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THERAPEUTIC POTENTIAL OF CULINARY SPICES

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ABSTRACT: Spices are herbs used as flavoring, aromatic, and coloring agents. The culture of various countries even involves the incorporation of spices daily, not just for their culinary potential but also for the health benefits they provide. Many age-old scriptures suggest incorporating the Indian System of Spices in everyday meals to counter many diseases and keep them at bay. The fact that dietary factors play an important role in the treatment as-well-as prevention of diseases makes it all the more important to conduct research and provide scientific evidence regarding the use of culinary species as potential agents with a therapeutic effect. Such culinary spices have various active phytoconstituents, which can have many therapeutic effects and also prove to be great antimicrobial, antidiabetic, anticancer, *etc*. Generally, most of allopathic drugs are taken individually. Still, unlike them, the spices are consumed in combinations to provide a possible synergistic effect that would be advantageous to us. Also, due to lesser chances of side effects and incorporation of mechanisms to treat any disease right from its root, it would be safer and more practical to head for herbal drugs like these culinary spices for treating all sorts of diseases and various other ailments too.

INTRODUCTION: Plants have been a valuable source of natural products for a long period of time to maintain health and wellbeing, especially with more research studies in the last decade for natural therapies. These culinary spices have been used for not only flavoring food and giving aroma but also to provide antimicrobial properties, relief from asthma, antioxidant power, analgesic activity, relief from Menopausal syndrome, and much more.

Some of the culinary spices studied for their therapeutic potential are mentioned in the following table along with their scientific profile and phytoconstituents that possess significant pharmacological properties.

The present review focusses on the detailed important pharmacological properties of these miniatures, which are potent in even small quantities, as reported by various researchers.

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TABLE 1: CULINARY SPICES AND THEIR PHYTOCONSTITUENTS

Common name	Scientific name	Family	Phytoconstituents present
Celery	*Apium graveolens*	Apiaceae	Flavonoids, Steroids, Carbohydrates, Phenols, Limonene , Selinene Frocoumarin ,Glycosides, Vitamin A, Vitamin C, Caffeic acid , p-coumaric acid ,Ferulic acid , Apigenin, Luteolin, Tannins Saponin, Kaempferol
Aniseeds	*Pimpinella anisum*	Schisandraseae	Shikimic acid, Linalool, Quercetin, Anethole, Gallic acid, Limonene
Lemon grass	*Cymbopogon citratus*	Poaceae	Geranial, Neral, Citronellal, Terpinolene, Geranyl acetate Myrcene, Terpinol, Methylheptenone, Flavonoids, Luteolin, Apigenin, Quercetin, Isoorientin 2'-O-rhamnoside
Bay leaves	*Laurus nobilis*	Lauraceae	Flavones, Flavonoids, Alkaloids, Linalool, Eugenol, Anthocyanin Methyl chavicol, Pinone, Sesquiterpene lactones, Phenols Carotenoids
Oregano	*Origanum vulgare*	Lamiaceae	Vitamin K, Vitamin E, Calcium,, Magnesium, Thymol, Carvacrol Linalool, Myrcene, Cymene, Terpinene, Caryophyllene
Nutmeg	*Myristica fragrans*	Myristicaceae	Myristicin, Licarin a-e, Nectandrin, Malabaricone B, Malabaricone C
Saffron	*Crocus sativus*	Iridaceae	Crocin, Picrocrocin, Safranal, α-crocetin, Lycopene, Zeaxanthin Vitamin B2
Rosemary	*Rosmarinus officinalis*	Lamiaceae	Rosmarinic acid, 1,8-cineole, Camphene , α-pinene, α-terpeniol Borneol, Luteolin, Hesperidin, Gallocatechin, Genkwanin.
Cayenne	*Capsicum annuum*	Solanaceae	Capsaicin , Dihydrocapsaicin , Nordihydrocapsaicin Homodihydrocapsaicin
Thyme	*Thymus vulgaris*	Lamiaceae	p-cymene, γ-terpinene, Thymol, Geraniol, Linalool, Carvacrol, Terpinen-4-ol
Parsley	*Petroselinum crispum*	Apiaceae	Apigenin, Apiin, Myristicin, Coumarins, Apiol
Sage	*Salvia officinalis*	Lamiaceae	Rosmarinic acid, Camphor, Borneol, Quercetin, Chlorogenic acid, Pinene, Thujone, Cineole, Rutin, Ellagic acid, Epicatechin.
Curry leaves	*Murraya koenigii*	Rutaceae	Linalool, Elemol, Geranyl acetate, Myrcene, Allo-Ocimene, α-Terpinene, Neryl acetate
Allspice	*Pimenta dioica*	Myrtaceae	Eugenol, Gallic acid, Ericifolin, Quercetin.
Wild mint	*Mentha longifolia*	Lamiaceae	Pulegone, Menthol, Menthone, Borneol, Isomenthone, 1,8-cineole
Jalapeno	*Capsicum annuum*	Solanaceae	Capsaicin, Dihydrocapsaicin, Coumaric acid, Cinnamic acid, Vanillin, Caffeic acid, Phenylalanine.
Liquorice	*Glycyrrhiza glabra*	Fabaceae	Glycyrrhizin, Glabridin A and B, 18β-glycyrrhetinic acid, Isoflavones
Chicory	*Cichorium intybus*	Asteraceae	Inulin, Coumarins, Sesquiterpene lactones, Anthocyanins, Tannins, Chlorogenic acids.
Marjoram	*Origanum majorana*	Lamiaceae	α-pinene, β-pinene, p-cymene, γ-terpinene, Terpinolene, α-phellandrene, β-phellandrene, Camphene, D-limonene, α-terpinene
Basil	*Ocimum basilicum*	Lamiaceae	Eugenol, ursolic acid, 1.8-cineole, linalool, β-caryophyllene

1. Celery: Celery is a plant native to the Mediterranean regions. Celery also strengthens the heart by reducing blood pressure and lipid content, thus helping prevent cardiovascular diseases.

Celery helps to reduce glucose levels in the body, prevents jaundice, liver ailments, urinary tract obstructions, rheumatic disorders, is antibacterial, and even provides relief from gout [1]. Following are the chemical structures of the phytoconstituents responsible for the therapeutic potential of celery.

FIG. 1: CELERY

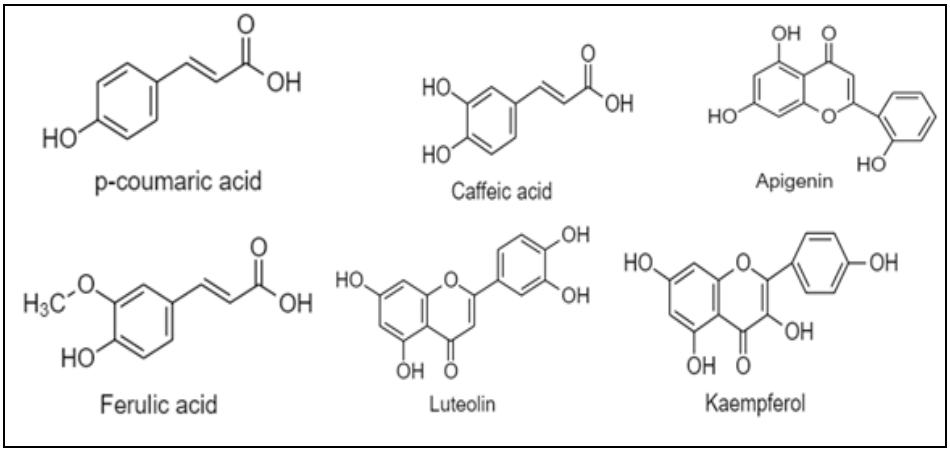

FIG. 2: PHYTOCONSTITUENTS OF CELERY

A study was conducted to determine the antioxidant activity of celery individually and in combination with doxorubicin in rats [2]. Ferric-reducing antioxidizing power (FRAP) and reduced glutathione in liver and blood homolysate were studied and analyzed. The contents of cytochrome p450 in liver homogenate were also studied. It was then found that doxorubicin alone did not have any effect on cytochrome p450, but the combination of doxorubicin with water of leaves and roots of celery showed protective effects which actually increased the ferric reducing antioxidant power in liver homogenate in comparison with animals which were only treated with doxorubicin.

Another study was conducted to investigate as well as analyze the *in-vivo* and *in-vitro* effect of antioxidant flavonoids that had been separated from celery [3]. After this, an ethanolic extract of celery was produced through techniques like column chromatography and crystallization. The IC_{50} values of DPPH, hydroxyl radical, and superoxide radical were found to be 68.0 µg/ml, 48.0 µg/ml, and 0.39 mg/ml, respectively. Also, the antioxidant activities were determined in vivo in the murein models. It was concluded that Apiin was a potent inhibitor of monodialdehyde and lipofuscin, strengthened Total antioxidant activity, and ameliorated the activity of Superoxide dismutase, glutathione peroxidase, and catalase.

The phytochemical screening of phytoconstituents of celery, like flavonoids, tannins, and saponins, was carried out to determine their antioxidant activity [4]. The total methanolic content was found to be higher, followed by ethanol and hexane fraction. The activity of FRAP was found to be higher in comparison with other extracts. Therefore, based on this investigation, it was concluded that the celery plant has antioxidant activity. Regarding the antimicrobial properties, the ethanolic fraction was found to be the most effective against the fungi *Aspergillus flavus*.

A study was conducted to determine the antioxidant activity of essential oil obtained from celery seeds [5]. The chemical compounds were first separated through hydrodistillation. They were then analyzed by mass spectrometry/gas chromatography. It was found that Limonene was the essential oil found in the highest concentration. The antioxidant activity of these essential oils was assessed and analyzed through DPPH and Rancimat apparatus. It was seen that the essential oils whether taken individually or together, both the cases showed antioxidant activity, thus highlighting the antioxidant activity of celery. From the results obtained it was concluded that essential oils of varying concentrations have antioxidant activity. A study was conducted to determine and investigate the antioxidant activity of seed extract obtained from celery [6]. Firstly, ether, water, and ethanol were used to prepare celery seed extracts. The activity of celery seeds was then analyzed using by DPPH assay method. The methanolic extracts showed the highest antioxidant activity. In fact, in the methanolic extract of the entire plant, the seed extract was found to have the highest antioxidant activity. The extracted luteolin and flavonoids could also reduce reactive oxygen. They could also increase superoxide dismutase enzymes which protect against damage. So, these compounds, too, may be responsible for antioxidant activity.

2. Aniseed: These are native to the Eastern Mediterranean regions, Spain, West Asia, Mexico, Egypt, and the Middle East. The main constituent of star anise is shikimic acid which is responsible for its anti-viral properties and use in Influenza A and B medication-Oseltamivir.

Star anise has broad spectrum pharmacological effects, like-GABA ergic, antibacterial, antifungal, antiviral, insecticidal, anticonvulsant, muscle relaxing, anti-spasmodic, reduction of menopausal hot flashes and pain in dysmenorrhea, anti-oxidant and increased glucose absorbing properties. Its hydrochloric extract provides properties [7].

Following are the chemical structures of the phytoconstituents responsible for the therapeutic potential of aniseed.

