World Journal of Pharmaceutical and Life Sciences
WJPLS
www.wjpls.org
SJIF Impact Factor: 6.129

CARDAMOM: THE QUEEN OF SPICES

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Article Received on 15/06/2021 **Article Revised on 05/07/2021** **Article Accepted on 25/07/2021**

ABSTRACT

Cardamom is a spice common in the Indian kitchen which comprises a number of active ingredients possessing many pharmacological effects. The general benefits are anti-microbial, anti-inflammation, analgesic, anti-nociceptive, anxiolytic and anti-cancer properties. In addition, 1,8-cineol prevents mucus formation, treats COPD and inhibits myeloperoxidase activity. Pinenes are advantageous in osteoarthritis, sleep enhancement and nephrological disorders. Alpha-terpineol is considered helpful in gastric disorders like ulcer, skin irritation and sciatic nerve pain. Humulene can help fight diabetes, fatty liver, obesity and tumours. Myrcene combats hypertension, diabetes and inflammation. Alpha-terpinyl acetate treats skin problems and inhibits cholinesterase enzymes. Menthone is used in curing irritable bowel syndrome. Sabinene can undo oedema and prevent fungal growth. Heptane has an adverse effect of deteriorating central nervous system coordination. Borneol is capable of angiogenesis and neurogenesis. Borneol and limonene can be used in nano-based drugs. So, the above properties and therapeutic effects of the ingredients of cardamom, these can be incorporated into medicines and used for treatment purposes**.** These properties enable provision of proper treatment in the concerned diseases.

KEYWORDS: Cardamom, 1,8-cineol, α-terpineol, Humulene, Menthone, Sabinene, Limonene.

INTRODUCTION

Cardamom, which is often regarded as the "queen of spices", is a flavour-enhancing agent, which improves the timber of the food to which it is added. For instance, curry, fried rice, pulao, tea and many sweets grow more delicious owing to the addition of Cardamom. It is sold either as intact pods or in the ground form. When in the ground form, it is available as Cardamom powder alone or as a constituent of the Indian spice called garam masala. Apart from being used in cookery, cardamom helps in proper digestion, mouth freshening, managing hypertension and diabetes,[1] prevents tooth cavities, combating bacterial infection inflammation, cancer, anxiety, liver diseases, maintains proper breathing dynamics and promotes weight loss.[2]

Sources

According to the plant sources of this spice, cardamom, there are three varieties commonly known as green, black and white cardamom. Elettaria cardamomum is the source of the green variety which gets bleached to give rise to the white variety. The black variety is obtained from Amomum sabulatum or Lanxangia tsaoko. If not otherwise mentioned, it is usually the green variety referred to.[3] It is a perennial plant which belongs to the Zingiberaceae family. The requirements are10-35^0 C temperature, 1500-4000mm of rainfall and humus-rich loamy soil. It is grown in the hills of Western Ghats, Karnataka, Kerala and Tamil Nadu, within India.[4]

Ingredients and Their Pharmacological Effects

1,8-cineol

1,8-cineol can lower neuropathic pain intensity involved with the P2X2 and P2X3 receptor-expression in the dorsal horn of spinal cord. Sometimes, other pain of nociceptive origin can be alleviated by this compound. According to report, further analysis must be made to ensure if the sole use of 1,8-cineol can abate pain or other interfering signals exist.[5] 1,8-cineol is effective in prevention of mucus-build-up and spasms caused either due to infection or inflammation. Hence, it is said to have anti-inflammatory properties. This potential of 1,8-cineol is exploited in the clinical treatment of respiratory diseases like asthma and chronic obstructive pulmonary disease (COPD).[6] The anti-inflammatory and analgesic properties may also be attributed to the ability of 1,8-cineol in lowering cytokine and prostaglandin production. It can also reduce opioid receptor related pain sensation. The decrease in activity of the central nervous system is another related effect.[7] 1,8-cineol has the unique property to penetrate the blood-brain barrier and suppress acetylcholinesterase activity. So, it can play a medicinal role in anxiety control, like other essential oils.[8] The anti-inflammatory feature during colon

inflammation (even in colon cancer) and in curing tongue oedema, as was reported in rats. 1,8-cineol is capable of replenishing glutathione levels, lowering myeloperoxidase activity, inhibiting tumour necrosis factor expression and consequently mitogen-activated protein kinase (MAPK).[9] In the gastrointestinal tract, 1,8-cineol can decrease peroxidation of lipids, maintain sulfhydryl groups along with its other effects, thus acting as an antioxidant in diseases like ulcer. Thus, it can confer a level of protection against digestive system disorders.[10]

