Review on Khadira (Acacia catechu Willd.) with special reference to Prameha (Diabetes)

Shweta Satpudke, Tabassum Pansare and Surekha Khandekar

Abstract

Prameha (Diabetes) is one amongst the refractory disease conditions recognised by medical scholars of ancient India. The prevalence of diabetes is increasing globally with a rise from about 30 million in 1985 to 177 million cases in 2000 and worldwide estimates project that more than 360 million people will be suffered diabetes by the year 2030. There are many ayurvedic formulations, herbs, minerals available for treatment of Prameha. Khadira is an important medicinal plant used in ayurvedic formulation and also well documented in Indian pharmacopoeia. Ayurvedic classics texts mentioned Khadira in treatment of Prameha due to its dominance of Tikta, Kashayarasa, Katuvipaka and Laghu, Rakshaguna and Kaphashoshan (Absorption of Kapha), Shophhara (Anti-inflammatory), Vranaropan (Wound healing), Medohara (Anti-obesity) actions. Modern research shows that Khadira possesses Flavonoids, Saponins and Alkaloids which work against diabetes. This review gives detail information regarding importance and role of Khadira in treatment of Prameha.

Keywords: Khadira, Acacia catechu, Prameha, diabetes

1. Introduction

Khadira belongs to family fabaceae which is also called pea family or legume family due to presence of single chambered legume in all species of this family. Acacia catechu is a small to moderate sized plant widely distributed throughout Asia [1]. The main origin of this plant is Pakistan, India, Thailand and Bangladesh [2]. It contains polyphenolic compounds, tannins, alkaloids, carbohydaraes and seeds of this plants are good source of protein. Catechin present in this plant plays a vital role as anti-oxidant. In vivo catechins are extensively and rapidly metabolized and impart to its anti-oxidant property [3]. Khadira is use in Vatajikasa (Dry cough), Krumikushtha (useful in skin diseases), Raktapitta (Urticaria), Vranashodhan (useful in wound), Mukharoga (useful in mouth disease), Dantaroga (beneficial for teeth), Sthavarishprativish (useful in poisoning), Swarbhedha (useful in horseness of voice), Visfota (beneficial for skin disease) [4]. Khadira is used in Ayurveda in treatment of diabetes. Khadira has multi targeted effects on various physiological system of human body [5]. During the intense search in classical texts of Ayurveda, it is found that Khadira is one the common drug has Pramehaginha (Anti-Diabetic) property And Acacia catechu showed its wide acceptance as an anti-diabetic effect. This review gives detail information about mode of action of Acacia catechu in Prameha (Diabetes). Its formulations in Prameha chikitsa (Treatment of Diabetes), Chemical compositions and Pharmacological actions which are works against Diabetes.

2. Prameha Samprapti (Pathophysiology)

In Ayurveda, Prameha is the condition caused by impairment of Kapha Dosha and Jala Mahabhoota i.e. Disturbed metabolism of water compartments in body giving laxity in body tissues especially in fats, muscle tissues giving them Abaddhba (lax or hypotonic) and Asamhat (not compact or loose) consistency. Kapha Dosha vitiation mainly hampers fat or lipid metabolism leading formation of Kleda (tissue waste products in liquid form dampening the body tissues). Excessive formation of Kleda, excessive evacuation of this Kleda in form of profuse, cloudy urine ‘Prabhit Avil Mutrata’ is cardinal symptom described. This excess Kleda bring Shaithilya in surrounding tissues like muscles, lymph, marrow, semen, fat and in advance stage putrefy them. Therefore these tissues are considered as Dushyas or target tissues of Prameha. Formation Kleda, disturbed lipid metabolismare key points in pathophysiology of Prameha although all three Dosha are involved in process [6].
3. Rasapanchaka of Khadira [7]
Rasa: Kashaya, Tikta
Vipaka: Kata
Veerya- Sheet
Guna: Laghu, Ruksa
Prabhav- Kushdhaghana (Useful in skin diseases).
Doshghnata- Kaphapitthshamak
Karma – Vranaropak, Shophahar, medoghna, Pramehaghna.

