention from researchers. Based on the previous studies, PPSO was extracted using conventional extraction methods, such as Soxhlet and cold press, and alternative advanced extraction methods, such as supercritical carbon dioxide. Different extraction processes were also applied in PPSO extraction, including maceration, autoclave, microwave and ultrasound-assisted extraction. However, conventional methods using Soxhlet extraction are the most reported methods in the literature, while limited studies have reported the used of advanced extraction methods. Based on the previous studies, the oil yield was found to be varied depending on the prickly pear cultivar in the first place and second on the extraction process. Several factors, including geographical origin, harvest period, fruit ripeness and extraction solvents are also included [16][17][2][6].

Moreover, the yield of PPSO varies depending on the extraction time applied from the same location, for example, when PPSO was extracted from prickly pear seeds from Algeria with n -hexane using the Soxhlet system, the yield of PPSO was 10.45 ± 0.10% when the extraction was carried out for 18 h [18], and the yield was 7.3–9.3% when the extraction was carried out for 9 h [19]. In contrast, the oil yield in Tunisian prickly pear seeds was approximately similar when the variation of the extraction time applied was low, and when the PPSO was extracted with n -hexane using the Soxhlet extractor for 10 h, the yield was reported to be 11.75% [16]. A similar PPSO yield (11%) was reported in another study by [20] of Tunisian PPSO extracted with n -hexane in a Soxhlet extractor for 9 h. However, a different Tunisian PPSO yield was reported between the PPSO extracted from seeds of wild prickly pear (10.32%) compared to cultivated prickly pear (8.91%) [21].

Few studies have reported the use of innovative methods such as supercritical fluid extraction, microwave extraction and ultrasound extraction in PPSO extraction. However, it is expected that they will be widely used for PPSO in the near future due to the importance of the health-promoting qualities of PPSO.

In addition, the extraction of PPSO using supercritical fluid extraction at different pressures ranging from 100 to 500 bar and different temperatures of 35–50 °C at a carbon dioxide flow rate of 50 g/min was reported with a yield of 6.5% [22]. In this context, a supercritical fluid extraction method in comparison with the Soxhlet method was applied to PPSO extract from two Tunisian prickly pear seed types—the spiny (wild) and thornless (cultivated) [21]. Supercritical fluid extraction was carried out at different temperatures of 35, 40, 45, 50, 60, and 70 °C, fixed pressure at 180 bar, and 15 mL/s of CO 2 flow rate for 135 min. The results of the optimized temperature in supercritical fluid extraction showed that a higher yield was obtained at 40 °C. Results obtained from this study show a significantly higher yield of 10.32% (wild) and 8.91% in Soxhlet with n -hexane compared to supercritical fluid extraction yielding 3.4% (spiny) and 1.94% (thornless) [21]. Green cactus pear seed oil was extracted using ultrasounds with an obtained yield of 3.75–6% [6]. The recovered extract obtained with supercritical fractionation of the defatted seeds of the prickly pear from Algerian Opuntia ficus - indica was rich in antioxidants catechin, epicatechin, and ferulic acid, which are known to be good for human health [23].

3. Characteristics of Prickly Pear Seed Oil

Few studies have reported the physicochemical properties of PPSO, including peroxide value, iodine value, acidity index, refractive index and saponification value. Physicochemical characteristics of PPSO, as reported in the literature, are summarized in **Table 1** .

Table 1. Physicochemical characteristics of prickly pear seed oil.

