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MEDICINAL PLANTS ON ANTIDIABETIC ACTIVITIES

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ABSTRACT

Gymnema sylvestre (Asclepiadaceae) also known as ‘gurmar’ or ‘sugar destroyer’ is a woody, climbing traditional medicinal herb which has many therapeutic applications in Ayurveda system of medicine. It is used for lowering serum cholesterol, triglycerides and blood glucose level (hypoglycaemic or antihyperglycemic), hyperlipidaemia, weight loss, stomach ailments, constipation, water retention and liver diseases, either high or low blood pressure, tachycardia or arrhythmias, and used as appetitive, purgative, in eye troubles, anti-inflammatory, smooth muscle relaxant, prevention of dental caries, cataract and as anticancer-cytotoxic agent. Bitter gourd (Momordica charantia L.; Family: Cucurbitaceae) is a vegetable with tropical and subtropical distribution. Bitter gourd fruit is a rich source of nutrients and ranks first among cucurbits for its nutritive value, being a good source of carbohydrates, proteins, vitamins, and minerals. Natural antioxidants in bitter gourd are primarily plant phenolics and polyphenolic compounds derived from fruits and seeds, and thus are alternatives to replace synthetic antioxidants to enhance food quality. Fruit contains as many as 14 carotenoids (five at the immature stage, and six and 14 in the mature-green and ripe stages, respectively) and cryptoxanthin, which is the principal chloroplast- and chromoplast-based pigment in ripe fruit. These plants are used to cure diabetes. They are best described as antidiabetic drugs.

INTRODUCTION

Diabetes mellitus (DM), commonly referred to as diabetes, is a group of metabolic disorders in which there are high blood sugar levels over a prolonged period. Symptoms of high blood sugar include frequent urination, increased thirst, and increased hunger. If left untreated, diabetes can cause many complications. Acute complications can include diabetic ketoacidosis, hyperosmolar hyperglycemic state, or death. Serious long-term complications include cardiovascular disease, stroke, chronic kidney disease, foot ulcers, and damage to the eyes.

Diabetes is due to either the pancreas not producing enough insulin or the cells of the body not responding properly to the insulin produced. There are three main types of diabetes mellitus.

- Type 1 DM results from the pancreas's failure to produce enough insulin. This form was previously referred to as "insulin-dependent diabetes mellitus" (IDDM) or "juvenile diabetes". The cause is unknown.
- Type 2 DM begins with insulin resistance, a condition in which cells fail to respond to insulin properly. As the disease progresses a lack of insulin may also develop. This form was previously referred to as "non insulin-dependent diabetes mellitus" (NIDDM) or "adult-onset diabetes". The most common cause is excessive body weight and insufficient exercise.
- Gestational diabetes is the third main form, and occurs when pregnant women without a previous history of diabetes develop high blood sugar levels.

Prevention and treatment involve maintaining a healthy diet, regular physical exercise, a normal body weight, and avoiding use of tobacco. Control of blood pressure and maintaining proper foot care are important for people with the disease. Type 1 DM must be managed with insulin injections. Type 2 DM may be treated with medications with or without insulin. Insulin and some oral medications can cause low blood sugar. Weight loss surgery in those with obesity is sometimes an effective measure in those with type 2 DM. Gestational diabetes usually resolves after the birth of the baby.

