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Review Article

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Therapeutic Applications of Salvadora Persica Plant in Medical Sciences: A Review Article

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ABSTRACT

The Salvadora persica plant has been used for medicinal purposes since ancient times. Many studies have demonstrated its potential as a therapeutic agent. Salvadora persica stick is commonly used to improve oral health. This plant has many benefits, including its antipathogenic, anti-inflammatory, anti-cancer, wound healing, metabolic, digestive, and contraceptive activities. The purpose of this study is to investigate the effects of Salvadora persica on therapeutic and medical aspects other than oral and dental hygiene.

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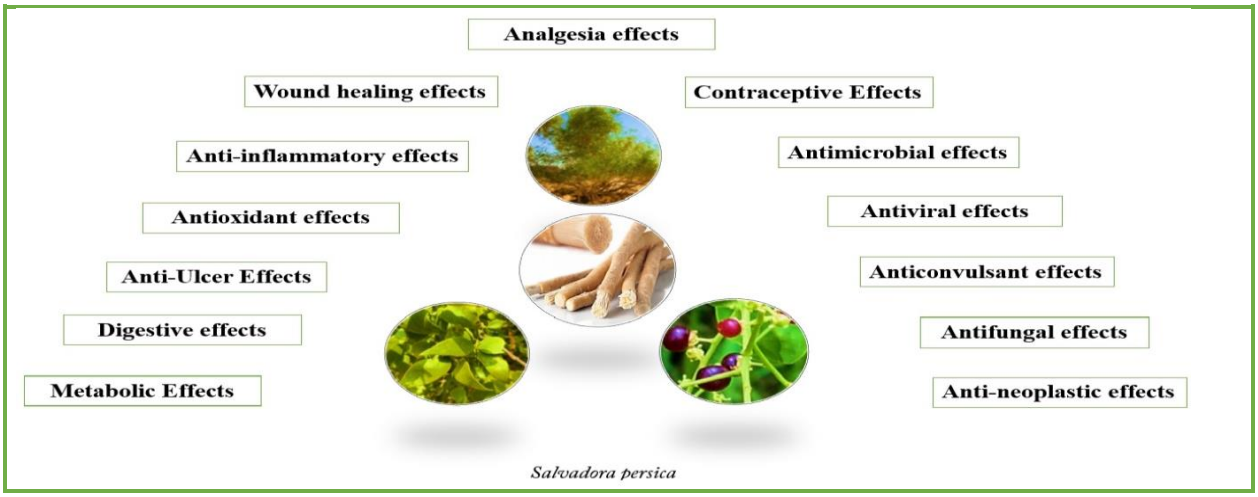
Graphical Abstract



Introduction

In recent years, global interest in using herbal medicines has increased due to their positive and encouraging effects as well as fewer side effects than chemical medicines [1]. Salvadora persica chewing sticks, also known as Arak stick, Miswak or Siwak, have various commercial forms which are available for public usage [2, 3].

In many developing countries, the traditional method of cleaning teeth using Miswak is being used due to its availability, cheapness, and simplicity [4]. In Muslim cultures, medicinal plants, including Salvadora persica (Miswak), have wide health-therapeutic applications and are still used for these purposes [5].

In the past, this plant has had various uses such as treating various infectious diseases, contraception, and veterinary applications [6].

The World Health Organization (WHO) has recommended using Salvadora persica as a chewing stick for cleaning teeth due to a wide range of known biological and therapeutic activities [7].

This review article discusses this plant's therapeutic and medical application besides its uses in oral and dental health.

Therapeutic applications of Salvadora persica

Analgesic effects

Salvadora persica can reduce pain sensation through interference with peripheral temperature and narcotic receptors in the body.

Likewise, the analysis done on the chemical substances in the Salvadora persica plant has confirmed the presence of analgesic agents [8].

Studies conducted investigating the analgesic effect of plant extract on rats in comparison to aspirin, indicated that Salvadora persica yielded even higher analgesic activity which could be attributed to β-Sitosterol, Campesterol, Avenasterol, Stigmasterol, and flavonoids existing in Salvadora persica [9, 10].

Anti-inflammatory effects

Various anti-inflammatory substances in Salvadora persica, including phenolic

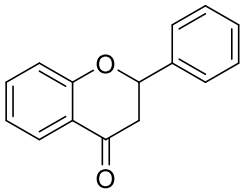
compounds such as: Gallic acid, hydroxy benzoic acid, chlorogenic acid, and cinamic acid and flavonoid factors like rutin and myricetin can reduce the production of inflammatory factors including interleukins, tumor necrosis factor, and transforming growth factor in the serum, providing the same anti-inflammatory effects as indomethacin which can be used as an effective anti-inflammatory agent [11] (Scheme 1).

