



Efficacy of *Nigella Sativa* L. in Prevention of Gestational Diabetes Mellitus: A Review

Tuba Razi^{1*}, Fahmeeda Zeenat¹

¹ Department of Amraz-e-Niswan wa Atfal, Faculty of Unani Medicine, Ajmal Khan Tibbiya College, Aligarh Muslim University, Aligarh

* tubarazi30095@gmail.com

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ABSTRACT

Background: India accounts for 17% of the world's diabetics, earning it the moniker "diabetes capital of the world." Gestational diabetes is one of the main risk factors of developing diabetes later in life. Along with increase in rate of diabetes mellitus there is parallel increase in cases of gestational diabetes mellitus as well. This alarming increase in rate of GDM is worrying because it not only increases morbidity and mortality rate of mother but the child also. It is managed by diet, physical exercise, hypoglycaemic drugs and insulin injections.

Despite the fact that conventional hypoglycaemic medications for the management of diabetes already exist, their unavailability, high cost, and related side effects in low-income countries continue to be serious concerns. As a result, finding alternate methods to manage diabetes has always been a top concern. *Nigella sativa* L. (Family: Ranunculaceae) has been well researched for its biological properties and is recognised as an important traditional treatment for diabetes management. In Unani medicine diseases are treated with less toxic herbal drugs. *Nigella sativa* is one of many important drugs mentioned in Unani literature for treatment of various ailments. **Method:** A systemic review of all relevant studies on conducted using electronic database such as PubMed, Scopus, Google Scholar etc. including manual search of textbooks available in the Institutional Library. **Results:** A thorough and critical examination of clinical research on the effectiveness, safety, and mechanism of action of *Nigella sativa* is provided in this systematic review. **Conclusion:** Given the results of the clinical studies and negligible side effects, *Nigella sativa* has a promising future in the creation of bioproducts for the treatment of gestational diabetes. To shed more light on thymoquinone's clinical application in the control of diabetes and gestational diabetes mellitus, additional research should examine the precise mechanism of actions through which it exerts its therapeutic antidiabetic benefits.

Key words: gestational diabetes, *Nigella.sativa*, diabetes mellitus.

Introduction

Gestational diabetes according to WHO, hyperglycaemia first detected at any stage during pregnancy should be classified as diabetes mellitus in pregnancy or gestational diabetes.¹

According to American association of diabetes (2022), gestational diabetes is diabetes diagnosed during 2nd or 3rd trimester of pregnancy, that was not clearly an overt diabetes prior to gestation.

According to national health survey data, the GDM rate increased by 30% between 2016 (6%) and 2020. (7.8 percent). From 2016 to 2019, the GDM rate increased by an average of 5% every year; from 2019 to 2020, it increased to 15%. In India, it is estimated that 4 million women currently suffer from GDM.²

Risk factors associated with GDM are obesity, family history of diabetes, having gestational diabetes in previous pregnancy, age of women i.e., advanced age at time of pregnancy (more than 30 years) and race (African -American, Asian, Hispanic, Pacific islanders)

Gestational diabetes is mainly managed by diet, physical exercise, hypoglycaemic medications (standard – metformin) and insulin injections. Since all these medications cause other side-effects in the long run and are costly therefore many people can't afford the treatment^{3,4}. So, it is need of the hour to formulate some new plant-based medications which are cost effective and cause fewer side-effects.

Pharmacological and therapeutic uses of *Nigella sativa* has been described in classical Unani literature. It was referred as Malathion by eminent Unani academics Hippocrates and Dioscorides. It is native to Egypt and they called it as Habbatul Sauda.⁵ It was traditionally used for variety of conditions and treatments related to respiratory health, stomach and intestinal health, kidney and liver function, circulatory and immune system support, and for general well-being. In Tibb-e-Nabvi (Prophetic Medicine), this plant has been described as a drug which can cure all diseases except death.

Consequences of GDM

Women with GDM are at increased risk of developing dm type 2 in future and so is the child. Others could be preeclampsia, macrosomia, problems with delivery, usually in association with foetal overgrowth including shoulder dystocia, and Erb's palsy and asphyxia, as well as increased rates of Caesarean section. It is observed that children born to diabetic mothers are 4 to 8 times more likely to develop diabetes mellitus 2 in future. It can Also lead to abortion, preterm labour, polyhydramnios, maternal and foetal distress.

Historical background of *Nigella sativa* Linn.

Nigella sativa originally comes from Latin word Niger which means black and sativa means cultivated.⁶The book of Isaiah in the Old Testament is regarded to contain the oldest documented mention to *Nigella sativa*. Easton's Bible dictionary asserts that the Hebrew word "Ketsah" unquestionably refers to *N. sativa*⁷.

