Ejemplos de evidencias de las actividades terapéuticas de los fitofármacos en forma de aceites esenciales.

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**Analgesic, antipyretic and anti-inflammatory activity of the essential oil of Artemisia caerulescens subsp. Gallica**
Authors: Moran A., Martin M.L., Montero M.J., Ortiz de Urbina A.V., Sevilla M.A., San Roman L.

Abstract
The essential oil of *Artemisia caerulescens* subsp. *gallica* was observed to have analgesic, antipyretic and anti-inflammatory actions when administered intraperitoneally to rats and mice at doses one-fourth to one-third that of its LD50 of 1.35 ml/kg. Lysine acetylsalicylate was used as a reference compound.

**Limonene-induced regression of mammary carcinomas**
Authors: Haag J.D., Lindstrom M.J., Cloud M.N.

Abstract
Dietary administration of the monocyclic monoterpenoid d-limonene causes complete regression of both dimethylbenz [alpha]anthracene- and N-nitroso-N-methylurea-induced rat mammary carcinomas. Carcinomas regress when limonene is added to the diet either when the tumor is small and still capable of spontaneously regressing or when it is large and progressed beyond the stage when it is susceptible to spontaneous regression. The limonene dose-tumor regression response relationship is steep. Significant regressions are not observed at 5% dietary levels, while a majority of tumors completely regress above a 7.5% dietary level. Limonene appears to act in a cytostatic fashion. Its removal from the diet results in a significant number of tumor recurrences. Regressing tumors have a unique histopathological appearance that is not associated with gross cytotoxicity, immune cell involvement, or apoptosis. Preliminary analysis suggests a remodeling/redifferentiation event underlying regression. The underlying mechanism of action of limonene in causing tumor regression is unknown. However, it should be noted that limonene can selectively inhibit the isoprenylation of small G proteins. Monoterpenoids such as limonene represent a novel class of anticancer drugs with the potential to cause tumor regressions with limited toxicity.
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**Limonene in trial cancer**
Authors: David McNamee

Abstract
Jirtle Rl, Haag Jd, Ariazi Ea, Gould MN. Increased mannose 6-phosphate/insulin-like growth factor II receptor and transforming growth factor β1 levels during monoterpen-induced regression of mammary tumours. *Cancer Res* 1993; 53:

**The induction of apoptosis in human melanoma, breast and ovarian cancer cell lines using an essential oil extract from the conifer Tetraclinis articulata**
Authors: Buhagiar, J.A., Camilleri Podesta, M.T., Wilson, A.P., Micallef, M.J., Ali S.
Editors: Anticancer Research 19- 1999: 5435-5444

Abstract
The cytotoxic effect of conifer Tetraclinis articulata essential oil (TAEO) on a number of human cancer cell lines and peripheral blood lymphocytes was assessed at various concentrations and time exposures. The cytotoxic effect showed the hallmarks of apoptosis confirmed by a variety of techniques including flow cytometry, an apoptosis-specific marker combined to fluorescent staining and DNA laddering. All cell lines tested were inhibited in a dose-dependent fashion and within a contact time of less than eight hours for the higher concentrations. Melanoma, breast and ovarian cancer cells gave IC50s of around 80 micrograms/ml whilst the IC50s on peripheral blood lymphocytes was almost double this value. We conclude that the essential oil contains components that are effective at inducing apoptosis. The advantages of using a mixture of monoterpenes (C10) as present in an EO over a single component, are discussed.
**Antiviral properties of isoborneol, a potent inhibitor of herpes simplex virus type 1**

Authors: Armaka M., Papanikolaou E., Sivropoulou A., Arsenakis M.
Editors: Brevier Science; VOL 43 ISS 2-1999 Sep: 79-92

Abstract:
Isoborneol, a monoterpene and a component of several plant essential oils, showed dual viricidal activity against herpes simplex virus 1 (HSV-1). First, it inactivated HSV-1 by almost 4 log10 values within 30 min of exposure, and second, isoborneol at a concentration of 0.06% completely inhibited viral replication, without affecting viral adsorption. Isoborneol did not exhibit significant cytotoxicity at concentrations ranging between 0.016% and 0.08% when tested against human and monkey cell lines. Isoborneol specifically inhibited glycosylation of viral polypeptides based on the following data: (1) the mature fully glycosylated forms of two viral glycoproteins gB and gD were not detected when the virus was replicated in the presence of isoborneol, (2) no major changes were observed in the glycosylation pattern of cellular polypeptides between untreated and isoborneol treated Vero cells, (3) isoborneol did not affect the glycosylation of gB produced from a copy of the gB gene resident in the cellular genome, and (4) other monoterpenes such as 1,8-cineole and borneol, a stereoisomer of isoborneol, did not inhibit HSV-1 glycosylation.

