Original Research Article

Evaluation of anti-diabetic activity of AHPL/AYTAB/0513 tablet in streptozotocin induced diabetes in rats

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Abstract

Background: Diabetes is a chronic, progressive disease associated with several complications leading to significant mortality and morbidity. Limitations and drawbacks of the conventional treatment generate need for safer, effective complimentary therapies to prevent complications, and maintain normoglycemic status.

Aim and Objectives: The aim of this study is to to evaluate antidiabetic activity of AHPL/AYTAB/0513 tablet alone, oral hypoglycemic agents (OHA[s]), and combination of AHPL/AYTAB/0513 tablet and OHA(s) in streptozotocin-induced diabetes in rats.

Materials and Methods: Totally, ten groups of animals were studied comparatively to evaluate antidiabetic activity of AHPL/AYTAB/0513 tablet, OHA(s), and combination of AHPL/AYTAB/0513 tablet and OHA(s). Blood glucose level (BGL), lipid profile, serum creatinine, serum insulin level, and histopathological characteristics of pancreas were studied to evaluate the efficacy of various formulations. Histopathological examination of kidney and heart was carried out to assess the ability of various formulations in preventing complications of diabetes.

Results: There was a significant decrease in mean BGL, serum triglycerides, serum total cholesterol, low-density lipoprotein (LDL), very LDL, and serum creatinine levels in all formulations groups. Significant increase in mean serum insulin level and high-density lipoprotein level was observed when compared to diabetic control (DC) group. Recovery of pancreatic beta cells and prevention of damage to heart and kidney cells was significant in all the formulation groups as compared to DC group. None of the formulations tested in nondiabetic rat showed hypoglycemia suggesting safety of all the formulations.

Conclusion: AHPL/AYTAB/0513 tablet alone and in combination with OHA(s) can be effectively used in the management of diabetes mellitus. In addition, AHPL/AYTAB/0513 tablet alone and in combination with OHA(s) help in prevention of diabetic complications. As an adjuvant to OHA(s), AHPL/AYTAB/0513 tablet can be more effective.

Keywords: Adjuvant to oral hypoglycemic agent, AHPL/AYTAB/0513 tablet, antidiabetic, diabetic complications, polyherbal, Type II Diabetes

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INTRODUCTION

Diabetes is a major noncommunicable epidemic of this century. The worldwide prevalence of diabetes for all age groups is projected to rise up to 4.4%, and the number of diabetics is bound to rise by double till 2030.[1,2]

Among various types of diabetes, majority of disease burden is with Type II diabetes mellitus (DM) comprising around 85% of the total cases. In this type of diabetes, peripheral insulin resistance leads to ultimate islet secretory dysfunction causing hyperglycemia.[2]

Since urbanization, obesity and various lifestyle-related factors are closely associated with increased the prevalence of diabetes,[1] lifestyle modification becomes the first step in Type II diabetes management. When these measures fail to provide sufficient DC pharmacological measures are employed. The main drawbacks of the present antidiabetic therapy are an increased incidence of hypoglycemic episodes and loss of efficacy over prolonged use.[3] Moreover, even with available pharmacotherapy, patients with DM, over the period, land up in several complications such as diabetic neuropathy, diabetic retinopathy, diabetic cardiomyopathy, and diabetic nephropathy. Hence, attention is focused on research and development of drugs that will achieve sustained glycemic control, encounter insulin resistance with less chances of hypoglycemia, and also help in delaying complications of DM.

Formulation AHPL/AYTAB/0513 is conceptualized and developed by Ari Healthcare Pvt. Ltd. It is a polyherbal combination containing Haridra (*Curcuma longa* Linn. [family - Zingiberaceae]),[4] Amalaki (*Emblica officinalis* [family - Euphorbiaceae]),[5] Jamboo (*Syzygium cumini* [family - Myrtaceae]),[6,7] Meshashringi (*Gymnema sylvestre* [family – Asclepiadaceae]),[8,9] Beejak (*Pterocarpus marsupium* Roxb. [family - Fabaceae])[10,11] and Karvellak (*Momordica charantia* [family - Cucurbetaceae]).[12,13] Most of these ingredients possess antidiabetic activity in isolation. Thus, the present study was planned to evaluate and comparatively assess antidiabetic activity of AHPL/AYTAB/0513 tablet, oral hypoglycemic agents (OHA[s]), and combination of AHPL/AYTAB/0513 tablet and OHA(s) in streptozotocin (STZ)-induced diabetes in rats. Similarly, their possible role in preventing complications of diabetes was also assessed in this study.

