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Mini review

# *Costus speciosus* and *Coccinia grandis*: Traditional medicinal remedies for diabetes

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ABSTRACT

Diabetes mellitus is a major illness which has been implicated with numerous clinical manifestations. Herbal medicines have become a popular form of therapy for this disease and are now being engaged in complementary means together with the usual chemical or biochemical agents due to the fact that they are less toxic at recommended dosages than synthetic counterparts. Plants have the ability to synthesize phytochemicals of medicinal value and these products in turn can be used for therapeutic purposes especially in developing countries where resources are meagre. *Costus speciosus* and *Coccinia grandis* are plants which contain reservoirs of anti-diabetic effects as well as other medicinal properties. These plants have been known to demonstrate pharmacological activities such as anti-inflammatory, anti-microbial, antioxidant, anti-dyslipidemic and anti-cancer. This review discusses the morphology of these two herbs, uses of these plants in medicinal practices, their traditional methods of administration and the bioactive compounds which have been identified to possess the anti-diabetic properties.



**Contents**



## 1. Diabetes: the current global landscape

Diabetes mellitus is an endocrinal disorder. It has been clinically identified as a global pandemic where an estimated 47 million of the world's population are victims of this disease condition (American Diabetes Association, 2011; WHO Fact Sheet, 2013). The disease initializes with a group of metabolic alterations characterized by hyperglycemia resulting from defects in insulin secretion, or a lack of physiological responses to insulin or both. It has already been established that chronic hyperglycemia in the diabetic condition is associated with long-term damage, dysfunction and eventually the failure of organs, especially the eyes, kidneys, nerves, heart and blood vessels (Halliwell and Gutteridge,

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1999). Diabetic patients are known to be five times more likely to develop heart diseases or have a stroke, as the long term effect of the disease condition causes damage to blood vessels in the body (UKPDS, 1998). Given the aetiology of the disease it can be further divided into three categories out of which Type I and Type II are the most frequent forms of the malady. In Type I diabetes, the body does not or is unable to produce insulin because of the autoimmune destruction of insulin-producing β-cells of the pancreas (Maritime, Sanders and Watkins, 2003). As a result, the glucose levels in the blood stream are increased. This condition can be predominantly seen in children and young adults as well, and in these instances, it is also known as juvenile diabetes. It is manifested by impaired glucose metabolism due to the total loss of insulin after destruction of pancreatic β-cells and is also known as insulin-dependent diabetes mellitus (IDDM). Type II diabetes is the more predominant form of the disease, in which the body does not produce sufficient amounts of insulin, or in some cases, the body is resistant to insulin (Baynes, 1991). It may also appear that the target tissues are insensitive to insulin (Atkinson and Maclaren, 1994). This type of diabetes is also known as non-insulin-dependent diabetes mellitus (NIDDM). The exact cause of diabetes is a mystery, although both lifestyle, genetic and environmental factors such as obesity and lack of exercise appear to play an important role (Atkinson and Maclaren, 1994).

### 1.1. The failures of current anti-diabetic medications

Untreated diabetes, in particular, IDDM, can lead to serious complications often resulting in a high rate of mortality. Treatment of patients with Type I diabetes normally involves daily doses of insulin administered either orally or by injections (Atkinson and Maclaren, 1994). Up to now, many kinds of anti-diabetic medicines have been developed for patients contracted with NIDDM, but almost all of them are chemical or biochemical agents conceived under laboratory environments. Despite these infinite initiatives, a complete recovery from Type 1 diabetes has not been reported to date (UKPDS, 1998). High rates of mortality have been witnessed in diabetic patients who are incessantly administered with chemically synthesized drugs, most often due to the inability of the drugs to curb the progression of the disease as well as reduce the occurrence of complications (Atkinson and Maclaren, 1994; Guyton and Hall, 2011; Tahrani and et al., 2011). As a result of these observed consequences, the global trend now is to use herbal medicine or to engage it as a complementary therapeutic option together with the usual chemical or biochemical agents (Trease and Evans, 1978; Betteridge, 1997; Okopien et al., 2003). Given the safety and reduced toxicity of therapeutic agents and bioactive compounds of phytochemical origin, these plant-based remedies are touted as promising replacements for the chemical drugs and insulin therapy (Baynes, 1991).

