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REVIEW

Potential of Secondary Metabolite Compounds of Black Cumin Seeds (*Nigella sativa* L.) as Therapeutic Agents for Chronic Diseases

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Abstract: Black cumin (*Nigella sativa*) has gained considerable attention in recent years due to its potential health benefits. This aromatic plant, native to the Middle East, North Africa, and South Asia, has long been used both as a culinary spice and as a traditional medicine. Ethnopharmacological studies highlight its antioxidant, anti-inflammatory, and antimicrobial properties. Recent research on the bioactive extracts, oils, and compounds derived from *N. sativa* seeds has demonstrated promising potential in the prevention and treatment of chronic diseases, including cancer, diabetes, and inflammatory disorders. This review aims to provide a comprehensive overview of the therapeutic potential of *N. sativa* seed compounds as reported in previous studies. The discussion covers their role in managing chronic diseases such as diabetes, cancer, and immune-related disorders, as well as their implications in overcoming drug resistance. In addition, this review examines the bioactivity of *N. sativa* seed extracts, oils, and isolated compounds, along with Structure Activity Relationship (SAR) studies, as a foundation for advancing research and development of natural therapeutic agents for chronic diseases.

Keywords: *Nigella sativa*, biological activities, secondary metabolite, chronic diseases

Introduction

Nigella sativa, commonly known as Jintan Hitam or Habbatussauda in Indonesia and Black Cumin in English, has a rich history of culinary and medicinal applications worldwide. This tiny flowering plant, native to Asia, Africa, and the Mediterranean, is celebrated for its small, distinctive black seeds.[1] These seeds have been valued for their pungent odor and potential health benefits and have played a significant role in traditional medicine and regional cuisines. As a spice and condiment in Middle Eastern, Indian, and North African cuisines, they are often sprinkled onto bread or incorporated into spice blends.[2]

N. sativa has a long history as a traditional remedy in various cultures. The seeds are believed to possess medicinal properties, and have been used to address a wide range of health issues, including digestive, respiratory, and skin ailments. Research on bioactive compounds found in *N. sativa* such as thymoquinone, suggest potential antioxidant, anti-inflammatory, and antimicrobial effects, making it a subject of interest in modern scientific exploration.[3,4] The extracts, oils, and some secondary metabolite compounds of *N. sativa* seeds have been tested in vitro and in cell culture against several chronic diseases, such as diabetes, cancer, and immunomodulation, showing promising results. These results demonstrate the potential for therapeutic applications in the management of diabetes, cancer, and immune-related diseases, considering that these diseases affect almost all people worldwide and are the leading causes of death.[5] The bioactivity of *N. sativa* seeds is supported by their secondary metabolites such as flavonoids, triterpenoids, alkaloids, and essential oils. The utilization of bioactive compounds from natural sources remains an important area of research, given the urgent need for safe and non-resistant drugs.[6,7]

This journal discusses the mechanisms of chronic diseases, including diabetes, cancer, immune related disorders, and drug resistance. It presents a special review on the bioactivity of N. sativa extracts, oils, and isolates, as well as structure activity relationship (SAR) studies of its compounds, which may serve as valuable references for the treatment of chronic diseases.

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Selected Chronic Diseases

Diabetes

Diabetes affects a significant proportion of the global population. Lifestyle factors and genetic predisposition are major contributors to the development of this disease. Diabetes is a life-threatening condition due to the challenges of maintaining blood glucose control and the need for lifelong treatment. Two major types of diabetes are recognized and remain important subjects of research. Type 1 diabetes results from autoimmune destruction of insulin-producing pancreatic β-cells, whereas type 2 diabetes is primarily associated with insulin resistance and progressive β-cell dysfunction.[8,9]

Type 1 Diabetes

Type 1 diabetes is primarily caused by the autoimmune mediated destruction of pancreatic β-cells by T lymphocytes. The resulting β-cell damage leads to reduced insulin production.[10,11] Current therapeutic approaches, such as T cell misreading repair therapy, aim to mitigate the pathogenic activity of T cells against β-cells; however, this strategy may introduce new complications by potentially enabling the proliferation of other malignant cells. The mechanism of T cell induced β-cell destruction is illustrated in Figure 1. [12] Current therapy trials are investigating both antigen specific and antigen nonspecific immune interventions, on the side strategies to restore β-cell mass through islet transplantation, neogenesis, regeneration, or a combination of these approaches.[13]

Type 2 Diabetes

Type 2 diabetes mellitus (T2DM) is a metabolic disorder characterized by impaired regulation of blood glucose, primarily resulting from insulin receptor dysfunction.[14] In addition, excessive or uncontrolled insulin secretion from pancreatic β-cells may further exacerbate receptor insensitivity. Insulin resistance is a key pathological hallmark of T2DM, driven by both established and emerging cellular mechanisms that collectively impair insulin receptor signaling in relation to circulating insulin levels. Hyperinsulinemia plays a critical role by producing a paradoxical state attenuated glucose-lowering efficacy alongside sustained lipid synthesis and lipoprotein secretion. Therefore, improving insulin sensitivity remains a central therapeutic target in the management of T2DM.[15,16]

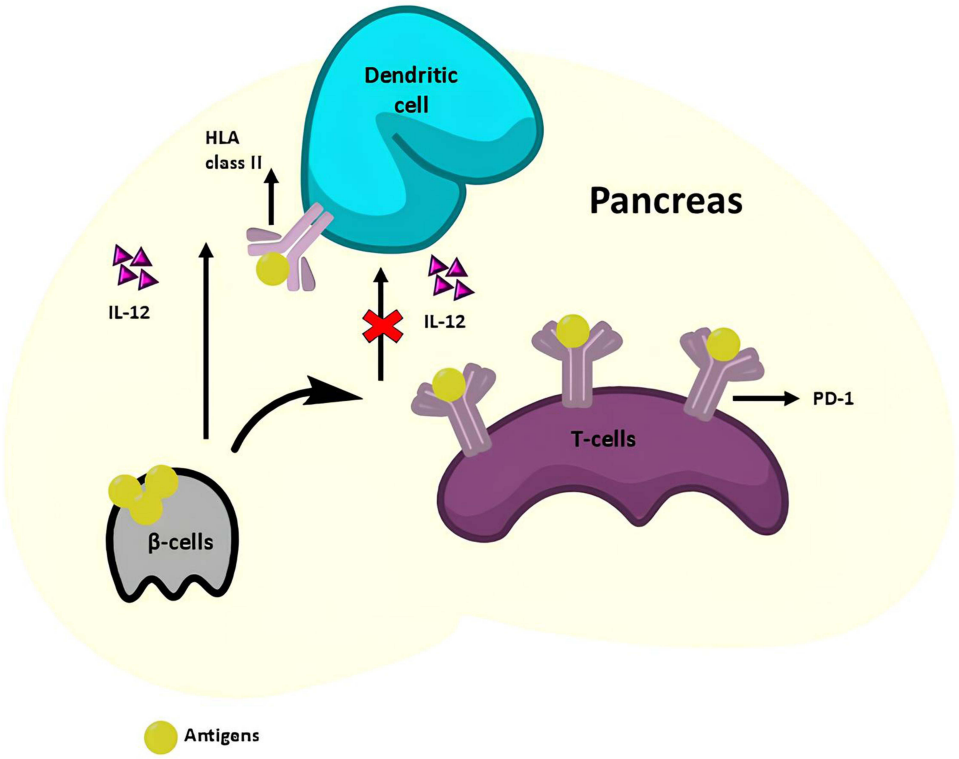

Figure 1 Mechanism of T cell inhibition of IL-22 synthesis by β cells in the pancreas.

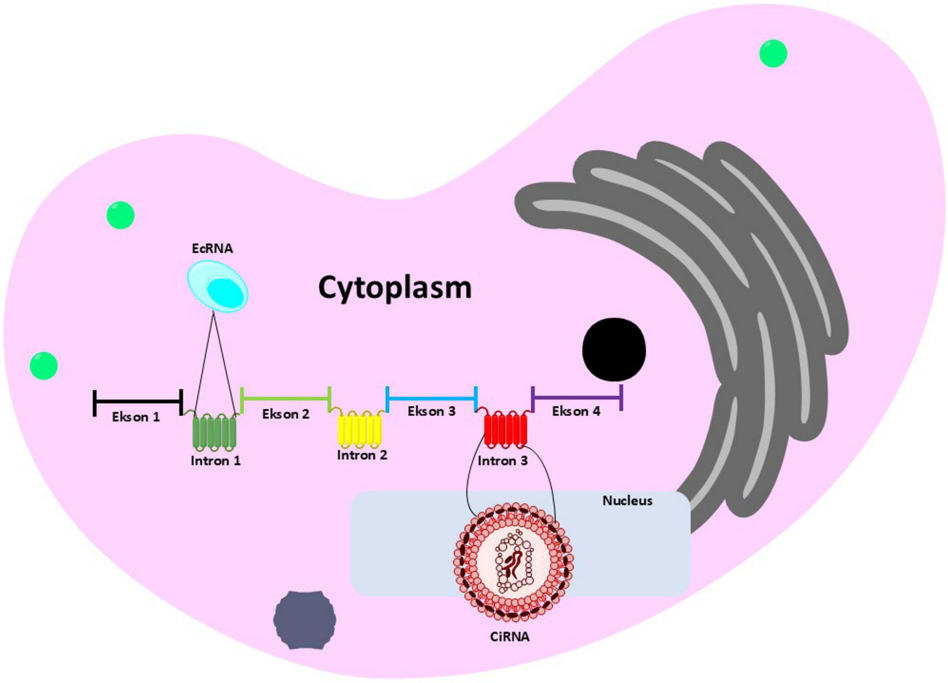

Figure 2 Mechanism of ciRNA template attachment to intron ends as an early stage of cancer cell coding.