MATERIALS AND METHODS

Ethics

The study was conducted, and analysis was done in December 2014 to May 2015. Before the initiation of the study, the Institutional Animal Ethics Committee (IAEC) approval was obtained, and the animals were used and treated strictly following Committee for the Purpose of Control and Supervision of Experiments on Animals guidelines (approval letter number: DYPISR/IAEC/14-15/P-01). Totally, 50 male Wistar rats of age 6–8 weeks weighing 180–250 g were used for the study.

Methodology

Evaluation of hypoglycemic activity of various formulations in nondiabetic rats

The overnight fasted Wistar albino rats were divided into nine groups of five animals each. Animals belonging to Group I served as normal control (NC) group and received saline solution at the dose of (1 ml/kg, p.o.); Animals belonging Group II and III served as standard and received glibenclamide (Emcure Pharmaceuticals Pvt. Ltd., Pune, India) (10 mg/kg, p.o.) and metformin (USV Ltd., Mumbai, India) (50 mg/kg, p.o), respectively; Group IV, V, and VI served as test groups and were administered with AHPL/AYTAB/0513 tablet (ARI Healthcare Pvt. Ltd., Pune, India) (111 mg/kg), (222 mg/kg), and (444 mg/kg) p.o, respectively. Animals in Group VII, VIII, and IX were administered with AHPL/AYTAB/0513 tablet (222 mg/kg, p.o) + glibenclamide (10 mg/kg, p.o), AHPL/AYTAB/0513 tablet (222 mg/kg, p.o) + metformin (50 mg/kg, p.o), and AHPL/AYTAB/0513 tablet (222 mg/kg, p.o) + glibenclamide (10 mg/kg, p.o) + metformin (50 mg/kg, p.o), respectively. After single-dose drug treatment, blood was withdrawn from the tail vein on 0^{th}, 30^{th}, 60^{th}, and 120^{th} min for estimation of blood glucose levels (BGLs) using glucometer (Manufactured by-Easy Care, Mumbai, India).

Oral glucose tolerance test in nondiabetic rats

The overnight fasted Wistar albino rats were divided into nine groups of five animals each. Animals belonging to Group I served as NC group and received saline solution at the dose of (1 ml/kg, p.o.); Animals belonging to Group II and III served as standard and received glibenclamide (10 mg/kg, p.o.) and metformin (50 mg/kg, p.o), respectively; while animals belonging to Group IV, V, and VI served as test group and were administered with AHPL/AYTAB/0513 tablet (111 mg/kg), (222 mg/kg), and (444 mg/kg) p.o, respectively. While animals belonging to Group VII to Group IX were administered with AHPL/AYTAB/0513 tablet (222 mg/kg, p.o) + glibenclamide (10 mg/kg, p.o), AHPL/AYTAB/0513 tablet (222 mg/kg, p.o) + metformin (50 mg/kg, p.o), and AHPL/AYTAB/0513 tablet (222 mg/kg, p.o) + glibenclamide (10 mg/kg, p.o) + metformin (50 mg/kg, p.o),

respectively. After drug treatment, animals were administered with 10% glucose solution (2 g/kg, p.o) and blood was withdrawn from the tail vein at 0th, 30th, 60th and 120th min for estimation of BGLs using glucometer.

Evaluation of antidiabetic activity in streptozotocin-induced diabetes in rats

Diabetes was induced to 18 h fasted rats by adminsitering by single dose of STZ (Hi-Media Lab. Pvt. Ltd., Mumbai, India) (55 mg/kg, intraperitoneally) after dissolving it in freshly prepared ice cold 0.1M citrate buffer (pH 4.5). After the injection, all the animals were given free access to feed and water and were provided with 5% glucose solution to drink overnight to counter the hypoglycemic shock. After 48 h of the STZ injection, the development of diabetes was confirmed by measuring glucose level using glucometer. The animals having fasting BGLs >200 mg/dl were selected for the experimentation.[14] The animals were divided into ten groups (n = 5) as follows:

- Animals belonging to Group I were NC, i.e., nondiabetic received saline solution at the dose of 1 ml/kg, p.o for 21 days
- Animals belonging to Group II served as DC and received saline solution (1 ml/kg, p.o.) for 21 days
- Animals belonging Group III and IV were diabetic and served as standard and received glibenclamide (10 mg/kg, p.o.) and metformin (50 mg/kg, p.o), respectively for 21 days
- While animals belonging to Group V to Group VII were diabetic and served as test groups and were administered with AHPL/AYTAB/0513 tablet (111 mg/kg), (222 mg/kg) and (444 mg/kg) p.o, respectively, for 21 days
- While animals belonging to Group VIII to Group X were diabetic and served as standards and test drug and given AHPL/AYTAB/0513 tablet (222 mg/kg, p.o) + glibenclamide (10 mg/kg, p.o), AHPL/AYTAB/0513 tablet (222 mg/kg, p.o) + metformin (50 mg/kg, p.o), and AHPL/AYTAB/0513 tablet (222 mg/kg, p.o) + glibenclamide (10 mg/kg, p.o) + metformin (50 mg/kg, p.o), respectively, for 21 days.

