

## Role of Curcumin in COVID-19

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### ABSTRACT

From ancient times herbs and spices have played a major role in lives of people from different parts of the world. Polyphenol, Curcumin is derived from a spice, Turmeric and has medicinal properties. It is used in the management of various disorders including inflammatory conditions, arthritis, hyperlipidemia, anxiety and metabolic syndrome. It plays a role in recovery from exercised induced inflammation and sore muscles in people who are physically active. These benefits are largely due to its antioxidant and anti-inflammatory effects. The bioavailability of curcumin is increased by 2000% if black pepper active component piperine is used. It is useful in viral infection including COVID-19. Recently, antiviral and antibacterial activity of curcumin was investigated, and it was shown to act against various important human pathogens like influenza virus, Hepatitis C virus, HIV, Staphylococcus and Pseudomonas.

### INTRODUCTION

Curcuma longa, turmeric is a rhizomatous herbaceous perennial plant of the ginger family. Curcumin, also called diferuloylmethane, constitutes the main natural polyphenol of curcuma longa (turmeric). It is traditionally used in Asian countries as a medical herb since it possesses antimicrobial, antimutagenic, anticancer, anti-inflammatory and antioxidant properties.<sup>1-5</sup> The polyphenol curcumin target multiple signaling molecules and benefits pain, metabolic syndrome, inflammatory conditions and management of degenerative eye conditions including benefit to the kidneys as shown in Figure 1.<sup>6</sup>

One of the major problems of ingesting curcumin alone is its poor bioavailability. Piperine, a product of black pepper is associated with an increase of 2000% in the bioavailability of curcumin.<sup>5,7</sup> Curries are made in India by addition of turmeric containing curcumin, in Thailand used in cosmetics, in China as a colorant, in Japan served in tea and in Korea served in drinks, in Malaysia as an antiseptic, in Pakistan as an anti-inflammatory agent and in

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USA in mustard sauce, cheese, butter and chips as a preservative and a colouring agent.<sup>8</sup>

The US Food and Drug Administration terms it as "Generally Recognized As Safe" (GRAS) and is approved by FDA. Clinical trials have shown good tolerability at doses between 400 and 800 mg per day.<sup>1,9</sup>

### Mechanism of Action

- 1. Antioxidant:** Curcumin improves systemic markers of oxidative stress and has anti-inflammatory properties. It is an efficient scavenger of peroxy radicals and serves as a chain breaking antioxidant.<sup>8-10</sup>
- 2. Anti-inflammatory:** The NF- $\kappa$ B activation is blocked by curcumin. It also suppresses inflammation through many different modalities.<sup>11,12</sup> Anti-viral properties against all viral strains including COVID-19 have been seen by researchers as shown in Table 1.<sup>6</sup>

3. **Arthritis:** Osteo-arthritis (OA) affects over 250 million people worldwide. Various studies have shown anti-arthritic effect of curcumin in OA and rheumatoid arthritis (RA).<sup>12,13</sup> Curcumin appears to be beneficial of several aspects of OA with a standardized curcumin dosage of 1000 mg per day has shown decrease in arthritic symptoms in 8 to 12 weeks.

**Metabolic Syndromes**

Metabolic syndromes include insulin resistance, hyperglycemia, hypertension, low high-density lipoprotein cholesterol, elevated triglyceride level and visceral obesity.<sup>14-17</sup> Curcumin has properties to improve insulin resistance, reduces fat accumulation and high

blood pressure, inflammation and oxidative stress.<sup>5,7,11</sup> In a double-blind trial, 36 obese adults were given 1-gram curcumin and 10 mg piperine or a placebo for 30 days.<sup>14</sup> It showed a significant reduction in serum triglyceride concentration.

**Healthy People**

In a study on muscle soreness after an intense physical workout in elite rugby players, 2-grams of curcumin and 20-grams of piperine offset the muscle pain.<sup>18</sup> It helps in sub-clinical anxiety and depression. Curcumin has no known side-effects. Numerous invitro and in vivo studies have shown curcumin is active against viruses, bacteria and fungi.

