Cedar of Lebanon – Cedrus Libani (young shoots)

and its

Many Incredible Topical Uses

Polycrest for Skin Homeostasis

By

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Dermatology–Allergy–Infectious Diseases: *Polycrest* for achieving skin homeostasis. The skin is the largest organ of the human body. The skin is rarely seen as a breathing organ for which it is and bigger than the lungs: the skin is 12-15% of body weight, with a surface area of 1-2 meters. Two distinctive layers exist in the skin: the epidermis and dermis. The basic cell type of the epidermis is the keratinocytes, which contain keratin, a fibrous protein. Basal cells are the innermost layer of the epidermis. Melanocytes produce melanin pigment, and are also in the inner layer of the epidermis. The dermis is a connective tissue under the epidermis, it contains capillaries, elastic fibers, nerve

endings, sensory receptors, collagen and elastin. The integumentary system has multiple roles in homeostasis, including protection, temperature regulation, sensory reception, biochemical synthesis, water balance, synthesis of vitamins and hormones and absorption (Farabee, 2006).

Cedar of Lebanon possesses profound activity on the integumentary system of the skin cell's renewal. It will interrupt abnormal skin cell's activity and is almost one hundred percent guaranteed to reestablish skin homeostasis (balance). When used PO at an adult dose of 15 gtts, tid, QD long term this plant has been shown and is considered the ***Systemic Botox Antiwrinkle Alternative*** without being a toxin and or having any of the risks associated with Botox, and without the same price tag while lasting longer than just six months. When used systemically it has been shown to be one of the best plants to increase collagen and elastin in addition to being the rejuvenator of dying cells – new cell renewal.

Topical use will get rid of almost ***any abnormal skin growth*** like that of psoriasis plaque among many others. Hyperkeratosis skin tags will eventually all shed, it effectively dissolved callouses and almost any skin fungus including nails - apply AM and PM sufficient amounts to cover afflicted area and let it dry and do not bathe or rinse for at least one hour. It is best used when the skin is clean such as right after a shower.

Avoid the eyes and if using on the face it must be diluted with at least 50 percent water. If any adverse reactions like that of skin burning or redness you need to discontinue or dilute furthermore. It is a very potent plant. When used for hyperkeratosis and psoriasis plaque use full strength. You will be amazed how well it works and noticeable improvement can be seen even within a few days of its use. In eczema where the skin is really raw, it is best to mix with a poly saturated fat like coconut oil; mix 1 Tbsp. of the oil with 10-25 drops of the extracts. You DO NOT NEED to use a massive amount of this plant, and it is recommended that you start small and increase using the appropriate amount that works for you. Not everyone is the same and on sensitive skin use even more diluted.

Topical antiinflammatory, and insecticide repellent. Antimicrobial activities include: antifungal, antiparasitic, antibacterial, anti-Candida; for scabies-ringworm infections and to heal wounds both in humans and domestic animals, both internally and externally. Himachalol from Cedrus Libani has shown potent anti-allergy activity. It is very effective for dry eczema - (dry white crusty skin) - psoriasis, pruritus, hyper-keratosis, chronic dermatitis, atopic dermatitis, lichenoid dermatosis, callosity, cuts that are infected or not healing, Buruli ulcer, Black Tongue/Lingua Villosa, diaper rash, jock itch/tinea cruris, athlete's foot/tinea pedis. Cedar is also effective in treating ***venereal warts*** or human papillomavirus (HPV) on the penis or sub prenuptial excrescences. NEVER EVER apply this plant straight and undiluted to any genitals sensitive areas - seek the advice of a knowledgeable physician expert in phytotherapy. It is known throughout the world that members within the cedar family treat abnormal skin growths, whether warts, eczema or psoriasis. This action harkens back to the fact this plant contains many phytochemicals that attack ***abnormal skin tissue growth***. Antiviral for infectious mononucleosis (EBV), viral tonsillitis, laryngitis and pharyngitis.

An *in vivo* study on the wound healing activity of Cedrus Libani was evaluated by linear incision and circular excision experimental wound models subsequently histopathological analysis. The healing potential was comparatively assessed with a reference ointment Madecassol®, which contains 1% extract of Centella asiatica. Additionally, acetic acid-induced capillary permeability test was used for Cedar of Lebanon antiinflammatory activity. The experimental study revealed that Cedrus Libani and Abies cilicica subsp. cilicica displayed remarkable wound healing and antiinflammatory activities (Tumen et al., 2011).

Cedrus Libani is of ***polycrest importance for any skin conditions but especially for the treatment of seborrheic keratosis,*** also known as "seborrheic verruca," and "senile wart," a benign skin condition. The growth originates in keratinocytes, the predominant type of cell in the epidermis. Although no treatment is necessary for seborrheic keratosis, it can be quite disfiguring when someone has many wart-likes growths all over their body. Systemically taken Cedrus Libani young shoots extract PO 10-15 gtts, tid, QD six months to one year will gradually and completely shed every seborrheic keratosis and restore the cellular keratinocytes skin homeostasis. This ability is unique to this plant. I suspect that Cedrus Libani, like many other embryonic plants that have been shown effective at inhibiting various genetic factors, is antagonistic to the fibroblast growth factor receptor 3 (FGFR3), a gene known to cause seborrheic keratosis (Hafner et al., 2007). Irrelevant of the cause of seborrheic keratosis, this plant has never once in my experience failed to greatly improve any and every skin condition.

It is an effective antiseborrheic (helps control the production of sebum), dermatitis herpetiformis (in Celiac disease), antiaging of the skin, dry skin, and antiwrinkle. It works on increasing *collagen and elastin* of the skin. Anti-furrow; furrows occur where there may be wrinkle lines complicated by the loss of subcutaneous fat and/or ligament support. It increases the ability of the skin and/or scalp to retain water. This is a Botox alternative when taken long term, six or more months, and is excellent for dry skin, hair loss, dandruff, dry skin accompanied with acne. For oily acne, use Elm or use both. Good for comedones (blackheads). Good for bruises. Himachalol from Cedrus Libani has shown potent anti-allergic activity, especially for allergic skin reactions. For leaf and bread molds which can cause phycomycotic diseases. It combats hair loss, alopecia areata.

Furuncles or folliculitis: Both are caused by Gram-positive Staphylococcus bacteria, which are normally found on the skin's surface. Damage to the hair follicle allows these bacteria to enter deeper into the tissues of the follicle and the subcutaneous tissue. Furuncles are also known as boils, skin abscess and inflamed sores. Cedar of Lebanon young shoot extracts are very effective in resolving furuncles.

The sesquiterpenes volatile oils have the ability to open up the blood vessels and deliver more immune cells to the damaged skin region, which in turn speeds up healing of old festering wounds. These sesquiterpenes attack abnormal tissue and leave normal tissue alone, thus warts disappear and the normal tissue remains unscathed.

The abietic types of acids have shown a more pronounced antibacterial activity than the pimaric and labdane acids when the disc diffusion method was used, but there was no inhibition of growth of Gram-negative bacteria. Among the individual resin acids, ***dehydroabietic acid*** was generally the most potent, when disc diffusion on agar was

used, and prediffusion increased the inhibitory effect. The composition of the pure resin acids dehydroabietic, neoabietic, and isopimaric acid did not change during the experiment, but abietic and levopimaric acid was converted into dehydroabietic acid by the addition of Müller-Hinton agar. In conclusion, the old tradition of treating wounds with pitch, sap, rosin, or rosin-containing tapes might have some antibacterial relevance (Söderberg et al., 1990).

