Original Article

Development And Evaluation Of Anti Diabetic Activity In Polyherbal Tablets Of Local Herbs

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Abstract

Diabetes is of the metabolic disorder that has become one of the major cause leading to morbidity and death around the globe. Anti-diabetic medications that are more effective and have adverse effects less frequently are currently being sought after. Much little study has been done on polyherbal compounds, irrespective of the fact that several individual herbs have been shown to have antidiabetic properties in studies or clinically. It is thought that herbal mixtures made of various plant products have synergistic anti-diabetic properties and may strengthen the intended results. Numerous polyherbal preparations have been investigated as potential therapeutics for the treatment of diabetes. A thorough assessment of the literature was conducted using many significant databases to characterize the present state of research on polyherbal substances for the treatment of diabetes. This research focused on the formulation and evaluation of polyherbal tablets containing extract from leaves of *Phyllanthus amarus***,** *Tinospora cordifolia*, *Momordica charantia***,** *Vinca rosea* available in the local areas of Sambalpur, Odisha, India. Invivo studies showed that the blood sugar lowering effect was found more pronounced in higher dose 500 mg/kg than lower dose 250 mg/kg. The efficacy of 500 mg/kg of the formulation was almost equal to that of standard therapy. Along with it oral glucose tolerance test showed increase in blood glucose level within a period of 30 mins from the starting of test as compared to the initial level of glucose concentration. This hyperglycemia was maintained until 60 min and then began to decrease. The polyherbal formulation proves to be an effective method of treatment of diabetes mellitus thus required to be explored further for better promising results.

Keyword: Diabetes Mellitus, Insulin, *Vinca Rosea*, Polyherbal Tablet, *Phyllanthus amarus*, *Tinospora cordifolia*, *Momordica charantia*

INTRODUCTION

Diabetes is a metabolic condition that affects how proteins, fats, and carbohydrates are processed. Nearly 10% of people worldwide have diabetes, according to a global survey. In the years to come, diabetes is anticipated to continue to pose a serious danger to public health. Reports from various survey conducted postulated that in developing countries like India and china nearly 500 million people will be affected by Diabetes and its compilations caused due to it. [1] Along with it prevalence of the disease will increase globally in the absence of efficient and economical therapies for both forms of diabetes, having a significant impact on the population of emerging nations. Although the preventative activity of these medications against the progressive nature of diabetes and its complications was moderate and not always effective, the positive effects on glycemic levels are widely documented in current medicine. Although insulin therapy provides efficient glycemic control, its limitations include its ineffectiveness when administered orally, short shelf life, need for constant refrigeration, and the risk of fetal hypoglycemia in the event of an excess dosage. Sulfonylurea and biguanide therapy also has negative side effects [2].

The use of alternative medicine has grown in popularity over the past few years for a number of reasons. According to surveys performed in Australia and the United States, respectively 48.5% and 34% of respondents have used at least one form of alternative medicine, including herbal remedies. WHO (1980) also suggested that in situations where we don't have access to safe contemporary pharmaceuticals, we evaluate how effective and appropriate plants are. The demand for herbal products with anti-diabetic properties and minimal adverse effects rises as a result. Additionally, because herbal medications have long been used as folk medicine, choosing ones to test for efficacy is not too difficult [3].

2. MATERIALS AND METHODS

2.1. Materials

2.1.1. Plant material

The leaves of *Phyllanthus amarus***,** *Tinospora cordifolia*, *Momordica charantia***,** *Vinca rosea* were collected from green valley nursery, Sambalpur (Odisha) in Feb, 2020. The plant material used in the sample was thoroughly washed under flowing tap water and then rinsed in purified water before being allowed to dry at room temperature. The plant material was then shade dried for 3 to 4 weeks without being infected. An automated grinder was used to process dried plant

material. Color, odour, flavor, and texture of powdered plant material were evaluated. For phytochemical and biological tests, dried plant material was sealed in an airtight container and stored [4].

2.2. Extraction Method

2.2.1. Extraction by maceration process

100gm of dried plant material were exhaustively extracted with methanolic solvent using maceration method. The extracts were evaporated above their boiling points and stored in an airtight container free from any contamination until it was used. Finally, the percentage yields were calculated of the dried extracts. Extraction of plant product of *Phyllanthus amarus, Tinospora cordifolia, Momordica charantia, Vinca rosea* were done by Maceration method [5].

