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Ayurvedic Naturoceuticals: Evidence Based Data and Clinical Implications. Part II

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1. INTRODUCTION

Ayurveda is a several millennia old Indian medical system. Data from experimental, epidemiological and clinical studies provide compelling evidence that several ayurvedic neutraceuticals not only provide prophylactic and therapeutic activity against several diseases, but may actually improve general health and promote longevity. These include herbs, oils, spices, plants, minerals and trace amounts of heavy metals. Although widely used in India, firm scientific evidence for their effectiveness has been lacking due to the small and often improperly done clinical trials. However more expansive and rigorous research is now being done, providing evidence based data on the effectiveness and safety of these natural products. In the United States, ayurvedic medications are regulated as dietary supplements. The second part of this four part series reviews another seven ayurvedic supplements.

2. DISCUSSION

This part of the article looks at cinnamon, coriander, fennel, fenugreek, guggulu, gurmar and neem. A review of all citations on PubMed regarding these ayurceuticals was done. We found entries as follows: cinnamon: 1321 entries dating back to 1945; coriander: 346 entries dating back to 1946; fennel: 478 entries dating back to 1946; fenugreek: 614 entries dating back to 1932; guggulu: 67 entries dating back to 1960; gurmar: 184 entries dating back to 1961 and neem: 769 entries dating back to 1951. Other pertinent scientific articles and studies with evidence based data were also reviewed.

2.1 Cinnamon

Cinnamon has been used as an herb by several cultural practices for centuries. It is obtained from the inner bark of several trees from the genus Cinnamomum. "True Cinnamon" refers to the dried inner bark of Cinnamomum verum. Other cinnamon species, C. cassia, C. loureiroi, and C. burmannii, commonly known as cassia, are also sold as cinnamon. Cinnamon is mainly produced in Sri Lanka where it is known as kurundu. It is used in cookery as a flavoring herb for both sweet and savory dishes and several beverages. Cinnamon bark and leaf oils also form the basis of a variety of synthetically derived chemicals used in cosmetic industries. (Wijesekera, 1978) The pungent taste and scent come from cinnamic aldehyde or cinnamaldehyde.

2.1.1 Evidence based data

The available in vitro and animal in vivo evidence suggests that cinnamon has anti-inflammatory, antimicrobial, anti-fungal, anti-viral, antioxidant, antitumor, cardiovascular, cholesterol-lowering, and immunomodulatory effects. (Gruenwald et al, 2010) It also exhibits blood-pressure lowering (Akilen et al, 2013) and gastro-protective properties. (Ozbayer et al, 2013) The anti-bacterial and anti fungal activity appears to be due to the chemical cinnamaldehyde in Cassia cinnamon. Cinnamon also contains beneficial polyphenols. The most impressive medical use of cinnamon appears to be in diabetes mellitus (Akilen et al, 2012; Ranasinghe et al, 2012) In vitro studies have demonstrated that cinnamon components act as insulin mimetics, potentiate insulin activity or stimulate cellular glucose metabolism. Heavy use of cinnamon may irritate the mouth and lips, causing sores. In some people, it can cause an allergic reaction. Applied to the skin, it might cause redness and irritation. Cinnamon use is however, generally safe. An internet promoted abuse, the cinnamon challenge in which a person tries to eat 1 tablespoon of Cinnamon without the use of water in less than 60 seconds has been associated with dangerous complications. (Grant-Alfieri et al, 2013)

2.1.2 Clinical Implications

Epidemiologic and clinical studies provide some evidence for the positive modulation of dysglycemia. The complementary use of this natural herb in the treatment of type 2 diabetes mellitus appears promising. The Cochrane review maintains that there is insufficient evidence at this time to support the use of cinnamon for type 1 or type 2 diabetes. (Leach et al, 2012) The therapeutic safety and efficacy in diabetes needs to be further established by more randomized and large clinical trials.