**Menthol: a natural analgesic compound**

Editors: Neuroscience Letters 322 (3) 145- 148

Abstract
Menthol, after topical application, causes a feeling of coolness due to stimulation of 'cold' receptors by inhibiting Ca++ currents of neuronal membranes. Since Ca++ channel blockers are endowed with analgesic properties, the aim of the present study was to investigate the potential antinociceptive effect of menthol. (-)-Menthol produced a dose-dependent increase in the pain threshold in the mouse hot-plate (3-10 mg kg (-1) p.o.) and abdominal constriction (3-10 mg kg (-1) p.o.; 10 microg per mouse intracerebroventricularly (i.c.v.)) tests. The antinociceptive effect of (-)-menthol was antagonised by the unselective opioid antagonist naloxone and by the selective kappa-
antagonist nor-NBI. Conversely, CTOP (mu-antagonist), 7-benzylidenedenal-trexone (delta(1) antagonist) and naltriben (delta(2) antagonist) did not prevent (-)-mentholantinociception. In both tests, (+)-menthol (10-50 mg kg (-1) p.o.; 10-30 microg per mouse i.c.v.) was unable to modify the pain threshold. These results indicate that (-)-mentholis endowed with analgesic properties mediated through a selective activation of kappa-opioid receptors.

The use of aromatherapy in Intrapartum Midwifery Practice
Authors: Burns E. Blamey C, Ersser SJ, Lloyd AJ, Barnetson L.
Editors: Report No. 7, Oxford Brookes University: Oxford Centre for Research and Development Health Care Practice

Abstract
The authors report the process and results of an evaluation of a midwifery aromatherapy service for mothers in labour: This study of 8058 mothers in childbirth, is the largest research initiative in the use of aromatherapy within a health-care setting. The study involved a wide range of participants, from mothers who experienced a low risk, spontaneous labour and birth, to those whose labour was induced, and those who had vaginal operative delivery and Caesarean section. The study took place over a period of 8 years, which enabled a more challenging test of the effect of aromatherapy on intrapartum midwifery practice and outcomes. In the study a total of 10 essential oils were used, plus a carrier oil, which were administered to the participants via skin absorption and inhalation. The study found little direct evidence that the practice of aromatherapy per se reduces the need for pain relief during labour, or the incidence of operative delivery. But a key finding of this study suggests that two essential oils, clary sage and chamomile are effective in alleviating pain. The evidence from this study suggests that aromatherapy can be effective in reducing maternal anxiety, fear and/or pain during labour. The use of aromatherapy appeared to facilitate a further reduction in the use of systemic opioids in the study centre, from 6% in 1990 to 0.4% in 1997 (per woman). Aromatherapy is an inexpensive care option. In 1997 when 1592 mothers used aromatherapy, the total cost was 769.17 Pounds. The study reports a minimal incidence of associated symptoms. Out of 8058 mothers, 1% (100) recorded an associated symptom. These were mild in nature. The successful model of integrated practice that this aromatherapy study presents, offers a useful example for other units to consider.
An evaluation of tea tree oil as an alternative microbicide
Author: Willcox M.
Source: Queen Alexandra Hospital, Portsmouth

Abstract
Tea tree oil is a popular ingredient in complementary medicines and beauty products. This literature review reveals some evidence of efficacy as an antiseptic, antibacterial and antifungal in topical application but also highlights dermatitis as a potential side-effect.

Toxicity of the essential oil of Melaleuca alternifolia or tea tree oil
Authors: Carson C.R, Riley.

