

MEDICAL MARIJUANA: ~~A NEW~~ ANCIENT OPTION IN PATIENT CARE.

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Taxonomy of Marijuana (MJ)

- ▣ Family Cannabaceae
 - Cannabis
 - Humulus
 - Celtis



Taxonomy of Marijuana

- ▣ Family Cannabaceae
 - Cannabis sp.
 - ▣ Sativa – narrow leaves, tall, fewer flowers, euphoric high
 - ▣ Indica – fat leaves, squat, abundant Flowers, heavy sedative high
 - ▣ Ruderalis – variant leaves, short, wild Type from central Asia



Taxonomy of Marijuana



MJ Archaeological Evidence

- ▣ 3500 BCE – Otzi, early report of cannabis seeds in pouch
- ▣ 2727 BCE – writings of Chinese Emperor Shen Nung⁵.
- ▣ 2459 BCE – Beaker culture grave near Hattemerbroek, NL. Large concentration of pollen⁶.
- ▣ 1450 BCE – Exodus 30:22-23 discusses use of Kaneh-Bosem (Cannabis) anointing oil¹⁰.
- ▣ 1213 BCE - Egyptians use for glaucoma, inflammation, and enemas.
- ▣ 700 BCE - Yanghai Tombs (Gobi Desert) near Turpan, China. 45 yo, blue eyed, shaman entombed with nearly 2lbs of MJ similar in quality to today³.
- ▣ 440 BCE – Herodotus's *Histories* refer to Scythians usage⁴.

Modern Historic Use of MJ

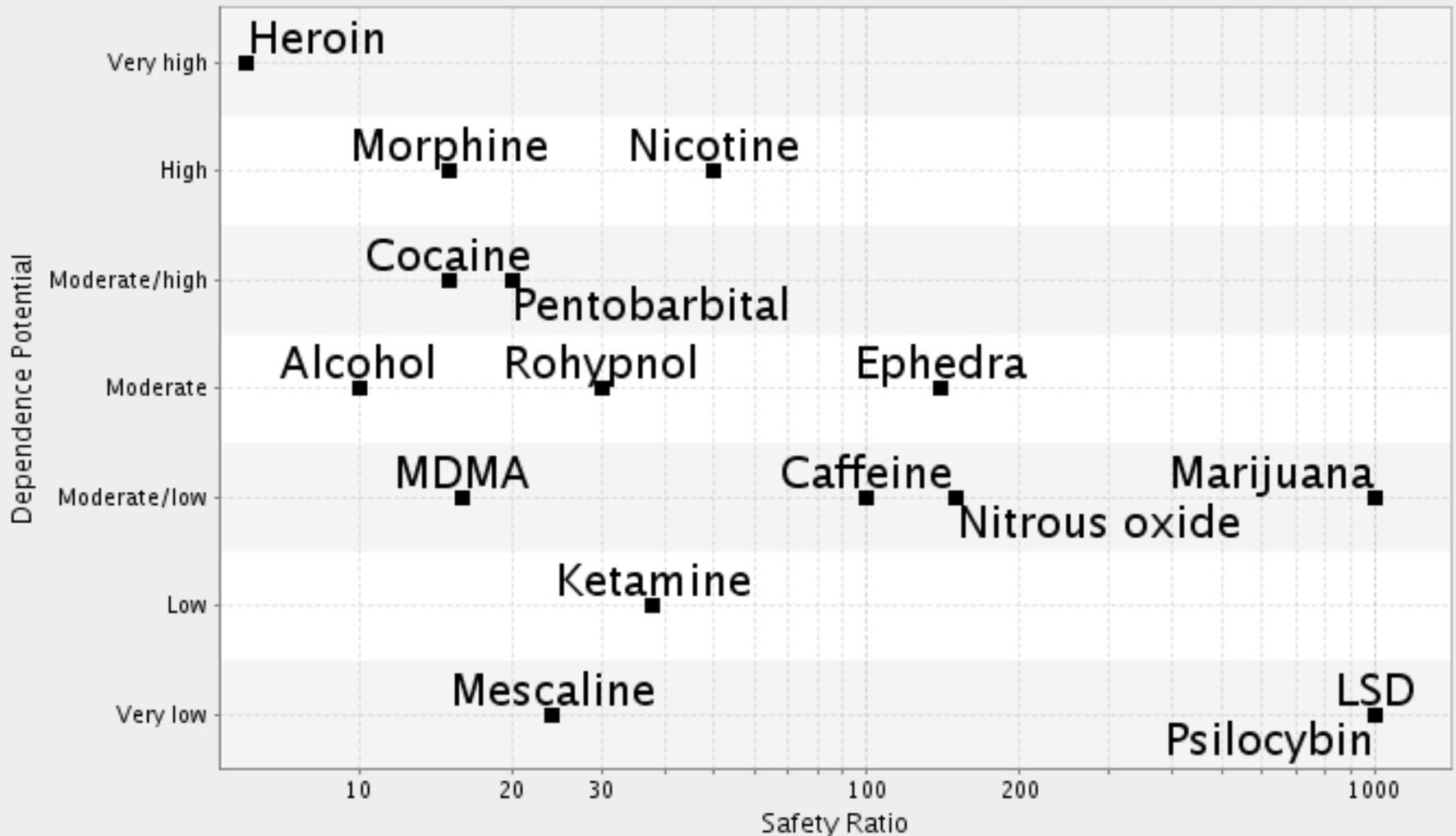
- ▣ 900 - Islamic physician Rhazès uses as analgesic and anaesthetic¹⁹.
- ▣ 1621 - The Anatomy of Melancholy by Burton recommends cannabis for depression²⁰.
- ▣ In US over 280 manufacturers were making nearly 2000 different cannabis medicines prior to 1937⁷.
- ▣ 1930 - Dr. W.B. O'Shaughnessy detailed use for pain, muscle spasm, and stomach cramps⁸.
- ▣ Dr. Albert Lockhart, beginning in 1964 eventually won the Jamaican Order of Merit for his work on MJ and vision. Brought first pharmaceutical cannabis to market in 1987 called Canasol⁹.
- ▣ 1970 - Synthetic THC called Marinol was approved in the US for use with chemotherapy associated nausea and AIDS associated anorexia¹⁰.

