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A REVIEW ON SOME PHYTOCHEMICALS ON DIABETES

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ABSTRACT

Diabetes Mellitus (DM) is one of the most prevalent metabolic disorders characterized by increased blood glucose levels and improper primary metabolism resulting from the defects in insulin secretion, insulin action, or both. It is one of the most common health problems worldwide, and the prevalence of this disease is rapidly increasing, leading to microvascular (retinopathy, neuropathy and nephropathy) and macrovascular (heart attack, stroke and peripheral vascular disease) complications. Phytochemicals identified from medicinal plants present an exciting opportunity for the development of new types of therapeutics for diabetes mellitus. Most prevalent among phytochemical groups are the alkaloids, glycosides, polysaccha- rides, and phenolics such as flavonoids, terpenoids and steroids. Medicinal plants are the main source of organic compounds such as polyphenols, tannins, alkaloids, carbohydrates, terpenoids, steroids and flavonoids. These organic compounds represent a source for the discovery and development of new types of antidiabetic molecules. Many compounds isolated from plant sources have been reported to show antidiabetic activity. They should be incorporated in food ingredients, dietary supplements, or drug preparations. Despite the availability of known antidiabetic medicines, remedies from phytochemicals are used with success to treat this disease. Use of antioxidants and phytochemicals can be a great help in tissue repair by quenching the free radicals generated due to oxidative stress. Hence, this article provides a comprehensive review of the available information on various aspects of phytochemicals, with special reference to their effectiveness in risk reduction of diabetes lipotoxicity. The key messages summarize some recent information in the field of antidiabetic phytochemicals.

Key words: Diabetes, Curcumin, Ellagic Acid, *Momordica charantia,* Tetrahydrocurcumin

INTRODUCTION

Diabetes mellitus (DM) or type 2 diabetes (T2 D) is a health problem affecting millions of individuals worldwide. In the past few decades, the global incidence and prevalence of diabetes has increased dramatically in the developing countries of Africa, Asia, and South America. Among the total population of diabetic patients more than 90% suffer from Type 2 Diabetes (T2 D). India is one of the leading countries for the number of people with diabetes mellitus and it is estimated that diabetes will affect approximately 57 million people by the year 2025 (Zimmet et al 2001). 'Diabetes mellitus' describes a metabolic disorder of multiple physiology characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both (Wang T et al 2007). The cause of type 2 diabetes ismultifactorial and includes both genetic and environmental factors that affect β-cell function and tissue (pancreas, muscles, liver, and adipose tissue) insulin sensitivity. Natural products such as plants and herbs have the capacity to reduce blood glucose values and ameliorate diabetes with reduced adverse side effects. They achieve this owing to the presence of phytochemicals such as flavonoids, saponins, alkaloids, tannins, glycosides, terpenes etc (Venkatesh et al., 2010).

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Medicinal plants are the main source of organic compounds such as polyphenols, tannins, alkaloids, carbohydrates, terpenoids, steroids and flavonoids. These organic compounds represent a source for the discovery and development of new types of antidiabetic molecules. Many compounds isolated from plant sources have been reported to show antidiabetic activity (Pareek et al., 2009; Meenakshi et al., 2010). The key messages summarize some recent information in the field of antidiabetic phytochemicals. In traditional practices medicinal plants were used to control diabetes mellitusin many countries. The ethnobotanical information reports about 800 plants worldwide which have been documented asbeneficial in the treatment of diabetes (Patil and Arvindekar, 2014). Themajority of traditional antidiabetic plantsawait proper scientific and medical evaluation for their ability to improve blood glucose control. However, a fewcomprehensive studies of traditionalantidiabetic plants have been carried out1. This has caused an increase in the number of experimental and clinical investigations directed toward the validation of the anti diabetic properties, which are empirically attributed to these remedies (Roman-Ramos et al., 1995). The antidiabetic activity of several plants has been confirmed along with their studies of mechanisms of hypoglycemic activity. Chemical studies directed to the isolation, purification and identification of the substances responsible for the hypoglycemic activity are being conducted. Management of diabetes without any side effects is still a challenge to the medical system. There is an increasing demand by patients to use the natural products with antidiabetic activity, because insulin and oral hypoglycemic drugs are having undesirable side effects (Kameswara Rao and

Appa Rao 2001). The plants with antidiabetic activities provide useful sources for the development of drugs in the treatment of diabetes mellitus. Medicinal plants with hypoglycemic activity were used for many centuries and some times as regular constituents of the diet, it is assumed that they do not have many side effects (Halim Eshart 2002). Phytochemicals isolated from plant source are used for the prevention and treatment of cancer, heart disease, diabetes, high blood pressure etc. (Mary et al. 2002).