Antioxidant effects

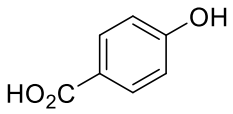
In laboratory studies, Salvadora persica plant extract has shown high antioxidant activity due to the presence of catalase, peroxidase, and polyphenol oxidase enzymes, which can protect cells against oxidative stress caused by free radicals [12]. As a result, due to the presence of substances like Catechin and Quercetin, compared to artificial chemical components, Salvadora persica can be safely used to prepare and manufacture medicines to treat oxidative stress-related disorders [13, 14] (Scheme 2).

Digestive effects

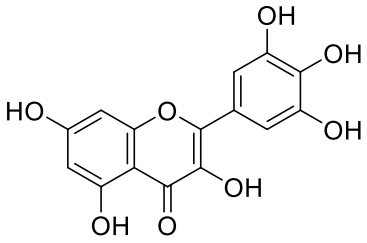
Thanks to anthraquinones existing in Salvadora persica, it can have antibacterial and mild laxative properties. Alongside with the role of Salvadora persica in keeping oral hygiene, it also assists in regulating peristaltic movements of the digestive system [15] (Scheme 3).



Flavonoid

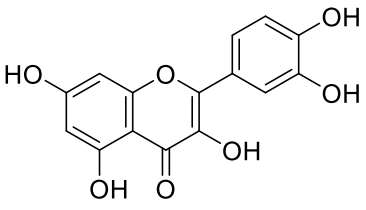


Hydroxy benzoic acid

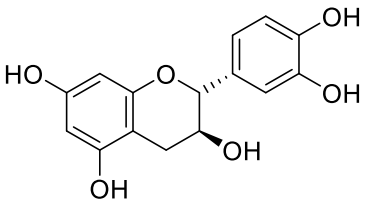


Myricetin

Scheme 1. Anti-inflammatory agents



Quercetin



Catechin

Scheme 2. Antioxidant agent

Furthermore, Salvadora Persica stimulates the gums and activates the gastro-colic reflex, thereby improving bowel movements and reducing constipation [16]. An investigation of Salvadora Persica's impact on patients with spinal cord injuries revealed that it can significantly reduce constipation [17]. Pakistanis also employ this plant to relieve abdominal pain [18].

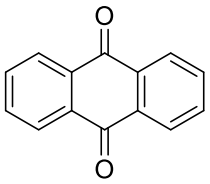
Metabolic effects

Researchers found that consuming Salvadora persica plant extract for 28 days led to a significant decrease in blood sugar levels and an increase in fat-reducing activity in diabetic mice; it further caused the regeneration of pancreatic beta cells [19]. According to a study, extracting stigmast–5–en–3-β–ol out of Salvadora persica stems, regular consumption of this substance in rats led to reduced LDL levels while increasing HDL levels in hyperlipidemic rats [20] (Scheme 4).

Contraceptive effects

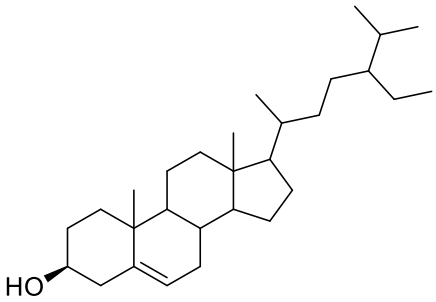
Indian women use this extract as a contraceptive [21, 22]. According to a study on female mice, Salvadora persica extract delayed menstruation by affecting levels of sex hormones and has the potential to be evaluated as a safe contraceptive in human [23].

Darmani *et al.* conducted a study to evaluate the effect of Salvadora persica plant extract on male and female mice's fertility mechanisms. Despite decreasing ovaries' weight, and increasing the uterus weight the plant extract could not bring about any significant contraceptive impact in the female rats. On the other hand, male mice that received this plant extract for 30 days had a lower fertility rate than control groups [24].



Anthraquinones

Scheme 3. Chemical with digestive effect



Stigmast-5-en-3β-ol

Scheme 4. Chemical agent with Metabolic effect

Antibacterial effects

It is believed that Salvadora persica has antibacterial properties due to presence of photochemical active substances such as benzyl isothiocyanate in it [25, 26].

