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Original Article

Parsley As a Potential Natural Remedy for Urolithiasis: A Review

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ABSTRACT
Urolithiasis, the formation of urinary calculi, is a common urological disorder. This abstract examines the potential of three plants - Parsley (*Petroselinum crispum*), Roselle (*Hibiscus sabdariffa*), and Gokhru (*Tribulus terrestris*) - as natural anti-urolithiatic agents. These plants have been traditionally used in various cultures for urinary health. Recent scientific studies have shown that they possess diuretic, anti-inflammatory, and antioxidant properties that may help prevent stone formation and promote stone expulsion. Parsley is rich in anti-oxidants and vitamin C, which may reduce crystal aggregation. High citric acid content of roselle could help to dissolve existing stones. Gokhru has demonstrated the ability to reduce stone-forming constituents in urine. Further research is needed to fully elucidate the mechanisms of action and establish standardized treatment protocols for these herbal remedies in urolithiasis management.

1. INTRODUCTION
Urolithiasis (nephrolithiasis) or kidney stones are the condition characterized by formation of urinary calculi in the urinary tract. The body naturally produces substances in urine that inhibit crystal formation. However, these protective agents aren't equally effective for all individuals, resulting in stone development for some people. It causes serious health problems such as severe pain at the end of urination, urinary-tract obstruction and infection. In general, urolithiasis affects all age groups from less than 1 year old to more than 70 yrs. The risk of stone formation is generally high in men 2–4 times, which could be due to the larger muscle mass of men as compared to women, enhancing capacity of testosterone and inhibiting capacity of oestrogen in stone formation[1]. Mankind has been afflicted by urinary stones since centuries dating back to 4000 B.C. A kidney stone is a cluster of crystals when they formed together to create a hard lump in one or both kidneys. They can vary in size from a few millimeters to several centimeters [2]. Oxalate-rich foods should be advised to avoid by the patients of kidney stone disease. Medicinal plants used in the treatment of urolithiasis (kidney stone) and they are safe and effective as compared to allopathic medicines [3].

Parsley: Parsley, or garden parsley (*Petroselinum crispum*) is a species of flowering plant in the family *Apiaceae* that is native to Greece, Morocco and the former Yugoslavia. The origin of parsley is from Mediterranean region, but today is cultivated wherever of the world. Parsley is biennial and glabrous. *Petroselinum crispum* seeds have been claimed to anti-urolithiatic, therefore used to treat or prevent kidney stone [4]. Hindi it is called as Ajmood, in Malayalam it is called as Seema mali and in Kannada it is called as Achu moda. In Swedish language, it is known as Persilja, in German, it is known as Petersilie, and in French, it is known as Persi[5]. *Petroselinum crispum* has been used as laxative, diuretic and anti-urolithiatic agents. The leaves are used against inflammatory condition, mastitis and haematomata. The seeds and roots of the plant have been used to treat numerous digestive problems including diarrhoea, ulcer, flatulence and colic pain. *Petroselinum crispum* is highly seasonal in nature and it is considered as a very rich source of vitamins C and E, β-carotene, thiamin, riboflavin and organic minerals [6]. *Petroselinum crispum* seeds have been claimed to be anti-microbial, anti-septic, astringent, gastrotonic, anti-dote, anti-spasmodic, carminative, digestive and sedative and are used for gastrointestinal disorder, inflammation, halitosis, kidney stone, and amenorrhoea. Myristicin and apiole are the two main components which are responsible for its antioxidant activity [7]. The anti-oxidative effect of the parsley was investigated by measuring the

activity of erythrocyte anti-oxidant enzymes. Parsley (*Petroselinum crispum*) contains large amounts of the flavone apigenin [8]. It is used in folk medicine for relief of bladder inflammation and to treat kidney ailments, increase lactation, resume menstruation, lessen gum and dental pains and for treatment of skin diseases [9]. Additional properties of *Petroselinum crispum* include regulating blood pressure, treating eczema and improving reproductive indices [10]. Parsley root *(Petroselinum crispum*) is a perennial plant. The methanolic extract from the aerial parts of *Petroselinum crispum* showed potent estrogenic activity [11] .