In Maceration plant materials were crushed and stored in a closed vessel. The vessel was filled with the selected menstruum or solvent. The crushed plant parts were allowed to stand still in the same position for 7 days with occasional shaking. After 7 days liquid were strained off and marc obtained were pressed to obtain the absorbed menstruum. The clarification of the solvent obtained were done by filtration and finally evaporated for getting a concentrated extract.

2.2.2. Preparation of Polyherbal Tablet

In the current study extract powder was taken that was properly dried. Methanolic leaves extract of *Phyllanthus amarus, Tinospora cordifolia, Momordica charantia,* and *Vinca rosea* were implemented by wet granulation in tablet form. Five formulations were prepared by taking combination of above extracts. Combination formulation given as PHF (Poly herbal formulation). Formulations have the following composition [6,7].

Table 2.1. Composition of Formulation of Polyherbal Extract

S.No	Ingredients	Formulations				
		F1	F2	F3	F4	F5
1	Powder of MEPA	75	75	75	75	75
2.	Powder of METC	75	75	75	75	75
3.	Powder of MEMC	75	75	75	75	75
4.	Powder of MEVR	75	75	75	75	75
2.	Dibasic Calcium Phosphate	75	70	65	60	55
3.	Micro Crystalline Cellulose	15	15	15	15	15
4.	Starch	40	45	50	55	60
5.	Magnesium Stearate	10	10	10	10	10
6.	Gelatin	5	5	5	5	5
6.	Talc	5	5	5	5	5
7.	Sodium Benzoate	5	5	5	5	5

MEPA-Methanolic Extract of *Phyllanthus amarus*, METC- Methanolic Extract of *Tinospora cordifolia*, MEMC-Methanolic Extract of *Momordica charantia*, MEVR- Methanolic Extract of *Vinca rosea.*

2.2.3. Evaluation of Tablets [8]

The various physical parameters were used to evaluate the tablets.

2.2.3.1. Organoleptic properties

Size (thickness), shape, color, taste was determined.

2.2.3.2. Weight Variation Test

For determination of weight variation take 20 tablets. Weight these 20 tablets and their average was determined. Compare the average of tablet weight with single tablet. [9]

Table 2.2 -Tolerance to uncoated tablet weight variance

Tablet average weight (mg)	Total deviation percentage allowed
130 mg or less	10 Percentage
130 mg to 324 mg	7.5 Percentage
More than 324 mg	5.0 Percentage

2.2.3.3. Tablet Hardness:

The tablet strength was represented as the capacity of the tensile (Kg/cm^2). The tablet crush load, in which the pressure force needed to break a tablet in half. A tablet hardness tester (Monsanto hardness tester) was used to calculate this. [9]

2.2.3.4. Friability

Friability testing was carried out to evaluate friction and shocks effect. This can often lead to chiping, caping, and breaking of tablets. For this reason, Roche friabilator was used. This machine puts many tablets under the cumulative impact of abrasion. The tablet was shaken in a plastic chamber which rotates with speed of 25 RPM. The tablets were dropped from

height of 6 inch per rotation. The tablets were again weight after dusting. The loss of weight of tablets should not more than 1 %. [9]

% Friability = (Initial weight - final weight) / (Initial weight) × 100

2.2.3.5. Disintegration Time (DT):

One tablet was mounted in each of the six DT apparatus. DT was performed at 37 $\pm 2^0$C Disintegration time defined as time required disintegrating and passing all fragments through the sieve (# 10). [9]

2.2.3.6. Drug Rekease Study:

Drug release was assessed by dissolution test under the following conditions: n = 6 (in triplicate), USP type II dissolution apparatus (Lab India, DISSO 2000) at 50 rpm in 900 ml of 0.1N HCl maintained at 37 ± 0.5˚C. The tablet was allowed to sink to the bottom of the flask before stirring. Special precaution was taken not to form air pockets on the surface of the tablet. Five milliliters of the sample was withdrawn by using a syringe filter at regular intervals and replaced with the same volume of pre warmed (37 ± 0.5°C) fresh dissolution medium. The drug content in each sample was analyzed after suitable dilution using UV spectrophotometer method at respective maximum wave length. The samples were analyzed by measuring the absorbance at 276 nm by UV-visible spectrophotometer (Shimadzu UV-1700). The cumulative percent drug release was calculated using an equation obtained from standard curve.