Reported Parameters	References				
	[24]	[25]	[13]	[18]	[19]
Physical state at room temperature	NR	NR	Liquid	Liquid	NR
Color	NR	NR	Greenish yellow	Yellow brown	NR
Odor	NR	NR	Slightly fruity	NR	NR
Property	NR	NR	Dry oil	NR	NR
Density at 20 °C (mass/volume)	NR	0.92 ± 0.01	0.91 ± 0.001	0.91 ± 0.01	0.90 ± 0.0
Refractive index at 20 °C	NR	1.47 ± 0.010	1.5 ± 0.001	1.48 ± 0.01	1.5 ± 0.0
Acid index	1.26 ± 0.5 3.02 ± 0.5	21.2 ± 0.5	1.95 ± 0.03	1.82 ± 0.01	NR
Peroxide index (meq O_2/kg of oil)	3.5 ± 1.5 8.6 ± 2.5	12.0 ± 0.4	2.23 ± 0.06	NR	NR
Iodine index (g I_2/100 g of oil)	131.5 ± 0.5 32 ± 0.3	NR	108.52 ± 0.25	93.45 ± 0.22	101.5 ± 1.0
Saponification index (mg of KOH/g oil)	NR	NR	171.40 ± 0.43	177.10 ± 0.05	169.0 ± 0.1
Extinction coefficient (K_{232})	2.8 ± 0.5 3.25 ± 0.5	0.08 ± 0.010	NR	NR	NR
K_{270}	0.51 ± 0.5 2.11 ± 0.5	0.13 ± 0.020	NR	NR	NR

NR = not reported.

Recently, the chemical and physical parameters of PPSO extracted by two different solvents—2-MeO and n -hexane—were reported [24]. The oil extracted by 2-MeO showed a higher acidity index (3.02 ± 0.5, g/100 g) compared to the n -hexane extracted oil (1.26 ± 0.5 g/100 g). The peroxide value was found to be high in the two different solvents (3.5 ± 1.5 in hexane oil and 8.6 ± 2.5 in 2-MeO), which can be an indicator for primary fat oxidation [26]. Additionally, the physicochemical characteristics of PPSO extracted with n -hexane using a Soxhlet apparatus were not different from the study of Gharby et al. [24], where the acid value was 1.82 ± 0.01, iodine value was 93.45 ± 0.22 (g of I2/100 g of oil), saponification value was 177.10 ± 0.05 (mg of KOH/g of oil), density was 2.04 ± 0.05 at 20 °C (mass/volume), and the refractive index was 0.909 ± 0.01, with a yellow-brown color [19].

In this context, the physicochemical characteristics of PPSO extracted with n -hexane in a Soxhlet extractor showed PPSO with a density of 0.903 ± 0.002, the refractive and iodine indices reported as 1.475 ± 0.002 at 20 °C. 101.5 ± 1.0, respectively, while the saponification index (mg of KOH/g oil) was 169.0 ± 0.1 [20]. In addition, the physicochemical characteristics of PPSO extracted by first cold pressing did not differ much from other studies previously mentioned: the PPSO was found to have a greenish-yellow-colored liquid, a density of 0.905 ± 0.001 at 20 °C, an acid index of 1.952 ± 0.034, an iodine index of 108.52 ± 0.250 (g I2/100 g oil), a peroxide index of 2.230 ± 0.061 (meq O 2/kg oil), a saponification index of 171.40 ± 0.430 (mg KOH/g oil), and a refractive index at 20 °C of 1.475 ± 0.001 [13]. However, the physical and chemical parameters of PPSO oil from Algeria extracted by cold pressing showed different results compared to other studies. The PPSO had an acidity of 21.2 ± 0.5 mg/g of oil (expressed as % of oleic acid), and the author explained the high acidity due to enzymatic hydrolysis during harvesting or the handling process. The peroxide value was found to be 12.0 ± 0.4 meq O 2/Kg. Compared to other studies on PPSO, the peroxide value reported in this study was also higher [25]. The authors have explained the elevated peroxide value as a result of unsatisfactory conditions used during the oil preparation.

4. Chemical Characterization of the Prickly Pear Seed Oil

From different reported studies, various factors have an influence on fatty acid content, including prickly pear variety, geographical location, methods and solvents used for oil extraction, cultivar, degree of maturity, and harvesting season. Recently, the fatty acid composition of the oil extracted by two different solvents using 2-MeO and n -hexane were found to be similar [24]; linoleic acid was the major fatty acid constituting up to 62%, followed by oleic acid (21%), linolenic acid (0.3%) with 84% counting as unsaturated fatty acid. Saturated fatty acid represented 16%, with palmitic acid counting as 11.70% and stearic acid 3.14% [24]. However, fatty acid content, especially linolenic acid and oleic acid, was found to be different depending on the extraction method. The fatty acids of PPSO were extracted from eight varieties of prickly pear from Mexico using two different methods—cold press and maceration [14]. The cold hydraulic press method showed slightly higher fatty acid contents when compared to the maceration method, where the oil analysis showed that linoleic acid was in the range of 66.5–76.1 and 60.5–78.8, followed by oleic acid in the range of 9.3–19.9 and 11.5–19.9 for hydraulic press and maceration methods, respectively.

