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Review Article

ANTIDIABETIC ROLE OF KUNDRU (*COCCINIA INDICA*): A REVIEW

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ABSTRACT
Diabetes mellitus is prevalent globally and is stated to be one of the important causes of death worldwide. Modern medicines, despite offering a variety of effective treatment options, can have several adverse effects. The role of traditional plants in the treatment of diabetes is already known and the anti diabetic effects of many plants have been scientifically established. Several medicinal plants have found potential use as hypoglycemic agents in the Indian system of medicine, including Ayurveda. One such plant is *Coccinia indica.*
Coccinia indica (*C. indica*) belongs to cucurbitaceae family, commonly known as '*Kundru'* and is famous for its safe anti diabetic properties. It is a perennial twin with tuberous roots, smooth stem with white flowers. This plant is grown all over India; different parts of this plant were traditionally used to treat various ailments. Triterpenes present in the *Kundru* powder (or extract) act like insulin. Anti diabetic activity of *Coccinia indica* can be initiated in two ways. Firstly, by increasing pancreatic secretion of insulin from existing B-cells, which decreases blood glucose levels due to the inhibition of glucose uptake in the intestine and insulinotropic activity of the powder extract. Secondly, by depressing the key gluconeogenic enzymes, Glucose-6-phosphatase and fructose-6-biphosphatase, which enhance glucose oxidation (by shunt pathway), activates principal enzyme G6PDH and thus, lowers blood glucose. The objective of the present paper is to review the available literature regarding the anti hyperglycemic effects of kundru in type 2 Diabetes Mellitus.

Keywords: *Coccinia indica, Diabetes Mellitus*

INTRODUCTION

Diabetes mellitus is a spectrum of common metabolic disorders, arising from a variety of pathogenic mechanisms, all resulting in hyperglycemia. The number of individuals with diabetes is rising rapidly throughout the world. Both genetic and environmental factors contribute to its pathogenesis, which involves insufficient insulin secretion, reduced responsiveness to endogenous or exogenous insulin, increased glucose production, and/or abnormalities in fat and protein metabolism.

Prevalence

Worldwide, the prevalence of diabetes mellitus is estimated to be 2.8% and is expected to rise to 4.4% by 2030. In India alone, the prevalence of diabetes is expected to increase from 30.9 million to 69.9 million by 2025. Despite the availability of many drugs for treatment for diabetes, its complications continue to be major medical problems. Currently available antidiabetic drugs are not completely effective and are associated with adverse effects both in the short and long run.
Incidence rates of prediabetes and type 2 diabetes mellitus have been increasing worldwide in recent decades and 80% of diabetes patients occur in middle-income countries(International Diabetes Federation) (IDF, 2013).
Plants have always been an exemplary source of drugs and many drugs currently available have been derived directly or indirectly from them. A vast majority of population particularly those living in villages depend largely on medicinal plants for treating and curing diseases. One such medicinal plant is *Coccinia indica* (Syn. Ivy gourd, *Coccinia grandis*, *Cephalandra indica*, *Coccinia cordifolia*)(Wight and Arnott, 2014). It is indigenous plant of Central Africa, India and Asia and is cultivated abundantly in India (Assam. Bihar, Orissa Maharashtra, Andhra Pradesh, Tamil Nadu) as a vegetable and its wild form is also found in many parts of India. This plant has been wildly used in traditional Indian medicinal system (Ayurvedic, Unani, Siddha). *Cephalandra indica* is a climbing shrub with white flower. Every part of the

plant exhibit pharmacological activities, and is annual employed for treating various human ailments. It belongs to Cucurbitaceae family and it is widely used for hypoglycemic and antidiabetic activities in ayurvedic system of medicine. Mainly its fruit has antidiabetic properties as compared to other parts of plant of Coccinia Indica, but the whole plant of *Coccinia indica* has pharmacological activities like analgesic, antipyretic, anti-inflammatory, antimicrobial, antiulcer, antidiabetic, antioxidant, hypoglycemic, hepatoprotective, antimalarial, antidyslipidemic, anticancer, antitussive, mutagenic.

The leaves of *Coccinia indica* plant are either pentagonal or triangular in shape and are arranged alternatively along the stem. The lower surface of the leaf is hairy while upper surface is hairless. Leaves have pale green underneath and bright green upper surface, with astringent taste and characteristic odour. Leaves are ovate, alternate, simple, subflashy, palmately 5 lobed with obtuse apex. It shows reticulate venation with glabrous surface (Mayank and Shashi, 2013).

