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Spices that heal: Review on untapped potential of lesser-known spices as immunity booster during COVID-19 pandemic

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Abstract

Herbs and spices are natural plant products that have been extensively used worldwide in cooking, home remedies and several industries. In current COVID-19 pandemic, herbal exploration is continually performed to reduce harmful effects of virus. Usual spices like turmeric, basil, cinnamon, *etc.*, have high antioxidant and antimicrobial activity which allow them to expand for their health benefits. But, there are other rare spices also, which can prove to be the most promising in curing serious ailments and enhancing immunity. This review is an attempt to highlight scientific evidence of three such spices, *viz.*, *Alkanna tinctoria* (Ratanjot), *Cleome viscosa* (Jakhiya), and *Nigella sativa* (Kalongi) that support the wisdom of ancestors throughout the ages.

1. Introduction

Phytomedicine or herbal medicine are plant derived substances which are utilized for therapeutic purposes and have great power and abundance (Sharma *et al.*, 2017). Among these, spices and herbs have historical importance in enhancing the flavour, colour and aroma of food along with boosting immunity and providing numerous health benefits (Grivetti, 2017). The terms spices and herbs are mostly used interchangeably, but can be prominently distinguished on the basis of part and origin of the plants used as well as ways of processing. Herbs are usually small green leaves and stems of herbaceous (non-woody) plants which grow on moderate climate whereas spices are derived from barks, buds, flower, fruits, rhizomes, roots, seeds, stamens and stems that grow in a warm and (sub) tropical climate (Sundar Raj *et al.*, 2014). Herbs are found fresh or dried, chopped or whole more subtle than spices that are made from dried and crushed portions rich in essential oils (Hogeback, 2022). The International Standards Organization Geneva has listed 109 spice and herb species which are useful as ingredients in food. There is different basis of spices classification: conventional, flavour based and parts of the plants used (Chhetri *et al.*, 2018). Rising applications are increasing their popularity progressively prompting intensive studies for natural therapies.

In the current worldwide COVID-19 pandemic scenario, there has been a lot of interest in strengthening immune system and taking precautions. Use of herbs and spices as home remedies may play a significant role to get away from viral infections. Thus, spices can

build a first line of defence against deadly virus (Singh *et al.*, 2021). Many common spices are known for their antiviral properties; for example, black paper, cinnamon, clove, ginger, tulsi and turmeric (Goothy *et al.*, 2020; Sharma *et al.*, 2017; Shrivastava, 2020; Srivastva *et al.*, 2020). Ministry of AYUSH, India have advised their use for selfcare during COVID-19. In this article, some of the recent scientific findings on *Alkanna tinctoria* (Ratanjot), *Cleome viscosa* (Jakhiya) and *Nigella sativa* (Kalongi) have been reviewed. These are uncommon spices in India, but actually can offer plethora of health benefits along with adding flavour to dishes. They can be utilized for building up the body's natural immunity in this global health emergency.

1.1 *Alkanna tinctoria* (L.) Tausch (Ratanjot)

Alkanna tinctoria L. Tausch belongs to family Boraginaceae (Gerardi *et al.*, 1998). It is a perennial herb which grows wild in many countries predominantly in arid maritime areas of Southern Europe, Northern Africa and Southwestern Asia including northern hills of India (Strid, 2016; Abdel-Gelil *et al.*, 2019). The origin of name *A. tinctoria* is from Spanish word *alcana* and Arabic *al-hena*, but it is widely known as dyers alkanet, languedoc or Spanish bugloss, orchanet. It has a bright blue flower and a dark red root of blackish appearance which accumulate a red colouring pigment, alkanin. It has been known since antiquity for its preventive and curative remedy for abscesses and inflammations due to the presence of alkanin in its roots (Kheiri *et al.*, 2017). It has been used as a cloth dye and to give colour to tinctures, varnishes, vegetable oils, wines, *etc.* It is also used today as food colouring (SabihOzer *et al.*, 2010; Elsharkawy *et al.*, 2013). Dried root of *A. tinctoria* is traditionally known as Ratanjot in India and are used to add flavour and natural colour to Indian food too. Its oil is popularly used as hair oil.

A large number of phytochemical compounds contained in *A. tinctoria* are associated with beneficial effects. It comprises of

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high amount of active pharmaceutical ingredients alkannin and shikonin (A/S) which are enantiomeric naphthoquinone. A/S are incredible source of antiaging, anti-inflammatory, antimicrobial, antioxidant, antitumoral and wound healing properties (Papageorgiou *et al.*, 2008; Rat *et al.*, 2021; Tung *et al.*, 2013). Therefore, it was chosen for the production of A/S for medical applications and strong wound healing medicines approved by the National Organization for Medicine in Greece. Nowadays, *Alkanna tinctoria* root extract based wound healing ointments such as helixderm and histoplastin red include A/S and related derivatives as active components (Papageorgiou *et al.*, 1999; Arampatzis *et al.*, 2019).

