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Original Paper

Evaluation of Hypoglycaemic, Hypolipidemic and Antioxidant Potential of *Trigonella foenum-graecum L.* (Fenugreek) Seeds in Type-2 Diabetics Living in Southern Rajasthan

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ABSTRACT

Background:

Diabetes mellitus is a syndrome characterised by disorders of carbohydrates, proteins and lipids metabolism due to insulin deficiency and/or insulin resistance. It has been noted with increasing frequency in India, where it is rising as an epidemic. According to ICMR-INDIAB-17 study, the prevalence of diabetes in India is 11.4%. It has therefore, rightly said that in the coming time, India is going to be the capital of diabetes.

Herbal remedies had been tried in the treatment of diabetes mellitus by the Traditional Indian system of medicine. A large number of herbal remedies have been subjected to scientific investigations by many research workers. These are Amla, Karela, Jambu, Giloy, Neem, Guggul, Guargurti Black Gram etc.

The effect of methi (Trigonella foenum-graecum L.) in diabetes (Madhumeh) has been mentioned in ancient scriptures like Susruta Samhita (2000-1000BC). Charak also found methi to be useful in this disease. The hypoglcemic property of methi has been demonstrated and confirmed by various scientific workers in last decade. In view of that, the present placebo controlled study was designed to evaluate the effect of methi on blood sugar, blood lipids and lipoprotein oxidation susceptibility in patients of type 2 diabetes from southern Rajasthan.

Methods:

This study was single blinded placebo controlled, conducted on thirty patients of type 2 diabetes, who were uncontrolled on oral hypolipidemic drugs. They were randomly divided into two groups of 15 each.

- ***Group 1:** Treated group (N=15) - Administered 25 gm of fenugreek seed powder with water 20 minutes before lunch and dinner for 1 month*
- ***Group II:** Control group (N=15) - Administered placebo for one month*
- *Blood samples were collected at day one (basal sample), at 15th day and at 30th day of the study and analysed for blood sugar, blood lipids and lipoprotein oxidation susceptibility.*

Results:

It was observed that administration of 25 gm fenugreek seeds resulted in significant decrease in fasting and postprandial blood sugar levels. However, the blood sugar levels were still in higher range. Fenugreek does not seem to have blood lipids

lowering effect on short term administration. However, it significantly increases HDL-C level at the end of one month. Lipoprotein oxidation susceptibility remained unaffected.

Conclusion:

Fenugreek seeds have potential antihyperglycemic activity without significant lipid lowering effect. The HDL-C raising property needs further attention. Study with higher doses and longer duration of treatment may bring more beneficial results.

KEYWORDS: Phytomedicine, Methi, Antihyperglycemic agents, Lipid peroxidation

INTRODUCTION

Diabetes has been known to mankind from ancient times. The Egyptian Papyrus ebers (circa 1500 BC) described an illness associated with passage of excessive urine and referred it the word, polyurea, which, the Egyptian physician may have meant diabetes. It was the Greek physician, the renowned Aretaous of Cappocia who gave the name diabetes to this illness. He made a complete clinical definition describing it as a melting down of flesh and limbs in urine. Nothing much happened in the understanding of the disease until the Beta cells of Islets were described by Langerhan's in 1889. Pure insulin was discovered by Banting and Best in 1922 which revolutionised the outlook for those suffering from the disease for the first time were able to live with the ailment for quite a long time. The spurt in research on diabetes has really begun with this epoch making discovery and within a span of 60 years there has been tremendous advances in all aspects such as a hereditary and environmental factors, metabolic abnormalities, pathophysiology of complications and management.

The exponential rise in the cases of diabetes all over the world is surprising. According to the International Diabetes Federation (IDF), one in ten adults around the world currently live with diabetes and the total number is predicted to increase to 783 million by 2045[1].It is a matter of serious concern that India has the second highest rate of diabetes in the world[2]. According to the ICMR-INDIAB-17 study, the prevalence of diabetes in India is 11.4% affecting 101 million people[3].

The syndrome of diabetes mellitus is characterised by disorders of metabolism of carbohydrates, proteins and lipids due to insulin deficiency and/or insulin resistance[4]. It is third commonest disease in the world next only to cardiovascular and oncological disorders, affecting at least 10.5% people throughout the world[1].

Some progress has been made in understanding the genetic form of the pathogenesis of type 2 diabetes. Studies of monozygotic twins have shown that genetic factors are more important in the development of type 2 than type 1. Type II (NIDDM) diabetes have two pathophysiologic defects (a) abnormal insulin secretion (b) resistance to insulin action in target tissue[5].

However, the role of oxygen free radicals in this disorder has only recently attracted the attention of many research workers in this field[6-8]. Also in the past three to four decades there had been increasing emphasis on different degrees of tissue damage caused by oxygen free radicals. A free radical can be defined as an atom(s) or a group of molecule capable of independent existence that contains one or more unpaired electrons. These can be formed by loss of a single electron from a non-radical or by gain of a single electron by a non-radical. Free radicals can occur as both organic and non-organic molecules are highly reactive and thus transient. Free radicals are generated in vivo, as a by product of normal metabolism, Because of the ubiquity of molecular oxygen in aerobic organisms and its ability to readily accept electrons, oxygen cantered free radicals are often the mediator of cellular free radical reactions.

In aerobes, during cellular metabolism an enormous number of reactions both enzymatic and non-enzymatic reduce the molecular oxygen (O_2), to superoxide radical (O2-), hydroxyl radicals (OH) and hydrogen peroxide (H_2O_2). The generation of free oxide radicals are responsible for wide spread and indiscriminate oxidation and peroxidation of proteins, lipids and DNA which lead to tissue damage and cell death.

Lipid peroxidation represents one form of tissue damage caused by oxygen free radicals. The unsaturated bonds of cell membrane lipids, cholesterol and fatty acids can readily react with free radicals and undergo peroxidation. Eventually it causes destruction of membrane lipids yielding lipid peroxides, lipid alcohol and aldehyde by-products. Peroxidation of fatty acids containing three or more double bonds will produce Malondialdehyde (MDA). The presence of MDA can be measured by thiobarbituric acid assay and it correlates with extent of lipid peroxidation[9].

Since free radicals are continuously being formed by normal process and cellular metabolism, they must be detoxified to keep body in physiologic tone. This detoxification done by two sets of substances:

(a) Several enzyme systems

1. Superoxide dismutase (SOD)
2. Catalase
3. Glutathione peroxidise

(b) Non-enzymatic free radical scavengers

Vit. E, C, Retinol, Mannitol, Selenium etc.

Superoxide dismutase is an enzyme which scavenges the superoxide radical by dismutation and thus provides defence against the free radical damage. Catalase is a haem containing enzyme, a scavenger of hydrogen peroxide, present in many tissues[9].

Recently free radicals have been implicated in the pathogenesis of diabetes mellitus and its long term complications suggesting there by the oxidative stress generated by free radicals may be a common factor in the diverse pathophysiological mechanisms leading to development of Diabetes mellitus as well as its long term complication[6-8].

Complications due to small blood vessels involvement is specific to diabetes. Hyperlipidemia is another major problem. Of all diabetics about 30-40 percent exhibits some degree of hyperlipidemia[10] and the incidence and severity of the derangement of lipid metabolism appears to be related to the severity and duration of diabetic state.

Although euglycemic state can be achieved in diabetes patients by conventional insulin and oral hypoglycemic drug treatment, this is only one facet in the management of diabetic syndrome. Correction of blood glucose abnormality does not necessarily mean lowering in the incidence of complications particularly the life threatening microvascular and neurological sequelae[11]. Insulin has also been reported to increase cholesterol synthesis[12] and secretion of very low density lipoprotein[13].

Adherence on carbohydrate restricted diets also tends to the development of insulin resistance and the serum-cholesterol are raised in diabetic patients[14]. These drugs have many side effects apart from being costly. Because of these limitations search is still going on to get drugs which are safe, effective and economic.

Since the time of Charaka and Sushruta several herbal remedies had been tried in the treatment of diabetes mellitus by the Indian system of medicine[15,16]. A large number of herbal remedies have been subjected to scientific investigations by many research workers. These are namely Amla, Karela, Jambu, Geloy Neem, Guggul black gram guargurti[17,18,19]. Epidemiological studies have shown that prevalence of diabetes is lower in the population with high fibre intake diet. Some studies have also reported decrease incidence of complications in those geographical area, like India and Japan where there is increase consumption of fibre in diet[20-22].

