Ethnobotanical review of *Bunium bulbocastanum* (Black Cumin) for the treatment of diseases: The clinical and mechanistic evidence

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Abstract:

Over many centuries, traditional medicines have been used by many countries throughout the world and reflect the vital part of healthcare. The use of traditional medicine has gained popularity in the last few decades and expanded globally. The traditional Indian medicine, Ayurveda being the most ancient yet promoting and supporting extensive research and therapies for various health needs. Bunium bulbocastanum, also known as kala jeera (black cumin), is a member of the Apiaceae family. Its fruit has been used for food for several years, and it can be consumed raw or cooked to add taste. This plant and its derivatives have antimicrobial, antioxidant, anti-inflammatory, anti-diabetes, antimicrobial and antifungal properties. Bunium bulbocastanum is also well known ayurvedic medicinal plant used to treat a variety of ailments including throat infections, cold, fever, and hyperglycemia. The previous studies have also explored that the aqueous and ethyl acetate fractions of the fruit extract of Bunium bulbocastanum have been shown to have anti-cancer activity on lung cancer and cervical cancer cell lines. Recently, traditional herbal medicinal plants and its derivatives have gained importance as they are easily accessible and have less than minimal risk of side effect. There is no review article which explored the potential health benefits of Bunium bulbocastanum. The present review focuses on a detailed survey of the literature on scientific researches of pharmacological activities of the seeds of this plant.

Keywords: *Bunium bulbocastanum*, medicinal herb, antioxidant, anticancer, antidiabetic, antifungal, antibiotic, black cumin

1. Introduction:

Plants have been used for medicinal purposes long before modern history. Since India has such a diverse flora, it's only natural that the conventional Indian medical system incorporates it. Despite western medicine's immense impact and reliance, as well as massive developments in synthetic medications, a substantial portion of the world's population still prefers products obtained from plants due to their accessibility, effectiveness, low cost and comparatively being devoid of serious toxic effects.(1) Plant-based chemicals have been the most effective forms of medicine since the dawn of humanity.(2) Herbal medicine is one of the most significant aspects of western medicine all over the world. Alkaloids, terpenoids, flavonoids, glycosides, and phenolics are phytochemicals derived from plants that have detailed physiological results.(3) The majority of these results are

positive and beneficial. These medicinal plants are thought to be very effective, since they have little or very little side effects. The notable point is that herbal therapy is independent of the person, age, or gender. Regular use of synthetic medications may lead to addiction, but plant-based products do not have these side effects and are thus safer than synthetic substances.(4)"

1.1 Morphology of plant:

Bunium bulbocastanum, also known as kala jeera (black cumin), is a member of the Apiaceae family. Black Cumin is a perennial aromatic spice found in dry temperate regions of northwest Himalayas, alpine areas of Himachal Pradesh, and Kashmir, and Uttaranchal.(5) The plant is branched, tuberous, leaves 2–3 pinnate and finely dissected. Flowers's white, borne on compound umbels. Its fruit has been used for food for several years, and it can be eaten raw or cooked to add flavor. *Bunium bulbocastanum* fruits (family Apiaceae) have long been used as a culinary spice.

Scientific Classification of Bunium bulbocastanum:

Kingdom: Plantae

Clade: Tracheophytes

Clade: Angiosperms

Clade: Eudicots

Clade: Asterids

Order: Apiales

Family: Apiaceae

Genus: Bunium

Species: B. bulbocastanum(9)

Bunium Bulbocastanum is also known as kala jeera or sahi jeera, among other names. Cumin seeds are divided into three forms in Ayurveda.

1. **Jeerak**

2. **Krishna Jeerak**

3. **Kaarvi** (also known as Sthula Jiraka, Upakunchika, Sushavi).

The seeds of the Cuminum cyminum plant, which belongs to the Apiaceae family, are used to make jeerak. Cumin, Jeera, Jeraka, Jira, Zeera, Zira, or Safed Jeera are some of the common names.(10) Two varieties of plants, *Bunium bulbocastanum* and Carum carvi, are used to give Krishna Jiraka.