Avicenna or Bu Ali Cena one of the most renowned unani physician wrote in his most famous book "the cannon of medicine" or AL qanoon fit tib the *Nigella sativa* is a seed that increases body energy and helps in recovery from many ailments. this is an example which indicates the use of *Nigella sativa* by Unani physicians since times immemorial.⁸

Morphological description of *Nigella sativa*

The plant is 30 and 60 cm tall. The leaves are thread-like pinnatisect, 2 to 5 cm long, and greyish in colour. Flowers have a greyish blue hue.⁹ The petals are eight in number, and the sepals are clawed. The fruit is a large, inflated capsule with many seeds within that is built up of three to seven connected follicles. Trigonous and rugose-tubercular describe the seeds. They have an exterior colour of black or brown, are oleaginous on the interior, and smell strongly, pleasantly, and somewhat like nutmeg. They taste peppery and pungent as well.¹⁰ Parts used are dried seeds and leaves¹¹



Nigella sativa leaves



Nigella sativa plant

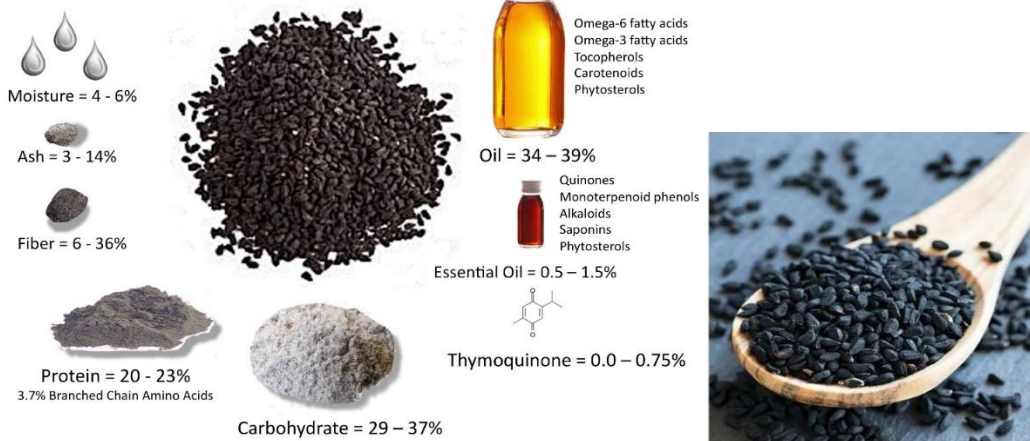


Nigella sativa flower



Nigella sativa seed pod

What's in *Nigella sativa* Seeds ?



Nigella sativa seeds

Chemical constituents present in *Nigella sativa*^{12,13,14,15}

CHEMICAL CONSTITUENT	PERCENTAGE OF CONSTITUENT
Oleic acid	3.4–6.3%
Volatile oil	0.5–1.6%
Ether extract	35.6–41.6%.
Thymoquinone	30–48%
carvacrol	6–12%
Protein	26.7%
Fat	28.5%
Carbohydrates,	24.9%
Total ash	4.8%

Physiological effects of *Nigella sativa* and its component TQ

Black seed oil extract effects a number of systems, including the uterine, smooth muscle, respiratory, cardiovascular, and gastrointestinal systems.

GALACTAOGOGUE: Ether extract of seeds when injected into lactating rats on balanced diet showed more powerful galactagogue action than oestrogen.¹⁶

ANTI-HISTAMINIC: Essential oil and nigellone protected guinea pigs against histamine induced bronchospasm.^{16,17}

BRONCHODILATORS: the crude extract of *Nigella sativa* seeds exhibited spasmolytic and bronchodilator actions, concentrated in the organic fraction of the extract and may have been mediated by calcium channel blockage.¹⁸

Evidence indicates that *Nigella sativa* oil has a protective role against gastric ulcers¹⁹

ANTIBACTERIAL ACTION: The essential oil of the seeds was active against *E. coli*, *Salmonella paratyphi*, *Staphylococcus aureus*, *Aspergillus flavus* and *Fusarium tenuis*.^{16,20}

ANTI-INFLAMMATORY ACTION: In a prospective and double-blind clinical trial study effects of *Nigella sativa* might lessen the occurrence of nasal mucosal congestion, nasal itching, runny nose, sneezing attacks, turbinate hypertrophy, and mucosal pallor.²¹

Results and Discussion:

NAME OF STUDY	RESULTS
Kooshki, et al. ²² Effect of <i>Nigella sativa</i> oil supplement on risk factors for cardiovascular diseases in patients with type 2	<i>Nigella sativa</i> supplements was significantly associated with decreased FBS (p .001), triglycerides (p .001), total cholesterol

