Food Bioactive Ingredients

Mohamed Fawzy Ramadan
Editor

Black Cumin (*Nigella sativa*) Seeds: Chemistry, Technology, Functionality, and Applications

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Dedicated to my beloved family

Preface

Nigella sativa (black cumin) is one of the most admired medicinal plants in history. Recently, black cumin has become an important topic for scientific research worldwide. *Nigella sativa* seeds are rich in bioactive phytochemicals (i.e., thymoquinone, tocols, sterols, polar lipids, and amino acids) with diverse biological and health-promoting traits. Extracts, essential oils, and fixed oils from *Nigella sativa* seeds have been used in pharmaceuticals, functional foods, and nutraceuticals. *Nigella sativa* is evident to promote health and it might serve to be a novel source for modern phytomedicine. This book project aims to build a multidisciplinary discussion on the advances in *Nigella sativa* chemistry, technology, cultivation practices, functional properties, health-promoting activities, as well as food and non-food applications.

Upon kind invitation from the Springer Nature, this book was edited. The book contains chapters that describe cultivation, composition, and applications of *N. sativa* seeds as well as the chemistry, technology, functionality, and applications of its extracts, fixed oil, and essential oil. Aiming to provide a major reference work for those involved in pharmaceuticals, nutraceuticals, and oil industry as well as undergraduate and graduate students, this volume presents a comprehensive review of the results that have led to the advancements in *Nigella sativa* chemistry, technology, and applications. I hope this book will be a valuable source for people involved in medicinal plants and functional foods.

I sincerely thank all authors for their valuable contributions and for their cooperation during book preparation. I highly acknowledge the support from Deanship of Scientific Research (Umm Al-Qura University, KSA). The help and support given to me by the Springer Nature staff, especially *Daniel Falatko* and *Arjun Narayanan*, was essential for the completion of my task and is appreciated.

"Let food be your medicine and medicine be your food" (Hippocrates)

Makkah, Saudi Arabia — Mohamed Fawzy Ramadan

Description

Nigella sativa seeds have an increasing number of applications in food and pharmaceutical industries. Black cumin is used worldwide in traditional medicine for treatment of several diseases. Bioactive phytochemicals with pharmacological properties have been identified in black cumin, including thymoquinone, *t*-anethol, alkaloids, and saponins.

Black Cumin (Nigella sativa) Seeds: Chemistry, Technology, Functionality, and Applications covers several specific topics with a focus on cultivation, composition, and applications of *Nigella sativa* seeds as well as the chemistry, technology, functionality, and applications of *Nigella sativa* extracts, fixed oil, and essential oil.

Edited by a team of experts, *Black Cumin (Nigella sativa) Seeds: Chemistry, Technology, Functionality, and Applications* brings together diverse developments in food science to chemists, nutritionists, and students of food science, nutrition, lipids chemistry and technology, agricultural science, pharmaceuticals, cosmetics, and nutraceuticals.

Black Cumin (Nigella sativa) Seeds: Chemistry, Technology, Functionality, and Applications is a key textbook for pharmaceutical and functional food developers as well as research and development (R&D) managers working in all sector using medicinal plants and vegetable oils. It is a useful reference work for companies reformulating their products or developing new products.

Key Features

- Broad coverage encompasses chemistry, technology, functionality, and applications of *Nigella sativa*
- Authored by international academics and industry experts
- Addresses growing application areas including pharmaceuticals, functional foods, nutraceuticals, and cosmetics

Readership

- Academics and students with a research interest in the area (pharmacologists, food chemists, lipid scientists, food scientists, and agronomists)
- Pharmaceutics, functional food developers, and R&D managers working in all sectors using medicinal plants and specialty oils

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Mohamed Fawzy Ramadan is a Professor in the Department of Agricultural Biochemistry, Faculty of Agriculture, at Zagazig University, Zagazig, Egypt. Since 2013, Prof. Ramadan has also been a Professor of Biochemistry and Consultant of International Publishing at the Deanship of Scientific Research, Umm Al-Qura University, Makkah, Saudi Arabia.

