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Nutraceutical Synergy in the Treatment of Polymorbid Pathology: Black Seed Supplementation in Hypertension, Diabetes, Knee Osteoarthritis and Anxiety - A Case Study

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Abstract

Introduction: Investigate combining black seed (*Nigella sativa*) and honey to manage hypertension, type-2 diabetes, knee osteoarthritis, and anxiety in a middle-aged woman.

Case Presentation: A 55-year-old woman, poorly controlled on allopathic meds for 4 months, had her BP and blood sugar monitored for 2 weeks. She then started a black seed-honey mix, and BP and blood sugar were monitored for another 2 weeks.

Significant reductions in BP and blood sugar levels were observed. The knee osteoarthritis score was halved, and anxiety was reduced from moderate to none. The patient continued the supplement with adjusted meds and experienced no adverse effects.

Conclusion: The black seed-honey mix shows promise as an adjunctive therapy for multiple conditions and warrants further investigation.

Keywords: Black seed; *Nigella sativa*; Honey, Hypertension; Type-2 diabetes mellitus; Osteoarthritis; Anxiety; Nutraceuticals; Blood pressure; Complementary medicine

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Introduction

Background

The management of chronic conditions such as hypertension, type-2 diabetes mellitus, knee osteoarthritis, and anxiety represents a significant global health challenge, necessitating a multifaceted approach to treatment [1, 2, 3]. In recent years, the exploration of nutraceuticals—biologically active compounds from natural origins—has gained traction as a promising adjunct to conventional therapies. This paper seeks insight into the potential therapeutic

synergy of two traditional remedies, black seed (*Nigella sativa*) and honey, in addressing the intricate web of multimorbidity.

Nutraceuticals, a fusion of "nutrition" and "pharmaceuticals," represent a diverse array of bioactive compounds derived from natural sources that offer therapeutic potential in the management of various health conditions [4]. These compounds, ranging from vitamins and minerals to herbal extracts and botanicals, have garnered increasing attention for their role in complementary and alternative medicine approaches to disease management [5]. Nutraceuticals bridge the domains of nutrition and pharmaceuticals, and their multifaceted pharmacological properties have positioned them at the forefront of complementary and alternative medicine strategies for managing a myriad of health conditions. Millions of people worldwide suffer from hypertension, a significant risk factor for cardiovascular disease [6], diabetes, knee osteoarthritis [7], and anxiety [8], which present noteworthy health challenges and necessitate diverse treatment approaches to alleviate consequences.

Against rising chronic disease burdens worldwide, traditional medicinal systems have long lauded the virtues of black seed and honey for their multifarious health benefits. Traditional medical systems have honoured black seed (*Nigella sativa*) and honey for their reputed health advantages for generations. Black seed, commonly referred to as "habbat al-barakah" or "the blessed seed," has anti-inflammatory, anti-hypertensive, and antioxidant properties due to its bioactive components, especially thymoquinone [9]. Similarly, honey's wide range of phytochemicals and enzymes, a natural sweetener made from floral nectar, gives it antioxidant, anti-inflammatory, antimicrobial, and wound-healing qualities [10,11].

The literature surrounding nutraceutical interventions for chronic diseases is expansive and multifaceted. Recent studies have increasingly focused on elucidating the mechanisms underlying the therapeutic effects of black seed and honey, particularly in the context of hypertension, diabetes, osteoarthritis, and anxiety. The therapeutic potential of *Nigella sativa*, particularly its seeds and thymoquinone (TQ), in various health conditions is acknowledged worldwide. Despite widespread interest, clinical utilization is hindered by the need for standardized preparations with known TQ content, impacting reproducibility and safety. Efforts to optimize and standardize these preparations are crucial for future therapeutic development. Thymoquinone emerges as an essential active ingredient, highlighting the necessity of its quantification in *Nigella sativa* formulations [12]. In diabetes management, black seed has garnered attention for its hypoglycemic effects, mediated by enhanced insulin sensitivity and β -cell function. Correspondingly, honey exhibits antidiabetic properties, with studies suggesting its role in improving glycemic control and lipid profiles in diabetic individuals [13]. In knee osteoarthritis, the anti-inflammatory properties of black seed have been explored as a potential therapeutic avenue for alleviating pain and improving joint function. Honey's anti-inflammatory and antioxidant properties may also offer synergistic benefits in mitigating osteoarthritic symptoms [14]. Furthermore, both black seed and honey have been investigated for their anxiolytic effects, with studies highlighting their potential to reduce anxiety levels and improve overall psychological well-being [15, 16].

