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HYPOGLYCEMIC, HYPOLIPIDEMIC AND ANTIOXIDANT PROPERTIES OF COMBINATION OF *CURCUMIN* FROM *CURCUMA LONGA*, Linn, AND PARTIALLY PURIFIED PRODUCT FROM *ABROMA AUGUSTA*, Linn. IN STREPTOZOTOCIN INDUCED DIABETES

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ABSTRACT

Dietary spice components of *Curcuma longa* and *Abroma augusta* have been screened for their protective effect against reactive oxygen species induced lipid peroxidation. They have been found to be efficient antioxidant when administered in combination . The purpose of the study was to investigate the effect of oral administration (300 mg / Kg) of the aqueous extract of turmeric whose active ingredient is *Curcumin* and *Abromine* powder as a hypoglycemic agent mixed with diet. The effect of this aqueous extract on blood glucose, lipid peroxidation (LPO) and the antioxidant defense system in rat tissues like liver, lung, kidney and brain was studied for 8 weeks in streptozotocin induced diabetic rats. The administration of an aqueous extract of turmeric and abromine powder resulted in a significant reduction in blood glucose and an increase in total haemoglobin. The aqueous extract also resulted in decreased free radical formation in the tissues studied.

The decrease in thiobarbituric acid reactive substances (TBARS) and increase in reduced glutathione (GSH) , superoxide dismutase (SOD) and catalase (CAT) clearly showed the antioxidant property of the mixture. It is suggested that these changes initially counteract the oxidative stress in diabetes however, a gradual decrease in the antioxidative process may be one of the factors which results in chronic diabetes. These results indicate that the mixture of the two plants have shown antidiabetic activity and also reduced oxidative stress in diabetes.A combination of *Abroma augusta and Curcuma longa* also restored the other general parameters in diabetic animals. The results were statistically analyzed and indicated that combination of herbal extracts showed better efficacy as compared to individual herbal plant extracts used.

KEYWORDS

Abroma augusta, *Curcumin*, diabetes mellitus ,hypoglycemia, hypolipidemic effect , lipid peroxidation , antioxidants

INTRODUCTION

Given a reasonable likelihood that medicinal plants with a long history of human use will ultimately yield novel drug prototypes, systematic and intensive search in plants for new drugs to treat Type 2 diabetes mellitus seem to be of great utility. This approach seems likely to increase the chances for discovering new drugs for the management of Type 2 diabetes mellitus. Out of the two types of diabetes, the incidence of non-insulin dependent diabetes mellitus (NIDDM) is much higher than the insulin dependent diabetes mellitus (IDDM).

Sulphonylureas and few biguanides are drugs used in the treatment of hyperglycemia in NIDDM, but they are unable to lower glucose concentration to within normal range and reinstate a normal pattern of glucose homeostasis permanently. Use of these therapies is restricted by their pharmacokinetic properties, secondary failure rates and accompanying side effects (1). Even insulin therapy does not reinstate a permanent normal pattern of glucose homeostasis, and carries an increased risk of atherogenesis and hypoglycemia. World Health

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Organization has recommended that medicinal plant research warrant attention (2).

Plants have been the major source of drugs in Indian system of medicine and other ancient systems in the world. Earliest description of curative properties of medicinal plants was found in Rig Veda (2500-1800 BC). Charaka Samhita and Sushruta Samhita give extensive description on various medicinal herbs. Information on medicinal plants in India has been systematically organized (3).

Medicinal plants have the advantage of having little or no side effects. Some of them are being used in traditional systems of medicine from hundreds of years in many countries of the world. Till today metformin is the only ethical drug approved for the treatment of NIDDM patients, which is derived from a medicinal plant *Galega officialis* and historically used for treatment of diabetes in medieval Europe (4).

There are many anti-diabetic plants, which might provide useful sources for the development of drugs, in the treatment of diabetes mellitus. The literature on medicinal plants with hypoglycemic activity is vast. As many of these plants 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. However chronic consumption of large amounts of traditional remedies must always be taken with caution as toxicity studies have not been conducted for most of these plants (5).

