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Original Article

Pathophysiology of Metabolic Syndrome – Its Management by Ayurvedic Formulation

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ABSTRACT

Metabolic syndrome (Met S) is a disorder of energy and storage containing of risk factor for various complications such as Type 2 diabetes mellitus and cardio vascular disease. In Met S combined effect of atherogenic property, insulin resistance, hypertension and obesity occur. Obesity significantly influences the onset of cardiovascular disorders particularly in the presence of type 2 diabetes mellitus giving rise to Met S. Various plant based remedies are known to treat metabolic syndrome by virtue of their antihyperlipidemic, antitumour, antioxidant, anorexia, anti-inflammatory and antihyperglycemic activities. Present study was designed to assess the effect of herbal test formulation of five plants *viz., Dioscorea bulbifera, Termenalia chebula, Termenalia arjuna, Hippophae rhamnoids and Nardostachys jatamansi* in hyperglycemic and hyperlipidemic (atherogenic property) albino Wistar rats. *D. bulbifera* (bulb), *T. chebula* (berries), *T. arjuna* (dried fruit pulp), *N. jatamansi (rhizome)* and *H. rhamnoids* (bulb) were collected, dried and powered. Distilled water and alcohol (60:40) were used to extract the active constituents present in the plant samples and were mixed in a definite proportion to make test formulation. Two studies were designed to assess the anti hyperglycemic and anti-atherogenic activity of the test formulation in high cafeteria and high cholesterol rich diet induced experimental rats respectively. In *study I* body weight, systolic blood pressure, total cholesterol, triglycerides, plasma insulin decreases significantly on the administration of ayurvedic formulation dose dependent with control group while in *study II* significantly reduction in LDL-c and increase in level of HDL –c giving treatment with conventional anti – obesity drug. Obesity is a multi factorial disorder and is a major risk factor for T2DM, hypercholesterolemia and ischemic heart disease. Present study revealed that the administration of test formulation in hyperglycemic and hyperlipidemic rat models mitigates the body weight, cholesterol, triglycerides, blood glucose, LDL-c, and HDL-c towards the normal values. The test formulation showed anti-hyperglycemic, insulin sensitivity enhancing, and anti atherogenic activity in hyperglycemic and hyperlipidemic induced rats.

Keywords: Metabolic syndrome, Ayurvedic formulation, Hyperlipidemia, Hyperglycemia, lipid profile.

INTRODUCTION

Metabolic syndrome is a disorder of energy and storage, its major factor is obesity and is a major public health problem worldwide [1]. Met S is an interrelated cluster of risk factor for cardiovascular diseases and Type 2 diabetes mellitus, such as hyperglycemia, raised blood pressure, elevated triglycerides level, low high density lipoprotein, cholesterol level and central obesity [2]. Our research group has reported the prevalence of the metabolic syndrome in Asian Indian population adolescents using population specific cut off points of various parameters such as BMI, waist circumference, cholesterol, triglycerides, and fasting hyperinsulinemia [3] (Vikram NK Mishra A, Pandey RM, Luthra K, Wasir JS, Dhingra V). Combined effect of atherogenic property, insulin resistance, hypertension and obesity occurs in metabolic syndrome. It is established that obesity is linked with metabolic syndrome significantly influence the onset of cardiovascular disorders particularly in the presence of type 2 diabetes mellitus [4]. Obesity is associated with decrease adiponectin and increase level of leptin hormone in adipose tissue. Insulin resistance in adipose tissue (fat cells) result in a flux of FFA (Free fatty acid) from the adipose tissue to the liver causing insulin resistance in the liver and the peripheral tissue. Fatty acid block glucose oxidation and glucose transport, but they also cause atherogenic activity by inducing production in the liver of very low

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density lipoprotein (LDL) particle that leads to the elevation of TG (triglycerides) and apolipoproteinB (Apo-B) and the lowering of high density lipoprotein (HDL-c). An increase in triglycerides in addition to high LDL-c levels, significantly increases the risk for coronary heart disease (CHD)[5] while low HDL-c is considered to be particularly key risk factor for CVD in both non-diabetic and diabetic individual which indicates HDL-c to be an strong independent risk factor contributor to CVD in humans, as compared diabetic with non-diabetic individuals [6 , 7]. It is reported that significantly low HDL-c and high triglycerides are frequently found with insulin resistance, with or without type 2 diabetes [8]. Study revealed that the complex lipid profile, observed with both type 2 diabetes and extremely high risk factor for CVD in case of metabolic syndrome [5, 9–12].

