REVIEW

Medicinal properties of jojoba (*Simmondsia chinensis*)

Zipora Tietel^a, Shirin Kahremany^b, Guy Cohen^{b,c} and Navit Ogen-Shtern^{b,c}

^aDepartment of Food Science, Gilat Research Center, Agricultural Research Organization, MP Negev 8531100, Israel; ^bThe Skin Research Institute, The Dead-Sea and Arava Science Center, Masada, 86910, Israel; ^cBen Gurion University of the Negev, Eilat Campus, Eilat 8855630, Israel

ABSTRACT

Jojoba, *Simmondsia chinensis* (Link) C.K. Schneider is an evergreen shrub widely grown in Israel, the Middle East, South America, Africa, India and Australia used as an agricultural crop for commercial purposes and as a source of its non-edible natural wax. It is widely used in pharmaceuticals and cosmetic formulation due to its unique structural characteristics and beneficial health effects. In addition, extensive work has been published on the plant's health-promoting activities, ranging from antioxidant activities to the treatment of cancer. Being a rich source of natural liquid wax, the majority of research regarding jojoba focuses on its applications, as well as on the ability to exploit the residual plant materials obtained in its production. To date, several potent phytochemicals have been attributed to its medicinal properties, e.g. simmondsin and phenolic compounds. The current review emphasizes the evidence-based medicinal qualities of the wax and plant extracts and highlights the gaps of knowledge in these research areas and the importance of acquiring additional understanding of jojoba distinctive traits.

ARTICLE HISTORY

Received 24 August 2020
Accepted 22 December 2020

KEYWORDS

Jojoba; medicinal properties;
antioxidant; dermatology;
bioactive molecules;
Simmondsia chinensis;
simmondsin

Introduction – Jojoba, the desert gold

Jojoba, *Simmondsia chinensis* (Link) C.K. Schneider (Fig. 1), is an ever-green dioecious shrub growing in arid and semi-arid areas. This desert shrub can be grown in harsh, low irrigation and high-temperature environment (Ash et al. 2005), and it is tolerant to various environmental conditions (Kumar et al. 2012; Arya & Khan 2016). Taxonomically, it is the single member of the Simmondsiaceae family (Chase et al. 2016). The plant is native to Baja California and the Sonoran Desert in north-central Mexico and the southwestern United States. It was first mentioned in the literature by the Mexican historian Clavijero (1789) as a plant used by native-Americans in Baja California for its medicinal properties and as currency for

the exchange of goods. A number of botanists, the first of whom was Link, presented initial descriptions of the plant and granted it its scientific name and taxonomic classification (Daugherty et al. 1958). Since the 1930s, jojoba has been scientifically studied. Research intensified during the 1950s, when jojoba wax was suggested as a substitute for banned whale sperm oil, and commercial interest in jojoba as a new agricultural industry emerged (Benzioni 2010). Due to its similarity to whale sperm oil, it was originally used mainly as a renewable non-animal substitute for industrial needs (Gisser et al. 1975). First successes in domesticating jojoba occurred in California and Arizona in the late 1960s and shortly after also in Israel (Benzioni 2010).

Figure 1. Jojoba, grown in kibbutz Hatzerim, Israel. Pictures by Yair Arazi.

Genetics and diversity

Being a dioecious plant, the genetic variability of jojoba is translated into hundreds of cultivated clones, which hardens obtaining homogenous desired features such as the quantity of seeds, and the quality and yield of the liquid wax. Hence, the majority of cultivation is performed using vegetative propagation of mother plants, which reduces genetic variability but paradoxically leads to genetic vulnerability (Al-Obaidi et al. 2017). In light of this, it is especially important to understand the genotypes responsible for the quality of jojoba propagation and the content of jojoba seeds, as well as additional compounds. Several studies were published in this regard. Of these, few demonstrated variability in the content and quality of jojoba oil, and additional compounds, such as simmondsin (will be later elaborated) content among different jojoba genotypes (Benzioni et al. 2005; Al-Soqeer et al. 2012). In parallel, several methods for detecting genetic polymorphism and providing genotypes with molecular fingerprinting have been published and described in more detail in (Al-Obaidi et al. 2017). Clearly, it is still worthwhile to place great emphasis on understanding the genetics of jojoba. In addition, the impact of cultivation seems to play a key role in its variable yields (Atteya et al. 2018; Khattab et al. 2019).

Market and usages

The uniqueness of the jojoba plant stems from the unusual presence, amount, and chemical structure of liquid wax in its seeds, which consists of approximately 50% of the seed weight (Al-Widyan & Al-Muhtaseb 2010). Jojoba wax, also termed jojoba oil, is comprised of long-chain esters. These can be exploited

in several industrial applications, most prominent are pharmaceuticals and cosmetics, due to the structural resemblance with human skin sebum and structural properties. Additional industrial uses that previously utilized whale sperm oil take advantage of jojoba oil in the production of plastics, detergents, renewable energy, and lubricants (Al-Widyan & Al-Muhtaseb 2010; Sandouqa & Al-Hamamre 2019; Vaillant et al. 2019). As a high yielding non-edible oil, its use as a raw material for the creation of biodiesel has been considered (Sandouqa & Al-Hamamre 2019). Of note, jojoba oil global production is growing rapidly, and has already exceeded 15,000 tons (2018) and is expected to reach 22,000 tons by 2022 (Worldwide analysis on the jojoba oil market; Bilin et al. 2018). This tremendous growth may be due to market demands, or alternatively, suggests an uncontrolled increase that will result in consequent over-supply, emphasizing the need to develop novel jojoba-based products and usages.