Nigella sativa seeds are referred to as Kaarvi, Kalaunji, Mangaraila, and Black Cumin (also known as Black Caraway). Mota Kalajira and Kalajira are the Bengali names for it, but structurally and botanically, Kalajira and Kalounji are very different. However, both are known as Black Cumin and are available. Kalounji (Nigella sativa) is a member of the Ranunculaceae (buttercup or crowfoot family), while KalaJira is a member of the Apiaceae family. While smaller than normal cumin, Kalajira (*Bunium bulbocastanum*) has a similar appearance. Nigella seeds are black, compressed, funnel-shaped seeds that don't resemble cumin seeds at all.

1.2 Traditional use of this miracle herb in folk medicine:

It's thought to help with blood sugar levels. It can also help with weight loss. There is no clinical evidence to support the fact that black cumin can help reduce cholesterol levels in the body. According to Ayurvedic doctrines, it aids in the equilibrium of Vata, Pitta, and Kapha Dosha.(15) According to public opinion, it's a good and effective cure for indigestion and diarrhea. Stomach aches, cramps, and gastric problems may all be relieved with black cumin seeds. For indigestion, and diarrhea, the seeds are crushed, and taken. In traditional medicine it is said to have protection against heart and brain disorders. The lack of empirical proof for certain of the arguments, researchers can dig further and come up with scientific evidence for the claims mentioned above. Ayurveda prescribes black cumin for a variety of intestinal problems.(12) It is a stimulant, anti-inflammatory, analgesic, anti-spasmodic, carminative, and lactation stimulant properties. They are used in treating diarrhea, dyspepsia, fever, flatulence, stomachic, hemorrhoids, and hiccoughs. It stimulates appetite, and digestion.(13) Black cumin is particularly beneficial for diabetes in herbal medicine because it not only regulates blood sugar levels but also lowers bad cholesterol.(8,14) Another species, *Bunium persicum* is commonly used as a flavoring agent in people's food, but there are no serious concerns regarding its toxicity. *Bunium bulbocastanum* has anti-diabetic effects as well as antioxidant properties.(8)

1.3 Pharmacological potential of *Bunium bulbocastanum*:

Bunium bulbocastanum has a lot of potential in the field of pharmacognosy and plant-based drug developmental researches. Medicinal use of *Bunium bulbocastanum* is not much explored and is lacking experimental evidences. However, *Bunium bulbocastanum* has not disappointed the researchers who have tried to elucidate its medicinal potential. Since there is lack of awareness on use if this herb a lot of studies needs to be done to come up with scientific evidence. This review tries to establish the clinical and mechanistic role of *Bunium bulbocastanum* in various health conditions.

2. Pharmacological action of *Bunium bulbocastanum* as therapeutic drug in health diseases:

It is well known that *Bunium bulbocastanum* has anticancer, antidiabetic, antimicrobial and antifungal properties, and this is because of its potent antioxidant activity and high phenolic content. (6) This plant and its derivatives have antimicrobial, antioxidant, anti-inflammatory, anti-diabetes, antihyperlipidemic and analgesic properties. Bunium bulbocastanum essential oil contains high levels of oxygenated monoterpenes, especially γ-Terpinene, cumin aldehyde, ρ-cymene and limonene, which have high antimicrobial and antioxidant effects. (7)