The adipokine hypothesis is one of the physiological mechanisms in reduction of metabolic syndrome related to type 2 diabetes and coronary heart disease, thus it used to explain how excess body fat leads to numerous health consequences. The inverse relationship between body fat and serum adiponectin levels has been demonstrated, and weight reduction can increase adiponectin levels as mentioned above [4,13]. It modulates glucose metabolism, decreases circulating free fatty acid concentrations and muscle triglyceride content [14-15]. Levels of adiponectin are reported to reduce in diabetics as compared to non diabetic individuals. Weight reduction significantly increases its circulating level [18]. It effects glucose flux hence, lipid catabolism [16-17], triglycerides clearance [19], protection from endothelial dysfunction, insulin sensitivity, weight loss, control of energy metabolism [20], upregulation of uncoupling protein [14], and reduction of TNFα. As endothelial dysfunction, TNFα act as inflammatory markers and they result as pathogenic features of atherogenic property and diabetic activity with metabolic disorders. Obesity and insulin resistance are associated with higher level of marker of inflammation and endothelial dysfunction (Visser et al ;1999;) . Adiponectin has potential to down regulate inflammatory response resulting in reduction of metabolic disorder. (Roy blat et al 2000). Adiponectin, act as hormone expressed in adipose tissue, plays an important role in regulating insulin senstivity glucose and lipid metabolism besides anti-inflammatory and anti-atherogenic properties. Recently anti-obesity drugs Sibutramine and Orlistat have been produced, which is an appetite suppressant [Mc Neely et al., 1998; Hvizdos et al.,1999]. Another drug Statin used to lower cholesterol level by inhibiting the enzyme HMG-COA reductase which is an inhibitor of fat absorption is being used for treatment of metabolic syndrome (Mc Neely et al., 1998; Hvizdos et al., 1999). Various botanical sources has been estimated for the treatment of metabolic syndrome including Dioscorea *bulbifera*, *Terminalia chebula, Terminalia arjuna, Nordostachys jatamansi* and *Hippophae rhamnoids* etc. *Dioscorea.bulbifera* (Dioscoreaceae) bulb possess profound therapeutic potential such as antihyperlipidemic, antitumour, antioxidant, anorexian, analgesic, anti-inflammatory, and antihyperglycemic activities [22-26]. Albuminoids, furanoids, norditerpenes, diosbulbins (A-H), Dihydrophenenthrene, tetrahydrophenenthrene, D-sorbitol, A dihydrophenenthrene 2, 4,6,7-tetrahydroxy, 9, 10 dihydroxy phenenthrene phytoestrogen are the active constituents found in *Diosorea. bulbifera*[27]. It is also known to low plasma cholesterol level through reduced cholesterol absorption by the liver. It is also known to reduce coronary heart disease factor involved with menopausal women (Dubey et al .,2008; Sauvaire et al .,1991).

Terminalia chebula (Combretaceae) has been reported to prevent obesity, insulin resistance, hyperglycemic and hyperlipidemia in spontaneously type 2 diabetes. Molecular mechanism lies behind these actions include inhibitory effects on lipid absorption, suppress absorption of triacylglycerol, and inhibit pancreatic lipase activity (MakhiharaH,Shimada T,Machida E). Besides, this plant is also known to have anti-inflammatory, anti-diabetic, antioxidant, glucose lowering activity, as well as inhibitory action on cyclooxygenase and lipooxygenase enzymes (Mahesh et al .,2009, Singh et al.,2009). Active phytoconstituents found in *Terminalia.chebula* involves flavonoids, glabridin, sennosides, triterpenoids, coumarin, gallic acid, chebulin, ellagic acid, tannin, chebulic acid and resin. *Terminalia. Arjuna* (Combretaceae) have potential to show the effects to regulate blood pressure and cholesterol levels and act as anti-atherogenic and anti-dyslipidemic (Bharani et al.,1995, Ram et al.,1997; karthikeyan et al 2003) . It increases the elimination of cholesterol by accelerating the turnover of LDL cholesterol in the liver, lowers the β –lipoprotein lipid oxidation and restores HDL components in hyperlipidemia and relieves hypertension. Tannins, triterpenoids, saponins, arjunic acid, arjunolic acid, oleanolic acid, arjungenin, arjunin, alavnnids, steroids, and β sitosterol are the active chemicals reported from *Termenalia. Arjuna* (Diwedi et al., 2005).