Virus	Family	Antiviral activity	References
CHIKV	Togaviridae	Entry inhibitor	Rhein et al., 2016
DENV	Flaviviridae	Entry inhibitor Particle production inhibition	Chen et al., 2013 Padilla-S et al., 2014
HBV	Hepadnaviridae	Replication inhibitor cccDNA inhibitor	Kim et al., 2009, 2011; Rechtman et al., 2010 Wei et al., 2017
HCV	Flaviviridae	Entry inhibitor	Anggakusuma et al., 2014
HIV	Retroviridae	Protease inhibitor Integrase inhibitor Tat protein inhibitor	Sui et al., 1993 Mazumder et al., 1995 Barthelemy et al., 1998; Balasubramanyam et al., 2004; Ali and Banerjea, 2016
HPV	Papillomaviridae	Gene expression inhibition	Maher et al., 2011; Mishra et al., 2015
HSV	Herpesviridae	Gene expression inhibition	Kutluay et al., 2008
IAV	Orthomyxoviridae	Entry inhibitor	Chen et al., 2010; Ou et al., 2013
JEV	Flaviviridae	Entry inhibitor Particle production inhibition	Chen et al., 2013 Padilla-S et al., 2014
MNV	Caliciviridae	Entry inhibitor	Yang M. et al., 2016
RSV	Pneumoviridae	Entry inhibitor Replication and budding inhibition	Yang X.X. et al., 2016; Yang et al., 2017
RVFB	Phenuiviridae	Replication inhibitor	Obata et al., 2013
ZIKV	Flaviviridae	Entry inhibitor	Narayanan et al., 2012 Mounce et al., 2017

Table 1: Antiviral activity of curcumin against several different viruses

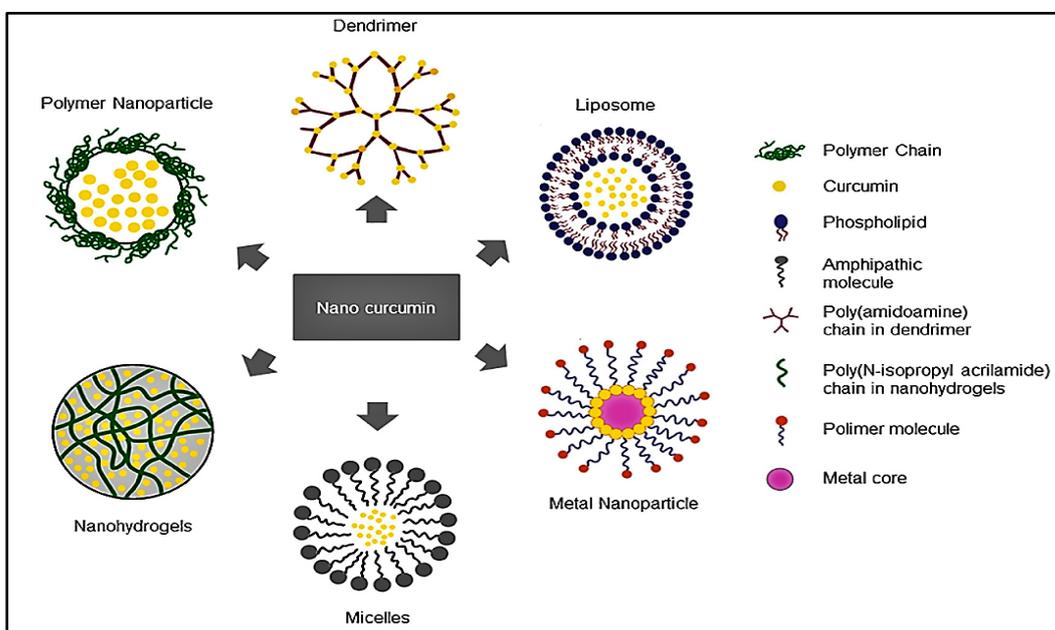


Figure 1. Nanocarrier systems encapsulating curcumin. Different nanoformulation strategies have been reported to improve the bioavailability and therapeutic efficacy of curcumin based on their chemical composition.