Prof. Ramadan obtained his Ph.D. (*Dr.rer.nat.*) in Food Chemistry from Berlin University of Technology (Germany, 2004). He continued his postdoctoral research at ranked universities in different countries, such as the University of Helsinki (Finland), Max-Rubner Institute (Germany), Berlin University of Technology (Germany), and the University of Maryland (USA). In 2010, he was appointed as Visiting Professor (100% research) at King Saud University in Saudi Arabia. In 2012, Prof. Ramadan was appointed as Visiting Professor (100% teaching) in the School of Biomedicine at Far Eastern Federal University in Vladivostok, Russian Federation.

Prof. Ramadan has published more than 250 research papers and reviews in international peer-reviewed journals as well as several books and book chapters (Scopus *h*-index is 40 and more than 4300 citations). He was an invited speaker at several international conferences. Since 2003, Prof. Ramadan has been a reviewer and editor of several highly cited international journals such as *Journal of Medicinal Food* and *Journal of Advanced Research*.

Prof. Ramadan received Abdul Hamid Shoman Prize for Arab Researcher in Agricultural Sciences (2006), Egyptian State Prize for Encouragement in Agricultural Sciences (2009), European Young Lipid Scientist Award (2009), AU-TWAS Young Scientist National Awards (Egypt) in Basic Sciences, Technology and Innovation (2012), TWAS-ARO Young Arab Scientist (YAS) Prize in Scientific and Technological Achievement (2013), and Atta-ur- Rahman Prize in Chemistry (2014).

Chapter 1
Introduction to Black Cumin (*Nigella sativa*): Chemistry, Technology, Functionality and Applications

Mohamed Fawzy Ramadan

Abstract *Nigella sativa* L. (botanical family, Ranunculaceae) is one of the most admired medical oilseeds in history. *Nigella sativa* seeds have been mentioned in the words of the Prophet Mohammed. *Nigella sativa* seeds contain active phytochemicals (i.e., phenolics, thymoquinone, fatty acids, tocols, sterols, polar lipids, amino acids…etc) with diverse biological effects. Functional extracts, essential oil, and fixed oil from *Nigella sativa* have been used in novel foods, nutraceuticals and pharmaceuticals. *Nigella sativa* is evident to promote health and it might serve to be a novel source for modern phytomedicine. Recently, black cumin has become an important topic for research worldwide. This book project aims to build a multidisciplinary discussion on the development and advances in *Nigella sativa* phytochemistry, cultivation practices, technology, functional characteristics, health-promoting activities as well as the food and non-food applications.

Keywords Ranunculaceae · Black seeds · UNSDG · Phyto-medicine · Functional properties · Essential oil · Fixed oil · Coronavirus (CoV) · Lipid technology · Lipid chemistry

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1 *Nigella sativa:* Chemistry, Technology, Functionality and Applications

The United Nations Sustainable Development Goals (UNSDG) were announced in 2015 (https://sustainabledevelopment.un.org). UNSDG offer a vision of a fairer, peaceful, more prosperous, and sustainable world. In foods, the way it is grown, processed, transported, stored, marketed, and consumed, lies the fundamental connection between people and the path to sustainable economic development. The third goal of UNSDG which called "*Good Health and Well-Being*" is aimed to promote human well-being and healthy life which is related to the use of health-promoting medical plants and herb as well as the environmental-friendly techniques in food processing.

Scientists are searching for new foodstuffs with novel traits that could be designed to improve their healthfulness. Current research being carried out, will have a great influence on the way we eat in the near future (McClements 2019). Aromatic and medical plants have been used to formulate nutraceuticals and pharmaceuticals. According to World Health Organization (WHO), about 80% of world population depends on conventional medicine, which uses plant extracts or phytochemicals to treat several diseases. With the developments in the field of nutrition, there is an increasing interest in herbs and medicinal plants as phytochemicals-rich sources for functional foods, nutraceuticals and drugs. The demand for extracting plants phytochemicals, oils, and bioactive compounds has recently increased due to the beneficial roles played by different bioactive phytochemicals. Research is recently focusing on studying the bioactive compounds and therapeutic traits as well as investigating the toxicological impacts and the mode of action of plant extracts, oils and bioactive phytochemicals (Ramadan and Moersel 2002a, b; Ramadan 2007; Ramadan and Wahdan 2012; Kiralan et al. 2014; Hassanien et al. 2015). The WHO is giving importance on the exploration of medical plants for the benefits of human health care. Emphasis have been provided on scientific results, on the quality assurance, quality control, safety, efficacy, toxicity of the species, dosage, clinical trials, therapeutic applications, and drug interactions.