Active chemical constituents of *Nordostachys. jatamansi* (Valerianaceae) have shown significant reduction in high Blood pressure in patients

suffering from moderate to severe hypertension (Hamid et., al 1962) and studied the effect of extract of this plant in experimental animal and reported the sedative action and hypotensive activity.

Hippophae.rhamnoids (Elaeagnaceae) contain Flavonoids, phytosterols, vitamin c, shows an reducing level of blood sugar and improving insulin sensitivity (Linn et al 2008). Thus this plant extraction used in Ayurvedic formulation had been resulted as therapeutic potential used in treatment of metabolic disorder.

MATERIAL AND METHOD

Extraction of plant material: The plant samples (*D. bulbifera, T. chebula, T. arjuna, N. jatamansi , H. rhamnoids*) were collected in the month of (september to november) and identified by professional Botanist. Distilled water and alcohol in the ratio of 60:40 was used to extract the active constituents present in the plant samples after several repetitions. The extracts were stored at 4^0C, until analysis was carried out.

Preparation of Ayurvedic formulation: Extracts of test samples *viz., D. bulbifera* (bulb), *T. chebula* (berries), *T. arjuna* (dried fruit pulp), *N.jatamansi (rhizome)* and *H. rhamnoids* (bulb) were used for the preparation of Ayurvedic test formulation. The hydro-ethanolic extracts of plants was mixed by adding additional additives (calcium carbonate and starch) to make capsule. The present Ayurvedic formulation was made by Baijnath Pharmaceuticals Pvt Ltd, Papraula , District Kangra ,Himachal Pradesh.

Experimental animals: The study was approved by institute ethical committee to conduct experimental trial. Animals (Wistar 30 female rats) 6-7 week old weighing 95-125g were taken in central animal house and housed three per polypropylene cage under standard laboratory condition (22±1˚C room temperature, 50-60% humidity with a 12 hours light/dark cycle). The animals were provided with pellet chow and water.

Experimental design for the pharmacological activity of test formulation

Study I

Group I: Rats were fed on normal laboratory diet for four weeks + normal chow diet (n=6)

Group II: High cafeteria diet (HCD 1.5g/kg body weight) for 4 weeks + Disease control group (n=6)

Group III: HCD + Test formulation (250 mg/kg/day) for a period of 4 weeks + treated group (n=6)

Group IV: HCD + Test formulation (500 mg/kg/day) for a period of 4 weeks + treated group (n=6)

Cafeteria diet used in the study includes 40 gm condensed milk + 40gm bread on 1st day,15gm chocolate + 30gm biscuit + 30gm dried coconut on the 2nd day and 40gm cheese + 50 gm boiled potato on 3rd day. The diet was given to rats of group II, III and IV. (Repeated successively up to 30 days) and given to 6 rats of Group II, III, IV. The test formulation was suspended in distilled water and administered orally in the dose of 250 mg (125 mg morning and 125mg evening) and 500 mg (250 mg morning and 250 mg evening) per kg body weight for 30 days. The rats were maintained at the above dietary regimen and their body weight were measured at every week. After 1 month all the four group rats were fasted overnight and blood was collected from retro orbital plexus. As such blood samples were collected at 1st, 15th and 30th day. The biochemical parameters like total cholesterol (TC), triglycerides (TG), and blood glucose were measured by using standard laboratory methods.