Although, for most reported studies from different varieties and different locations, the main fatty acids were linoleic and oleic acids, and the content of fatty acid was different. Moreover, differences were found in the oil composition of the PPSO derived from various places. In this context, the fatty acids analysis of PPSO extracted from seven Spanish prickly pear cultivars showed differences between fatty acid content in different varieties, which were attributed to genetic factors [27]. The major fatty acid was linoleic (57.72–63.11%), followed by oleic acid (19.37–21.79%), linolenic acid (0.23–1.10%), palmitic acid (12.47–15.06%) and stearic acid (2.56–4.10%). In this regard, the analysis of fatty acid of PPSO from different places in Morocco showed unsaturated fatty acids of 83.0%, where the major fatty acids were linoleic acid (60.2–64.6 g/100 g), oleic acid (18.2–22.3 g/100 g), linolenic acid (0.3 g/100 g), and palmitic acid (11.6–12.4 g/100 g) [28]. In addition, fatty acid content was varied due to time collection from different locations and provinces of Turkey [29]. The unsaturated fatty acids included mainly linoleic (49.3–62.1%), oleic acid (13.0–23.5%) and vaccenic acids (5.0–6.3%). Saturated fatty acids mainly include palmitic acid contents of seed oils (10.6–12.8%) and stearic acid (3.3–5.4%).

Geographical location also has an impact on fatty acid content of PPSO, especially the content of linoleic acid, even though the PPSO is extracted with the same method. A study on the fatty acid profile of Algerian PPSO extracted by cold press indicated that Algerian PPSO contains linoleic acid (49.7–56.1%), oleic acid (15.6–19.3%), vaccenic acid (4.30%) and α-linolenic acid (0.24%). Saturated fatty acid mainly includes palmitic acid (10.08%) and stearic acid (2.97%) [25]. Fatty acid composition of Egyptian PPSO extracted with methanol in a Soxhlet apparatus showed that linoleic acid was found to be the major unsaturated fatty acid (54.03%), followed by oleic acid (22.41%) and linolenic acid (0.63%); whereas, the major saturated fatty acid was palmitic acid (17.11%) and stearic acid (3.5%) [30]. However, the fatty acid content of Tunisian PPSO extracted using the cold press method as well was found to contain higher linoleic acid (61.6%) and higher oleic acid (21.18%). Linolenic acid was counted as 0.2%. Furthermore, the saturated fatty acids were higher, representing 16%, which included palmitic acid (12.2%) and stearic acid (3.3%) [13]. In this context, the fatty acid composition of PPSO from Sicilian yellow fruit extracted from the seeds using cold pressing was in the range of the reported studies. Unsaturated fatty acids represent 83.79%, with 58% linoleic acid content, 18% oleic acid, 6.29% vaccenic acid, and 0.3% arachidic acid. Saturated fatty acids counted for 16.31%, where palmitic acid content of 12% and stearic acid of 4% were the major ones [31]. The results from this study also reported that the oil obtained in Sicily contained significant amounts of some unsaturated fatty acids, which have been known for their health-benefiting properties, including trans-13-octadecenoic, 7Z, 10Zhexadecadienoic, and gadoleic acid.