Tetrahydrocurcumin: *Curcuma longa* is commonly used in the treatment of diabetes by ayurvedic physicians. Curcumin is a biologically active component isolated from the rhizome of *Curcuma longa* that posses antihyperglycemic activity (Arun and Nalini 2002), hypolipidemic action (Suresh Babu and Srinivasan 1997) and anti - renal lesion effect (Suresh Babu and Srinivasan 1998). The use of Curcumin is recommended for the prevention of advanced glycated endproducts (AGE) accumulation, and the associated complications of diabetes (Sajithal et al. 1998). Tetrahydrocurcumin (THC) (fig.1) is one of the major colourless metabolites of curcumin. THC has been reported to exhibit the same physiological and pharmacological properties of curcumin (Majeed et al. 1995 and Sugiyama et al. 1996). THC is the rapidly metabolized product of curcumin during absorption from the intestine (Ravindranath and Chandrasekara 1980). THC has the strongest antioxidant activity among all curcuminoids (Osawa et al. 1995). Several studies in experimental animals indicate that THC also prevent cancer (Lin and Lin-Shiau 2001), as well as a protective agent against inflammation (Nakamura 1998 and Hong et al. 2004), atherosclerotic lesions (Naito et al. 2002) and hepatotoxicity (Pari and Murugan 2004). In our previous study, we have demonstrated the antidiabetic effect of THC in streptozotocin induced diabetic rats (Pari and Murugan 2005). Since THC might also contribute to the pharmacological activities of curcumin, in this study we explored the role of THC in prevention of streptozotocin induced hyperglycemia and related lipid complications.

Ellagic Acid: An organic heterotetracyclic compound resulting from the formal dimerisation of gallic acid by oxidative aromatic coupling with intramolecular lactonisation of both carboxylic acid groups of the resulting biaryl. It is found in many fruits and vegetables, including raspberries, strawberries, cranberries, and pomegranates. Ellagic acid (EA) is known for its antioxidant properties. That means it removes toxins from your body and protects against harmful molecules known as free radicals. Plants also produce this antioxidant compound as a defense mechanism against infection and pests. Natural polyphenol compound, has potent anti-diabetic, anti-inflammatory, and neuroprotective properties. The present study was aimed to explore the potential protective effects EA against diabetes-associated behavioral deficits and verified possible involved mechanisms. EA could potentially serve as a novel, promising, and accessible protective agent against diabetes-associated behavioral deficits, owing to its anti-hyperglycemic, anti-inflammatory, and neurotrophic properties. Ellagic acid (2,3,7,8-tetrahydroxy-chromeno [5,4,3-cde] chromene-5, 10-dione) (EA) is a natural polyphenolic compound that is commonly found in fruits, such as raspberries, pomegranates, grapes and blackcurrants as well as in nuts. Our group has recently shown that EA improves vascular function in blood vessels exposed to hyperglycemic conditions through the reduction of oxidative stress. In rodent models of hepatic ischemia reperfusion and aging, EA has been demonstrated to have beneficial effects on the liver by decreasing oxidative stress (Kapan et al., 2012).

Momordica charantia

Momordica charantia **L. (**M. charantia**),** a member of the Cucurbitaceae family, is widely distributed in tropical and subtropical regions of the world. It has been used in folk medicine for the treatment of diabetes mellitus, and its fruit has been used as a vegetable for thousands of years. Momordica charantia (MC) is one such herbal drug which is a part of various traditional systems of medicine. The current investigation aims to focus on the opulence of MC with respect to its phytoconstituents and pharmacological activities. More than 200 medicinal compounds have been isolated from its leaves, stems, pericarp, entire plants, callus tissues and seeds. These biologically dynamic chemicals include various glycosides, saponins, alkaloids, fixed oils, triterpenes, proteins, steroids, inorganic compounds, carotenoids, carbohydrates etc. The pharmacological profile of MC exhibits its potential as antidiabetic, antibacterial, antiviral, anticancer, antifertility, antiulcer, immunomodulator, antipsoriasis, analgesic, anti-inflammatory, hypotensive, hypocholesterolemic, antioxidant, cardioprotective, anthelmintic and antimalarial agent. Various findings have also suggested its utility in the treatment of eczema.