Study II

The study was designed to evaluate the atherogenic dyslipidemia effect of test formulation in atherogenic high cholesterol diet (30% peanut oil and 5 % cholesterol) induced hyperlipidemia and atherogenic property in experimental rats.

Group I: Rats were fed on normal laboratory diet for 30 days act as untreated group (n=6)

Group II: High cholesterol diet (30% peanut oil and 5 % cholesterol) + untreated group (n=6).

Group III: High cholesterol diet (30% peanut oil and 5 % cholesterol) + Test formulation (250 mg/kg /day) twice in a day (125mg/kg/morning, 125 mg /kg evening) for 30 days (n=6).

Group IV: High cholesterol diet (30% peanut oil and 5 % cholesterol) + Drug Statin (2.5mg/kg/day) for 30 days + treated group (n=6).

Collection of blood and assessment of biochemical parameters: After 30 days the experimental rat groups of study II, were fasted every night and blood was collected from retro-orbital plexus . Blood samples were also collected on 1st, 15th and 30th day was allowed to clot and then centrifuged at 2000 rpm for 10 min to obtain clear serum. Blood glucose in serum plasma was estimated by glucose oxidase method [38]. On 30th day changes in biochemical parameters were determined in serum viz., triglycerides (TG), serum insulin, total cholesterol (TC), glucose tolerance, and systolic blood pressure were measured from serum sample using standard laboratory method. TC was estimated by the enzymatic method as described by Allan et al, [42-41], (TGs)were

determined by the enzymatic colorimetric method [39-41]. In blood samples of study II rats, total cholesterol, LDL-c, HDL-c and triglycerides concentration were estimated using standard laboratory methods on 1st, 15th and 30th day, HDL-c was determined by the phosphotungstate method [42,43-46] LDL was calculated by using Friedwald et al .1972 formula [47]. Body weight of each group of both the study animals was recorded at the interval of every one week.

Statistical analysis: Data were evaluated by Student unpaired t-test one way analysis of variance (ANOVA) or two way analysis of variance where appropriate. The level of high statistical significance was set at P <0.001. Data was presented as mean ±SEM.

RESULTS

Study I: Administration of high cafeteria diet (HCD) in rats exhibited marked increase in parameters under investigation like total cholesterol, triglycerides, plasma insulin etc. In addition the high carbohydrate fed rats showed impaired glucose tolerance following standard oral glucose administration (Table 1-4). Table (1-4) depicts the antihyperglycemic effect of test formulation in high cafeteria diet rats at initial, 15th, 30th days. Test formulation was evaluated at 250 mg/kg/day and 500 mg/kg/day. Table showed significant changes in parameters of control group where normal chow diet was given. The lowest dose level showed less significant reduction P<0.01 whereas highest dose 500 mg showed highly significant antihyperglycemic effect P<0.001 in comparison to high cafeteria diet control. The total body weight (TBW) in group III and IV was comparatively less in comparison to group II. Dose dependent decrease in TBW was observed in group III and IV animals. The results also showed that the test formulation mitigates the level on TC, TG and plasma insulin towards normal values in cafeteria diet induced hyperglycemia in rats (Table 1-3).

TABLE 1: Pattern of various parameters associated with metabolic syndrome (Before initial day)

Groups	Parameters				
	TBW (g)	SBP (mmHg)	TC (mg/dl)	TG (mg/dl)	PI (µg/ml)
Group I	138.91±19.45	118.63±3.75	96.42±12.32	109.42±9.72	21.55±5.97
Group II	145.64±20.91	124.90±4.04	90.35±11.45	101.83±8.45	22.86±5.88
Group III	134.93±18.64	121.83±3.94	92.42±10.93	99.62±10.03	22.79±5.88
Group IV	151.82±19.11	120.64± 3.85	93.86±11.68	97.35±8.60	20.62±4.60

Abbreviations: TBW-total body weight, SBP-systolic blood pressure, TC-total cholesterol, TG-triglycerides, and PI-plasma insulin.