diabetes mellitus. <i>Phytother. Res.</i> 2020, 34, 2706–2711.	(p .001), low-density lipoprotein cholesterol (p .001), serum hs-CRP, and increased serum levels of high-density lipoprotein cholesterol (p .001).
Kaatabi, et al. ²³ <i>Nigella sativa</i> improves glycaemic control and ameliorates oxidative stress in patients with type 2 diabetes mellitus: Placebo controlled participant blinded clinical trial. <i>PLoS ONE</i> 2015, 10, e0113486	FBG in <i>Nigella sativa</i> and HbA1c both significantly decreased over time as compared to placebo. Similar differences were seen in the levels of c-peptide, insulin resistance.
Bamosa, et al. ²⁴ Effect of <i>Nigella sativa</i> seeds on the glycaemic control of patients with type 2 diabetes mellitus. <i>Indian J. Physiol. Pharmacol.</i> 2010, 54, 344–354.	conclusion of the 12-week therapy period, at dose of 2 g/day as an adjuvant to oral hypoglycaemic medications HbA1c decreased by 1.52% (p <0.0001). insulin resistance was considerably decreased (p0.01)
Heshmati et al. ²⁵ <i>Nigella sativa</i> oil affects glucose metabolism and lipid concentrations in patients with type 2 diabetes: A randomized, double-blind, placebo-controlled trial. <i>Food Res. Int.</i> 2015,70, 87–93.	Fasting blood sugar, glycated haemoglobin, triglycerides, and low-density lipoprotein cholesterol all decreased significantly in the intervention group when compared to the placebo group (p<0.05)
Rachman et al. ²⁶ .The efficacy of black cumin seed oil and hypoglycaemic drug combination to reduceHbA1c level in patients with metabolic syndrome risk. <i>IOP Conf. Ser. Mater. Sci. Eng.</i> 2017, 259,012018.	Black seed oil in the dose of 1.5 ml and 3ml/day for 20 days resulted in a decreased value of Hba1c (p<0.05).
Darand. M et al. ²⁷ The effects of black seed supplementation on cardiovascular risk factors in patients with non-alcoholic fatty liver disease: A randomized, double-blind, placebo-controlled clinical trial. <i>Phytother. Res.</i> 2019, 33, 2369–2377	At a dose of 2g/day resulted in significant decreases in serum glucose (-7.95 vs. -1.22; p =.041), serum insulin (-3.87 vs. 1.07; p =.027), and a significant rise in the quantitative insulin sensitivity check index (-0.03 vs.0.006; p=0.002).
Moustafa, H.A.M et al. ²⁸ Effect of <i>Nigella sativa</i> oil versus metformin on glycaemic control and biochemical parameters of newly diagnosed type 2 diabetes mellitus patients. <i>Endocrine</i> 2019, 65, 286–294	At a dose of 1.35 g/day for 3 months in newly diagnosed td2 patients was inferior to metformin (2 g/day) in lowering fbg ,2 h ppg and hba1c but was comparable to metformin in lowering fasting insulin (-1.7 vs. -1.2), insulin sensitivity (+7.6 vs. +16.7%), and insulin resistance (-0.39 vs. -0.29).
Najmi, A.; Nasiruddin, M.; Khan, R.A.; Haque, ²⁹ S.F. Effect of <i>Nigella sativa</i> oil on various clinical and biochemical parameters of insulin resistance syndrome. <i>Int. J. Diabetes Dev. Ctries.</i> 2008, 28, 11.	At a dose of 5ml/day for 6 weeks <i>Nigella sativa</i> group demonstrated a marginally higher decrease in fbg (-29.24 ± 6.09 vs. -18.46 ± 6.77 mg/dl) and ppg (-23.39 ± 8.54 vs. -19.87 ± 6.22 mg/dl) compared to standard therapy.
Ali, S.M et al. ³⁰ Thymoquinone (TQ) with metformin decreases fasting, post prandial glucose, and HbA1c in type 2 diabetic patients. <i>Drug Res.</i> 2021, 71, 302–306	Compared to diabetic mice treated with only metformin, those given with a combination of TQ and metformin had significantly lower blood sugar levels.
Dalli, M et al. ³¹ Chemical Composition Analysis Using HPLC-UV/GCMS and Inhibitory Activity of Different <i>Nigella sativa</i> Fractions on Pancreatic α -Amylase and Intestinal Glucose Absorption. <i>BioMed Res. Int.</i> 2021, 2021, 9979419.	Results showed that the high-dose <i>Nigella sativa</i> seed polysaccharides could significantly lower the levels of fbg, glycosylated serum protein (gsp), triglycerides (TQ), total cholesterol (tc), low-density lipoprotein cholesterol (ldl-c) and significantly increased insulin

Conclusions:

Review of classical Unani literature highlights the importance of *Nigella sativa* as described by eminent Unani academics Hippocrates and Dioscorides. It was traditionally used for variety of conditions and treatments related to respiratory health, stomach and intestinal health, kidney and liver function, circulatory and immune system support, and for general well-being.

The effectiveness of *Nigella sativa* and its compound TQ in the clinical therapy of diabetes mellitus was discussed in this review. Based on the results, *Nigella sativa* can be regarded as a highly bioactive medicinal plant. A bioproduct should be made from *Nigella sativa* and pharmacologically verified through in vivo and clinical investigations. It would be quite effective to administer *Nigella sativa* in the prevention of gestational diabetes. Although very little to no research has been done to determine *Nigella sativa*'s effectiveness in avoiding gestational diabetes, the studies on DM have created a research need in this area. Numerous studies have demonstrated *Nigella sativa*'s effectiveness in drastically lowering blood glucose levels, which

support its use in the treatment of gestational diabetes. Further studies should be done to find its significance which can really be beneficial in near future.

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