

CLINICAL STUDIES ON THE FOLLOWING INGREDIENTS:

Oregano

Antibacterial and Antifungal Activities of Spices *

Abstract

Infectious diseases caused by pathogens and food poisoning caused by spoilage microorganisms are threatening human health all over the world. The efficacies of some antimicrobial agents, which are currently used to extend shelf-life and increase the safety of food products in food industry and to inhibit disease-causing microorganisms in medicine, have been weakened by microbial resistance. Therefore, new antimicrobial agents that could overcome this resistance need to be discovered. Many spices-such as clove, oregano, thyme, cinnamon, and cumin-possessed significant antibacterial and antifungal activities against food spoilage bacteria like *Bacillus subtilis* and *Pseudomonas fluorescens*, pathogens like *Staphylococcus aureus* and *Vibrio parahaemolyticus*, harmful fungi like *Aspergillus flavus*, even antibiotic resistant microorganisms such as methicillin resistant *Staphylococcus aureus*. Therefore, spices have a great potential to be developed as new and safe antimicrobial agents. This review summarizes scientific studies on the antibacterial and antifungal activities of several spices and their derivatives.

Source: Qing Liu, Xiao Meng, Ya Li, Cai-Ning Zhao, Guo-Yi Tang, Hua-Bin Li. "Antibacterial and Antifungal Activities of Spices" International Journal of Molecular Medicine (2017): 18(6):1283.

Natural Therapy of Fungal and Nail Disease *

Nails are the unique part of body, besides it's a dead tissue it also have role in serving the human beauty. It protects the fingertip and tissues from injuries and also enhances the precise movements of distal digits, but it has also been cursed with many diseases and ailments including serious infections. Most common types are of Fungal or Yeast infections resulting in Onychomycosis and if it is left untreated, the nail plate may separate from the nail bed. Other infections include Paronychia, Tinea Unguis, and *Pseudomonas* bacterial infection. Different nail disorders are Onychatrophia resulting from injury, Leuconychia cause by trapping of tiny bubbles of air, Melanonychia known as nail moles and can be sometimes serious. For a physician physical appearance of nail is important which can reveals many disorders like Malnutrition, Liver disease, etc. Nail infections can be treated with natural products which are mainly Oregano oil, Lemongrass oil, Horopito. One of the latest and modern treatment to treat fungal infections of nails is Ozone treatment but it is not frequently used and quite costly. Like others body parts nails also required a good source of nutrients to maintain their complexions and healthiness, Vitamin A, Vitamin D and calcium help in maintaining moisture content of nails and avoid brittleness, Besides this Proteins and fatty acids like Linoleic acids are also essential.

Source: Dr. Bharat Parashar, Virendra Yadav, Brajesh Maurya, Love Sharma, Manav Bharti. "Natural Therapy of Fungal Nail Disease" The Pharma Innovation (2012) Vol 1, No 4.

Old-pressed oregano (*Origanum vulgare*) oil: a rich source of bioactive lipids with novel antioxidant and antimicrobial properties

Abstract

In this investigation, cold-pressed oregano (*Origanum vulgare*) oil (OO) was studied for its lipid classes, fatty acid profile, tocopherols, and phenolics contents. Radical scavenging potential against DPPH \cdot and galvinoxyl radicals was determined. Antimicrobial properties of OO against foodborne bacteria, food spoilage fungi, and dermatophyte fungi were also evaluated. The level of neutral lipids in OO was the highest, followed by glycolipids and phospholipids. The main fatty acids in OO were linoleic, oleic, stearic and palmitic acids. γ -Tocopherol constituted 32.1 % of total measured tocopherols followed by α -tocotrienol (25.8 %) and γ -tocotrienol (21.3 %). OO contained high amounts of phenolic compounds (5.6 mg/g as GAE). OO had strong antiradical action wherein 72 % of DPPH \cdot radicals and 60 % of galvinoxyl radicals were quenched after 60 min of incubation. Rancimat assay showed that induction time (IT) for OO/sunflower oil blend (1:9, v/v) was 6 h, while OO/sunflower oil blend (2:8, v/v) recorded higher IT (8 h). OO inhibited the growth of all tested microorganisms. The highest antimicrobial activity of OO was recorded against the dermatophyte fungi including *T. mentagrophytes* (42 mm) and *T. rubrum* (38 mm), followed by food spoilage fungi including *A. flavus* (36 mm) and *C. albi* (32 mm) with minimal lethal concentration (MLC) ranging between 40 and 320 μ g/mL. OO exhibited also broad-spectra activity against foodborne pathogen bacteria (*S. aureus*, *E. coli*, *S. enteritidis*, and *L. monocytogenes*) with MLC ranging between 160 and 320 μ g/mL. The results suggest that OO could be used economically as a valuable natural product with novel functional properties in food, cosmetics, and pharmaceutical industries.

Source: Assiri, Adel MA, et al. "Cold-pressed oregano (*Origanum vulgare*) oil: a rich source of bioactive lipids with novel antioxidant and antimicrobial properties." European Food Research and Technology 242.7 (2016): 1013-1023.

