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REVIEW PAPER

INDIAN SPICES BOOST THE IMMUNE SYSTEM AGAINST COVID-19

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Abstract
Since 12th December 2019, the epidemic outbreak of an unknown acute respiratory tract infection has emerged in Wuhan City, China. The World Health Organization (WHO) discovered that this outbreak was caused by the 2019 novel coronavirus (2019-nCoV) or the extreme acute respiratory coronavirus 2 syndrome (SARS-CoV-2). No vaccine or no specific anti-viral treatment against COVID-19 has been made available so far. Therefore, COVID-19 can be prevented by enhancing the body's immune system and fighting off the symptoms. Nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) is one of the essential transcription factors in humans which are responsible for the regulation of immune cell, synthesis of pro-inflammatory cytokines and gene expression of inflammatory molecules and reactive oxygen species (ROS). Phytochemicals derived from Indian spices (turmeric, garlic, ginger, etc.) can modulate the gene expression in the NF-κB pathway. In the midst of pandemic COVID-19, adding spices to food (eg. 'Rasam') can boost up the body's immune system. Indian spices are emerging as potential agents for the prevention of COVID-19.

Keywords: SARS-CoV-2, COVID-19, NF-κB, Indian spices, 'Rasam'

Introduction

The novel 2019 coronavirus (2019-nCoV) or the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a major threat to public health. It has been spreading rapidly from Huanan South China Seafood Market at Wuhan City, Hubei Province, China to other countries such as Thailand, South Korea, Japan, Taiwan, Singapore, Italy, Iran, Canada, France, Vietnam and the United States of America (USA) since 12th December 2019 (Guo *et al.*, 2020). The Government of China reported to World Health Organization (WHO) about the cluster cases of unknown pneumonia in Wuhan City on 31st December 2019 (World Health Organization, 2020a). The Chinese

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scientists took the sample from a patient and analysed the genome sequence of the virus on 7th January 2020. They shared the full genetic sequence of SARS-CoV-2 publicly on 12th January 2020 (World Health Organization, 2020a). The World Health Organization (WHO) named the SARS-CoV-2 infectious disease as coronavirus disease 2019 (COVID-19) on 11th February 2020 (World Health Organization, 2020a). They announced COVID-19 as a pandemic outbreak on 12th March 2020. It is a highly pathogenic virus. Till 6th October 2020, about 214 countries and territories around the world and two international conveyances had been affected by COVID-19 (World Health organization, 2020a). As of 6th October 2020, a total of 36,041,783 coronavirus cases; 1,054,604 death cases and 27,145,526 recovered cases have been reported throughout the world (Coronavirus outbreak, 2020). In the United States of America (USA), more than 7 million (7,722,746) people were affected by COVID-19 (Coronavirus outbreak, 2020). Worldwide, the highest number of death cases (215,822) has been confirmed in the USA (Coronavirus outbreak, 2020). The number of new cases is growing exponentially in the USA, India, Brazil, Russia, Colombia, Spain, Peru, Argentia and Mexico.

SARS-COV-2

Morphology and Genome Characterization

Coronaviruses are classified into four genera, which are alpha (α), beta (β), gamma (ɤ) and delta (Δ) coronavirus. There are six possible human coronaviruses (α-HCoV-NL63, α-HCoV-229E, β -HCoV-OC43, β -HCoV-HKU1, β -SARS-CoV, and β -MERS-CoV. β -SARS-CoV and β -MERS-CoV) cause severe respiratory tract infections (Lim *et al*., 2016). The other four human coronaviruses lead to mild respiratory symptoms like a common cold due to their low pathogenicity. β -SARS-CoV and β -MERS-CoV share some common viral structural protein features, such as spike glycoprotein (S), envelope (E), membrane (M) and nucleocapsid (N) (Lim *et al*., 2016).

The SARS-CoV-2 β-coronavirus belongs to the Coronaviridae family, Coronavirinae suborder, which is classified under the Nidovirales order. It is an enveloped, non-segmented positive-sense and single-stranded RNA virus (Richman *et al*., 2016). It contains a large RNA genome of about 30kb. The viral particle (virion) is spherical, 60-140 nm in diameter, with spikes of about 9-12 nm. The mRNA transcript comprises a 5’ terminal cap structure and a 3’ poly A-tail. SARS-CoV-2 consists of a mRNA transcript wrapped in a helical symmetrical nucleocapsid which is surrounded by an envelope comprising a 150 kDa surface/spike glycoprotein, a 25-30 kDa membrane protein and an 8-12 kDa envelope small membrane protein pentamer. The rep gene (viral replicase gene) encodes the first two open reading frames (orf1a and orf1b). Orf1a and Orf1b are polyproteins involved in the co-translation proteolysis process. It consists of two-third of the genome at the 5’ end. The accessory proteins (Orf3a, Orf6, Orf7a, Orf8 and Orf10) contribute to pathogenesis. Table 1 describes the genome characterization of SARS-CoV-2 (Lim *et al*., 2016; Fehr and Perlman, 2015).