As a result of their antibacterial componds like Astragalin, Kaempferol-3-rhamnoside, Luteolin, Apigenin, miswak sticks have bacteriostatic effects on resistant species like methicillin-resistant *Staphylococcus aureus* (MRSA), which can cause pneumonia and other life-threatening infections like sepsis [27]. In addition, Salvadora persica is used to treat kidney infections [28] (Scheme 5).

Antiviral effects

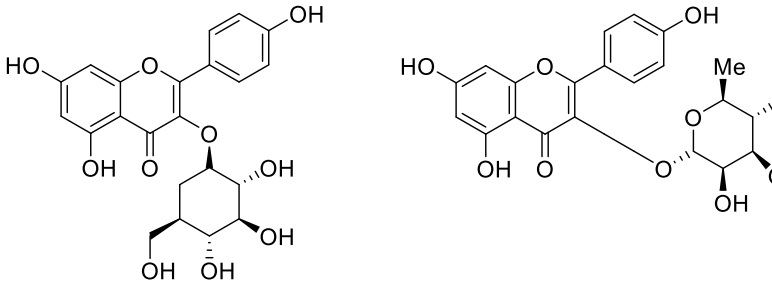
Salvadora persica plant was investigated for its effect on the Covid-19 virus during the outbreak of the Covid pandemic, including one study in which active flavonoids including: mauritianin, narcissin, and astragalin were discovered to bind to proteases responsible for

virus transcription in Salvadora persica plant extract with antiviral activity equal to Remdesivir. Salvadora persica stick can secrete its effective substances into saliva which act as antiviral agents [29, 30] (Scheme 6).

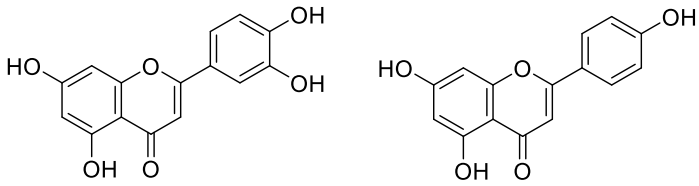
Antifungal effects

The antifungal activity of Salvadora persica has been confirmed in some studies. There is evidence that Salvadora persica plant extract inhibits the growth of pathogenic Candida species [31].

Various studies have investigated and confirmed the potential fungicidal effect of Salvadora persica plant extract on pathogenic Aspergillus species and different Candida species, including Candida albicans, Candida glabrata, and Candida parabacillus. This extract has the potential to be used as an antifungal agent against aspergillosis [32].

