# TERPENES AND TERPENOIDS IN CANNABIS


Marco Troiani

Digamma Consulting

In Collaboration with Lief Therapeutics

In Collaboration with MCR Laboratories


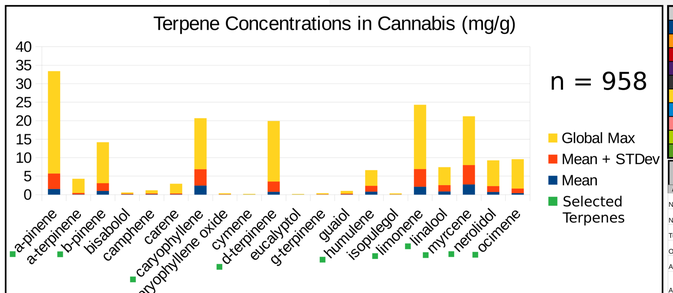


**Figure 1** - Terpene Concentrations in Cannabis - Data from a set of 958 samples of cannabis flower. Displayed are mean, standard deviation, and global maximum for 20 terpenes. The 10 most prevalent terpenes are denoted in green for further statistical analysis.

| Terpene | Found In | Smell |
|---|---|---|
| Nerolidol | neroli, ginger, jasmine | wood, fresh bark |
| Humulene | hops | hoppy |
| Caryophyllene | cloves, hops, black pepper | spicy, sweet |
| Linalool | lavender, basil | lavender, flowery |
| d-Terpinene | juniper, myristica | musky, diesel |
| Limonene | lemon, orange | citrus, fruity, sharp |
| Ocimene | basil | sweet, herbal |
| Myrcene | bay leaf, hops, mango | sweet, musky |
| b-Pinene | pine trees, hops | pine, green wood |
| a-Pinene | pine trees, rosemary | pine, wood |

**Figure 2** – Table illustrating the 10 terpenes selected from Figure 1 and their associated plant sources and smell. Listed is also color labels used in Figure 3 and Tables 1-9.

THESIS: Data science can allow doctors to prescribe specific strains of cannabis to patients based on their medical condition.

The medical benefits of cannabis are becoming more evident in the medical research community. Many of the studies that study cannabis focus on cannabinoids, such as tetrahydrocannabinol (THC) and cannabidiol (CBD). Many studies have found that cannabinoids can help treat inflammation, cancer, chronic pain, neurological dysfunction and many mental health issues.

Although cannabinoids are most likely the major component of the medical efficacy of cannabis, anecdotal evidence from medical patients in the United States indicate that some strains of cannabis are beneficial for certain aliments, conditions, or particular patients, while others are not. This strain variation cannot be accounted for by cannabinoid composition because the large majority of United States medical cannabis is 90% or greater THC by cannabinoid composition. What does vary greatly from strain to strain of cannabis is the chemical profile of terpenes and terpenoids found on the plant.

Terpenes and terpenoids are a class of volatile hydrocarbon compounds produced by many species of plants. Terpenes often responsible for the smell that humans associate with various plants, and are responsible for the unique smell of each strain of cannabis. Terpenes are present in the trichomes of the plant and are chemically bound to cannabinoids forming crystalline structures.

Terpenes also have many medical benefits, even when not associated with cannabinoids. Using databasing technology, it is possible to bridge the gap of knowledge between the medical benefits of terpenes found in cannabis and the chemical knowledge of each cannabis strain's terpene profile. To accomplish this, we built two custom databases: one to organize medical research papers on cannabis, and one to organize chemical data on cannabis samples. Using both of these data sets, it is possible to give doctors and patients the tools to understand the relationship between their cannabis' terpene profile and its medical benefits.

## CHEMICAL ANALYSIS

Terpene data was taken from two analytical laboratories in distant parts of the United States: Massachusetts and Nevada. These labs were participating in their state's medical marijuana program and generated data over a span of over 18 months. The cannabis samples were analyzed by headspace-gas chromatography-mass spectrometry (HS-GC-MS). Laboratories were screened based on proper quality control, certifications, and GLP and ISO standards. All data is reported in mg/g, which is equivalent to per mille (‰) or part per thousand.

## DATABASING

Chemical data entries were collected as samples and organized by strain and terpene values. These values were analyzed for statistical mean, standard deviation, and global maximum and this data was used to find 10 prevalent terpenes in cannabis samples for further statistical analysis (**Figure 1**). The data set was analyzed for the 14 most common strain names, and the 10 selected terpenes were graphed as normalized values (**Figure 3**). Values were normalized to the total mass of the 10 selected terpenes.

Medical data entries were collected as medical research publications and organized by publication data (author, date, etc), cannabinoids studied, terpenes studied, and associated medical disorders. This data set was restricted to papers focusing specifically on terpenes with an associated medical disorder, and organized by terpene (**Tables 1-9**). Totals of the numbers of paper referencing each terpene, and the subtotals for the following medical disorders were generated: cancer, anxiety, depression, pain, insomnia, and infection.

