PHYTOCHEMICAL AND PHARMACOLOGICAL PROFILE OF MISWAK(*salvadora persica* Linn salvadoraceae): AN OVERVIEW

Wasimuzzama Khan, Mujib Atar, Tausif Shaikh, Rashmi Tambe, S. Katekar, Rukhsana A. Rub*

Dept. of Pharmacognosy, M.C.E. Society's Allana college of Pharmacy, 2390, KB Hidayatullah Road, Azam Campus, Camp, Pune, (M.S) India-411001

Summary

Miswak (*Salvadora persica*) is a desert plant of Salvadoraceae family and is commonly known as toothbrush tree as its roots and branches are used as tooth cleaning sticks in many third world countries.It is also known as Mustard tree, Arak tree, Peelu tree etc. It is a small evergreen tree with numerous, drooping and finely striated branches, with opposite, fleshy, elliptic-lanceolate or ovate leaves and drupe, 3mm diameter globose, smooth fruits. The phytochemical review suggests the presence of wide range of chemical constituents in various parts of the plant like; Salvadorine, trimethylamine, α-tocopherol, α-lonone, Salvadourea, β-sitosterol, Salvadoricine, rutin and quercetin, Benzylamides, 1-8-cineole, α-caryophellene, β- pinene, benzylisothio-cyanate etc.

Phytoconstituents like Trimethylamine and Salvadorine have been reported to have antibacterial, antiphlogistic and gingiva-stimulating effect.The various extracts of the stem have been found to exhibit strong antimicrobial activity against wide range of gram positive and gram negative bacteria

especially residing in oral flora. The stem is also reported to have significant anti-inflammatory and analgesic activity justifying its use in dental preparations. The plant also has great antiplaque, antifungal, antipyretic, hepatoprotective, antioxidant, anti-ulcer, hypolipidemic and anticonvulsant activities.

Keywords: *Salvadora persica,* Miswak, phytochemistry, pharmacological studies.

Introduction

Miswak consists of dried roots and dried above ground parts of *Salvadora persica* Linn, family Salvadoraceae.

It is commonly known as toothbrush tree, Mustard tree, Arak tree, Peelu tree etc. *Salvadora persica* is usually a small evergreen tree with numerous, drooping and finely striated branches, with opposite, fleshy, elliptic-lanceolate or ovate leaves and drupe, 3mm diameter globose, smooth red fruits when ripe. Habitat is in saline soils and littoral forests, commonly found in drier parts of India, Sindh, Ceylon, dry regions of West Asia, Egypt and Abyssinia.[1]

It is one of the earliest mentioned plants in recorded literature especially amongst Islamic literature where its roots and branches are reported to be used as tooth cleaning sticks.[2]

Fruit are used as aphrodisiac, alexiteric, stomachic, appetizer, useful in biliousness, also used as deobstruent, carminative and diuretic.

Leaves are bitter, corrective, astringent to bowels, tonic to liver, diuretic analgesic, anthelmintic, useful in nose troubles, piles, scabies, leucoderma, lessen inflammation, strengthen teeth. Seeds are purgative and improve diuresis. Leaves are also used as an external application in rheumatism. Root-bark is remarkably acrid, when applied to the skin acts as external stimulant, sometimes it raises blisters. Stem-bark is warm and acrid and is given in decoction in low fever and as a stimulant and tonic in amenorrhoea. Shoots and leaves are given as antidote to all poisons; leaf-juice is given in scurvy.[1]

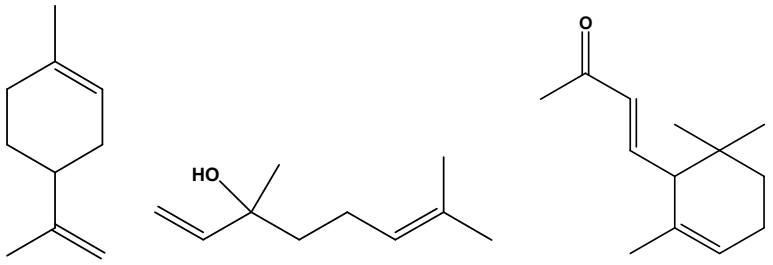
Phytochemical review

1. The seeds of *Salvadora persica* contain about 40% oil with a fatty acid composition (lauric-20%, myristic-55%, palmitic 20% and oleic-5%) which can make an excellent soap.[3] seeds also contain fluoride and silica.[4]

