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RESEARCH ARTICLE

AN ANTI-HYPERLIPIDEMIC AND HYPOGLYCEMIC EFFECT OF KALONJI (NEGILLA SATIVA) IN ALLOXAN INDUCED DIABETIC EXPERIMENTAL WISTAR ALBINO RATS

[1]Arati Chikaraddi and [2]Yasmeen Maniyar

[1]Associate Professor, Department of Pharmacology, S Nijalingappa Medical College, Bagalkote, Karnataka
[2]Professor and Head, Department of Pharmacology, S Nijalingappa Medical College, Bagalkote, Karnataka

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Corresponding author:
Arati Chikaraddi

ABSTRACT

Background: India is facing heavy burden of NCDs (Non-Communicable Diseaes) because of explosion in the epidemiological transition worldwide. In that mainly diabetes, obesity and cardiometabolic risk factors like dyslipidemia plays a important role in the prevalence of NCDs and hence, increase in the cardio vascular events like atherosclerosis and ischemic heart disease. ***Objective:*** In present study the effect of Kalonji (Negilla Sativa) seed oil is experimented on cardiometabolic risk factors partly i,e dyslipidemia in alloxan induced diabetic albino rats. ***Materials and Methods:*** wistar albino rats of wt 200-250gms were selected and fed with high fat diet for a period of four weeks to induce insulin resistance later direct diabetis was induced by alloxan monohydrate. After induction of diabetes animals fed with standard drug atorvastatin, different doses of Kalonji 200mg/kg, 400mg/kg and 600mg . The data was collected by estimating Bl. glucose levels on day 0, 7, 14 and on 30th day. Lipid profile done with higher dose of kalonji 600/kg body wt. on Day Zero (before treatment) and day 30 (after treatment). ***Results and Conclusion:*** It is observed that high dose 600mg/kg body wt. of kalonji showed significant hypolipidemic activity as compare to control and standard drug atorvastatin 10mg/kg body wt. It showed decrease in total cholesterol and LDL levels significantly as that of standard drug Atorvastatin 10mg/kg. And also Hypoglycemic effect of Kalonji at 600mg has shown a potent action as compared to 200mg and 400mg. Kalonji also has not produced any toxic changes with high. Hence kaloonji (negilla sativa) proves that it has both hepato toxicity, rensl toxicity activity which helps in decreasing the risk factors in the development of CVDs and NCDs.

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INTRODUCTION

Diabetes mellitus (DM) is a global disease, reaching a epidemic proportion worldwide. It is class of metabolic disorder characterized by hyperglycemia as a result of which disturbances in carbohydrate, fat and protein metabolism due to defect in the insulin secretion, insulin action or both[(1)]. This metabolic disorder usually associates with dyslipidemia, .Consequence of this, fat deposition occurs in bl vessels. Abnormal accumulation of fat in bl. vessels called atherosclerosis causing severe complications like blindness, renal failure, cerebro -vascular accidents, ischemic heart diseases etc[(2)] . In addition to this, persistent hyperglycemia inhibits angiogenesis leading to development of vascular complications. More than 80% of deaths occur due to diabetes and its complications in low or middle economic countries [(3)]. According to 10th edition of IDF Diabetic Atlas, the prevalence of diabetes was estimated for the year 2021 and projected to the year 2030 -2045 estimated that 537 million adults have DM hadiabetes, and by 2030 643 million and 2045 783 million adults are projected to be living with DM.

It also showed prevalence is more seen in middle income countries [(4)] like India. India also called "Diabetic capital of world as it has largest number of diabetics. The ICMR 2023 Indian study estimated prevalence in India to be 10.1 Crores. Largest prevalence was observed in Goa (26.4%), Puducherry (26.5%) and Kerala (25.5%) [(5)].It is steadily increasing in the last decade in asian countries mainly due to urbanization lack of physical activity [(6, 7, 8)], increased obesity and hence insulin resistance is the main characteristic feature of Asian Indians. The costs involved in diabetics care are also considerable both for the patient and healthcare system representing 11.5% of the total global health spending. The medical cost occurred in diabetics care for a person are two to five fold higher than those in cured by the people without diabetics. Diabetes is rising in India, because of genetic predisposition and family history, the risk prevalence significantly influence by the presence of obesity, lack of physical activity, changing lifestyle, improved standard of living, erratic working hours, sedentary habits, early availability of fast food are sources reasons why, told by Rohu Baxi,consultant diabetologist at Bombay hospital to BBC.