Geographical location with a different extraction method has an effect on the fatty acid composition; in this regard, analyses of fatty acid composition in PPSO from prickly pear seeds cultivated in Yemen extracted using the maceration method with n -hexane was investigated [1] and unsaturated fatty acids were found to be the majority of fatty acid content, representing up to 81% in oil with linoleic acid content of 57.5% and oleic acid content of 22.30%. On the other hand, the major saturated fatty acids of PPSO were palmitic (14%) acid and stearic acid (3%). In this regard, a high percentage of unsaturated fatty acids was reported in the PPSO from Tunisia extracted using n -hexane with a Soxhlet system in which linoleic acid was the major component making up 70%, followed by 17% oleic acid. Saturated fatty acid represents 12.4%, and palmitic acids (9%) and stearic (3%) were the major saturated fatty acids [11]. Moreover, it was found that the fatty acid content of PPSO varied due to different locations and provinces of Turkey, and also, based on the time collection, the content of linoleic ranged from 49.3 to 62.1%, oleic acid from 13.0 to 23.5% and vaccenic acids from 5.0 to 6.3%. Saturated fatty acids mainly include palmitic acid contents of seed oils of 10.6–12.8% and stearic acid 3.3–5.4% [29].

5. Potential Health Benefits of Prickly Pear Seeds Oil

The potential health benefits of PPSO have attracted increasing attention. The authors of a number of studies have suggested that the primary benefit of PPSO is due to its polyunsaturated fatty acids, sterols and antioxidant activity. The biological activity of PPSO reported in the literature, conducted mainly in animal studies, showed that the PPSO exerts several health benefits.

5.1. Antioxidant Activity of Prickly Pear Seeds Oil

In vitro antioxidant activity of PPSO was determined using different methods, including DPPH, ABTS and the molybdate method, and the findings varied from one study to another study, mainly due to different analytical methods, solvent, and methods used for PPSO extraction.

Brahmi et al. [25] indicated that PPSO extracted by the cold press method showed antioxidant activity of 0.56 ± 0.01 AU, as determined using the molybdate method, and radical free radical scavenger ability of 37.0 ± 4.2%, as determined using the DPPH method. The reported antioxidant activity from this study is considered weak compared to another reported study [13], which showed that compared with vitamin C, PPSO extracted by cold pressing has 88% and 87% scavenging activity on DPPH (10-4M) and ABTS, respectively. In this regard, a study was performed by Berraaouan et al. [9], who showed that the Moroccan PPSO extracted by cold press exhibited a good antioxidant effect in DPPH scavenging assay (0.001%; *w*/*v*) with an IC_{50} value of 0.96 mg/mL. In this study, the antioxidant activity of PPSO extracted by ultrasound extraction ranged from 55.84 to 68.37 mg AAE/100 g for ABTS and 101.63 to 289.26 µmol TE/100 g for DPPH, which showed to be different from that extracted by the Soxhlet method with scavenging activity of 54.33 ± 0.84 mg AAE/100 g and 266.60 ± 1.97 µmol TE/100 g in ABTS and DPPH methods, respectively [6]. In addition, the antioxidant activity of PPSO extracted by supercritical fluid extraction showed an EC50 value of 140 mg extract/mg DPPH for inhibition of free radical formation, and that was better than the antioxidant activity of oil extracted by the Soxhlet method, which showed an EC50 value of 307 (mg extract/mg DPPH), as reported in [23].

Moreover, the antioxidant activity of PPSO is also influenced by the solvent used for extraction. The results of the free radical scavenging activity of PPSO extracted by different solvents, *n*-hexane, petroleum ether and chloroform-methanol (2:1, *v*/*v*), in comparison with antioxidant of vitamin E was reported [1]. The study clearly showed that the oil extracted using chloroform-methanol (2:1, *v*/*v*) exhibited higher antiradical activity (87%) towards the DPPH radical compared to *n*-hexane (86%) and petroleum ether (76%). In this regard, the antioxidant activity of PPSO from Algerian prickly pear seeds was reported. According to Chaalal et al. [32], the best results of antioxidant capacity were obtained when the seeds were extracted with 75% acetone (among ethanol, methanol, and water 50%, *v*/*v*), which had an antioxidant capacity of 95%.

Limited studies have reported on the antioxidant activity of PPSO in vivo. However, more recently, this was reported in [4]. (The findings obtained from their research showed that PPSO had significant antioxidant action in rats induced with acute inflammation, where the tested antioxidative parameters that advanced the oxidation protein product, including malondialdehyde, were significantly lower in treated rats with PPSO compared to untreated rats, and the level of these parameters returned to the normal level). Furthermore, PPSO has shown a significant evaluation of antioxidant enzyme activity compared to untreated rats, and the activity of superoxide dismutase, catalase and glutathione peroxidase reached the normal level with the group of animals that were not induced with inflammation [4].

