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ORIGINAL ARTICLE

ANTIDIABETIC ACTIVITY OF *CATHARANTHUS ROSEUS* IN ALLOXAN INDUCED DIABETIC RATS

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ABSTRACT

The present study is aimed to investigate the blood glucose and serum protein in the alloxan induced diabetic rats. The alloxan was induced to rats to analyse the blood glucose. The plant extract, *Catharanthus roseus* was treated to alloxan induced rats to reduce the blood glucose and the serum protein recovered the normal level. The present study is concluded that the *Catharanthus roseus* reduce the blood glucose level to the rats

Keywords: Alloxan, *Catharanthus roseus* Glucose, Protein, Rats

1.INTRODUCTION

Diabetic mellitus is a complex and multifarious group of disorders that disturbs the metabolism of carbohydrates, fats and protein. It results from shortage or lack of insulin secretion or reduced sensitivity of the tissue to insulin. It is a chronic metabolic disorders characterized by hyperglycemia caused by insulin deficiency, often combined with insulin resistance. Insulin is a hormone released from the cells of pancreas and glucose to glycogen thus maintaining the glucose level in the body. The deficiency of insulin leads to increase of glucose level in blood and urine. Diabetic mellitus is one of the common metabolic disorders with micro and macro vascular complications that results in significant morbidity and morality. It is a major disease characterized by derangement in carbohydrate, fat and protein metabolism, affecting nearly 10% of the population. In recent years, many hyperglycemic agents are introduced, still the diabetes and the related complication continue to be a major medical problem not only in developed countries (Kirithikar *et al.*, 1995).

Diabetes mellitus is one of the common metabolic disorders with micro-and macrovascular complications that results in significant morbidity and mortality. It is considered as one of the five leading causes of death in the world (Vats et al., 2004; Kumar et al., 2006). In modern medicine no satisfactory effective therapy is still available to cure diabetes mellitus [Sumana and Suryawashi ,2001]. There is increasing demand by patients to use natural products with antidiabetic activity due to side effects associated with the use of insulin and oral hypoglycemic agents [Holman and Turner, 1991; Kameswara Rao, et al., 2001). Diabetes is a disease in which levels of blood glucose, also called blood sugar, are above normal. Over the passage of time, high blood glucose, also called hyperglycemia, damages nerves and blood vessels, which can lead to complications such as heart disease, stroke, kidney disease, blindness, nerve problems, gum infections, and amputation. It is a fast growing medical problem in affluent societies and critically attacks the metabolic activity of patient. It is a major crippling disease in the world leading to huge economic losses. In recent years, developed nations have witnessed an explosive increase in the prevalence of diabetes mellitus (DM) predominantly related to lifestyle changes and the resulting surge in obesity. In India, this disorder is on alarming condition as compared to most of the developed countries.

Alloxan, a well- known diabetogenic agent is widely used to induce type 2 diabetes in animals [Viana et al., 2004]. The drug and its reduction product dialuric acid establish a redox cycle with the formation of superoxide radicals. These radicals undergo dismutation to hydrogen peroxide. Thereafter, highly reactive hydroxyl radicals are formed by fenton reaction. The action of reactive oxygen species with a simultaneous massive increase in cytosolic calcium concentration causes rapid destruction of β cells [Szkudelski et al., 2001]. Alloxan induced diabetes mellitus serve as a pathological biomodel for testing a substance with supposed antioxidant activities ***in vivo*** [Bartosikova et al., 2003].

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In recent years, many drugs have been isolated from natural sources as the modern medicine system treats the symptoms and suppresses the disease but does little to ascertain the renal cause. Drugs usually hinder the self-healing efforts of the body and make recovery more difficult. Therefore, the current scenario is to isolate the active constituents present in the plant material to develop medicinally drugs are having rare changes of adverse effects.

Many traditional plants are used for diabetic's treatment. Traditional anidiabetic plants might provide new oral hypoglycemic compounds , which can counter the high cost and poor availability of the current medicines/ /present day drugs for many rural populations in developing countries. India is well known its herbal wealth. Medicinal plants like *Allium sativum* and *Gymnema slyvestre* have been studied for treatment of diabetic mellitus (Grover et al., 2002).

In modern medicine, the beneficial effects on glycemic level are well documented and preventing activity of these drugs against progressive nature of diabetes and its micro and macro vascular complications are modest (Kasiviswanath et al., 2005).several studies on enzyme involved in hepatic glucose metabolism in rats with alloxan and streptozotocin diabetes have shown well defined changes, which consist primarily of a decrease in the activity of glucokinase and hexokinase (Sheela and Augusti,1992).

Catharanthus roseus (L) G. Don(Madgaskar periwinkle) of the Apocynaceace family is widely grown in tropical and subtropical regions of the world. The plant produces several pharmaceutically important alkaloids (Jaleel and Panneerselvam 2007). Catharanthus roseus is a species of catharanthus native and endemic to Madagascar. Synonyms include Vinca rosea, Ammocallis rosea and Lochnera rosea; Other English names occasionally used Cape Periwinkle, Rosy Periwinkle and Old maid. In the wild, it is an endangered plant ; the main cause of decline is habitat destruction by slash and burn agriculture. It is also however widely cultivated and naturalized in subtropical areas of the world.