The effect of methi in diabetes (Madhumeh) has been mentioned in ancient scriptures like Susruta Samhita (2000-1000BC). Charak also found methi to be useful in this disease[23-25]. This property of methi on blood sugar has been demonstrated and confirmed by various scientific workers in the past[26-29]. Currently, the applicability of fenugreek seeds in diabetes has been studied from various part of the world, including Asia[30], India[31], the Middle East[32], and North America[33].

The exact mechanism by which methi lower the blood sugar is not known. Their blood sugar lowering effect may have been brought about by their possible antioxidant property and high fibre content. According to Fuller et al 2015[34], disogenin, a steroidal saponin, maintains insulin signalling and glucose homeostasis. The abundant dietary fibre of fenugreek such as galactomannan, inhibits glucose and lipid absorption in the digestive tract. Seeds of methi is also have mucilaginous, demulcent, diuretic, tonic, galactogogue, carminative, emmenogogue, astringent, emollient, aphrodisiac properties[25]. Based on these facts and observations, the present study is an attempt to observe the effect of methi on blood glucose, blood lipid and lipid peroxidation in patients of type 2 diabetes mellitus.

LITERATURE SURVEY

FENUGREEK *(Trigonella foenum-graecum L.)*[23-25]

The plant of fenugreek; botanically known as Trigonella foenum-graecum belongs to family Fabaceae. It is locally known as Methi and cultivated throughout India, for culinary, fodder and medicinal purpose. There are two types of methi:

1. The ordinary methi or desi methi
2. The scented methi known as kasurimethi. The flowers of desi methi are white. The pods are straight and 6-7 cms long while kasturimethi bears bright, orange yellow flowers and smaller sickle shaped pods. Unlike desi methi, the cultivation of kasturimethi is confined to northern India particularly Punjab and Rajasthan.

Chemical Composition[35]

The chemical composition of seeds (mg/100gm) is as follows:

Moisture	13.7%	Fibre	7.2%
Fat	5.8%	Ash	3%
Crude protein	26.2%	Thiamine	0.34mg%
Calcium	160mg%	Nicotinic acid	1.1mg%
Phosphorus	370mg%	Sodium	19.0mg%
(Phytin P 151 mg)			
Iron	14.1 mg	Potassium	530 mg%
(lonised 1.5)			
Carbohydrate	44.1%	Carotene	96µg%
Riboflavin	0.29mg%	Folic acid	84µg%
		(Free 14.5µg)	

Germinating seeds also contain pyridoxine, cyanocobalamin, calcium pantothenate, biotin and vitamin C. It is a good source of vitamins and germination brings about an increase in vitamins.

CARBOHYDRATES

Young seeds contain small amount of low molecular weight carbohydrates consisting mainly of sucrose, glucose, fructose, myoinositol, galactinol, stachyose and traces of galactose and raffinose. Two galactose containing compounds tentatively identified as verbascose and digalactosylmyoinositol are reported to be present. With increase in maturity of seeds the proportion of stachyose increases, whereas that of sucrose, glucose and galactinol decreases. Very little myoinositol is present in mature seeds. The seeds are reported to contain small amount of xylose and arabinose[36].

Proteins

The seeds contain 30 percent of crude protein. The common protein solvents are distilled water, saline solution and 70 percent alcohol extract respectively contain 15, 25 and 5 percent of the total protein nitrogen of the seeds. The analysis of albumin, globulin and prolamin extracted by these solvents have essential aminoacids which have following values:[37]

- Lysine 4.9, 1.7, 0.5
- Histidine 2.8, 11.6, 0.4
- Cystine 1.2, 0.6, 3.0
- Arginine 9.3, 11.2, 2.3
- Tyrosine 2.0, 5.7, 4.3
- Tryptophan traces 0.5, 2.4

An analysis of the total protein of seeds (extracted by 0.2 percent NaOH) for its amino acids give the following value of percent protein, lysine 8, Histidine 1.1, arginine 8, tyrosine 3, aspartic acid 9, glutamic acid 9, serine 6, glycine 9.5, threonine 5, alanine 5.9, phenylalanine 1, leucine 11, proline 1 and valine + methionine 6. The limiting amino acid is tryptophan[38].

The globulin is characterised by a surprisingly high content of histidine which is about four and a half times the average amount contained in other related globulins obtained from leguminous seeds. The albumin appears to contain phosphorus and sulphur in the molecule. In this respect the composition of the fraction approaches the casein of milk. The protamin contains a low percentage of cystine and tryptophan. The nutritive value of the protein as assessed by WHO/FAO 1965 scoring procedure (based on the pattern of essential amino acids in eggs protein) is 65.

Fats

The seeds contain 6-8 percent fatty oil with a foetid odour and bitter taste. The component of fatty acids in oil are (weight % of total acids) palmitic 9.6, stearic 4.9, arachidic 2, behenic 0.9, oleic 35, linoleic 33.7, linolenic acid 13.8. The unsaponifiable matter contains a lactation stimulating factor[39].

Other Components

Reutter has noted the presence of several alkaloids such as methylamine, dimethylamine and trimethylamine as well as choline, neurine and betaine which are derived from the splitting of lecithins. Its chemical composition resembles that of Cod liver oil, owing to its containing substance rich in phosphates, lecithin and nucleo-albumin. It also contains considerable quantities of iron in an organic form which enables it to be readily absorbed.

The seeds contain four flavonoid compound (2 glycosides and 2 aglycons) and 2 steroidal saponinsdiosgenin and gitogenin in 9:1 ratio. Another sapogenintigogenin is reported to be present in traces. The presence of a few more sapogenius including yamogenin is also reported. An alcoloidtrigonelline and choline is also present in seeds[40].

Actions

Seeds are mucilaginous, demulcent, diuretic, tonic, galactagogue, carminative, emmenogogue, astringent, emollient, and aphrodisiac. Like the alkaloids of cod liver oil, the alkaloids of fenugreek seeds stimulate the appetite by their action on the nervous system, and also produce a diuretic or ureopoietic effect[24].

Uses[40]

1. The seeds are used as a condiment and for flavouring food preparations.
2. They have a strong odour and slight bitter taste. They may be eaten raw or cooked. They are constituent of curry powder.
3. In South India seeds are widely used as a partial substitute for dehusked black gram in preparation of butter for dosa. In Egypt, ground seeds are, mixed with wheat flour for making bread. In Switzerland they are used for flavouring cheese. Roasted seeds are used as a substitute for coffee in some parts of Africa. In USA seeds are used in the preparation of chutneys and in various spicy blends.
4. Fenugreek extract is used as a flavouring ingredient of imitation maple syrup.
5. They are used externally in poultices for boils, abscesses, and ulcers and internally as emolient for inflammation of intestinal tract.
6. They find application also in veterinary medicine and are used in poultices, ointment, plasters and form a constituent of "condition powders" for horses, cattle and sheep.
7. The aqueous extract of the seeds shows antibiotic activity against micrococcus pyogens versus auscus.
8. The seeds are used in colic, flatulence dysentery, diarrhoea, dyspepsia with loss of appetite, diarrhoea chronic cough, dropsy.
9. Blum stated that fenugreek can be employed as substitute for cod liver oil in every case in which later is indicated such as lymphalism, scrofula, rickels, debilily following diseases or neurasthenia, as well as in gout and diabetes in which it may be combined with insulin[24].
10. Growth and nitrogen balance studies on rats have revealed that supplementation of raw or germinated fenugreek at 10

percent level increases the biological value of the food mixture containing rice and black gram.

11. Hypoglycemic effect: When 25 grams of fenugreek seeds were administered to diabetic patients for 21 days, a significant improvement in plasma glucose response was observed. Their insulin requirement was also reduced from 56 units/day to 20 units/day after 8 weeks of treatment.

Khosla *et al.* studied the effect of fenugreek on blood glucose on diabetic rats. Fenugreek was administered 2 and 8 grams/kg dose orally to normal and alloxan induced diabetic rats. It produces a significant fall ($p<0.05$) in blood glucose level in the normal as well as diabetic rats and the hypoglycemic effect was dose related[26].

National Institute of Nutrition (NIN), Hyderabad conducted controlled trials in man and experimental animals aimed at studying the effects of fenugreek on lowering of blood glucose and hypercholesterolemia. When rats fed on cholesterol risin raising diet were given. Fenugreek at 60, 30 and 15 percent levels, elevation of serum cholesterol was prevented, LDL and VLDL cholesterol was lowered. HDLc and triglycerides were not affected. Ratio of HDL-cholesterol to total cholesterol was significantly increased ($p<0.01$). Thus it has cholesterol lowering effect on exogenous cholesterol but not on endogenous cholesterol[27].

