# Studies on Hypoglycaemic Activities of Cow Derived Products (Panchgavya) with Selected Medicinal Plants in Alloxan Induced Diabetic Mice

''बेटी बचाओ, बेटी पढ़ाओ''

**A Synopsis Submitted by**

***In partial fulfilment for the award of the degree***

**of**

**Doctor of Philosophy in Zoology**


**Supervised By:**

**JV'n Dr. Krishan Kumar**

**Submitted By:**

**JV'n Ranju Rajput**

**JVR-I/17/10045**

**Department of Food and Biotechnology**

**Faculty of Agriculture and Veterinary Science**

**Jayoti Vidyapeeth Women's University, Jaipur (Rajasthan)**


**2018**

## INTRODUCTION

Diabetes mellitus is a common term for miscellaneous disturbances of metabolism for which the main finding is chronic hyperglycaemia. The cause of diabetes is either erronious insulin secretion or imperfect insulin action or both. (Kerner and Bruckel, 2014)

The term diabetes mellitus defined a metabolic disorder of multiple aetiology characterized by chronic hyperglycaemia with disorder of carbohydrate, protein and fat metabolism resulting from imperfection in insulin secretion, insulin action, or both. Long– term damage, dysfunction and failure of various organs are the effects of diabetes mellitus. Diabetes mellitus may showed characteristic symptoms such as polyuria, thirst, blurring of vision, and weight loss. People who suffer from diabetes are at increased risk of cardiovascular, peripheral vascular and cerebrovascular disease. (WHO, 1999)

### Classification

WHO in 1980 (WHO, 1980) and, in modified form, in 1985 (WHO, 1985), The first widely accepted classification of diabetes mellitus was published. Clinical classes and two statistical risk classes are included in the 1980 and 1985 classifications of diabetes mellitus and allied categories of glucose intolerance. Expert Committee proposed two major classes of diabetes mellitus in 1980 and named them, IDDM or Type 1, and NIDDM or Type 2 diabetes. Study Group Report the terms in 1985 Type 1 and Type 2 were ommited, but the classes IDDM and NIDDM were retained, and introduced a class of Malnutrition–related Diabetes Mellitus (MRDM). Other classes of diabetes included, Other Types and Impaired Glucose Tolerance (IGT) as well as Gestational Diabetes Mellitus (GDM) in both the 1980 and 1985 reports,. In 1991, these were reflected in the subsequent International Nomenclature of Diseases (IND), and in 1992, the tenth revision of the International Classification of Diseases (ICD–10). Classification of 1985 was widely accepted and is internationally used. (WHO, 1999)

### 1. Type 1 Diabetes

It is also called Immune-Mediated Diabetes (Kerner and Bruckel; 2014). Type 1 diabetes, which also called juvenile diabetes, develops most often in young people; however, in adults, type 1 diabetes may also develop. In type 1diabetes, the body no longer makes insulin or

enough insulin in type 1 diabetes because the body's immune system, which generally protects the body from infections by getting rid of bacteria, viruses, and other harmful substances, has attacked and destroyed and damage the cells that make insulin. (Your Guide to Diabetes 2013). Type 1 diabetes may also caused by the absolute deficiency of insulin secretion. Individuals are at high risk in evolution of this type of diabetes. Diabetes can often be recognised by serological evidence of an autoimmune pathologic process occurring in the pancreatic islets and by genetic markers (Diagnosis and Classification of Diabetes Mellitus. 2014).

- Destruction of the b-cell which cause the absolute insulin deficiency.
- Generally mediated by immune mechanisms.
- Latent autoimmune diabetes in adults (LADA) is classified as type 1 diabetes. (Kerner and Bruckel, 2014)

**2. Type 2 Diabetes**

Type 2 diabetes, which is called as adult-onset diabetes, that can affect people at any age, even the children. However, type 2 diabetes evolved mostly in middle aged and older people. Over weighted and inactive people are more chances to develop the type 2 diabetes. Type 2diabetes generally begins with insulin resistance-a situation that happens when fat, muscle, and liver cells do not use insulin to carry glucose into the body's cells to use for energy. As a result, the body needs insulin in high quantity to help glucose enter cells. First of all, the pancreas maintain with the added demand by making more insulin. When the level of sugar in the blood increases after the meal, the pancreas does not make enough insulin (Your Guide to Diabetes, 2013).