A series of C14-hydroxy derivatives of dehydroabietic acid were synthesized from commercial abietic acid and evaluated for their cytotoxic, antimycotic, and antiviral activities. From these C14-hydroxy derivatives, triptoquinone C-4 epimers were obtained and their immunomodulatory activity was additionally evaluated. None of the tested compounds showed antiviral activity against herpes simplex virus type 1 (HHV-1), nor did they display antimycotic activity against certain Aspergillus, spp. except for one compound, abieta-8,11,13-trien-14,18-diol. Interestingly, two triptoquinone epimers showed cytotoxic activity, and one of them induced mitochondrial potential loss, DNA damage and cell cycle distribution alterations in Jurkat cells, but not in human peripheral blood mononuclear cells. In addition, these compounds inhibited monocyte differentiation and production of pro-inflammatory cytokines, IL-1β and TNF-α, and the antiinflammatory cytokine IL-10 in the presence of LPS. In conclusion, one of the triptoquinone molecules could be a promising scaffold for the development of novel anticancer agents, and two of them could be potential antiinflammatory agents (Zapata et al., 2013).

Antibacterial activity of dehydroabietic acid, against multidrug-resistant strains. Evidenced bactericidal activity against Staphylococcus epidermidis (American Type Culture Collection 14990) within 24 h. On the basis of these results, dehydroabietic acid plays an important part in the search for novel sources of agents that can act against multiresistant bacteria (Leandro et al., 2014).

All atlantones have been shown to possess antifungal activity against Aspergillus flavus, A. niger, A. ochracoeus, A. parasiticus, and A. sydowii. A weak activity was also recorded against A. parasiticus, A. sydowii and Trichophyton rubrum (Chaudhary et al., 2012). Acaricidal activity against Tetranychus urticae (Neves et al., 2011).

Ampelopsin, a small molecule inhibitor of HIV-1 infection targeting HIV entry. Ampelopsin could protect sensitive cells against HIV-1 infection and dramatically reduce HIV-1 antigen P24 expression. HIV-1SF33 attaching to MT-4 cells was interfered by ampelopsin, and the EC_{50} was 0.175 mg/mL for cellular protection and 0.024 mg/mL for P24 inhibition. At co-cultivating phase, EC_{50} was 0.229 mg/mL and 0.197 mg/mL respectively. Furthermore, the EC_{50} was 0.179 mg/mL and 0.348 mg/mL in acute infection. Human PBMCs migration was induced after being challenged with ampelopsin or chemokines, and synergistic action was observed during co-treatment. Ampelopsin alone resulted in maximal chemotaxis at 1 mg/mL. HIV-1 co-receptor CXCR4 on the surface of PBMCs was decreased by internalization, which indicated the effect of ampelopsin on CXCR4. About 70% CXCR4 was reduced by ampelopsin at 1 mg/mL. Ampelopsin also augmented cellular immunological functions in immunosuppressive mice. Ampelopsin demonstrated a strong inhibitive role during HIV-1 absorption, incubation and acute infection. These results are coincident with its immune enhancement (Liu et al., 2004).

Astragalin is good for the treatment of allergies, atopic dermatitis and hyperkeratosis. Immunologic studies have determined the capacity of spleen T cells to produce both IL-4 and IL-13, but not IFN-gamma, was downregulated by astragalin (Kotani et al., 2000).

Astragalin glucosides exhibited 8.3-60.6% higher inhibitory effects on matrix metalloproteinase-1 expression, 18.8-20.3% increased antioxidant effects, and 3.8–18.8% increased inhibition activity of melanin synthesis (Kim et al., 2012).

Aziridines and oxazolines: valuable intermediates in the synthesis of unusual amino acids. Aziridines show activity as protease inhibitors; for example, 2-(4-amino-4-carboxybutyl)aziridine-2-carboxylic acid is a potent irreversible inhibitor of the bacterial enzyme diaminopimelic acid epimerase, while 2-(3-carboxypropyl)aziridine-2-carboxylic acid is an irreversible inhibitor of glutamate racemase. Aziridine-2,3-dicarboxylates have been introduced in peptidomimetics as modified aspartic acid moieties for the purpose of preparing cysteine protease inhibitors (Cardillo et al., 2003).

Aziridine-2,3-dicarboxylate is a peptidomimetic cysteine protease inhibitors with antileishmanial activity. In this study, it was demonstrated that the cysteine protease inhibitors aziridine-2,3-dicarboxylates 13b and 13e impaired promastigote growth at mid-micromolar concentrations and decreased the infection rate of peritoneal macrophages at concentrations 8- to 13-fold lower than those needed to inhibit parasite replication. Simultaneous treatment of infected cells with compound 13b and gamma interferon resulted in an even further reduction of the concentration needed for a significant decrease in macrophage infection rate. Notably, treatment with the compounds alone modulated the cytokine secretion of infected macrophages, with increased levels of interleukin-12 and tumor necrosis factor alpha. Furthermore, the decreased infection rate in the presence of compound 13b correlated with increased nitric oxide (NO) production by macrophages. Importantly, at the concentrations used herein, compounds 13b and 13e were not toxic against fibroblasts, macrophages, or dendritic cells. Together, these results suggest that the aziridine-2,3-dicarboxylates 13b and 13e are potential antileishmanial lead compounds with low toxicity against host cells and selective antiparasitic effects (Ponte-Sucre et al., 2006).

The protozoan parasite Trypanosoma brucei causes Human African trypanosomiasis, which is fatal if left untreated. Due to the toxicity of currently used drugs and emerging drug resistance, there is an urgent need for novel therapies. The major trypanosome papain-like cysteine protease expressed by the parasite (e.g., rhodesain in T. b. rhodesiense) is considered an important target for the development of new trypanocidal drugs. Series of aziridine-2,3-dicarboxylate-based cysteine protease inhibitors have been tested, most of them inhibiting rhodesain in the low micromolar range. Among these, ***only dibenzyl aziridine-2,3-dicarboxylates*** display trypanocidal activity being equipotent to the drug eflornithine. The Leu-Pro-containing aziridinyl tripeptides 13a-f are the most promising as they are not cytotoxic to macrophages up to concentrations of 125microM (Vicik et al., 2006).

A synergistic bactericidal activity of essential (EO) containing β-bisabolene with ampicillin against Staphylococcus aureus was observed in a time-kill assay. EO and β-bisabolene have the potential to restore the effectiveness of ampicillin against resistant S. aureus (Nascimento et al., 2007).

Antifungal activities of α-himachalene and β-bisabolene were the highest, particularly for dermatophytes and Cryptococcus neoformans, with MIC values of 0.16–0.64 μL mL (Maxia et al., 2009).

For the treatment of fungal skin diseases such as tinea, ringworm, and athlete's foot, benzoic acid helps prevent infection caused by bacteria and fungus (Wilson et al., 2004).

The effects of benzoic acid in the preservative-resistant yeast Zygosaccharomyces bailii were studied. The results suggested that the primary action of benzoic acid in Z. bailii is to cause a general energy loss, by adenosine triphosphate (ATP) depletion. Benzoic acid inhibits the growth of mold, yeast and some bacteria (Warth, 1991). It is also effective against Candida albicans.