2.2.4 *In-vivo* anti-diabetic activity of Polyherbal Tablet

2.2.4.1. Animals

The animal experimental protocol was approved by the Institutional Animals Ethical Committee (IAEC), Oriental University, Indore (M.P.). Approval Reference Number, IAEC/ 2019-20/RPO-06. Male & female Wistar albino rats (12-160g) were provided by Oriental University, Indore (M.P.), India. The animals were housed in standard conditions of temperature (25±2^0C) and 12:12h light-dark cycle. The rats were fed with commercial diet and water *ad Libitum*.

2.2.4.2. Acute oral toxicity study [10]

Acute oral toxicity study was evaluated as per OECD guidelines (425) on Wistar albino rats. Animals were provided by Oriental University, Indore (M.P.) and experiment was done in the lab. Before experimentation rats were fasted overnight with water *ad libitum*.

All the animals were weighed and divided into three groups of six animals each. Animals in Group I were control and that were left untreated whereas Group II and Group III were the test groups of polyherbal tablet, respectively. One day prior to the administration of the plant extract, all the animals were fasted for 12 h but had access to water ad libitum.

Each animal of both the test groups (Group II and III) which receives dose of 2000mg/kg. All three animals were received dose of 2000 mg/kg body weight of polyherbal tablet by gavage using oral cannula (limit test). Animals were observed individually for any toxicity sign of gross changes like convulsion, tremor, circling, depression, and mortality. The observations were made at 30 min, 60 min, 2 h, 4 h, 6 h, 24 h and then animals were kept for further 14 days under observation. Administered dose was found tolerable (as no death found). Therefore, two dose levels 250 mg/kg & 500 mg/kg was selected for anti-diabetic activity.

2.2.4.3. Sub-acute Toxicity Study

Sub-acute oral toxicity study was performed as per OECD guideline 407 using adult albino rats. Animals were divided into four different groups where each group contained 6 rats, (3 male & 3 female). For every 28 days fresh dose was prepared by suspending formulation in CMS 2% with vigorous mixing and given once in a day to animals at different dose levels using a feeding needle. Animals were kept under eye for throughout the course of study. All the observation recorded systematically. The visual observations included skin changes, food and water consumption, body weight, aggressiveness, mobility, sensitivity to sound and pain as well mortality. Blood was collected from each animal to analyzed hematological parameters.

2.2.5. *In-Vivo* pharmacological activity

2.2.5.1. Induction of diabetes:

Animals were acclimatized about two weeks before initiation of experiment. Type-II Diabetes was induced to all animals except rats of group-I (Normal control) by giving 10% fructose solution instead of drinking water for three weeks, after third week single dose of 40 mg/kg of STZ was injected i.p. to fasted rats. STZ was freshly prepared in 0.1M citrate phosphate buffer (pH 6.3). Blood glucose level was determined after 48 h, animals having blood glucose level higher than 250 mg/dl were divided in following groups [11].

2.2.5.2 Experimental Design

In the experiment, a total of 30 rats were used. The rats were divided into 5 groups comprising of 6 animals in each group as follows:

Group I: Normal control group
Group II: Diabetic control, Streptozotocin (60 mg/kg b.w.)
Group III: Diabetic rats treated with polyherbal preparation (250 mg/kg)
Group IV: Diabetic rats treated with polyherbal preparation (500 mg/kg)
Group V: Diabetic rats treated with glibenclamide (0.25 mg/kg).

2.2.5.3. Sample collection

Blood samples were collected on day 3, day 7 and day 14 by tail vein and blood glucose levels were estimated using an electronic glucometer (Gluco chek).

Figure 1: Blood collection from animals for determination of Blood Glucose Level

Figure 2: Measurement of Blood Glucose Level with Glucometer

2.2.5.4. Statistical Analysis

All the values were expressed as mean ± S.E.M. The data were statistically analysed by two-way ANOVA followed by Post Bonferrono test. P values < 0.05 were considered as significant.