Sengul *et al.* (2009) screened crude extracts from aerial parts of some medicinal plants including *A. tinctoria* for their antimicrobial and antioxidant activities by using disc diffusion and α -carotene bleaching assay. The methanol extract of *A. tinctoria* showed antimicrobial activity against nine out of 32 food borne microorganisms with highest inhibition zone against *Alcaligenes faecalis* and observed antioxidant capacity was 79.80 per cent. Their results provided evidence that *A. tinctoria* might be a potential source of potent, safe and natural antioxidant and antimicrobial agents for developing new therapeutic drugs. Also, in earlier studies genus alkanna was reported as antioxidant rich (Assimopoulou *et al.* 2004). Zannou and Koca (2020) evaluated the antioxidant properties of alkanet root in hydrophilic natural deep eutectic solvents sodium acetate: lactic acid and sodium acetate: formic acid revealing more extractability and stability of phytochemicals and bioactive compounds in these solvents.

Khan *et al.* (2015) carried out an investigation to evaluate the potential of anti-multidrug resistant activity of *A. tinctoria* leaves extract against human pathogenic bacteria by well diffusion method. They also performed qualitative phytochemical screening of different extracts. The result of inhibitory zone demonstrated considerable antibacterial activity of aqueous and ethanol leave extracts of *A. tinctoria* against four multidrug resistant isolates which include *Acinetobacter baumannii*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Staphylococcus aureus*. These extracts also showed good solubility of phytochemicals especially alkaloids, flavonoids and carbohydrates exhibiting potential antibacterial activity as compared to broad spectrum antibiotic Imipenem. Their findings suggested the future therapeutic use of *A. tinctoria* leaves to treat infectious diseases caused by resistant bacteria. In another study done by Jaloob (2017), hot water extracts (300 mg/ml) of *A. tinctoria* roots showed excellent antibacterial activity against bacteria isolated from patients with burn infections, suggesting it as a raw material for the manufacture of ointment for treatment of burn infections.

1.2 *Cleome viscosa* L. (Jakhiya)

Cleome viscosa L. is an invasive species of family Cleomaceae (Gupta and Rao, 2012). It is considered native in Australia and widely distributed in warm and humid regions across America, Africa and Asia including Uttarakhand and Terai regions of India and Nepal (Akbari-Gelvardi *et al.*, 2021; Singh *et al.*, 2015). In some regions of northern India, the dried seeds of *C. viscosa* (Jakhiya) are used for tempering many vegetables and curries. It is considered to have many useful properties for treatment of variety of ailments as documented in Ayurveda and Unani system of medicine and ethnobotanical surveys (Mali, 2010). It is also documented to remove "Kapha" (phlegm) and to treat diarrhea, fever and ulcers

(Anonymous, 2001). Traditionally, the whole plant and its parts (leaves, seeds and roots) were well known for its medicinal importance among tribes for cure of different infections as they possess different antimicrobial activities (Upadhyay *et al.*, 2008). Thus, it has been explored by various researchers to justify its utility to cure numerous diseases.

C. viscosa is found safe as wild edible plant for humans and also have nutritive value (Upadhyay, 2015). Also, various pharmacological activities have been reported due to variety of phytoconstituents and other biologically active chemicals it contains such as cleomiscosin A, cleomiscosin B, coumarinolignoids etc. (Upadhyay, 2015; Singh *et al.*, 2015). In several studies, it was found effective in treatment of blood diseases, convulsions, diarrhea, fevers due to indigestion, helminthic infections, leprosy, malarial fevers and skin diseases (Maikhuri *et al.*, 2000; Mali *et al.*, 2007).

Williams *et al.* (2003) evaluated leaves and stem extracts of *C. viscosa* with hexane for various biological activities such as antibacterial, antifungal, contact insecticidal and nematocidal. According to the thin layer chromatography autobiographic assay, a 14-member ring cembranoid diterpene was isolated and found to be a potent antibacterial agent against *Bacillus subtilis* (gram-positive) and *Pseudomonas fluorescens* (gram-negative). It demonstrated a pyrethroid type of contact insecticidal activity on adult *Cylas formicarius elegantulus* summer and had a high nematocidal activity with abbot's value of 72.69% on the plant parasitic nematode, *Meloidogyne incognita* Chitwood. It did not inhibit the growth of fungus, *Cladosporium cucumerum*. Jana and Biswas (2011) isolated and purified lactam nanoic acid from the root exudates of *C. viscosa* and tested its aqueous solution on different infectious bacteria and fungi, suggesting important role of *C. viscosa* as a source of bacteriostatic agent and in ecological network.

Gupta *et al.* (2011) revealed that leaves of *C. viscosa* have high phenolic (66.38 ± 0.82 mg/g) and flavonoid content (0.54 ± 0.04 mg/g), inhibition of \hat{A} carotene bleaching (antioxidant activity: 77.30%), reducing power and free radical scavenging activity, correlating relationship of these secondary metabolites to possible biological activities and evaluating *C. viscosa* as a potential source of natural bioactive chemicals. Another study done by Yarrappagaari *et al.* (2022) showed the firm antihyperglycemic impact of methanol extract of whole plant to inhibit key carbohydrate hydrolyzing enzymes (α -glucosidase and α -amylase), suggesting it as a significant system in the administration of diabetes. Besides this, they additionally assessed non-enzymatic glycosylation of Hb and glucose uptake by yeast cell method.