Phytochemicals including proteins, polysaccharides, flavonoids, triterpenes, saponins, ascorbic acid and steroids have been found in this plant. Various biological activities of M. charantia have been reported, such as antihyperglycemic, antibacterial, antiviral, antitumor, immunomodulation, antioxidant, antidiabetic, anthelmintic, antimutagenic, antiulcer, antilipolytic, antifertility, hepatoprotective, anticancer and anti-inflammatory activities. However, both in vitro and in vivo studies have also demonstrated that M. charantia may also exert toxic or adverse effects under different conditions. MC is commonly known as bitter gourd, bittermelon, balsam pear or bitter cucumber in English (Dasgupta et al., 2009), karela in Hindi and karavella in Sanskrit. Momordica means, 'to bite' signifying the jagged margins of the leaves, which appear as if bitten. The entire plant has a characteristic odour and a bitter taste. MC is a monoecious annual climber which is cultivated throughout India, Malaya, China, Tropical Africa and America. The fruits are consumed with other vegetables, stuffed, stir-fried or added in small quantities to beans and soups to provide a slightly bitter flavor. Fruits, flowers and young shoots are also used as flavoring agents in various Asian dishes. Young MC shoots and leaves are also cooked and eaten as leafy vegetables, leaf and fruit extracts are used in the preparation of tea (Reyes et al., 1994; Tindall, 1983).

MC has been the entity of research since many decades. Till date, more than 200 phytoconstituents have characterized from different parts of MC including its leaves, fruits, seeds and stems in different laboratories in India, Japan, USA, Thailand, Egypt, China, Taiwan, Australia, Nigeria, Pakistan, Brazil, Nepal, Philippines and Peru (Day et al., 1990).Ayurvedic Pharmacopoeia describes its medicinal uses as Bhedana (purgative), Laghu (easily digestable), Tikta (bitter), Jvara (fever), Asradosa (dyscarasia), Paandu (anaemia), Prameha (obstinate urinary diseases including diabetes) and Krimi (worm infestation). It is a monoecious annual climber with a slender, branched, angled and grooved stem that grows up to

5m. Its leaves are alternate, petiolate, orbicular, 5-7 lobed, 5-12cm in diameter, both surfaces glabrous and prominently nerved. Tendrils are simple and slender. Flowers pale yellow to orange, solitary and unisexual. Fruits dark green to whitish pepo, 5-25 cm long, the current review exhibits the phytochemical and pharmacological profile of MC. Nutrient Profle (Joseph and Jini, 2013; Bakare et al., 2010)The analysis of the fruits of MC depicted the following nutritional facts (per 100 gm of fruit).

Moisture: 83.2%
Protein: 5.3g
Total Carbohydrate: 3.3g
Phosphorus: 99mg
Ascorbic acid: 88mg
Magnesium: 85mg
Calcium: 84mg
Iron: 2.04mg
Niacin: 1.11mg
Riboflavin: 0.362mg
Thiamin: 0.181mg
Folate: 128ìg
Nicotinic acid: 0.5 ìg
Vitamin A: 1734^{IU}

Conclusion

Management of diabetes without any side effects is still a challenge to the medical system. There is an increasing demand by patients to use the natural products with antidiabetic activity, because insulin and oral hypoglycemic drugs possess undesirable side effects. Plants with antidiabetic activities provide useful sources for the development of drugs in the treatment of diabetes mellitus. Phytochemicals isolated from plant source are used for the prevention and treatment of cancer, heart disease, diabetes and high blood pressure etc. Use of antioxidants and phytochemicals can be a great help in tissue repair by quenching the free radicals generated due to oxidative stress. If the mechanism for stress generated hyperglycemia is revealed, target driven therapeutic approach can be performed involving phytochemicals.

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