On day 21st, the blood from the retro-orbital plexus was withdrawn under mild ether (Hi Media Lab. Pvt. Ltd., Mumbai, India) anesthesia using fine glass capillary and collected in eppendorf tubes from overnight fasted rats.[15] Fasting blood sugar level (BSL) was estimated using glucometer. The animals were then sacrificed and pancreas, heart, kidney were removed for histopathological examination.

The blood samples were centrifuged (using Cooling Centrifuge Manuf: REMI C24, Mumbai, India) and serum was estimated for determination of serum insulin, serum triglyceride, Serum total cholesterol, serum high-density lipoprotein (HDL), serum low-density lipoprotein (LDL), serum very LDL (VLDL), and serum insulin level (biochemical kits for triglycerides, cholesterol estimation were obtained from Bio Lab Diagnostics Pvt. Ltd., Mumbai, India, while biochemical kits for HDL, VLDL, and LDL estimation were obtained from Ebra Diagnostics, Mannheim, Germany).

The data obtained from above study was expressed as mean ± standard error of the mean and statistically analyzed by one-way ANOVA followed by Dunnett's test.

RESULTS

In nondiabetic rats treated with single dose of formulations, no significant reduction in BSL was observed after 120 min as compared to the initial BSL of the respective group [Table 1].

Similarly, when the oral glucose tolerance test (OGTT) was performed in single-dose treated-nondiabetic rats, it was observed that all the formulation groups effectively reduced and normalized BGL on 120th min of OGTT when compared with NC group. When compared between

Table 1: Effect of various formulations on plasma glucose level in nondiabetic rats

Groups (n=5)	Plasma glucose level (mg/dl)			
	0 min	30 min	60 min	120 min
Group I: NC	81±3	85.6±2.46	81.2±1.2	81.8±2.267
Group II: Glibenclamide	81±0.9	75.6±2.99	77.6±2.11	82±2.191
Group III: Metformin	74±1.2	77.8±3.04	76.4±4.14	75.6±2.249
Group IV: AHPL/AYTAB/0513 tablet (111 mg/kg)	84±0.9	76.8±2.78	77.2±3.57	81.4±2.462
Group V: AHPL/AYTAB/0513 tablet (222 mg/kg)	79±1.6	75.8±1.562	77.8±0.86	80.2±2.577
Group VI: AHPL/AYTAB/0513 tablet (444 mg/kg)	76±3.5	76±3.11	75.6±2.98	77.8±1.772
Group VII: AHPL/AYTAB/0513 tablet (222 mg/kg) + glibenclamide	76±3.6	78.4±1.21	73±3.01	71.4±1.887
Group VIII: AHPL/AYTAB/0513 tablet (222 mg/kg) + metformin	82±2.8	80±1.92	78±1.38	80.2±2.267
Group IX: AHPL/AYTAB/0513 tablet (222 mg/kg) + glibenclamide + metformin	83±1.7	77±3.85	80.6±2.94	81.4±1.99

n=5, values are expressed as mean±SEM. Statistically analyzed by one-way ANOVA followed by Dunnett's test. SEM: Standard error of mean, NC: Normal control

the groups, no statistically significant difference was noted [Table 2].

In STZ-induced diabetic rats, all the formulation groups effectively reduced BGL on 21st day, which was close to the BGL of non-DC group. Highest percentage reduction in BGL was observed in the combination group of glibenclamide + metformin + AHPL/AYTAB/0513 tablet 222 mg/kg [Table 3]. The mean body weight of the rats significantly reduced in STZ-induced diabetic group. The results indicate that, on treatment with the formulations, the mean body weight of STZ-induced diabetic rats was preserved [Table 4].

Moreover, all the treatment groups significantly increased serum insulin level [Graph 1], mean body weight, and HDL cholesterol levels after 21 day treatment with these formulations in STZ-induced diabetic rats [Graph 2]. Serum creatinine [Table 5], serum triglycerides, total cholesterol, LDL, and VLDL levels were found to be significantly decreased in all the treatment groups [Graph 2].