Table 1. The genome characterization of SARS-CoV-2.

	SARS-CoV-2
Length of DNA nucleotides	29,903
Open reading frame (orf)	Orf1a, Orf1b, Orf3a, Orf6, Orf7a, Orf8, Orf10
Structural protein	4 (S, E, M, N)
Spike protein (S)	21562-25383
Envelope protein (E)	26244-26471
Matrix protein (M)	26522-27190
Nucleocapsid protein (N)	28273-29532
Accessory proteins	5 (Orf3a, Orf6, Orf7a, Orf8, Orf10)
A characteristic gene order	5'- replicase Orf1a, Orf 1b, spike, Orf3a, envelope, membrane, Orf6, Orf7a, Orf8, nucleocapsid, Orf10-3' with short untranslated regions (UTRs) at both termini

The spike protein is actively involved in binding between the host cell receptor and the virion. It allows the viral particles to enter the host cells. It is the main therapeutic target for drug designing. The membrane protein maintains the shape of the virion. It also enhances the curvature of the membrane and helps in binding to the nucleocapsid. The envelope protein actively participates in the assembly and release of virions. The ion-channel activity in the SARS-CoV-2 E protein is vital for pathogenesis. The nucleocapsid protein is essential for RNA synthesis and packaging the genome into virions (Fehr and Perlman, 2015; Ou *et al*., 2020).

A respiratory sample from a COVID-19 patient was analysed using the next sequencing tool. The Chinese scientists found that SARS-CoV-2 is a novel member of the beta coronavirus family that infect humans using phylogenetic tree analysis. It is a deadly virus. It has a genetic similarity with SARS-CoV and MERS-CoV. The SARS-CoV-2 shares 79% sequence similarity with SAR-CoV, while 50% is identical to MERS-SARS (Singhal, 2020; Moreno *et al*., 2017; Xu *et al*., 2020; Song *et al*., 2019). However, it is still different from coronaviruses that cause SARS-CoV and MERS-CoV in humans.

In 2013, the scientists identified that the genome sequence of SARS-CoV-2 was about 96.3% genetically homologous to a Yunnan *Rhinolophus affinis* (bat) coronavirus RaTG13. SARS-CoV-2 is more closely related to bat SARS-like-virus-CoVZC45 (MG772933.1) (more than 85% homology identity) and bat-SL-CoVZXC21 (MG772934) which has 89% genome similarity. Bat-SL-CoVZXC21 was obtained from the Southwest of China (Moreno *et al*., 2017; Xu *et al*., 2020; Song *et al*., 2019). Bats are the natural reservoirs for human pathogenic diseases like SARS, MERS and COVID-19. Researchers from the South China Agriculture University found that pangolins may be one of the intermediate sources for SARS-CoV-2. They isolated the virus from the pangolin, analysed and reported that the virus was 99% identical to the human SARS-CoV-2 strain using metagenomic RNA sequencing (Xu *et al*., 2020).

Pathogenesis

The virus infection is initiated by the attachment of SARS-CoV-2 virus particles to the Human Angiotensin-converting enzyme 2 (hACE2) through the spike protein (Ceccarelli *et al*., 2020). hACE2 is an entry host receptor for SARS-CoV and SARS-CoV-2. It is a zinc-binding carboxypeptidase transmembrane glycoprotein. It mostly targets the lungs and host immune system.

The spike protein consists of two domains, which are S1 and S2. The binding between the S1 domain and its linked receptor enhances the S protein's conformational change. After that, it triggers the interaction between the viral particle and the host cell membrane via the S2 domain. Finally, the virus enters the host cell through the endosomal pathway. The cysteine protease cathepsin L1 (CTSL1) can also help in the membrane fusion between the virion and the host cell at the low pH in the cellular environment. This host protease promotes the endosomal virus entry into the cell membrane during the SARS-CoV-2 infection via proteolytic cleavages which activate the S protein. The transmembrane protease serine 2 (TMPRSS2) and trypsin-like protease (TMPRSS11D) are human airway proteases. They are located on the host cell surface membrane which carries out the cleavage of the S1/S2 domain, to trigger the S protein for the entry of the virus into the host cells via the non-endosomal pathway (Lim *et al*., 2016; Fehr and Rehman, 2015; Ou *et al*., 2020).