Among various components of fenugreek only fibre and saponin components of seeds showed cholesterol lowering activity[41]. Fenugreek shown was to bring about hypocholesterolemic effect through increased excretion of faecal bile acids and sterols; depletion of cholesterol stores in liver also involved. Technological Research Institute at Mysore showed that dietary fenugreek stimulates bile formation in liver and could also connect cholesterol into bile salts[42].

Sauvaire and associate observed and found the implication of steriodsaponins, and sapogenins, in the hypocholesterolemic effect of fenugreek. The transformation of fenugreek subtractions, rich in steroid saponins, was studied upon their passage through the digestive tract to determine the contribution of saponins and/or diosgenin and other stroidsapogenins to the hypocholesterolemic effect of fenugreek seeds. Feces of alloxan diabetic dogs fed fenugreek sub-fractions were analyzed, and diosgenin, smilagenin and gitogenin were identified and measured using capillary gas chromatography/mass spectrometry. Our results show that saponins are, in part (about 57%), hydrolyzed into sapogenins in the digestive tract. It appears that saponins may be implicated, alone or together with diosgenin, in the observed hypocholesterolemic effect of fenugreek seeds in diabetic dogs[43].

Diabetes and Hyperlipidemia[44,45]

In general, the major classes of plasma lipids are cholesterol, cholesterol esters, triglycerides and phospholipids. Lipids are insoluble in water and for this transportation in blood they need carrier proteins known as apoproteins or lipoproteins. Lipids are complexing with apolipoproteins becomes a molecule known as lipoproteins. The lipoproteins present in plasma are chylomicrons, very low density lipoproteins (VLDLs), low density lipoproteins (LDLs) and high density lipoproteins (HDLs).

Of all diabetics about 30-40 percent exhibits some degree of hyperlipidemia that can be attributed to-

- Triglyceride over production related to increased hepatic lipogenesis from carbohydrates
- Delayed clearance of plasma triglycerides due to decreased peripheral action of insulin.
- Decreased lipoprotein lipase activity especially of tissue lipase
- Increased endogenous synthesis of cholesterol due to excess of immediate precursors such as acetyl CoA and HMG-CoA.

Although recent advances have been obtained in the understanding of lipid abnormality in diabetic subjects during last decade or so, it was as early as in 1916 that Bloor commented that marked increase of blood lipids could occur in severe and long standing diabetic patients.

Chase and Glasgow have incriminated that premature ischemic heart disease which occurs in diabetic patients is due to the lipid abnormalities[44]. Robinowitch observed that hyperlipidemia in diabetics was closely related with duration and severity of diabetes mellitus[45].

Bannion et al. observed that hyperlipidemia is more marked in patient of maturity onset diabetes mellitus, probably because of enhanced cholesterol production due to obesity, uncontrolled hyperglycemia which may be independent and additional cause, hyperinsulinemia due to insulin resistance leading to over production of VLDL and decreased removal of VLDL due to deficiency of lipoprotein lipase[46]. Abnormally raised lipids in diabetes needs attention because they can cause diabetic complications such as diabetic peripheral neuropathy[47] and diabetic retinopathy. Furthermore, the presence of dyslipidemia in diabetes further increases the risk of developing cardiovascular disease[48].

In 1972 Santen et al, reported that insulin treated diabetes on an average do not differ from age-matched non-diabetics in regard to serum cholesterol (LDL) and triglyceride (VLDL). The only consistent and most significant finding was an increase of mean HDL-cholesterol levels in diabetics than non-diabetics[49].

Free Radical and Lipid Peroxidation[50-54]

Oxygen has two faces, one benign and other malignant, we are so accustomed to an aerobic life and tend to forget that oxygen and some of the partial reduction products of oxygen can be very dangerous substances. Organisms that require oxygen commonly require it within relatively narrow limits of concentration. Many obligate anaerobes can be killed by high concentration of oxygen.

Because of the ubiquity of oxygen and its ability to readily accept the electrons oxygen cantered free radicals are often the mediators of cellular free radical reactions. The various oxygen free radicals are superoxide 'anion radical (O_2-), hydroxyl radical (OH*) and singlet oxygen (O_2*).

A free radical in an atom or molecule with an unpaired electron. A related term reactive oxygen species is used to describe collectively not only the oxygen derived free radicals but also the non-radical oxidants like hydrogen peroxide (H_2O_2), hypochlorous acid (HOCI) which are not unpaired electron[54].

Molecular oxygen in its ground state contains two unpaired electrons which spins in the same directions. Singlet oxygen is formed when absorption of energy shifts one of these electrons in an orbit of higher energy with inversion of spin[55].

1) Superoxide Radicals:

When oxygen accepts one electron it is converted to superoxide anion (O_2-) radical that can act as an oxidant and reductant. When it acts as an oxidant it is reduced to hydrogen peroxide (H_2O_2) and when it acts as a reductant it is oxidized to molecular oxygen.

Superoxide anion can be formed in the cells by any number of enzymatic and non-enzymatic oxidation of molecular oxygen. The various studied reactions as sources of superoxide are:

- Xanthine oxidase reaction
- Autooxidation of haemoglobin
- Oxidation of epinephrine
- NADPH cytochrome-C reductase
- Oxidase of flavins and flavoprotein
- Polymorphonuclear. Leukocytes produce superoxide radicals during ingestion of bacteria.

Superoxide radicals are involved in mechanism of lipid peroxidation. Superoxide radical is far less harmful than hydroxyl radical and produce direct injury at few cellular sites. Superoxide radical lead to generation of hydroxyl radicals, H_2O_2 and singlet oxygen.

2) Hydrogen peroxide: Hydrogen peroxide is another mediator of free radical induced cell injury. It may be formed by the following reactions:

a) Divalent reduction of oxygen in presence of enzymes-urate oxidase, glycolate-oxidase etc.

b) Univalent reduction of oxygen to oxide radicals and formation of H_2O_2

Hydrogen peroxide readily reacts with superoxide to form hydroxyl radical.

$H_2O_2+O_2 \rightarrow O_2+OH^* + OH^*$ (Haber Weiss Reaction)

In biological system it reacts with metallic ions like ferrous to form hydroxyl ions

$Fe_2+ + H_2O_2 \rightarrow Fe_3+ + OH^* + OH^*$ (Fenton reaction)

3) Hydroxyl Radicals:

Hydroxyl radical cause maximum damage to biological system

$OH- + H_2O_2 \rightarrow HO_2- + H_2O$

Free Radical Toxicity: Oxygen free radicals are capable of reversibly or irreversibly damaging compounds of all biochemical classes including nucleic acids, proteins and free amino acids, lipids and lipoproteins, carbohydrates and connective tissue macromolecules. These have impact on cell activities such as membrane function metabolism and gene expression[54].

The primary damage' can lead to depletion of NADH, reduced glutathione, ATP and to rises in cytosolic calcium ions all of which can cause cell damage. There has been extensive evidence to implicate free radicals in playing some role in development of many diseases. Much of the evidence is based on the experimental data, indicating increased rates of lipid peroxidation in diseased tissue and anchorating effects of antioxidant or both[56].

Diseases associated with increased free radical production[56]

1) Degenerative Diseases

- Ageing
- Atherosclerosis
- Cataract
- Parkinsonism

2) Ischemic and Cardiovascular Diseases

- Cerebrovascular Ischaemia (Stroke)
- Coronary Heart Disease
- Hypertension
- Incomplete Ischemia
- Multisystemic Organ Failure (hepatic, renal, pulmonary)
- Reperfusion and Complete Ischemia
- Acute Tubular Necrosis
- Cardiopulmonary Bypass
- Circulatory Bypass

3) Inflammatory Diseases

- Arthritis
- Behcet's Disease

4) Progressive Systemic Sclerosis

- Immunological Diseases
- Connective Tissue Diseases

- Diabetes mellitus including Diabetic Microangiopathy, and Retinopathy
- Hepatitis
- Immune Deficiencies
- Vasculitis

5) Infectious Diseases

- Mucocutaneouslymphnode Syndrome (Kawasaki's disease)
- Chronic and Severe Viral Eruptions

6) Gastrointestinal

- Crohnn's Disease
- Peptic Ulcer
- Ulcerative Colitis

7) Chemical Induced

- Alcoholic Liver
- Bleomycin
- Paraquat

8) Respiratory Disease

- ARDS (Adult Respiratory Distress Syndrome)

9) Skin and Appendages

- Burn and Wounds
- Dermatitis
- Dermatitis Herpetiform

10) Environmental

- Chemical Carcinogens
- Smoking and Air Pollutants
- Radiation from;
- Excessive Exposure to Sun
- Nuclear Reactors Radiotherapy

11) Miscellaneous

- Carcinogenesis, Mutagenicity, Cytotoxicity
- Eclampsia
- Organ Transplantation, Organ Preservation
- Retrolental Fibroplasia

Lipid peroxidation has been suggested to be associated with a variety of pathological processes. The mechanism of free radical mediated lipid peroxidation involves at least three distinct phases.