These studies have employed diverse methods, including in vitro experiments, animal models, and clinical trials, to provide a comprehensive understanding of the therapeutic potential of black seed and honey across various disease states.

Research Problem

Despite advancements in conventional treatments, managing chronic conditions like hypertension, type-2 diabetes mellitus, knee osteoarthritis, and anxiety remain challenging. There is a need to explore alternative and complementary therapies to improve outcomes and alleviate symptoms. The efficacy and safety of combining black seed (*Nigella sativa*) and honey as nutraceuticals in managing these conditions have not been extensively studied. Thus, the research problem lies in investigating the therapeutic potential of this natural remedy to address the multifaceted aspects of these chronic conditions and enhance overall patient well-being.

Objectives

To highlight the potential of incorporating natural medicines into comprehensive patient care approaches, this paper aims to clarify the nutraceutical role of black seed and honey in healing various multifactorial health issues. Through a comprehensive literature review and a detailed clinical case presentation, we provide insights into the therapeutic potential of black seed and honey combination therapy with allopathic medicine in addressing multiple chronic health conditions.

Case Presentation

General Background

This case study details the therapeutic results of a middle-aged woman who, in addition to standard allopathic medicine, was prescribed ground black seed combined with honey for her poorly controlled diabetes, osteoarthritis in her knees, anxiety, and hypertension.

Study Design

A single-case study was conducted to assess the impact of supplementing conventional medication with ground black seed mixed with honey on blood pressure, blood sugar levels, osteoarthritis severity, and anxiety levels.

Participants

Mrs. F, a 55-year-old female, presented to the medicine outpatient department of Holy Family Hospital, a teaching hospital of Rawalpindi Medical University, Rawalpindi, Pakistan with a history of moderate to high blood pressure, type-2 diabetes mellitus, knee pain, and anxiety. She had been on a regimen of Losartan (100mg), Amlodipine (10mg), Atenolol (50mg), and Metformin (1500mg) daily for the last 4 months.

Interventions/Variables

Baseline measurements of blood pressure and blood sugar levels were recorded for 2 weeks before and 2 weeks with the intervention. The patient supplemented her conventional medication regimen with one teaspoon of ground black seed mixed with honey twice daily.

Data Collection

The patient supplemented her conventional medication regimen with one teaspoon of ground black seed mixed with honey twice daily. The severity of arthritis was assessed using the Osteoarthritis Score, and anxiety levels were measured using the Anxiety Symptoms Questionnaire (ASQ) pre-and post-intervention.

Data Analysis

Data was recorded in pre-made questionnaires and evaluated using SPSS Software version 26. Each reading was taken in triplicate. Mean and SD were measured for each, and the Value was calculated. p values at $p < 0.001$ were considered significant.

Mrs F reported inadequate control of her hypertension, diabetes, and knee pain despite adherence to allopathic medications. She also experienced anxiety and tension due to her health condition. Upon examination, Mrs. F appeared anxious but otherwise stable. Vital signs revealed elevated blood pressure and random blood sugar levels.

Blood pressure and blood sugar levels were monitored for 14 days before initiating black seed supplementation. The patient's baseline osteoarthritis severity was assessed using the Osteoarthritis Score, and her anxiety levels were evaluated using a standard questionnaire (ASQ).

Mrs. F was advised to supplement her existing allopathic medications with one teaspoon (around 5 grams) of black seed grounded and mixed with honey twice daily. The treatment plan aimed to improve blood pressure control, glycemic control, knee pain, and anxiety symptoms.

Blood pressure and blood sugar levels were monitored for 14 days after initiating black seed supplementation. On day 14th, osteoarthritis severity and anxiety levels were re-evaluated.

Following black seed supplementation, Mrs F experienced a significant reduction in a mean of 14 days systolic blood pressure from 195 ± 27 mmHg to 130 ± 10.8 mmHg and diastolic blood pressure from 105 ± 9 mmHg to 85 ± 10.7 mmHg ($P < 0.001$ in all cases). Random blood sugar levels decreased from 354.3 ± 106.9 mg/dl to 122.1 ± 22.9 mg/dl ($P < 0.001$). The Osteoarthritis Score improved by 50%, and anxiety levels decreased from moderate to none.

Fig 1. graph showing the effect of Powered black seed mixed with honey over 14 days on blood pressure, random blood sugar, osteoarthritic score, and anxiety levels.