Then, the viral RNA is released into the cytoplasm. Orf 1a and Orf 1b are translated via the ribosomal frameshifting mechanism to generate polypeptide 1a (pp1a) and polypeptide 1b (pp1b). The polypeptides are cleaved by the host and the viral proteases to produce non-structural proteins (NSPs). Afterwards, they are assembled to form the RNA replicase-transcriptase complex. This complex mainly participates in the replication of the virus. The sub-genomic RNAs are transcribed and translated to build the structural and accessory proteins. The viral progeny particles are packaged and assembled from genomic RNA containing nucleocapsid and other structural proteins, such as the S, E and M proteins in the cytoplasm. Then, they bud into the lumen of the endoplasmic reticulum-Golgi intermediate compartment (ERGIC) and come out as a smooth-wall vesicle on the plasma membrane through exocytosis. Lastly, the matured virions are released from the infected cell and spread to new host cells (Lim *et al*., 2016; Fehr and Rehman, 2015; Ou *et al*., 2020). The viral infectious cycle will begin again

Transmission and clinical manifestations

SARS-CoV-2 is a highly pathogenic virus. It spreads easily from human to human. It is transmitted via respiratory secretions such as fluid droplets when an infected person coughs or sneezes (Singhal, 2020; Adhikari *et al*., 2020; Yang and Wang, 2020). In the early stage, it causes fever, dry cough and tiredness; Later on there are subsequent onsets of respiratory clinical manifestations such as shortness of breath and lung infection. In severe cases, it causes life-threatening pneumonia, bronchiolitis and organ failure (eg. kidney, heart and liver) (Huang *et al*., 2020). Centres for Disease Control and Prevention have found new signs of COVID-19, such as aches and pains, nasal congestion, headache, conjunctivitis, sore throat, diarrhoea, loss of taste or scent, skin rash or finger or toe discoloration (World Health Organization, 2020b). Some patients may get these less common symptoms. The SARS-CoV-2 infection might leads to the disruption of the immune system by decreasing the innate immune responses with delayed activation of pro-inflammatory signals from the chemokines and cytokines.

Elderly people, pregnant ladies, children, immune-compromised patients (*e.g*. human immunodeficiency virus (HIV) and cancer patients) and people with chronic diseases like hypertension, diabetes, lung, kidney and heart problems are highly susceptible to the SARS-CoV-2 infection.

Preventive measures

As the growth of positive COVID-19 cases in the world has been increasing gradually, preventive measures against COVID-19 are essential. Some of the most important preventive measures are: avoid handshaking; wear a mask and gloves; wash hands regularly with soap and water; use hand sanitizer frequently especially before and after touching the lock key, keyboard, mouse, keys, credit cards, lift buttons, laptop and hand phone; avoid using a cloth mask because it is not as effective as the surgical mask or N95 respirators; avoid going to crowded place such as restaurants, markets, parks, shopping malls, cinema theatres, etc.; thoroughly cook meat and eggs; avoid attending mass events or gatherings like weddings, conferences, etc.; cover the mouth and nose when coughing or sneezing; avoid contact with anyone who coughs or sneezes; maintain social distancing (about 1 metre); stay at home when not feeling well; stop hunting, selling and eating wild animals such as bats, snakes, pangolins, etc.; avoid travelling to COVID-19 affected areas and countries; undergo health screening for COVID-19 after returning home from overseas; self-quarantine by staying at home for 14 days after getting back home from abroad, or developing fever, dry cough, shortness of breath, chills, frequent shaking with chills, muscle pain, headache, sore throat and loss of taste or odour; avoid spreading false information about COVID-19 through social media such as Facebook, Instagram, Twitter, etc; throw the used masks and gloves into the dustbin. Some countries are still enforcing the 'Movement Control Order' such as Singapore, Malaysia, India, etc. to control the spread of the virus infection. Some countries have announced that it will be mandatory for people to wear face masks in public places such as markets, restaurants, shopping malls, religious places (temples, churches and mosques), and public transportation like on the bus, train and taxi. People failing to observe this act are fined. The immigration department of some countries banned nationals from countries which had a high numbers of COVID-19 cases such as the USA, India, Brazil, Russia, Colombia, Peru, Spain, Argentina, Mexico, South Africa, etc., from entering their countries. Worldwide, digital technologies are used to raise the awareness of the public health response to fight against COVID-19, such as monitoring and tracing contact, positive case identification, etc. Currently, at least 29 countries are using digital technology (mobile data) to trace contacts. For example, South Korea implemented a contact tracing application successfully. This application allows nationals to record their locations. Besides, it draws on data from credit card and telecommunication companies. In Singapore, they launched the 'TraceTogether' application on 20th March 2020 to curb the spread of

COVID-19 cases. In Malaysia, three major mobile applications such as Gerak Malaysia, MySejahtera and MyTrace have already been launched to the purpose of contact tracing.