Aside from the oil, other parts of the jojoba plant possess properties that may become valuable (Wisniak 1994), e.g. jojoba meal and leaves were found to have various other potential uses. The meal is rich in proteins and fibers, and as such, has the potential to be used as food or staple feed. However, it contains anti-nutritional factors, a problem that still has to be industrially overcome (Reddy & Chikara 2010). The meal was also suggested as an anti-rodent agent (Al-Obaidi et al. 2017). In addition, leaves were found to possess potential medicinal properties, as further described in detail below. From an ecological perspective, the plant can also contribute to combat desertification due to its ability to grow in arid areas (Al-Obaidi et al. 2017). Like its usages, jojoba-based analyses can be roughly divided into two main sections: evaluation of its liquid

wax and identification of phytochemicals in other plant parts, including the jojoba meal obtained following the extraction process.

Oil extraction methods and concomitant composition

As mentioned earlier, jojoba wax is comprised of approximately 50% seed weight. However, to obtain pure oil, several steps are required. After the initial harvest, jojoba seeds are first cleaned to remove rough debris, such as dust and leaves, and are then typically left to dry and dehull (Arya & Khan 2016). To obtain a high yield, a combination of mechanical pressure and chemical extraction using hexane (or other organic solvents) is necessary (Wisniak 1994). The downside of this process is the environmental impact and economic price of the organic solvent. Usage of other solvents, such as chloroform and isopropanol has been tested and found to be less efficient and occasionally with leftover traces in the oil (Wisniak 1994; Abu-Arabi et al. 2000). Supercritical CO₂, which is a solvent-free method, showed similar or higher oil yield, however, typically its initial establishment price is high. In addition to its pre-mentioned disadvantages, solvent extraction also results in lower quality wax. Thus, jojoba oil is currently mechanically extracted by cold-press method, at low heat, to conserve its quality characteristics, e.g. tocopherol contents (El-Mallah & El-Shami 2009). Naturally, the oil yield of this method is relatively low, as some oil is retained in the meal (Kibbutz Hazerim, personal communication), but the resulting wax is of high quality.

Jojoba oil is a mixture of long-chain (C36–C46) esters of fatty acid and fatty alcohol, distinguishing it from other vegetable oils, which are triglyceride-based (Figure 2) (Mokhtari et al. 2019). This gold-yellow odorless oxidation-resistant wax is liquid at room tempera-

ture, which is another unique characteristic differentiating it from other natural waxes used in cosmetics (Le Dréau et al. 2009; Zięba et al. 2015).

Meticulous analysis demonstrated that the main fatty chains composing the wax are C20:1 and C22:1 of both acids and alcohols, with changes of the exact percentage linked to both genetic and environmental factors (Busson-Breysse et al. 1994; Agarwal et al. 2018). Trace elements have also been reported in the wax (Agarwal et al. 2018). Free fatty acids, also present in the wax, are negatively correlated with wax quality (El-Mallah & El-Shami 2009). Tocopherols and phytosterols, two other groups of bioactive medicinal molecules, have also been observed in jojoba oil. Tocopherols are common in oil crops, serving as lipophilic antioxidants and oil stabilizers that also possess health-promoting properties. In jojoba oil, they were reported at relatively high concentrations of 417 ppm, with gamma-tocopherol as the main form (79.2%), and alpha, beta and delta-tocopherol at lower concentrations (El-Mallah & El-Shami 2009). Phytosterols are another group of characteristic compounds of oil, with structural resemblance to cholesterol. Thus, their consumption is recommended as cholesterol-lowering treatment. In jojoba, various types were recorded, including sitosterol, campesterol and stigmasterol (Busson-Breysse et al. 1994; Ogbe et al. 2015).

Chemical parameters for wax quality analysis have not been established yet, although such parameters are very common in other oil crops, e.g. olive oil. Quality grading might allow growers to receive better compensations for their high-quality wax.

Jojoba meal and other plant part

The remaining cake after oil extraction process (jojoba meal) is rich in dietary fibers and proteins.

Figure 2. Jojoba oil (wax) structure.

Figure 3. Simmondsin and derivatives.

However, the presence of simmondsin, a unique jojoba secondary metabolite and a principal bioactive component of jojoba, and its derivatives, prevents its use as food or animal feed purposes. Simmondsin, 2-(cyanomethylene)-3-hydroxy-4,5-dimethoxycyclohexyl-beta-D-glucoside (Figure 3) is present in seeds, hulls, leaves, twigs and roots of jojoba. Approximately 5% of jojoba meal is simmondsin with additional 0.5–1% of derivatives, of which the 2'-ferulate is the main one. Isolated and characterized by Elliger et al. almost thirty years ago, this unique molecule is toxic at high concentrations and has an anorexic action at lower levels (Elliger et al. 1973). Due to its cyano group, it is listed as an antinutritional compound and thorough removal of its content is required prior to usage as animal feed. Thus, several methodologies have been investigated for the neutralization/removal of this agent prior to usage as feed supplements, including chemical and enzymatic approaches (Verbiscar et al. 1981; Bouali et al. 2008; Elsanhoty et al. 2017). However, usage of simmondsin at low and at non-toxic range may be harnessed as a health-promoting agent as specified below. Unlike its well-characterized oil, other parts of jojoba plant are yet to be fully explored for their phytochemical composition. So far, research was mainly performed on simmondsin and derivatives, and on selected bioactive polyphenolic compounds (described below). To date, comprehensive in-depth metabolomic evaluation of the leaf, roots, twigs and meal is still lacking and therefore other unique compounds may be discovered in the near future.