5.2. Antimicrobial Activity of Prickly Pear Seeds Oil

Few studies have reported the antimicrobial activity of PPSO. In general, PPSO showed weak antimicrobial activity in some reported studies, no activity in other studies and good activity in other studies.

Recently, the antimicrobial activity of Algerian PPSO at a concentration of 100 µL extracted by cold press was investigated [25]. Two Gram-positive strains (*Methicillin-resistant Staphylococcus aureus (MRSA) ATCC 43300* and *MRSA ATCC 29213*), two Gram-negative strains (*Escherichia coli* and *Pseudomonas aeruginosa*) and six fungal strains (*Aspergillus niger*, *Aspergillus flavus*, *Mucor rammaniarrus*, *Aspergillus ochraceus*, *Aspergillus parasitus* and *Candida albicans*) were selected to determine the antifungal activity. Findings from this study have indicated that the PPSO did not show antimicrobial activity against bacteria and fungi selected in this study. The authors have explained that the weak antimicrobial activity could have been due to the evaluation method used, which could influence the results, or the low content of phenolic compounds found in the studied oils, which could also be responsible for their inefficiency. However, a study of AbdelFattah et al. [7] indicated that PPSO extracted by methanol at 100 µL of 50% dilution (*v/v* methanol) reduced the growth of *Salmonella*, *Escherichia coli*, *Bacillus subtilis*, *Bacillus cereus*, yeast and mycotoxins metabolites while there is no significant effect response to yeast spores. In this regard, the antimicrobial activity of PPSO originated from Tunisia was tested against 10 microorganisms that have been known to be clinically pathogenic in humans; four bacterial strains, including *Escherichia coli*, *Staphylococcus aureus*, *Streptococcus agalactiae*, and *Enterobacter cloacae*, three yeast strains, including *Candida albicans*, *Candida parapsilosis*, and *Candida sake*, and three fungi, including *Aspergillus niger*, *Penicillium digitatum*, and *Fusarium oxysporum*, were studied [5]. Incubation with the PPSO at doses of 50 µL for 24 h for bacterial strains, 48 h for yeast, and 3–4 days for fungi at 28 °C indicated that PPSO showed antibacterial activity against *Enterobacter cloacae*, *Candida parapsilosis* and *Candida sake*, whereas no activity was shown against the three bacterial strains tested, including *Staphylococcus aureus*, *Streptococcus agalactiae*, and *Escherichia coli*. The oil also showed antifungal activity against three opportunistic cutaneous molds, including *Penicillium*, *Aspergillus*, and *Fusarium.* Moreover, the antimicrobial activity of the PPSO extracted from two Mexican varieties (green: *Opuntia albicarpa* and red: *Opuntia ficus indica*) with different solvents was reported [8]. In their study, the antimicrobial activity of PPSO was examined against different bacteria, including *Candida albicans*, *Escherichia coli*, *Staphylococcus aureus*, *Listeria monocytogenes*, *Pseudomonas aeruginosa*, *Saccharomyces cerevisiae* and *Salmonella Typhi*. Both PPSO from the two Mexican varieties produced a microbial inhibition zone in most of the microorganisms against Gram-positive and Gram-negative bacteria, and the effect was comparable to antimicrobial compounds such as ampicillin, streptomycin, and sulfamethoxazole/trimethoprim.

It is well-known that the presence of biofilm in pathogenic microbes makes these pathogens hard to treat. In this regard, a study by Nazzaro et al. [33] evaluated the ability of PPSO at 1 to 8 µL/mL obtained through cold pressure to form biofilm using different types of bacteria, (including *Listeria monocytogenes*, *Escherichia coli*, *Pseudomonas aeruginosa*, and the phytopathogen *Pectobacterium carovotorum*). PPSO at 1 to 8 µL/mL was able to inhibit the biofilm of *Escherichia coli*, *Pseudomonas aeruginosa* and *Pectobacterium carotovorum* at 38.75%, 71.84% and 63.06% inhibition, respectively. The action of the PPSO was also 64.97% effective at blocking the metabolism of *Listeria monocytogenes* cells. When the PPSO was tested against *Pectobacterium carotovorum*, the microbial cell metabolism was completely inhibited with 8 µL/mL (96.26%). These findings indicate an interesting applicative versatility of this oil, with potentialities for food, agriculture and health purposes.