Medical plants, especially those showing multiple biological effects, are of great interest. Black seeds or black cumin (*Nigella sativa*, family Ranunculaceae), is of importance due to its widespread food and medical applications (Ramadan et al. 2003; Ramadan and Moersel 2004; Hassanien et al. 2014; Kiralan et al. 2016). *Nigella sativa* is used worldwide for the treatment of several diseases. These findings were stimulated by the talks of Prophet of Islam religion (Prophet Mohammad) who said that the black seeds contain all kinds of remedies except death (Ahmad et al. 2013; Islam et al. 2019). In the traditional medicine, *Nigella sativa* seeds have been used to manage dispiritedness and fatigue, and chronic headache. Roasted *Nigella sativa* seeds with honey or butter are prescribed for colic and cough and considered a novel lactagogue and antiseptic agents to treat eye infection. World attentions has been directed to the outbreak of coronavirus disease (COVID-19) that was first reported from Wuhan, China, on 31 December 2019. The effect of *Nigella*

sativa extract on the replication of coronavirus (CoV) and on the expression of TRP-gene during CoV infection was evaluated (Ulasli et al. 2014). *Nigella sativa* extract exhibited an impact virus load and TRP-gene expression after CoV infection. Effective using of black cumin in therapeutic applications and for trade is markedly depend on yield (raw product, oils, seeds, and active compounds) and quality (Yimam et al. 2015).

Numerous bioactive phytochemicals that possess many pharmacological properties have been identified in black cumin including thymoquinone (TQ), dithymoquinone, thymohydroquinone, *t*-anethol, alkaloids (nigellicines and nigelledine), saponins (α-hederin), flavonoids, and monoterpenes such as *p*-cymene and *α*-piene (Ramadan and Moersel 2003; Ramadan et al. 2012; Ramadan 2016). *Nigella sativa* also contains important ingredients including oils, essential fatty acids, vitamins, carbohydrates, minerals, proteins, and essential amino acids. These bioactive compounds exhibited cardiovascular supportive, antidiabetic, anticancer, analgesic, anti-inflammatory, antiepileptogenic, antioxidant, anti-schistosomiasis, immunomodulatory, gastroprotective, hepatoprotective and nephron-protective activities. Black seed's antimicrobial properties included those on gram-positive bacteria, gram-negative bacteria, parasites, viruses, and fungi pathogens (Ramadan et al. 2012; Ramadan 2016).

Nigella sativa seed oil (fixed or volatile) is widely used in many foodstuffs, cosmetics and pharmaceutical products (Kiralan et al. 2017). Black seed oil is a popular natural painkiller and used as an antiseptic and analgesic remedy and for treatment of joint's pain and stiffness. *Nigella sativa* seed oil and sesame oil blend is used for abdominal disorders, jaundice, dermatosis, cough, fever, liver ailments, headache, sore eyes and hemorrhoids. Thymoquinone (TQ) is the main active constituent in *N. sativa* essential oil, and most of the *Nigella sativa* traits are attributed to it (Kiralan et al. 2018). Thymoquinone protects the human cells from oxidation and gives recovery to cells by inhibiting from harmful impacts. Thymoquinone exerts high potential on carcinogenesis, eicosanoids production, and membrane lipid oxidation. In addition, TQ working as an effective chemo-protective agent with a hyperproliferative action in the experimental animals. Thymoquinone shows antiproliferative impacts on cancer cell lines of colon, ovary, larynx, breast, lung, myeloblastic leukemia, and osteosarcoma. Moreover, TQ protects from several diseases and prevents from weakening the immune system (Ramadan 2016).