2.2 Coriander

Coriander (Coriandrum sativum L.), is a valued herbal plant in Ayurvedic medicine. It has also been used therapeautically in a host of disorders in different civilizations. It is grown in several parts of the world, including countries of India, China, Central and Eastern Europe, Italy and the Netherlands. It is widely used for its culinary properties. The dried fruits or seeds (Coriandri fructus) are also used as a condiment in several foods. Its pleasant flavor is also utilized in the manufacture of medicines and tobacco. Its aroma is commonly incorporated in cosmetics and soaps.

2.2.1 Evidence based data

Due to the presence of a multitude of bioactives, a wide array of pharmacological activities have been ascribed to different parts of this herb, which include anti-microbial, anti-oxidant, anti-hyperglycemic, anxiolytic, anti-epileptic, anti-depressant, anti-mutagenic, anti-inflammatory, anti-dyslipidemic, and neuro-protective. Coriander also demonstrates lead-detoxifying potential. (Pathat et al, 2011; Sahib et al, 2012) Studies have also established gut modulatory, blood pressure lowering and diuretic activities. (Jabeen et al, 2009) It also possesses anti-fungal properties. (Soares et al, 2012) More commonly it is used to treat common gastrointestinal symptoms such as nausea, loss of appetite, diarrhea and flatulence. Folk uses include treatment of measles, toothaches, joint pains and infections. It has also been touted to increase milk flow in breast feeding women. The phytopharmaceutical ingredients in the coriander plant include monoterpenes, α-pinene, limpnene, γ-terpinene, p-cymene, borneol, citronellol, camphor, geraniol, coriandrin, dihydrocoriandrin, coriandronsA-E, flavonoids and essential oils. (Pathat et al, 2011) Coriander is safe to use and studies reveal a lack of toxicity. (Burdock, 2009)

2.2.2 Clinical Implications

Epidemiological and clinical studies provide suggestive evidence for the positive modulation of a host of medical disorders, especially gastrointestinal. However, clinical studies providing evidence based data in humans are lacking.

2.3 Fennel

Fennel (Foeniculum vulgare) is a hardy, perennial, highly aromatic and flavorful herb. (Zeller et al, 2006) It bulb, foliage and seeds are widely used in cooking all over the world. Fennel seeds and essential oils are often used in food products such as liqueurs, bread, cheese, and an aromatic

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ingredient of soaps and cosmetics. It is also used to flavor and reduce the side effects of some pharmaceutical products, such as laxatives. Its medicinal properties have been well recognized in Ayurveda.

2.3.1 Evidence based data

Historically, fennel has been used as an analgesic, antispasmodic, antioxidant, anti-inflammatory, antimicrobial, antimutagenic, antithrombotic, bronchodilatory, cytotoxic, diuretic, emmenagogue, estrogenic, galactagogue, gastroprotective, hepatoprotective, hypotensive, integrator, lithotriptic, memory enhancing, secretomotor and secretolytic. (Rahimi et al, 2013) It has been used as an eye lotion and topically as a poultice for snake bites. Fennel has also been ingested to speed the elimination of poisons. Fennel contains anethole, which may account for most of its medicinal actions.(Raal et al, 2012) Recent experimental studies have confirmed a broad spectrum antioxidant and antiplatelet activity, clot destabilizing effect and vasorelaxant action associated with fennel. (Tognolini, 2007) Studies also suggest antioxidant, antimicrobial and antitumor effects. (Shahat et al, 2007; Mohamad et al, 2011) As a complimentary modality, it is commonly used to treat gastrointestinal ailments such as indigestion, bloating, heart burn, gas and loss of appetite. It also appears to calm cough and reduce symptoms in upper respiratory tract infections. Its evidence based therapeutic use has been validated in colic in breast fed infants (Perry et al, 2011) and painful menstrual cramps. (Omidvar et al, 2012) Fennel ingestion is safe. Rare cases of allergic reactions have been recorded. Suspected carcinogic potential of estragole, an ingredient common in fennel tea, has never been proven and appears to be negligibly small. (Gori et al, 2012)

2.3.2 Clinical Implications

Clinical studies provide evidence for the beneficial use of fennel in infantile colic and primary dysmenorrhea. It has been used historically for a host of other conditions, but evidence based data is lacking, primarily due to a paucity of clinical studies.