## RESULTS

The chemical database contained 958 cannabis flower samples with data for 20 terpenes. Of these, ten were identified to be more prevalent in cannabis: nerolidol, humulene, caryophyllene, linalool, d-terpinene, limonene, ocimene, myrcene, and alpha and beta pinene. These terpenes were selected form the set of 20 based on global maximum, standard deviation and mean, which have been illustrated in **Figure 1**. The remaining 10 terpenes can be said to consistently be present in trace quantities in cannabis over the data set examined.

**Figure 2** displays the 10 terpenes selected for further examination. Each is displayed with a color label, a non-cannabis plant source, and a qualitative term for each terpene's smell and aroma.

**Figure 3** displays the results of the 14 most popular cannabis strains illustrated by terpene profile. Each bar in each bar graph represents a unique sample of cannabis submitted to the cannabis laboratory, with many bars indicated a higher data set. The data is normalized, showing the percentage of each terpene out of the combined mass of the ten terpenes being examined. Visually, the data shows patterns in the terpene profile that are consistent with each strain, though natural variation is readily apparent. These patterns allow medical professionals to quickly see which terpenes are major components of each cannabis strain. Continued terpene testing on each batch of medicine would ensure that strains are both labeled accurately and contain necessary amounts of certain terpenes. Larger integrated data systems would allow for real-time information about cannabis strains available at local dispensaries and pharmacies, and to search and organize those available strains by desired terpene content.

The medical database contained 431 publications from 251 Journals. After restricting the data set to entries which address both at least one specific terpene and at least one specific medical disorder, 130 publications remained. Tables 1-9 display the data from the restricted dataset organized by terpene. The totals at the bottom allow a quick review of the total number of publications for each terpene, with a subtotals by disorder. These tables allow the relative effectiveness of each terpene at treating different disorders to be reviewed at a glance. This data is designed to help inform medical professionals of which terpenes may be beneficial to their patient based on their disorder and general condition. Combined with Table 3, this allows for a medical professional to recommend strains based on a patient's condition.

Table 1 — Nerolidol

| Author Last Name | Year | Title | Journal | Disorders |
|---|---|---|---|---|
| Mohd-Shukri | 2011 | THE EFFECTS OF NEROLIDOL, ALLICIN AND BERENIL ON THE MORPHOLOGY OF Trypanosoma evansi IN MICE : A COMPARATIVE STUDY USING LIGHT AND ELECTRON MICROSCOPIC APPROACHES | Malaysian Applied Biology Journal | antimicrobial, antiparasitic, infection |
| Khakpour | 2014 | Effect of Citrus aurantium L. Essential Oil and Haloperidol on Anxiety in Male Mice | World Journal of Neuroscience | anxiety |
| Saketi | 2014 | Effect of Citrus aurantium L. Essential Oil and Its Interaction with Fluoxetine on Anxiety in Male Mice | Journal of Behavioral and Brain Science | anxiety |
| Hanusova | 2015 | The effect of Myrcia rubra essential oil and its components a-humulene and trans-nerolidol on adhesion and apoptosis of colorectal cancer cells | Cancer Cell and Microenvironment | cancer, colon cancer |
| Ferreira | 2012 | Nerolidol effects on mitochondrial and cellular energetics | Toxicology in Vitro | cancer, liver cancer |
| Das | 2012 | Antioxidative effects of the spice cardamom against non-melanoma skin cancer by modulating nuclear factor erythroid-2-related factor 2 and NF-kB signalling pathways | British Journal of Nutrition | cancer, non-melanoma skin cancer |
| Russo | 2011 | Taming THC: potential cannabis synergy and phytocannabinoid-terpenoid entourage effects | British Journal of Pharmacology | inflammation, memory, cognition, pain, depression, anxiety, addiction, epilepsy, cancer, fungal and bacterial infections, MRSA, entourage |
| Nokhodchi | 2007 | The effect of terpene concentrations on the skin penetration of diclofenac sodium | International Journal of Pharmaceutics | skin permeability, transdermal, absorption, diffusion |
| Celik | 2016 | Beneficial effects of nerolidol on thioacetamide-induced damage of the reproductive system in male rats | Biomedical Research | testicular damage |

| Total | cancer | anxiety | depression | pain | insomnia | infection |
|---|---|---|---|---|---|---|
| 9 | 4 | 3 | 1 | 1 | 0 | 2 |

