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Opuntia stricta (Haw): A review on its chemical composition, putative *in-vitro* antidiabetic mechanism of action and potential pharmacological uses in chronic disease

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Abstract
Opuntia species, which belong to the Cactaceae family, are well-known and have long been utilized in folk medicine. Scholars have been interested in the stems, fruits, and cladodes of *Opuntia* species in recent years because of their possible nutraceutical content and therapeutic properties. While *Opuntia stricta* (*O. stricta*) is a well-known Cactaceae family member, it is a relatively unknown herbal plant in Zambia, where it is viewed primarily as a flower and only a few local people use it as a complementary herbal medicine to manage chronic illnesses such as diabetes mellitus. Much is not known about its chemical composition and putative *in-vitro* antidiabetic pharmacological action. Therefore, this review provided experimental data regarding chemical composition, *in-vitro* pharmacological mechanism, and potential indications of *O. stricta* in the prevention and management of various chronic conditions.

Keywords: *Opuntia stricta*, antidiabetic mechanism, potential pharmacological

Introduction
Opuntia species (sp) (Cactaceae) are well-known and important, and are widely utilized in diverse indigenous systems of medicine to treat a variety of disorders such as asthma, inflammatory diseases, ulcers, and diabetes [1, 2]. The genus *Opuntia* contains about 200 species, mostly shrubby to low-growing clump-forming plants with flattened jointed stem segments called "pads" or "cladodes" that are usually covered with little prickly glochids with bigger spines every now and then [2, 3]. The majority of *Opuntia* species are native to North, Central, and South America, but they have also been introduced to Kenya, South Africa, Yemen, Ethiopia, and Madagascar [4-6].
The surge in demand for nutraceuticals has prompted further research into the chemical makeup and nutritional benefits of natural plants like *Opuntia* species [7]. The stem, fruit, and cladode of *Opuntia* species have been shown to contain significant levels of vital nutrients like antioxidants, betalains, and amino including taurine, vitamins, and minerals [6, 7].

Scientific, alternative and English names of *Opuntia stricta*
The scientific name for *O. sricta* is *Opuntia stricta* (Haw.) and it is also known by other alternative names (synonyms) like *Cactus dillenii*, *Cactus Opuntia* var. *inermis*, *Cactus strictus* Haw, *Opuntia anahuacensis* Griffiths, *Opuntia dillenii* (Ker Gawl.) Haw, *Opuntia dillenii* var. *tehuantepecana*, *Opuntia inermis* (DC.) DC., *Opuntia horrida* Salm-Dyck ex DC. *Opuntia maritima* Raf, *Opuntia Opuntia vulgaris* var. *balearica and stricta* var. *dillenii*. *Opuntia stricta* is also known by the common and English names: Sweet Prickly-Pear, Erect Prickly Pear, Erect Prickly-Pear, Erect Pricklypear, Common Pest Pear, Coastal PricklyPear, Common Prickly Pear, Australian Pest Pear, Araluen Pear, Coastal Prickly-Pear, Eltham Indian-Fig,Cactus, Gayndah Pear, Pest Pear Of Australia, Pest Prickly-Pear,Sour Prickly Pear, Southern Spineless Cactus, Spineless Prickly Pear and Spiny Pest Pear [10]. *O. stricta* is also known in vernacular. In Germany, it is known as Feigenkaktus, Spain; Chumbera, Nopal Estricto, *Afrikaan*: Suurturksvy; *Chinese*: Xiang-Ren-Zhang, Hsian-Jen-Chang, Xian-Tao, Hsian-T'ao; *Mexico*: Yaaxpakan (Spanish); *Portuguese*: Opúntia, Palma-De-Espinho, Palmatória and India: Nagajemudu, Nagadali (Andhra Pradesh), Nagphana (Bengal), Chorhathalo (Gujrat), Nagphan, Chhittarthor (Himachal Pradesh), Hathhathoria, Naghhana (Hindi), Papaskalli, and Chappatigalli (Karnatka) [5].

