

## Thymoquinone (Nigella Sativa) : Nature's Miracle Herb - A Review



### Medical Science

**KEYWORDS :** Thymoquinone ,Anti-Inflammatory, Anti-Oxidant ,Bactericidal

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### ABSTRACT

*Nigella Sativa* , commonly known as Black seed/ cumin is an annual plant which belongs to Ranunculacea family and traditionally used in Indian subcontinent, Arabian countries and Europe for medicinal purposes like skin diseases, jaundice, hypertension, diabetes, rheumatism, headache , fever, influenza ,asthma ,cough , gastrointestinal problems, anorexia and paralysis. *Nigella Sativa* seeds contain diverse but well characterized chemical components, capable of inducing beneficial pharmacological effects in Humans. *Nigella Sativa* includes essential oils, proteins, alkaloids and saponins. Most of the properties of *Nigella Sativa* are attributed to thymoquinone (2-isopropyl-5 methyl 4- benzoquinone).Thymoquinone exhibits inhibitory and bactericidal effects on both gram positive and gram-negative bacteria and also a synergistic effect with other antibiotics. This review focuses on the thymoquinone properties like anti-inflammatory, anti oxidative and capability of inhibition of proinflammatory cytokines that are thought to play a significant role in preventing the initiation and progression of Periodontitis.

### INTRODUCTION:

Periodontitis is an inflammation of periodontium that extends beyond the gingiva and destroys the connective tissues to which teeth attaches<sup>1</sup>. Bacteria associated with dental plaque has been widely accepted for the cause of inflammatory periodontal diseases<sup>1,2</sup>.With increasing our knowledge and understanding of bacterial diseases, a more direct antimicrobial agent has become an important aspect of periodontal therapy<sup>2</sup>. The treatment of chronic Periodontitis focuses on arresting the destruction of periodontal support through the removal of some pathogenic bacteria present in the periodontal pocket<sup>1</sup>. Mechanical scaling and root planning accomplish this goal<sup>1</sup>.Presence of tortuous and deep pocket often results in considerable variation in the effectiveness of scaling and root planning. Which is one reason to employ antimicrobial agent in management of chronic Periodontitis<sup>3</sup>. Presence of tortuous and deep pocket often results in considerable variation in the effectiveness of scaling and root planning<sup>3</sup>.Which is one reason to employ antimicrobial agent in management of chronic Periodontitis<sup>3</sup>. To over come some of the adverse effects caused by antimicrobial agent , WHO advocates researchers to investigate the possibility of using natural products such as plant extracts and herbs as alternative <sup>4</sup>. *Nigella sativa* , commonly known as Black seed/ cumin is an annual plant belongs to Ranunculacea family and traditionally used in Indian subcontinent , Arabian countries and Europe for medicinal purposes<sup>1,5</sup>.*Nigella sativa* seed contains diverse but well characterized chemical components , capable of inducing beneficial pharmacological effects in humans<sup>1,5</sup>. *Nigella sativa* ,includes essential oils ,proteins , alkaloids and saponins<sup>1</sup>.Most of the properties of *Nigella sativa* are attributed to Thymoquinone(2 isopropyl-5 methyl 4-benzoquinone).Thymoquinone exhibit inhibitory and bactericidal effects on both gram positive and gram negative bacteria and also synergistic effects with other antibiotics <sup>1,6</sup>. This review focuses on the thymoquinone properties like anti-inflammatory , anti oxidative , immune modulatory , anti cancer and capability of proinflammatory cytokines that are thought to play a significant role in preventing the initiation and progression of Periodontitis.

### PHARAMCOGNOSTICAL CHARACTERISTICS :

#### 1.plant morphology

*Nigella Sativa* is an Annual flowering plant grows 20-90 cm tall, with finely divided leaves, the leaf segment narrowly linear to thread like . Flower are delicate and usually colored white , pink, pale blue or pale purple with 5-10 petals .Fruit is large and inflated with capsule composed of 3-7 United follicles , each containing numerous seeds<sup>7</sup>.





## 2.characteristics of seed

They are small dicotyledonous, trigonous , angular , regulose- tubercular , 2- 3.5 mm X 1-2 mm, black externally and white inside. Transverse section of seed show single layered epidermis consisting of elliptical ,thick walled cells covered externally by a papillose cuticle and filled with dark brown content<sup>5,7</sup>. Epidermis is followed by 2-4 layers of thick walled tangentially elongated paranchymatous cells , followed by a reddish elongated cells. inner to the pigment layer , is present a layer composed of thick walled rectangular elongated or nearly columnar, elongated cells<sup>5,7</sup>.

