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Review Article

Role of Clove in Human Medical History

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Abstract: The clove is usually known as "lavang". Due to the increase in nutrition and medicinal properties, Plants' importance in human life has increased every day. Clove is the topical evergreen Myrtaceae family tree native to the islands of Maluka in east Indonesia. It is commonly used for tooth care. Clove is used extensively in dental care for relieving toothache, sore gums and oral ulcers. Gargling with clove oil can also aid in sore throat conditions and bad breathe. This is commonly used as an expectorant for the treatment of dental discomfort, the digestive problem, oral ulceration, mosquito repellent. Clove is a pharmacologically active medicinal plant that includes Anti-oxidant, anti-pyretic, anti-viral, anti-microbial, anti-diabetic, anti-inflammatory, analgesic, anti-platelet, anti-stress, anti-disease, and anti-carcinogenic in cervical cancer. Clove is amongst the most essential sources of Phenolic compounds, including eugenol (80% -90%), eugenyl acetate (15% -17%), and beta-caryophyllene (5% -12%), alpha-humulene (0.55%), alpha-terpenyl acetate (0.1%), and methyl eugenol (0.2%). The clove oil extracted from the dried floral buds of the clove provide as a topical treating pain and as a healing factor. The flowers, stalks and clove tree leaves are obtained from the distillation of clove oil. Eugenol is the clove's principal bioactive ingredient. For oral diseases, it is used as an antiseptic. Cloves are used in the cuisine of Asian, African, Middle East countries and used to give aromatic and flavor qualities to hot beverages. A mine component of clove plant parts is eugenol, that it has not been classified for its potential toxicity. Other important essential oil of clove is acetyl eugenol, beta-caryophyllene and vanillin, crategolic acid, tannins such as bicornin, gallotannic acid, methyl salicylate, the flavonoids eugenin, kaempferol, rhamnetin, and eugenitin, triterpenoids such as oleanolic acid, stigmasterol, and campesterol and several sesquiterpenes. Thus, foods should be preserved against the microbial spoilage throughout the storage periods. In addition to clove extracts could affects as anti-oxidative, fungicidal, and antibacterial effects on foods. It has been reported that clove essential oil is one of the natural fungicides and antibacterial phytomaterial. The active essential oil in clove, eugenol, has been shown to act as an effective platelet inhibitor, preventing blood clots. The major constituents in bud and leaf oils were reported to be eugenol and caryophyllene. Main constituent's flower buds of clove essential oil are phenylpropanoids such as carvacrol, thymol, eugenol and cinnamaldehyde. Clove bud oil contained primarily eugenol, eugenyl acetate and caryophyllene. The high concentration of eugenol in leaf and buds oil makes it potentially useful in the medicines because they exhibit antibacterial, antifungal, anti-inflammatory activity, insecticidal and antioxidant properties, and are used traditionally as flavouring agent and antimicrobial material in food. Clove (*Syzygium aromaticum* L.) buds and flowers are utilized for its essential oil. Eugenol is the main component of clove oil, which has strong antioxidant activity. Eugenol is the chief bioactive constituent of clove, which is present in concentrations ranging from 9 381.70 to 14 650.00 mg/100 g of fresh plant weight. With regard to the phenolic acids, gallic acid is found in higher concentration (783.50 mg/100 g fresh weight). Cloves contain appreciable amounts of volatile oil (used for flavouring foods and pharmaceuticals), which is mainly confined in aerial parts of plant. Other phenolic acids found in clove are caffeic, ferulic, elagic and salicylic acids. Flavonoids including kaempferol, quercetin and its derivates (glycosilated) are also found in trace amounts. Appreciable amounts of essential oil are present in aerial parts of clove. Good quality clove bud contains volatile oil (15 to 20%), which mainly comprises of eugenol (70 to 85%), eugenyl acetate (10 to 15%), and beta-caryophyllene (5 to 12%). Approximately, 15-20% volatile oil can be produced from dried buds. Clove improves memory by relieving mental fog, drowsiness, and depression. Clove oil is mosquito repellent. Clover oil exhibited significant inhibition against tested strains, with minimum inhibitory concentrations ranging from 0.312-1.25% (v/v) for clove oil, and 0.312- 5% (v/v) for rosemary oil.