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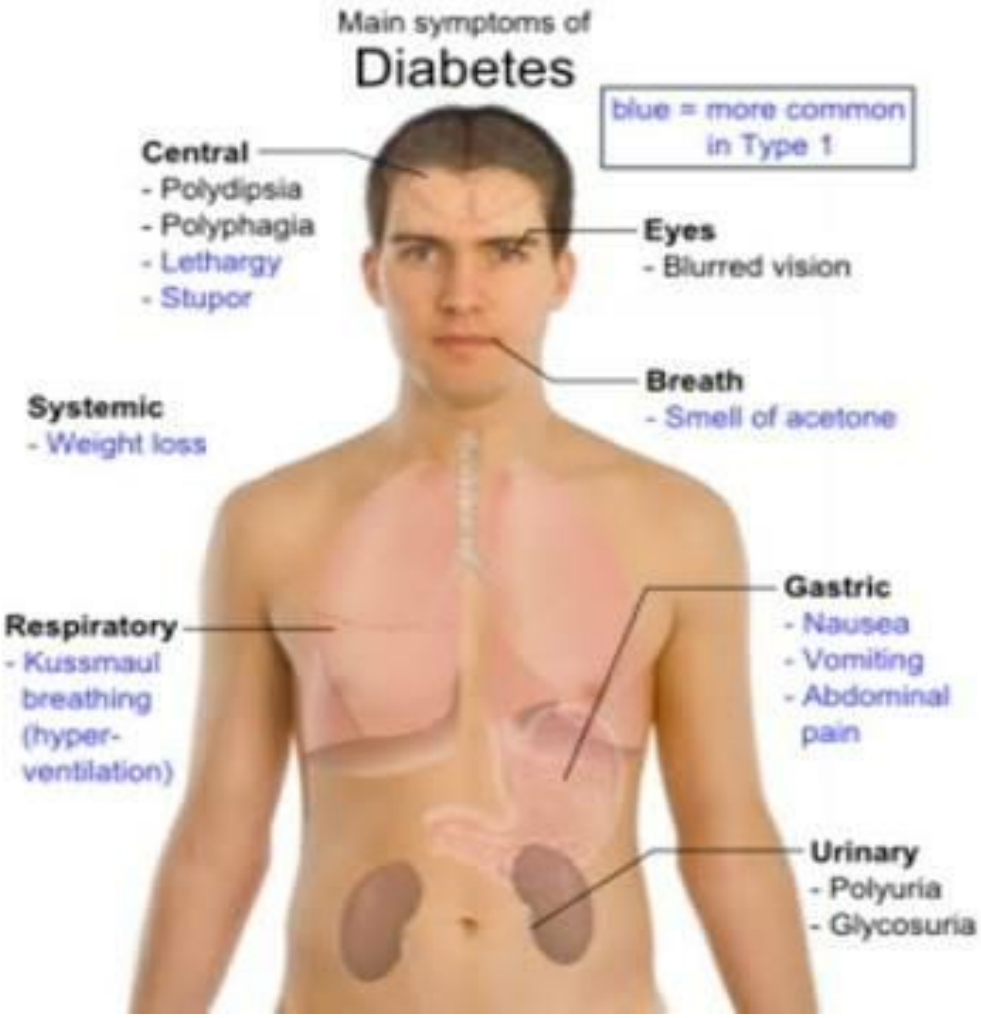
The classic symptoms of untreated diabetes are weight loss, polyuria (increased urination), polydipsia (increased thirst), and polyphagia(increased hunger). Symptoms may develop rapidly (weeks or months) in type 1 DM, while they usually develop much more slowly and may be subtle or absent in type 2 DM.

Several other signs and symptoms can mark the onset of diabetes although they are not specific to the disease. In addition to the known ones above, they include blurry vision, headache, fatigue, slow healing of cuts, and itchy skin. Prolonged high blood glucose can cause glucose absorption in the lens of the eye, which leads to changes in its shape, resulting in vision changes. A number of skin rashes that can occur in diabetes are collectively known as diabetic dermadromes.



PATHOPHYSIOLOGY

Insulin is the principal hormone that regulates the uptake of glucose from the blood into most cells of the body, especially liver, adipose tissue and muscle, except smooth muscle, in which insulin acts via the IGF-1. Therefore, deficiency of insulin or the insensitivity of its receptors play a central role in all forms of diabetes mellitus.