## Chemical Composition Of Black Seeds<sup>5,8,12</sup>

### NS Oil Composition

Fundamental oil composition	Nigella sativa
Thymoquinone	30-48%
Thymohydroquinone, dithymoquinone, p-cymene	7-15%
4- terpeneol	2-7%
Carvacrol	6-12%
Alkaloids- nigellicime, nigellicime N-oxide , Saponins- potential anticancer agent , lamonene	Traces amount

## Saturated and unsaturated fatty acids:

Saturated acid	18.1%
Monounsaturated acid	23.8%
Polyunsaturated acids	58.1%

## Nutritional values:

protein	26.7 %
Fats	28.5 %
Carbohydrates	24.9 %
Total ash	4.8%
vitamins	Carotene Riboflavin, Thiamin
minerals	Cu, Zn ,P, Fe ,

## Fatty acids:

saturated	Unsaturated
Linoleic acid- 50-60%	Palmitic acid
Oleic acid - 20 %	Stearic acid
Eicodadienoic acid – 3 %	
Dihomolinoelic acid-10%	

## TRADITIONAL USES:

*Nigella sativa* has been traditionally used in treatment of variety of disorders , diseases and conditions pertaining to Respiratory system, Digestive tract, Liver function, Cardio-vascular function, immune system, kidney function ,as well as for general well-being<sup>7</sup>.

Avicenna refers to black seed in the “canon of medicine”, as seeds stimulate the body’s energy and helps recovery from fatigue and dispiritedness. The seeds traditionally used in Southeast Asian and the Middle East countries for the treatment of several diseases and ailments including asthma , bronchitis , rheumatism and inflammatory diseases<sup>7</sup>. A tincture prepared from black seed is useful in indigestion , loss of appetite , diarrhea, dropsy , amenorrhea and dysmenorrhea and in treatment of warms and skins<sup>5,7</sup>. Externally the oil is used as an antiseptic and local anesthetic . Roasted black seeds are given internally to stop the vomiting<sup>7</sup>.

## PHARMACOLOGICAL PROPERTIES

### 1.Antibacterial activity

Antibacterial properties of *Nigella Sativa* is due to its constituents particularly Thymoquinone and melanin<sup>10</sup>. In vitro studies of anti bacterial activity shows Ethanol extract of seed inhibited the growth of *methicillin resistant staphylococcus aureus* (MRSA)<sup>9,10</sup> . *methanol, chloroform extract ,essential oil* shows significant anti bacterial activity against *staphylococcus aureus* and *E.coli*. All oil samples were more active against gram positive than gram negative bacteria. Crude alkaloid and water extract are more effective against gram negative (16) than gram positive (6) bacteria<sup>7,9,10</sup>. Methanol extract of seed exhibit antiplaque action by inhibiting *streptococcus mutant* ,thus preventing caries formation<sup>9</sup>. It was found to exhibit antibacterial activity against *Bacillus pumilus* , *B. subtilis* , *streptococcus mutans* , *staphylococcus aureus* ,*P.aeruginosa*<sup>9</sup> . It was shows that thymoquinone possess clinically useful anti *H. pylori* activity, comparable to triple therapy<sup>7</sup>.

### 2.Anti inflammatory effects

The crude fixed oil of *Nigella sativa* seed, have been found to inhibit the eicosanoid generation and measure lipid per oxidation , through the inhibition of cyclooxygenase (COX) and 5-lipoxygenase (LO) pathways of arachidonate metabolism thus responsible for its anti-inflammatory activity<sup>9</sup>. It helps in reduction of MCP-1, TNF-alpha, Interleukin (IL) 1 beta and cox-2<sup>9,11</sup>. TQ as a novel inhibitor of proinflammatory pathways provides a promising strategy that combines anti inflammatory and proapoptotic modes of action<sup>7</sup>.

### 3.Anti oxidative effects

TQ is a rich source of Phytochemical due to which it shows anti-oxidative properties. Thymoquinone induces antioxi-

dant responses through the scavenging capability of various free radicals( ROS)<sup>11</sup>. It's scavenging power being as effective against superoxide dismutase<sup>11</sup>. The anti-oxidant action of *Nigella Sativa* may explain its claimed usefulness in folk medicine . The essential oil of *Nigella Sativa* was tested for a possible antioxidant activity. The essential oil , thymoquinone and other components like *carvacrol* , *anethole* and *4-terpineol* demonstrated respectable *Radical scavenging property*(ROS).<sup>12</sup>

#### 4. Immunomodulatory activity

The radio protective potential of NS crude oil against hemopoietic adverse effect of gamma irradiation was evaluated. Oral administration of *Nigella Sativa* oil before irradiation considerably normalized significant increase of malondialdehyde concentration with significant decreases in plasma glutathione peroxidase , catalase , Erythrocyte superoxidase dismutase activities promising natural protection against immunosuppressive and oxidative effects of ionizing radiation<sup>9</sup>.