Table 2: Effect of various formulations on blood glucose level in oral glucose tolerance test in nondiabetic rats

Groups (*n*=5)	BGL (mg/dl)				Percentage increase in BGL on 120th min
	0 min	30 min	60 min	120 min	
Group I: NC	81±3	139.4±2.08	128.2±0.66	118.6±2.44	46.41
Group II: Glibenclamide	81±0.9	128.6±3.09**	112.2±1.24**	82±2.47**	1.23
Group III: Metformin	85±1.2	128.6±1.66**	116.4±1.6**	80.6±1.47**	−5.17
Group IV: AHPL/AYTAB/0513 tablet (111 mg/kg)	84±0.9	130.2±1.28*	120.4.8±1.37**	109.4±2.98**	30.23
Group V: AHPL/AYTAB/0513 tablet (222 mg/kg)	79±1.6	127.2±1.06**	114.2±1.393**	98.2±2.24**	24.30
Group VI: AHPL/AYTAB/0513 tablet (444 mg/kg)	76±3.5	130.6±2.73*	119.6±1.503**	94±2.81**	23.68
Group VII: AHPL/AYTAB/0513 tablet (222 mg/kg) + glibenclamide	76±3.6	129.2±1.06**	114.8±0.86**	80.4±3.4**	5.79
Group VIII: AHPL/AYTAB/0513 tablet (222 mg/kg) + metformin	82±2.8	126.4±2.06**	118±1.46**	87.2±1.98**	6.34
Group IX: AHPL/AYTAB/0513 tablet (222 mg/kg) + glibenclamide + metformin	83±1.7	129.8±1.59**	119.4±1.63**	86.4±2.24**	4.09

n=5, values are expressed as mean±SEM. *$P<0.05$, **$P<0.01$ when compared with NC group. Statistically analyzed by one-way ANOVA followed by Dunnett's test. SEM: Standard error of mean, NC: Normal control, BGL: Blood glucose level

Table 3: Effect of various formulations on blood glucose levels in streptozotocin-induced diabetes in rats

Groups (*n*=5)	BGL (mg/dl)			Percentage reduction of BGL at the end of treatment
	0 day	15th day	21st day	
Group I: NC	88.8±4.14	88.8±4.14	88.8±4.14	-
Group II: DC	355.6±11.021	382±3.86##	420±8.319##	-
Group III: Glibenclamide	357.6±8.756	174.8±2.267**	80±5.161**	77.63
Group IV: Metformin	379.2±7.385	169.8±2.417**	89±5.099**	76.53
Group V: AHPL/AYTAB/0513 tablet (111mg/kg)	366.4±7.801	232±2.915**	112.2±6.726**	69.38
Group VI: AHPL/AYTAB/0513 tablet (222 mg/kg)	384.8±9.785	218.4±1.806**	92±5.607**	76.09
Group VII: AHPL/AYTAB/0513 tablet (444 mg/kg)	366.6±3.092	213.45±2.31**	96.8±6.822**	73.59
Group VIII: AHPL/AYTAB/0513 tablet (222 mg/kg) + glibenclamide	374.6±2.159	164.8±1.985**	84.4±5.046**	77.47
Group IX: AHPL/AYTAB/0513 tablet (222 mg/kg) + metformin	356±10.134	183.6±3.894**	85.8±6.028**	75.89
Group X: AHPL/AYTAB/0513 tablet (222 mg/kg) + glibenclamide + metformin	387.4±3.043	178.2±2.577**	86±6.063**	77.80

n=5, values are expressed as mean±SEM. ##Significant decrease,**$P<0.01$ when compared with DC group. Statistically analyzed by one-way ANOVA followed by Dunnett's test. SEM: Standard error of mean, NC: Normal control, DC: Diabetic Control, BGL: Blood glucose level

Table 4: Effect of various formulations on body weight in streptozotocin-induced diabetes in rats

Groups (*n*=5)	Body weight (g)		
	1st day	15th day	21st day
Group I: NC	184.4±1.965	192±3.742	200.2±3.169
Group II: DC	180±0	150.8±1.594##	142±1.342##
Group III: Glibenclamide	184.4±1.806**	169.2±1.8**	180.8±1.985**
Group IV: Metformin	186.4±3.458**	162.2±3.262**	186±0.4**
Group V: AHPL/AYTAB/0513 tablet (111 mg/kg)	183±3.661**	154.4±2.449**	168±2**
Group VI: AHPL/AYTAB/0513 tablet (222 mg/kg)	182±2.025**	167.6±3.742**	175±3.317**
Group VII: AHPL/AYTAB/0513 tablet (444 m/kg)	186.4±1.691**	168.6±3.852**	174.8±3.338
Group VIII: AHPL/AYTAB/0513 tablet (222 mg/kg) + glibenclamide	180±4.472**	164.2±2**	186.6±3.855**
Group IX: AHPL/AYTAB/0513 tablet (222 mg/kg) + metformin	187±1.844**	170.4±2.449*	193±1.871**
Group X: AHPL/AYTAB/0513 tablet (222 mg/kg) + glibenclamide + metformin	179±2.324**	162.8±2.34**	196±3.742**

n=5, values are expressed as mean±SEM. ##Significant decrease,*$P<0.05$, **$P<0.01$ when compared with DC group. Statistically analyzed by one-way ANOVA followed by Dunnett's test. SEM: Standard error of mean, NC: Normal control, DC: Diabetic control, BGL: Blood glucose level

