Constituents :
Nigellone has the chemical formula C18H22O4.
1- Volatile oil (up to 1.4%) : Thymoquinone (the major component of the volatile oil), nigellone (carbonyl
polymer of thymoquinone, C18H22O4), carvone, a-pinene, b-pinene, sabinene, p-cymene, and others.
2- Fixed oil (27-40%) :
3- Saturated fatty acids (18.1%) : Myristic (0.5%), palmitic (13.7%), stearic (2.6%), and arachidic (13.7%).
Unsaturated fatty acids :
a)Monounsaturated acids (23.8%) : Palmitoleic (0.1%) and oleic (23.7%).
b)Polyunsaturated acids (58.1%) : Linoleic (Omega - 6,57.9 %) and linolenic (alpha - linolenic, omega -
3,0.2%).
Black seed oil is one of the few oils containing gamma linolenic acid (makesprostaglandins of the one series).
Lipid contents of N. Sativa are neutral lipids which are predominant, glycolipids
and phospholipids which are present in lower quantities. Glycolipids consisted of monogalactosyl diglyceride, digalactosyl diglyceride, sterylgalactoside and acetylated
sterylgalactoside, while the phospholipids comprised of phosphatidy1-choline,phosphatidylethanolamine,
phosphatidylinositol,phosphatidylglycerol,candiolipin,Lysophosphatidylethanolamine
and lysophosphatidylcholine.
4 - Alkaloids : Isoquinoline alkaloids (nigellimine and nigellimine N-oxide), nigellidine (indazole alkaloid) and igellicine.
5-Saponin : Melantin (melanthin).
Proximate analysis of Nigella sativa seeds showed a composition of around 21% protein (fifteen amino acids make up the protein content of the black seed, including eight of the nine essential amino acids. Glutamic acid, arginine and aspartic acid were the main amino acids present. Black seed contains arginine which is essential for infant growth), 38% fat (linoleic and oleic acids were the major unsaturated fatty acids while palmitic acid was the main saturated one), 4% moisture, 4% ash, 8% crude fibre and 32% total carbohydrates. Potassium, phosphorus, sodium and iron were the prominent elements present. Zinc, calcium, magnesium, manganese and copper were found at lower levels. Lead, cadmium and arsenic were not detected in the seeds.
Actions and uses :
History and folklore :
Black seed was found in the tomb of Tutankhamun, but its role in ancient Egypt, medicinal or otherwise, is unknown, Dioscorides, a greek physician of the 1st century AD, recorded that black cumin seeds were taken to treat headaches, nasal congestion, toothache, and intestinal worms, and, in large quantities, as a diuretic, a promoter of menstruation, and to increase breast-milk production. In cooking, the seeds can be used as a substitute for pepper and can be sprinkled on

bread and cakes. The distilled essential oil is used as a flavouring in confectionery.

Seeds mixed with honey and taken first thing in the morning to stimulate appetite (appetizer); seeds are remedy for eczema, toothache, stiffness in joints, headaches, intestinal parasties especially in children antipoison, taenicide, also take part in treatment of influenza, migraine sinustitis, asthma, respiratory affections, paralysis, soothing stomach pain leprosy, general antidote for poisonous bites, for delayed menses emmenagogue, flatulence (carminative), diuretic, galactagogue (used in India to increase breast milk), antispasmodic, gout, liver hypofunction and bleeding disorders including epistaxis and haemophilia. The seeds are also used as condiment and for treating conjunctivitis and polio. The seeds are claimed to have digestive, diaphoretic, antipyretic and antidiarrhoeal properties. In Yemen the seeds are used for constipation and haemorrhoids and worn in amulets to protect against evil spirits.
Herbalists in several Middle Eastern countries claim several therapeatic uses for Nigella sativa L. expressed oil. The expressed oil is commonly used for treatment of bronchial asthma, respiratory oppression and as an antitussive, and as ear drops for earache treatment. Topically, the oil is used as an- analgesic for headache, to reduce
inflammation and to treat psoriasis. The vapour from oil added to boiling water is inhaled as a remedy for various respiratory tract conditions such as colds, influenza and bronchial asthma. Rheumatic diseases are treated by massaging the warm oil on the affected area.
Different studies :
Seed extracts of Nigella sativa exhibit antibacterial, anti-inflammatory CNS depressant and analgesic activities. The seed oil has been used as a local anaesthetic. In studies with rats and mice, the oil showed significant CNS - depressant activity and a very marked analgesic effect at 1 ml/kg, p.o. No evidence of toxicity was noted at 10 times this dosage. It is suggested that the analgesic activity may be due to the presence of an opioid principle in the oil. In tests with 37 isolates of Shigella species (S .dysenteriae, S. Flexneri. S. sonnei, and S. boydii) and 10 strains of V. cholerae and E.coli, the volatile seed oil of N. sativa showed promising activity against all the strains except one of S. dysenteriae. The minimum inhibitory concentration of the oil was between 50 and 400 mug/ml for the various strains. These results indicate that the seed oil has therapeutic potential for the treatment of diarrhoea.
Seed extracts and seed oil from N. sativa, exhibit insecticidal antibacterial, bronchodilator, hypotensive and immunostimulant properties. The spasmolytic effects of an EtOH extract, and the