**Table1 Differential Diagnostic Criteria for Type1 and Type2 Diabetes**

| | Type 1 Diabetes | Type 2 Diabetes |
|---|---|---|
| Manifestation age | Mostly children, adolescents and young adults | Mostly middle and old age |
| Onset | Acute to subacute | Usually gradual |
| Symptoms | Frequently polyuria, polydipsia, weight loss, fatigue | Frequently no complaints |

| | | |
|---|---|---|
| Body weight | Usually normal | Usually overweight |
| Predisposition to ketosis | Pronounced | None or only slight |
| Insulin secretion | Reduced or none | Below normal to high, qualitatively always impaired |
| Insulin resistance | None (or only low) | Often pronounced |
| Frequency in patient's family history | Usually negative | Typically positive |
| Concordance with identical twins | 30 to 50 % | Over 50 % |
| Heredity | Multi factorial (polygenetic) | Multi factorial (most likely polygenetic, but genetic heterogeneity is possible) |
| Associated with HLA (leukocyte antigen) system | Present | Not present |
| Antibodies associated with diabetes | Approx. 90-95 % at onset (GAD, ICA, IA-2, IAA) | None |
| Metabolism | Unstable | Stable |
| Response to insulin secretion stimulating anti diabetics | Usually none | Usually good at first |
| Insulin therapy Usually not required until insulin secretion has decreased after years of disease | Required | Usually not required until insulin secretion has decreased after years of disease |

- The LADA (latent autoimmune diabetes of adults) is associated with slower loss of beta cell function. Rapid failure of oral anti diabetics is to be expected. Analysis of GAD antibodies is recommended for cases of suspicion of LADA. (Kerner and Bruckel, 2014)

### 3. Gestational Diabetes

It is an operational classification (rather than a pathophysiologic condition) which identifying in women who develop diabetes mellitus during gestation. During the pregnancy, women who develop type 1 diabetes mellitus and women with undiagnosticate asymptomatic Type 2 diabetes mellitus that is developed during pregnancy are termed as Gestational Diabetes

Mellitus. The disorder has its onset in the third trimester of pregnancy, in most women who develop Gestational Diabetes Mellitus. (Baynes, 2015)

**4. Other Specific Types of Diabetes**

- Endocrinopathies (e. g. Cushing syndrome, acromegaly, pheochromocytoma)
- Diseases of the exocrine pancreas (e. g. pancreatitis, cystic fibrosis, hemochromatosis)
- Genetic defects of the β-cell function (e. g. MODY forms)
- Genetic defects of insulin action
- Drug induced (e. g. glucocorticoids, neuroleptics, alpha-interferons, pentamidine)
- Infections
- Rare forms of auto-immune mediated diabetes
- Other genetic syndromes which can be associated with diabetes. (Kerner and Bruckel, 2014).

**Symptoms of Diabetes mellitus**

Symptoms of the diabetes are includes-

- Polydipsia, polyuria, weight loss, sometimes with polyphagia, and blurred vision.
- Loss of growth and susceptibility to some infections may also accompany chronic hyperglycemia.
- Hyperglycemia are acute, life-threatening consequences of uncontrolled diabetes with ketoacidosis or the nonketotic hyperosmolar syndrome.
- Long-term complications of diabetes include nephropathy leading to renal failure; retinopathy with potential loss of vision; autonomic neuropathy causing gastrointestinal, genitourinary, and cardiovascular symptoms, sexual dysfunction and peripheral neuropathy with risk of foot ulcers, amputations, and Charcot joints.
- Increased incidence of atherosclerotic cardiovascular, peripheral arterial, and cerebrovascular disease are often found in diabetic patients.
- Patient with diabetes have an hypertension and abnormalities of lipoprotein metabolism.
- The chronic hyperglycemia of diabetes is allied with long-term damage, dysfunction, and failure of various organs of body, specifically the eyes, nerves, kidneys, heart, and blood vessels (Diagnosis and Classification of Diabetes Mellitus. 2014).

