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A review on Malaysian medicinal plants having anti-hyperglycemic activity

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ABSTRACT

The use of natural products as a source of remedies has long history since ancient times. Currently, medicinal plants are traditional practices for an extensive range of therapeutics and pharmacological activities like hypoglycemic, immunological, antiviral, anti-inflammatory, anti-hepatic, cardiovascular and central nervous effect. In the past, the use of plant based medicines was mainly restricted to developing countries because of insufficient resources, but currently the trend is changed and natural products as a source of medicines are growing rapidly in developed countries. It is confirmed from research articles that nearly about 75%–80% of the reserved zone inhabitants used natural products for their health remedies. In all, about 250 000–500 000 species of plants exist worldwide and almost 800 plants have been documented for use in folklore systems of medicine. Regarding to this, Malaysia is being accepted as one of the largest biodiversity countries. In Malaysia, 12 000 species of natural products exist and 1 200 are documented to have remedial potential against various diseases. In the market, a variety of allopathic drugs are available, but are linked to various side effects. Hence, there is rising interest in the direction to plant based medicines remedies with a basic tactic towards the nature. The anti-diabetic drugs from natural products source in current use and their same way of producing action are preferred mainly due to affordable price, easy availability and minor harmful effect on human beings. Therefore, the aim of the present research work was to review various Malaysian medicinal plants having potential in attenuation of high level of blood glucose. All over the world, diabetes mellitus is claimed to be one of the most common chronic hereditary non-communicable disease, fourth leading cause of mortality in the most developed countries. The disease is also spreading in many developing and newly industrialized nations. According to International Diabetes Federation, the diabetes will affect 592 million people in 2035.

1. Introduction

Diabetes mellitus is an endocrine hereditary chronic metabolic syndrome that has produced mortality and disability all over the world. In diabetes mellitus, an abnormal metabolism of carbohydrate, protein and fat occurs in body that is linked with decreased level of insulin and results in damaging the peripheral nerves muscles, blurred vision, neuron muscles and heart muscles,

leading to stroke, heart attack and peripheral vascular disease problems[1,2]. The generation of excessive free radicals in human body caused the pathogenesis of hundred chronic disorders including diabetes, arthritis, cancer, hypertension, AIDS, heart attack, aging, inflammation and other degenerative diseases. A number of enzymatic and non-enzymatic anti-oxidative mechanisms occur in human body, which stabilize and deactivate the generation of excessive free radicals responsible for various degenerative diseases like diabetes, thus diminishing the high possibilities of inflammation, cancer, heart disease, arthritis and hyperglycemia[3]. Worldwide, diabetes mellitus is most rapidly increasing disease and will affect 592 million people in 2035 as documented by International Diabetes Federation[4]. It was reported by Patel *et al.*[5], that type I insulin dependent diabetes mellitus and

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type II non-insulin dependent diabetes mellitus are the main types of diabetes. Type II is the most common and about 90%–95% of diabetic patients have type II in which the body fails to use insulin properly due to damage in beta cell function[1]. In spite of achieving an extensive progress in the remedy of diabetes by allopathic drug like oral hypoglycemic and insulin drug, an exploration for innovative medicines keeps on due to various serious toxic effects of the existing allopathic drugs.

Globally, 250 000–500 000 species of plants are available and 800 are used in folklore systems of medicine. The research on plants continues on identification and isolation of active ingredients, rather than to study medicinal properties of whole plant. In addition, the bioactive compounds derived from medicinal plants are used for heart diseases such as angina pectoris, hypertension, asthma, pain, and other human health-related problems.

About 12 000 species of plants exist in Malaysia, from which 1 200 are claimed to have remedial potential against various diseases that affect the health of human beings.

Several native Malaysian plants have been well known to be beneficial in managing and controlling diabetes mellitus successfully. The drugs obtained from natural products have always been an excellent source of remedies in various ailments and the available allopathic drugs are directly or indirectly derived from natural products source.

The plant based medicine is well known for the remedy of diabetes mellitus and hyperlipidemia in developing countries because of insufficient resources and high cost of allopathic medicines. All over the world, several medicinal plants have been confirmed and approved as a remedy for diabetes and hyperlipidemia, and their mechanisms of hypolipidemic and hypoglycemic activity of these natural products are being studied. The advantages of medicinal plants over allopathic drug are that these are easily accessible and inexpensive.