Benzoic acid is used for the treatment of skin irritation and inflammation caused by burns, insect bites, fungal infections, and eczema.

The antimicrobial and antitumor activity of the E. macrorrhiza essential oil containing high amounts of β-Cedrene against Staphylococcus aureus, Escherichia coli, Candida albicans and Caco-2 cells were evaluated. Among all the tested microorganisms and Caco-2 cells, the essential oils showed the strongest inhibitory effect on Staphylococcus aureus (MIC = 2.8 μg/mL) and Caco-2 cell (IC_{50} = 11.86 μg/mL), whereas no effect on Escherichia coli and Candida albicans. The data of this study suggested that the essential oils have great potential as a natural medicine for microbial infections and cancers (Lin et al., 2012).

A study reports that cedrol, in particular, a compound found in the essential oil of cedar, seems to have a high toxicity to cercariae (Schistosoma mansoni), a parasite found in humans (Naples et al., 1992).

The major chemical components of western juniper (cedrol and α- and β-cedrene) and Alaska cedar (nootkatin) were also tested. In western juniper, α- and β-cedrene were found to be active antimicrobial compounds effective against Fusobacterium necrophorum, Clostridium perfringens, Actinomyces bovis and Candida albicans (Johnston et al., 2001).

Cedrol was shown to accelerate fibroblast growth in a dose-dependent manner and increased the production of ***type 1 collagen*** and ***elastin***. Phosphorylation of p42/44 extracellular signal-regulated kinase, p38 mitogen-activated protein kinase, and Akt was markedly increased by cedrol, indicating that enhanced extracellular matrix (ECM) production is linked to activation of intracellular signaling cascades. These results indicate that cedrol enhances ECM production in dermal fibroblasts in a MAPK-dependent manner with applications for the maintenance of skin texture (Jin et al., 2012).

Cyclohexane is antimicrobial, antibacterial against multidrug resistance in Salmonella enterica (Bailey et al., 2008) and used as a repellents and ascaricides as personal protection measures in the prevention of tick-borne diseases (Cisak et al., 2012).

The potent antibacterial activity of dehydroabietic acid was shown effective against Staphylococcus aureus and Bacillus subtilis comparable to positive control (Gu et al., 2012).

Another study confirms that dehydroabietic acid, an abietane-type diterpene, inhibits Staphylococcus aureus biofilms *in vitro*. Three active compounds were identified: nordehydroabietylamine (1), (+)-dehydroabietic acid (2) and (+)-dehydroabietylamine (3) that prevented biofilm formation in the low micromolar range, and unlike typical antibiotics, only 2 to 4-fold higher concentrations were needed to significantly reduce viability and biomass of existing biofilms. Compound 2, (+)-dehydroabietic acid, was the most selective towards biofilm bacteria, achieving high killing efficacy (based on log Reduction values) and it was best tolerated by three different mammalian cell lines. Since (+)-dehydroabietic acid is an easily available compound, it holds great potential to be used as a molecular probe in biofilms-related studies as well as to serve as inspirational chemical model for the development of potent drug candidates (Fallarero et al., 2013).

Dehydroabietic acid reverses TNF-α-induced the activation of FOXO1 and suppression of TGF-β1/Smad signaling in human adult dermal fibroblasts. These results suggested that DAA could be useful in improving the diabetic wound healing.

A study showed that oils containing germacrene D have antimicrobial activity against Gram-negative bacteria and Candida glabrata, with minimal inhibitory concentration (MIC) values between 50 and 1000 µg/ml (de Carvalho et al., 2014).

β-Caryophyllene, germacrene D, and germacrene B were shown to possess antiplasmodial activity against the W2 strain of Plasmodium falciparum (Boyom et al., 2011).

Hyperoside is a potent inhibitor of Hepatitis-B (HbsAg) and HBeAg secretion in 2.2.15 cells and DHBV-DNA levels in the HBV-infected duck model. The inhibition of the peak of viremia was maximum at the dose of 0.10 g-kg-1·d-1 and reached 60.79% on d 10 and 69.78% on d 13, respectively (Wu et al., 2007).

It is an effective antiviral herpes simplex (HSV1); molluscicidal, and activity for scabies. Phytochemical analysis demonstrates that the main constituents of Cedar of Lebanon young shoots extract are two monoterpenes: α-pinene and β-myrcene Khan et al. (2005), reported that some monoterpenes such as isoborneol tested against HSV-1 inactivated very effectively the herpes virus by a mechanism which involved the inhibition of glycosylation of viral polypeptides. At the same time the borneol a stereoisomer (isomer of isoborneol) did not inhibit the glycosylation but completely inhibited viral replication, a ***protease inhibitor*** without affecting viral adsorption. Topical application is excellent for cold sores.

Cedrus Libani antiviral activity against viral infections. This study reported the phytochemical composition analyzed by GC–MS of essential oil and cones and leaves ethanol extracts. The main components were himachalol (22.50%), β-himachalene (21.90%), and α-himachalene (10.50%). Ethanol extract leaves were characterized by a high content of germacrene d (29.40%). The same extract obtained from cones essentially contained α-pinene (51.0%) and β-myrcene (13.0%). Moreover, they investigated extracts, essential oil, and identified compounds for their *in vitro* antiviral activities against herpes simplex virus type 1 (HSV-1). Cytotoxicity was evaluated by MTT assay in Vero cells. Cones and leaves ethanol extracts exhibited an interesting activity with IC50 of 0.50 and 0.66 mg/ml, respectively, at non-cytotoxic concentration. A

comparable activity was found when essential oil was tested (IC50 of 0.44 mg/ml), (Loizzo et al., 2008).

α-Himachalene novel antimicrobial activity against Gram-positive bacteria Bacillus subtilis, Micrococcus luteus and Staphylococcus aureus, and mycotoxigenic fungi Aspergillus parasiticus, A. ochraceousand A. sydowii (Chaudhary et al., 2014).

Antifungal activities of α-himachalene and β-bisabolene were the highest, particularly for dermatophytes and Cryptococcus neoformans, with MIC values of 0.16–0.64 μL mL (Maxia et al., 2009). It was shown to inhibit HIV-1 replication in cultured monocytes, macrophages, and mononuclear cells, perhaps by inhibition of HIV-1 protease inhibitor activity (Battinelli et al., 2003).

A study demonstrated that β-himachalene produced a significant inhibition of compound 48/80 and nystatin-induced rat paw edema. It also inhibited heat- as well as hypotonic solution-induced hemolysis of erythrocytes *in vitro*. The antiinflammatory activity of the oil could be due to its membrane stabilizing action (Shinde et al., 1999).

Isopimaric acid was assayed against multidrug-resistant (MDR) and methicillin-resistant Staphylococcus aureus (MRSA). The minimum inhibitory concentrations (MIC) were 32-64 microg/mL and compared with a commercially obtained resin acid, abietic acid, with MICs of 64 microg/mL. Resin acids are known to possess antibacterial activity and are valued for their antiseptic properties in festering wound healing. These results show that isopimaric acid is active against MDR and MRSA strains of S. aureus, which are becoming increasingly resistant to antibiotics. Both compounds were evaluated for modulation activity in combination with antibiotics, but did not potentiate the activity of synthetic antibiotics tested (Smith et al., 2005).