Basil and Oregano

Antimicrobial Activity of Basil, Oregano, and Thyme Essential Oils *

For centuries, plants have been used for a wide variety of purposes, from treating infectious diseases to food preservation and perfume production. Presently, the increasing resistance of microorganisms to currently used antimicrobials in combination with the appearance of emerging diseases requires the urgent development of new, more effective drugs. Plants, due to the large biological and structural diversity of their components, constitute a unique and renewable source for the discovery of new antibacterial, antifungal, and antiparasitic compounds. In the present paper, the history, composition, and antimicrobial activities of the basil, oregano, and thyme essential oils are reviewed.

Introduction One of the actions to counter the emergence of the drug resistance problem is the development of new antimicrobials. Plant essential oils are explored as a promising substitute to currently used antimicrobials, and to date, many plant essential oils have been reported to present considerable antimicrobial activity. This activity is attributed to their ability to synthesize aromatic substances, the majority of which are phenols or oxygen-substituted derivatives. The antimicrobial, antiseptic, and other therapeutic applications of plants are well recognized since the prehistoric times, widely used by all civilizations throughout the millennia [1]. Interestingly, according to the World Health Organization, approximately 80% of the world population, mostly in developing countries, still relies on medicinal plants and their extracts for primary health care [2, 3]. The contemporary pharmaceuticals, cosmetics, and food industries are founded on the knowledge of the properties of medicinal plants that can be used for applications from treating infectious, systematic, and inflammatory diseases to food preservation and perfume production [4]. The aim of the present paper is to review the antimicrobial activities of three essential oils; namely, the basil, oregano, and thyme essential oils.

Source: Hercules Sakkas, Chrissanthi Papadopoulou. "Antimicrobial Activity of Basil, Oregano, and Thyme Essential Oils" Journal of Microbiology and Biotechnology (2017): 27(3), 429–438.

Basil Leaf

Sensitivity of *Candida albicans* to essential oils: are they an alternative to antifungal agents? *

Abstract

Aims: *Candida albicans* is an important opportunistic pathogen, responsible for the majority of yeast infections in humans. Essential oils, extracted from aromatic plants, are well-known antimicrobial agents, characterized by a broad spectrum of activities, including antifungal properties. The aim of this work was to assess the sensitivity of 30 different vaginal isolated strains of *C. albicans* to 12 essential oils, compared to the three main used drugs (clotrimazole, fluconazole and itraconazole).

Methods and results: Thirty strains of *C. albicans* were isolated from vaginal swab on CHROMagar™ *Candida*. The agar disc diffusion method was employed to determine the sensitivity to the essential oils. The antifungal activity of the essential oils and antifungal drugs (clotrimazole, itraconazole and fluconazole) were investigated using a microdilution method. Transmission and scanning electron microscopy analyses were performed to get a deep inside on cellular damages. Mint, basil, lavender, tea tree oil, winter savory and oregano essential oils inhibited both the growth and the activity of *C. albicans* more efficiently than clotrimazole. Damages induced by essential oils at the cellular level were stronger than those caused by clotrimazole.

Conclusions: *Candida albicans* is more sensitive to different essential oils compared to the main used drugs. Moreover, the essential oil affected mainly the cell wall and the membranes of the yeast.

Significance and impact of the study: The results of this work support the research for new alternatives or complementary therapies against vaginal candidiasis.

Source: E. Bona, S. Cantamessa, M. Pavan, G. Novello, N. Massa, A. Rocchetti, G. Berta, E. Gamalero. "Sensitivity of *Candida albicans* to essential oils: are they an alternative to antifungal agents?" Journal of Applied Microbiology (2016): 121(6):1530-1545.

Antifungal Activity of the Essential Oil of Basil (*Ocimum basilicum*)

Abstract

The antifungal and fungicidal effects of two chemotypes of basil (*Ocimum basilicum*) oil and its major individual components were studied in a series of in vitro and in vivo experiments. Mycelial growth of the plant pathogenic fungus *Botrytis fabae* was reduced significantly by both the methyl chavicol chemotype oil and the linalol chemotype oil, and the major individual components of the oils all reduced fungal growth, with methyl chavicol, linalol, eugenol and eucalyptol reducing growth significantly. Combining the pure oil components in the same proportions as found in the whole oil led to very similar reductions in fungal growth, suggesting that the antifungal effects of the whole oils were due primarily to the major components. When the fungus was exposed to the oils in liquid culture, growth was reduced by concentrations considerably smaller than those used in the Petri dish studies. *Botrytis fabae* and the rust fungus *Uromyces fabae* were also controlled in vivo, with the whole oils of both chemotypes, as well as pure methyl chavicol and linalol, reducing infection of broad bean leaves significantly. Most effective control of fungal infection was achieved if the treatments were applied 3 h postinoculation.

Source: Oxenham, S. K., K. P. Svoboda, and D. R. Walters. "Antifungal activity of the essential oil of basil (*Ocimum basilicum*)" *Journal of phytopathology* (2005): 153.3 174-180.

