

A brief review on anti diabetic plants: Global distribution, active ingredients, extraction techniques and acting mechanisms

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ABSTRACT

A study has been conducted with the aim to provide researchers with general information on anti diabetic extracts based on relevant research articles collected from 34 reliable medical journals. The study showed that Asian and African continents have 56% and 17% share of the worldwide distribution of therapeutic herbal plants, respectively. In Asia, India and China are the leading countries in herbal plants research, and there has been an increase in medicinal research on plants extract for diabetes treatment since 1995 in these regions. The information collected shows that plant leaves are about 20% more favorable for storing active ingredients, as compared to other parts of herbal plants. A brief review on the extraction techniques for the mentioned parts is also included. Furthermore, the acting mechanisms for the anti diabetic activity were described, and the related active ingredients were identified. The findings reveal that most of the anti diabetic research is focused on the alteration of glucose metabolism to prevent diabetes.

Key words: Active ingredient; Anti diabetic treatment; extraction technique; herbal plants extract

INTRODUCTION

Research on diabetes treatment is gaining ground as the world population with diabetes is rising each year, and is expected to hit 439 million adults by 2030.^[1] The awareness on the issue has led to a vast discovery of new medications as well as natural products extracted from herbal plants. Many active ingredients extracted from herbal plants possess therapeutic values, i.e. hypoglycemic activity, antioxidant action, etc and they are yet to be discovered. In view of that, a study has been performed on anti diabetic plant extracts and the focuses are on: the global distribution of the plants; the parts in which therapeutic elements are located; and, also the acting mechanism for diabetic treatment. This study not

only provides researchers with the information pertaining to anti diabetic plants, but also to evaluate their related research activities. The papers reviewed in this article are selected from the medicinal journals as tabulated in Table 1 due to their popularity and reliable reputation in medicinal research on herbal plant extract. The research papers were extracted from the selected journals under key words of "Plant extract for diabetes treatment".

The information extracted from the 34 journals listed was compiled and arranged into respective sections as guidance for any interested parties.

GLOBAL DISTRIBUTION OF ANTI DIABETIC PLANTS

Anti diabetic plants were widely distributed in six continental regions, and some specific regions around the world such as in Caribbean, Mediterranean and Middle East. This section lists the areas of distribution of the anti diabetic plants with the intention to identify and deduce their locations. The worldwide distribution of anti diabetic plants is depicted in Figure 1. This figure shows that Asia (56%) and Africa (17%) dominated the global distribution of the anti diabetic plants. This is not surprising as the two continents are located in the tropic and sub-tropic regions, and have large coverage of tropical rain forests. Moreover, these regions have their long established traditional medicine systems. As the activity of herbal plant researches in

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Table 1: The selected 34 medicinal journals for the study

- Antiviral Research
- Asian Pacific Journal of Tropical Medicine
- Biochemical and Biophysical Research Communication
- Bioorganic and Medicinal Chemistry
- Biotechnology
- Cancer Letters
- Carbohydrate Polymer
- Chemico-Biological Interaction
- Clinical Research and Review
- Diabetes Research and Clinical Practise
- Environmental Toxicology and Pharmacology
- European Journal of Integrative Medicine
- European Journal of Pharmacology
- Fitoterapia
- Food and Chemical Toxicology
- Food Chemistry
- Free Radical Biology and Medicine
- General Pharmacology
- International Immunopharmacology
- Journal of Biological Sciences
- Journal of Controlled Release
- Journal of Ethnopharmacology
- Journal of Food Composition and Analysis
- Journal of Urology
- Life Sciences
- Metabolism
- Neuroscience Letter
- Nutrition
- Nutrition Research
- Nutrition, Metabolism and Cardiovascular Diseases
- Parasitology International
- Pharmacological Research
- Phytomedicine
- South African Journal of Botany

Data was extracted from 1990 up to June 2010.

certain regions is proportional to the plant distribution, American continent has a 10% research performed on the medicinal plants. European countries led by Germany are closely behind with 6%. Besides, some strategic regions such as Caribbean, Mediterranean and Middle East, have individually engaged to around 2 to 4% research on herbal plants, and Australian continent has contributed 1 % to the anti diabetic herbal plants research.