Chemical profile, antifungal, antiaflatoxin and antioxidant activity of Citrus maxima Burm. and Citrus sinensis (L.) Osbeck essential oils and their cyclic monoterpene, DL-limonene (Singh et al., 2010). Limonene has well-known antifungal activity, in synergy with the rest of this plant's composition; *γ*-terpinene, and terpinolene are effective against Malassezia resistance, which is a causative factor for the skin condition seborrheic dermatitis. In this study, limonene possesses antifungal activity against Malassezia furfur and Malassezia pachydermatis. The results revealed that the minimum fungicidal concentration (MFC) value of limonene is lower than the value for itraconazole. The MFC value of limonene was seen to be 7.81 μg/mL against M. furfur and 3.90 μg/mL against M. pachydermatis. MFC values of itraconazole against M. furfur and M. pachydermatis were 62.50 μg/mL and 31.25 μg/mL, respectively. In addition, it was noted that limonene was not toxic to Beas-2B cells with normal morphology at a concentration of 100 μg/mL. However, itraconazole exhibited weak toxicity at the same concentration. Results indicate that limonene could potentially be effective at controlling M. furfur and M. pachydermatis infections with no cytotoxicity (Lee et al., 2011).

Fractionation with n-hexane/ethyl acetate (1:1 v/v) by open column chromatography of the oleoresin from Pinus oocarpa Schiede yielded two diterpenes, pimaric acid (1) and dehydroabietic acid (5), the sesquiterpene longifolene (3) and a diterpenic mixture containing pimaric acid (1), isopimaric acid (4) and dehydroabietic acid (5). Subsequently, the isolated compounds, the mixture of 1, 4 and 5, the oleoresin and the dehydroabietic acid methyl ester (2), were tested *in vitro* against epimastigotes of Trypanosoma cruzi,

the causative agent of Chagas disease. The most active compounds were 1, 3 and the oleoresin, being as active as nifurtimox, a drug effective in the treatment of acute infection by American trypanosomiasis and used in this work as positive control (Rubio et al., 2005).

A study demonstrated the antidermatophytic activity of Nigella sativa essential oil strong antimicrobial activity against Microsporum gypseum, Trichophyton rubrum and Trichophyton simii with diameter of inhibition zone and activity index 38 mm (AI: 1.90), 20 mm (AI: 1.33) and 35 mm (AI: 1.09), respectively as compared with Chrysosporium. This antidermatophytic activity was attributed to *p*-cymene (54.13%), α-thujene (10.43%), hydrocarveol (10.40%), longifolene (6.97%), β-pinene (3.10%), and other components present in *trace amounts* (Sunita et al., 2013). Please note that Cedrus Libani also contains most of these compounds.

Juniperus communis is a plant which has been reported as a traditional cure for tuberculosis (TB) and other respiratory diseases. The aim of this study was to isolate and identify the constituents responsible for the activity of the n-hexane extract of Juniperus communis roots against Mycobacterium tuberculosis H(37)Rv and Juniperus communis aerial parts against Mycobacterium aurum. Subsequently, it was to evaluate the activity of the pure isolated compounds against (i) drug-resistant Mycobacterium tuberculosis variants, (ii) non-replicating Mycobacterium tuberculosis and (iii) a range of non-tuberculous mycobacteria (NTM). Longifolene and totarol were most active against the rifampicin-resistant variant (MICs of 24 and 20.2 microM, respectively). The antimycobacterial activity of Longifolene and trans-communic acid, and the activity of totarol against Mycobacterium aurum, Mycobacterium fortuitum and Mycobacterium phlei, was reported for the first time. The effect of these compounds on drug-resistant variants and non-replicating Mycobacterium tuberculosis has never been published before. The presence of antimycobacterial terpenoids in Juniperus communis aerial parts and roots justifies, to some extent, the ethnomedicinal use of this species as a traditional anti-TB remedy (Gordien et al., 2009).

The chemical composition of the essential oil obtained from the leaves of Piper ovatum Vahl by hydrodistillation was analyzed by GC–MS. The main constituents found were δ-amorphene (16.5%), ***cis-muurola-4(14),5-diene*** (14.29%) and γ-muurolene (13.26%). The crude extracts and isolated compounds were screened for their antimicrobial activity. Hydroalcoholic extracts of different parts of Piper ovatum Vahl, essential oil and amides isolated from leaves were tested against Gram-positive and Gram-negative bacteria and Candida species. All extracts and amides were active against Bacillus subtilis and Candida tropicalis, including clinical strains. Essential oil was active against C. tropicalis. These amides showed an inhibitory effect on the adherence of C. tropicalis ATCC 28707 on cover glasses at 10 µg/mL, but did not show morphological alterations at the tested concentrations. Amides were identified as piperovatine and piperlonguminine, and showed MIC values of 15.6 and 31.2 µg/mL to B. subtilis and 3.9 µg/mL to C. tropicalis, and low toxic effects to Vero cells and macrophages (Silva et al., 2009).

Another study demonstrated antibacterial activity effective against Bacillus cereus and antifungal activity against Aspergillus niger (Hassanzadeh et al, 2010).

The antimicrobial activity of α-muurolene was investigated for Staphylococcus aureus, Escherichia coli, Candida albicans and Caco-2 cells (human colorectal carcinoma). Among all the tested microorganisms and Caco-2 cells, the essential oils showed the strongest inhibitory effect on Staphylococcus aureus (MIC = 2.8 µg/mL) and Caco-2 cell (IC50 = 11.86 µg/mL) antitumor properties, whereas no effect on Escherichia coli and Candida albicans (Lin et al., 2012).

The antiplasmodial and antimicrobial activities of some essential oils containing myrcene were individually evaluated against eleven microorganisms, using the agar diffusion method, by determination of MIC values. The investigated oils exhibited moderate antimicrobial activity. Maximum activity of the oils was observed against Nocardia asteroides, Staphylococcus aureus and Enterococcus faecalis. Fungicidal activity against Candida albicans was also found for both oils (Laouer et al., 2009).

Both α- and β-pinene are highly toxic to Candida albicans, killing 100% of inoculum within 60 min (da Silva et al., 2012). After treatment with α-pinene the fungal morphology and ultrastructure showed obvious changes: their cell wall and cytoplasmic membrane were ruptured; intracellular components released out and the cell residue fused to form irregular masses. In addition, the synthesis of DNA, RNA, and polysaccharides of cell walls and ergosterol of cytoplasmic membranes was inhibited. It is indicated that these changes are related to the antifungal mechanism of α-pinene (Xia et al., 1999).

The bacteriostatic and bactericidal activities of six components of conifer essential oils (α and β pinene, R- and S-limonene, 1,8 cineole, borneol) were tested on Listeria monocytogenes serovars 4b and 1/2c. α Pinene was the most active component with an average minimal inhibitory concentration (MIC) of 0.019% against L. monocytogenes 4b. Given that these products are highly active against L. monocytogenes, they might be used to kill this species or to prevent its growth (Mourey et al., 2002).

Antimicrobial activity of *trans*-pinocarveol remarkably inhibited the growth of tested Gram-positive bacteria Enterococcus hirae and both tested fungi. This oil has shown an antioxidant activity equivalent to 18% of the reference compound a-tocopherol (Juteau et al., 2002).