Keywords: lavang, clove, *Syzygium aromaticum* L, flavouring foods, glycosilated.

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INTRODUCTION

Clove is used extensively in dental care for relieving toothache, sore gums and oral ulcers. Gargling with clove oil can also aid in sore throat conditions and bad breathe. Arabic traders brought the buds to Europe in 4th century A.D., and in the seventh and eighth century A.D. Europe, cloves became very popular as a medicinal flower, due to their ability to preserve foods, and mask the smell of poorly-kept foods (International Organization for Standardization, 2002). The active essential oil in clove, eugenol, has been shown to act as an effective platelet inhibitor, preventing blood clots (Körfers *et al*., 2009). Preliminary studies suggest that clove oil may play a chemo preventive role, particularly in cases of lung, skin and digestive cancers (Schönfelder *et al*., 2004).

Clove bud oil has biological activities, such as antibacterial, antifungal, insecticidal and antioxidant properties, and are used traditionally as flavouring agent and antimicrobial material in food (Lee and Shibamoto, 2001; Huang *et al*., 2002; Velluti *et al*., 2003). Importantly, Lee and Shibamoto, 2001, reported that clove oil might also be used as an anti-carcinogenic agent due to its antioxidant properties. Their results also suggested that clove oil might be of use as a potential chemo preventative agent. Syzygium species have been reported to possess antibacterial (Shafi *et al*., 2002) and anti-inflammatory activity (Muruganadan *et al*., 2001). Recently, flavonoid triglycosides have been isolated (Nassar, 2006). The major constituents in bud and leaf oils were reported to be eugenol and caryophyllene (Srivastava *et al*., 2003; Raina *et al*., 2001; Wenqiang *et al*., 2007). Kamel *et al.* (2007) reported the main constituent's flower buds of clove essential oil are phenylpropanoids such as carvacrol, thymol, eugenol and cinnamaldehyde. Amla et al. (2007) also reported that the bud oil contained primarily eugenol, eugenyl acetate and -caryophyllene.

The high concentration of eugenol in leaf and buds oil makes it potentially useful in the medicines because they exhibit antibacterial, antifungal, anti-inflammatory activity, insecticidal and antioxidant properties, and are used traditionally as flavouring agent and antimicrobial material in food (Huang *et al*., 2002; Velluti *et al*., 2003; Shafi *et al*., 2002; Muruganadan *et al*., 2001). Clove (*Syzygium aromaticum* L.) buds and flowers are utilized for its essential oil. In Indonesia, clove is classified into four main varieties: Siputih, Sikotok, Zanzibar, and Ambon (Luthfi, 2017). The Zanzibar variety produces more buds than other varieties and considered the most superior and cultivated variety (Rukmana and Yudirachman, 2016). A clove bud is a single flower with a length of 1-2 cm, while a clove flower has eight stages of clove bud development, namely young bud, budding-1, budding-2, budding-3, full-budding, flowering, initial fruiting, and full fruiting (Rukmana and Yudirachman, 2016 and Razafimamonjison *et al*., 2013). Eugenol is the main component of clove oil, which has strong antioxidant activity (Laitupa and Susane, 2010).

There are obvious physiological differences between unstable and stable growth stage. However, studies on its yield and quality as essential oil are limited. Particularly, young trees at 3-4 years old had the first flowering period (Semangun and Karwur, 2014), which makes the flower buds an interesting material for experiment. The highest oil yield in young trees was also reported in several previous studies on other plant species (Pujiarti *et al*., 2011 and Pambudi *et al*., 2016). Composition of the vacuole structures led to high oil yield in young clove trees. Essential oil is one of the secondary metabolites stored in plant vacuoles (Campbell and Reece, 2012). Small vacuoles merge to form a single large structure as the plants grow (Evert, 2006). The biosynthesis starts from the first budding stage, meaning the transformation of the droplet into bubble occurs along with the budding stages (Kridati *et al*., 2012). Optical rotation of oil extracted from young trees was higher than that from mature trees, which was similar to that found in eucalyptus oil (Runtunuwu *et al*., 2016). According to Pujiarti et al. (2011), tree age has a diverse influence on the optical rotation of essential oils. Changes in the polarization angle increase with the decrease in the viscosity of the material (Nuraniza *et al*., 2013).