1. Initial Step:

When free radicals interact with polyunsaturated fatty acids (PUFA) and extract a proton forming fatty acid radical.

2. Propagation Step:

Fatty acid radical reacts with oxygen, generating a fatty acid peroxyradical which reacts with other lipids, proteins or free radicals perpetuating the transfer of protons with subsequent oxidation of substrates.

3. Terminal Step:

a) Glutathione peroxidase can enzymatically reduce the lipid hydroperoxides to non- reactive hydroxyfally acids.

b) The bond rearrangement in fatty acids may cause formation of diene conjugates or degradation products such as malondialdehyde, 4-hydroxyenal.

c) Free radical scavengers can also terminate the radical chain reaction by reducing the level of peroxide radicals.

Malondialdehyde (MDA)

In response to oxidative stress when lipid peroxidation occurs, a great variety of aldehydes are formed by breakdown of lipid hydroperoxides in biological system. Some of the aldehydes are highly active and may be considered as second toxic messengers which disseminate and augment initial free radical reaction.

Among many aldehydes which can be formed during lipid peroxidation, the most intensively studied are:

- Malondialdehyde (MDA)
- Hydroxyalkenals (HNE)

In aqueous form MDA can occur in various forms depending on pH. In acidic pH it is in tautomeric enol form and in alkaline pH it is in enolate form. MDA in biological sample results mainly from the oxidative degradation of PUFA with more than two double bonds. In humans, the precursor for MDA is therefore the arachidonic acid.

In the mechanism proposed by Esterbaner (1991) the principal steps of MDA formation in case of arachidonic acid involve a successive degradation of fatty acid chain to hydroperoxyaldehyde which yield MDA.

In liver MDA is oxidatively metabolised to CO_2 and H_2O. In this process mitochondrial aldehyde dehydrogenase first converts MDA to malonic acid semi-aldehyde which spontaneously decarboxylates to acetaldehyde. This is oxidized to acetate further to CO_2 and H_2O. Level of MDA has been frequently used as an indicator of lipid peroxidation in various disease states.

Antioxidants

Since the free radicals are continuously being formed in small amounts by normal process of cellular metabolism, all aerobic cells possess mechanism to mitigate their harmful effects. Cells contain various enzyme system as well as free radical scavengers for removing oxygen free radicals and their products. The balance between the production and catabolism of free radicals by cells and tissue is critical for the maintenance of their biological integrity.

Various Defence Mechanisms include:

a) Enzyme Systems

- Superoxide dismutase (SOD)
- Catalase
- Peroxidases e.g., glutathione peroxidase

b) Non-enzymatic (Free radical scavengers)

- Alphatocopherol (Vit. E)
- Ascorbate (Vit. C)
- Beta carotene
- Flavinoids
- Plasma proteins
- Mannitol
- Selenium
- Uric acid
- Bilirubin etc.

c) Drugs

- Chelating agents – Desferoxamine
- Allopurinol
- ACE Inhibitor – Captopril
- Pentoxyphylline etc.

There are various studies showing that free radicals and excessive oxidative stress have been implicated in the pathogenesis of diabetes and more importantly in causing its long term complications[6,51-53]. Supplimentation with Vit. C and Vit. E tends to significant decrease in the levels of diene conjugates, lipidperoxides and significant increase in the level of reduced glutathione[50,57,58].

In one study conducted by Raheja *et al.* (1991) concluded that free radicals and excessive oxidative stress have been implicated in the pathogenesis of diabetes and more importantly, in causing the long term complications. Diabetes has been shown to have significant increased levels of free radical activity as well as oxidative stress. Supplimentation with vitamin C leads to a significant decrease in the levels of diene conjugates ($P<0.005$), lipid peroxides ($P<0.01$) and significant increase in the levels of reduced glutathione ($P<0.010$)[53].

MATERIALS AND METHODS

This study was approved by institutional ethical committee and conducted on thirty patients of type 2 diabetes, who were uncontrolled on oral hypoglycemic drugs. They were randomly divided in two groups of 15 each:

- Group 1: Study group (N=15) - Administered 25 gm of fenugreek seed powder with water 20 minutes before lunch and dinner for 1 month
- Group II: Control group (N=15) - Administered placebo for one month

Criteria for diagnosing diabetes were taken from American Diabetes Association. These includes fasting sugar >126 mg/dl, postprandial/ random sugar >200 mg/dl. These cases did not have any other associated illness. Detailed clinical history was recorded and detailed clinical examination done.

Each patient was followed for one month and during that period he was advised not to take any other hypoglycemic drug and any herbs possibly having blood sugar lowering effect and allowed to take fixed diabetic diet of 1800 calories/day calculated on the weight and height basis. Blood samples were collected at day one (basal sample), at 15th day and at 30th day of the study and analysed for:

- Blood sugar fasting and postprandial[59]
- Serum cholesterol[60]
- Serum Triglycerides[61]
- HDL-C[62]
- Lipid peroxidation[63]

Collection and Processing of Blood Samples:

Disposable syringes were used and 10 ml. of blood withdrawn from antecbital vein. 2ml. blood collected in EDTA vial for blood sugar estimation and rest of the blood in plane vial from which serum was separated for lipids and LOS estimation.

Blood glucose was estimated by glucose oxidase/ peroxidise (GOD/POD) method[59]. Blood lipids (cholesterol, triglycerides, HDL-C) were estimated by enzymatic methods using Reckon diagnostic P. Ltd. kits[60-62]. LOS was measured chemically as prescribed below.

Lipoprotein Oxidation Susceptibility Test (LOS)[63]

The LOS was measured based on the principle that the hydrolysis of plasma lipoperoxide forms MDA (Malondialdehyde) which reacts with thiobarbituric acid to form a red 2:1 Thiobarbituric acid Malondialdehyde adduct,

this coloured complex absorbs maximally at 532 nm and optical density will be measured by spectrophotometry[23].

Reagents Used:

1. Dextran sulphate
2. Copper chloride
3. Magnesium chloride
4. Bovine albumin
5. Barbituric acid
6. Trichloracetic acid
7. Hydrochloric acid
8. Sodium chloride
9. n-Butanol

Reagents:

1. **Dextran Sulphate:** 1.0 gm of dextran sulphate was dissolved in 100 ml of distilled water and 0.2 mM of solution of dextran sulphate was prepared
2. **Copper Chloride:** 8.52 mg of copper chloride dissolved in 100 ml of distilled water. 0.5 nm of copper chloride was prepared
3. **Magnesium Chloride:** 10.2 mg of magnesium chloride dissolved in 100 ml of distilled water and 0.5 M magnesium chloride solution was prepared
4. **Bovine Albumin:** 3 gm of bovine albumin dissolved in 50 ml of distilled water thus 6.0 per cent of bovine albumin solution was prepared
5. **Hydrochloric Acid:** 2.2 ml of HCL dissolved in distilled water and 0.25 N of HCI solution was prepared
6. **TBARS Reagent:** This reagent contained 26 nm of Thiobarbituric acid (TBA) and 0.92 M trichloroacetic acid in 0.25N HCI. The TBA was added first, heated and stirred. After it was dissolved, the TCA was added to the solution and was brought to volume with HCI. This reagent was stored in a dark bottle at room temperature.
7. **Sodium Chloride:** 4 g of sodium chloride dissolved in 100 ml of distilled water to give 4.0 per cent of sodium chloride solution.

Procedure

- **Step I:** LOS test serum (not plasma) was used in this test. A 500 µ lit serum sample was treated with 50µ lit solution containing 0.2 nm dextran sulphate (MW = 50,000 Genzyme, Cambridge MA) and 0.5 M MgCl2.H2O to precipitate the apo. B containing lipoproteins (LDL and VLDL)
- **Step II:** After centrifugation at 3,000 rpm at 20°C for 10 minutes. The supernatant was removed
- **Step III:** 1 ml of 6% bovine serum albumin (BSA) and another 50µ lit. of dextran sulphate magnesium solution was added
- **Step IV:** Solution was vortexed and re-centrifuged as above to wash away any residual serum proteins and HDL
- **Step V:** The supernatant was again removed and the remaining precipitate (containing LDL and VLDL) was dissolved in 4% NACI
- **Step VI:** A volume of re-dissolved precipitate containing 100 mg of non-HDL cholesterol was combined with sufficient 4 % NaCl to give a total volume 500µ lit.
- **Step VII:** 50µ lit of 0.5 mM CuCl2.2H2O solution was added (Final Copper Concentration was 46 µM)
- **Step VIII:** Samples were incubated at 37°C in a shaking water bath for 3 hours
- **Step IX:** Next 2 ml of TBARS reagent was added to each tube
- **Step X:** The mixture was heated at 100°C in a water bath for 15 minutes
- **Step XI:** After removing and cooling the tubes 2.5 ml n-Butanol was added. The tubes were vortexed and then centrifuged for 15 minutes at 3,000 rpm at room temperature
- **Step XII:** The pink upper layer was removed and the optical density was determined in a spectrophotometer at 532 nm.