### 1.2. Edible plants as anti-diabetic remedies

Medicinal plants are known to be of great importance in human culture to meet the primary health care needs, as indicated by their usage throughout history and in traditional medicinal systems. Nearly 25% of the world's population relies on traditional medicinal systems for different aspects of primary health care (Prabhakar, 2008). These traditional systems like Ayurveda, Traditional Chinese Medicine and tribal medicines use plants as the primary means of disease prevention. Plants are capable of producing phytochemicals which are able to extend therapeutic properties (Patel et al., 2012). These phytochemicals are relatively non-toxic and safe for consumption, provided the correct dosages being administered. Better yet, in recent years, despite the origin of the remedies in the East, there has been an increasing interest in herbal medicines as they have increased in popularity in the West as well (Mullarkey et al., 1990). This popularity is mostly due to the fact that the herbal products are more abundant and cheaper than synthetic products. Many higher order plants have been observed to be the major sources of natural products (secondary metabolites) such as terpenes, alkaloids and cardiac glycosides which possess pharmaceutical importance (Golbidi et al., 2011). Many new bioactive drugs, isolated from plants, have demonstrated anti-diabetic effects which are even more potent than known oral hypoglycaemic agents such as daonil, tolbutamide and chlorpropamide (Devasagayam et al., 2004). The present therapeutic pathways of medicinal plants are focused on controlling and lowering blood glucose through the following means:

- Stimulation of β-cells in the pancreatic islets to release insulin
- Increasing the quantity of insulin receptors
- Decreasing gluconeogenic enzymes, thereby controlling blood glucose levels
- Fighting against free radicals by behaving as antioxidants and thereby, decreasing cell damage
- Inhibition of enzymes responsible for increased blood glucose levels

Out of these mechanisms, the inhibition of enzymes could be deemed as a more novel aspect when it comes to plant-based anti-diabetic remedies.

### 1.3. Costus speciosus and Coccinia grandis as anti-diabetic remedies

*C. grandis* and *C. speciosus* are two medicinal plants which have been used throughout history in traditional medicinal practices, especially in South Asia, to treat diabetic patients. At present, many scientific studies have been carried out or are ongoing on these two plants to exploit their beneficial effects for commercial purposes, although many of these studies are still in in vitro or in vitro phases, and not progressed onto human trials. In this aspect, toxicological studies of the two herbs are also underway. Despite their relative lack of scientific evidence, both herbs are consumed in South Asia for general health and wellness purposes and not only during the contraction of a disease condition, mostly due to their historical applications. In contrast with most medicinal plants, both species do not carry a repulsive flavour which deters them from being consumed in raw form or as a salad. They are abundantly found in the tropics and do not require special means of nurturing or harvesting. They have a very high growth rate where they might even be considered as weeds. Administration of these two plants is simple for medicinal purposes and does not require extensive preparation methods. Given the ease of cultivating these two plants, their therapeutic value, non-toxic nature and availability, this review is an attempt to emphasize the importance of *C. speciosus* and *C. grandis* as effective herbal remedies, especially to reduce the incidence of diabetes as well as to reduce the progression of the disease.

## 2. *C. grandis*

### 2.1. Morphology and applications

Fig. 1 shows the fresh, mature plant leaves and the fruit of *C. grandis*. *C. grandis* belongs to the family Cucurbitaceae. It is native to East Africa and has been widely spread in tropical Asian countries. This plant has become naturalized in these parts of the world because it is capable of thriving well in warm, humid, tropical regions (Arunvanan et al., 2013). *C. grandis* has many names such as baby watermelon, little gourd or Tindora and Kowakka as it is commonly known in Sri Lanka. This plant is a fast-growing perennial and herbaceous climber which grows into several metres covering lands that readily cover shrubs and small trees. The shape of the leaves varies from heart to pentagon, and the leaves are arranged alternately along the stem. The upper surface of the leaf is hairless whereas the lower surface is hairy (Pekamwar et al., 2013). Flowers are large, white and star-shaped, and the fruits are smooth and green. When the fruits ripen, they turn bright red, and have an ovoid to ellipsoid shape (Ediriweera and Ratnasooriya, 2009).There are 3–8 glands on the blade near the leaf stalk. Tendrils of the plant are simple. It has an extensive tuberous root system and succeeds in any soil but prefers a sunny sheltered position in a humus-rich open soil, while it is necessary

