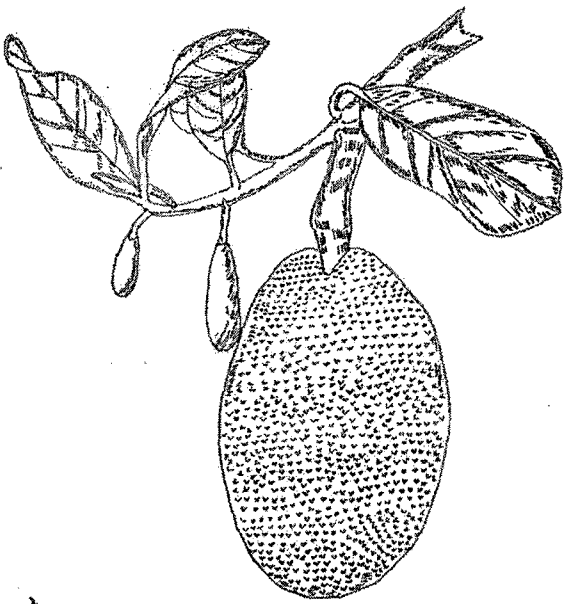
CHAPTER – V

Artocarpus heterophyllus Lam.

Artocarpus heterophyllus Lam.
Plate No: 5



Fruit

Flower bud

Artocarpus heterophyllus. Lam

Syn: *Artocarpus integrifolius* auct. non L. f.

Family: Moraceae

Sanskrit name: Panasah

Trade name: Jack fruit tree

A large evergreen tree, bark black mottled green, smooth. Leaves oblong, coriaceous, dark green, inflorescence cauliflorous and also from the main branches, tender heads enclosed by glabrous leafy scales which fall off leaving annular scars at the base. Fruit very large elliptic-oblong, covered with spinous projections, seeds smooth, ovoid.

Medicinal Uses: The Chinese use jackfruit pulp and seed tonic for cooling the system and it is also useful in overcoming the influence of alcohol in the body. The seed starch is given to biliousness and the roasted seeds are regarded as aphrodisiac. The ash of the leaves, corn and coconut shells, are mixed with coconut oil to heal ulcers. The dried latex yields artostenone, convertible to artosterone, a compound with marked androgenic action. The latex when mixed with vinegar promotes healing of abscesses, snakebite and glandular swellings. The roots are used in skin diseases and asthma. An extract of the root is taken in cases of fever and diarrhea. Heated leaves are placed on wounds. The wood has a sedative property; its pith is said to produce abortion (Julia, 1987).

Root Bark:

The root bark contains prenyl flavones, heterophyllin, cycloheterophyllin, heteroflavanone A ($C_{19}H_{20}O_7$) and B, artonins A, B, C, D, J, K, and L. 2', 4', 6'-Trioxygenated flavanone, heteroflavanone C ($C_{23}H_{26}O_6$), prenyl flavonoid, cycloartocarpin A ($C_{26}H_{26}O_6$), tridecyl docosanoate, 9-hydroxy tridecyl docosanoate ($C_{35}H_{70}O_3$), β-sitosterol, betulin, ursolic acid, betulinic acid and a phenolic compound heterophylol have also been isolated from the root bark (Hano *et a.l,*1990; Lu & Lin,

1993, 1994). A new flavanone (artocarpanone A), a new prenylflavone (artocarpetin A), heterophylol (a phenolic compound) and 9 known flavonoids were isolated from the roots (bark and heartwood) (Lin *et al.,* 1995). Six prenyl flavonoids, including 2 new compounds, were reported from the root bark. The new prenyl flavones were characterized as 8-(γ,γ-dimethylallyl)-5,4'-dihydroxy-7,2'-dimethoxy-flavone and 3,3'-di-(γ,γ-dimethylallyl)-5,7,2',5'-tetrahydroxy 4'methoxyflavone (Chung *et al.,* 1995).

Fruit:

Fruit pulp contains several volatile flavor constituents of which esters represent 31.9%; carboxylic acids (13.5%) and carbonyl compounds (6%) are also present. The main flavor components are 3-methylbutan-1-ol, 37.1%; 3-methylbutanoic acid, 13.5%; 3-methylbutyl-3-methylbutanoate, 10.3%; ethyl-3-methylbutanoate, 6.7%; isoamyl acetate, 4.6%; butan-1-ol, 3.8%; 3-phenyl-propanal, 3.4%; 3-phenylpropan-1-ol, 3.1%; propyl-3-methylbutanoate, 2.9%; and methyl -3- methylbutanoate, 2.1%. The yield of total volatiles were 36 mg/kg of pulp (Wong *et al.,* 1992).

The aqueous extract of the edible part of the fruit contains glucose, galactose, mannose and biologically important compounds, D-glucuronic acid, D-mannitol and succinic acid. Six carotenoids were detected in fruit kernel. The carotenes such as β -carotene, α -carotene, β -zeacarotene, α -zeacarotene and β -carotene-5, 6-epoxide and a dicarboxylic carotenoid, crocetin, were identified. Fruit is a good source of pro vitamin A carotenoids. Serum retinol concentrations in rats supplemented with fruit carotenoids were significantly higher ($p=0.008$) compared with the control group. The same was true for liver retinol ($p=0.006$). Increased consumption of ripe jackfruit prevents and controls vitamin A deficiency (Chandrika and Warnasuriya, 2005). Fructose, glucose and sucrose were the major sugars in all parts of the fruit, except in the outer spiny rind, which was devoid of glucose. Capric, myristic, lauric, palmitic, oleic, stearic, linoleic and arachidic acids were the major fatty acids, with varying proportions in different parts of the fruit (Chowdhury *et al.,* 1997).

Seed:

Seeds contain two tetrameric lectins, jacalin and artocarpin. Jacalin was the first lectin found to exhibit the beta-prism I fold, which is characteristic of the lectin in Moraceae family (Pratap *et al.,* 2002). Artocarpin, a mannose-specific lectin, is a homotetrameric protein devoid of covalently attached carbohydrates and consist of four isolectins. A neutrophil migration-including lectin (KM) has been isolated from the saline extracts of the seeds. It can be used as a tool to study protein-carbohydrate interaction during neutrophil migration through the extracellular matrix. A reinvestigation of the carbohydrate-binding properties revealed that artocarpin, from the seeds, behaves as a polyspecific lectin.

Kernel and Heart wood:

The kernel yields starch (29.5%) which may be used as a source for the industrial production of maltose. The methanolic extract of the heart wood showed antibacterial activity. Two active compounds which were identified from the heart wood are 6 - (3-methyl-1-butenyl) - 5, 2' ,4' – trihydroxy - 3- isoprenyl - 7 - methoxyflavone and 5, 7, 2', 4'-tetrahydroxy - 6 isoprenylflavone. Both isolates completely inhibited the growth of primary cariogenic bacteria. These phytochemical isoprenylflavones would be potent compounds for the prevention of dental caries (Sato *et al.*, 1996). A new natural Diels-Alder-type adducts, named artonin X, and 2 known Diels-Alder type adducts (kuwanon R and artonin D), were isolated from the bark (Shinomiya *et al.,* 1995).

Latex:

The fatty acid ester 4-hydroxy undecyl docosanoate and a crystalline protease, artocarpin have been isolated from the latex of the fruit (Prasad & Virupaksha, 1990). Tertracyclic triterpenoids, 9, 19-cyclolanost-3-one-24-25-diol (24R) ($C_{30}H_{50}O_3$) and 9, 19-cyclolanost-3-one-24, 25-diol (24S) and the monoacetate, cycloartenol ($C_{34}H_{54}O_5$) have been isolated from the latex (Barik *et al.*, 1994).

Leaf:

The glycosyl transferase inhibitors (+)-catechin, procyanidine B_3, procyanidine C_1 and afzelechin-(4-α→8)-catechin have been isolated from the leaves; these substances are useful as anti-plaque agent (Fernando & Thabrew, 1990; Fernando *et al.,* 1991).

The matured leaf exhibited hypoglycemic activity and exerted no adverse effects on liver function, haemoglobin concentration, and reproductive ability in experimental animals. It also exerted no adverse effect on the histology of heart, lungs, kidney, intestine and pancreas of the animals. The hot water extract of the leaves enhances the glucose tolerance capacity in diabetic patients. Administration of the leaf extract prior to glucose loading resulted in a significantly increased glycogen content in the liver (by 70%) and muscle (by 100%) and the triacylglycerol content in the adipose tissue (by 30%) in comparison with rats treated only with the glucose load. The leaf extract was also able to markedly inhibit the activity of insulinase. Pretreatment of fasted rats with the leaf extract had no significant effect on the gluconeogenic capacity of kidney slices. The leaf extract had no effect on the intestinal glucose absorption (Fernando and Thabrew, 2001).
The present study is therefore undertaken to reinvestigate the hypoglycemic activity of the matured fresh leaf extract of *A. heterophyllus* and to observe the activities of antioxidants, carbohydrate metabolizing enzymes and lipid profile in alloxan induced diabetic rats.

Results:

Pharmacognostic characters:

Micromorphology:

The leaves are hypostomatic with anomocytic stomata. Latex ducts were found on the lower surface. Spharaphides were found on the epidermal cell. The average size of the epidermal cell was from 23.10x15.18μm on lower epidermis and 25.08x21.12μm on upper epidermis. The average size of the stomata was 21.12x 11.88μm and the size of the crystal was 9.9x8.58μm on lower epidermal layer and on the upper epidermal layer was 10.9x9.22 μm (Fig 3).

Stomatal complex

Stomatal Index/mm^2 was 16.2, Stomatal Frequency/mm^2 was 31.7, Palisade ratio was 10.5, Vein Islet number/mm^2 was 15.9 and Vein Termination number/mm^2 was 14.

Anatomy

Midrib

In the midrib the epidermis consist of square cells containing starch grains. The cortex contains hypodermal collenchymatus and chlorenchymatus cells with starch grains and spharaphides; below this were parenchymatic cells containing latex cells and spharaphides. These layers were also found on the lower side of the midrib. The sclereids are seen surrounding the whole vascular bundle. In the vascular bundle the phloem was seen on both sides of the xylem which contains latex cells and starch grains. The latex cell, starch grains and spharaphides were also seen in the xylem medullary rays. The lower epidermis contains elongated cells with starch grains. The size of cells were: upper epidermal cells 14.52x8.58μm; lower epidermal cells 15.56x5.08μm; sclereids 11.22x14.52μm; collenchyma 13.20x14.52μm; parenchyma 20.46x23.10μm; xylem rays 19.14x19.80μm; crystals 17.80x22.40μm; xylem vessels 23.10x22.40μm. The mesophyll is differentiated in to palisade and spongy cells containing starch grains. Palisade tissue was two layered. Patches of collenchyma were seen between the palisade cells. The epidermal layer contains latex sac. The spongy cells were of two types arranged in two regions, the cells of upper region was loosely packed while the lower layer contains closely packed cells. (Fig 2).

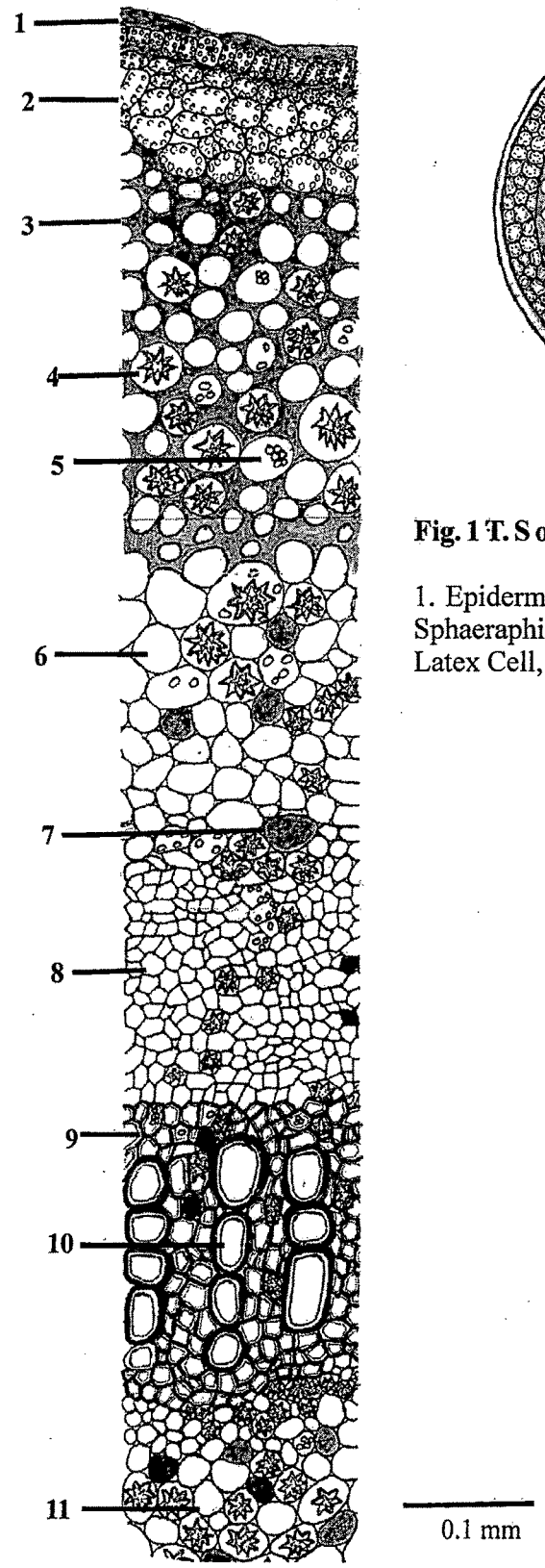
Petiole

The epidermal layers contain chloroplast. The cortex consists of hypodermal chlorenchyma and inner parenchyma containing latex cells, spharaphides and starch grains. The middle layer collenchyma also contains spharaphides and starch grains. In the vascular bundle phloem and xylem rays contain spharaphides, starch grains and latex cells. The pith region is abundantly filled with spharaphides; it also contains starch grains and latex cells. The length and breath of the cells were: upper epidermal cell

17.82x8.58μm, lower epidermal cell 17.82x9.10μm, collenchyma 30.36x31.68μm, parenchyma 28.38x35.64μm, xylem rays 25.08x15.84μm, crystals 17.80x21.10μm, xylem vessel 19.80x19.80μm, and pith cells 40.90x4.90μm. (Fig 1)

Powder characteristics

Powdered leaf was analyzed under the microscope. Fragments of palisade tissues, stomata, veins, fibres, latex sacs, starch grains, rosettes of calcium oxalate crystals, spirally coiled tracheids, fragment of sclereids are depicted in (Fig.4)