Histopathology of pancreas

Histopathological examination of pancreatic tissues of STZ-induced diabetic rats presented disturbed cellular architecture with signs of necrosis, inflammation, and hemorrhage. The scarcity of beta cells indicated reduction in endocrine tissue of pancreas when compared with non-DC group. There was significant regression in the features of inflammation, necrosis, hemorrhage with preserved cellular architecture, and abundance of islet cells when compared to the diabetic group. This suggests probable regeneration of islet cells in diabetic pancreatic tissue as a result of provided treatment. When compared between the groups, combination of standard drugs (glibenclamide and metformin) with AHPL/AYTAB/0513 tablet provides better results in terms of preservation of histopathological features of pancreas [Figure 1].

Histopathology of kidney

On histopathological examination of kidney tissues, the tissues of diabetic group were found to possess disturbed cellular architecture, signs of necrosis, and hemorrhage along with congested blood vessels. All these signs were absent in the tissue of NC group of nondiabetic rats. Deranged histopathological features were completely reversed in the groups treated with high-dose formulation (444 mg/kg) and groups treated with combination of standard drug and 222 mg/kg formulation. All the treatment groups showed significant improvement in terms of preservation of kidney tissue when compared to diabetic group. When compared between the formulation groups, the high-dose formulation (444 mg/kg) and combination groups of standard drugs and formulation proved more effective [Figure 2].

Histopathology of heart

Similarly when the heart tissue was studied; the groups treated with formulations displayed regression of pathological damage caused by STZ-induced diabetes, which was manifested by preservation of normal cellular architecture, absence of necrosis, inflammation, hemorrhage, and normal blood vessels. When compared between the formulation groups, medium dose formulation group and combination of standard drugs with formulation proved superior to any other group [Figure 3].

DISCUSSION

The study was carried out in nondiabetic and STZ-induced diabetic rats to evaluate hypoglycemic/antidiabetic activity of AHPL/AYTAB/0513 tablet alone and as an adjunct to OHAs.

On single-dose administration of all the formulations in nondiabetic rats, none of the groups showed a significant reduction in fasting BGL. In all the groups, BSL was within normal limit. This suggests that none of the formulation produces hypoglycemia in nondiabetic rats. All the drugs were tolerated well by the rats. Surprisingly, high dose (444 mg/kg) of AHPL/AYTAB/0513 tablet did not produce hypoglycemia, suggesting the safety of the formulation at high dosage level also. Further, the results of OGTT in nondiabetic rats suggest that all the formulations help to improve glucose tolerance in nondiabetic rats.

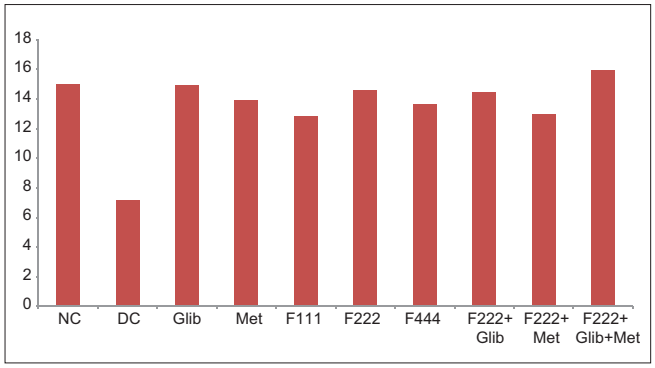
In STZ-induced diabetes study, there was a significant increase in BSL in DC group. However, all other treatment groups effectively reduced BSL when compared to their initial BSL. When compared to DC group, the reduction in BSL was statistically significant in all the treatment groups. When compared between the treatment groups, no significant difference was observed. Highest percentage reduction in BSL was seen in the group treated with glibenclamide + metformin + AHPL/AYTAB/0513 tablet (222 mg/kg). This confirms that as an adjuvant, AHPL/AYTAB/0513 was able to enhance the efficacy of OHA(s).

All the ingredients present in AHPL/AYTAB/0513 tablet have been effectively used in Ayurveda for the management of various types of Prameha (diabetes). *E. officinalis*[5] *S. cumini*,[6,7] *G. sylvestre*,[8,9] *P. marsupium*,[10,11] *C. longa*,[4,16] *and M. charantia*[12,13] possess antidiabetic activity. *S. cumini* enhances peripheral utilization of glucose,[6] *G. sylvestre*[9] and *M. charantia*[13] inhibit absorption of glucose from intestine, *P. marsupium* helps in conversion of proinsulin to insulin, and *G. sylvestre*[8,9] helps to release insulin from pancreatic beta cells. These multidimensional activities of ingredients of AHPL/AYTAB/0513 tablet could have helped bring down BGL effectively.

