

Nigella sativa medicine for treatment of diabetes mellitus

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ABSTRACT

Nigella sativa (*N. sativa*) Family Ranunculaceae is a widely used medicinal plant throughout the world. *Nigella sativa* is an annual flowering plant. It grows to 25–30 cm tall and has linear lanceolate leaves. The delicate flowers have 5-10 petals and the colors are usually yellow, white, pink, pale blue or pale purple. The fruit of plant is large and inflated capsule composed of 3-7 united follicles, that each of them has numerous seeds. The black colored seeds are flattened, oblong and angular, funnel shaped, with the length of 0.2 cm and 0.1 cm wide

Nigella sativa seeds have wide therapeutic effects and have been reported to have significant effects against many ailments. It is very popular in various traditional systems of medicine like homeopathic. Seeds and oil have a long history of folklore usage in various systems of medicines and food. The seeds of *N. sativa* have been widely used in the treatment different types of diseases and ailments. It is considered as one of the greatest forms of healing medicine. It has been recommended for using on regular basis in Tibb-e-Nabwi (Prophetic Medicine). It has been widely used as antihypertensive, liver tonics, diuretics, digestive, anti-diarrheal, appetite stimulant, analgesics, anti-bacterial and in skin disorders. Extensive studies on *N. sativa* have been carried out by various researchers and a wide spectrum of its pharmacological actions have been explored which may include antidiabetic, anticancer, immunomodulator, analgesic, antimicrobial, anti-inflammatory, spasmolytic, bronchodilator, hepato-protective, renal protective, gastro-protective, antioxidant properties, etc. Due to its miraculous power of healing, *N. sativa* has got the place among the top ranked evidence based herbal medicines. This is also revealed that most of the therapeutic properties of this plant are due to the presence of thymoquinone which is major bioactive component of the essential oil. The present review is an effort to provide a detailed survey of the literature on scientific researches of pharmacognostical characteristics, chemical composition and pharmacological activities of the seeds of this plant.

Diabetes mellitus is a common chronic disease affecting millions of people world wide. Standard treatment is failing to achieve required correction of blood glucose in many patients. Therefore, there is a need for investigating potential hypoglycemic drugs or herbs to improve glycemic control in diabetic patients. *Nigella sativa* seeds were used as an adjuvant therapy in patients with diabetes mellitus type 2 added to their anti-diabetic medications. A total of 57 patient were recruited and divided randomly into three dose groups. Capsules containing *Nigella sativa* were administered orally in a dose of 1, 2 and 3 gm/day for three months. The effect of *Nigella sativa* on the glycemic control was assessed through measurement of fasting blood glucose (FBG), blood glucose level 3 hours postprandially (3 hPG), and glycosylated

hemoglobin (HbA1c). Serum C-peptide and changes in body weight were also measured. Insulin resistance and beta-cell function were calculated using the homeostatic model assessment (HOMA2). Nigella sativa at a dose of 2 gm/day caused significant reductions in FBG, 2hPG, and HbA1 without significant change in body weight. Fasting blood glucose was reduced by an average of 45, 62 and 56 mg/dl at 4, 8 and 12 weeks respectively. HbA1C was reduced by 1.52% at the end of the 12 weeks of treatment ($P < 0.0001$). Insulin resistance calculated by HOMA2 was reduced significantly ($P < 0.01$), while B-cell function was increased ($P < 0.02$) at 12 weeks of treatment. The use of Nigella sativa in a dose of 1 gm/day also showed trends in improvement in all the measured parameters but it was not statistically significant from the baseline. However, no further increment in the beneficial response was observed with the 3 gm/day dose. The three doses of Nigella sativa used in the study did not adversely affect either renal functions or hepatic functions of the diabetic patients throughout the our study period.

Keywords: Nigella sativa, Miracle herb, Ranunculaceae, Habat-ul-Sauda, Thymoquinone, Tibb-e-Nabwi, Black seeds, Anti-diabetic, Antioxidant

INTRODUCTION

Nigella sativa (N. sativa) Family Ranunculaceae is a widely used medicinal plant throughout the world. Nigella sativa is an annual flowering plant. Botanical name is Nigella sativa. It is believed to be indigenous to the Mediterranean region but has been cultivated into other parts of the world including the Arabian peninsula, northern Africa and Asia. Nigella sativa seeds have wide therapeutic effects and have been reported to have significant effects against many ailments such as skin diseases, jaundice, gastrointestinal problems, anorexia, conjunctivitis, dyspepsia, rheumatism, diabetes, hypertension, intrinsic hemorrhage, paralysis, amenorrhea, anorexia, asthma, cough, bronchitis, headache, fever, influenza and eczema.