Based on the records for 20 years of research on plants possessing anti diabetic properties [Figure 2], Asia and Africa demonstrate an increase in the trends and research activities since 1995, and this rise is further expected to continue. Comparing between these two continents, the increment of the research on herbal plants in Asia is about 40% higher than that in the African continent. On the other hand, North America, South America and Europe show stable increase in the research activity towards the year 2010, whereas Australia remains unchanged in its research activity on anti diabetic plants for the last 20 years. From this figure, it is clear that Asia and Africa which are rich in plants effective for diabetes treatment, have carried out maximum research in the past few years.

The distribution in Figure 2 indicates that Asia has the most

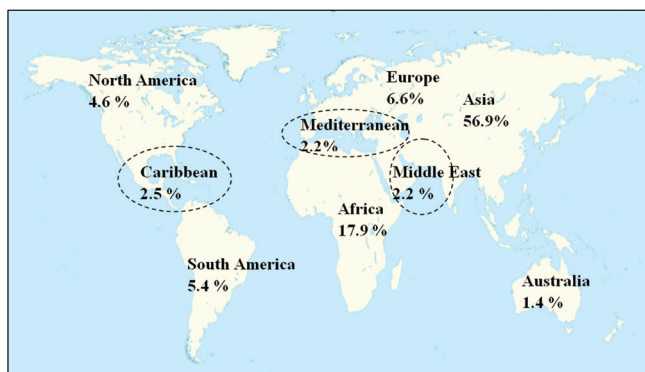


Figure 1: Distribution of plants for diabetes treatment as seen in the study

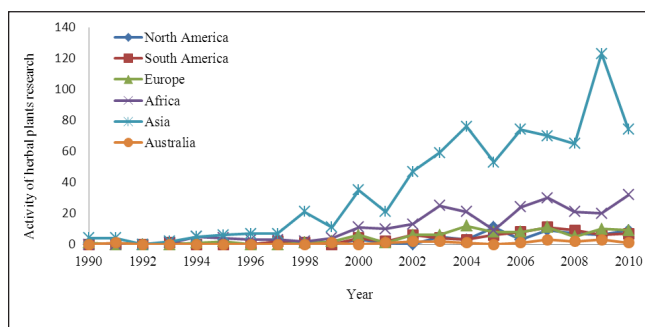


Figure 2: Activity of plant-based research for anti diabetic treatment in the past 20 years as seen in the study

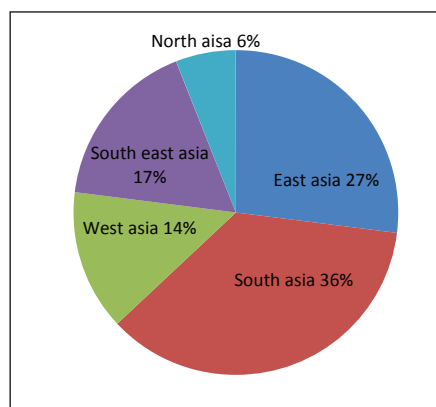


Figure 3: The distribution of anti diabetic plants in Asia as seen in the study

herbal plants which corresponds to the large numbers of researches conducted in the region. The detail distribution of the anti-diabetic herbal plants in this continent is charted in Figure 3. South Asia has a large distribution of 36% followed by East Asia and South East Asia which dominate 27% and 17% respectively. The leading countries for the herbal plant research here are India and China. Many of the research hypotheses have been based on traditional medicine system such as Chinese Herbology and *Ayurveda*. These two traditional medicine systems are the foundation for the herbal plant medicinal research in their respective regions. Northern Asia has the least distribution of the herbal plants due to its temperate zone and Siberian influence

whilst, South Asia and East Asia are the potential regions of herbal plants, and so is their intermediate, South East Asia.

DISTRIBUTION OF ACTIVE ANTI DIABETIC COMPOUNDS IN PLANTS AND THEIR EXTRACTION TECHNIQUES

The parts of plants that possess active compounds for diabetic treatment and various types of extraction techniques applied are presented in this section. In some cases in which the active ingredients are scattered all over the plants, the entire plants were prepared and extracted for the desired ingredient. More than 80 plants with printed records from the 34 related journals reviewed in this manuscript involved the extraction of the whole plant for desired compounds in the last one decade. Generally, leaves are the favorable storage site for desired compounds and more than 35% of the plants extractions for diabetic treatment can be obtained from these parts as illustrated in Figure 4. Besides, fruits contain substantial amount of active ingredients, and thus, in many occasions they are consumed as juice via oral administration to obtain the desired compounds. Other parts of plants that can be extracted for therapeutic compounds are root, aerial parts, flowers, seeds, stem barks, etc.