MJ Antitumoral Potential

- ▣ Cannabinoid extracts have been shown to specifically inhibit glioma growth and stop associated angiogenesis¹¹.
- ▣ When used as an adjunct extracts increase the tumor cell death from radiation¹¹.
- ▣ Cannabis extracts demonstrate cytotoxic activity on colon cancer cells, but reduced activity on normal colon cell¹².
- ▣ Synergistic interactions were found between different extracts¹².

MJ Safety and Dependence

Safety Ratio and Dependence Potential of Psychoactive Drugs



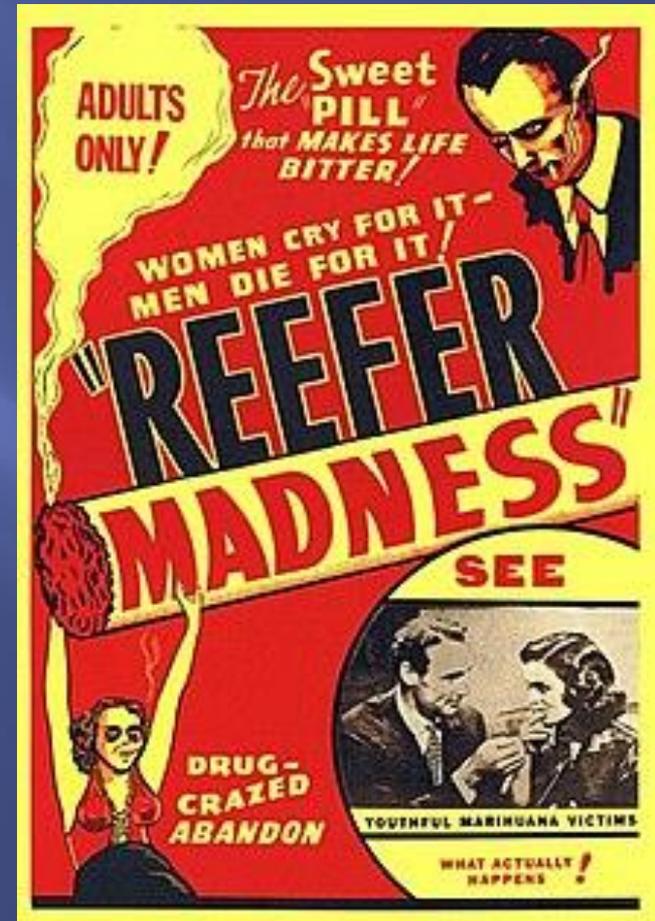
Safety ratio defined as $\text{Active dose} / \text{Lethal dose}$.²