## BLACK PEPPER

Black pepper (*Piper nigrum* Linn.) is the world's most common spice and known as the "King of Spices." Pepper is a perennial vine and a native of South India. In its dried form, the fruit is often referred to as peppercorns. Peppercorns, and the powdered pepper derived from grinding them, may be described as black pepper, white pepper, red/pink pepper, and green pepper. The sole use of black pepper is in the seasoning of food owing to its aroma and pungency. In traditional medicines, this spice is also reported to have digestive power, to improve appetite, and to cure cold, cough, dyspnea, diseases of the throat, intermittent fever, colic, dysentery, worms and piles. The uses of black pepper in traditional medicine as an antipyretic and anti-inflammatory are supported by modern science. In folk medicine, black pepper is also used against epilepsy and snake bite. An electuary prepared from the seed is said to help hard tumors, while a salve prepared from the seed is said to help eye indurations and internal tumors.<sup>6</sup>

## CARDAMOM

Cardamom consists of two genera of the ginger family Zingiberaceae, namely *Elettaria* and *Amomum*. In South Asia green cardamom is called *elaichi* in Marathi, Hindi and Urdu. It is called *elakkaay* in Telugu and *elam* in Tamil. All these cardamom species are used as cooking spices.

Medically, cardamom is used for flatulent indigestion and to stimulate the appetite in people with anorexia. Moreover, in Ayurvedic medicine it is used as a carminative, diuretic, stomachic and digestive, and for cough, colds and cardiac stimulation. Cardamom has been used in traditional medicine against kidney and urinary disorders,<sup>6</sup> and as a gastrointestinal protective. Cardamom oil has reported anti-inflammatory and antibacterial uses. In India, green cardamom (*A. subulatum*) is broadly used to treat infections of the teeth and gums, to prevent and treat throat trouble, congestion of the lungs and pulmonary tuberculosis, asthma, heart disease, inflammation of the eyelids and digestive disorders. When mixed with neem and camphor, cardamom is used as a nasal preparation to treat colds. An infusion of cardamom can be used as a gargle to relieve sore throats, which has led to its use in cough sweets. Cardamom is also reportedly used as an antidote for both snake and scorpion venom and for food poisoning. In traditional Chinese medicine it is used to treat stomachache, constipation, dysentery, and other digestion problems. Cardamom pods, fried and mixed with mastic and milk, are used for bladder problems. The seeds are popularly believed to be an aphrodisiac.<sup>19</sup>

## CINNAMON

Cinnamon (*Cinnamomum verum* or *C. zeylanicum*) is native to India, Sri Lanka, Bangladesh, and Nepal. The name "cinnamon" comes from Greek *kinnámōmon*, itself ultimately from Phoenician. The botanical name for the spice, *Cinnamomum zeylanicum*, is derived from Sri Lanka's former (colonial) name, Ceylon. In Sinhala (Sri Lanka), it is known as *kurundu*, Sanskrit as *tvak* or *darusita*, Hindi as *dalchini*, and in Gujarati as *taj*. In Malayalam cinnamon is called *karuva* or *elavarngam*. The dried skin (*karuvappatta/elavarngappatta*) of *karuva* is an important part of spicy curries. This spice is regarded as antipyretic, antiseptic, astringent, balsamic, carminative, diaphoretic, fungicidal, stimulant, and stomachic.<sup>20</sup> The powdered bark of this spice in

water is applied to alleviate headaches and neuralgia. Cinnamon is often combined with ginger to stimulate circulation and digestion. In addition, among people of Kashmiri origin, cinnamon is used to treat infectious diseases. It has been regarded as a folk remedy for indurations (of spleen, breast, uterus, liver and stomach) and tumors (especially of the abdomen, liver and sinews).