**Fig. 1.** Fresh leaves and the fruit of mature *Coccinia grandis* plant (sample obtained from the Royal Botanical Gardens, Peradeniya, Sri Lanka).

to keep the plant well-watered in the growing season (Modak et al., 2007). Since *C. grandis* is dioecious, male and female plants must be grown if seed and fruits are required. The seed usually germinates within 2–4 weeks at 20 °C (Jayaweera, 1982). Since the fruits are edible, several birds act as dispersers of seeds. Immature fruits are used in Asian cooking where young leaves and long slender stem tops of the plant are cooked and eaten as a pot herb or added to porridge (Jayaweera, 1982; Ediriweera and Ratnasooriya, 2009). Young and tender green fruits are used either as raw salads or cooked and added to curries. This plant is also used as a garden ornament. The aqueous extract of *C. grandis* is hypothesized to reduce the blood glucose level by stimulating gluconeogenesis, or inhibiting glycogenolysis with prolonged treatments in Ayurvedic medicinal treatments, which is very popular in Asian countries such as India and Sri Lanka (Shibib et al., 1993). It also has the ability to reduce the cholesterol levels as demonstrated in a few animal studies (Munasinghe et al., 2011). Some countries in Asia such as Thailand prepare traditional tonic-like drinks for medicinal purposes using the leaves of this plant (Trease and Evans, 1978).

### *2.2. Bioactive compounds present in C. grandis*

*C. grandis* is rich in secondary metabolites such as phenolic compounds and alkaloids as shown in many studies using High-Performance Liquid Chromatography–Mass Spectrometry (HPLC-MS) and Nuclear Magnetic Resonance (NMR) (Shibib et al., 1993; Ng et al., 2000; Tamilselvan et al., 2011). The phytochemicals of this plant include saponins, flavanoids, glycosides, xyloglucan, taraxerol, carotenoids and cryptoxanthin (Tamilselvan et al., 2011). Saponins in combination with phytochemicals can provide a high anti-diabetic activity, as shown in various other instances (Ng et al., 2000). They are widely distributed plant metabolites which can be isolated from the leaf extracts of *C. grandis* (Munasinghe et al., 2011). The existence of flavonoids adds value to this herb since they are a group of compounds which are known to exhibit antioxidant, and thereby, anti-diabetic activities (Halliwell and Gutteridge, 1999; Ng et al., 2000). The antioxidant activity of *C. grandis* is hypothesized to be exerted through its reducing power, hydrogen peroxide scavenging potential owing to the existence of flavonoids (Halliwell and Gutteridge, 1999). It has also shown an α-amylase inhibitory activity of 81.1%, also owing to the existence of flavonoids (Ng et al., 2000; Tamilselvan et al., 2011), although this aspect is effective only against Type II diabetes. It has been found that *C. grandis* stimulates gluconeogenesis, or inhibits glycogenolysis in diabetic rat liver (Munasinghe et al., 2011). Selected research reports based on animal studies support that compounds in this plant inhibit the enzyme glucose-6-phosphatase which is one of the key liver enzymes involved in regulating glucose metabolism (Shibib et al., 1993; Munasinghe et al., 2011). In summary, reducing glucose metabolism and absorption from the gut, increasing the insulin production from the pancreas, and reducing glucose uptake by fat and muscle cells are hypothesized to be probable mechanisms of action by which *C. grandis* exerts its anti-diabetic effects, although these hypotheses are yet to be verified. Some studies have also shown that pectin from the fruit of this plant is able to reduce the blood glucose by decreasing its absorption from the intestine and increasing liver glycogen by decreasing glycogen phosphorylase in animal models (Sastri, 1962).