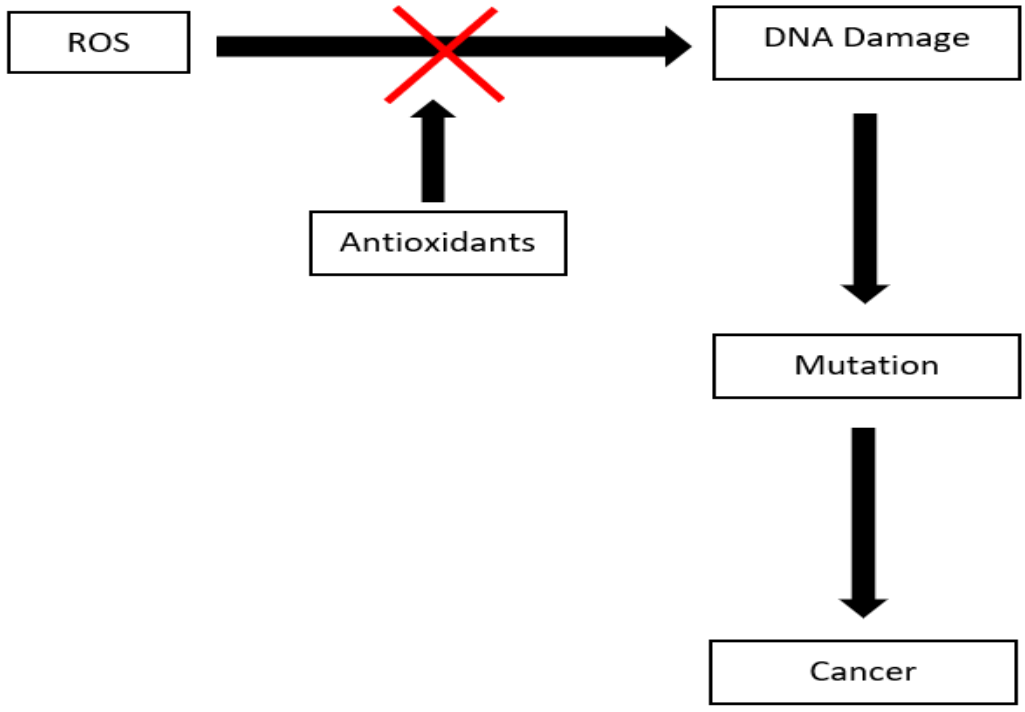
2.1: *Bunium bulbocastanum* as Chemotherapy agent:

Cancer is characterized by unchecked, uncontrolled and abnormal cell growth. The most common being stomach cancer, lung cancer, breast cancer, prostate cancer, and lymphoma. Symptoms differ depending on the type of cancer (16). Tumors are tissue masses that form as mutated cells multiply uncontrollably (Except in the case of Leukemia). Metastasis occurs when tumor cells invade the blood vessels and lymph nodes and seeds the cancerous cells into the nearby and distant organs. For the last 40 years, cancer-related mortality has risen by almost 40%. In the next 15 years, another 60% rise is anticipated, with 13 million people expected to die of cancer by 2030.(16) Chemotherapy, radiation, and/or surgery will all be used to cure this condition. Chemotherapy involves the use of chemicals that disrupt cell division by damaging proteins or DNA, causing tumor cells to die. These drugs attack all rapidly dividing cells (not only cancer cells), but normal cells can rebound from most compound-induced damage, while tumour cells cannot(17). Since drugs spreads across the entire body, chemotherapy is most often used to cure cancer that has spread or metastasized. It is used as a treatment in a few cases of leukaemia and lymphoma. Chemotherapy is administered in cycles to enable the body to heal between procedures.

However, chemotherapy and radiotherapy are associated with side effects such as nausea, fatigue, hair loss, exhaustion, and vomiting are also present.(17) Different types of chemotherapy or chemotherapy combined with other therapeutic methods are often used in blend therapies.

Reactive Oxygen Species (ROS) plays major role in pathogenesis of cancer. The ROS can be combated with the help of antioxidants. Since antioxidant properties are important in reducing oxidative stress, which has been shown to be a major factor in cancer pathogenesis. An imbalance between the generation of free radicals and reactive metabolites, also known as oxidants or reactive oxygen species (ROS), and their removal by protective mechanisms, such as antioxidants, is described as oxidative stress. Damage to essential biomolecules and cells occurs as a result of this imbalance, which has the ability to affect the entire body. ROS are byproducts of natural cellular metabolism, and they play an important role in the activation of signaling pathways in plant and animal cells in response to changes in intracellular and extracellular environmental conditions. The main source of ROS is endogenous metabolism occurring in the mitochondria especially the electron transport chain. (18)

Fig 2: Anti cancerous activity of *Bunium bulbocastanum* in Cancer treatment



The mitochondrial respiratory chain also releases nitric oxide (NO) under hypoxic conditions, which can result in reactive nitrogen species (RNS). By inducing excessive lipid peroxidation, RNS may produce other reactive species, such as reactive aldehydes like malondialdehyde and 4-hydroxynonenal. Proteins and lipids are also important targets for oxidative attack, and their modification can increase the risk of mutagenesis(18). ROS is formed over a long period of time in response to prolonged environmental stress, and this may cause substantial damage to cell structure and function, as well as somatic mutations and neoplastic transformation. Indeed, oxidative stress has been related to cancer initiation and development by increasing DNA mutations or causing DNA disruption, genome instability, and cell proliferation.