Various researchers have documented that natural products having ability of restoring the function of pancreatic tissues due to increased insulin output or inhibiting the absorption of glucose in intestine (due to blocking Na^+/K^+ ATPase activity) or facilitating the metabolites in insulin dependent processes which is claimed for having anti-diabetic activity[6].

Natural product based medicine having anti-hyperglycemic ability may act through either secretagogues or insulin-mimetic properties as reported by Patel *et al.* and Hung *et al.*[6,7].

The literature has confirmed about the availability of 400–800 medicinal natural products having beneficial effect in attenuation of blood glucose level and presently available experimental techniques. In spite of this, to find new hypoglycemic drugs from medicinal plants is even now attractive as they have many substances which validate alternative and reliable effects on diabetes mellitus. The majority of natural products contain terpenoids, flavonoids, glycosides and alkaloids, which are regularly involved as having anti-diabetic effect.

This review article concentrates on the function of current Malaysian natural products for the remedy of diabetes mellitus and other ailments which have disturbed the life of human beings on this planet. The folklore medicaments suggest great capability for the discovery and innovation of novel anti-diabetic remedies.

2. Common medicinal plants of Malaysia having approved anti-diabetic properties

2.1. *Pericampylus glaucus* (Lam.) Merr (*P. glaucus*)

The plant *P. glaucus* belongs to the family of Menispermaceae. The plant is commonly known as akar chuping and distributed throughout Malaysia. Oral administration of *P. glaucus* at dose of 400, 600 and 800 mg/kg (body weight) significantly reduced high level of lipid profiles and blood glucose in both normal and streptozotocin (STZ) induced diabetic rats which were fed with high fats diets. The crude plant extract of *P. glaucus* produced dose dependent attenuation in blood glucose level. The ethanolic extract of *P. glaucus* at dose 800 mg/kg (body weight) produced significant ($P < 0.001$) attenuation in the level of blood glucose [4.2 ± 0.5 mmol/L], respectively in normal rats after 4 h of treatment that became significant (3.7 ± 0.1 ; $P < 0.001$) after 6 h. In STZ induced high fats diabetic rats, ethanolic extract of *P. glaucus* at same dose (800 mg/kg body weight) produced reduction in blood glucose (14.4 ± 0.2 ; $P < 0.05$) after 2 h of the treatment that became ($P < 0.001$) more significant after 4 h as compared to diabetic untreated group. In long term study, the *P. glaucus* also caused significant ($P < 0.05$, $P < 0.01$, $P < 0.001$) attenuation in blood glucose level at dose 400, 600 and 800 mg/kg (body weight) in STZ induced diabetic high fats diets rats[1].

2.2. *Ougeinia oojeinensis* (Roxb.) (*O. oojeinensis*)

The plant *O. oojeinensis* belongs to the family of Fabaceae, commonly known as Atimukta and distributed throughout the southeast region of Asia including India, Malaysia, and Bangladesh *etc.*

Oral administration of ethanolic bark extract of *O. oojeinensis* at dose of 200 mg/kg (body weight) significantly ($P < 0.001$) produced the hypolipidemic and anti-hyperglycemic effect in alloxan induced diabetic rats (150 mg/kg body weight) as compared to untreated diabetic control groups. The anti-hyperglycemic activity produced by ethanolic extract of *O. oojeinensis* was noted more as compared to standard drug glibenclamide. The blood glucose value for standard drug glibenclamide was 128 mg/dL (60.89%) and ethanolic extract of *O. oojeinensis* was 84.17 mg/dL (74.28%) on fourteen days of receiving the extract. The positive result was also produced by ethanolic extract of *O. oojeinensis* on biochemical parameters. The effect of extract on various biochemical parameters at 200 mg/kg was significant attenuations of all lipid profiles parameters except for high density lipoprotein (HDL) that was increased in diabetic model rats.

A significant percentage in attenuations of low density lipoprotein (LDL) (64.85%), total cholesterol level (59.91 triglycerides level) (22.58%) and very low density lipoprotein (22.36%) in ethanolic extract treated was comparative to standard drug treated groups [total cholesterol (66.55%), LDL (79.50%), triglycerides level (26.68%) and very low density lipoprotein (26.57%)] and reached normal value. However, the HDL level increased with treatment of extract and glibenclamide group respectively[8].

