WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 6.805
Volume 5, Issue 3, 826-837. Research Article ISSN 2277– 7105

EFFECT OF CO-ADMINISTRATION OF THE EXTRACTS OF *BOUGAINVILLEA SPECTABILIS* AND *CATHARANTHUS ROSEUS* ON PROTEIN AND GLYCOGEN CONTENTS OF DIABETIC ALBINO RATS.

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Article Received on
25 Dec 2015,

Revised on 15 Jan 2016,
Accepted on 06 Feb 2016

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ABSTRACT

Bougainvillea spectabilis and *Catharanthus roseus* extracts are part of various herbal formulations for the treatment of diabetes. The present study aims to determine the biochemical alterations due to Co-administration of *Bougainvillea spectabilis* and *Catharanthus roseus* leaf extracts on female diabetic albino rats. *Bougainvillea spectabilis* and *Catharanthus roseus* leaves extracted with methanol and administered to both normal and alloxan induced diabetic rats. The protein and glycogen levels were measured at 7, 14 and 21 days at a dose level of 300 mg/kg b.wt. In the present study, effect of Methanolic extract of combination of *Bougainvillea spectabilis* and *Catharanthus roseus* in various organs of diabetic albino rats significantly increased the protein as well as glycogen content at 300mg/kg b.wt for intervals of 7, 14 and 21 days. It may be due to the presence of certain phytoconstituents of plants such as flavonoids, Saponins etc.

KEYWORDS: *Bougainvillea spectabilis*, *Catharanthus roseus*, alloxan, protein, glycogen.

1. INTRODUCTION

The medicinal plants are of great importance to human health. Medicinal plants are widely used in management of diseases all over the world.[1] Many medicinal plants are used daily in Ayurvedic practices. In India more than 7,000 medicinal plant species are known. Plants have

always been part of the medicinal science from the beginning of human civilisation to the present modern world of synthetic medicines.

Bougainvillea spectabilis belongs to the family Nyctaginaceae. It is a familiar ornamental plant commonly grown in Indian gardens. *Bougainvillea* is a genus of flowering plants native to South America from Brazil west to Peru and south to southern Argentina. The *Bougainvillea* leaves are reported to have medicinal properties *viz.* antiviral, antibacterial etc.[2,3] It is also reported that ethanolic extract of *Bougainvillea spectabilis* leaves have beneficial effect on serum cholesterol concentration reduction.[4] This traditional plant has also antidiabetic potential. The alcoholic extract of the leaf has been reported to possess hypoglycemic effect and has been used for the management of diabetes mellitus. The hypoglycemic principle of the leaf extract has been isolated and named Pinitol.[5]

Catharanthus Roseus is known with various names (Madagascar periwinkle; *Vinca rosea; Lochnera rosea*) in India and all over world. *Catharanthus roseus* contains more than 400 known alkaloids, some of which are approved as antineoplastic agents to treat leukemia, Hodgkin's disease, malignant lymphomas, neuroblastoma, rhabdomyosarcoma, Wilmer's tumor and other cancers. Water decoction of the leaves and /or the whole plant is used as household remedy for diabetes in several countries *viz.* Brazil, Cook Islands, Dominica, England, Jamaica, Pakistan, Taiwan, and West Indies.[6] The flower extract of *Catharanthus roseus* is reported to have wound healing activity in Sprague Dawley rats.[7]

2. MATERIALS AND METHODS

2.1 Plant Material

Bougainvillea spectabilis and *Catharanthus roseus* leaves were collected from the Bundelkhand University Campus Jhansi (U.P) and adjacent area. The leaves were removed from the stalk and air dried at room temperature (25 - 30 ^{0}C) after which it was ground and sieved to fine powder and made into extract with methanol used for the experiment.

2.2 Animal used

Albino rats of Wister strain weighing about 300±10 gms. The study was carried out at Department of Zoology, Institute of Basic science, Bundelkhand University campus, Jhansi. The study was conducted in sexually mature albino rats (300±10gm/kg b.wt.), purchased from DRDE (Defence Research Development Establishment) Gwalior. Prior to study, the

ethical clearance was obtained from the animal ethical committee, (CPCSEA, MOEF, and Government of India). Proposal No. BU/Pharm/IAEC/12/035.