Cancer

Cancer is a life-threatening disease that affects populations worldwide, with nearly every country reporting a substantial burden of cancer cases. In the United States alone, more than one million new cases were recorded in 2021.[17] Recent advances have highlighted the role of circular RNAs (circRNAs), particularly through their single-stranded transcription processes, in the molecular mechanisms underlying cancer. Dysregulation of circRNA gene expression (ciRNA) has been implicated in various types of cancer, as illustrated in Figure 2.[18] Circular RNAs (circRNAs) constitute a unique class of noncoding RNAs with covalently closed loop structures that confer high stability and resistance to exonuclease degradation. Once considered transcriptional by-products, they are now recognized as critical regulators of gene expression through diverse mechanisms, including acting as microRNA sponges, interacting with RNA-binding proteins, and modulating transcriptional and post-transcriptional processes. In cancer biology, circRNAs have been shown to influence key oncogenic pathways, such as cell proliferation, apoptosis, metastasis, and therapeutic resistance.[19]

Immune Diseases

Immune-related diseases have been increasingly linked to circular intronic RNA (ciRNA) regulatory systems.[20] The underlying mechanisms often involve abnormalities in the central dogma of molecular biology, particularly in transcriptional and post-transcriptional processes. Dysregulated transcription of nuclear factor kappa B (NF-κB) and aberrant nuclear translocation may lead to coding errors that trigger maladaptive autoimmune responses. Beyond its role in antitumor activity, the immune system also contributes to the dysregulation of other critical protein networks, including the suppression of pancreatic β-cell function, which ultimately predisposes individuals to diabetes.[21]

Chronic Disease Treatments Often Face Complications and Resistance

Insulin Therapy

Insulin therapy remains the primary treatment option for patients with type 1 diabetes mellitus who are unable to produce endogenous insulin. While exogenous insulin administration is essential for optimizing insulin activity and maintaining glucose homeostasis, adherence to a healthy lifestyle also plays a pivotal role in effective disease management. Despite

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these approaches, no definitive cure for diabetes has yet been identified. Moreover, insulin therapy is often associated with complications, particularly the risk of hypoglycemia.[22–24]

Tirzepatide

Tirzepatide is one of the most recently developed therapeutic agents for diabetes and is administered via a once-weekly subcutaneous injection. It exerts its effects by enhancing insulin sensitivity and reducing blood glucose levels, demonstrating high clinical efficacy. Nevertheless, concerns remain regarding treatment dependence and the transient nature of its therapeutic effects, which limit its potential as a definitive solution. Furthermore, the relatively large molecular structure of tirzepatide, derived from the synthesized human glucose-dependent insulinotropic polypeptide (GIP) hormone, poses significant challenges in its formulation and large-scale preparation.[25–28]

Antioxidants

Antioxidants are known to confer multiple health benefits, including maintaining overall physiological fitness. Among cancer-preventive agents, flavonoids and phenolic antioxidants have attracted considerable attention. Polyphenolic compounds exert their effects by donating electrons, thereby stabilizing free radicals and reducing oxidative stress, which plays a role in carcinogenesis. Importantly, these compounds are generally derived from natural sources and are not associated with the adverse side effects often observed in synthetic agents.[29]

Bioactivity of N. sativa

The bioactivities of *Nigella sativa* are summarized in Table 1, along with the corresponding mechanisms discussed in this manuscript. The plant's extracts, oils, and isolated compounds have demonstrated a wide range of pharmacological properties, including antimicrobial, antioxidant, anticancer, antidiabetic, antiviral, anti-inflammatory, anti-obesity, anti-hypothyroid, immunomodulatory, protective, and oral health-promoting effects.

Table 1 Bioactivity of *N. sativa* by Various Assays

No.	Extact/Compound	Activity	Test Results
1	Ethanol extract	Antimicrobial[30]	*Staphylococcus aureus*, *Candida glabrata*, *Candida albicans*, *Staphylococcus haemolitycus*, and *Escherichia coli* with MIC: 250 to 500 μg/mL
2	Butanol extract	Antimicrobial[31]	*C. albicans* with MIC: 0.125 μL/mL
3	Methanolic extract	Antimicrobial[32]	*S. mutans* with MIC: 12.5 μg/mL
4	Oils	Antimicrobial[33]	*S. aureus* with inhibition zone: 15.5 mm
5	Seed oil	Antioxidant[34]	DPPH EC_{50}: 6.7 μg/mL
6	Seed oil	Anticancer[35]	Cell MCF7 with LC_{50} values of 1.6 μg/mL
7	Methanol extract	Cytotoxicity[36]	AGS and pancreatic PANC-1 cell lines, with IC50 values of 43.31 and 144.4 μg/mL
8	Hydroalcoholic extracts	Cytotoxicity[37]	C6 cell line with IC_{50} values of 260 μg/mL
9	Thymoquinone	Anticancer[38]	COS31 cell inhibition at 25 μM concentration
10	Ethanol extract	Wound healing[39]	Significantly expedited the process of wound healing
11	Oil	Antidiabetic[40]	Reduction of SOD, MDA and TAC levels with the administration of were given 2g/day
12	*Nigella sativa* oil (NSO)	Antidiabetic[41]	Increasing the bioavailability of gliclazide by 29%
13	*Nigella sativa* oil (NSO)	Antivirus[42]	COVID-19 virus cure with a percentage of 62%
14	Petroleum ether extract	Anti-inflammatory[36]	Suppressed iNOS release in RAW264.7 cells with a concentration of 320 μg/mL

(*Continued*)

Table 1 (Continued).

No.	Extact/Compound	Activity	Test Results
15	NSE and NSO	Anti-hypothyroidism[43]	Inhibits thyroid hormone synthesis
16	*N. sativa* extract	Immune system[44]	Boosts the immune system at a concentration of 1 g
17	NSO	Protectivity[45]	Reduced the toxicity effect induced by LPS at a concentration of 40 μg/mL.

Antimicrobial

The ethanol extract of *Nigella sativa* exhibited inhibitory effects against clinical isolates of *Klebsiella pneumoniae, Acinetobacter baumannii*, and *Pseudomonas aeruginosa* at a concentration of 50 mg/mL, as determined by the well diffusion method. Additionally, the extract demonstrated antimicrobial activity against *Staphylococcus aureus, Staphylococcus haemolyticus, Escherichia coli*, as well as the fungi *Candida glabrata* and *Candida albicans*, with minimum inhibitory concentration (MIC) values ranging from 250 to 500 μg/mL.[30,39,46,47] The in vivo antimicrobial efficacy of a 33% *Nigella sativa* seed extract was evaluated in 40 neonates with pustular staphylococcal skin infections and compared to the standard treatment with mupirocin. The neonates were randomly assigned to either the experimental group (treated with *N. sativa* extract) or the control group (treated with mupirocin), and recovery times were recorded. The results showed no statistically significant difference in recovery time between the two groups. The *N. sativa* extract demonstrated comparable clinical efficacy to mupirocin and was not associated with any observable side effects.[31]

The aqueous extract and oil of *Nigella sativa* demonstrated notable inhibitory activity against a broad spectrum of bacterial strains, with inhibition zone diameters ranging from 25 to 31 mm and minimum inhibitory concentration (MIC) values between 1280 and 5120 μg/mL. Notably, the seed oil exhibited antimicrobial activity against several pathogenic microorganisms, including *A. niger, C. albicans, A. flavus, S. aureus, F. oxysporum, B. subtilis, E. coli, P. mirabilis*, and *B. licheniformis*. Among these, *E. coli* was found to be particularly susceptible to the seed oil.[48–51]

The antibacterial effects of *Nigella sativa* essential oil (EO) were evaluated in a murine model infected with two bacterial strains, *S. aureus* and *E. coli*. The EO was administered at a dose of 0.3 g/kg. Remarkably, the treatment resulted in complete (100%) inhibition of both bacterial strains in the infected mice, indicating a strong bactericidal effect. Compared to the control group, which received a saline solution and showed no signs of bacterial inhibition, the EO treatment demonstrated significantly superior efficacy in suppressing bacterial growth and activity.[52]

Ishikawa et al investigated the effect of *N. sativa* oil on the activity of L-methionine-γ-lyase in *Fusobacterium nucleatum*. L-methionine-γ-lyase is an enzyme commonly found in various bacterial species and is responsible for catalyzing the degradation of L-methionine, resulting in the production of methyl mercaptan, α-ketobutyrate, and ammonia. To evaluate the inhibitory effect of *N. sativa* oil, the researchers measured the concentrations of α-ketobutyric acid and ammonia as indicators of enzymatic activity. Treatment with *N. sativa* oil at a concentration of 10 μg/mL significantly reduced the levels of both α-ketobutyric acid and ammonia, suggesting a strong inhibitory effect on enzyme function. Enzyme kinetics further revealed that *N. sativa* oil exhibited a mixed-type inhibition pattern against L-methionine-γ-lyase, indicating interaction with both the active site and allosteric sites of the enzyme. Overall, the findings demonstrate that *N. sativa* oil not only inhibits L-methionine-γ-lyase activity in *F. nucleatum* but also contributes to the reduction of malodor by suppressing methyl mercaptan production.[53]

Encapsulated hydrodistillation extracts and hexane/acetone fractions of *N. sativa* demonstrated moderate antimicrobial activity against *P. aeruginosa, E. coli, C. albicans, M. luteus, S. aureus*, and *L. innocua*. Notably, all extracts exhibited enhanced inhibitory effects against *M. luteus* and *S. aureus*. Among the tested samples, the 3% hexane fraction showed the highest antimicrobial efficacy, producing an inhibition zone of 20 mm.[54]

Nanocomposite films incorporating *N. sativa* seed oil exhibited excellent mechanical flexibility, withstanding over 300 folding cycles without structural failure. In addition, these films demonstrated broad-spectrum antimicrobial activity against a range of pathogenic microorganisms, including *S. aureus, E. faecalis, E. coli, P. aeruginosa, P. mirabilis, K. pneumoniae, A. baumannii*, and *C. albicans*. These properties highlight the potential of *N. sativa* oil-based nanocomposite films for use in antimicrobial packaging materials and wound dressing applications.[55]

Anti-Oxidant

N. sativa seed oil exhibited significant antioxidant activity as determined by the DPPH assay, with a half-maximal effective concentration (EC_{50}) of 6.7 μg/mL. Similarly, the non-volatile fraction of *N. sativa* showed an EC_{50} of 7.7 μg/mL, with no statistically significant difference between the two. This comparable activity may be attributed to the similar total phenolic content present in both extracts.[44] In a separate study, *N. sativa* seed oil exhibited notable antiradical activity, as demonstrated by both the DPPH and FRAP assays. The oil showed an IC_{50} value of 0.017 mg/mL in the DPPH assay and an EC_{50} value of 0.119 mg/mL in the FRAP assay. These antioxidant capacities were comparable to those observed for standard reference antioxidants, indicating the potential of *N. sativa* seed oil as a natural source of effective radical scavengers.[48] In an in vivo rat model, *N. sativa* oil demonstrated antioxidant activity by significantly reducing levels of malondialdehyde (MDA) and oxidized glutathione (GSSG), while enhancing hydrogen donor capacity compared to the control group. These findings suggest that *N. sativa* oil may mitigate oxidative stress through modulation of key oxidative biomarkers.[32] *N. sativa* oil-based emulsions containing coumaric acid or its C10-ester demonstrated superior free radical scavenging activity against superoxide anions and hydrogen peroxide when compared to extra virgin olive oil (EVO). In addition, the emulsions significantly suppressed the expression of proinflammatory cytokines, including interleukin-1β (IL-1β) and monocyte chemoattractant protein-1 (MCP-1), indicating potential anti-inflammatory effects.[56]

Biosynthesized silver nanoparticles (AgNPs) derived from *N. sativa* exhibited strong antioxidant activity, as evaluated by DPPH, FRAP, and total antioxidant capacity (TAC) assays. Among the assays, the DPPH assay demonstrated the highest radical scavenging activity, particularly at an AgNP ratio of 1:2. In the FRAP assay, the AgNPs effectively reduced $Fe^{3}+$ to $Fe^{2}+$, with peak activity observed at the same optimal ratio. Similarly, the TAC assay recorded elevated antioxidant capacity at this ratio. Notably, the AgNPs achieved 89% radical scavenging activity at a concentration of 100 μg/mL in the DPPH assay. Furthermore, their antioxidant capacity increased in a dose-dependent manner across all assays.[57]

