Review of antidiabetic activity of “RangJeud” 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.

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 ethnombotanical 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 (Rubiacaceae), Dioscoreas erythroclada (Rubiacaceae), Mimoso 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. Semenya et al. (2012) identified 24 medicinal plant species in South Africa belong to 20 families, mostly from the Astereæaceae (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 Leguminosæae, Euphorbiaceae, Apocynaceae, Cucurbitaceae, Moraceae and Rutaceae. The most prominent in the preparation of anti-diabetic recipes are Senna alata, Curculigo pilosa, Cucurmeropsis manni, Anthocleist spp, Vernonina 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, Cuscusa reflexa, Dillenia indica, Diplazium esculentum, Lectua gracilis, Millingtonia hortensis, Oxalis griffithii, Saccharum spontaneum, and Solanum viarum. Mootooosamy 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,
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

guarana and 2,000 m (Phyu and Tangpong, 2013).

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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 (Rojsga et al., 2012), phenolic acids such as caffeic acid, gallic acid, protocatechuic acid, and chlorogenic acid (Thongsard et al., 2005; Oonsivilai et al., 2007). Two novel iridoid glucosides of 8-epi-grandifloric acid and 3'-O-β-glucopyranosyl-stilbericoside, with seven known grandifloric acid compounds: benzyl β-glucopyranoside, benzyl β-(2'-O-β-glucopyranosyl)-glucopyranoside, grandifloric acid, (E)-2-hexenyl-β-glucopyranoside, hexanol-β-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-β-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 (Suwanchaikasem et al., 2013 and 2014), anticancer activities (Jetawattana et al., 2015), detoxifying (Chattaviriya et al., 2010; Palipoch et al., 2011a and 2011b; Roejjanasaroj et al., 2014), and associated diseases such as hepatological (Wonkchalee et al., 2012) and neurological diseases (Thongsard 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).
Laovitthayanggoon 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 β-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 β-cell of Langerhans islets or emancipating insulin from the bound form. More additional researches, Pitooolpong 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 (Chowdhary 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, glycyrhiza-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 (Akcellar 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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