Origin and Distribution

O. sricta is widely distributed around the world and is endemic to Ecuador, the United States, the Caribbean, Mexico, Colombia, and Venezuela, among other places. Some *O. stricta* species, such as *O. stricta* var. dillenii, are only found in the drier Caribbean Islands, while their presence on the mainland USA has been confirmed (Louisiana and Georgia). Many more nations, including Spain, South Australia, Sri Lanka, Yemen, France, Italy, South Africa, Tanzania, Kenya, Namibia, Zambia, Zimbabwe, and Ethiopia, have been introduced to *O. stricta*. It has swiftly naturalized and grown invasive in several countries. *O. stricta* has been reported in significant invasions in Australia, South Africa, and Namibia [2, 6, 11].

Taxonomic classification and description

O. stricta var. *stricta* and *O. stricta* var. *dillenii* are the two varieties (or sub-species) of *Opuntia stricta* Haworth that are now widely considered as a single species [5, 10]. Plants are spreading or erect succulent shrubs with many branches that reach a height of 1- 2 m and shallow fibrous roots. The stems are green to bluish-green, with a succession of flattened cladodes that are around 30 cm long by 15 cm wide and commonly 7-15 cm wide, as illustrated in figure 1. The cladodes' border appears scalloped between elevated areoles from which strong, somewhat curved yellowish spines emerge, ranging in number from completely missing to groups of one or more or clusters [5]. The spine clusters in *O. stricta* var. *dillenii* are yellow and small, measuring about 2- 5 mm long. The vivid yellow blooms, which resemble those of a cactus, bloom during the summer months. With yellowish inner tepals, filaments, anthers, and style and stigma lobes, the flowers are about 6–8 cm across [10]. *O. stricta* Haworth is most recognized by its barrel-shaped skin and red to purplish fruit, which is typically 4-6 cm long and 2-3 cm wide, as illustrated in figure 2. Except for a few glochids lodged in the little areoles, its outer surface is smooth and spineless. Seeds with a diameter of 4-5mm are embedded in a purple-colored pulp. The pulp has a sour flavor and approximately 60 hard-coated seeds [6, 10]

Fig 1: *Opuntia Sricta*, stem and cladodes

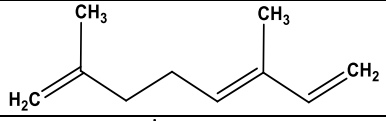
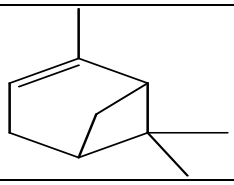
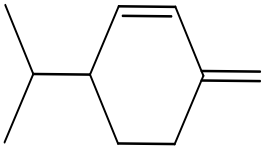
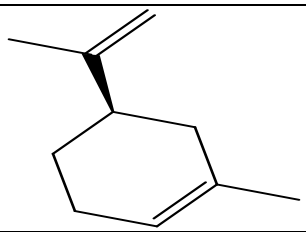
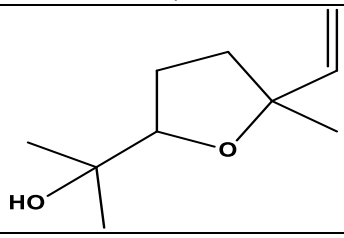
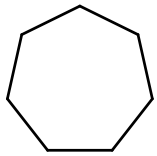
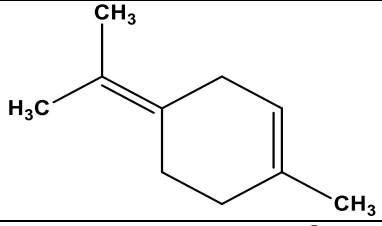
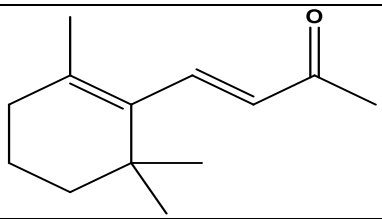
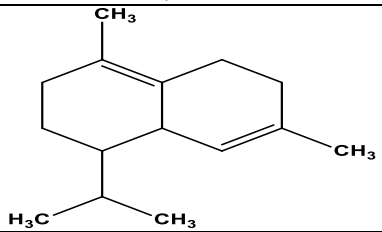
Fig 2: *Opuntia Sricta*, fruits and cladodes [12]

Chemical Composition of Cladodes

Opuntia species have a high nutritional value, owing to their mineral, vitamin, dietary fiber, and phytochemical content [13, 14]. The cladodes of *O. stricta* include essential oils, dietary fibers, antioxidants, carbohydrates, different flavonoids, vitamins, free radical scavengers, and certain phytochemicals, according to the body of knowledge [14, 15]. The chemical composition of cladodes is currently known to be affected by harvest season, maturity stage, postharvest treatment type of species, and environmental circumstances [8, 16]. According to one study, medium-aged cladodes of *Opuntia ficus indica* contained more total saponins, phytosterols, and indigestible fiber than younger and older cladodes, while young cladodes contained the most hydrolyzable and condensed tannins [8].