Anticancer

N. sativa seed oil and its non-volatile fractions were evaluated for cytotoxic effects against MCF7 and A325 breast cancer cell lines. The seed oil induced cell death in a concentration-dependent manner, with LC_{50} values of 1.6 μg/mL for MCF7 cells and 1.3 μg/mL for A325 cells. In contrast, the non-volatile fraction exhibited no cytotoxicity against either cell line, even at the highest concentration tested.[34] Further analysis of *N. sativa* extract on MCF7 cells revealed a downregulation in the mRNA expression of nuclear factor kappa B (NF-κB) subunits (p50 and RelB) and inhibitor of kappa B kinase (IKK) subunits (IKKα and IKKβ). This suggests that the extract may exert anti-inflammatory effects in breast cancer cells through modulation of NF-κB signaling pathways.[58]

The methanolic extract of *N. sativa* demonstrated cytotoxic activity against gastric (AGS) and pancreatic (PANC-1) cancer cell lines, with IC_{50} values of 43.31 μg/mL and 144.4 μg/mL, respectively. These findings indicate the potential of *N. sativa* extract to inhibit the proliferation of gastric and pancreatic cancer cells.[59]

The hydroalcoholic extract of *N. sativa* seeds exhibited cytotoxic activity against the rat glioma C6 cell line, with an IC_{50} value of 260 μg/mL. In addition to its cytotoxic effects, the extract significantly upregulated mRNA expression of the anti-inflammatory cytokine interleukin-10 (IL-10), while downregulating the expression of proinflammatory markers interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and transforming growth factor-beta 1 (TGF-β1) in both C6 cells and fibroblasts. These findings suggest that *N. sativa* extract may exert anti-inflammatory effects alongside its cytotoxic properties.[60]

Thymoquinone (TQ), a major bioactive compound in *Nigella sativa*, exhibited significant anticancer activity against COS31 cells at a concentration of 25 μM. Within 6 hours of treatment, TQ induced apoptosis, indicating its pro-apoptotic potential. In addition to triggering programmed cell death, TQ caused a marked alteration in cell cycle distribution. Specifically, treatment resulted in a reduction in the proportion of cells in the S phase, accompanied by an accumulation of cells in the G1 phase, suggesting cell cycle arrest at the G1 checkpointThis dual action-induction of apoptosis and G1 phase arrest-demonstrates TQ's potential to inhibit COS31 cell proliferation by disrupting both survival and replication mechanisms.[33]

Antidiabetic

In an in vivo study on type II diabetic mice, *Nigella sativa* seed extract powder (NSSP) was administered to evaluate its therapeutic effects. High-dose NSSP treatment significantly ameliorated diabetic parameters by reducing fasting blood glucose (FBG), glycosylated serum protein (GSP), triglycerides (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), malondialdehyde (MDA), and pro-inflammatory cytokines including tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interleukin-1β (IL-1β). Concurrently, NSSP increased insulin (INS) levels, high-density lipoprotein cholesterol (HDL-C), total antioxidant capacity (T-AOC), and antioxidant enzyme activities, namely superoxide dismutase (SOD) and catalase (CAT). These beneficial effects were attributed to modulation of the PI3K/AKT signaling pathway and alterations in the gut microbiota composition.[61]

Rahmani et al investigated the effects of *N. sativa* oil supplementation in hemodialysis patients with diabetes. Administration of 2 g/day of *N. sativa* oil resulted in significant improvements in oxidative stress and metabolic parameters, including increased superoxide dismutase (SOD) activity and total antioxidant capacity (TAC), as well as decreased levels of malondialdehyde (MDA), high-sensitivity C-reactive protein (hs-CRP), glycosylated hemoglobin (HbA1c), and fasting blood sugar (FBS).[62]

Dalli et al investigated the inhibitory effects of various *Nigella sativa* fractions on α-amylase activity and intestinal glucose absorption through both in vitro and in vivo experiments. The fractions demonstrated significant inhibition of α-amylase in both settings. Notably, the acetone fraction of SA3 exhibited potent inhibitory activity against intestinal α-glucosidase. Furthermore, the acetone fractions displayed inhibitory effects on pancreatic α-amylase comparable to those of acarbose, with the SA2 fraction showing particularly strong inhibition.[63,64]

Adiwidjaja et al investigated the pharmacokinetic and pharmacodynamic interactions between *Nigella sativa* oil (NSO) and the antidiabetic drug gliclazide. Co-administration of NSO with gliclazide significantly increased systemic exposure to gliclazide, as evidenced by a 29% enhancement in its bioavailability. Bioavailability refers to the fraction of an administered drug that reaches systemic circulation. Additionally, NSO decreased gliclazide clearance by 20%, indicating prolonged drug retention in the body and potentially enhancing therapeutic efficacy. Pharmacodynamically, pretreatment with NSO in healthy rats potentiated the glucose-lowering effect of gliclazide by up to 50% compared to gliclazide alone. However, this synergistic effect was not observed in insulin-resistant rats, suggesting that the interaction between NSO and gliclazide may be influenced by the metabolic status of the subject. In summary, the study demonstrates that NSO enhances gliclazide exposure through increased bioavailability and reduced clearance, resulting in improved glycemic control in healthy, but not insulin-resistant, rats.[65]

The seed extract of *Nigella sativa* has demonstrated the ability to enhance insulin secretion in isolated pancreatic islets, indicating its potential to positively modulate insulin release a critical hormone in glucose homeostasis. This effect suggests that *N. sativa* may serve as a promising candidate for antidiabetic therapy by improving glycemic control. Additionally, *N. sativa* has been shown to reduce postprandial glucose levels and exert beneficial effects on gastrointestinal function, further supporting its role in managing diabetes.[66,67]

Antivirus

In a clinical trial evaluating the effects of *Nigella sativa* oil (NSO) in patients with mild COVID-19, the NSO-treated group demonstrated a significantly higher recovery rate (62%) compared to the control group (36%). Moreover, the average duration of illness was shorter in the NSO group, with a mean recovery time of 10.7 days, versus 12.3 days in the control group. These findings suggest that NSO may contribute to improved clinical outcomes and faster recovery in patients with mild forms of COVID-19.[68]

The alcoholic extract of *Nigella sativa* exhibited antiviral activity against the Peste des petits ruminant virus (PPRV), a pathogen that affects small ruminants. Compared to the negative control group, treatment with the extract significantly reduced viral plaque formation, indicating its potential as an antiviral agent targeting PPRV.[69]

An extract derived from *Nigella sativa* seeds exhibited notable antiviral activity in HepG2 cells, a hepatocellular carcinoma cell line commonly used in liver disease and viral infection studies. The extract effectively inhibited viral infection at concentrations ≥ 30 μg/mL.[70] Additionally, various *N. sativa* derivatives including seed extracts, thymol-rich

fractions, fixed oils, and volatile oils have also demonstrated antiviral properties against hepatitis viruses, further supporting the therapeutic potential of *N. sativa* in managing hepatic viral infections.[71]

N. sativa has shown potential in supporting the management of hepatitis C, with beneficial effects observed in both diabetic and non-diabetic patients. Supplementation with *N. sativa* was associated with improvements in several clinical parameters, including total protein, albumin, red blood cell (RBC) count, platelet count, fasting blood glucose, and postprandial blood glucose levels. Additionally, *N. sativa* demonstrated antioxidant properties by reducing oxidative stress and was effective in lowering hepatitis C viral load. Importantly, it was well tolerated, indicating its safety for therapeutic use.[70] Further research has demonstrated that a specific hexane extract of *Nigella sativa*, applied at a concentration of 32,000 ppm, inhibited 64.45% of hepatitis C virus (HCV) RNA helicase activity. While other extracts, such as those obtained using ethyl acetate and methanol, also exhibited inhibitory effects, their potency was notably lower compared to the hexane extract. These findings suggest that the bioactive compounds responsible for helicase inhibition are likely to be lipophilic in nature, potentially belonging to the terpene or fatty acid classes.[72]

Anti-Inflammatory

The anti-inflammatory activity of *Nigella sativa* extract was assessed in RAW264.7 murine macrophage cells. Upon lipopolysaccharide (LPS) stimulation, the extract inhibited the release of inducible nitric oxide synthase (iNOS) in a concentration-dependent manner. At the highest tested concentration (320 µg/mL), the extract achieved 35.08% inhibition of iNOS expression, demonstrating its potential anti-inflammatory properties.[59]

Administration of lipopolysaccharide (LPS) induced marked increases in inflammatory and oxidative stress markers, along with histopathological alterations in lung tissue. Treatment with ethanol seed extract of *Nigella sativa* in rats significantly attenuated these effects in a dose-dependent manner. The extract reduced total white blood cell (WBC) counts, including eosinophils, neutrophils, basophils, and monocytes, as well as oxidative stress biomarkers and pro-inflammatory cytokines such as transforming growth factor-β1 (TGF-β1), interferon-γ (IFN-γ), and prostaglandin E2 (PGE2). These results highlight the anti-inflammatory and antioxidant potential of *N. sativa* seed extract in mitigating LPS-induced pulmonary inflammation.[73]

Further in vivo investigation of the anti-inflammatory potential of *Nigella sativa* extract was conducted using the carrageenan-induced rat paw edema model. Administration of the extract resulted in a dose-dependent reduction in paw swelling. The maximum inhibition of paw edema (29.66%) was observed at 4 hours post-carrageenan injection following treatment with 800 mg/kg of the extract, confirming its anti-inflammatory activity.[74]

The anti-inflammatory activity of *N. sativa* oil in combination with essential oils was evaluated using the human red blood cell (HRBC) membrane stabilization assay. The combined oil formulation demonstrated 60.11% inhibition of erythrocyte lysis, indicating membrane-stabilizing and anti-inflammatory effects. Notably, its activity was not significantly different from that of the standard anti-inflammatory drug diclofenac sodium, suggesting comparable efficacy.[75]

Anti-Obesity

Esmail et al investigated the therapeutic effects of *N. sativa* and L-carnitine in a rat model of high-fat diet (HFD)-induced obesity. HFD-fed rats exhibited characteristic features of obesity, including significant dyslipidemia (elevated cholesterol and triglyceride levels), increased body weight, and elevated serum markers such as the atherogenic index (AI) and alanine transaminase (ALT), an enzyme indicative of hepatic injury.

Over a 6-week treatment period, rats received either *N. sativa* or L-carnitine. Both treatments significantly improved the lipid profile, with reductions in total cholesterol and triglyceride levels. Additionally, final body weight was reduced, and elevated serum AI and ALT levels were normalized. Histopathological analysis revealed that the HFD induced hepatic steatosis, characterized by fat accumulation in hepatocytes. Notably, *N. sativa* administration mitigated these histological abnormalities, suggesting a hepatoprotective effect.

In summary, *N. sativa* effectively ameliorated HFD-induced metabolic disturbances by improving lipid metabolism, reducing body weight, and protecting against liver damage, supporting its potential as a natural intervention for obesity-related disorders.[76]

Anti-Hypothyroidism

Hassan et al evaluated the therapeutic potential of *Nigella sativa* aqueous extract (NSE) and *N. sativa* oil (NSO) in a methimazole-induced hypothyroidism model. Both treatments were orally administered for four weeks. The results demonstrated a significant reduction in thyroid-stimulating hormone (TSH) levels following administration of NSE and NSO, indicating decreased pituitary stimulation of the thyroid gland, a hallmark of hypothyroidism.