FIG. 3: ANISEED

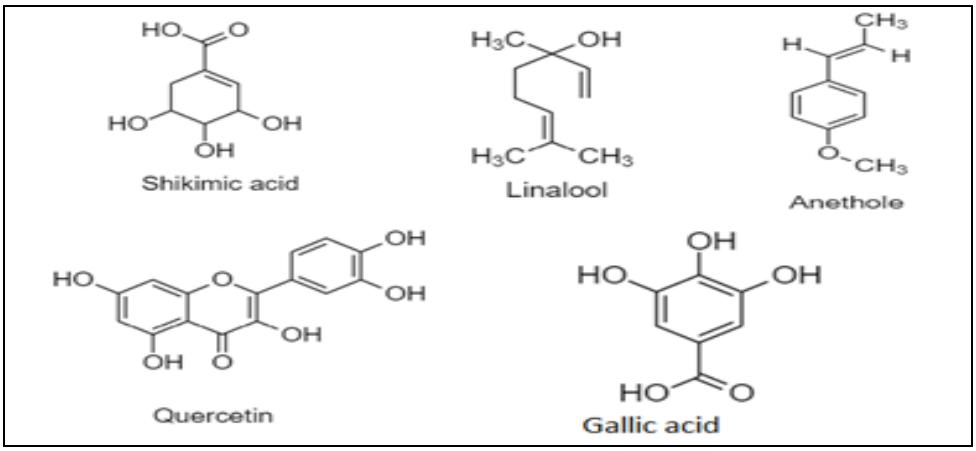

FIG. 4: PHYTOCONSTITUENTS OF ANISEED

A study was conducted wherein the *in-vitro* antibacterial activity of *Pimpinella anisum* fruits extracts was investigated against some pathogenic bacteria [8]. Extracts of its fruit were prepared in different solvents like water, petroleum ether, 50% (v/v) methanol and acetone to test its antibacterial activity against four pathogenic bacteria, *Streptococcus aureus*, through disc diffusion method. It was found that acetone and petroleum ether extracts could not exhibit any antibacterial activity against these bacteria. On the contrary, both aqueous and methanolic extracts exhibited some antibacterial activity. The aqueous extract was found to exhibit better antibacterial properties than methanolic extract.

A study was conducted to investigate the antimicrobial effect of ethanolic and water extract of aniseeds against *Candida albicans* and other bacterial species through disc diffusion method [9]. The antibacterial effect of water extract was found to be effective against *Candida albicans* and against other gram-negative bacteria like *Pseudomonas aeruginosa* and *Escherichia coli*. On the contrary, the ethanolic extract of aniseeds did not show antibacterial activity against *Candida albicans* but other tested bacteria.

Another study was conducted to investigate the effect of anise oil on broiler performance as in broiler nutrition and growth-promoting substances in place of antibiotics [10]. The control group was administered with 0.1% Avilamycin antibiotic. The study groups were administered 100 mg/kg, 200 mg/kg, and 400 mg/kg of anise essential oil. The results revealed that the addition 400 mg/kg of anise essential oil improved the daily live weight gain by 15% compared to the control group. In the control group, only 7% improvement was seen. The screening of antioxidant properties of seven Umbelliferae fruits including *Pimpinella anisum* obtained from Iran was performed in study [11]. Out of all the extracts, *Pimpinella anisum* extract exhibited the strongest antioxidant and free radical scavenging activity. The total flavonoid content of all extracts was also determined by aluminium

chloride technique, which revealed that the extract of *Pimpinella anisum* had the highest amount of flavonoid content. Its ethyl acetate fraction was found to have the highest antioxidant activity as-well-as flavonoid content. Also, antioxidant potency and flavonoid content were found to be directly correlated with each other.

3. Lemon Grass: Lemon grass is a plant native to tropical countries, mainly South-east Asia. It has antifilarial, anti-inflammatory, antidiarrheal, antimutagenic, hypolipidemic, antioxidant, hypocholesterolemic, and hypoglycemic properties [12]. Following are the chemical structures of the phytoconstituents responsible for the therapeutic potential of lemongrass.

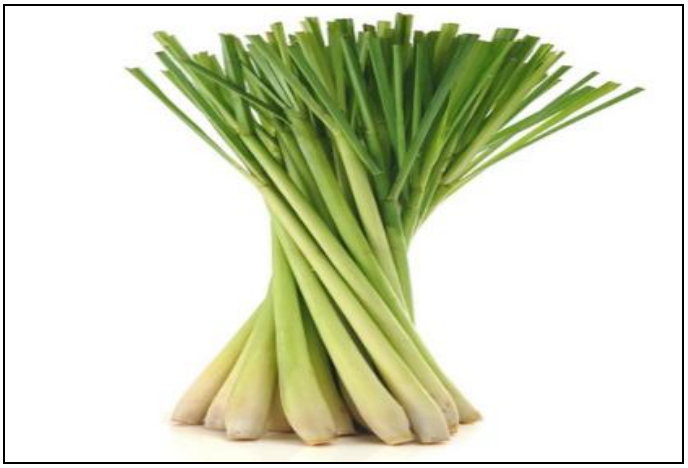

FIG. 5: LEMON GRASS

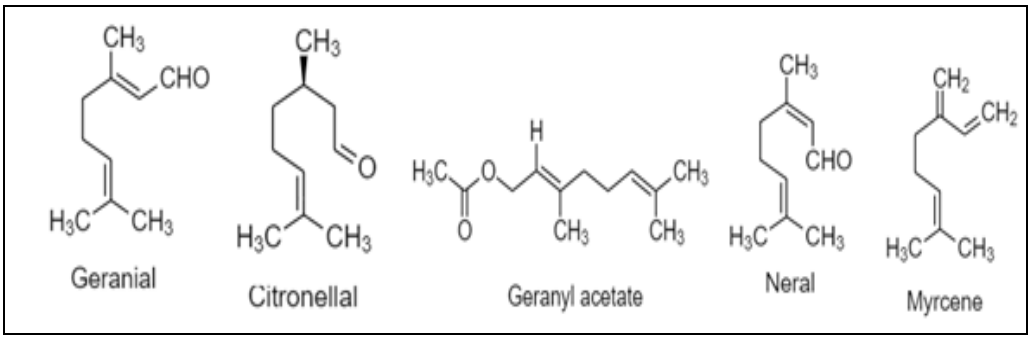

FIG. 6: PHYTOCONSTITUENTS OF LEMON GRASS

A study was performed to determine the anti-microbial activity of essential oils from various Brazilian plants, including *Cymbopogon citrates* [13]. The aerial parts of the plants were steam distilled. Further, the test was conducted by the GC/MS method. The essential oils were tested as ethanol+ water solutions [20 mg/ml]. Streptomycin and Amphotericin B were positive control groups for antibacterial and antifungal effects, respectively. The essential oil of *Cymbopogon citratus* showed significant antibacterial and antifungal against *Bacillus subtilis* and *T. mentagrophytes*, respectively.

On the contrary, it showed marginal/lesser antibacterial and antifungal effects against *M. smegmatis* and Aspergillus, respectively. The *in-vivo* antimalarial effect of essential oil of *Cymbopogon citratus* and *Ocimum gratissimum* on *Plasmodium berghei* infected mice was determined in study [14]. Both plants' essential oils showed significant antimalarial activity against *Plasmodium berghei*. For the positive control group, rats were administered 10 mg/kg of chloroquine, which showed a suppressive activity of 100%. The essential oil of *Cymbopogon citratus* showed maximum antimalarial activity at concentrations 200, 300 and 500 mg/kg of mouse. At same concentrations, the essential oil of *Ocimum gratissimum* suppressed the malarial effect by 55.0%, 75.2% and 77.8%. A study was conducted to investigate the anti-fungal activity of lemon grass oil against some dermatophytes like *Epidermophyton floccosum*, *T. rubrum*, *Trichophyton mentagrophytes* and *Microsporum gypseum* [15].

The antifungal activity of lemon grass essential oil was measured through agar diffusion method, after which the zone of inhibition was measured. The values recorded and it was found that *M. gypseum* showed the maximum values of MIC [235 µgrams/ml] and MLC [310 µgrams/ml], followed by *T. rubrum*, *T. mentagrophytes* and *E. floccosum*. Another study was performed on albino rats to investigate the hypocholesterolemic effect of ethanolic extract of fresh leaves obtained from *Cymbopogon citrates* [16]. Before the extract

administration, physical activities, food intake, and body weight increased. Also, the rat's induced hypercholesterolemia by feeding them egg yolk for 14 days. The doses of 100 mg/kg and 200 mg/kg of body weight were administered orally in the two control groups for 7 continuous days. It was observed that the cholesterol level in rats was reduced after dose-dependent administration of the extract, which further explains its potency as an agent to treat and manage heart diseases. Studies were performed to determine the antioxidant and free radical scavenging effects of *Cymbopogon citrates* [17].

DPPH and superoxide anion assays were conducted which revealed that values ranging between 40 and 68% and 15-32% at 33 and 50 µgms/ml respectively inhibited lipid peroxidation in erythrocytes by 19-71% at 500 µgms/ml but was inactive towards xanthine oxidase at 50 µgms/ml. IC_{50} value came out to be 9-10 µM and inhibited lipid peroxidation in erythrocytes by 70% at a concentration of 100 µgms/ml. In superoxide anion scavenging, the IC_{50} value was 68.8 and 54.2 µM. Caffeic acid inhibited lipid peroxidation by 85% at 100 µgms/ml. A study was conducted to determine the hypolipidemic and hypoglycemic effects of aqueous extract of fresh leaves obtained from *Cymbopogon citratus* [18]. Daily oral dosing of 125-500 mg/kg of fresh leaf aqueous extract was administered in male Wistar rats for 42 days. It was noticed that when administered in rats, the fresh leaf aqueous extract of lemon grass lowered the total cholesterol, low density lipoprotein, very low density lipoprotein and fasting plasma glucose level in a dose-dependent manner. It also increased the plasma high-density lipoprotein dose-dependently but did not show any effects on the level of plasma triglycerides. The neurobehavioral effect of lemon grass essential oil was also studied in mice [19]. The essential oil was obtained from fresh leaves by hydrodistillation method and then administered to Swiss male mice 30 min before beginning the experiment. 0.5 Or 1.0 g/kg dose of essential oil was studied for its anxiolytic effect. The results showed that the essential oil increased sleep duration, delayed PTZ-induced clonic seizures, and blocked the maximal electroshock-induced tonic extensions. It also increased the time spent in open arms of the elevated plus model. These results were recorded in the absence of any motor impairment through rota rod apparatus and open field test.

4. Bay Leaves: Bay leaves are generally cultivated in European, sub-tropical, tropical, and Asian countries. Bay leaves have a variety of phytoconstituents that can decrease the blood cholesterol level and uric acid level, are anti-inflammatory, improve functions of the liver, have anticonvulsant and anti-oxidant properties, produce sedative effects, treat diabetes and migraines, have also been used in traditional medicines to treat rheumatism, sprains, indigestion, used to treat blood dysentery and congestion of kidney, relieve indigestion, constipation, and sore throat and have wound-healing properties [20]. Following are the chemical structures of the phytoconstituents responsible for the therapeutic potential of bay leaves.

FIG. 7: BAY LEAVES

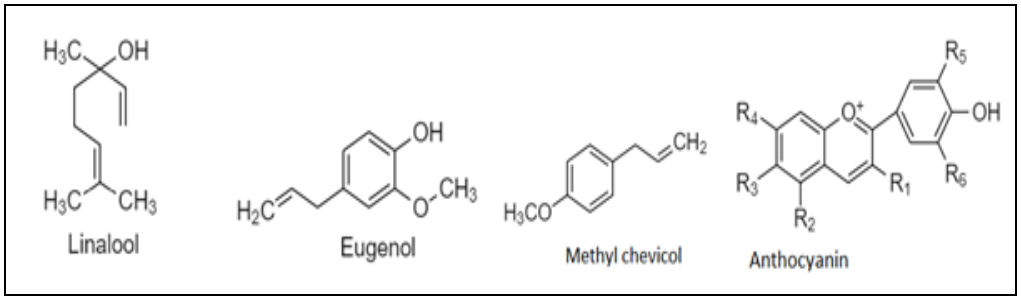

FIG. 8: PHYTOCONSTITUENTS OF BAY LEAVES

A study was conducted to determine and compare the wound-healing activities of *Allamanda cathartica,* and *Laurus nobilis* extracts in Sprague Dawley rats [21]. Many excision and incision wound healing models were used for the same. Four groups were formed, wherein groups 1 and 2 were used as a reference and 3 and 4 as control. Group 3 animals were administered 150 mg/kg/day of *Allamanda,* and group 4 animals were treated with 200 mg/kg b.w. /day of *Laurus nobilis* for 14 days, respectively. For studying incision wound healing, groups 3 and 4 animals were administered doses of *Allamanda* and *Laurus nobilis* respectively for 10 days. In the animals treated with bay leaves extract, the wound closure rate was higher along with more weight of granulation tissue and more content of hydroxyproline content of granulation tissue than animals treated with *Allamanda* extracts. The animals treated with bay leaf extract had a higher number of inflammatory cells and lesser collagen production than those treated with *Allamanda* extract.