Garlic Bulb

Fungal infection control by garlic extracts (*Allium sativum* L.) and modulation of peritoneal macrophages activity in murine model of sporotrichosis *

Abstract

Garlic (*Allium sativum* L.) is grown all over the world as seasoning and medicinal vegetable since 3,000 BC. Allicin is the main component of garlic, being attributed to it the most of its biological activities, such as bactericidal, antifungal and antiviral actions. However, other compounds of garlic present antioxidant, hypocholesterolemic, vasodilator activities, protective action against different types of cancer, and immunomodulatory. Fungal infections are important causes of morbidity and mortality in people mainly in immunosuppressed ones. *Sporothrix schenckii*, the causing agent of Sporotrichosis (most common subcutaneous mycosis in Latin America), is dimorphic fungus, of saprophytic life in soil or plants, infecting people and animals mainly through skin injuries and bruises. The main of this work was to evaluate the influence of garlic consuming on immune modulation of healthy and infected Swiss mice in induced way by *S. schenckii*, since these animals functioning of peritoneal macrophages as well as the nitric oxide and cytokines' production (IL-1 β , IL-10 and IL-12) and to evaluate the antifungal potential of garlic with *S. schenckii* through minimum inhibitory concentration test and colony-forming units. The results showed that garlic offers antifungal potential with *S. schenckii*. The oral taking of garlic extracts influences the releasing of cytokines by macrophages, regular consuming shows anti-inflammatory effect, and its acute use may take to an inflammatory response. Mice that consumed garlic responded more effectively to fight against the infection.

Source: J.P. Burian, L.V.S. Sacramento, I.Z. Carlos. "Fungal infection control by garlic extracts (*Allium sativum* L.) and modulation of peritoneal macrophages activity in murine model of sporotrichosis" *Brazilian Journal of Biology* (2017): 77(4):848-855.

Investigating the therapeutic effect of vaginal cream containing garlic and thyme compared to clotrimazole cream for the treatment of mycotic vaginitis *

Abstract

Background: Vaginitis is the most prevalent gynecological problem for which women look for treatment and is responsible for 10 million physician visits annually. Use of herbal treatments has been recorded in many of patient groups as well as in general populations to increase health level. The present study was conducted with the purpose of determination and comparison of the effect of vaginal cream containing garlic and thyme compared to clotrimazole cream for the treatment of mycotic vaginitis.

Methods: This clinical trial is a prospective, multivariate, single-blind, two-stage, two-group study with randomized assignment of samples into the two groups. From the clinics in Isfahan in 2010, 64 cases (32 individuals in each group) entered the study. Data collection was accomplished by demographic information questionnaire and clinical performance checklist, and data analysis was performed by SPSS 16.0 software.

Results: Abundance distributions of clinical symptoms (vaginal discharge; vulval erythema and edema), patients' complaints (secretions, itching, dyspareunia, painful urination, and vaginal irritation) and clinical symptoms (existence of germinating hypha, acidity under 4.5, and culture of vaginal secretions) were different in each group prior to and after the intervention; these factors however were not different between the two groups before and after the intervention.

Conclusions: The vaginal cream containing garlic and thyme is effective as much as clotrimazole vaginal cream for the treatment of candida vaginitis and there is no difference between responses to treatment by these two drugs.

Source: Parvin Bahadoran, MSc, Fatemeh Karimzadeh Rokni, Fariba Fahami, MSc. "Investigating the therapeutic effect of vaginal cream containing garlic and thyme compared to clotrimazole cream for the treatment of mycotic vaginitis" *Iranian Journal of Nursing and Midwifery Journal* (2010): (Suppl1): 343-349.

Apple Cider Vinegar

In Vitro Assessment Of Antifungal Potential Of Apple Cider Vinegar And Acetic Acid Versus Fluconazole In Clinical Isolates Of Otomycosis *

Abstract

Background: There has been an increase in the prevalence of otomycosis in recent years. This has been linked to the extensive use of antibiotics, use of immunosuppressant drugs and steroids for a variety of malignant and immunological diseases. Treatment of otomycosis is challenging, and requires a close follow-up; in addition treatment with topical or systemic antifungal drugs might be associated with problems of resistance, mucosal irritation, and systemic toxicities. *Candida albicans* and *Aspergillus niger* are the most commonly identified organisms. Aim: the aim of this study is to investigate the antifungal potential of apple cider vinegar and acetic acid in a hope to find a safer alternative to traditional antifungal drugs in treatment of otomycosis.

Patients and methods: ear swaps were collected from 18 patients attending otolaryngology outpatient clinic-Al-Habboobi Hospital who presented with aural symptoms suggestive of otomycosis. Fungal identification was done depending on microscopical and colonial morphology. Antifungal effect of the tested agents was assessed by agar well-diffusion assay.