Since older times *Curcuma longa* (Turmeric) (Family *Zingeberaceae),* commonly known as *Haldi* in Hindi has been used as spice and coloring agent. In Ayurveda the traditional Indian system of medicine it has been used in several ways namely (i) as an ingredient in the preparation of medicinal oils, ointment and poultice, (ii) in diabetes and leprosy, iii) for stomachache, carminative, tonic, laxative, antirheomatic, blood purifier, vermicide, antiseptic and cure for liver ailments. (iv). The raw juice is used to tear in gallstones, gall bladder complaints, and dental-troubles and for sore throat and common cold parasitic skin diseases and pile cure. Curcumin, its major constituent has also been found to show anti-rheumatic action. The anti-rheumatic activity of 1200 mg of curcumin has been found to be comparable to that of 300 mg of phenylbutazone. The anti-inflammatory activity of curcumin analogues such as feruloyl, 4-hydroxy cinnamoyl methane and bis 9, 4-hydroxycinnamoyl methane was found to be comparable with sodium curcuminate and phenyl butane. (Figs. 1, 2)

Demethylated derivatives of curcumin and ferric acid viz. 3,4 dihydroxy cinnamoyl methane and caffeic acid are known potent inhibitors of lipid peroxidation (6). While conducting studies on the inhibition of ß-hydroxydeoxygeranasine formation by curcumin (Fig1), in mouse fibroblast cells, it was revealed that the compound was able to inhibit RA- induced tumor promotion by functioning as an hydroxyl radical scavenger to prevent 8-OH d6 formation within the DNA molecule (6). The *C. longa* rhizomes have been reported to possess anti-diabetic properties as its alcohol extract possesses active constituents showing blood glucose lowering activity in alloxan induced diabetic rats. (5).

Oxidative stress has been associated particularly with the development of complications in diabetes (6). Curcumin, (5- 50 µ molar) inhibited lipid peroxidation in a dose dependent manner. This inhibition was however reversed by adding high concentration of Fe^{2+}. One of the major consequences of increased oxidative stress in lipid peroxidation is the oxidative degradation of lipids with more than two double bonds (C= C).

Endothelial injury in the vascular wall has been shown to be the initial event in atherosclerosis and related problems of coronary heart diseases. Lipid droplet deposits in the aortic wall undergo peroxidative changes in presence of reactive species of oxygen, which eventually produce endothelial injury. Thus, compounds that can scavenge the reactive species of oxygen and inhibit peroxidation of lipids could be useful as preventive agents against atherosclerosis.

Curcumins have also been reported to exhibit inhibitory effects on lipid peroxidation induced by air on linoleic acid. They also inhibited the hemolysis of erythrocytes induced by hydrogen peroxide at low concentrations. It was inferred that the effects of the curcuminoids on hemolysis and lipid peroxidation of erythrocytes was presumably different from those of dl-1-tocopherols (7). Anti-oxidative components in the methanol extract of the rhizomes *of C. longa* were identified as curcumins as their 50% inhibitory concentrations for the air oxidation of linoleic acid were significant, and were comparable to those of tocopherol. An extract of the crude Japanese drug "Ukon" containing rhizomes of *C. longa* exhibited intense preventive activity against carbon tetrachloride -

induced liver injury. Turmeric based crude drugs were also found to exhibit anti-hepatotoxic activity (8).

Although *C. longa* has been investigated for its various medicinal properties, detailed studies on its anti-diabetic, antioxidant potential, lipid peroxidation level in diabetic rats are still lacking. The present paper reports studies on the effect of *C. longa* and *A. augusta* constituents on hyperglycemic oxidative stress and lipid peroxidation levels in diabetic rats.

MATERIALS AND METHODS

Plant *Abroma augusta* was purchased from Khasia Mountains in Assam and *C. longa* was purchased from Delhi market. The whole plant of *A. augusta* and *rhizome* of *C.longa* were air dried, powdered in a grinder, and mixed in equal proportions before use.

INDUCTION OF DIABETES IN RATS

Healthy adult albino Wistar rats of both sexes weighing between 150-200 gm were obtained from the Centre for Cellular and Molecular Biology (CCMB), Hyderabad and used in this study. The animals were fed on a pellet diet (Hindustan Lever. India) and water provided *ad libitum*.