Alpha-pinene and beta-pinene

Alpha-pinene can free a patient from nociceptive pain triggered by capsaicin that is mediated by GABA A and mu-opioid receptors, as is evident from the experiment on the dental extract of rats.[11] Alpha pinene is thought to play protective roles in cancer. It can reduce pancreatic and pulmonary myeloperoxidase activity if pre-treated with cerulein. Alpha-pinene can reduce inflammation due to balanced liberation of tumour necrosis factor-alpha, interleukin 1-beta and interleukin-6.[12] Alpha-pinene are used in bacterial infection treatment (by destroying membrane compactness and heat-shock proteins), dementia cure and dilating the bronchus and bronchioles. It can suppress activity acetylcholinesterase.[13] Alpha pinene is known for its uses in the ministration of urinary stones and other renal and nephrological diseases.[14] It can be used to cure anxiety. This molecule can bind with the same active site of the GABA A-benzodiazepine receptor to which benzodiazepine binds; if it does, the duration of non-rapid eye movement (non-REM) sleep is increased due to delayed synaptic impulse flow through GABAergic neurons.[15] Alpha-pinene can be helpful in schizophrenia and other neuron-induced psychopathological disorders.[16] Alpha-pinene, especially the + enantiomeric form, can be a novel medicine for prevention of osteoarthritis and inflammation of the cartilage.[17] The other positive specific effects of alpha and beta pinene have been identified in coagulative diseases, tumour-genetic cells, bacterial infection (Leishmania), other pathogenic infection, malaria and pain disorders.[18]

Alpha-terpineol

Alpha-terpineol can expand the diameter of blood vessels by regulated voltage-gated and receptor-mediated calcium transport, thus known for its anti-hypertensive properties. Alpha-terpineol can prevent formation of superoxide radicals by triggering monocytic activity, hence it is as good as an antioxidant. It can also cause cessation of cell cycle, in cases of lung cancer and other malignant tumours. This effect is achieved by inhibiting tumour necrosis factor along with the administration of other apoptotic agent. Alpha-terpineol can prevent fungal growth by maltreating the mitochondria and destroying the cell membrane. It can decrease pain intensity originating from the central and peripheral portions. This is done by lowering the concentration of prostaglandins, substance P, serotonin, bradykinin, histamine and other mediators of pain-cum-inflammation. Alpha-terpineol is naturally resistant against gastric disorders and can be put to use during ulcer treatment. Other treatment fields include bronchitis, chronic obstructive pulmonary disease and skin irritation.[19] The anti-cancer activity of alpha-terpineol involves blockage of NF-kappaB pathway.[20] These compound and associated molecules treat make a patient suffering from nociceptive pain, when the stimulus is mechanical, by increasing the level of pain sensation to decide a perception as “painful” at a much higher threshold.[22] Alpha-terpineol is often considered effective during pathogenic infection and proliferation.[22] It can peroxidise lipids, but development of fatty liver and cerebral ischemia can be the unwanted side-effects, as per reports.[23] Alpha-terpineol can delay the generation of compound action potential and consequently the neuronal action potential in sciatic and other peripheral nerves. This molecule has been identified as an integral part of aromatherapy and traditional folk medicinal purposes.[23]

Humulene

Humulene is also known as caryophyllene. The trans isomeric from of caryophyllene can inhibit the expression of platelet-activating factor and prevent oedema caused due to ovo-albumin or bradykinin. On the other hand, oedema caused due to histamine can be decreased by alpha-humulene. Alpha-humulene and trans-caryophyllene can lower tumour necrosis factor (TNF-alpha) and IL-1beta, while trans-caryophyllene alone can lower the TNF-alpha levels. Both these compounds can modulate the concentrations of prostaglandins, nitric oxide synthase and cyclooxygenase-2. Due to these effects, humulene can be used in the treatment of inflammatory diseases.[24] Alpha-humulene is anti-carcinogenic and this feature gets boosted by the usage of beta-caryophyllene.[25] The anti-oxidation potential of humulene often gets switched-off to initiate death of cancerous cells. Humulene can help fight high body weight, diabetes, tumours. It can inhibit hunger sensation.[26]

