



# International Journal of **Biological Chemistry**

ISSN 1819-155X



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## Antihyperlipidemic and Antioxidant Effect of Hyponidd in the Brain of Streptozotocin Induced Diabetic Rat

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**Abstract:** Hyponidd, a herbomineral formulation composed of 10 medicinal plants extracts. We have investigated the hyponidd on prevention of oxidative stress and antihyperlipidemic effect in streptozotocin (STZ) induced diabetic rat brain. Rats were rendered diabetic by STZ (45 mg kg<sup>-1</sup> body weight). After induction of diabetes rats were treated with hyponidd (100 and 200 mg kg<sup>-1</sup>) for 45 days. After 45 days treatment, significant reduction in fasting blood glucose, thiobarbituric acid reactive substances, hydroperoxides and lipid profiles (Cholesterol, Triglycerides and Free fatty acids). Hyponidd also caused a significant (p<0.05) increase in reduced glutathione, superoxide dismutase, catalase and glutathione peroxidase in the brain of STZ-induced diabetic rat, suggesting its role in protection against lipid peroxidation induced membrane damage. The results clearly showed that the hyponidd effectively restores antioxidant status and lipid profiles in the brain of STZ-diabetic rat.

**Key words:** Herbal formulation, antioxidant, cholesterol, catalase, streptozotocin

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### INTRODUCTION

Free radicals may also be a contributory factor in a progressive decline in the function of the immune system (Pike and Chandra, 1995). Excessive production of free radicals is believed to be involved in many diabetic complications, including diabetic neuropathy in diabetes mellitus. It has been established that diabetes is a risk factor for cerebral ischemia and the relative risk of cerebral ischemia in diabetic patients is approximately twice as much as in patients without diabetes (Baird *et al.*, 2002). In addition, diabetes is strongly related to early brain injury and to the poor outcome after cerebral ischemia (Bravata *et al.*, 2003). Clinical studies on diabetic patients showed that hyperglycemia augments brain lesions associated with cerebral ischemia (Srinivasan *et al.*, 1997). In animal models of cerebral ischemia, hyperglycemic animals suffered greater neurological deficit with extensive brain damage and widespread necrosis than non-hyperglycemic animals (Yorek, 2003). One of the mechanisms of diabetes-enhanced brain injury is oxidative stress caused by hyperglycemia. Reactive oxygen species-mediated oxidative stress is believed to produced tissue injury in wide variety of disease including diabetes (Yorek, 2003).

In recent years, there has been renewed interest in the treatment against different diseases using herbal drugs as they are generally non-toxic (Momin, 1987). Many indigenous drugs have been used by practitioners of Ayurvedic system for the treatment of diabetes mellitus in India. World Health Organization (WHO), has also recommended the evaluation of the effectiveness of plans in condition where there is lack of safe modern drugs (Pari and Amarnathsathesh, 2004). A hypoglycemic action

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from some plant treatments has been confirmed in animal models and non-insulin-dependent diabetic patients and various hypoglycemic compounds have been identified. A botanical substitute for insulin seems unlikely, but traditional treatments may provide valuable clues for the development of new oral hypoglycemic agents and simple dietary adjuncts (Bailey and Day, 1989). A wide array of plant derived active principles representing numerous chemical compounds has demonstrated activity consistent with their possible use in the treatment of diabetes mellitus (Mukherjee *et al.*, 2006). Many kinds of natural products, such as alkaloids, glycosides, polysaccharides, peptidoglycans, flavonoids, tannins, steroids, glycopeptides, terpenoids and inorganic ions have been identified (Mukherjee *et al.*, 2006). The introduction of these indigenous herbal compounds in the management of diabetes mellitus will greatly simplify the management and make it less expensive. In traditional Indian medicine, plant formulation and several cases of combined extracts of plants are used as drugs of choice rather than individual active principle or plant. Many herbal formulations such as Trasina, Diamed, Diasulin, Cogent db and D-400 exhibit antidiabetic effect (Subash Babu and Prince, 2004).