The ability of Indian spices to enhance the immune system against COVID-19

Scientists from different countries are still working on finding the vaccine or effective medicine for COVID-19. However, no vaccine or no specific anti-viral treatment against COVID-19 has been available so far. Thus, the SARS-CoV-2 infection can be prevented by blocking inflammation and enhancing the body's immune system. The inhibition of inflammatory mediators on the transcriptional level can block the inflammation. NF-κB is a major transcription factor which regulates several vital physiological processes such as inflammation, oxidative stress, immune responses, certain viral gene expression, cell growth and apoptosis (Gilmore and Herscovitch, 2006). It is actively involved in the development of adaptive and innate immunity (Golan-Goldhirsh and Gopas, 2014). Therefore, NF-κB could be a potential target for inflammation-based viral therapy.

Plant compounds are able to target the multiple steps in the NF-κB pathway. They hinder the phosphorylation or the ubiquitination of signalling molecules. Therefore, they inhibit the degradation of the NF-κB inhibitor (IκB). They interfere with the NF-κB translocation from the cytoplasm to the nucleus, and modify the expression of the pro-inflammatory transcription genes such as cytokines, lipoxygenase, nitric oxide synthases (NOS) and cyclooxygenase (COX). They also block the interaction between the NF-κB and the target DNA. The plant compound binds to the target DNA and shuts off the transcriptional activity of NF-κB (Seo *et al*., 2018).

Since 5000 B.C., spices have been extensively used for medical treatment, or as colouring agents, flavouring agents and preservatives in cooking (Kunnumakkara *et al*., 2018). Indian food cannot possibly be imagined without spices. Moreover, numerous studies have reported that phytochemicals derived from spices (*e.g.* cardamom, fennel seed, chilli, clove, cassia bark, black pepper, long pepper, cumin, coriander, nutmeg, bay leaf, star anise, onion, mustard, asafoetida, mint, fenugreek, turmeric, garlic, ginger, etc.) prevent and cure different types of chronic diseases via targeting inflammatory pathways. Indian spices have been identified as a class of promising anti-inflammatory, anti-oxidative, anti-viral and immunomodulatory agents. Table 2 shows the Indian spices and their mode of action (Yahfoufi *et al*., 2018; Tzeng *et al*., 2015; Chojnacki *et al*., 2015; Thummuri *et al*., 2015; Gruenwald *et al*., 2010; Zhai *et al*., 2016; Iacobellis *et al*., 2005; Lee *et al*., 2009; Cianciulli *et al*., 2016; Tang *et al*., 2015; Bachiega *et al*., 2012; Schmitz *et al*., 2015).

Table 2. Indian spices and their mode of actions.

Spices	Scientific name	Family	Part of plant	Bioactive compound	Chemical formula	Agent	Mechanism
Cardamom	*Elettaria cardamomum*	Zingiberaceae	Seeds	1,8-Cineole	$C_{10}H_{18}O$	-Anti-inflammatory	Blocks the interaction between NF-κB and target DNA
Clove	*Syzygium aromaticm*	Myrtaceae	Flowers and buds	Eugenol	$C_{10}H_{12}O_2$	-Anti-inflammatory	Modify the inflammatory signalling molecules such as TNF-α, IL-1, IL-6, COX-2, PGE2, NF-κB
Cassia bark	*Cinnamomum zeylanicum*	Lauraceae	Bark	Cinnamaldehyde	C_9H_8O	-Anti-inflammatory -Immunomodulatory	Inhibits the activation of NF-κB
Black pepper	*Piper nigerum*	Piperaceae	Fruit	Piperine	$C_{17}H_{19}NO_3$	-Anti-inflammatory -Immunomodulatory	Inhibits extracellular signal-regulated kinase 1 or 2, NF-κB, IκB-kinase α/β, cAMP response element binding and the expression of caspase-3 and Ki-67
Cumin	*Nigella sativa*	Ranunculaceae	Seeds	Thymoquinone	$C_{10}H_{12}O_2$	-Anti-inflammatory -Anti-oxidant	Downregulates NF-κB
Coriander	*Corriandrum sativum*	Apiaceae	Leaves and seeds	Linalool	$C_{10}H_{18}O$	-Anti-inflammatory	Inhibits the activation of NF-κB
Nutmeg	*Myristica fragrans*	Myristicaceae	Seeds	Eugenol	$C_{10}H_{12}O_2$	-Anti-inflammatory	Modify the inflammatory signalling molecules such as TNF-α, IL-1, IL-6, COX-2, PGE2, NF-κB
Mustard	*Brassica hirta*	Brassicaceae	Seeds	Sulforaphane	$C_6H_{11}NOS_2$	-Anti-inflammatory	Hinders pro-inflammatory signalling genes such as NOS, COX, lipoxygenase and cytokines
Fenugreek	*Trigonella foenum-graecum*	Fabaceae	Seeds	Diosgenin	$C_{27}H_{42}O_3$	-Anti-oxidant -Anti-inflammatory -Anti-viral	Suppresses inflammatory factors such as NOS-2 and COX-2
Turmeric	*Curcuma longa*	Zingiberaceae	Rhizome	Curcumin	$C_{21}H_{20}O_6$	-Anti-oxidant -Anti-inflammatory -Anti-viral	Hinders phosphorylation of IκBα and p65; acetylation and translocation of NF-κB to the nucleus