2.3. *Azadirachta excelsa* (*A. excelsa*)

A. excelsa belongs to the family of Meliaceae and is commonly known as sentang in Malaysia. The plant is native to Peninsular Malaysia, Sumatra, Borneo, and Sulawesi but also found in lowland humid region of South East Asian. Oral administration of ethanolic extract of *A. excelsa* at dose of 500 mg/kg (body weight) produced significant ($P < 0.001$) anti-hyperglycemic activity as compared to diabetic control group induced by alloxan monohydrate at dose 130 mg/kg body weight. The percentage in reduction of blood glucose with treatment of ethanolic extract of *A. excelsa* was 60.7%, while the diabetic rats treated with standard metformin at a dose of 50 mg/kg body weight was 31.3% reduction in their blood glucose[9].

2.4. *Tetracera indica merr* (*T. indica*)

T. indica belongs to the family of Dilleniaceae and is commonly known as Mempelas minyak or Mempelas paya. The plant is widely found in rain forest climber of Malaysia and Indonesia. Oral administration of aqueous and methanol extracts of *T. indica* leaves at a dose of 250 and 500 mg/kg body weight significantly ($P < 0.001$) reduced the blood glucose level in normal and alloxan induced diabetic rats. The significant hypoglycemic activity was noted with aqueous extract at the dose of 250 mg and 500 mg/kg body weight at 8 h after receiving the extract, respectively. While the reduction in blood glucose level with aqueous extract was observed less than the oral glibenclamide drug. The anti-hyperglycemic effect in diabetic rats with methanol extract was only noted at dose of 500 mg/kg body weight after 6 and 8 h of treatment as compared to the standard glibenclamide treated group. However, the methanolic extract of *T. indica* at a dose of 250 mg/kg body weight exhibited the highest anti-hyperglycemic activity after 8 h of receiving the *T. indica* extract. The percentage in attenuation of blood glucose with methanolic extract was 58.2% and 55.3% ($P < 0.05$) at dose of 500 and 250 mg/kg body weight after 8 h of treatment, respectively. Similarly, the percentage in reduction of blood glucose level with aqueous and methanol extracts (77.4%) and (74.1%) at 250 mg and 500 mg/kg body weight after 8 h of receiving the both extracts of *T. indica*[10].

2.5. *Leptospermum flavescens* (*L. flavescens*)

The plant *L. flavescens* belongs to the family of Myrtaceae. The plant is widely distributed throughout Malaysia and the common name is 'Gelam Bukit' in Malaysia. A dose dependent attenuation in level of blood glucose was produced after oral administration of *L. flavescens*. The aqueous extract prepared from the leaves and stems produced more significant effect in reduction of fasting plasma glucose level at a dose of 500 mg/kg (body weight) diabetic animal in which diabetes was induced by alloxan. The percentage in attenuation of blood glucose with extract was 61.9% at a dose of 500 mg/kg body weight. Similarly, single oral administration of leaves and stem aqueous extract at a dose of 200 mg/kg produced hypoglycemic effect but was less significant as compared to 500 mg/kg body weight. The leaves extract of *L. flavescens* after 60 min of administration at dose of 500 mg/kg body weight caused

significant decrease in blood glucose level as compared to dose 200 mg/kg body weight of *L. flavescens* extract and normal control group. There was significant increase in fasting blood glucose levels in untreated diabetic group as compared with the normal control group. A non significant ($P > 0.05$) glucose lowering effect was noted on Day 0 of receiving extract (*L. flavescens*), but considerable attenuation in blood glucose levels was produced by plant extract (*L. flavescens*) on the 20th day of treatment at both dose 250 and 500 mg/kg (body weight). The glucose lowering activity of extract at dose 200 mg/kg remained statistically significant in comparison to untreated diabetic control. The leaves and stem aqueous extract of *L. flavescens* decreased the fasting plasma glucose level in a dose-dependent manner. There was more significant reduction in fasting plasma glucose levels in diabetic animals that were treated with standard drug glipizide as compared to diabetic control group[11].