Flowers are star shaped, white and large. Flower is rarely in axillary clusters of 3 pedicle and each flower has three stamens (Gupta et al., 2008).

Seeds are slightly papillose, yellowish grey, much compressed and ovoid rounded at the apex. Fruits are green in colour but when ripe it becomes glabrous and red in colour. The fruit is pulpy, ovoid to ellipsoid shaped and slimy in touch (Gupta *et al.*, 2008).

Roots break with a fibrous fracture and areflexible; the fresh root is long tapering, thick, and tuberous. The cork is composed of rows of cells. Parenchyma is full of starch grains and permeation of parenchyma with vascular elements is observed (Kirtikar and Vasu, 1976).

Nowadays herbal plants are used in preparation of many drugs. *Coccinia indica* is a marvelous plant which is used to cure many ailments.

Antidiabetic Activity of Coccinia indica

Kuriyan (2008) suggested that *Coccinia indica* extract has a potential hypoglycemic action in patients with mild diabetes. It was a double-blind, placebo controlled, randomized trial. A total of sixty type 2 diabetic subjects (aged 35–60 years) were tested from St. Johns Medical College Hospital, Bangalore, India. The subjects were randomly assigned into the placebo or experimental group and were provided with 1 g alcoholic extract of the herb for 90 days. There was a significant decrease in the fasting, postprandial blood glucose and A1C of the experimental group compared with that of the placebo group. The fasting and postprandial blood glucose levels of the experimental group at day 90 significantly decreased, by 16 and 18%, respectively.

Hypoglycemic activities of leaves of *Coccinia grandis* were tested with 90% alcoholic extract. Diabetes was induced by a single intraperitoneal injection of freshly prepared streptozotocin 55 mg/kg body weight of rats in 0.1 M citrate buffer (pH 4.5). Alcoholic extract 600 mg/kg body weight was injected orally to mice. Oral administration of alcoholic extract of leaves of *C. grandis* showed significant hypoglycemic effect on blood glucose level in normal fasting rats (Ajay, 2009).

It is proved that there is an insulin stimulatory effect of C. indica leaves from existing b-cells in diabetic rats. Terpenoids are found to be responsible for antidiabetic activity. Despite the broad use of C. indica in traditional medicine, very few systematic pharmacological and phytochemical studies are reported till date assessing its therapeutic properties (http://www.pharmacophorejournal.com/).

Mallick (2007) evaluated combined extracts of Musa paradisiaca and *Coccinia indica* aqueous extract of leaf for antidiabetic activity in streptozotocin induced diabetes rats. The ethanolic extract of the aerial part decreases blood glucose levels and lipid parameters in streptozotocin induced diabetic rats at 100 or 200 mg/kg. Chronic administration of fruit extract 200 mg/kg for 14 days reduces the blood glucose level in alloxan induced diabetic rat (Gunjan *et al.*, 2010).

The aqueous extract of *Coccinia indica* reduced the blood glucose level and also reduced the cholesterol, protein and urea with prolonged treatment. *Coccinia grandis* stimulated gluconeogenesis, or inhibited glycogenolysis in the diabetic rat liver. Treatment with *Coccinia* extract increases the total protein, SGPT, SGOT (Doss *et al.*, 2008).