Medicinal properties

Antioxidant capacity

When evaluating the medicinal properties of a plant, one of the most basic and simple characterizations relies on the evaluation of its antioxidant capacity and total phenolic content. Indeed, several studies have evaluated jojoba antioxidant activity with various methods and extraction methodologies.

Kara has evaluated the scavenging capacity of methanolic and ethanolic extract of both the seed and leaf of jojoba by the 2,2'-Diphenyl-1-picrylhydrazyl (DPPH) method (Kara 2017). This colorimetric method uses a stable free radical, which becomes discolored in the presence of an anti-oxidant, either transferring an electron or donating hydrogen (Brand-Williams et al. 1995). In this system, all jojoba extracts were found to possess similar scavenging efficacy (approximately 40% at 500 µg/ml). However, when determined by linoleic acid bleaching assay, the antioxidant activity of the methanolic and ethanolic leaf extracts was twice as much as those measured for the seeds (45 nmol/g). These conflicting results may be due to the inherent difference between the methods and the favor of lipophilic moieties in the second system. An interesting study by Wagdy et al. investigated the possible usage of the seed hull extract and found a considerable scavenging effect in similar methodologies described above (Wagdy & Taha 2012). This approach is of high interest, as typically the hulls are a waste product of jojoba wax production, while these authors showed that the hulls may provide additional value in the industry. The impact of cultiva-

Figure 4. Bioactive flavonoids isolated from jojoba leaf (adapted from Abdel-Mageed et al. 2014).

tion conditions on the antioxidant properties has also been investigated, and it was reported that jojoba antioxidant activity of the methanolic leaf extract could be increased by 50% in enriched cultivation conditions (addition of putrescine and *Moringa* extract) in comparison to control conditions (Taha et al. 2015).

Abdel-Wahhab *et al.* investigated the hepatoprotective impact of jojoba ethanolic seed extract *in vivo*. Both low and high dosage (0.5 and 1 mg/kg, respectively) attenuated liver oxidative stress in mycotoxin-induced damage model. Malondialdehyde (MDA) levels, an important ROS-derived lipid peroxidation product of polyunsaturated fatty acids, was doubled in the mycotoxin group but dropped upon jojoba treatment. Concomitantly, the liver levels of the anti-oxidant enzyme superoxide dismutase (SOD) were raised to those of the control group (Abdel-Wahhab et al. 2015). However, these impressive results may not be exclusively attributed to direct jojoba antioxidant capacity, and can result from secondary action of jojoba extract, as it also reduced inflammation and hepatocellular necrosis in that model (Abdel-Wahhab et al. 2015).

The majority of studies regarding jojoba do not pinpoint the active compound assigned for the antioxidant capacity of the above-mentioned extracts. In-depth chemical analysis is still required in order to gain insight into the active molecule or molecules. A comprehensive work was performed by Abdel-Mageed et

al, identifying flavonoid aglycones from the ethanolic leaf extract of jojoba (Abdel-Mageed et al. 2014). Quercetin 3-methyl ether (isorhamnetin), quercetin 3,3-dimethylether, and quercetin showed strong antioxidant activity and lipoxygenase inhibition (Fig. 4). In a recent study conducted in hyperglycemia-induced oxidative stress model, it was found that simmondsin, one of the principal bioactive components in jojoba mentioned above, is sufficient to reduce pancreatic beta-cell damage, which may explain the protective antioxidant properties of jojoba extract. The contribution of tocopherol on the antioxidant capacity of the oil should also be evaluated. The collective results demonstrate that mainly leaf and hull extracts of jojoba, may possess strong antioxidant properties that can be used as a remedy for oxidative stress-related pathologies. However, it should be noted that the safety of such extracts should be clinically validated for both their safety and efficacy prior to usage as food supplements or other health-promoting products.

Anti-fungal and anti-microbial properties

New antimicrobial agents are of constant need due to the rise in antibiotic-resistant germs. The hypothesis that jojoba may present such properties has been investigated by several research groups. Jojoba extracts derived from hulls (extracted in 80% methanol, ethanol,

acetone, isopropanol and ethyl acetate) showed significant anti-bacterial properties (Wagdy & Taha 2012); *Escherichia coli*, *Staphylococcus aureus*, *Bacillus cereus*, *Listeria monocytogenes* and *Salmonella typhimurium* growth was inhibited in various degrees of efficacy. The authors suggested that this phenomenon is in correlation with ethnobotanical knowledge. However, the active molecule(s) or mechanism of action (MOA) were not elucidated in this preliminary evaluation. Abu-Salem and Ibrahim have also shown high efficacy on both bacteria and fungi of root extract and latex of the plant (Abu-Salem & Ibrahim 2014). In separate works, antibacterial and antifungal activities were also found for jojoba oil (Pooja Umaiyal et al. 2016; Al-Ghamdi et al. 2019). Thus, it seems that the active agent(s) are not restricted to a specific part of the plant. However, it is important to mention that several other reports evaluating similar extracts found no noticeable antimicrobial activity. This discrepancy may be due to the bacterial strains used, as well as the cultivating and genetic differences between the plants (Elnimiri & Nimir 2011; Al-Qizwini et al. 2014). In addition, although all researchers used routine evaluation systems (agar diffusion assay, disc diffusion assay and minimal inhibitory concentration (MIC)), these models may be different between laboratories and any modification may affect the obtained results significantly (Balouiri et al. 2016).