Diabetes was experimentally induced to produce diabetic retinopathy(6). Overnight fasted animals were injected with STZ (60mg/kg dissolved in 3 mM citrate buffer pH 4.5) intraperitoneally (i.p). After 10 days only those rats which showed plasma glucose levels > 300 mg/dl were classified as diabetic and were included in the study as described earlier by our laboratory (7). The diabetic rats were further divided into two groups of untreated and treated (five each). One group of untreated diabetic rats was orally administered saline daily 0.1ml/ 100mg b.w. and the other (treated group) was orally administered daily water extract of a combination of the two plants in the morning for 8 weeks by bulged steel tube. The body weight was recorded weekly. At the end of the experiment, animals were killed and tissues collected and stored in deep freeze (- 4 ° C).

ESTIMATIONS

Blood (5 ml) was collected from the vein at the beginning and end of the experiment. Erythrocytes and plasma were separated. Plasma glucose, total cholesterol, LDL-, VLDL- and HDL- cholesterol and triglycerides were estimated as described earlier by us (8). Lipid peroxidation products were estimated as thiobarbituric acid reactive substance (TBARS) in plasma and tissues (9). Among the antioxidants, reduced glutathione was determined by the method of Hussein *et al* (10). Superoxide dismutase and catalase were estimated as given in (11). Assay of antioxidant enzymes and protein were conducted as described earlier by us (12).

Statistical analysis :

All the data were statistically evaluated and the significance calculated using student's 't' test. All the results were expressed as mean ±S.D.

RESULTS AND DISCUSSION

Many plants have been used for the treatment of diabetes mellitus in Indian system of medicine and in other ancient systems of the world. Out of these, only a few have been evaluated as per modern system of medicine. From many such plants only extracts have been prepared and their usefulness evaluated in experimental diabetes in animals. Most of them seem to act directly on the pancreas (pancreatic effect) and stimulate insulin level in the blood. Some have extra pancreatic effect by acting directly on tissues like liver, muscle etc. and alter favorably the activities of the regulatory enzymes of glycolysis, gluconeogenesis and other pathways. Many of its products / chemical constituents are known to possess wide array of medicinal properties. This study demonstrated the hypoglycemic and hypolipidemic effect of *Curcuma longa* constituents and *Abroma augusta* (Linn) on blood glucose profile and antioxidant properties of *STZ – induced diabetic rats.*

The present study has shown that fasting plasma glucose (FPG) values, before and after treatment for 8 weeks in normal, diabetic untreated and diabetic treated with water extract of one plant only (*A. augusta or C. longa*) or both the plants *A. augusta and C. longa* are shown in (table 1). The fasting plasma glucose (FPG) values remained more or less the same in normal i.e. 93.4 ± 24.3 mg/dl before and 89 .4 ± 6.22 mg/dl after 8 weeks. In diabetic rats even the initial (0 week) FPG values were higher (176 ± 50.2 mg/dl) which increased to 290.5± 10.7 mg/dl by 8 weeks. However after treatment with 300 ml of water extract of *A. augusta and C. longa the* high initial FPG values (162.4 ± 22.6mg/dl) came back to normal level (89 .4 ± 6.22). There was improvement after treatment with the aqueous extract of both the plants. The same was

observed in the glucose tolerance test after 8 weeks.

Results (in table 2) show the mean FPG values of normal, diabetic untreated and diabetic treated rats subjected to glucose tolerance test after 8 weeks. The fasting blood glucose values for normal, diabetic untreated and diabetic treated with both the extracts are 82.3 ± 20.0, 295.5 ± 11.1 and 72.2 ± 1.0 mg/dl. In the glucose tolerance test in the case of normal animals the peak values were obtained in ½ hr and were 290.5 ±11.1 mg/dl and returned back to initial values in 2 hours.

We identified that this effect of combination of *Curcuma longa* and *Abroma augusta* not only showed anti-hyperglycemic effect but also hypolipidemic effect. Results (in table 2) showed the effect of water extract of *A. augusta* on the fasting plasma glucose (FPG) of normal and untreated diabetic rats. 92.3 ± 20.0, 295.5 ± 11.1 and 72.2 ± 1.0 mg/dl. However in *Abroma augusta* plus *Curcuma longa. The zero values were normal (*72.2 ± 1.0 mg/dl) In the case of diabetic untreated animals the blood values remained at high level (above 270 mg/dl). This shows that treatment with *Abroma augusta* + *Curcuma longa* for 8 weeks improved glucose tolerance.