Thus, the aqueous extract of bay leaves was found to have better wound-healing activity than Allamanda's. Another study was conducted to investigate the anti-oxidant, and free radical scavenging activity of bay leaf extracts [22]. When bay leaf extract was taken in concentrations of 20, 40, and 60 µgrams/ml in linoleic acid emulsion, it was observed that the concentration of 60 µgrams/ml showed maximum inhibition of peroxidation of lipids-98.6%, which corresponded to strong anti-oxidant activity. The bay leaf extract also showed strong reducing power, DPPH radical scavenging activity, superoxide anion radical scavenging, hydrogen peroxide scavenging, and metal chelating activities at 20, 40, and 60 µgrams/ml. Thus, the bay leaf extract showed strong anti-oxidant activities due to the presence of phenolic compounds. A study was conducted to determine the antimutagenic activity of 3-kaempferyl p-coumarate against Trp-P-2 [23]. IC_{50} value of Trp-P-2 was found to be 1.9 µgrams. This value was found to be close enough to those of existing antimutagens like flavones and flavonols. After its experimental identification, it was separated through the process of chromatography. The desmutagenic action converts the metabolically activated form of Trp-P-2 into its carcinogenic form, which is responsible for the antimutagenic action. Also, this compound was found to have weak bioantimutagenicity and could also suppress the mutagenic action of direct mutagens. A research study investigated the composition and ascaricidal activity of *Laurus nobilis* and *Laurus novocanariensis* essential oils against *Psoroptes cuniculi* [24]. The oils of plants were analyzed with gas chromatography with FID GC/MS detection. Disks of filter paper soaked up with diluted concentrations of 50 µL essential oils. The mortality rates corresponding to different concentrations of essential oils were recorded after 24 hours of contact with mice and were reported and it was found that essential oil from *L. novocanariensis* was found to be better than *L. nobilis* at concentrations of 5% and 10% where it showed mortality rates of 100% at both the concentrations. A pharmacological review of *Laurus nobilis* was performed to determine its antifungal effect against seven strains of fungi pathogenic to plants [25]. This was conducted in *in-vitro* conditions and in 50, 125 and 250 micrograms/ml concentrations. A very effective antifungal activity was observed against the fungus *Botrytis cinerea* using 250 micrograms/ml of *L. nobilis*.

5. Oregano: Oregano is a herb native to Mediterranean hills. Many researches have also been conducted to evaluate the anti-inflammatory, anti-microbial, antiproliferatvie, cytotoxic, cardiovascular preventive properties, and some positive conclusions could be made from the same [26]. Following are the chemical structures of the phytoconstituents responsible for the therapeutic potential of oregano.

FIG. 9: OREGANO

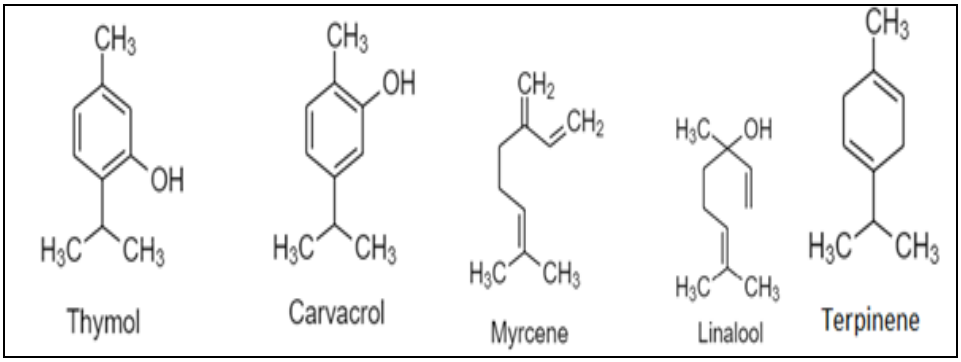

FIG. 10: PHYTOCONSTITUENTS OF OREGANO

A study was conducted to investigate the effect of chitosan in boosting the antimicrobial activity of oregano essential oil in fresh pork meat packed in a modified atmosphere having 70% O_2, 10% N_2, and 20% CO_2 and then stored at a temperature of 4°C for 15 days [27]. Upon observation, it was noticed that a decrease was recorded in the growth of *L. monocytogenes* after treatment with chitosan individually or with oregano essential oil. Also, growth inhibition was seen for up to 15 days with chitosan and 4% oregano essential oil. The total count of viable cells and spoilage bacteria was also found to be reduced. Chitosan and oregano essential oil applied individually also reduced lipid peroxidation [0.62-0.75 mg malondialdehyde/ kg of meat] as compared to control [0.99 mg malondialdehyde/ kg of meat].

Conclusively, the treatment with chitosan and oregano essential helped extend meat's shelf life compared with the control, whose commercial shelf life was 10 days. The research was conducted to study the effect of ethanolic extract of *Origanum vulgare* in treating *Propionibacterium acnes* induced ear edema in mice [28]. For this, they took ICR mice. The test group administered 2 mg/ µl of ethanolic extract from oregano, along with 5% DMSO [dimethyl sulfoxide]. The control group administered a vehicle named DMSO [5%]. 6×10^7 CFU/ 10 µL PBS of *P.acnes* was administered in the right ear by intradermal injection, and 10 µl of PBS [Phosphate-buffered saline] was injected in the right ear. After 24 hours, the ear swelling in mice was measured, and the mice were then euthanized. The results showed that essential oregano oil reduced ear swelling by 32% and ear weight by 37%. A study was conducted to evaluate the effects of ethyl acetate extracts of *Origanum vulgare* in preventing streptozotocin-induced diabetes in C57BL/6 mice [29]. Streptozotocin was administered intra-peritoneally in multiple low doses for 5 consecutive days and at a concentration of 40 mg/kg/day. On the other hand, oregano ethyl extract was also administered intraperitoneally at a concentration of 2 mg for 10 consecutive days, with same-day administration of both. During the evaluation, it was observed that when taken alone, streptozotocin induced the development of 80% of hyperglycemia, and ethyl acetate extract of oregano successfully reduced hyperglycemic development to 15% of mice.

After administration of ethyl acetate extract of oregano, the increased/decreased levels of various cytokines and other important substances were recorded as follows in **Table 1** [51].

TABLE 2: EFFECT OF ETHYL ACETATE EXTRACT OF OREGANO ON INFLAMMATORY CYTOKINES AND OTHER IMPORTANT

Increased Levels	Decreased Levels
Concentration of TNF	Number of F4/80 macrophages
Concentration of IL-10 cytokine	Concentration of IL-1β, IFN-γ, IL-17 and IL-6 cytokines Cell counts of Th1 and Th17

A study was conducted in male Wistar rats and Swiss mice to evaluate the anti-inflammatory and anti-ulcer properties of carvacrol, a major monoterpene in oregano essential oil [30]. The results of dextran and histamine-induced paw edema were recorded, and it was found that under the influence of carvacrol [50 mg/kg] and cyproheptadine [10 mg/kg], histamine showed the highest reduction in edema by 46% and 61% respectively. The results obtained in substance P-induced paw edema were recorded, and it was found that carvacrol [100 mg/kg] showed a higher percentage reduction in edema of 46% as compared to ruthenium red [3

mg/kg]. The results obtained from TPA-induced ear edema were recorded, and it was found that indomethacin [0.5 mg/ear] showed a higher reduction in edema of 55%, compared to Carvacrol [0.1 mg/ear].The results obtained from arachidonic acid-induced ear edema model were recorded, and it was found that indomethacin [2 mg/ear] showed a higher reduction in edema of 57% as compared to Carvacrol [0.1 mg/ear]. Finally, the results obtained from the acetic acid-induced gastric lesions test were recorded, and it was found that 50 mg/kg of carvacrol showed the highest reduction in the area of lesion, the value is 91% reduction.

6. Nutmeg: Nutmeg is an age-old spice first described in the mid-18th century French colonies on the Maluku islands [31]. Its therapeutic effects have been used to treat problems and ailments like gastrointestinal disorders, painful wounds and rheumatic pain and it has also been used as a calming agent. Various pre-clinical trials have been conducted wherein studies focusing on their anxiolytic, anti-infective, anti-oxidative, and anti-inflammatory actions were reported [32]. Following are the chemical structures of the phytoconstituents responsible for the therapeutic potential of nutmeg-

FIG. 11: NUTMEG

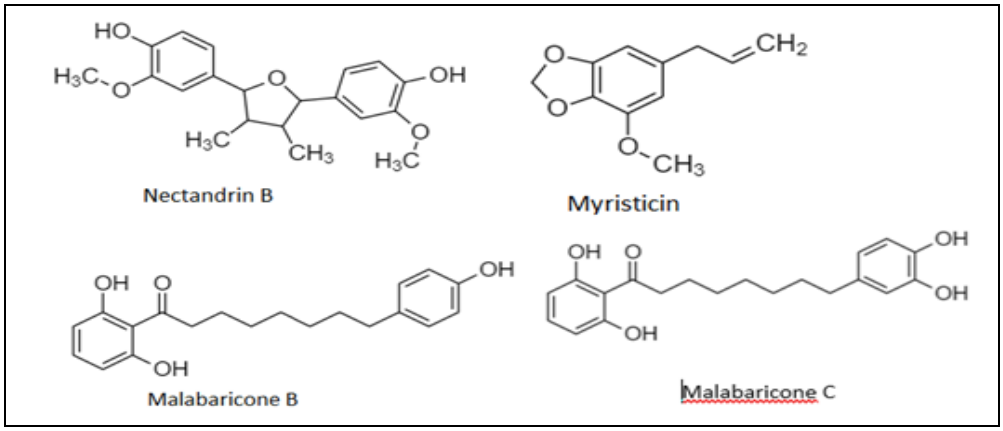

FIG. 12: PHYTOCONSTITUENTS OF NUTMEG

A study was conducted to investigate the hypoglycaemic and hypolipidaemic effects of aqueous nutmeg extract [33]. For this, the rats were given 100 mg/kg dose of nutmeg extract orally, for 30 days after which they were given subcutaneous injections of isoproterenol [85 mg/kg] for 2 consecutive days. In rats administered with isoproterenol, there was an increase in blood glucose level, plasma lipids and lipoprotein lipase activity along with appearance of hyalinization of tissue compared to rats pretreated with nutmeg extract. Also, it was observed that in rats pretreated with aqueous nutmeg extract, the damage to heart tissue was reduced after inducing myocardial infarction by injecting isoproterenol subcutaneously. A research study was conducted to determine the antifungal effects of lignans obtained from *Myristica fragrans* on various pathogenic fungi [34]. It was observed that the foliar infection of *M. grisea*, *P. infestans* and *P. recondita* were controlled to some extent by a dose of 500 mg/l of all three lignans extracted from nutmeg. Also, the barley powdery mildew caused by *B. graminis* could be suppressed to a large extent by 1 day dose of EA6. MDA and NB were found to show significant antifungal effects against plant pathogens causing rice blast and wheat leaf rust and moderate effects against rice sheath blast and tomato late blight. The three lignans of nutmeg could also inhibit and fight these infections *in-vivo* against crown gall *A. tumefaciens*, rice grain rot *B. glumae*, bacterial leaf light of konjac plant *A. konjaci*. The effect of macelignan, a phytoconstituent obtained from nutmeg, was studied in inhibiting melanosome transfer mediated by protease activated receptor-2 in keratinocytes [35].