5.3. The Antidiabetic Properties of Prickly Pear Seeds Oil

The antidiabetic effect of PPSO is the most longstanding claimed pharmacological effect of PPSO. Thus far, most of the reported studies have addressed different mechanisms of action; however, the only scientific demonstration of a possible antidiabetic activity has been in rats.

Recently, in the study reported by AbdelFattah et al. [7], feeding male albino rats a diet supplemented with PPSO at 5% (*w/w*) for two months was stated to decrease the serum glucose concentration by 4.88 and 11.43% after 30 and 60 days, respectively, and to increase liver glycogen levels significantly by 53.94 and 125.85% compared to the control group. The suggested mechanism of action was due to increased insulin secretion, which stimulates glucose incorporation into glycogen in skeletal muscles and liver for the regulation of blood glucose. In addition, oral glucose test tolerance was performed on healthy Sprague Dawley rats. Oral administration of either aqueous or hydro-ethanol cactus seed extracts at 400 mg/kg for a period of 0.5–3 h, induced a reduction of blood glucose levels with a maximum decrease at an hour and a half compared to the control group by 62% [10]. Moreover, the antidiabetic effect of PPSO with its molecular mechanisms in streptozotocin (STZ)-induced diabetic rats was investigated [1]. Oral administration of PPSO at doses of 0.4 and 0.6 g/kg for 21 days to STZ rats caused a significant reduction of the blood glucose level compared to STZ untreated rats, and furthermore, the effect was approximately similar to the standard drug for blood glucose reduction, glibenclamide, at the end of the experiment period. The author has stated that treatment with PPSO elicited an increase in the expression level of glucose transporter 2 gene but reduced the expression of the phosphoenolpyruvate carboxykinase gene, which are key genes in the glucose metabolism. In this regard, the evaluation effect of PPSO treatment at 2 mL/kg of body weight on the incidence of alloxan-induced diabetic Swiss albino mice for seven days was studied [34]. Their

results have shown that the administration of PPSO significantly decreased the incidence of alloxan-induced hyperglycemia in the PPSO-treated group compared to the untreated group. The authors suggested that this effect might be due to the synergism of the antioxidant compounds in quenching free radicals and the capacity of their unsaturated fatty acid in PPSO to enhance the antioxidant status in pancreatic b cells.

Moreover, an oral glucose test tolerance was performed on healthy or streptozotocin-induced diabetic rats as envisaged [9]. PPSO was administered to the rats at a dose of 0.8 mL/kg body weight, and glibenclamide was used as a standard drug at 2 mg/kg body weight. An evaluation of serum glucose level was carried out at 30, 60, 120, 240, and 360 min after treatment. The findings from their study indicated significant inhibition on the hyperglycemia that follows glucose loading at 90 min for treated rats. The author suggested that the mechanism of reduction of the glucose level could be due to inhibition of intestinal glucose absorption by the action of unsaturated fatty acid that presented in PPSO, where it has been known that fatty acids disturb the absorption function of enteric cells when they are present in the luminal space [35]. In another study, the effect of PPSO supplementation to healthy adult male rats of the Wistar strain at 25 mg/kg body weight for 2 months was investigated [11]. The obtained findings from this study indicated that PPSO caused a significant decrease in serum glucose concentration (22%), and that was parallel with the significant increase in liver glycogen levels as compared to the control group. The author has suggested the increase of glycogen levels in liver and muscle with the increase in insulin secretion, which stimulates glucose incorporation into glycogen in skeletal muscles and liver for the regulation of blood glucose.

5.4. Effect of Prickly Pear Seed Oil on Lipid Profile and Cholesterol Regulation

Hypercholesterolemia is associated with an increased risk of adverse cardiovascular outcomes. Limited studies reported the effect of PPSO on regulating the cholesterol and lipid profile, while there were several studies that reported the benefits of other parts of prickly pear, including fruits, leaves, pulp fractions and prickly pear pectin for cholesterol regulation and management of body weight in human and animal studies.