Table 2 — Humulene

| Author Last Name | Year | Title | Journal | Disorders |
|---|---|---|---|---|
| Lin | 2013 | Extraction of biologically active compounds by hydrodistillation of Boswellia species gum resins for anti cancer therapy | OA Alternative Medicine | cancer |
| Legault | 2003 | Antitumor Activity of Balsam Fir Oil: Production of Reactive Oxygen Species Induced by α-Humulene as Possible Mechanism of Action | Planta Medica | cancer |
| Silva | 2007 | Cytotoxic evaluation of essential oil from Zanthoxylum rhoifolium Lam. leaves | Acta Amazonica | cancer, cervical cancer, lung cancer, colon cancer |
| Hanusova | 2015 | The effect of Myrcia rubra essential oil and its components a-humulene and trans-nerolidol on adhesion and apoptosis of colorectal cancer cells | Cancer Cell and Microenvironment | cancer, colon cancer |
| Lan | 2011 | Death receptor 5-mediated TNFR family signaling pathways modulate Â -humulene-induced apoptosis in human colorectal cancer HT29 cells | Oncology Reports | cancer, colon cancer |
| Ramadan | 2015 | Essential oils from Egyptian aromatic plants as antioxidant and novel anticancer agents in human cancer cell lines | Grasas y Aceites | cancer, liver cancer, breast cancer, prostate cancer, colon cancer, lung cancer |
| Kumar | 2000 | Hypericum perforatum: Nature's mood stabilizer | Indian Journal of Experimental Biology | depression, anxiety, infection |
| Rogerio | 2009 | Preventive and therapeutic anti-inflammatory properties of the sesquiterpene a-humulene in experimental airways allergic inflammation | British Journal of Pharmacology | inflammation, allergey |

| Total | cancer | anxiety | depression | pain | insomnia | infection |
|---|---|---|---|---|---|---|
| 8 | 6 | 1 | 1 | 0 | 0 | 1 |

Table 3 — Caryophyllene

| Author Last Name | Year | Title | Journal | Disorders |
|---|---|---|---|---|
| Al Monsouri | 2014 | The cannabinoid receptor 2 agonist, β-caryophyllene, reduced voluntary alcohol intake and attenuated ethanol-induced place preference and sensitivity in mice | Pharmacology, Biochemistry, and Behavior | alcoholism, addiction |
| Novak | 2001 | Essential oils of different cultivars of Cannabis sativa L. and their antimicrobial activity | Flavor and Fragrance Journal | antimicrobial, infection |
| Nissen | 2010 | Characterization and antimicrobial activity of essential oils of industrial hemp varieties (Cannabis sativa L.) | Fitoterapia | antimicrobial, infection |
| Sepahvand | 2014 | C hemicalcomposition, antioxidant activity and antibacterial effect of essential oil of the aerial parts of S alvia sclareoides | Asian Pacific Journal of Tropical Medicine | antioxidant, infection |
| Kumar | 2016 | AROMA THERAPY IN MAJOR DEPRESSIVE DISORDERS (MDD): AN ASSESSMENT | World Journal of Pharmacy and Pharmaceutical Sciences | anxiety, depression |
| Bahi | 2014 | -Caryophyllene, a CB2 receptor agonist produces multiple behavioral changes relevant to anxiety and depression in mice | Physiology and Behavior | anxiety, depression, stresscb |
| Lehmer | 2005 | Ambient odors of orange and lavender reduce anxiety and improve mood in dental office | Physiology and Behavior | anxiety, mood |
| Radulescu | 2011 | CHEMICAL COMPOSITION AND CANCER CHEMOPREVENTIVE EFFECT OF VOLATILE OIL ISOLATED FROM THYMUS PULEGIODES L. | Farmacia | cancer |
| Lin | 2013 | Extraction of biologically active compounds by hydrodistillation of Boswellia species gum resins for anti cancer therapy | OA Alternative Medicine | cancer |
| Duran | 2016 | SYNERGISTIC ACTIVITIES OF THE ESSENTIAL OILS HYPERICUM PERFORATUM WITH METHOTREXATE ON HUMAN BREAST CANCERC ELL LINE MCF-7 | ICAMS | cancer, breast cancer |
| Silva | 2007 | Cytotoxic evaluation of essential oil from Zanthoxylum rhoifolium Lam. leaves | Acta Amazonica | cancer, cervical cancer, lung cancer, colon cancer |
| Ramadan | 2015 | Essential oils from Egyptian aromatic plants as antioxidant and novel anticancer agents in human cancer cell lines | Grasas y Aceites | cancer |
| Jung | 2015 | Caryophyllene potently inhibits solid tumor growth and lymph node metastasis of B16F10 melanoma cells in high-fat diet–induced obese C57BL/6N mice | Carcinogenesis | cancer, metastasis, melanoma, obesity, metabolism |
| He | 2006 | Gum mastic inhibits the expression and function of the androgen receptor in prostate cancer | Cancer | cancer, prostate cancer |
| Herrera-Ruiz | 2006 | Antidepressant and anxiolytic effects of hydroalcoholic extract from Salvia elegans | Journal of Ethnopharmacology | depression, anxiety |
| Kumar | 2000 | Hypericum perforatum: Nature's mood stabilizer | Indian Journal of Experimental Biology | depression, anxiety, infection |
| McPartland | 2001 | Cannabis and Cannabis Extracts: Greater Than the Sum of Their Parts? | | entourage |
| Jianu | 2013 | Chemical Composition and Antimirobial Activity of Essential Oils of Lavender (Lavandula angustifolia) and Lavandin (Lavandula x intermedia) Grown in Western Romania | International Journal of Agriculture & Biology | infection, antibacterial, antifungal, Shigella, Staphylococcus, Escherichia, Salmonella, Streptococcus |
| Jardak | 2017 | Chemical composition, anti-biofilm activity and potential cytotoxic effect on cancer cells of Rosmarinus officinalis L. essential oil from Tunisia | Lipids in Health and Disease | infection, antibacterial, cancer, cervical cancer, breast cancer |
| Burstein | 2009 | Cannabinoids, Endocannabinoids, and Related Analogs in Inflammation | AAPS Journal | inflammation |
| Gertsch | 2008 | Anti-inflammatory cannabinoids in diet | Communicative & Integrative Biology | inflammation, crohns, atherosclerosis, osteoarthritis |
| Russo | 2011 | Taming THC: potential cannabis synergy and phytocannabinoid-terpenoid entourage effects | British Journal of Pharmacology | inflammation, memory, cognition, pain, depression, anxiety, addiction, epilepsy, cancer, fungal and bacterial infections, MRSA, entourage |
| Russo | 2003 | Cannabis is more than simply Δ9-tetrahydrocannabinol | Psychopharmacology | inflammation, pain, anxiety, depression, autoimmune, immunodeficiency, antioxidant |
| Benito | 2011 | -Caryophyllene Inhibits Dextran Sulfate Sodium-Induced Colitis in Mice through CB2 Receptor Activation and PPAR Pathway | American Journal of Pathology | inflammation, ulcerative colitis |
| Horvath | 2012 | -caryophyllene ameliorates cisplatin-induced nephrotoxicity in a cannabinoid 2 receptor-dependent manner | Free Radical Biology and Medicine | nephrotoxicity, renal failure, kidney disease, inflammation, oxidative stress |
| Guimaraes-Santos | 2012 | Copaiba Oil-Resin Treatment Is Neuroprotective and Reduces Neutrophil Recruitment and Microglia Activation after Motor Cortex Excitotoxic Injury | Evidence-Based Complementary and Alternative Medicine | neuroprotective, excitotoxicity, inflammation |
| Ghelardini | 2001 | Local anaesthetic activity of -caryophyllene | Il Farmaco | pain |
| Fine | 2013 | The Endocannabinoid System, Cannabinoids, and Pain | Rambam Maimonides Medical Journal | pain, chronic pain |
| Klauke | 2014 | The cannabinoid CB2 receptor-selective phytocannabinoid beta-caryophyllene exerts analgesic effects in mouse models of inflammatory and neuropathic pain | European Neuropsychopharmacology | pain, neuropathic pain, infammation |