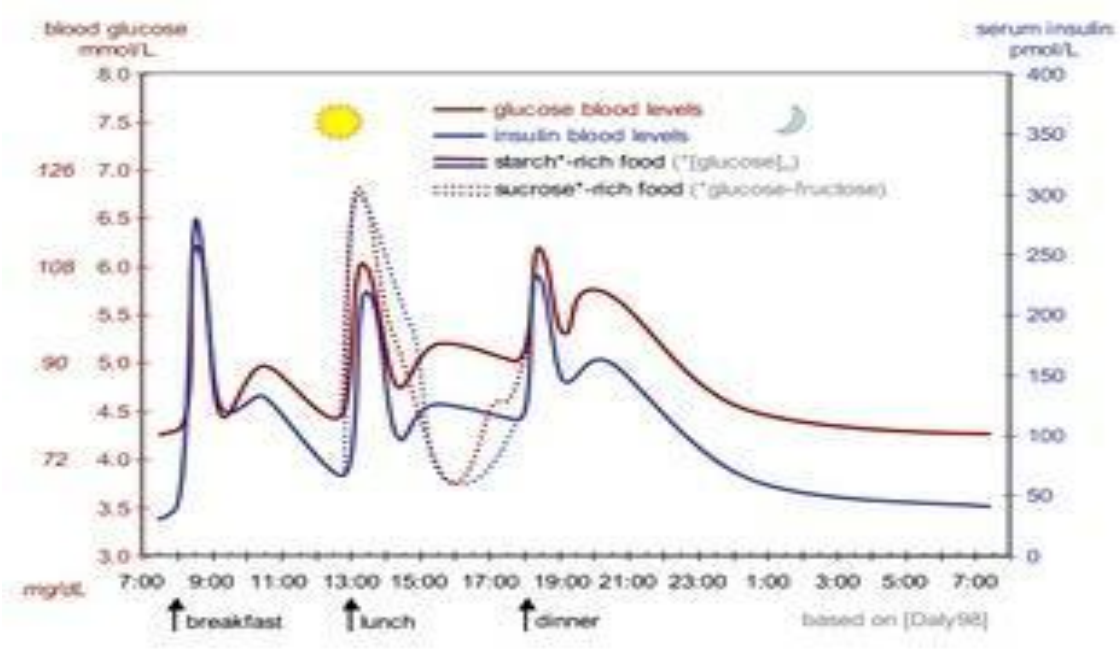
The body obtains glucose from three main sources: the intestinal absorption of food; the breakdown of glycogen, the storage form of glucose found in the liver; and gluconeogenesis, the generation of glucose from non-carbohydrate substrates in the body. Insulin plays a critical role in balancing glucose levels in the body. Insulin can inhibit the breakdown of glycogen or the process of gluconeogenesis, it can stimulate the transport of glucose into fat and muscle cells, and it can stimulate the storage of glucose in the form of glycogen.

Insulin is released into the blood by beta cells(β-cells), found in the islets of Langerhans in the pancreas, in response to rising levels of blood glucose, typically after eating. Insulin is

used by about two-thirds of the body's cells to absorb glucose from the blood for use as fuel, for conversion to other needed molecules, or for storage. Lower glucose levels result in decreased insulin release from the beta cells and in the breakdown of glycogen to glucose. This process is mainly controlled by the hormone glucagon, which acts in the opposite manner to insulin.

If the amount of insulin available is insufficient, or if cells respond poorly to the effects of insulin (insulin insensitivity or insulin resistance), or if the insulin itself is defective, then glucose will not be absorbed properly by the body cells that require it, and it will not be stored appropriately in the liver and muscles. The net effect is persistently high levels of blood glucose, poor protein synthesis, and other metabolic derangements, such as acidosis.

When the glucose concentration in the blood remains high over time, the kidneys will reach a threshold of reabsorption, and glucose will be excreted in the urine (glycosuria). This increases the osmotic pressure of the urine and inhibits reabsorption of water by the kidney, resulting in increased urine production (polyuria) and increased fluid loss. Lost blood volume will be replaced osmotically from water held in body cells and other body compartments, causing dehydration and increased thirst (polydipsia).



GYMNEMA SYLVESTRE

Despite the use of several types of oral anti-diabetic drugs, treatment of type-2 diabetes is still a major problem due to therapy failure (DeFronzo, 1999). Such failure is evident in a

majority of patients after 10 years treatment with sulfonylurea, a widely used class of drugs that stimulate insulin release by closure of B-cell K-ATP channel (DeFronzo, 1999; Brown et al., 2004). Herbal medicines known to be useful in diabetes treatment may be able to lead to compounds with such a combination of ideal therapeutic properties (Gupta, 1961; Jain and Sharma, 1967; Reddy et al., 1989; Stocklin, 1969; Liu, 1992; Sinsheimer and Manni, 1965). Yet, according to an earlier review of herbs and nutrient. supplements that were claimed to improve glycemic control few plants were supported by rigorous clinical evidence. The herbs that did demonstrate positive clinical effects were Gymnema sylvestre. Of particular interest was the herb Gymnema, because of its long history as a treatment for diabetes, and its range of unique and varied effects.