2.2.6. Hypoglycaemic Activity [12]

2.2.6.1. Oral Glucose Tolerance Test

Animals used for oral glucose tolerance test were categorized into five different groups six (6 Rats) each were used for the study. Different doses of plant extracts will be administered 60 min prior to oral glucose load (2.0 g/kg). Animals were randomly assigned into following groups of six animals each.
Group I: Control received Glucose (2g/kg)
Group II: received Glucose + Glibenclamide (10 mg/kg)
Group III: received Glucose + ayurvedic marketed formulation
Group IV: received Glucose + Polyherbal tablets (250mg/kg)
Group V: received Glucose + Hydroalcoholic extract (500mg/kg)
Blood samples were collected from the tail prior to drug administration and at 0, 30, 90 and 120 minutes after glucose loading. Blood glucose levels were measured using one touch Glucometer (Bayer).

2.2.7. Induction of non-insulin dependent diabetes mellitus:

High-fat diet (HFD) rats develop insulin sensitivity though neither hyperglycaemia nor diabetes. Rats given a high-fat diet develop insulin resistance but neither hyperglycaemia nor diabetes. Streptozotocin (STZ) is now often used to induce both insulin-dependent and noninsulin-dependent diabetes mellitus by inducing cell death via DNA alkylation [13]. Although elevated STZ has been demonstrated to significantly alter insulin secretion, mimicking type 1 diabetes, low-dose STZ has been shown to produce a mild impairment of insulin secretion, mimicking type 2 diabetes in its latter stages. The rats were divided into two different dietary regimens by feeding either normal or high fat diet (HFD) for the initial period of two weeks (52% Fats, 28% proteins and 20% carbohydrates) [14]. After two weeks of dietary manipulation, the body weight and biochemical estimations such as plasma glucose (PGL), triglycerides (TG), total cholersterol and plasma insulin were carried out and the groups of rats fed with HFD was injected intraperitoneally (i.p) with a single low dose of STZ (30 mg/kg b.w) dissolved in 0.1M cold citrate buffer, pH 4.5. After one week Streptozotocin (STZ) the rats was selected for blood glucose levels. Rats having fasting blood glucose (FBG) > 250mg/dl that exhibited random hyperglycaemia and glycosuria were selected for the experiment. The rats were permitted to continue eating their different diets until the end of the experiment.

Table 2.3: Composition of High Fat Diet (HFD)

Ingredients	Diet (g/kg)
Powdered Normal Palates Diet	392
Lard	321
casein	210
cholesterol	15
Vitamin and mineral mix	60
Yeast powder	01
Sodium Chloride	01

*The composition of normal pellet diet (NPD): 4.1% fat, 22.2 % protein and 12.1% carbohydrates, as a percentage of total kcal

2.2.7.1. Experimental Protocol

30 Wistar rats were randomly divided into 5 groups:
Group I: Control group (2g/kg)
Group II: High-fat diet group (HFD)
Group III: High-fat diet + STZ injection group
Group IV: HFD-STZ induced diabetic rats treated with polyherbal tablet (250 mg/kg body weight/rat/day) for 30 days.
Group V: HFD-STZ induced diabetic rats treated with polyherbal tablet (500 mg/kg body weight/rat/day) for 30 days.
At the end of the trial, each group received an oral glucose tolerance test (OGTT) and an insulin tolerance test (ITT); fasting plasma was taken for further evaluation of triglyceride (TG), total cholesterol (TC), and glucose. The insulin sensitivity index (ISI) was determined using fasting insulin and glucose levels.

2.2.7.2. Oral Glucose Tolerance Test (OGTT)

At the end of the experimental period, an OGTT was performed in overnight fasted rats. Fasting blood samples (0 min) were collected and then all rats were administered glucose (2 g/kg, p.o.) in aqueous solution. Blood samples were then collected at 30, 60, 90 and 120 min. The glucose levels in all blood samples were estimated by the method of Sasaki et al. (1972). The level of insulin in the blood samples collected at the fasting and 60th min was determined using the ELISA kit for rat insulin according to the manufacturer instructions (Thermofisher scientific, USA).

2.2.7.3. Insulin tolerance test (ITT)

At the end of the experimental period rats were fasted for 6 h and injected with Insulin (0.75 IU/kg, IP) and then blood samples were collected at 0, 30, 60, and 120 minutes for the measurement of plasma glucose (Zhang et al., 2008). The values are presented as a percentage of initial plasma glucose level.