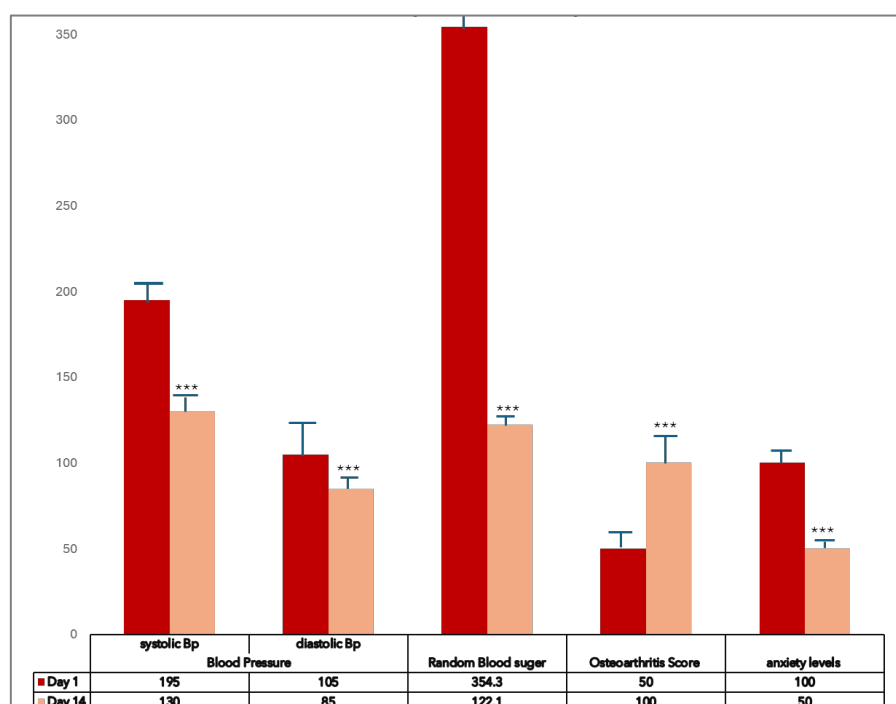


Figure 1. Effects of Powered Black Seed Mixed with Honey on Blood Pressure, Blood Sugar, Osteoarthritic Score, and Anxiety Levels Over 14 Days

Note. Denotes significance difference at $p < 0.001$.

Discussion

The case report provides compelling evidence supporting the therapeutic potential of a combined regimen of black seed and honey in the management of hypertension, diabetes, knee osteoarthritis, and anxiety in a female patient. Black seed has been esteemed for centuries in various cultures for its medicinal properties. Rich in bioactive compounds like thymoquinone, black seed has garnered attention for its antioxidant, anti-inflammatory, and cardioprotective effects. A daily dose of 2 grams of black seeds is ideal for achieving health advantages in multiple clinical trials. Nevertheless, replication or additional research has yet to confirm several positive clinical trial results [17,18].

A possible explanation for the controversial results in these studies could be using sub-therapeutic doses and/or evaporation of volatile oil active components in capsule formation, the usual dosage form of ground powder of black seed used in most of these clinical trials. To overcome this problem, the black seed was ground in a manual grinder, and the powder was immediately mixed with an equal amount of honey. A thick mixture prepared this way can be quickly taken with a teaspoon, containing about 2.5-3 grams of black seed, i.e. around 5-6 grams daily. Moreover, such preparation can be easily made at home at a low cost and gives better compliance because of the improved taste of honey. Half-teaspoon of honey, with black seed and after meals does not increase blood sugar levels.

Hypertension, a prevalent cardiovascular risk factor, was effectively managed in our patient by administering black seed and honey. Previous studies have highlighted the antihypertensive properties of black seed due to its vasodilatory effects and ability to modulate endothelial function and oxidative stress. Additionally, honey has been shown to possess hypotensive effects attributed to its vasodilatory and anti-inflammatory properties. In our patient, black seed and honey supplementation allowed a decrease in the requirement of antihypertensive medications from Losartan (100mg), Amlodipine (10mg), and Atenolol (50mg) to Losartan (100mg), and Atenolol (50mg) daily.

Similarly, our patient experienced improvements in glycemic control, as evidenced by reductions in fasting blood glucose levels following treatment with black seed and honey. Black seed has been reported to regulate blood glucose levels through mechanisms such as inhibiting glucose absorption, stimulating insulin secretion and increasing insulin sensitivity [19]. Honey, on the other hand, may improve glycemic control by promoting glucose uptake by tissues and enhancing pancreatic beta-cell function [20, 21]. The combined effect of black seed and honey in regulating glucose metabolism suggests a promising adjunctive therapy for individuals with diabetes, which permits the reduction of Metformin dose from 1500mg to 500mg daily.