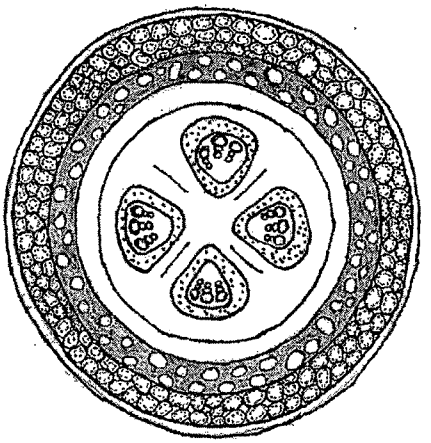


Fig. 1 T. S of Petiole *Artocarpus heterophyllus*

1. Epidermis, 2. Chlorenchyma, 3. Collenchyma, 4. Sphaeraphides, 5. Starch grains, 6. Parenchyma, 7. Latex Cell, 8. Phloem, 9. Medullary rays, 10. Xylem,

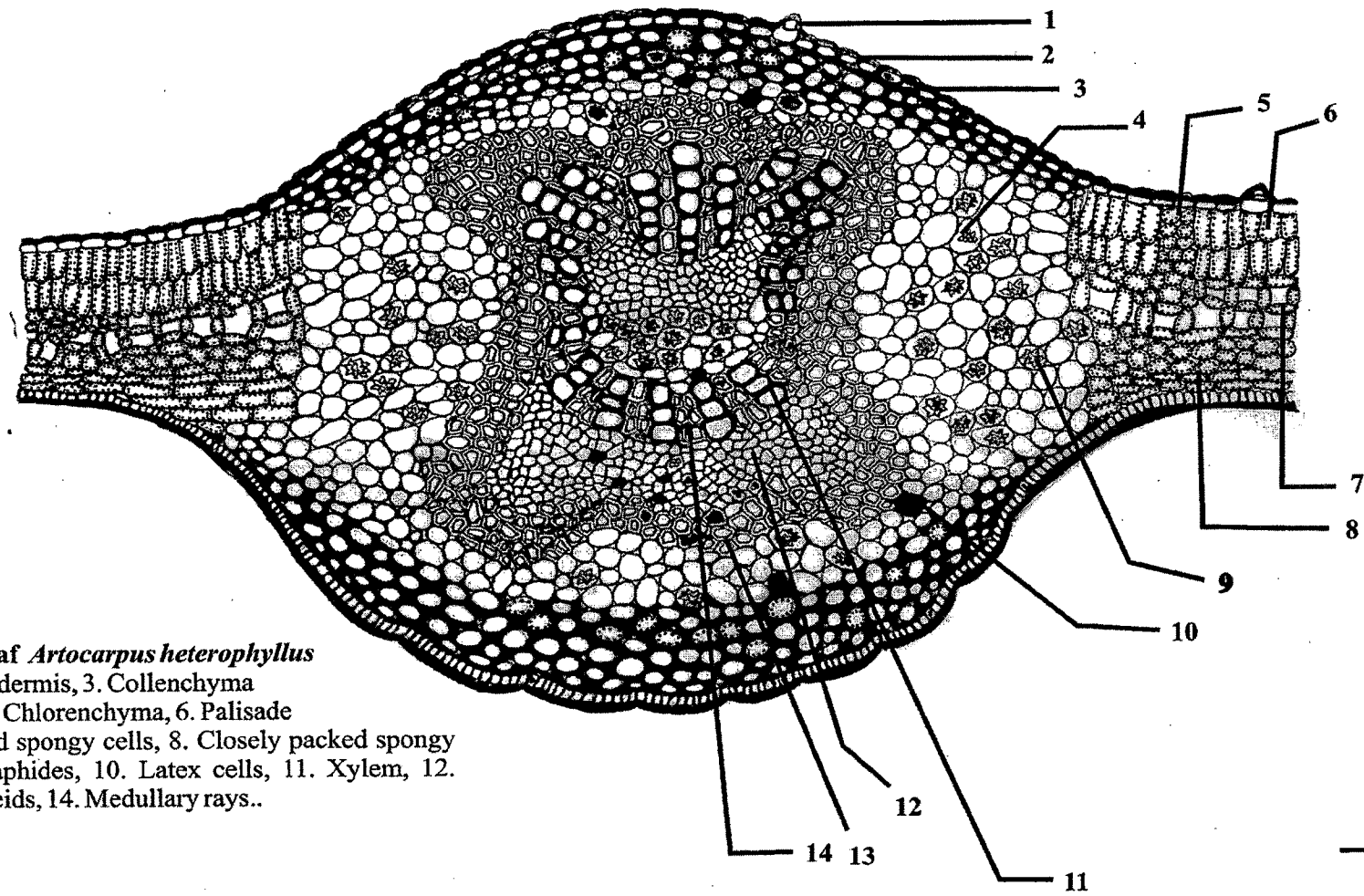


Fig. 2 T. S. of leaf *Artocarpus heterophyllus*
1.Latex sac, 2. Epidermis, 3. Collenchyma
4. Starch grains, 5. Chlorenchyma, 6. Palisade
7. Losely arranged spongy cells, 8. Closely packed spongy cells, 9. Sphaereaphides, 10. Latex cells, 11. Xylem, 12. Phloem, 13. Sclereids, 14. Medullary rays..

Fig. 3

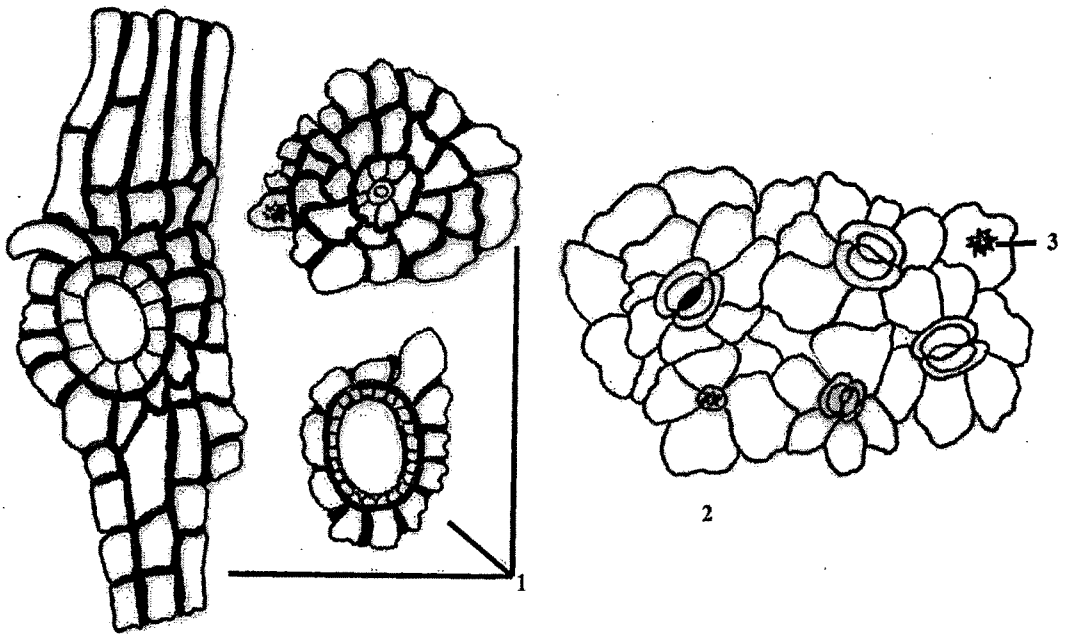


Fig. 4

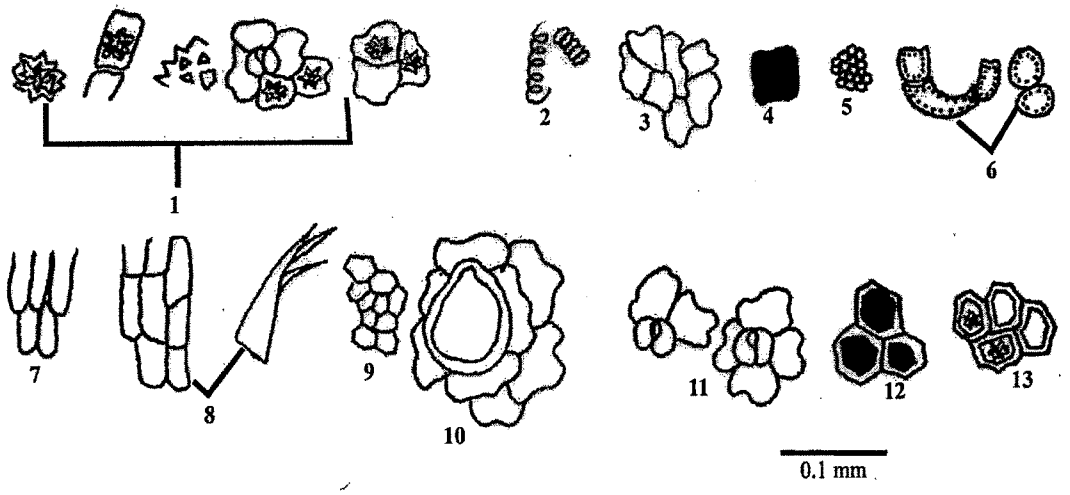


Fig. 3 Lower epidermal layer *Artocarpus heterophyllus*
1. Latex sac, 2. Anomocytic stomata, 3.Rosettes of calcium oxalate crystals.

Fig 4 Powder characters: 1. Rosettes of calcium oxalate crystals, 2. Tracheids, 3. Epidermal cells, 4. Latex cells, 5. Starch grains, 6. Spongy cells, 7. Palisade, 8. Vein, **9**. Sclereides, 10. Latex sac, 11. Stomata, 12. Latex filled sclereides, 13. Calcium oxalate crystals in sclereides

Phytochemistry

The phytochemicals present in the leaves are as follows: flavonoids such as 4'- OMe apigenin and 3', 4'- di - OMe -luteolin were found and phenolic acid such as vanillic and syringic acids were detected. Quinones, steroids, proanthocyanidins, and tannins were present and alkaloids were absent.

Pharmacology:

Result and Discussion:

The present study was to evaluate the antidiabetic activity of *A. heterophyllus* and to validate the use of this plant in controlling diabetes mellitus and also to detect the effect of the extract in the enzymatic and the non enzymatic antioxidants, carbohydrate metabolizing enzymes, in plasma and tissues apart from this, plasma lipids, plasma urea, uric acid, creatinine and blood urea nitrogen (BUN) were also checked.

Preliminary studies were carried out to determine the time taken to produce peak hypoglycaemic condition in normal rats after oral administration of the leaf extracts (Table 1 to 7). It was observed that the peak hypoglycemia occurred two hours after the administration of the extract. After continuous treatment of the extract for 30 days there was a significant fall (by 13%) in the fasting blood glucose level and there was no significant changes observed in the body weight, food intake and water intake respectively. Maximum glucose tolerance (57-58%) was observed in 90 minutes after the extract administration in normal glucose loaded rats.

The result shows that the fresh leaf extract reduces blood glucose levels in glucose loaded and in alloxan diabetic rats (Table 8 and 9); the normal rats did not show any significant changes. All the doses tested showed a reduction in the plasma glucose concentration (by 1.5 - 2.5%) but a significant reduction was observed in the dose 400mg and 600 mg/kg body weight respectively (4-7%). The optimum time of action observed in the extract was three hours after the administration. This implies that the activity of the crud extract might be of short duration. However, since multiple doses are also effective in reducing the plasma glucose concentrations after glucose challenge. The long term effect is also

evident. The exact reason for the reduction can not be explained. There was a reduction in the body weight (by 31.7%) in diabetic rats. This was recovered after the treatment with the plant extract 400mg, 600mg and glibenclamide (by 36.4%, 32.8% and 30.2%) respectively. The hypoglycemic activity of this plant did not show any significant changes in the normal rats.

The next phase of the study illustrate the effect of the extract on the enzymatic and non enzymatic antioxidants, carbohydrate metabolizing enzymes, plasma lipids, urea, uric acid and creatinine levels in alloxan induced diabetic rats (Table 10 - 21).

In the present study there is an increased level of TBARS in plasma (by 56.1%), liver (by 57.7%), kidney (by 56.7%) and brain (by 57.7%) of diabetic rats when compared to the control rats. Increased level of TBARS suggests increased OFRs. An increased level of TBARS is an index of lipid peroxidation. This study clearly shows that the administration of *A. heterophyllus* extract 400mg, 600mg and glibenclamide decreases the level of TBARS in plasma by (16.6%, 19.4% and 52.7%), in liver the percentage of decrease observed was (13.8%, 11.1% and 50%), in kidney the percentage of decrease observed was (13.5%, 8.1% and 51.3%) and in brain the observed decrease was (5%, 23.4% and 55.1%) but the result was not statistically significant when compared to the untreated diabetic rats.

The level of enzymatic and non enzymatic antioxidants in plasma, liver, kidney and brain of alloxan induced diabetic rats were decrease in the present study. There are ample evidences which confirm that the elevation in glucose concentration may depress natural antioxidant defenses such as vitamin C and glutathione (Yoshida *et al.*, 1995; Armstrong *et al.*, 1996). The imbalance between the generation of OFRs and in the antioxidant defense system may increase the oxidative stress which can damage the macromolecules such as DNA, protein and lipids.

In the present study, it is observed that the total glutathione concentration declines in the plasma (34.8%), liver (47.9%), kidney (73.7%) and brain (62.4%) of alloxan induced diabetic rats when compared to the control rats, which represent increase utilization due

to oxidative stress, and after the treatment with the extract 400mg, 600mg and glibenclamide the level of glutathione was increased in plasma (17.2%, 17.2% and 29%), liver (32.9%, 41.6% and 47.9%), kidney (59.7%, 60.2% and 68.4) and brain (47.6%, 48.6% and 56.5%), of experimental rats when compared to the untreated diabetic rats. Glutathione is known to protect the cellular system against the toxic effects of lipid peroxidation. Other workers have also reported decreased level of plasma GSH in STZ diabetic rats (Garg *et al.*, 1996).

In the present study, it is observed that the level of ascorbic acid was decreased in the plasma (58.4%), liver (40%), kidney (50%) and brain (47.6%) of diabetic rats. The reduction may be due to increased utilization of vitamin C as an antioxidant defense against increased reactive oxygen species. Vitamin C is known to act as an antioxidant in both *in vivo* and *in vitro*. It functions as a free radical scavenger and successfully prevents detectable oxidative damage under all type of oxidative stress. The treatment with the plant extract 400mg, 600mg and glibenclamide elevated the level of vitamin C in Plasma: 19%, 27.6% and 52.3%; liver: 4.25%, 4.25% and 34.7%; kidney: 11.7%, 18.9% and 46.4% and brain: 18.5%, 21.4% and 36.2% respectively in experimental rats when compared to the untreated diabetic rats.