Most of the extractions used in plants extract research are associated with the conventional techniques. The techniques employed in the extraction are tabulated in Table 2. In conventional extraction, the release of the desired compounds traditionally required soaking and maceration in mild solvents. In traditional Chinese medicine practices, decoction in water is broadly employed and is an effective method to be considered in cases where the presence of a chemical solvent is undesired.^[2-6] In addition to the soaking/maceration technique, percolations using methanol and ethanol on the stem were also applied.^[7-12] Other solvents such as acetone, petroleum ether and hexane have also been used as solvents in the conventional extraction.^[13-15] Moreover, extraction by liquid nitrogen was also witnessed in some research works.^[16] The soxhlet technique for extracting anti-diabetic ingredient was not popular until 2005, after which the extraction technique was incorporated with ethanol and light petroleum.^[17,18] Other than solvent extraction, techniques such as lyophilization^[19,20] and sonification^[21,22] have also been employed. Furthermore, supercritical fluid extraction and microwave assisted techniques have also been used in recent years. For instances, supercritical fluid extraction on lotus gem were carried out by Taiwanese research teams to investigate the antioxidant activity of the extract,^[23] and microwave-assisted extraction was employed to investigate the bioactivity of tea flower polysaccharides.^[24] These two advanced, non conventional techniques offer attractive advantages of short extraction time and solvent free active compounds, respectively. The extraction techniques normally used in plant research are lacking in the involvement of the engineering aspect as well, and hence the processes are not optimized. As a result, the therapeutic efficacy of the plants under investigation might be affected.

THE PLANT EXTRACTS FOR DIABETES TREATMENT AND RELATED ACTING MECHANISM

Most of the medicinal researches have aimed to evaluate the therapeutic value of plants and to identify the related active ingredients extracted. The active ingredients from flavonoids (e.g. quercetin and kaempferol), alkaloids such as dieckol, etc which are potential for diabetes treatment have been discovered and their therapeutic functions have been described in Table 3. Besides that, some polysaccharides^[25,26] from plants are also beneficial to humans in fighting diabetes.

In this study, the anti diabetic acting mechanisms of the active ingredients are categorized into 6 groups for the ease of compilation as shown in Figure 5. The acting mechanisms are namely: alteration of glucose metabolism; hypolipidemic effect; pancreatic effect; antioxidative effect; diabetes complication treatment; and, insulin-like effect. Figure 5 gives an overall picture on the trend of plant research for anti diabetic treatment based on the information gathered for the past 20 years. The figure indicates the percentage distribution of anti diabetic acting

Table 2: Various techniques employed in plant extraction as seen in the study

Conventional extraction	Non conventional extraction
Water Soaking	Soxhlet extraction involved solvents
Maceration by water, ethanol, methanol	Lyophilization
Solvent extraction (ethanol, methanol, petroleum ether, hexane, acetone, and etc)	Sonification
Percolation by water	Supercritical fluid extraction (carbon dioxide)
	Microwave assisted Extraction

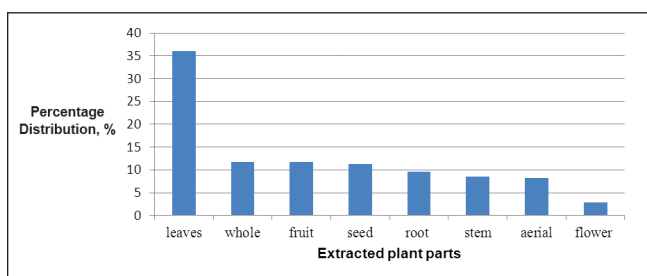


Figure 4: The percentage distribution of anti diabetic ingredients in plant parts as seen in the study

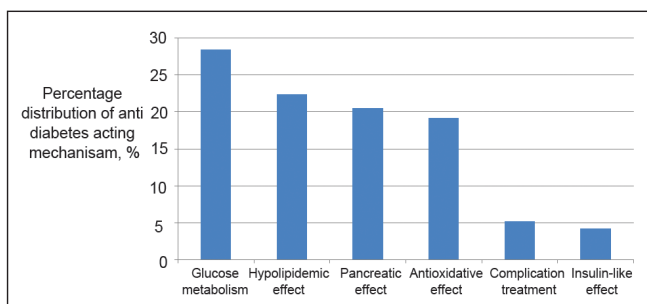


Figure 5: The percentage distribution of various anti diabetic acting mechanisms as seen in the study