Body weight. There was a decrease in body weight of diabetic rats and after treatment showed gain in weight as in control animals. Treatment of diabetic rats with an extract of these two plants showed considerable improvement in glucose tolerance also (table 1 and 2) and these results point out that the diabetic rats showed abnormal glucose pattern. The effect of weight on treatment for 8 weeks with water extract *of A. augusta* and *Curcumin* on urea, creatinine, cholesterol and protein in STZ diabetic rats is shown in table 3. Kidney mass plasma creatinine, glucose, Na^+K^+ concentration urinary Na^+ K^+ Creatinine excretion are shown in table 4.

Turmeric *(Curcuma longa*), as well as its active constituent Curcumin, inhibits lipid peroxidation. *Curcumin* and *Abroma augusta* also decreases serum cholesterol levels in hyperlipidaemic rats. (Table 3)

The results presented in table 3, confirm the lipid peroxide scavenging activity of *Curcumin* administration. Scavenging activity of *Curcumin* administration also reduces lipid peroxidation (14). Curcumin has been shown to inhibit cyclooxygenase activity (15). From table 4, it is seen that the mixture of the extracts of the two plants *A.augusta* + *turmeric* has shown promising results by lowering the food intake and reduction in body weight, and kidney mass. Analysis of blood creatine and urinary creatine and urinary sodium levels showed positive effect in diabetic rats (table 7). Positive effect of the extracts was also noticed in plasma cholesterol, phospholipids and erythrocyte cholesterol and phospholipid levels as seen in table 6.

The effect of water extract of a combination of *A. augusta* and *C. longa* for 8 weeks on lipidperoxidation, SOD and CAT activities in erythrocytes in STZ diabetic rats (table 5). That glucose induces LPO in liver is comparable with diabetes in which hyperglycemia induces peroxidation of membrane lipids and causes cellular injury. The increase in SOD in liver at lower concentration of glucose could be the protective response by the liver cells to counteract the peroxidative stress in the tissue. Exposure of liver to elevated glucose levels result in the decreased activities of SOD, CAT, GST and GSH, which contributed to the increased lipid peroxides in the liver. It has been demonstrated that polyunsaturated fatty acids of mammalian tissues and body fluids undergo lipid peroxidation (20).

The positive effect of the two extracts was also seen in other biochemical parameters analyzed (TC, LDL-HDL and TAG) as presented in (Table 6). Normally diabetic rats tend to loose weight but after treatment with the two extracts, the body weight did not decline significantly (table 7.8). It is therefore clear that *Curcumin* + *A. augusta* are a good combination for reducing not only the overall physiological and biochemical effects due to diabetes but also physical effects like body weight food and water intake.

Effect of water extract of *A. augusta* and *C. longa* on total hemoglobin, change in blood and urine sugar of normal and experiment rats (tables 8,9,10). Treatment of rats with STZ / Alloxan is an established model for type I or Insulin - dependent diabetes. Diabetes is associated with profound alterations in the plasma lipid and lipoprotein profile and with an increased risk of coronary heart disease (16). The liver and some other tissues participate in the uptake, oxidation and metabolic conversion of free fatty acids, synthesis of cholesterol and phospholipids and secretion of specific classes of plasma lipoproteins.

Lowering of serum lipid levels through dietary or drug therapy seems to be associated with a decrease in the risk of vascular disease and related complications (17). Many herbs and plant products have been shown to have antihyperglycemic and antihyperlipidemic property (18). In the preliminary chemical examination, besides determining the % extractives and the ash content, the roots of *Abroma augusta* (Linn) have been shown to contain some alkaloid bases, reducing sugars and some phytosterols but glycosides have been found to be absent. An alkaloid, abromine m.p. 283°-285°, with decomposition, its hydrochloride m.p. 230°and a phytosterol($C_{30}H_{52}O_2$), m.p. 153-157°has been isolated. We plan to conduct further studies to understand the mechanisms of action of this medicinal plant. There is every possibility of developing a few useful drugs from medicinal plants with a long history of human use.