Myrcene

Besides inducing sleep, myrcene can be of therapeutic value in case of diseases like osteoarthritis, hypertension, pain, diabetes, diarrhea, dysentery and other inflammatory disorders. Since, myrcene compounds can percolate through the skin, it can be used in the dermatological treatment.[27] Myrcene can inhibit motor task activities and at very high concentration it lead to building of anxiety.[28] Myrcene can alleviate peripheral pain but does not cause any habituation towards the prolonged or regular doses, unlike morphine, as was reported in rats.[29] However, the role of this molecule in relieving pain both due to inflammation and neuropathy have been known, along with the promotion of better immune responses.[30] The analgesic properties can be owed to the fact that TRPV 1 channels (transient receptor potential channel type 1) serves as the primary target of this compound and help in pain-management by

modulation calcium entry and exit through the concerned cells.[31] It can be used as an antibiotic. The uses of myrcene has also been implicated in combatting tumour cells and cancer, when administered in combination with other terpenes and cannabinoids.[32]

Alpha-terpinyl acetate

Alpha-terpinyl acetate is an anti-oxidant molecule which can stop the functioning of acetylcholinesterase, butyrylcholinesterase and reduce oxidative stress caused by hydrogen peroxide. The plausible causes might be the ability of alpha-terpinyl acetate to form complexes with beta-amyloid peptides, free radicals and cholinester-degrading enzymes. Since, the molecule can bind with many ligands, it can be utilized to design a new drug which may have multi-faceted binding possibilities indicating that alpha-terpinyl acetate can be a initiative in the advent of Alzheimer's disease treatment.[33] Alpha-terpinyl acetate can competitively block the activity of P450 2B6, a human cytochrome, whose purpose is to hydroxylate bupropion.[34] Alpha-terpinyl acetate, considered a derivative of the essential oils of cardamom, can prevent proliferation in skin fibroblastic cells. These mentioned group of compounds, if administered, can increase the levels of tissue inhibitor of metalloproteinase 1 (TMP1), while lower the formation of VCAM1 (vascular cell adhesion molecule 1) and M-CSF (macrophage-colony stimulating factor) during the dermal pathogenesis. In this way, it can antagonize inflammation and elevate immune responses.[35] Alpha-terpinyl acetate is anti-fungal and anti-dermatophytic but lesser pronounced effects are known against bacteria and yeast. So, it can be used in the treatment of mycosis.[36]

Limonene

Limonene can both enhance and inhibit either aggravation or slowing down of tumour growth. It inhibits the expression of anti-apoptotic proteins like BCl2 and increases the expression of apoptotic proteins like BAX, caspase, etc. and during the process regulate a balance between cell death in relation to other processes. Due to these effects, limonene can prevent inflammation and can be used in nano-technological drugs.[37] d-limonene can be used to deliver medicines into the layers of skin, for its high transdermal passage. d-limolene can be administered after surgery to dilute and diffuse remnant cholesterol gallstone content. However, it can constrict bronchiolar conduits and cause eye irritation.[38] If d-limone and ethanol are embalmed on the skin as a combination in an ointment medicine, absorption of indomethacin is increased.[39] Limonene is an anti-oxidant molecule and it prevents microbial infection, nociceptive pain and cancer (breast cancer, skin cancer, lung cancer). It can inhibit 5-lipoxygenase enzyme responsible for anti-inflammation while the pain management property is due to release of inflammatory mediators.[40] Limonene is expected to treat weight loss and bronchitis but far more studies are required in support of these uses.[41]

Menthone

Menthone, along with other suitable compounds like menthol and isomenthol, can prevent microbial infection specially against organisms like *E. Coli* and *Salmonella typhimurium.* The other effects exerted by these group of compounds include combating pain, fever; inhibiting acetylcholinesterase enzyme; curing abdominal pain, vomiting, diarrhoea; reducing execution of free radical functioning; maintaining L. Casei cheese during storage; preventing mutations and cancer [42]. Menthone is significant in the treatment of cough, irritable bowel syndrome, enhancement of bile secretion and relaxation of smooth muscles.[43]

