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The Promise Between Ancient Wisdom and Modern Science for Nigella sativa as a Multimodal Agent in Healthspan Extension: A Narrative Review

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Abstract

Longevity medicine increasingly focuses on extending healthspan rather than lifespan alone, and *Nigella sativa* (black seed), with its long history of traditional use, along with thymoquinone (TQ), its principal bioactive compound, has drawn growing interest for its effects on several pathways implicated in aging. To summarize the evidence for *N. sativa* as a potential healthspan-promoting agent, we conducted a narrative review of the peer-reviewed literature from PubMed, Scopus, and Web of Science, together with classical Islamic medical texts and authenticated Prophetic narrations, considering in vitro studies, animal studies, and human randomized controlled trials, with a focus on aging-related mechanisms, human evidence, Islamic medical tradition, and remaining research gaps. Case reports and case series were excluded.

TQ shows antioxidant, anti-inflammatory, metabolic, neuroprotective, and cellular effects relevant to several hallmarks of aging, and human studies show modest improvements in cardiometabolic risk factors, inflammatory markers, oxidative stress, and some cognitive measures. Overall, *N. sativa* is a promising multimodal candidate for healthspan research, but evidence that it extends human healthspan is not yet established, and longer trials using standardized preparations and aging-specific outcomes are needed.

Categories: Nutrition, Integrative/Complementary Medicine, Geriatrics
Keywords: aging, cardiometabolic, healthspan, ibn sina, inflammaging, islamic medicine, longevity medicine, neuroprotection, nigella sativa, thymoquinone

Introduction And Background

Nigella sativa (called al-ḥabbah al-sawdāʾ in Arabic, meaning "the black seed") has been used for more than two thousand years in traditional medicine, including Islamic, Greco-Arabic, and Ayurvedic traditions [1,2]. Modern longevity research is now asking a more specific question: can its biological effects help preserve healthspan?

Longevity medicine has shifted from simply extending lifespan toward preserving health, physical function, metabolic stability, and cognition [3]. In this context, "healthspan" refers to the period of life spent in good health, free of serious chronic disease or disability, as distinct from lifespan, the total length of life regardless of health status. The "hallmarks of aging" are a set of interconnected biological processes, including genomic instability, telomere attrition, epigenetic alterations, loss of proteostasis, deregulated nutrient sensing, mitochondrial dysfunction, cellular senescence, stem cell exhaustion, and altered intercellular communication, that together drive age-related functional decline [4]. Because aging involves interconnected biological processes, interventions that influence several pathways may have particular value.

This is where *N. sativa* becomes scientifically interesting. Many current approaches to aging focus on individual pathways: rapamycin targets mechanistic target of rapamycin (mTOR), metformin activates AMPK, and nicotinamide adenine dinucleotide (NAD+) precursors support sirtuin enzymes involved in DNA repair and metabolic regulation [5]. Aging, however, involves multiple interconnected processes, including oxidative stress, chronic inflammation, mitochondrial dysfunction, and cellular senescence [4]. Thymoquinone (TQ), the principal bioactive compound in black seed oil, appears to influence several of these processes.

This review examines *N. sativa* through the lens of longevity medicine, focusing on mechanisms relevant to aging, human clinical evidence, its place in Islamic medical tradition, and the major gaps that remain.

Review

Methods

This is a narrative review and was not registered or conducted according to a systematic review protocol; therefore, PRISMA 2020 reporting was not applied. The review follows the general principles of scale for the assessment of narrative review articles (SANRA). No formal risk-of-bias or Grading of Recommendations Assessment, Development and Evaluation (GRADE) assessment was performed. Meta-analytic estimates should therefore be interpreted in the context of the original studies' confidence intervals, heterogeneity, and certainty assessments. Classical Islamic texts and Hadith were included only for historical context, not as clinical evidence. Hadith citations are based on Sahih al-Bukhari and Sahih Muslim, and translations of classical Arabic texts are the author's own unless otherwise indicated.