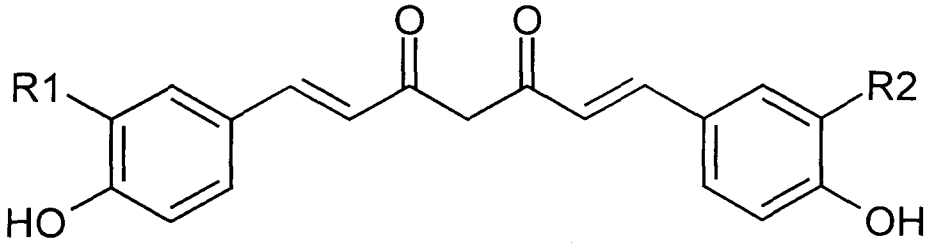


Fig 1 :

R1= R2= OCH: Curcumin

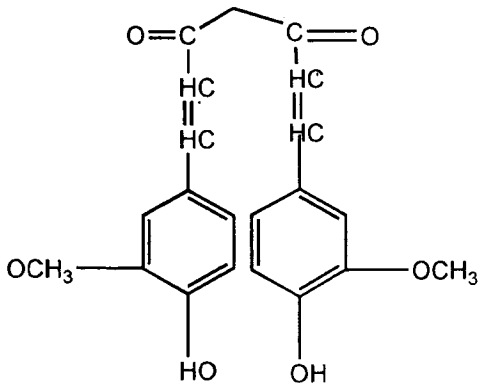
R1 = H R2 = OCH : 4 – Hydroxycinamoyl (feruloyl) methane

R1 = R2 = H: Bis (4 – hydroxycinamoyl) methane

Structure of the Curcuminoids.

Curcumin, 4 – hydroxycinnamoyl (feruloyl) methane and bis (4 – hydroxycinnamoyl) methane , as isolated from rhizomes of *Curcuma longa* (L.), have been shown to have inhibitory effects on the lipid peroxidation. In the present study, the action of the natural curcuminoids was investigated on the lipid peroxidation of erythrocytes.

This figure shows the three curcuminoids isolated from *Curcuma longa* rhizomes. The side chains R1 and R2 of curcumin are two methoxy groups. 4 – Hydroxycinnamyl (Feruloyl) methane has only one methoxy group at R2. Bis (4- hydroxycinnamoyl) methane has a proton on both side chains R1 and R2.



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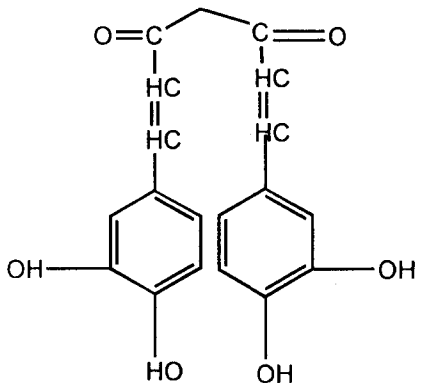

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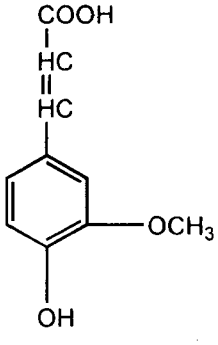

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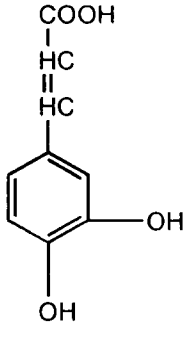

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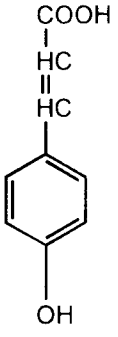

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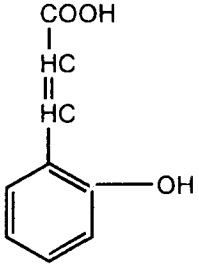

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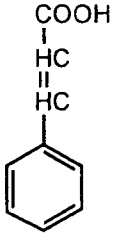