Another study on the antimicrobial activity of trans-pinocarveol demonstrated the strongest activity against Enterococcus faecalis and Staphylococcus aureus, Pseudomonas aeruginosa and Escherichia coli (Elaissi et al., 2012).

All fungal infections are characterized with intense itching. Jock Itch or Tinea Cruris occurs when a particular type of fungus grows and multiplies in the groin area, and develops almost exclusively in adult men. The fungus that causes Tinea Cruris thrives in warm, moist areas and can be triggered by friction from clothes and prolonged wetness in the groin area such as from sweating. It may also be contagious and can be passed from one person to the next by direct skin-to-skin contact or contact with unwashed clothing. Tinea Cruris is characterized by red, raised, scaly patches that may blister and ooze. The patches often have sharply-defined edges and are often redder around the outside with normal skin tone in the center. Other causes of itching in the groin include Lichen simplex chronicus, or pubic lice (crabs), chemical irritation, etc.

Typhoid fever, also known as enteric fever, bilious fever, Paratyphoid, Salmonella Infection or Yellow Jack, is an illness caused by the bacterium Salmonella enterica serovar Typhi. Common worldwide, it is transmitted by the ingestion of food or water contaminated with feces from an infected person. The bacteria then perforate through the intestinal wall and are phagocytosed by macrophages. Salmonella Typhi then alters its structure to resist destruction allowing it to exist within the macrophage. This renders it resistant to damage by PMN's, complement and immune response. The organism is then spread via the lymphatic system while inside the macrophages. This gives it access to the ***reticulo-endothelial system*** and then to the different organs throughout the body. The organism is a Gram-negative short bacillus that is motile due to its peritrichous flagella. The bacteria grow best at 37 °C/99 °F – human body temperature.

For whooping cough and the common cold. Campylobacter infection organisms are spiral-shaped bacteria that can cause disease in humans and animals. Amoebiasis is caused by protozoa. Amoebiasis is also known as amoebic dysentery, bloody flux, flux and dysentery. Amoebiasis is commonly spread by water contaminated by feces or from food served by contaminated hands. It can also spread to other organs like the liver, and brain by invading the venous system of the intestines. The most common symptoms of Amoebiasis are diarrhea, stomach cramps and fever and also effective for Giardiasis.

Crude Cedrus Libani extracts and metabolites have been found to possess various biological activities including insecticidal, juvenile hormone, antitumor, antiulcerogenic, antiinflammatory, antihypertensive, antitussive, antimicrobial and central nervous system activities (Yang et al., 2008). Particularly Abies cilicia and Cedrus Libani extracts were shown to possess antimicrobial activity against Bacillus megaterium, Bacillus subtilis, Bacillus cereus, Klebsiella pneumoniae, Enterobacter aerogenes, Staphylococcus aureus, Mycobacterium smegmatis, Proteus vulgaris, Listeria monocytogenes, Pseudomonas aeruginosa, Candida albicans, Candida tropicalis and Penicillium italicum. When the results of this study were compared with an ampicillin standard, it was found that the microorganisms studied were generally susceptible (Digrak et al., 1999).

Many phytochemicals contribute to the antibacterial and antifungal potent activity of this plant against MRSA and all dermatophytes.

Cedrus Libani was shown to display remarkable wound healing and potent antiinflammatory activities (Tumen et al., 2011).

Cedar of Lebanon young shoots and Sweet Chestnut when combined are very effective in treating ***venereal warts*** human papillomavirus (HPV) on the penis or sub prenuptial excrescences for the treatment of abnormal skin growths, whether warts or psoriasis. This action harkens back to the fact that plants have phytochemicals that attack ***abnormal tissue growth***. Topical application of Sweet Chestnut buds on penile wart(s) 2 times daily is also required to complete treatment. Mixed the extract with some coconut oil to not burn the skin.

Systemic Dosage: For other related skin fungal infections, take 10-30 drops, 3 times daily for 1 week to 2 weeks depending on the severity. Cedar of Lebanon young shoots extracts are very effective in resolving many fungal skin infections. Cedar of Lebanon young shoots extracts are a natural substitute for conventional antibiotics like Ciprofloxacin, Roxithromycin, Doxycycline or other penicillin derivatives.

Topical repellent and DEET alternative: due to a ***novel sesquiterpenes complex that contributes to its effective repellency against*** ticks and mosquitoes.

Mix the following plant extracts with equal amount of distilled water into a glass or BPA free plastic spray bottle:

- 15 ml of Cedar of Lebanon – Cedrus Libani (young shoots)
- 15 ml of Juniper – Juniperus Communis (young shoots)
- 15 ml Lemon Tree – Citrus Limonum (bark)
- 15 ml Rosemary – Rosmarinus Officinalis (young shoots)

Directions: Shake well each time and use as a natural repellent for ticks and mosquitoes. Keep away from the eyes. It can be used on animals in place of toxic products. Spray a generous amount to all exposed areas including the neck. For double security you can also spray on top of your clothes. Must be used daily and every time you wash or bathe. Reapply with sweating profusely. It should be stored in a dry cool dark place. It is good only for three months once diluted with the distilled water.

Topical use: Antibacterial for cuts that are infected, antifungal infections of the nails, Microsporum, Epidermophyton and Trichophyton. Use a Q-tip to apply the extract to the infected nail(s) 2 times daily. The synergistic use of Boxwood – Buxus Sempervirens (young shoots) with Cedar of Lebanon makes it a very effective treatment for topical nail fungus without any toxicity like that of over the counter (OTC) antifungal drugs.

For Scabies - **Ringworm, and Candida.** Use 1-2 drops of straight tincture on each affected area every 2 hours 4 to 6 times per day. It takes around 10-20 applications to be eradicated. For scabies, practice the necessary clothing sterilization to achieve full eradication of infestation.

It is also good topical use for ***cracked nipples*** or ***chafing of the skin***.

Buruli ulcer or Bairnsdale ulcer is a chronic, slowly spreading disease of the dermis. Buruli ulcer leads to the wasting of the dermal layers. Bairnsdale Ulcer is caused by Mycobacterium ulcerans. Initially the disease manifests as solid, non-tender, nodules about 1-2 cm in diameter in the subcutaneous layers. Over the next two months, these areas become widespread. Numerous painless, undetermined ulcerations appear. The ulcerations in Buruli ulcer can be extensive, involving as much as 15% of the skin surface. There are many manifestations of Buruli ulcer which include atrophy of nerves, appendages, and blood vessels, and it can occasionally invade the bone. The lesions heal ultimately, but lead to extensive scarring. Cedar of Lebanon young shoots extracts are very effective in resolving the Buruli ulcer or Bairnsdale ulcer. Cedar of Lebanon young shoots extract are a natural substitute for conventional antibiotics like Ciprofloxacin, Roxithromycin, Doxycycline or other penicillin derivatives.