In this study, the level of α- tocopherol was increased in plasma (33.6%) and decreased in the tissues (liver: 37%, kidney: 63.2% and brain: 40%) during diabetic condition. There can be an increased utilization of vitamin E due to increased level of TBARS. α-tocopherol is the most important lipid soluble, radical scavenging antioxidant. It reduces lipid hydroperoxide generated during the process of peroxidation and protects the cell structures against damage (Kinalski *et al.*, 2000). The treatment (leaf extract 400mg, 600mg and glibenclamide) restores the diabetic induced changes observed in the level of vitamin E in the experimental rats, the level of vitamin E in plasma was decreased (22.4%, 22.4% and 19.6%) and it was increased in liver (24.4%, 26.1% and 34.6%), kidney (46.2%, 44% and 53.3%) and brain (26.1%, 31.2% and 35%) when compared to the untreated diabetic rats.

The antioxidant defense system is significantly altered in diabetes. In the present study a significant decrease in SOD, CAT and GPX activities was observed in the liver (63.9%, 57.9% and 53.9%) and brain (53.2%, 56.9% and 44.8%) of diabetic rats when compared with control rats, Kono *et al.*,(1982) explained that this condition can result in a number of deleterious effects due to the accumulation of superoxide radicals (O_2^-) and hydrogen peroxides (H_2O_2). Catalase causes reduction of H_2O_2 where as GPx reduces H_2O_2 and lipid peroxides. In this study, it was observed that the level of GPx was increased in the kidney (by 46.1%) of diabetic rats where as the activity of SOD (60.32%) and CAT (56.9%) was decreased. The increased GPx activity and decreased catalase and SOD activity in the kidney suggests that there may be a compensatory mechanism among the antioxidant enzymes in response to increased oxidative stress so that tissues lacking significant catalase activity may be critically dependent on the activity of GPx. Administration of the leaf extract 400mg, 600mg and glibenclamide showed a significant ($p<0.05$) increase in the activity of SOD (brain: 26.8%, 34.4% and 48.6%; liver: 46.3%, 52.4% and 59.5%; kidney: 19.82%, 34.2% and 56.3%) but the changes observed in the level of CAT and GPX was not significant statistically. The level of CAT was increased in brain (11.2%, 10.4% and 45.2%), liver (8.3%, 13.8% and 48.6%) and kidney (21.6%, 28.8% and 53.05) and the level of GPX was decreased in kidney (27.7%, 25% and 44.4%) and increased in brain (15.78%, 20% and 37.6%) and liver (22.6%, 28.1% and 48.7%) in the experimental rats when compared to the untreated diabetic rats.

In the present study the hexokinase activity was decreased (50%) in alloxan induced diabetic rats which may be due to insulin deficiency (insulin stimulates and activates hexokinase D). Hexokinase is universally present in the cells of all types. Hepatocytes also contain a form of hexokinase called hexokinase D or Glucokinase which is more specific for glucose and differs from other forms of hexokinase in kinetic and regulatory properties (Lehninger *et al.*, 1993). Glucokinase (also called hexokinase IV) catalyze the conversion of glucose to glucose-6-phosphate and plays an important role in the maintenance of glucose homeostasis. In liver, the enzyme is an important regulator of glucose storage and disposal (O'Doherty *et al.*, 1999). Treatment with the fresh leaf extract 400mg, 600mg and glibenclamide elevated the activity of hexokinase (8.3%,

8.3% and 26.6%) in the liver. *A. heterophyllus* like glibenclamide may stimulate insulin secretion which may activate hexokinase, there by increasing utilization of glucose leading to decrease blood sugar level. As there is no accumulation of glucose-6-phosphate, hexokinase activity is not inhibited by auto-regulation, as in the case of diabetic rats. Hence the activity of hexokinase was increased in *A. heterophyllus* and glibenclamide treated diabetic rats.

In the present study there was an increased activity of glucose-6-phosphatse and fructose-1, 6- bisphosphatase in the liver of alloxan induced diabetic rats which may be due to insulin insufficiency. Murray *et al.*, (2000) explained that, insulin decrease gluconeogenesis by decreasing the activity of the key enzyme, such as glucose-6-phosphatase, fructose-1, 6-bisphosphataes, phosphoenolpyruvate carboxykinase. Here in this study it is observed that treatment with the leaf extract 400mg, 600mg and glibenclamide significantly reduced the activity of glucose-6-phosphatase (29%, 29% and 45.16%) and fructose-1, 6-bisphosphatase (32.4%, 37% and 44.4%) in the experimental rats when compared to the diabetic control rats; this may be due to increased insulin secretion which is responsible for the repression of gluconeogenic key enzyme.

There was an increased level of creatinine (83.7%), urea (70.3%) and blood urea nitrogen (70.4%) in the plasma of diabetic rats. After the treatment with the leaf extract (400 and 600mg) and glibenclamide the level of urea (27.4%, 36.9% and 48.6%), creatinine (66.5%, 75.1% and 78.6%) and BUN (27.2%, 37% and 48.7%) was decreased, which indicates that the plant extract can partially inhibit renal damage caused by diabetes. Uric acid is considered to be one of the non enzymatic antioxidant, but increased production of uric acid means, increased free radical production due to activation of the xanthine oxidase enzyme system (Nemeth *et al.*, 2002). In this experiment uric acid (84.8%) levels were increased in diabetic rats. This may be due to metabolic disturbance in diabetes reflected in high activities of xanthine oxidase and lipid peroxidation (Madianov *et al.*, 2000); it was observed that the level of uric acid was decreased (21.8%, 31.1% and 65.5%) after the treatment with the leaf extract 400mg, 600mg and glibenclamide respectively when compared to the untreated diabetic rats.

During diabetic condition the level of cholesterol (71.9%), free fatty acids (61.4%), phospholipids (42.3%), triglycerides (60.7%), LDL-c (85%) and VLDL-c (60.9%) was in increased with a decrease in HDL-c. After the treatment with the leaf extract 400mg, 600mg and glibenclamide, a significant decrease in the lipid profile (cholesterol: 21.1%, 33.7% and 45.6%; free fatty acid: 1.5%, 4.5% and 43.9%; phospholipids: 3.5%, 11.1% and 32.9%; triglycerides: 26.5%, 33.8% and 54.12%; LDL-c: 28%, 42% and 62.3%; VLDL-c: 26.5%, 33.7% and 54.1%) with increase in HDL cholesterol (39.8%, 45.9% and 63.4%) levels was observed. The extract was able to control the hyperlipidaemic state of diabetes this could be due to the direct effect of some of the chemical constituent present in the plant extract on lipid metabolism by affecting absorption, synthesis or utilization of lipid levels.

For all the parameters studied, aqueous extract of *A. heterophyllus* at a dose 400 and 600 mg/kg body weight had the same effect and the effect was less than the standard drug glibenclamide.

Conclusion:

In conclusion the fresh leaves extract showed hypoglycemic activity but the effect was less than the standard drug and significant changes were observed in the OGTT of normal rats. The plant extract did not show any significant changes in the activity of CAT and GPX this can be because the level of TBARS was also not reduced after the treatment but there were significant changes observed in antioxidants such as GSH, vitamin C, vitamin E and SOD. The activity of carbohydrate metabolizing enzymes was significantly restored after the treatment. The plant extract could also lower the plasma lipids and restore the level of urea, uric acid and creatinine there by protecting the diabetic rats from renal damage. Traditionally ayurvedic formulation is mostly a combination of drugs. The fresh matured leaves of *A. heterophyllus* can be used in the combination since there is no much effect observed in the antioxidants the effect can be compensated with a combined formulation.

Table: 1 Effect of *A.heterophyllus* aqueous leaf extract on blood glucose levels in fasted normal rats.

Groups	Treatment (Dose/Kg body weight)	Blood glucose (mg/dl)			
		Fasting	**1h**	**2h**	**3h**
1	Control (received 2% gum acacia)	67.7 ± 1.7^{a}	68.25 ± 3.2^{a}	68.5 ± 2.3^{a}	66.7 ± 2.75^{b}
2	*A.heterophyllus* 100mg	67.7 ± 1.7^{a}	67.5 ± 1.7^{a}	68.2 ± 1.7^{a}	69.2 ± 0.95^{b}
3	*A.heterophyllus* 200mg	71.0 ± 2.7^{a}	69.7 ± 4.0^{a}	65.5 ± 1.0^{a}	69.2 ± 0.95^{b}
4	*A.heterophyllus* 400mg	68.0 ± 1.8^{a}	67.2 ± 2.2^{a}	66.5 ± 1.0^{b}	65.5 ± 4.4^{c}
5	*A.heterophyllus* 600mg	68.7 ± 0.95^{a}	67.5 ± 1.7^{b}	63.5 ± 3.4^{c}	64.2 ± 4.9^{d}
6	*A.heterophyllus* 800mg	66.7 ± 1.5^{a}	66.7 ± 1.5^{b}	69.0 ± 1.15^{c}	63.5 ± 4.3^{d}
7	*A.heterophyllus* 1000mg	60.7 ± 2.9^{a}	61.5 ± 4.4^{b}	61.5 ± 1.91^{c}	64.5 ± 3.3^{d}

Table: 2 Effect of continuous administration of aqueous extract of *A.heterophyllus* on blood glucose levels in normal fasted rats.

Groups	Treatment (Dose/Kg body weight)	Blood glucose (mg/dl)			
		Initial Day	**4th Day**	**7th Day**	**15th Day**
1	Control (received 2% gum acacia)	67.2 ± 2.2^{a}	68.2 ± 1.7^{a}	67.0 ± 2.1^{a}	67.5 ± 1.9^{b}
2	*A.heterophyllus* 100mg	66.7 ± 2.06^{a}	68.0 ± 0.8^{a}	65.5 ± 1.2^{a}	68.0 ± 1.6^{b}
3	*A.heterophyllus* 200mg	66.2 ± 1.8^{a}	66.2 ± 1.2^{a}	64.2 ± 1.7^{a}	67.0 ± 1.4^{b}
4	*A.heterophyllus* 400mg	65.7 ± 2.2^{a}	64.5 ± 1.7^{b}	62.2 ± 2.06^{b}	64.5 ± 3.1^{a}
5	*A.heterophyllus* 600mg	65.2 ± 1.25^{a}	62.0 ± 1.63^{b}	60.2 ± 1.25^{c}	56.7 ± 1.5^{d}
6	*A.heterophyllus* 800mg	67.5 ± 1.9^{a}	62.0 ± 1.63^{b}	57.5 ± 1.29^{c}	57.0 ± 1.15^{d}
7	*A.heterophyllus* 1000mg	66.2 ± 1.8^{a}	63.25 ± 1.5^{b}	61.0 ± 1.15^{c}	57.2 ± 1.5^{d}

Values are means $\pm$ S.D for six animals in each group.
Values not sharing a common superscript differ significantly at $p<0.05$.
Duncan's Multiple Range Test (DMRT)

Table: 3 Effect of *A.heterophyllus* aqueous leaf extract on oral glucose tolerance in normal fasted rats (2g/kg body weight).

Groups	Treatment (Dose/Kg body weight)	Blood glucose (mg/dl)			
		Fasting	**30 min**	**60 min**	**90 min**
1	Control (received 2% gum acacia) + glucose	69.5 ± 1.9^{a}	171.2 ± 2.9^{b}	167.5 ± 2.8^{a}	162 ± 3.5^{a}
2	*A.heterophyllus* 100mg + glucose	68.5 ± 1.0^{a}	169.0 ± 1.15^{b}	163.7 ± 3.5^{b}	160.5 ± 1.91^{c}
3	*A.heterophyllus* 200mg + glucose	68.25 ± 2.3^{a}	167.7 ± 2.06^{b}	164.2 ± 1.5^{b}	161.7 ± 2.3^{c}
4	*A.heterophyllus* 400mg + glucose	69.0 ± 1.15^{a}	168.7 ± 2.9^{b}	165.7 ± 2.8^{c}	163 ± 2.4^{d}
5	*A.heterophyllus* 600mg + glucose	70.0 ± 1.6^{a}	170.0 ± 1.6^{b}	167.7 ± 2.06^{c}	163.7 ± 2.5^{d}
6	*A.heterophyllus* 800mg + glucose	68.2 ± 2.8^{a}	168.2 ± 2.8^{b}	161.25 ± 2.9^{c}	158.7 ± 2.9^{d}
7	*A.heterophyllus* 1000mg + glucose	69.5 ± 1.9^{a}	170.0 ± 1.63^{b}	165 ± 2.4^{c}	160 ± 1.63^{d}

Table: 4 Effect of *A.heterophyllus* aqueous leaf extract on oral glucose tolerance test in normal fasted rats after 30 days of continuous drug administration (2g/kg body weight).

Groups	Treatment (Dose/Kg body weight)	Blood glucose (mg/dl)			
		Fasting	**30 min**	**60 min**	**90 min**
1	Control (received 2% gum acacia)	68.25 ± 2.3^{a}	173.7 ± 3.5^{b}	171.2 ± 3.7^{b}	167 ± 2.9^{b}
2	*A.heterophyllus* 100mg	68.0 ± 2.1^{a}	169.7 ± 4.5^{b}	166.7 ± 4.2^{b}	167.2 ± 3.7^{c}
3	*A.heterophyllus* 200mg	67.7 ± 2.06^{a}	169.2 ± 2.5^{b}	166.2 ± 3.5^{b}	164.2 ± 2.8^{c}
4	*A.heterophyllus* 400mg	73.2 ± 5.3^{a}	170.2 ± 3.3^{b}	165.5 ± 3.3^{c}	161.5 ± 4.4^{d}
5	*A.heterophyllus* 600mg	67.2 ± 4.5^{a}	170.0 ± 4.3^{b}	166.2 ± 3.5^{c}	160.7 ± 2.9^{d}
6	*A.heterophyllus* 800mg	65 ± 2.4^{a}	160.7 ± 5.05^{b}	156.7 ± 3.9^{c}	156 ± 4.5^{d}
7	*A.heterophyllus* 1000mg	66.5 ± 1.7^{a}	162.2 ± 2.06^{b}	161 ± 2.0^{c}	158.2 ± 2.8^{d}

Values are means $\pm$ S.D for six animals in each group.
Values not sharing a common superscript differ significantly at $p<0.05$.
Duncan's Multiple Range Test (DMRT)

Table: 5 Effect of continuous administration of *A.heterophyllus* aqueous extract on body weight changes in normal rats.