Nigella sativa, Hindi name (Mangaraila) and Arabi (Kalonji) is an annual flowering plant. It grows to 25–30 cm tall and has linear lanceolate leaves. The delicate flowers have 5-10 petals and the colors are usually yellow, white, pink, pale blue or pale purple. The fruit of plant is large and inflated capsule composed of 3-7 united follicles, that each of them has numerous seeds. The black colored seeds are flattened, oblong and angular, funnel shaped, with the length of 0.2 cm and 0.1 cm wide



This plant is known by different names in different country, for example black cumin (English), black caraway seeds (USA), shonaiz (Persian) and kalajira (Bangali).

Characteristics of the Nigella Sativa Seeds

Macroscopically, seeds are small dicotyledonous, trigonus, angular, regulose-tubercular, 2-3.5mm×1-2 mm, black externally and white inside, odor slightly aromatic and taste bitter. Microscopically, transverse section of seed shows single layered epidermis consisting of elliptical, thick walled cells, covered externally by a papillose cuticle and filled with dark brown contents. Epidermis is followed by 2-4 layers of thick walled tangentially elongated parenchymatous cells, followed by a reddish brown pigmented layer composed of thick walled, rectangular elongated cells. Inner to the pigment layer, is present a layer composed of thick walled rectangular elongated or nearly columnar, elongated cells. Endosperm consists of thin walled, rectangular or polygonal cells mostly filled with oil globules. The powder microscopy of seed powder shows brownish black, parenchymatous cells and oil globules.