Evidence of the effect of PPSO in reducing the total cholesterol, LDL, and serum glucose levels in male Albino rats fed with a diet supplemented with PPSO at 5% (*w*/*w*) for two months compared to control animals was reported [7]. This study also indicated that PPSO had no significant effect on body weight gain but caused a decrease in feed conversion efficiency. The effect was shown to be due to the presence of different compounds in PPSO, including β-sitosterol and other compounds, such as unsaturated fatty acid, β-carotene and vitamin E, which have been reported in the literature to have a lowering effect on the lipid profile. In this regard, the modulation effect of Schottenol and Spinasterol, two sterols presented in PPSO as well as sterol extracts from PPSO on cholesterol metabolism in the Murine microglia BV2 cell line (BV2) at a concentration range from 12.5 to 50 µM for 24 and 48 h was reported [36]. PPSO modulated the gene expression of two nuclear receptors (liver X receptor (LXR)-α and LXRβ) and their target genes (ABCA1 and ABCG1), which have been known to be involved in regulating cholesterol metabolism. In addition, feeding adult male rats of Wistar strain a diet supplemented with PPSO (2.5%, *w*/*w*) for nine weeks resulted in a significant reduction in total cholesterol, triglyceride level, atherogenic index and average gain of body weight compared to the control group. The results from this study have also indicated that the fatty acid analysis in the liver of treated animals with PPSO showed that a significant increase in oleic acid levels resulted in an increase of MUFA in rats fed with a PPSO diet compared to other groups [37]. In this regard, Ennouri et al. [11] also indicated a reduction in plasma total cholesterol and LDL, VLDL cholesterol with no effect on HDL-cholesterol concentrations in male Wistar rats fed a diet supplemented with PPSO at 2.5% (*w*/*w*) for 2 months. This effect was suggested due to phytosterols presented in oil, especially β-sitosterol, where many studies have reported in the literature that phytosterols induce a decrease in lipoprotein cholesterol levels in total plasma.

5.5. Cytotoxic and Apoptotic Effects of Prickly Pear Seed Oil

A recent study [7] investigated the in vitro chemoprevention effect of PPSO at different concentrations (0.01, 0.1, 1, 10, 100 µM) against the growth of Colo-205 and HepG2 cells for 72 h. PPSO has potent activity (IC_{50} = 0.052 µM) toward HepG2, while this PPSO exhibited active but not potent activity (IC50 = 29.5 µM) against colorectal cancer (Colo-205) cell line. (The authors also found the inhibition effect of cell growth in cells that were treated with PPSO to be parallel with an increase of ROS in the cells, suggesting a ROS-induced cell death likely due to the pro-oxidant effects of the extracts). However, the PPSO was effective at inhibiting Colo-320 and Colo-741 growth [12], where the apoptotic effects of spiny (wild) and thornless (cultivated) forms of *Opuntia ficus indica* L. grown in Cyprus were studied against Colo-320 and Colo-741 cells for 48 h. Cell growth and cytotoxicity were measured by MTT assays. The spiny and thornless PPSO (1:16 dilution) were found to be active against the inhibition of Colo-320 and Colo-741 cell growth for 48 h. The author suggested that the inhibitory effect of thornless PPSO is due to the high linoleic acid content, which is a known compound with an anticancer effect in cancer cells. However, in some studies, the PPSO and its composition did not show a

cytotoxic effect in vitro. In this regard, the sterol extract prepared from PPSO was screened for its cytotoxic effect against the Murine microglia BV2 cell line at a concentration range of 12.5–50 µM for 24 and 48 h using MTT assay; the findings indicated that sterol extract was not toxic to Murine microglial BV2 cells [38]. In addition, another study reported [39] that the prickly pear seed extracts obtained from different cultivars of prickly pear did not show any toxicity on breast, prostate and colon cancer cells in a concentration range of 0.2–0.16 g/mL assessed by the MTT assay, and it was toxic towards the MOLT-4 leukemia cells with an IC50 value of 5 mg/mL by one of the tested varieties.