2. GEOGRAPHICAL SOURCE

Parsley [*Petroselinum Crispum*] –

Figure: Parsley [*Petroselinum crispum*]

Parsley (*Petroselinum crispum*) is native to the Mediterranean region but now it is cultivated worldwide. Parsley is grown widely as a spice, a herb and a vegetable in the following countries: Pakistan, India, Madagascar, Thiland, Indonesia, Egypt, Morocoo, France, Israel, Bulgaria, USA, Southern Italy, Portugal, Greece, Spain, Algeria, Malta, Morocco and Tunisia, Russia and South Africa, Turkey, Germany, Hungary and Poland[12].

3. PHYTO CHEMISTRY

Parsley [*Petroselinum Crispum*] –

Parsley [*Petroselinum Crispum*] Contains Flavanoid, Carbohydrates, Essential oil components, Coumarin compounds and Miscellaneous compounds.

1. Flavanoids

Flavanoids are dominant compounds of this plant[13]. Flavanoids including Apigenin, Luteolin, Chrysoeriol, Quercetin, Isorhamnetin are detected from cell suspension of *Petroselinum crispum*[14]. Apigenin, Cosmosiin, Oxypencedanin hydrate, Apiin are detected from aqueous extract of *Petroselinum crispum* leaves[15]. 6-Acetylapiin, A flavone glycoside, Petroside are detected from methanol extract of *Petroselinum crispum* arial parts. Myristicin, Apiol, Cnidilin, Isoimperatorin, Diosmetin, 7-O-β-D-glucopyrananoside, Kaempferol-3-O- β-glucopyranoside are detected from the arial extract of *Petroselinum crispum*. Kaempferol, Apigenin are detected from leaf of *Petroselinum crispum*[16].

2. Carbohydrates

D-glucose and Apiose are detected from cell suspension of *Petroselinum crispum*. Apiose is a sugar, detected in seed, stem and leaf of *Petroselinum crispum*. This sugars are mostly contribute in the structure of flavonoid glycosides[17].

3. Essential oil components

Myristicin and Apiol are two main components responsible for antioxidant activity of parsley. α-pinene, sabinene, β-pinene, ρ-cymene, limonene, β-phellandrene, γ-terpinene, myristicin, elemicin, 1-allyl-2,3,4,5-tetramethoxy-benzene, carotol, eugenol and apiol were identified in *Petroselinum crispum* seed[18]. Leaf essential oil contained β-elemene, β-caryophyllene, phenylacetaldehyde, γ-elemene, α-terpineol, α-pinene, α-thujene, toluene, camphene, hexanal, β-pinene, sabinene, 3-carene, m- and/or ρ-xylene, myrcene, α-phellandrene, β-phellandrene, α-terpinene, limonene, 2-pentylfuran, cis-β-ocimene, γ-terpinene, trans-β-ocimene, ρ-cymene, α-terpinolene, ρ-1,3, 8-menthatriene, cis-Hex-3-en-l-ol, 4-isopropenyl-1-methylbenzene, α-cubebene, benzaldehyde, α-copaene, cryptone, β-bisabolene, α-elemene, 2-(ρ-Tolyl) propan-2-ol, δ-cadinol and elemicin[19]. Analysis of volatile oil from *Petroselinum crispum* plant, callus and cell culture showed that monoterpenes were the main constituent. ρ-1,3,8-menthatriene was high abundant compound among monoterepenes followed by β-phellandrene and apiol. Moreover, aldehydes (nonanal and decanal) and also fatty acids (Free and bound) were found in the volatile oil[20].

4. Coumarins

Oxypeucedanin is the major furocoumarin of *Petroselinum crispum.* Photoder-8-methoxypsoralen, 5-methoxypsoralen and imperatorin are other furocoumarins isolated from its leaf and root[21].