### *2.3. Other uses and applications of C. grandis*

In traditional medicine, fruits of this plant are used to treat leprosy, fever, asthma, bronchitis and jaundice (Sastri, 1962). β-sitosterol—a compound isolated from several parts of this plant has the ability alone and in combination with similar phytosterols, to reduce blood cholesterol levels and is sometimes used in the treatment of hypercholesterolemia (Pekamwar, 2013). *C. grandis* is also rich in beta-carotene which is used to reduce the risk of breast cancer in women before menopause, and the risk of age-related macular degeneration (Pekamwar, Kalyankar and Kokate et al., 2013). The juice from the stem is dripped in to the eye to treat the cataracts (Patel et al., 2012), while the leaves are used as a poultice in treating skin eruptions (Pekamwar, Kalyankar and Kokate et al., 2013) and the roots are used in treating vomiting (Neelesh, Sanjah and Sappa, 2010). The fruit extract of *C. grandis* is used for reducing inflammation (Shibib, 1993). The aqueous extract of leaves of this plant is used for the anti-bacterial activity against *Shigella flexneri*, *Bacillus subtilis*, *Escherichia coli*, *Salmonella choleraesuis*, *Shigella dysenteries*, and *S. flexneri* (Jayaweera, 1982; Pekamwar et al., 2013). Aqueous extract of *C. grandis* has been known to display more significant anti-bacterial activity in comparison to ethanol extract (Munasinghe et al., 2011). Thus, chemical characterization of *C. grandis* has demonstrated this herb to be an important source of many pharmacological and medicinally important chemicals, most of them which are in existence in other plants as well and have shown therapeutic effects.

## **3. *C. speciosus***

### *3.1. Morphology and applications*

Fig. 2 shows the fresh plant leaves of *C. speciosus*. It is an ornamental, rhizomatous and perennial plant belonging to the family Costaceae

**Fig. 2.** Fresh leaves of mature *Costus speciosus* plant (sample obtained from the Royal Botanical Gardens, Peradeniya, Sri Lanka).

(Zingiberaceae). This family consists about 52 genera and more than 1300 species (Pawar and Pawar, 2012). This is a plant native to South East Asia although it is currently more abundantly found In India, Sri Lanka, Indonesia and Malaysia. Nevertheless, it has been naturalized in some tropical areas such as Hawaii as well (Pawar and Pawar, 2012). The plant is commonly referred to as crepe ginger or spiral flag in English, Kemuka, Kushta, Kashmira, in Sanskrit, Keukand, Keu in Hindi and Bengali, Chenhalya Koshta in Telengu and Thebu in Sinhalese. It is an erect, succulent herb up to 2.7 m high, arising from a horizontal rhizome (Arunvanan et al., 2013). Red stems emerge from the rhizome, which bear large and soft, variegated leaves. The leaves are elliptical to oblong or oblong-lancoelate, spirally arranged and silky beneath. They are large, white, approximately 1.5″ in diameter with thick, cone-like terminal spikes, bright red bracts and lip-white with a yellowish centre, crisped, concave disk and a turf of hair at the base (Modak et al., 2007). There are many more different species in this family such as *Costus barbatus*, *Costus chartaceus*, *Costus cuspidatus*, *Costus giganteus*, *Costus igneus*, *Costus asae* and *Costus spectabilis*, where the differences lie in the flower or colour (Arunvanan et al., 2013). Some varieties contain flowers and bracts which appear with compact cones, while others are shaped like a pineapple or soft crepe coming out of green cones (Trease and Evans, 1978). There are also differences in leaves as some leaves are pubescent on an axial surface, while others are smooth and purplish (Arunvanan et al., 2013).