Serum Insulin level in diabetic group was reduced to 7.2 ± 0.687 which was significantly lower than that of NC group. This is in agreement with the fact that STZ causes hyperglycemia in the rats through its direct cytotoxic action on pancreatic beta cells.[15,17] Degeneration of beta cells leads to insulin deficiency. However, when serum insulin level of all other treatment groups was studied, it was found that all the groups effectively increased the serum insulin level in diabetic rats. This suggests probable mechanism of regeneration of pancreatic islets cells with the treatment, which is also supported by the histopathological findings of pancreas. The histopathological studies of the rat pancreas showed recovery of the STZ-induced damage of the insulin-secreting pancreatic beta cells, improvement

in necrosis (mild to moderate architecture), and fibrotic changes by AHPL/AYTAB/0513 tablet alone and in combination with standard drugs, i.e., glibenclamide and metformin.

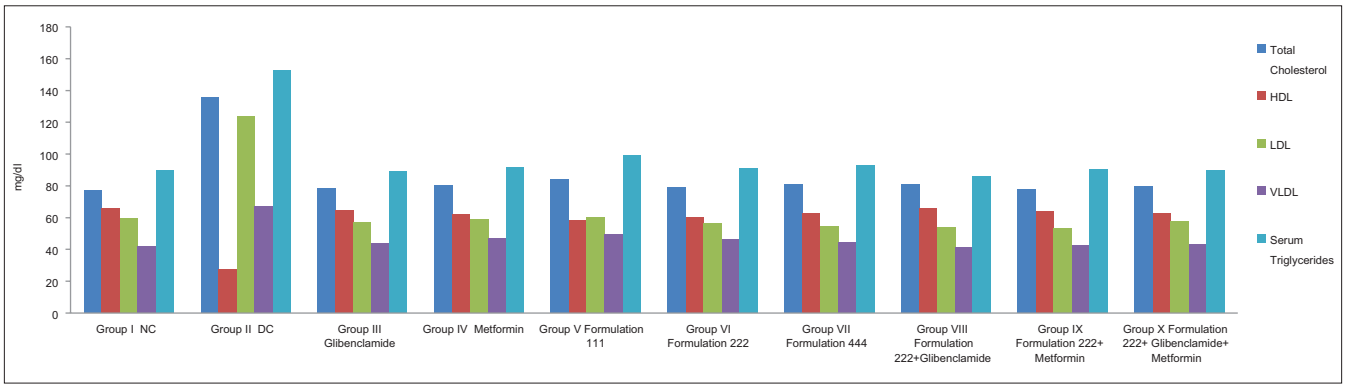
When compared between the groups, highest insulin levels were observed in the group treated with glibenclamide + metformin + AHPL/AYTAB/0513 tablet (222 mg/kg). Ingredients of AHPL/AYTAB/0513 tablet such as *S. cumini*,[6] *G. sylvestre*,[7] *P. marsupium*,[18] *C. longa*,[18] and *M. charantia*[18] either protect or help to regenerate pancreatic beta cells. Ingredients such as *G. sylvestre*[8,9] and *P. marsupium*[10,11,19] help in release of insulin from pancreatic beta cells. The synergistic activities of these ingredients have helped in regeneration of pancreatic beta cells in rats and subsequent release of insulin from beta cells.



Graph 1: Effect of various formulations on serum insulin level in streptozotocin-induced diabetic rats

Uncontrolled DM is a common cause of weight loss wherein utilization of fats for energy generation along with extracellular and cellular water loss due to osmotic diuresis and glycosuria lead to weight loss.[20] Findings of the study support this fact where reduction in mean body weight was observed in diabetic group. All the treatment groups prevented such weight loss in diabetic rats and effectively either preserved or increased the mean body weight in the rats.

It was observed that AHPL/AYTAB/0513 tablet alone or in combination with OHA(s) can correct dyslipidemia in diabetic rats. As an adjuvant to OHA(s), AHPL/AYTAB/0513 tablet is more effective in terms of correcting deranged lipid levels. Most of the ingredients of AHPL/AYTAB/0513 tablet possess antihyperlipidemic activity.[4,8] The ingredients of AHPL/AYTAB/0513 tablet could have act synergistically to correct the deranged lipid levels in the rats.



