

# Review of antidiabetic activity of “Rang Jeud” *Thunbergia laurifolia*

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## ABSTRACT

Diabetes mellitus still is the serious medical problem to human health due to rapid increase and lead the cause of death in the developed and developing countries. It characterizes by hyperglycemia because there is the defect in insulin secretion, or the reduced sensitivity of the tissue to insulin. The clinical reports revealed that diabetes cannot be cured completely. The newer anti-hyperglycemic drugs continue searching because the existing synthetic drugs have several limitations. Traditional medicinal plants and their phytochemical substances have been used in the treatment of diabetes mellitus and associated secondary complications more than a century, but only a few of these have proofed their safe and efficacious. The aim of this review article is focused *Thunbergia laurifolia* one of the medicinal plants used for antioxidant activities. *T. laurifolia* contains several kinds of glycosides, flavonoids, gallic acid and phenolic compounds. Many researches have evaluated that these phytochemical substances have the major impact on diabetes. In conclusion this review focuses on the hypoglycemic activity of this plant and clear that it has the potential to be considered as a candidate for preparing new treatment of diabetes mellitus.

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## INTRODUCTION

Globally, it is estimated that 387 million people suffer from diabetes mellitus for a prevalence of 8.3% in 2014 (IDF, 2014). The future trend indicates that more than 60% of the world's diabetic population will be in Asian countries because of the rapidly occurrence in socioeconomic and industrialization growths (Ramachandran *et al.*, 2012). Diabetes mellitus, one of the fastest-growing health problems is concerned about the use of anti-hyperglycemic drugs because of undesirable pathological conditions in the example the adverse effect of metformin is gastrointestinal discomfort, pioglitazone with bladder cancer and heart failure, sulfonylureas with hypoglycemia and weight gain (Valeron and de Pablos-Velasco, 2013). There are the ethnobotanical studies of medicinal plants used in the treatment of diabetes mellitus in many countries. Manosroi *et al.* (2011) reported the hypoglycemic activity of five Thai medicinal plants, including *Anogeissus acuminata* (Combretaceae), *Catunaregam tormentosa* (Rubiaceae), *Dioecrescis erythroclada* (Rubiaceae), *Mimosa pudica* (Fabaceae), and *Rauwolfia serpentina* (Apocyanaceae), which have been traditionally used in the

Northern part of Thailand. Maroyi (2011) identified 61 medicinal plant species in Zimbabwe belong to 45 genera and 28 families, mostly from the Fabaceae, Anacardiaceae, Ebenaceae, Euphorbiaceae, Tiliaceae, Loganiaceae, and Moraceae are exclusively used against diabetes. Semanya *et al.* (2012) identified 24 medicinal plant species in South Africa belong to 20 families, mostly from the Asteraceae (13%), Cucurbitaceae and Sapotaceae (8%). *Plumeria obtuse* and *Momordica balsamina* are exclusively used. Soladoye *et al.* (2012) identified 132 medicinal plant species in South-Western Nigeria from 56 families in the treatment of diabetes. The families with most antidiabetic plants were Leguminosae, Euphorbiaceae, Apocynaceae, Cucurbitaceae, Moraceae and Rutaceae. The most prominent in the preparation of anti-diabetic recipes are *Senna alata*, *Curculigo pilosa*, *Cucurmeropsis mannii*, *Anthocleist spp*, *vernonia amygdalina* and *Allium spp*. Tag *et al.* (2012) identified 46 medicinal plant species in Northeast India and reported the new 11 plant species on antidiabetic efficacy as *Begonia roxburghii*, *Calamus tenuis*, *Callicarpa arborea*, *Cuscuta reflexa*, *Dillenia indica*, *Diplazium esculentum*, *Lectuca gracilis*, *Millingtonia hortensis*, *Oxalis griffithii*, *Saccharum spontaneum*, and *Solanum viarum*. Mootosamy and Fawzi Mahomoodally (2014) identified 111 medicinal plant species in Mauritius from 56 families in the treatment of diabetes. The families with most antidiabetic plants were Asteraceae. According to 8 quantitative indexes,