Spices	Scientific name	Family	Part of plant	Bioactive compound	Chemical formula	Agent	Mechanism
Fennel seed	*Foeniculum vulgare*	Apiaceae	Seeds	Anethole	$C_{10}H_{12}O$	-Anti-inflammatory	Reduces the expression of NF-κB
Chilli	*Capsicum annuum*	Solanaceae	Fruit	Capsaicin	$C_{18}H_{27}NO_3$	-Anti-inflammatory	Suppresses inflammatory cytokines such as IL-1β, IL-6, and TNF-α
Ginger	*Zingiber officinale*	Zingiberaceae	Rhizome	6-Gingerol	$C_{17}H_{26}O_4$	-Anti-inflammatory -Anti-oxidant	Downregulates TNF-α, and IL-6, and NF-κB
Garlic	*Allium sativum*	Amaryllidaceae	Bulb	Diallyl sulphide (DAS)	$C_6H_{10}S$	-Anti-inflammatory	Inhibits inflammatory factors such as ROS, NF-κB, 8-hydroxy-2′-deoxyguanosine, 8-iso-prostaglandin F2α; and increases the Nrf2 activation
Long pepper	*Piper longum*	Piperaceae	Fruit	Piperine	$C_{17}H_{19}NO_3$	-Anti-inflammatory -Anti-viral	Inhibits extracellular signal-regulated kinase 1 or 2, NF-κB, IκB-kinase α/β, cAMP response element binding and the expression of caspase-3 and Ki-67
Bay leaf	*Laurus nobilis*	Lauraceae	Leaf	1,8-Cineole	$C_{10}H_{18}O$	-Anti-inflammatory	Blocks the interaction between NF-κB and target DNA
Star anise	*Pimpinella anisum*	Apiaceae	Seed pod	Eugenol	$C_{10}H_{12}O$	-Anti-inflammatory	Reduces the expression of NF-κB
Onion	*Allium cepa*	Amaryllidaceae	Bulb	Quercetin	$C_{15}H_{10}O_7$	-Anti-oxidant -Anti-inflammatory	Downregulates NF-κB
Asafoetida	*Ferula asafetida*	Umbelliferae	Rhizome	Diallyl-disulphide (DAS)	$C_6H_{10}S$	-Anti-inflammatory	Inhibits inflammatory factors such as ROS, NF-κB, 8-hydroxy-2′-deoxyguanosine, 8-iso-prostaglandin F2α; and increases the Nrf2 activation
Mint	*Mentha spicata*	Lamiaceae	Leaf	Carvone	$C_{10}H_{14}O$	-Anti-oxidant -Anti-inflammatory	Downregulates NF-κB

Major components of Indian spices and their role in the inflammation pathway

1,8-Cineole

1,8-Cineole (Eucalyptol) is a natural organic compound derived from different types of plants, such as cardamom and bay leaf. It is a cyclic ether and monoterpene oxide. It has a significant pharmacological activity against respiratory ailments, such as anti-inflammatory and bronchodilatory conditions. It is used to treat a variety of respiratory and inflammatory disorders (Galan *et al*., 2020). Moreover, it has been proven that it downregulates the NF-κB expression in humans. Based on the study by Li *et al*. (2016), it was shown that 1,8-Cineole protects against infection with the influenza virus in mice by modulating pulmonary inflammatory signalling responses. 1,8-Cineol significantly reduced the expression of interleukin(IL)-4, IL-5, IL-10, and monocyte chemotactic protein-1 (MCP-1) in nasal irrigation fluids, and the expression of IL-1β, IL-6, tumour necrosis factor-alpha (TNF-α), and interferon gamma (IFN-γ) in the lung tissues of mice infected with influenza virus. Moreover, the study proved that 1,8-Cineol efficiently lowered the level of NF-κB p65, ICAM-1, and VCAM-1 in lung tissues. According to Müller *et al*. (2016), 1,8-Cineol increased the anti-viral transcription factor IRF3 expression in a human *ex vivo* model of rhinosinusitis. At the same time, it lowered the activity of the pro-inflammatory NF-κB in that model. Brown *et al.* (2017) reported that chronic obstructive pulmonary disease (COPD) patients who took 200 mg 1,8-cineole orally, three times per day for six months, showed a significant reduction in their symptoms like coughing, dyspnea and breathing issues.