Literature search strategy

PubMed, Scopus, and Web of Science were searched for peer-reviewed English-language publications on *N. sativa*, TQ, aging-related mechanisms, and clinical outcomes, supplemented by reference-list screening. The literature search was carried out during manuscript preparation over approximately one month, without a fixed date restriction, using the keywords neuroprotection, cardiometabolic aging, Ibn Sina, Islamic medicine, nuclear factor erythroid 2-related factor 2 (Nrf2), inflammaging, healthspan, TQ, *N. sativa*, and longevity medicine. Peer-reviewed in vitro studies, animal studies, human randomized controlled trials, and published systematic reviews or meta-analyses addressing aging-related mechanisms or outcomes were included. Case reports and case series were excluded. Specific search strings and formal screening counts were not recorded, consistent with the narrative design.

Nigella sativa in the Islamic medical tradition: a scientific heritage

N. sativa has a long history in Islamic medicine. Its place rests on a Prophetic tradition (Hadith) preserved in Sahih al-Bukhari and Sahih Muslim, which has shaped the continued use and study of black seed [6]. Physicians of the Islamic Golden Age, including Ibn Sina and Ibn al-Qayyim al-Jawziyyah, described its traditional uses centuries before modern pharmacology [1,7]. The principal passages are quoted in Box 1. The 16th-century physician Dawud al-Antaki also listed black seed among the medicinal substances in his medical encyclopedia [2]. These historical accounts are not evidence of anti-aging efficacy, but they provide context for the long-standing clinical interest in the plant, which predates the modern hallmarks of aging (Figure *1*).

Hadith Sahih al-Bukhari, Kitab al-Tibb (Book of Medicine), Hadith No. 5688; Sahih Muslim, Hadith No. 2215 [6]

"You should use this black seed, for it contains a cure for every disease except death." "'Alaykum bi-hādhihi al-ḥabbah al-sawdā', fa-inna fīhā shifā'an min kulli dā'in illā al-sāma"

Ibn al-Qayyim al-Jawziyyah (1292-1350 CE), al-Tibb al-Nabawi (Prophetic Medicine), 14th century CE [1]

"Black seed heats and dries to the third degree. It is beneficial against cold and phlegm, relieves headache, opens obstructions, and strengthens all faculties of the body." "Al-ḥabbah al-sawdā' tusakhkhinu wa-tujaffif fī al-darajah al-thālithah"

Ibn Sina (Avicenna, 980-1037 CE), al-Qanun fi al-Tibb (The Canon of Medicine), Vol. 2, 11th century CE [7]

"Black seed activates innate body heat, strengthens the stomach, and removes cold and dampness." "Al-ḥabbah al-sawdā' tunashshiṭu al-ḥarārah al-gharīziyyah wa-tuqawwī al-ma'idah"

FIGURE 1: Classical sources quoted in the review (English rendering and transliteration)

CE, Common Era

The molecular architecture of black seed: what makes it work

The broad biological activity of *N. sativa* reflects its complex chemical composition. TQ is the best-studied component, but other constituents may contribute complementary effects (Table *1*) [8-10].

Bioactive compound	Chemical class	Key longevity-relevant actions	Refs
TQ	Quinone terpene	Antioxidant via Nrf2; anti-inflammatory via NF-κB; neuroprotective; anti-senescence; SIRT1 activator	[4,8,11,12,13]
Thymohydroquinone	Quinone	Acetylcholinesterase inhibition, cognitive protection against age-related cholinergic decline	[14]
Thymol	Monoterpene phenol	Antioxidant; antimicrobial; cardiovascular endothelial protection	[9,10]
Carvacrol	Monoterpene phenol	Anti-inflammatory; neuroprotective; modulates gut microbiome with aging implications	[9,10]
α-Hederin	Saponin	Immunomodulation; promotes autophagy, cellular waste clearance essential in aging	[9,10]
Nigellicine/Nigellidine	Alkaloid	Anti-inflammatory; analgesic; mild anxiolytic properties	[9,10]
Linoleic acid (omega-6)	Polyunsaturated fatty acid	Membrane fluidity maintenance; lipid metabolism support	[9,10]
Vitamin E (tocopherols)	Fat-soluble antioxidant	Membrane lipid peroxidation protection; synergizes with TQ antioxidant activity	[9,10]

TABLE 1: Major bioactive constituents of Nigella sativa and their longevity-relevant biological activities

TQ, thymoquinone; NF-κB, nuclear factor kappa-light-chain-enhancer of activated B cells; SIRT1, sirtuin 1

TQ accounts for much of the experimental evidence, but whole seeds or cold-pressed oil may also benefit from interactions among co-occurring phytochemicals [10].