Additionally, free triiodothyronine (FT3) levels significantly increased in both treatment groups, reflecting improved thyroid hormone activity. NSO treatment also significantly elevated free thyroxine (FT4) levels, whereas the increase in FT4 following NSE treatment was not statistically significant. These findings suggest that both *N. sativa* extract and oil possess potential therapeutic effects against hypothyroidism, with NSO exhibiting a more pronounced influence on thyroid hormone regulation.[77]

Immune System

Salem et al investigated the immunomodulatory effects of *N. sativa* seeds using an in vitro THP-1 monocyte model. Notably, the immunomodulatory activity of roasted seeds was significantly diminished. A molecular docking analysis was performed to evaluate the interaction between *N. sativa* phytochemicals and inducible nitric oxide synthase (iNOS), a key protein involved in immunomodulatory pathways. The results revealed that roasting substantially reduced the binding affinity scores of certain compounds toward iNOS.

To assess safety, the cytotoxicity of four distinct *N. sativa* fractions was evaluated on THP-1 cell viability via the MTT assay, with none of the fractions exhibiting cytotoxic effects. Upon lipopolysaccharide (LPS) stimulation, gene expression analyses demonstrated that all four *N. sativa* fractions significantly downregulated the expression of iNOS, COX-2, NF-κB, AP1, and SP1 compared to the positive control.

Furthermore, the *N. sativa* fractions markedly suppressed pro-inflammatory cytokines including IL-1β, IL-6, IL-8, and TNF-α, while simultaneously upregulating the anti-inflammatory cytokine IL-10, suggesting a potent immunomodulatory effect with anti-inflammatory potential. Comparative analysis between polar fractions of raw and roasted *N. sativa* revealed that the polar fraction from raw seeds more effectively reduced IL-1β and TNF-α levels and increased IL-10 expression relative to the roasted counterpart.[78]

In a clinical trial assessing the immunomodulatory effects of *N. sativa*, subjects were administered capsules containing *N. sativa*, followed by blood collection and immunological analysis. Administration of a 1 g dose of *N. sativa* resulted in a significant enhancement of several immune parameters. Specifically, the absolute lymphocyte count increased from 1850 to 2170 cells/μL, CD3+ T cell counts rose from 1184.4 to 1424 cells/μL, and CD4+ helper T cell counts increased from 665.6 to 841 cells/μL. Interestingly, this stimulatory effect on T cell populations was not observed at the higher 2 g dose. Other immunological parameters measured did not show statistically significant changes across different dosing regimens. These findings suggest a dose-dependent immunopotentiating effect of *N. sativa*, with 1 g identified as the optimal dose for enhancing helper T cell-mediated immunity in the studied young population.[79]

Dietary supplementation with *N. sativa* significantly enhanced cell-mediated immune responses, as evidenced by improved weight gain and feed conversion ratio (FCR). Additionally, *N. sativa* administration resulted in notable increases in total antioxidant capacity (TAC), catalase (CAT) activity, and the production of key cytokines including interleukin-12 (IL-12), gamma interferon (γ-IFN), and tumor necrosis factor-alpha (TNF-α). Histopathological analysis of phytohemagglutinin (PHA)-stimulated foot pads demonstrated a dose-dependent increase in leukocyte infiltration and edema. These collective findings indicate that *N. sativa* seeds exhibit potent immunostimulatory effects, likely mediated through their antioxidant properties, enhanced cytokine production, upregulation of CD8 expression, and attenuation of splenic apoptosis.[80]

Protectivity

In a study evaluating the protective effects of *Nigella sativa* oil (NSO) against sodium arsenate (NaAs)-induced toxicity, multiple biochemical parameters were assessed in intestinal mucosal homogenates across treatment groups. Both enzymatic and non-enzymatic antioxidants, carbohydrate metabolism, and activities of brush border membrane marker enzymes were analyzed. Intestinal brush border membrane vesicles (BBMV) were isolated to measure the activity of specific membrane enzymes, including alkaline phosphatase (ALP), γ-glutamyltransferase (GGTase), leucine aminopeptidase (LAP), and sucrase. Kinetic parameters (Km and Vmax) of these enzymes were also evaluated. Additionally, enterocyte DNA integrity

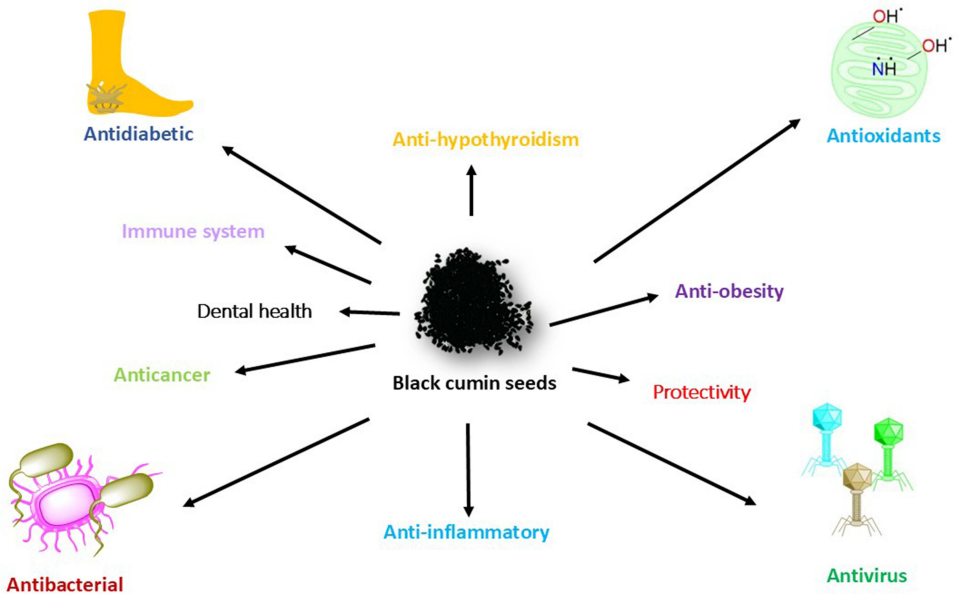

Figure 3 Illustrates the bioactive extracts and major compounds identified in *N. sativa* seeds.

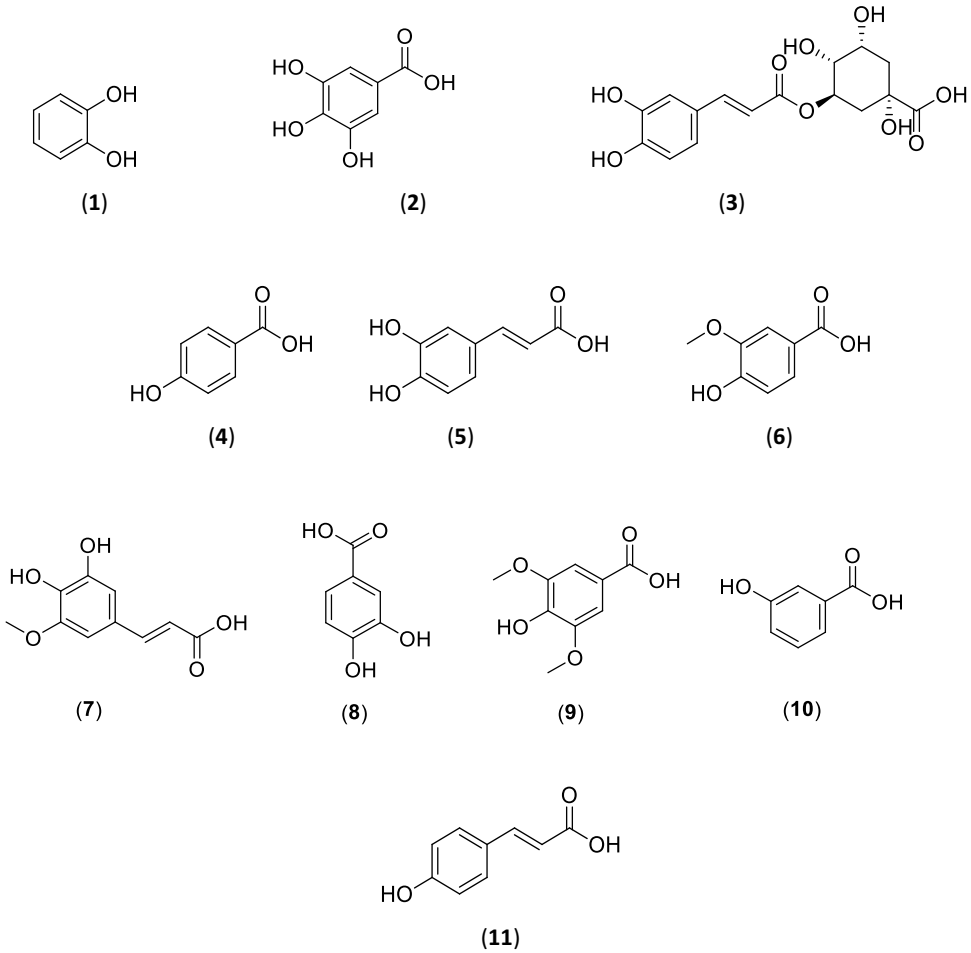

Figure 4 Phenolic compounds from *N. sativa* such as catechol (**1**), gallic acid (**2**), chlorogenic acid (**3**), 4-hydroxy benzoic acid (**4**), caffeic acid (**5**), vanillic acid (**6**), 5-hydroxyferulic acid (**7**), protocatechuic acid (**8**), syringic acid (**9**), 3-hydroxybenzoic acid (**10**), *p*-coumaric acid (**11**).[91,92]

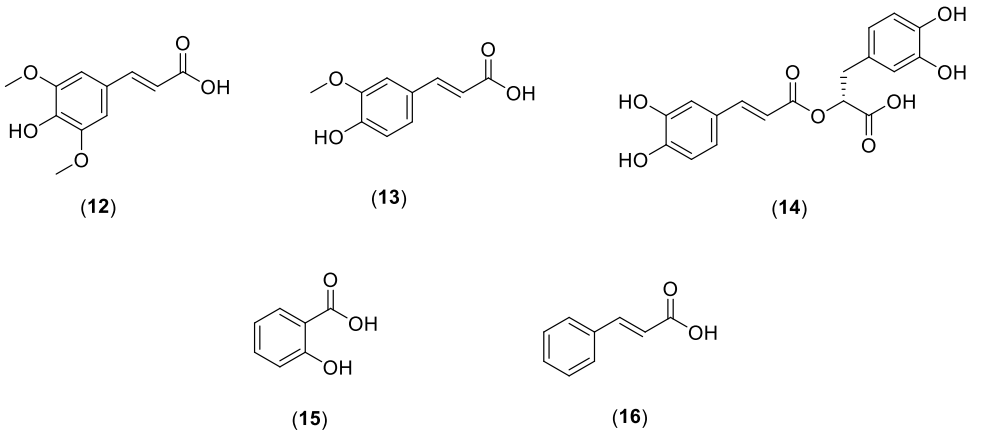

Figure 5 Phenolic compounds from *N. sativa* such as sinapinic acid (**12**), ferulic acid (**13**), rosmarinic acid (**14**), salicylic acid (**15**), and *trans*-cinnamic acid (**16**).[91,92]