Eugenol

Eugenol (allyl chain-substituted guaiacol) is the phenolic component derived from essential oil. Clove, cinnamon, nutmeg, basil, bay leaf and black pepper are well-known sources of eugenol. It inhibits the activity of the COX-2 and TNF-α in cells. It also suppresses the activation of NF-κB. Furthermore, it blocks the pro-inflammatory cytokine expression in macrophages. The inhibitory effect on the synthesis of prostaglandin and the chemotaxis of neutrophils/ macrophages actively participate in its anti-inflammatory mechanism mode. Tragoolpua and Jatisatienr (2007) found that eugenol could destroy the virions' envelopes and block viral replication at the early stage of the infectious cycle. The active phytocomponent, eugenol from the clove extracts (flower buds and essential oil) showed anti-viral activity against HSV-1 and HSV-2. Based on Lane *et al.* (2019), it was concluded that a low concentration of eugenol (EC50 of 1.3 μM) could kill the Ebola virus. Another study on the administration of eugenol at 5 and 10 mg kg^{-1} in lipopolysaccharide induced acute lung injury mice showed significant results for anti-inflammation activity (Huang *et al*., 2015). This was because eugenol suppressed the expression of the pro-inflammatory cytokines. Pramod *et al*. (2010) found that clove oil (200mg/kg) could prevent macrophages from producing cytokines in lung injured-mice. Furthermore, it was shown it acts as an anti-viral agent for feline calicivirus, tomato yellow leaf curl virus, human influenza A (HIA) virus and four airborne diseases.

Cinnamaldehyde

Cinnamaldehyde is a natural phenylpropanoid component of essential cinnamon oil. It has a variety of pharmacological uses, such as anti-inflammatory, anti-viral, anti-oxidant, anti-immunomodulatory, anti-bacterial, anti-cancer and anti-cholesterol. Li *et al*. (2017) carried out an experiment on the administration of cinnamaldehyde in mice infected with coxsackievirus B3 (CVB3). The results showed that the active component of cinnamon decreased the viral titre. It inhibited the viral replication in mice. It also downregulated the expression of nitric oxide (NO), NF-κB and pro-inflammatory cytokines in the CVB3 infected mice. Based on Zhang *et al*. (2018), cinnamaldehyde increased the level of IL-6, TNF-α, IFN-γ, and NO, while decreasing the expression of the IL-2, SOD and GSH in the lung of viral pneumonia infected mice. It reduced viral production and inflammation in lung damaged tissues. Another study concluded that cinnamaldehyde exerted anti-viral activity against HSV-2 (Toujani *et al*., 2018). The study proved that the lowest EC_{50} value (2.3 µg/ml) suppressed the viral particles' infectiousness in the human cell.

Piperine

Piperine is an amide alkaloid derived from the fruits of the black, white and long pepper extracts. It has been reported to have different types of biological and pharmaceutical therapeutic effects, such as anti-inflammatory, anti-viral, analgesic, anti-convulsant and anti-cancer. It is also used to treat gastrointestinal diseases, inflammatory disorders like asthma, Alzheimer's disease (AD), Parkinson's disease, arthritis, gastritis and endometritis. The anti-inflammatory properties of piperine suppress the inflammatory signalling expression in chronic disorders through NF-κB, MAPK, AP-1, COX-2, NOS-2, IL-1β, TNF-α, PGE2 STAT3. According to Rathee *et al.* (2018), the Aegle marmelos plant extract in combination with piperine shows promising results of hepatoprotective activity via the anti-oxidant and anti-inflammatory effects. Mair *et al*. (2016) showed that the piperine phytocomponent from the *Piper nigrum* fruit extract inhibited the CVB3 activity at IC_{50} of 10.6 µg/ml.

Thymoquinone

Thymoquinone is a monoterpene compound found in the seeds of black cumin. It possesses a variety of pharmaceutical activities, such as anti-oxidant, anti-inflammatory, anti-cancer, immunomodulatory, anti-viral and anti-bacterial. Umar *et al.* (2016) demonstrated that thymoquinone combined with curcumin exerts anti-viral activity against the avian H9N2 virus in turkeys. The combination therapy decreased the pro-inflammatory cytokine expression; and it simultaneously inhibited the pathogenic mechanism of the H9N2 virus. Another study (2013) reported that a hepatitis C virus (HCV) patient was given 450 mg of black cumin oil three times per day, for three months continuously (Barakat *et al*., 2013). The results showed that the black cumin reduced the viral titre and improved the oxidative stress in the patient.