A 10 M preparation of macelignan, obtained from nutmeg was suggested to be used as a natural depigmenting agent because of its ability to inhibit melanosome transfer and dendrite formation in B16F10 melanoma cells. A study was conducted to analyze constituents found in nutmeg that can inhibit locomotor activity in mice in a wheel cage [36]. When administered at a dose of 0.5 ml/cage, the inhibition of locomotion was highest, and the value of locomotion inhibition was 68.32%. After administration of 0.1 ml/cage nutmeg essential oil, its concentration at different intervals was recorded. After 2 hours of time intervals, the plasma concentration of Myristicin was found to be the highest, the value being 7.1 mg/ml. Conclusively, the plasma concentration of these essential oil components could be correlated with the extent to which inhibition of locomotor activity was exhibited by nutmeg essential oil extract.

7. Saffron: Saffron is a herb cultivated extensively in Iran [37]. It's among the world's most precious and expensive spices. Saffron may be effective in treating a wide spectrum of diseases like coronary heart diseases, stomach diseases, dysmenorrhea, hypertension, and even memory and learning impairments. It can also be used as an antitussive, anticonvulsant, antialzheimer, anti-inflammatory, anti-genotoxic, anti-spasmodic, anti-sclerotic, and anti-oxidant agent [38]. Following are the chemical structures of the phytoconstituents responsible for the therapeutic potential of saffron.

FIG. 13: SAFFRON

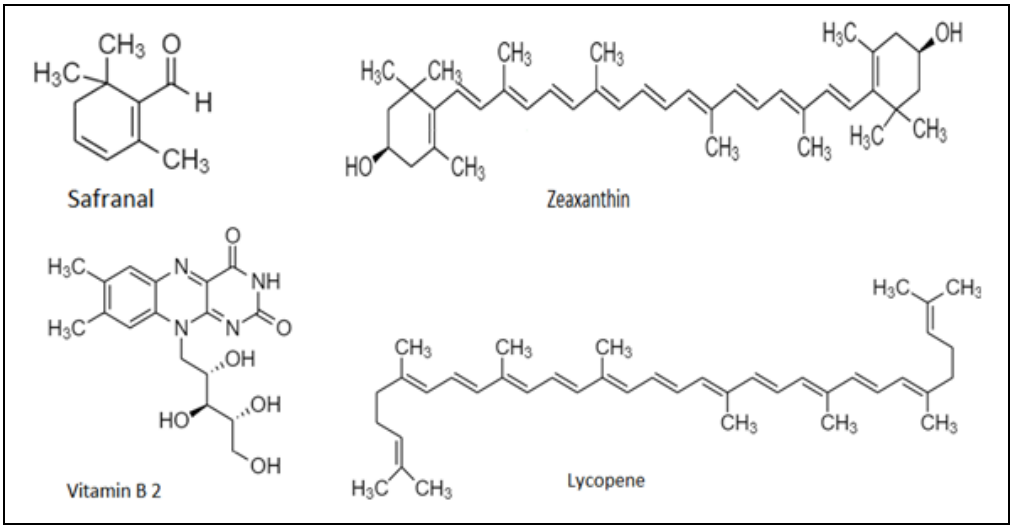

FIG. 14: PHYTOCONSTITUENTS OF SAFFRON

A study was conducted to determine the effects of saffron in chemical-induced convulsions in rats [39]. The anti-convulsant activity of saffron was compared to that of sodium valproate in Wistar albino rats. After injecting 700mg/kg body weight i.v. of Pentylenetetrazol in rats, the test group was administered with 200, 400 and 800 mg/kg body weight of dried powder of saffron and its effects were compared to those of sodium valproate [300 mg/kg body weight] in standard drugs group. It was observed that dried sample of saffron powder delayed the occurrence of convulsions as-well-as delayed the duration of clonic convulsions at concentrations 400 and 800 mg/kg. Another study was conducted to determine the antioxidant properties of saffron through FRAP analysis and Trolox-equivalent antioxidant capacity and inhibitory properties through thioflavin T-based fluorescent assay and DNA binding shift assay [40]. Water: methanol [50:50, V/V] extract of saffron was prepared and was found to exhibit higher antioxidant properties compared with carrots and tomatoes, and also inhibited the amyloid beta fibrillogenesis in a time-dependent manner. Thus,

the study showed promising results regarding using saffron as a potent anti-oxidant and inhibitor of amyloid beta fibrillogenesis. A study was conducted to evaluate the safety of saffron stigma aqueous extract and Crocin in schizophrenic patients wherein a double-blind placebo-controlled trial was performed on them [41].

Along with the normal treatment, one group of male patients was administered 2 doses of aqueous saffron extract at a concentration of 15 mg/day daily. In contrast, the placebo group was administered with 2 doses of Crocin at a concentration of 15 mg/day daily. Upon completion of the trial, it was observed that the aqueous extract of saffron produced no side effects and increased the WBC cell count, which was of no clinical significance as it was under the normal range only.

A study was conducted to evaluate the effects of ethanolic and aqueous extracts of saffron, along with its constituents Safranal and Crocin, in hyperalgesia and allodynia induced by chronic constriction injury model of neuropathic pain in mice using von Frey filaments and acetone drop and radiant heat tests which were performed to evaluate the extent and degree of mechanical allodynia, thermal allodynia, and thermal hyperalgesia respectively [42]. The open-field test was used to evaluate ambulatory behavior. For this, a seven-day trial was carried out using ethanolic and aqueous extracts using concentrations of 50, 100, and 200 mg/kg i.p. Safranal was administered at concentrations of 0.025, 0.5 and 0.1 mg/kg i.p. It was found that dose-dependent these could lessen the behavioral symptoms caused by neuropathic pain.

8. Rosemary: Rosemary is one of the most popular perennial spices native to the Mediterranean region and cultivated worldwide. The antioxidant property of rosemary extract has also been certified by the European Union.

Rosemary has been suggested to exhibit various pharmacological properties, including antibacterial, anticancer, anti-nociceptive, anti-diabetic, anti-inflammatory, antiulcerogenic, anti-thrombotic, antidiuretic, anti-carcinogenic, and hepatoprotective properties [43]. Following are the chemical structures of the phytoconstituents responsible for the therapeutic potential of rosemary.

FIG. 15: ROSEMARY

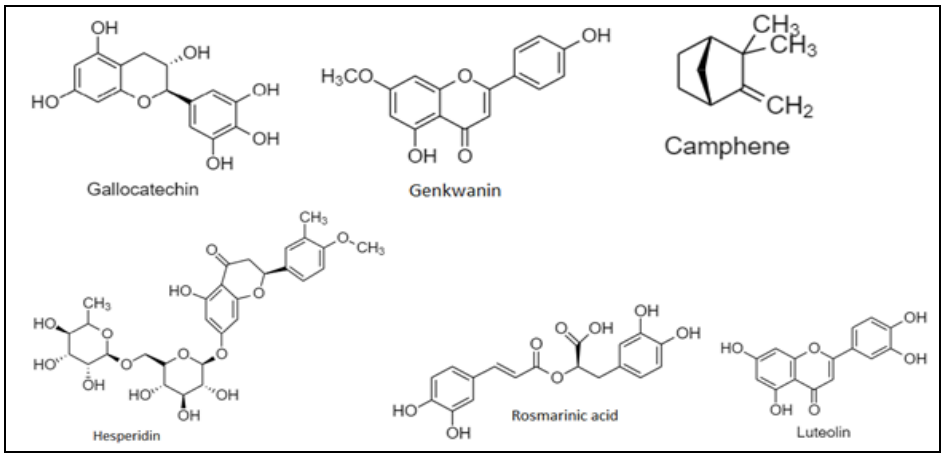

FIG. 16: PHYTOCONSTITUENTS OF ROSEMARY

A study was conducted to investigate the fluoxetine-like anti-depressive behavior of hydroalcoholic extract of rosemary without altering the learning deficit in olfactory bulbectomized [OB] mice [44]. Hydroalcoholic extract and fluoxetine were administered at 10-300 mg/kg and 10 mg/kg p.o., respectively, and for 14 days in the first set of experiments. In the second set of

experiments, serum glucose, hippocampal and cerebrocortical AChE was determined by administering hydroalcoholic extract and fluoxetine at 10 mg/kg each. Upon observation, it was found that hydroalcoholic extract at a concentration of 10-300 mg/kg could reduce the OB-induced hyperactivity and increased anhedonic and exploratory behavior, just like fluoxetine. Another study was conducted to investigate the effects of butylated hydroxytoluene [BHT] and butylated hydroxyanisole [BHA] on the growth and production of aflatoxin in Aspergillus [45]. For the experiment, BHT and BHA were administered in toxigenic and non-toxigenic groups of *Aspergillus flavus*. BHT was administered at a concentration of 0.005-0.020 grams/plate and showed no significant inhibitory effects. BHA administered in the same concentration showed a significant inhibitory effect on the growth and toxigenesis of the sample under investigation.

A study was conducted to determine the effects of Chrysamine G [CG] and its derivatives in reducing amyloid beta-induced neurotoxicity in mice [46]. First, a new compound, HCG, having a low affinity for amyloid beta, was synthesized from the monovalent structure of CG. At a concentration of 0.1-1 µM, it was found that both CG and HCG were equally successful in reducing the deaths caused due to amyloid beta-induced neurotoxicity. This action of CG was attributed to its antioxidant activity. A research study determined the enhanced anti-oxidant effect of α-tocopherol with rosemary extract in inhibiting the oxidation caused due to Fe^{2+} and hemoprotein [47]. A mixture of α-tocopherol and rosemary extract was prepared by mixing 0.035% of each constituent and was then administered in the sardine oil model. During observations, it was noticed that this mixture produced a quite strong antioxidant effect which was better than either extract. The mixture also prolonged the induction period for 10-16 days when compared to the individual effects of α-tocopherol and rosemary extract. Also, compared to the effects of rosemary extract and α-tocopherol alone, the mixture could reduce the decomposition rate of highly unsaturated fatty acids, myoglobin, triglycerides, and hemoglobin.

9. Cayenne: A type of red pepper originated in South America. It has been used as a part of traditional medicine for treating ailments like sore throat, cough, toothache, rheumatism, parasitic infections *etc.* [48]. It may also be used as an antiseptic, appetite-stimulant, antitussive, *etc.* [49]. Following are the chemical structures of the phytoconstituents responsible for the therapeutic potential of cayenne.

FIG. 17: CAYENNE

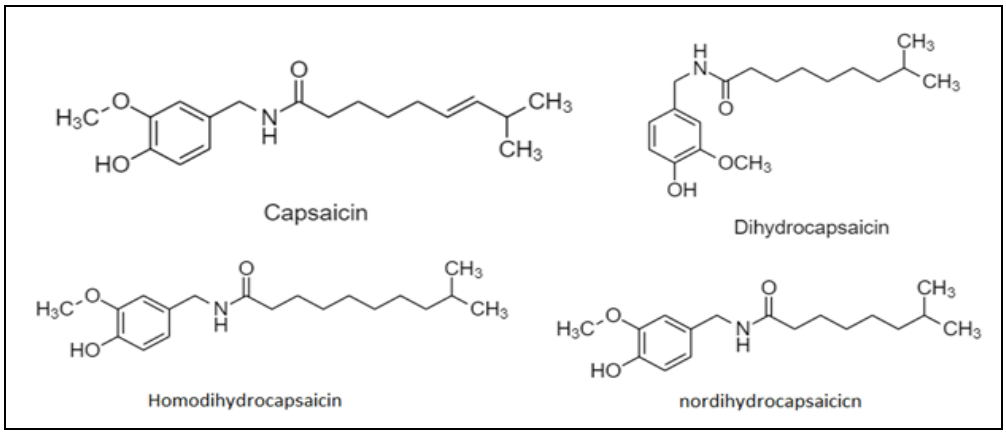

FIG. 18: PHYTOCONSTITUENTS OF CAYENNE

A study was conducted to investigate if plant extracts could stimulate the activity of PPARα receptor, which is responsible for improving the lipid profile through various mechanisms [50]. It was found that along with the extracts of 3 other plants, cayenne was successful in stimulating the

transactivational activities of PPARα receptor. Its phytoconstituent exhibited an EC_{50} value of 49 µM. Thus, the study was concluded with promising results regarding its effects shown on lipid profile, especially for diseases like dyslipidemia which is the major cause of cardiovascular diseases. Another study was conducted to determine the effect of *Aspergillus oryzae*-fermented kochujang on serum cholesterol in hyperlipidemia patients [51]. In this, subjects were divided into kochujang and placebo group. The subjects were administered either 34.5 grams/day of kochujang or placebo, each thrice a day for 12 days. Upon observation, it was noticed that after the administration of kochujang, there was a decrease in total cholesterol and LDL cholesterol levels. At the same time, no such effect was seen on HDL and triglyceride levels.