2.3 PREPARATION OF DOSE

Doses were prepared with Gum acacia in saline (0.9%). The dose was prepared according to 300mg/kg b.wt. Concentration and then it is given orally to rats for different duration and their effect was studied after 7, 14 and 21 days of daily administration.

2.4 ROUTE OF ADMINISTRATION

The dosages were given to the animals via oral route by gastric feeding needles. The entry normally obtained without anaesthesia. Feeding needle with a ball tip was used to prevent introduction of the needle into the trachea and prevent trauma to the oral cavity.

2.5 EXPERIMENTAL DESIGN

Present study has been planned to study the effect of the methanolic extract of *Bougainvillea spectabilis* and *Catharanthus roseus*. The diabetic induced animals were divided into four groups. One group served as experimental, which received dose of plant extract at a level of 300mg/kg b.wt., the second group received the dose of Standard drug (Glibenclamide) at 5mg/kg b.wt, third group served as diabetic experimental (Alloxan) and simultaneously fourth group served as normal control which received vehicle only. The animals were kept in same environment conditions after daily 7, 14, and 21 days of treatment. The biochemical parameters viz. protein,glycogen were studied by standardized techniques or methods.

Alloxan was injected through the penial vein at a dose of 5 mg alloxan/ kg b.wt after a 24-hour fast, and confirmation of an elevated blood sugar was done 3 days later.

2.6 Estimation of various biochemical parameters

The tissues (Liver, Kidney, uterus and pancrease) were weighed and homogenized in a glass homogenizer at a concentration of 25mg/ml in chilled hypotonic solution of Sodium bicarbonate ($NaHCO_3$). The homogenate was then kept in ice box and suitable aliquots for different estimation were taken. Protein and Glycogen levels were estimated by (Lowry *et al,* 1951) and (Seifter *et al,*1950) respectively.

2.7 Statistical analysis

The results were expressed as Mean ± S.E. Significance of differences as compared to the control was the significance determined using student's t-test.

3. RESULTS AND DISCUSSION

Diabetes mellitus is a metabolic disorder characterized by multi groups of disorders that disturb the metabolism of carbohydrates, fat and protein.[8, 9] Its syndrome is characterized by the loss of glucose homeostasis and storage and lack of insulin secretion.[10, 11] Inspite of introduction of various hypoglycemic agents, diabetes and its complication continue to be a major problem in the world population.[12] The disease complication is mainly associated with a risk of antherosclerosis,[13] coronary heart disease,[14] stroke and peripheral vascular disaease.[15, 16]

3.1 EFFECT ON PROTEIN CONTENT

In the present study, effect of Methanolic extract of combination of *Bougainvillea spectabilis* and *Catharanthus roseus* in various organs of diabetic albino rats significantly increased the protein content at 300mg/kg b.wt for intervals of 7, 14 and 21 days as shown in Table-I. It may be due to the presence of certain phytoconstituents of plants such as flavonoids, Saponins etc. During Alloxan induced at 100mg/kg b.wt, the protein content were significantly reduced as compared to the normal values. Alloxan was chosen to induce diabetes in the rat, because Alloxan causes severe necrosis of pancreatic β-cells with consequent lack of insulin secretion, possibly through generating excessive reactive oxygen species.[17] In other words Alloxan caused a massive reduction in insulin release by the destruction of beta cells of islets of Langerhans and thus induce hyperglycemia. However administration of plant extract (combination of *Bougainvillea spectabilis* and *Catharanthus roseus*) and Glibenclamide caused marked improvement of serum and total protein content. Proteins play a vital role in the physiology of living organisms. All the functions of an organism are regulated by enzymes and hormones, which are generally proteins. If any alteration takes place in the protein turnover, it may have an adverse effect on the important and complex groups of biological materials, comprising the nitrogenous constituents of the body and food intake and thus performing different biological events to maintain homeostasis of the cells. Therefore the protein content of a cell can be considered as a diagnostic tool to determine the physiological phases of a cell.[18] This parameter shows great degree of alterations in vital organs. Numbers of toxicants of chemical or synthetic origin are known to decrease the protein contents through the process of degradation. As these compounds elicit a significant alteration in the physiological functions, it is expected that these changes are maintained through the transformation or degradation of new proteins. Plant extracts of medicinal values are known to increase the total proteins contents in vital as well as