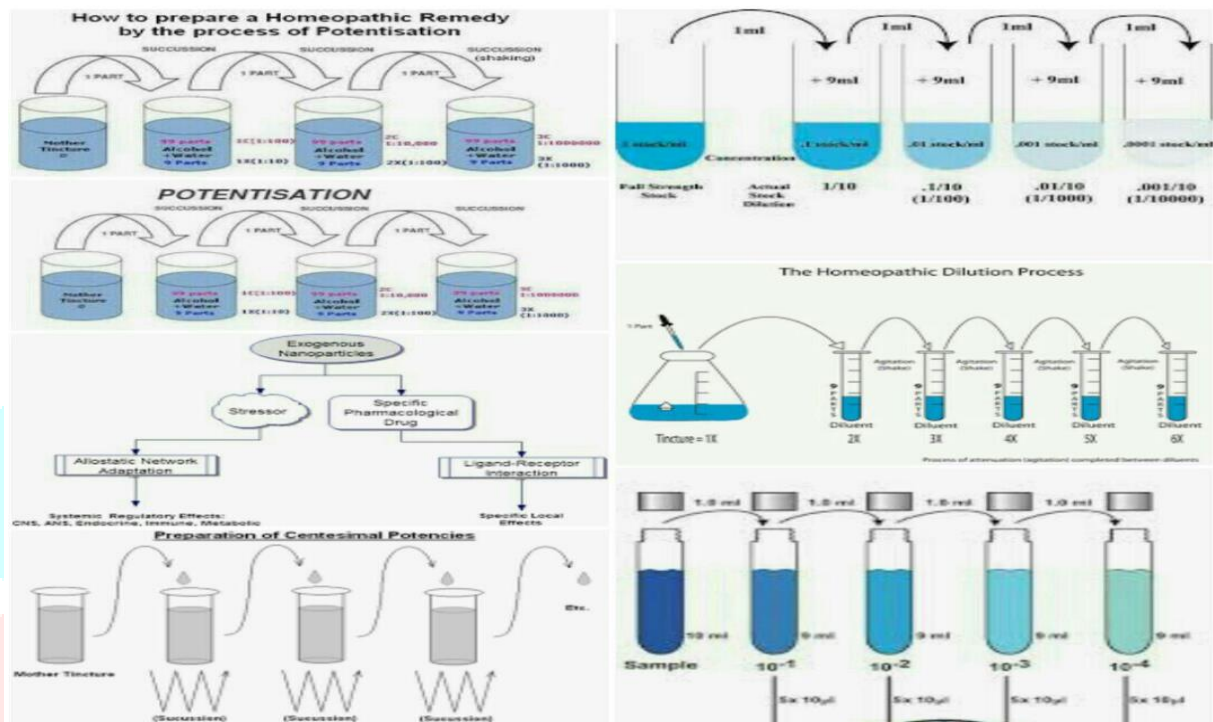
Nigella Sativa Seeds

Homoeopathy Drug Proving

Drug Proving is the method of stupifying the scientific properties of the drug substance i.e. (NIGELLA SATIVA) . In other hand we can say that it is the systematic process of investigating the pathogenic power of drug by administering the same in to the healthy individuals of different age and both sex , different geographical areas and should be trustworthy , honest ,healthy as well as mentally who can narrates symptoms exactly or may be physician as a well provers.

Background: The methodology of drug Proving has envolved considerable since the times of Dr Hahnemann standarisation of Proving process and quality of Proving studies has been a major considaration for research over years. Proving guidelins have been developed by various international bodies such as Homoeopathic Pharmacopeia committee of United States (HPCUS), European Commission of Homoeopathy (ECH) and LigaMedicorumHomoeopathica Internationalis (LMHI) and in our country a major research activities of the Central Council for Research in Homoeopathy (CCRH) are also doing vast work.Dr. Hahnemann has clearly indicated his views and given his instructions regarding the preparation of Homoeopathy mother tincture from various sources in his Organon of Medicine at aphorism 269 and 271 including foot notes. We shall examine them here and classified those plant materials in four groups depending upon the quantity of juice. They contained most juicy, moderately juicy, less juicy and dry plant samples. Class I Tincture is prepared with equal parts by weight of juice and alcohol. This mixture is allowed to stand for 8 days in a well - stoppered bottle, in a dark cool place, and is then filtere. This prepared tincture denoted by Q and known by Mother Tincture.The Homoeopathy Medicines are potentised in three scale namely 1. Decimal scale , 2. Centisimal scale, 3. Fifty Millisimal

scale. Decimal Scale: As the mother tincture in this method contains 1/ 10 of drug concentration, it corresponds to 1x potency. One drop of mother tincture and 9 drops of plane alcohol and given 10 downward strokes on the palm in equal proportion, it becomes 1X Potency. The next higher potencies are prepared with one drop of preceding Potency and nine drops of alcohol and do usual process it becomes 2X Potency. The medicine prepare under Decimal Scale are called 1X, 2X, 3X etc. And medicines are prepare under Centesimal Scale called 1,2,3,30,200,1M etc. whereas medicines are prepare under the Fifty Millisimal Scale called 0/1, 0/2, 0/3, etc.



Now a days Diabetes mellitus is increasing rapidly throughout over world, so my try to control easily and safely from this challenges. The Diabetes Mellitus (DM) is a metabolic disorder. It is increasing with the frightening rate globally. The incidence of diabetes, regardless of age, was estimated to be 8.8% in 2015 and predicted to be 10.4% in 2040 throughout the world. However, type 1 DM is less common than type 2 DM and accounts for approximately 5–10% of the entire diabetes cases worldwide. Fifty to eighty percent of diabetic patients die due to cardiovascular disorders induced by the diabetes. In addition to it, diabetes is a primary cause of blindness, kidney failure and amputation. Type 1 DM, also called as insulin dependent diabetes, is a chronic illness in which the islets produce either low or no insulin due to destruction of beta cells. Some genetic factors also involved in it. The beta cells are destroyed due to autoimmune responses. There are beta cell antigens, released from beta cells that cause the activation of immune system. These antigens are first processed then presented to T-helper 1(Th1) by the antigen presenting cells (APCs). While, Th1 cells produces some cytokines especially interferon gamma and interleukin-2 which cause the initiation of inflammation of the islet cells that ultimately results in Type 1 DM. Patients suffering from it have to take insulin on regular basis . Nigella sativa (N.s) belonging to family Ranunculaceae is an extensively used medicinal plant throughout the world . It is evident from the studies that N.s has a wide spectrum of activities including anti-diabetic, anti-cancer, immunomodulating, analgesic, anti-bacterial, anti-fungal, anti-viral, anti-parasitic,