2.6. *Nypa fruticans Wurmb. vinegar* (*N. fruticans*)

N. fruticans belongs to the family of Arecaceae, commonly known as nipa palm. The plant is being used in traditional system of medicine for treating diabetes and other chronic diseases in Malaysia. The plant is primarily throughout the East Asian region. Oral dose of administration of *N. fruticans* and their extracts did not produce any significant ($P > 0.05$) effect in both normal and diabetic rats. However, aqueous extract of nipa palm vinegar displayed the most notable blood glucose lowering effect (56.6%) and a significant improvement in serum insulin levels (79.8%, $P < 0.05$) in long term study, compared with untreated diabetic control group[12].

2.7. *Cinnamomum iners* (*C. iners*)

The plant *C. iners* is locally identified by the names of medang kemangi, kayu manis hutan and teja and belongs to the family of Menispermaceae. The plant is commonly found in humid areas of Malaysia, Myanmar, Thailand, Singapore, Brunei, India, Indonesia and Philippines. Oral administration of petroleum ether, chloroform, methanol and water extract of *C. iners* reduced the high level of blood glucose induced by *i.p.* injection of streptozotocin. Later, methanol extract was fractionated to obtain ethyl acetate, *n*-butanol, chloroform and aqueous fraction. A *C. iners* leaf active portion standardized using cinnamic aldehyde active portion produced significant anti-diabetic activity by measuring glucose absorption from the intestine[13].

2.8. *Curculigo latifolia* (*C. latifolia*)

The plant *C. latifolia* is a shrub tree and commonly identified as Lemba by the Malaysian. The plant belongs to the family of Hypoxidaceae and mainly grows under rubber tree. The plant is found in all regions of Malaysia and comprises berry like fruit that shows both taste modifying and sweet tasting activities. The anti-diabetic effects of *C. latifolia* were confirmed in high fat diet treated animals after a low dose of 40 mg STZ by *i.p.* routes through expression of lipid and glucose metabolisms. Oral administration

of *C. latifolia* fruit and root extracts for a period of 28 days in diabetic treated animals caused a significant ($P < 0.05$) decrease in level of blood glucose, triglycerides, total cholesterol, LDL, gamma-glutamyltransferase and alanine transaminase levels and significantly increased the level of insulin followed by adiponectin, HDL and body weight[14].

2.9. *Amaranthus spinosus* Linn (*A. spinosus*)

The *A. spinosus* plant belongs to the family of Amaranthaceae and is approved in animal's model for having anti-diabetic and hypolipidemic activity for a long time. The plant was used in traditional system of medicines for the ailments of diabetes mellitus. The plant is widely found in tropical and sub-tropical regions of Malaysia and India. Oral administration of methanolic extract of *A. spinosus* at the doses of 250 and 300 mg/kg body weight caused significant anti-hyperglycemic and anti-hyperlipidemic activity in alloxan induced albino rats after a single dose of alloxan monohydrate by *i.p.* route at dose of 150 mg/kg body weight. The methanol extract caused significant ($P < 0.001$) hypoglycemic activity by oral administration of *A. spinosus* at the dose of 250 and 500 mg/kg body weight after receiving the extract for fifteen days respectively as compared to normal untreated diabetic rats. The attenuation of blood glucose level by oral glibenclamide drug was found more significant ($P < 0.001$) as compared to methanolic extract of *A. spinosus*. The anti-hyperlipidemic effect in diabetic rats with methanol extract was also significant ($P < 0.01$) against total cholesterol, triglycerides, phospholipids, low density, very low density and high density lipoprotein[15].

3. Conclusions

It is well documented that diabetes mellitus is a serious chronic disorder that has affected majority of the population worldwide. It's associated with alteration in carbohydrate, fat and protein metabolism that results in elevated blood glucose level. The plant based medicines have been used in traditional system of medicines for individuals suffering diabetes mellitus in both insulin dependent and non insulin dependent diabetes mellitus, since from ancient time. In recent review article, we present lists of those medicinal plants that have been approved for having anti-hyperglycemic properties in animal's model and can be used to treat various types of secondary problems resulted from diabetes mellitus. Natural products are being claimed to be an effective and good source of remedies for the treatment and management of various diseases that have affected human being. But, still a variety of natural products and bioactive components obtained from medicinal plants have not been well investigated and characterized. It needs more investigational studies in order to evaluate the exact mechanism of action of medicinal plants with anti-diabetic and insulinomimetic activity.

Conflict of interest statement

We declare that we have no conflict of interest.

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