G. sylvestre (Asclepiadaceae) a vulnerable species is a slow growing, perennial, medicinal woody climber found in central and peninsular India. Its leaves, called “Gurmar” in India, are well known for their sweet taste suppressing activity (Kapoor, 1990) and are used for the treatment of diabetes mellitus (Dixit and Pandey, 1984; Gupta, 1961; Jain and Sharma, 1967; Reddy et al., 1989) for over 2000 year, hence the name “Gurmar” meaning 'sugar destroying'. It is used in food additives against obesity.

G. sylvestre is a woody, climbing herb indigenous to the tropical forests of central and southern India. The plant belongs to Kingdom Plantae with Division Angiospermae and Class Dicotyledoneae. Gymnema is native to south-Indian forests. It is a large tropical liana native to central and western India and can be also found in tropical Africa and in Australia (Stocklin, 1969). The current review is aimed at providing an overview on ethnomedicinal, pharmacological studies including clinical and experimental studies, hypoglycemic and anti-hyperglycemic activities of plants, active hypoglycemic compounds and constituents along with their available toxicity status.

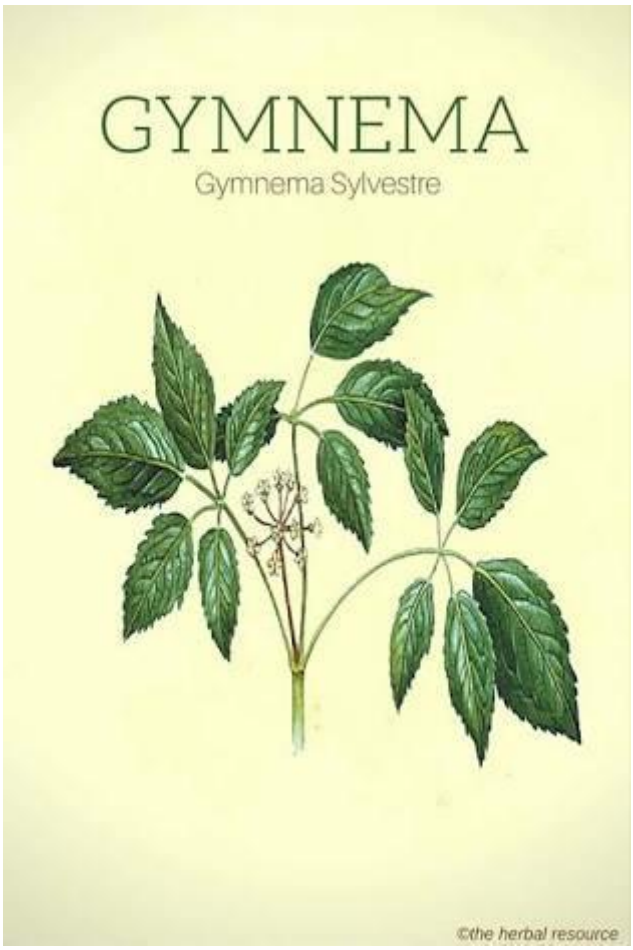
CHEMICAL CONSTITUENTS AND BIOACTIVE COMPONENTS

The anti-diabetic array of molecules has been identified as a group of closely related gymnemic acids after it was successfully isolated and purified from the leaves of G. sylvestre (Liu 1992; Sinsheimer and Manni, 1965). Later, the phytoconstituents of G. sylvestre were isolated, and their chemistry and structures were studied and elucidate (Sinsheimer and Manni, 1965; Sinsheimer et al., 1970; Yoshikawa et al., 1989; Yoshikawa et al., 1992). Gymnemic acids, a group of triterpenoid saponins belonging to oleanane and dammarene classes. Oleanane saponins are gymnemic acids and gymnemasaponins, while dammarene

saponins are gymnemasides. Gymnemic acids I-VI were isolated and characterized from aqueous leaf extracts and gymnemic acids XV-XVIII from the saponin fraction of the leaves. Gymnemic acids VIII-XII have been elucidated as glucosideuronic acid derivatives of gymnemagenin (Porchezhian and Dobriyal, 2003). Gymnemic acids are thought to be responsible for the antidiabetic activity of G. sylvestre; gymnemic acid VIII was the major component of an extract shown to stimulate insulin release from the pancreas (Persaud et al., 1999).