2. Seeds bark and leaves are reported to have fatty acid methyl ester (FAME), tocopherol (γ-tocopherol, α-tocopherol, vitamin E, and γ-tocotrienols), sterol (phytosterol, sistosterol, β-sisterol, campestrol, stigmasterol, 5-Avenastrol) and phenolic compound. [5,6] The plant contain sulphur,[7] organic sulphur compounds,[8] ascorbic acid,[9,10,11,12] and small amount of saponin.[13] The chemical analysis of miswak sticks showed the presence of fluoride, calcium, phosphorus and silica.[14]

3. Fruits contain large amount of sugar, fat, colouring matter and an alkaloid, oil-cake from the seeds contains nitrogen 4.8% potash 2.8% and phosphoric anhydride 1.05%, ash contains large amount of chlorine.[15]

4. The phytochemical screening revealed the occurrence of carbohydrates, glycosides, sterols, terpenes, flavonoids and alkaloids.It also contains 0.16% volatile oil from which heptadecene β-carbonic acid is the major constituent. The other volatile component are D-limonene, Linalool, Linalyl acetate, Benzaldehyde, E-2-decanal, 2-Undecanone, 6-10-dimethyl, Delta (7) methanone-2, 2-Cyclohexen-1-one 3-methyl-6-(1-methyl ethanyl), β-Damascenone, 5-9-Undecadien0z-one 6-10-dimethyl, α-lonone, Indole, Hedycaryol, 2-Pentadecanone-6-10-14-trimethyl, Nonaoic acid, Delta-silinene, β-Eudesmol, Tricosane, Dedecanoic acid, 2-Hexadecen-1-ol-3-7-11-15-tetramethyl, Octadecanoic acid, Nonadecane, Tetra dedecanoic acid, 9-Octadecanoic acid, 9-12-Octadedecenoic acid, Hexadecanoic acid.[4,16]

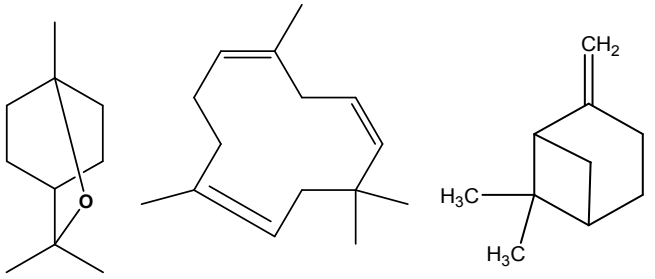


D-Limonene **Linalool** **Alpha lonone**

5. Root stem and seeds are reported to have volatile compound like cis-2-methylcyclohexanol, Benzaldehyde, Chloromethylbenzene, benzylalcohol, N-Acetylpiperidine, 3-Methyl-2-furancarboxylic acid, Nonanal, 2-3-Dihydro-3-5-dihydroxy-6-methyl-(4H)-pyran-4-one, Benzoic acid pentyl ester, Pyridine derivative, Tetradecene, Octadecanol, 3-4-5-Trimethoxyphenol, Tetradecanoic acid, (E)-9-Octadecenoic acid, 9-12-Octadecadienoic acid, Hexadecanoic acid, (Z)-9-Ictadecenoic acid, (Z)-9Octadecenoic acid ethyl ester etc.[16]

6. The major essential oil components identified in the leaves are benzyl nitrile, eugenol, thymol, isothymol, eucalyptol, isoterpinolene, and β-caryophyllene.[17]

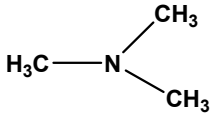
7. The oil obtained by hydro distillation of stem was determined as a mixture of monoterpene hydrocarbon (11%), oxygenated monoterpenes (54%) and sesquiterpene hydrocarbons (21%). The major components identified were 1-8-cineole (eucalyptol) (46%), α-caryophellene (13.4%), β- pinene (6.3%) and 9-epi-(e)caryophellene.[18]