4. Botanical Description of Khadira
Acacia catechu willd.Is also known as black catechu. Word acacia came from Greek word ‘thrones’ meaning ‘point or a bar’. The species name is derived from word ‘cutch’ which is tanning extract obtained from heartwood of acacia catechu [8].

5. Khadira in Pramehachikitsa
The formulations of Khadira are described in ayurvedic classics as following

5.1 Charaka Samhita: Khadira described in Kashtagna mahakashaya and Kashayskandha [9].

Table 1: Showing formulation of Khadira in Charaka Samhita.

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Diseases</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. khadira kwatha</td>
<td>Kaphaja Premeha</td>
<td>Charak Samhita Chakitsastana 6/28</td>
</tr>
<tr>
<td>2. Trikanadi Sneha</td>
<td>Vataja Premeha</td>
<td>Charak Samhita Chakitsastana 6/38</td>
</tr>
<tr>
<td>3. Sarodaka</td>
<td>Premeha</td>
<td>Charak Samhita Chakitsastana 6/46</td>
</tr>
</tbody>
</table>

5.2 Sushruta samhita: Arjuna described in Salsaradigana [10].

Table 2: Showing formulation of Khadira in Sushruta Samhita.

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Diseases</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
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<td>Sushruta Samhita Chititsastana-11/8</td>
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<tr>
<td>2. Khadira kwatha</td>
<td>Kshodrameha</td>
<td>Sushruta Samhita Chititsastana-11/9</td>
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<tr>
<td>3. Salsaradieha</td>
<td>Premeha</td>
<td>Sushruta Samhita Chititsastana-13/10</td>
</tr>
<tr>
<td>4. Loharichita</td>
<td>Premeha</td>
<td>Sushruta Samhita Chititsastana-13/12</td>
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</tbody>
</table>


Table 3: Showing formulation of Khadira in Ashtanghridayayam.

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Diseases</th>
<th>Reference</th>
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<td>Ashtang Hridaya Chakitsastana 12/77</td>
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<tr>
<td>2. Khadira kwatha</td>
<td>Premeha</td>
<td>Ashtang Hridaya Chakitsastana 12/18</td>
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<td>3. Khadira churna</td>
<td>Premeha</td>
<td>Ashtang Hridaya Chakitsastana 12/42</td>
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<tr>
<td>4. Khadira kwatha</td>
<td>Premeha</td>
<td>Ashtang Hridaya Chakitsastana 12/31</td>
</tr>
</tbody>
</table>

5.4 HaritaSamhita [12]

Table 4: Showing formulation of Khadira in Harita Samhita.

<table>
<thead>
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<th>Diseases</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
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<td>Madhuneha</td>
<td>Chakra Datta-33/13</td>
</tr>
<tr>
<td>Khadira kwatha</td>
<td>Pramehapidaka</td>
<td>Chakra Datta-33/49</td>
</tr>
</tbody>
</table>

5.5 Chakradatta: Khadira has been described in different formulation to treat various disorders. Reference of Khadira in Prameha are mentioned below [13].

Table 5: Showing formulation of Khadira in Chakradatta.

<table>
<thead>
<tr>
<th>Preparation</th>
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<td>Bhavprakash Madhyam Khand-38/44</td>
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<td>Premeha</td>
<td>Bhavprakash Madhyam Khand-38/46</td>
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<td>Khadira kwatha</td>
<td>Premeha</td>
<td>Bhavprakash Madhyam Khand-38/108</td>
</tr>
</tbody>
</table>

5.6 Bhavprakash: Khadira has been described in the form of various preparations which are indicated for Prameha treatment [14].

Table 6: Showing formulation of Khadira in Bhavprakash.

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Diseases</th>
<th>Reference</th>
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</thead>
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<td>Bhaishayai Ratnawali-Pramehachikitsa-20/</td>
</tr>
<tr>
<td>Khadira kwatha</td>
<td>Shanaimeha</td>
<td>Bhaishayai Ratnawali-Pramehachikitsa-27/</td>
</tr>
<tr>
<td>Kshodrameha</td>
<td>Premeha</td>
<td>Bhaishayai Ratnawali-Pramehachikitsa-28/</td>
</tr>
</tbody>
</table>

5.7 Bhaisajyaratnavali: Khadira described as below [15].

Table 7: Showing formulation of Khadira in Bhaisajyaratnavali.