Treatment of diabetes many of the years there have been many attempts to use herbal medicines, the source of medicinal products has been phytotherapy. Various medicinal plants and preparations have been exhibited to act at main points of glucidic metabolism (Paolo. et al., 2018). The antidiabetic activity of medicinal plants is quality to the presence of flavonoids, polyphenols, terpenoids, coumarins and other constituents which exhibit the decrement in glucose levels in blood (Patel *et al.,* 2012).

Some of the new bioactive drugs isolated from plants exibited antidiabetic activity with more efficacy than oral hypoglycemic agents used in clinical therapy during the past few years. Benefits of medicinal plants have been confirmed by the various studies with hypoglycemic effect in management of diabetes mellitus. The effects of the medicinal plants may delay the improvement of diabetic complications and heal the metabolic abnormalities (Neelesh Malviya *et al.,* 2010).

Indian cow or Kamdhenu (Bos indicus) is worshipped as a holy animal in Hindu religion. Amazing therapeutic values of cow derived products like cow milk, cow milk curd, cow (butter) ghee, cow urine, cow dung and a combination of these products called as Panchgavya that is the reason for worshipping cow. In ancient Ayurvedic texts like Charak samhita, Shushruta samhita, Brahad-Wagbhatt etc.the use of these products has been well defined. (Kaushik *et al.,* 2017)

All the five cow derived products are individually called “Gavya” and collectively called as “Panchgavya” in Sanskrit. In the scripts of Vedas (divine scripts of Indian wisdom) and Vrkshyurveda (Vrksha means plants and Ayurveda means health system) panchgavya had reverence. Indian cow breeds are unique and specific species, in their characteristics and appearance.

Cow urine concoction (CUC) is having anticonvulsive and hypoglycemic effects; and useful against inflammations and anemia; liver disorders and fever (Dhama *et al.,* 2013). Cow urine has many valueable and profitable properties particularly in the therapeutics and agriculture field. Therapeutic properties of cow urine Uses in the cure of Skin diseases, Stomach, kidney and heart diseases, Stones, Diabetes, Liver problems, Jaundice, Athletes’ feet, Immunostimulant, Anticonvulsant agent, Cysts, Bioenhancer, Anti-cancer properties. Cow urine act as a disinfectant and thus clearify atmosphere and improves the fertility of the soil (Khan, *et al.,* 2015).

Cow milk is pondered as a healthy food and is found to be efficient in treating fever and pain; tumors; diabetes; kidney disorders and weaknesses and crucially act as a medium to administer medicine. It have also fungicidal properties; when utilize with medicinal herbs contain aphrodisiac quality and milk fat has anticancer activities (Dhama K, *et al.,* 2013). Cow's milk possess elements like vitamin A, vitamins of B complex group, vitamin C and carotenes. It also possess elements like sterols, flavones and phenols. In aging, these chemical agents delay the process. It shows Bio-Protective Role in Human Health, Immunity, Vision, Anti-cancer properties, Natural anti-oxidants, Absorption of nutrients, anti Diabetic properties, Tonic for health etc. (Khan *et al.*, 2015).

Cow milk curd is pondered blood purifier, "Vatanashak" and "Tridoshnashak" and it is found useful in "pitta", blood related problems like, piles and gastro-intestinal disorders. It is an proficient and powerful probiotic, there is a hope to control the infections without using the drug. Dahi (cow curd) or Matha (whey or butter milk) is pondered as nutritive, digestive and useful in gastrointestinal ailments by controlling the growth and population of harmful micro organism. Many Lactobacillus bacteria (lactic acid producing) is present in curd and buttermilk that produces antifungal metabolites viz. cyclic dipeptides, phenyllactic acid as well as proteinaceous compounds and 3-hydroxylated fatty acid (Dhama, K *et al.*, 2005 and Schnurer and Magnusson, 2005)

Cow ghee contains immune stimulatory properties (Dhama K. *et al.*, 2013). Cow ghee (butter-fat) is traditionally considered to enhance memory, intelligence, voice, vision and body's resistance to infections. It shows the antichollestric and immunostimulant activity. Ayurvedic practitioners consider that cow's milk and ghee are boost the memory. Cow ghee is beneficial for eye sight and digestion. It is 'Tridosh Nashak', energetic, madhuri, cold, brain tonic, tonic, fragrant, and over all the best of the 'ghee' (butter milk). It contains antiageing factors. The modern doctors recommend for cholestrol patients not using any fat except cow ghee. It does not increment in cholesterol and has neither bad effect on heart. Cow butter (ghee) act as a blood purifier and beauty enhancer. Cow ghee has the property that may heal the wounds. The ghee obtained by the cow milk is very much useful for weak eyesight person. In experimental animals, Cow ghee as well as urine has been seen to promote immune processes. (Khan et al., 2015)