In a very interesting examination, the two glucosides, simmondsin and simmondsin 2-ferulate have been isolated from jojoba, and tested for their bioactivity (Abbassy et al. 2007). In that study, both agents showed high efficacy with moderated potency (Half maximal effective concentration (EC_{50}) of approximately 150 mg/l) against plant pathogenic fungi. Similar studies are required in order to attribute the antimicrobial properties to simmondsin, its derivatives, and other compounds.

Dermatology and skin care

The skin is a vital homeostatic organ that acts as a physical, chemical, and biological barrier (Gvirtz et al. 2020; Kahremany et al. 2020). As chronically exposed to deleterious actions of the environment, its appearance may be affected and extrinsic aging of the skin may become visible (Choi 2019; Ogen-Shtern et al. 2020). Jojoba oil has long been used in dermo-cosmetic products. Amongst its main functions, jojoba is a key component of the oil phase in numerous topical

formulations (Di Berardino et al. 2006). In addition to its structural importance to the formulation stability, jojoba oil also serves as a carrier and enhancer of the active compounds (Nasr et al. 2016). In addition, the antioxidant and tocopherol content of jojoba mentioned above may be used to reduce skin-related oxidative stress (Kahremany et al. 2019). However, it should be noted that jojoba can also exert contact dermatitis (Wantke et al. 1996; Di Berardino et al. 2006) and may be absorbed systemically if high topical amounts are applied (Yaron et al. 1980; Matsumoto et al. 2019).

Numerous dermo-cosmetic products use jojoba as part of their formulation and to date, almost 200 International Nomenclature of Cosmetic Ingredients (INCI) entries are listed with jojoba and derivatives. However, its beneficial potential as an active agent in skin care has not been thoroughly investigated, including the lack of large control trial supporting its effectiveness while used in massage, a key end-usage in the current jojoba oil market.

Several clinical cosmetic trials have investigated the properties of jojoba dermal applications. For instance, it was reported that the addition of jojoba hydrolyzed ester to lotions can enhance skin hydration by reduction of trans-epidermal water loss (TEWL) (Meyer et al. 2008). In a separate study, increasing concentrations of jojoba oil in cream formulations enhanced their moisturizing properties (Zięba et al. 2015). Nevertheless, it is exceedingly difficult to elucidate the impact of jojoba in this setup, separating its impact from the rest of the formula. Thus, to evaluate whether this liquid wax has direct action on epidermal and dermal layers, a more direct approach is of need. To address this, Ranzato et al. have used the scratch assay, in which a wound is inflicted by a tip on dermal keratinocytes and fibroblast cell monolayers (Ranzato et al. 2011). Their data demonstrated that jojoba wax is safe at a wide range of concentrations and may enhance wound closure in both keratinocytes and fibroblasts cultures. They also have shown that jojoba treatment triggers collagen synthesis in fibroblasts. Ca^{2+} dependent mechanism that requires the involvement of the PI3K–Akt–mTOR pathway and of the p38 and ERK1/2 was suggested by the authors.

Interestingly, the beneficial impact of jojoba oil on psoriasis has also been suggested (Pazyar & Yaghoobi 2016). This chronic inflammatory skin disease is typically displayed as plaques, covered with thick, silvery, shiny scales that hampers the quality of life of the patients (Rendon & Schäkel 2019). El Mogy suggested

that jojoba oil without or with 2% salicylic acid can improve psoriatic skin (El Mogy 2005). In two clinical trials, jojoba oil-based microemulsion was used as a platform for enhancing the action of commercial drugs (Nasr et al. 2016; Ramez et al. 2018). Further *in vitro* and clinical studies are required to understand the potential use of jojoba in psoriasis.

Acne-prone, lesioned skin is the result of combined excessive sebum production, bacterial settlement, and inflammation. Results of a study by Meier et al. show that treatment with jojoba oil clay facial masks can reduce pustules, papules, cysts and comedones (Meier et al. 2012). Importantly, the study demonstrated the impact of dermatological conditions on quality of life at a cost-effective treatment regime. Other animal-studies experiments, demonstrating anti-inflammatory action of jojoba oil (see below) may also be relevant to the effect on acne.

Metabolic syndrome and metabolism

The metabolic syndrome is a set of metabolic abnormalities such as insulin resistance, nonalcoholic fatty liver disease, glucose intolerance, obesity and type 2 diabetes. A recent study by Belhadj et al. demonstrated that incorporation of jojoba seed in the diet of rats might reduce the deleterious effects of a high-fat diet and high fructose diet (Belhadj et al. 2020). In their study, a marked reduction was observed in insulin resistance, fat mass and renal complications in the treatment group. These findings were accompanied by reduction in the rat body mass, and thus the author concluded that this anorexic impact is the main cause of the jojoba regimen. Their results are also in line with previous studies demonstrating that jojoba leaf extract may reduce body weight in rats (Makpoul et al. 2017). Interestingly, simmondsin, present in both jojoba oil and leaf extracts, has already been shown to reduce food intake in rats, suggesting that the impact of jojoba on appetite is mediated by this unique molecule (Cokelaere et al. 1995). In addition, a direct effect of simmondsin was observed in pancreatic beta-cells, suggesting a multi-site action of the molecule (Belhadj et al. 2018).