| Total | cancer | anxiety | depression | pain | insomnia | infection |
|---|---|---|---|---|---|---|
| 29 | 9 | 7 | 6 | 5 | 0 | 7 |

Table 4 — Linalool

| Author Last Name | Year | Title | Journal | Disorders |
|---|---|---|---|---|
| Cavanagh | 2002 | Biological Activities of Lavender Essential Oil | Phytotherapy Research | antibacterial, antifungal, infection, sedative, depression, anxiety |
| Mitic-Culafic | 2016 | Antigenotoxic potential of plant monoterpenes linalool, myrcene and eucalyptol against IQ-and PhIP- induced DNA damage | Botanica Serbica | antimutagenic, mutation, antioxidant, cancer |
| Sepahvand | 2014 | C hemicalcomposition, antioxidant activity and antibacterial effect of essential oil of the aerial parts of S alvia sclareoides | Asian Pacific Journal of Tropical Medicine | antioxidant, infection |
| Perrucci | 1996 | The Activity of Volatile Compounds from Lavandula angustifolia Against Psoroptes cuniculi | Phytotherapy Research | antiparasitic, Psoroptes |
| Bradley | 2007 | Anxiolytic effects of Lavandula angustifolia odour on the Mongolian gerbil elevated plus maze | Journal of Enthnopharmacology | anxiety |
| Souto-Maior | 2011 | Anxiolytic-like effects of inhaled linalool oxide in experimental mouse anxiety models | Pharmacology, Biochemistry, and Behavior | anxiety |
| Kumar | 2016 | AROMA THERAPY IN MAJOR DEPRESSIVE DISORDERS (MDD): AN ASSESSMENT | World Journal of Pharmacy and Pharmaceutical Sciences | anxiety, depression |
| Saki | 2014 | The effect of most important medicinal plants on two important psychiatric disorders (anxiety and depression) - a review | Asian Pacific Journal of Tropical Medicine | anxiety, depression |
| Rombola | 2017 | Bergamot Essential Oil Attenuates Anxiety-Like Behaviour in Rats | Molecules | anxiety, mood |
| Lehmer | 2005 | Ambient odors of orange and lavender reduce anxiety and improve mood in dental office | Physiology and Behavior | anxiety, mood |
| Lopes Campelo | 2011 | Sedative, anxiolytic and antidepressant activities of Citrus limon (Burn) essential oil in mice | Die Pharmazie | anxiety, stress, depression |
| Boskabady | 2005 | RELAXANT EFFECTS OF OCIMUM BASILICUM ON GUINEA PIG TRACHEAL CHAINS AND ITS POSSIBLE MECHANISM(S) | DARU Journal of Pharmaceutical Sciences | bronchodilation |
| Radulescu | 2011 | CHEMICAL COMPOSITION AND CANCER CHEMOPREVENTIVE EFFECT OF VOLATILE OIL ISOLATED FROM THYMUS PULEGIODES L. | Farmacia | cancer |
| Ramadan | 2015 | Essential oils from Egyptian aromatic plants as antioxidant and novel anticancer agents in human cancer cell lines | Grasas y Aceites | cancer, liver cancer, breast cancer, prostate cancer, colon cancer, lung cancer |
| Das | 2012 | CYTOTOXIC AND APOPTOGENIC PROPERTIES OF DRACOCEPHALUM KOTSCHYI AERIAL PART DIFFERENT FRACTIONS ON CALU-6 AND MEHR-80 LUNG CANCER CELL LINES | Farmacia | cancer, lung cancer |
| Zhou | 2014 | Antioxidative effects of the spice cardamom against non-melanoma skin cancer by modulating nuclear factor erythroid-2-related factor 2 and NF-kB signalling pathways | British Journal of Nutrition | cancer, non-melanoma skin cancer |
| El-Alfy | 2012 | Anti-depression effect of Chimonanthus salicifolicus essential oil in chronic stressed rats | Journal of Medicinal Plant Research | depression |
| Guzman-Gutierrez | 2012 | Nature Against Depression | Current Medicinal Chemistry | depression |
| Herrera-Ruiz | 2006 | Antidepressant activity of Lisea glaucescens essential oil: Identification of b -pinene and linalool as active principles | Journal of Enthnopharmacology | depression |
| Perry | 2006 | Antidepressant and anxiolytic effects of hydroalcoholic extract from Salvia elegans | Journal of Enthnopharmacology | depression, anxiety |
| McPartland | 2001 | Aromatherapy in the Management of Psychiatric Disorders | CNS Drugs | depression, anxiety, panic, stress, sexual dysfunction, convulsions |
| De Martino | 2001 | Cannabis and Cannabis Extracts: Greater Than the Sum of Their Parts? | | entourage |
| de Rapper | 2009 | Chemical Composition and in Vitro Antimicrobial and Mutagenic Activities of Seven Lamiaceae Essential Oils | Molecules | infection, antibacterial, antifungal |
| d'Auria | 2013 | The In Vitro Antimicrobial Activity of Lavandula angustifolia Essential Oil in Combination with Other Aroma-Therapeutic Oils | Evidence-Based Complementary and Alternative Medicine | infection, antibacterial, MRSA, Staphylococus, Enterococcus, Pseudomonas, Crytpococcus, Candida, antifungal |
| Adam | 2013 | Antifungal activity of Lavandula angustifolia essential oil against Candida albicans yeast and mycelial form | Medical Mycology | infection, antifungal, Candida |
| Navarra | 1998 | Antifungal Activity of Essential Oils and Active Principles from Chemotypes of Lippia alba (Mill.) N.E. Brown | Journal of Agricultural and Food Chemistry | infection, antifungal, Malassezia, Trichophyton, Trichosporon |
| Danh | 2015 | Comparison of Chemical Composition, Antioxidant and Antimicrobial Activity of Lavender (Lavandula angustifolia L.) Essential Oils Extracted by Supercritical CO2, Hexane and Hydrodistillation | Frontiers in Pharmacology | infection, inflammation, cancer, anxiety, neuroprotective, pain, cardiovascular |
| Peana | 2012 | Evaluation of the anti-inflammatory, anti-catabolic and pro-anabolic effects of E-Anti-depression effect of Chimonanthus salicifolicus essential oil in chronic stressed rats | Food and Bioprocess Technology | infection, S. aureus, E. coli, E. faecalis, C. albicans |
| Russo | 2002 | Anti-inflammatory activity of linalool and linalyl acetate constituents of essential oils | Phytomedicine | inflammation, edema |
| Peana | 2011 | Taming THC: potential cannabis synergy and phytocannabinoid-terpenoid entourage effects | British Journal of Pharmacology | inflammation, memory, cognition, pain, depression, anxiety, addiction, epilepsy, cancer, fungal and bacterial infections, MRSA, entourage |
| Peana | 2004 | Effects of (?)-linalool in the acute hyperalgesia induced by carrageenan, L-glutamate and prostaglandin E2 | European Journal of Pharmacology | pain |
| Peana | 2004 | Profile of spinal and supra-spinal antinociception of (-)-linalool | European Journal of Pharmacology | pain |
| Ghelardini | 1999 | Local Anaesthetic Activity of the Essential Oil of Lavandula angustifolia | Planta Medica | pain, anaesthesia |
| Barocelli | 2004 | Antinociceptive and gastroprotective effects of inhaled and orally administered Lavandula hybrida Reverchon bGrossoG essential oil | Life Sciences | pain, antinociceptive, analgesic, gastroprotection, gastric ulcers, GI |
| Johnson | 2016 | The effectiveness of nurse-delivered aromatherapy in an acute care setting | Complementary Therapies in Medicine | pain, nausea, anxiety |
| Yu | 2017 | Lavandula angustifolia Mill. Oil and Its Active Constituent Linalyl Acetate Alleviate Pain and Urinary Residual Sense after Colorectal Cancer Surgery: A Randomised Controlled Trial | Evidence-Based Complementary and Alternative Medicine | pain, urinary symptoms |
| Nakamura | 2009 | Stress Repression in Restrained Rats by (R)-(-)-Linalool Inhalation and Gene Expression Profiling of Their Whole Blood Cells | Journal of Agricultural and Food Chemistry | stress, blood disorders, anxiety |
| Meehan-Atrash | 2017 | Toxicant Formation in DabbintL The Terpene Story | ACS Omega | toxicity, toxic breakdown products |