RESULT AND DISCUSSION

3.1 Evaluation of Developed Polyherbal Formulation

3.1.1 Evaluation of Powder Blends

Table 3.1 Evaluation of Powder Blends

Formulation	Bulk Density (g/mL)	Tapped Density (g/mL)	Carr's Index (%)	Hausner's Ratio	Angle of repose
F1	0.43	0.54	20.37	1.25	25.63
F2	0.47	0.55	14.54	1.17	23.46
F3	0.41	0.57	28.07	1.39	24.42
F4	0.45	0.53	15.09	1.17	25.52
F5	0.46	0.56	17.85	1.21	23.28
F6	0.42	0.58	27.58	1.38	26.62
F7	0.48	0.57	15.78	1.18	24.81
F8	0.46	0.54	14.81	1.17	23.52

3.1.2 Evaluation of Polyherbal Tablets

Table 3.2: Evaluation of Polyherbal Tablets

Parameter	PHF				
	F1	F2	F3	F4	F5
Weight variation	±5.13	±5.36	±4.15	±4.36	±4.03
Hardness (kg/cm^2)	5.28±0.39	5.16±0.48	4.91±0.63	4.33±0.63	4.96±0.83
Friability	0.74±0.06	0.68±0.09	0.83±0.06	0.73±0.04	0.85±0.03
Dissolution Time	25.42±0.27	19.48±0.58	15.39±0.48	18.63±0.63	10.63±0.73
Drug Content	93.26±0.76	95.73±0.48	93.74±0.53	97.58±0.73	98.46±0.57

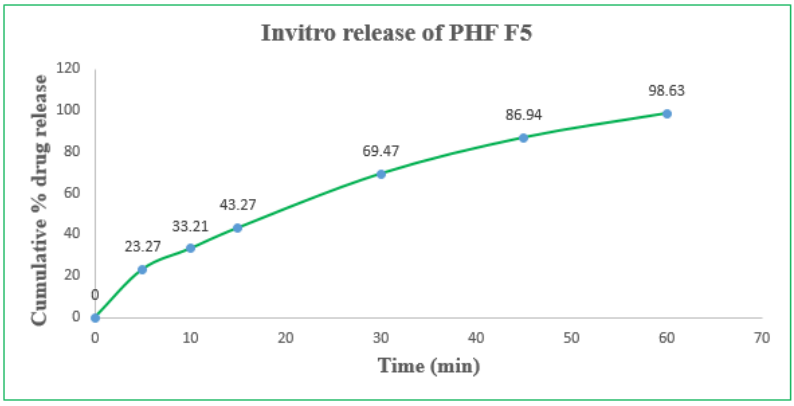

Figure 3: Invitro release of optimized formulation containing PHF

3.2 Stability Study

Table 3.3: Stability Study of Polyherbal Tablet

Physical Parameter	Stability Study for			
	Initial	1 month	2 month	3 month
Colour	Green	Green	Green	Green
Appearance	Smooth	Smooth	Smooth	Smooth
Average Weight (mg)	425	427	426	426
Thickness (mm)	6.05	6.05	6.05	6.05
% Friability	0.82	0.85	0.87	0.87
Disintegration Time (min)	15.35	15.73	16.13	16.36

3.3 Pharmacological Evaluation of the Developed Formulation

3.3.1 Acute Toxicity Study

Table 3.4. Single Dose Acute Toxicity Study of Polyherbal Tablet

Groups	No. of animals	Dose (mg/kg)	Results
1	6	500	No toxic sign
2	6	1000	No toxic sign
3	6	2000	No toxic sign

Table No.3.5:- Effect of optimized polyherbal formulation *on* body weight of diabetic rats.

Groups	Treatment	Body weight (gm)		
		Initial	Day 7	Day 14
I	Normal Control	127.5±3.55	127.0±3.44	127.33±2.5
II	Diabetic Control	235.5±3.53	282.5±2. 5	271.33±2.4 4
III	Glibenclamide, 5mg/kg	286.0±3.38	205.5±2.66	182.5±2.8
IV	PHF, 250mg/kg	274.5±2.5	218.5±2.33	193.5±2.8
V	PHF, 500mg/kg	276.33±2.54	221.5±2.45	183.66±2.5

All values are mean ± SEM, n = 6

Table No.3.6:- Effect of optimized polyherbal formulation on blood glucose level in diabetic rats.