A random, double-blind, and placebo-controlled trial was conducted to determine the effects of red pepper and turmeric on oxidative stress biomarkers and inflammation in overweight and obese women [52]. The red pepper was administered at a dosage of 1 gram/day while turmeric at 2.8 grams/day. Upon observation and analysis, it was found that there was no difference between pre to post-supplementation measures of oxidative stress biomarkers and inflammation when compared with the placebo. Also, the scores recorded through PLS-DA analysis were quite insignificant.

10. Thyme: Thyme is a plant native to the Mediterranean region. The ancient Egyptians used it in the process of embalming. Thyme has been found to possess various pharmacological properties and can be used as an antimicrobial, antitussive, expectorant, antibroncholitic, carminative, diuretic, carminative, anti-spasmodic, anthelmintic, antioxidant agent, *etc* [53]. Following are the chemical structures of the phytoconstituents responsible for the therapeutic potential of thyme.

FIG. 19: THYME

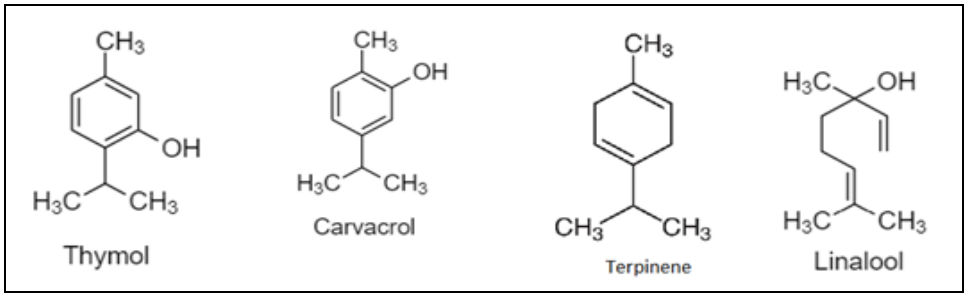

FIG. 20: PHYTOCONSTITUENTS OF THYME

A research study examined the antimicrobial effects of thyme essential oil [54]. The oil was extracted through the process of hydrodistillation. It was observed that at a concentration of 16-256 mg/ml, the oil showed strong inhibitory action against *Streptococcus pyogenes* (MIC-1.9 mg/ml) and *Streptococcus mutans* (MIC-3.6 mg/ml). Also, the MIC values of *C albicans, A. actinomycetemcomitans,* and *P gingivalis* were 16.3, 32 and 32 mg/mL, respectively. Another research was conducted to evaluate the anti-diabetic effect of thymus aqueous extract [55]. For this, 20 grams/day of thymus aqueous extract was administered. After this, it was observed that there was a significant decrease in HB A1C and fasting blood glucose levels. A research study was performed to investigate the chemical composition and antibacterial activity of *Thymus vulgaris* [56]. The essential oil was extracted through hydrodistillation and then analyzed through GC/MS and GC/FID. The major components identified from the essential oil were camphor, camphene, Borneol, β-pinene, α-pinene, and 1, 8-cineole. It was then tested for its antibacterial activity against six gram-positive and gram-negative bacteria. Thyme essential oil exhibited significant antibacterial activity with and MIC range of 0.33-2.67 mg/ml. Also, the essential oil

showed greater antibacterial effects on gram-negative bacteria but poor effects on gram-positive bacteria. A study was conducted to examine the anti-radical, anti-inflammatory, and anti-fungal effects of essential oils extracted from *Apium graveolens* (0.14%) and *Thymus vulgaris* (0.32%) [57]. It was observed that at SC_{50} values of 0.41 and 0.06 grams/l, *Apium graveolens* and *Thymus vulgaris* showed antiradical activity, respectively, while at IC_{50} value of 0.19 grams/l, an anti-inflammatory effect was shown. Also, out of the fungi tested, *Cryptococcus neoformans* was found to be the most sensitive to anti-fungal of *Apium graveolens* and *Thymus vulgaris*. A research study was carried out to examine the effects of thyme on broiler diet and cytokines' efficiency in their gene expression profile [58]. It was observed that at a concentration of 5 g/kg, thyme improved body weight, feed intake, increased white blood cell, lymphocyte count, nitric oxide and IgG levels while enhancing the performance of broilers and their immunity.

11. Parsley: Parsley, a culinary herb native to the Mediterranean region. A lot of extensive research has revealed that it can be used as a menorrhagic, antimicrobial, antianemic, anticoagulant, antihyperlipidemic, hypoglycaemic, hypouricemic, antihepatotoxic, antioxidant, antihypertensive, diuretic effects *etc.* [59]. Following are the chemical structures of the phytoconstituents responsible for the therapeutic potential of parsley.

FIG. 21: PARSLEY

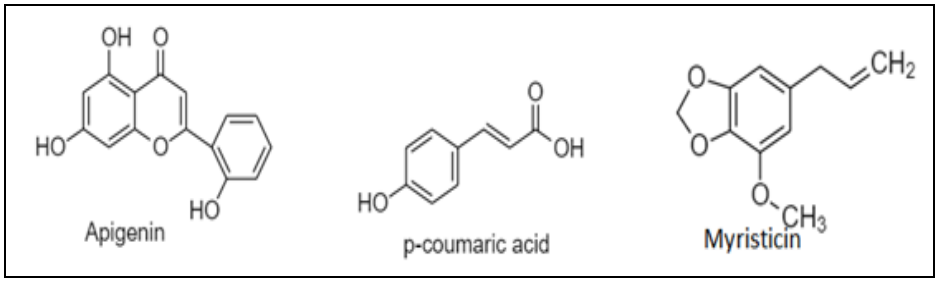

FIG. 22: PHYTOCONSTITUENTS OF PARSLEY

The *in-vivo* anti-diabetic and hepato-protective effects of leaves obtained from parsley were examined in a research study [60]. For this, their aqueous was prepared and administered in STZ-induced diabetic rats at a dose of 5 g/kg for 28 days. The study showed promising results wherein no change in body weight was recorded, while the levels of blood glucose and serum ALT and ALP had decreased significantly compared to the control group. Further, the hepatocytes were improved, and the degenerative changes were also reduced. A study was performed to examine the in-vitro antibacterial effect of hot water and cold water extract of leaves obtained from parsley[61]. For this, 100, 150, 200, and 250 mg/ml of parsley extracts were administered in *Staph pyogenes*, *Staph aureus* and *Pseudomonas aeruginosa*, which were taken from a patient suffering from burn infection. The study showed promising results, wherein both extracts showed anti-bacterial activity. Also, the inhibition zone of hot water extract was found to be better and larger than that of cold water extract. A research study was performed to analyze the antibacterial and antifungal effects of essential oil extracted from parsley along with its chemical composition [62]. After essential oil extraction through hydrodistillation and chemical composition determination through gas chromatographic-mass spectroscopic analysis, the major compounds were apiol, myristicin, and phenylpropanoids terpenoid and β-phellandrene. After performing antibacterial assays, it was found that parsley essential oil was successful in inhibiting the growth of all test bacteria and had MICs ranging from 0.04-1.00 mg/ml. It also showed bacteriostatic activity at lower concentrations than at least one of the controls. After performing antifungal assays, parsley essential oil showed fungistatic effect on

the growth of all fungi. Also, its fungicidal concentrations were found to be 5-62.5 times higher than those of controls.

12. Sage: Sage is a plant native to Mediterranean and the Middle East. It has been found to exhibit an array of pharmacological effects and thus can be used to treat seizures, gout, rheumatism, ulcers, hyperglycemia, inflammation, tremor, dizziness, diarrhea, paralysis, *etc.* It can also be used an anti-cancer, anti-nociceptive, anti-inflammatory, antioxidant, antimutagenic, antimicrobial agent *etc.* [63].

Following are the chemical structures of the phytoconstituents responsible for the therapeutic potential of sage.

FIG. 23: SAGE

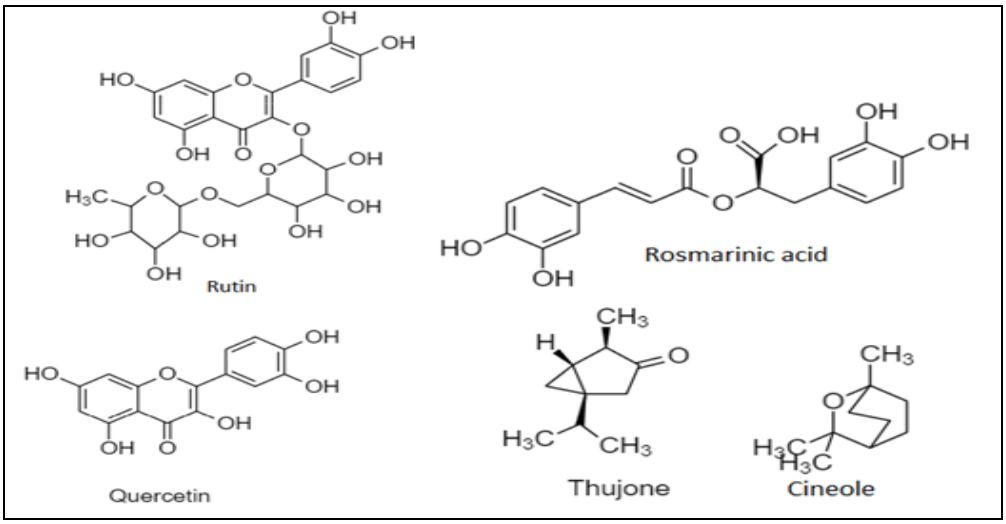

FIG. 24: PHYTOCONSTITUENTS OF SAGE

A research study was performed to investigate the effects of the alcoholic extract of sage on memory and cognitive functions in patients suffering from mild to moderate Alzheimer's disease [64].

For this, randomized and placebo-controlled trials were carried out wherein the patients were administered with 60 drops of the alcoholic extract every day for 16 weeks. After the specified period, it was observed that there was a significant improvement in the memory and cognitive functions in patients administered with the extract, while more frequent agitation was observed in patients of placebo.

Another study was conducted to examine the nephroprotective effect of rutin (a phytoconstituent of sage) on hexachlorobutadiene (HCBD) induced nephrotoxicity in female rats [65].

24 hours after administration of 100, 500 and 100 mg/kg i.p. of rutin followed by 100 mg/kg i.p. injection of HCBD after 1 hour, it was noticed that there was a decrease in protein, serum creatinine and urea. Further, no such effect was seen on the levels of urine glucose. Pretreatment with rutin was also successful in reversing the depletion in thiol content and elevation in lipid peroxidation due to injection of HCBD. Another study was conducted to investigate the effect of sage hydroalcoholic (HA) extract on vincristine-induced neuropathy in NMRI male mice [66].