| Total | cancer | anxiety | depression | pain | insomnia | infection |
|---|---|---|---|---|---|---|
| 38 | 7 | 14 | 10 | 8 | 0 | 9 |

Table 5 — d-Terpinene

| Author Last Name | Year | Title | Journal | Disorders |
|---|---|---|---|---|
| Novak | 2001 | Essential oils of different cultivars of Cannabis sativa L. and their antimicrobial activity | Flavor and Fragrance Journal | antimicrobial, infection |
| Nissen | 2010 | Characterization and antimicrobial activity of essential oils of industrial hemp varieties (Cannabis sativa L.) | Fitoterapia | antimicrobial, infection |
| Turkez | 2015 | Genotoxic and oxidative damage potentials in human lymphocytes after exposure to terpinolene in vitro | Cytotechnology | antioxidant |
| Okumura | 2011 | Terpinolene, a component of herbal sage, downregulates AKT1 expression in K562 cells | Oncology Letters | cancer |
| Aydin | 2013 | ANTICANCER AND ANTIOXIDANT PROPERTIES OF TERPINOLENE IN RAT BRAIN CELLS | Archives of Industrial Hygiene and Toxicology | cancer, antioxidant |
| Afoulous | 2011 | Helichrysum gymnocephalum Essential Oil: Chemical Composition and Cytotoxic, Antimalarial and Antioxidant Activities, Attribution of the Activity Origin by Correlations | Molecules | cancer, breast cancer |
| Jardak | 2017 | Chemical composition, anti-biofilm activity and potential cytotoxic effect on cancer cells of Rosmarinus officinalis L. essential oil from Tunisia | Lipids in Health and Disease | infection, antibacterial, cancer, cervical cancer, breast cancer |
| Macedo | 2016 | Association of terpinolene and diclofenac presents antinociceptive and anti-inflammatory synergistic effects in a model of chronic inflammation | Brazilian Journal of Medical and Biological Research | pain, inflammation |
| Johnson | 2016 | The effectiveness of nurse-delivered aromatherapy in an acute care setting | Complementary Therapies in Medicine | pain, nausea, anxiety |

| Total | cancer | anxiety | depression | pain | insomnia | infection |
|---|---|---|---|---|---|---|
| 9 | 4 | 1 | 0 | 2 | 0 | 3 |