Hyponidd, a herbomineral formulation composed of eleven medicinal plants, they were known to possess antidiabetic effect and have been used in the indigenous system of medicine to treat diabetes mellitus (Table 1). In our previous study, we have reported the antihyperglycemic and antioxidant

Table 1: Name of plants, composition, their phytochemicals and effects of the constituents of Hyponidd (Subash Babu and Prince, 2004)

Plant species	Concentration (mg tablet <sup>-1</sup> )	Phytochemicals	Effects observed
<i>Momordica charantia</i>	12	Charantin, momordicosides A and B, acylglucosyl sterols, P-insulin, V-insulin, stigmasterol	Antidiabetic effect
<i>Swertia chirata</i>	15	Polyoxygenated xanthenes, mangiferin, swertinin, swertianin, swerchirin, chiratin, chirataini	Antioxidant effect
<i>Melia azadirachta</i>	75	$\beta$ -carotene, nimbin, azadirachtin, nimbidiol, quercetin, nimbidin and nimbatiktam	Antioxidant effect
<i>Pterocarpus marsupium</i>	75	Pteroside, pterisoauroside, marsuposide, vijayosin, sesquiterpene; pterosupin, pterostilbene, marsupin	Antidiabetic effect
<i>Tinospora cordifolia</i>	75	Tinosporin, isocolumbin, palmatine, tinocordiside (X), tinocordifolioside (XI), cordioside, $\beta$ -sitosterol	Antidiabetic and antihyperlipidemic effect
<i>Gymnema sylvestre</i>	112.5	Gymnemic acids, saponins, stigmasterol, quercitol, betaine, choline, trimethylamine	Antidiabetic effect
<i>Enicostemma littorale</i>	112.5	Vanillic acid, ferulic acid, p-coumaric acid, apigenin, genkwanin, isovitexin, swertisin, saponarin	Antidiabetic effect
<i>Emblica officinalis</i>	150	Phyllemblin, gallic acid, ellagic acid, phyllantidine, phyllantine, lupeol, emblicanin A and B	Antioxidant effect
<i>Eugenia jambolana</i>	150	Gallic acid, ellagic acid, corilagin, ellagitannins, quercetin	Antidiabetic effect
<i>Cassia auriculata</i>	225	Flavonoids, anthracene derivatives, dimeric procyanidins, myristyl alcohol, $\beta$ -D-glucoside, quercetin 3-O-glycoside, rutin	Antidiabetic and antioxidant effect
Curcuma longa	300	Curcumin, desmethoxy curcumin, bisdemethoxy curcumin, dihydrocurcumin, $\alpha$ and $\beta$ -turmerones, eugenol, campesterol, stigmasterol	Antioxidant effect
<b>Powders</b>			
Yashad bhasma (Zinc calx)	37.5		Used in the treatment of diabetes mellitus in Ayurvedic system
Aspaltham	37.5		

effect of hyponidd in STZ-induced diabetic rats (Subash Babu and Prince, 2004). In view of the above facts, the present study was undertaken to evaluate the effect of hyponidd on antihyperlipidemic and antioxidant effect of hyponidd in the brain of streptozotocin induced diabetic rat. The effect of hyponidd was compared with glibenclamide, a well known hypoglycemic drug.

## **MATERIALS AND METHODS**

### **Animals, Test Drug and Chemicals**

Female Wistar rats with a body weight of 180-200 g were procured from the central Animal House, Raja Muthiah Medical College and Hospital and Annamalai University in October 2005. The animals were fed on standard pellet diet (Hindustan Lever, India) and water *ad libitum*. Hyponidd, a herbomineral formulation composed of ten medicinal plants extracts (*Momordica charantia*, *Melia azadirachta*, *Pterocarpus marsupium*, *Tinospora cordifolia*, *Gymnema sylvestre*, *Enicostemma littorale*, *Embllica officinalis*, *Eugenia jambolana*, *Cassia auriculata* and *Curucuma longa*). And it is purchased from recognized pharmacy, Cuddalore District, manufactured by Charak Pharmaceuticals (I) Private Ltd., Haryana, India. Streptozotocin was purchased from Sigma chemical company Inc. (St. Louis, MO) USA. All other biochemicals and chemicals used in this experiment are of analytical grade.

### **Experimental Induction of Diabetes**

The rats were injected intraperitoneally with freshly prepared streptozotocin (45 mg kg<sup>-1</sup> body weight) in 0.1 M citrate buffer (pH 4.5) in a volume of 1 mL kg<sup>-1</sup> b.wt. (Subash Babu and Prince, 2004). After 48 h of streptozotocin administration, blood glucose levels of each rat were determined. Rats with blood glucose range of 250-300 mg/100 mL were considered diabetic and included in the study. Blood was collected from the eyes (venous pool).