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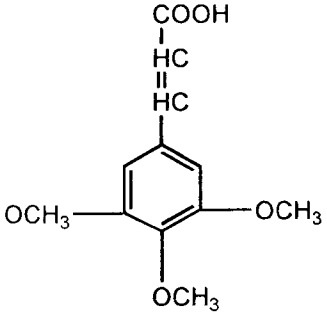

(8)

Fig. 2: Structures of curcumin and related compounds: 1. Curcumin (trans, trans): 2. Bis- **3, 4-Dihydroxycinnamoylmethane (trans, trans); 3. Ferulic acid (trans); 4. Caffeic acid (trans) 5. P-Hydroxycinnamic acid (trans); 6. o-Hydroxycinnamic acid (trans); 7. Cinnamic acid (Trans); 8. 3.4.5-Trimethoxycinnamic acid (trans).**

Table .1 a. Effect of water extract of *A.augusta* and *C. longa* on the fasting plasma glucose level in rats.

Plasma glucose mg/dl. (Mean±SD)		
Group	**0 week**	**8 weeks**
Normal	93.4 ± 24.3	83.0 ± 24.2
Diabetic untreated	176 ± 50.2[a]	290.5± 10.7[a]
Diabetic + *Abroma* treated	162.3±24.5[a]	104.5± 26.4
Diabetic + *Curcuma longa* treated	1705±6.40[a]	110.0±7.0[a]
Diabetic +*Abroma and Turmeric treated*	162.4 ± 22.6[a]	89 .4 ± 6.2 2

[a] = $p < 0.001$

Group of 5 animals were used for each set of experiments.

All the data were statistically evaluated and the significance was calculated using student's 't'– test. All the results were expressed as mean ± S.D.

Table 1 b. Effect of water extract *A. augusta* and *C. longa* on total hemoglobin, and Urine sugar of normal and experimental rats

Group	Hemoglobin	Urine sugar
Normal	15.5 ± 4.0	–
Diabetic Untreated	11.5 ± 1.5	+++
Diabetic + *Abroma*	13.9 ± 2.5	–
Diabetic + *C. longa*	14.5 ±1.9	–
Diabetic + Mixture	15.8 ±4.6	-

Table. 1 c. Effect of water extract *A. augusta* and *C. longa* on various treatments on the body weight of rats

Group	Initial	Change in body weight (g)
Normal	190±11.2	210± 7.0
Diabetic Untreated	160.5 ± 7	200± 5.0*
Diabetic + *Abroma*+ *C-longa*	175.9 ± 2.5	210± 1.0

p< 0.05

Table .2. Effect of water extract of *A. augusta* and Turmeric (*300-mg/kg-body wt*) in combination or individually on glucose tolerance test (GTT) in untreated and treated rats.

Blood glucose (mg/dl), mean ± S.D					
Group	**0 hr.**	**0.5 hr.**	**1 hr.**	**1.5 hr.**	**2 hr.**
Normal	82.3 ± 20.0	140.2 ± 11.2	132.6 ± 27.3	116.2 ± 10.0	102.0 ± 12.0
Diabetic untreated	295.5 ± 11.1[a]	245.0 ± 8.6	273.4 ±89.3[a]	290.6 ±82.6[a]	250.5.0 ± 9.2[a]
Diabetic + A. augusta	80.9 ± 25.6	112.2 ± 20.6	114.3 ± 15.0	100.0 ± 10.3	92.6 ±24.0
Diabetic + Turmeric treated	85.0 ± 4.2	86.0 ± 4.3	81.0 ± 3.9	82.0 ± 3.2[a]	83.0 ±3.2[a]
Diabetic + A. augusta + Turmeric treated	79.0 ± 3.5[a]	83.0 ± 4.3[a]	85.0 ± 3.2	81.0 ±3.6[a]	72.2 ± 1.0

[a] = $p < 0.001$ compared with initial blood glucose (0hr) of normal rats.

The blood was collected at 0, 0.5 , 1, 1.5, and 2 hrs.Plasma glucose was estimated in all samples.

Table. 3. Effect of treatment for 8 weeks with water extract of *A. augusta* and Curcumim *(Combination/ individually)* on urea, creatinine, cholesterol and protein in STZ diabetic rats.