1,8-cineole **Alpha-caryophyllene** **Beta Pinene**

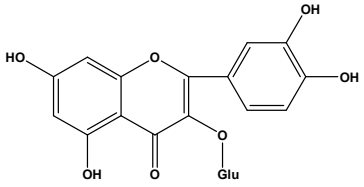
8. Roots and leaves of *Salvadora persica* showed presence of Salvadourea,[19] β-sisterol [20]

9. The alkaloid Salvadorine,present in roots and bark of *Salvadora persica* yields trimethylamine on hydrolytical cleavage. [9,15,21,22]

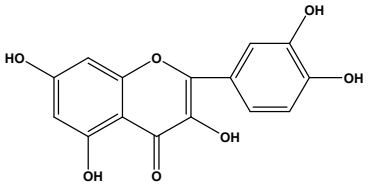


Trimethylamine

10. Three Lignan glycosides [23] and flavonoids rutin and quercetin were detected in the stems of *Salvadora persica*.[24]

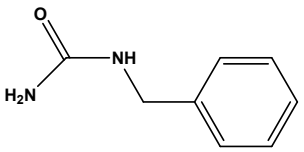


Rutin

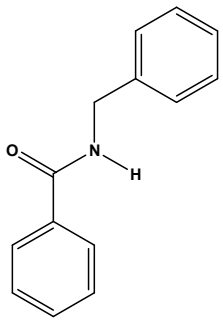


Quercetin

11. Four Benzylamides ; butanediamide-N-N-bis(phenylmethyl-2-hydroxy-butanediamide, N-benzyl-2-phenylacetamide, N-benzylbenzamide, and benzylurea were isolated from the stem of plant [25]

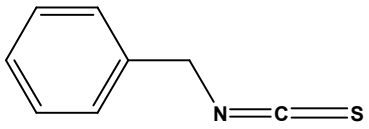


Benzylurea



N Benzylbenzamide

12. Extract of roots, twigs or stem is reported to contain high amount of sodium chloride and potassium chloride as well as salvadourea and salvadorine, saponin, tannins, vitamin C, silica and resin, in addition to cyanogenic glycoside and benzylisothio-cyanate.[26]



Benzylisothiocyanate

Pharmacological review

1. Ethnomedical literature reports the use of plant *Salvadora persica* as a toothbrush,[27,28] dentrifice,[9] and a chewing stick.[29]

2. *Salvadora persica* extract is comparable to other oral disinfectants and anti-plaque agents like triclosan and chlorhexidine gluconate.If used at a high concentration, extracts of bark, pulp & whole miswak (bark & pulp) show strong inhibition against *Streptococcus faecalis,*

Streptococcus mutans, at 5%, 10% & 50% v/v.[30, 31] Extracts have also been reported to exhibit significant antibacterial,[32]antifungal,[33] antiplasmodial,[34]antiplaque[35,36,37]anticaries and antiperiodontopathic effects.[38]

3. Aqueous & methanolic extract of stem of *Salvadora persica* was also investigated for antimicrobial activity against isolated oral pathogens like *Staphylococcus aureus, , Streptococcus pyogenis, Lactobacillus acidophilus, Pseudomonas aeruginosa and Candida albicans.*At 12.5, 25, 50, 100 & 200 mg/ml, aqueous extract inhibited all the isolated microorganism and was more effective than methanol extract which was resisted by *Lactobacillus acidophilus* and *Pseudomonas aeruginosa*.[39]

4. Phytoconstituents like Trimethylamine and Salvadorine have been reported to have antibacterial, antiphlogistic and gingiva-stimulating effect.[29]

5. 50% ethanolic extract of leaves & stem bark of *Salvadora persica* showed activity against *Neisseria gonorrhoeae*.[40]

6. Methanolic & aqueous extract of root bark of *Salvadora persica* linn showed anti-candida activity against Candida albicans (ATCC 90028) with average inhibition zone of 10mm.[33,41]

7. Methanolic, chloroform and aqueous extract of *Salvadora persica* was reported to have significant antifungal activity as compared to other 11 medicinal plants used in folklore medicine in Saudi Arabia, investigated against *Aspergillus flavus, Aspergillus fumigates, Aspergillus niger and Candida albicans*.[42]