Cow dung has the properties that kill the germs of malaria and tuberculosis and it has also antifungal properties (Dhama et al., 2013). Cow dung contains antiseptic and disease preventive properties (prophylactic). Cow dung may use as skin tonic. Cow dung mixed with crushed neem leaves and spread on the skin it good for boils and heat rashes. Cow dung (cow dung ash) used as tooth polish because it relieve in the toothaches, so instead of toothpaste which is made of chemicals and dead bones of animals, it is a good alternative against chemical toothpaste (Dhama et al., 2005).

## OBJECTIVES

- To investigate the individual and combined effect of leaf extracts of the study plants *Psidium Guajava* (Guava), *Cannabis sativa* (Hemp) and *Citrus Limon* (Lemon) and Cow derived products on biochemical parameters.
- To study the effect of leaf extracts and Cow derived products on some enzymological parameters.
- To study the effect of leaf extract and Cow derived products on lipid profile of diabetic mice.
- To compare the effect of plants leaf extract and Cow derived products with standard drug Glibenclamide.

# REVIEW OF LITERATURE

Mahida *et al.,* (2017) (Protective Effect of Cow Urine Distillate in Streptozotocin Induced Type I Diabetes in Rats) was reported on his study was undertaken to validate antidiabetic property of cow urine. His study conducted on 36 adult male albino Wistar rats. Streptozotocin (STZ) injected on the male albino Wistar rats. Blood serum was used for various biochemical investigations. Induction of diabetes with streptozotocin significantly decreased the body weight of rats as compared to normal and control groups. Induction with Streptozotocin significantly elevated the blood glucose, total cholesterol, creatinine and triglyceride levels in comparison to control groups. Cow urine Treated rats significantly reduced the elevated blood glucose, total cholesterol, creatinine and triglyceride levels in comparison to Streptozotocin control group. The study estimated that cow urine distillate has a protective effect in diabetic rats.

Jarald *et al.,* (2008) was reported on his study was undertaken to validate antidiabetic property of the preparations containing cow urine. Rats were supplied with standard pellet diet and water ad libitum. The treated rats were monitored for 14 days for mortality and general behavior. The results showed, after 21 days, values of blood glucose were decreased in all the treated groups. In diabetic control group's value remained stable preparations exhibited activity in a dose-dependent manner. For 21 days Normal rats treated with cow urine did not show any increment in their glucose levels in blood. Comparatively, the preparations containing cow urine were found to be better than the herbal preparation prepared using distilled water.

Bhavani (2014) (Antidiabetic activity medicinal plant *Aegle marmelos* (linn.) on alloxan induced diabetic rats) estimated this study was performed to evaluate the hyperglycemic effect of aqueous extract of *A. marmelos* leaves on diabetic rats. Male Wister Albino rats are used in this experiment. Alloxan monohydrates induced diabetes mellitus was produced in a batch of hypogenic male albino rats by injecting intrapreophrea; cavity a single dose of 2% alloxan monohydrates solution in saline, after these have been fasted for 24hours. The rats showed the following signs of the condition: Polydipsia, Polyuria, weight loss, asthenia weakness, Dehydration. Inhibition in blood sugar could be seen from 7th day after continuous administration of the extract and on 28th day, sugar levels in blood were found to be decreased by 54%. The *A. marmelos* leaves (ethanolic extract) have a promising antidiabetic activity against alloxan – induced diabetic rats.

Shukla K and Dubey PK (2009) (Antidiabetic Activity of *Psidium Guajava* (Guava) Leaves Extract), investigated the *Psidium guajava* leaves extracts were exhibited the hypoglycemic activity. Aqueous and ethanolic extract of *Psidium guajava* leaves were prepared and screened for hypoglycemic activity. The mean percentage reduction in blood glucose level was found to be 18.88 % and 9.19+% for both ethanolic and aqueous leaves extracts, in diabetic albino rats. Ethanolic extract was showed the better hypoglycemic effect in mice than the aqueous extract. Electron-microscopic studies and blood glucose monitoring verifying the *Psidium guajava* exhibits its beneficial activity by the ß-cell rejuvenation, stimulation and regeneration. Leaves extracts of *P. guajava* produces blood glucose homeostasis and it also reversed metabolic and pathologic changes in pancreatic islets.