Parameters	**Normal**	**Normal + Mixture**	**Diabetic**	**Diabetic + Mixture**
Urea (mg/dl)	26.8±3.2	28.5±5.4	68.8±3.1	43.6 ± 2.0
Creatinine (mg/dl)	0.43±0.02	0.41±0.03	0.66±0.04	0.49±0.02
Cholesterol (mg/dl)	86±2.7	95±3.4	198±2.2	100±6.0
Protein (g/dl)	7.3±0.2	7.4±0.3	6.5 ± 0.1	7.00±0.08

Table. 4. Plasma and urine levels of Na^+, K^+ and Creatinine in treated and untreated STZ induced diabetic rats

Analysis	Non- diabetic Untreated	Diabetic treated
Plasma [Na^+] mmol)	139 ± 2	134± 0.9*
Urinary Na^+excreted (mmol/1/2 4h)	750 ± 40	12.0± 45*
Plasma [k^+] (mmol/1)	5.0± 0.32	4.50 ± 0. 20
Urinary Creatinine Excreted /ml/24h	4.0 ± 0.2	4.5 ± 2.5
Plasma [creatinine] mmol/1	30 ± 3.5	37 ± 3*

*** = p < 0.05**

Table 5. Effect of water extract of the combination of *A. augusta and C. longa* for 8 weeks on lipid peroxidation, SOD and CAT activities in erythrocytes of STZ diabetic rats

Group	LOP U/ml	SOD U/ml	CAT U/ml
Control	286.6±4.7	320 ±24.0	279.9 ±5.1
Diabetic untreated	410.9 ± 7.2	269.5 ±8.2	200.1±2.2
Diabetic + A. augusta	205± 11.2	293 ±10	258.0±10.0
Diabetic + C. longa	211± 14	310.4 ± 1.8	269.2±4.6
Diabetic + A. augusta + C. longa	209.5±10.8	330.5±2.00	395± 11.0

Table. 6. Effect of aqueous extract of *Abroma augusta* and *Curcuma longa* on lipid profile in different conditions of rats.

Group	TC (mg/dl)	LDLC (mg/dl)	HDLC (mg/dl)	LDLC/HDLC	TAG (mg/dl)
1. Normal	156.0 ± 13.4	80.2±8.79	45.87±8.4	1.5 ± 0.13	104.6±5.2
2.Diabetic untreated	245.0 ± 16.0[a]	170.84±7.9	49.35±2.50	3.93 ± 0.19[a]	190.1± 6.30[a]
2. Diabetic + Abroma *augusta* and *Curcuma longa*	163.0 ± 1.54	92.15 ± 10.84	46.6±18.45	1.56± 0.03	130.0 ± 12.0[a]

[a] = $p < 0.001$ *when compared with normal group.*

TC, LDLC, HDLC= total , low density and high density lipoprotein cholesterol respectively.

Table 7 : The combination of *A. augusta* and *C. longa* on general parameters of STZ diabetic rats.

General Parameters

	Control	Diabetic	Diabetic + *C. longa*	Diabetic + *A.* augusta	Diabetic + *C. longa* + *A. augusta*
Bodyweight (g)	215±10	140±8.0	182±1.4	210±3.0	213±3.5
Liverweight (g)	5.2±0.2	5.0±0.1	5.5±0.1	6.0±0.1	5.7±0.1
Kidney weight (g)	1.5±0.3	1.6±0.04	1.3±0.06	1.5±0.05	1.4±0.06
Protein (g/dl)	7.0±0.4	6.3±.02	6.2±.01	7.5±.3	6.8±0.07