5. Miscellaneous compounds

Carotenoids including β-carotene, lutein, violaxanthin and neoxanthin were detected in *Petroselinum crispum* leaf and stem[22]. Moreover, ascorbic acid is identified in *Petroselinum crispum*[23] Ethanol extract of Petroselinum crispum seed have crispane and crispanone[24]. Moreover, l-methyl-4-(methylethenyl)-2,3-dioxabicyclo [2.2.2]oct-5-ene and 4-methyl-7-(methylethenyl)-3,8-dioxatricyclo [5.1.02-4] octane were isolated from leaves[25].

4. PHARMACOLOGICAL ACTIVITIES

Parsley [*Petroselinum crispum*] -

1. Anti-oxidant activity

Adding *Petroselinum crispum* leaves to the diet of 14 people for one week caused significant increase in anti-oxidant enzymes compared with their levels in the basic diet received group. Apigenin was demonstrated to be the main compound responsible for this activity *Petroselinum crispum*[26]. Different extracts from *Petroselinum crispum* leaves and stems exhibited antioxidant properties in various in vitro models[27]. The essential oil from seed showed in vitro anti-oxidant activity. Apiol and myristicin were two components responsible for its anti-oxidant activity[28].

2. Anti-diabetic activity

Various extract from *Petroselinum crispum* leaves enhanced the liver and blood anti-oxidant function in normal mice. On the other hand in carbon tetrachloride (CCl(4)) induced oxidative stress mice, the extracts showed both protective and deteriorative activity on liver and blood anti-oxidant function. *Petroselinum crispum* leaves decreased blood glucose level and demonstrated hepatoprotective activity in diabetic rats via anti-oxidant activity. The anti-hyperglycemic activity of *Petroselinum crispum* is not due to improvement and regeneration of secretory granules and β-cells of pancreas islets. *Petroselinum crispum* improves hyperglycemia- induced heart and aorta oxidative damage via its anti-oxidant activity in the heart and aorta tissue. However, it did not showed significant effect on non-enzymatic glycosylation of skin proteins in diabetic rats[29].

3.Immunomodulating activity

Essential oil from *Petroselinum crispum* seed suppressed humoral and cellular immune response via inhibiting splenocytes and macrophages function[30].

4. Analgesic and spasmolytic activity

Petroselinum crispum seed hydroalcoholic extract revealed analgesic activity in mice. It also reduced KCl- and CaCl2 induced contractions on rat isolated ileum dose dependently via blocking voltage-gated calcium channels. Different extracts from aerial parts demonstrated anti-spasmodic activity on spontaneous and acetylcholine induced contractions of rat isolated ileum[31].

5. Gastrointestinal activity

Ethanol extract from *Petroselinum crispum* leaves executed beneficial effects on different models of peptic ulcer in rats via its anti-secretory and cytoprotective activity. Aqeoues extract from *Petroselinum crispum* seeds demonstrated laxative activity in rat by significant absorption of sodium and water and also enhancing NaKCl2 transporter activity in the colon[32].

- **Roselle [*Hibiscus sabdariffa*]** and **Gokhru [*Tribulus terrestris*]** are herbal plants and also used to treat urolothiasis.

1. Roselle [*Hibiscus sabdariffa*]

Figure: 1 Roselle [*Hibiscus sabdariffa*]

Roselle (*Hibiscus Sabdariffa*) is a member of *Malvaceae* family. The effect of Hibiscus sabdariffa in the treatment of hyperlipidaemia, apoptosis and hypertension [33]. The plant can be found in almost all warm countries such as India, Saudi Arabia, Malaysia, Indonesia, Thailand, Philippines, Vietnam, Sudan, Egypt and Mexico. Roselle leaves are used for their, antimicrobial, emollient, antipyretic, diuretic, anti-helmentic, sedative properties. H. sabdariffa can be utilized to treat kidney disease and bladder stones [34]. This plant can live for one year or multiple years, taking the form of a small shrub with a woody base. It can reach heights of 2 to 2.5 meters (7 to 8 feet). Its leaves, which are 8 to 15 centimeters long. The plant contains various chemical compounds, including alkaloids, flavonoids, phenols, saponin, steroids, tannins, terpenoids, glycosides, and phlobatannins [35]. Plants are also now being explored as sources of natural pigments to be used as food colorants [36].