Table 6 — Limonene

| Author Last Name | Year | Title | Journal | Disorders |
|---|---|---|---|---|
| van Vuuren | 2007 | Antimicrobial activity of limonene enantiomers and 1,8-cineole alone and in combination | Flavor and Fragrance Journal | antimicrobial, infection |
| Ibrahim | 2001 | Insecticidal, repellent, antimicrobial activity and phytotoxicity of essential oils: With special reference to limonene and its suitability for control of insect pests | Agriculture and Food Science in Finland | antimicrobial, infection |
| Novak | 2001 | Essential oils of different cultivars of Cannabis sativa L. and their antimicrobial activity | Flavor and Fragrance Journal | antimicrobial, infection |
| Nissen | 2010 | Characterization and antimicrobial activity of essential oils of industrial hemp varieties (Cannabis sativa L.) | Fitoterapia | antimicrobial, infection |
| Bai | 2016 | Protective Effect of D-Limonene against Oxidative Stress-Induced Cell Damage in Human Lens Epithelial Cells via the p38 Pathway | Oxidative Medicine and Cellular Longevity | antioxidant |
| Pimenta | 2012 | Naturally occurring anxiolytic substances from aromatic plants of genus citrus | Journal of Medicinal Plants | anxiety |
| Leite | 2008 | Behavioral effects of essential oil of Citrus aurantium L. inhalation in rats | Brazilian Journal of Pharmacognosy | anxiety |
| Hatano | 2012 | Anxiolytic effects of repeated treatment with an essential oil from Lippia alba and (R)-(-)-carvone in the elevated T-maze | Brazilian Journal of Medical and Biological Research | anxiety |
| Khakpour | 2014 | Effect of Citrus aurantium L. Essential Oil and Haloperidol on Anxiety in Male Mice | World Journal of Neuroscience | anxiety |
| Saketi | 2014 | Effect of Citrus aurantium L. Essential Oil and Its Interaction with Fluoxetine on Anxiety in Male Mice | Journal of Behavioral and Brain Science | anxiety |
| Lehmer | 2000 | Ambient odor of orange in a dental office reduces anxiety and improves mood in female patients | Physiology and Behavior | anxiety |
| Khanum | 2010 | Anxiety-Herbal Treatment: A Review | Research and Reviews in Biomedicine and Biotechnology | anxiety |
| Costa | 2013 | Citrus aurantium L. essential oil exhibits anxiolytic like activity mediated by 5-HT1A-receptors and reduces cholesterol after repeated oral treatment | BMC Complementary & Alternative Medicine | anxiety, cholestrol, cardiovascular |
| Kumar | 2016 | AROMA THERAPY IN MAJOR DEPRESSIVE DISORDERS (MDD): AN ASSESSMENT | World Journal of Pharmacy and Pharmaceutical Sciences | anxiety, depression |
| Gargano | 2008 | Essential Oils Against Lung and Liver Cancer Cells | Phytomedicine | anxiety, epilepsy, pain |
| Rombola | 2017 | Bergamot Essential Oil Attenuates Anxiety-Like Behaviour in Rats | Molecules | anxiety, mood |
| Lehmer | 2005 | Ambient odors of orange and lavender reduce anxiety and improve mood in dental office | Physiology and Behavior | anxiety, mood |
| Moraes Pultrini | 2005 | Effects of the essential oil from Citrus aurantium L. in experimental anxiety models in mice | Life Sciences | anxiety, obsessive compulsive disorder, OCD |
| Lima | 2012 | Anxiolytic-like activity and GC-MS analysis of limonene fragrance, a natural compound found in foods and plants | Pharmacology, Biochemistry, and Behavior | anxiety, stress |
| Lopes Campelo | 2011 | Sedative, anxiolytic and antidepressant activities of Citrus limon (Burn) essential oil in mice | Die Pharmazie | anxiety, stress, depression |
| Garcia | 2010 | The anticancer drug perillyl alcohol is a Na/K-ATPase inhibitor | Molecular and Cellular Biochemistry | cancer |
| Russin | 1989 | Inhibition of rat mammary carcinogenesis by monoterpenoids | Carcinogenesis | cancer, breast cancer |
| Odeh | 2012 | THE CYTOTOXIC EFFECT OF ESSENTIAL OILS CITRUS AURANTIUM PEELS ON HUMAN COLORECTAL CARCINOMA CELL LINE (LIM1863) | Journal of Microbiology, Biotechnology and Food Sciences | cancer, colon cancer |
| Da Fonesca | 2007 | Preliminary results from a phase I/II study of perillyl alcohol intranasal administration in adults with recurrent malignant glioma | Surgical Neurology | cancer, glioma |