2.4 Fenugreek

Fenugreek (Trigonella foenum-graecum L. Leguminosae) is a plant with small round leaves and is a common ingredient in dishes from the Indian subcontinent. It is also one of the oldest medicinal plants, with a long history of use in Ayurvedic medicine. It is commonly used in cooking, as an herb, spice or vegetable. In India it is also consumed as a condiment. (Yoshikawa et al, 1997)

2.4.1 Evidence based data

Traditional medicine ascribes several therapeutic benefits to fenugreek. These include labor induction, digestive aid, and as a general tonic to improve metabolism and health. Fegnugreek has several documented therapeutic actions. (Puri, 1998) These have been well studied. (Ulbright et al, 2007; Basch et al, 2003) Fenugreek has found therapeutic use in patients with diabetes mellitus. (Haber et al, 2013) Fenugreek decreases insulin resistance in mild type-2 diabetic patients and helps improve dysglycemia. (Gupta et al, 2001) There are also favourable effects on lipids, with reductions in serum total cholesterol, LDL and VLDL cholesterol and triglycerides. (Sharma et al, 1990) Fenugreek is also a good source of fiber which contributes to its glycemic and antilipid effects. (Madar, 1987; Roberts, 2011) Fenugreek seeds exhibit galactagogue porperties and increase milk supply in lactating women. (Zapantis et al, 2012) There is also an increase in libido in male patients attributed to their ingestion. (Steels et al, 2011) Although fenugreek has traditionally been considered safe and well tolerated, allergic reactions are known to occur, with some cross-reactivity with chickpea allergy. (Patil et al, 1997) Other reported side effects include transient diarrhea and flatulence, dizziness and hypoglycemia.

2.4.2 Clinical implications

Several animal and human trials suggest a therapeutic potential of the hypoglycemic and antihyperlipidemic properties of oral fenugreek seed powder. (Basch et al, 2003) The stimulation of lactation and the increase in libido also appear promising for clinical integration of this plant.

2.5 Guggul

The guggul (Commiphora mukul) plant is a short, horny shrub. It is commonly found in South Asia. Its resin has significant medicinal properties. It has been used in ayurveda for more than 2000 years to treat a variety of human ailments.

2.5.1 Evidence based data

Gum resin from Commiphora mukul, known as guggul, has been used for centuries in Ayurveda to treat several ailments including obesity, liver disorders, malignant sores and ulcers, urinary complaints, intestinal worms, leucoderma , edema and sudden paralytic seizures. The resin contains minerals, volatile oils, terpenes, sterols, ferulates, ferrulates, flavones, sterones, and many other active bio-chemical substances. (Shah et al, 2012) Guggulsterone, a steroid, is the major bioactive constituent responsible for guggul's therapeutic effects. Modern therapeutic focus of guggul has been primarily on its hypolipidemic effects (Urizar et al, 2003) and cardiovascular benefits. (Deng, 2007) Guggulsterone has also demonstrated anti-inflammatory effects (Sharma et al, 1977) and may play a role in the treatment of arthritis. (Singh et al, 2003) It has also been shown to have antioxidant properties and some anti-cancer activity. (Shishodia et al, 2008) In animal studies, Guggulsterone has also been shown to attenuate cardiotoxicity due to Doxorubicin, a commonly used antineoplastic drug. (Wen-Ching et al, 2012) Guggul is generally safe. It may cause stomach discomfort or allergic rash. It should be avoided in pregnant or breast-feeding women and in children. Safety of use beyond 4 months has not been well studied.

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2.5.2 Clinical Implications

Several studies provide suggestive data that guggul supplementation may have clinically relevant cardiovascular effects. (Deng, 2007) However robust evidence based human studies remain lacking. (Szapary et al, 2003). Guggul also appears to have therapeutic potential for treating acne.