volatile oil, of seeds, were tested in vitro using isolates segments of rabbit intestinal smooth muscle. Both substances inhibited spontaneous movements of rabbit intestine, and the volatile oil inhibited contractions which were induced by high potassium (K+ solutions or acetylcholine. This inhibition was dose-dependent, reversible and not affected by the addition of calcium to the organ bath. These data suggest that the seed volatile oil has an antispasmodic effect, possibly due to a calcium antagonistic activity.
The seeds of N. sativa are used in a herbal preparation used to treat diabetes mellitus. The effects of the volatile oil, extracted from the seeds, on the levels of glucose and insulin in rabbits were investigated and the administration of 50 mg/kg i.p. to fasting normal and alloxan-diabetic rabbits produced significant hypoglycaemic effects. These effects were consistent and time-dependent. In

normal animals, 15% and 23% decreases, and in diabetic rabbits, 12% and 21% decreases in fasting plasma glucose levels were detected 4h and 6h, respectively, after treatment. The administration of the volatile oil did not alter basal insulin levels in all animal groups, which might suggest a non-insulin-mediated mechanism of action for the hypoglycaemic activity.
Seed samples of Indian, Ethiopian, Turkish and unknown geographical sources of N. sativa were examined by thin-layer and gas chromatography for content of fixed oils and thymoquinone (a major component of the volatile oil), and these substances were tested as possible inhibitors of eicosanoid generation and membrane lipid - peroxidation. The crude fixed oil and pure thymoquinone both inhibited the cyclooxygenase and 5 lipoxygenase pathways of arachidonate metabolism in rat peritoneal leukocytes stimulated with calcium ionophore A2318, as shown by dose-dependent inhibtion of thromboxane B2 and -leukotriene B4, respectively. Thymoquinone was very potent, with approximate IC50 values against 5 lipoxygenase and cyclooxygenase of < 1 and 3.5 g/ml, respectively. Both substances also ihibitied non-enzymatic peroxidation in ox brain phospholipid lioposomes, but thymoquinone was about ten times more potent. However, the inhibition of eicoasnoid generation and lipid peroxidation by the fixed oil of N. sativa is greater than is expected from its content of thymoquinone (ca. 0.2% w/v), and it is possible that other components such as the unusual C20:2 unsaturated fatty acids may contribute also to its anti-eiocosanoid and antioxidant activity. These biological properties of the oil support the traditional use of N. sativa and its derived products as a treatment for rheumatism and related inflammatory diseases.
The effect of the volatile oil of N. sativa seeds on the cellular

polypeptides of Jurkat T leukaemia cells was analyzed using two-dimensional polyacrylamide gel electrophoresis (2-D PAGE) and silver staining. Two polypeptide spots, with a MW of 24 kDa and isoelectric points of 5.3 (acidic protein) and 5.8 (basic protein), were changed in their intensity following treatment. The basic protein was decreased and the acidic protein was increased after 10 min of N. sativa volatile oil treatment. The 2 protein spots had a pinkish colour after silver staining. Analysis of (32P)-labelled Jurkat cells did not reveal any radioactivity in the vicinity of these 2 proteins. Analysis
of lymphoid and non-lymphoid cell lines treated with activating and differentiating agents did not reveal any-changes in these 2 proteins. Several normal cells and neuroblastoma tumours with and without N-myc gene amplification expressed the basic protein only. Immature leukaemic cells expressed the acidic protein in addition to the basic protein spot. These results suggest that the changes in these protein spots as a result of N. sativa treatment may reflect a role in its biological effect (s), perhaps, through posttranslation modification of the protein.
Nigella sativa seeds and the oil extract but not the water extract from them, showed antibacterial activity against all 5 tested strains of listeria monocytogenes; the inhibitory effect was similar on all 5 strains, with the minimum inhibitory concentration being 0.5 and 1.5% for seeds and oil extract respectively. The inhibitory property of the oil extract was not affected by C/15 min. when seeds or oil extract were added C/15 or 30 min; or 121 C/30 min, 100 heating at 65 to processed cheese contaminated with about 4X 104 c.f.u. L. monocytogenes/g, the listeria were C/24 h compared with an increase in count to about completely eliminated after incubation at 37 108/g in control cheese.