Legality

- ❑ 1906 - Many states labeled as a poison.
- ❑ 1920 - International Opium Convention begins prohibitions.
- ❑ 1930 - Uniform State Narcotic Drug Act. Regulated as a drug in every state. Formation of the Federal Bureau of Narcotics.
- ❑ 1937 - Marihuana Tax Act. Put under Federal control. AMA opposed.
- ❑ 1956 - Narcotics Control Act established first mandatory minimum sentencing for possession. Repealed 1970.
- ❑ 1970 - Controlled Substances Act made Schedule I and illegal for any use including medical.
- ❑ 1968 - “War on Drugs” used by Nixon as a political tool against anti-war protestors.
- ❑ 1973 - DEA formed by President Richard Nixon.
- ❑ 1984 - Comprehensive Crime Control Act per Pres. Reagan re-established mandatory minimums, created “3 strikes”, and prison time.
- ❑ 1998 - Proposition 215 to legalize medical cannabis first passed in California.
- ❑ 2014 - Rohrabacher–Farr amendment (first proposed in 2001) passed after 6 failed attempts settled the medical marijuana issue in California.

Marijuana Hysteria

- 1936 - Reefer Madness



Marijuana Hysteria

- ▣ Case of Victor Licata
 - October 1933
 - Murdered his parents, two brothers and sister while they slept with an axe
 - Had pre-existing mental illness
- ▣ Media
 - Tampa Bay Times made claims Licata was “addicted” to marijuana cigarettes for more than six months¹⁵.
- ▣ Police
 - Tampa Police Chief pledges himself to marijuana prohibition

Medical Marijuana Florida

- ▣ March 20th, 2014
- ▣ Florida House of Representatives Budget Committee passed (CS/HB 843) known as Charlotte's Web measure.
- ▣ Limits the ability to prosecute for possession of Marijuana with <0.5% THC and >15% CBD used to treat seizures¹⁶.

Medical Marijuana Florida

- ▣ Medical marijuana now legal in the State of Florida
- ▣ Florida statute 381.986 - Medical use of marijuana
- ▣ Passed November 8, 2016
 - 71.3% for versus 28.7% against

Medical Marijuana Florida

- ▣ Who can prescribe medical marijuana?
 - A Medical Director

- ▣ “Medical director” means a person who holds an active, unrestricted license as an allopathic physician under chapter 458 or osteopathic physician under chapter 459¹⁴

Medical Marijuana Florida

- ▣ Qualifying conditions¹⁴
 - Cancer
 - Epilepsy
 - Glaucoma
 - HIV
 - AIDS
 - Post-traumatic stress disorder (PTSD)
 - Amyotrophic lateral sclerosis (ALS)
 - Crohn's disease
 - Parkinson's disease
 - Multiple sclerosis (MS)

Plus...

Medical Marijuana Florida

- ▣ Qualifying conditions cont¹⁴
 - Medical conditions of the same kind or class as or comparable to those above
 - A terminal condition diagnosed by a physician other than the qualified physician issuing the physician certification
 - Chronic nonmalignant pain caused by a qualifying medical condition or that originates from a qualifying medical condition and persists beyond the usual course of that qualifying medical condition

Medical Marijuana Florida

- ▣ Forms of medical marijuana available
 - Oral – capsules
 - Topical/Transdermal – creams, patches
 - Sublingual – oils, tinctures
 - Inhalation – vaporization
 - Rectal - suppositories

MM Registry Florida

▣ Certification

Physician Certification

Do you have a voluntary and informed written consent signed by patient? Yes No

Is this patient pregnant? Yes No

Did you conduct a physical exam in person for this Certification? Yes No

Certification Start Date:

DurationDays:

Certification End Date:

A physician Certification may include up to three 70-day orders. Be sure to set your certification for a long enough period of time, should you wish to have orders like that.

You cannot change the certification date range once you save the Certification.

A qualified physician must evaluate an existing qualified patient at least once every 30 weeks before issuing the next physician certification.