Results: 18 samples were examined, 13 (72%) of them were positive for fungal growth, 6 were *Aspergillus niger*, 1 was *Aspergillus flavus*, 2 were *Candida albicans*, and the other 4 were Non- *Candida albicans*. Apple cider vinegar(5%) inhibits growth of *Aspergillus niger*, *Aspergillus flavus*, *Candida albicans* and Non- *Candida albicans* with average diameter of inhibition zones of 15mm, 13mm, 17.5mm, 17 mm respectively, while the average diameters noted with acetic acid 2% were 10.5mm, 11mm, 13mm, 13.5mm respectively. Fluconazole (5mg/ml) inhibits growth of the *Aspergillus niger*, *Aspergillus flavus* with average diameters of 14mm,20mm respectively,while cause no inhibition of *Candida albicans* and Non- *Candida albicans*.

Conclusion: Apple cider vinegar and acetic acid have significant antifungal activity at the tested concentrations against *Aspergillus niger*, *Aspergillus flavus*, and fluconazole resistant *Candida albicans* and Non- *Candida albicans*.

Source: Haydar Badr Jabir, Fatin Naeem Abbas, Rana Muhsin Khalaf. "In Vitro Assessment Of Antifungal Potential Of Apple Cider Vinegar And Acetic Acid Versus Fluconazole In Clinical Isolates Of Otomycosis" Thi-Qar Medical Journal (2011): Vol 5, Issue 1, 126-133.

Apple Cider Vinegar for Fungus Infections

Antifungal Activity of Apple Cider Vinegar on Candida Species Involved in Denture Stomatitis

Abstract

Apple cider vinegar showed antifungal properties against *Candida* spp., thus representing a possible therapeutic alternative for patients with denture stomatitis.

Source: Mota, Ana Carolina Loureiro Gama, et al. "Antifungal activity of apple cider vinegar on *Candida* species involved in denture stomatitis." Journal of Prosthodontics 24.4 (2015): 296-302.

In Vitro Assessment Of Antifungal Potential Of Apple Cider Vinegar And Acetic Acid Versus Fluconazole In Clinical Isolates Of Otomycosis

Abstract

Background: There has been an increase in the prevalence of otomycosis in recent years. This has been linked to the extensive use of antibiotics, use of immunosuppressant drugs and steroids for a variety of malignant and immunological diseases. Treatment of otomycosis is challenging, and requires a close follow-up; also treated with topical or systemic antifungal drugs might be associated with problems of resistance, mucosal irritation, and systemic toxicities. *Candida albicans* and *Aspergillus niger* are the most commonly identified organisms. Aim: This study aims to investigate the antifungal potential of apple cider vinegar and acetic acid in a hope to find a safer alternative to traditional antifungal drugs in the treatment of otomycosis. Patients and methods: ear swaps were collected from 18 patients attending otolaryngology outpatient clinic-Al-Habboobi Hospital who presented with aural symptoms suggestive of otomycosis.fungal identification was done depending on microscopical and colonial morphology. Antifungal effect of the tested agents was assessed by agar well diffusion assay. Results: 18 samples were examined, 13 (72%) of them were positive for fungal growth, 6 were *Aspergillus niger*, 1 was *Aspergillus flavus*, 2 were *Candida albicans*, and the other 4 were Non- *Candida albicans*.Apple cider vinegar(5%) inhibits the growth of *Aspergillus niger*, *Aspergillus flavus*, *Candida albicans* and non- *Candida albicans* with average diameter of inhibition zones of 15mm, 13mm, 17.5mm, 17 mm respectively, while the average diameters noted with acetic acid 2% were 10.5mm, 11mm, 13mm, 13.5mm respectively. Fluconazole (5mg/ml) inhibits the growth of the *Aspergillus niger*, *Aspergillus flavus* with average diameters of 14mm,20mm respectively, while cause no inhibition of *Candida albicans* and non- *Candida albicans*.Conclusion: Apple cider vinegar and acetic acid have significant antifungal activity at the tested concentrations against *Aspergillus niger*, *Aspergillus flavus*, and fluconazole-resistant *Candida albicans* and Non- *Candida albicans*.

Source: Jabir, Hayder Badr, Fatin Naeem Abbas, and Rana Muhsin Khalaf. "In vitro assessment of the antifungal potential of apple cider vinegar and acetic acid versus fluconazole in clinical isolates of otomycosis." Thi-Qar Medical Journal 5.1 (2011): 126-133.

Wormwood (*Artemisia absinthium*)

Chemical Composition of the Essential Oils of Serbian Wild-Growing *Artemisia absinthium* and *Artemisia vulgaris* *

Abstract

The chemical composition of the aerial and root essential oils, hydrodistilled from *Artemisia absinthium* L. and *Artemisia vulgaris* L. (wild-growing populations from Serbia), were studied by gas chromatography, gas chromatography-mass spectrometry, and ¹³C nuclear magnetic resonance. During the storage of plant material under controlled conditions, a significant decrease of essential oil yields (isolated directly after drying and after 1 year of storage) and significant differences in their chemical compositions were observed. A possible mechanism for the observed oil component interconversion

has been discussed. The noticeable differences in the chemical composition of the oils isolated from roots and aerial parts of *A. absinthium* and *A. vulgaris* were also correlated with the diverging biosynthetic pathways of volatiles in the respective plant organs. The antimicrobial activities against the common human pathogens of all of the isolated oils were tested according to National Committee on Clinical Laboratory Standards. The oils showed a broad spectrum of antimicrobial activity against the tested strains. Therefore, these oils can be used as flavor and fragrance ingredients.