Groups	Treatment (Dose/Kg body weight)	Body weight changes (gm)			
		Initial day	**4th Day**	**7th Day**	**15th Day**
1	Control (received 2% gum acacia)	157.5 ± 3.7^a	160.2 ± 3.5^a	163.7 ± 2.5^a	167.2 ± 1.5^a
2	*A.heterophyllus* 100mg	162.2 ± 2.06^a	165.5 ± 1.7^a	167.7 ± 2.06^a	169.5 ± 1.91^b
3	*A.heterophyllus* 200mg	159.7 ± 2.9^a	160.7 ± 4.5^a	163.7 ± 3.5^a	166.0 ± 3.65^b
4	*A.heterophyllus* 400mg	158.7 ± 2.9^a	161.0 ± 2.5^a	163.0 ± 3.4^a	165.0 ± 2.4^a
5	*A.heterophyllus* 600mg	158.2 ± 2.87^a	160.2 ± 3.3^a	162.5 ± 3.7^a	165.0 ± 3.46^b
6	*A.heterophyllus* 800 mg	160.5 ± 4.2^a	163.0 ± 4.16^a	165.5 ± 4.43^a	167.0 ± 4.7^b
7	*A.heterophyllus* 1000mg	158.7 ± 2.9^a	161.0 ± 2.58^a	163.5 ± 3.41^b	166.0 ± 2.82^b

Table: 6 Effect of continuous administration of aqueous extract of *A.heterophyllus* leaf on food intake in normal rats.

Groups	Treatment (Dose/Kg body weight)	Food intake (g/week)			
		Initial day	**4th Day**	**7th Day**	**15th Day**
1	Control (received 2% gum acacia)	77.7 ± 1.7^a	76.0 ± 1.4^a	77.0 ± 1.15^a	77.5 ± 1.91^b
2	*A.heterophyllus* 100mg	77.7 ± 1.7^a	78.0 ± 2.9^a	78.25 ± 2.87^a	79.5 ± 4.2^b
3	*A.heterophyllus* 200mg	71.1 ± 4.3^a	73.5 ± 4.1^a	75.5 ± 4.12^a	78.0 ± 3.5^b
4	*A.heterophyllus* 400mg	72.7 ± 3.2^a	74.5 ± 3.0^a	76.5 ± 1.7^a	81.0 ± 1.15^b
5	*A.heterophyllus* 600mg	71.7 ± 2.8^a	74.5 ± 3.3^a	77.0 ± 3.4^a	80.2 ± 3.5^b
6	*A.heterophyllus* 800mg	74.5 ± 1.7^a	77.2 ± 1.5^a	79.5 ± 1.0^a	81.0 ± 2.0^b
7	*A.heterophyllus* 1000mg	71.0 ± 3.8^a	73.2 ± 3.9^a	75.5 ± 4.1^a	78.0 ± 3.5^b

Values are means $\pm$ S.D for six animals in each group.
Values not sharing a common superscript differ significantly at $p<0.05$.
Duncan's Multiple Range Test (DMRT)

Table: 7 Effect of continuous administration of aqueous extract of *A.heterophyllus* leaf on water intake in normal rats.

Groups	Treatment (Dose/Kg body weight)	Water intake (L/week)			
		Initial day	**4th Day**	**7th Day**	**15th Day**
1	Control (received 2% gum acacia)	4.62 ± 0.47	5.52 ± 1.08	5.75 ± 0.95	6.1 ± 1.09
2	*A.heterophyllus* 100mg	4.52 ± 0.20	4.45 ± 0.26	4.9 ± 0.42	4.9 ± 0.42
3	*A.heterophyllus* 200mg	4.9 ± 0.4	5.02 ± 0.35	5.05 ± 0.30	4.7 ± 0.52
4	*A.heterophyllus* 400mg	4.95 ± 0.36	4.7 ± 0.21	5.17 ± 0.43	4.8 ± 0.69
5	*A.heterophyllus* 600mg	4.65 ± 0.17	5.2 ± 0.30	4.9 ± 0.40	4.8 ± 0.43
6	*A.heterophyllus* 800mg	4.50 ± 0.24[a]	4.7 ± 0.33[a]	4.9 ± 0.20[a]	4.7 ± 0.20[b]
7	*A.heterophyllus* 1000mg	4.57 ± 0.28[a]	4.7 ± 0.33[a]	5.02 ± 0.33[a]	5.1 ± 0.38[b]

Table: 8 Effect of *A.heterophyllus* aqueous leaf extract on blood glucose level in streptozotocin diabetic rats.

Groups	Treatment (Dose/Kg body weight)	Blood glucose (mg/dl)			
		Fasting	**1h**	**2h**	**3h**
1	Control (received 2% gum acacia)	69.7 ± 1.7[a]	68.5 ± 3.4[a]	70.2 ± 3.5[a]	66.7 ± 2.06[a]
2	Diabetic control	276.2 ± 33.5[a]	280.0 ± 34.6[a]	286.2 ± 41.9[a]	282.2 ± 34.9[a]
3	Diabetic + *A.heterophyllus* 400mg	264.0 ± 30.68[a]	258.2 ± 28.0[a]	252.0 ± 25.3[b]	238.7 ± 14.3[c]
4	Diabetic + *A.heterophyllus* 600mg	249.0 ± 2.58[a]	247.2 ± 2.2[b]	246.0 ± 1.41[c]	244.2 ± 3.3[d]
5	Diabetic + glibenclamide (600 µg/ kg body weight)	251 ± 2.58[a]	248.7 ± 2.9[b]	245.7 ± 4.34[c]	242.5 ± 3.3[d]

Values are means ± S.D for six animals in each group.
Values not sharing a common superscript differ significantly at $p<0.05$.
Duncan's Multiple Range Test (DMRT)

Table: 9 Effect of continuous administration of *A.heterophyllus* aqueous leaf extract for 30 days on blood glucose level in alloxan diabetic rats.

Groups	Treatment (Dose/Kg body weight)	Blood glucose (mg/dl)			
		Initial day	**4th Day**	**7th Day**	**15th Day**
1	Control (received 2% gum acacia)	70.0 ± 4.39^{a}	70.0 ± 3.5^{a}	71.25 ± 2.9^{a}	70.2 ± 3.8^{a}
2	Diabetic control	264.2 ± 23.9^{a}	268.0 ± 28.0^{a}	270.7 ± 29.5^{a}	273.0 ± 30.0^{b}
3	Diabetic + *A.heterophyllus* 400mg	235.7 ± 8.09^{a}	235.0 ± 7.39^{a}	233.7 ± 6.23^{b}	230.7 ± 6.5^{c}
4	Diabetic + *A.heterophyllus* 600mg	253.0 ± 2.16^{a}	250.5 ± 1.91^{b}	248.2 ± 2.36^{c}	246.0 ± 2.8^{d}
5	Diabetic + glibenclamide (600 µg/ kg body weight)	253.7 ± 3.5^{a}	251.5 ± 3.1^{b}	249.2 ± 3.77^{c}	246.7 ± 4.27^{d}

Table: 10 Effect of *A. heterophyllus* on blood glucose level and body weight

Groups	Treatment (Dose/Kg body weight)	Blood glucose (initial)	Blood glucose (final)	Body weight (initial)	Body weight (final)
1	Control (received 2% gum acacia)	81.8 ± 6.17	97.5 ± 4.2^{a}	185.8 ± 26.15	189 ± 12.8^{a}
2	Diabetic + control	283 ± 14.35	337.5 ± 20.9^{b}	190 ± 17.8	129 ± 19^{b}
3	Diabetic + *A. heterophyllus* (400mg)	287 ± 19.93	181.8 ± 16.9^{c}	205.8 ± 23.3	203 ± 18^{c}
4	Diabetic + *A. heterophyllus* (600mg)	284 ± 19	180.8 ± 35^{c}	184 ± 17.4	192 ± 19.4^{c}
5	Diabetic + Glibenclamide (600µg/kg body weight)	305 ± 27	135 ± 17.3^{a}	182 ± 20.4	185 ± 28^{c}

Values are means $\pm$ S.D for six animals in each group.
Values not sharing a common superscript differ significantly at $p<0.05$.
Duncan's Multiple Range Test (DMRT)

Table: 11 Effect of *A. heterophyllus* on TBARS, GSH, Vitamin C, and Vitamin E in plasma of alloxan induced diabetic rats

Groups	Treatment (Dose/Kg body weight)	TBARS (n mol /ml)	GSH (µg /dl)	Vitamin C (µg /dl)	Vitamin E (µg /dl)
1	Control (received 2% gum acacia)	1.58 ± 0.56^{a}	23 ± 3.2^{a}	1.95 ± 0.18^{a}	0.71 ± 0.04^{a}
2	Diabetic + control	3.6 ± 0.39^{b}	14.98 ± 2.3^{b}	0.81 ± 0.098^{b}	1.07 ± 0.038^{b}
3	Diabetic + *A. heterophyllus* (400mg)	3 ± 0.44^{b}	18.08 ± 2.3^{d}	1.0 ± 0.22^{c}	0.83 ± 0.045^{c}
4	Diabetic + *A. heterophyllus* (600mg)	2.9 ± 0.70^{b}	18.08 ± 2.4^{d}	1.12 ± 0.13^{c}	0.83 ± 0.040^{c}
5	Diabetic + Glibenclamide (600µg/kg body weight)	1.7 ± 0.51^{a}	21.1 ± 2.3^{a}	1.7 ± 0.18^{a}	0.86 ± 0.016^{d}

Table: 12 Effect of *A. heterophyllus* on TBARS, GSH, Vitamin C, and Vitamin E in liver of alloxan induced diabetic rats

Groups	Treatment (Dose/Kg body weight)	TBARS (n mol /ml)	GSH (µg /dl)	Vitamin C (µg /dl)	Vitamin E (µg /dl)
1	Control (received 2% gum acacia)	1.52 ± 0.52^{a}	13.9 ± 3.25^{a}	0.75 ± 0.01^{a}	5.4 ± 0.28a
2	Diabetic + control	3.6 ± 0.39^{b}	7.24 ± 2.5^{b}	0.45 ± 0.04^{b}	3.4 ± 0.19^{b}
3	Diabetic + *A. heterophyllus* (400mg)	3.1 ± 0.68^{b}	10.8 ± 1.6^{c}	0.47 ± 0.02^{c}	4.5 ± 0.37^{c}
4	Diabetic + *A. heterophyllus* (600mg)	3.2 ± 0.66^{b}	12.4 ± 1.9^{c}	0.47 ± 0.02^{c}	4.6 ± 0.43^{c}
5	Diabetic + Glibenclamide(600µg/kg body weight)	1.8 ± 0.40^{a}	13.9 ± 3.24^{a}	0.69 ± 0.03^{d}	5.2 ± 0.04^{d}

Values are means ± S.D for six animals in each group.
Values not sharing a common superscript differ significantly at $p<0.05$.
Duncan's Multiple Range Test (DMRT)

Table: 13 Effect of *A. heterophyllus* on TBARS, GSH, Vitamin C, and Vitamin E in Kidney of alloxan induced diabetic rats

Groups	Treatment (Dose/Kg body weight)	TBARS (n mol /ml)	GSH (µg /dl)	Vitamin C (µg /dl)	Vitamin E (µg /dl)
1	Control (received 2% gum acacia)	1.6 ± 0.47^{a}	11.8 ± 3.6^{a}	$0.60 \pm .024^{a}$	3.8 ± 0.46^{a}
2	Diabetic + control	3.7 ± 0.33^{b}	3.1 ± 1.67^{b}	$0.30 \pm .054^{b}$	1.40 ± 0.14^{b}
3	Diabetic + *A. heterophyllus* (400mg)	3.2 ± 0.25^{b}	7.7 ± 1.6^{d}	$0.34 \pm .060^{b,c}$	2.6 ± 0.29^{c}
4	Diabetic + *A. heterophyllus* (600mg)	3.4 ± 0.69^{b}	7.8 ± 1.6^{d}	$0.37 \pm .016^{c}$	2.5 ± 0.46^{c}
5	Diabetic + Glibenclamide (600µg/kg body weight)	1.8 ± 0.66^{a}	9.83 ± 2.3^{a}	0.56 ± 0.015^{a}	3.0 ± 0.17^{d}

Table: 14 Effect of *A. heterophyllus* on TBARS, GSH, Vitamin C, and Vitamin E in Brain of alloxan induced diabetic rats

Groups	Treatment (Dose/Kg body weight)	TBARS (n mol /ml)	GSH (µg /dl)	Vitamin C (µg /dl)	Vitamin E (µg /dl)
1	Control (received 2% gum acacia)	1.6 ± 0.70^{a}	14.9 ± 4.5^{a}	0.84 ± 0.05^{a}	5.5 ± 1.14^{a}
2	Diabetic + control	3.79 ± 0.65^{b}	5.6 ± 2.3^{b}	0.44 ± 0.045^{b}	3.3 ± 0.11^{b}
3	Diabetic + *A. heterophyllus* (400mg)	3.8 ± 0.91^{b}	10.7 ± 2.5^{b}	0.54 ± 0.01^{c}	4.47 ± 0.34^{c}
4	Diabetic + *A. heterophyllus* (600mg)	2.9 ± 0.72^{b}	10.9 ± 4.2^{b}	0.56 ± 0.02^{c}	4.8 ± 0.28^{c}
5	Diabetic + Glibenclamide (600µg/kg body weight)	1.7 ± 0.65^{a}	12.9 ± 3.05^{a}	0.69 ± 0.02^{d}	5.08 ± 0.32^{d}

Values are means $\pm$ S.D for six animals in each group.
Values not sharing a common superscript differ significantly at $p<0.05$.
Duncan's Multiple Range Test (DMRT)

Table: 15 Effect of *A. heterophyllus* on SOD, CAT and GPX in brain of alloxan induced diabetic rats

Groups	Treatment (Dose/Kg body weight)	SOD U/mg protein	CAT U/mg protein	GPx U/mg protein
1	Control (received 2% gum acacia)	11.77 ± 0.21^{a}	166 ± 34.85^{a}	8.7 ± 0.63^{a}
2	Diabetic + control	5.47 ± 1.7^{b}	71.5 ± 10^{b}	4.8 ± 0.79^{b}
3	Diabetic + *A. heterophyllus* (400mg)	7.48 ± 1.29^{c}	80.5 ± 9.7^{b}	5.7 ± 0.57^{b}
4	Diabetic + *A. heterophyllus* (600mg)	8.34 ± 1.08^{c}	79.8 ± 4.07^{b}	6.0 ± 0.62^{b}
5	Diabetic + Glibenclamide (600µg/kg body weight)	10.65 ± 0.37^{a}	130.5 ± 17.8^{c}	7.7 ± 0.97^{a}

Table: 16 Effect of *A. heterophyllus* on SOD, CAT and GPX in liver of alloxan induced diabetic rats

Groups	Treatment (Dose/Kg body weight)	SOD U/mg protein	CAT U/mg protein	GPx U/mg protein
1	Control (received 2% gum acacia)	12.01 ± 0.32^{a}	163.2 ± 24.36^{a}	8.9 ± 1.8^{a}
2	Diabetic + control	4.33 ± 0.68^{b}	68.76 ± 8.24^{b}	4.1 ± 0.78^{b}
3	Diabetic + *A. heterophyllus* (400mg)	8.07 ± 0.96^{c}	75.01 ± 6.9^{b}	5.3 ± 0.73^{b}
4	Diabetic + *A. heterophyllus* (600mg)	9.1 ± 0.47^{c}	79.8 ± 20.6^{b}	5.7 ± 0.57^{b}
5	Diabetic + Glibenclamide(600µg/kg body weight)	10.7 ± 0.38^{d}	134.01 ± 13.25^{c}	8 ± 0.82^{a}