The clove is usually known as "lavang."Due to the increase in nutrition and medicinal properties, Plants' importance in human life has increased every day. The term clove is derived from 'clove' and 'clou' meaning 'nail.' This is used mainly in Ayurvedics (Hussain and Trak, 2019). Clove is the topical evergreen Myrtaceae family tree native to the islands of Maluka in east Indonesia. The color is small brown, floral buds, and a spice is used. It was used as food preservatives, flavoring agents and nutritional additives, medicinal coloring agents (Cortés-Rojas *et al*., 2014). Health, cosmetic, nutritional and agricultural use clove. It is commonly used for tooth care (Chaieb *et al*., 2007). This is commonly used as an expectorant for the treatment of dental discomfort, the digestive problem, oral ulceration, mosquito repellent (Thangaselvabai *et al*., 2010). Clove is a pharmacologically active medicinal plant that includes Anti-oxidant, anti-pyretic, anti-viral, anti-microbial, anti-diabetic, anti-inflammatory, analgesic, anti-platelet, anti-stress, anti-disease, and anti-carcinogenic in cervical cancer. The clove is available in three types of essential oil (Jain, 2019). Clove is amongst the most essential sources of Phenolic compounds, including eugenol (80% -90%), eugenyl acetate (15% -17%), and beta-caryophyllene (5% -12%), alpha-humulene (0.55%), alpha-terpenyl acetate (0.1%), and methyl eugenol (0.2%) (Yunusa *et*

al., 2018). The clove oil extracted from the dried floral buds of the clove provide as a topical treating pain and as a healing factor. The flowers, stalks and clove tree leaves are obtained from the distillation of clove oil (Khalil *et al*., 2017). Eugenol is the clove's principal bioactive ingredient. For oral diseases, it is used as an antiseptic (Overly, 2019).

The clove tree is an evergreen plant. Cloves flower consist of a long calyx that terminates in four spreading sepals, and four unopened petals that form a small central ball with aromatic scent (Bhuiyan *et al*., 2010). The original clove zone is in Indonesia and Philippines (Danthu *et al*., 2014). Cloves are used in the cuisine of Asian, African, Middle East countries and may be used to give aromatic and flavor qualities to hot beverages. A mine component of clove plant parts is eugenol, that it has not been classified for its potential toxicity (Bendre *et al*., 2016). Other important essential oil of clove is acetyl eugenol, beta-caryophyllene and vanillin, crategolic acid, tannins such as bicornin, gallotannic acid, methyl salicylate, the flavonoids eugenin, kaempferol, rhamnetin, and eugenitin, triterpenoids such as oleanolic acid, stigmasterol, and campesterol and several sesquiterpenes (Bendre *et al*., 2016). Thus, foods should be preserved against the microbial spoilage throughout the storage periods (Goni *et al*., 2009). In addition to clove extracts could affects as anti-oxidative, fungicidal, and antibacterial effects on foods (Goni *et al*., 2009). It has been reported that clove essential oil is one of the natural fungicides and antibacterial phytomaterial (Ayoola *et al*., 2008).

The garden strawberry need to remain on the plant to fully ripen because they do not continue to ripen after being picked (Raina *et al*., 2001). Rotted and overripe berries are removed to minimize insect and disease problems (Sallato *et al*., 2007). The berries do not get washed until just before consumption. In large operations, strawberries are fall victim to a number of diseases like powdery mildew, leaf spot, leaf blight and slime molds (Pleasant, 2011). The use of biocontrol agents with plant extracts in plant disease control has been employed by Zeng et al. (2012) suggested that clove extract might be a viable alternative to synthetic fungicides to extend the postharvest storage period and maintain fruit quality of navel orange too. Weight loss occurred during storage regardless the type of fruit or vegetable evaluated. However, the rate of water loss was dependent on the type of crop evaluated, and was greatly related to the physiological and morphological characteristics of each individual fruit or vegetable, and with of each individual fruit or vegetable, and with the expected shelf life under the environmental conditions used in this study (Pino et al., 2001 and Tournas and Katsoudas, 2005).