Formalin induced pain response in first and second phase, while administration of HA extract before it was effective in decreasing its pain response in second phase. Vincristine increased pain responses in the second phase and HA extract was effective in treating that too.

When compared with the analgesic effects of morphine, it was observed that morphine showed such effects in first phase while HA extract showed the effects in second phase. A randomized,

placebo-controlled trial was conducted to investigate the effects of ethanolic extract of sage in improving memory and attention of healthy old volunteers [67]. 167-1332 mg of this ethanolic extract was administered 1, 2.5, 4 and 6 hours before checking for results which revealed improved attention and memory in the volunteers.

13. Curry Leaves: Curry leaves are herb of Indian origin and are of great medicinal importance. They can be used as anti-inflammatory, anti-tumor, anti-oxidant, hypoglycemic, anticancer agents, *etc*. Curry leaves have also been used extensively in the Ayurvedic system of medicine [68]. The phytoconstituents responsible for the therapeutic potential of curry leaves are.

FIG. 25: CURRY LEAVES

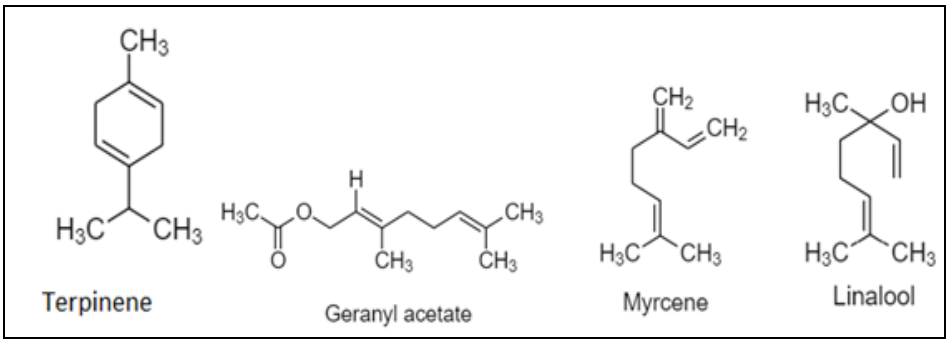

FIG. 26: PHYTOCONSTITUENTS OF CURRY LEAVE

A study was conducted to investigate the antioxidative effects of curry leaves in palm olein using deep-frying and accelerated studies [69]. In tests such as free fatty acid, Oxidative Stability Index, polar and polymer compound content, anisidine value and iodine value, it was observed that 0.2% extract was successful in slowing down the deterioration of oil oxidation and was slightly less efficient than 0.02% butylated hydroxytoluene. In the case of fries, it was observed that the extracts successfully improved the flavour, colour, acceptability and quality of fries.

Studies were also conducted to determine curry leaf extracts' anti-inflammatory and anti-cancer effects in male Swiss albino mice [70]. DAL (Dalton's Ascitic Lymphoma) cells were injected i.p. in mice, 2 days after which 7 mg/kg of SU II was injected while 20mg/kg of 5-fluorouracil was used as reference.

It was found that on 16th day after injection, a reduction in the number of cancer cells and tumour weight was observed, which is suggestive of the protective effect in DAL. A study was performed to examine the wound healing effects of *Murraya koenigii* leaves extract[71]. 65 mg/kg of leaf extract was administered in male albino rats. After its administration, it was found that the leaf extract acted against the inflammatory cells and also caused a reduction in the deposition of collagen. The anti-amnesic effect of curry leaves extract was investigated through a study conducted in aged mice [72]. The aged mice were given a diet containing 2%, 4%, and 8% w/w extract for a time period of 30 days.

After 30 days, it was observed that different concentrations of extracts were successful in reducing the amnesia caused due to diazepam (1 mg/kg i.p.) and scopolamine (0.4 mg/kg i.p.). Also, the extract successfully reduced the total cholesterol levels and brain cholinesterase activity.

14. Allspice: Allspice is a plant native to the tropical forests of South and Central America, the West Indies, and Southern Mexico. It is known to exhibit anti-bacterial, anti-neuralgic, analgesic, anti-hypertensive, anti-prostate cancer, anti-breast cancer properties *etc.* [73]. Following are the chemical structures of the phytoconstituents responsible for the therapeutic potential of allspice.

FIG. 27: ALLSPICE

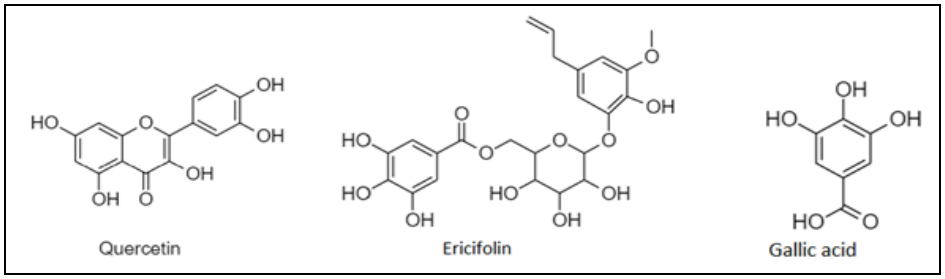

FIG. 28: PHYTOCONSTITUENTS OF ALLSPICE

A study was conducted to investigate the antioxidative effects of polyphenols obtained from berries of allspice [74]. In the DPPH radical scavenging test, it was observed that all the isolated compounds, except for kaempferol and its glycosides, showed high radical scavenging activity in the concentration range of 3.125-50 µM. A research study was conducted to determine the anti-plasmodial effects of eugenol, a phytoconstituent found in allspice [75].

When tested against Plasmodium falciparum (FCR-3), a chloroquine-resistant strain, it was found that eugenol showed an IC50 value of 753 µM. This value was far less than those recorded for other phytoconstituents. A study was conducted to investigate the antiviral activity of eugenol against HSV-1 and HSV-2 viruses [76]. It was found that eugenol inhibited the growth of HSV-1 and HSV-2 with IC_{50} Values of 25.6 µg/mL and 16.2 µg/mL, respectively.

The study also revealed the presence of some interactions between eugenol and acyclovir, an antiviral drug. Further, eugenol also successfully delayed the development of keratitis induced in mouse models due to herpes-virus. Another study was conducted in ICR mice to determine the analgesic activity of eugenol [77]. It was observed that when administered orally in a concentration of 1-10 mg/kg, it exhibited anti-nociceptive activity in a dose-dependent manner as evident from the contractions produced in the body. The effect could be maintained for a minimum of 30 min. The effect of Gallic acid was investigated in an animal model of Parkinson's disease (PD) through a research study [78].

Animals of the test group received 8 µg/2 µL 6-hydroxydopamine dissolved in normal saline containing 0.01% ascorbate or vehicle in the right Medial forebrain Bundle (MFB), which led to an impairment in motor functions and pallidal electrical power. After administration of 200 mg/kg of Gallic acid, it was observed that it could improve motor dysfunctions and gamma wave power in rats having PD.

15. Wild Mint: Wild mint is a plant native to the Mediterranean regions, Australia, North Africa, and Europe. Some extensive research have revealed that it can exhibit a myriad of pharmacological properties which means it can be used as an anti-microbial, anti-hemolytic, anti-bacterial, anthelmintic, antioxidant agent *etc* [79]. Following are the chemical structures of the phytoconstituents responsible for the therapeutic potential of wild mint.

FIG. 29: WILD MINT

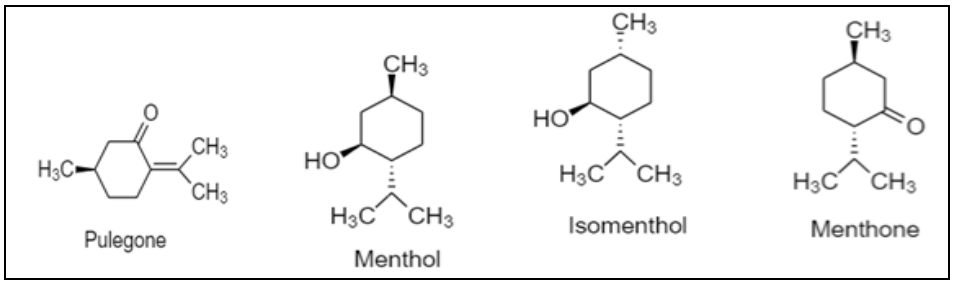

FIG. 30: PHYTOCONSTITUENTS OF WILD MINT

A study was conducted to determine the medicinal use of *M. longifolia* in diarrhoea and gut spasm through its Calcium channel-blocking activity [80]. It was observed that at a concentration range of 100-1000 mg/kg, *M. longifolia* crude extract provided a protection of 31-80% from diarrhoea in castor oil-induced diarrhoea model. The effects produced by it were similar to those of loperamide. Further, in isolated rabbit jejunum preparation, *M. longifolia* crude extract inhibited spontaneous as-well-as-high K^+ induced contractions, with respective EC_{50} values being 1.80 and 0.60 mg/ml.

Another study was conducted to determine the antipyretic and anti-nociceptive activity of aqueous leaf extract of *Mentha longifolia* in rats and mice [81]. The investigations were done using lipopolysaccharide (LPS)-induced pyrexia in rats and acetic acid and hot plate analgesia tests in mice. It was observed that at a concentration of 37.5-150 mg/kg i.p. the aqueous leaf extract reduced LPS quite significantly. At a concentration of 6.25-100 mg/kg i.p. it reduced the writhes induced by 3% acetic acid. Further, at a concentration of 25-400 mg/kg i.p., the leaf aqueous extract delayed the reaction time of mice in the hot plate test in mice. A study was conducted in rats to examine the ileal relaxation induced by leaf extract of wild mint [82]. The; last portion of the ileum of a rat was first mounted on an organ bath and was then contracted by carbachol (CCh, 10 microM), KCl (60 mM), and BaC12 (4 mM). After this, it was treated with 0.0625-1 mg/ml of hydroalcoholic extract of leaves obtained from *M.longifolia*. It was observed that in cumulative concentrations and with the same potency, the extract successfully inhibited the contractions induced by carbachol, barium chloride, and potassium chloride. Also, when tested against concentrations induced by calcium chloride, the extract inhibited those, too, in a concentration-dependent manner (0.25-1 mg/ml).

16. Jalapeno: Jalapeno is a type of pepper native to Mexico [83]. Some extensive research has revealed that various extracts and volatile oils obtained from jalapeno can be used as strong and potent anti-bacterial agents [84]. Following are the chemical structures of the phytoconstituents responsible for the therapeutic potential of jalapeno.

FIG. 31: JALAPENO

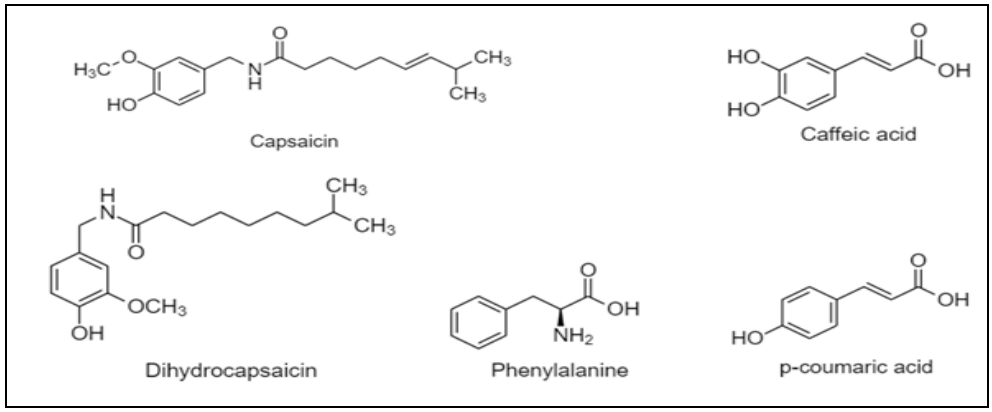

FIG. 32: PHYTOCONSTITUENTS OF JALAPENO

A study was conducted to determine the antimicrobial properties of different extracts of jalapeno prepared in sterilized hot water and varying concentrations of methanol and ethanol (70% and 95% in both) [85]. The antibacterial assays were conducted against *Listeria monocytogenes*, *Escherichia coli* O157:H7, and *Salmonella enterica*. The diameter of growth inhibition was then measured. It was observed that *Listeria monocytogenes* was more susceptible to the extracts than *E. coli* or *Salmonella* isolates. Also, the ethanolic and methanolic extracts were found to exhibit better results than sterilized hot water. Another study was conducted to investigate the antimicrobial activities of carvacrol and Cinnamic acid-phytoconstituents of jalapeno, in freshly-cut melon and kiwi fruit at a temperature of 4°C and 8°C [86].