The coefficient of variation of method was 4% intra assay and 9% inter assay.

Normal Value: 66±22 nmol. MDA/mg. of non HDL-C

Statistical Analysis

All data are expressed as mean + SE. The results were analyzed with Student's t test for paired data. p value of <0.05 was considered statistically significant[64].

OBESERVATIONS

Table I shows that the basal fasting and postprandial blood sugar level are 204.2±62.7 265.4±65.7 mg percent respectively. After 15 days of administration of fenugreek seeds powder postprandial blood sugar falls to 239.53±95.9 mg percent, which is around 10% but statistically not significant (P>0.1).

Table 1: Effect of Fenugreek (25g Bid) on Blood Sugar (mg Percent) in Type 2 Diabetes Patients

BLOOD SUGAR (mg%)					
	Basal		15th Day	30th Day	
	Fasting	Postprandial	Postprandial	Fasting	Postprandial
Mean	204.2	265.4	239.53	165.06	210.26
SD±	62.7	65.7	95.9	46.1	62.7
Mean change % change			-25.9 ↓ 9.74%	-39.1↓ 19.16%	-55.1↓ 20.77%
SE±	16.20	16.97	14.614	6.997	6.816
P			>0.1	<0.001	<0.001

P - As compared to basal levels

At 30th day, fasting and postprandial blood sugar levels decreased to 165.06±46.1 and 210.26±62.7 mg percent respectively. The decrease in fasting (39.1 mg%) and postprandial (55.1 mg%) blood sugar levels are statistically significant (P<0.001) [Figure 1]

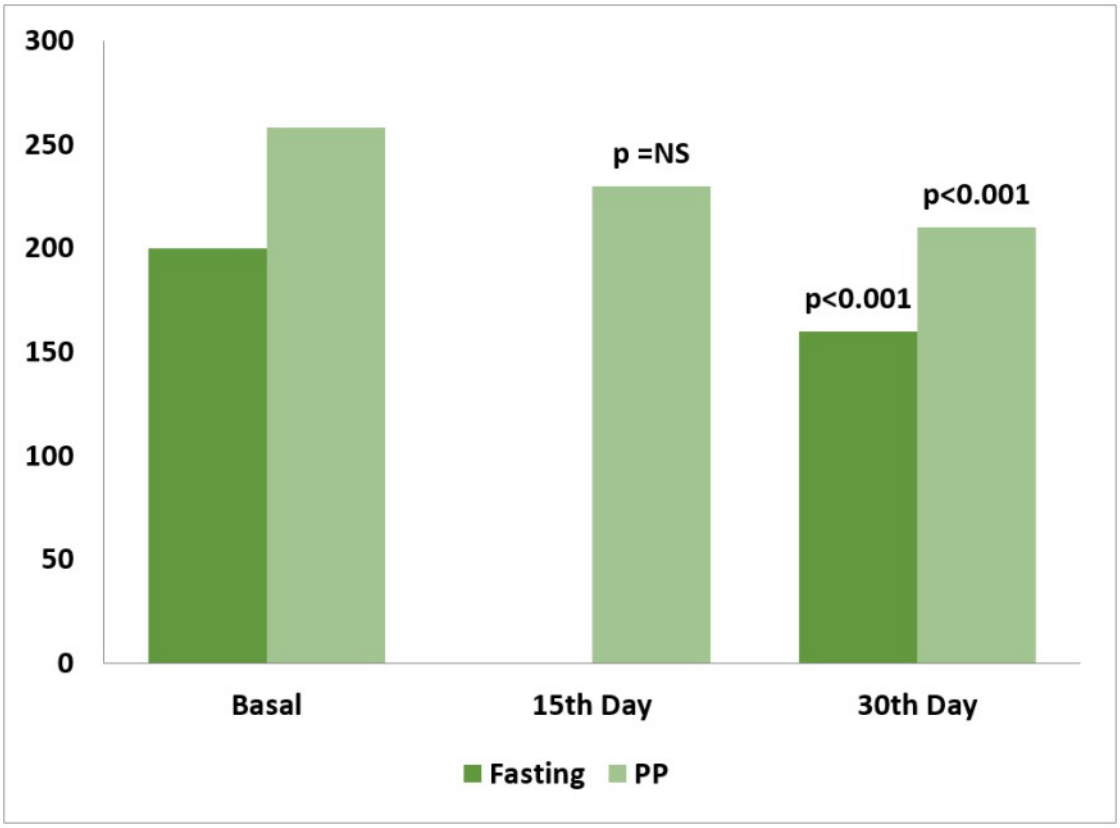

Figure 1: Effect of Fenugreek on Blood Sugar in Type 2 Diabetes Patients

Table 2: Effect of Placebo on Blood Sugar (mg%) in Type 2 Diabetes Patients (Control Group)

BLOOD SUGAR (mg%)					
C. No.	**Basal**		**15th Day**	**30th Day**	
	Fasting	Postprandial	Postprandial	Fasting	Postprandial
Mean	198.66	244.6	277.26	207.0	279.8
SD±	37.5	39.5	57.5	25.6	65.2
Mean change % change			+32.6↑ 13.35%	+8.34↑ 4.19%	+35.2↑ 14.39%
SE±	9.68	10.20	7.616	6.403	9.863
P			<0.001	NS	<0.01

P - As compared to basal levels; NS - Not significant

The Table 2 shows the blood sugar levels in control group. It points out that the postprandial blood sugar levels rose to the significantly higher values on the 15th and 30th day of study as compared to the basal levels [Figure 2]. The percent change in postprandial sugar at 15th and 30th day in treated and control groups have been shown in Figure 3.

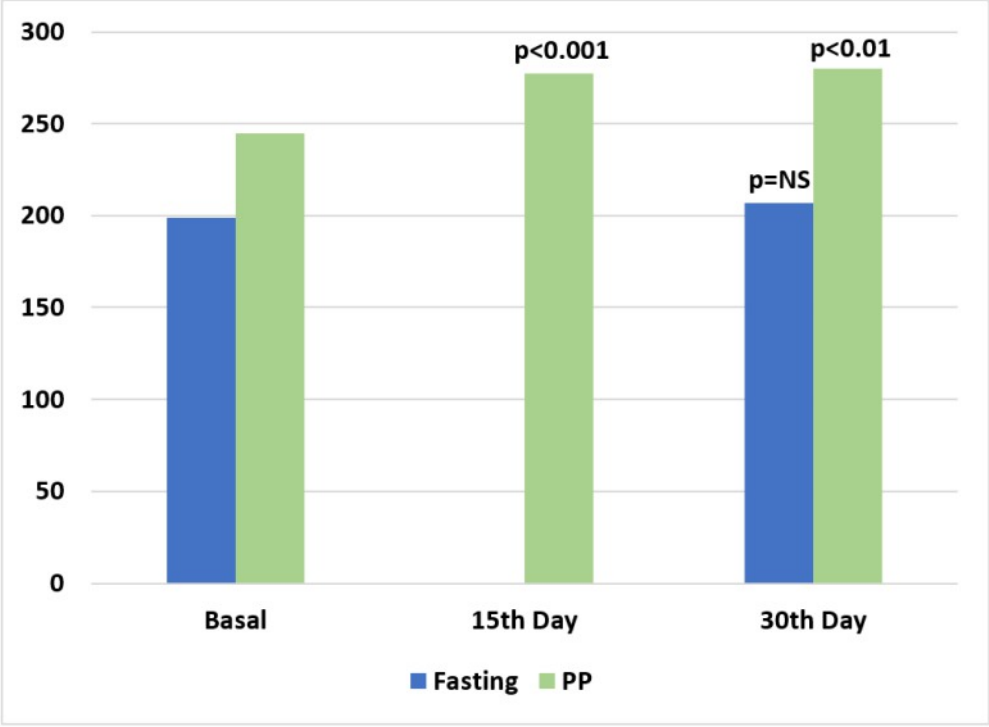

Figure 2: Effect of Placebo on Blood Sugar in Type 2 Diabetes Patients

While looking at the effect of the administration of fenugreek over a month on serum lipids [Table 3] it was observed that the levels of serum cholesterol and triglyceride did not go down, rather, there was statistically significant (P<0.01) rise in the level of serum cholesterol from 204.33±46.1 mg percent to 227.20±46.9 mg percent.