Clove enhances memory retention. It is recommended for relieving brain fog, lethargy and depressive state of mind. Research has shown that clove oil is an effective mosquito repellent (Trongtokit *et al*., 2005). Clove oil showed antimicrobial activity against some human pathogenic bacteria resistant to certain antibiotics (Lopez *et al*., 2005). Clove oil and its main component eugenol show considerable antifungal activity against Candida Aspergillus and dermatophyte species. It also shows activity against clinically relevant fungi including fluconazole- resistant strains (Pinto *et al*., 2009). Clove is a potent antiviral agent. Eugenin isolated from clove buds showed antiviral activity against Herpes Simplex virus at a concentration of 10 µg /ml (Chaieb *et al*., 2007). It also down regulates the expression of some growth promoting proteins, viz, COX^{-2}, cMyc, Hras (Banerjee *et al*., 2006). Oral administration of aqueous infusions of clove at the dose of 100 µl /mouse/day not only delayed the formation of papilloma but also reduced the incidence of papilloma as well as the cumulative number of papillomas per mouse (Banerjee *et al*., 2005).

Clove and Eugenol possess strong antioxidant activity, which is comparable to the activities of the synthetic antioxidant, BHA (butylated hydroxyl anisole) and Pyrogallol (Dorman *et al*., 2000). It also showed a significant inhibitory effect against hydroxyl radicals and act as an iron chelator (Gulcin *et al*., 2004). Cloves showed the highest DPPH radical scavenging activity & highest FRAP values (Yadav and Bhatnagar, 2007). The antioxidant activity of clove bud extract and its major aroma components, eugenol and eugenol acetate were comparable to that of the natural antioxidant α-tocopherol (Lee and Shibamoto, 2001). Eugenol inhibited 5-lipoxygenase activity and leukotriene C-4 in human PMNL cells (Raghavenra *et al*., 2006). A more global analysis of gene expression by DNA microarray analysis revealed that clove and insulin regulated the expression of many of the same genes in a similar manner (Prasad *et al*., 2005). Clove also contains a variety of flavonoids, including kaempferol, rhamnetin and β-caryophyllene which also contributed to clove's anti -inflammatory and antioxidant properties (Ghelardini *et al*., 2001). Clove extract was also effective in increasing the latency of anoxic stress induced convulsions in mice (Singh *et al*., 2009).

It has been found that ethanolic extract of clove (50%) produced a significant and sustained increase in the sexual activity of normal male rats, without any conspicuous gastric ulceration and adverse effects (Tajuddin *et al*., 2004). Culex quinquefasciatus and Anopheles dirus under laboratory conditions using human subjects (Trongtokit *et al*., 2005). The clover leaf and bud oils showed potent insecticidal activity against the human head louse (Pediculus capitis) (Yang *et al*., 2003). Clove in particular has attracted the attention due to the potent antioxidant and antimicrobial activities standing out among the other spices (Shan *et al*., 2005). For centuries the trade of clove and the search of this valuable spice stimulated the economic development of this Asiatic region (Kamatou *et al*.,

2012). The collection could be done manually or chemically-mediatedusing a natural phytohormone which liberates ethylene in the vegetal tissue, producing precocious maturation (Filho *et al*., 2013). Nowadays, the larger producer countries of clove are Indonesia, India, Malaysia, Sri Lanka, Madagascar and Tanzania specially the Zanzibar Island (Kamatou *et al*., 2012). In Brazil, clove is cultured in the northeast region, in the state of Bahia in the regions of Valença, Ituberá, Taperoá, Camamu and Nilo Peçanha, where approximately 8 000hectares are cultivated, producing near 2500 tons per year (Oliveira *et al*., 2007 and 2009).