Hibiscus sabdariffa, with an attractive flower, is widely grown in many developing countries. More than 300 species are distributed in tropical and subtropical regions around the world[37]. They are originally native from India, to Malaysia[38]. where it is commonly cultivated and was carried at an early date to Africa. It is also cultivated in Sudan, Egypt, Nigeria, Mexico, Saudi Arabia, Taiwan, West Indies and Central America[39]. In India it is widely grown by the tribal in the villages of Madhya Pradesh, Maharashtra, Orissa, West Bengal, Assam, Meghalaya and Andhra Pradesh[40].

2. Gokhru [Tribulus terrestris]

Figure: 2 Flower of Gokhru

Gokhru *(Tribulus Terrestris)* is a member of *Zygophyllaceae* family. It consists of some medicinal properties such as diuretic, anti-urolithic, immunomodulatory, anti-cancer, aphrodisiac, analgesic, stomachic, anti-hypertensive, diuretic, lithontriptic, urinary anti-infective, cardiotonic, anti-bacterial, anti-inflammatory, anti-spasmodic, anthelmintic, larvicidal, and anti-carcinogenic [41]. *Tribulus terrestris* increases testosterone through increasing luteinizing hormone (LH) [42] *Tribulus terrestris* is a plant that grows especially in South Africa, Australia, India, and Europe [43]. Its diuretic activity helped in the treatment of stones along the urinary tract [44]. The stems are rich in starch, fructose and sucrose [45].

The extract of *Tribulus terrestris* contains protodioscin (PTN), a steroidal saponin, that has been extensively used for the treatment of various ailments, such as urinary, cardiovascular[46]. and gastrointestinal disorders[47]. Administration of *Tribulus terrestris* to humans and animals improves libido and spermatogenesis[48]. PTN has been reported to upregulate the levels of testosterone and leuteinizing hormone[49] dehydroepiandrosterone[50] dihydrotestosterone, and dehydroepiandrosterone sulfate[51] *Tribulus terrestris* has a proerectile effect[52]. Saponin from *Tribulus terrestris* is also known for its hypoglycemic effect[53].

MARKETED FORMULATION

Figure: 1 Gokhru Capsules

Figure: 2 Gokhru Supplements

Figure:3 Parsley Leaf

Figure: 4 Roselle Extract

REFERENCE

1. Arya P, Pandey S, Verma V. "Kidney stones formation and use of medicinal plants as antiurolithiatic agents." *Universal Journal of Pharmaceutical Research*. **2017**;36-41.
2. Raikwar D, Patel MK. "Role of herbal medicines in the treatment of Kidney stone: A brief review." *Adv Pharm J.* **2022**;7(5):149-154.
3. Malabadi RB, Meti NT, Chalannavar RK. "Updates on herbal remedy for kidney stone chronic disease." *International Journal of Research and Scientific Innovation.* **2021**;8(2):122-134. MI
4. Farzaei MH, Abbasabadi Z, Ardekani MR, Rahimi R, Farzaei F. "Parsley: a review of ethnopharmacology, phytochemistry and biological activities." *Journal of traditional Chinese medicine.* **2013** 1;33(6):815-826.
5. Sarwar S, Ayyub MA, Rezgui M, Nisar S, Jilani. "Parsley: A review of habitat, phytochemistry, ethnopharmacology and biological activities." *International Journal of Chemical and Biochemical Sciences IJCBS*. **2016** ;9:49-55.
6. El-Sayed MM, Metwally NH, Ibrahim IA, Abdel-Hady H, Abdel-Wahab BS. "Antioxidant activity, total phenolic and flavonoid contents of Petroselinum crispum Mill." *Journal of Applied Life Sciences International*. **2018** ;22;19(2):1-7.
7. Piras A, Porcedda S, Falconieri D, Fais A, Era B, Carta G, Rosa A. "Supercritical extraction of volatile and fixed oils from Petroselinum crispum L. seeds: chemical composition and biological activity." *Natural Product Research*. **2022** 3;36(7):1883-1888.
8. Nielsen SE, Young JF, Daneshvar B, Lauridsen ST, Knuthsen P, Sandström B, Dragsted LO. "Effect of parsley (Petroselinum crispum) intake on urinary apigenin excretion, blood antioxidant enzymes and biomarkers for oxidative stress in human subjects." *British Journal of Nutrition*. **1999**;81(6):447-455.
9. Said-Al Ahl HA, Abou-Ellail M, Omer EA. "Harvest date and genotype influences growth characters and essential oil production and composition of Petroselinum crispum plants." *J. chem. pharm. Res*. **2016** ;6;8(5):992-1003.