Gymnema saponins I-V, groups of anti-sweet principles with a novel D-glucoside structure are also present in gymnema extracts. Besides this, other plant constituents are flavones, anthraquinones, hentri-acontane, pentatria contane, α and β- chlorophylls, phytin, resins, d-quercitol, tartaric acid, formic acid, butyric acid, lupeol, β-amyrin related glycosides and stigmasterol. The plant extract also tests positive for alkaloids. The structure of gurmarin, another anti-sweet agent found in gymnema, has been elucidated as a polypeptide comprising 35 amino acid residues (Fletcher et al., 1999).

Mechanism of Action of Gymnemic Acids The main constituent of gymnema is believed to be gymnemic acid, a mixture of at least 17 different saponins. Gymnemic acid formulations have been found useful against obesity, according to recent reports (Yoshikawa et al., 1993). This is attributed to the ability of gymnemic acids to delay the glucose absorption in the blood. The atomic arrangement of gymnemic acid molecules is similar to that of glucose molecules. These molecules fill the receptor locations on the taste buds thereby preventing its activation by sugar molecules present in the food, thereby curbing the sugar craving. Similarly, Gymnemic acid molecules fill the receptor location in the absorptive external layers of the intestine thereby preventing the sugar molecules absorption by the intestine, which results in low blood sugar level.



BITTERGOURD

In the last few years there has been an exponential growth in the field of herbal medicine and these drugs are gaining popularity both in developing and developed countries because of their natural origin and less side effects. Many traditional medicines in use are derived from medicinal plants, minerals and organic matter.[1]

In Indian systems of medicine most practitioners formulate and dispense their own recipes.[2]

The World Health Organization (WHO) has listed 21,000 plants, which are used for medicinal purposes around the world. Nepal, a repository of wild flora and fauna, harbors 2.2% of world‘s flowering plants in spite of sharing only 0.1% of the total land area of the world. Out of the 7000 species of higher plants available in Nepal, recent literature claims that, more than 1400 are of medicinal value.[3,4,5] Moreover, neighboring country India is the largest producer of medicinal herbs and is called botanical garden of the world. Among 2500 medicinal species in India, 150 species are used commercially on a fairly large scale.[2]

Diabetes mellitus is the one of the five leading causes of death in the world.6 It is a major global health problem with a projected rise in prevalence from 171 million in 2000 AD to 366 million in 2030 AD with majority still remaining undiagnosed.[7]

It is a syndrome of disordered metabolism, usually due to a combination of hereditary and environmental causes, resulting in abnormally high blood sugar levels.[8]

Etiologically, it is due to relative or absolute lack of insulin, the insensitivity of insulin or both. Momordica charantia is the most common plant used in alternate medicines as anti-diabetic. Extracts and Active Ingredients Today around 228 different medicinal compounds have been isolated from the stems, leaves, pericap, entire plant, aerial parts of the plant, endosperm, callus tissues, cotyledons and mainly the seeds and unripe fruit in different laboratories in India, Japan, USA, Thailand, Egypt, China, Taiwan, Australia, Nigeria, Pakistan, Brazil, Nepal, Philippines and Peru.[22] Medicinal value of Momordica charantia has been attributed to phenols, flavonoids, isoflavones, terpenes, anthroquinones, and glucosinolates, all of which confer a bitter taste.[19]

Medicinal Uses Anti-Inflammatory Action

Ganesan et al. demonstrated that anti-inflammatory activity of dried leaves were comparable to 10 mg/kg of indomethacin.[23]

Further, Sharma et al. reported wound healing capacity of fruit powder were comparable to those of povidone iodine ointment in an excision, incision and dead space wound model in rats.