8. *In vitro* investigation on the efficacy of *Salvadora persica* extract showed significant inhibition on growth of the oral pathogens like *Candida albicans, Streptococcus mutans, Actinobacillus actinomycetemcomutans, Lactobacillus acidophilus, Actinomyces naeslundii* and *Prophyromonas gingivalis*.[43]

9. Antimicrobial effect of alcoholic extract of *Salvadora persica*(1%, 5%, and 20%), Sodium hypochlorite(5.25%) , chlorhexidine(0.2%) was studied and found that all concentractions of *Salvadora persica* extract, sodium hypochlorite, and chlorhexidine had a significant antimicrobial effect against aerobic and anaerobic bacteria recovered from teeth with necrotic pulps, The best antimicrobial effect for *Salvadora persica* extract was noticed at 15% conc. according to broth microdilution method.[44]

10. Aqueous twig extract of *Salvadora persica* showed significant (84%) reduction in adherence of *Streptococcus mutans* to Buccal epithelial cells as compared to 45% adhesion inhibition with chlorhexidine digluconate.[45]

11. Antimicrobial evaluation of methanolic extract of *Salvadora persica* showed significant inhibition against *Staphylococcus aureus* (ATCC 29213), *Escherichia coli* (ATCC 25922), *Micrococcus flavus* (SBUG16), *Bacillus subtilis* (ATCC 6059) and *Pseudomonas aeruginosa* (ATCC 27853) with MIC 500, 500, 500, 1000, 1000µg/ml respectively.[46]

12. Decoction of *Salvadora persica* posseses significant anti-inflammatory effect on carrageenin-induced paw edema in rats, the percentage of inhibition of paw edema from the first to the third hour was observed as 31.07$\pm$ 1.0% ($P < 0.05$); 31.39 $\pm$ 0.9% ($P < 0.05$); 32.43 $\pm$ 0.7% ($P < 0.05$). [47,48]

13. Decoction of roots & branches of Miswak was evaluated for analgesic test (hot plate, writhing reflex and tail flick), and was found to lowers mice's response to chemical and thermal stimuli in dose dependent manner. The effective doses (ED50) were 3.5, 4.5, and 5.5 ml/kg for hot plate, tail flick and writhing reflex test respectively.[49]

14. The aqueous extract of polyherbal Ayurvedic preparation of *Salvadora persica* exhibited significant antipyretic, analgesic properties during rodent experiments while exhibiting low toxicity and ulcerogenicity. The clinical trial showed that fever was rapidly and substantially reduced after oral administration of polyherbal Ayurvedic

preparation of *Salvadora persica* and this antipyretic effect was more sustained and highly significant ($P < 0.001$) when compared to Aspirin.[50]

15. Anti-ulcer activity of *Salvadora persica* on Acetyl Salicylic Acid induced ulcer in rats showed that the mechanism of antiulcerogenicity may be attributed to the attenuation of aggressive factors and the facilitation of a defensive factor. *Salvadora persica* appears to strengthen the mucosal barrier which is the first line of defence against endogenous and exogenous ulcerogenic agents. It can be categorized as cytoprotective agent. On the other hand, as ASA is a cyclooxygenase inhibitor, the beneficial antiulcer effects of the *Salvadora persica* could be mediated by prostaglandins.[47]

16. Antioxidant studies on hydroalcoholic and aqueous extract of *Salvadora persica* on various models showed significantly high scavenging ability on DPPH radical, 2-2-azino bis (3-ethylbenzothiazoline-6-sulphonic acid) radical, superoxidentroblue-tetrazoliun (NBT) radical and reduction of ferric ion solution.[51]

17. The extract of the stem of *Salvadora persica* is reported to possess hypoglycemic[52] and hypolipidemic activitiy also.[53]

18. The toxic effects of an extract of Miswak from *Salvadora persica* was investigated on the reproductive system of the mouse for 30 days,which showed that exposure to Miswak extract did not have much effect on female mouse fertility, however exposure of male mice to Miswak extract resulted in a 72% reduction in pregnancies in untreated females impregnated by test males. The relative weights of the testes and preputial glands were significantly increased and that of the seminal vesicles was significantly decreased in test males. [54]

19. Benzylisothio-cyanate and related compound from *Salvadora persica* was reported to have inhibition of carcinogenic effects of polycylic hydrocarbons.[55]

Conclusion

Miswak is one of the most important plants mentioned in Islamic and other traditional literature and have been found to have huge pharmacological potential and tremendous scope for its phytochemical research, as suggested in this extensive review on the plant.