10. Roshankhah S, Jalili C, Salahshoor MR. "Protective effects of Petroselinum crispum on ischemia/reperfusion-induced acute kidney injury in rats." *Physiology and Pharmacology*. **2019** 10;23(2):129-139.
11. Schröder L, Koch J, Kost B, Mahner S, Jeschke U, Haumann J, Schmedt J, Richter DU. "The effects of Petroselinum crispum on estrogen receptor positive benign and malignant mammary cells." *Geburtshilfe und Frauenheilkunde*. **2017**;76(04): 39-42.
12. Wong PY, Kitts DD. "Studies on the dual antioxidant and antibacterial properties of parsley (Petroselinum crispum) and cilantro (*Coriandrum sativum*) extracts."*Food chemistry*. **2006** ;1;97(3):505-515.
13. Pápay ZE, Kósa A, Boldizsár I, Ruszkai A, Balogh E, Klebovich I, Antal I. "Pharmaceutical and formulation aspects of Petroselinum crispum extract." *Acta Pharmaceutica Hungarica.* **2012** 1;82(1):3-14.
14. Kreuzaler F, Hahlbrock K. "Flavonoid glycosides from illuminated cell suspension cultures of Petroselinum hortense. Phytochemistry." **1973** 1;12(5):1149-1152.
15. Chaves DS, Frattani FS, Assafim M, de Almeida AP, Zingali RB, Costa SS. "Phenolic chemical composition of Petroselinum crispum extract and its effect on haemostasis." *Natural Product Communication*s **2011** l;6(7):400-404.
16. Yoshikawa M, Uemura T, Shimoda H, Kishi A, Kawahara Y, Matsuda H. "Phytoestrogens from the aerial part of Petroselinum crispum MIll.(Parsley) and structures of 6"-acetylapiin and a new monoterpene glycoside, petroside." *Chemical and pharmaceutical bulletin*. **2000**;1;48(7):1039-1044.
17. Hudson CS. "Apiose and the glycosides of the parsley plant." *InAdvances in Carbohydrate Chemistry* **1949**;(4): 57-86.
18. Bruneton J. "Pharmacognosy, phytochemistry, medicinal plants."*Springer Science & Business Media* **1993**; 907-915.
19. Zhang H, Chen F, Wang X, Yao HY. "Evaluation of antioxidant activity of parsley (Petroselinum crispum) essential oil and identification of its antioxidant constituents." *Food research international*. **2006** 1;39(8):833-839.
20. Wagner H, Bladt S. "Plant drug analysis: a thin layer chromatography atlas." *Springer Science & Business Media.* **1996.**
21. Kasting R, Andersson J, von Sydow E. "Volatile constituents in leaves of parsley. Phytochemistry." **1972** 1;11(7):2277-82.
22. Lopez MG, Sanchez-Mendoza IR, Ochoa-Alejo N. "Compartive study of volatile components and fatty acids of plants and in vitro cultures of parsley (Petroselinum crispum (Mill) nym ex hill)." *Journal of agricultural and food chemistry.* **1999** 16;47(8):3292-3296.
23. Chaudhary SK, Ceska O, Tétu C, Warrington PJ, Ashwood-Smith MJ, Poulton GA. "Oxypeucedanin, a major furocoumarin in parsley, Petroselinum crispum." *Planta medica*. **1986**;52(06):462464.
24. Francis GW, Isaksen M. "Droplet counter current chromatography of the carotenoids of parsley Petroselinum crispum." *Chromatographia*. **1989**;27:549-551.
25. Davey MW, Bauw G, Van Montagu M. "Analysis of ascorbate in plant tissues by high-performance capillary zone electrophoresis". *Analytical biochemistry*. **1996** 15;239(1):8-19.
26. Nielsen SE, Young JF, Daneshvar B, Lauridsen ST, Knuthsen P, Sandström B, Dragsted LO. "Effect of parsley (Petroselinum crispum) intake on urinary apigenin excretion, blood antioxidant enzymes and biomarkers for oxidative stress in human subjects." *British Journal of Nutrition*. **1999**;81(6):447-55.
27. Popovic M, KaurinoviÇ B, Jakovljevic V, Mimica-Dukic N, Bursac M. "Effect of parsley (Petroselinum crispum (Mill.) Nym. ex AW Hill, Apiaceae) extracts on some biochemical parameters of oxidative stress in mice treated with CCl4." *Phytotherapy research*. **2007**;21(8):717-723.