### **Experimental Design and Drug Administration**

In the experiment, a total of 42 rats (12 normal, 30 STZ-diabetic surviving rats) were used. The rats were divided into 7 groups of six each. Hyponidd tablets were powdered, suspended in distilled water and different doses of hyponidd were administered orally using an intragastric tube. Group 1: Normal untreated rats; Group 2: Normal rats treated with Hyponidd (200 mg kg<sup>-1</sup> b.wt.) in distilled water; Group 3: Streptozotocin treated diabetic control rats; Groups 4: STZ treated diabetic rats administered with hyponidd (50 mg kg<sup>-1</sup> b.wt.) in distilled water; Group 5: STZ treated diabetic rats administered with hyponidd (100 mg kg<sup>-1</sup> b.wt.) in distilled water; Group 6: STZ treated diabetic rats administered with Hyponidd (200 mg kg<sup>-1</sup> b.wt.) in distilled water; Group 7: STZ treated diabetic rats given glibenclamide orally (600 µg kg<sup>-1</sup> b.wt.) in distilled water using an intragastric tube.

All doses were given two days after injection of STZ. No irritation or restlessness was observed after each drug or vehicle administration. No noticeable adverse effect (i.e., respiratory distress, abnormal locomotion and catalepsy) was observed in any animal after the drug administration. Blood glucose levels were estimated every week to ascertain the status of diabetes in different groups of rats. At the end of 45 days, all the rats were killed by decapitation under phenobarbitone sodium anesthesia (60 mg kg<sup>-1</sup>). Blood was collected in two different tubes (i.e.,) one with whole blood for serum separation and another with anticoagulant -potassium oxalate and sodium fluoride for plasma insulin assay. Brain, Liver and Kidney were dissected out, washed in ice-cold saline and weighed.

### **Biochemical Analysis**

#### **Estimation of Blood Glucose**

Fasting blood glucose was estimated by the o-toluidine method of Sasaki *et al.* (1972).

### Estimation of Tissue Thiobarbituric Acid Reactive Substances (TBARS) and Lipid Hydroperoxides (HP)

Tissue Thiobarbituric Acid Reactive Substances (TBARS) and lipid hydroperoxides were estimated by the methods of Fraga *et al.* (1988) and Jiang *et al.* (1992), respectively.

### Assay of Antioxidant Enzymes

The activity of Superoxide Dismutase (SOD) was assayed by the method of Kakkar *et al.* (1984). Catalase by the method of Sinha (1972). The activity of glutathione peroxidase was assayed by the method of Rotruk *et al.* (1973). Glutathione was estimated by the method of Ellman (1959). Protein content in the tissue homogenate was measured by the method of Lowry *et al.* (1951).

### Estimation of Lipid Profiles

Lipids were extracted from the tissues by the method of Folch *et al.* (1957), Serum and tissue total cholesterol (Zak *et al.*, 1953), triglycerides (Rice, 1970) and free fatty acids (Falholt *et al.*, 1973) were estimated.

### Statistical Analysis

Statistical analysis was performed using SPSS software package, version 6.0. The values were analyzed by one way Analysis of Variance (ANOVA) followed by Duncan's Multiple Range Test (DMRT) (Duncan, 1957). All the results were expressed as mean±SD for six rats in each group; p-values <0.05 were considered as significant.

## RESULTS

Table 2 shows the levels of body weight, food intake, water intake and fasting blood glucose in normal and experimental groups. The STZ-treated diabetic rats showed a significant increase in blood glucose compared to the normal rats. Oral administration of Hyponidd to diabetic rats exceptionally maintained the blood glucose levels to near normal in diabetic rat.

Table 3 shows the changes in the concentration of TBARS, HP, SOD, CAT, GSH and GPx in normal and experimental groups. The STZ-treated diabetic rats showed a significant increase in TBARS

Table 2: Effect of hyponidd on change of body weight, food and water intake and blood glucose levels in normal and diabetic rats