The review renders elaborate data on the range of chemical constituents like ; Salvadorine, trimethylamine, α-tocopherol, α-lonone, Salvadourea, β-sisterol, Salvadoricine, rutin and quercetin, Benzylamides, 1-8-cineole, α-caryophellene, β-pinene, benzylisothio-cyanate present in various parts of the plant.

Phytoconstituents like Trimethylamine and Salvadorine are reported to have significant antibacterial, antiphlogistic and gingiva-stimulating effect. Thus the plant has great antiplaque, antifungal, antipyretic, hepatoprotective, antioxidant, anti-ulcer, hypolipidemic and anticonvulsant activity.

Thus the crude extracts or the isolated phytoconstituents of the herb can be exploited for designing effective herbal formulations for aforesaid indications. The areas where still more focus is needed are, pharmacognostic evaluation, and thorough phytochemical investigation to explore the presence of valuable phytoconstituents rendering therapeutical potential to the plant.

References

1. Bombay State Gazetter (Botany) Page No. 186
2. Sahih Muslim, Volume 1, Book of Wudhu.
3. FAO http://www.fao.org/docrep/x5327e/x5327elj. htm
4. Salah Sayed Ahmed, Soaad Esmaeil Essawy El-Gengaihi, Mohamed El-Sayed Ibrahim and Ewald Schnug, Preliminary phytochemical and propagation trial with Salvadora persica L., Agriculture and Forestry Research 2008, 1/2, (58), 135-138

5. Abdalbasit Adam Mariod, Bartrand Mathaus, I. H. Hussein, Chemical characterization of the seed and antioxidant activity of various parts of *Salvadora persica*., Journal of the American oil chemist's society, Research Library: 2009, 86,9
6. Awasthi CY, Mitra CR, *Salvadora oleoides*, constituents of the fruit and seed, Indian oilseeds Journal, 1964, 8; 289-292.
7. Cornu A, Massot R, Compilation of Mass spectra data, 1975, vol. I, 171 A.
8. Daxenbichler ME, Spencer GF, Carlson DG, Rose GB, Brinker AM, Powell RG, Glucosinolate composition of seeds from 297 species of wild plants, Phytochemistry, 1991, 30:2623-2638.
9. Farooqi MIH, Srivastava JG, the tooth brush tree, Quart J Crude Drug Res, 1968; 8, 1297-1299.
10. Boulos L, Medicinal plants of North Africa, Reference publications, Michigan, Inc., Algonac, 1983, 158-162.
11. Etkin NL: A Hausa herbal pharmacopoeia: Biomedical evaluation of commonly used plant medicines. J Ethanopharmacology, 1981, 4; 75-98.
12. Kapoor LD, Handbook of Ayurvedic medicinal plants, Boca Raton, Florida, CRC Press. Inc., 1990
13. Von Kampf R, Uber Miswak, eine zur Zahnreingigung verwendete Drogeder arabischen Volksmedizin, Pharm Acta hely, 1975, 50; 350-352.
14. Kerharo J, Adam JG, La Pharmacopee Senegalaise Traditionnelle plantes medicinales et Toxiques Vogpt-Freres, Paris, 1974, 716-719.
15. Dr. K. M. Nadkari, the Indian Matria Medica, Popular Prakashan Volume I, Page No. 1092
16. Howaida F. Abdel Rahman, Nils Skaug, Ann Margot Whyatt and George W Francis, Volatile compounds in crude *Salvadora persica* extracts, Pharmaceutical biology, 2003, Vol. 41, No. 6, 399-404.
17. Alali F, Al-Lafi, GC/MS analysis and bioactivity testing of the volatile oil from the leaves of the tooth brush tree *Salvadora persica* L. Nat prod Res, 2003, 17; 189-194.
18. Alali F, Hudaib M, Aburjai T, Khairallah and Al-Hadidi N, GC-MS analysis and antimicrobial activity of the essential oil from the stem of the Jordanian toothbrush tree *Salvadora*

persica, Pharmaceutical Biology, 2004, Vol.42, No. 8, 577-580.