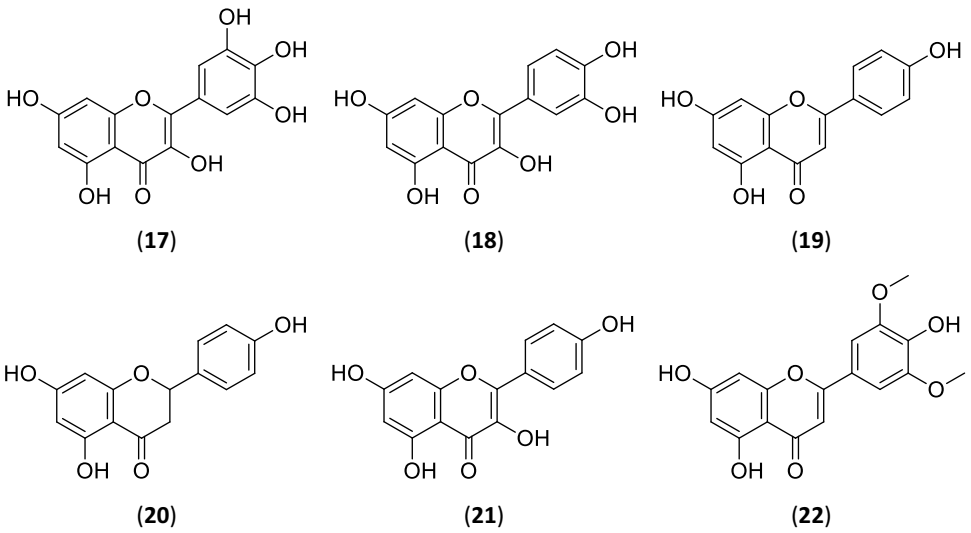

Figure 6 Flavonoid compounds from *N. sativa* such as myricetin (**17**), quercetin (**18**), apigenin (**19**), naringenin (**20**), kaempferol (**21**), chrysin (**22**).[45]

was examined via comet assay, and histopathological analysis of intestinal tissue was performed to assess structural alterations caused by chronic arsenic exposure and the modulatory effect of NSO supplementation. The results demonstrated that oral administration of NSO significantly ameliorated the detrimental effects of sodium arsenate, enhancing antioxidant defenses and energy metabolism, thereby strengthening the intestine's resilience against free radical-mediated arsenic toxicity.[81]

Ates et al investigated the hepatoprotective effects of *Nigella sativa* oil (NSO) against bisphenol A (BPA)-induced liver toxicity in rats. NSO was administered orally via gavage over a 30-day period. At the end of the study, blood samples were collected under anesthesia, and serum was isolated to measure liver toxicity markers, including alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and gamma-glutamyl transferase (GGT), which are key indicators of liver function and damage. Histological analysis of liver tissue was also performed. The results demonstrated that NSO supplementation significantly improved both liver histology and biochemical markers of liver function, indicating that NSO effectively ameliorates BPA-induced hepatic damage and supports liver structural and functional integrity.[35]

NSO demonstrated efficacy in mitigating the toxic effects of lipopolysaccharide (LPS) across all tested concentrations. Specifically, NSO at concentrations ranging from 10 to 40 μg/mL significantly reduced levels of key inflammatory markers, including TNF-α, PGE2, IL-1, and IL-6, in LPS-exposed microglial cells. Pretreatment with NSO also decreased inducible

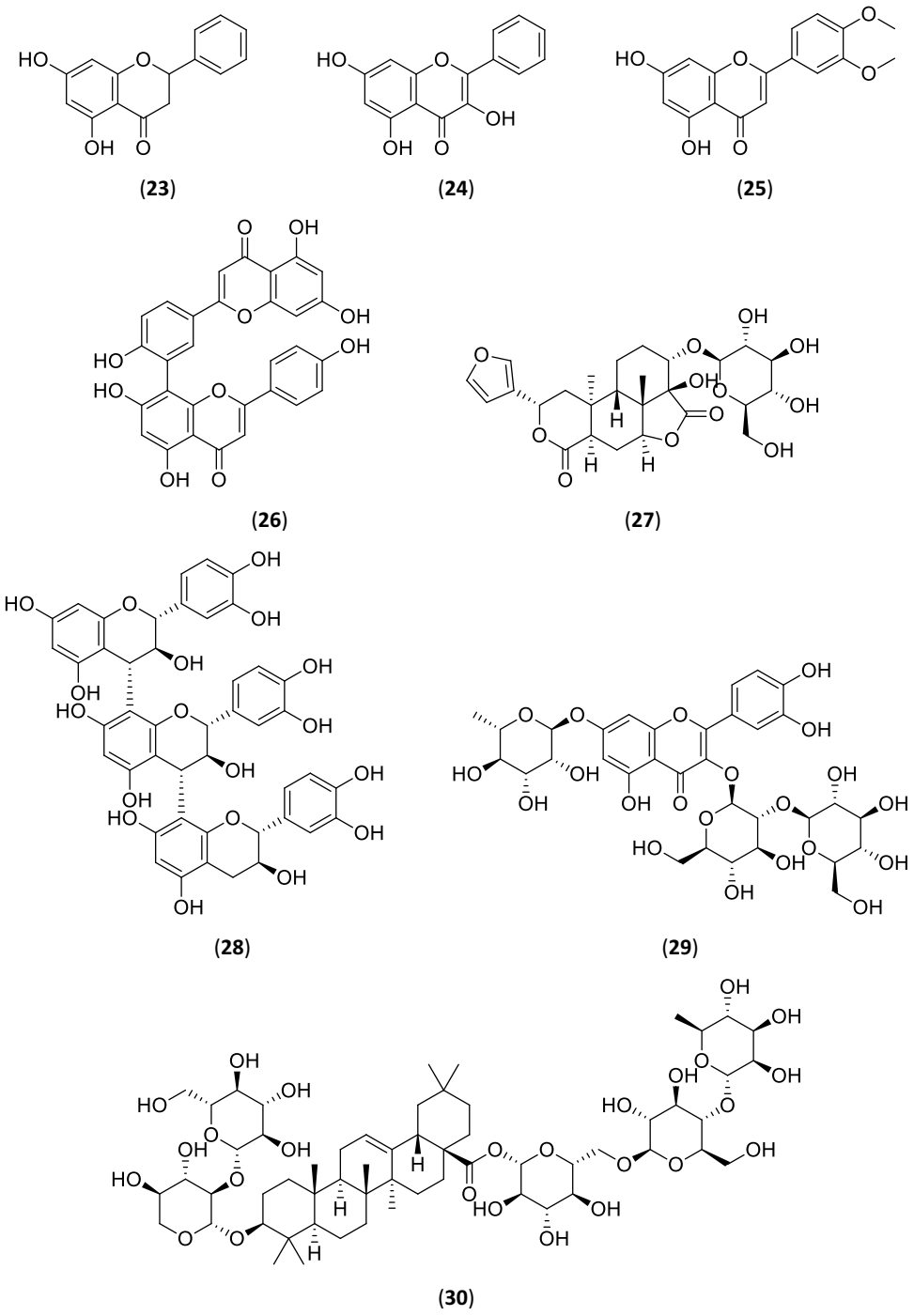

Figure 7 Flavonoid compounds from *N. sativa* such as pinocembrin (**23**), and galangin (**24**) 5,7-Dihydroxy-3′,4′-dimethoxyflavone (**25**), amentoflavone (**26**), borapetoside A (**27**), procyanidin C2 (**28**), and quercetin3-*O*-sophoroside-7-*O*-rhamnoside (**29**), flaccidoside III (**30**).[45]

nitric oxide synthase (iNOS) expression and increased arginase-1 (Arg1) levels, suggesting a shift toward an anti-inflammatory microglial phenotype. These results indicate that NSO has potent immunomodulatory properties and may promote microglial polarization towards the M2 phenotype, which is associated with neuroprotection. Therefore, NSO holds promise as a therapeutic agent for neurodegenerative diseases characterized by chronic inflammation.[36]

N. sativa demonstrated protective effects against hypercholesterolemia-induced damage in the submandibular salivary glands. Histological and immunohistochemical analyses confirmed the superior protective role of *N. sativa*. Rats fed a high-cholesterol diet and orally administered *N. sativa* seeds exhibited nearly normal histological architecture in their

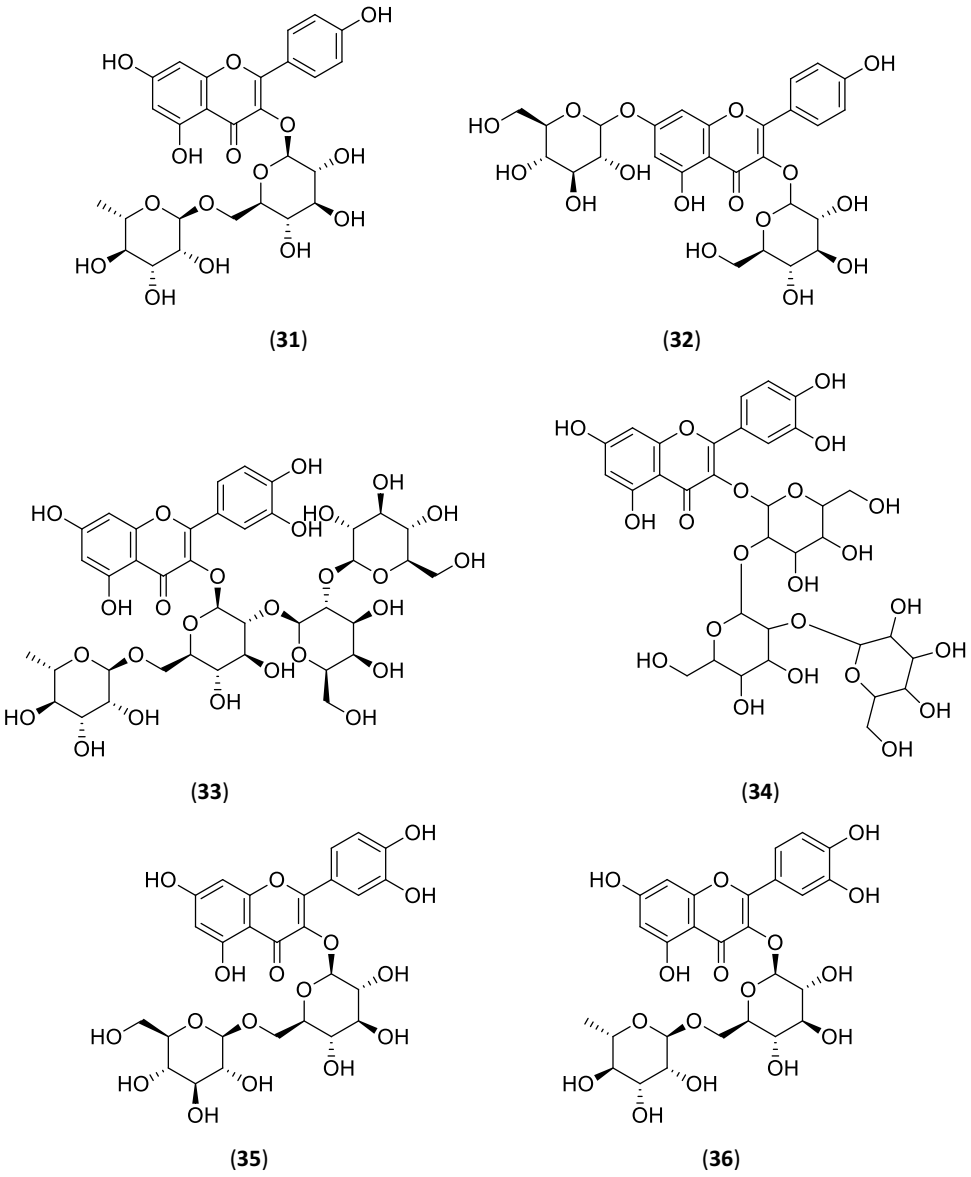

Figure 8 Flavonoid compounds from *N. sativa* such as kaempferol-3-*O*-rutinoside (**31**), kaempferol-3,7-diglucoside (**32**), nigelflavonoside B (**33**), quercetin sphorotrioside (**34**), quercetin-3-gentiobiosides (**35**), rutin (**36**).[42,91,93]