Additional medicinal values and the future of jojoba research

Other scattered reports have shown additional health beneficial impacts of jojoba oil and extracts. For

instance, jojoba has been reported to possess anti-inflammatory properties, both *in vitro* and *in vivo* (Habashy et al. 2005). This may be linked to the ability of the plant extract and simmondsin to inhibit with high potency both lipoxygenase (LOX) and cyclooxygenase (COX), key enzymes in the inflammation cascade. LOX and COX are responsible mainly for the metabolism of arachidonic acid, generating its downstream signaling and inflammatory mediators, such as prostaglandins, leukotrienes and lipid peroxidation by products (Cohen et al. 2013; Abdel-Mageed et al. 2014, 2016). Furthermore, jojoba leaf extracts at as low as EC_{50} 2 μ g/ml have been reported to present an anti-viral effect on herpes simplex viruses type 1 and 2 (HSV-1, HSV-2) and varicella-zoster virus (Yarmolinsky et al. 2010). Anti-cancer cytotoxicity was also demonstrated in human melanoma (MV 3), breast (MCF 7), and colorectal (HCT 116) tumor cell lines as well as inhibition of angiogenesis, required for tumor growth (D'oosterlynck & Raes 2008; Al-Qizwini et al. 2014; Al-Obaidi 2019).

Generally, jojoba usage may be separated roughly into two branches: the use of its unique oil, and the use of extracts obtained from other parts of the plant. Currently, the jojoba liquid wax is mainly used as a substrate for the formulation or as an ingredient with an active role. However, as it was demonstrated, the whole plant, including leaves, roots and hulls can be used as a source of bioactive molecules and this direction should also be developed. A thorough investigation using metabolomic tools may reveal more unique active compounds. Another difficulty in jojoba research is the current scarcity of commercially available simmondsin and derivatives, thus more sources are of need in order to understand the entire pharmaceutical potential.

Acknowledgments

This study was supported by "Nitzan" industrial collaboration grant from the ministry of Agriculture and Rural Development (Israel, grant no 20-06-0072) and Jojoba Desert (kibbutz Hazerim). G.C, N.O.S. (Regional R&D Center, 580458776) and SK (Scholarship number 3-16752) are partially supported by the Israeli ministry of science and technology. The authors would like to thank Dr. Sarit Melamed and Dr. Arnon Dag for their vital perspective intertwined in this review.