Linalool

Linalool is a monoterpene isolated from the coriander leaf extract. It is also present in cinnamon, rosemary, basil, cardamom and thyme. Lee *et al.* (2018) administered linalool (5.2 mg/kg) in endotoxin-injected mice. The results showed that it promisingly decreased the expression levels of IL-1β, IL-18, TNF-α and IFN-γ in the infected mice. Forouzanfar *et al*. (2014) carried out an experiment on the anti-inflammatory effect of linalool in Wistar rat-induced paw edema. It repressed the secretion of the cytokine by activated T-cells. It also lowered the IL-2, TNF-α and IFN-γ expression in the infected rat.

Sulforaphane

Sulforaphane is the active anti-inflammatory compound of mustard leaf extract. It is an isothiocyanate (group of sulphur containing organic compounds). According to Furuya *et al*. (2016), it was reported that sulforaphane suppressed the human immunodeficiency virus (HIV) infection via the transcription of the regulator Nrf2 in macrophages. Sulforaphane blocked the infection before the formation of long terminal repeat (2-LTR) viral DNA circles in HIV infected cells. Yu *et al*. (2016) demonstrated that sulforaphane inhibited the expression of HCV protein and RNA in replicon cells with the minimum inhibitory concentration (IC_{50}) of 5.7 µm by degrading the phosphorylation of PI3K via Nrf2/HO-1 signalling pathway.

Diosgenin

Diosgenin is a steroidal sapogenin phytocompound isolated from fenugreek seed extract. It has been reported to play a vital pharmalogical role in a variety of diseases as an anti-viral, anti-oxidant, anti-inflammatory, anti-diabetic, or in hypercholesterolemia and gastrointestinal disorders. Wang *et al*. (2011) evaluated the effect of diosgenin against the anti-viral activity of HCV. They found that disogenin suppressed the replication of HCV at the lowest concentration (EC50) of 3.8 µM. Diosgenin decreased the expression of the viral mRNA and subsequently the viral replication via lowering the expression of STAT3. Kim *et al.* (2016) concluded that diosgenin significantly reduced phthalic anhydride (PA)-induced skin inflammation in mice by repressing the level of IL-4 and IL-6.

Curcumin

Curcumin is a natural polyphenol bioactive compound present in the turmeric plant. It has been shown to possess pharmalogical therapeutic effects, like anti-inflammatory, anti-oxidant, anti-viral, anti-bacterial and anti-fungal. Avasarala *et al*. (2013) performed an experiment on the anti-inflammatory effects of curcumin in reovirus induced-acute respiratory distress syndrome (ARDS) infected mice. The infected mice were treated with curcumin (50mg/kg) for five days. Curcumin significantly reduced the expression of pro-inflammatory cytokines such as IL-6, IL-10, IFNc, and MCP-1 via decreasing the phosphorylation of NF-κB p65. Moreover, curcumin blocked the reovirus pathogenesis in infected mice by lowering the expression of the TGFß Receptor II, which is important in the TGFß signalling pathway. According to Xu and Liu (2017), it was demonstrated that curcumin decreased the expression of pro-inflammatory cytokines in influenza A

(IA) virus infected-human macrophages and mice immune cells through the NF-κB signalling pathway. Curcumin triggered the expression of NF-κB1 and IκBα inhibitors. Finally, it impeded the translocation of p65 from the cytoplasm to the nucleus in order to prevent the viral replication of the IA.

Anethole

Anethole is a natural aromatic compound (phenlypropanoid) derived from essential oils. It is present in star anise and fennel seed. Wang *et al*. (2018) evaluated the anti-inflammatory effects of anethole in chronic constriction injury (CCI)-induced neuropathic pain in mice. They found that anethole suppressed the TNF-α, IL-6 and IL-1β expression in infected mice. At the same time, the expression of anti-inflammatory cytokine (IL-10) increased. Another study stated that anethole manifested anti-viral activity against HSV-1 via inhibited the viral production. It decreased the viral infectiousness by >99% (Marinov and Valcheva-Kuzmanova, 2015).

Capsaicin

Capsaicin is a phytocompound isolated from the chili peppers. Based on Zhang *et al*. (2019), capsaicin (1 mg/kg) was administered in concanavalin A (Con A)-induced hepatitis mice. The results showed a significantly reduced level of the IL-1β, IL-6, and TNF-α, while enhancing the expression of the liver X receptor α (LXRα) in the infected mice. Zheng *et al*. (2018) investigated the anti-inflammatory effects of capsaicin in lipopolysaccharide-stimulated BV2 microglial cells. They reported that capsaicin decreased the expression of the NO, TNF-α and IL-1β in cells. Furthermore, it promoted the IκBα expression while blocking the translocation of NF-κB p65 from the cytoplasm to the nucleus. It also inhibited the NOS and COX-2 activities in cells. It hindered the activation of NF-κB. Thus, it blocked the pro-inflammatory signalling responses in the infected cells.