## CLOVES

Cloves (*Syzygium aromaticum*, or *Eugenia aromaticum* or *Eugenia caryophyllata*) are the aromatic dried flower buds of a tree in the Myrtaceae family. Cloves are native to Indonesia and are used as a spice in cuisine all over the world. The name derives from the French "clou," (meaning "nail") as the buds vaguely resemble small irregular nails in shape. The spice is used in Ayurveda, Chinese medicine and Western herbalism and dentistry, where the essential oil is used as an anodyne (painkiller) for dental emergencies. It has been reported as analgesic, anesthetic, antibacterial, antiparasitic, antidotal, antioxidant, antiperspirant, antiseptic, carminative, deodorant, digestive, rubefacient, stimulant, stomachic, tonic and vermifugal. Cloves are used as a carminative to increase hydrochloric acid in the stomach and to improve peristalsis. Cloves are also said to be a natural antihelminthic. The essential oil is used in aromatherapy, especially for digestive problems. Topical application of this spice over the stomach or abdomen will warm the digestive tract. In Chinese medicine cloves are considered acrid, warm and aromatic, entering the kidney, spleen and stomach meridians, and are notable in their ability to warm the middle, direct stomach qi (energy flow) downward, treat hiccough and fortify the kidney. Because the herb is so warming, it is contraindicated in any persons with fire symptoms. As such it is used in formulas for impotence or clear vaginal discharge, for morning sickness together with ginseng and patchouli, and for vomiting and diarrhea due to spleen and stomach coldness. Clove oil is used in various skin disorders like acne and pimples, to treat severe burns and skin irritations, and to reduce the sensitiveness of the skin. Cloves are used for the treatment of dog and cat ear problems in British Columbia, Canada. The essential oil extracted from cloves is used as an ointment to relieve pain and promote healing in herbal medicine. Cloves are also employed as a fragrance in flavoring industries.<sup>21</sup>

## CORIANDER

*Coriandrum sativum* L. Apiaceae (Umbelliferae) (coriander, also known as cilantro, cilantrillo, Arab parsley, Chinese parsley, Mexican parsley, *Dhania* and *Yuen sai*), is native to southwestern Asia and regions west to north Africa. The name "coriander" derives from the French *coriandre* through Latin *coriandrum* and in turn from Greek *κοριαννον*. John Chadwick notes the Mycenaean Greek form of the word, *koriadnon*, "has a pattern curiously similar to the name of Minos' (Minos became a judge of the dead in Hades in Greek mythology) daughter Ariadne," and this explains how the word might have been corrupted later to *koriannon* or *koriandron*. It is an annual herb commonly used in Middle Eastern, Mediterranean, Indian, Latin American, African and Southeast Asian cuisine. Coriander leaves are referred to as cilantro (United States and Canada, from the Spanish name for the plant), *dhania* (Indian subcontinent, and increasingly in Britain), *kindza* (in

Georgia), Chinese parsley or Mexican parsley. All parts of the plant are edible, but the fresh leaves and the dried seeds are the most common parts used in cooking. As heat diminishes their flavor quickly, coriander leaves are often used raw or added to the dish right before serving. In Indian traditional medicine, coriander is used in the disorders of digestive, respiratory and urinary systems as it has diaphoretic, diuretic, carminative and stimulant activities. The plant is recommended for relief of anxiety and insomnia in Iranian folk medicine, and it is a common plant included in the Mexican diet, usually consumed uncooked, the oil being used as an antimicrobial agent and as a natural fragrance. It is also recommended for urethritis, cystitis, urinary tract infection, urticaria, rash, burns, sore throat, vomiting, indigestion, nosebleed, cough, allergies, hay fever, dizziness and amebic dysentery. Locally known as "Maadnousse" in Morocco, coriander has been documented as a traditional treatment for diabetes, indigestion, flatulence, insomnia, renal disorders and loss of appetite, and as a diuretic.<sup>22</sup>