Graph 2: Effect of various formulations on total cholesterol, high-density lipoprotein, low-density lipoprotein, very low-density lipoprotein, and serum triglycerides in streptozotocin-induced diabetes in rats

Table 5: Effect of various formulations on serum creatinine in streptozotocin-induced diabetic rats

Groups (*n*=5)	Serum creatinine (mg/dl)
Group I: NC	0.479±0.056
Group II: DC	1.869±0.060##
Group III: Glibenclamide	0.468±0.033**
Group IV: Metformin	0.569±0.084**
Group V: AHPL/AYTAB/0513 tablet (111 mg/kg)	0.585±0.088*
Group VI: AHPL/AYTAB/0513 tablet (222 mg/kg)	0.460±0.089**
Group VII: AHPL/AYTAB/0513 tablet (444 mg/kg)	0.475±0.089
Group VIII: AHPL/AYTAB/0513 tablet (222 mg/kg) + glibenclamide	0.403±0.082**
Group IX: AHPL/AYTAB/0513 tablet (222 mg/kg) + metformin	0.465±0.111**
Group X: AHPL/AYTAB/0513 tablet (222 mg/kg)+ glibenclamide + metformin	0.400±0.087**

n=5, values are expressed as mean±SEM. ##*P*<0.01 when DC group compared with NC, **P*<0.05, ***P*<0.01 all groups were compared with DC group except normal control group. Statistically analyzed by one-way ANOVA followed by Dunnett's test. SEM: Standard error of mean, NC: Normal control, DC: Diabetic control

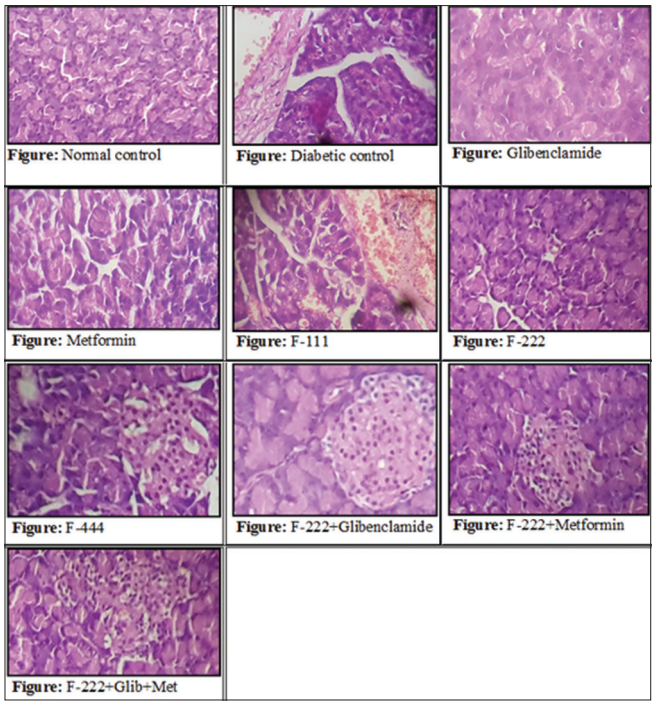


Figure 1: Histopathological representation of pancreas in streptozotocin-induced diabetes in rats treated with various formulations (H and E, ×40) (Reproduction size: at column width)

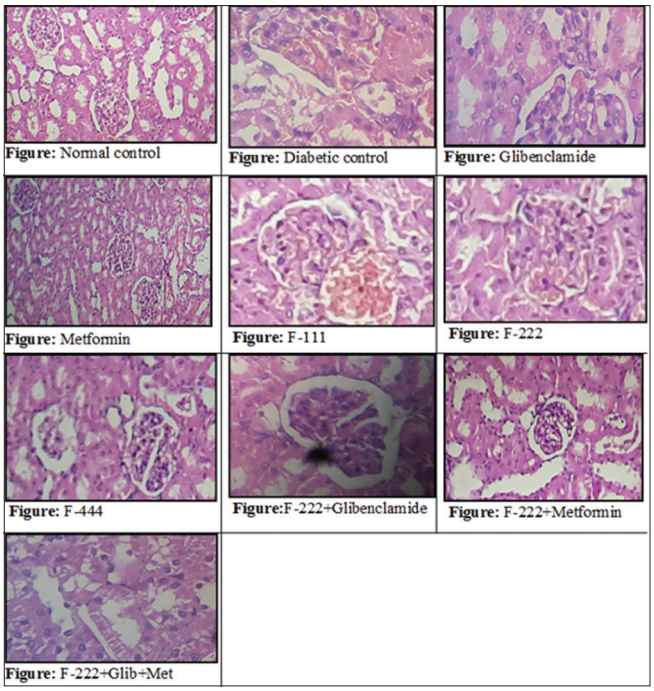


Figure 2: Histopathological representation of kidney in streptozotocin-induced diabetes in rats treated with various formulations (H and E, ×40) (Reproduction size: at column width)