The plant is mainly cultivated in the rainy season and it grows well on fertile moist soil or clayey loam soil in shady areas. A high humidity and low temperature (circa. 13 °C) are the best conditions for cultivation of this plant (Modak et al., 2007). It can be propagated by different vegetative methods such as using rhizome pieces, division of culms, stem cutting or via seeds dispersed by birds (Trease and Evans, 1978). As multiplication rate, percentage of seed germination and seed viability are low in this plant and also as delayed rooting of vegetative methods is shown, for large-scale production in preservation and commercial cultivation, biotechnological approaches such as tissue culture and germplasm preservation are currently being taken into consideration (Neelesh, Sanjah and Sappa, 2010).

### 3.2. Bioactive compounds present in C. speciosus

*C. speciosus* is widely used in several indigenous systems of medicine to treat various ailments not only limited to diabetes and its associated conditions. The leaves have been demonstrated to possess hypoglycemic properties and insulin potentiating action in addition to decreasing blood glucose levels in C57BLKS/J *db*/*db* mice (Neelesh, Sanjah and Sappa, 2010). Traditionally, it is known that the diabetic people eat one leaf of *C. speciosus* per day to regulate blood glucose levels (Oliver, 1980). *C. speciosus* is a rich reservoir of many phytochemicals which possess sensory properties such as bitter, astringent, aphrodisiac, purgative, anti-helmintic, depurative, febrifuge and expectorant (Devi and Urooj, 2010). Major secondary metabolites of this plant are alkaloids, flavanoids, glycosides, phenols, sterols and sesquiterpenes (Van Wyk and Wink, 2004). HPLC-MS has demonstrated significant amounts of saponins to be present in the herb, where the major saponins which have been isolated from the seeds of this plant include diosgenin, dioscin and gracillin (Jayaweera, 1982; Bavarva and Narasimhacharya, 2008). It has been found that diosgenin—a steroid, is the major constituent isolated from this plant and that the rhizome is the major source of this compound (Bavarva and Narasimhacharya, 2008). The maximum quantity of diosgenin reported in the stem is 0.65%, in the leaves 0.37%, and in the flower 1.21% (Bavarva and Narasimhacharya, 2008). The chemical structures of Diosgenin and Eremanthin—the two most potent bioactive compounds present in *C. speciosus* are shown in Fig. 3. G2-tocopherol and quinines have also been isolated from the seeds (Ediriweera and Ratnasooriya, 2009). Eremanthin isolated from *C. speciosus* has resulted in reduced plasma glucose level in streptozotocin-induced diabetic Wistar rats (Eliza et al., 2009). Rhizomes of this plant are also rich in dioscin, gracillin, β-sitosterol and β-D-glucoside as demonstrated from characterization using HPLC-MS and NMR (Devi and Urooj, 2010; Pawar and Pawar, 2012). In addition, some essential oils can be isolated from the rhizomes (Arbonnier, 2004). Different terpene compounds such as lupeol palmitates, β-amyrin, and α-amyrinsterate have been isolated from the leaves (Devi and Urooj, 2010). The plant is also known to contain high amounts of several antioxidants such as ascorbic acid, β-carotene, α-tecophenol, glutathione, phenol and flavonoids (Van Wyk and Wink, 2004). Two new quinones—di-hydrophytic plastoquinone and its methyl derivatives as well as α-tocopherol have been known to be present in the seeds as shown by NMR characterization (Devi and Urooj, 2010). Complementing the evidence from traditional medicinal systems, scientific evidence has been provided that the rhizome extract has the ability to reverse diabetics and its complications, and improve hepatic antioxidant enzyme activity acting on neurotransmitters and monoamine oxidase activity (Moosmann and Behl, 2002).