Source: Polina Blagojevic, Niko Radulovic, Radosav Palic, Gordana Stojanovic. "Chemical Composition of the Essential Oils of Serbian Wild-Growing *Artemisia absinthium* and *Artemisia vulgaris*" *Journal of Agriculture and Food Chemistry* (2006): 54, 13, 4780–4789.

Screening of chemical composition and antifungal and antioxidant activities of the essential oils from three Turkish artemisia species *

Abstract

The compositions of essential oils isolated from the aerial parts of *Artemisia absinthium*, *Artemisia santonicum*, and *Artemisia spicigera* by hydrodistillation were analyzed by GC-MS, and a total of 204 components were identified. The major components of these essential oils were camphor (34.9-1.4%), 1,8-cineole (9.5-1.5%), chamazulene (17.8-nd%), nuciferol propionate (5.1-nd%), nuciferol butanoate (8.2-nd%), caryophyllene oxide (4.3-1.7%), borneol (5.1-0.6%), alpha-terpineol (4.1-1.6%), spathulenol (3.7-1.3%), cubenol (4.2-0.1%), beta-eudesmol (7.2-0.6%), and terpinen-4-ol (3.5-1.2%). The antifungal activities of these essential oils were tested against 11 plant fungi and were compared with that of a commercial antifungal reagent, benomyl. The results showed that all of the oils have potent inhibitory effects at very broad spectrum against all of the tested fungi. Pure camphor and 1,8-cineole, which are the major components of the oils, were also tested for antifungal activity against the same fungal species. Unlike essential oils, these pure compounds were able to show antifungal activity against only some of the fungal species. In addition, the antioxidant and DPPH radical scavenging activities of the essential oils, camphor, and 1,8-cineole were determined in vitro. All of the studied essential oils showed antioxidant activity, but camphor and 1,8-cineole did not.

Source: Saban Kordali, Ahmet Cakir, Ahmet Mavi, Hamdullah Kilic, Ali Yildirim. "Screening of chemical composition and antifungal and antioxidant activities of the essential oils from three Turkish artemisia species" *Journal of Agriculture and Food Chemistry* (2005): 53(5):1408-16.

Composition and antimicrobial activity of the essential oil of *Artemisia absinthium* from Croatia and France *

Abstract

The essential oils obtained by steam distillation from the aerial parts of two populations of *Artemisia absinthium*, from France and from Croatia, were analyzed by GC and GC-MS. The oils of *A. absinthium* of French origin contain (Z)-epoxyocimene and chrysanthenyl acetate as major components while the oils of Croatian *A. absinthium* contain mainly (Z)-epoxyocimene and beta-thujone. Analysis of oils before and after anthesis showed some quantitative differences. Analysis of separated leaves and flowering heads showed only few differences among these organs. As they contain no thujone, antimicrobial screening was performed on samples of French origin and showed that *A. absinthium* oil inhibited the growth of both tested yeasts (*Candida albicans* and *Saccharomyces cerevisiae* var. *chevalieri*).

Source: Fabien Juteau, Igor Jerkovic, Veronique masotti, Mladen Milos, Josip Mastelic, Jean-Marie Bessier, Josette Viano. "Composition and antimicrobial activity of the essential oil of *Artemisia absinthium* from Croatia and France" *Planta Medica* (2003): 69(2):158-61.

Turmeric Root

Antifungal activity of turmeric oil extracted from *Curcuma longa* (Zingiberaceae) *

Abstract

Turmeric oil and curcumin, isolated from *Curcuma longa* L., were studied against fifteen isolates of dermatophytes, four isolates of pathogenic molds and six isolates of yeasts. The inhibitory activity of turmeric oil was tested in *Trichophyton*-induced dermatophytosis in guinea pigs. The results showed that all 15 isolates of dermatophytes could be inhibited by turmeric oil at dilutions of 1:40-1:320. None of the isolates of dermatophytes were inhibited by curcumin. The other four isolates of pathogenic fungi were inhibited by turmeric oil at dilutions of 1:40-1:80 but none were inhibited by curcumin. All six isolates of yeasts tested proved to be insensitive to both turmeric oil and curcumin. In the experimental animals, turmeric oil (dilution 1:80) was applied by dermal application on the 7th day following dermatophytosis induction with *Trichophyton rubrum*. An improvement in lesions was observed in 2-5 days and the lesions disappeared 6-7 days after the application of turmeric oil.

Source: A. Apisariyakul, N. Vanittanakom, D. Buddhasukh. "Antifungal activity of turmeric oil extracted from *Curcuma longa* (Zingiberaceae)" *Journal of Ethnopharmacology* (1995): 49(3):163-9.