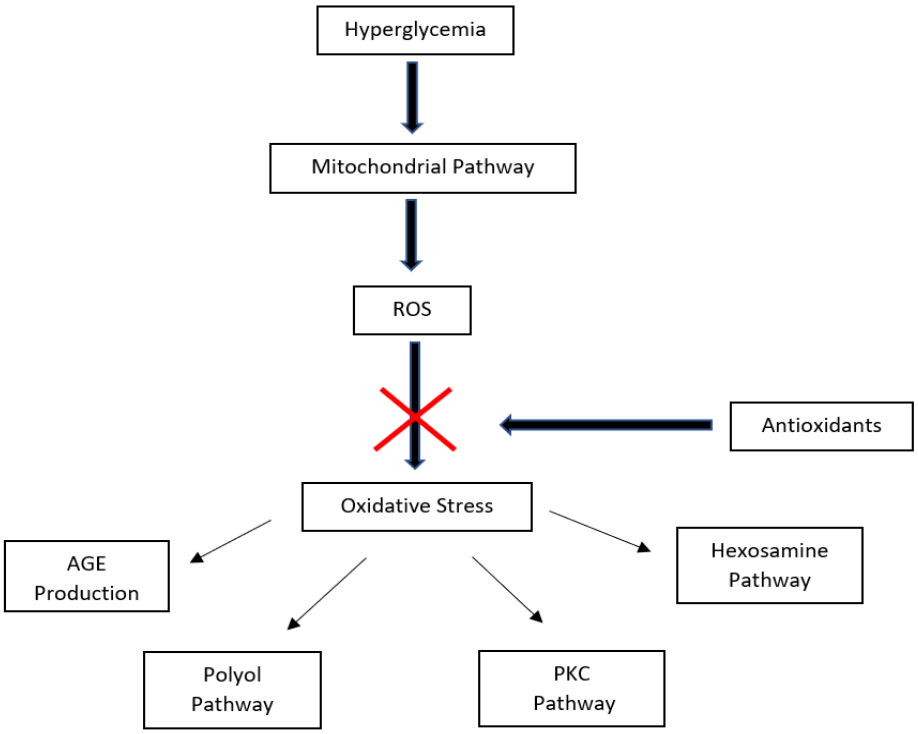
The study done by Hazarika I, Das A (2016), showed cytotoxic effect of ethyl acetate and aqueous fractions of extract of *Bunium bulbocastanum*. The evidence highlighted the potential of *Bunium bulbocastanum* to stop the uncontrolled proliferation of the cancer cells. It is well known that, *Bunium bulbocastanum* extract has a higher antioxidation propensity than the normal (ascorbic acid). Furthermore, various studies had showed the potency of ethyl acetate fraction of *Bunium bulbocastanum* as a stronger anticancer agent in the screening of anticancer activity, implying that the anticancer activity is attributed to its antioxidant property. (5)

2.2: *Bunium bulbocastanum* as Hypoglycemic drug in diabetes mellitus:

Diabetes, a non-communicable disease, is the leading cause of death worldwide, and particularly involving low- and middle-income countries(19). Diabetes affected 8.5 percent of people aged 18 and up in 2014. Diabetes claimed the lives of 1.5 million people in 2019. Diabetes mellitus (DM) is a carbohydrate metabolic condition that develops when either pancreas fails to produce insulin (type 1 DM) or when the extrahepatic cells become resistant to insulin (type II DM). Insulin is a hormone that helps to keep blood sugar levels in check. Uncontrolled diabetes causes significant damage to the nerves and blood vessels, over time leading to micro and macrovascular complications such as retinopathy, nephropathy, arteriosclerosis or myocardial infarction, and peripheral neuropathy. However, lot of deaths are because of cardiovascular disease, chronic kidney disease, ketoacidosis or some other diabetes related complications. The progression of diabetes complications, both microvascular and coronary, is influenced by oxidative stress. (6) Diabetes causes mitochondrial superoxide overproduction in endothelial cells in both large and

small arteries, as well as in the myocardium. This increased superoxide synthesis activates five main pathways implicated in the pathogenesis of complications: polyol pathway flux, increased AGE development, increased expression of the advance glycated end products (AGE) receptor and its activating ligands, activation of protein kinase C isoforms, and overactivity of the hexosamine pathway. In type 2 diabetes, pathway-selective insulin resistance, which enhances mitochondrial ROS synthesis from free fatty acids and inactivates antiatherosclerosis enzymes, contributes to atherosclerosis and cardiomyopathy. (14)