<table>
<thead>
<tr>
<th>Preparation</th>
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<th>Reference</th>
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<tbody>
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</tr>
<tr>
<td>Khadira kwatha</td>
<td>Shanaimeha</td>
<td>Bhaishayai Ratnawali-Pramehachikitsa-27/</td>
</tr>
<tr>
<td>Kshodrameha</td>
<td>Kshodrameha</td>
<td>Bhaishayai Ratnawali-Pramehachikitsa-32/</td>
</tr>
</tbody>
</table>

5.8 Yogratnakara: In this, Khadira is mentioned as Pramehaghya dravya [16].

5.9 Nighantas
Bhavprakash Nighantu- Khadira is described as Medoghna (anti-obesity) and Mehaghna (anti-diabetic) dravya [17].

Raj Nighantu – Khadira is described as Kaphghna, Shophhara (anti-inflammatory) and Vranashodhana (wound healing) dravya [18].

Kaidev Nighantu - Khadira is mentioned as Kaphghna, Shophghna (anti-inflammatory), Mehahar (anti-diabetic) and medohar (anti-obesity) dravya [19].

Shodhal Nighantu – Khadira is explained as Medoghna (anti-obesity) and Mehaghna (anti-diabetic).

5.10 Dhanvantari Nighant: Khadira is described as a Kaphaghnadrayya [20].

6. Chemical constituents [21]

Heartwood: Flavanoids- Epigallocatechin, epicatechingallate, Catechin (-) epicatechin, epigallocatechingallate, rocatchin, phloroglucinol, procatechuc acid, catecutannic acid, quercetin.

Leaves -Alkaloids: Kaempferol, dihydrokaempferol, taxifolin, (+)-afzelchin gum.
Fruit- Fruit is a strap-shaped pod, 5-8.5 cm x 1-1.5 cm, flat, tapering at both ends, shiny, brown, dehiscent, 3-10 seeded; seeds broadly.

7. Mode of Action of Khadira In Prameha
The diseases Prameha defined in classics as the Kaphavata predominance. Even though all three Dosha are involved in the Prameha manifestation, the Vata predominance is understood with hypo functioning of Agni (Mand) or Vishamagni [22]. This improper Agni influence the Kapha and Aam production into the body. Further, due to unwholesome diet and regimen (Apathyadhavahiha) Kapha, Manssa, Meda get aggravated and cause the obstruction. (Margavarodha) Khadira with Kashayarasa clears the channels due to kaphoshoshan (Absorption of kapha) as well as decreases the Kleda. Katuipaka helps to increases the digestion. Thus it stimulates the Jatharagni and regularizes the Mandagni which is the main cause of Prameha. Laghu and Ruksha guna clears the Mala, Kleda from strotas and alleviates. So the Khadira is capable of correcting the Dhatuvitiatision (Satihityata). Due to Kashaya rasa, sheet Veerya and Ruksha guna, it acts as sthambhaka hence performs Mutrasangrahayantikarma ie. Reduces the amount of Mutra thus restore the normal Ambu. Khadira has ‘Tikta’ rasa in addition to Kashayarasa. Tiktarasa has predominance of Akasha and Vayumahabhoota. So it has ability of permeate to sушмастротасас. Due to this drug can reach at cellular level and help to reduce meda and Kleda. Thus, helps in breakdown of Pramehasampranti and reduces related symptoms [23]. Many atimes diabetes existed along with obesity and diabetic wound. Properties of Khadira like Pramehaghna (Anti-diabetic), Mehaghna(Anti-obesity) and Vrana ropan (wound healing) properties are well explained in ayurvedic classics.

8. Relation between chemical compositions and Prameha Flavonoids: It is important antioxidant and promotes several health effects. Flavonoids in Diabetes usually alternate the diabetes treatment by reducing the aldose ructcase, regenerating the pancreatic cells, enhancing insulin release and increasing calcium ion uptake [24]. The role flavonoids are quite important in fighting with complications of diabetes mellitus than any other method of treatment [25]. Also, Flavonoids stimulated glycogen synthesis in rats soleus muscle through mechanisms well known to insulin signal transduction [26].