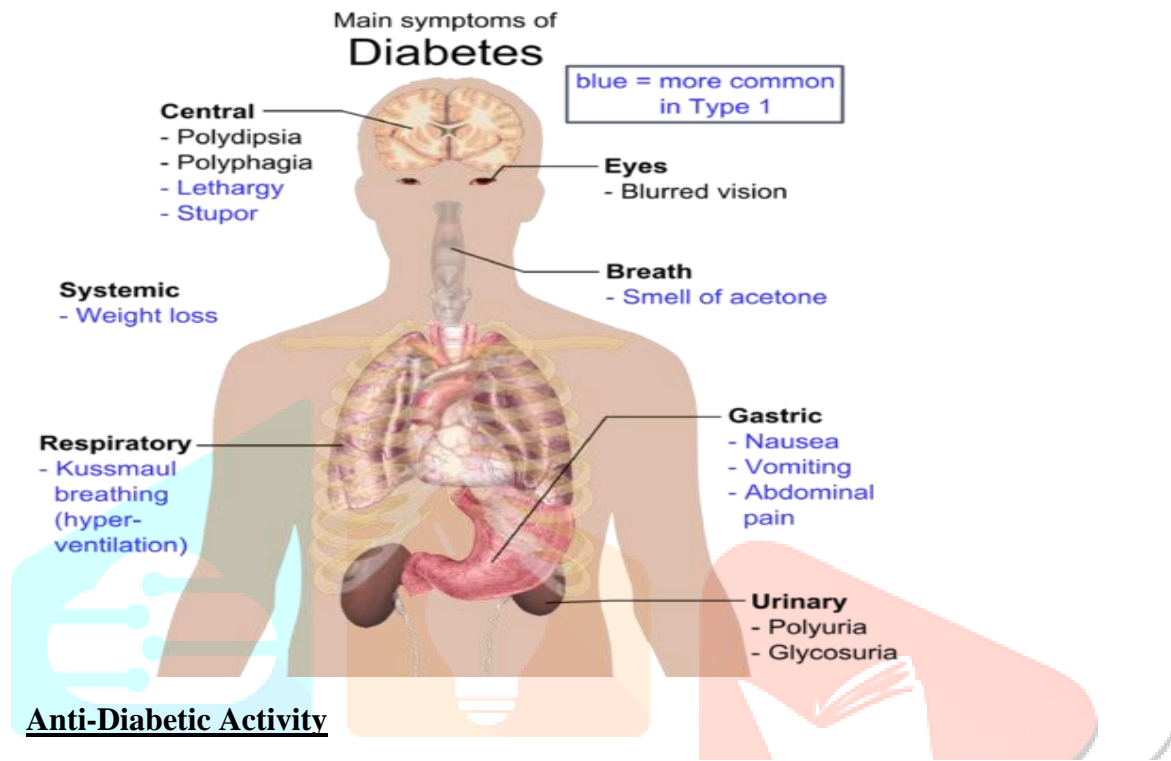
antiinflammatory, spasmolytic, anti-asthmatic, bronchodilation, anti-allergic, anti-hypertensive, hepato-protective, renal protective, cardioprotective, gastro-protective, anti-epileptic and antioxidant properties.

Diabetes is a chronic condition characterized by high levels of sugars in the blood. It affects 28.5 million people, or 8.3 percent of the U.S. population, according to the National Diabetes Information Clearinghouse. The disease occurs due to reduced production of the pancreatic hormone insulin, or due to reduced sensitivity of muscle, liver and fat cells to the hormone. Common symptoms include blurred vision, frequent urination, fatigue, weight loss and thirst. Along with a healthy diet, exercise and medications, certain herbs such as black seeds