Naim *et al.,* (2012) (Comparative Study of Antidiabetic Activity of Hexane-Extract of Lemon Peel (*Limon citrus*) and Glimepiride in Alloxan-Induced Diabetic Rats) investigated the antidiabetic activity of the lemon peel. He has compare the antidiabetic activity of hexane extract of lemon peel *(Citrus Limon*) with that of glimepiride (a marketed product), in alloxan-induced diabetic rats. The investigation was performed by the measurement of glucose level in blood using a glucometer. He was found that the hexane extract of lemon peel exhibited antidiabetic activity compared to that of glimepiride. It can thus be concluded that the lemon peel extract contains significant antidiabetic activity.

Arumugama and Kavimanib (2008) (Antidiabetic activity of leaf and callus extracts of *Aegle marmelos* in rabbit) reported the treatment of crude aqueous extract of the *Aegle marmelos* leaf and the three month-old callus brought about a significant reduce in blood sugar. Among the different types of extracts, the methanol extracts of the leaf and callus brought about the highest anti-diabetic effect. The results advise that both the leaf and callus contain anti-diabetic active principles, which would decrease the level of sugar in STZ-diabetic rabbits. These findings demonstrate that the methanol extract of the callus powder of *Aegle marmelos* is as effective as the leaf extract in the management of diabetes.

Al-Bahrani (2016) (The Role of *Momordica charantia* in Reducing the Level of Glucose in Mice) investigated the effects of aqueous and alcoholic extract of Momordica charantia on the level of serum glucose were studied on 40 mature male rats. All male rats distributed into 5 equal groups and they fed basal diets. The results showed the effect on the glucose level of the serum, at 0.30mg/ml of water extract of *Momordica charantia.* On the other side, no any

effects showed on the glucose level at the higher dosages of methanolic Momordica charantia extract.

Ramachandran and Srividya (2014) Studied “in Vitro antidiabetic activity and in vivo post prandial glycemic response of aloe gel enriched Curd”. In vitro anti diabetic activity of dahi enriched with aloe gel powder (AG) at different concentrations became carried out in terms of amylase and α glucosidase inhibition. Dahi with 0.15% aloe gel (0.15 AG) was selected for the in vivo study to evaluate the post prandial glycemic response. Blood glucose measurements were carried out at periodic intervals. This investigation gives clinical evidence for the improved glucose reducing efficacy of a curd containing Aloe gel. This research shows the potential of utilizing Aloe gel for commercial formulation of low glycemic dairy products.

# METHODOLOGY

**Collection of Samples-** Different types of Medicinal plant leaf samples and Cow derived products will be collected in University campus and will bring to laboratories for further analysis.

1. **Extracts Preparation of Selected Plants-** The extracts will be prepared by using different solvents, i.e. Methanol and Ethanol.
2. **Investigation of the some biochemical parameters**

**Test for Blood Glucose**

i. Glucose oxidase- peroxidise Method (GOD-POD Method) (Trinder, 1969).

**Test for the Blood Urea**

i. Diacetyl Monoxime Method (DAM-TSC Method).

**Test for the Serum Creatinine**

i. Jaffe's Method (Jaffe, 1886).

**Tests for Proteins**

Lowry's method (Lowry *et al.,* 1951).

**3. Perform Some Enzymological Parameters-**

**a. Test for serum alkaline phosphatase activity**

The serum alkaline phosphatase estimation by King's Method. (King and Armstrong, 1934)

**b. Test for serum glutamate Pyruvate Transaminase Activity**

The serum glutamate Pyruvate Transaminase estimation by Reitman and Frankel Method **(Stanley Reitman and Sam Frankel, 1957)**

**c. Test for serum glutamate Oxaloacetate Transaminase (SGOT) Activity**

The serum glutamate oxaloacetate Transaminase estimation by Reitman and Frankel Method (Stanley Reitman and Sam Frankel, 1957)

**4. Lipid Profile Test**

**Test for Cholesterol**

Zak's Method (Zak *et al.,* 1954)

**Test for HDL**

PEG- CHOD- PAP, end point assay with lipid clearing factor (LCF).