The *Coccinia indica* leaf extract exerts hypoglycemic activity on blood glucose and cholesterol, TG, LDL, VLDL level in alloxan induced diabetic rats (Manjula *et al.*, 2007).
Ethanolic extract of *Coccinia indica* decreased the blood glucose level in diabetic rats. Pectin from fruit reduces the blood glucose by decreasing the absorption of glucose from the intestine and increasing liver glycogen and decreasing glycogen phosporylase (Ramakrishnan *et al.*, 2011).
Alcoholic extract of *Coccinia grandis* leaves (Jose and Usha, 2010) and stem have the capacity to lower the blood glucose level in normal fasted rats (Doss *et al.*, 2008).
Ethyl acetate extract and petroleum ether extract of *Coccinia* contains triterpines, alkaloid, flavonoid, B-carotene which is responsible for it's hypoglycemic activity (Islam et al., 2011).Dried extract of *Coccinia* indica (500 mg kg/ body weight) were administered to diabetic patients for six weeks. Oral administration of *Coccinia indica* leaves showed significant hypoglycemia in alloxanized diabetic dogs and increased glucose tolerance (Ahad *et al.*, 2010).
Results of a study conducted by ujjwal *et al.*, (2017) *C. indica* and *M. balsamina* fruits possess beneficial effects in diabetes by lowering elevated blood glucose level. Six cucurbitane-type triterpenoids were isolated from bioactive extracts of *C. indica* and *M. balsamina* .
The dietary fiber content of CGF (*Coccinia grandis* fruit) extract was analyzed by the enzymatic-gravimetric method and the extract showed good amounts of both soluble (11.65 ± 0.93 mg/g) and insoluble fibers (38.42 ± 1.56 mg/g). Oral administration of pectin isolated from *C. grandis* fruits was shown to have a significant hypoglycemic effect in normal rats. Pectin is a soluble fiber that affects blood glucose levels either by decreasing the transit time or indirectly through the production of short chain fatty acids (SCFAs). Acetate, propionate, and butyrate are the commonly produced SCFAs obtained by anaerobic fermentation of dietary fiber components by the microflora in the large intestine. Thus, the high dietary fiber content of CGF extract recorded in the present study correlate the beneficial effects of CGF in the diabetic condition (Gao *et al.*, 2009 and Smith *et al.*, 1998)
Being a part of Indian traditional medicine for ages, *Coccinia indica* has been widely used in reducing blood sugar among various other uses. Hyperglycemia was induced in overnight fasted healthy adult Wister albino rats by a single intraperitoneal injection of Streptozotocin made in citrate buffer. The diabetic rats in groups received treatment with two different concentrations of the extract, the standard drug and saline. The effectiveness of extract in the maintenance of blood glucose level in both normal and diabetic rats is indicated by significant reduction of the elevated blood sugar level after 10 days of treatment (up to 41.87%) which is comparable to that of standard drug glibenclamide (43.50%) under similar conditions. The results from the experimental studies reflect the efficiency of extract to control blood glucose levels, thereby ascertaining the anti hyperglycaemic activity of methanol extract of *Coccinia indica* and its potential for safe use in the antidiabetic therapy (Ghosh and Roy, 2013).
Feeding of water soluble alkaioid fraction of alcohol extract (1 gm/kg) of *Coccinia indica* leaves to normal fasting guinea pigs showed hypoglycemic activity of short duration and the effect was attributed to the presence of beta sitosterol. Oral administration (2 gm/kg/day) of pectin isolated from C. indica fruit showed a significant hypoglycemic action in normal rats due to stimulation of glycogen synthetase activity and reduction of phosphorylase activity (Kumar *et al*, 1993).
Orally administered pectin materials isolated from fruit extracts of *C. indica* at dose = 200 mg/100 g body weight/day caused hypoglycemia in normal rats. The study noted that pectin materials caused significant reduction in blood glucose and an increase in the liver glycogen as a result of increase in hepatic glycogen synthetase activity and corresponding reduction in phosphorylase activity. Hypoglycemic effect of ethanolic extract of *C. indica* is partly due to the repression of the key gluconeogenic enzyme (glucose-6-phosphatase), but did not affect alanine aminotransferase and aspartate amino transferase activities, in starved male rats (Hossain, *et al*, 1992).
The hypoglycaemic effect of orally administered extracts of leaves and roots of *Coccinia indica* has been reported earlier. The oral administration of the pectin isolated from the fruit of *Coccinia indica* at a dose of 200 mg/100 g BW/day showed a significant hypoglycaemic action in normal rats. Pectins isolated from

many other plants have also been reported to have hypoglycaemic actions. The pectin administration resulted in a significant reduction in blood glucose and an increase in the liver glycogen. Glycogen synthetase activity was highly significant. Incorporation of labelled glucose into hepatic glycogen was also found to be higher. A significant reduction in phosphorylase activity was noted in the pectin-administered groups (Kumar et.al 1993).

Effect of aqueous leaf extract of *C. grandis* on serum/blood glycemic parameters and regenerative potential of islet cells in the pancreas of streptozotocin induced diabetic rats revealed that there was a statistically significant decrease in the percentage of glycosylated hemoglobin together with a concomitant increase in the concentrations of serum insulin and C-peptide in plant extract and glibenclamide treated diabetic rats ($p<0.05$). The β-cell regeneration in *C. grandis* extract treated diabetic rats was noted through an increase in the percentage of insulin secreting β-cells and an increase in islet profile diameter ($p<0.05$). The findings of the present investigation helps to scrutinize the therapeutic benefits of the *C. grandis* extract in the management of diabetes mellitus in traditional medicine (Attanayake *et al.*, 2015).