Comparison

*vs**	P>0.05	P>0.05	P>0.05	P<0.001	P>0.05
*vs***	P>0.05	P>0.05	P>0.05	P>0.05	P>0.05
*vs****	P>0.05	P>0.05	P>0.05	P>0.05	P>0.05
vs*	P>0.05	P>0.05	P>0.05	P>0.05	P>0.05
vs**	P>0.05	P>0.05	P>0.05	P>0.05	P>0.05

TABLE 2: Effect of test formulation on metabolic markers in experimental study of metabolic syndrome.(After 15 days treatment)

Groups	Parameters				
	TBW(g)	SBP (mmHg)	TC(mg/dl)	TG (mg/dl)	PI (µg/ml)
GROUP 1	135.72±20.40	116.90±5.02	94.10±6.22	105.64±17.01	21.04±4.87
GROUP II	157.66±18.22	131.62±6.32	121.45±4.13	194.73±43.85	31.64±3.90
GROUPIII	81.20±12.45	121.45±4.90	95.12±6.45	167.94±36.90	26.42±3.14
GROUP IV	76.09±11.75	123.84±5.31	96.78±7.11	158.63±33.75	25.36±5.02

Abbreviations: TBW-total body weight, SBP-systolic blood pressure, TC-total cholesterol, TG-triglycerides, and PI-plasma insulin.

Comparison

*vs**	P>0.05	P<0.01	P>0.05	P<0.01	P<0.01
*vs***	P>0.05	P>0.05	P>0.05	P<0.01	P>0.01
*vs****	P<0.05	P>0.05	P>0.05	P<0.01	P>0.05
vs*	P>0.05	P>0.05	P>0.05	P<0.01	P>0.05
vs**	P>0.05	P>0.05	P>0.05	P<0.01	P>0.05

TABLE 3: Effect of test formulation on various markers in metabolic syndrome animal model (After 30th days)

Groups	Parameters				
	TBW (g)	SBP(mmHg)	TC (mg/dl)	TC(mg/dl)	PI(µg/ml)
GROUP I	133.42±15.82	118.94±5.42	97.94±8.12	98.32±20.42	21.64±3.42
GROUP II	172.25±13.98	143.64±6.11	131.42±7.90	288.42±95.68	43.90±5.11
GROUP III	85.38±12.42	125.90±4.87	98.22±4.97	183.45±71.32	30.42±4.82
GROUP IV	81.45±10.86	125.66±4.95	97.35±5.11	177.94±66.45	29.60±4.16

Abbreviations: TBW-total body weight, SBP-systolic blood pressure, TC-total cholesterol, TG-triglycerides, and PI-plasma insulin.

Comparison

*vs**	P>0.05	P<0.001	P>0.05	P<0.01	P<0.001
*vs***	P<0.05	P<0.05	P>0.05	P<0.05	P<0.01
*vs****S	P<0.05	P>0.05	P<0.05	P<0.05	P<0.01
vs*	P<0.05	P>0.05	P>0.05	P>0.05	P<0.01
vs**	P>0.05	P<0.01	P>0.05	P>0.05	P<0.01

TABLE 4: Glucose tolerance test following 15 days and 30 days test formulation treatment

Group	After 15 days				After 30 days			
	0 min	50 min	100 min	150 min	0 min	50 min	100 min	150 min
GROUP I	78.10±7.4	71.35±10.2	……	73.86±5.09	…….	75.82±6.32	68.22±8.01	79.32±6.90
GROUP II	79.45±6.35	188.42±44.10	160.45±17.23	136.82±16.28	124.40±8.25	196.70±25.97	174.22±21.64	148.30±13.45
GROUP III	83.42±7.32	153.94±39.62	133.52±15.2	112.36±11.20	107.98±20.42	141.38±19.90	119.35±16.45	98.42±7.25
GROUP IV	87.10±6.93	147.44±30.18	129.73±16.13	108.94±9.75	105.22±9.68	135.65±8.90	106.35±9.64	93.82±8.33