There are evidences show that improve in the nutrition, overweight, obesity and change in unhealthy life styles will decrease the development of diabetes and its complications chronically. It is an urgent need to address these changes at primordial, primary and secondary prevention of diabetes. Primordial prevention can be done by regular health checkups, healthy dietary habits like including low saturating fats and white sugar, more complex carbohydrates and use of nutrients which have very low hypoglycemic index protect against development of cardiovascular complications and diabetes, even in presence of strong genetic predisposition. At primary level, it can be done by modifying the risk factors like obesity, physical activities, and lifestyle modifications in different ethnic groups. Lastly secondary prevention are concerned with anti diabetic drugs with least adverse effects and in future with gene therapy

Considering these point of view, we conducted a study in experimental animals to see the effect of small nutrient i.e. Kalonji or Negilla Sativa in obese diabetic induced model. Plant extract was chosen because as the increased trend towards traditional medicines with plant resources which are often cheaper, easily available and prepared easily. Kalonji plant seed oil is obtained from traditional medicinal store to see the effect on hyperlipidemia and diabetes in high fat induced diabetic wistar albino rats. Kalonji has been widely used as medicinal value for various reasons. It is also called as black cumin, family of Ranunculaceae. It is an annually flowering plant distributed all over India. It has shown medicinal properties as an astringent, diuretic, anthelimentic, antidiabetic, antioxidant, anti-inflammatory, anticancer and many more. In this study the hypoglycemic and hypolipidemic activity of kalonji, were observed at different doses and compared with standard drugs.

MATERIALS AND METHODS

The materials required are standard drugs ATORVASTATIN and GLIBENCLAMIDE. For glucose estimation Glucometer and hyperlipidemic kits were used for lipid estimations. To induce diabetes-alloxan monohydrate and high fat diet was served to become obese.

STUDY ANIMALS:

Wistar albino rats (200-250 gms) of either sex were selected for the study from central animal house S Nijalingappa Medical College bagalkote, Karnataka. They were housed under standard laboratory conditions maintained at 25 degree Celsius and under 12/12 hour/light/dark cycle and fed with high fat diet, water and libitum. Before starting the study the experimental protocol was approved by the institutional animal ethics committee by the animal regulatory body of the Indian government.

PLANT MATERIAL: The pure form of Kalonji seed oil (Negilla Sativa Seed oil) obtained from traditional medicinal store.

ACUTE TOXICITY: Acute toxicity studies already established by previous studies, has shown safe even at higher doses 2gm/kg body weight. From this 3 doses were chosen as 200mg, 400mg and 600mg/kg body weight for further experimentation.

DIABETES INDUCTION: The induction of diabetes was done by using alloxan monohydrate in the dose of 160mg/kg body weight dissolved in chilled normal saline and given intraperitonially to overnight fasted animals. The rats were kept on 10% of glucose solution in water bottles to prevent death from hypoglycemia. On day 5 fasting blood glucose levels were measured using glucometer. The glucose level less than 250mg/dl were rejected

INDCTION OF HYPERLIPIDEMIA: All group of animals fed with high fat diet for period of 4 weeks to induce insulin resistance. After 4 weeks of high fat diet diabetes was induced into same animals. The basal readings of serum TG, cholesterol and LDL were collected before the induction of DM.

GROUPING OF ANIMALS

GROUP 1: Normal non hyperlipidemic and non diabetic rats fed with normal saline

GROUP 2: Diabetic (DM) controls rats fed with 0.5ml of normal saline

GROUP 3: DM rats treated with GLIBENCLAMIDE 5mg/kg body wt

GROUP 4: DM rats treated with Kalonji (Negilla Sativa) 200mg/kg body wt.

GROUP 5: DM rats treated with Kalonji 400mg/kg body wt.

GROUP 6: DM treated with Kalonji 600mg/kg body weight orally.

BLOOD SAMPLING AND BL.GLUCOSE & LIPID ESTIMATION: Fasting bl. glucose levels were estimated by using glucometre on day 0, 5, 14 and day 30. A 26 gauze size needle was used and it was pricked into one of the tail vein to obtain a drop of blood which was dropped on the strip target site, within 30 secs. bl.sugar levels were displayed in the glucometre. It requires a very less amount of blood, simple and easy procedure. The strips can be stored even at room temp. The results can be correlated with venous bl glucose level by laboratory methods with co-efficient of variation ±10%.

Statistical analysis: Data were presented in the form of ±mean ±SD using SPPS software 15th version.

RESULTS

The study helped to evaluate the effect of Kalonji seed oil in alloxan induced diabetic rats with dyslipidemia. Wistar albino rats of either sex were selected (36 in no.) for the study and marked separately. For the first five groups diabetes was induced by alloxan monohydrate in the dose of 160mg/kg.body wt. and to all the groups high fat diet was given for a period of 4wks later diabetes was induced and high fat diet was continued throughout the study. All the animals were fed with different dose of Kalonji seed oil 200,400 and 600mg/kg body wt. on empty stomach. The bl.glucose levels were obtained on day 7, 14 and 30th day and on day 30 along with bl. glucose estimation, lipids like TG, Cholesterol and LDL levels were estimated for the group VI.

Table 1 explains lipid profile estimation before and at the end of the study with group VI compared to normal group. Negilla sativa 600mg/kg body wt. has shown decrease in the lipid level in blood gradually.