Sabinene

Sabinene, in association with other compounds, can prevent fungal growth and superoxide radical formation. Sabinene can block the synthesis of nitric oxide in the lipopolysaccharide enzymatic pathway and macrophages stimulated by gamma-interferons, and consequently exerts anti-inflammation.[44] Sabinene in combination with other relevant compounds can prevent Staphylococcus aureus which is resistant towards methicillin. However, role of sabinene in this aspect is lower as compared to other components of this group involved in this action.[45] Sabinene is antibacterial, specifically against Salmonella typhi. Sabinene, in combination with terpinen-4-ol can exert antagonising inflammatory activity in oedema caused by carrageenan evident from the paws of rats.[46]

Heptane

When animals are treated with n-heptane, changes like prolonged sleep, reduced hepatic glucose-6-phosphate levels altering microsome functioning and an increase in peroxidation of lipids occur after about one to two days of administration. Other liver proteins and the quantity of sulfhydryl groups get lowered.[47] If the n-heptane is induced through inspiration, then NADPH-diaphorase increases and RNA content falls in the brain at the most nominal threshold. If application is continued, then NADPH diaphorase is restored, but other proteins present in the brain are disintegrated. Although, these levels get altered, degree of alteration may not be such that might lead to neurological disorder.[48] However, adverse effects like lack of alertness, loss of reflexes, nausea, drowsiness, irritation of mucous membrane, light-headed and lack of equilibrium of nervous system activities might be produced.[49] This molecule can worsen skin cuts.[50]

Other Trace Components of Oil

Borneol

The (-) borneol (or l-borneol) form can act as a sedative, lower pain intensity, prevent blood coagulation, antagonize inflammation and dilate blood vessels. The smooth muscles, particularly the aorta, gets relaxed by the action of borneol.[51] The healing of damaged tissues, regeneration of cells, removal of rotten smell are other useful effects of borneol.[52] Borneol has the capacity to

channelize a drug to its particular target (be it hypothalamus or hippocampus) thus making the action of drug more effective. The intricacy of tight junctions can be decreased in some regions of the blood brain barrier using borneol that might allow entry of certain drugs like cisplatin. Borneol can enhance passage of substances through epithelial tissues and trafficking of medicines embedded within nanoparticles.[53] Osthole is a natural coumarin compound that helps in fighting neuropathy, osteoporosis, inflammation, diabetes and stroke. Borneol boosts the activity of osthole. Borneol can act as an anti-oxidant too.[54] Borneol performs the loosening of the blood-brain barrier by altering the activity of ATP-binding cassette transporters like P-glycoprotein.[55] Borneol, can bestow upon an individual, a protective shield against cerebral ischemia due to its ability to increase angiogenesis and neurogenesis, but additional factors affecting these pathways should be considered. (l-Borneol Exerted the Neuroprotective Effect by Promoting Angiogenesis Coupled with Neurogenesis via Ang1-VEGF-BDNF Pathway.[56]

Beta-phellandrene

Although beta-phellandrene is documented as an ingredient of cardamom spice, and present in combination in other species as well, its specific uses are yet to be discovered.

CONCLUSION

Cardamom is a commonly-used spice which can be of three different varieties green, black and white. Depending on the plant source; whether it is Elettaria cardamomum, Amomum subulatum or Lanxangia tsaoko, the colour differs. The ingredients of cardamom include 1,8 cineol, alpha-pinene, beta-pinene, alpha-terpineol, humulene, myrcene, limonene, menthone, sabinene, alpha-terpinyl acetate, heptane, beta-phellandrene and borneol. All these components have beneficial pharmacological effects which include anti-oxidant activity, anti-inflammation, and analgesic property. The diseases like respiratory obstruction, urinary stones, psychopathy, diabetes, high blood pressure, pathogenic infection, ulcer, skin ailments, tumour and Alzheimer's disease can be treated using these ingredients of cardamom in various combinations with other chemical compounds. There are enzymatic involvements as well, stimulatory at some point of time and inhibitory at the other. The enzymes whose activity are altered are lipopolysaccharide, cholinesterases, nitric oxide synthase, apoptotic proteins and P-glycoprotein. So, the above properties and therapeutic effects of the ingredients of cardamom, these can be incorporated into medicines and used for treatment purposes**.**

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