28. Fejes SZ, Blazovics A, Lemberkovics E, Petri G, Szöke E, Kery A. "Free radical scavenging and membrane protective effects of methanol extracts from Anthriscus cerefolium L.(Hoffm.) and Petroselinum crispum (Mill.) Nym. ex AW Hill." *Phytotherapy Research*. **2000**;14(5):362-365.
29. Ozsoy-Sacan O, Yanardag R, Orak H, Ozgey Y, Yarat A, Tunali T. "Effects of parsley (Petroselinum crispum) extract versus glibornuride on the liver of streptozotocin-induced diabetic rats." *Journal of ethnopharmacology.***2006** 8;104(1-2):175-81.
30. Yanardağ R, Bolkent Ş, Tabakoğlu-Oğuz A, Özsoy-Saçan Ö. "Effects of Petroselinum crispum extract on pancreatic B cells and blood glucose of streptozotocin-induced diabetic rats." *Biological and Pharmaceutical Bulletin.* **2003**;26(8):1206-1210.
31. Sener G, Saçan Ö, Yanardag R, Ayanoglu-Dülger G. "Effects of parsley (Petroselinum crispum) on the aorta and heart of STZ induced diabetic rats." *Plant for HFoods uman Nutrition*. **2003**;58:1-7.
32. Sener G, Saçan Ö, Yanardag R, Ayanoglu-Dülger G. "Effects of parsley (Petroselinum crispum) on the aorta and heart of STZ induced diabetic rats." *Plant Foods for Human Nutrition*. **2003**;58:1-7.
33. Riaz G, Chopra R. "A review on phytochemistry and therapeutic uses of Hibiscus sabdariffa L." *Biomedicine & Pharmacotherapy*. **2018** 1;102:575-586.
34. Singh P, Khan M, Hailemariam H. "Nutritional and health importance of Hibiscus sabdariffa: a review and indication for research needs." *Journal of Nutritional Health & Food Engineering*. **2017**;6(5):125-128.
35. Okereke CN, Iroka FC, Chukwuma MO. "Phytochemical analysis and medicinal uses of Hibiscus sabdariffa." *International Journal of Herbal Medicine.* **2015**:16-19.
36. Jabeur I, Pereira E, Barros L, Calhelha RC, Soković M, Oliveira MB, Ferreira IC. "Hibiscus sabdariffa L. as a source of nutrients, bioactive compounds and colouring agents." *Food Research International*. **2017;** 1;100:717-723.
37. Ilyas RA, Sapuan SM, Kirubaanand W, Zahfiq ZM, Atikah MS, Ibrahim R, Radzi AM, Nadlene R, Asyraf MR, Hazrol MD, Sherwani SF. "Roselle: production, product development, and composites in Roselle." *Academic Press* **2022;** 1-23.
38. Mahadevan N, Kamboj P. "Hibiscus sabdariffa Linn.–an overview." *Acta Pharmaceutica Hungarica..* **2009** 77-86
39. Ismail A, Ikram EH, Nazri HS. "Roselle (Hibiscus sabdariffa L.) seeds nutritional composition protein quality and health benefits."*Natural Product Communication*s **2008**;2(1):1-6.
40. Singh RK, Sureja AK, Singh D. "Amta and Amti (Hibiscus sabdariffa L.)-Cultural and agricultural dynamics of agrobiodiversity conservation."*Natural Product Communication*s **2006**;556-560.
41. Choudhary SH, Kaurav HE, Chaudhary GI. "Gokhru (tribulus terrestris and pedalium murex): medicinal importance of chota gokhru and bada gokhru in ayurveda and modern science." *Asian J. Pharm. Clin. Res.* **2021** ;29;14(6):6-13.
42. Hussain AA, Mohammed AA, Ibrahim HH, Abbas AH. "Study the biological activities of Tribulus terrestris extracts." *World Academy of Science, Engineering and Technology.* **2009;** 24;57:433-435.
43. Ștefănescu R, Tero-Vescan A, Negroiu A, Aurică E, Vari CE. "A comprehensive review of the phytochemical, pharmacological, and toxicological properties of Tribulus terrestris L." *Biomolecules*. **2020** 12;10(5):752-757.
44. Chhatre S, Nesari T, Somani G, Kanchan D, Sathaye S. "Phytopharmacological overview of Tribulus terrestris pharmacognosy review." *International Journal of Herbal Medicine* **2014**;8(15):4549.
45. Adaikan PG, Gauthaman K, Prasad RN. "History of herbal medicines with an insight on the pharmacological properties of Tribulus terrestris." *The aging male*. **2001** 1;4(3):163-169.