References

- Abbassy MA, Abdelgaleil SAM, Belal ASH, Rasoul MAAA. 2007. Insecticidal, antifeedant and antifungal activities of two glucosides isolated from the seeds of *Simmondsia chinensis*. *Ind Crops Prod.* 26(3):345–350. DOI 10.1016/j.indcrop.2007.04.005.
- Abdel-Mageed WM, Bayoumi SAH, Radwan AA, Salem-Bekhit MM, Abd-Alrahman SH, Basudan OA, Sayed HM. 2014. *Simmondsia chinensis*: A rich source of bioactive flavonoids and lignans. *Ind Crops Prod.* 60:99–103. DOI 10.1016/j.indcrop.2014.06.007.
- Abdel-Mageed WM, Bayoumi SAL, Al-Wahaibi LH, Li L, Sayed HM, Abdelkader MSA, El-Gamal AA, Liu M, Zhang J, Zhang L, Liu X. 2016. Noncyanogenic Cyanoglucoside Cyclooxygenase Inhibitors from *Simmondsia chinensis*. *Org Lett.* 18(8):1728–1731. DOI 10.1021/acs.orglett.6b00206.
- Abdel-Wahhab M, Joubert O, El-Nekeety A, Sharaf H, Abu-Salem F, Rihn B. 2015. Dietary incorporation of jojoba extract eliminates oxidative damage in livers of rats fed fumonisin-contaminated diet. *Hepatoma Res.* 2:78–86. DOI 10.4103/2394–5079.168078.
- Abu-Arabi MK, Allawzi MA, Al-Zoubi HS, Tamimi A. 2000. Extraction of jojoba oil by pressing and leaching. *Chem Eng J.* 76(1):61–65. DOI 10.1016/S1385-8947(99)00119-9.
- Abu-Salem FM, Ibrahim HMA. 2014. Antimicrobial Activity and Phytochemicals Screening of Jojoba (*Simmondsia chinensis*) Root Extracts and Latex. *Int J Biol Biomol Agric Food Biotechnol Eng.* 8(5):516–22. DOI 10.5281/zenodo.1094407.
- Agarwal S, Arya D, Khan S. 2018. Comparative fatty acid and trace elemental analysis identified the best raw material of jojoba (*Simmondsia chinensis*) for commercial applications. *Ann Agric Sci.* 63(1):37–45. DOI 10.1016/j.aas.2018.04.003.
- Al-Ghamdi A, Elkholy T, Abuhelal S, Al-Abbadi H, Qahwaji D, Khalefah N, Sobhy H, Abu-Hilal M. 2019. Against antibacterial and antifungal activity of jojoba wax liquid (*Simmondsia chinensis*). *Pharmacogn J.* 11(1):191–194. DOI 10.5530/pj.2019.11.31.
- Al-Obaidi JR. 2019. Contribution of Jojoba (*Simmondsia chinensis*) Products in Human Health. In: *Plant Hum Heal.* Vol. 2. Cham: Springer International Publishing; p. 303–312. DOI 10.1007/978-3-030-03344-6_12.
- Al-Obaidi JR, Halabi MF, AlKhalifah NS, Asanar S, Al-Soqeer AA, Attia MF. 2017. A review on plant importance, biotechnological aspects, and cultivation challenges of jojoba plant. *Biol Res.* 50(1):25. DOI 10.1186/s40659-017-0131-x.
- Al-Qizwini H, Al-Khateeb E, Mhaidat NM, Maraqa A. 2014. Antioxidant and antimicrobial activities of Jordanian *Simmondsia chinensis* (link) ck schneid. *Eur Sci J.* 10(27):229–241.
- Al-Soqeer A, Motawei MI, Al-Dakhil M, El-Mergawi R, Al-Khalifah N. 2012. Genetic variation and chemical traits of selected new jojoba (*Simmondsia chinensis* (Link) Schneider) genotypes. *JAOCS, J Am Oil Chem Soc.* 89(8):1455–1461. DOI 10.1007/s11746-012-2034-x.
- Al-Widyan MI, Al-Muhtaseb MA. 2010. Experimental investigation of jojoba as a renewable energy source. *Energy Convers Manag.* 51(8):1702–1707. DOI 10.1016/j.enconman.2009.11.043.
- Arya D, Khan S. 2016. A review of *simmondsia chinensis* (jojoba) “the desert gold”: A multipurpose oil seed crop for industrial uses. *J Pharm Sci Res.* 8(6):381–388.
- Ash GJ, Albiston A, Cothier EJ. 2005. Aspects of Jojoba Agronomy and Management. In: *Adv Agron.* p. 409–437. DOI 10.1016/S0065-2113(04)85007-7.
- Atteya AKG, Al-Taweel SK, Genaidy EAE, Zahran HA. 2018. Effect of gibberellic acid and zinc sulphate on vegetative, flowering, seed yield and chemical consistent of jojoba plant (*Simmondsia chinensis*). *Indian J Agric Res.* 52(5):542–547. DOI 10.18805/IJARE.A-349.
- Balouri M, Sadiki M, Ibnsouda SK. 2016. Methods for in vitro evaluating antimicrobial activity: A review. *J Pharm Anal.* 6(2):71–79. DOI 10.1016/j.jpha.2015.11.005.
- Belhadj S, Dal S, Khaskhoussi F, Maillard-Pedracini E, Hentati O, Sigrist S. 2020. Anorexic and metabolic effect of jojoba: Potential treatment against metabolic syndrome and hepatic complications. *Nutr Metab.* 17(1):1–10. DOI 10.1186/s12986-020-00441-3.
- Belhadj S, Hentati O, Hamdaoui G, Fakhreddine K, Maillard E, Dal S, Sigrist S. 2018. Beneficial effect of Jojoba seed extracts on hyperglycemia-induced oxidative stress in RINm5f beta cells. *Nutrients.* 10(3):834. DOI 10.3390/nu10030384.
- Benzioni A. 2010. Jojoba Domestication and Commercialization in Israel. *Hortic Rev (Am Soc Hortic Sci).* 17:223–266. DOI 10.1002/9780470650585.ch7.
- Benzioni A, Mills D, Van Boven M, Cokelaere M. 2005. Effect of genotype and environment on the concentration of simmondsin and its derivatives in jojoba seeds and foliage. *Ind Crops Prod.* 21(2):241–249. DOI 10.1016/j.indcrop.2004.04.005.
- Bilin M, Alshanaheh F, Evcil A, Savas MA. 2018. A Comparative Examination of the Quality of Jojoba Seed Oil Harvested on the Mesaoria Plain of Cyprus Island. In: *ISMSIT 2018—2nd Int Symp Multidiscip Stud Innov Technol Proc.* p. 1–4. DOI 10.1109/ISMSIT.2018.8567052.
- Bouali A, Bellirou A, Boukhatem N, Hamal A, Bouammali B. 2008. Enzymatic detoxification of jojoba meal and effect of the resulting meal on food intake in rats. *Nat Prod Res.* 22(7):638–647.
- Brand-Williams W, Cuvelier ME, Berset C. 1995. Use of a free radical method to evaluate antioxidant activity. *LWT—Food Sci Technol.* 28(1):25–30. DOI 10.1080/14786410701614341.
- Busson-Breyse J, Farines M, Soulier J. 1994. Jojoba wax: Its esters and some of its minor components. *J Am Oil Chem Soc.* 71(9):999–1002. DOI 10.1007/BF02542268.
- Chase MW, Christenhusz MJM, Fay MF, Byng JW, Judd WS, Soltis DE, Mabberley DJ, Sennikov AN, Soltis PS, Stevens PF, et al. 2016. An update of the Angiosperm Phylogeny Group classification for the orders and families of flowering plants: APG IV. *Bot J Linn Soc.* 181(1):1–20. DOI 10.1111/boj.12385.
- Choi EH. 2019. Aging of the skin barrier. *Clin Dermatol.* 37(4):336–345. DOI 10.1016/j.jclindermatol.2019.04.009.
- Cohen G, Riahi Y, Sunda V, Deplano S, Chatgililoglu C, Ferreri C, Kaiser N, Sasson S. 2013. Signaling properties of 4-hydroxyalkenals formed by lipid peroxidation in diabetes. *Free Radic Biol Med.* 65:978–987. DOI 10.1016/j.freeradbiomed.2013.08.163.