### FENUGREEK

Fenugreek (*Trigonella foenum-graecum*) is commonly known as maithray (Bangla, Gujarati), methi or mithi (Hindi, Nepali, Marathi, Urdu and Sanskrit). In traditional medicines it is used as an aphrodisiac, astringent, demulcent, carminative, stomachic, diuretic, emmenagogue, emollient, expectorant, lactagogue, restorative, and tonic. Fenugreek is used for a variety of health conditions, including digestive problems, bronchitis, tuberculosis, fevers, sore throats, wounds, arthritis, abscesses, swollen glands, skin irritations, diabetes, loss of appetite, ulcers and menopausal symptoms, as well as in the treatment of cancer. An infusion of the leaves is used as a gargle for recurrent mouth ulcers. As an emollient it is used in poultices for boils, cysts and other complaints. It is used to reduce blood sugar level and to lower blood pressure. Fenugreek has been demonstrated to relieve congestion, reduce inflammation and fight infection. Fenugreek is used for treating sinus and lung congestion, and loosens and removes excess mucus and phlegm.<sup>23</sup> The Chinese use the seed for abdominal pain, chilblains, cholecystitis, fever, hernia, impotence, hypogastrosis, nephrosis, and rheumatism.

### GARLIC

Garlic (*Allium sativum* L.) is a species in the onion family, Alliaceae. One of the oldest dietary vegetables, it has been used as early as 3000 BC for the treatment of intestinal disorders and is now known for its fibrinolytic activity and its possible role in lowering blood cholesterol. Dietary patterns in the Mediterranean characterized by high consumption of fruits and vegetables, especially garlic, are believed to be beneficial to the regional patterns of atherosclerotic disease. The spice has also been used in folk medicine for the treatment of diabetes and inflammation. A well-known remedy for local pain is to crush garlic bulbs, apply the crushed garlic to the site of pain and then put a bandage over it. This practice is done by "naturopathic physicians" worldwide and as part of traditional "Arabic Medicine" in the Middle East. In Nepal, East Asia and the Middle East it has been used to treat all manner of illnesses including fevers, diabetes, rheumatism, intestinal worms, colic, flatulence, dysentery, liver disorders, tuberculosis, facial paralysis, high blood pressure and bronchitis. In Ayurvedic and Siddha medicine garlic juice has been used to

alleviate sinus problems.<sup>24</sup> In Unani medicine, an extract prepared from the dried bulb is inhaled to promote abortion or taken to regulate menstruation. Unani physicians also use garlic to treat paralysis, forgetfulness, tremor, colic pains, internal ulcers and fevers.

### GINGER

Ginger (*Zingiber officinale*) is commonly used as a cooking spice throughout the world. It is also known as zanjabil (Arabic), aadu (gujarati), shunti (Kannada), allam (Telugu), inji (Tamil and Malayalam), alay (Marathi), aduwa (Nepali), and adrak (Hindi and Urdu). The rhizome of ginger has long been used in Ayurvedic and traditional Chinese medicine to treat a wide range of ailments including gastrointestinal disorders, mainly nausea and vomiting associated with motion sickness and pregnancy, abdominal spasm, as well as respiratory and rheumatic disorders. As a home remedy, ginger is widely used for dyspepsia, flatulence, abdominal discomfort and nausea. It has been recommended by herbalists for use as a carminative (an agent that reduces flatulence and expels gas from the intestines), diaphoretic (an agent that produces or increases perspiration), antispasmodic, expectorant, peripheral circulatory stimulant, and astringent (an agent that causes shrinkage of mucous membranes or exposed tissues and that is often used internally to check discharge of blood serum or mucous secretions).<sup>25</sup> Ginger has a reputation for its anti-inflammatory properties. In traditional medicine, ginger has been used to treat a wide array of ailments including sore throats, stomachaches, diarrhea, toothache, gingivitis, arthritis (inflammation of the joints), bronchitis (an acute inflammation of the air passages within the lungs), muscle pains, sprains, constipation dermatitis, hypertension, dementia, fever, infectious diseases, helminthiasis, stroke, constipation, diabetes and asthmatic respiratory disorders.