It could also be due to dietary soluble fibers [14] and sterols [15] in kalonji which decreases dietary absorption of cholesterol from gut .and high content of PUFAs decrease serum triglycerides [16,17].

Table 1. Lipid profile in high fat diet induced with alloxan induced diabetic rats of group Kalonji 600mg/kg compared with standard group atorvastatin and normal animals

Group	Total Triglycerides in mg/dl		Total Cholesterol in mg/dl		Total LDL in mg/dl	
	Before treatment	*After treatment*	*Before treatment*	*After treatment*	*Before treatment*	*After treatment*
Normal control	90.18±4.26	98.8±5.4	78.32±4.1	86 .43±1.2	60.4±4.28	64.4±4.43
Atorvastatin 10mg /kg	94.62±3.0	87.32±3.5	75.65±4.2	60.34±4.7	78.5±5.2	52.7±3.24
Extract of N. Sativa highs dose600mg/dl	108.24±8.24	99.4±4	79.54.	68.72±3.1	76.8±4.62	61.5±6.84

Table 2. Blood glucose in mg/dl expressed as MEAN ±SD

	Normal	Control	Standard	Kalonji 200mg/kg	Kalonji 400mg/kg	Kalonji 600mg/kg
Day zero	95.67±15.9	106.00±10.7	92.33±13.5	112.67± 11.7	99.67±9.5	96.50±4.9
Day 7	127.17±24.9	337.67± 50.4	230.17±53.9	294.17± 91.3	198.67±84.2	118.00±43.5
Day 14	94.17±17.394	332.00± 54.3	207.00±61.3	278.67± 87.9	162.83±60.4	118.83±27.7
Day30	101.83±17.4	375.33± 91.3	112.50±6.6	200.50±81.4	93.17±15.6	83.67± 5.8

DISCUSSION

Dm is a chronic progressive endocrine disorder as a result of impaired insulin secretion, insulin resistance and increased glucose production. This usually associated with dyslipidemia means altered levels of lipid and lipoproteins in diabetic patients called diabetic dyslipidemia. It is characterized by elevated levels of triglycerides, cholesterol and VLDL with reduced HDL. Indians develop diabetes at younger age due to fast urbanization of rural areas, improved standard of living in rural area and unhealthy life styles. By analysts it is observed that obesity was the concomitant factor with DM in 60-80% of patients. Recents studies say that prevalence of obesity has been tripled in the last 20 years in developing countries as compared to developed countries. As a result of this vascular complications are seen more in chronic diabetics at an earlier age like CVDs (Cardio Vascular Diseases), which is the single leading cause of death globally. The management of type 2 DM is aimed at control of bl. glucose level to normal and minimize hypoglycemia caused by anti diabetic drugs so as to prevent development of long term complications mainly vascular complications like atherosclerosis and CVDs. Presence of chronic low grade inflammation is a new concept in the pathogenesis of DM [9]

The Current American association of Diabetics [10] and Indian diabetic association for the study of guidelines in the management recommends start of anti diabetic agents with life style modification at diagnosis. Because of severe adverse effects occur with anti diabetic drugs now; the people are shifting to traditional medicine or herbal medicine. As they are easily available, easily prepared and consumed with less or least toxicity and adverse effects. The herbal medicines that commonly used for diabetes are neem, jamun fruit, papaya zinger etc. In this pipe line our study with Kalonji has shown potent hypolipidemic property with hypoglycemic activity at thre dose of 600mg/kg body wt..The hypolipidemic activity was due to presence of thymoquinone which was shown to inhibit non enzymetic lipd peroxidation in liposomes [11] and works as antioxidant. Many recent studies reveal that antioxidants capable of neutralizing free radicals are effective in preventing experimentally induced diabetes in animal models [12,13].

The hypoglycemic role seen could be due to anti inflammatory action on pancreas increase insulin secretion and its due to increased peripheral utilization of glucose[18,19] .So this can be used as adjuvant to oral antidiabetic drug in diabetic control. The most widely used pharmacological agents for the treatment of dysplipidemia in patients of CAD are “statins”. Hepatotoxicity has been described with all statins and usually manifests as asymptomatic elevation of serum transaminases (aminotransferases). Persistent elevation greater than three times the upper limit of normal are considered significant and treatment should be discontinued if this occurs (Zhao et al., 2019)[20]. Hence naturally available drugs having multifold properties such as lipid-lowering and anti-oxidant activities and other are in more demand. In this study it clearly mentions that even with very high dose of kalonji seed oil has shown no toxic effects on major systems on liver and kidney. So naturally, easily available resources will be a main platform for the synthesis and development of new medicine for the betterment of society especially in developing or low socio-economic countries like India.

Glossary

CVD: Cardio Vascular Disease
DM: Diabetes mellitus
NCD: Non Communicable Disease

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