Spicing up” of the immune system by curcumin *

Abstract

Curcumin (diferuloylmethane) is an orange-yellow component of turmeric (*Curcuma longa*), a spice often found in curry powder. Traditionally known for its anti-inflammatory effects, curcumin has been shown in the last two decades to be a potent immunomodulatory agent that can modulate the activation of

T cells, B cells, macrophages, neutrophils, natural killer cells, and dendritic cells. Curcumin can also downregulate the expression of various proinflammatory cytokines including TNF, IL-1, IL-2, IL-6, IL-8, IL-12, and chemokines, most likely through inactivation of the transcription factor NF-kappaB. Interestingly, however, curcumin at low doses can also enhance antibody responses. This suggests that curcumin's reported beneficial effects in arthritis, allergy, asthma, atherosclerosis, heart disease, Alzheimer's disease, diabetes, and cancer might be due in part to its ability to modulate the immune system. Together, these findings warrant further consideration of curcumin as a therapy for immune disorders.

Source: Ganesh Chandra Jagetia, Bharat B. Aggarwal. "Spicing up" of the immune system by curcumin" Journal of Clinical Immunology (2007): 27(1):19-35.

Turmeric (Curcuma Longa L.): A promising spice for phytochemical and pharmacological activities

Abstract

Turmeric (*Curcuma longa*) is a small rhizomatous perennial herb belonging to Zingiberaceae family originating from South-Eastern Asia, most probably from India. The plant produces fleshy rhizomes of bright yellow to orange color in its root system, which is the source of the commercially available spice turmeric. In the form of root powder, turmeric is used for its flavoring properties as a spice, food preservative and food-coloring agent. Turmeric has a long history of use in Ayurvedic medicine as it is credited with a variety of important beneficial properties. Turmeric constituents include the three curcuminoids: Curcumin (diferuloylmethane; the primary constituent and the one responsible for its vibrant yellow color), demethoxycurcumin and bisdemethoxycurcumin, as well as volatile oils (turmerone, atlantone, and zingiberene), sugars, proteins, and resins. Several studies using the modern techniques have authenticated turmeric used as anti-inflammatory, antimicrobial, anti-fertility, anticancer, anti-diabetic, antioxidant, hypolipidemic, anti-venom, anti-hepatotoxic, nephroprotective, anticoagulant, etc.. Most importantly, the plant has shown to possess anti-HIV activity which could be of great value to combat AIDS particularly in third world countries. In this present work, we make an overview of the phytochemistry and pharmacological activities of turmeric, showing its importance.

Source: Yadav, Deepika, et al. "Turmeric (*Curcuma longa* L.): A promising spice for phytochemical and pharmacological activities." International Journal of Green Pharmacy (IJGP) 7.2 (2013).

Olive Leaf Extract

Phenolic Compounds and Antimicrobial Activity of Olive (*Olea europaea* L. Cv. Cobrançosa) Leaves

Abstract

We report the determination of phenolic compounds in olive leaves by reversed-phase HPLC/DAD, and the evaluation of their in vitro activity against several microorganisms that may be causal agents of human intestinal and respiratory tract infections, namely Gram-positive (*Bacillus cereus*, *B. subtilis* and *Staphylococcus aureus*), Gram-negative bacteria (*Pseudomonas aeruginosa*, *Escherichia coli* and *Klebsiella pneumoniae*) and fungi (*Candida albicans* and *Cryptococcus neoformans*). Seven phenolic compounds were identified and quantified: caffeic acid, verbascoside, oleuropein, luteolin 7-O-glucoside, rutin, apigenin 7-O-glucoside and luteolin 4'-O-glucoside. At low concentrations, olive leaf extracts showed an unusual combined antibacterial and antifungal action, which suggests their great potential as nutraceuticals, particularly as a source of phenolic compounds.

Source: Pereira, Ana, et al. "Phenolic compounds and antimicrobial activity of olive (*Olea europaea* L. Cv. Cobrançosa) leaves." Molecules 12.5 (2007): 1153-1162.

In vitro antimicrobial activity of olive leaves

Abstract

We investigated the antimicrobial effect of olive leaves against bacteria and fungi. The microorganisms tested were inoculated in various concentrations of olive leaf water extract. Olive leaf 0.6% (w/v) water extract killed almost all bacteria tested, within 3 h. Dermatophytes were inhibited by 1.25% (w/v) plant extract following a 3-day exposure whereas *Candida albicans* was killed following a 24 h incubation in the presence of 15% (w/v) plant extract. Olive leaf extract fractions, obtained by dialysis, that showed antimicrobial activity consisted of particles smaller than 1000 molecular weight cutoffs. Scanning electron microscopic observations of *C. albicans*, exposed to 40% (w/v) olive leaf extract, showed invaginated and amorphous cells. *Escherichia coli* cells, subjected to similar treatment but exposed to only 0.6% (w/v) olive leaf extract showed destruction. These findings suggest an antimicrobial potential for olive leaves.

Source: Markin, D., L. Duek, and I. Berdicevsky. "In vitro antimicrobial activity of olive leaves. Antimikrobielle Wirksamkeit von Olivenblättern in vitro." Mycoses 46.3-4 (2003): 132-136.