### KALONJI

Kalonji (*Nigella sativa*) is an annual flowering plant, native to southwest Asia. The scientific name is a derivative of Latin niger meaning "black." In English, *Nigella sativa* seed is variously called black cumin, fennel flower, nutmeg flower, Roman coriander, blackseed, black caraway, or black onion seed. In English-speaking countries with large immigrant populations, it is also known as kalonji (Hindi), kezah (Hebrew), chernushka (Russian), çörek otu (Turkish), habbat albarakah (Arabic "seed of blessing") or siyah daneh (Persian). It is regarded as an aromatic, carminative, diaphoretic, digestive, diuretic, emmenagogue, excitant, lactagogue, laxative, expectorant, antipyretic, antihelminthic, resolvent, stimulant, sudorific, parasiticide, stomachic, tonic, and vermifuge. The herb may be more important to Muslims than to Christians and Jews. Prophet Muhammad once stated that the black seed can heal every disease — except death. In Ayurvedic medicine, it is used as purgative adjunct. In Unani, it is considered an abortifacient and a diuretic and is used for ascites, coughs, eye-sores, hydrophobia, jaundice, paralysis, piles and tertian fever. The Lebanese take the seed extract for liver ailments. In Indonesia, the seeds are added to astringent medicines for abdominal disorders. In Malaya, the seeds are poulticed to treat abscesses, headaches, nasal ulcers, orchitis, and rheumatism. Arabian women use the seeds as a galactagogue.

Kalonji seeds and oil, alone or in combination with other drugs, are highly effective in alopecia, vitiligo and other skin ailments. Continuous use of kalonji is effective in mad dog bites. It is useful in paralysis, facial palsy, migraine, amnesia and palpitation. Its powder if taken with water is effective in treating hemorrhoids. If Kalonji seeds are boiled in vinegar and this solution is applied to the gums and teeth, it can reduce inflammation of the gums and also relieve pain. It has been reported that in a fine powder form it is effective if applied in early stages of cataract. Black seed oil has been a women's beauty secret since ancient times. Black cumin and its oil have been used to purge parasites and worms, detoxify, ameliorate amebic dysentery, shigellosis, abscesses, old tumors, ulcers of the mouth, and rhinitis.<sup>26</sup> For external use, the seed is ground into a powder and mixed with sesame oil, and can be used to treat abscesses, hemorrhoids and orchitis. Finally, the powdered seed has been used to remove lice from the hair.

### KOKUM

The genus *Garcinia* of the Clusiaceae family includes around 200 species, of which *Garcinia indica* is the most common. *Garcinia indica* is also known as *Brindonia indica*, *Stalagmitis purpurea*, *Garcinia purpurea*, *Garcinia microstigma*, *Stalagmitis indica*, *Garcinia celebica*, and *Oxycarpus indica*. *Garcinia indica*, primarily of Indian origin, is known by many names: bindin, biran, bhirand, bhinda, kokum, katambi, panarpuli, ratamba, and amsol. In the English language, it is commonly known as mangosteen, wild mangosteen, or red mango. The extract and rind of *Garcinia cambogia* is used as a curry condiment in India. In traditional medicine, such as Ayurveda, kokum is prescribed for edema, rheumatism, delayed menstruation, constipation and other bowel complaints, and intestinal parasites. The extract of *Garcinia cambogia* is used as an herbal appetite suppressant and weight-loss supplement.<sup>27</sup>