Saponins- Saponins have been found having Pharmaceutical properties of anti-inflammatory, anti-fungal, anti-bacterial, antiviral and anti-diabetes. In the aspect of anti-diabetes, saponins activates AMPK in a calcium-dependent manner, thus regulating gluconeogenesis and glucose uptake. Saponins effectively alleviated hyperglycemia in diabetic rats by up-regulating the expression of glucose transporter type 4(GLUT4) while down-regulated the expression of G6P in insulin signal pathway [27].

Triterpenoids- The therapeutic approach of Triterpenoids to treating DM is to decrease postprandial glucose levels. It can be achieved through the inhibition of α-glucosides and α-amylases which delay the absorbance of carbohydrates in postprandial insulin level [28].

Bitter principle- Compound stimulate peripheral and skeletal muscle glucose utilization and inhibits intestinal glucose uptake and shows hypoglycemic effect [29].

9. Research on Pharmacological Actions of Khadira
9.1 Anti-oxidant activity
As the Khadira contain many potent flavonoids such as catechin present in this plant plays a vital role as anti-oxidant. Catechins and rutin are most importance constituents which are free radical scavengers. Anti-oxidant principles of Acacia catechu willd were analysed by Dot-blot assay and quantitative analysis by DPPH radical scavenging assay which ascorbic acid as standard [30, 31].

9.2 Anti-diabetic activity
In type 2 diabetes, insulin is secreted in lesser amounts than required, thus causing much of the sugars to remain in the blood stream. Acacia also increase the level of beta cells, thus encouraging them to secrete more insulin. This is helpful for type 2 diabetes mellitus. It is also help to lose body weight. Its adrenergic amine content stimulates beta- receptors to break down the lipids in the body. This, in turn, enhances the rate of metabolism as cholesterol is broken down and hunger is curved [32].

9.3 Anti- hyperlipidemic activity
In eastern traditional medicine Acacia catechu Willd is extensively used in management of diabetes in combinations with other medicinal plants. Polar as well as non-polar components of Acacia catechu Willd shown hypoglycaemic activity. Hypoglycemic activity of extract of Khadira (Acacia catechu Willd) is assumed to be due to the presence of flavonoids which also show inhibition of cyclooxygenase and regenerate β cells. In an experiment, ethyl acetate extract of Acacia catechu Willd at a concentration of 500mg/kg/day used for 7 days, significantly decreases blood glucose level of normal as well as alloxa induced diabetic albino rats but it was not effective as that of standard drug. Studies show that myricetin, quercetin and catechin-gallateinhbit insulin stimulated glucose transporters in cells [33].

9.4 Anti-obesity activity
The bark of Acacia catechu Willd family Fabaceae, maintains healthy fat metabolism and reduces the conversion of carbohydrates to fats. In studies of rats fed on a diet containing cholesterolyoloeate, betel nut extracts significantly lowered cholesterol and triglycerides [34].

Diabetic wound healing property
9.5 Wound healing property
Crushed bark of acacia catechu is used topical on wounds as it is very potent wound healing medicinal plant. It has astringent effect and also cause precipitation of skin which makes it very good wound healing plant. Furthermore it also exhibits antimicrobial property which prevent growth of microbes on wounds. This property is due to presence of tannins, flavonoids and other active ingredients [35].

9.6 Antibacterial activity
Khadira (Acacia catechu Willd) heartwood extract is found to be an effective antibacterial agent. A study conducted in ethanolic and aqueous heartwood extract of Khadira, proved its efficacy as a potent anti-bacterial agent. Taxifolin present in heartwood of Khadira is found to be responsible for its antibacterial effect. In vitro, Acacia catechu Willd is reported to have broad spectrum antimicrobial and antifungal activity. Phytochemical studies of Khadira leaves shows the presence
of alkaloids, carbohydrates, flavones, glycosides, phenolic compounds, saponins, steroids and tannins which may be responsible for its antimicrobial activity. Its Methanolic extract having antimicrobial activity against pathogenic as well as non-pathogenic bacteria e.g. Bacillus subtilis, Staphylococcus aureus, Salmonella typhi, Escherichia coli, Pseudomonas aeruginosa and Candida albicans. It is effective against gram positive as well as gram negative bacterium.[36].