2 *Nigella sativa* Market

Increasing demand for pharmaceuticals with natural phytochemicals owing to their health benefits is likely to propel *Nigella sativa* market size in the near future (www.gminsights.com). *Nigella sativa* fixed seed oil is a source of bioactive lipids, tocols, sterols, vitamins, folate, phosphorous, calcium, copper, zinc and essential fatty acids, which helps in improving digestion and boosting immune system. This product is usually organic (cold pressed extract), contain low calorie and could be used

in flavoring and cooking, and stimulating industry size. In addition, increasing interest for novel natural products in bakery products is likely to stimulate *Nigella sativa* seed oil market size.

On the other side, *Nigella sativa* essential oil have been used in novel foods, and nutraceuticals. *Nigella sativa* essential oil (in form of oil or capsules) contain thymoquinone (TQ), *p*-cymene, β-pinene, α-pinene, longifolene, α-thujene and carvacrol, which are essential in the nutraceutical formulation. Nutraceuticals market is expected to surpass 550 billion USD by 2025, owing growing e-commerce and consumer awareness, which is anticipated to drive the market size of *Nigella sativa*.

Due to the consumption needs of the rapidly increasing world population, *Nigella sativa* has a large international market. *Nigella sativa* seed oil market size was more than USD 15 million in 2018, and by 2025 industry expects to surpass USD 25 million. Moreover, at the end of 2025, *Nigella sativa* oil market size from cosmetic applications and personal care is projected to surpass 700 tons (https://www.gminsights.com/industry-analysis/black-seed-oil-market). Recently, the global market size, sales, share, and growth analysis report of *Nigella sativa* oil industry was released (www.marketwatch.com).

3 *Nigella sativa* in the International Literature

Being a spacious habitual and rich in bioactive phytochemicals, black cumin is considered as a weapon to the drug discovery and drug development. Several studies have been done on *Nigella sativa* and its oils as well as its bioactive compounds, especially on TQ and its derivatives (Islam et al. 2019). A search with the keyword "*Nigella sativa*" in PubMed database (February 2020) showed 1334 published contributions belonging to *Nigella sativa* extracts (water/organic/water-organic solvents), essential oil, fatty acids, seed oil, and isolated bioactive constituents.

When *Nigella sativa* was used as a keyword to search in Scopus or ISI Web of knowledge databases, about 2890 articles and reviews have been found (till February 2020). A careful search on *Nigella sativa* (as keywords) in the title, abstract and keywords among contributions in the Scopus database (www.scopus.com) revealed that the total number of scholarly outputs published is high (*ca.* 2890 till February 2020). Apart from the total published scholarly outputs *ca*. 2550 were research articles, *ca*. 227 reviews, and 14 book chapters. Figure 1.1 shows the scholarly output on *Nigella sativa* since 2000. It is clear that the scholarly outputs published annually on *Nigella sativa* are markedly increased from 20 contributions in 2000 to 252 article in 2019. These measurable indicators reflect the importance of *Nigella sativa* as a topic in the international scientific community.

The publications were mainly related to the subject areas of pharmacology, toxicology and pharmaceutics, agricultural and biological sciences, medicine, biochemistry, genetics and molecular biology, chemical engineering, chemistry, and engineering. Scienticts form Iran, Egypt, India, Saudi Arabia, Turkey, Pakistan and United States have emerged as main contributors. Most prolific journals were