Abstract
Objectives: The aim of this study was to investigate the antimicrobial activity of a range of commercially available tea tree oil (TTO) products and to evaluate whether formulation plays a significant part in their antiseptic activity. Methods: The antimicrobial activity of the purchased products and control TTO solutions was assessed against Escherichia coli, Staphylococcus aureus, Salmonella typhimurium, Pseudomonas aeruginosa, and Candida albicans using well diffusion, broth microdilution, and broth macrodilution assays. Results: Zone sizes obtained by the agar well diffusion assay ranged from 0 to 49.8 mm, with the more viscous and lipophilic products producing the smallest zones. Micro- and macrodilution methods showed that eight products had minimum inhibitory concentrations that were lower than the nonformulated TTO control. The remaining three products showed activity equivalent to the TTO control. Conclusions: In general, the commercially available antiseptic TTO products showed antimicrobial activity that was equivalent to, or greater than the nonformulated TTO control. This suggests that the TTO within these products has retained its antimicrobial activity. Furthermore, the enhanced activity of the products may be attributed to other antimicrobial excipients within the products such as preservatives, or to synergistic antimicrobial interactions between the TTO and other product excipients. The observation that the commercially available antiseptic TTO products tested in this study retained adequate antimicrobial activity emphasizes the importance of considering how product bases and excipients may interact with the active compound during formulation.
to ensure efficacy of the final product. Finally, the current data suggest that these TTO products may also be active in vivo. However, this can only be determined through further studies and in clinical trials.

Research on the chemical composition and aspects of the pharmacological action of the essential oil of Kochi thyme (Thymus kotschyanus Boiss)
Authors: Guseinov D.Ia., Kagramanov K.M., Kasumov F.Iu., Akhundov R.A.
Editors: Farmakol Toksikol – 1987 Mar-Apr; 50 (2): 73-4 Russian

Abstract
In experiments on white mice, guinea pigs and rabbits it was found that ethereal oil of Kochi thyme is non-toxic. At concentrations of 0.5-5.0% (1 mg/kg) it produced in rabbits hypotensive and cardiotonic effects.

Application of Origanum majorana L. essential oil as an antimicrobial agent in sausage
Source: Department of Food Engineering, URI-Campus de Erechim, Av. Sete de Setembro 1621, CEP 99700-000, Erechim, RS, Brazil.

Abstract
This work reports on the antimicrobial activity in fresh sausage of marjoram (Origanum majorana L.) essential oil against several species of bacteria. The in vitro minimum inhibitory concentration (MIC) was determined for 10 selected aerobic heterotrophic bacterial species. The antimicrobial activity of distinct concentrations of the essential oil based on the highest MIC value was tested in a food system comprising fresh sausage. Batch food samples were also inoculated with a fixed concentration of Escherichia coli and the time course of the product was evaluated with respect to the action of the different concentrations of essential oil. Results showed that addition of marjoram essential oil to fresh sausage exerted a bacteriostatic effect at oil concentrations lower than the MIC, while a bactericidal effect was observed at higher oil concentrations which also caused alterations in the taste of the product.
Aromatherapy: evidence for sedative effects of the essential oil of lavender after inhalation
Authors: Buchbauer G., Jirovetz L., Jager W., Dietrich H. Plank
Editors: Z Naturforsch {C};46(11-12)-1991 Nov-Dec:1067-72

Abstract
The sedative properties of the essential oil of Lavender (Lavandula angustifolia Miller) and of its main constituents--linalool and linalyl acetate--were investigated in mice followed up in a series of experimental procedures. The significant decrease in the motility of female and male laboratory animals under standardized experimental conditions is found to be closely dependent on the exposure time to the drugs. Nevertheless after an injection of caffeine into mice a hyperactivity was observed which was reduced to nearly a normal motility only by inhalation of these fragrance drugs. In particular the correlation of the motility of the animals to linalool in serum is experimentally proven, thus furnishing evidence of the aromatherapeutical use of herbal pillows employed in folk medicine since ancient times in order to facilitate falling asleep or to minimize stressful situations of man.