MM Registry Florida

▣ Certification

- Cancer
- Epilepsy
- Glaucoma
- Positive status for human immunodeficiency virus
- Acquired immune deficiency syndrome
- Post-traumatic stress disorder
- Amyotrophic lateral sclerosis
- Crohn's disease
- Parkinson's disease
- Multiple sclerosis
- Medical conditions of the same kind or class as or comparable to those enumerated in paragraphs (a)-(j)
- Terminal condition diagnosed by a physician other than the qualified physician issuing the physician certification. "Terminal condition" means a progressive disease or medical or surgical condition that causes significant functional impairment, is not considered by a treating physician to be reversible without the administration of life-sustaining procedures, and will result in death within 1 year after diagnosis if the condition runs its normal course.
- Chronic nonmalignant pain

Go Back

Save Certification

MM Registry Florida

Orders – Recommendations (Rx)

Physician Certifications

New Certification

Show 10 entries

Search: Search

	Certification Status	Start Date	End Date	Order Count	Physician	
Collapse	Active	7/2/2018	1/28/2019	2	CHAPMAN, GLENN	View

New Order

Show 10 entries

Search:

Expand	Order Status	Start Date	Purchase Device	Days	End Date	Edit
▼	Open	08/01/2018	False	60	09/30/2018	Edit Cancel
▼	Expired	07/02/2018	False	30	08/01/2018	Edit

You have placed 2 order(s) in this Certification, and have 1 order(s) remaining to place.

Previous **1** Next

MM Registry Florida

Orders – Recommendations (Rx)

Expand	Order Status	Start Date	Purchase Device	Days	End Date	Edit
^	Open	08/01/2018	False	60	09/30/2018	Edit Cancel

Medical Cannabis - Sublingual

Route: Sublingual

Total Amount Ordered: 3600 milligrams

Amount Per Dose: 20 milligrams

Doses Per Day: 3

Note:

Dispensed On	At	Via	Amount Dispensed	Status
08/29/2018 03:33 PM	Curaleaf	Heger, Eric	300 mg	Given to Patient
Amount Remaining: 3300				
08/09/2018 03:47 PM	Curaleaf	Hunt, Leigh	600 mg	Given to Patient
Amount Remaining: 2700				

MM Registry Florida

▣ Orders – Recommendations (Rx)

Create New Order for Certification starting on 7/2/2018 and ending on 1/28/2019.

Start Date

09/09/2018

Purchase Delivery Device

Duration Days

Select Days of Duration

End Date

09/09/2018

Go Back

Save Order

Add Route

MM Registry Florida

▣ Orders – Recommendations (Rx)

New Order Route ▼

Order is for

Low THC

Medical

Route of Administration

Select Form

Order Notes

Amount (in mg) of CBD per dose

of doses per day

Amount Remaining

0

MM Registry Florida

▣ Orders – Recommendations (Rx)

New Order Route ▾

Order is for

- Low THC
- Medical

Route of Administration

Select Form

Select Form

- Oral
- Topical
- Sublingual
- Inhalation
- Rectal

Amount (in mg) of CBD per dose

of doses per day

Amount Remaining

0

Mj Delivery Method Choices

- ▣ Oral²¹ – capsules
 - Onset – 1-2 hrs
 - Duration – 4-6 hrs
 - Dose consistency – high
 - Benefits – easy to travel with, flavor not an issue

Mj Delivery Method Choices

- ▣ Topical/Transdermal²¹ – creams, patches
 - Onset – 30 min – 1.5 hrs
 - Duration – 6-8 hrs
 - Dose consistency – low in cream, high in patches
 - Benefits – can limit dose and apply directly to region, avoids enteral metabolism

Mj Delivery Method Choices

- ▣ Sublingual²¹ – oils, tinctures
 - Onset – 30 min – 1.5 hrs
 - Duration – 6-8 hrs
 - Dose consistency – low due to delivery
 - Benefits – easy to adjust dose, duration of effect vs inhaled

Mj Delivery Method Choices

- ▣ Inhalation²¹ – vaporization
 - Onset – seconds
 - Duration – 30 min to 2 hrs
 - Dose consistency – poor due to variable inhalation
 - Benefits – rapid onset, easy to travel with

Mj Delivery Method Choices

- ▣ Rectal²¹ - suppositories
 - Onset – 15-30 min
 - Duration – 4-8 hrs
 - Dose consistency – high
 - Benefits – if oral/inhaled route not available, no enteral metabolism

Constituents of Marijuana

- ▣ Cannabinoids²³ – diverse organic chemical compound that act on cannabinoid receptors
 - Endocannabinoids - produced naturally in the body
 - Phytocannabinoids - found plants
 - Synthetic cannabinoids – manufactured
- ▣ Terpenes²⁴ – large, diverse class of organic compounds found in plants and insects. Often have a strong smell.