It is evergreen subshrub or herbaceous plant growing to 1 m tall. The leaves are oval to oblong, 2.5-9 cm long; and 1-3.5 cm broad, glossy green, hairless, with a pale midrib and a short petiole 1-1.8 cm long; they are arranged in opposite pairs. The flowers are white to dark pink with a darker red centre, with a basal tube 2.5-3 cm long and a corolla 2-5 cm in diameter with five petal-like lobes. The fruit is a pair of follicles 2-4 cm long and 3 mm broad.The species has been cultivated for herbal medicine and as an ornamental plant. In traditional Chinese medicine, extract from it have been used to treat numerous disease including diabetes, malaria.the substances such as vinblastine and vineristine extracted from the plant are used in the treatment of leukemia.

2.MATERIALS AND METHODS

Fresh leaves of *Catharanthus roseus* were collected from Thanjavur District of Tamilnadu, India. The leaves *Catharanthus roseus* were collected and dried under shade. The dried materials were mechanically powdered using mixer grinder and stored in air tight container. About 100 gms of course powder was weighed and subjected for extraction with methanol by continuous stirring for 48 hrs. After 48 hrs, solvent was filtered and is subjected to Soxlet apparatus for 11 hrs. the extracts evaporated to dryness under vaccum desicator. After the extract preparation, the extract is given to diabetic induced rats.

Male albino rats weighing 100-150 g were obtained from Tamilnadu Animal House. Male albino rats were housed under standard housing conditions of 5ºC relative humidity 60% and photo period of 12 h dark/12 h light standardized pellet diet. The animals were divided into four groups containing four rats in each group. Group I – Rats were kept as control; Group II- rats were alloxan drug treated (120 mg/kg body wt.)' Group III- rats were alloxan drug treated (120 mg/kg body wt.)+ *Catharanthus roseus* treated (250 mg / kg body wt.); Group IV- rats were alloxan drug treated (120 mg/kg body wt.)+ insulin (5 mg/ kg body wt.). The animals are injected to intraperitonial injection. After the treatment, the blood samples were collected for heart puncture. The collected blood was centrifuged at 3000 rpm for 10 minutes. The serum was collected and stored in cool temperature and used for estimation of various biochemical parameters.

Analysis of Glucose level

The glucose was estimated by Gluco Chek (Blood Glucose monitoring system). The procedure as follows.The blood sample was collected in the tail portion of the albino rats. Wash the tail with warm, soapy water. Rinse well and dry them thoroughly. Tail was also clean with an alcohol pad to dry before testing. Prepare the launching device. Take one test strip out of the test strip vial replace the vial cap immediately and close it tightly. Insert the test strip into the test strip of the meter. The meter turns on automatically, the code number appears the test strip vial or can press the strip symbol which will instruct after to insert a test strip. Insert test strip within 1 minute then the meter will display the code number. Place the lancing device in rat's tail and press the trigger, gently squeeze the rat tail until get a drop of blood. The blood sample will be drawn into the test strip automatically, hear a beep letting know the test has begun. The blood glucose level displays on the monitoer.

Estimation of Protein

The total protein content in serum and tissues was estimated by adopting the method of Lowry *et al*. (1951)

0.5 ml of serum-in case of serum separated from blood) was mixed with 4.0 ml of alkaline copper reagent. This was allowed to stand at room temperature for 10 minutes. Then 0.5 ml of Folin-ciocalteau reagent was added and mixed well. The absorption of blue colour developed was read in an UV spectrophotometer at 620 nm. Standards in the concentration range of 20-100 µg were treated in a similar manner along with blank containing 1.0 ml of distilled water. The protein content was expressed as g/dl in serum

Statistical analysis

Statistical significance was evaluated by Mean and Standard Deviation by Zar (1984).

3.RESULTS

Figure 1 shows the glucose level in the blood. Glucose level was estimated in all four groups. The group I rats glucose level was noted on 1st ,3rd and 7th as 115.75±4.34, 116.25±4.19 and 116.5±5 mg/dl respectively. Similarly, the glucose in group II was noted on 1st ,3rd and 7th as 119.75±7.41,284.75±20.12 and 393±11.97 mg/dl respectively. The group III (*Catharanthus roseus*) noted the glucose level. The glucose level was increased in 1st day (386.66±5.68 mg/dl) when compared to control rats. At the same time, the glucose level was significantly decreased at 3rd day (252.25±19.92 mg/ dl) and 7th day (118.25±7.67 mg/dl). The group IV noted the glucose level. The glucose level was increased in 1st day (391.66±4.16 mg/dl), 3rd day 241.25±6.13 mg/dl and 7th day 104 ±11.88 mg/dl. Figure 2 shows the protein level in the serum of rats. The protein level was decreased in group II as 5.79±0.11 mg/dl when compared to Group I (6.57±0.10). During the Group II and Group IV, the protein level was significantly was increased as 6.83±0.06 and 6.98±0.09 mg/dl respectively.