submandibular salivary glands, highlighting the beneficial impact of the treatment. Additionally, quantitative assessments showed a highly significant reduction in α-SMA and NF-κB expression in the *N. sativa*-treated group, indicating its effectiveness in mitigating hypercholesterolemia-related inflammatory and fibrotic changes in these glands.[82]

The administration of *Nigella sativa* oil (NSO) exhibits gastroprotective effects in experimental models of ethanol-induced gastric ulcers. NSO increases gastric mucus production, which protects the stomach lining, and reduces gastric juice acidity, a factor that contributes to ulcer formation. In tests using two oral doses of NSO (50% and 100% at 1 mg/kg), both doses showed protective benefits. Additionally, subacute oral administration of NSO did not cause any significant toxicity or adverse effects in the animals, indicating that NSO is safe for oral use over a short period. In a subacute toxicity study, oral administration of *Nigella sativa* oil (NSO) was well tolerated by the test animals over an extended period. Throughout the study, the animals exhibited normal behavior with no significant changes in body

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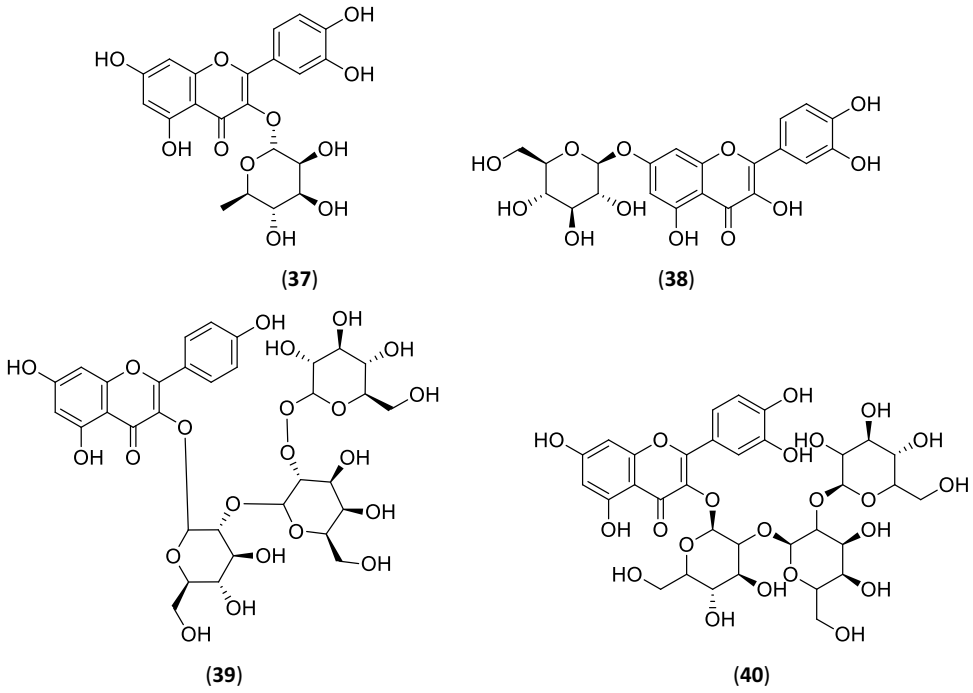


Figure 9 Flavonoid compounds from *N. sativa* such as quercetin-3-*O*-α-L-rhamnoside (**37**), quercetin-7-*O*-β-D-gluco- pyranoside (**38**), kaempferol 3-glucosyl-(1-2)-galactosyl -(1-2)-glucoside (**39**), quercetin 3-(6-feruloylglucosyl)-(1-2)-galactosyl-(1-2)-glucoside (**40**).[42,91,93]

weight, water consumption, or food intake. No adverse effects or signs of toxicity were observed, indicating that NSO is safe for subacute oral use in this animal model.[83]

A clinical trial assessing *Nigella sativa* supplementation in patients with type 2 diabetes mellitus (T2DM) demonstrated significant improvements compared to the placebo group. Supplementation was associated with reductions in fasting blood sugar (FBS), triglycerides, total cholesterol, low-density lipoprotein cholesterol (LDL-C), serum high-sensitivity C-reactive protein (hs-CRP), and malondialdehyde (MDA) levels. Additionally, levels of high-density lipoprotein cholesterol (HDL-C) were increased. These findings suggest that *N. sativa* oil supplementation provides cardiovascular protective effects in T2DM patients by improving lipid profiles and glycemic control, reducing systemic inflammation, and limiting oxidative stress.[37,84]

Nigella sativa in Dental Health

N. sativa demonstrated significant antibacterial activity against the key periodontal pathogens *Porphyromonas gingivalis* and *Prevotella intermedia*. Although its efficacy was slightly lower than that of tetracycline (which showed inhibition zones of 15.3 mm and 16.5 mm, respectively), the methanolic extract of *N. sativa* exhibited notable antibacterial effects. At 25 mg/mL, inhibition zones measured 5.4 mm against *P. gingivalis* and 7.4 mm against *P. intermedia*, increasing to 9.4 mm and 10.1 mm, respectively, at 50 mg/mL. These results indicate that *N. sativa* possesses potent antibacterial properties against these periodontal pathogens.[38,85]

In an in vivo rat model infected with *Porphyromonas gingivalis, Nigella sativa* toothpaste significantly reduced inflammatory cell counts and activity, while also protecting the periodontal extracellular matrix from destruction.[86] A clinical trial further demonstrated that *N. sativa* oil (NSO) was more effective than eugenol in promoting soft tissue healing and reducing inflammation in patients suffering from dry socket complications.[87] Additionally, *N. sativa* paste used for direct pulp capping in rabbit teeth accelerated hard tissue formation and caused less inflammation compared to calcium hydroxide, indicating its potential for improved dental pulp healing.[40]

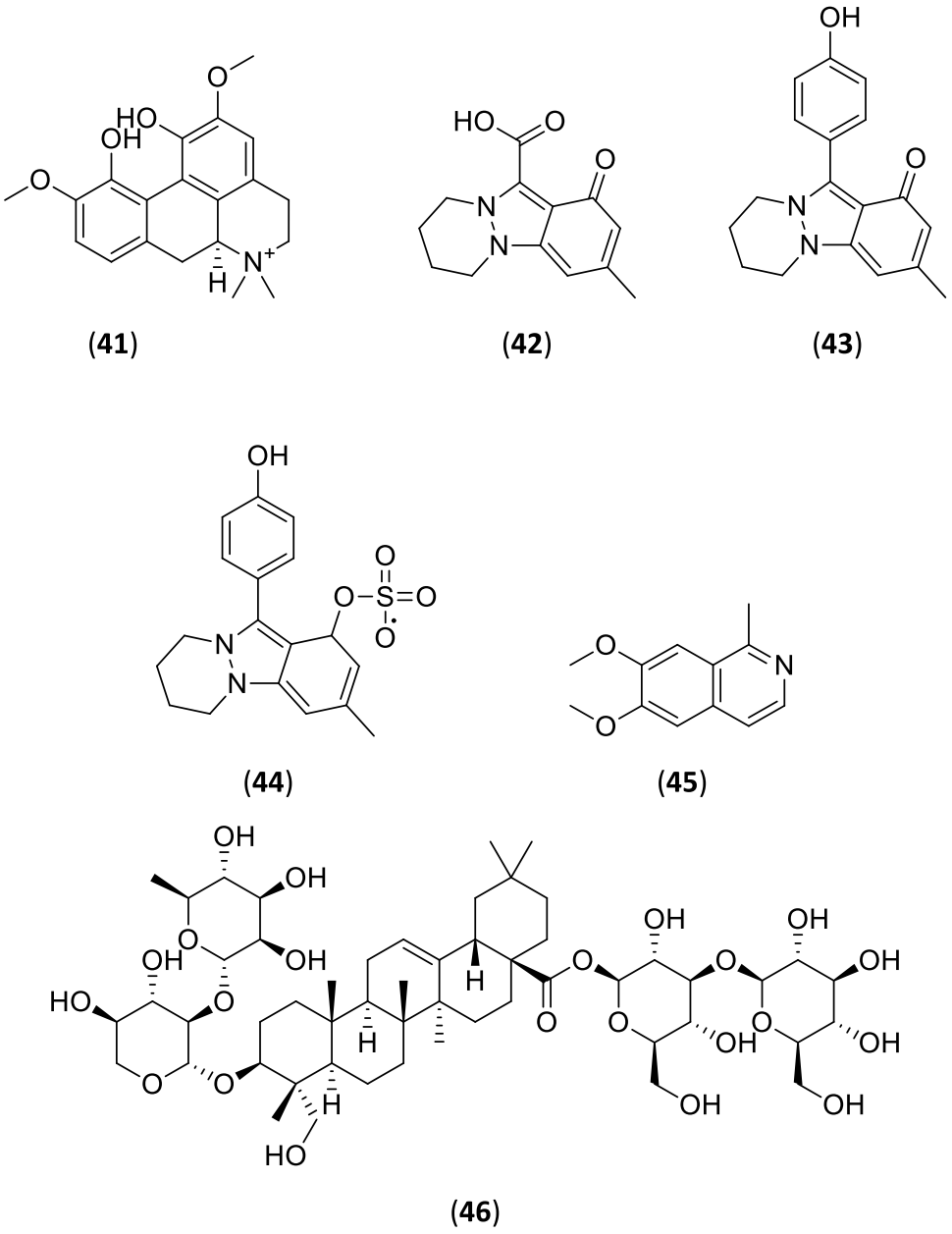


Figure 10 Alkaloid compounds from *N. sativa* such as magnoflorine (**41**), nigellicine (**42**), nigellidine (**43**), nigellidine-4-*O*-sulfite (**44**), nigellimine (**45**), and nigelloside (**46**).[91,94–98]