Diabetic nephropathy is one of the commonly encountered microvascular complications in uncontrolled long-term diabetes leading to end-stage renal disease. Serum creatinine level is indicator of renal damage. The results of the study showed that all the treatment groups significantly reduced the serum creatinine level; however, the combination of conventional OHA(s) with AHPL/AYTAB/0513 tablet (222 mg/kg) was more successful in maintaining normal serum creatinine level. This was also evident from the histopathological evaluation of the kidney that AHPL/AYTAB/0513 tablet in combination with OHA(s) was more effective in terms of prevention of hyalinization and maintaining structure of glomeruli as compared to DC group. Ingredients of AHPL/AYTAB/0513 tablet such as *C. longa*[16] and *M. charantia*[21] possess nephroprotective action. These herbs are being used effectively in the management of diabetic nephropathy. In addition, most of the ingredients of AHPL/AYTAB/0513 tablet possess antioxidant activity.[4,8] Thus, these multiple activities of the ingredients could have helped in protecting the kidney from damage in STZ-induced diabetes in rats.

Histopathological examination of the heart showed that AHPL/AYTAB/0513 tablet alone and in combination with standard drugs, i.e., glibenclamide and metformin significantly prevented myonecrosis as is evident from significant reduction in the infiltration and inflammatory cells, vascular changes as compared to DC group.

From the results, it is evident that AHPL/AYTAB/0513 tablet helps to normalize BGL, improve insulin secretion, and response to conventional OHAs. In addition, AHPL/AYTAB/0513 tablet helps to protect heart and kidney from damage due to diabetes. Thus, AHPL/AYTAB/0513 tablet is safe for effective management of newly diagnosed mild to moderate cases of Type II DM and as an adjuvant to OHAs in established cases of Type II DM. AHPL/AYTAB/0513 tablet also helps to delay complications of diabetes.

CONCLUSION

It can be concluded that AHPL/AYTAB/0513 tablet possesses a significant antidiabetic activity. AHPL/AYTAB/0513 tablet in combination with standard drugs, i.e., glibenclamide and metformin has shown enhanced antidiabetic effect. AHPL/AYTAB/0513 tablet in combination with standard drugs, i.e., glibenclamide and metformin showed better recovery of beta pancreatic cells than AHPL/AYTAB/0513 tablet or standard drugs alone. No hypoglycemic episodes and any other adverse effects were observed in rats treated with AHPL/AYTAB/0513 tablet alone or in combination with OHA(s) indicating the safety of AHPL/AYTAB/0513 tablet alone and as an adjuvant to OHAs. AHPL/AYTAB/0513 tablet along with standard drug(s) showed promising results in

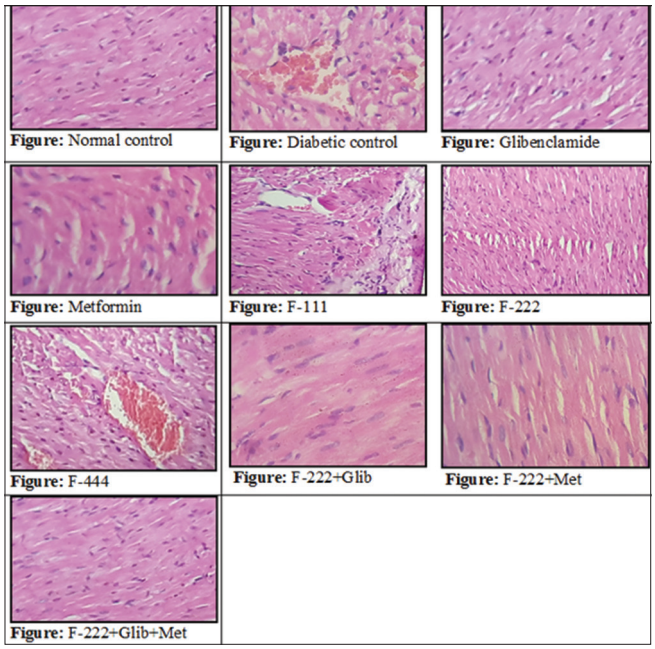


Figure 3: Histopathological representation of heart in streptozotocin-induced diabetes in rats treated with various formulations (H and E, ×40) (Reproduction size: at column width)

diabetic complications such as diabetic nephropathy and cardiovascular complications.

AHPL/AYTAB/0513 tablet alone and in combination with OHA(s) can be effectively used in the management of DM. In addition, AHPL/AYTAB/0513 tablet alone and in combination with OHA(s) helps in prevention of diabetic complications. As an adjuvant to OHA(s), AHPL/AYTAB/0513 tablet can be more effective.

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Conflicts of interest

There are no conflicts of interest.

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