Nigella sativa seeds and Dregea volubiis leaves are used in Ayurvedic medicine to treat various disorders and are considered to have galactogogue activity. Aqueous extracts of N. sativa seeds and mature D. volubilis leaves were therefore administered orally to rats and histopathological changes in the liver in both treatment groups at the end of 14 days were compared with a control group which received distilled water under identical conditions for 30 days and with a group of normal animals. Degenerative changes in hepatocytes were seen following administration of D. volubilis while consistent significant histopathological changes were not evident following administration of N. sativa.
Topical application of extracts of N. sativa and Crocus - sativus (saffron), inhibited two-stage skin carcinogenesis in male Swiss mice (initiation and promotion with dimethylbenz [a] anthracene and croton oil]. When the extracts were applied at 100 mg/kg body

weight, onset of papilloma formation was delayed and mean number of papillomas per mouse was reduced. Mice were given a subcutaneous injection of 745 nmol 20-methylcholanthrene (MCA) on 2 days to initiate soft tissue sarcomas. After
30 days they were given N. sativa extract intraperitoneally or saffron by mouth at 100 mg/kg. Controls were given saline. The spices restricted neoplasm incidence to 33.3 and 10%, respectively, compared with 100% in controls.
The diethyl ether extract of N. sativa seeds (24-400 mg extract/filter paper disc) caused concentration - dependent inhibition of Gram-positive bacteria (Staphylococcus aureus), Gram negative bacteria (Pseudomonas aeruginosa and Escherichia coli) and Candida albicans. The extract also showed antibacterial synergism and additive activity when combined with various antibiotics. It successfully eradicated a non-fatal subcutaneous S. aureus infection in mice when injected at the site of infection.
42 Sheep positive for Moniezia expansa infection by examination of faecal samples (by a direct smear method) were selected for studying the efficacy of powdered N. sativa seeds. The powder was suspended in 2% gum tragacanth and given orally to the experimental sheep at doses of 1.5, 2.0 or 2.5 g/kg body weight. Extracts in ethanol or water were given at dosages containing 2.5g powder / kg body weight. Extracts in ethanol or water were given at dosages containing 2.5 g powder / kg body weight. Niclosamide (0.01 g/kg) was given to treat a control group of sheep. The results were evaluated by faecal egg counts on days 3, 10 and 15 after treatment. No effects on egg counts were seen on day 3, but on day 15 the powdered seeds at 2.5 g/kg, the equivalent given as an ethanol extract, and the niclosamide were equally effective in treating the sheep.
A preventative for dental caries contains at least 1 of a lower alcohol extract, aqueous lower alcohol extract or water extract obtained from e.g. Myristica fragrans Van Hout., Peucedanum graveolens Benth., N. sativa L., Sida cordifolia L., Embelia ribes Bunn., Azdirachta indica A. Juss., Pongamia glaba Vent., Strychnos nux-vomica L., Quercus infectoria Oliv., Blettaria cadamomus Maton, Tephrosia purpurea Pres. and Coscinium fenestratum Colebr. To prevent dental caries, Streptococcus mutans, Streptococcus sanguis and Streptococcus mitis etc. must be destroyed. The preparation which is based on herbal medicine is safe and effective. The plant listed are used in Sri Lanka, and extracts of the plants may be used in toothpaste, gargles, ointments or chewing gum etc.

In mice, an extract of Crocus sativus stigmas partially prevented the decreases in body weight, haemoglobin levels and leucocyte counts caused by 2 mg cisplatin (a cytotoxic drug) i.p. for 5 days.