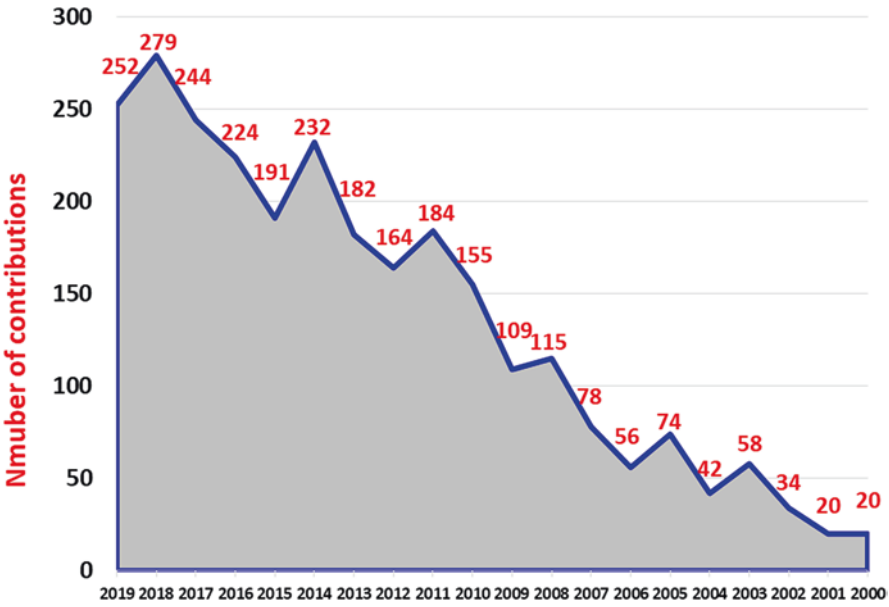

Fig. 1.1 Scholarly output on *Nigella sativa* since 2000. (www.scopus.com)

Journal of Ethnopharmacology, Phytotherapy Research, Pakistan Journal of Pharmaceutical Sciences, International Journal of Pharmacy and Pharmaceutical Sciences, Pharmaceutical Biology, Evidence Based Complementary and Alternative Medicine, Industrial Crops and Products, and BMC Complementary and Alternative Medicine.

Several books already published on the composition and functional properties of herbs, oilseeds, and medicinal plants. However, it is hard to find a book focused on the cultivation, composition and functionality of *Nigella sativa*. This book is planned to contain comprehensive chapters focusing on *Nigella sativa*, which contain unique bioactive components that have led to their being considered health-promoting seeds. The main goal of editing this book was to discuss the phytochemical composition, therapeutic properties and functionality of high value oils, phytochemicals, nutrients, extracts and volatiles of *Nigella sativa* seeds, to explore their useful uses in pharmaceuticals, nutraceuticals, novel foods, natural drugs, and feed. *Nigella sativa* seeds have unique phytochemical profile and characteristics that make them a novel source for nutraceuticals, pharmaceuticals and functional foods. Book chapters are designed to have the following main sections:

1. Cultivation, Composition and Applications of *N. sativa* seeds
2. Chemistry, Technology, Functionality and Applications of *N. sativa* fixed oil
3. Chemistry, Technology, Functionality and Applications of *N. sativa* essential oil
4. Chemistry, Technology, Functionality and Applications of *N. sativa* extracts

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Part I
Nigella sativa Seeds: Cultivation, Composition and Applications

Chapter 2
Effect of Cultivation, Fertilization and Irrigation Practices on *Nigella sativa* Yield and Quality

Enas Mohamed Wagdi Abdel-Hamed

Abstract *Nigella sativa* (black cumin) seeds are used as a food additive, and in medical proposes. Considering the importance of *Nigella sativa* plant, large-scale production is important. Phytochemical profile changes during germination because biochemical activities produce energy and essential constituents, wherein some phytochemicals transform into active constituents. Few studies reported on the impacts of cultivation conditions on the growth, yield and biochemical constituents of *Nigella sativa*. This chapter summarizes and highlights the impact of different cultivation, fertilization and irrigation regimes on the yield and quality of *Nigella sativa* seeds.

Keywords Water-use efficiency · Salinity · Drought stress · Geometrical properties · Plant growth characters · Germination · Seed treatment · Gibberellic acid

Abbreviations

AET	Actual evapotranspiration
Cd	Cadmium
DAE	Days after emergence
EO	Essential oil
G × E	Genotype × Environment
GA_3	Gibberellic acid
K	Potassium
KIN	Kinetin
MAD	Maximum allowable depletion
N	Nitrogen

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