Comp*vs**	P>0.05	P<0.001	P<0.001	P<0.001	P<0.001	P<0.001	P<0.01	P<0.001
vs*	P>0.05	P<0.001	P<0.001	P<0.001	P<0.001	P<0.05	P<0.01	P<0.01
vs*	P<0.05	P<0.001	P<0.001	P<0.001	P<0.001	P<0.01	P<0.001	P>0.05
vs**	P>0.05	P>0.05	P<0.05	P<0.05	P<0.01	P>0.05	P<0.01	P<0.001
vs**	P>0.05	P>0.05	P<0.05	P<0.05	P<0.05	P<0.05	P<0.001	P>0.05

Study II

Atherogenic diet produced a significant increase in body weight along with marked increase in serum cholesterol and other lipoprotein such as LDL-c with a decrease in HDL-c during the 30 days of treatment with atherogenic diet. A significant mean increase in body weight was recorded in group II. In group II the increase in body weight was significantly higher in comparison to group I. It was observed that co-administration of test

formulation with atherogenic diet, the body weight returned towards normal after 30 days (Table1-4). Table (5-8) depicts the effect of test formulation in cholesterol diet (30% peanut oil and 5 % cholesterol) induced atherogenic activity in rats at initial, 15th, and 30th days. Test formulation and standard drug statin treatment as given in study II experimental design. The conventional drug statin and test formulation both influenced the levels of the parameters and revealed suppressed atherosclerotic process among the treated animal (Table 5-8).

TABLE 5: Role of hydro alcoholic test formulation on Total Cholesterol among high cholesterol diet treated rats.

Groups	TC level(mg/dl)		
	Initial	After 15 days	After 30 month
GROUP II	64.32±7.89	63.80±6.52	64.70±8.42
GROUP II	……	895.42±49.75	480.82±40.72
GROUP III	……	738.44±90.85	378.50±38.20
GROUP IV	……	691.52±78.85	167.42±16.80

Abbreviation- TC total cholesterol

Comparison

*vs**	P>0.05	P<0.001	P<0.001
vs*	…….	P<0.001	P<0.001
vs*	…….	P<0.001	P<0.001

TABLE 6: Effect of test formulation on triglycerides level among high cholesterol diet induced rats.

Groups	TG level (mg/dl)		
	Initial	After 15 days	After 30 days
GROUP I	26.85±8.70	30.32±7.85	28.4±5.52
GROUP II	…..	340.70±64.80	298.50±39.32
GROUP III	…….	260.55±69.85	174.93±21.78
GROUP IV	…….	228.50±31.80	112.85±19.30

Abbreviation – TG Triglycerides

Comparison

*vs**	P>0.05	P<0.001	P<0.001
vs*	…..	P<0.05	P<0.001
vs*	…..	P>0.05	P<0.05

TABLE 7: Effect of test formulation on HDL-c level among high cholesterol diet treated rats

Groups	HDL –c level (mg/dl)		
	Initial	After 15 day	After 30 days
GROUP I	22.5±4.33	23.32±2.85	22.37±3.85
GROUP II	……	17.82±5.32	13.85±1.85
GROUP III	…..	19.6±3.85	21.2±3.85
GROUP 1V	……	20.32±4.85	21.85±3.85

Abbreviation: HDL - High density lipoprotein

Comparison

* vs**	**P<0.05**	P<0.05	P<0.001
vs*	**…..**	P<0.05	P<0.001
vs*	**…..**	P<0.05	P<0.05

TABLE 8: Effect of test formulation on LDL-c level among high cholesterol diet treated rats.

Groups	LDL-C level (mg/dl)		
	Initial	After 15 days	After 30 days
GROUP I	85±4.78	22.75±5.72	24.22±6.85
GROUP II	…...	341.50±62.32	314.40±48.34
GROUPIII	…….	274.50±41.93	142.55±32.08
GROUP IV	……..	255.8±37.38	106.85±16.85