Values are means $\pm$ S.D for six animals in each group.
Values not sharing a common superscript differ significantly at $p<0.05$.
Duncan's Multiple Range Test (DMRT)

Table: 17 Effect of *A. heterophyllus* on SOD, CAT and GPX in Kidney of alloxan induced diabetic rats

Groups	Treatment (Dose/Kg body weight)	SOD U/mg protein	CAT U/mg protein	GPx U/mg protein
1	Control (received 2% gum acacia)	11.72 ± 0.18^{a}	75.7 ± 7.1^{a}	3.88 ± 0.50^{a}
2	Diabetic + control	4.65 ± 1.17^{b}	32.6 ± 6.68^{b}	7.2 ± 0.88^{b}
3	Diabetic + *A. heterophyllus* (400mg)	$5.8 \pm 1.5^{b,c}$	41.6 ± 5.8^{b}	5.2 ± 0.65^{b}
4	Diabetic + *A. heterophyllus* (600mg)	7.07 ± 0.62^{c}	45.8 ± 5.26^{b}	5.4 ± 0.77^{b}
5	Diabetic + Glibenclamide(600µg/kg body weight)	10.64 ± 0.21^{a}	69.45 ± 17.8^{c}	4 ± 0.59^{c}

Values are means ± S.D for six animals in each group.
Values not sharing a common superscript differ significantly at $p<0.05$.
Duncan's Multiple Range Test (DMRT)

Table: 18 Effect of *A. heterophyllus* on Hexokinase, Glucose-6-phosphatase and Fructose-1, 6-bisphosphatase of alloxan induced diabetic rats

Groups	Treatment (Dose/Kg body weight)	Hexokinase (U^{a}/ mg protein)	Glucose-6-phosphatase (U^{b}/mg protein)	Fructose-1, 6-bisphosphatase (U^{c}/mg protein)
1	Control (received 2% gum acacia)	0.22 ± 0.01^{a}	0.16 ± 0.01^{a}	0.55 ± 0.02^{a}
2	Diabetic + control	0.11 ± 0.01^{b}	0.31 ± 0.06^{b}	1.08 ± 0.04^{b}
3	Diabetic + *A. heterophyllus* (400mg)	0.13 ± 0.008^{b}	0.22 ± 0.02^{c}	0.73 ± 0.06^{c}
4	Diabetic + *A. heterophyllus* (600mg)	0.13 ± 0.01^{b}	0.22 ± 0.01^{c}	0.68 ± 0.025^{c}
5	Diabetic + Glibenclamide(600µg/kg body weight)	0.15 ± 0.05^{c}	0.17 ± 0.01^{a}	0.60 ± 0.05^{a}

Values are means ± S.D for six animals in each group. Enzyme units are expressed as units/mg protein
[a] µmol of glucose phosphorylated/h
[b] µmol of liberated / min
[c] µmol of pi liberated / min
Values not sharing a common superscript differ significantly at $p<0.05$.
Duncan's Multiple Range Test (DMRT)

Table: 19 Effect of *A. heterophyllus* on plasma Urea, Uric acid, creatinine, and BUN on alloxan induced diabetic rats

Groups	Treatment (Dose/Kg body weight)	Urea (mg/dl)	Uric acid (nmol/ml)	Creatinine (mg/dl)	Blood Urea Nitrogen (mg/dl)
1	Control (received 2% gum acacia)	19.6 ± 5.8^{a}	3.1 ± 0.42^{a}	0.7 ± 0.4^{a}	9.1 ± 2.7^{a}
2	Diabetic + control	66 ± 6.8^{b}	20.5 ± 0.87^{b}	4.3 ± 1.05^{b}	30.8 ± 3.1^{b}
3	Diabetic + *A. heterophyllus* (400mg)	47.9 ± 5.9^{c}	16.03 ± 2.47^{c}	1.44 ± 0.61^{c}	22.4 ± 2.7^{c}
4	Diabetic + *A. heterophyllus* (600mg)	41.6 ± 4.1^{c}	14.13 ± 1.2^{c}	1.07 ± 0.36^{c}	19.4 ± 1.9^{c}
5	Diabetic + Glibenclamide(600µg/kg body weight)	33.9 ± 2.3^{d}	7.06 ± 1.03^{d}	0.92 ± 0.48^{d}	15.8 ± 1.06^{d}

Table: 20 Effect of *A. heterophyllus* on plasma Cholesterol, Free fatty acid, Phospholipids and Triglycerides on alloxan induced diabetic rats

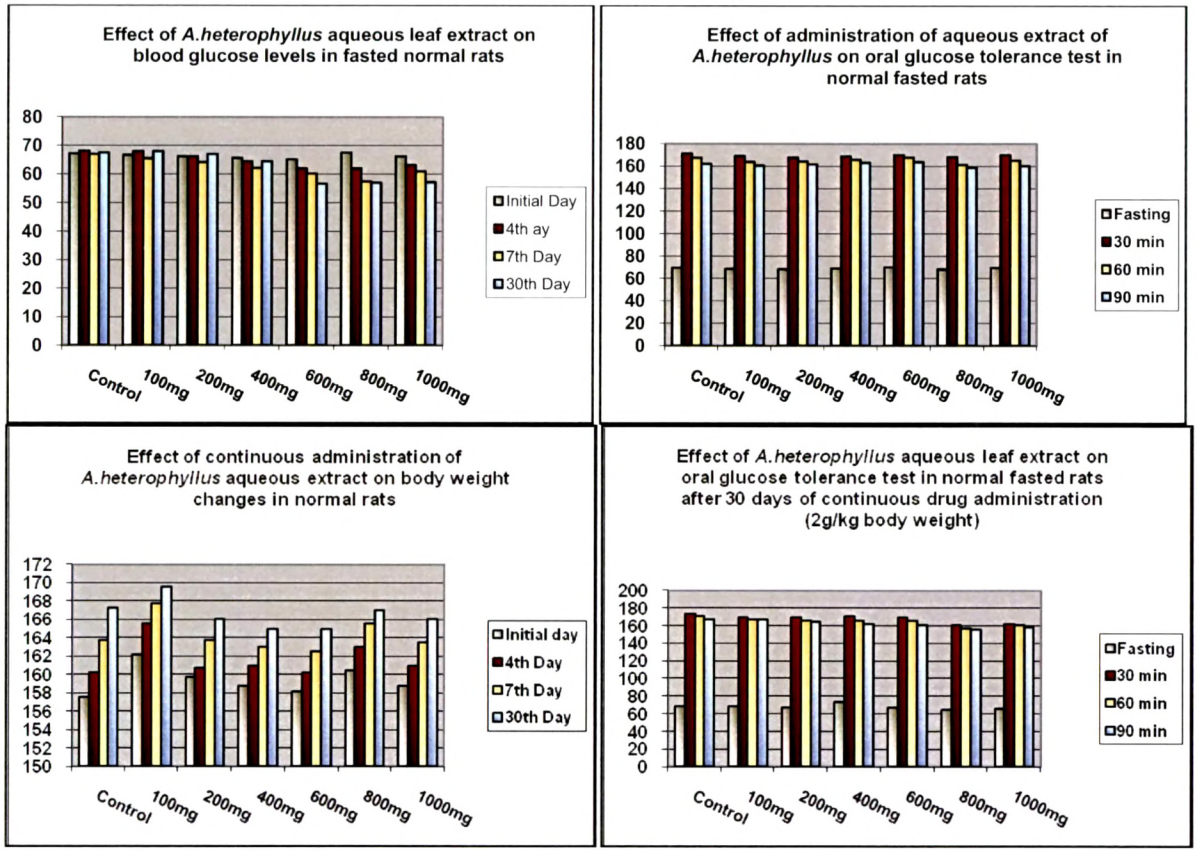
Groups	Treatment (Dose/Kg body weight)	Cholesterol (mg/dl)	Free fatty acids (mg/dl)	Phospholipids (mg/dl)	Triglycerides (mg/dl)
1	Control (received 2% gum acacia)	63.9 ± 10.9^{a}	50.9 ± 2.2^{a}	121.3 ± 1.17^{a}	59.9 ± 21.8^{a}
2	Diabetic + control	228 ± 27^{b}	132 ± 1.7^{b}	210.4 ± 6.51^{b}	152.6 ± 12.7^{b}
3	Diabetic + *A. heterophyllus* (400mg)	180 ± 93.6^{c}	130 ± 7.8^{c}	203 ± 5.5^{c}	112.14 ± 17.7^{c}
4	Diabetic + *A. heterophyllus* (600mg)	151 ± 62.8^{d}	126 ± 7^{c}	187 ± 10.2^{c}	101 ± 21.6^{c}
5	Diabetic + Glibenclamide(600µg/kg body weight)	124 ± 13.3^{e}	74 ± 13.3^{d}	141 ± 3.5^{d}	70 ± 14.1^{d}

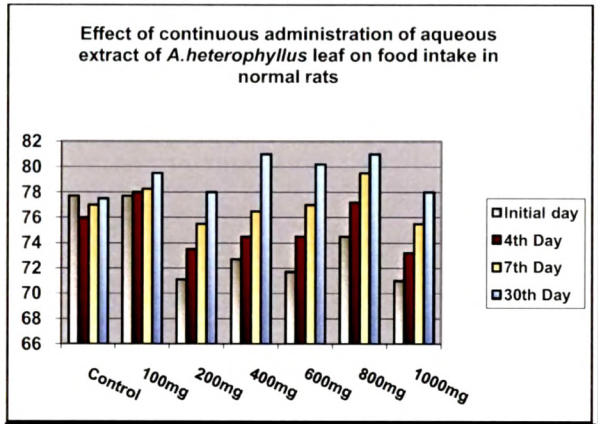
Values are means $\pm$ S.D for six animals in each group.
Values not sharing a common superscript differ significantly at $p<0.05$.
Duncan's Multiple Range Test (DMRT)

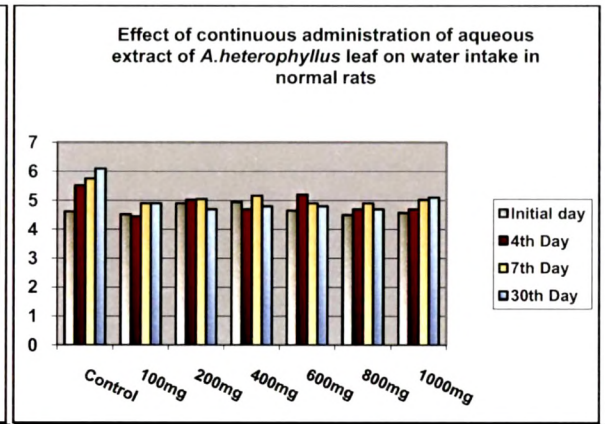
Table: 21 Effect of *A. heterophyllus* on plasma HDL-C, LDL-C and VLDL-Con streptozotocin induced diabetic rats

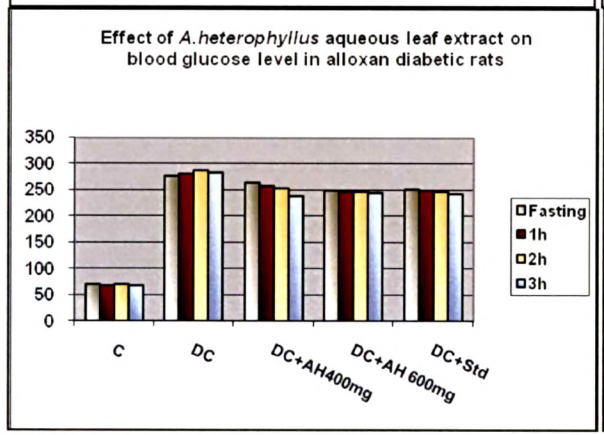
Groups	Treatment (Dose/Kg body weight)	HDL-C (mg/dl)	LDL-C (mg/dl)	VLDL-C (mg/dl)
1	Control (received 2% gum acacia)	39.9 ± 4.6^{a}	35.9 ± 7.2^{a}	11.9 ± 4.3^{a}
2	Diabetic + control	17.2 ± 6.6^{b}	242 ± 20^{b}	30.5 ± 2.5^{b}
3	Diabetic + *A. heterophyllus* (400mg)	28.6 ± 1.2^{c}	174 ± 91^{c}	22.4 ± 3.5^{c}
4	Diabetic + *A. heterophyllus* (600mg)	31.8 ± 2.6^{c}	140 ± 61^{c}	20.2 ± 4.3^{c}
5	Diabetic + Glibenclamide(600µg/kg body weight)	47.1 ± 1.3^{d}	91 ± 9.1^{d}	14.0 ± 2.8^{d}

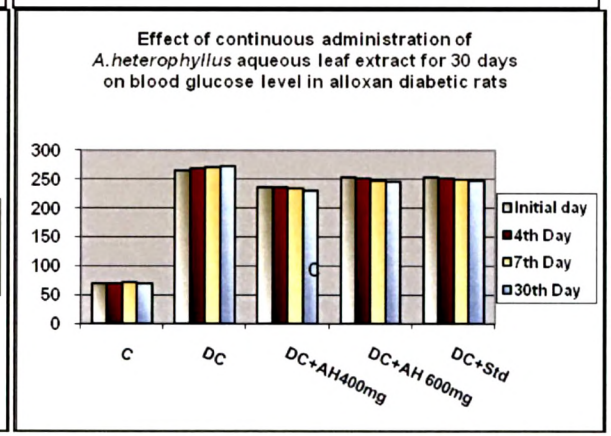
Values are means $\pm$ S.D for six animals in each group.
Values not sharing a common superscript differ significantly at $p<0.05$.
Duncan's Multiple Range Test (DMRT)

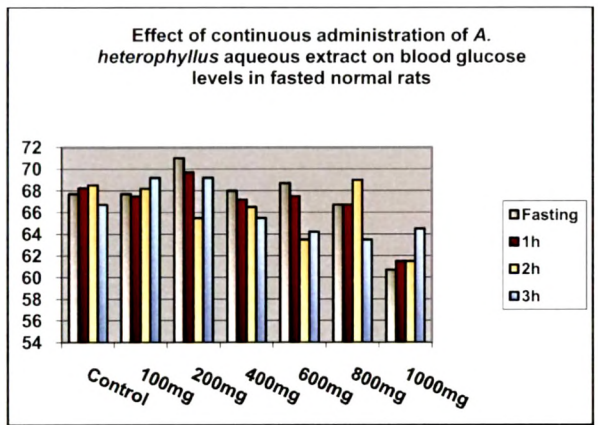

Effect of A.heterophyllus aqueous leaf extract on blood glucose levels in fasted normal rats
80
70
60
50
40
30
20
10
0
Control
100mg
200mg
400mg
600mg
800mg
1000mg
Initial Day
4th ay
7th Day
30th Day
Effect of administration of aqueous extract of A.heterophyllus on oral glucose tolerance test in normal fasted rats
180
160
140
120
100
80
60
40
20
0
Control
100mg
200mg
400mg
600mg
800mg
1000mg
Fasting
30 min
60 min
90 min
Effect of continuous administration of A.heterophyllus aqueous extract on body weight changes in normal rats
172
170
168
166
164
162
160
158
156
154
152
150
Control
100mg
200mg
400mg
600mg
800mg
1000mg
Initial day
4th Day
7th Day
30th Day
Effect of A.heterophyllus aqueous leaf extract on oral glucose tolerance test in normal fasted rats after 30 days of continuous drug administration (2g/kg body weight)
200
180
160
140
120
100
80
60
40
20
0
Control
100mg
200mg
400mg
600mg
800mg
1000mg
Fasting
30 min
60 min
90 min