1.3 *Nigella sativa* L. (Kalongi)

Nigella sativa L. belongs to family Ranunculaceae (Lal and Meena, 2018). It is a small annual flowering plant which originated in Middle East, South and South West Asia (Zohari *et al.*, 2012). In India, it is grown in Jammu and Kashmir, Himachal Pradesh, Punjab, Uttar Pradesh, Rajasthan, Madhya Pradesh, Bihar, Assam, West Bengal and Tamil Nadu (Lal *et al.*, 2020). The dried seeds of *N. sativa* (Kalongi) are used as a spice in many cuisines and its oil which is 32 to 40% of the total composition of seeds is utilized by cosmetic industries (Eid *et al.*, 2017). Its excessive therapeutic properties are revealed in various religious and old literature dated more than 2000 years back, it was usually applied in ancient Unani remedy in

countries of Middle East and Asia (Sharma *et al.*, 2005; Goreja, 2003). Due to miraculous power of healing and a rich historical and religious background, Kalongi is also known as seed of blessing (Srivastava, 2014). Thus, extensive studies have been carried out for exploring its pharmacological actions and therapeutic uses.

N. sativa have significant positive therapeutic effects on humans and animals against many ailments (Assi *et al.*, 2016). Most of these effects are due to active quinine constituents, of which thymoquinone is mainly abundant and has beneficial properties (Tavakkoli *et al.*, 2017). Thus, these seeds are utilized as analgesics, anticancer, anti-diarrheal, antihypertensive, anti-inflammatory, antimicrobial, appetite stimulant, diuretics, immunomodulator, liver tonics and skin diseases (Lal *et al.*, 2020; Thakur *et al.*, 2021). *N. sativa* is also reported effective against lethal virus infections like avian influenza (H9N2), Broad bean mosaic virus, chistosoma mansonii infection, hepatitis C virus, human immunodeficiency virus, PPR virus, papaya ring spot virus and zucchini yellow mosaic virus (Shamim Molla *et al.*, 2019; Salem and Hossain, 2000).

Salem (2005) reviewed immunomodulatory and therapeutic properties for the crude oil of *N. sativa* seeds and its active ingredients particularly thymoquinone, concluding that the immunotherapeutic efficacy of ingestion or administration of the whole seed, oil or its purified constituents should be measured by the nature of disease. Sayeed *et al.* (2013) demonstrated the beneficial effects of *N. sativa* seeds on memory, attention and cognition in forty healthy human volunteers using neuropsychological tests along with its safety profile during the nine-week study period. Biochemical assay of kidney, liver and heart were determined which do not show any statistically significant changes. They recommended extensive investigations of *N. sativa* on patients with Alzheimers disease and for novel drug discovery for treating cognitive disorder. Koshak *et al.* (2017) reviewed the medicinal benefits of *N. sativa* in bronchial asthma by searching various medical databases and highlighted future research priorities utilizing well-characterize chemical preparations of *N. sativa* for well-designed large clinical studies.

Umar *et al.* (2016) determined the possible effects of *N. sativa* on immune response and pathogenesis of H9N2 avian influenza virus in 130 non-vaccinated mixed-sex turkey poult. They divided turkeys into five experimental groups. Group A had non-infected and a non-treated negative control, infected and non-treated positive controls were in group B and group C, D and E contain infected and treated turkeys. They found significantly higher antibody titre against H9N2 AIV in turkeys fed 6 per cent *N. sativa* seeds powder showing its immunomodulatory nature and increased cytokine gene expression lead to suppressed pathogenesis of H9N2 viruses. In a review article by Khazdair *et al.* (2021), preliminary data of molecular docking, animal and clinical studies showed that *N. sativa* and thymoquinone reduced the level of proinflammatory mediators including interleukins 2, 4, 6 and 12, while enhancing interferon α , serum levels of immunoglobulins IgG1 and IgG2 a and improved pulmonary function tests in restrictive respiratory disorders. It suggested the randomized clinical trials for the efficacy of *N. sativa* and thymoquinone on infected patients with COVID-19 as these might have beneficial effects on the treatment or control of COVID-19.

2. Conclusion

Using herbs and spices in diet is a great way to maintain healthy life. *Alkanna tinctoria* (Ratanjot), *Cleome viscosa* (Jakhiya) and *Nigella sativa* (Kalongi) are rare spices which have not been explored much as compared to others. These were an integral part of ancient system of medicines, but as a result of globalization and modernization, there have been a nutrition transition resulting a decrease in their utilization. There are wide range of bioactives and nutrients in them, which may contribute not only as natural therapies for many diseases but also ramp up the immunity in case of COVID-19 type diseases.

Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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