### 3.3. Other uses and applications of C. speciosus

*C. speciosus* has been found to possess a diverse number of pharmacological activities such as anti-bacterial, anti-fungal, anti-choline esterase, antioxidant, anti-hyperglycemic, anti-inflammatory, analgestic, antipyretic, antidiuretic, larvicidal, anti-stress and estrogenic activities (Shobana and Naidu, 2000). The rhizome of this plant is used as a vegetable and has also been used in production of pickles, while in some countries drinks are prepared using flowers and leaves (Van Wyk and Wink, 2004). The rhizome which is widely used in Ayurveda is known to be given to patients with pneumonia, constipation, skin diseases, fever, asthma, bronchitis, inflammation, anaemia, rheumatism, dropsy, cough, urinary diseases and jaundice (Moosmann and Behl, 2002). The rhizome juice of this plant is given internally to treat leprosy, while it is also known to have anti-fertility and anabolic properties (Shobana and Naidu, 2000). As for the anti-bacterial activities, it has been observed that the rhizome extract is effective against gram positive (*Staphylococcus aureus*, *Staphylococcus epidermidis*) and gram negative bacteria (*E. coli*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*)—a property associated with the presence of diosgenin (Oliver, 1980). Some parts of the plant such as the young stem and sap from leaves are used internally for eye and ear infections (Maritim et al., 2003). The leaves of *C. speciosus* are given as a treatment for mental disorders (Moosmann and Behl, 2002; Maritim et al., 2003). Tribal and rural people use this plant extracts for snake bites, bites of rabid dogs and jackals (Van Wyk and Wink, 2004). Bruised leaves are applied in fever, and decoctions of the stem are used in fever and dysentery (Oliver, 1980). The stems are also made into a paste and applied on blisters (Van Wyk and Wink, 2004). Larvicidal activity against mosquito larvae has been shown by aqueous extracts from leaves (Pellicano et al., 2008). In Japan, the Rhizome extracts are used for controlling syphilis, while in Malaysia it is used for treatment of small pox (Van Wyk and Wink, 2004). Costunolide—a sesquiterpene compound isolated from *C. speciosus*, has been known to exhibit preventive effects against intestinal carcinogenesis (Prabhakar and Doble, 2008). Costunolide also possesses the ability to decrease serum total cholesterol, triglyceride, LDL-cholesterol and at the same time increase plasma insulin, tissue glycogen, HDL-cholesterol and serum protein (Al-Aboudi and Afifi, 2011; Wazaify et al., 2011).

## 4. Commercial usage of *C. grandis* and *C. speciosus*

Although not as popular as *Momordica charantia* (bittergourd) and *Salacia reticulata*, *C. grandis and C. speciosus* have a similarly significant history of evidence where they have been successfully used for the prevention and treatment of diabetes and its associated complications. Despite the lack of scientific evidence on their efficacy and toxicological effects, traditional medicinal systems have always been effective against combating diseases of complicated nature while the remedial effects

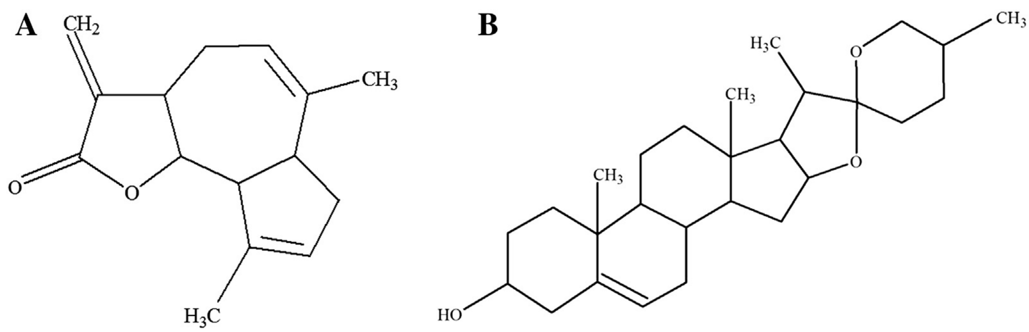


**Fig. 3.** The two most potent bioactive compounds present in *Costus speciosus*: (A) Eremanthin and (B) Diosgenin.

have always been holistic and side-effects have been minimum. Through the addition of scientific findings, an increase in the consumption of these edible plant species across the world can be made possible in such a way that they can be subjected to broad studies for diabetes management. Increasing demand of edible plants with therapeutic properties, on the other hand, may create extra pressure on natural habitats, especially given the availability of arable land. Thus, prior to using edible plants such as *C. grandis and C. speciosus* for commercial means, systematic cultivation is needed in order to ensure the sustainable utilization and conservation as well as form means of legal and diplomatic protection from exploitation of these species and its bioactive constituents.

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