Treatment with the C. sativus extract prolonged the life span of cisplatin-treated mice almost 3-fold. In contrast, an extract of N. sativa seed only tended to protect from cisplatin induced falls in hemoglobin levels and leucocyte counts.
The volatile oil of N. sativa seeds inhibited the contractions of rabbit aortic rings induced by norepinephrine stimulation in Ca2+ - containing solution, but not in Ca2+ - free solution. This inhibition was dose dependent and reversible. Also, the volatile oil inhibited the contraction of rabbit aortic rings induced by high potassium (K+) solution. These data suggest that the volatile oil of N. sativa seeds possesses a direct vascular smooth muscle relaxant effect, possibly by interfering with the influx of extra-cellular Ca2+ . (calcium antagonistic activity).Anticestodal effect of N. sativa seeds was studied in children infected naturally with worms, the activities were judged on the basis of percentage reductions in the faecal eggs per gram (EPG) counts. Single oral administration of 40 mg/kg of N. sativa, equivalent amount of its ethanolic extract and 50 mg/kg of niclosamide reduced the percentage of EPG counts not significantly different from each other on the days 7 and 15. Therefore, it is conceivable that the N. sativa contain active principles effective against cestodes. The crude did not produce any adverse side effects in the doses tested.
Plant mixture extract comprising of N. sativa, myrrh, olibanum asafoetida and aloe have a blood glucose lowering effect. The anti-diabetic action of the plants extract may, at least partly, mediated through decreased hepatic gluconeogenesis. The extract may prove to be a useful therapeutic agent in the treatment of non-insulin dependent diabetes mellitus (NIDDM).
Volatile oil of N. sativa induced respiratory effects, mediated via release of histamine with direct involvement of histaminergic mechanisms and indirect activation of muscarinic cholinergic mechanisms. Removal of thymoquinone from volatile oil may provide a potential centrally acting respiratory stimulant.
Nigella sativa seeds fatty acids showed 50% cytotoxicity to Ehrlich ascites carcinoma, Dalton's lymphoma ascites and Sarcoma 180 cells at a concentration of 1.5
micrograms, 3 micrograms respectively with little activity against lymphocytes. Tritiated thymidine incorporation studies indicated the possible action of an active principle at DNA level. In vivo Ehrlich ascites carcinona tumour development was completely inhibited by the active principle at the dose of 2 mg /mouse per day x 10 .
Nigellone in relatively low concentrations is very effective in inhibiting histamine release. The mechanism of action seems to be through decreasing intracellular calcium by inhibiting its uptake and stimulating the efflux, and by an inhibition on protein kinase C. There is also indication for a mild inhibition of oxidative energy metabolism contributing to some inhibition of the release.

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The volatile oil of N. sativa induced cardiovascular depressant effects, mediated mainly centrally via indirect and direct mechanisms. The direct mechanisms may be due to the presence of thymoquinone in the volatile oil. The volatile oil seemed to possess the potential of being a potent centrally acting antihypertensive agent.
The volatile oil of N. sativa seeds inhibited the spontaneous movements of rat and guinea pig uterine smooth muscle and also the contractions induced by oxytocin stimulation. These effects were concentration-dependent and reversible by tissue washing.

Therefore volatile oil of N sativa may have some anti-oxytocic potential.
Diethyl ether extract of N. sativa seeds caused concentration - dependent inhibition of Gram positive bacteria represented by Staphylococcus aureus. Gram negative bacteria represented by Psendomonas aeruginosa and Escherichia coli (but not Salmonella typhimurium and a pathogenic yeast Candida albicans. The extract showed antibacterial synergism with streptomycin and gentamicin and showed additive antibacterial action with spectinomycin, erythromycin, tobramycin, doxycycline, chloramphenicol, nalidixic acid, ampicillin, lincomycin and sulphamethoxyzole-trimethoprim combination. The extract successfully eradicated a non-fatal subcutaneous staphylococcal infection in mice when injected at the site of infection.
Some antibacterial properties of the N. sativa seeds active principle with some clinical applications have been carried out as the following:
Using the direct incoulation of several strains of Gram positive and Gram negative bacteria into the crude oil of N. sativa L. seeds showed that the crude oil became completely sterile after 24 hours except with Pseudomonas pyocyanea strains which all survived (10 strains). Paraffin oil tubes inoculated with the same organisms acted as controls.