When dipped in a 5-15 mM carvacrol solution, the total viable counts in kiwi fruit were reduced, but some discoloration and bad odour were observed. Further, at 1 mM concentration of carvacrol solution or Cinnamic acid, the total viable count was reduced at both 4°C and 8°C. Further, treatment of honeydew melon with 1 mM solution of carvacrol and Cinnamic acid also extended the lag phase of microbes. Also, on day 3 of treatment, the viable counts were further reduced. A study was conducted a study to determine the inhibitory effects of jalapeno extracts on food borne pathogenic bacteria [87]. Different Capsaicinoids were separated from jalapeno. Upon observation, it was found that m-coumaric acid and Cinnamic acid were effective in showing inhibitory activity on four of the tested bacteria. It was observed that *B. sereus* and *S. sereus* were the most susceptible to these compounds with an inhibition diameter of and 8.2 and 6 mm for cinnamic acid and 10 and 9.8 mm for m-coumaric acid. Listeria was also inhibited by m-coumaric (6.2 mm) acid and Cinnamic acid (5 mm). The antimicrobial properties of *Capsicum* species were also examined in a research study [88]. Two phytoconstituents separated, capsaicin and Dihydrocapsaicin were also tested for their antimicrobial properties. Further, the plain and heated extracts of *Capsicum* species were tested for their antimicrobial properties using filter disk assay. It was observed that in the presence of extracts, a stimulatory effect was produced on *C.albicans*. Also, both cooked and uncooked extracts partially inhibited *Bacillus cereus* and *Bacillius subtilis*. Most of the cooked and uncooked extracts partially or completely inhibited *C. tetani* and *Clostridium sporogenes*. Similarly, *Streptococcus pyogenes* was also inhibited due to the effect of both cooked and uncooked extracts of fresh *Capsicum* leaves.

17. Liquorice: Liquorice is a plant native to the Mediterranean regions, India, China and Russia. It has a lot of therapeutic potentials and thus can be used as an anti-bacterial, antidiabetic, anti-inflammatory, anti-viral, anti-oxidant *etc.* [89]. Following are the chemical structures of the phytoconstituents responsible for the therapeutic potential of Liquorice.

FIG. 33: LIQUORICE

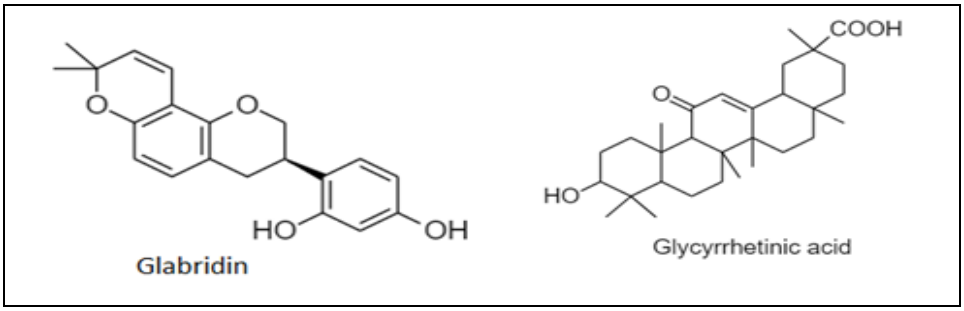

FIG. 34: PHYTOCONSTITUENTS OF LIQUORICE

A study was conducted to determine the effects of Glabridin, obtained from liquorice, in reversing learning and memory deficit in diabetic rats [90]. 5, 25 and 50 mg/kg of Glabridin was injected p.o. in streptozotocin-induced diabetic rats, and the results were evaluated 30 days later. It was observed that at a dose of 25 and 50 mg/kg, there was an improvement in the learning and memory of non-diabetic rats. In contrast, the same dose successfully reverses the learning and memory deficits of diabetic rats. Further, no improvements were recorded at low dose. A study was conducted to investigate the efficacy of liquorice root extract in decreasing the transaminase activities in non-alcoholic fatty liver through a randomized controlled trial [91].

After 2 months of administering a capsule of 2 grams aqueous root extract/day, it was observed that the mean alanine aminotransferase (AMT) and mean aspartate aminotransferase (ALT) levels had decreased significantly. No significant difference was recorded in the levels of BMI, before and after the study was conducted. Another study was conducted to examine the hepatoprotective effects of liquorice aqueous extract against CCl_4 induced oxidative damage in a rat model [92]. The extract was administered at a concentration of 100-300 mg/kg for a period of 15 days. The extract exhibited promising results wherein it was observed that the aqueous extract of liquorice was successful in arresting inflammatory cytokine production and in the stimulation of anti-oxidant enzymes. A study was conducted to investigate the effects of Glabridin, a phytoconstituent of liquorice extract in potentiating the effects of potentiation on GABAA receptor-mediated responses in dorsal raphe neurons [93]. A dose of 10-12-10-8 M of Glabridin was administered in isolated dorsal raphe neurons of rats. The extract showed promising results, wherein it successfully produced sedative and hypnotic effects by potentiating GABAergic inhibition in dorsal raphe neurons by the $GABA_A$ receptor. The research was conducted to study and examine the various topical agents available for managing hyperpigmentation [94]. *In-vivo* double-blind clinical trials were conducted in human patients wherein 20% of glycyrrhizinic acid, a phytoconstituent of liquorice, was administered at a dose of 20% for 2 weeks. After 2 weeks, it was observed that in patients administered the dose, there was a reduction of erythema, oedema and itching sores. Another study was conducted to determine the antiviral effects of water extract of Glycyrrhiza in inhibiting enterovirus 71, in the cell line of human fibroblast cell [95]. The study administered 0.1 µg/ml of extract in an *in-vitro* human foreskin cell line. It was observed that the dose was successful in protecting the host cells from enterovirus 71. Further, it was also found that the extract at a concentration of 3000 µg/ml produced only 30% cytotoxicity in the host cells.

18. Chicory: Chicory is a plant grown mostly in India, north-western Europe, South Africa, and Chile. It may exhibit a lot of health-promoting activities and thus can be used as an anti-bacterial, anthelmintic, antiviral, antimutagenic, antifungal, antihepatotoxic, anticarcinogenic, anti-oxidative, immune-stimulant properties, *etc.* [96]. Following are the chemical structures of the phytoconstituents responsible for the therapeutic potential of chicory.

FIG. 35: CHICORY

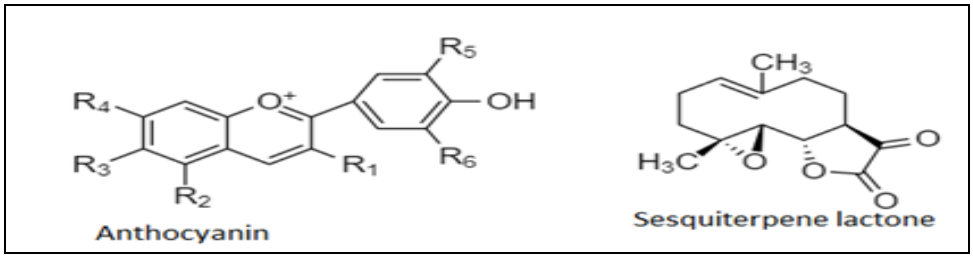

FIG. 36: PHYTOCONSTITUENTS OF CHICORY

A study was conducted to determine the anti-hyperuricemic effects of chicory [97]. It was found that after the administration of 16.7g/kg per day pf chicory, 13.3g/kg per day of chicory, and 6.6g/kg per day of chicory had decreased the serum urate levels in rats induced with hyperuricemia using 10% fructose. Another study was conducted to determine the effects of microwave cooking on antioxidant effects of chicory leaves for the first time [98]. Increase in bio actives responsible for enhancing consumer health was found in food after it was chicory leaves were pre-treated in a microwave. The research was conducted to determine chicory's cardioprotective effects by inhibiting oxidative stress and inflammatory response [99]. It was found that after administering 250 mg and 500 mg/kg of chicory seed extract, its cardioprotective effects were observed through inhibition of inflammatory response and oxidative stress. A study was conducted to determine the larvicidal activity of chicory against the mosquito vectors of dengue fever, malaria, and filariasis [100]. It was found that the methanol extract of roots of *C.intybus* exhibited and LC_{50} value of 64.56, 40.15 and 18.88 and LC_{90} values of 247.54, 231.28 and 107.16 µg/ml against *Cx. quinquefasciatus*, *Ae. aegypti* and *An. stephensi*. Another study was conducted to determine the anthelmintic effects of chicory extract on *C.oncophora* eggs [101]. It was observed that a dose of 2500 µg extract/ml of chicory inhibited the eggs by 95% at EC_{50} value of 619 µg extract/ml. Further, after 12 hours of incubation with ≥500 µg extract/ml of chicory, the adult worms were totally paralyzed. Also, after 48 hours of incubation with ≥250 µg extract/ml of chicory, worm motility was completely inhibited.

19. Marjoram: Marjoram is a herb cultivated in the regions of Asia, North Africa, Hungary, Portland, Spain, Egypt, Portugal, Germany, and France. It might act as a cardioprotective, antioxidant, anti-platelet, antiprotozoal, antifungal, antibacterial, antimetastatic, antiatherosclerosis, antitumor, antiulcer, anti-cholinesterase activity *etc.* [102]. The chemical structures of the phytoconstituents are responsible for the therapeutic potential of marjoram.

FIG. 37: MARJORAM

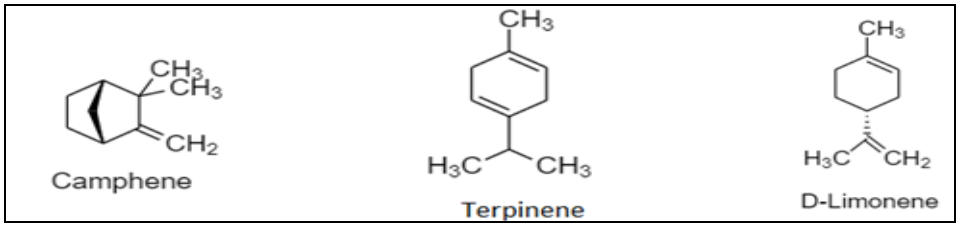

FIG. 38: PHYTOCONSTITUENTS OF MARJORAM

A study was conducted to test and determine the antibacterial effect of *O. majorana* essential oil against *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas aeruginosa* [103]. For this, 2000 µg/ml of essential oil was tested against a standard of 50 µg/ml of amoxicillin and a control of 2% DMSO. It was concluded from the results that *E. coli* and *P. aeruginosa* were more sensitive to the essential oil (MIC 31.25 µg/ml) as compared to *S. aureus*. A study was conducted to determine the

antidiabetic activity of *O. majorana* ethanolic extract [104]. For this, different doses- 100, 200, and 400 mg/kg, of the extract were administered. The results concluded that the extracts had lowered the blood glucose level while also enhancing the serum insulin levels in STZ diabetic rats. Further, compared to the untreated diabetic rats, there was also a decrease in total cholesterol, triglycerides, VLDL and LDL levels in treated diabetic rats along with enhanced HDL levels in the same. Another study was conducted to determine the antifungal effect of *O. majorana* essential oil against *Botrytis cinerea*, *Aspergillus niger*, *Penicillium expansum* and *Monilinia fructicolia* [105].