Cedar of Lebanon contains significant amounts of lauric acid 36.91% (Loizzo et al., 2007). The strong bactericidal properties of lauric acid (C12:0), a middle chain-free fatty acid commonly found in natural products, have been shown in a number of studies. However, it has not been demonstrated whether lauric acid can be used for acne treatment ***as a natural antibiotic*** against Propionibacterium acnes (P. acnes), which promotes follicular inflammation (inflammatory acne). This study evaluated the antimicrobial property of lauric acid against P. acnes both *in vitro* and *in vivo*. Incubation of the skin bacteria P.

acnes, Staphylococcus aureus (S. aureus), and Staphylococcus epidermidis (S. epidermidis) with lauric acid yielded minimal inhibitory concentration (MIC) values against the bacterial growth over 15 times lower than those of benzoyl peroxide (BPO). The lower MIC values of lauric acid indicate stronger antimicrobial properties than that of BPO. The detected values of half maximal effective concentration (EC_{50}) of lauric acid on P. acnes, S. aureus, and S. epidermidis growth indicate that P. acnes is the most sensitive to lauric acid among these bacteria. In addition, lauric acid did not induce cytotoxicity too human sebocytes. Notably, both intradermal injection and epicutaneous application of lauric acid effectively decreased the number of P. acnes colonized with mouse ears, thereby relieving P. acnes-induced ear swelling and granulomatous inflammation. The obtained data highlight the potential of using lauric acid as an alternative treatment for antibiotic therapy of acne vulgaris (Nakatsuji et al., 2009).

Monolaurin, a monoester formed from lauric acid (medium chain fatty acids), has profound antimicrobial activities: antibacterial, antifungal, antiprotozoal, and antiviral properties.

Antibacterial	Antifungal	Antiparasitic	Antiviral
Gram-negative	Candida albicans	Giardia lamblia	Cytomegalovirus (CMV)
Gram-positive organisms	Dermatophytes: Ringworm		Epstein-Barr virus (EBV)
Groups A, B, F, and G streptococci	Tinea corporis		Herpes simplex virus-1 (HSV-1)
Helicobacter pylori(gram-negative)	Tinea cruris: jock itch		Herpes simplexvirus-2 (HSV-2)
Haemophilus influenza(gram-negative)	Tinea pedis: athletes foot		Herpes viridae(all)
Listeria monocytogenes			Human immunodeficiency virus HIV-1, HIV+
Propionibacterium acnes			Human lymphotropic viruses (type 1)
Staphylococcus aureus			Influenza virus
Streptococcus agalactiae			Measles virus
			Pneumonovirus
			Rubella virus
			Sarcoma virus
			Syncytial virus
			Vesicular stomatitis virus
			Visna virus

Table created by Dominique Richard, 2015

In addition to the lauric acid content found in Cedrus Libani, its many monoterpenes and sesquiterpenes also contribute greatly to its antibacterial, antifungal, antiparasitic and antiviral activities.

The antimicrobial activities of the isomers (equal) and enantiomers (opposite) of pinene were studied against bacterial and fungal cells. The agar diffusion test showed that only the positive (+) enantiomers of the a- and β-isomers of pinene were active. The minimal inhibitory concentration (MIC) and minimal microbicidal concentration (MMC) of these monoterpenes were also determined, confirming that the positive enantiomers exhibited microbicidal activity against all fungi and bacteria tested with MICs ranging from 117 to 4,150 µg/mL. However, no antimicrobial activity was detected with the negative (-) enantiomers even when as high as 20 mg/mL (da Silva et al., 2012).

By contrast, antibacterial activity against MRSA occurred after 6 h. The combinatorial use of conventional antibiotics like ciprofloxacin, plus (+)-a-pinene or (+)-β-pinene, provided synergistic activity against MRSA whereas an indifferent effect against all fungi was detected when amphotericin B was combined with the positive enantiomers of pinene. Both pinenes in micromolar amounts are sufficiently potent as a standalone treatment against mycosal infections. The potential of (+)-a-pinene and (+)-β-pinene are phospholipase inhibitors and the esterase activities was also evaluated, and the best inhibition results were obtained with *Cryptococcus neoformans*, which can cause lung infection in AIDS patients, and is also seen in meningitis and encephalitis. *Candida albicans* biofilm formation was prevented with the MIC concentration of (+)-a-pinene and twice the MIC value of (+)-β-pinene. Finally, the cytotoxicity of the positive enantiomers of pinene to murine macrophages was evaluated, and 250 µg/mL of (+)-a-pinene and (+)-β-pinene reduced the cell viability by 66.8% and 57.7%, respectively (da Silva et al., 2012).

The antibacterial activity of eugenol, α-pinene and β-pinene inhibiting the growth of potential ***infectious endocarditis*** caused by gram-positive bacteria was studied. *Staphylococcus aureus, S. epidermidis, Streptococcus pneumoniae* and *S. pyogenes* strains were used as test microorganisms. The assayed phytochemicals showed effectiveness in inhibiting all assayed bacteria strains presenting MIC values between 2.5 and 40 µL/mL. Eugenol showed the lowest MIC values which were between 2.5 and 5 µL/mL for the most bacteria strains. MIC values found to the phytochemicals were able to inhibit the cell viability of S. aureus, providing a total elimination of the bacteria inoculum in a maximum time of 24 hours of exposure. α-Pinene and β-pinene were effective at a 20 mcg per mL. This study showed the interesting antibacterial property of the assayed phytochemicals, and supports their possible and rational use in antimicrobial therapy (Leite et al. 2007).

β-Pinene has high activity against Bacillus cereus and Enterococcus faecalis (Fehr, 1981).

Quinic acid (QA) is a versatile chiral starting material for the synthesis of new pharmaceuticals. As a sugar compound, it is found in many different plants. It is a ***neuraminidase inhibitor*** for the treatment of influenza A and B strains marketed under the brand name Tamiflu. Quinic acid is also thought to displace binding of the mu opioid receptor antagonist. Shikimic acid and quinic acid are key intermediates for the biosynthesis of aromatic compounds in living systems (Buchler, 2008)

A study demonstrated synergistic activity of quinic acid as it augments the antibacterial activity of ampicillin, ciprofloxacin, vancomycin, and cefepime against S. aureus, and activated the effects of ampicillin and vancomycin against E. coli (Gohari et al., 2010).

High-rhamnose-containing plants have been shown to have antiwrinkle properties. Research studies done by Professor Jaggi Rao from the University of Alberta, found rhamnose had a protective effect, allowing for regeneration of the skin by stimulating the papillary dermis, causing it to produce new skin cells, collagen and elastin. The latest weapon against wrinkles (Alleyne, 2011), rhamnose is also recognized in pharmacology for its soothing and antiinflammatory properties. Rhamnose may have a protective effect through antioxidant activity (Racco, 2011).

A study demonstrated that terpinen-4-ol is the most active ingredient of tea tree oil (TTO) to kill Demodex mites followed by α-Terpineol, 1,8-Cineole and Sabinene. At a mere concentration of 1%. Terpinen-4-ol exhibited a significant synergistic effect with Terpinolene, but an antagonistic effect with α-Terpineol in killing mites (both $P < 0.05$). *In vivo*, Terpinen-4-ol was shown to eradicate mites. Terpinen-4-ol can be of great benefits as an ascaricide to treat a number of ocular and cutaneous diseases caused by demodicosis (Tighe et al., 2013).

Resistance against antiectoparasitic compounds is increasing. Treatment failure against itch mite Sarcoptes scabiei var hominis with lindane, crotamiton, and benzyl benzoate has been reported, as well as likely emerging resistance to 5% permethrin and oral ivermectin. This concern advocates for the identification and development of novel ascaricidal drugs. Tea tree oil is a membrane-active biocide extracted from the tree M alternifolia. It is a principal antimicrobial in a wide range of pharmaceuticals sold in Australia, with the main active component being oxygenated terpenoids. The results suggest a potential role as a new topical ascaricide and confirm terpinen-4-ol as the primary active component (Walton et al., 2004).