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*Bryophyllum pinnatum* had the highest fidelity level value (FL=100%). *Allium sativum* had the highest relative importance value (RI=2.00). *Aloe vera* had the highest relative frequency of citation value (RFC=0.61), the cultural importance index value (CII=0.64) and the highest cultural agreement index value (CAI=0.635). *Psidium guajava* had the highest quality use agreement value (QUAV=0.961). *Allium cepa* had the highest quality use value (QUV=0.965). *Morinda citrifolia* had the highest use value (UV=1.21) (Mootoosamy and Fawzi Mahomoodally, 2014). From these previous surveys, *Thunbergia laurifolia*, one of the medicinal plants has been used in ethnomedicine. *T. laurifolia*, synonym with *T. grandiflora* and *T. harissi*, has been widely used as “Traditional Medicinal Plant” in Central and Southern Africa, Asia, and Central America to relieve symptoms of various diseases (Singtonat and Osathanunkul, 2015). It is commonly known as laurel clock vine, blue trumpet vine, babbler’s bill, purple allamanda, sky flower. It belongs to the family Acanthaceae. There are around 200 global species belonging to the genus *Thunbergia* whose names after the Swedish botanist, Carl Peter Thunberg (1743-1822) (Nordenstam, 2013). The vernacular name of *T. laurifolia* is also known as kukua loti (Assanese), neel lota (Bengali), liane mauve (French), neel lata (Hindi), kar tuau (Malay), rang jeud, rang yen, nam nong (Thai) (Chan and Lim, 2006).

### Morphological characters

*T. laurifolia* is a woody climbing and ornamental plant (Fig. 1A). It is a long-lived vine with tuberous roots that grows up to 15 m in height. Its younger stems are square in cross-section and bear oppositely arrange leaves on stalks up to 6 cm long. Older stems are quite thick when mature and usually become rounded. Its flowers are trumpet-shaped, with 5-7 rounded and pale purplish-blue petals, and a yellow throat. The flower is up to 8 cm long and 6-8 cm across (Fig. 1B). Its leaves are dark green, opposite, heart-shaped, with a pointed tip and slightly serrated leaf margin. The leaf blade can grow up to 20 cm in length and 16 cm in width with a petiole up to 6 cm in length. Leaves are thin and bright green in color when young, and tend to be darker green, thick and slightly variegated as they mature (Fig. 1C). Its seed pod is cone-shaped, 1 cm long, with a round base (Chan *et al.*, 2011). It is native to India, Indochina, Southern China, Taiwan,

the sub-continent, Southeastern Asia, and Northern Australia (Chan *et al.*, 2011). However, now it is cultivated and can be easily found in worldwide.

### Phytochemical substances

*T. laurifolia* contains several kinds of iridoid glucosides (Kanchanapoom *et al.*, 2002), alkaloids, flavonoids (Rojsanga *et al.*, 2012), phenolic acids such as caffeic acid, gallic acid, protocatechuic acid, and chlorogenic acid (Thongsaard *et al.*, 2005; Oonsivilai *et al.*, 2007). Two novel iridoid glucosides of 8-*epi*-grandifloric acid and 3'-*O*- $\beta$  glucopyranosyl-stilbericoside, with seven known grandifloric acid compounds: benzyl  $\beta$ -glucopyranoside, benzyl  $\beta$ -(2'-*O*- $\beta$ -glucopyranosyl)-glucopyranoside, grandifloric acid, (*E*)-2-hexenyl- $\beta$ -glucopyranoside, hexanol- $\beta$ -glucopyranoside, 6-*C*-glucopyranosyl apigenin and 6,8-di-*C*-glucopyranosyl apigenin were reported by Kanchanapoom *et al.* (2002). The flavonoids extracted from *T. laurifolia* as apigenin, apelin casmosiin, delphinidin-3-5-di-*O*- $\beta$ -D-glucoside and chorogenic acid (Kanchanapoom *et al.*, 2002). A phenolic profiling of water extract of leaves of *T. laurifolia* showed the presence of apigenin and apigenin glucosides, as well as phenolic acids of caffeic, gallic and protocatechuic (Chan *et al.*, 2012).

### Biological activities

*T. laurifolia* is traditionally used for anti-inflammation (Boonyarikpunchai *et al.*, 2014), antimicrobial (Wonkchalee *et al.*, 2012; Khobjai *et al.*, 2014), antidiabetic (Aritajat *et al.* 2004), antioxidant (Suwancaikasem *et al.*, 2013 and 2014), anticancer activities (Jetawattana *et al.*, 2015), detoxifying (Chattaviriyi *et al.*, 2010; Palipoch *et al.*, 2011a and 2011b; Rocejanasaroj *et al.*, 2014), and associated diseases such as hepatological (Wonkchalee *et al.*, 2012) and neurological diseases (Thongsaard and Marsden, 2013; Phyu and Tangpong, 2013).

The chronic oral administration in rat with 20, 200, 1,000 and 2,000 mg/kg/day for six months of *T. laurifolia* did not show any affect the body weight, food consumption, behavior or general health of the animals. The hematological and biochemical parameters increased, however, these were within the normal range. No histological alteration of the visceral organs was observed (Chivapat *et al.*, 2009).