A clinical trial on patients with chronic generalized gingivitis demonstrated that *Nigella sativa* intervention significantly reduced gingival and plaque indices. Additionally, it lowered levels of the inflammatory marker IL-6 and decreased pathogenic bacterial counts.[88] Furthermore, the use of an *N. sativa* oil-based mouthwash following nonsurgical periodontal therapy led to a reduction in matrix metalloproteinase-8 (MMP-8) levels in patients with chronic periodontitis. The mouthwash also improved clinical outcomes, including plaque index (PI), clinical attachment loss (CAL), probing pocket depth (PPD), and bleeding on probing (BoP) after two weeks of use, highlighting its therapeutic potential for periodontal health.[41,89]

Collectively, these studies suggest that *N. sativa* and its derivatives hold promising potential for improving oral and dental health. Their benefits include reducing inflammation, promoting tissue healing, and offering protection against

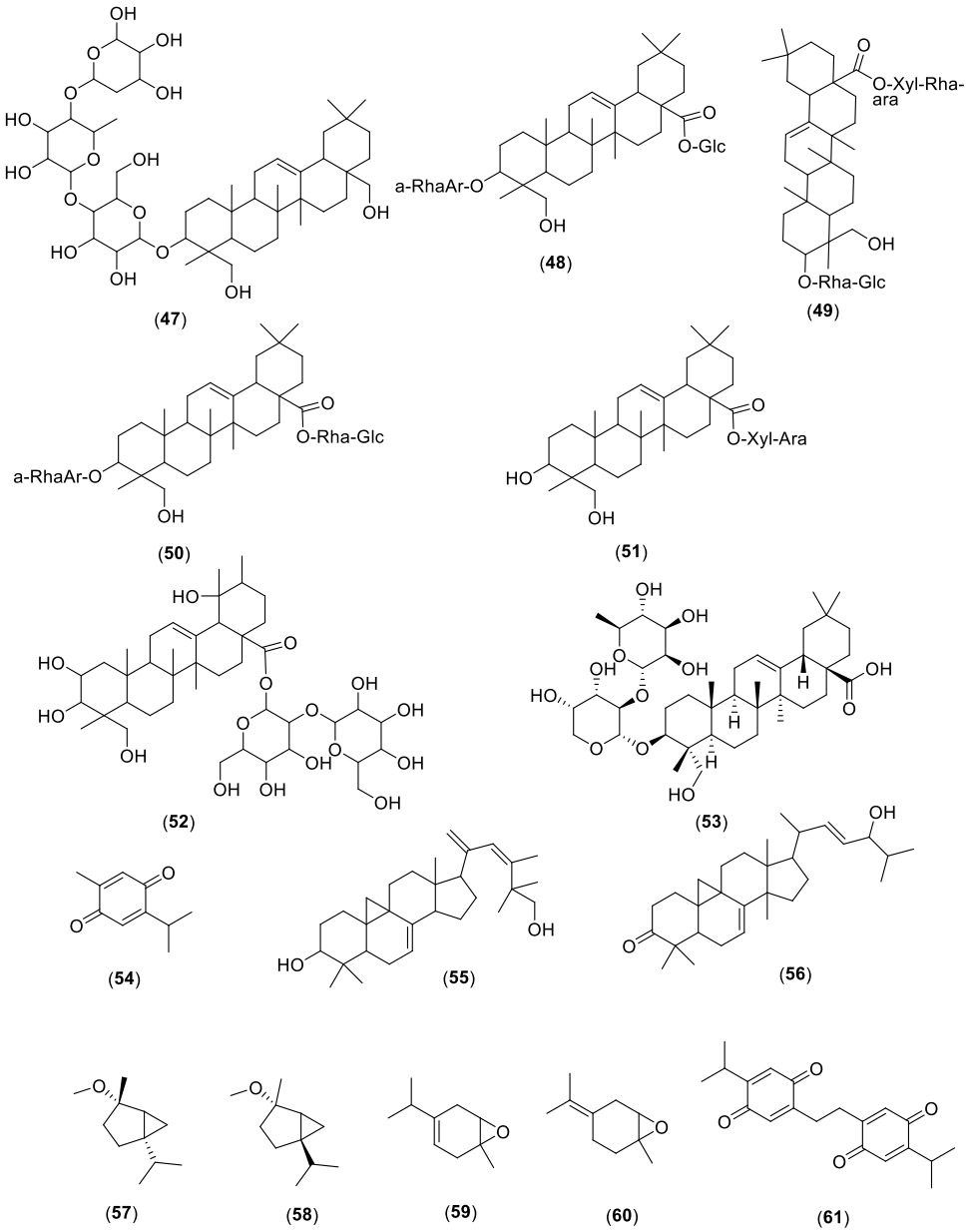
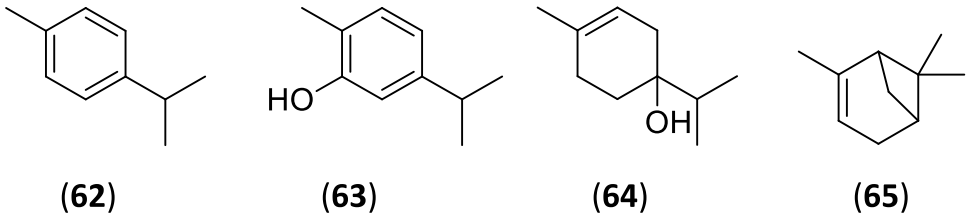


Figure 11 Terpenoid compounds from *N. sativa* such as 3β,23,28-trihydroxyolean-12-ene-3-O-α-L-arabinopyranoside(1→4)-a-rhamnopyranosyl,(1→4)-β-D-gluco-pyranoside (**47**), 3-O-α-L-rhamnopyranosyl-(1→2)-α-L-arabinopyranpsyl]-28-O-β-D-gluco-pyranosyl hederagenin (**48**), 3-O-(β-D-xylopyranosyl-(1-3)-α-L-rhamnopyrnaosyl-(1-2)-α-L-arabinopyranosyl]-28-O-(α-L-rhamno-pyranosyl-(1-4)-β-D-glucopyranosyl-(1-6)-β-D-glucopyranosyl] hederagenin (**49**), 3-O-α-L-rhamnopyranosyl-(1→2)-α-L-arabinopyranpsyl]-28-O-α-L-rhamnopyranosyl-(1→4)-β-D-glucopyranosyl-(1→6)-β-D-glucopyranosyl] hederagenin (**50**), 3-O-(β-D-xylopyranosyl-(1-3)-α-L-rhamnopyrnaosyl-(1-2)-α-L-arabinopyranosyl-hederagenin (**51**), tetrahydroxy-urs-12-en-28-O-[β-D-glucopyranosyl (1-2)-β-D-glucopyranosyl] ester (**52**), α-Hederin (**53**), thymoquinone (**54**), cycloart-23-methyl-7,20,22-triene-3β,30-diol (**55**), cycloart-3-one-7,22-diene-24-ol (**56**), *trans*-sabinene hydrate methyl ether (**57**), *cis*-sabinene hydrate methyl ether (**58**), 1,2-epoxy-menth-4-ene (**59**), 1,2-epoxy-menth-4(8)-ene (**60**), and dithymoquinone (**61**).[43,45,91,99–103]

a range of dental and oral conditions.[90] An overview of the bioactive extracts and principal compounds from *Nigella sativa* seeds is provided in Figure 3.

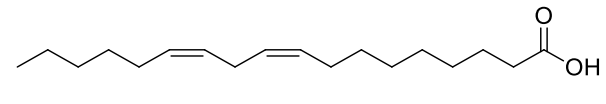
Chemical Componds

The exploration of *Nigella sativa* has been the focus of extensive research aimed at elucidating its broad spectrum of biological activities. Numerous studies have consistently emphasized the critical role of its phytochemical constituents as primary mediators of these bioactivities. The complex interplay between the chemical profile of *N. sativa* and its

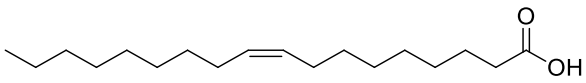


(**62**) (**63**) (**64**) (**65**)

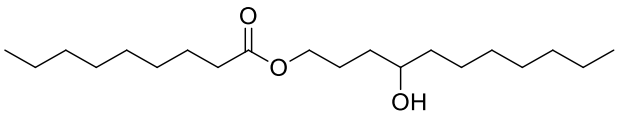
Figure 12 NSO from *N. sativa* such as *p*-cymene (**62**), carvacrol (**63**), 4-terpineol (**64**), and α-pinene (**65**).[42,104]



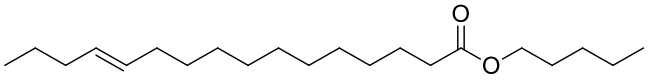
(**66**)



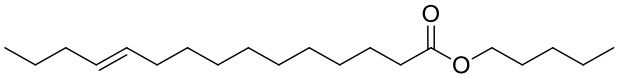
(**67**)



(**68**)

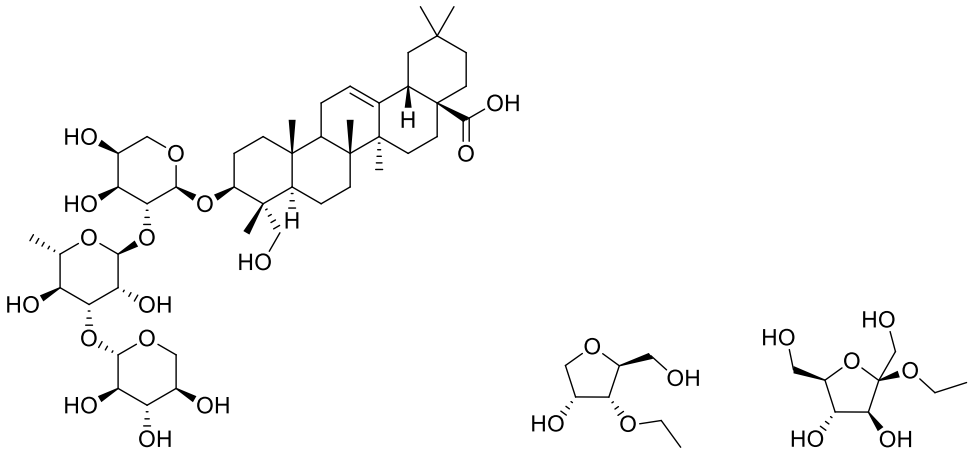


(**69**)



(**70**)

Figure 13 Fatty acid and other compounds from *N. sativa* such as Linoleic acid (**66**) and oleic acid (**67**), including 4-hydroxy undecyl nonanoate (**68**), pentyl hexadic-12-enoate (**69**) and pentyl pentadic-11-enoate (**70**).



(**71**) (**72**) (**73**)

Figure 14 Fatty acid and other compounds from *N. sativa* such as sapindoside B (**71**), Ethyl-α-D-furaarabinose (**72**) and ethyl-β-D-fructofuranoside (**73**).