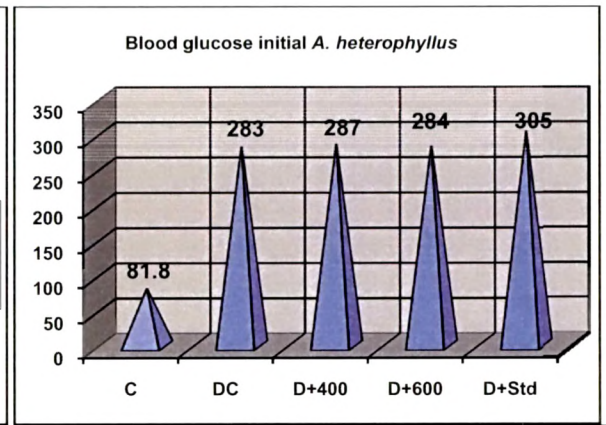

Effect of continuous administration of aqueous extract of A.heterophyllus leaf on food intake in normal rats
82
80
78
76
74
72
70
68
66
Control
100mg
200mg
400mg
600mg
800mg
1000mg
Initial day
4th Day
7th Day
30th Day

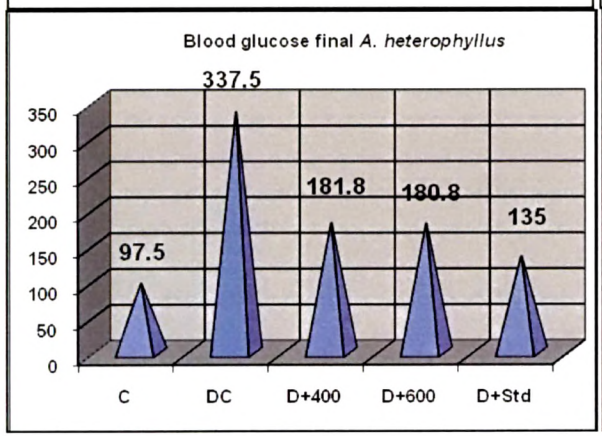

Effect of continuous administration of aqueous extract of A.heterophyllus leaf on water intake in normal rats
7
6
5
4
3
2
1
0
Control
100mg
200mg
400mg
600mg
800mg
1000mg
Initial day
4th Day
7th Day
30th Day

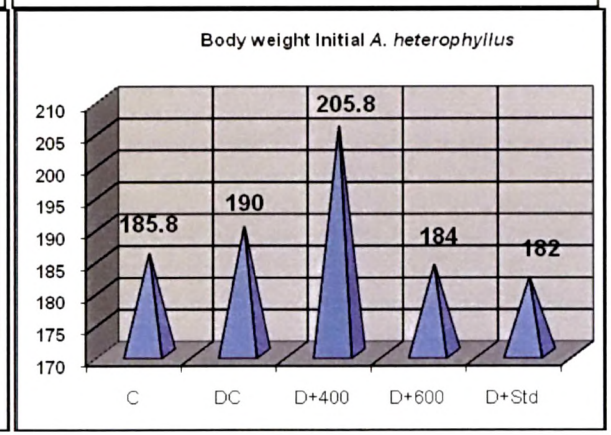

Effect of A.heterophyllus aqueous leaf extract on blood glucose level in alloxan diabetic rats
350
300
250
200
150
100
50
0
C
DC
DC+AH400mg
DC+AH 600mg
DC+Std
Fasting
1h
2h
3h

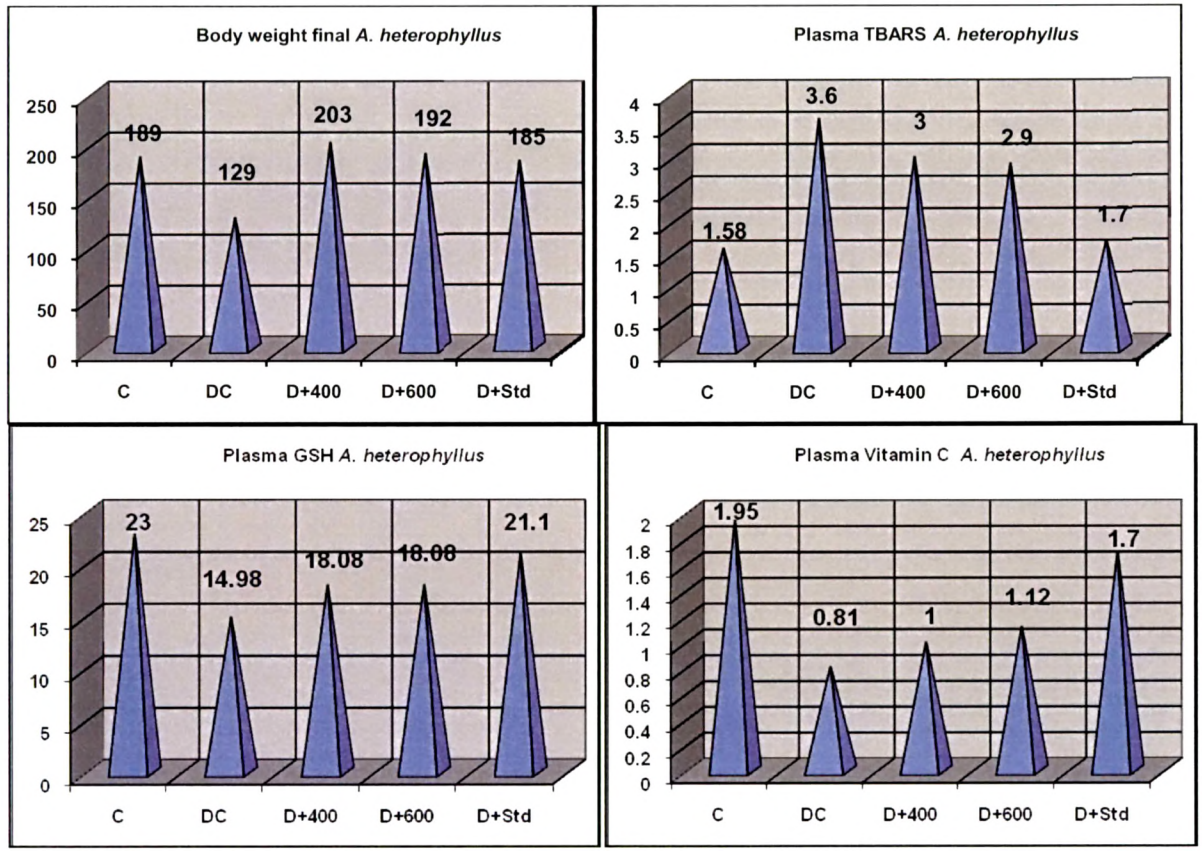

Effect of continuous administration of A.heterophyllus aqueous leaf extract for 30 days on blood glucose level in alloxan diabetic rats
300
250
200
150
100
50
0
C
DC
DC+AH400mg
DC+AH 600mg
DC+Std
Initial day
4th Day
7th Day
30th Day

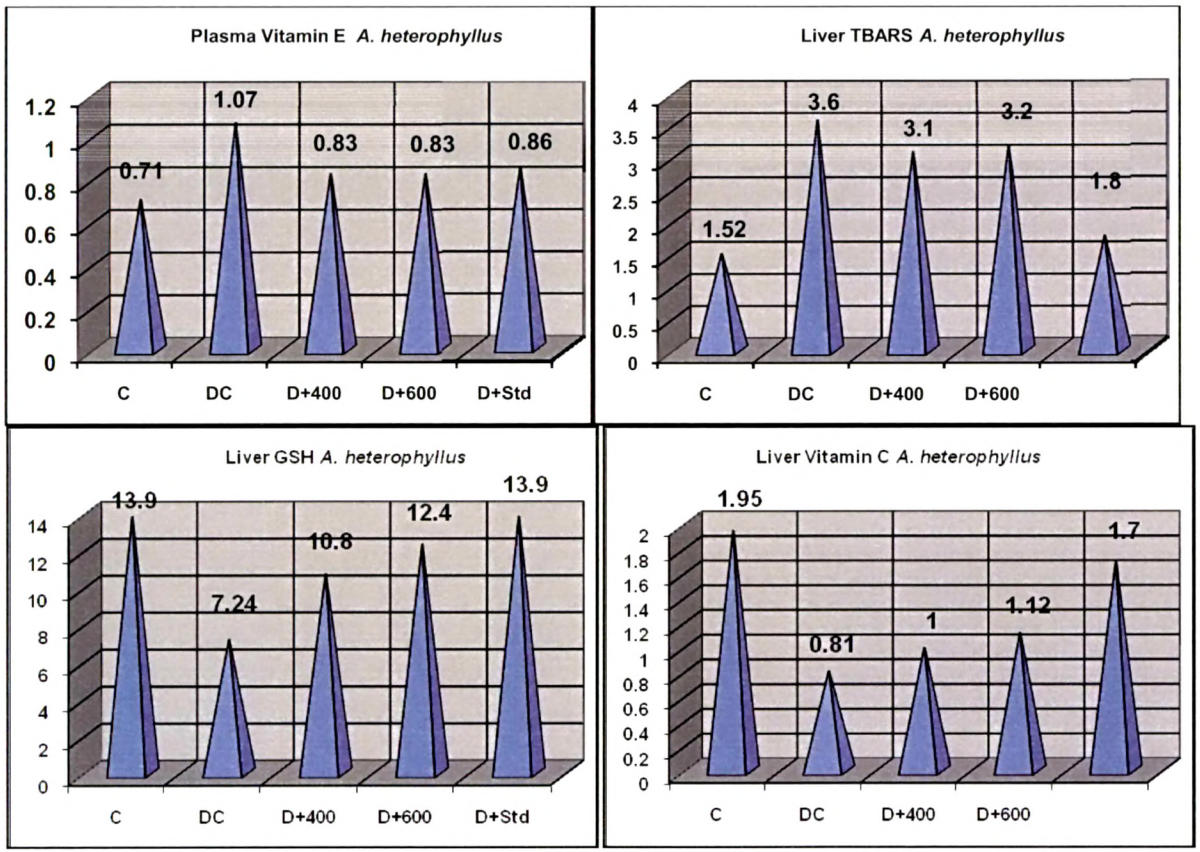

Effect of continuous administration of A. heterophyllus aqueous extract on blood glucose levels in fasted normal rats
72
70
68
66
64
62
60
58
56
54
Fasting
1h
2h
3h
Control
100mg
200mg
400mg
600mg
800mg
1000mg

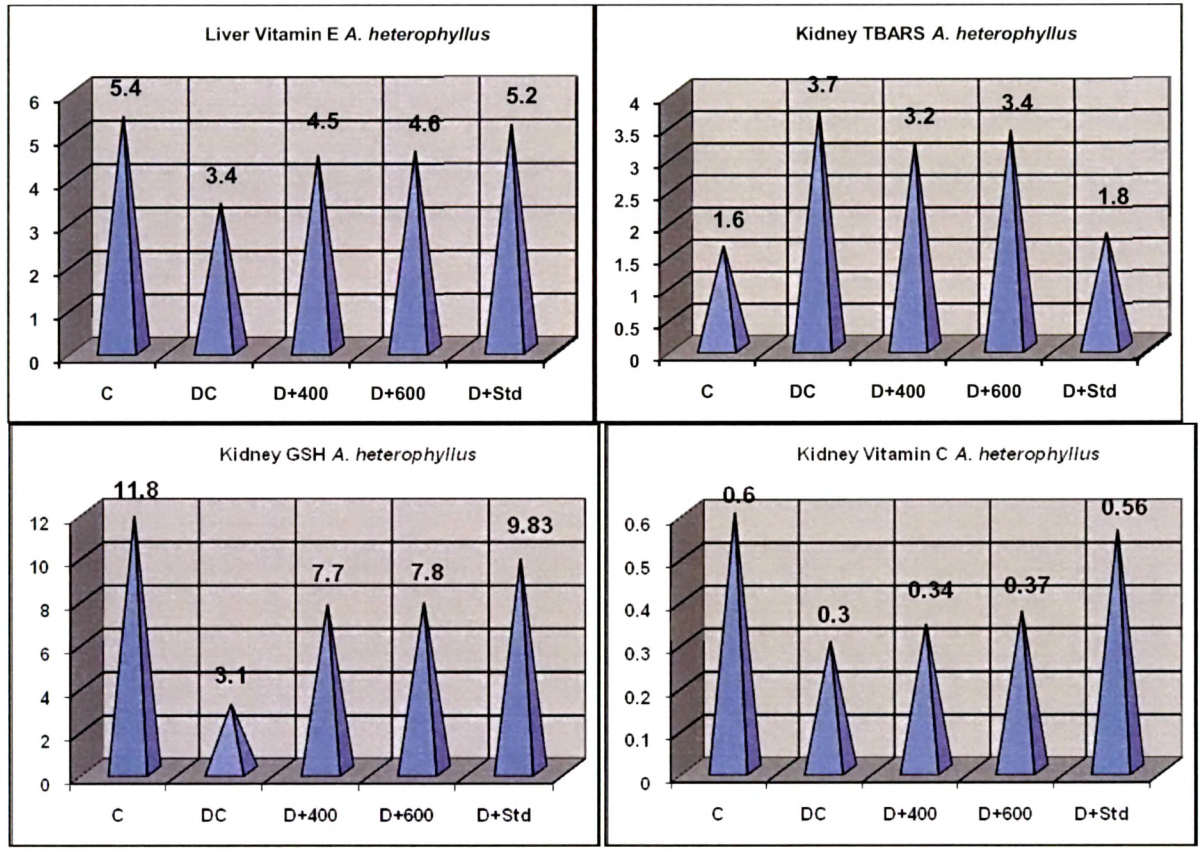

Blood glucose initial A. heterophyllus
350
300
250
200
150
100
50
0
81.8
283
287
284
305
C
DC
D+400
D+600
D+Std