Furthermore, our patient reported significant alleviation of knee pain and improvement in joint function after initiating treatment with black seed and honey. Knee osteoarthritis, characterized by cartilage degeneration and joint

inflammation, poses challenges in pain management and functional impairment. The patient had to discontinue Mefenamic acid (Ponstan) because of stomach upset.

The anti-inflammatory and analgesic properties of black seed and honey may have contributed to the observed symptomatic relief in our patient, highlighting their potential as complementary therapies in osteoarthritis management. The analgesic potential of black seed extracts was demonstrated by an increase in hot plate reaction time and a reduction in abdominal constrictions produced by acetic acid in mice. The anti-inflammatory activity of these extracts was elucidated by the prevention of carrageenan-induced paw oedema in albino rats [22,23].

The analgesic and anti-inflammatory activity mechanism was reported to be associated with polyphenols present in the black seed, e.g., ferulic acid, p-coumaric acid, kaempferol, and quercetin. Ferulic acid and other phenols were shown to inhibit the formation of precursor phospholipids required for the synthesis of arachidonic acid and then Prostaglandins and Leukotrienes, the critical mediators of pain and inflammation. Moreover, most components of black seed reduced the expression of COX1 and COX2, enzymes needed for synthesising prostaglandins [24].

Honey's anti-inflammatory properties have been implicated in managing conditions characterized by chronic inflammation, such as osteoarthritis [25,26].

Additionally, our patient experienced notable reductions in anxiety symptoms following supplementation with black seed and honey. Anxiety, a prevalent mental health disorder, significantly impacts psychological well-being and quality of life. The anxiolytic properties of black seed and honey, attributed to their effects on neurotransmitter systems and stress response pathways, may have contributed to the observed improvements in anxiety symptoms. This suggests a potential role for black seed and honey in mental health support and anxiety management. Both the black seed and honey's neuroprotective effects have been investigated in the context of anxiety and stress-related disorders, with preliminary evidence suggesting anxiolytic potential [27,28].

While our case report provides promising insights into the therapeutic efficacy of black seed and honey combination therapy, several limitations warrant consideration. Firstly, as a single case report, our findings may not be generalizable to all individuals with similar health conditions, although few similar studies have been reported previously [29]. Further studies involving larger sample sizes and controlled clinical trials are needed to validate our observations and elucidate the underlying mechanisms of action. Additionally, the potential interactions and safety profile of black seed and honey require further investigation to ensure their suitability for long-term use in clinical practice. However, black seed has shown a wide margin of safety in acute and chronic toxicity studies in small laboratory animals.

Limitations of the study

The current study is not limited, as it is a single case report, and the positive results have prompted the initiation of a 60-patient study to elucidate the mechanism of action.

Conclusions and Implications

In conclusion, our case report underscores the potential of black seed and honey combination therapy as a novel nutraceutical approach in the management of hypertension, diabetes, knee osteoarthritis, and anxiety. The synergistic effects of these natural remedies offer multifaceted benefits in addressing multiple chronic health conditions, highlighting their potential as complementary therapies alongside conventional treatments. Further research is warranted to validate our findings and establish the clinical utility of black seed and honey in disease management.

Suggestions for Future Research

The current study has laid a foundation for further investigation into the therapeutic potential of combining black seed (*Nigella sativa*) and honey in managing multiple chronic conditions. As a next step, a clinical trial involving 60 patients is underway to evaluate the mechanism of action and efficacy of this combination therapy. This trial aims to provide deeper insights into how black seed and honey when supplemented with allopathic medicines, benefit hypertension, type-2 diabetes, knee osteoarthritis, and anxiety. By rigorously examining the outcomes and mechanisms of action in a larger patient population, this clinical trial seeks to validate the initial study's findings and uncover additional benefits or therapeutic pathways. The results of this ongoing research endeavour hold promise for advancing our understanding of natural remedies for chronic diseases. They may pave the way for developing novel treatment options.

Declarations

Author Contributions

Conceptualization, Akram Randhawa, methodology, Akram Randhawa; formal analysis, Asma Umer Khayam; investigation, Haseeba; writing—original draft preparation, Asma Umer Khayam.; review, Asma Umer Khayam, Haseeba and Akram Randhawa. All authors have read and agreed to the published version of the manuscript.

Data Availability Statement

Data is available upon request due to ethical restrictions. The data presented in this study are available on request from the corresponding author.

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Institutional Review Board Statement

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board (or Ethics Committee).

Informed Consent Statement

Informed consent was taken from the patient on a written consent form.

Conflicts of Interest

The author declares that there is no conflict of interest regarding the publication of this manuscript.

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