With the gutter technique the crude oil diluted 1/10 inhibited the growth of all Gram positive bacteria tested above i.e. 7 strains of Staphylococcus aureus, 5 strains of Streptococcus pyogenes, 3 strains of Streptococcus faecalis, 3 strains of Pseudo-anthrax bacillli, 2 strains of Streptococcus pneumoniae, 3 strains of Staphylococcus albus and 2 strains of Diphtheroid bacilli. No inhibition of growth was noted with 26 strains of Pseudomonas Pyocyaneas, 5 strains of Friedlander's bacillus, 7 strains of Bacterium coli, 4 strains of Paracolon bacilli, 4 strains of Faecalis alkaligenes 16 strains of Proteus, 1 strains of Salmonella typhi and one strain of each of Salmonella paratyphi A,B,C.
Fractionation of the crude oil into a volatile oil and a fixed oil and their subsequent testing showed that the antimicrobial activity was confined solely to the volatile oil. In the same way the total fatty acids fraction, the non-saponifiable matter fraction and the non-acidic fraction of the volatile oil were found to have no activity. Further fractionation showed that the phenolic fraction was responsible for the antimicrobial activity and all the other fractions except the acidic fraction were found to be inactive in the this respect.
The incorporation of the crude oil into media in which viable counts were performed showed that for staphylococci as representative of

Gram positive organisms, the concentration needed to inhibit growth varied between 0.4-0.6 % V/V. For Gram negative bacilli as examplified by strains of Bacterium coli, the concentration had to be raised up to more than 6% to obtain an appreciable inhibition. The volatile oil was inhibiting in 0.04 -0.06% concentration for staphylococci and 0.6-0.8% for B. coli. The phenolic fraction was as active as the volatile oil towards staphylococci but was inactive towards B. coli.

In propylene glycol, it was found that the active concentration of the phepnlic fraction could be lowered to 0.1% in which concentration all types of bacteria were inhibited. Below this concentration, the Gram negative bacteria were the first to escape inhibition. This may be attributed to an increased niscibility of the culture media with the active principle in an organic phase, as propylene glycol is devoid of any antibacterial effect.

In most essential oils which investigated for the possible antiseptic or germicidal action it was observed that: direct contact of the bacteria with the oils appeared to be more effective than the vapours. From the bacteriological investigations, this seems to be true also for N. sativa essential oil as direct contact of various Gram positive and Gram negative bacteria with the oil itself leads to their disappearance after 24 hours except for Pseudomonas pyocyanea. As would be expected with antiseptics, the activity of the phenolic fraction was found to be diminished in the presence of blood and serum.

The phenolic fraction when injected in relatively high doses (2000mg /kg body weight) in rats was found to be completely nontoxic (immediate or late effects). In dogs, this fraction was found to have no effect on the blood pressure or respiration. Similarly, it had no effect on the isolated toad's heart when it was perfused with Ringer's solution containing 2mg% of this fraction and perfused even for more than 30 minutes.

The causative microorganisms of external otitis are varied, and complex. Usually streptococcus, P. pyocyaneas, Plaut Vincent organism, staphylococcus and rarely diphtheria.

Ointments and creams of various kinds have been recommended for the treatment of external otitis containing such drugs as ammoniated mercury, resorcin and many others. Inevitably sulphonamides, penicillin and other antibiotics have been incorporated in these remedies and as in other cases good results have been reported and also many failures. The bacteriology of otitis external is also so complex that treatment in the absence of thorough bacteriological investigations must be to some extent, on a basis of trial and error and it must be realized that no specific remedy has yet been discovered.