Nigella sativa effects on biological aging processes

Oxidative Stress: The Rust of Human Biology

Oxidative damage accumulates with age and affects DNA, proteins, and lipid membranes, contributing to cellular dysfunction and senescence [15]. A major cellular defense is the Nrf2 pathway, which regulates antioxidant enzymes, including superoxide dismutase, catalase, glutathione peroxidase, and heme oxygenase-1. Nrf2 activity declines with age, reducing antioxidant defenses [4,11]. TQ can activate Nrf2 through modification of Keap1, promoting antioxidant gene expression. In animal models, TQ increased hepatic antioxidant enzyme activity, including quinone reductase and glutathione transferase [16]. In a randomized trial of patients with type 2 diabetes, 2 g/day of *N. sativa* oil for 12 weeks improved total antioxidant capacity and oxidative stress markers [17]. A meta-analysis of five randomized controlled trials found that *N. sativa* supplementation significantly increased superoxide dismutase activity, with no significant changes in malondialdehyde or total antioxidant capacity [18]. Ibn al-Qayyim's earlier description of black seed as supporting the body's vital faculties provides an interesting historical parallel [1].

Inflammaging: The Slow Fire That Ages Us

Inflammaging refers to the chronic, low-grade inflammation that develops with aging and contributes to many age-related diseases [19]. Persistent increases in inflammatory mediators such as IL-6, tumor necrosis factor-alpha (TNF-α), IL-1β, and C-reactive protein (CRP) can impair metabolic signaling and vascular health. Early pharmacological work showed that fixed oil of *N. sativa* and TQ inhibit eicosanoid generation in leukocytes, an upstream contributor to inflammatory signaling [20].

Nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) is a central regulator of this inflammatory response and a well-characterized target of TQ. TQ can inhibit NF-κB activation [12]. A meta-analysis of five randomized controlled trials found that *N. sativa* significantly reduced serum CRP (WMD, -0.55 mg/L; 95% CI, -1.02 to -0.08), although heterogeneity was substantial [21].

Ibn Sina described black seed in terms of reducing internal heat and correcting illness [7]. While these concepts differ from modern inflammatory biology, they illustrate the long history of observations

concerning its effects.

Cardiometabolic Health: Protecting the Engine of Longevity

Cardiovascular and metabolic health are closely linked to biological aging. Dyslipidemia, insulin resistance, hypertension, and visceral obesity increase cardiovascular risk and contribute to broader age-related decline [22].

Human evidence for *N. sativa* is particularly notable for cardiometabolic outcomes (Table *2*). Meta-analyses and randomized trials report lower LDL and total cholesterol levels, improved HbA1c and fasting glucose levels in individuals with prediabetes and type 2 diabetes, lower systolic blood pressure, and modest reductions in body weight and BMI [23-27].

Study	Journal	Design/N	Dose and duration	Key findings
Sahebkar et al. (2016) [23]	Pharmacol Res	Meta-analysis (n=17 RCTs)	Variable, 1-3g/day	↓ TC (WMD -4.78 mg/dL), LDL (WMD -7.69 mg/dL), TG; modest ↑ HDL
Namazi et al. (2018) [27]	Phytother Res	Meta-analysis (n=11 RCTs)	Variable	Significant ↓ BMI, waist circumference, body weight across all included studies
Ardiana et al. (2020) [18]	Sci World J	Meta-analysis (n=5 RCTs; 293 participants)	Variable	Significant ↑ SOD (WMD 48.19, 95% CI 30.30-66.08); no significant change in MDA or TAC
Askari et al. (2019) [25]	Phytother Res	Meta-analysis of clinical trials (n=17 RCTs)	Variable	Improved glycemic control across the included trials
Saadati et al. (2022) [24]	Front Nutr	Meta-analysis (n=11 RCTs; 666 participants), prediabetes and T2DM	Variable	↓ LDL (WMD -20.12 mg/dL), total cholesterol (WMD -23.84 mg/dL), HbA1c (WMD -0.54%) and fasting glucose (WMD -24.18 mg/dL); no significant change in triglycerides or HDL
Sahebkar et al. (2016) [26]	J Hypertens	Meta-analysis (n=11 RCTs; 860 participants)	Variable, mean 8.3 weeks	↓ Systolic BP (WMD -3.26 mmHg, 95% CI -5.10 to -1.42); ↓ diastolic BP (WMD -2.80 mmHg, 95% CI -4.28 to -1.32)
Kaatabi et al. (2015) [17]	PLoS One	RCT (n=114)	2g/day oil, 12 weeks	↑ Total antioxidant capacity; ↓ oxidative stress markers; ↓ LDL; ↑ HDL
Bin Sayeed et al. (2013) [31]	J Ethnopharmacol	RCT (n=40)	2g/day, 9 weeks	Improved memory and attention scores; reduced anxiety; good tolerability