**Test for LDL**

**Test for VLDL**

**Test for Tri Gliceride**

Enzymatic-colorimetric end point method

5. **Comparable study of plants leaf extract and Cow derived products with standard drug Glibenclamide.**

## REFERENCES


Abul-Fadl M.A.M. and King E.J. (1949). Properties of the acid phosphatases of erythrocytes and of the human prostate gland. Biochem. J.; 46: 51-60.

Al-Bahrani M.H.A. (2016). The Role of *Momordica charantia* in reducing the level of glucose in mice. Int.J.Curr.Microbiol.App.Sci. 5(8): 470-478.

Arumugama S., Kavimanib S., Kadalmanic B., Ahmedd A.B.A., Akbarshac M.A. (2008). Antidiabetic activity of leaf and callus extracts of *Aegle marmelos* in rabbit. Science Asia; 34: 317-321.

Baynes H.W. (2015). Classification, Pathophysiology, Diagnosis and Management of Diabetes Mellitus. J Diabetes Metab; 6(5): 41.

Bhavani R. (2014). Antidiabetic activity medicinal plant *Aegle marmelos* (linn.) on alloxan induced diabetic rats. IRJPBS; 1 (1): 36-44.

Bradford M.M. (1976). A rapid and sensitive method for the quantitation of microgram quantities of protein utilizing the principle of protein-dye binding. Anal Biochem; 72: 248-254.

Dhama K., Chakraborty S. and Tiwari R. (2013). Panchgavya therapy (Cowpathy) in safe guarding health of animals and humans – A review. Res. Opin. Anim. Vet. Sci., 3(6), 170-178.

Dhama K., Rathore R., Chauhan R.S. and Tomar S. (2005a). Panchgavya: an overview. International Journal of Cow Science, 1(1): 1-15.

Dhama, K., Rathore, R., Chauhan, R.S. and Tomar, S. (2005a). Panchgavya: an overview. International Journal of Cow Science, 1(1): 1-15.

Diagnosis and classification of diabetes mellitus. Diabetes Care Volume 37, Supplement 1; 81-83: DOI: 10.2337/dc14-S081

Governa P., Baini G., Borgonetti V., Cettolin G., Giachetti D., Magnano A.R., Miraldi E. and Biagi M. (2018). Phytotherapy in the Management of Diabetes: A Review. Molecules; 23(1): 105.

Gururaja M.P., Joshi A.B., Joshi H., Sathyanarayana D., Subrahmanyam E.V.S., Chandrashekhar K.S. (2011). Antidiabetic potential of cow urine in streptozotocin- induced diabetic rats. Asian Journal of Traditional Medicines; 6 (1): 8-13.

Jaffe M. (1886). Uber den Niederschlag, welchen Pikrinsäre in normalem Harn erzeugt und uber eine neue Reaction des Kreatinins. Zeitschrift für physiologische Chemie; 10 (5): 391–400.

Jarald E.E., Edwin S., Tiwari V., Garg R. and Toppo E. (2008). Antidiabetic activity of cow urine and a herbal preparation prepared using cow urine, Pharmaceutical Biology; 46(10-11): 789-792.

Kaushik, J. Jain and Rai P. (2017). Therapeutic potentials of cow derived products- a review. International journal of pharmaceutical sciences and research 7(4).1383-90

Kerner W., Bruckel J. (2014). Definition, classification and diagnosis of diabetes mellitus. Exp Clin Endocrinol Diabetes; 122(7): 384–386.

Khan M.Y., Roy M., Saroj B. K. and Dubey S. (2015). A Review- Benefits of Panchgavya therapy (Cowpathy) for health of humans. Asian J. Res. Pharm. Sci. 5(2); 115-125

Kim G.N., Shin J.G. and Jang H.D. (2009). Antioxidant and antidiabetic activity of *Dangyuja* (*Citrus grandis* Osbeck) extract treated with *Aspergillus saitoi.* Food Chemistry; 117(1): 35-41.