Terpinen-4-ol is the main constituent of essential oil known for its biocidal and antiinflammatory properties. The possibility of fabricating polymer thin films from terpinen-4-ol using radio frequency (RF) plasma polymerization for the prevention of the growth of Pseudomonas aeruginosa was investigated, and the properties of the resultant films compared against their biologically active precursor. Films fabricated at 10 W prevented bacterial attachment and EPS secretion, whilst polyterpenol films deposited at 25 W demonstrated no biocidal activity against the pathogen (Bazaka et al., 2010).

Antiviral activity against influenza A/PR/8 virus subtype H1N1, and against HSV-1 and HSV-2. The antiviral activity against influenza A/PR/8 virus subtype H1N1 has been principally attributed to terpinen-4-ol, the main active component (Garozzo et al., 2009).

α-Ylangene antimicrobial and the antioxidant activity against free radical, antibacterial activity against both Gram positive (Staphylococcus epidermidis, Staphylococcus aureus, Bacillus subtilis) and Gram negative (Escherichia coli, Pseudomonas aeruginosa, Proteus vulgaris) bacteria. The essential oil showed antibacterial effect against all the gram (+) bacteria and gram (−) bacteria tested. These results show many essential oil could be considered as a natural alternative to food antioxidants and preservatives (Chen et al., 2011).

Plant oils and their compounds were screened *in vitro* for antibacterial and antifungal activity by disc diffusion method. Minimum Inhibitory Concentrations (MICs) of oils (% v/v) against bacteria and fungi were determined by agar dilution method. Results showed that potential antimicrobial activity was demonstrated by geranium oil, geraniol, and terpineol. These oils and oil components were active against Gram-positive and Gram-negative bacteria pathogens. Antifungal activity was also observed against dermatophytes, yeasts and Aspergillus species. Antimicrobial formulations containing geranium oil, geraniol and terpineol showed strong antibacterial and antifungal activity (Singh et al., 2010).

The fraction containing terpinen-4-ol showed high antibacterial activity toward all strains tested on the growth of food-borne pathogens. Tests with authentic samples showed that ***terpinen-4-ol played a major role in the antibacterial activity of essential oil***, and in a mice test, the oil actively minimized inflammation by S. aureus. The test strains were Klebsiella pneumoniae, Listeria monocytogenes, Salmonella typhimurium, Staphylococcus aureus, Escherichia coli, Legionella pneumophila, and Methicillin-resistant Staphylococcus aureus. Antibacterial activity was estimated by measuring bacterial growth inhibition. It inhibited the growth of all test strains and exhibited the strongest antibacterial activity against L. monocytogenes (Park et al., 2010).

The inhibitory activities of terpinen-4-ol and pyrrolidine were similar to amoxicillin ($P>0.05$). *Only when found in high concentration* does it possess antimicrobial activity against drug-resistant strains of Helicobacter pylori. Most of these compounds are being reported for the first time and may represent new sources of therapeutically useful compounds against H. pylori. In the stem bark of Sclerocarya birrea (Anacardiaceae) most of the compounds were essential oils, with terpinen-4-ol being the most abundant agent (35.83%), followed by pyrrolidine (32.15%), aromadendrene (13.63%) and α-gurjunene (8.77%). MIC_{50} ranges for amoxicillin, terpinen-4-ol and pyrrolidine were 0.0003-0.06 µg/mL, 0.004-0.06 µg/mL and 0.005-6.3 µg/mL, respectively (Njume et al., 2011).

The aim of this study was to examine the effect of five naturally occurring compounds from essential oils on 10 different species of mycotoxigenic fungi involved in several plant diseases. The ***antifungal activities of terpinen-4-ol, eugenol, carvone, 1,8-cineole (eucalyptol) and thymol*** were observed i*n vitro* on Fusarium subglutinans, Fusarium cerealis, Fusarium verticillioides, Fusarium proliferatum, Fusarium oxysporum, Fusarium sporotrichioides, Aspergillus tubingensis, Aspergillus carbonarius, Alternaria alternata and Penicillium sp. The naturally occurring compounds tested showed toxic effects on *in vitro* mycelium growth of all fungal species but with different level of potency. This proves the antifungal synergistic activities of many essential oils and their components (Morcia et al., 2012).

Terpinen-4-ol should be considered for inclusion as a single agent in products formulated for topical treatment of methicillin-resistant Staphylococcus aureus (MRSA) infection and coagulase-negative staphylococci (CoNS) and their toxicity against human fibroblast cell. Terpinen-4-ol exhibited significantly greater bacteriostatic and bactericidal activity, as measured by minimum inhibitory and bactericidal concentrations, against both MRSA and CoNS isolates. Although not statistically significant, time-kill studies also clearly showed that terpinen-4-ol exhibited greater antimicrobial activity than tea tree oil (TTO). Comparison of the toxicity of terpinen-4-ol and TTO against human fibroblasts revealed

that neither agent, at the concentrations tested, were toxic over the 24-h test period (Loughlin et al., 2008).

The essential oils (Eos) were tested for antifungal activity against Aspergillus flavus, Rhizoctonia solani, Penicillium commune, and Fusarium oxysporum. Two samples were weakly effective against Aspergillus flavus. Furthermore, terpineol and α-terpineol, two of the major components of EO of Pistacia lentiscus L., totally inhibited the mycelian growth of Aspergillus flavus. Quite good antioxidant activity of the EO was also found (Barra et al., 2007).

Terpinen-4-ol, an active component of tea tree oil, exhibits broad-spectrum antimicrobial activity. However, the high volatilization of terpinen-4-ol and its no wettability property have limited its application. The objective of this study was to synthesize novel nanocarriers to deliver and protect terpinen-4-ol. The polyethylene glycol (PEG)-stabilized lipid nanoparticles were prepared and characterized by scanning electron microscope, Zetasizer, and differential scanning calorimetry. These nanoparticles had an average diameter of 397 nm and a Z-potential of 10 mV after being modified by glycine. Results showed that homogeneous particle size, high drug loading, stability, and targeting were obtained by the nanoparticles. Liquid chromatography/mass spectrometry showed a sustained release trend from nanoparticles for terpinen-4-ol. Minimum inhibitory concentration and ***minimum biofilm eradication*** concentration were tested ***against Candida albicans*** ATCC 11231. Studies on isolated mitochondria showed the blockage of biofilm respiration and inhibition of enzyme activity. The effects can be ascribed to localization of terpinen-4-ol on the membrane of mitochondria (Sun et al., 2012).

A study data suggests that terpinen-4-ol is a likely mediator of the *in vitro* and *in vivo* activity of tea tree oil. This is the first *in vivo* demonstration that terpinen-4-ol could control Candida albicans vaginal infections. Terpinen-4-ol compound holds promise for the treatment of vaginal candidiasis, and particularly the azole-resistant forms (Mondello et al., 2006).

Plants with increased concentrations of terpinen-4-ol have displayed enhanced antimicrobial activity. High levels of terpinen-4-ol and enhanced p-cymene appeared to correlate with increased activity especially Candida albicans (Williams et al., 1993).