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REFERENCES

1. Melinda A., (1988) Non insulin dependent diabetes mellitus treatment with sulphonylureas in Clinical Endocrinology and metabolism. Des natures, M. and Hale, P., Balliere- Tindall, London. ; P, 443-453.
2. World Health Organization. (1980) Expert committee diabetes mellitus. Technical Report Second Series. No.646, WHO.Geneva, p. 61.
3. Satyavati, G.V. and Gupta, A. K. (1987) Medicinal plants of India eds Indian Council , New Delhi; Vol. II. Shankar, TNB; Shanta N.V., Ramesh. H.P.; Murthy I.A.S., Murthy V.S., 1987 Ind. J. Exp. Biol. 1980; 18, 73.
4. Oubre, A.Y., Carlson, T.J., King, S.R. and Reaven, G.M. (1970) from plant to patient, an Ethanomedical approach to the identification of new drugs for the treatment of NIDDM. Diabetologia; 4 0 (5): 614-617.
5. Shnkar, TNB; Shanta N.V., Ramesh. H.P; Murthy I.A.S. Murthy V.S., (1980) . Toxicity Studies on Turmeric (Cuecuma longa): Acute Toxicity studies in rats, Guineapigs& Monkeys. Ind. J. Exp. Bio. 1980; 18 (1): 73-75.
6. Shih, C.A., Lin J.K. (1980) Inhibition of 8-Hydroxydeoxyguanosive formation by curcumin in mouse fibroblast cells. carcinogenrsis. 14 (4) 709-712
7. Tank R, Sharma N, Sharma, I. Dixit. VP (1989) Anti-diabetic activity if *C.longa* in alloxan Induced diabetic rats - Indian drugs; 27 (11) 587-589.
8. Hakino, H. (1985) Anti hepatotoxic activity of crude drugs. Yakugaku Zasshi .105 (2) 109-118.
9. Soudamini, K. K., Kuttan, R, (1989) Inhibition of chemical carcinogenesis byCurcumins. J Ethnopharmacology; (27): 227-233.
10. Hussein, H.E.M.A., Jamil, K. and Rao, M. (2001) Preliminary studies on the Hypoglycemi effect of *Abroma augusta* in alloxan diabetic rats. Ind. J. clin. Biochem 16 (1). 77-80.
11. Poliodoro, G.D.T., Arduini., R.G.L A. and Federici, G. (1984) Superoxide dissimulates, reduced Glutathione and TBA- reactive products in erythrocytes of patients with multiple sclerosis. Int. J. Biochem. 16 (50): 505-509.
12. Hiroshi, O., Nobuko, O. and Kunio, V. (1979) Assay for lipid peroxides in animal tissues by thiobarbituric acid reaction. Anal. Biochem. 5. 351-358.
13. Wendell, A. (1981) Glutathione peroxidase. In: Methods in Enzymology, Ed. Jakoby, W.B. Academic Press, New York, USA Vol. (77): P. 327-333.
14. Hussein, H.E.M.A., Jamil, K. and Rao, M (2001) Hypoglycemic, hypolipidemic and antioxidant properties of tulsi (Ocimum *sanctum* Linn) on streptozotocin induced diabetes in rats. Ind. J. clin. Biochem. 16 (2). 190-194.
15. Salimath BP, Sundaresh C.S. Srinivas L. (1985) Dietary compounds inhibit lipid peroxidation in erythrocyte membrane .Nut Res; (6): 1171-1178
16. Huang MT, Smart RC, Wong CQ. Conney AH. (1988) inhibitory effect of Curcumin, chlorogenicacide.Coffeic acid, and ferric acid on tumour promotion in mouse skin by 12-0-tertradecanoyl . phorobol,; 13(48) : 5941-5946.
17. Betteridge J. (1997) Lipid disorders in diabetes mellitus, in: J C. Pickup, G. Willams (Eds.) textBook of Diabetes, sec. Ond ed., Blackwell Science, London; PP, (31). 1- 55.
18. Brown G.B. Xue-Qiao, Sacco, D.E.and Alberts, J.J. (1993) Lipid lowering and plaque regression. New insights into prevention of plaque disruption and clinical events in coronary disease, Circulation; (87): 1781-1791.
19. Karunanayake, E.H. Tendon, K.H. (1993) Search of novel hypoglycemic agents from medicinal plants, in: AK Sharma (Ed.) Diabetes Mellitus and Its Complications. An update, macmillan India LTD, New Delhi, India, pp. 192-205.
20. Mata P, Alonso R, Lopez- Fare A, Orders JM, Lahore C, Caramel C, Codices R, Blanquez E, DE, Ova M (1996). Effect of dietary fat saturation on LDL oxidation and monocyte adhesion too human Endothelial cells in vitro. Arterioscler Thromb Vasc Biol; 16: 1347- 1355.