The organisms cultured from the external ear inflammation and the results of treatment are as the following:
Staphylococcus aureus was isolated in most cases, giving very good response to treatment with 1% phenolic fraction in propylene glycol with marked improvement within three days for the secretions, desquamative process and itching. The desquamative plug in the canal was fully inhibited. Cure occurred in about one week. No recurrence occurred in 8 months follow up. Only three cases relapsed and required further use of 1 % solution of the essential oil itself. Streptococcal cases did not respond quickly and a longer treatment period was necessary. Gram negative bacilli proteus and Pseudomonas pyocyanea were very slightly affected by the active fraction and although some cases showed improvement, yet the organisms could be found in the external ear in all these cases and we fell that the apparent improvement in symptoms was a mere subsidence phase in the course of the disease. It is interesting to note that in cured Gram positive cocci cases, when controlling the external ear organisms, the culture was completely sterile even for ordinary inhabitants and remained so for variable periods of time.
In cases of the patients complaining of maxillary sinusitis it was found that the patients treated with the phenolic fraction in the above mentioned concentrations, the opacity disappeared and the sinus remained free later.
According to the amount of muco-pus aspirated from the sinus and the degree of pathological changes of the mucosa, the cases under treatment were divided into three groups:
All Gram positive cocci encountered (Staphylococcus aureus, streptococcus and Pneumonia cocci) were strongly affected by the phenolic fraction and were not recovered by culture from sinus aspirate in the three types. This accounted for the high percentage of cure in the mild and moderate types. In the advanced cases although the organism was not recultured from the aspirate, yet the persistence of discharge in spite of being lesser in amount condemned this group as not cured. We attribute this to the advanced pathological changes in the mucosa with cystic or polypoid changes.
This was also confirmed radiologically. The Gram negative bacilli {Paracolon bacilli. Influenza bacilli and Friedlanders bacillius) were cultured from the sinus aspirates and were responsible for the failure in treatment. Being accompanied by improvement of symptoms; headache and discharge indicated that they were affected to a limited degree by the active fraction. The rapidity of cure was proportional to the concentration used. Thus cases in which 1% phenolic fraction was used needed a smaller number of punctures than using 0.2% or 0.5% and cases which did not respond to the first concentrations responded well when the higher concentration was used.

During the treatment of all cases with the phenolic fraction in its different concentration; no side action or inconvenience was recorded.

In other words, it can be concluded that, the antibacterial activity of the crude N. sativa oil was tested by different methods and it was found that the oil inhibited the growth of many strains of Gram positive and Gram negative bacteria except some strains of Pseudomonas pyocyaneas. The fractionation of the oil into several fractions and their subsequent testing showed that the activity was confined solely in the phenolic fraction of the essential oil. The incorporation of the active fraction in propylene glycol lowered the active concentration of the drug towards different microorganisms. The biological data of this active fraction showed that it is non-toxic. Clinically the phenolic fraction was used in the treatment of thirty seven cases of chronic external otitis and thirty three of chronic purulent maxillary sinusitis. In cases of external otitis, the phenolic fraction was used as drops in propylene glycol instilled repeatedly in the ear. In cases of maxillary sinusitis, the drug was instilled in the sinus repeatedly by punctures. Control cases of maxillary sinusitis were punctured and propylene glycol was instilled to exclude its action if any.

The drug was highly effective in curing external otitis and moderate cases of maxillary sinusitis in the concentration mentioned especially where the affecting microorganism was a Gram positive bacterium. However in cases where the affective organism was a Gram negative bacillus, there was improvement associated with subsidence of symptoms but the microorganisms could always be recovered by culture. This applies also to the advanced cases of positive cocci entailing cystic or polypoidal changes of the mucosa. In chronic maxillary sinusitis, it was found that the action of the drug is more potent than that of systemic antibiotics. This was demonstrated 'by the radiological reopacity of the sinus previously treated with antibiotics and by the clearance of that opacity when the drug was instilled.

The effect of thymoquinone, from N. saliva, on ifosfamide (IFO)-induced Fanconi syndrome (FS) and its antitumour activity were investigated in rats and mice, respectively. In rats, administration of IFO (50 mg /kg, i.p., for 5 days) induced FS and decreased creatinine clearance rate. Administration of thymoquinone in the drinking water (5 mg /kg per day) for 5 days before and during IFO treatment ameliorated the severity of IFO induced renal damage. Thymoquinone significantly improved IFO-induced phosphaturia, glucosuria, elevated serum creatinine and urea, and significantly normalized creatinine clearance rate. Moreover, thymoquinone significantly prevented IFO induced renal glutathione depletion and lipid peroxide accumulation. In mice bearing Ehrlich ascites

carcinoma (EAC) xenograft, thymoquinone (10 mg /kg per day, p.o.) significantly enhanced the antitumour effect of IFO (50 mg/kg per day, i.p. on days 1 - 4 and 15-18). Mice treated with IFO in combination with thymoquinone showed less body weight loss and a lower mortality rate compared with IFO single therapy. Thymoquinone may improve the therapeutic efficacy of IFO by decreasing IFO-induced nephrotoxicity and improving its antitumour activity.