A study highlights the role of plant volatile organic compounds, found in essential oils, for the treatment of bacteria-related inflammation. This report is focused on terpinen-4-ol. Analysis of the published literature shows that many essential oils have significant antibacterial, antifungal and antiinflammatory effects. Some of their major components, such as terpinen-4-ol, act by inhibiting pro-inflammatory cytokine expression while stimulating production of antiinflammatory cytokines. Such observations may be exploited to encourage ***biotherapy against mastitis***. In the context of inflammation and related mammalian responses, understanding the interplay between volatile organic compounds, especially terpinen-4-ol, and cytokines during bacteria related inflammation should clarify their mode of action to control mastitis (Taga et al., 2012).

α-Terpinene possesses antibacterial activity, and therefore, it could be used as a natural preservative ingredient in food and/or pharmaceutical industries against Escherichia coli (Eteghad et al., 2009). Another study demonstrated antimicrobial activity against four pathogens strains: Listeria monocytogenes, Streptococcus pyogenes, Proteus vulgaris

and again confirmed effectiveness against Escherichia coli. The result of this study revealed that both cell wall and membrane of the treated gram-negative and gram-positive bacteria were significantly damaged by not only α-terpinene but the rest of the terpenes found in most essential oils. This is most likely due to their synergistic potentiating effects (Oyedemi et al., 2009).

γ-Terpinene exhibited a broad spectrum of fungitoxic behavior against all tested fungi such as Aspergillus niger, Aspergillus flavus, Aspergillus oryzae, Aspergillus ochraceus, Fusarium monoliforme, Fusarium graminearum, Pencillium citrium, Penicillium viridicatum, Pencillium madriti, and Curvularia lunataas absolute mycelial zone inhibition was obtained at a 6 µL dose of the essential oil containing various monoterpenes (Thangam et al, 2003).

Essential oils extracted by hydro distillation from fruits of Cuminum cyminum L. and Carum Carvi L., the antibacterial activity, determined with the agar diffusion method, was observed against Gram-positive and Gram-negative bacteria species in this study. The activity was particularly high against the genera Clavibacter, Curtobacterium, Rhodococcus, Erwinia, Xanthomonas, Ralstonia, and Agrobacterium, which are responsible for plant or cultivated mushroom diseases worldwide. In general, a lower activity was observed against bacteria belonging to the genus Pseudomonas. These results suggest the potential use of the above essential oils for the control of bacterial diseases (Iacobellis et al., 2005). Another study demonstrated that *γ*-terpinene exhibited a potent antimicrobial activity against Streptococcus pyogenes ATCC 19615 (Sati et al., 2012).

The mechanism of antimicrobial activity of essential oils components; α-terpineol, *γ*-terpinene and eugenol was studied to evaluate their effect on the bacterial membrane against four strains of bacteria: Listeria monocytogenes, Streptococcus pyogenes, Proteus vulgaris and Escherichia coli. The study was done to observe changes in membrane composition by assaying for the leakage of protein and lipid using Bradford and van Handel's method respectively. The oils components were capable of inducing cell lysis by the leakage of protein and lipid contents. Eugenol at 2 × MIC was highly effective toward protein content leakage after 120 min of exposure. Alpha terpineol and γ-terpinene showed similar effect at 2 × MIC under the same condition. ***Gamma terpinene displayed the highest activity*** toward lipid content leakage at 2 × MIC while α-terpineol and eugenol showed similar effect after 120 min of exposure. The result revealed that both cell wall and membrane of the treated Gram-negative and Gram-positive bacteria were significantly damaged (Oyedemi et al., 2009).

Monoterpene compounds α-terpinene, *γ*-terpinene, α-pinene, *p*-cymene, terpinen-4-ol, α-terpineol, thymol, citral and 1,8-cineole were examined for their antiviral activity against herpes simplex virus type 1 (HSV-1) *in vitro*. These essential oils were able to reduce viral infectivity by 96%; the monoterpenes inhibited HSV by about 80%. The mode of antiviral action has been determined, only moderate antiviral effects were revealed by essential oils and monoterpenes when these phytochemicals were added to host cells prior to infection or after entry of HSV into cells. However, both essential oils and monoterpenes exhibited high anti-HSV-1 activity by direct inactivation of free virus particles. All tested drugs interacted in a dose-dependent manner with herpesvirus particles thereby inactivating viral infection. Among the analyzed compounds,

monoterpene hydrocarbons were slightly superior to monoterpene alcohols in their antiviral activity, α-pinene and α-terpineol revealed the highest selectivity index. However, mixtures of different monoterpenes present in natural plants essential oil revealed a ten-fold higher selectivity index and a lower toxicity than its isolated single monoterpene analogues (Astani et al., 2010).

The antibacterial activity of essential oils and their major constituents against respiratory tract pathogens by gaseous contact for which *γ*-terpinene was shown effective.

The antifungal activity is increased by the rest of this plant's total composition synergy; *γ*-terpinene and terpinolene are especially effective against Malassezia resistance and a known causative factor in seborrheic dermatitis. The antifungal activity was attributed to the complex composition of essential oil including: α-thujene, α-terpinene, *p*-cymene, gamma-terpinene, terpinolene, 1-terpineol, α-calacorene, α-phellandrene, and terpinen-4-ol explain the higher antifungal effect the doses of fungicides required for control of the Fusarium species (Sampietro et al., 2014).

To investigate the inhibitory effects of Artemisia princeps Pamp. (family Asteraceae) essential oil (APEO) and its main constituents against bacterial vaginosis and vulvovaginal candidiasis, their antimicrobial activities against Gardnerella vaginalis and Candida albicans *in vitro* and their anti-inflammatory effects against G. vaginalis-induced vaginosis and vulvovaginal candidiasis were examined in mice. APEO and its constituents eucalyptol and α-terpineol were found to inhibit microbe growths. α-Terpineol most potently inhibited the growths of G. vaginalis and C. albicans with MIC values of 0.06 and 0.125% (v/v), respectively. The antimicrobial activity of α-terpineol was found to be comparable to that of clotrimazole. Intravaginal treatment with APEO, eucalyptol, or α-terpineol significantly decreased viable G. vaginalis and C. albicans numbers in the vaginal cavity and myeloperoxidase activity in mouse vaginal tissues compared with controls. These agents also inhibited the expressions of proinflammatory cytokines (IL-1 β, IL-6, TNF-α), COX-2, iNOS, and the activation of NF- κB and increased expression of the anti-inflammatory cytokine IL-10. In addition, they inhibited the expressions of proinflammatory cytokines and the activation of NF- κB in lipopolysaccharide-stimulated peritoneal macrophages, and α-terpineol most potently inhibited the expressions of proinflammatory cytokines and NF- κB activation. Based on these findings, APEO and its constituents, particularly α-terpineol, ameliorate bacterial vaginosis and vulvovaginal candidiasis by inhibiting the growths of vaginal pathogens and the activation of NF- κB (Trinh et al., 2011).

A study demonstrated the effective antifungal activity of Cedar of Lebanon young shoots extract against the dermatophyte Trichophyton mentagrophytes being more active than amphotericin B and nystatin. This was attributed to the synergistic activity of α-pinene, α-bisabolol and *trans*-verbenol (Al-Jafari et al., 2011).