2.6 Gurmar

Gurmar (gymnema sylvestre), a climbing shrub, grows in the tropical forests of India and Africa. It is an important member of the Ayurvedic medicine pharmacopeia. It is also known as gurmari, gurmarbooti, gymnema, cowplant, Australian cowplant, periploca of the woods, meshasringa, bhetki cha pala, shardunika, vishani and miracle fruit. It has an ability to make the tongue unable to taste sweets, especially when its leaves are chewed. Its name literally means "sugar killer" or "destroyer of sugar." Extracts of this plant are widely used in traditional Australian, Japananese and Vietnamese medicine. (Porchezhian et al,2003)

2.6.1 Evidence based data

Gymnemic acids exhibits anti-sweet activity, (Yoshikawa et al, 1993; Liu et al, 1992) with anti-diabetic effects. (Nahas et al, 2009; Jachak, 2002) These appear to be related to a decreased intake of sugar, decreased absorption of sugar from the intestine, increased insulin production, possibly from regeneration of pancreatic cells and decreased glucose production by the liver. It has also been noted to reduce intestinal transport of maltose in rats. It also suppresses sweet taste resulting in appetite reduction and leading to weight loss. (Kumar et al, 2012) A cardioprotective effect has been noted in rats. (Kumar e al, 2012) 5. It may also have antiviral, anti-allergic and lipid lowering effects. It has some use in digestive disorders and as a laxative. It has also been used for malaria, as an antidote for snake bites, and as a diuretic and antitussive.*The beneficial effects of G. sylvestre* are attributed to a host of phytochemicals. The leaves contain acidic glycosides and anthroquinones and their derivatives and triterpene saponins belonging to oleanane and dammarene classes. Other plant constituents include flavones, anthraquinones, hentri-acontane, pentatriacontane, α and β-chlorophylls, phytin, resins, *d*-quercitol, tartaric acid, formic acid, butyric acid, lupeol, β-amyrin related glycosides, alkaloids and stigmasterol. (Manni et al. 1965; Kanetkar et al, 2007))

2.6.2 Clinical Implications

Experimental and small clinical studies suggest that gymnema sylvestre suppresses the taste of sugar and may play a potential complementary therapeutic role in the management of obesity, metabolic syndrome and diabetes mellitus. Large scale human studies are indicated.

2.7 Neem

Neem (Azadirachta indica) is widely recognized as a wonder tree due its extensive array of documented medical benefits. (Brahmachari, 2004) It has been used in Ayurveda for centuries. Besides its biomedical properties, it is also finding increasing commercial use as an insecticide, pesticide and an agrochemical agent. Sacred rituals in many South Asia cultures incorporate neem leaves. The tree grows in tropical and semi-tropical regions and is native to India, Pakistan, and Bangladesh.

2.7.1 Evidence based data

All parts of the neem tree- leaves, flowers, seeds, fruits, roots and bark have been used traditionally for the treatment of inflammation, infections, fever, skin diseases and dental disorders. Its fruits and seeds are the source of neem oil. Neem twigs are often used for brushing teeth by the indigenous Indian population. Villagers use neem leaves in different parts of India for curing gastrointestinal disorder such as diarrhea and cholera. (Thakurta e al, 2007) More than 140 compounds have been isolated from different parts of neem, especially its leaves. These have demonstrated immunomodulatory, anti-inflammatory, antihyperglycaemic, antiulcer, antimalarial, antifungal, antibacterial, antiviral, antioxidant, antimutagenic and anticarcinogenic properties. (Subapriya et al, 2005) Although some liver, kidney and testicular toxicity has been documented in lab animals with high doses of neem oil, (Deng et al, 2013) use of neem products in humans appears to be relatively safe. (Bandyopadhyay et al, 2004; Mbah et al, 2007)

2.7.2 Clinical Implications

Neem gel has been documented to reduce gingivitis. It may also reduce plaque. (Chatterjee et al, 2011) Several research papers have also documented a therapeutic activity against hyperacidity and a tendency to help heal stomach and intestinal ulcers. (Maity et al, 2009; Bandyopadhyay et al, 2004) Other medical benefits still require evidence based clinical verification.

3. CONCLUSIONS

Ancient medicine was based on naturopathic principles, and recent well organized clinical trials are providing evidence based legitimacy to these ancient claims. This four part article evaluates twenty eight ayurvedic naturoceuticals (ayur-ceuticals) which have been garnering clinical interest and appreciation they deserve. However, more robust studies need to be done, to define doses and investigate side effects, so that more targeted guidelines are made available for their clinical intergration.

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