Groups	Body weight (g)		Food intake (g day <sup>-1</sup> )	Water intake (mL day <sup>-1</sup> )	Blood glucose (mg dL <sup>-1</sup> )	
	Initial	Final			Initial	Final
Normal	180.91±7.12	205.70±9.36 <sup>a</sup>	55.3±3.8	221.6±18.2	93.28±7.24	98.31±6.26 <sup>b</sup>
Normal + hyponidd (200 mg kg <sup>-1</sup> )	186.55±9.20	221.80±13.61 <sup>b</sup>	60.8±2.0	240.3±17.2	101.83±8.74	95.27±5.56 <sup>a</sup>
Diabetic control	206.43±8.74	168.70±7.91 <sup>b</sup>	69.2±4.2	278.8±10.9	324.83±13.86	351.09±21.05 <sup>c</sup>
Diabetic + hyponidd (100 mg kg <sup>-1</sup> )	178.60±9.38	189.32±8.20 <sup>c</sup>	62.8±4.3	255.1±8.3	294.51±16.68	148.98±8.04 <sup>b</sup>
Diabetic + hyponidd (200 mg kg <sup>-1</sup> )	185.61±6.26	203.80±8.79 <sup>c</sup>	59.3±3.5	232.5±13.2	299.24±14.01	98.51±8.42 <sup>b</sup>
Diabetic + glibenclamide (600 µg kg <sup>-1</sup> )	181.49±9.20	198.44±8.16 <sup>c</sup>	62.8±2.8	238.4±17.3	289.43±15.34	108.39±7.39 <sup>b</sup>

Each value is mean±SD for 6 rats in each group, Values not sharing a common superscript differ significantly at p<0.05 (DMRT)

Table 3: Effect of hyponidd on TBARS, HP, SOD, CAT, GPX and GSH levels in normal and diabetic rat brain

Groups	TBARS	HP	SOD	CAT	GSH	Gpx
Normal	1.58±0.11 <sup>a</sup>	62.38±3.55 <sup>a</sup>	7.96±0.69 <sup>a</sup>	2.93±0.29 <sup>a</sup>	11.82±0.53 <sup>a</sup>	6.91±0.47 <sup>a</sup>
Normal + hyponidd (200 mg kg <sup>-1</sup> )	1.55±0.12 <sup>a</sup>	62.17±3.10 <sup>a</sup>	7.24±0.61 <sup>ab</sup>	3.05±0.34 <sup>a</sup>	10.28±0.81 <sup>b</sup>	6.83±0.51 <sup>a</sup>
Diabetic control	2.89±0.18 <sup>b</sup>	98.83±4.16 <sup>b</sup>	3.28±0.27 <sup>c</sup>	0.83±0.05 <sup>b</sup>	5.72±0.36 <sup>c</sup>	2.90±0.19 <sup>b</sup>
Diabetic + hyponidd (100 mg kg <sup>-1</sup> )	1.84±0.10 <sup>a</sup>	73.59±2.48 <sup>c</sup>	5.98±0.43 <sup>d</sup>	1.92±0.19 <sup>c</sup>	8.46±0.47 <sup>d</sup>	3.87±0.22 <sup>c</sup>
Diabetic + hyponidd (200 mg kg <sup>-1</sup> )	1.62±0.02 <sup>a</sup>	67.44±1.82 <sup>ac</sup>	6.84±0.53 <sup>bd</sup>	2.35±0.21 <sup>d</sup>	9.93±0.39 <sup>b</sup>	5.37±0.37 <sup>d</sup>
Diabetic + glibenclamide (600 µg kg <sup>-1</sup> )	1.67±0.02 <sup>a</sup>	69.38±1.08 <sup>c</sup>	6.21±0.47 <sup>d</sup>	2.12±0.20 <sup>cd</sup>	8.89±0.28 <sup>d</sup>	4.81±0.33 <sup>c</sup>

UNITTS = (TBARS - nmoles/100 g tissue; Hydroperoxides- n moles/100 g tissue; GSH-nmoles g<sup>-1</sup> wet tissue; GPx-µg of GSH consumed min<sup>-1</sup> mg<sup>-1</sup> protein; CAT-µmols of H<sub>2</sub>O<sub>2</sub> consumed min<sup>-1</sup> mg<sup>-1</sup> protein; SOD-One unit is defined as the enzyme concentration required to inhibit the O.D at 560 nm of chromogen production by 50% in one min<sup>-1</sup> mg<sup>-1</sup> protein) Each value is mean±SD for 6 rats in each group, Values not sharing a common superscript differ significantly at p<0.05 (DMRT)

Table 4: Effect of hyponidd on total cholesterol, triglyceride and free fatty acids levels in normal and diabetic rat brain