### MINT

*Mentha* (mint) is a genus of about 25 species (and many hundreds of varieties) of flowering plants in the family Lamiaceae (mint family). The word "mint" descends from the Latin word *menthe*, which is rooted in the Greek word *minthe*, mentioned in Greek mythology as Minthe, a nymph who was transformed into a mint plant. There are different types of mint including *Mentha aquatica* — water mint or marsh mint; *Mentha arvensis* — corn mint, wild mint, Japanese peppermint, field mint or pudina; *Mentha asiatica* — asian mint; *Mentha australis* — Australian mint; *Mentha citrata* — bergamot mint; *Mentha crispata* — wrinkled-leaf mint; *Mentha diemenica* — slender mint; *Mentha laxiflora* — forest mint; *Mentha longifolia* or *Mentha sylvestris* — horse mint; *Mentha piperita* — peppermint; *Mentha requienii* — Corsican mint; *Mentha sachalinensis* — Garden mint; *Mentha spicata* — *M. cordifolia*, spearmint, curly mint; *Mentha suaveolens* — apple mint, pineapple mint, and *Mentha vagans* — gray mint. Mint leaves are used in teas, beverages, jellies, syrups, candies, and ice creams. In Middle Eastern cuisine mint is used in lamb dishes. In British cuisine, mint sauce is popular with lamb. Mint is a necessary ingredient in Touareg tea, a popular tea in northern African and Arab countries. The plant is commonly used as a herbal agent in the treatment of loss of appetite, common cold, bronchitis,

sinusitis, fever, nausea and vomiting, and indigestion.<sup>28</sup> Peppermint plants have been used as a herbal medicine for the same conditions, and others. *Mentha arvensis* is known to possess abortifacient properties in folk medicine (Casey and Satyavati) and is commonly used as a folk remedy for pregnancy termination.

### RED CHILI

Red chili, belonging to the plant genus *Capsicum*, is among the most heavily consumed spices throughout the world. The name, which is spelled chili, chile, or chilli, comes from Nahuatl *chilli* via the Spanish word *chile*. Red chili has been used as an alternative medicine for the treatment of inflammation, diabetes, low back pain and also in homeopathy medicine to treat acute tonsillitis. Moreover, capsicum plaster, which contains powdered capsicum and capsicum tincture, has been used in Korean hand acupuncture to reduce postoperative nausea, vomiting and sore throat.<sup>29</sup>

### ROSEMARY

Rosemary (*Rosmarinus officinalis*) is native to the Mediterranean region. The name "rosemary" derives from the Latin name *rosmarinus*, which literally means "dew of the sea." In traditional European medicine, rosemary was used as a tonic, a stimulant, and a carminative to treat flatulence, as well as a diuretic, cholagogue (an agent which promotes the discharge of bile from the system), hepatoprotective, antirheumatic, expectorant, and mild analgesic. Rosemary has a number of therapeutic applications in folk medicines to treat a wide range of diseases such as headaches, epilepsy, poor circulation, diabetes mellitus, respiratory disorders, eczema, stomach problems and inflammatory diseases, and to stimulate growth of hair. It has been recommended for its positive effects on human fertility. It works as a digestion aid for the treatment of dyspepsia and mild gastrointestinal upsets, and it has been used in renal colic and dysmenorrhea because of its antispasmodic effects. Its aroma is used against coughs and colds. In traditional European medicine, it was believed that the eating of the rosemary flower comforts the brain, the heart and the stomach. It is used to improve memory and concentration, and to boost energy. The leaves of the plant are commonly used as a spice and as a source of antioxidant compounds employed in food conservation; the essential oil is used as a food additive.<sup>30</sup>

### CONCLUSION

Spices, including black pepper, cardamom, cinnamon, ginger, kalongi, red chillies, Kokomo, mint, rosemary have been shown to be indispensable for daily human health. Besides adding flavor and taste to dishes, they help prevent and alleviate various health problems. Over the last few years several bioactive compounds have been isolated from spices, providing a scientific basis for the use of spices in our diet.

Curcumin has multiple health benefits due to its antioxidant and anti-inflammatory mechanism. a combination of curcumin and piperine increases the bioavailability significantly. It helps in the management of oxidative and inflammatory conditions including arthritis, hyperlipidemia, metabolic syndromes and anxiety. Muscle soreness is relieved by ingesting curcumin. Finally, low doses of curcumin can provide health benefits to healthy patients.

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