5.6. Anti-Inflammatory Effect of Prickly Pear Seed Oil

Prickly pear seed oil showed a potential anti-inflammatory effect and reduced the inflammatory biomarkers in vivo, as reported recently [4]. In their study, acute inflammation was induced by carrageenan in adult male Wistar rats by administration of 100 µL of 1% freshly prepared solution of carrageenan in normal saline in the right hind paw of each rat. Rats were treated with PPSO at 25 µL/paw. The obtained results showed a significant reduction in the size of the edema in the oil-treated group, compared to all the studied groups, and the reduction effect was even better than the reference drug groups. PPSO also significantly reduced inflammatory biomarkers, including the number of white blood cells, blood platelets, C-reactive protein and plasma fibrinogen concentration compared to untreated animals. The author has explained that this effect is due to the antioxidant properties of PPSO and other bioactive compounds such as phytosterols, tocopherols, polyphenols, and carotenoids. In addition, PPSO was shown to have wound healing potential in vivo, as reported in [5]. The findings from this study have shown that the topical application of PPSO at 0.6 µL/mm^2 accelerated skin closure and improved the healing process significantly compared to the reference and the control groups. The authors explained that the wound healing effect of the PPSO is due to the active components that are present in the oil, including unsaturated fatty acids, triacylglycerols, phytosterols, and tocopherols; these compounds work to enhance the speed of wound contraction, complete reepithelialization, and improve the external scar's aspect. Moreover, Benattia et al. [10] investigated the anti-inflammatory effect of the prickly pear seed extract (aqueous and hydro-ethanolic) at a dose of 500 mg/kg in male Sprague Dawley rats. The seed extract showed a significant inhibition of the edema of paw in the rats induced by carrageenan with 25% inhibition for 3 h after pretreatment compared to untreated induced rats. The author suggested that the efficacy of the hydro-ethanolic extract from the seeds was due to the presence of polyphenolic compounds, among which flavonoids were reported to be able to inhibit the oxidants released by leukocytes and other phagocytes in the inflammatory site [34]. Flavonoids are also well-known to reduce the effect of prostaglandins, which cause the late phase of acute inflammation and pain perception [40].

5.7. Anti-Ulcer Activity of Prickly Pear Seed Oil

The only study that investigated the anti-ulcer activity of PPSO is [5]. The administration of PPSO at two different doses of 3.5 and 7 mL /kg/body to the male albino Wistar rats induced with 1% absolute ethanol was found to protect gastric mucosa against the ulcerating effect of ethanol. PPSO showed high efficiency in the protection of the cytoarchitecture and function of the gastric mucosa against the severe damages provoked by ethanol intake. PPSO showed healing of 91% on day 2 and 99% on day 3, and complete healing was attained on the fourth day under PPSO treatment. The anti-ulcer effect of PPSO was explained due to its richness in beneficial compounds, including tocopherols, linoleic acid, oleic acid, and β-sitosterol, which act in synergistic and complementary ways to ensure gastroprotection and gastric mucosal.

5.8. The Effect of Prickly Pear Seed Oil against UV-C Radiation

Even though a viable PPSO on the market is used mainly as a cosmetic ingredient, studies that have shown the activity of PPSO as a good cosmetic product are very limited. In this regard, the authors of [15] investigated the effect of PPSO on human dermic fibroblasts using a primary fibroblast culture of human skin. PPSO was applied at 10, 50, 100, and 200 µM, and then the culture cells were submitted to UV radiation in a crosslink for 15 min after that. PPSO at 50 µM reduced cell death due to UV radiation of human dermic fibroblasts. The authors explained that the protective effect of the PPSO against UV-C radiation was due to the action of the mixture of components that are present in PPSO against UV radiation, such as the antioxidants and polyunsaturated fatty acid. In addition, PPSO was suggested to be able to protect against UV-B and UV-A ranges, as reported in [19]. Findings from this study indicated that PPSO strongly absorbs UV-C radiation within a range of 100–290 nm and shows some absorbing properties in the UV-B range of 290–320 nm and UV-A ranges of 320–400 nm, where ultraviolet light is responsible for the most cellular damage.

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