Groups	Total cholesterol (mg g <sup>-1</sup> wet tissue)	Triglyceride (mg g <sup>-1</sup> wet tissue)	Free fatty acids (mg g <sup>-1</sup> wet tissue)
Normal	12.89±0.82 <sup>a</sup>	1.89±0.08 <sup>a</sup>	1.32±0.15 <sup>a</sup>
Normal + hyponidd (200 mg kg <sup>-1</sup> )	13.47±1.29 <sup>a</sup>	1.94±1.14 <sup>ab</sup>	1.61±0.29 <sup>a</sup>
Diabetic control	23.89±0.81 <sup>b</sup>	3.64±0.20 <sup>c</sup>	2.93±0.20 <sup>b</sup>
Diabetic + hyponidd (100 mg kg <sup>-1</sup> )	16.68±1.13 <sup>c</sup>	2.49±0.17 <sup>d</sup>	2.01±0.07 <sup>c</sup>
Diabetic + hyponidd (200 mg kg <sup>-1</sup> )	13.29±1.04 <sup>a</sup>	2.04±0.07 <sup>ab</sup>	1.47±0.09 <sup>ad</sup>
Diabetic + glibenclamide (600 µg kg <sup>-1</sup> )	14.53±1.04 <sup>ac</sup>	2.27±0.13 <sup>bd</sup>	1.58±0.07 <sup>ad</sup>

Each value is mean±SD for 6 rats in each group, Values not sharing a common superscript differ significantly at p<0.05 (DMRT).

and HP and there was a significant reduction in SOD, CAT, GSH and GPx in diabetic rat brain. Oral administration of Hyponidd to diabetic rats showed significantly restored the peroxides and antioxidant levels in diabetic rat brain.

Table 4 shows the levels of lipids profiles in normal and STZ-induced diabetic rats. There was a significant increase in the levels of total cholesterol, triglycerides and free fatty acids in diabetic rats compared to normal rats. Administration of Hyponidd brought back the levels of lipids significantly (p<0.05) to near normal.

For all the parameters studied, Hyponidd at a dose of 100 and 200 mg kg<sup>-1</sup> b.wt. showed a significant effects with the higher dose giving a far better effect. Glibenclamide also showed a significant effect in all the parameters studied in diabetic rats. However, the effect exerted by Hyponidd (200 mg kg<sup>-1</sup> b.wt.) was more effective than glibenclamide. Oral administration of Hyponidd (200 mg kg<sup>-1</sup> b.wt.) to normal rats had no significant effect.

## DISCUSSION

Hyperglycemia generates reactive oxygen species which in turn cause lipid peroxidation and membrane damage (Hunt *et al.*, 1988). Reactive oxygen species are an important part of the defense mechanism against infection, but excessive generation of free oxygen radicals may damage tissue (Steinberg *et al.*, 1989). Formation of lipid peroxides by the action of free radicals on unsaturated fatty acids has been implicated in the pathogenesis of atherosclerosis and vascular disease (Stinger *et al.*,

1989). Many studies have evaluated the effects of oxidative stress and antioxidant systems in the central and peripheral nervous system in diabetes mellitus (Baydas *et al.*, 2002). Membrane abnormalities in human diabetes are well established (Giugliano *et al.*, 1996). Superoxide radicals have been implicated in the tissue injury (Bayners, 1991). Increase of superoxide radical and/or hydrogen peroxide has been observed in diabetes mellitus and treatment with antioxidant can lower plasma glucose in streptozotocin-induced diabetic rats (STZ-diabetic rats) (Johnson *et al.*, 1993). Role of free radicals in the pathogenesis of organ damage from Insulin-dependent Diabetes Mellitus (IDDM) has also been documented (Oberley, 1988). However, brain contains large amounts of enzymes to protect brain against oxidative damage. Living cells possess three protective enzymes, superoxide dismutase (SOD), Catalase (CAT) and Glutathione Peroxidase (GPX), to help the cells against a variety of oxidative stress (Huang *et al.*, 1999). Application of these defense enzymes may reduce the damage induced by acute hyperglycemia.

A marked increase in the concentration of TBARS and hydroperoxides are observed in diabetic rat brain. An increase of lipid hydroperoxides is related to induced diabetes also (Subash Babu and Prince, 2004). Lipid hydroperoxides are molecules with high toxicity potential for destroying enzymes and cell membranes. This may be due to a decrease in the activities of antioxidant enzymes, which is a favorable factor for uncontrolled generation of free radicals and subsequent generation of lipid hydroperoxides. Increased in lipid peroxide concentration in tissues of diabetic animals has also been observed (Venkateswaran and Pari, 2003). Oral administration of hyponidd lowers the TBARS and hydroperoxides in the brain of STZ-diabetic rat.