Herbal combination of N. sativa, Leptadena reticulata, Foeniculum vulgare, Pueraria tuberosa, and Asparagus racemosus were clinically effective in curing >95% of cases of four types of primary indigestion (alkaline indigestion, impaction, acidic indigestion and bloat) in 144 lactating Murrah buffaloes. This herbal preparation provided a potent stimulation for early restoration of milk production without any adverse effect.
Powdered N. sativa seeds given daily for 10 days at a level of 100 mg /kg body weight to goats with agalactia were significantly increasing the milk yield during treatment and post- treatment (20 days). Nigella sativa may be a useful galactagogue.
Aqueous extract of N. sativa seeds reduced the ulcer index of acetyl salicylic acid -treated rats. The extract decreased the volume of gastric juice but did'not affect mucin activity or peptic activity. There is qualitative changes in hexose and fucose contents of carbohydrates.
The volatile oil of N. sativa seeds inhibits the contractions of quinea pig tracheal smooth muscle induced by histamine stimulation and the contractions of rabbit tracheal smooth muscle induced by acetylcholine stimulation. This inhibition was dose -dependent and reversible. Also, the volatile oil inhibited by high potassium (K+) solution. Meanwhile, the volatile oil did not inhibit the contractions of guinea pig and rabbit tracheal smooth muscle induced by histamine and acetylcholine, respectively, in Ca+-free solution. These data suggest that the volatile oil of N. sativa has a calcium antagonist effect.
o The fixed oil of N. sativa seeds produced dose-dependent inhibition of the generation of thromboxane B2 (TXB2) and leukotriene B4 (LTB4) via exerting an inhibitory activity on cyclooxygenase and 5-lipoxygenase pathways respectively. Inhibition of TXB2 and LTB4 synthesis occurred in parallel. Thymoquinone, an active constituent present in the volatile oil of N. sativa was also inhibitory, it resulted in dose-dependent inhibition of TXB2 and LTB4 production. Thymoquinone at 5 mg /ml results in 79.3% and 100 % inhibition of the production of TXB2 and LTB4 respectively, while at 50mg /ml it results in 94.3% inhibition of TXB2 generation. In comparison, the oil at 5 mg /ml was found to

result in 45.1% inhibition of TXB2 and no inhibitory effect was observed for LTB4 production at this concentration. At 50 mg /ml the oil resulted in 100% inhibition of the production of both TXB2 and LTB4. Although thymoquinone was found to possess great inhibitory activities on both cyclooxygenase and 5-lipoxygenase enzymes, it is not the sole constituent that accounts for the inhibitory activities exhibited by N. sativa fixed oil.
These biochemical actions of decreased eicosanoids production may explain some of the plant's claimed therapeutic actions.
N. sativa seeds fixed oil at 12 mg /ml causes a 50% inhibition of eicosanoid generation. Up to this point the fixed oil was more active at inhibiting the production of TXB2 than LTR4. At a concentration higher than 12 mg /ml the fixed oil was more active at inhibiting the generation of LTB4 than TXB2. However, it was evident that the inhibitory effects of N. saliva fixed oil were dose-dependent. Both TXB2 and LTB4 synthesis were inhibited in a parallel fashion. Thymoquinone more active at inhibiting the synthesis of LTB4 than TXB2. The inhibition of eicosanoid production by thymoquinone was also found to be dose-dependent.

Inhibition of TXB2 and LTB4 generation by the fixed oil in a parallel fashion points to phospholipase A2 as a possible site of action, because this enzyme is of major importance in the formation of arachidonic acid which is then metabolized via cyclooxygenase and 5-lipoxygenase pathways. However, direct actions of N. sativa fixed oil and thymoquinone on both cyclooxygenase -and 5-lipoxygenase enzymes cannot be ruled out.
In other words, it can be concluded that although thymoquinone was found to possess great inhibitory activities on both cyclooxygenase and, 5-lipoxygenase enzymes, it is not the sole constituent that accounts for the inhibitory activities exhibited by N. sativa fixed oil.
In conclusion various active constituents in N. sativa fixed oil are capable of strongly suppressing the generation of eicosanoids by inhibiting both cyclooxygenase and 5-lipoxygenase pathways. Highlighting the fact that .V. sativa fixed oil blocks both cyclooxygenase and 5-lipoxygenase pathways it can be classified as a dual blocker.
According to what has been discussed above the inhibitory actions. exhibited by N. sativa fixed oil may explain the uses of the plant seeds and the fixed oil of the seeds in Middle East folk medicine for the treatment of headache, pain, bronchial asthma and psoriasis which are conditions related to the biological effects of products of arachidonate metabolism via both cyclooxygenase and 5-lipoxygenase pathways.
In one series of 27 volunteers, the black seed taken in the amount