46. Wang B, Ma L, Liu T. "406 cases of angina pectoris in coronary heart disease treated with saponin of Tribulus terrestris." *Zhong xi yi jie he za zhi= Chinese journal of modern developments in traditional medicine*. **1990**1;10(2):85-87.
47. Tomova M, Gjulemetova R, Zarkova S, Peeva S, Pangarova T, Simova M. "Steroidal saponins from Tribulus terrestris L. with a stimulating action on the sexual functions". *InFirst International Conference on Chemical, Biotechnological and Biologically Active Natural Products*r. **1981**; 299-303.
48. Gauthaman K, Adaikan PG. "Effect of Tribulus terrestris on nicotinamide adenine dinucleotide phosphate-diaphorase activity and androgen receptors in rat brain." *Journal of ethnopharmacology*. **2005**;1-2:127-32.
49. Adimoelja A, Ganeshan AP. "Protodioscin from herbal plant Tribulus terrestris L improves the male sexual functions, probably via DHEA." *Int J Impot Res.* **1997** 1-70.
50. Gauthaman K, Adaikan PG, Prasad RN, Goh VH, Ng SC. "Changes in hormonal parameters secondary to intravenous administration of Tribulus terrestris extract in primates." *International Journal of Impotence Research*. **2000**;1:6.
51. Adaikan PG, Gauthaman K, Prasad RN, Ng SC. "Proerectile pharmacological effects of Tribulus terrestris extract on the rabbit corpus cavernosum." *Annals of the Academy of Medicine, Singapore*. **2000**:22-26.
52. Li M, Qu W, Wang Y, Wan H, Tian C. "Hypoglycemic effect of saponin from Tribulus terrestris." *Journal of Chinese medicinal materials*. **2002**:420-422.
53. Adeghate E. "Effect of subcutaneous pancreatic tissue transplants on streptozotocin-induced diabetes in rats." *Morphological studies on normal, diabetic and transplanted pancreatic tissues*. **1999:**66-72.