9.7 Antifungal activity
Ethanol extract of Heartwood of Acacia catechu Willd was tested for antifungal (antimycotic) activity against Candida albicans, Aspergillus Niger, Aspergillus fumigates, Mucor spp and Penicillium marneffei. Disc diffusion technique was followed for screening antifungal activity. The discs were loaded with 50μl of ethanolic extracts at different concentrations [25μg/disc, 250μg/disc and 500μg/disc]. Positive controls used were fluconazole (10mcg/disc) and amphotericin B (100 units/disc). After incubation at 28 °C for 48 hours, the zone of inhibition was measured. The extract at different concentrations showed varying degree of antifungal activity against the micro-organisms tested compared to standard. Assay was conducted to check antifungal activity of the aqueous and methanol extract of Acacia catechu Willd against fourteen human pathogenic fungi using agar disc diffusion method. The methanol extract of Acacia catechu Willd was established most promising, and found active against Candida, Dermatophytes and Aspergillus species therefore stressing the need to locate the active principle [37].

9.8 Anti-microbial activity
In vitro Khadira (Acacia catechu Willd) is reported to have broad spectrum anti-microbial and antifungal activity. Phytochemical studies of Acacia catechu Willd leaves shows the presence of alkaloids, carbohydrates, flavones, glycosides, phenolic compounds, saponins, steroids and tannins which may be responsible for its anti-microbial activity. Its Methanolic extract of has Anti-microbial activity against pathogenic as well as non-pathogenic bacteria e.g Bacillus subtilis, Staphylococcus aureus, Salmonella typhi, Escherichia coli, Pseudomonas aeruginosa and Candida albicans. It was found to be most effective against Staphylococcus aureus with about 20mm zone of inhibition at minimum bactericidal concentration (MBC) of the crude extract 1,000 lg/ml. Experiments shows that anti-microbial activity of Khadira (Acacia catechu Willd) depends on nature of solvent used for extraction, thus organic solvents used in extraction of leaves are most effective than any other [38].

9.9 Anti-inflammatory properties
The chief major active chemical components of Khadira (Acacia catechu Willd) are flavonoids which inhibit Cyclooxygenase and 5-Lipoxygenase and hence decrease inflammation. Mixed extract of Scutellaria baiacalensis and Acacia catechu inhibit Prostaglandin E2 generation in human osteosarcoma cells which express COX-2, and leukotriene production is also inhibited in human cell lines, immortalized THP-1 monocyte and HT-29 colorectal adenocarcinoma. Baicalin from Scutellaria baiacalensis and catechin from Acacia catechu Willd are responsible for dual inhibition of Cyclooxygenase and 5-Lipoxygenase. Baicalin and catechin are found to inhibit COX1, COX2 and 5-LOX. Baicalin also down regulates the expression of cytokines and PGE2, nitric oxide formation, and neutrophil invasion in a carrageenan-induced paw edemamsodel [39].

10. Conclusion
Due to Kashyarasara, Katuvipaka, it shows kaphashoshan property (Absorption of kapha), Clears the channels by reducing obstructions, and improves the hypo functioning of Agni. Due to tika rasa Khadira shows Aampachan, Angnideepana and Srotoshodhana properties. So it is useful in Prameha. Main chemical constituents of Acacia catechu are Flavonoids, Tannins, Saponins, Alkaloids, Glycosides which shows anti-diabetic activity. Khadira has been shown to possess multifarious medicinal properties such as Anti-oxidant, Anti- hyperlipidemic, Anti-diabetic, Anti-obesity, Wound healing property, Analgesic activity, Antifungal activity, Anti-inflammation activities which are help against Diabetes. With anti-diabetic activity, Khadira also screened for effective in diabetes associated with obesity and diabetes. Wound. We hope this review article will help the scientists working of Khadira in the area of traditional medicines against Diabetes.

11. References
34. Muhammad anis Hashmat. A review on Acacia catechu willd, Interdisciplinary journal of contemporary research in business, 2015;(1):593-59