19. Ray A B, Chand L, and Dutta S C, Salvadourea, new urea derivative from *Salvadora persica,* Chem Ind., 1975, 12, 517-518
20. Malik S, Ahmad S. S, Haidar S.I, and Muzaffar A, Salvadoricine, A new alkaloid from the leaves of *Salvadora persica,* Tetrahedron lett.,1987, 28,163-164
21. Ra'ed Al Sadhan, Khalid Almas, Miswak (chewing stick): A cultural and Scientific Heritage, Saudi Dental Journal, volume 11 Number 1999, 2:80-88
22. Dorland WA Newman, Dorland's Illustrated Medical Dictionary, 27th edition, Philadlphia: W. B. Saunders Co., 1988.
23. Kamel M.S, Ohtani K, Assaf M. H, Kasai R, El-Shanawani M A, Yamasak K, Ali A A, and Tanaka O, Lignan glycosides from stems of *Salvadora persica*, Phytochemistry, 1992, 31, 2469-2471
24. Abdel-Wahab S.M, Selim M. A, and El-Fiki N M, Investigation of the flavonoid content of *Salvadora persica* L. Bull, Fac Pharm.(Cairo Univ), 1990,28,67-70
25. Ashraf Taha Khalil, Benzylamides from *Salvadora persica*, Arch Pharm Res,2006 Vol. 29, No.11, 952-956.
26. Ezmirly ST, El-Nasr MS, Isolation of glucopraeolin from *Salvadora persica* L. Chem Soc. Pakistan, 1981:3:9-12.
27. Al-Said MS, Traditional medicinal plants of Saudi Arabia, American Journal of Chinese Medicine, 1993, 21, 291-298.
28. Johns T, Mhoro EB, Sanaya P, Food plants and masticants of the Batemi of Ngorongoro district Tanzania, Economic Botany, 1996, 50, 115-121.
29. Hattab F. N. Miswak: the natural tooth brush Journal of Clinical Dentistry, 1997:8, 125-129
30. Khalid Almas and Nasir H. Al Bageih, The antimicrobial effects of bark and pulp extracts of miswak, *Salvadora persica*. Biomedical Letters, the Faculty press, 1999 :(60), 71-75
31. Dr. K. Almas, The antimicrobial effects of seven different types of Asian chewing sticks, Odonto-stomatologie tropicale 2001- No. 96, 17-20

32. Al-Lafi, Ababneh H, The effect of the extract of miswak (chewing stick) used in Jordan and the Middle East on oral bacteria, Int. Dent. J, 1995, 45; 218-222
33. Al-Bagieh NH, Idowu A, Salako NO, Effect of aqueous extract of miswak on the in vitro growth of Candida albicans, Microbios Lett, 1994, 80; 107-113.
34. Ali H, Konig CM, Khalid SA et al. Evaluation of selected Sudanese medicinal plants for their in vitro activity against hemoflagellates selected bacteria, HIV-1-RT and tyrosine kinase inhibitory, and for cytotoxicity, J Ethnopharmacol, 2002 83; 219-228
35. Mohammad ER, Mehrdad R, The antiplaque effects of Salvadora persica and Padina essential oil solution in comparison to Chlorhexidine in human gingival disease; a randomized placebo-controlled clinical trial, International Journal of Pharmacology, 2005; 1(4); 311-315.
36. Gazi MI, Lambourne A and Chgla AH, The antiplaque effect of of tooth paste containing *Salvadora persica* compared with Chlorhexidine gluconate, Clin. Prev. Dent., 1987; 9; 3-8.
37. Mahommad Batwa, The effectiveness of miswak chewing stick on plaque removal, Karolinska institutet, Odontologiska Institutionen, Stockholm 2004, Nr. 68, 1-33
38. Al-Samh DAA, Al-Bagieh NH, A study of antimicrobial activity of the miswak ethanolic extract in vitro, Biomedical Letters, 1996, 53;225-238
39. Firas A, Al-Bayati, Khudir Sulaiman, In vitro antimicrobial activity of *Salvadora persica* L. extracts against some isolated oral pathogens in Iraq, Turk J Biology, 2008; 32, 57-62.
40. P. Shokeen, M. Bala, V. Tandon, Evaluation of the activity of 16 medicinal plants against Neisseria gonorrhoeae, International Journal of Antimicrobial agents, Elsevier, 2009, 33; 86-91
41. Deborah KB Runyoro, Mecky IN Matee, Olipa D Ngassap, Cosam C Joseph and Zakaria H Mbwambo, Screening of Tanzanian medicinal plants for anti-Candida activity, BMC Complementary and Alternative medicine, BioMed Central, 2006, 6: 11, 1-10