| Da Fonesca | 2010 | Case of Advanced Recurrent Glioblastoma Successfully Treated with Monoterpene Perillyl Alcohol by Intranasal Administration | Journal of Cancer Therapy | cancer, glioma, glioblastoma |
| Sani | 2017 | CYTOTOXIC AND APOPTOGENIC PROPERTIES OF DRACOCEPHALUM KOTSCHYI AERIAL PART DIFFERENT FRACTIONS ON CALU-6 AND MEHR-80 LUNG CANCER CELL LINES | Farmacia | cancer, lung cancer |
| Das | 2012 | Antioxidative effects of the spice cardamom against non-melanoma skin cancer by modulating nuclear factor erythroid-2-related factor 2 and NF-kB signalling pathways | British Journal of Nutrition | cancer, non-melanoma skin cancer |
| Zetola | 2002 | CNS activities of liquid and spray-dried extracts from Lippia alba Verbenaceae (Brazilian false melissa) | Journal of Enthnopharmacology | convulsions, stress, anxiety |
| Zhou | 2014 | Anti-depression effect of Chimonanthus salicifolicus essential oil in chronic stressed rats | Journal of Medicinal Plant Research | depression |
| McPartland | 2001 | Cannabis and Cannabis Extracts: Greater Than the Sum of Their Parts? | | entourage |
| Viana | 2000 | Anticonvulsant Activity of Essential Oils and Active Principles from Chemotypes of Lippia alba (Mill.) N.E. Brown | Biological and Pharmaceutical Bulletin | epilepsy, seizures, anticonvulsant |
| Angioni | 2006 | Chemical Composition, Seasonal Variability, and Antifungal Activity of Lavandula stoechas L. ssp. stoechas Essential Oils from Stems/Leaves and Flowers | Journal of Agricultural and Food Chemistry | infection, antifungal, Aspergillus, Rhizotonia, Fusarium |
| Adam | 1998 | Antifungal Activities of Origanum vulgare subsp. hirtum, Mentha spicata, Lavandula angustifolia, and Salvia fruticosa Essential Oils against Human Pathogenic Fungi | Journal of Agricultural and Food Chemistry | infection, antifungal, Malassezia, Trichophyton, Trichosporon |
| Kaefer | 2008 | The Role of Herbs and Spices in Cancer Prevention | Journal of Nutritional Biochemistry | infection, antioxidant, inflammation, cancer |
| Navarra | 2015 | Citrus bergamia essential oil: from basic research to clinical application | Frontiers in Pharmacology | infection, inflammation, cancer, anxiety, neuroprotective, pain, cardiovascular |
| Chaudhary | 2009 | Perillyl alcohol attenuates Ras-ERK signaling to inhibit murine skin inflammation and tumorigenesis | Chemico-Biological Interactions | inflammation, cancer |
| Russo | 2011 | Taming THC: potential cannabis synergy and phytocannabinoid-terpenoid entourage effects | British Journal of Pharmacology | inflammation, memory, cognition, pain, depression, anxiety, addiction, epilepsy, cancer, fungal and bacterial infections, MRSA, entourage |
| Russo | 2003 | Cannabis is more than simply Δ9-tetrahydrocannabinol | Psychopharmacology | inflammation, pain, anxiety, depression, autoimmune, immunodeficiency, antioxidant |
| Cheng | 2009 | Neuropharmacological activities of phytoncide released from Cryptomeria japonica | Journal of Wood Science | insomnia, anxiety, pain |
| Johnson | 2016 | The effectiveness of nurse-delivered aromatherapy in an acute care setting | Complementary Therapies in Medicine | pain, nausea, anxiety |
| Williams | 1991 | Terpenes and the Lipid-Protein-Partitioning Theory of Skin Penetration Enhancement | Pharmaceutical Research | skin permeability, absorption, transdermal |
| Williams | 1991 | The enhancement index concept applied to terpene penetration enhancers for human skin and model lipophilic (oestradiol) and hydrophilic (5fluorouracil) drugs | International Journal of Pharmaceutics | skin permeability, absorption, transdermal |
| Nokhodchi | 2007 | The effect of terpene concentrations on the skin penetration of diclofenac sodium | International Journal of Pharmaceutics | skin permeability, transdermal, absorption, diffusion |
| d'Alessio | 2014 | Anti-Stress Effects of d-Limonene and Its Metabolite Perillyl Alcohol | Rejuvenation Research | stress, anxiety |
| Meehan-Atrash | 2017 | Toxicant Formation in DabbintL The Terpene Story | ACS Omega | toxicity, toxic breakdown products |