Table 3: Potential anti diabetic active compounds extracted from plants in the study

Active ingredients	Plants	Therapeutic function	References
Quercetin	<i>Euonymus alatus</i> (leaves), <i>Kalanchoe pinnata</i> (leaves), <i>Eucommia ulmoides</i> (leaves)	Exhibit hypoglycaemic effect through stimulation of insulin for glucose uptake, regeneration of the pancreatic islets and prevent against dementia associated with vascular and neurodegenerative disorders.	[27-31]
kaempferol	<i>Gynura procumbens</i> (leaves), <i>Euonymus alatus</i> (leaves), <i>Equisetum myriophyllum</i> (aerial parts)	Promote hypoglycaemic effect	[27,32,33]
4-hydroxybenzoic acid	<i>Pandanus odoratus</i> (roots)	Enhance serum insulin level and liver glycogen content	[34]
3-hydroxymethyl xylitol	<i>Casearia esculenta</i> (roots)	Possess antihyperglycaemic effect	[35]
Malvidin-3-O-glucoside	<i>Vaccinium angustifolium</i> Aiton (fruits)	Exhibit hypoglycaemic activity	[36]
Apigenin	<i>Tinospora cispa</i> (stems)	Improve glucose tolerance and increase plasma insulin level	[37]
Bassic acid	<i>Bumelia sartorum</i> (root bark)	Enhance secretion of insulin from the islets of Langerhans, increase glucose uptake process and glycogen synthesis.	[38]
Catechin	<i>Cassia fistula</i> (bark), green tea (leaves)	Exhibit hypoglycaemic, glucose oxidizing and insulin mimetic activities	[39,40]
Chlorogenic acid	<i>Cecropia pachystachya</i> (leaves), <i>cecropia obtusifolia</i> (leaves)	Possess hypoglycaemic effect	[41,42]
Comatin	<i>Coprinus comatus</i> broth (whole plants)	Maintain a low level of blood glucose and improve glucose tolerance	[43]
Curcumin	<i>Curcuma longa</i> (rhizomes)	As an adjuvant therapy for the prevention and treatment of diabetic encephalopathy	[44]
Dieckol	<i>Ecklonia cava</i> (whole plants)	Potential inhibitor for α -glucosidase and α -amylase	[45]
Enhydrin	<i>Smallanthus sonchifolius</i> (leaves)	Exhibit hypoglycaemic effect	[46]
Eremanthin	<i>Costus speciosus</i> (rhizomes)	Possess hypoglycaemic and hypolipidemic activities	[47]
Gensenoside	<i>Panax ginseng</i> (roots)	Enhance glucose uptake, anti hyperglycaemic and anti obese activities by improving insulin and leptin sensitivity	[48,49]
Gugulsterone	<i>Commiphora mukul</i> (barks)	Exhibit hypoglycaemic and hypolipidemic effect	[50]
Gugulipid	<i>Commiphora whightii</i> (barks)	Potential anti dementia drug	[51]
Gymnemic acid	<i>Gymnema sylvestre</i> (leaves)	Increase the regeneration of β -cells	[52]
Lsoorientin	<i>Gentiana olivieri</i> (leaves), <i>Cecropia pachystachya</i> (leaves), <i>Cecropia obtusifolia</i> (aerial parts)	Exhibit hypoglycaemic and anti hyperglycaemic activity	[41,42,53]
Kinsenoside	<i>Anoectochilus roxburghii</i> (whole plants)	Repairing β -cells in pancreatic islet injury and improving its function	[54]
Anthocyanins (Malvidin, delphinidin, cyanidin, petunidin, peonidin) 3-glucoside	<i>Vitis vinifera</i> (fruits)	Possess inhibitory effect for lens opacity	[55]
Mangiferin	<i>Slacia oblonga</i> (stems)	Decrease fasting blood glucose level	[56]
Naringenin	<i>Ajuga iva</i> (whole plants)	Reducing lipid peroxidation and enhancing antioxidant Enzymes activities in plasma erythrocytes and tissues	[57]
Pongamol	<i>Pongamia pinnata</i> (fruits)	Possess significant anti hyperglycemic activity	[58]
Karangin	<i>Pongamia pinnata</i> (fruits)	Possess significant anti hyperglycemic activity	[58]
Genistein	soy bean	Beneficial for correcting the hyperglycaemia and preventing diabetic complications	[59]
Coumarin	<i>Hemionitis arifolia</i> (whole plants), <i>Clausena anisata</i> (roots)	Exhibit hypoglycaemic effect through stimulation of pancreatic β -cells and subsequent secretion of insulin	[60,61]
Lignans (isotaxiresinol, secoisolariciresinol and taxiresinol)	<i>Taxus yunnanensis</i> (wood)	Exhibit blood glucose lowering effect	[62]
Ursolic acid	<i>Leandra lacunosa</i> (aerial parts)	Inhibit the increase in blood glucose level	[63]

mechanisms possessed by herbal plant extracts in descending order.