Concentrations up to 18%of essential oil can be found in the clove flower buds. Roughly, 89%of the clove essential oil is eugenol and 5%to 15%is eugenol acetate and β-cariofileno (Jirovetz *et al*., 2006). The antioxidant activity of aqueous extracts of clove has been tested by different in vitro methods as 2, 2-diphenyl-1-picrylhydrazyl (D P P H); 2, 2'-azino-bis (3-ethylbenzothiazoline-6-sulphonic acid) (ABTS), oxygen radical absorbance capacity, ferric reducing antioxidant power, xanthine oxidase and 2-deoxiguanosine. Clove and plants as pine, cinnamon, and mate proved its enormous potential as food preservative among the other 30plants analyzed (Dudonné *et al*., 2009). The powerful antioxidant activity of both extracts may be attributed to the strong hydrogen donating ability, metal chelating ability and scavanging of free radicals, hydrogen peroxide and superoxide (Gülçina *et al*., 2004). Gülcin *et al.* (2011) studied the antioxidant activity of eugenol by several in vitromethods and discusses the structure-activity relationship (Gülçina *et al*., 2011). Listeria monocitogenes, results reinforces the employment of eugenol to inhibit the growth of these microorganisms in surfaces in contact with food (Pérez-Conesa *et al*., 2014).

Rana *et al.* determined the antifungic activity of clove oil in different strains and reported this scale of sensibility Mucorsp. > Microsporum gypseum > Fusarium monoliforme NCIM 1100 > Trichophytum rubrum > Aspergillussp. > Fusarium oxysporum MTCC 284 (Rana *et al*., 2011). The chromatographic analyses showed that eugenol was the main compound responsible for the antifungic activity due to lysis of the spores and micelles. A similar mechanism of action of membrane disruption and deformation of macromolecules produced by eugenol was reported by Devi *et al.* (2010). The activities of clove oil against different dermatophytes a s Microsporum canis (K C T C 6 5 9 1), Trichophyton mentagrophytes (KCTC 6077), Trichophyton rubrum (KCCM60443), Epidermophyton floccosum (KCCM 11667) and Microsporum gypseumwere tested and results indicate a maximum activity at concentration of 0.2mg/ml with an effectiveness of up to 60%(Park *et al*., 2007). Pure clove oil or mixes with rosemary (Rosmarinus officinalis spp.) oil were tested against Staphylococcus epidermidis, Staphylococcus aureus, Bacillus subtilis, E. coli, Proteus vulgaris, Pseudomonas aeruginosaand results showed minimum inhibitory concentrations between 0.062%and 0.500% (v/v) which is promising as antiinfenccious agents or as food preservative (Fu *et al*., 2007).

The anticandidal activity of eugenol and carvacrol was tested in a vaginal candidiasis model, microbial and histological techniques were employed to compare the samples with the controls. The results suggest that eugenol and carvacrol could be a promising antifungal agent for treatment and prophylaxis of vaginal candidacies (Chami *et al*., 2004). In addition to the wide spectrum of activity of eugenol against bacteria, a study showed that eugenol and cinnamaldehyde at 2 µg/mLinhibited the growth of 31strains of Helicobacter pylori, after 9h and 12h of incubation, respectively, being more potent that amoxicillin and without developing resistance. The activity and stability of those compounds was checked at low pvalues since Helicobacter pyloriresides in the stomach (Ali *et al*., 2005). The results showed the increase in the therapeutic effectiveness of eugenol and the modification of the release when administrated as solid lipid nanoparticles (Garg and Singh, 2011). Beta-cyclodextrin inclusion complexes containing eugenol and clove bud extracts were tested against two common foodborne pathogens, Salmonella entericaserovar Typhimurium LT2and Listeria innocua (Hill *et al*., 2013).

The mechanism evolved has been attributed to the activation of calcium and chloride channels in ganglionar cells (Healthcare, 2004). The voltage dependant effects of eugenol in sodium and calcium channels and in receptors expressed in the trigeminal ganglio also contributed to the analgesic effect of clove (Li *et al*., 2008). The peripheral antinociceptive activity of eugenol was reported by Daniel et al. showing significant activity at doses of 50, 75and 100mg/kg (Daniel *et al*., 2009). This factor is activated by free radicals and results in the expression of gens that suppress apoptosis and induce cellular transformation, proliferation, invasion, metastasis among others (Aggarwal and Shishodia, 2006). With regard to toxicity, eugenol presented strong genotoxic effects (DNA-damaging) on human VH10fibroblast, medium genotoxic effects on Caco-2colon cells and non DNA-damaging effects on HepG2hepatome cells (Slamenová *et al*., 2009). Nevertheless the National Toxicology Program based on several long term carcinogenicity studies concluded that eugenol was not carcinogenic to rats (Ghosh *et al.*, 2005). The cytotoxicity, reactive oxygen species (ROS) production, and intracellular glutathione levels in a human submandibular cell line (HSG cells) of eugenol and isoeugenol was studied by Atsumi *et al*. (2005).