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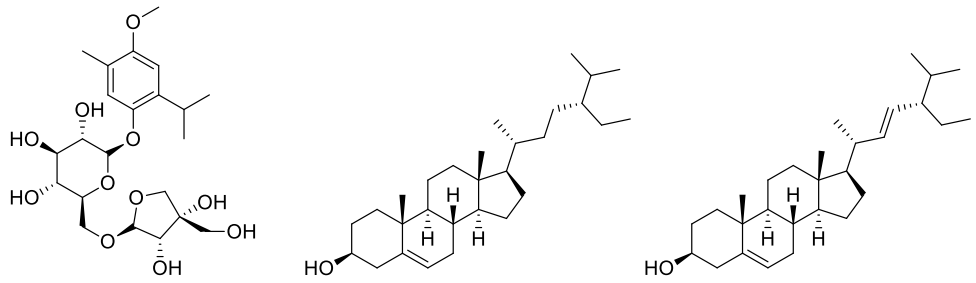

Figure 15 Fatty acid and other compounds from *N. sativa* such as 3-methoxythymol-6-O-β-D-apiofuranosyl-(1-6)-β-D-glucopyranoside (**74**), β-sitosterol (**75**) and stigmasterol (**76**).

therapeutic effects on various physiological systems has attracted considerable scientific interest, underscoring its potential in promoting health and well-being.

Phenolic

The utilization of advanced analytical techniques, such as ultra-high-performance liquid chromatography-mass spectrometry (UHPLC-MS), has revealed the presence of phenolic compounds in *N. sativa* (Figures 4 and 5).

Flavonoid

N. sativa is rich in flavonoids, which have various biological functions. The flavonoid compounds in *N. sativa* obtained by UHPLC-MS are shown in Figures 6–9.

Compound **31** showed antioxidant activity in an α-glucosidase assay with an IC_{50} of 214.5 μM. Meanwhile, compound **33** also exhibited antioxidant properties, as measured by the DPPH and FRAP assays, with IC_{50} of 32.7 and 95.18 μM, respectively.[42,91,93]

Alkaloid

Alkaloids are a class of naturally occurring organic compounds that typically contain basic nitrogen atoms. *N. sativa* has been reported to contain alkaloids (Figure 10). In particular, nigellidine from *N. sativa* exhibited antiviral properties against Cov19 in in silico and in vitro assays.[91,94–98]

Terpenoid

Naturally, *N. sativa* is enriched in terpenoid compounds. These were identified as shown in Figures 11 and 12.

Compound **48** exhibited anti-diabetic properties in a protein tyrosine phosphatase (PTP1B) assay with an IC_{50} value of 91.30 μM.[91] Compound **53** displayed a dose-dependent increase in its inhibitory effect on regrowth compared with that in the group treated with cyclophosphamide, with statistically significant improvements observed on days 8 and 15. This suggests that this compound has the potential to inhibit regrowth.[99] Compound **54** derived from *N. sativa* demonstrated a substantial reduction in the number of viable cancer cells, even at the lowest concentration compared to the **54** standard. Furthermore, the incidence of cell death was significantly higher in the groups treated with **54** than in untreated cancer cells. It also exhibited dose-dependent anti-proliferative activity against HeLa cells.[100] This compound showed strong antibacterial properties against a range of bacteria, particularly against gram-positive cocci, such as *Staphylococcus aureus* and *S. epidermidis*. It inhibited biofilm formation at concentrations of 22 μg/mL for *S. aureus* and 60 μg/mL for *S. epidermidis*. In addition, compound **54** affected the oxidative activity of the bacterial cells and prevented their adhesion to the surface.[105]

Compounds **57, 58**, and **60** were observed to possess antioxidant properties as they were found to inhibit oxidative stress in human skin WS-1 fibroblasts. These compounds exhibited IC_{50} values of 0.32, 0.005, and 0.43, respectively, indicating their efficacy in combating oxidative stress.[43]

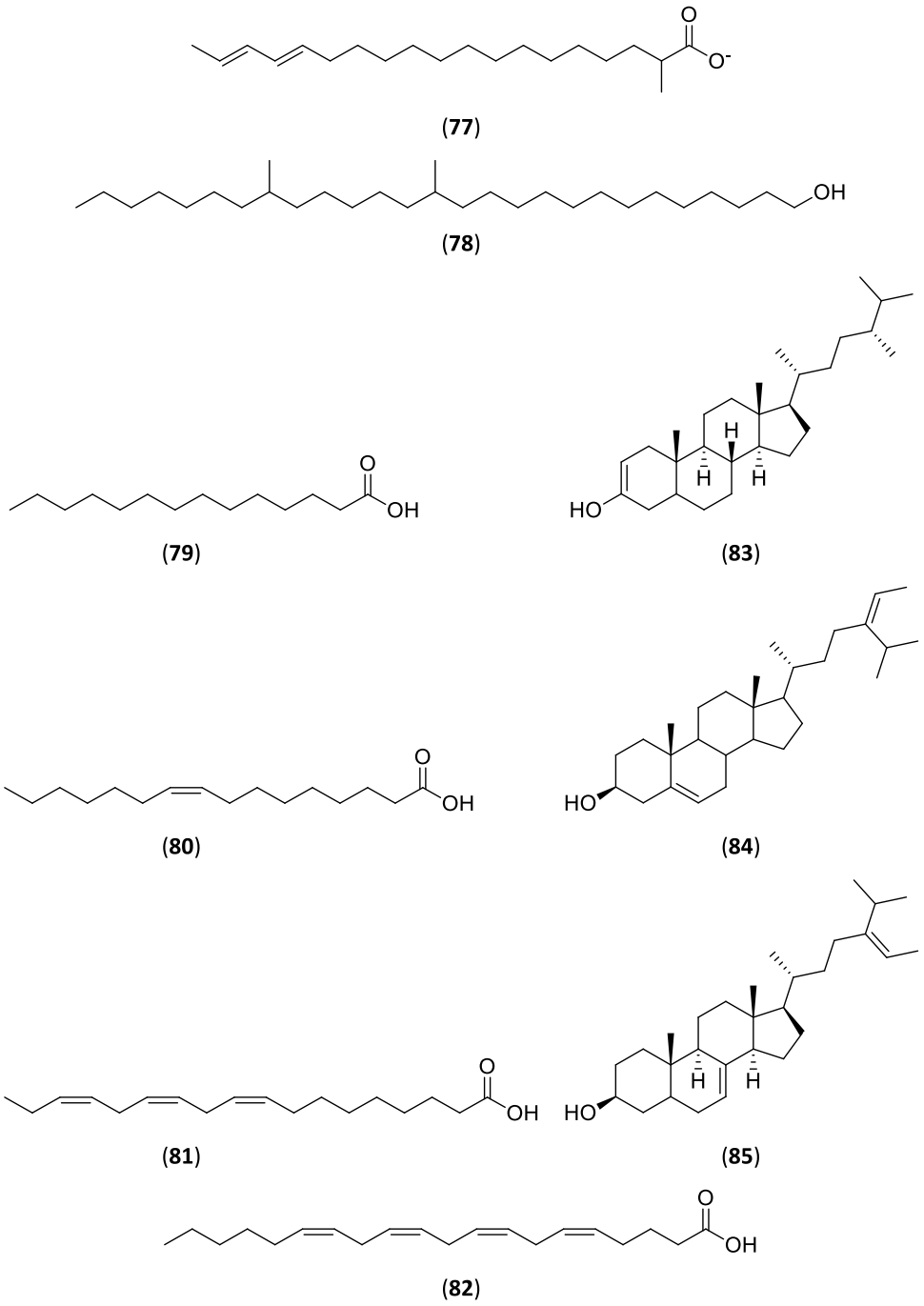

Figure 16 Fatty acid and other compounds from *N. sativa* such as methylnonadeca-15,17-dienoate (**77**), 14,20-dimethyl heptacosanol (**78**), myristic acid (**79**), palmitoleic acid (**80**), linolenic acid (**81**), arachidonic acid (**82**), campesterol (**83**), 5-avenastrol (**84**) and 7-avenasterol (**85**).

Fatty Acid and Other Compounds

Linoleic acid (**66**) and oleic acid (**67**) derived from *N. sativa*, particularly its oil, exhibited antibacterial activity against *S. aureus*. Furthermore, *N. sativa* yielded ester compounds including 4-hydroxy undecyl nonanoate (**68**), pentyl hexadic-12-enoate (**69**), pentyl pentadic-11-enoate (**70**), and sapindoside B (**71**). The structures of these compounds are shown in Figures 13–17.

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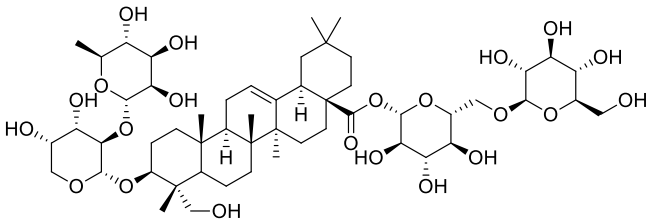

(**86**)

Figure 17 Fatty acid and other compounds from *N. sativa* such as tauroside E3 (**86**).

Notably, **69** and **70** demonstrated antibacterial activities that were similar to those of **66** and **67**.[42,44,106] Ethyl-α-d-furaarabinose (**72**) and ethyl-β-d-fructofuranoside (**73**), both monosaccharides isolated from *N. sativa*, and 3-methoxythymol-6-O-β-D-apiofuranosyl-(1-6)-β-d-glucopyranoside (**74**). Compounds, **72** and **73**, have been shown to possess bidirectional regulatory effects on immunity and anti-inflammation by modulating the nuclear factor-κB (NF-κB) signaling pathways.[107]

The compounds (**75**) and (**76**) are known to be present in *N. sativa*. In addition, lipid compounds such as methylnonadeca-15,17-dienoate (**77**) and 14,20-dimethyl heptacosanol (**78**) were identified in *N. sativa*. Notably, compounds **75, 76**, and **77** demonstrated antibacterial activities against *S. aureus*.[106]

Compounds identified as myristic acid (**79**), palmitoleic acid (**80**), linolenic acid (**81**), and arachidonic acid (**82**) were fatty acids that could be isolated from *N. sativa* seed oil. Other sterol compounds found in NSO are campesterol (**83**), 5-avenastrol (**84**), and 7-avenasterol (**85**).[108] Tauroside E3 (**86**), a bile acid conjugate, is a bile component that plays a role in digestion, and can be isolated from *N. sativa*.[42]

Conclusion

Extracts and bioactive compounds from Nigella sativa seeds hold significant potential for development as therapeutic agents against chronic diseases, including diabetes, cancer, and immune-related disorders. Both in vitro and in vivo studies have demonstrated promising pharmacological activities, particularly thymoquinone, the major constituent of *N. sativa*, which exhibits potent antioxidant, anti-inflammatory, and antimicrobial effects. Owing to its relatively simple chemical structure, thymoquinone can be efficiently isolated from *N. sativa* or synthesized, making it a highly promising candidate for overcoming drug resistance and for further exploration in the development of novel treatments for chronic diseases.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas, took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors declare no conflict of interest.

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