Coccinia indica (C. indica) extracts recover the activities of enzyme lipoprotein lipase (LPL) and glucose-6-phosphatase and lactate dehydrogenase, which were raised in untreated diabetics [Kamble SM 1998]. Oral administration of 500 mg/kg of C. indica leaves exhibits significant hypoglycemia in alloxanized diabetic dogs and increased glucose tolerance in normal and diabetic dogs (Devendra *et al.*, 2015).

Anti Dyslipidemic Activity of Coccinia indica

Ethanol extract of *Coccnia grandis* showed significant triglyceride and cholesterol-lowering effects in dyslipidemic hamster model. Ethanolic extract was fractionated into chloroform, n-butanol and water-soluble fractions (250 mg/ kg body weight) which were used to evaluate the anti dyslipidemic activity. Standard drug fenofibrate at the dose of 108 mg/kg was used. Golden Syrian hamsters (Mesocricetus auratus), male, 12-week-old, (110-120 g) body weight were used. Chloroform fraction was found to possess significant lipid-lowering activity followed by increase in high density lipoprotein-cholesterol and total cholesterol ratio. Chloroform soluble fraction which acts as active component was subjected to repeated column chromatography for the isolation of a polyprenol compound and characterized as C60-polyprenol. Polypernol was the first compound isolated from this plant. The polyprenols, which were isolated from chloroform fraction, showed anti dyslipidemic activity (Singh *et al.*, 2007, Bhatia *et al.*, 2003).

A study was designed to evaluate the hypoglycemic and hypolipidemic effect of *Coccinia indica* aqueous extract in diabetic rats. Diabetes was induced by alloxan. The study concluded that continuos administration of *Coccinia indica* reduces the increased level of serum lipids secondary to the diabetic state (Josh and Usha, 2017).

Evaluation of the antidiabetic activity of methanolic polyherbal extract of *Coccinia indica* leaves in diabetic rats was carried out on groups of Diabetic rats. They were given two concentrations of the extract (150 and 300 mg/kg, p.o.) with standard drug and saline, under similar conditions When compared to glibenclamide after 10 days of treatment there was a significant reduction of elevated blood sugar level. The results showed that the polyherbal extracts of leaves of *Coccinia indica* shows distinct antidiabetic property (Gosh and Roy, 2013).

The leaf extract (ethanolic) of Coccinia grandis significantly decreased Serum triglyceride, glycerol and total cholesterol and in high fat diet (HFD)-fed dyslipidemic hamsters at a dose of 50 mg/kg body weight. According to this study the leaves of *Coccinia grandis* contain polyprenol and exhibits marked antidyslipidemic activity (Singh *et al.*, 2007).

Singh *et al.*, (2007) evaluated Coccinia grandis leaf extract for antidyslipidemic activity in hamsters. Chloroform extract of *Coccinia grandis* leaves containing polyprenol, lowers the plasma lipid profile and increases high density lipid cholesterol and total cholesterol ratio. It drastically decreased serum triglycerides by 42%, total cholesterol 25% and glycerol 12%, in high fat diet fed dyslipidemic hamsters

at the dose of 50 mg/kg body weight. Aqueous and ethanolic extracts of leaves can be used for control of obesity (Mishra *et al.*, 2012).

CONCLUSION

As we know, India has become the diabetic capital and diabetes itself is a big risk factor for other morbidities, it is of utmost importance that natural treatment options that are effective, available and safe for consumption are explored.

In view of the onset of modern medicine, the traditional plant medicine has taken a back seat although they still play vital remedial roles more in developing countries than in the developed countries. These plants possess phytoconstituents like polyphenols, flavonoids, tannins saponins, alkaloids, steroids, amino acids, essential oils etc. and have negligible side effects. In India, use of the different parts of several medicinal plants to cure specific aliments has been practiced from ancient time. A vast majority of population, particularly those living in rural areas depends largely on medicinal plants for treatment of diseases.

Therefore, this study is being undertaken to probe into the possibilities of using *Coccinia indica* for their antidiabetic effects in adults with T2DM.

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