6-Gingerol

6-Gingerol is a major bioactive component of the turmeric plant. It has been described as possessing anti-inflammatory, anti-viral, anti-bacterial, anti-diabetic, anti-oxidant and anti-cancer effects. El-Deeb *et al.* (2018) investigated 6-gingerol effects in HCV infected peripheral blood mononuclear cells. The result showed that 6-gingerol modulated the expression of TNF-α, IL-2 & IL-8 in the infected cells. It decreased the production of the pro-inflammatory cytokines in the cells. Another study demonstrated that 6-gingerol (100 μmol/L) may be administered to non-alcoholic steatohepatitis (NASH) infected mice (Tzeng *et al*., 2015). 6-gingerol lowered the expression of the MCP-1, TNF-α, IL-6 and NF-κB in infected mice.

Diallyl sulphide (DAS)

Diallyl trisulfide is an organosulphur compound isolated from garlic. It possesses a variety of pharmaceutical properties, like anti-viral, anti-inflammation, anti-bacterial, anti-cholesterol and anti-oxidant. It has been used to treat asthma, cancer, heart disease, osteoarthritis and acute or chronic liver injury. Hall *et al*. (2017) carried out an experiment on the anti-viral activity of DAS against the dengue virus (DENV). They treated the human cells infected with DENV-2 NGC (New Guinea

C) virus with four different concentrations (10, 50, 250, 1000 μM) of DAS compounds. The results showed that DAS suppressed the pro-inflammatory immune responses (TNF-α, IL-8 & IL-10). It blocked the viral pathogenesis by inhibiting the production of NO, oxidative injury and the expression of ROS. According to Li *et al*. (2019), CCL_4 induced mice were fed with three varying concentrations of DAS (100, 200, or 400 μmol kg^{-1}) to study the anti-inflammatory effects of DAS on liver injured mice. They concluded that DAS triggered the phosphorylation of IκBα and reduced the expression of NF-κB p65 in the cytoplasm. Therefore, it blocked the translocation of NF-κB p65 from the cytoplasm to the nucleus. Furthermore, it lowered the TNF-α expression in liver injured mice.

Quercetin

Quercetin is a polyphenol (flavonoid) derived from onion. It has pharmalogical properties such as anti-viral, anti-inflammatory, anti-microbial, anti-allergic, anti-asthmatic and anti-oxidant. Based on Ganesan *et al*. (2012), it was reported that quercetin suppressed the phosphorylation of Akt, and the pro-inflammatory cytokines (IL-8) and interferon (IFN) signalling responses in mice infected with the rhinovirus (RV). It also blocked viral endocytosis, viral replication, the formation of RV capsid protein, RV-induced eIF4GI cleavage abrogation, and upregulated eIF2α phosphorylation. It inhibited the infectious and pathogenetic mechanism of RV and enhanced the lung function in the infected mice. According to Yu *et al*. (2007), it was shown that quercetin inhibited HIV-1 reverse transcriptase activity at the low concentration (IC_{50}) of 60 μM. Therefore, it blocked the HIV-1 virus replication.

Carvone

Carvone is a bioactive compound isolated from Peppermint oil (essential oil). Its applications as anti-viral, anti-bacterial, anti-inflammatory, anti-cancer and anti-oxidant are well known, due to its pharmalogical and biological properties. Based on Jusoh *et al*. (2018), carvone could be a potential neuraminidase (NA) inhibitor. Carvone bound successfully with the neuraminidase active site of the influenza virus at the lowest binding energy of 8.30 kcal/mol measured using a computational biology tool. It blocks the NA function via preventing the viral endocytosis action.

Conclusions

During the COVID-19 pandemic outbreak, the consumption of good food is very important to maintain a healthy life. Fresh vegetables (e.g. carrots, spinach, broccoli, cauliflower, beetroot, etc.) and fruits (guava, apple, lemon, orange, etc.) always protect us against diseases. A strong immune system acts as a barrier against any pathogen entering our body. There is no specific food that can cure COVID-19. However, adding spices to food can boost up the immune system. 'Rasam' is a South Indian soup that is made with tomatoes, tamarind, along with spices such as cumin, fennel seed, garlic, black pepper, chilli, turmeric, coriander, mustard and curry leaves. This soup mainly consists of spices. It is also called herbal soup. It helps to fight off the COVID-19 symptoms and enhance the body's immune system. Rasam is normally served with plain rice. It can be the main dish or just a drink after the meal. All the South Indian restaurants serve rasam with plain rice. It helps in digestion, combating flu, cough and regulates an upset stomach. In conclusion, spices regulate immunity by interfering with the inflammatory factors such as COX, NOS, cytokines, lipoxygenase, growth factors (TNF-α, interleukins) in the NF-κB pathway. They may be viewed as promising anti-viral agents for the prevention of the COVID-19 disease.

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