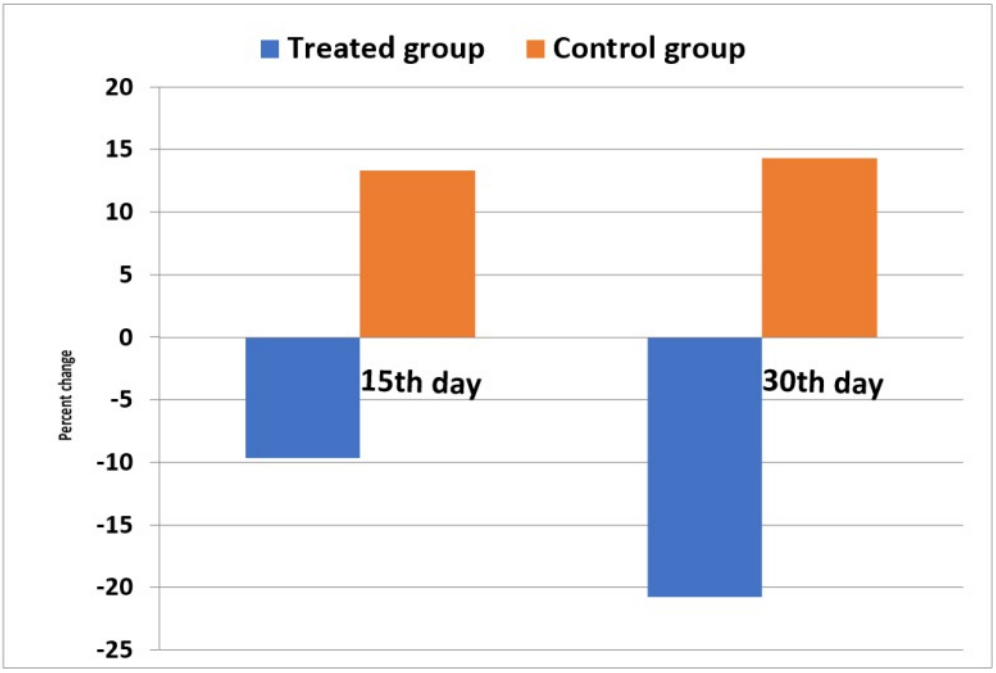

Figure 3: Percent Change in Postprandial Blood Sugar at 15th and 30th Day in Treated and Control Groups

Table 3: Effect of Fenugreek on Blood Lipids and Lipoprotein Oxidation Susceptibility in Type 2 Diabetes Patients

C. No.	Serum Lipids						Lipid Peroxidation Nmol MDA/mg of non-HDL-C	
	Serum Cholesterol (mg%)		Triglycerides (mg%)		HDL-C (mg%)			
	Basal	30th Day	Basal	30th Day	Basal	30th Day	Basal	30th Day
Mean	204.33	227.20	168.86	179.93	52.8	57.1	58.3	64.0
SD±	46.1	46.9	61.2	61.4	9.4	11.5	14.7	11.0
Mean change % change	+22.8↑ 11.19%		+11.0↑ 6.55%		+4.3↑ 8.14%		+3.6↑ 9.77%	
SE±	7.616		5.964		1.394		3.64	
P	<0.01		<0.1		<0.01		NS	

P - As compared to basal levels; NS - Not significant

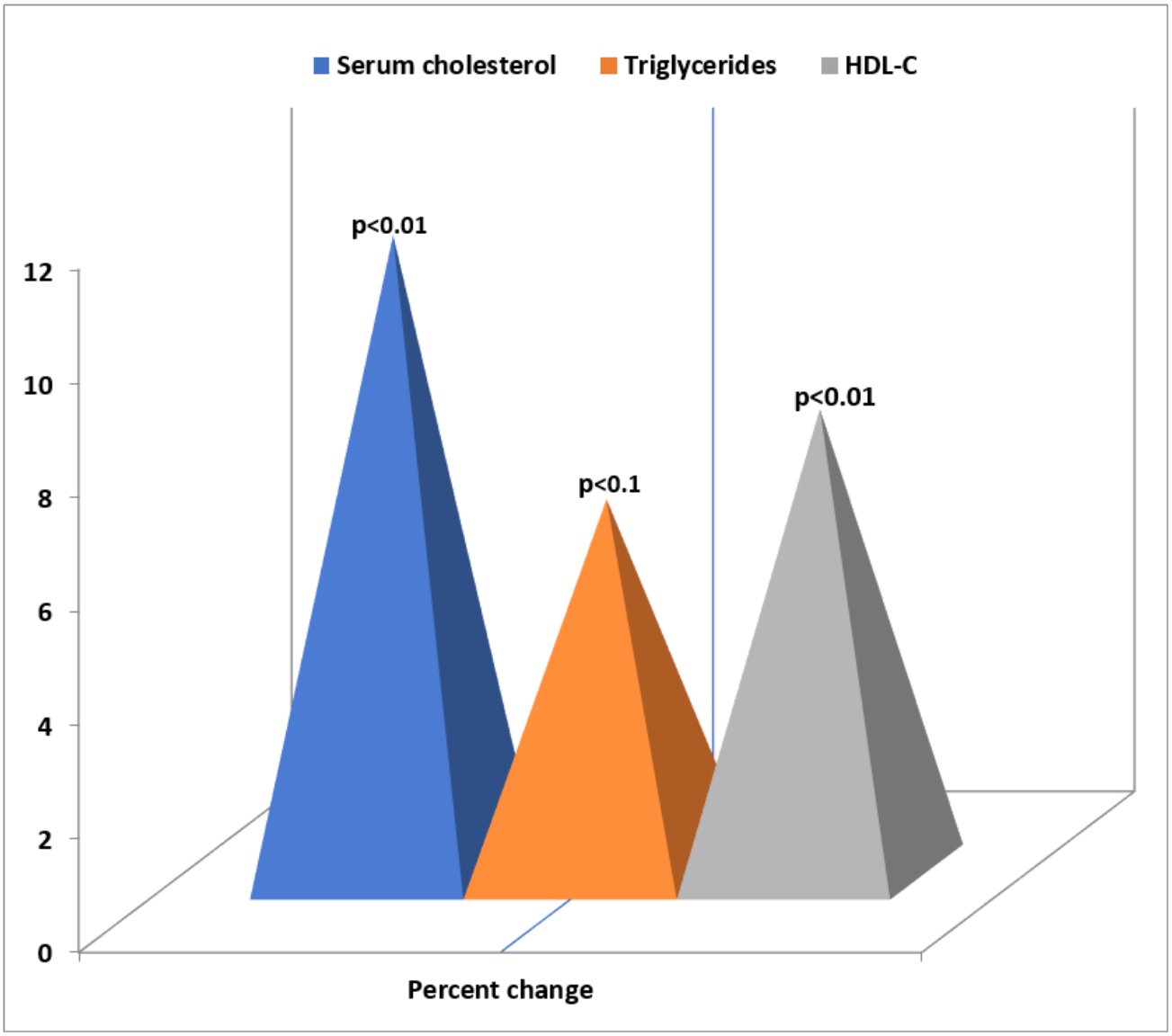

Figure 4: Percent Change in Blood Lipids at 30th Day of Administration of Fenugreek (25 g BID)

The triglycerides also increased but their rise was statistically not significant (P<0.1). However, there is significant (P<0.01) rise in HDL-C for a mean of 52.8±9.4 to 57.1±11.5 mg percent. The rise in serum cholesterol and HDL-C has maintained the status quo in cholesterol:HDL-C ratio [Figure 4]. Lipid peroxidation has not been altered significantly (P=NS) after fenugreek administration at the end of the study [Table 3, Figure 6].