Fig 3: Anti diabetic role of *Bunium bulbocastanum*



There have been no antiglycation studies on *B. bulbocastanum* fruits. Ahmad H. Khan (2014) (3) discovered that the chloroform and ethyl acetate fractions have antiglycation and antioxidation properties. The chloroform fraction was the most effective antiglycation agent for the antiglycation in vitro assay. Antioxidation activity of the ethyl acetate and aqueous fractions showed a promising result. In therapeutics, the chloroform fraction of *B. bulbocastanum* fruits could be used as an

antiglycation agent. Further studies on *Bunium bulbocastanum* fruits extracts could lead to therapeutics for reducing diabetic complications. (8)

2.3: *Bunium bulbocastanum* as antimicrobial agent:

Antibiotic resistance is a major issue today, and isolating phytochemicals with strong antimicrobial activity against a variety of species will aid in the potential development of antimicrobial agents that can be used therapeutically.(20) The study of various antimicrobial phytochemicals derived from plant extracts can aid in the development of drugs that target particular photogenic microorganisms while causing the least amount of damage to the body's natural flora. (21)

Foodborne infections can be exacerbated by the introduction of pathogenic microorganisms in food. Recent increases in the prevalence of multidrug- and disinfectant-resistant bacteria in various food commodities have resulted in a rise in morbidity and mortality. Chemical preservatives are potentially dangerous to humans and can lead to health problems, leaving consumers at greater risk.(3) Furthermore, chemical preservatives only have an effect on a few pathogenic bacteria in food, such as *Listeria monocytogenes*, which fail to prevent the development of spoilage microorganisms. Antibiotic resistance bacteria, on the other hand, are limiting the efficacy of antibiotics, so treatment opportunities for common infectious diseases are dwindling. As a result, natural antimicrobials are gaining attraction as viable alternatives to synthetic antimicrobial therapeutics and chemical preservatives, owing to their low risk of side effects and effectiveness against human pathogens. Such data shows that they may be a reservoir of antimicrobial agents against certain foodborne pathogens, and that they may be good candidates for food preservatives. Many phytochemicals present in *Bunium bulbocastanum* can be researched upon for the discovery of new generation of antibiotics. (20)

2.4: *Bunium bulbocastanum* as Antifungal agent:

Resistance to medicines by different fungal species is one of the most pressing issues in the world of mycology today. Any of the available fungicides have severe side effects, and resistance has been observed in a variety of photogenic fungal species. Fungicides used to combat pathogenic fungal species have been found to have side effects in studies. Scientists are experimenting with various approaches in order to discover new and novel antimicrobial agents that can treat infections with little to no side effects.

Mycotoxins are secondary metabolites produced by fungi, some of which have been shown to be toxic to humans and animals. Only the chloroform (CHCl3) fraction had poor activity (15%) against *F. oxysporum*, according to scientific evidence. *Bunium Bulbocastanum* has a poor antifungal property, according to the available evidence. (18) More research on various fractions of different sections of the plant, such as seeds and leaves, is required.

Conclusion:

Bunium bulbocastanum has been used as a drug for several years in various forms. Its medicinal value is mentioned in many ancient texts. A considerable amount of study has gone into elucidating the different medicinal applications of this plant extract. It has been demonstrated to be an effective anticancer, antidiabetic, antimicrobial, and antifungal agent. It is a powerful antioxidant that aids in the reduction of oxidative stress. As a result, *Bunium bulbocastanum* plant extract can be used as a preventive therapy for cancer and diabetes patients. The antimicrobial activity of the plant extract is very high. Antimicrobial activity's mode of action is unknown, and further research is required. The plant extract does not seem to have much antifungal properties. Detailed study elucidating the various phytochemicals present in the various fractions and their mode of action can help for drug development with drugs acting on specific targets.

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