Abbreviation – LDL – low density lipoprotein

Comparison

*vs**	P>0.05	P<0.001	P<0.001
vs*	…..	P<0.05	P<0.001
vs*	…..	P>0.05	P<0.05

DISCUSSION

Obesity is a multi-factorial disorder linked with metabolic syndrome and is a major risk factor of Type 2 diabetes mellitus and Cardio vascular disease therefore ayurvedic formulation and anti-obesity drug targeted not only to reduce body weight but also exert beneficial effectors for high blood pressure, insulin resistance and lipid metabolism. As selection of plants were taken on their bases of chemical constituents, possessing profound pharmacological activity on various targets involved with obesity T2DM and CVD, Insulin resistance and hyperlipidemia . The active chemical constituents present in test formulation which were extracted from various botanical herbal plants have the capability to inhibit lipid metabolizing enzyme (Agarwal et al.,2000)In this paper we discussed the role of ayurvedic formulation inducing in high cafeteria diet experimental wistar rats in the treatment of metabolic syndrome leading with obesity causing type 2 diabetes and coronary heart disease. As this Ayurvedic formulation contain five plant extracts – D.bulbifera one of the ingredient plant present in test formulation found to inhibit the α- amylase and α- glucosidase which effects post prandial hyperglycemia(Ghosh et al ;2011) posseses anti-hyperglycemic and anti-hyperlipidemic activity[51].T. arjuna contain flavonoids and sterols components used as a cardioprotective agent by reducing atherogenic activity as it result in reduction of cholesterol,shows anti-hypertensive and antioxidant effects (Agrawal et al 2000;Chopraet al 1969;Tiwari et al ; 1989; Gupta et al ;2001).T.chebula extract contain triterpenes and flavonoids components used in reduction in blood glucose and absorption of triglycerides ,inhibiting pancreatic lipase activity (Makhihara H.Shimada T.Machida E.),shows activity of anti-hyperlipidemic and anti-hypercholesterolemia. [55][56]. H.rhamnoids contain flavonoids ,vitamin C ,zeaxanthin which shows therapeutic activity in lowering the level of blood sugar and improving insulin sensitivity (Linn et al 2008, Joanta et al .,2009). N. jatamansi have shown significantly reduction in high blood pressure in patients suffering from moderate to severe hypertension (Hamid et al .,1962).It has been discussed the role of ayurvedic formulation and conventional drug used in treatment of metabolic syndrome. According to present study it shows significance evaluation of anti-hyperglycemic and anti-atherogenic activity. Aqueous extract of plant used in preparation of ayurvedic formulation showed a dose dependent anti-hyperglycemic effect in high cafeteria diet rats inducing 250mg/kg/day and 500mg/kg/day doses at point of measurements of initial ,15^{th} days and 30^{th} days and glucose tolerance parameters in study 1 ,shows significance results P<0.001 lowering the level of body weight , total cholesterol ,systolic blood pressure ,triglycerides and enhancing plasma insulin shown in (Table 1-4) whereas in study II inducing conventional drug statin dose dependent showed significant result P<0.001 more effective rather than compare to ayurvedic formulation given to experimental rats showing less effectiveness result shows significance about P<0.01 as shown in (Table 5-8) as anti –obesity drug result in much faster lowering the level of total cholesterol content ,LDL-c and triglycerides and increase the level of HDL-c. The experimental groups treated with the Ayurvedic formulation and anti-obesity drug shows decrease in parameters such as blood glucose, total cholesterol ,triglycerides and insulin resistance result in the treatment of metabolic disorders.

CONCLUSION

It is concluded that metabolic syndrome plays major role in obesity leading with clusters of conditions T2DM and cardiovascular disease . As demonstrated that test formulation taken from botanical source often contain natural active components that act upon various targets, providing an opportunity to simultaneously correct multiple defects associated with metabolic syndrome. Study, demonstrated that test formulation and conventional drugs statin contain pure principles responsible for anti-hyperglycemic and anti – atherogenic property , reduced the effects of parameters and there is an improvement in insulin sensitivity along with increase in circulating adiponectin and adipocyte insulin responsiveness after long term treatment with test formulation . It is observed that test formulation did not reduce the food intake rather it decreases the leptin level and enhances adiponectin with the result it has anti obesity, anti–atherogenic property ,anti inflammatory and anti hyperglycemic potentials and is effective in the management of metabolic syndrome.

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