	Groups	Blood glucose (mg/dl)		
		3rd day	7th day	14th day
I	Normal Control	112.33±4.33	114.33±2.45	113.5±3.66
II	Diabetic Control	163.33±2.43	184.66±3.35a***	190.33±3.33a***
III	Glibenclamide, 5mg/kg	140.66±3.66	133.33±2.66 a***, b***	130.5±2.55 a***, b***
IV	PHF, 250mg/kg	158.66±4.55	169.5±3.66 a***, b***	175.33±2.33a***, b***
V	PHF, 500mg/kg	164. 5±3.85	168.5±3.64 a***, b***	170.66±2.33 a***, b***

Values are mean± SEM, n=6. *p<0.05, **p<0.01, ***p<0.001
a- significant difference as compared to control
b- Significant difference as compared to diabetic control

Table 3.7. Effect of optimized polyherbal formulation in Oral Glucose Tolerance (OGTT) Method.

Group	Drug treatment	Initial glucose level(mg/dl)	Final glucose level(mg/dl)		
			0.5 hr	1hr	2 hr
1	Normal	83.6±3.52	92.2±5.84	95.1±7.83	94.6±7.72
2	Diabetic Control	89.6±3.52	136.2±4.11	129.3±5.62	116.6±5.82
3	PHF, 250mg/kg	86.3±4.62*	126.6±8.62*	98.3±7.62*	94.4±7.82*
4	PHF, 500mg/kg	92.5±3.47	129.1±6.56*	108.3±6.52*	98.3±5.48*
5	Glibenclamide (5mg/Kg)	97.3±4.53*	125.3±5.63*	106.6±5.74*	92.3±6.75*

The values are expressed as mean under the curve ±SEM in each group (n=6). Data were analyzed by one way ANOVA followed by Dunnett's test. *P<0.05.

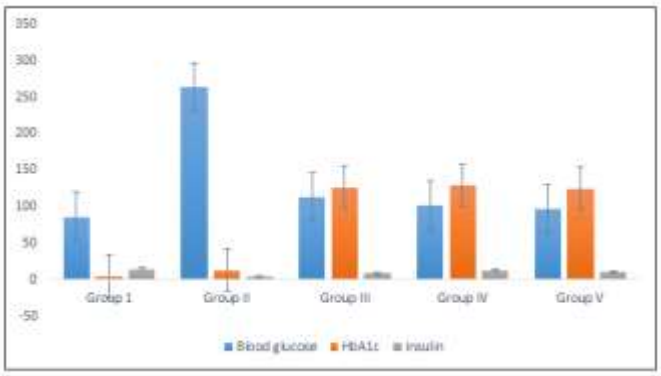

Figure 3.1: Effect of blood glucose, glycosylated haemoglobin (HbA1c) and plasma insulin in control and experimental groups of rats

Table 3.8: Effect of optimized polyherbal formulation in HFD in Oral Glucose Tolerance (OGTT) Method.

Group	Drug treatment	Initial glucose level(mg/dl)	Final glucose level(mg/dl)		
			30 min.	60 min.	120 min.
1	Normal	83.6±3.52	92.2±5.84	95.1±7.83	94.6±7.72
2	Diabetic Control (HFD fed - low dose STZ)	256.3±2.83	328.6±3.62	292.5±6.72	262.3±3.21
3	PHF, 250mg/kg	132.6±3.64*	158.5±4.73*	115.4±4.73*	98.2±7.74*
4	PHF, 500mg/kg	134.5±4.73	162.5±5.73*	108.3±6.52*	98.3±5.48*
5	Glibenclamide	138.5±5.53*	145.4±3.63*	105.6±4.74*	94.6±4.73*

	(5mg/Kg)				

ANTIDIABETIC ACTIVITY

In present study, the effect of various concentrations of formulation was compared to metformin at different time intervals in the Streptozotocin induced hyperglycemic rats. The experimental rats showed a marked increase in blood sugar level after 8th day of induction of diabetes, which was reduced significantly ($p < 0.01$) 50% at twelfth day. The blood sugar lowering effect was found more pronounced in higher dose 500 mg/kg than lower dose 250 mg/kg. The efficacy of 500 mg/kg of the formulation was almost equal to that of standard therapy.