Table 4: Effect of Placebo on Serum Lipids and Lipoprotein Oxidation Susceptibility in Type 2 Diabetes Patients (Control Group)

C. No.	Serum Lipids						Lipid Peroxidation Nmol MDA/mg of non-HDL-C	
	Serum Cholesterol (mg%)		Triglycerides (mg%)		HDL-C (mg%)			
	Basal	30th Day	Basal	30th Day	Basal	30th Day	Basal	30th Day
Mean	221.9	232.1	139.8	148.2	52.7	48.8	54.3	55.4
SD±	53.0	49.8	54.1	55.8	7.6	8.1	11.9	10.8
Mean change % change	+10.2↑ 4.59%		+8.3↑ 6.00%		-3.9↓ 7.4%		+1.1↑ 2.02%	
SE±	2.32		1.239		0.800		1.058	
P	<0.001		<0.001		<0.01		NS	

P - As compared to basal levels; NS - Not significant

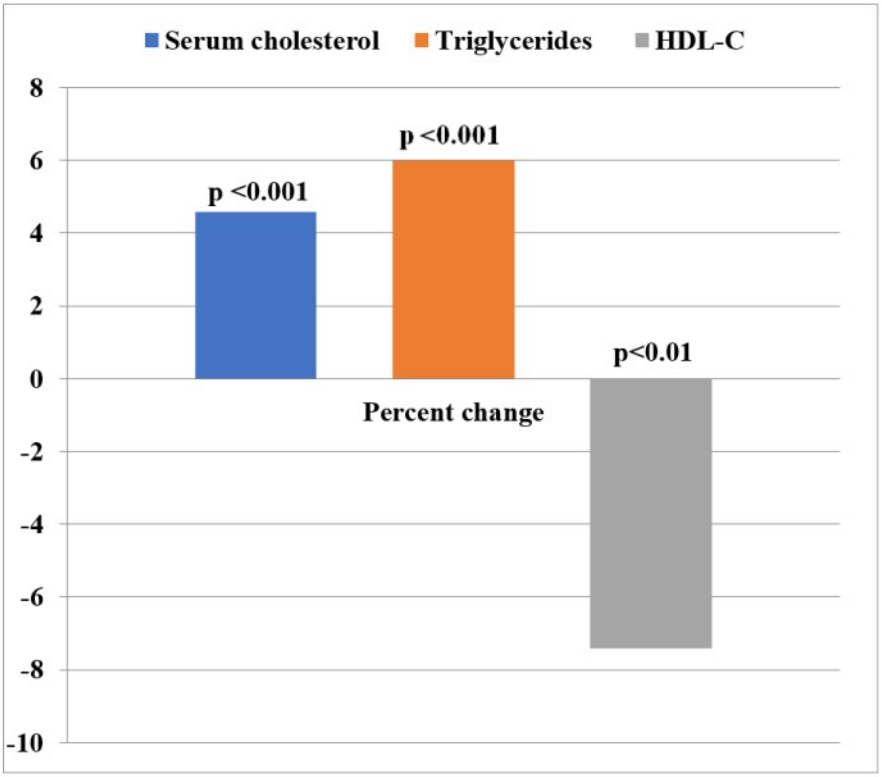

Figure 5: Percent Change in Serum Cholesterol, Triglycerides and HDL-C after 30th day in Control Group

In the placebo group, the rise in serum triglyceride level is also significant (P<0.001). HDL-C level on the other hand has significant (P<0.01) fall from 52.70±7.6 to 48.8±8.10 mg percent at the end of one month [Table 4, Figure 5] Lipoprotein oxidation susceptibility however was unaltered (P>0.1) [Figure.6].

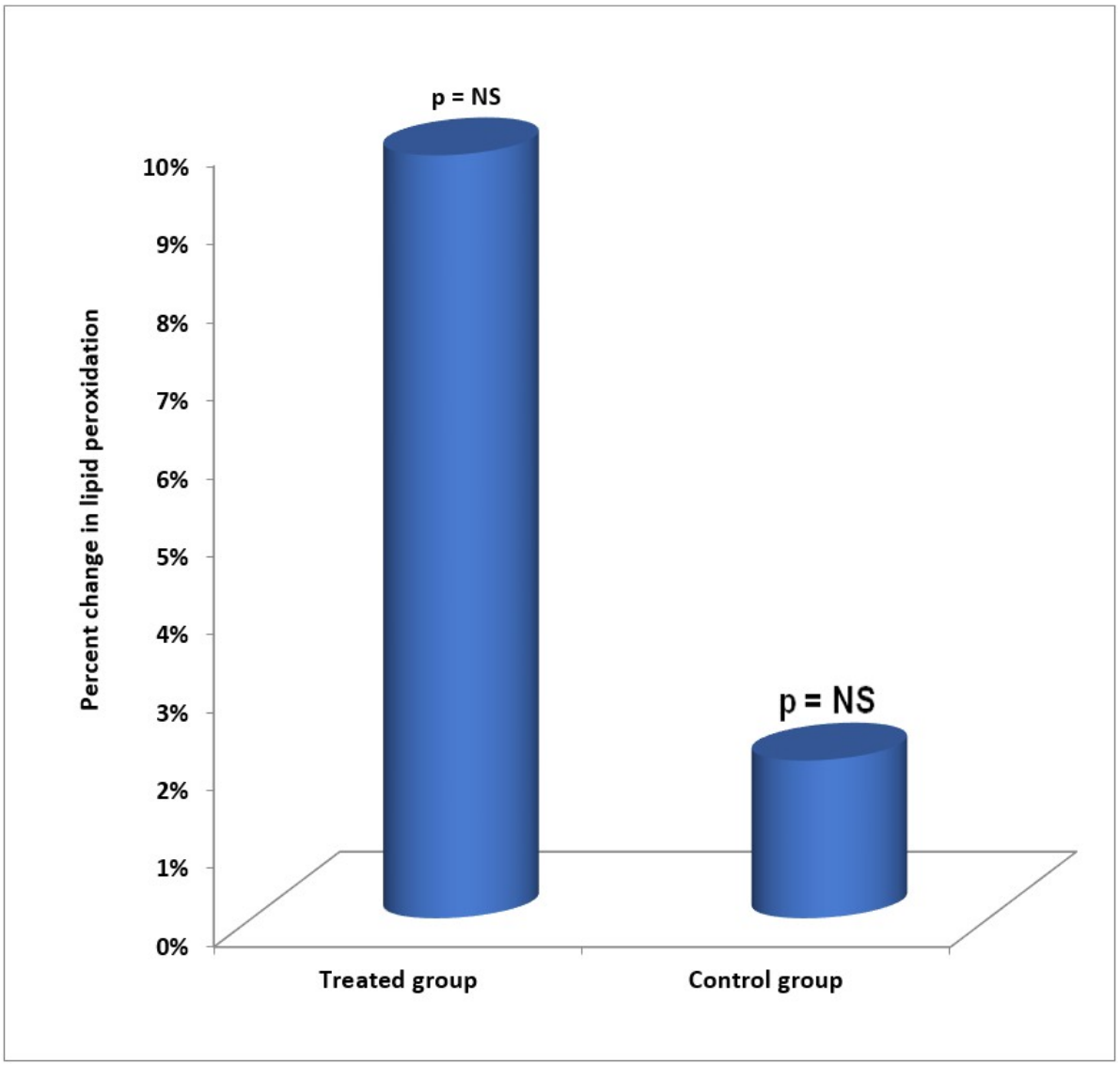

Figure 6: Percent Change in Lipid Peroxidation at 30th day in Both Treated and Control Groups

DISCUSSION

The present study was planned to evaluate the effect of fenugreek (*Trigonella foenum-graecum*) powder on blood sugar, blood lipids and antioxidant status in type 2 diabetes cases.

The study was conducted on 30, type 2 diabetes patients. They were divided into two groups of 15 each. Group 1 received 25g of fenugreek seed powder, 20 minutes before lunch and dinner. Group II received placebo before lunch and dinner. Group II was taken as a control group to whom placebo was given. All the patients were followed for a period of one month. Blood samples were collected at day one (basal), at 15th day and at 30th day of the study and analysed for blood sugar, serum cholesterol, serum triglyceride and HDL cholesterol level and for lipid peroxidation.

Effects of Fenugreek

(a) Effect on blood sugar:

In the present study it was found that fenugreek on the 30th day of administration causes a decrease in fasting blood sugar levels from 204.2±62.7 to 165.06±46.1 mg percent, a mean fall of 39.1 mg percent which is highly significant statistically (P<0.001). The fall in the blood sugar levels on the15th day of administration was from 265.40±65.7 to 239.53±95.9 mg percent, the mean fall is 26.1 mg percent which is statistically not significant (P=NS). The fall in postprandial blood sugar levels on the 30th day is highly significant (P<0.001), being reduced to 210.26±62.7 mg percent, with a mean fall of 55.4 mg percent.

Khosle *et al.* observed the effect of fenugreek on blood sugar in

normal and diabetic rats (alloxan induced) after administration of seed powder in a dose of 2 and 8 gm/kg dose orally respectively. It produced a significant fall in ($P<0.05$) blood glucose, both in normal as well as diabetic rats and the hypoglycemic effect was dose related[26].