Caprylic Acid (MCT Powder)

Short-Term Antifungal Treatments of Caprylic Acid with Carvacrol or Thymol Induce

Synergistic 6-Log Reduction of Pathogenic *Candida albicans* by Cell Membrane Disruption and Efflux Pump Inhibition *

Background/aims: Although naturally-derived antifungals have been investigated for their ability to inactivate *Candida albicans*, which is a major cause of candidiasis, they have shown a less than 3 log reduction in *C. albicans* or required treatment times of longer than 3 h. Thus, the naturally-derived antifungals used in previous studies could not substantially eradicate *C. albicans* within a short period of time.

Methods: To improve the fungicidal effects of naturally derived antifungals against *C. albicans* within short time periods, we developed composites showing antifungal synergism using caprylic acid (CA), carvacrol (CAR) and thymol (THM) for 1-10 min at 22/37°C. Using flow cytometry, we examined the mode of action for the synergism of these compounds on membrane integrity and efflux pump activity.

Results: Whereas the maximum reduction by individual treatments was 0.6 log CFU/ml, CA + CAR/THM (all 1.5 mM) eliminated all pathogens (> 6.8 log reduction) after 1 min at 37°C and after 10 min at 22°C. The flow cytometry results showed that exposure to CA damaged the membranes in 15.7-36.5% of cells and inhibited efflux pumps in 15.4-31.3% of cells. Treatments with CAR/THM slightly affected cell membranes (in 1.8-6.9% of cells) but damaged efflux pumps in 14.4-29.6% of cells. However, the combined treatments clearly disrupted membranes (> 83.1% of cells) and pumps (> 95.0% of cells). The mechanism of this synergism may involve membrane damage by CA, which facilitates the entry of antifungals into the cytoplasm, and the inhibition of efflux pumps by CA, CAR or THM, causing their accumulation within cells and, leading to cell death.

Conclusion: Antifungal composites (CA + CAR/THM) showing synergism (i.e., an additional 6 log reduction) within minutes at room/body temperature can be used to treat candidiasis and improve the microbiological safety of facilities contaminated with fungi as a novel alternative to synthetic antifungals.

Source: Yoon Seol Bae, Min Suk Rhee. "Short-Term Antifungal Treatments of Caprylic Acid with Carvacrol or Thymol Induce Synergistic 6-Log Reduction of Pathogenic *Candida albicans* by Cell Membrane Disruption and Efflux Pump Inhibition" *Cellular Physiology and Biochemistry* (2019): 53(2):285-300.

Caprylic acid in the effective treatment of intractable medical problems of frequent urination, incontinence, chronic upper respiratory infection, root canalled tooth infection, ALS, etc., caused by asbestos & mixed infections of *Candida albicans*, *Helicobacter pylori* & cytomegalovirus with or without other microorganisms & mercury *

Abstract

There are many causes of frequent urination. Whenever water or fluids are consumed, the patient has to urinate within 10 or 20 min. Often urinary bladder examinations & blood tests show no significant abnormalities, & treatment by anti-bacterial or anti-viral agents does not improve the symptoms significantly. In intractable frequent urination with difficulty holding urine, as well as other intractable medical problems such as frequent coughing, white pus in gingiva, infection of the apex of a root canalled tooth, slow-healing wounds, & ALS, the authors often found coexisting mixed infections of *Candida albicans* (C.A.), *Helicobacter pylori* (H.P.), & Cytomegalovirus (CMV) with or without additional bacterial (*Chlamydia trachomatis*, etc.) or viral infections & increased Asbestos, with or without Hg deposits. We often found various degrees of mixed infections with C.A., H.P., & CMV in the external sphincters of the urethra & in the Trigone of the urinary bladder which consists of (1) a horizontal, band-like area between the 2 ureter openings & (2) the funnel shaped part of the Trigone at the lower half of the urinary bladder. In the coexistence of significant amounts of C.A., H.P. & CMV, the infection cannot be reduced by otherwise effective medicines for H.P. & CMV. However, one optimal dose of Diflucan, or Caprylic acid taken orally or externally applied, rapidly reduced the symptoms significantly. We found the best treatment is to give a combination of an optimal dose of Caprylic acid orally in the form of "CaprilyCare" or "Caprylic Acid," with a capsule of Omega-3 Fish Oil as an anti-viral agent, Amoxicillin, Substance Z & a Cilantro tablet. We found that an optimal dose of Caprylic acid increases normal cell telomere (NCT) to a desirable 750 ng BDORT units while Diflucan increases NCT by only 25 ng BDORT units, & with Omega-3 fish oil, leads to a mutual cancellation of both drugs. Thus, Caprylic acid is superior to & less expensive than Diflucan, & has potential application for anti-cancer, anti-aging, anti-Alzheimer's disease, anti-Autism, anti-infection, & general circulatory improvement.

Source: Yoshiaki Omura, Brian O'Young, Marlyn Jones, Andrew Pallow, Harsha Duvvi, Yasuhiro Shimotsuura. "Caprylic acid in the effective treatment of intractable medical problems of frequent urination, incontinence, chronic upper respiratory infection, root canalled tooth infection, ALS, etc., caused by asbestos & mixed infections of *Candida albicans*, *Helicobacter pylori* & cytomegalovirus with or without other microorganisms & mercury" *Acupuncture and Electrotherapeutics Research* (2011): 36(1-2):19-64.