Cladodes of *Opuntia* species have been found to be a good source of dietary fibers [14, 17], which have been associated to lowering blood glucose levels by binding to dietary lipids and boosting excretion [18, 19]. The calcium (Ca) content of *Opuntia* cladodes has also been reported to be higher than that of vegetables, fruits, and nuts [20, 21]. Vitamin A, E, and C levels of *O. stricta* cladode per 100g of dry extract were 711.2 mg, 231.4 mg, and 2.9 mg, respectively, according to one study [15].

Table 1: Some chemical composition and their pharmacological properties of *Opuntia stricta* cladodes [15]

Name	Structure	Pharmacological action
Alpha-ocimene		Anti-inflammatory
Alpha-Pinene		Antineoplastic, anti-inflammatory. Antioxidant
beta-Phellandrene		Antineoplastic, anti-inflammatory. Antioxidant
Sylvestrene		*
Linalool oxide		Antineoplastic, anti-inflammatory. antioxidant
Cycloheptane		*
Terpinolene		Antineoplastic, anti-inflammatory. Antioxidant
beta-Ionone		Antineoplastic, anti-inflammatory. Antioxidant
delta-Amorphene		Antineoplastic, anti-inflammatory

*Pharmacological action not reported at the time of the study

Chemical Composition of Fruits

The fruit of *O. stricta* is one of the edible portions of the plant. Protein, calcium, nitrogen, moisture, energy, fat, copper, iron, magnesium, zinc, sodium, phosphorus, niacin, and vitamin are among the nutrients found in Stricta fruit [10, 22]. The nutritional value of *O. stricta* fruit per 100g was also recorded in one study. Proteins, oil, fiber, and carotenoids were found in larger concentrations in the seeds than in the

pulp and peal [22, 23]. Cactus pulp is also high in ascorbic acid, phosphate, calcium, iron, salt, sucrose, glucose, and fructose, according to the study [23].

Opuntia stricta fruit juice was discovered to be a possible source of betacyanin pigments and could be used as a natural red-purple food colorant in one of the studies. Only betanin and isobetanin (betacyanins) were found in *O. stricta* fruits, but no betaxantins [24]. The primary components of *O. stricta* fruit peels were likewise discovered to be trans-linalool oxide, cis-linalool oxide, and linalool [25].

Nutritive and medicinal uses

Nutritive properties

The fruits of *O. stricta* are edible raw and are widely cultivated [23]. Commercially, the fruits are used to make alcoholic beverages, candies, juices, teas, and jellies. Flowers produce a good amount of honey. *O. stricta* platyclads have been used to produce candy. Betacyanin pigments are found in *Opuntia stricta* fruit juice and are utilized as a natural red-purple culinary colorant [6, 10, 26]. The young leaves of *O. stricta* are commonly used in salads and as healthy vegetables. Mock-gherkins are made from the immature fruits [26].

Pharmacological properties of *Opuntia stricta* and other *Opuntia species*

The body of knowledge has suggested that *Opuntia* species might be of value in the management certain chronic diseases.

Antidiabetic effects

As shown in table 2, studies that have been conducted so far have shown that *Opuntia* species extract reduces blood glucose levels in diabetic induced rats [9, 23]. Therefore, these studies have supported the traditional use of *Opuntia* species in the treatment of diabetes mellitus type 2 by local people in many parts of the world [16, 27]. In one study, stems of *Opuntia ficus indica* stems reduced postprandial levels of glycemia in wistar rats and polysaccharides were identified to be responsible for the hypoglycemic effect [28]. It was also reported that the cactus acid fruit (xoconostle) that contained phenols and flavonoids bioactive compounds had inhibitory activities against alpha amylase and alpha glucosidase enzymes suitable for absorption of carbohydrates in the gastrointestinal tract (GIT) [29]. Very few studies have investigated, putative *in-vitro* antidiabetic mechanism of action of *Opuntia* species.