Cannabinoid Receptors

- ▣ Membrane bound receptors found in mammals, birds, fish and reptiles.
- ▣ Human brain has more cannabinoid receptors than any other G protein-coupled receptor (GPCR) type.
- ▣ Types
 - Cannabinoid receptor type 1 (CB₁)
 - ▣ Primarily in brain, including anterior eye and retina. Absent in medulla oblongata
 - Cannabinoid receptor type 2 (CB₂)
 - ▣ Primarily in immune cells, subpopulation in microglia in cerebellum. Responsible for anti-inflammatory effect.

Cannabinoids

- ▣ 113 different cannabinoids isolated from cannabis²²
- ▣ Best known and researched: THC and CBD
- ▣ Examples
 - THC (Tetrahydrocannabinol)
 - THCA (Tetrahydrocannabinolic acid)
 - CBD (Cannabidiol)
 - CBDA (Cannabidiolic Acid)
 - CBN (Cannabinol)
 - CBG (Cannabigerol)
 - CBC (Cannabichromene)
 - CBL (Cannabicyclol)
 - CBV (Cannabivarin)
 - THCV (Tetrahydrocannabivarin)
 - CBDV (Cannabidivarin)
 - CBCV (Cannabichromevarin)
 - CBGV (Cannabigerovarin)
 - CBGM (Cannabigerol Monomethyl Ether)
 - CBE (Cannabielsoin)
 - CBT (Cannabicitran)

THC

- ▣ Primary psychoactive component of the Cannabis plant²³
- ▣ Metabolism mainly in the liver by microsomal hydroxylation and oxidation catalyzed by enzymes of the cytochrome P-450 (CYP2C9 and CYP3A4)
- ▣ Highly protein bound at 95-99%
- ▣ Lipophilic with fat being the major long term storage site
- ▣ At peak of cognitive effect on 1% found in brain
- ▣ Crosses the placenta
- ▣ Found in breast milk²⁵

THC and CBD

- ▣ The synergistic effect of THC with CBD is due to the inhibition of the CYP-450 3A enzyme by CBD
- ▣ Induction and inhibition can occur and are responsible for interactions with other drugs
- ▣ The majority of drug interactions are theoretical.
- ▣ In practice there are no major drug interactions.

Cannabis Drug Interactions

- ▣ CYP2C9 inhibitors that would be expected to inhibit THC elimination³⁰
 - Amiodarone
 - Cimetidine
 - Metronidazole
 - Fluoxetine
 - Fluvoxamine
 - fluconazole

Cannabis Drug Interactions

- ▣ CYP3A4 inhibitors expected to increase in THC concentrations³⁰
 - Clarithromycin
 - Erythromycin
 - Cyclosporine
 - Verapamil
 - Itraconazole
 - Boceprevir

Cannabis Drug Interactions

- ▣ Rifampin (CYP3A4 inducer) has been reported to reduce THC levels by 20% to 40%
- ▣ Omeprazole (modest inhibitor of CYP2C19) did not alter the plasma concentration of CBD in one study³⁰

CBD et. al.

- ▣ Cannabidiol (CBD)
 - Substrate of CYP3A4 and CYP2C19
 - Non-psychotropic
 - Poor affinity for CB1 and CB2 receptors but acts as an indirect antagonist of cannabinoid agonists
 - 5-HT1A receptor agonist hence effects on sleep
 - Shown to play a role in preventing the short-term memory loss associated with THC²⁷
 - Ketoconazole was noted to increase the plasma concentration of CBD by about 2-fold
 - Rifampin reduced CBD levels by 50%
 - Omeprazole (modest inhibitor of CYP2C19) did not alter the plasma concentration of CBD³⁰

CBD et. al.

- ▣ Cannabinol (CBN)
 - Primary product of THC degradation. Increases as MJ degrades.
 - Mildly psychoactive
 - affinity to the CB2 > CB1

CBD et. al.

- ▣ Cannabigerol (CBG)
 - Non-psychoactive
 - Shown to promote apoptosis in cancer cells and inhibit tumor growth in mice²⁸
 - α 2-adrenergic receptor agonist
 - 5-HT1A receptor agonist

CBD et. al.