Bioperine

Recent Developments in Delivery, Bioavailability, Absorption and Metabolism of Curcumin: the Golden Pigment from Golden Spice *

Abstract

Curcumin (diferuloylmethane) is a yellow pigment present in the spice turmeric (*Curcuma longa*) that has been associated with antioxidant, anti-inflammatory, anticancer, antiviral, and antibacterial activities as indicated by over 6,000 citations. In addition, over one hundred clinical studies have been

carried out with curcumin. One of the major problems with curcumin is perceived to be the bioavailability. How curcumin should be delivered *in vivo*, how bioavailable is it, how well curcumin is absorbed and how it is metabolized, is the focus of this review. Various formulations of curcumin that are currently available are also discussed.

Piperine

Besides these natural compounds have been also used to increase the bioavailability of curcumin. One of them is piperine, a major component of black pepper, known as inhibitor of hepatic and intestinal glucuronidation and is also shown to increase the bioavailability of curcumin. This effect of piperine on the pharmacokinetics of curcumin has been shown to be much greater in humans than in rats. In humans, curcumin bioavailability was increased by 2,000% at 45 minutes after co-administering curcumin orally with piperine, whereas in rats, it has been found that concomitant administration of piperine 20 mg/kg with curcumin 2 g/kg increased the serum concentration of curcumin by 154% for a short period of 1-2 hours post drug. The study shows that in the dosages used, piperine enhances the serum concentration, extent of absorption and bioavailability of curcumin in both rats and humans with no adverse effects [95].

Another study also showed that piperine (20 mg/kg orally) when administered with curcumin (2 g/kg orally) enhances the bioavailability of the latter up to 20-fold more in epileptic rats [111]. Enhanced bioavailability of curcumin was also evidenced by other researcher when curcumin was administered orally concomitant with piperine. Intestinal absorption of curcumin was also found relatively higher when administered concomitantly with piperine, and it stayed significantly longer in the body tissues [112]. In view of these findings, curcumin-piperine (Cu-Pi) nanoparticles has been prepared by various methods [113]. The bioavailability, cellular uptake and biological effects of this nanoparticles are being tested.

Source: Sahdeo Prasad, PhD, Amit K. Tyagi, PhD, Bharat B. Aggarwal, PhD. "Recent Developments in Delivery, Bioavailability, Absorption and Metabolism of Curcumin: the Golden Pigment from Golden Spice" *Cancer Research and Treatment* (2014): 46(1): 2–18.

Anti-inflammatory and antiarthritic effects of piperine in human interleukin 1 β -stimulated fibroblast-like synoviocytes and in rat arthritis models *

Abstract

Introduction: The objective of this study was to determine the anti-inflammatory, nociceptive, and antiarthritic effects of piperine, the active phenolic component in black pepper extract.

Methods: The *in vitro* anti-inflammatory activity of piperine was tested on interleukin 1 β (IL1 β)-stimulated fibroblast-like synoviocytes derived from patients with rheumatoid arthritis. The levels of IL6, matrix metalloproteinase (MMPs), cyclo-oxygenase 2 (COX-2), and prostaglandin E2 (PGE₂) were investigated by ELISA and RT-PCR analysis. The analgesic and antiarthritic activities of piperine were investigated on rat models of carrageenan-induced acute paw pain and arthritis. The former were evaluated with a paw pressure test, and the latter by measuring the squeaking score, paw volume, and weight distribution ratio. Piperine was administered orally to rats at 20 and 100 mg/kg/day for 8 days.

Results: Piperine inhibited the expression of IL6 and MMP13 and reduced the production of PGE₂ in a dose dependant manner at concentrations of 10 to 100 μ g/ml. In particular, the production of PGE₂ was significantly inhibited even at 10 μ g/ml of piperine. Piperine inhibited the migration of activator protein 1 (AP-1), but not nuclear factor (NF) κ B, into the nucleus in IL1 β -treated synoviocytes. In rats, piperine significantly reduced nociceptive and arthritic symptoms at days 8 and 4, respectively. Histological staining showed that piperine significantly reduced the inflammatory area in the ankle joints.

Conclusions: These results suggest that piperine has anti-inflammatory, antinociceptive, and antiarthritic effects in an arthritis animal model. Thus, piperine should be further studied with regard to use either as a pharmaceutical or as a dietary supplement for the treatment of arthritis.

Source: Jun Soo Bang, Da Hee Oh, Hyun Choi, Bong-Jun Sur, Sung-Jig Lim, Jung Yeon Kim, Hyung-In Yang, Myung Chul Yoo, Dae-Hyun Ham, Kyoung Soo Kim. "Anti-inflammatory and antiarthritic effects of piperine in human interleukin 1 β -stimulated fibroblast-like synoviocytes and in rat arthritis models" *Arthritis Research Therapy* (2009): 11(2): R49.

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