Sharma *et al.* observed the effect of fenugreek on blood sugar level in diabetics, by administrating fenugreek seeds 100g/day in two divided doses, before lunch and dinner, followed for 10 days. They found that fenugreek diet significantly reduced fasting blood sugar level and improved glucose tolerance test [27]. Fenugreek is now considered to be an established co-prescription with anti-diabetic drugs in the treatment of this common endocrinal disorder. Our finding in this regard is in agreement with Khosle *et al*[26] and Sharma *et al*[27].

Overview of literature shows that administration of fenugreek seeds decreases blood sugar levels in type 2 diabetes when given in different doses and for different duration. The doses employed were 5gm.twice a day for two months, 2.5 gm. twice a day for 3 months (mild type 2 diabetes), 10 gm. daily for six months and 15gm.daily as well. All studies have shown reduction in blood sugar levels in type 2 diabetes with some GI side effects.

(b) Effect on blood lipids:

In the present study there is a rise in serum cholesterol level from 204.33±46.1 to 227.20±46.9, mean rise is 22.8 mg percent; increase in serum triglycerides is from 168.86±61.2 to 179.93±61.4, mean rise is 11.0 mg percent and rise in HDL cholesterol is from 52.8±9.4 to 57.10±11.5 mg percent, mean rise is 8.0 mg percent. The rise in serum cholesterol and serum HDL cholesterol is significant statistically ($P<0.01$) but the rise in triglyceride is not significant [Table 3, Figure 4].

Sharma *et al.* observed the effect on blood lipids after 100 gm/day of fenugreek seed powder in two divided doses, to NIDDM patients for 10 days. They found that serum cholesterol; LDL and VLDL cholesterol and serum triglycerides were significantly reduced. The HDL cholesterol fraction, however remain unchanged[27].

In the present study the serum lipid showed a slight rise on consumption of fenugreek, although the rise is statistically insignificant but this finding is not in conformity with the work of Sharma *et al*[27]. It is difficult for us to explain the difference. This difference may perhaps be due to short interval of 10 days of Fenugreek administration by Sharma *et al*. This statement obviously needs confirmation by other studies.

A meta-analysis study performed recently (January 2000 to December 2019) to evaluate the effect of fenugreek seeds supplementation on human lipid profile showed that it significantly decreases total cholesterol, LDL-C and increases HDL-C compared with the control group. However, in the non-controlled studies, there was no significant difference in TC, TG, LDL-C between pre and post fenugreek studies. One observation was consistent, whether there was controlled or without control studies, that there was significant (.ooo1) increase in mean HDL-C[65].

(c) Effect on lipid peroxidation:

There is no significant effect on lipoprotein oxidation susceptibility after administration of 20 gm. fenugreek seeds [Table 3, Figure 6].

In an animal experimental study on alloxan diabetic rats revealed that increased lipid peroxidation was observed in the diabetic rats along with significant lowered levels of glutathione, ascorbic acid and beta-carotene with increase in alpha-tocopherol. Supplementation of fenugreek seeds lowered lipid peroxidation and the levels of glutathione and beta-carotene were increased and the alpha-tocopherol was decreased. However, the level of ascorbic acid remained unaltered[66].

Effects of Placebo

In the control group where only placebo was given it was found that there was significant rise in postprandial blood sugar level on the 15th and 30th day, however the rise in the fasting blood sugar level after 30 days was not statistically significant [Table 2, Figure 2]. This insignificant rise in fasting blood sugar may be partly explained by regular exercise which these patients were undertaking and the strict regulation of their diets and the effect of OHA, they were taking.

While recording the changes in lipid levels, it was found that there is rise in serum cholesterol and serum triglyceride level, mean rise is 10.2 mg percent and 8.3 mg percent respectively, both of which were statistically highly significant ($P<0.001$), while there is a fall in HDL-C level, mean fall is 3.0 mg percent is significant ($P<0.01$) [Table 4, Figure 5]. There is a rise in lipid peroxidation status. The mean rise is of 1.1 nmol MDA/mg non HDL-C which is statistically not significant [Figure 6].

Although, Fenugreek has an established hypoglycemic effect but apparently has no profound effect on serum cholesterol and triglycerides. The proportionately higher rise in the level of HDL-cholesterol as compared to the rise in triglycerides seems to us of some significance. Long term studies should be carried out to see the effect of fenugreek on HDL-cholesterol and other lipids. This is particularly important as there are only few agents available which increase HDL-C level. We have seen that in the apparent absence of antioxidant action of fenugreek, its blood sugar lowering effect and HDL raising property seems to us of promise in future.

A recently published systemic review and meta-analysis of randomized controlled studies on the effect of fenugreek in type 2 diabetes has concluded that fenugreek significantly reduced fasting, two hours postprandial blood sugar and HbA1c levels. However, it did not decrease insulin resistance. Moreover, there was significant improvement in total cholesterol, triglycerides and HDL-C without any significant effect on LDL-C[67]. Many of the findings in the present study follow the same pattern with some exceptions.

The exact mechanism, by which it lowers blood sugar level is not known and also not an aim of our study, but probably it may be attributed to its high fibre content like in other legumes and

acts by following mechanisms:

1. Fibre delays gastric emptying thereby the rate of food stuff available to small intestine for absorption is slowed down[68].
2. Fibre may also increase viscosity of the unstrapped layers between the food and intestinal brush border surface so as to reduce the rate of carbohydrate absorption[69].
3. Antinutrients in legumes like phytates, lactine and enzyme inhibitors reduce the absorption of carbohydrates[70,71].
4. Starch complex of whole wheat flour and legumes has delayed absorption due to tightly bound carbohydrate as compared to wheat flour which is devoid of this complex[72].

During the one month follow up three patients on fenugreek complained of anorexia, distaste, bloating, constipation and nausea. These symptoms were present on the initial few days of the administration of fenugreek after which they subsided. Five patients on fenugreek experienced increased wellbeing and body strength. A systemic review of ten studies which included 706 participant of type 2 diabetes, when analysed for adverse effects and toxicity of fenugreek, reported that there were no adverse effects in two studies[73,74]. Gholaman *et al*[73], concluded that fenugreek is safe to administer. Most of the studies indicated the absence of hepatic and renal dysfunctions. Three studies[75-77] reported abdominal distension, stomach discomfort, nausea and diarrhoea. These symptoms, as in the present study, resolved spontaneously without the need of any special treatment.

The present study is an attempt to confirm the hypoglycemic effect of fenugreek. We have successfully demonstrated statistically significant reduction in the blood sugar levels in type 2 diabetics who were supplemented with fenugreek with their existing OHA therapy. Attempt was also made to discuss the possible mechanism of action of Fenugreek.

Another important finding of the present study was the statistically significant rise in HDL-C level observed with fenugreek. However, no beneficial effect was observed on serum cholesterol and serum triglyceride levels.

SUMMARY & CONCULSION

Our study is an attempt in finding the antioxidant status of well known indigenous herbs fenugreek. It has been observed the world over that increased oxidative stress has a role in the etiopathogenesis and evolution of long term complications of diabetes mellitus. Many herbs which have been found to have antioxidant properties are found to be useful in diabetes as well.

It was observed that fenugreek caused significant reduction in fasting and postprandial blood sugar levels. This reduction in blood sugar levels has also been observed by many other workers[26,27,67]. It was interesting to note the statistically significant rise in HDL-C level within 1 month of administration of fenugreek. The significance of this finding is obvious. However, contrary to findings of others[27,65], we did not find any reduction in serum cholesterol and triglyceride level. It can be argued that further research on fenugreek and its active ingredients like linolenic acid, saponins and sapogenins may help us in our quest for a potent antidiabetic and antilipid herbal drug.

CONCLUSION

It can be concluded that, fenugreek administered in the dose of 25 gm. twice a day before meals has significant fasting and postprandial blood sugar lowering effect. Fenugreek does not seem to have significant cholesterol and triglyceride lowering effect on short term administration. However, it causes significant rise in HDL-C levels. In the prescribed doses schedule for a short duration of one month, it has no significant antioxidant potential. With the exceptions of few transient gastrointestinal side effects, it was tolerated well without any severe adverse effects.

In a nutshell, when Fenugreek was added to the oral hypoglycaemic regimen to patients with type 2 diabetes, it is beneficial in further lowering of blood sugar levels and raising the HDL-C levels without any persistent side effects. The present study is a pointer in the right direction in the quest of an effective indigenous herb capable of raising HDL-C levels as well as of tackling the problem of hyperglycemia.

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