- Cokelaere MM, Busselen P, Flo G, Daenens P, Decuyper E, Kühn E, Van Boven M. 1995. Devazepide reverses the anorexic effect of simmondsin in the rat. *J Endocrinol.* 147(3):473–477. DOI 10.1677/joe.0.1470473.
- Daugherty PM, Sineath HH, Wastler TA. 1958. Industrial raw materials of plant origin. IV. A survey of *Simmondsia chinensis* (Jojoba). *Econ Bot.* 12(3):296–304. DOI 10.1007/BF02859773.
- Di Berardino L, Di Berardino F, Castelli A, Della Torre F. 2006. A case of contact dermatitis from jojoba. *Contact Dermatitis.* 55(1):57–58. DOI 10.1111/j.0105-1873.2006.0847e.x.
- D'oosterlyncx A, Raes S. 2008. Simmondsin for use as angiogenesis inhibitor. U.S. Patent No. 7,387,999.
- Elliger CA, Waiss ACJ, Lundin RE. 1973. Simmondsin, an unusual 2-cyanomethylenecyclohexyl glucoside from *Simmondsia californica*. *Chem Informationsd.* 1:209–2212. DOI 10.1002/chin.197401405.
- El-Mallah MH, El-Shami SM. 2009. Investigation of liquid wax components of Egyptian jojoba seeds. *J Oleo Sci.* 58(11):543–548. DOI 10.5650/jos.58.543.
- El Mogy NS. 2005. Medical effect of jojoba oil. U.S. Patent No. 6,846,499.
- Elnimiri K, Nimir H. 2011. Biological and chemical assessment of the Sudanese jojoba (*Simmondsia chinensis*) oil. *Int J Nat Prod Pharm Sci.* 2(1):28–39.
- Elsanhoty RM, Al-Soqeer A, Ramadan MF. 2017. Effect of detoxification methods on the quality and safety of jojoba (*Simmondsia chinensis*) meal. *J Food Biochem.* 41(5):e12400. DOI 10.1111/jfbc.12400.
- Gisser H, Messina J, Chasan D. 1975. Jojoba oil as a sperm oil substitute. *Wear.* 34(1):53–63. DOI 10.1016/0043-1648(75)90308-7.
- Gvartz R, Ogen-shtern N, Cohen G. 2020. Kinetic cytokine secretion profile of LPS-induced inflammation in the human skin organ culture. *Pharmaceutics.* 12(4):299. DOI 10.3390/pharmaceutics12040299.
- Habashy RR, Abdel-Naim AB, Khalifa AE, Al-Azizi MM. 2005. Anti-inflammatory effects of jojoba liquid wax in experimental models. *Pharmacol Res.* 51(2):95–105. DOI 10.1016/j.phrs.2004.04.011.
- Kahremany S, Babaev I, Gvartz R, Ogen-Stern N, Azoulay-Ginsburg S, Senderowitz H, Cohen G, Gruzman A. 2019. Nrf2 Activation by SK-119 Attenuates Oxidative Stress, UVB, and LPS-Induced Damage. *Skin Pharmacol Physiol.* 32(4):173–181. DOI 10.1159/000499432.
- Kahremany S, Hofmann L, Gruzman A, Cohen G. 2020. Advances in understanding the initial steps of pruritoceptive itch: How the itch hits the switch. *Int J Mol Sci.* 21(14):1–45. DOI 10.3390/ijms21144883.
- Kara Y. 2017. Phenolic Contents and Antioxidant Activity of Jojoba (*Simmondsia chinensis* (Link). Schindler. *Int J Second Metab.* 4(2):142–147. DOI 10.21448/ijsm.309538.
- Khattab EA, Afifi MH, Amin GA. 2019. Significance of nitrogen, phosphorus, and boron foliar spray on jojoba plants. *Bull Natl Res Cent.* 43(1):66. DOI 10.1186/s42269-019-0109-7.
- Kumar S, Mangal M, Dhawan AK, Singh N. 2012. Biotechnological advances in jojoba [*Simmondsia chinensis* (Link) Schneider]: Recent developments and prospects for further research. *Plant Biotechnol Rep.* 6(2):97–106. DOI 10.1007/s11816-011-0211-2.
- Le Dréau Y, Dupuy N, Gaydou V, Joachim J, Kister J. 2009. Study of jojoba oil aging by FTIR. *Anal Chim Acta.* 642(1–2):163–170. DOI 10.1016/j.aca.2008.12.001.
- Makpoul KR, Ibraheem AA, Shokry AM. 2017. Assessment of nutritional value, chemical composition and anti-obesity effect of dried Jojoba leaves in North Sinai. *J Nutr Hum Heal.* 1(1):11–16. DOI 10.35841/nutrition-human.1000102.
- Matsumoto Y, Ma S, Tominaga T, Yokoyama K, Kitatani K, Horikawa K, Suzuki K. 2019. Acute effects of transdermal administration of jojoba oil on lipid metabolism in mice. *Med.* 55(9):594. DOI 10.3390/medicina55090594.
- Meier L, Stange R, Michalsen A, Uehleke B. 2012. Clay jojoba oil facial mask for lesioned skin and mild acne-results of a prospective, observational pilot study. *Forsch Komplementarmed.* 19(2):75–79. DOI 10.1159/000338076.
- Meyer J, Marshall B, Gacula M, Rheins L. 2008. Evaluation of additive effects of hydrolyzed jojoba (*Simmondsia chinensis*) esters and glycerol: A preliminary study. *J Cosmet Dermatol.* 7(4):268–274. DOI 10.1111/j.1473-2165.2008.00405.x.
- Mokhtari C, Malek F, Manseri A, Caillol S, Negrell C. 2019. Reactive jojoba and castor oils-based cyclic carbonates for bio-based polyhydroxyurethanes. *Eur Polym J.* 113:18–28. DOI 10.1016/j.eurpolymj.2019.01.039.
- Nasr M, Abdel-Hamid S, Moftah NH, Fadel M, Alyoussef AA. 2016. Jojoba Oil Soft Colloidal Nanocarrier of a Synthetic Retinoid: Preparation, Characterization and Clinical Efficacy in Psoriatic Patients. *Curr Drug Deliv.* 14(3):426–432. DOI 10.2174/1567201813666160513132321.
- Ogbe RJ, Ochalefu DO, Mafulul SG, Olaniru OB. 2015. A review on dietary phytosterols: Their occurrence, metabolism and health benefits. *Pelagia Res Libr Asian J Plant Sci Res.* 5(4):10–21.
- Ogen-Shtern N, Chumin K, Cohen G, Borkow G. 2020. Increased pro-collagen 1, elastin, and TGF- β 1 expression by copper ions in an ex-vivo human skin model. *J Cosmet Dermatol.* 19(6):1522–1527. DOI 10.1111/jocd.13186.
- Pazyar N, Yaghoobi R. 2016. The Potential Anti-Psoriatic Effects of Jojoba Extract. *J Dermatological Res.* 1(1):14–15. DOI 10.17554/j.issn.2413-8223.2016.01.6.
- Pooja Umaiyal M, Gayathri R, Vishnupriya V, Geetha R V. 2016. Anti microbial activity of jojoba oil against selected microbes: An invitro study. *J Pharm Sci Res.* 8(6):528.
- Ramez SA, Soliman MM, Fadel M, Nour El-Deen F, Nasr M, Youness ER, Aboel-Fadl DM. 2018. Novel methotrexate soft nanocarrier/fractional erbium YAG laser combination for clinical treatment of plaque psoriasis. *Artif Cells, Nanomedicine, Biotechnol.* 46(sup1):996–1002. DOI 10.1080/21691401.2018.1440236.
- Ranzato E, Martinotti S, Burlando B. 2011. Wound healing properties of jojoba liquid wax: An in vitro study. *J Ethnopharmacol.* 134(2):443–449. DOI 10.1016/j.jep.2010.12.042.
- Reddy MP, Chikara J. 2010. Biotechnology advances in jojoba (*Simmondsia chinensis*). In: *Desert plants*. Springer; p. 407–421. DOI 10.1007/978-3-642-02550-1_19.
- Rendon A, Schäkel K. 2019. Psoriasis pathogenesis and treatment. *Int J Mol Sci.* 20(6):1475. DOI 10.3390/ijms20061475.
- Sandouqa A, Al-Hamamre Z. 2019. Energy analysis of biodiesel production from jojoba seed oil. *Renew Energy.* 130:831–842. DOI 10.1016/j.renene.2018.07.015.