Therefore, it can be concluded that the cytotoxicity of eugenol occurs in a ROS-independent

manner in the presence of oxidative stress. In another work, it was reported that eugenol inhibits the enzyme MMP-9which is related to metastasis in human fibrosarcoma cells suggesting its application for prevention of metastasis related to oxidative stress (Nam and Kim, 2013). Danio rerioand Poecilia reticulatathe medium lethal concentrations (LD50) at 96h were (18.2-5.52) mg/mLin Danio rerioand (21.7-0.8) mg/mLin Poecilia reticulate (Doleželová *et al*., 2011). Eugenol is easily absorbed when administrated by oral route reaching rapidly plasma and blood with mean half-lives of 14.0h and 18.3h, respectively. Acumulative effect has been hypothesized and associated to relieve of neuropathic pain after repeated daily administrations (Guénette *et al*., 2007). Park and Shin (2005) reported the possibility of employment of clove essential oil to control the japonesse terminte Reticulitermes speratus (Kolbe *et al*., 2009). In the same way, Eamsobhana et al. (2009) found that clove essencial oil at 5%posses 100%of repellent activity against the chigger Leptotrombidium imphalu which could be a safer and cheaper alternative to synthetic repelents commonly associated to harmful side effects (Sritabutra *et al*., 2011). The larvicidal methods are one of the most effective strategies to combat dengue, since there is not drug for treatment or a vaccine. Eugenol exhibited interesting results and could be a promising alternative to common insecticide (Barbosa *et al*., 2013). Eugenol, eugenol acetate and beta-caryophyllene were effective in repellency of red imported fire ants Solenopsis invicta (Hymenoptera: Formicidae), being eugenol the fastest acting compound (Zhang *et al*., 2013). Clove oil was also effective spatial repellent for pestiferous social wasps Vespula pensylvanica (Saussure) and paper wasps mainly Polistes dominulus (Christ) (Javahery *et al*., 2012).

Clove oil can also serve as an anesthesia for a variety of fish. However, lengthy exposures can cause mortality and sub-acute morbidity (Hekimoğlu and Ergun, 2012). Clove oil could be employed as suppressor of potato tuber germination by affecting the lipid peroxidation and the enzymes activities of catalase, glutathione-S-transferase, peroxidase, polyphenol oxidase and superoxide dismutase (Afify *et al*., 2012). Syzygium is the largest genus of Mirtaceae family, comprising of about 1200 to 1800 species of flowering plants, which are widely distributed in tropical and subtropical areas of Asia, Africa, Madagascar, and throughout Pacific and Oceanic regions (Cock and Cheesman, 2018). Cloves contain appreciable amounts of volatile oil (used for flavouring foods and pharmaceuticals), which is mainly confined in aerial parts of plant. The yield and composition of volatile oil are variable and are thought to be linked to growing conditions, genetic factors, different chemotypes, geographic origins, and differences in the nutritional status of plant (Al-Maskri *et al*., 2011; Arshad *et al*., 2014 and Hanif *et al*., 2019). Clove is known by different vernacular names in different languages. It is known as qaranful (Arabic), Karamfil (Bulgarian), Ding xiang (Chinese), Kruidnagel (Danish), Garifalo (Greek), Mikhaki (Georgian), Nelke (German), Szegfu (Hungarian), Cengkeh (Indonesian), Choji (Japanese), Jeonghyang (Korean), Krustnaglinas (Latvian), Lwaang (Nepalese), Carvo de India (Portuguese), Mikhak (Persian), Kala (Pashto), Gvosdika (Russian), Clavo (Spanish), Carenfil (Turkish), Garn ploo (Thai), Dhing huong (Vietnamese), and Laung (Urdu/Punjabi/Hindi) (Milind and Deepa, 2011).