Table 2: Mechanism of actions of some *Opuntia* species investigated by certain studies

Authors	Evidence	Mechanism of action
Kunyanga *et al.*, 2014 [23]	*Opuntia stricta* cladode aqueous extract (1 mg/kg) significantly reduced blood glucose levels *in vivo*	**
Manzano *et al.*, 2017 [28]	*Opuntia ficus indica* stems reduce postprandial levels of glycemia in wistar rats	**
Hwang *et al.*, 2017	*Opuntia ficus-indica* showed antdiabetic activities in low-dose streptozotocin induced diabetic rats fed a high-fat diet	Inhibition of α-Glucosidase enzyme
Abdallah, 2008 [41]	*Opuntia. dillenii* fruit juice reduced bold glucose levels on streptozotocin induced diabetic rats	Proliferation of cells of Langerhans islets might have explained hypoglycaemic activity due to antioxidant activity
Patel *et al.*, 2017	*Opuntia* elatior fruit juice reduced blood glucose levels in diabetic induced albino rats	Not conducted
Leem *et al.*, 2016 [27]	*Opuntia ficus-indica* var. saboten significantly reduced blood glucose levels in rats	inhibiting glucose absorption from the intestine and enhancing glucose uptake from insulin-sensitive muscle cells through the AMPK/p38 MAPK signalling pathway
Hassan *et al.*, 2011 [33]	*Opuntia ficus-indica* fruit juice possessed hypoglycaemic effects in in alloxan-induced diabetic rats	**
Mokua *et al.*, 2016	prickly pear cactus cladode extracts lowered blood glucose levels in alloxan induced diabetes rats	**
Nunez-Lopez *et al.*, 2013	Medium and small cladode flours of *Opuntia ficus-indica* lowered postprandial blood glucose in streptozotocin-induced diabetic rats,	**
Bouhrim *et al.*, 2019 [30]	Seed oil of *Opuntia* dillenii reduced blood sugar levels in streptozotocin-induced diabetic rats [30]	**
Halmi *et al.*, 2012	*Opuntia ficus-indica* cladodes aqueous extract reduced blood sugar levels in diabetes induced albino rabbits	**

**: Not investigated

Anti-hyperlipideamic effects

The ability of various *Opuntia* species to minimize the risk of atherosclerotic diseases has been proven [31]. 160 dyslipidemia patients were placed into two groups in one study: a control group and an experimental group. For a month, an experimental group's diet was supplemented with 100g of *Opuntia* cactaceae. The results showed that the group receiving *Opuntia* cactaceae in their diet had considerably lower cholesterol and triglyceride levels [32]. Another study looked at the nutritional value, antioxidant activity, and effect of cactus pear (*Opuntia ficus-indica*) fruit juice on biochemical parameters, enzyme activities, and lipid peroxidation in alloxan-induced diabetic rats. Cactus pear fruit juice was also found to have hypocholesterolemic and antiatherogenic characteristics in this study [33].

Antibacterial effects

Moosazadeh *et al*. found that the essential oil of *Opuntia stricta F*. had antibacterial efficacy against standard strains of Pseudomonas aeruginosa, Bacillus cereus, Escherichia coli, Candida albicans, and Bacillus licheniformis in a fascinating study. The presence of thymol, which was identified as the primary component, was linked to the antibacterial activity, although the mechanism of action was unknown [12]. In another investigation, *Opuntia ficus-indica* cladodes were found to inhibit the growth of gram-positive bacteria and the generation of Staphylococcus aureus biofilms. There were a lot of phenolic chemicals in the cladodes, particularly p-hydroxybenzoic acid derivatives [34]. When compared to aqueous extracts of stem and fruit, methanol fruit extracts of *Opuntia ficus-indicas* cladodes displayed strong bacterial

inhibitory activity against *Bacillus subtilis*, *Pseudomonas aeruginosa*, and *Escherichia coli* [35].

Anti-viral effect

At concentrations of 25 g/ml and 20 g/mL, *Opuntia dillenii* floral extract showed potent antiviral activity against herpes simplex 1 and vaccinia [36]. The cactus plant *Opuntia streptacantha* was utilized in another investigation to stop intracellular virus replication and inactivate extracellular viruses. Viruses like the Equine herpes virus, pseudorabies virus, influenza virus, respiratory syncitial illness virus, HIV-1, and Herpes simplex virus Type 2 had both RNA and DNA replication inhibition [37]. Both research didn't look into the exact mechanism of action or the active inhibitory bioactive components in the extracts of the two *Opuntia* species.