Role of Nigella sativa Seeds in the Management of Diabetes

Diabetes as a metabolic syndrome is associated with multiple complications. Neuropathy nephropathy and retinopathy are the most common complications associated with diabetes. Diabetic peripheral neuropathy affects up to 50% of diabetic patients. It is a major cause of morbidity. Its major clinical features include neuropathic pain and insensitivity, which makes the patient more susceptible to injuries, burns and foot ulceration. Currently, serotonin norepinephrine reuptake inhibitors are used to relieve the neuropathic pain in diabetic patients. It is evident from studies that N.s oil also normalizes the value of norepinephrin, serotonin and dopamine in the brain. It suggests that N.s oil also plays a significant role in the management of diabetes associated neuropathy. Thymoquinone and N.s seed extract ameliorates the morphology of sciatic nerve and preserves the myelin sheath of axons. Hyperglycemia also induces oxidative stress in epithelial cells of renal tubules where reactive oxygen species (ROS) cause the damage and produce the fibrosis that is a typical feature of diabetic nephropathy which progressively results in renal failure. N.s, in combination with proanthocyanidin, shows protective effect against diabetic nephropathy . Osmotic imbalance, advanced glycation end products formation and oxidative stress act synergistically in the development of lens opacity in diabetes. Researchers have investigated the effect of ethanolic seed extract of N.s against diabetes induced cataract on goat eye lens. Photographic examination of eye lens revealed that ethanolic extract decelerates the development of lens opacification. Diabetic patients are more susceptible to bone fractures due to the development of osteopenia and osteoporosis resulting from enhanced urinary excretion of magnesium and calcium, production of advanced glycation end products, oxidative stress and altered osteoblast function. A study showed that combination of human parathyroid hormone (6 µg/kg/day) and N.s oil (2 ml/kg/day) is very useful in the treatment of diabetes induced osteopenia in STZ induced diabetic rats which cause to decrease the bone volume and trabecular connectivity. Anaemia is commonly seen in diabetic patients due to decreased red blood cells number. Decreased white blood cell count is responsible for immuno suppression in diabetic patients. Studies have exposed that N.s seeds can significantly increase the lowered values of RBC and WBC counts, neutrophil and packed cell volume in diabetic animal model. It shows that N.s is also useful in the management of diabetes induced hematological disturbances. Histopathological studies of diabetic rat aorta show that N.s reduces the apoptosis in vascular structures. Hydro alcoholic extract of N.s is effective against atherosclerosis and it also shows hepatoprotective action in diabetic rats. Diabetes affects the testosterone level resulting in sexual dysfunction in men. Currently, testosterone replacement therapy is recommended in such patients . Water extract of N.s seeds enhance the testosterone level in alloxan induced diabetic rodent models due to its stimulating effect on the interstitial cells of the testes. Epidemiological studies have clearly indicated that

diabetes increases the risk of numerous types of cancer including liver, pancreas, breast, urinary tract, colorectal, and female reproductive organs. Obesity, hyperglycemia, and increased oxidative stress contribute to it majorly Diabetic patients are more prone to cell mutation due to increased oxidative stress.



The therapeutic potentials of α -lipoic acid (α -LA), L-carnitine, and *N. sativa* or combination of them in carbohydrate and lipid metabolism was evaluated in a Rat model of diabetes which was induced by single *i.p.* injection of streptozocin (STZ) 65 mg/kg. For evaluation of glucose metabolism, fasting blood glucose, insulin, insulin sensitivity, HOMA, C-peptide, and pyruvate dehydrogenase activity were determined. Either α -LA or *N. sativa* significantly reduced the elevated blood glucose level. The combination of 3 compounds significantly increased the level of insulin and C-peptide. Combination of α -LA, L-carnitine and *N. sativa* will contribute significantly in improvement of the carbohydrate metabolism in diabetic rats, thus increasing the rate of success in management of DM. The effects of *N. sativa* aqueous extract and oil, as well as TQ, on serum insulin and glucose concentrations in streptozotocin diabetic rats were studied. Serum insulin and glucose concentrations, SOD levels, and pancreatic tissue malondialdehyde (MDA) were determined. Electron microscopy was used to identify any subcellular changes. Diabetes increased tissue MDA and serum glucose levels and decreased insulin and SOD levels. Treatment of rats with *N. sativa* extract and oil, as well as TQ, significantly decreased the diabetes-induced increases in tissue MDA and serum glucose and significantly increased serum insulin and tissue SOD. Ultrastructurally, TQ ameliorated most of the toxic effects of streptozotocine (STZ), including segregated nucleoli, heterochromatin aggregates (indicating DNA damage), and mitochondrial vacuolization and fragmentation. The aqueous extract of *N. sativa* also reversed these effects of STZ, but to a lesser extent. The *N. sativa* oil restored normal insulin levels, but failed to decrease serum glucose concentrations to normal. The biochemical and ultrastructural findings suggest that *N. sativa* extract and TQ have therapeutic and protect against STZ-diabetes by decreasing oxidative stress, thus preserving pancreatic β -cell