The chemical composition and biological activity of clove essential oil, Eugenia caryophyllata (Syzygium aromaticum L. Myrtaceae): a short review.
Authors: Chaieb K, Hajlaoui H, Zmantar T, Kahla-Nakbi AB, Rouabha M, Mahdouani K, Bakhrouf

Abstract
The essential oil extracted from the dried flower buds of clove, Eugenia caryophyllata L. Merr. & Perry (Myrtaceae), is used as a topical application to relieve pain and to promote healing and also finds use in the fragrance and flavouring industries. The main constituents of the essential oil are phenylpropanoids such as carvacrol, thymol, eugenol and cinnamaldehyde. The biological activity of Eugenia caryophyllata has been investigated on several microorganisms and parasites, including pathogenic bacteria, Herpes simplex and hepatitis C viruses. In addition to its antimicrobial, antioxidant, antifungal and antiviral activity, clove essential oil possesses antiinflammatory,
Eugenol--from the remote Maluku Islands to the international market place: a review of a remarkable and versatile molecule.

Authors: Kamatou GP, Vermaak I, Viljoen AM.

Abstract
Eugenol is a major volatile constituent of clove essential oil obtained through hydrodistillation of mainly Eugenia caryophyllata (=Syzygium aromaticum) buds and leaves. It is a remarkably versatile molecule incorporated as a functional ingredient in numerous products and has found application in the pharmaceutical, agricultural, fragrance, flavour, cosmetic and various other industries. Its vast range of pharmacological activities has been well-researched and includes antimicrobial, anti-inflammatory, analgesic, anti-oxidant and anticancer activities, amongst others. In addition, it is widely used in agricultural applications to protect foods from micro-organisms during storage, which might have an effect on human health, and as a pesticide and fumigant. As a functional ingredient, it is included in many dental preparations and it has also been shown to enhance skin permeation of various drugs. Eugenol is considered safe as a food additive but due to the wide range of different applications, extensive use and availability of clove oil, it is pertinent to discuss the general toxicity with special reference to contact dermatitis. This review summarises the pharmacological, agricultural and other applications of eugenol with specific emphasis on mechanism of action as well as toxicity data.
Ejemplos de evidencias de las actividades terapéuticas de los fitofármacos en forma de aceites esenciales.

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Authors: Park MJ, Gwak KS, Yang I, Choi WS, Jo HJ, Chang JW, Jeung EB, Choi IG.
Editors: Department of Forest Sciences, College of Agriculture and Life Sciences Seoul National University, Seoul, Republic of Korea. Published in: J Microbiol. 2007 Oct;45(5):460-5.

Abstract
This study was carried out in order to investigate the potential of using plant oils derived from Leptospermum petersonii Bailey and Syzygium aromaticum L. Merr. Et Perry as natural antifungal agents. The antifungal effects of essential oils at concentrations of 0.05, 0.1, 0.15, and 0.2 mg/ml on the dermatophytes Microsporum canis (KCTC 6591), Trichophyton mentagrophytes (KCTC 6077), Trichophyton rubrum (KCCM 60443), Epidermophyton floccosum (KCCM 11667), and Microsporum gypseum were evaluated using the agar diffusion method. The major constituents of the active fraction against the dermatophytes were identified by gas chromatography-mass spectrometry and high-performance liquid chromatography analysis. The antifungal activities of S. aromaticum oil (clove oil) against the dermatophytes tested were highest at a concentration of 0.2 mg/ml, with an effectiveness of more than 60%. Hyphal growth was completely inhibited in T. mentagrophytes, T. rubrum, and M. gypseum by treatment with clove oil at a concentration of 0.2 mg/ml. Eugenol was the most effective antifungal constituent of clove oil against the dermatophytes T. mentagrophytes and M. canis. Morphological changes in the hyphae of T. mentagrophytes, such as damage to the cell wall and cell membrane and the expansion of the endoplasmic reticulum, after treatment with 0.11 mg/ml eugenol were observed by transmission electron microscopy (TEM). At a concentration of 0.2 mg/ml, L. petersonii oil (LPO) was more than 90% effective against all of the dermatophytes tested, with the exception of T. rubrum. Geranial was determined to be the most active antifungal constituent of L. petersonii oil. Taken together, the results of this study demonstrate that clove and tea tree oils exhibited significant antifungal activities against the dermatophytes tested in this study.
Phytochemical composition of Cymbopogon citratus and Eucalyptus citriodora essential oils and their anti-inflammatory and analgesic properties on Wistar rats.
Authors: Gbenou JD, Ahounou JF, Akakpo HB, Laley A, Yayi E, Gbaguidi F, Baba-Moussa L, Darbouz R, Dansou P, Moudachirou M, Kotchoni SO.