- Taha LS, Taie HAA, Hussein MM. 2015. Antioxidant properties, secondary metabolites and growth as affected by application of putrescine and moringa leaves extract on jojoba plants. *J Appl Pharm Sci*. 5(01):030–036. DOI 10.7324/JAPS.2015.50106.
- Vaillant S, Peralta RD, Ramos LF, Wisniak J. 2019. Jojoba Oil (*Simmondsia Chinensis*) as a Natural Plasticizer for Ethylene Propylene Diene Monomer Elastomers. *Ind Eng Chem Res*. 58(43):20147–20153. DOI 10.1021/acs.iecr.9b03955.
- Verbiscar AJ, Banigan TF, Weber CW, Reid BL, Spencer Swingle R, Trei JE, Nelson EA. 1981. Detoxification of Jojoba Meal by *Lactobacilli*. *J Agric Food Chem*. 29(2):296–302. DOI 10.1021/jf00104a020.
- Wagdy SM, Taha FS. 2012. Primary assessment of the biological activity of jojoba hull extracts. *Life Sci J*. 9(2):244–253.
- Wantke F, Hemmer W, Götz M, Jarisch R. 1996. Contact dermatitis from jojoba oil and myristyl lactate/maleated soybean oil. *Contact Dermatitis*. 31(1):71–72. DOI 10.1111/j.1600-0536.1996.tb02126.x.
- Wisniak J. 1994. Potential uses of jojoba oil and meal—a review. *Ind Crops Prod*. 3(1–2):43–68. DOI 10.1016/0926-6690(94)90077–9.
- Worldwide analysis on the jojoba oil market. <https://finance.yahoo.com/news/worldwide-analysis-jojoba-oil-market-150615323.html>.
- Yarmolinsky L, Zaccai M, Ben-Shabat S, Huleihel M. 2010. Anti-Herpetic Activity of *Callissia fragrans* and *Simmondsia chinensis* Leaf Extracts In Vitro. *Open Virol J*. 4:57–62. DOI 10.2174/1874357901004010057.
- Yaron A, Benzioni A, More I. 1980. Absorption and distribution of jojoba wax injected subcutaneously into mice. *Lipids*. 15(11):889–894. DOI 10.1007/BF02534410.
- Zięba M, Małysa A, Noga A. 2015. Evaluation of selected quality features of creams with addition of jojoba oil designed for dry skin. *Polish J Cosmetol*. 18(2):132–137.