King E.J., Armstrong A.R. (1934). A convenient method for determining serum and bile phosphatase activity. Can Med Assoc J.; 31(4): 376–381.

Lowry O.H., Rosebrough N.J., Farr A.L., and Randall R.J. (1951). Protein measurement with the Folin Phenol Reagent. J. Biol. Chem; 193: 265-275.

Mahida N.R., Mandali G.C., Raval S.K. and Joshi B.P. (2017). Protective effect of cow urine distillate in streptozotocin induced type I diabetes in rats. The indian journal of veterinary sciences & biotechnology; 12(3): 127-131.

Malviya N., Jain S. and Malviya S. (2010). Antidiabetic potential of medicinal plants. Acta Poloniae Pharmaceutica Drug Research; 67(2): 113-118.

Mohammady I., Elattar S., Mohammed S. and Ewais M. (2012). An evaluation of anti-diabetic and anti-lipidemic properties of *Momordica charantia* (bitter melon) fruit extract in experimentally induced diabetes. Life Science Journal; 9 (2): 363-374.

Naim M., Amjad F.M., Sultana S., Islam S.N., Hossain M.A., Begum R., Rashid M.A., and Amran M.S. (2012). Comparative study of antidiabetic activity of hexane-extract of lemon peel (*limon citrus*) and glimepiride in alloxan-induced diabetic rats. Bangladesh Pharmaceutical Journal 15(2): 131-134.

Patel D.K., Prasad S.K, Kumar R. and Hemalatha S. (2012). An overview on antidiabetic medicinal plants having insulin mimetic property. Asian Pacific J. Tropical Biomed. 2(4): 320-330.

Ramachandran P. and Srividya N. (2014). In vitro antidiabetic activity and in vivo post prandial glycemic response of aloe gel enriched curd. 3(1): 38-46.

Rapaka D., and Vennam S.R. (2012). Evaluation and comparison of anti-diabetic activity of hydroalcoholic extracts of fresh and dry leaves of *Psidium guajava* in type-II diabetes mellitus. Int. Res J Pharm. App Sci.; 2(4): 62-65.

Reitman S., and Frankel S. (1957). A colorimetric method for the determination of serum glutamic oxalacetic and glutamic pyruvic transaminases. American journal of clinical pathology; 28(1): 56–63.

Schnurer J. and Magnusson J. (2005). Antifungal lactic acid bacteria as biopreservatives–review. Trends in Food Science and Technology, 16(1-3): 70-78.

Shukla K. and Dubey P.K. (2009). Antidiabetic activity of *psidium guajava* (guava) leaves extract. Research J. Science and Tech.; 1(1): 13-15.

Trinder P. (1969). Determination of blood glucose using an oxidase-peroxidase system with a non-carcinogenic chromogen. J. Clin. Pathol; 22, (2): 158-161.

Tripathi P., Gupta P.P. and Lal V.K. (2013). Interaction of *Momordica charantia* with metformin in diabetic rats. American journal of pharmacology and toxicology; 8 (3): 102-106.

Weiss L., Zeira M., Reich S., Har-Noy M., Mechoulam R., Slavin S., & Gallily R. (2006). Cannabidiol lowers incidence of diabetes in non-obese diabetic mice. Autoimmunity; 39(2): 143–151.

Weiss L., Zeira M., Reich S., Slavin S., Raz I., Mechoulam R., and Gallily R. (2008). Cannabidiol Arrests Onset of Autoimmune Diabetes in NOD Mice. Neuropharmacology. 54(1): 244–249.

WHO (1980). WHO Expert committee on diabetes mellitus. Second Report. Geneva. technical report series 646.

WHO (1985). World Health Organization. Diabetes mellitus: Report of a WHO Study Group. Geneva: Technical Report Series 727.

WHO (1999). Definition, diagnosis and classification of diabetes mellitus and its complications: report of a WHO consultation. Part 1, Diagnosis and classification of diabetes mellitus. World Health Organization. Dept. of Non communicable Disease Surveillance. Geneva; p 2-8.

Your Guide to Diabetes: Type 1 and Type 2 (2013). National institute of diabetes and digestive and kidney diseases, national diabetes information clearinghouse, NIH Publication No. 14–4016

Zak B., Moss N., Boyle A.J., and Zlatkis A. (1954). Anal. Chein. 26, 776.