42. Abdalmoniem, M A Saadabum, Antifungal activity of some Saudi plants used in traditional Medicine, Asian Journal of Plant sciences, 2006, 5(5), 907-909
43. Abdel Rahman HE, Skanig N, Francis GW, In vitro antimicrobial effects of crude miswak extracts on oral pathogens, Saudi Dental J., 2002, 14; 26-32
44. Nawal AK Al-Sabawi, Abdul-Khalik K, Al Sheikh Abdal, Mahmoud Y Taha, The antimicrobial activity of salvadora persica solution (Miswak-siwak) as root canal irrigant (a comparative study), University of Sharjah Journal of Pure & Applied sciences, 2007, volume 4, No. 3; 69-91.
45. Hammad and A-K Sallal, Inhibition of Streptococcus mutans adhesion to buccal epithelial cells by an aqueous twigs extract of *Salvadora persica*, Pharmaceutical Biology, 2005, vol 43, No.2, 121-124.
46. Mohamed Al-Fatimi, Martina W, Gudrun S, Ulrike Lindequiest, Antioxidant, antimicrobial and cytotoxic activities of selected medicinal plants from Yemen, Journal of ethnopharmacology, 2007; 111, 657-666.
47. Monforte MT, Miceli N, Mondello MR, Sanogo R, Rossitto A and Galati EM, Antiulcer activity of *Salvadora persica* on experimental ASA- induced ulcer in Rats: Ultrastructural modifications, Pharmaceutical Biology, 2001, Vol. 39, No. 4, 289-292.
48. Ezmirly, S T, Cheng JC, and Wilson SR, Saudi Arabian medicinal plants*: Salvadora persica,* Planta Med, 1979, 35, 191-192
49. Sulaiman MI, Al-Khateeb TL, Al-Mazaraoo AA, The analgesic effects of Miswak, The Saudi Dental Journal, 1996, vol. 8, No.3, 140-144.
50. Gupta M, Shaw BP and Mukharjee A, Evaluation of antipyretic effect of a traditional polyherbal preparation: A double-blind, Randomized clinical trial, International Journal of pharmacology, 2008, 4(3), 190-195.
51. Arora S, Kaushik D, Free radical scavenging activity of *Salvadora persica* Linn., Asian Journal of Chemistry, 2007, Vol.19 (6), 4638-4644.
52. Travato A, Galati EM, Rossitto A, Monforte MT, D'Aquino A, and Forestieri AM, Hypoglycemic effects of *Salvadora persica* in the rat Phytomedicine, 1998, 5, 129-132.

53. Galati EM, Monforte MT, Forestieri AM, Miceli N,Bader A and Trovato A, *Salvadora persica* L: hypolipidemic activity on experimental hyper cholesteremia in rat, Phytomedicine, 1999, 6, 181-185.
54. Darmani H, Al-Hiyasat S, Elbetieha AM, Alkofahi A, The effect of an extract of *Salvadora persica* (Miswak chewing stick) on fertility of male and female mice, Phytomedicine, 2003, 10; 62-65
55. Wattenberg IW, Inhibition of carcinogenic effects of polycyclic hydrocarbon by benzylisothiocyanate and related compounds, J National Cancer Inst., 1977; 58, 395-398