Figure 5 show that 28% of the anti diabetic researches emphasized on the alteration of glucose metabolism. By altering

the glucose metabolism, it helps to regulate the blood sugar levels to normal and thus prevent diabetes, whereas other anti diabetic mechanisms assist in treating diabetes and its complications. Several active ingredients belonging to this category are: basic acid, an active compound isolated from *Bumelia sartorum*, and,

natural flavonoids such as quercetin and kaempferol as they can promote hypoglycemia through increase glucose uptake and glycogen synthesis.^[27,33,38] Recently, researchers found that dieckol, a compound isolated from *Ecklonia cava*, is a potential inhibitor for α -glucosidase and α -amylase. It exhibits hypoglycaemia by reducing the impact of carbohydrates on blood sugar and is claimed to be comparable to Acarbose, a medical anti diabetic drug.^[45] In addition, the effect of enhancing glucose tolerance and homeostasis have been reported in the root extracts of *Berberis aristata* and in comatin, an active ingredient extracted from *Coprinus comatus* broth. Both extracts can prevent diabetes by reducing the severity of insulin resistance.^[43,64]

The second, third and fourth categories of the acting mechanisms respectively focus on hypolipidemic effect, pancreatic effect and antioxidative effect. The interactions among them are important focal points for anti diabetic research; for instance, a common secondary cause of hyperlipidemia is associated with diabetes. On one hand, some herbal plants extract such as guggulsterone isolated from *Commiphora mukul* and isoorientin obtained from *Gentiana olivieri* possess hypoglycemic and hypolipidemic properties which are suitable for obese diabetes patients;^[50,53] on the other, herbal plants extract with pancreatic effect helps to enhance insulin secretion through insulin sensitizing mechanism. Furthermore, it has been reported that mangiferin and procyanidins, the natural compounds found in several plants like apple, grape and mango, exhibit hypoglycaemic activity through enhancing insulin signaling pathway.^[65,66] As for antioxidative effect, plant extracts such as green tea, *Ajuga iva* aqueous extract and Chlorogenic acid from *Cecropia pachystachya* are capable of reducing oxidative stress and protecting against tissue damage in diabetes.^[41,57,67] Another acting mechanism based on antioxidants such as kinsenoside, gymnemic acid and quercetin are helpful in preventing and treating Type I diabetes as they can regenerate the beta cells in islets of Langerhans in pancreas.^[29,52,54,68]

The last two acting mechanisms associate with diabetic complication treatment and insulin-like active ingredients administration. There are a lot of diabetic complications; however, only a few are involved in research attributing to their severity. For example, *Pterocarpus marsupium* extract is more effective compared to *Ocimum sanctum* extract as it exhibits better anti cataract effect for diabetic complication treatment.^[69] Moreover, some extracts, i.e. garlic and ginger extracts, can be used to prevent and attenuate the development of nephropathy.^[70] In addition, extracts isolated from Syzigium plants, i.e. *S. cumini* and *S. aromaticum*, are potential active ingredients for insulin substitutes.^[71,72]

CONCLUSIONS

The identified sources of plants with therapeutic value indicate that Asia has dominated more than 50% of the distribution followed by African continents which are estimated to be at 17%. Asian giants, e.g. India and China lead the research on anti diabetic plants, and correspondingly shown an increase in the related

anti diabetic research trend. From the information gathered on various parts of plant, leaves are the most favorable storage sites for active ingredients. The extraction methods commonly employed in anti diabetic plant extraction are conventional methods involving solvents. However, the engineered extraction techniques such as supercritical extraction and microwave assisted extraction are gaining more attention due to the high efficiency of these techniques, and also because they produce a better yield of the active ingredients. This review article also implies that the alteration of glucose metabolism by herbal plants is crucial as far as preventing diabetes is concerned.

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