2000, 1000 and 500 ppm of the essential oil were tested against a positive control of azoxystrobin (80 µl/100ml) and negative control of Tween 20(0.2%). It was thus concluded that at a concentration of 2000 ppm, the essential oil showed effects against *Aspergillus niger*, *Penicillium expansum*, and *Monilinia fructicolia*. Further, the Fungal Spore Germination Assay results also showed that the essential oil showed dose-dependent inhibitory action on spore germination of *Monilinia fructicolia.* A study was performed to determine the antiproliferative effects of *O. majorana* ethanolic extract against human colorectal cell lines HT-29 and Caco-2 [106]. It was found that the extract showed antiproliferative activity against human cell lines HT-29 at IC_{50} value of 342 µg/ml and against human colorectal cell lines at IC50 value of 296 µg/ml. Another experiment was conducted to determine the antioxidant activity of ethanol/water extracts produced by ultrasound-assisted extraction, and pressurized liquid extraction of *O. majorana leaves* [107]. It could be concluded from the results that the TEAC value was 1.81 ± 0.02 mmol TE g/L dry extract and 1.52 ± 0.04 mmol TE g/L dry extract for pressurized liquid extraction (ethanol/water) and ultrasound-assisted extraction (ethanol/water), respectively. A study was conducted to determine the antioxidant activity of *O. majorana* essential oil [108]. The methods used: iron-chelating power, radical scavenging DPPH and reducing power assay. It was found that good anti-DPPH, reduction power and the iron-chelating effect was shown with the respective IC_{50} values being 0.3 mg/ml, 0.4 mg/ml and 23 mg/ml. The individual values of anti-DPPH, reduction power and iron-chelating effect of ethanolic extract were found to be 11.5 mg/ml, 5.6 mg/ml, and 67.2 mg/ml.

20. Basil: Basil, also known as the 'Elixir Of Life' and 'Queen Of Herbs' in Ayurveda, is a herb grown mainly in the Indian subcontinent[109]. It is known to keep the body free of all ailments and problems. It has been reported to be an agent for curing bronchitis, pyrexia, rheumatism, epilepsy, asthma, hematological diseases, parasitic infections, cardiovascular diseases, and neurocognitive disorders [110, 111]. Following are the chemical structures of the phytoconstituents responsible for the therapeutic potential of basil.

FIG. 39: BASIL

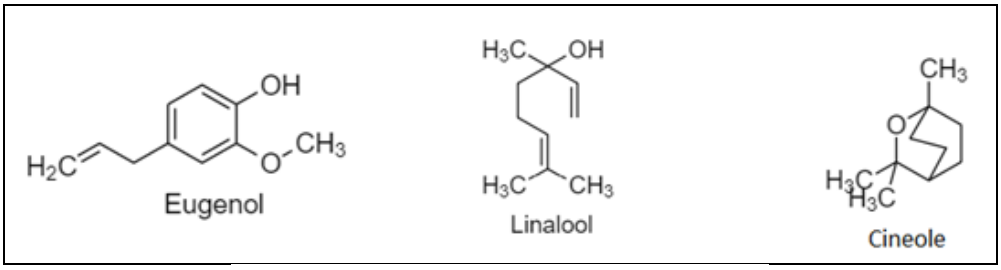

FIG. 40: PHYTOCONSTITUENTS OF BASIL

A randomized controlled clinical trial was conducted to determine the effects of Tulsi powder in patients with hyperglycemia [112]. Male adults were given 3 g of Tulsi leaves capsules before

meals for 6.5 weeks. After the time period, it was observed that there was a significant drop in the fasting glucose level and postprandial glucose level in males administered with the capsules. A randomized parallel-group clinical trial was conducted to determine the effects of Tulsi on liver enzymes and metabolic parameters in young and overweight obese subjects [113]. For the same, adults were given 250 mg of Tulsi leaves capsules twice daily before a meal and for 8 weeks. It was observed that there was an improvement in the BMI, levels of serum triglycerides, HDL, LDL, VLDL, plasma insulin, and insulin resistance. A study was conducted in depression-induced rats to determine the beneficial effects of hydroethanolic extract of *Ocimum basilicum* L on enzymatic and non-enzymatic antioxidants [114].

It was observed that administration of 250-500 mg/kg of body weight extract leads to an increase in the brain pool of non-enzymatic and enzymatic antioxidants, thus relating the anti-depressant activity of the extract to this phenomenon. Another study was conducted to determine the antithrombotic effect of ethanolic extract of *Ocimum basilicum* in mice model carrageenan-induced blood coagulation [115]. Upon administration of 100-400 mg/ml of extract, it was found that the fibrinolytic systems were activated and thus antithrombotic effects were produced, which led to the cardioprotective action of the *Ocimum basilicum* leaf ethanolic extract. A research study was performed in male albino rats to determine the wound-healing effects of ethanolic extract of *Ocimum basilicum* leaves [116]. After a 12-day observation period, it was concluded that when an ointment containing 5% w/w ethanolic extract of *Ocimum basilicum* was applied to the excised wound base, it produced wound-healing effects and reduction in mean wound area, which was as effective as that produced by 5% w/w povidone-iodine ointment.

Challenges Associated With the Usage of Culinary Spices in Healthcare: Even though many spices have been proven to possess a myriad of health benefits and show great potential in being used as agents for curing different diseases and ailments, still some more solid evidence is needed which includes conducting regulated and monitored pre-clinical and clinical trials to qualify spices as potential agents for curing health problems. Also, every spice must be used in a certain quantity and to a certain extent. Even the frequency of consuming the spices has to be taken off. If overused, it can cause more harm than good. To state a few examples, the KADHA recipe, which gained a lot of popularity due to its health benefits in preventing CoVID-19 and normal flu virus, is a mixture of many herbs and spices prepared by boiling the mixture in water. But, some studies have also shown that this kadha, if consumed daily, might cause problems in the functioning of the liver and kidneys because of the presence of turmeric.

Also, if consumed in excess amounts, the same kadha can cause gastrointestinal and stomach-related problems like acidity and problems in urinating, as kadha also contains various spices like black pepper, ginger, cloves, and black cardamom, which produce heat in the body. In a similar way, many other spices have to be consumed only after knowing their right amounts, or else the body will have to face the harmful effects. To determine the right concentration and amount of consumption, many more pre-clinical and clinical trials along with extensive studies have to be conducted, which would not only establish a firm ground for their usage in healthcare but would also provide correct information regarding the exact concentration and frequency of using these spices as therapeutic agents. Conclusively, it can be said that without proper research and studies, the right concentration and frequency of consumption of spices cannot be determined and continuous research and studies are required to establish their role as therapeutic agents in the field of healthcare.

The Role of the Indian Government in Controlling the Usage of Spices as Therapeutic Agents in Healthcare: In India, the Ministry of Ayush ensures the optimal development and propagation of Ayush systems of healthcare which includes Ayurveda, Unani, Homeopathy, Naturopathy, and Siddha systems of medicine and Yoga too [63]. On having a closer look at the India scenario, it is found that, unfortunately, no such proper guidelines have been issued by the Ministry of Ayush regarding the optimum concentration and frequency of administration of spices, especially in a country like India, which is the birth place of such Ayurvedic practices and recipes.

Here again, if we consider the example of Kadha, a maximum number of people are still unaware of what all spices should be added in what quantity to prepare a kadha. They are also not aware of the contraindications if any when many different types of spices have to be consumed together in a kadha. As a result, when preparing this decoction, people cannot follow a standardized recipe and procedure as it is unavailable. In such a scenario, it is the government's responsibility to release the standard guidelines for the preparation and administration of Ayurvedic recipes, including kadha and different spices consumed daily, especially in a country like India where spices are an integral component of people's daily diet. No wonder it has been claimed that plant-based drugs and products like spices have been proven to possess myriad therapeutic uses. Still, it is the sole responsibility of the government to make people aware of the standardized preparation procedure and frequency of administration of such herbal products.

The Global Scenario of Usage of Spices as Therapeutic Agents: The usage of spices is not just limited to India but is now prevalent in many other parts of the world too. Different countries worldwide have realized the benefits of using spices in healthcare, and quite many people prefer using spices as a natural remedy for some sudden ailments. With increasing awareness of the health benefits of spices, the demand for spices is likely to increase shortly. Presently, many companies sell spices and herbs in different forms for easy administration by the people. Spices like turmeric, cumin seed, black pepper powder cinnamon, organic ginger, licorice root, cardamom powder, and paprika are being sold in powdered as-well-as capsulated forms. Many of these companies buy spices from most the south-east Asian countries, after which they mold those spices into a suitable form for easy administration and then sell it to people around the world. Countries like the USA, the UK, Northern America, and Europe have started importing a lot of spices, not just for seasonings but also for preventing illnesses. The following chart depicts the amount of spices likely to be consumed shortly.

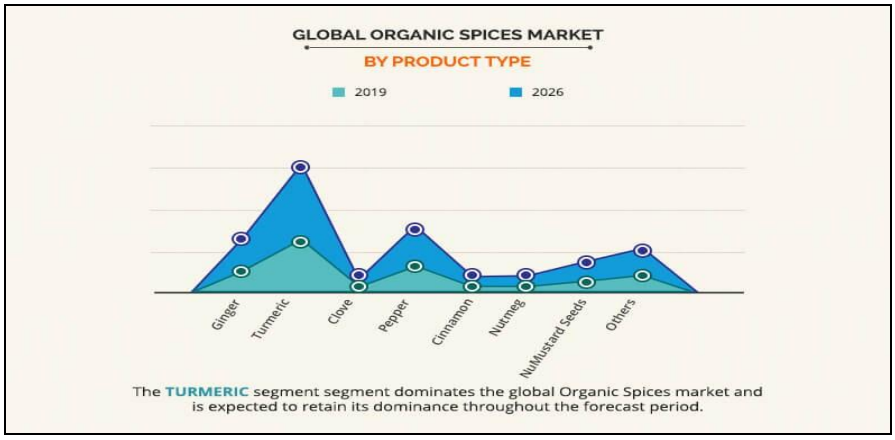

FIG. 41: AMOUNT OF SPICES LIKELY TO BE CONSUMED IN FUTURE

CONCLUSION: According to these spices' scientific profile, the phytoconstituents they possess are of utmost importance. Some extensive research were conducted to determine the therapeutic potential of these spices, and the results have concluded that each of these spices has a myriad of pharmacological properties which can be beneficial for treating diseases and problems of gastro intestine, wounds, rheumatic pain, excessive CNS activity, inflammation, anxiety, oxidation, infection, *etc*. They were also found to exhibit anti-oxidant, cardio-protective, anti-Alzheimer, anti-convulsant, anti-sclerotic, anti-proliferative, anticancer, anti-nociceptive, anti-diabetic, anti-cytotoxic properties. With strong evidence from more clinical trials, these spices can be expected to be used worldwide as therapeutic agents. The research and studies conducted till now have provided essential data regarding the therapeutic and pharmacological properties of the spices mentioned. It is clear that these spices can provide long-term benefits with minimal side effects as they are complete of plant origin. Apart from this, while cultivating such spices, the raw materials should be chosen judiciously to avoid foreign material interference in the therapeutic

phytoconstituents these spices have been proven to possess. But, still, more extensive research and exhaustive studies have to be undertaken *in-vivo* as-well-as in-vitro environments to establish a more convincing and solid ground of evidence regarding their therapeutic potential and adverse effects. In addition, it is the responsibility of the government to standardize, regulate and make people aware of the usage of spices and herbal ingredients, especially those which can be prepared in domestic households. Reliable data and results of clinical studies should be provided to the public so as to promote the usage of spices for therapeutic purposes without causing any side effects or adverse reactions.

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CONFLICT OF INTEREST: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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