reproductive organs. The rise in protein content due to administration of combination of *Bougainvillea spectabilis* and *Catharanthus roseus* may alter certain key enzymes which are needed for protein synthesis. Even plant of *Cucumis metuliferus* fruit power revealed that there was a significant dose dependent increase in the levels of the total proteins as compared to the control.[19] Proteins are structurally and functionally most diverse and dynamic molecules with exquisite specificity. Acute and sub chronic toxicity of the essential oil of *Ocimum gratissimum* L. leaf, through oral administration leads to less hepatic injury thereby not affecting the biochemical parameters to significant level.[20,21] has also studied the polyherbal combination of *Tomarix gallica, Capparis spinosa, Cichorium intybus, Solanumn igrumand, T. arjuna* on liver and these medicinal herbs alone or in combination can influence in restoration of the cellular functions and structural integrity of liver. Similarly, doses of *Ageratum conyzoides* (goat weed) significantly increased the level of total protein in rats i.e, plant may not pose any toxicological treat to the liver when used in traditional medicine at doses investigated.[22] While aqueous extract of plant *Catharanthus roseus, Psidium guajava* and *Sorghum bicolor* were also reported to show the increased level of serum proteins, which suggest the hepatotoxic effects in rats.[23, 24] Most plant foods have low amount of protein concentration available during digestion and absorption in the intestines to contribute to serum protein levels such as *Ocimum gratissimum* significantly reduced the total serum protein.[25] Similarly,[26] showed the reduction of total protein concentration just at high dose of Abamectin and *Bacillus thuringiensis* in male albino rats.

Therefore, it is assumed that there may be a common mechanism which increases the protein contents in all the organs. Probably the Co-administration of *Bougainvillea spectabilis* and *Catharanthus roseus* may alter certain key enzymes which are needed for protein synthesis. Also *Bougainvillea spectabilis* and *Catharanthus roseus* are rich in phytoconstituents due to which protein content is increased in various organs.

3.2 Effect on Glycogen Content

Liver is considered as a metabolic centre for the synthesis of glucose from glycogen and is used whenever it is required. Although the breakdown of glycogen into glucose and vice-versa is a normal phenomenon in liver but when any toxicant or a xenobiotic enters into the liver, it disturbs the glycogen synthesis. It has been reported that disruption of glycogen storage is associated with dysfucnctional and dystrophic changes in the liver and kidney due to inhibition of key enzymes in carbohydrate metabolism such as hexokinase, glucokinase,

and phosphoglucomutase.[27] In the present study, effect of methanolic extract of combination of *Bougainvillea spectabilis* and *Catharanthus roseus* significantly increased the glycogen content in various organs of diabetic albino rats at a dose level of 300mg/kg b.wt for intervals of 7, 14 and 21 days as shown in Table-II. It may be due to the presence of certain phytoconstituents of plant such as flavonoids, saponins etc. During alloxan induced at 100mg/kg b.wt the glycogen content were significantly reduced as compared to the normal rat. Alloxan caused a massive reduction in insulin release by the destruction of beta-cells of islet of Langerhans and thus induce hyperglycemia, however administration of plant extract and Glibenclamide caused a marked improvement of serum and total glycogen content. Authors has reported in present findings that after chronic administration of combination of *Bougainvillea spectabilis* and *Catharanthus roseus*, the glycogen contents were increased significantly at all doses and durations and it was noticed that increase in glycogen is gradual and successive. The results support the finding of Saini et al, 1985, that an indigenous plant preparation, Liv.52 is believed to be hepatoprotective. A prophylactin action of Liv.52 against hapatotoxins such as acetaminophen, alcohol, carbon tetrachloride, and antibiotics is well documented.[28, 29] In diabetes, the glycogen contents were significantly decreased but extract of *Bougainvillea spectabilis* and *Catharanthus roseus* recouped the disease and managed the content of glycogen in tissues. In diabetes, the glycogen content markedly depleted.[30] Similarly, *Trigonella foenumgraecum* plant also prevented various alterations in glycogen content that were occurred during diabetes.[31] Since destruction of beta-cells of islets of Langerhans resulting in marked decrease in insulin levels, it is rational that glycogen levels in tissues decreased as they depend on insulin for influx of glucose. Therefore, normal levels in tissues decreased as they depend on insulin for influx of glucose. Insulin is a potent activator of the enzyme glycogen phosphorylase responsible for glycogenolysis in liver and muscles. That also agreed the findings of[32] who reported that due to administration of polyherbal drug “Diashis”, there were significant recoveries in the level of glycogen in the level of glycogen in the liver and skeletal muscle in diabetic rat towards the control levels.[33] also reported that the level of glycogen content in liver is reduced to 49% in diabetic rats as compared to the normal control rat, but treatment with different fractions of *Magnifera indica* improved the level of glycogen content to their normal level. Depletion of liver glycogen content was seen in the diabetic control group. A significant increase in the glycogen content of liver was observed after administration of alcoholic leaf extract of *Barlaria prionitis*.[34] It was also observed that ethanolic extract of chamomile *recutila capitula* has reversal effects on the level of glycogen in paracetamol hepatotoxicity.[35] In diabetes, glycogen content