**Fig. 1:** *Thunbergia laurifolia* is a woody climbing plant (A), flower (B) and leaves (C).

Laovithayangoon *et al.* (2007) reported the lead and mercury, heavy metal residues in commercial *T. laurifolia* tea was in the acceptable levels (<10 mg/kg), and no mutagenic effect. Those results indicated that *T. laurifolia* is safe in its oral effective dose.

### Hypoglycemic activity

Medicinal plants and their derivatives represent more than 50% of all the drugs in modern therapeutics (Pan *et al.*, 2013). However, there are still not many data available about the hypoglycemic activity of this medicinal plant, *T. laurifolia*. During the review searches were done on the search engine of scientific databases i.e., Biomed Central, Science Direct, Scirus, SpringerLink, PubMed, Google Scholar, Wiley Journals and etc. Different combinations of keywords were used during the searches. Aritajat *et al.* (2004) studied the effects of *T. laurifolia* leave. They designed the experiment using alloxan induced diabetic rats and treated with 60 mg/ml/day of *T. laurifolia* leave for 15 days. The results showed *T. laurifolia* leave extract included insulin-like substance significantly decreased the levels of blood glucose. In addition, they mentioned *T. laurifolia* leaves extract can recover  $\beta$ -cell structure in the islet of Langerhans of the pancreas. Hypoglycemic action can be potentiating the insulin by enhancing the pancreatic secretion of it from  $\beta$ -cell of Langerhans islets or emancipating insulin from the bound form. More additional researches, Pitoopong *et al.* (2014) studied the effects of 500 mg/kg/day *T. laurifolia* leave for 28 days in hyperglycemic cats. The results showed *T. laurifolia* leave extract significantly decreased the levels of blood glucose. The other species from the same genus *Thunbergia* have been reported for hypoglycemic or anti-hyperglycemic activity as *T. grandiflora* (Chowdhury *et al.* 2012), *T. coccinea* (Victoria *et al.*, 2012). Electronic searches were conducted that many active hypoglycemic constituents isolated from the medicinal plants such as abromine from *Abroma augustum*, berberine from *Berberis aristata*, casesalpinianone from *Caesalpinia bonduc*, leucopelargonin from *Ficus bengalensis*, glycyrrhiza-flavonol A from *Glycyrrhiza glabra*, gymnemic acid from *Gymnema sylvestre*, pterostilbene from *Pterocarpus marsupium*, and cuminyl from *Syzygium cumini* (Saravanamuttu and Sudaranam, 2012). *T. laurifolia* possesses the antidiabetic effect using multiple pathways. From the literature reviews that can be summarized these pathways as following:

#### Insulin elevation

The hypoglycemic activity is due to the stimulation of synthesis of insulin from pancreatic beta cells (Aritajat *et al.*, 2004).

#### Antioxidant properties

Many researchers reviewed the most phytochemical substances with anti-diabetes activity. Gallic acid, one of the components in many plants, is a potential antihyperglycemia (Punithavathi *et al.*, 2011; Jayamani and Shanmugam, 2014). The two flavonoids, apigenin and delphinidin were reported to act as antioxidants by scavenging reactive oxygen species and/or

chelating metal iron, which is responsible for the generation of reactive oxygen species (Jin *et al.*, 2009). Apelin was demonstrated to actively modulate angiogenesis and stimulate endothelial cell proliferation, migration and tube formation in diabetic rat (Akcilar *et al.*, 2015).

#### Inhibit enzyme

One of the diabetic treatments is the alpha-amylase inhibition since this enzyme is known as one of the key enzyme in human digestive system to degrade starch to monosaccharides and cause the rise in blood glucose. Jaiboon *et al.* (2011) reported *T. laurifolia* showed 99.05% of this alpha-amylase inhibitory activity.

#### Increased hepatic metabolism

The hypoglycemic activity is thought to be due to increased hepatic metabolism. This plant is significantly enhanced liver cell recovery by bringing hepatic triglyceride and transaminases back to normal (Pramyothin *et al.*, 2005).

In conclusion, apart from the conventional medicines, traditional or alternative therapy plays a significant role in treating diabetes mellitus. It needs to know how to use and what the phytochemical constituents are. This review article has attempted to compile the new medicinal plant, *T. laurifolia*, to be the one of choice in the treatment. All of this information will help researchers explore its scientific evidence. It has been suggested that oxidative stress can play an important role in tissue damage associated with diabetic complications. Oxidative stress in diabetes and increased of free radicals are generated which cause injury or destruction of pancreatic beta cells, which can repair or regenerated by using potent antioxidant. The hypoglycemic activity of *T. laurifolia* based on the antioxidant phytochemical constituents, thus is the aim of the present review.

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