integrity. The hypoglycemic effect observed could be due to amelioration of β -cell ultrastructure, thus leading to increased insulin levels. *N. sativa* and TQ may prove clinically useful in the treatment of diabetics and in the protection of β -cells against oxidative stress. The protective effects of the volatile oil of *N. sativa* seeds on insulin immunoreactivity and ultrastructural changes of pancreatic β -cells in STZ-induced diabetic rats was reported by Kanter *et al.* 2009. STZ was injected intraperitoneally at a single dose of 50 mg/kg to induce diabetes. Increased intensity of staining for insulin, and preservation of β -cell numbers were apparent in the *N. sativa*-treated diabetic rats. The protective effect of *N. sativa* on STZ-diabetic rats was evident by a moderate increase in the lowered secretory vesicles with granules and also slight destruction with loss of cristae within the mitochondria of β -cell when compared to control rats. It is evident that *N. sativa* treatment exerts a therapeutic protective effect in diabetes by decreasing morphological changes and preserving pancreatic β -cell integrity. The antihyperglycemic potential of TQ on the activities of key enzymes of carbohydrate metabolism in streptozotocin (STZ)-nicotinamide (NA)-induced diabetic rats was evaluated. Oral administration of TQ at 20, 40, 80 mg/kg body weight for 45 d, dose dependently improved the glycemic status in STZ-NA induced diabetic rats. The levels of insulin, Hb increased with significant decrease in glucose and HbA_{1c} levels. The altered activities of carbohydrate metabolic enzymes were restored to near normal. These results proved that TQ at 80 mg/kg body weight is associated with beneficial changes in hepatic enzyme activities and thereby exerts potential anti-hyperglycemic effects. The *N. sativa* showed the synergistic effect with human parathyroid hormone in improving bone mass, connectivity, biomechanical behavior and strength in insulin-dependent diabetic rats and found to be more effective as compared to the treatment with *N. sativa* or human parathyroid hormone alone. In a clinical study, the adjuvant effect of *N. sativa* oil on various clinical and biochemical parameters of the insulin resistance syndrome were investigated. *N. sativa* oil was found to be effective as an add-on therapy in patients of insulin resistance syndrome. *N. sativa* oil has a significant activity in diabetic and dyslipidemic patients. *N. sativa* is of immense therapeutic benefit in diabetic individuals and those with glucose intolerance as it accentuates glucose-induced secretion of insulin besides having a negative impact on glucose absorption from the intestinal mucosa. The effects of the TQ in STZ-induced diabetes in rats were investigated. The Effect of *N. sativa* seeds on the glycemic control of patients with type 2 diabetes mellitus was investigated in 2010. *N. sativa* seeds were used as an adjuvant therapy in patients with diabetes mellitus type 2 added to their anti-diabetic medications. *N. sativa* at a dose of 2 gm/day caused significant reductions in fasting blood glucose, 2 h postprandially (2 hPG), and glycosylated hemoglobin (HbA_{1c}) without significant change in body weight. The results indicate that a dose of 2 gm/day of black seed might be a beneficial adjuvant to oral hypoglycemic agents in type 2 diabetic patients. The *in vivo* antidiabetic activity of *N. sativa* seed ethanol extract (NSE) was evaluated in diabetic Meriones shawi. Plasma lipid profile, insulin, leptin, and adiponectin levels were assessed. ACC phosphorylation and Glut4 protein content were determined in liver and skeletal muscle. NSE animals showed a progressive normalization of glycaemia. It was also demonstrate that *in vivo* treatment with NSE exerts an insulin-sensitizing action by enhancing ACC phosphorylation, a major component of the insulin-independent AMPK signaling pathway, and by enhancing muscle Glut4 content.

Conclusion

The use of herbal drugs as complementary medicine is prevalent and gaining world wide popularity. Many drugs are derived directly from plants; while the others are chemically modified natural products. The original research articles published so far have confirmed the pharmacological potential of *N. sativa* and extracts and some of its active principles, particularly TQ and alpha-hederin possess remarkable *in vitro* and *in vivo* pharmacological activities against a large variety of diseases and found to be relatively. But I found during my research according to principle of Homoeopathy many unique benefits found, especially in Diabetes Mellitus, carcinoma, GIT disorder and non healing ulcer recover very soon and safely.

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