Increased lipid peroxidation under diabetic condition may be due to increased oxidative stress in the cells as a result of the depletion of antioxidant scavenger systems. Diminished levels of both enzymic and non-enzymic antioxidants are noted in diabetic rat brain in the present study. GSH, being the most important biomolecule against chemically induced toxicity, can participate in the elimination of reactive intermediates by reduction of hydroperoxides in the presence of GPx. GSH also functions as free radical scavenger and in the repair of radical cause biological damage (Meister, 1984). Administration of Hyponidd increased the content of GSH in the brain of STZ-diabetic rat. Activities of GPx decrease significantly in diabetic rats. GPx an enzyme with selenium catalyses the reduction of hydrogen peroxide and hydroperoxide to non toxic products (Bruce *et al.*, 1982). Administration of Hyponidd increased the content of GPx in the brain of STZ-diabetic rat.

Activities of Superoxide Dismutase (SOD) and Catalase (CAT) in tissues have been reduced in diabetic rats. SOD catalyses the dismutation of the highly reactive Superoxide anion to oxygen and hydrogen peroxide (Mc Cord *et al.*, 1976). Hemoprotein catalase which catalyze the reduction of hydrogen peroxide and protects the tissues from highly reactive hydroxyl radicals (Chance *et al.*, 1952). i.e., Reduction in the activities of SOD and CAT may result in a number of deleterious effects due to the accumulation of Superoxide anion radicals and hydrogen peroxide. Reports have shown that the activities of SOD, Catalase and GPx were lowered in diabetic rat brain (Latha and Pari, 2003). Administration of Hyponidd increased the activities of SOD and CAT in the brain of diabetic rat.

Lipids play a vital role in the pathogenesis of diabetes mellitus. The most common lipid abnormalities in diabetes are hypertriglyceridemia and hypercholesterolemia (Hjerrild and Gravholt, 2006). In our study, we have noticed elevated levels of serum lipids such as cholesterol and triglycerides in diabetic rats. These observations are in line with other reports (Krishnakumar *et al.*, 2000). Diabetes-induced hyperlipidaemia is attributable to excess mobilization of fat from the adipose tissue due to the under utilization of glucose (Krishnakumar *et al.*, 2000). The levels of increased lipids in diabetes represent a risk factor for coronary heart disease (Al-Shamaony *et al.*, 1994). Under normal circumstances, insulin activates lipoprotein lipase and hydrolyses triglycerides (Shirwaikar *et al.*, 2004). Insulin increases uptake of fatty acids into adipose tissue and increases triglyceride synthesis. Moreover, insulin inhibits lipolysis. In case of insulin deficiency lipolysis is not inhibited and we have

increased lipolysis which finally leads to hyperlipidemia. In insulin deficient diabetes, the concentration of free fatty acids is elevated as a result of free fatty acid outflow from fat depots, where the balance of the free fatty acid esterification-triglyceride lipolysis cycle is displaced in favor of lipolysis (Shirwaikar *et al.*, 2004). The regression of the diabetic state on Hyponidd administration increases the utilization of glucose, thereby depressing the mobilization of fat.

In the present study, Hyponidd, a herbomineral formulation significantly restored the antioxidant enzymes and lipid profiles in STZ-induced diabetic rat brain. Phytochemical studies of the constituent plants of hyponidd (Table 2) reveal the presence of various alkaloids, flavonoids, terpenoids, sterols and polyphenolic compounds. Studies have shown that the constituents of Hyponidd such as *Cassia auriculata*, *Melia azadirachta*, *Momordica charantia*, *Pterocarpus marsupium*, *Tinospora cordifolia*, *Gymnema sylvestra*, *Emblica officinalis* and *Eugenia jambolana* possess strong antioxidative and antihyperlipidemic effect in diabetic animals (Subash Babu and Prince, 2004). On the basis of above results, it could be concluded that Hyponidd, a combination of eleven herbal plants exert a significant antioxidant and antihyperlipidemic effect in diabetic rat brain. This could be due to different types of active principles, each with a single or a diverse range of biological activities, which serves as a good adjuvant in the present armamentarium of antidiabetic drug with decrease the risk of secondary complication.

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