TABLE 2: Key randomized controlled trials and meta-analyses of Nigella sativa: cardiometabolic, oxidative-stress, and cognitive outcomes

RCT, randomized controlled trial; T2DM, type 2 diabetes mellitus; WMD, weighted mean difference; TC, total cholesterol; TG, triglycerides, HDL, high-density lipoprotein; SOD, superoxide dismutase; MDA, malondialdehyde TAC, total antioxidant capacity; LDL, low-density lipoprotein; HbA1c, glycated hemoglobin (hemoglobin A1c); BP, blood pressure

These effects may involve AMPK activation, improved pancreatic β-cell function, greater peripheral glucose uptake, and increased endothelial nitric oxide availability [28]. Ibn Sina also described black seed in relation to digestive and metabolic function [7].

Neuroprotection and the Longevity of the Mind

Preserving cognitive function is a central component of healthspan. Cognitive aging reflects interacting

processes, including oxidative stress, neuroinflammation, mitochondrial dysfunction, and abnormal protein accumulation [29].

TQ has shown neuroprotective effects in experimental models. In Alzheimer's disease models, it reduced amyloid-β burden, supported cholinergic function, and reduced neuronal oxidative damage [30]. Thymohydroquinone, a TQ metabolite, also inhibits acetylcholinesterase [14]. Ibn al-Qayyim described black seed as being used for forgetfulness and weakness of the mind in older adults [1]. In a randomized trial, healthy adults receiving 2 g/day of *N. sativa* for nine weeks showed improved memory scores and reduced anxiety compared with those receiving placebo [31]. TQ has also been reported to increase brain-derived neurotrophic factor (BDNF) expression, a pathway relevant to cognitive resilience. This remains an area requiring dedicated, TQ-specific confirmation rather than extrapolation from general aging research findings [32]. These findings are promising but require confirmation in larger and longer clinical studies.

Cellular Senescence: Clearing the Body's Aging Cells

Senescent cells accumulate with age and release inflammatory and tissue-remodeling factors collectively known as the senescence-associated secretory phenotype (SASP) [4]. Emerging evidence suggests that TQ may have partial senolytic or senomorphic activity. In cellular models, TQ has been shown to selectively induce apoptosis in pre-senescent cells while sparing healthy proliferating cells, operating through p53/p21 pathway modulation and suppression of anti-apoptotic B-cell lymphoma 2 (Bcl-2) family proteins [12]. Equally importantly, TQ suppresses the secretion of SASP components, including Interleukin (IL)-6, IL-8, and matrix metalloproteinase (MMP)-3, through NF-κB inhibition, reducing the paracrine aging signals that senescent cells transmit to surrounding healthy tissue [12]. TQ has also been shown to activate sirtuin (SIRT) 1 and promote autophagic flux through peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1α), potentially supporting the removal of damaged cellular components [13]. These findings provide a plausible link between traditional observations and modern longevity pathways, although the evidence remains largely experimental and derives substantially from cancer cell models rather than models of physiological aging; therefore, extrapolation to healthspan-relevant senescence should be made cautiously.

Genomic Stability and Telomere Protection

Telomere shortening is an established feature of biological aging, and oxidative stress can accelerate this process [33]. Direct long-term human data on *N. sativa* are lacking.

The Human Evidence: What Clinical Trials Tell Us

It would be premature to claim that *N. sativa* has been proven to extend human healthspan. However, randomized trials and meta-analyses show a consistent pattern of modest improvements in several risk factors and biomarkers associated with aging (Table *2*).