Abstract
Cymbopogon citratus and Eucalyptus citriodora are widely used herbs/plants as a source of ethnomedicines in tropical regions of the world. In this work, we studied the anti-inflammatory and gastroprotective effects of C. citratus and E. citriodora essential oils on formol-induced edema, and acetic acid induced abdominal cramps in Wistar rats. To fully understand the chemically induced anti-inflammatory properties of these plants, we first analyzed the chemical composition of the essential oils. A total of 16 chemical constituents accounting for 93.69 % of the oil, were identified in C. citratus among which, Geranial (27.04 %), neral (19.93 %) and myrcene (27.04 %) were the major constituents. For E. citriodora, 19 compounds representing 97.2 % of the extracted oil were identified. The dominant compound of E. citriodora essential oil was citronellal (83.50 %). In vivo analysis and histological assay showed that the two essential oils displayed significant dose dependent edema inhibition effect over time. They displayed strong analgesic and antipyretic properties similar to that induced by 50 mg/kg of acetylsalicylate of lysine. However, the E. citriodora essential oil was more effective than that of C. citratus. We identified significant numbers of aldehyde molecules in both essential oils mediating antioxidant activity that may contribute to the anti-inflammatory effects observed on the rats. Altogether, this work demonstrates the anti-inflammatory property of C. citratus and E. citriodora suggesting their potential role as adjuvant therapeutic alternatives in dealing with inflammatory-related diseases.
Synergistic properties of the terpenoids aromadendrene and 1,8-cineole from the essential oil of Eucalyptus globulus against antibiotic-susceptible and antibiotic-resistant pathogens.

Authors: Mulyaningsih S, Sporer F, Zimmermann S, Reichling J, Wink M.


Abstract
The aim of the present study was to investigate the chemical composition of the essential oil of the fruits of Eucalyptus globulus and to examine the potential application of the fruit oil against multidrug-resistant bacteria. GLC/MS analysis in the fruit oil showed that aromadendrene was the main compound followed by 1,8-cineole and globulol. The three most abundant components of the fruit oil were also tested individually against microorganisms. In addition, the synergistic effects of combinations of the major constituents (aromadendrene and 1,8-cineole) of the fruit oil were also investigated. All Gram-positive bacteria were susceptible to the fruit oil with different degrees of susceptibility as determined by microdilution method. The oil exerted a marked inhibition against multidrug-resistant bacteria such as methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin-resistant enterococci (VRE) Enterococcus faecalis. The results indicated that aromadendrene might be responsible for the antimicrobial properties, whereas 1,8-cineole and globulol exhibited low activities. The checkerboard assay demonstrated that combinations of 1,8-cineole and aromadendrene reduce the MIC in most cases in an additive way, whereas the time-kill assay indicates a synergistic effect.
Essential oils from aromatic herbs as antimicrobial agents.  
Authors: Solórzano-Santos F, Miranda-Novales MG.  

Abstract
Bacterial resistance to multiple antibiotics is a health problem. Essential oils (EOs) possess antibacterial properties and have been screened as potential sources of novel antimicrobial compounds. Terpenes and terpenoids are components derived from EOs. Some of these EOs show inhibitory activity against Staphylococcus aureus. Carvacrol has specific effects on S. aureus and Staphylococcus epidermidis. Perilla oil suppresses expression of α-toxin, Staphylococcus enterotoxin A and B and toxic shock syndrome toxin. Geraniol shows good activity in modulating drug resistance in several gram-negative species. EOs could act as biopreservatives, reducing or eliminating pathogenic bacteria and increasing the overall quality of animal and vegetable food products. Although clinical studies are scarce, the uses of EOs for topical administration and as penetration enhancers for antiseptics are promising. Little information exists for oral administration.