Eugenol is the chief bioactive constituent of clove, which is present in concentrations ranging from 9 381.70 to 14 650.00 mg/100 g of fresh plant weight. With regard to the phenolic acids, gallic acid is found in higher concentration (783.50 mg/100 g fresh weight) (Shan *et al*., 2005). Other phenolic acids found in clove are caffeic, ferulic, elagic and salicylic acids. Flavonoids including kaempferol, quercetin and its derivates (glycosilated) are also found in trace amounts. Appreciable amounts of essential oil are present in aerial parts of clove. Chemical profile of this oil is generally found by GCMS analysis (Ahmad *et al*., 2008; Hanif *et al*., 2011and Javed *et al*., 2012). Good quality clove bud contains volatile oil (15 to 20%), which mainly comprises of eugenol (70 to 85%), eugenyl acetate (10 to 15%), and beta-caryophyllene (5 to 12%). Other minor constituents including methyl amyl ketone, kaempferol, gallotannic acid, α-humulene, β-humulene, methyl salicylate, crategolic acid, and benzaldehyde are responsible for the characteristic pleasant fragrance of clove (Mittal *et al*., 2014). Drying may take 4 to 5 days. Well dried buds are hard, crisp and dark brown, having moisture content (<12%), which can be stored for 1 to 2 years in gunny bags. Approximately, 15-20% volatile oil can be produced from dried buds (Thangaselvabai *et al*., 2010). Clove improves memory by relieving mental fog, drowsiness, and depression. Clove oil is mosquito repellent (Trongtokit *et al*., 2005).

Clover oil exhibited significant inhibition against tested strains, with minimum inhibitory concentrations ranging from 0.312-1.25% (v/v) for clove oil, and 0.312- 5% (v/v) for rosemary oil (Abdullah *et al*., 2015). Clove oil was tested against five dermophytes including Trichophyton rubrum, Epidermophyton floccosum, Microsporum canis, Microsporum gypseum, and Trichophyton mentagrophytes. Maximum inhibitory effect (≈60%) against all fungal strains was shown at dose of 0.2mg/ml (Park *et al*., 2007). Results revealed the maximum inhibitory action of clove, mustard, and cinnamon at 1% concentration. Garlic showed good inhibitory action at 3% concentration. However, mint and ginger had negligible inhibition at same concentration (Sofia et al., 2007). Essential oils of Piper nigrum, Syzygium aromaticum, Pelargonium graveolens, Myristica fragrans, Origanum vulgare, and

Thymus vulgaris were evaluated for antimicrobial activity against twenty five bacterial strains, including food borne, animal, and plant pathogens considerable inhibitory action was observed by the volatile oils in a dose dependent behavior (Dorman and Deans,2000). It was also verified that the citotoxic potential of eugenol was more powerful than borneol. With regard to toxicity, eugenol exhibited strong DNA damaging effects on human fibroblast (VH10), medium damaging effects on colon cells (caco-2) and non genotoxic effects on hepatome cells (HepG2) (Slameňová *et al*., 2009).

Generally phenolic and flavonoids are responsible for antioxidant activities of the oil (Khan et al., 2012). Among all, clove showed maximum, whereas, onion showed minimum inhibitory potential (Shobana and Naidu, 2000). Essential oils were added to soybean oil at doses of 0.006 and 0.01g/ml, for thirty days, at accelerated oxidation level. Among all examined oils, the clove oil showed more potent ($p<0.05$) antioxidant activity followed by oregano and sage oils (Ghadermazi *et al*., 2017). Eugenin isolated from clove bud essential oil exhibited a potent inhibitory effect against herpes simplex virus at a dose of 10µg/ml (Chaieb *et al*., 2007). The degree of hepatic damage was evaluated by increased levels of cytopalsmic enzymes (aspartate aminotransferase and alanine aminotransferase). Clove extract restored the normal concentrations of enzymes in serum (Thuwaini *et al*., 2016). The toxicity of clove oil was evaluated in aquarium fish species, Poecilia reticulata and Danio rerio. The LD50 values were (18.2±5.52) mg/ml and (21.7±0.8) mg/ml in Danio rerio and Poecilia reticulate, respectively, at 96 h (Doleželová *et al*., 2011).

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