of two grams a day (1 g twice daily) for four weeks improved the ratio between the Helper T cells (T4) and Suppressor T cells (T8) by 55% and 30% average enhancement of the natural killer (NK) cell activity. In a second series of 19 volunteers, the black seed taken in the same amount improved the Helper T cell to Suppressor T cell ratio by 72% while the control groups showed no apparent improvement. The black seed also improved the Natural Killer cell activity by an average of 74%. These findings may be of great practical significance since a natural immune enhancer like the black seed could play an important role in the treatment of cancer, AIDS, and other disease conditions associated with immune deficiency states.

Toxicity studies in animals showed the N. sativa extract to be free of any irritant or toxic effect, even when injected in large doses. The extracts of the N. sativa seeds by natural fat and petroleum ether caused shortening of clotting time. In studying the effect of black seed on the first time of the cellular defence of the body i.e. the phagocytes, showed significant enhancement of ingestion (ingestion is one of the most important function of the immune system and the easiest to test) in the tested mice as shown by the higher per centage of macrophages ingesting the organism. Nigellone in relatively low concentration is very effective in inhibiting histamine release from the mast cells.

Intravenous administration of volatile oil or thymoquinone to rats decreased the arterial blood pressure and the heart rate in a dose - dependent manner. The volatile oil induced cardiovascular depressant effects were mediated mainly via indirect and direct mechanisms, that involved both 5-hydroxytryptaminergic and muscarinic mechanisms. The volatile oil seemed to possess the potential of being a potent centrally acting antihypertensive agent. The direct mechanism may be due to the presence of thymoquinone in the volatile oil.

The petroleum ether extract of the seeds at 1000 -62.5 ppm concentration was found to have the same activities as growth regulating juvenile hormone when tested against the fifth instar larvae of Dysdercus similis.

The extract of N. sativa seeds when used properly is useful in treating cancer, preventing toxicity of anticancer drugs in human body (i.e. it protects the bone marrow against the chemotherapy and at the same time it can act as anti-cancer agent), protecting the normal cells from the cytopathic effects of the virus and in increasing immune function (increases antibody producing B cells). N. sativa seed extract also has been found to help restore immune competent cells in immunosupressed cancer patients and to over stimulate bone marrow formation in normal individual. N. sativa seed extract, rather than the increase of the immune competent cell number, has been found to help free tumor antigen binding sites on

B cells, there by elevating the CD19 (Cluster Differentiation 19. These are antibodies which help detect B lymphocytes. Elevation in CD19 indicates an elevation in B lymphocytes and vice versa) and associated cell population. When antigen binding site on the immunoglobulin molecule on the surface of B cells is free because of N. sativa treatment, it binds to the tumor associated antigen thereby generating an immune response against the antigen.
Protection of human amniotic " WISH " cells from cytopathic effect of vesicular stomatitis virus (VSV) was also observed upon administration of N. sativa seed extract.
Additionally, the serum interferon level is found to increase; and hence, the N. sativa extract has interferon like antiviral activity. This is an example of interferon level increasing in the circulation, preventing viral diseases and, in addition possibly curing viral diseases.
N. sativa promotes anti-tumor activity. Data from pharmacosensitivity screening indicates anti-tumor activity of N. sativa seeds extract mainly against melanoma and colon cancer types N. sativa seed extract destroys tumor cells and leaves normal cells alone possibly because of its ability to bind to cell surface asialofeutin (lectin) in diseased cells, which causes aggregation and clumping of tumor cells.
It also blocks enzymes and inappropriate gene products involved in nucleic acid synthesis and metabolism.

Administration:

The extract of N. sativa may be administered by itself or in admixture with an appropriate excipient or carrier.
The preparation may be administered to the patient by enteral, such as oral or rectal and parentral such as intraperitoneal, intramascular, intravenous or subcutaneous route.
The preparation may also be administered in combination with supplements, such as antiviral agents, immune modulators, antibodies, other chemotherapeutic agents or combination thereof.