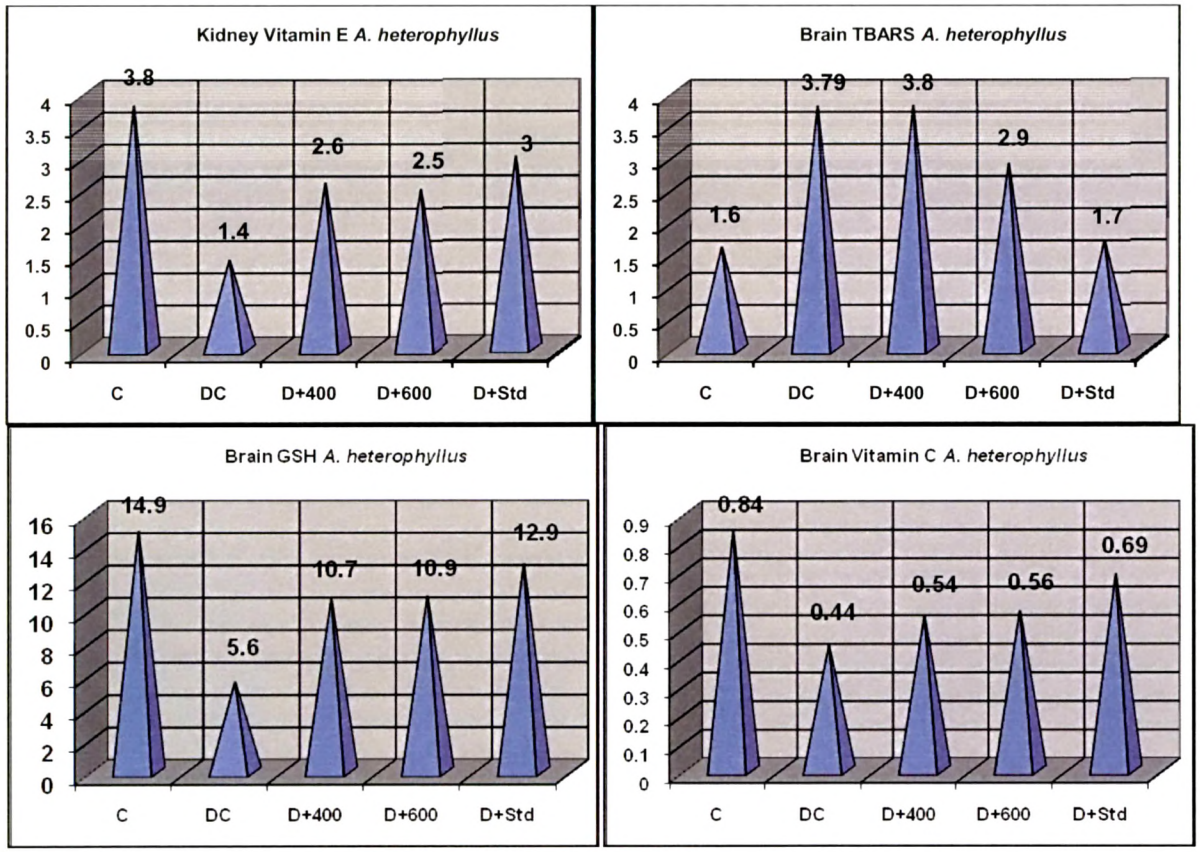

Blood glucose final A. heterophyllus
350
300
250
200
150
100
50
0
97.5
337.5
181.8
180.8
135
C
DC
D+400
D+600
D+Std

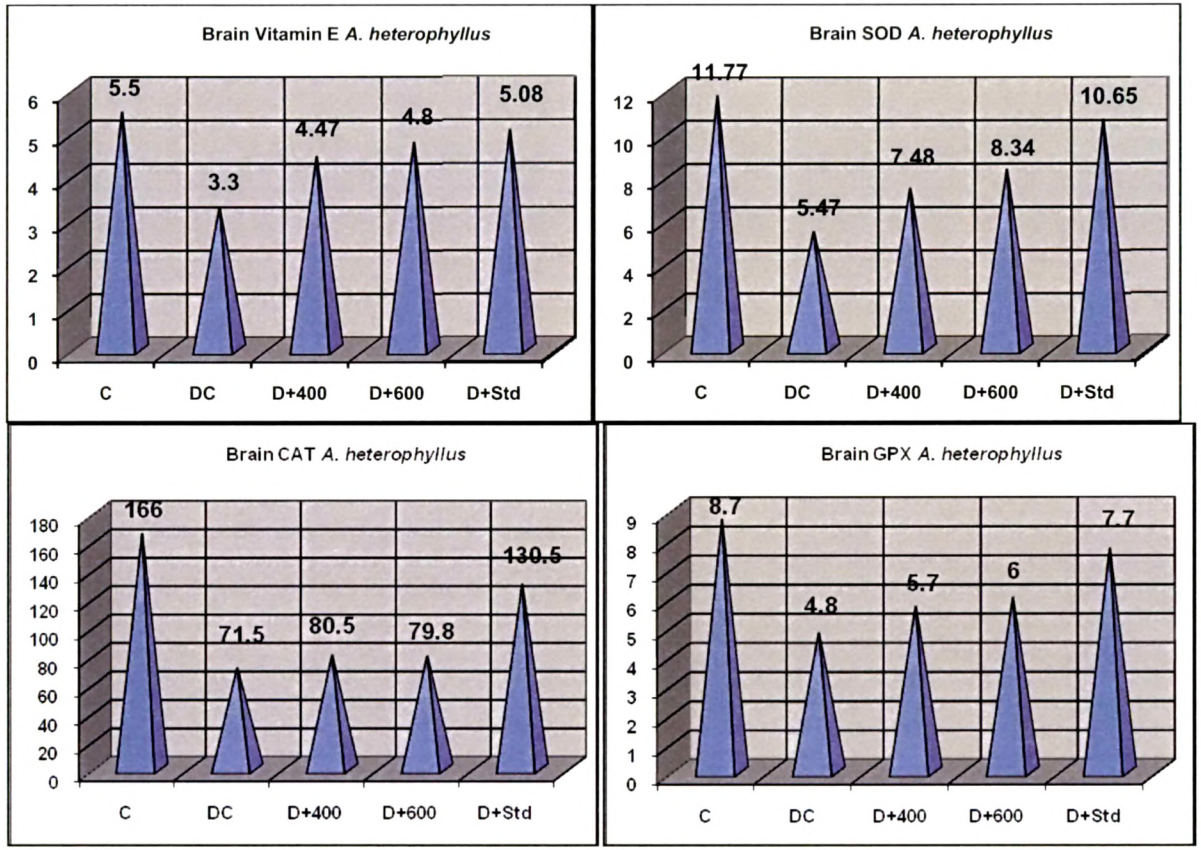

Body weight Initial A. heterophyllus
210
205
200
195
190
185
180
175
170
185.8
190
205.8
184
182
C
DC
D+400
D+600
D+Std

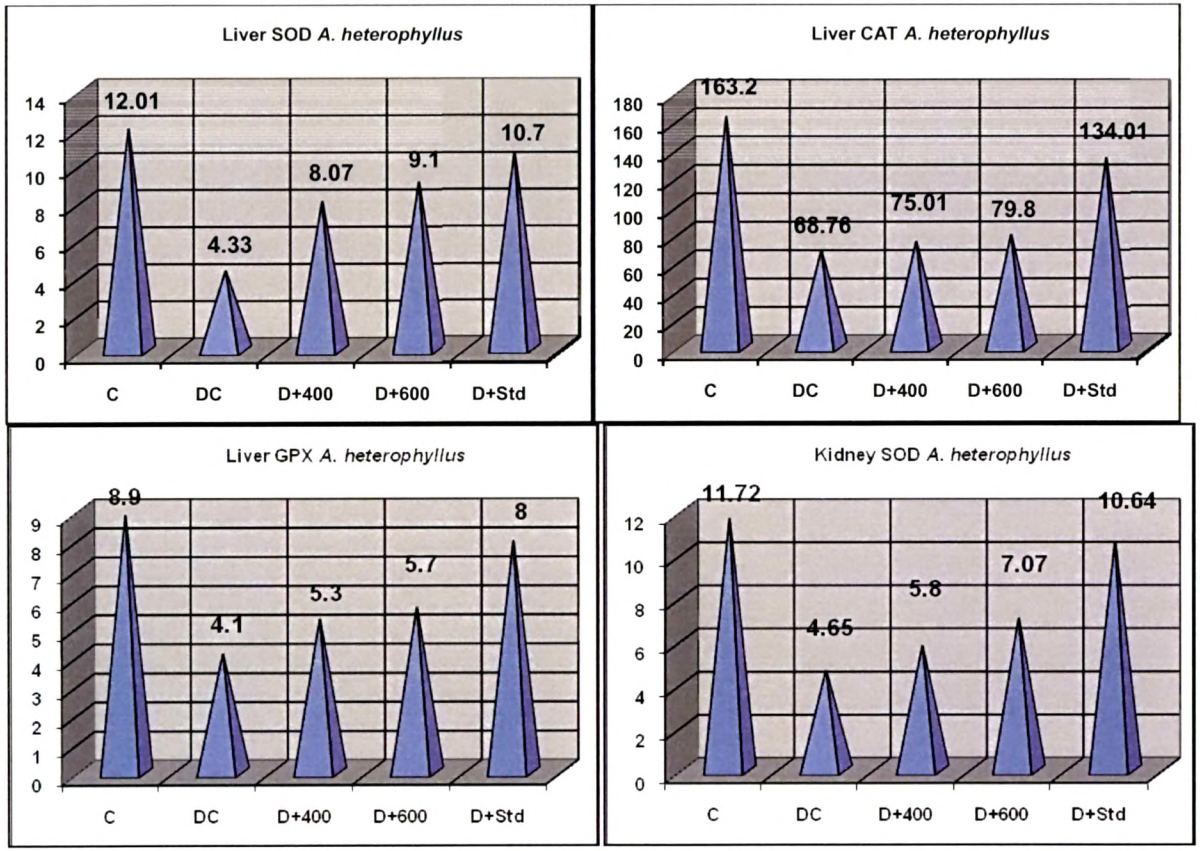

Body weight final A. heterophyllus
250
200
150
100
50
0
189
129
203
192
185
C
DC
D+400
D+600
D+Std
Plasma TBARS A. heterophyllus
4
3.5
3
2.5
2
1.5
1
0.5
0
1.58
3.6
3
2.9
1.7
C
DC
D+400
D+600
D+Std
Plasma GSH A. heterophyllus
25
20
15
10
5
0
23
14.98
18.08
18.08
21.1
C
DC
D+400
D+600
D+Std
Plasma Vitamin C A. heterophyllus
2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
1.95
0.81
1
1.12
1.7
C
DC
D+400
D+600
D+Std

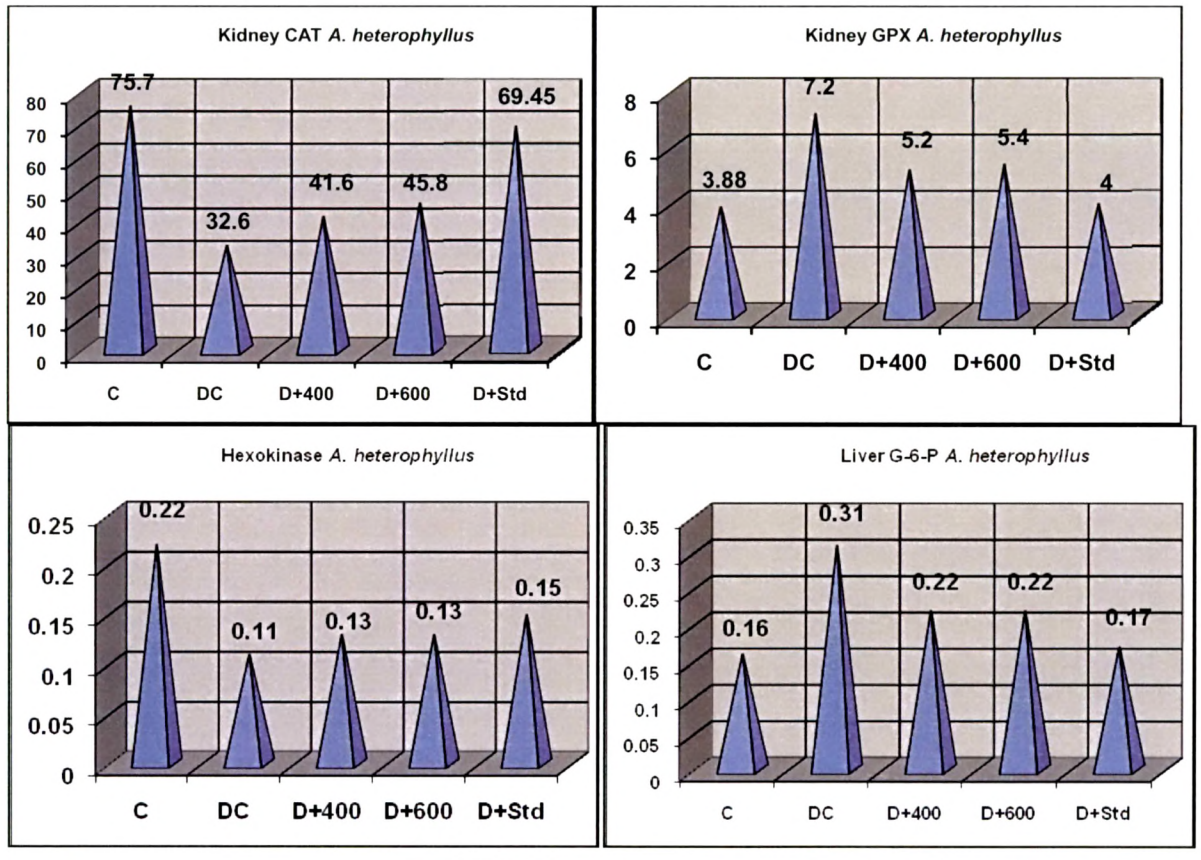

Plasma Vitamin E A. heterophyllus
1.2
1
0.8
0.6
0.4
0.2
0
0.71
1.07
0.83
0.83
0.86
C
DC
D+400
D+600
D+Std
Liver TBARS A. heterophyllus
4
3.5
3
2.5
2
1.5
1
0.5
0
1.52
3.6
3.1
3.2
1.8
C
DC
D+400
D+600
Liver GSH A. heterophyllus
14
12
10
8
6
4
2
0
13.9
7.24
10.8
12.4
13.9
C
DC
D+400
D+600
D+Std
Liver Vitamin C A. heterophyllus
2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
1.95
0.81
1
1.12
1.7
C
DC
D+400
D+600