- ▣ Tetrahydrocannabivarin (THCV)
 - Prevalent in certain central Asian and southern African strains of Cannabis
 - Antagonist of THC at CB1 receptors and lessens the psychoactive effects of THC²⁹

CBD et. al.

- ▣ Cannabichromene (CBC)²³
 - Non-psychoactive
 - Does not affect the psychoactivity of THC
 - Shown antitumor effects in breast cancer xenopants in mice
 - Common in tropical cannabis varieties

Terpenes

- ▣ B-Caryophyllene
- ▣ B-Myrcene
- ▣ Eucalyptol
- ▣ Humulene
- ▣ Limonene
- ▣ Linalool
- ▣ Pinene
- ▣ Terpeneol

Terpenes

- ▣ B-Caryophyllene³¹
 - Medical effects
 - ▣ Anti-inflammatory
 - ▣ Neuropathic pain
 - ▣ Anti-spasmodic
 - ▣ Anti-bacterial
 - ▣ Anti-fungal
 - Other effects
 - ▣ Large contributor to entourage effect
 - ▣ Suggested benefit with ulcers/GI complaints
 - Flavor/scent
 - ▣ Spicy
 - ▣ Woodsy aroma

Terpenes

- ▣ B-Myrcene³¹
 - Medical effects
 - ▣ Anti-inflammatory
 - ▣ Analgesic
 - ▣ Anti-spasmodic
 - ▣ Anti-bacterial
 - ▣ Anti-fungal
 - Other effects
 - ▣ Relaxing/sedating
 - ▣ Enhances permeability of blood brain barrier
 - ▣ May modulate endogenous opioid system without tachyphylaxis
 - Flavor/scent
 - ▣ Musky, fruity, clove

Terpenes

- ▣ Eucalyptol³¹
 - Medical effects
 - ▣ Anesthesia
 - ▣ Anti-proliferative
 - ▣ Antioxidant
 - ▣ Anti-inflammatory (COX effects)
 - ▣ Analgesic
 - ▣ Anti-spasmodic
 - ▣ Anti-bacterial
 - ▣ Anti-fungal
 - Other effects
 - ▣ Blocks nerve hypersensitivity
 - ▣ Improves transdermal delivery
 - Flavor/scent
 - ▣ Eucalyptus smell

Terpenes

- ▣ Humulene³¹
 - Medical effects
 - Anti-inflammatory
 - Analgesic
 - Anti-bacterial
 - Other effects
 - Appetite suppressant
 - Flavor/scent
 - Spicy, woody, earthy, hoppy

Terpenes

- ▣ Limonene³¹
 - Medical effects
 - ▣ Anti-reflux
 - ▣ Antioxidant
 - ▣ Anti-inflammatory (COX effects)
 - ▣ Analgesic
 - ▣ Anxiolytic
 - ▣ Antidepressant
 - ▣ Anti-fungal
 - Other effects
 - ▣ Helpful with reflux/heartburn
 - ▣ Improves transmucosal delivery
 - Flavor/scent
 - ▣ Citrus

Terpenes

- ▣ Linalool³¹
 - Medical effects
 - ▣ Anesthesia
 - ▣ Anti-inflammatory
 - ▣ Analgesic
 - ▣ Anticonvulsant
 - ▣ Anxiolytic
 - Other effects
 - ▣ Improves sleep
 - Flavor/scent
 - ▣ Floral aroma

Terpenes

- ▣ Pinene³¹
 - Medical effects
 - ▣ Anti-inflammatory
 - ▣ Anti-asthmatic
 - ▣ Anti-bacterial
 - ▣ Alertness (inhibits acetylcholinesterase)
 - ▣ Bronchodilator
 - Other effects
 - ▣ Most commonly occurring terpene in nature
 - ▣ Memory enhancing
 - Flavor/scent
 - ▣ Pine smell

Terpenes

- ▣ Terpeneol³¹
 - Medical effects
 - ▣ Anti-proliferative
 - ▣ Antioxidant
 - ▣ Anti-inflammatory
 - ▣ Analgesic
 - Other effects
 - ▣ Sedating
 - ▣ Attenuate withdrawal effects from morphine
 - ▣ Reduce tolerance to analgesic effects of morphine
 - Flavor/scent
 - ▣ Lilac

Resources

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QUESTIONS