Results obtained from the oral glucose tolerance test showed increase in blood glucose level within a period of 30 mins from the starting of test as compared to the initial level of glucose concentration. This hyperglycemia was maintained until 60 min and then began to decrease (Table 3.6). Polyherbal tablets of optimised formulation significantly prevented the increase in blood glucose levels after 60 min of glucose administration at the doses of 50 mg/kg. Glibenclamide also blocked the increase in blood glucose levels after 30 min.

Table 3.8 shows the levels of blood glucose, glycosylated haemoglobin and plasma insulin in control and experimental groups of rats. In diabetes, fasting hyperglycemia is primarily due to the excessive release of glucose from liver. Liver plays a vital role in the maintenance of normal blood glucose levels and is the primary organ responsible for endogenous glucose production. In fasting condition, liver produces glucose whereas in postprandial state it stores excess glucose in the form of glycogen [15]. Insulin controls hepatic glucose production by regulating the key enzymes involved in gluconeogenesis and glycogen metabolism [16]. Under physiological conditions, HbA1c is formed by nonenzymatic, irreversible covalent bonding of glucose with haemoglobin in the circulation. In diabetes, the level of glycosylated haemoglobin is elevated because of increased glycation of haemoglobin due to persistent hyperglycemia.

Table 7.33 shows the blood glucose levels of control and experimental groups of rats after an oral glucose load. The oral glucose tolerance test (OGTT) is a measure of effective glucose utilization by the system and generally aids in the early diagnosis of diabetes [17]. Diabetic rats showed significantly elevated fasting blood glucose levels compared with control rats. There is no significant difference between control and drug control rats. After the oral glucose load, blood glucose levels peaked at 60 min in diabetic rats and did not return to basal levels over the next 60 min.

Treatment of HFD-STZ diabetic rats with optimized polyherbal tablets as well as glibenclamide resulted in a significant decrease in blood glucose concentrations (at 0 (fasting), 30 and 60 min) when compared with untreated HFD-STZ diabetic rats. In addition, blood glucose levels returned to basal levels 120 min after the oral glucose load in polyherbal tablets as well as Glibenclamide treated HFD-STZ diabetic rats. The result of the OGTT exemplifies the positive impact of polyherbal tablets complex in glucose homeostasis [18].

Many studies have reported that the rats fed with high fat diet (HFD) develop insulin resistance but not frank hyperglycemia or diabetes [19,20]. To investigate the effect of polyherbal tablet formulation on insulin sensitivity, insulin (0.75 IU/kg) was injected intraperitoneally to the control as well as experimental rats and blood was collected at different time intervals 0, 30, 60, 90 and 120 min for the measurement of glucose concentration **table 3.8**. The glucose concentration in diabetic rats was not reduced even after 120 min.

CONCLUSION

Novel methods of treatment for diabetes is essential due to increasing incidents of the disease conditions. Glycation of body proteins brought on by persistent hyperglycemia results in secondary problems that impact the heart, eyes, kidneys, and nerves. It has been consistently demonstrated that regulating blood glucose can postpone the early development of diabetes problems. However, to avoid their consequences, multi-drug regimens made up of drugs from several classes are necessary for multifactorial metabolic illnesses like diabetes. Utilizing polyherbal formulations may help to solve this issue and stop any further consequences. Data from animal research demonstrate that the polyherbal formulations can improve insulin and glucose tolerance in diabetic rodents as well as lower serum glucose. Treatment of diabetes mellitus through herbal methods of treatment are one the highly explored alternative in modern day treatment methods. Various herbal extracts have been studied for the therapeutic effects toward the lowering of blood glucose levels. Based on the extensive literature study different herbal plants were selected for their therapeutic effects towards lowering of glucose levels. The polyherbal tablets formulation were prepared using extract from leaves of Phyllanthus amarus, Tinospora cordifolia, Momordica charantia, Vinca rosea. The results obtained gave a satisfactory conclusion in lowering of blood glucose levels in rodents as well as oral glucose tolerance effects. However further studies are required in evaluation of other qualitative parameter in therapeutic effects as well as better efficacy towards the treatment.

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