Anti-oxidant properties

The antioxidant capabilities of vegetables and fruits have been considered to be responsible for their beneficial health effects [32, 38, 39]. Several antioxidants have been discovered in *Opuntia* species, including ascorbic acid, vitamin E, beta-carotene, carotenoids, betanin, indicaxanthin, quercetin, kaempferol, isorhamnetin, beta-Phellandrene, cysteine, reduced glutathione, and taurine [15, 33, 36]. Extracts of *Opuntia stricta* were shown to be high in phonolic biochemical components and to have good antioxidant activity in a recent study [15]. Another study used a 1, 1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging assay to reveal that the isolated non-polar chemicals from *O. stricta* fruit peels had substantial antioxidant activity [25]. Extracted polysaccharides from *O. stricta* fruit peels were found to have excellent antioxidant activity, and chemical analysis of the fruit peel extract revealed arabinose, mannose, galactose galacturonic acid, rhamnose, and glucose [40]. The antioxidant capabilities of *Opuntia* species have been linked to antibacterial, hypogylacemic, and antiinflammatory effects in some studies [25, 33, 41].

Anti-inflammatory properties

Plants from the *Opuntia* genus have been used for generations to treat inflammatory disorders like rheumatism and asthma [15, 42]. RAW 264.7 cells were used in a South African investigation to investigate the anti-inflammatory effect of *O. stricta* cladodes. Aqueous, ethanol, and acetone extracts of *O. stricta* cladodes were found to have anti-inflammatory effects [15]. The pharmacological effects of ethanol extracts of the fructus and stem of *Opuntia ficus-indica* were investigated in another investigation. In the CMC-pouch model in rats, the results demonstrated suppression of carrageenan-induced rat paw edema as well as a substantial inhibition of leukocyte migration [43]. In a follow-up study, the anti-inflammatory activity of *Opuntia elatior* Mill fruits was assessed in Albino wistar rats utilizing carrageenan-induced paw edema and neutrophil adhesion assays. *Opuntia* fruits were discovered to have anti-inflammatory activities that were dose-dependent [44].

Analgesic action

Writhing and tail-immersion tests in Albino wistar rats were used to assess the analgesic qualities of *Opuntia* fruit juice (OFJ). When compared to the control group, the OFJ at doses of 5, 10, and 15 ml/kg per oral inhibited the writhing responses of rats caused by intraperitoneal acetic acid administration, and at the dose of 15 ml/kg established a significant reduction in painful sensation caused by tail immersion in warm water [44]. In another study, hot plate and tail flick procedures were used to test extracts from *Opuntia ficus-indica* cladodes for their most popular application as an analgesic. Cladode extracts demonstrated significant analgesic effect at intraperitoneal dosages of 300, 500, and 1000 mg/kg body weight, according to the findings [45]. This data gives credence to the traditional use of *Opuntia ficus-indica* cladodes as an analgesic.

Antiulcerogenic effect

Antiulcerogenic abilities have been discovered in *Opuntia* species [13]. The juice of full *Opuntia ficus indica* (L.) Mill. fruits was studied in one study. Ascorbic acids, polyphenols, and flavonoids were found in the juice, according to the data. The researchers also discovered that preventing the ulcerogenic activity of ethanol in rats with the juice of *Opuntia ficus indica* (L.) Mill.) increased mucus production and restored normal mucosal architecture using light microscopy [46].

In another study, the protective *Opuntia ficus indica var. saboten* fruit juice and its main constituent, betanin, were evaluated against stress-induced acute gastric lesions in rats. Gastric mucosal lesions with bleeding were induced in Sprague–Dawley rats after six hours of water immersion restraint stress. The results showed that lyophilized powder that contained *Opuntia. ficus indica var. saboten* fruit juice, and maltodextrin, and betanin at a dose of 800–1600 mg/kg considerably exerted gastro protective activity against stress-induced gastric lesions by maintaining gastric mucus [47]. In addition, the methanolic floral extract (OMFE) of *Opuntia ficus indica f. inermis* was tested in rats to see if it might prevent ethanol-induced stomach ulcers. The results demonstrated that pre-treatment with OMFE (250, 500, and 1000 mg/kg) protected against ethanol-induced gastric ulcers by preventing the deep necrotic lesions of the gastric epithelium in a dose-dependent manner [48].

