



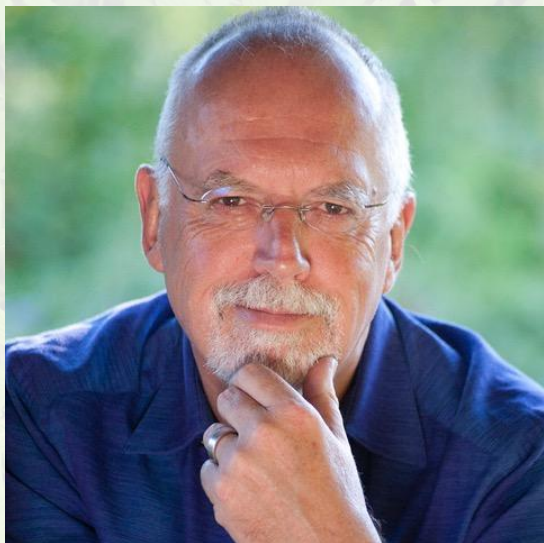
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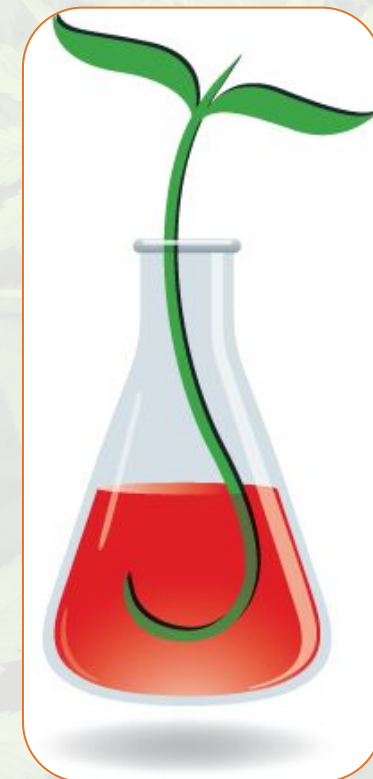
Cannabis Terpenes + Herbal Synergy



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Medical Herbalism Defined

- Based on biomedical science
- Multidisciplinary: Natural plant chemistry +
phytopharmacology + botany + plant physiology
- Combined with Western herbal medicine perspective





The Full Terpene Story

- Plant skin + bark + floral components contain terpenes
- Extracted at low temperatures (steam distillation)
- Application in aromatherapy, cooking, perfumes





Hemp Oil Defined

- Two types of cannabis plants
 - Hemp variety provides nutritive, cold pressed hemp oil, pressed from seed
 - Sinsemilla variety cultivated for medicine + adult use
- Rich in linoleic + linolenic fatty acids
- Analysis shows no cannabinoids or terpenes (unless by contamination)





Hemp Essential Oil Defined

- Hemp essential oil, cannabis essential oil + hemp oil often used interchangeably + incorrectly
- Essential oil is Steam distillate of cannabis flower
- Not widely available or used
- Rick Simpson “Oil” (RSO) is a concentrated cannabis plant extract, not an oil





Cannabis “Oil” Defined (RSO)

- Solvent Extract of cannabis flowers
- Usually available as semi-solid concentrate, (with solvent removed)
- Cannabis oil is NOT cannabis essential oil, hemp oil, or hemp seed oil





Terpenes Defined

- Hydrocarbons derived from isoprene
- Isoprene is short-chain molecule made of 5-carbon units
- Terpene sub-classes defined by number of isoprene units
 - Monoterpenes, sesquiterpenes, diterpenes, triterpenes
- Mevalonic pathway allows terpene medicinal properties to be metabolized





Why the Mevalonate Pathway?

- Common to plant and animal cells.(eukaryotes)
- Humans + animals utilize synthesize cholesterol, carotenoids, retinoids
- Terpenes are produced by plants cells in this pathway
- Implication: plant + human terpene physiology are similar
 - Terpenes are important to cellular development + differentiation
 - Cellular process influences disease such as cancer





World of Terpenes

- Over 10,000 documented
- THC + CBD are terpenophenolics (have combined/hybrid molecular structure)
- 150-200 terpenes in cannabis





Terpenes in Cannabis

- Terpenes comprise 10% of trichome content
- Monoterpenes are 50-90% + some sesquiterpenes
- Common in many foods + cannabis
 - Monoterpene: myrcene, pinene, limonene (lemons, pineapple, apricots)
 - Sesquiterpene: beta-caryophyllene (black pepper, cloves)





Terpene Loss

- Terpene loss over time via evaporation (30% in 3 months)
- Heat contributes to terpene loss
- Monoterpenes account for strain specific odors





Terpenes Work at Low Levels

- Physiological changes can occur with olfactory use at low doses
- Most research has been focused on high terpene levels





Patients Should Care about Terpenes

- Using a wine analogy, medicinal users should consider the value of terpenes in selecting cultivars
- Cannabis quality matters when it comes to terpenes





Herbal Synergy or Entourage Effect

- Herbs are complex mixtures of many different chemicals
- Complementing herbs to enhance or counter-balance their effects
- Senna (irritant laxative) + ginger (antispasmodic) = positive outcome





Herbal Medicine Is Polypharmacy

- Herbal medicine is complete medicine
- As complex mixtures, herbs treat complex conditions
- Synergy can occur between active compounds within same class





Synergy among Dissimilar Compounds

- Active + inactive compounds can create a supra-additive effect ($1 + 1 = 3$)
- Purified, active forms may not yield best results
- Whole plant berberine extract versus purified berberine sulfate
- Disruption cell transporter pump changes outcomes + drug resistance





Full Plant Spectrum

- Sum of all constituents underlies herbal actions
- Yarrow: no one single ingredient accounts for its net effect
- Other herbal effects are dominated by single molecules for example...





Synergistic Effects

- Effect of tropane alkaloid plant (belladonna) determined by those alkaloids
- Effect of cannabis may be
 - Between cannabinoids + terpenoids
 - Among cannabinoids only
 - Between cannabinoids + unknown compounds
- Analysis needed to quantify these effects





Measuring Synergy

- Isobologram measures compounds with independent but similar action
- Moved to statistical analysis for more accuracy
- Pharmacokinetic animal data can be extrapolated to humans
(details in Boik reference)





Synergy in Action

- Limonene: high dose needed for anti-inflammatory effect – not feasible
- Adding myrcene + pinene at lower doses + limonene = synergistic effect less limonene needed





Science of Today

- Transcriptomic approach to synergy: analysis of messenger RNA expression in experimental cell models exposed to herbs or herbal compounds
- Allows for complete characterization of additive and subtractive effects





Maximizing Synergy

- Opioids + cannabis = additive combination allowing for lower opioid dose
- CBD reduces psychoactive effect of THC
- Some synergies are well established, others need quantifiable research





Terpene Cannabinoid Synergy

- How much is needed for therapeutic effect?
- Some monoterpenes
 - Limonene metabolizes to perillyl alcohol in humans
 - Perillic acid can reverse + inhibit tumor growth
- Required high doses are unrealistic with side effects but herbal synergy may help





Sesquiterpene Beta-Caryophyllene (BCN) Potential

- BCN is unique :the only known non cannabinoid compound from cannabis to bind with CBR2
- Hence directly influences endocannabinoid system without psychoactive effects
- Pharmaceutical research is focused on anti-cancer drug development by modifying the BCN molecule





Proceed with Caution

- Herbal synergy is an established reality in cannabis but not enough studies have been done
- Practitioners can include cannabis as one component in a holistic healing plan
- Give clients a realistic view of the entourage effect