Discussion

The overall profile of *N. sativa* is notable not because of one isolated effect, but because several of its reported actions overlap with processes involved in aging: oxidative stress, chronic inflammation, metabolic dysfunction, neurodegeneration, cellular senescence, and longevity signaling [4,34].

Compared with agents that target a single aging pathway, TQ appears to act across several biological systems. Rapamycin primarily inhibits mechanistic target of rapamycin complex 1 (mTORC1), metformin targets AMP-activated protein kinase (AMPK), and NAD+ precursors support sirtuin activity [5]. TQ may influence several of these pathways simultaneously, although generally with less potency and far less clinical evidence than dedicated pharmacological agents [35].

Islamic medical tradition provides valuable historical context for the long-standing use of *N. sativa*. This history should not be treated as equivalent to clinical trial evidence, but it can help explain the plant's sustained use and the early documentation of its indications and cautions [1].

Safety and Practical Considerations

Safety is especially important for a proposed longevity intervention because many users may be otherwise healthy. Overall, *N. sativa* appears well tolerated, although important caveats remain [36]. Clinical trials generally use 1-3 g/day of seed or 1-2.5 mL of cold-pressed oil. Reported adverse effects are usually mild gastrointestinal symptoms, such as nausea, bloating, and loose stools [37].

Potential interactions should also be considered. TQ may have antiplatelet effects and could increase the effects of anticoagulants such as warfarin [37]. Its glucose-lowering effects may be additive with those of insulin or sulfonylureas, and its antihypertensive effects may add to those of blood pressure medications [17,25,38]. High-dose animal studies suggest possible uterotonic effects, so supplemental use during

pregnancy should be approached cautiously [1].

A practical challenge that deserves emphasis is the significant variation in TQ content across commercial preparations. Studies have found TQ concentrations varying by up to tenfold between products, an issue that has important implications for both clinical trials and individual use [39].

Limitations

Notably, this review has several limitations. Most clinical trials have lasted only 8-16 weeks and have focused on disease-related outcomes rather than aging itself. Human data on epigenetic age, telomere length, and senescent-cell burden are lacking. TQ also has limited aqueous solubility and substantial first-pass metabolism, which may restrict oral bioavailability [40].

As this is a narrative rather than a systematic review, no formal risk-of-bias assessment, search-strategy log, or GRADE certainty rating was performed, and no original quantitative synthesis was undertaken. The pooled effect estimates quoted in Table *2* are drawn directly from the cited meta-analyses and should be interpreted alongside those sources' confidence intervals and heterogeneity statistics. Several cellular mechanistic findings for TQ, particularly those related to apoptosis and senescence pathways, derive from cancer cell models rather than models of physiological aging; extrapolation to healthspan-relevant senescence should therefore be made cautiously.

Future directions

The most important next step is a longer randomized trial using a standardized *N. sativa* preparation with verified TQ content. Ideally, such a study would follow middle-aged adults for several years and assess biological aging markers alongside cardiometabolic, cognitive, and patient-reported healthspan outcomes. This would help determine whether the promising mechanistic and short-term clinical evidence translates into meaningful effects on healthy aging.

Conclusions

The evidence reviewed here suggests that ancient interest in *N. sativa* has a plausible modern scientific basis, although its potential role in longevity remains unproven. Modern molecular and clinical research provides plausible explanations for several traditional observations: *N. sativa* and TQ can influence oxidative stress, inflammation, cardiometabolic risk, cognitive function, and cellular pathways relevant to aging, but most of the evidence remains short-term or preclinical. For longevity medicine, *N. sativa* is best viewed as a promising multimodal candidate rather than an established anti-aging therapy. It may help support healthspan through several biological pathways, but it is not a cure for aging, and traditional Hadith should not be interpreted as a literal clinical claim. The next step is rigorous, long-term clinical research using standardized preparations and aging-specific outcomes to determine whether the biological promise of black seed translates into meaningful improvements in human healthspan.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Alawi A. Al-Attas

Acquisition, analysis, or interpretation of data: Alawi A. Al-Attas

Drafting of the manuscript: Alawi A. Al-Attas

Critical review of the manuscript for important intellectual content: Alawi A. Al-Attas

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