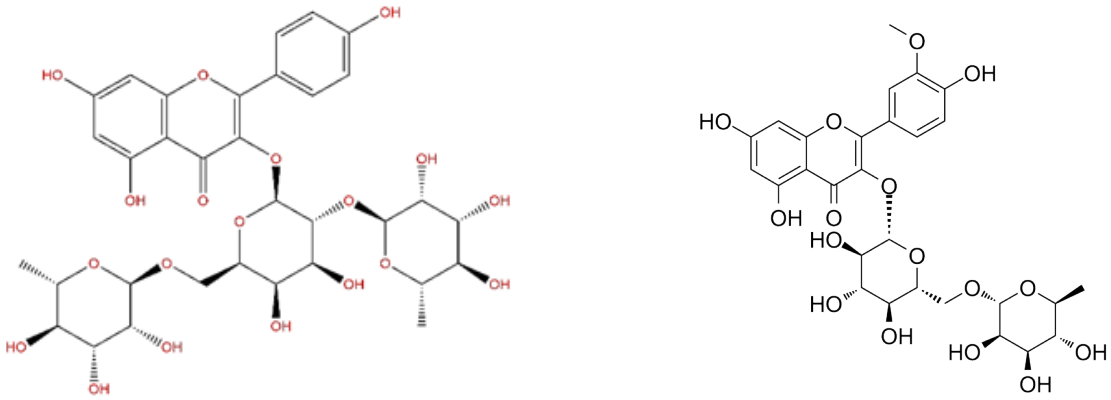


Astragalin **Kaempferol-3-rhamnoside**



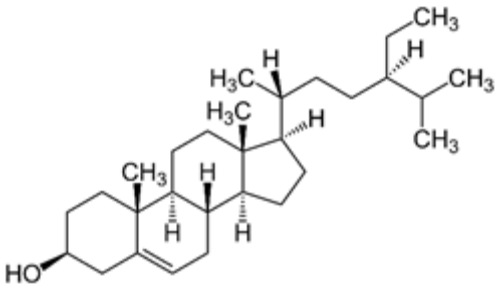
Luteolin **Apigenin**

Scheme 5. Agents with antibacterial properties

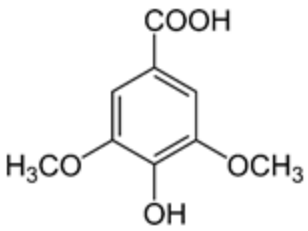


Mauritianin ***Narcissin***

Scheme 6. Agents with antiviral activity



Beta-Sitosterol



Syringic acid

Scheme 7. Anti-neoplastic agents

Anti-neoplastic effects

Studies have found that Salvadora persica contains active anti-neoplastic compounds like: Beta-Sitosterol, Gallic acid, Syringic acid, and Pyro catechol [33-35] (Scheme 7).

According to a study investigating Salvadora persica plant extract on epithelial cancer cells and oral squamous cells, this plant possess potential anti-neoplastic effects on these cells [36].

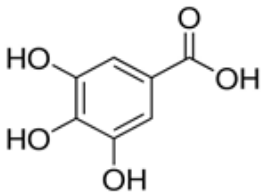
The plant has been found to treat breast, ovarian, and colon cancers and reduce the size of melanoma tumors in mice through various mechanisms [20, 33, 35].

Wound healing effects

Salvadora persica has been tested for its effects on wounds caused by surgical incisions in rats, which showed wound healing effect through proliferation of cells by the presence of effective ingredients such as phenolic constituent including Gallic acid and other chemical compounds like: tannins, saponins, flavonoids, and sterols [37-39] (Scheme 8).

Compared with solcoseryl gel, herbal ointments containing 10% Salvadora persica extract significantly improved wound healing process [40].

In addition, results of a study examining the efficacy of the hydro alcoholic extract of Salvadora persica on mice with second-degree burns revealed that on day fourteen of the wound healing process, mice treated with the hydroalcoholic extract of this plant showed a significant improvement in wound healing compared to rats treated with silver sulfadiazine ointment [41].



Gallic acid

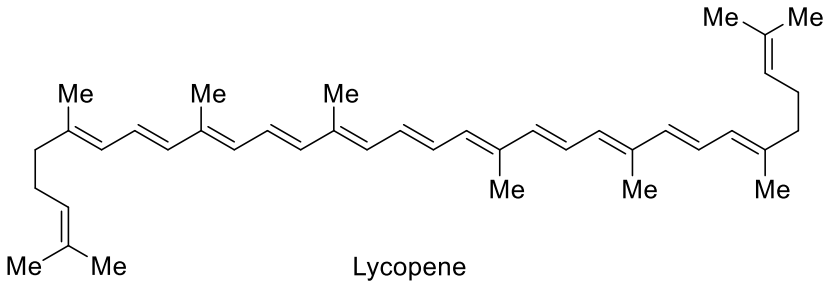
Scheme 8. Wound healing compound

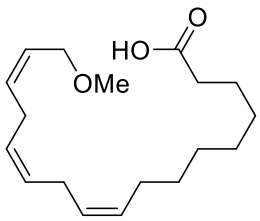
Anti-ulcer effects

The researchers found that Salvadora persica prevented stomach ulcers caused by salicylic acid or ethanol in rats by decreasing inflammatory mediators, increasing tissue growth factor, and enhancing oxidative defense due to the presence of antioxidant factors like: lycopene, α-linolenic acid, oleic acid, lycoxanthin, retinoic acid, furan, vitamin C, tannin, saponin, and sulfur compounds. These changes could possibly strengthen the mucosal barrier which protects stomach from existing acid and preventing peptic ulcer [42,43] (Scheme 9).

Anticonvulsant effects

Monforte et al. conducted a study to investigate the anticonvulsant effects of Salvadora persica on pentylenetetrazole-induced seizures. Taking Salvadora persica extract orally or by injection reduced convulsion frequency and duration and reduced mortality caused by convulsions [44].





Scheme 9. Anti-ulcer agents

Conclusion

The findings of this review article showed that the Salvadora persica as a unique plant can play an important role in the health care system in the future in addition to oral and dental health application. It is important to note that its consumption in healthy people can have beneficial and preventive effects on human health. Although various studies have shown the beneficial and prominent effects of this medicinal plant on mice, more experimental studies are needed to investigate its effects on humans.

Disclosure Statement

No potential conflict of interest was reported by the authors.

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Authors' Contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

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