Antispermatogenic properties

The weights of seminal vesicles, ventral prostate testes, and epididymides were significantly reduced after oral administration of *Opuntia dillenii* phylloclade extract at a concentration of 250 mg/kg to male rats. Rats treated with *Opuntia dillenii* had their spermatid production reduced by 88.06%, preleptotene spermatocytes reduced by 59.7%, spermatogonia reduced by 61.65%, and secondary spermatocytes reduced by 63.32%, according to the findings. The *Opuntia dillenii* phylloclade extract was found to have a 100% reduction in male rat fertility [49].

Male rats were given the methanol fruit extract of *Opuntia* elatior Mill orally at doses of 300 and 900 mg/kg body weight for 60 days in another study. The epididymal sperm count, blood testosterone levels, spermatogenesis, and testicular hydroxysteroid dehydrogenase activity were all used to assess fertility. Mating treated rats with normally cycling virgin females was used to test fertility, and the reversal of infertility in male rats was tested by stopping treatment for two weeks. The researchers discovered that in male rats treated for 60 days, epididymal sperm count and motility were lowered by up to 75% to 80%. The results also demonstrated that stopping the medication for two weeks resulted in infertility reversal [50].

Antineoplastic properties

Opuntia species have anticancer effects, according to the body of knowledge. Betanin, which is present in most *Opuntia* species, is thought to cause apoptosis in K562 cells

via the intrinsic mechanism. Betanin is thought to work by causing the release of cytochrome c from mitochondria into the cytosol and the cleavage of ADP ribose polymerase [51]. Another study used the trypan blue assay to evaluate the anticancer activities of various *Opuntia ficus indica* peel extracts. The results showed that chloroform and ethanol extracts caused the largest percentages of antineoplastic activity, with 96 and 83 percent, respectively [52].

Toxicology of *Opuntia stricta*

Opuntia species have been reported to be typically well tolerated when given orally [53]. An acute toxicity research was carried out in one of the investigations in accordance with the report obtained from Kumar *et al*. [54]. The mice were put into three groups of six mice each, aged 6 to 8 weeks, and fasted overnight. The control group received 33.3 ml/kg of distilled water, whereas the second and third groups received 5g/kg of mucilage suspension of *Opuntia ficus-indica* and *O stricta*. The test mice did not demonstrate any changes in behavior for 4 hours after receiving mucilage dispersions from two *Opuntia* species, and no death was observed after two weeks of follow-up [55].

This study, however, didn't report the very low acute toxicity that was observed. In books of traditional folk medicines and case studies, *Opuntia ficus-indica* has been reported to cause headache, abdominal fullness, increased stool frequency volume, mild diarrhoea, nausea, and low colonic obstruction [56, 57]. Even though most people believe that herbal medicines are comparatively safe since they are "natural", there is unusually little data to give credence to this assumption [53]. Nevertheless, there is a huge possibility that side effects may also occur because of contamination of herbal products due to heavy metals such as arsenic, copper, lead, mercury, and other undisclosed pharmaceutical ingredients added to the herbs to produce a desired effect. Microorganisms, microbial toxins, and genetic factors are among other factors that can affect the content of active biochemicals in herbal products [53, 57]. It is against that background that more investigations are launched to assess the risks and benefits of using *Opuntia stricta*.

Conclusion

Contemporary medicine may be available in most parts of the world for the treatment of many chronic degenerative ailments. However, most people around the world are still relying on the use of folk medicine. This review article revealed that while *Opuntia* species are among the most widely studied plants in the world, there is an in-depth gap in information regarding the isolation of the active ingredients responsible for the reported pharmacological properties and their postulated mechanism of action. Furthermore, there is generally insufficient data on the pharmacodynamics and pharmacokinetics of *Opuntia stricta*. Therefore, more studies are required to characterize the reported pharmacological properties and the safety of *Opuntia* species, keeping in mind that the reported pharmacological properties in different studies, both *in-vitro* and in-vivo, may differ as a result of the different geographical environments and species. This review also revealed that *O. stricta* has been domesticated in some parts of the world, a situation which may further cause the exhibition of variations in both the biochemical composition and properties.

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