#### 5. Antidiabetic activity

Studies on the plant mixture containing *Nigella Sativa* revealed that the blood glucose lowering effect was due to inhibition of hepatic gluconeogenesis and the plant extract mixture may prove to be useful therapeutic agent in treatment of non-insulin dependent diabetes mellitus<sup>12</sup>.

#### 6. Anti cancer activity

Cancers are the abnormal cell growth caused by genetic alteration. Any agent which has anti-cancer activity ,either protect genetic material from alteration or kill the genetically altered cancer cells<sup>13</sup>. Thymoquinone acts on cancer cell to help to kill them by several molecular pathways. The possible mechanism of thymoquinone action on cancer cells are i) TQ induces apoptotic cell death in cancerous tissues by up regulating expression of apoptotic genes ( caspase-3,8,9 and bax) and down regulating expression of anti apoptotic genes(bcl-2). ii) TQ suppresses AKT activation by dephosphorylation and thus block cancer cell survival. iii) TQ protects normal cells injury caused by ionizing radiation in the treatment of cancer. iv)TQ prevents CYP450 enzyme from environmental damage and protects cell from cancer, v) TQ increases the activities of antioxidant enzymes and protects cell against cancer<sup>13</sup>.

The first report of anticancer activity of thymoquinone was noted against Ehrlich's ascites carcinoma, Daltons lymphoma ascites and sarcoma-180 cells<sup>11</sup>. Thymoquinone showed anti-cancer activity against hepatocellular carcinoma by the inhibition of HepG2 cells in a dose –dependent manner<sup>11</sup>.

#### 7. Effects On Alkaline Phosphate

Thymoquinone reduces the level of Alkaline Phosphates when given intraperitoneally<sup>11</sup>.

#### 8. Hepatoprotective Activity

Oral administration of 1ml/kg seed oil every day for one week prior to carbon tetrachloride(CCL<sub>4</sub>) injection alleviated ccl<sub>4</sub>-induced suppression of CYP2B, CYP3A2, CYP2C11 and CYP1A2, and also down regulated the ccl<sub>4</sub> induced iNOS mRNA and up regulated IL-10 mRNA. These results suggest that this protective effect is partly due to the down regulation of the anti inflammatory IL-10<sup>9,14</sup>.

#### 9.Gastroprotective Effects

Thymoquinone has protective role against gastric ulcers and its function is relative to keep the oxidation –reduction balanced of with gastric mucosa. It also help to protect gastric mucosa against the injurious effects of absolute alco-

hol and promote ulcer healing. TQ inhibit stomach tumor which created due to BP and relatively might decrease proliferation 67-70%<sup>11,15,16</sup>.

#### 10. Effects On Bacterial Biofilm

Thymoquinone prevents plaque Biofilm formation 90% -*Staphylococcus aureus*, *Staphylococcus epidermidis* ,*Enterococcus faecalis* , <50% - *Pseudomonas aeruginosa*. Thymoquinone has same antibacterial activity as gentamycin and erythromycin .Gram negative bacilli resist to Thymoquinone action are *Salmonella enterica* , *Pseudomonas aeruginosa* , *Escherichia coli*<sup>17</sup>.

#### 11. Effects On Periodontitis

Thymoquinone used in chitosan based chip in treatment of Periodontitis shows Significant improvement in plaque index, Reduction in *periodontal pocket depth* as compared with chlorhexidine chip and scaling and root planning, increased in *clinical attachment level* as compared with chlorhexidine chip and scaling and root planning. As concentration of thymoquinone in chitosan based chip increase shows better results as compared with Chlorhexidine and SRP<sup>11,18</sup>.

Oral administration of thymoquinone diminishes alveolar bone resorption in rat Periodontitis model when administered by gastric feeding<sup>11</sup>.

Periodontal chip containing thymoquinone can be used at same appointment as scaling and root planning or during periodontal maintenance appointments. Periodontal chip formulated from thymoquinone incorporated in a chitosan base as a targeted method of drug delivery system provide clinical benefits that are achieved when using these chip as an adjunct to conventional scaling and root planning in management of chronic Periodontitis<sup>11,18</sup>.

#### CONCLUSION:

All finding discussed above indicate that thymoquinone (*Nigella sativa*) have antimicrobial, anti-inflammatory, antioxidant, anticancer, anti diabetic ,Immunomodulatory effects. Considering anti-inflammatory & antioxidant properties & capability of significantly inhibiting the expression of proinflammatory cytokines, thymoquinone thought to play a significant role in preventing the initiation and progression of Periodontitis. Further studies are required to study the effects of thymoquinone on Periodontitis in humans.

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