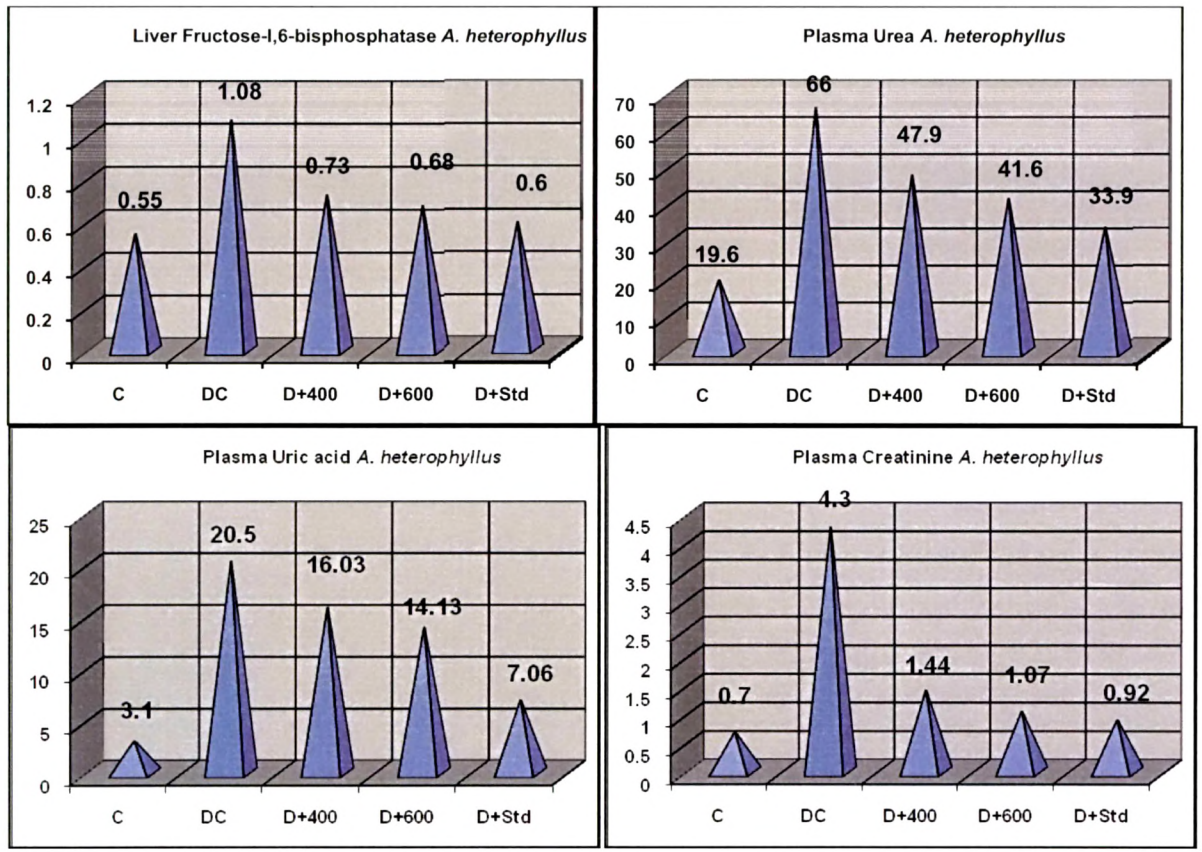

Liver Vitamin E A. heterophyllus
5.4
3.4
4.5
4.6
5.2
6
5
4
3
2
1
0
C
DC
D+400
D+600
D+Std
Kidney TBARS A. heterophyllus
1.6
3.7
3.2
3.4
1.8
4
3.5
3
2.5
2
1.5
1
0.5
0
C
DC
D+400
D+600
D+Std
Kidney GSH A. heterophyllus
11.8
3.1
7.7
7.8
9.83
12
10
8
6
4
2
0
C
DC
D+400
D+600
D+Std
Kidney Vitamin C A. heterophyllus
0.6
0.3
0.34
0.37
0.56
0.6
0.5
0.4
0.3
0.2
0.1
0
C
DC
D+400
D+600
D+Std

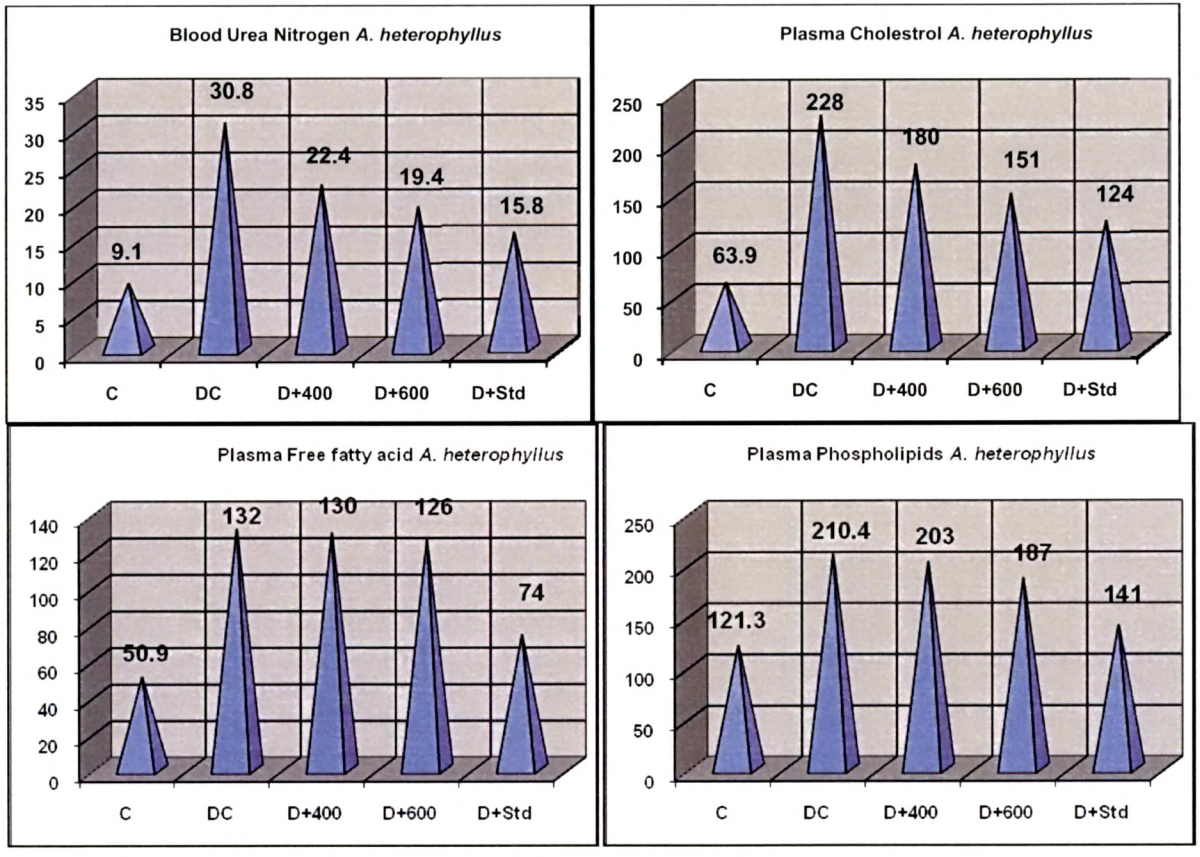

Kidney Vitamin E A. heterophyllus
3.8
1.4
2.6
2.5
3
4
3.5
3
2.5
2
1.5
1
0.5
0
C
DC
D+400
D+600
D+Std
Brain TBARS A. heterophyllus
1.6
3.79
3.8
2.9
1.7
Brain GSH A. heterophyllus
14.9
5.6
10.7
10.9
12.9
16
14
12
10
8
6
4
2
0
Brain Vitamin C A. heterophyllus
0.84
0.44
0.54
0.56
0.69
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1

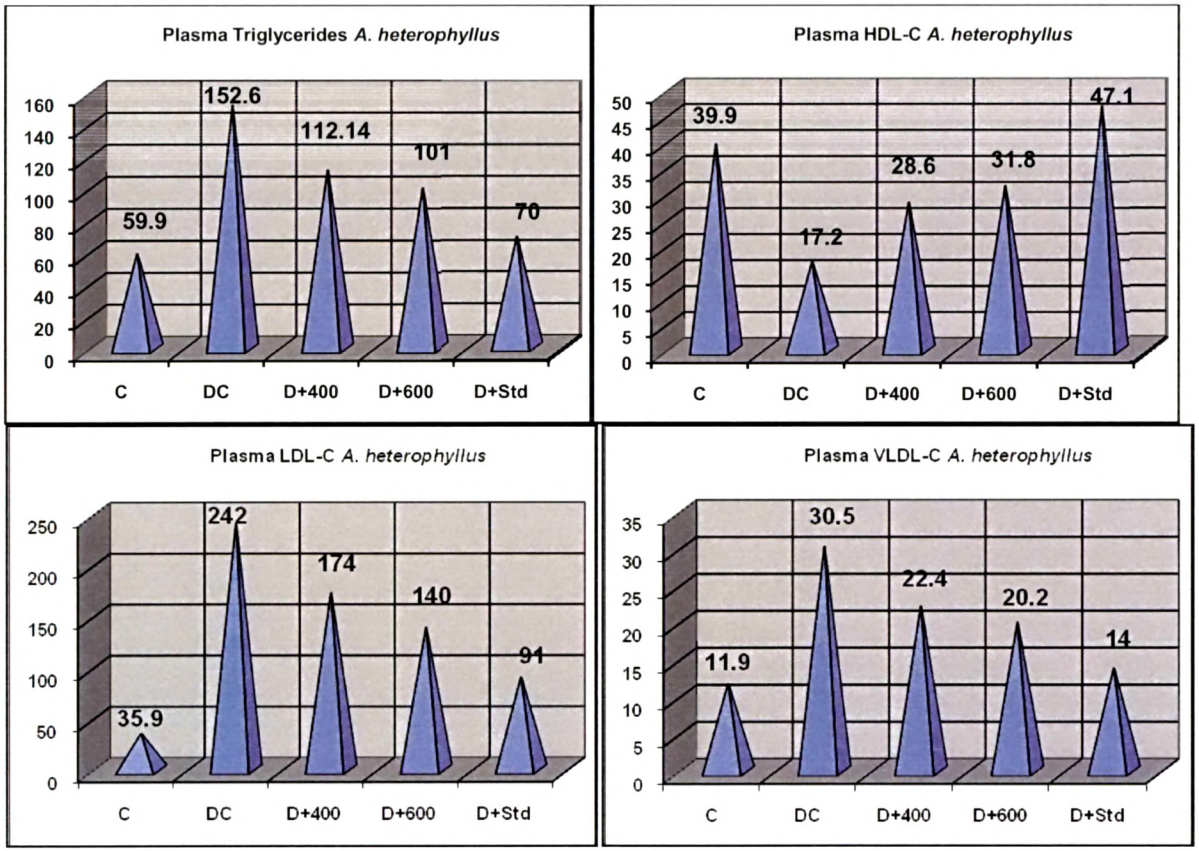

Brain Vitamin E A. heterophyllus
5.5
3.3
4.47
4.8
5.08
0
1
2
3
4
5
6
C
DC
D+400
D+600
D+Std
Brain SOD A. heterophyllus
11.77
5.47
7.48
8.34
10.65
0
2
4
6
8
10
12
C
DC
D+400
D+600
D+Std
Brain CAT A. heterophyllus
166
71.5
80.5
79.8
130.5
0
20
40
60
80
100
120
140
160
180
C
DC
D+400
D+600
D+Std
Brain GPX A. heterophyllus
8.7
4.8
5.7
6
7.7
0
1
2
3
4
5
6
7
8
9
C
DC
D+400
D+600
D+Std


Liver SOD A. heterophyllus
14
12
10
8
6
4
2
0
12.01
4.33
8.07
9.1
10.7
C
DC
D+400
D+600
D+Std
Liver CAT A. heterophyllus
180
160
140
120
100
80
60
40
20
0
163.2
68.76
75.01
79.8
134.01
C
DC
D+400
D+600
D+Std
Liver GPX A. heterophyllus
9
8
7
6
5
4
3
2
1
0
8.9
4.1
5.3
5.7
8
C
DC
D+400
D+600
D+Std
Kidney SOD A. heterophyllus
12
10
8
6
4
2
0
11.72
4.65
5.8
7.07
10.64
C
DC
D+400
D+600
D+Std


Kidney CAT A. heterophyllus
75.7
32.6
41.6
45.8
69.45
80
70
60
50
40
30
20
10
0
C
DC
D+400
D+600
D+Std
Kidney GPX A. heterophyllus
3.88
7.2
5.2
5.4
4
8
6
4
2
0
C
DC
D+400
D+600
D+Std
Hexokinase A. heterophyllus
0.22
0.11
0.13
0.13
0.15
0.25
0.2
0.15
0.1
0.05
0
C
DC
D+400
D+600
D+Std
Liver G-6-P A. heterophyllus
0.16
0.31
0.22
0.22
0.17
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
C
DC
D+400
D+600
D+Std


Liver Fructose-l,6-bisphosphatase A. heterophyllus
1.2
1
0.8
0.6
0.4
0.2
0
0.55
1.08
0.73
0.68
0.6
C
DC
D+400
D+600
D+Std
Plasma Urea A. heterophyllus
70
60
50
40
30
20
10
0
19.6
66
47.9
41.6
33.9
C
DC
D+400
D+600
D+Std
Plasma Uric acid A. heterophyllus
25
20
15
10
5
0
3.1
20.5
16.03
14.13
7.06
C
DC
D+400
D+600
D+Std
Plasma Creatinine A. heterophyllus
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
0.7
4.3
1.44
1.07
0.92
C
DC
D+400
D+600
D+Std


Blood Urea Nitrogen A. heterophyllus
35
30
25
20
15
10
5
0
9.1
30.8
22.4
19.4
15.8
C
DC
D+400
D+600
D+Std
Plasma Cholestrol A. heterophyllus
250
200
150
100
50
0
63.9
228
180
151
124
C
DC
D+400
D+600
D+Std
Plasma Free fatty acid A. heterophyllus
140
120
100
80
60
40
20
0
50.9
132
130
126
74
C
DC
D+400
D+600
D+Std
Plasma Phospholipids A. heterophyllus
250
200
150
100
50
0
121.3
210.4
203
187
141
C
DC
D+400
D+600
D+Std


Plasma Triglycerides A. heterophyllus
160
140
120
100
80
60
40
20
0
59.9
152.6
112.14
101
70
C
DC
D+400
D+600
D+Std
Plasma HDL-C A. heterophyllus
50
45
40
35
30
25
20
15
10
5
0
39.9
17.2
28.6
31.8
47.1
C
DC
D+400
D+600
D+Std
Plasma LDL-C A. heterophyllus
250
200
150
100
50
0
35.9
242
174
140
91
C
DC
D+400
D+600
D+Std
Plasma VLDL-C A. heterophyllus
35
30
25
20
15
10
5
0
11.9
30.5
22.4
20.2
14
C
DC
D+400
D+600
D+Std