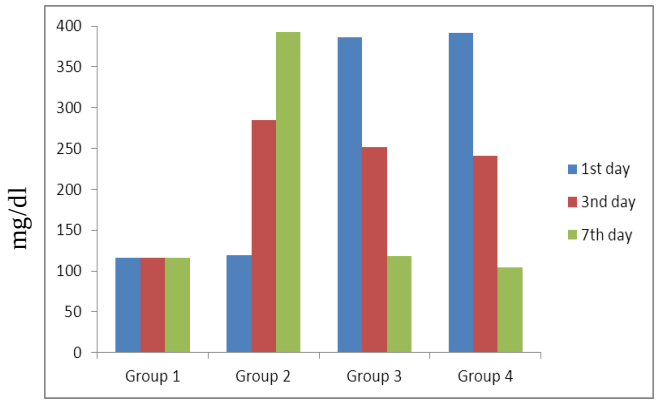

Fig. 1 Effect of *Catharanrhus roseus* on the blood glucose level in normal and alloxan induced diabetic rats

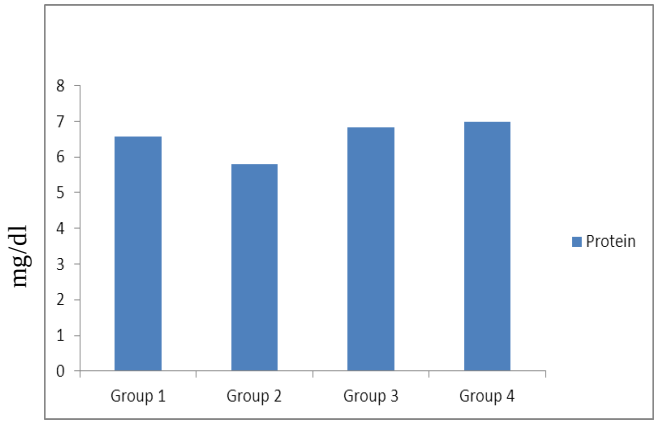

Fig. 2 Effect of *Catharanrhus roseus* on the serum protein level in normal and alloxan induced diabetic rats

4.DISCUSSION

In the present study, alloxan has been used to induce diabetes in rats. The administration of alloxan resulted in the steady increase in the blood glucose level during seven days experimental period, indicating hyperglycemia. These observation similar to Dixit et al., (1986) and Nagappa et al., (2003) who have used alloxan to induce diabetes in a variety of species. During Catharanthus roseus treatment, the increased level of glucose was decreased in diabetic rats. The renewal of β cells in diabetes have been studied in several animal models. The total β cell mass reflects the balance between the renewal and loss of these cells. It was also suggested that regeneration of islet ß cells following destruction by alloxan may be the primary cause of the recovery of alloxan-injected guinea pigs from the effects of the drug [Gorray et al., 1986]. *Vinca rosea* whole plant alcoholic extracts has been shown to act by β cell regeneration. Similar effects in streptozotocin-treated diabetic animals were reported by pancreas tonic [Rao et al., 1998], ephedrine [Xiu et al., 2001], and *Gymnema sylvestre* leaf extracts [Shanmugasundaram et al., 1995]. Ahmed et al., (2010)reported that , the damage of pancreas in alloxan-treated diabetic control rats (Figure 1 Group II) and regeneration of β cells by glibenclamide (Figure 1 Group V) was observed. It is found that methanolic whole plant extract at high dose (500 mg/kg) is more effective than whole plant extract at low dose (300 mg/kg) after 14 days of treatment. Hence the above discussion revels that methanolic whole plant extract at high dose (500 mg/kg) is more effective and shows similar curative effect as standard that is, glibenclamide (5mg/kg). This could be due to the possibility that some β-cells are still surviving to act upon by *Vinca rosea* extract to exert its insulin releasing effect. Histopathological studies reinforce the healing of pancreas, by *Vinca rosea* extracts, as a possible mechanism of their antidiabetic activity.

Ahmed et al., (2010)reported that concluded that alcoholic whole plant extracts of *Vinca rosea* at high dose (500 mg/kg) exhibited significant antihyperglycemic activity than whole plant extract at low dose (300 mg/kg) in alloxan-induced diabetic rats. These extracts also showed improvement in parameters like body weight and lipid profile as well as regeneration of β cells of pancreas and so might be of value in diabetes treatment.

Proteins are important organic constituents of the animal cells. It plays a vital role in the process of interactions between intra and extra-cellular media being a part of cell membrane and an enzyme. It participates the intricately balanced sub-ceullar fraction (Amudha *et al*., 2002; Ramalingam *et al*., 2002). Proteins are important organic substances required by an organism in the tissue building, the cellular organelles repair and also cellular metabolism (Yeragi *et al*., 2000). In the present study, the level of protein was increased in alloxan induced rats when compared to control rats. The similar results also reported by Jayanthi et al., (2010) in alloxan induced rats. During Catharanthus roseus treatment, the increased level of protein was decreased in diabetic rats.

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