| Total | cancer | anxiety | depression | pain | insomnia | infection |
|---|---|---|---|---|---|---|
| 45 | 11 | 22 | 5 | 5 | 2 | 9 |

Table 7 — Ocimene

| Author Last Name | Year | Title | Journal | Disorders |
|---|---|---|---|---|
| Cavanagh | 2002 | Biological Activities of Lavender Essential Oil | Phytotherapy Research | antibacterial, antifungal, infection, sedative, depression, anxiety |
| Sepahvand | 2014 | C hemicalcomposition, antioxidant activity and antibacterial effect of essential oil of the aerial parts of S alvia sclareoides | Asian Pacific Journal of Tropical Medicine | antioxidant, infection |
| Hui | 2010 | Chemical composition of lavender essential oil and it santioxidant activity and inhibition against rhinitis-related bacteria | African Journal of Microbiology Research | antioxidant, infection, antibacterial, Staphylococcus, Micrococcus, Proteus, Escherichia |
| Lehmer | 2005 | Ambient odors of orange and lavender reduce anxiety and improve mood in dental office | Physiology and Behavior | anxiety, mood |
| Boskabady | 2005 | RELAXANT EFFECTS OF OCIMUM BASILICUM ON GUINEA PIG TRACHEAL CHAINS AND ITS POSSIBLE MECHANISM(S) | DARU Journal of Pharmaceutical Sciences | bronchodilation |
| Radulescu | 2011 | CHEMICAL COMPOSITION AND CANCER CHEMOPREVENTIVE EFFECT OF VOLATILE OIL ISOLATED FROM THYMUS PULEGIODES L. | Farmacia | cancer |
| Herrera-Ruiz | 2006 | Antidepressant and anxiolytic effects of hydroalcoholic extract from Salvia elegans | Journal of Enthnopharmacology | depression, anxiety |
| Taran | 2010 | Antimicrobial activity of essential oils of Ferulago angulata subsp. carduchorum | Jundishapur Journal of Microbiology | infection |
| Vaseghi | 2013 | Hypnotic Effect of Salvia reuterana Boiss for Treatment of Insomnia | Journal of Medicinal Plants | insomnia |
| Andalib | 2011 | SEDATIVE AND HYPNOTIC EFFECTS OF IRANIAN TRADITIONAL MEDICINAL HERBS USED FOR TREATMENT OF INSOMNIA | EXCLI Journal | insomnia |

| Total | cancer | anxiety | depression | pain | insomnia | infection |
|---|---|---|---|---|---|---|
| 10 | 1 | 3 | 2 | 0 | 2 | 4 |

Table 8 — Myrcene

| Author Last Name | Year | Title | Journal | Disor