Anxiolytic Action

Ganesan et al. proved anxiolytic activity of methanol extract of dried leaves of Momordica charantia in elevated plus maze test.[30]

Antidepressant Action

Ganesan et al. during evaluation of swimming behavior of the animals elucidated that the antidepressant effect of orally administered methanol extract of Momordica charantia leaves is comparable to the standard drug imipramine.[30]

Antifeedent and Antioviposition Action

Lee et al. reported that the methanol extract of Momordica charantia leaves exhibited strong oviposition deterrent activity against Liriomyza trifolii female, a kind of pest.[31]

Mosquito Larvicidal Action

Singh et al. demonstrated larvicidal property of Momordica charantia against three mosquito species— anopheles stephensi, Culex quinquefasciatus and Aedes aegypti.[32]

Anti-viral action

In vitro studies have shown that Momordica charantia fruit-extracts inhibit infection and growth of several viruses, including HIV[33] Herpes simplex and Epstein Barr virus.[34,35]

Anti-bacterial and Anti-Protozoal Action

Momordica charantia extracts also inhibit the growth of numerous gram-negative and gram-positive bacteria, including E. coli, Salmonella, Shigella,[36]

Staphylococcus, Pseudomonas, Streptobacillus, Streptococcus, and H. pylori,[37] and protozoal organisms such as E. histolytica and Plasmodium falciparum.[38]

Hypolipidemic Activity

Kumar et al. reported that the Momordica charantia decreases "bad" cholesterol and increases "good" cholesterol.[39] Ahmed et al.[40] and Yadav et al.[41] proved hypolipidemic as well as hypoglycemic effects of Momordica charantia fruit in the STZ-induced diabetic rat.

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REFERENCES

1. Abdel-Barry JA, Abdel-Hassan IA, Al-Hakiem MH. Hypoglycaemic and antihyperglycaemic effects of Trigonella foenum-graecum leaf in normal and alloxan induced diabetic rats. J Ethnopharmacol, Nov1997; 58(3): 149–155.
2. Adachi Y, Yoshida J, Kodera Y, Katoh A, Takada J, Sakurai H. Bis(allixinato)oxovanadium(IV) complex is a potent antidiabetic agent: studies on structure-activity relationship for a series of hydroxypyrone-vanadium complexes. J Med Chem, 2006 Jun; 49(11): 3251–3256.
3. Uprety Y, Poudel RC, Shrestha KK, Rajbhandary S, Tiwari NN, Shrestha UB, et al. Diversity of use and local knowledge of wild edible plant resources in Nepal, 2012; 8: 16.

4. Kunwar RM, Mahat L, Acharya RP Bussmann RW. Medicinal plants, traditional medicine, markets and management in far-west Nepal. J Ethnobiol Ethnomed, 2013; 9: 24.
5. Manandhar NP, Manandhar S. Plants and People of Nepal. New york, USA: Timber Press, 2002.
6. Joseph B, Jini D. Insight into the hypoglycaemic effect of traditional Indian herbs used in the treatment of diabetes. Res J Med Plant, 2011; 5(4): 352-376.
7. Longo D, Fauci A, Kasper D, Hauser S, Jameson J, Loscalzo J. Harrison‘s Principles of Internal Medicine. 18th ed. USA: Mcgraw-hill, 2011.
8. Shaw JE, Sicree RA, Zimmet PZ. Global estimates of the prevalence of diabetes for 2010 and 2030. Diabetes Res Clin Pract, Jan 2010; 87(1): 4–14.
9. Zimmet P. Globalization, coca-colonization and the chronic disease epidemic: can the Doomsday scenario be averted? J Intern Med, Mar 2000; 247(3): 301–10.
10. Zimmet P, Shaw J, Alberti KGMM. Preventing Type 2 diabetes and the dysmetabolic syndrome in the real world: a realistic view. Diabet Med, Sep 2003; 20(9): 693–702.
11. Homoeopathy ID of IS of M. The ayurvedic pharmacopoeia of India, Volume 1, Part 2. 1 st ed. New Delhi: Govt. of India, Ministry of Health and Family Welfare, Dept. of ISM and H, 2007.
12. Kirtikar KR, Basu BD. Indian Medicinal plants,Volume I. Dehra Dun: International Book distributors, 1999.
13. Nadkarni KM. Indian materia medica. Vol. I. Bombay: Popular Prakashan; 1976.
14. Williamson EM. Major herbs of Ayurveda. 1st ed. Ghaziabad: The Dabur research Foundation and Dabur ayurvet limited, 2002; 182.
15. Taylor L. Herbal Secrets of the Rainforest: The Healing Power of Over 50 Medicinal.