decreases due to enhanced glycogenolysis and the normal capacity of the liver to synthesize glycogen is impaired, which is due to insulin deficiency.[36] However,[37] have reported that ethanolic extract of seed kernel of *Caesalpinia bonducella* caused an increase in concentration of glycogen synthetase and hexokinase, both of which contribute to increase glycogen synthesis. The increase in liver glycogen may also have been brought about by inhibition of the enzyme glucose-6-phosphatase leading to accumulation of glucose-6-phosphatase, which allosterically inhibited the enzyme glycogen phosphorylase. Though,[38] have reported that *Gymnemia sylvestre* caused significant decrease in glucose content in kidney.

4. ACKNOWLEDGEMENT

The authors express their sincere thanks to Department of Zoology, Osmania University and Department of Zoology, Bundelkhand University Hyderabad For their constant support and encourangement throughout the study.

Table I: Showing effect of daily administration of Methanolic extract of combination of *Bougainvillea spectabilis* and *Catharanthus roseus* on diabetic female albino rats indicating the content of protein (mg/100mg). Values are given as Mean ± SE of 6 animals in each group.

S. No.	TISSUES	CONTROL	DIABETIC CONTROL	7 DAYS		14 DAYS		21 DAYS	
				D.C+P.E	D.C+STD	D.C+P.E	D.C+STD	D.C+P.E	D.C+STD
1.	LIVER	16.0±0.32	12.3±0.11*	13.2±0.7	18.8±0.7	17.3±1.4*	21.2±1.2	28.1±0.7	29.0±0.7*
2.	KIDNEY	26.0±0.12	20.2±0.13*	24.8±0.4	26.8±0.87	32.1±0.4	36.5±0.6	40.7±1.1	49.3±0.9
3.	UTERUS	20.8±0.19	15.1±0.14*	16.5±0.6	18.5±0.5	26.1±3.5	28.3±1.3	37.3±1.2	39.2±0.8
4.	PANCREASE	19.5±0.21	11.2±0.11*	17.5±0.6	20.4±0.9	22.4±0.7	32.0±0.7	30.4±1.0	41.5±0.6*

Where

D.C- Diabetic Control

P.E- Plant Extract

STD- Standard Drug

Table II: Showing effect of daily administration of Methanolic extract of combination of *Bougainvillea spectabilis* and *Catharanthus roseus* on female diabetic albino rats indicating the content of glycogen (mg/100mg). Values are given as Mean ± SE of 6 animals in each group.

S.No.	TISSUES	CONTROL	DIABETiC CONTROlL (D.C)	7 DAYS		14 DAYS		21 DAYS	
				D.C+P.E	D.C+STD	D.C+P.E	D.C+STD	D.C+P.E	D.C+STD
1.	LIVER	34.52±0.21	25.56±1.50*	31.45±0.42	36.56±0.57	38.45±3.6	44.35±0.5*	42.75±3.41*	49.75±1.06*
2.	KIDNEY	17.5±0.11	8.95±0.77*	11.81±0.46	15.46±1.21	18.18±1.39*	27.59±0.97*	29.98±0.78*	37.5±0.35*
3.	UTERUS	18.01±0.17	11.20±0.96*	19.5±1.31	24.6±1.19	26.5±0.14*	30.4±1.22*	32.4±0.57*	36.5±1.28*
4.	PANCREASE	24.5±0.42	13.45±0.83*	21.19±0.12	26.65±1.58*	28.78±0.5*	35.75±0.65*	35.75±1.93*	42.57±0.65*

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