Barriers to Cannabis Research

Roger Kern, Ph.D. and Suzanne Sisley, MD

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Challenges and Barriers in Conducting Cannabis Research

- Despite changes in state policy and the increase use of cannabis, the federal government has not legalized cannabis
- The government continues to enforce restrictive regulations on research into the health harms or benefits of cannabis products
- Patients, health care professionals, and policy makers without the evidence to make sound decisions
- This poses a public health risk

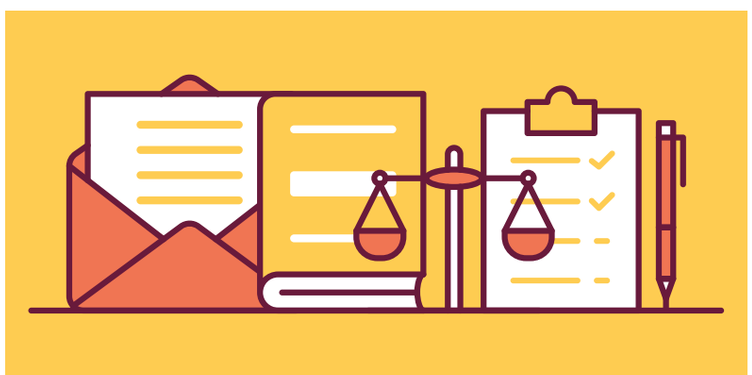
Let’s Identify the Barriers to Research

1. Regulatory and Policy Challenges
2. Cannabis Supply
3. Variation of Administration Options
4. Limited Funding
5. Product Standardization

Regulatory and Policy Changes

Scientists who plan to conduct research on cannabis or cannabinoids must navigate a series of review processes that may involve many hurdles of approvals:

- The National Institute on Drug Abuse (NIDA)
- The U.S. Food and Drug Administration (FDA)
- The U.S. Drug Enforcement Administration (DEA)
- Institutional and state government review boards
- State boards of medical examiners



The Limitations of Cannabis Supply

Cannabis research is available only through the NIDA Drug Supply Program

- This means the focus is on the consequences of addiction and not on the potential beneficial health effects of cannabis

- All cannabis that NIDA provides is sourced from the University of Mississippi, (currently the sole cultivator since 1968)

- The cannabis available at University of Mississippi does not reflect the variety of products used by consumers, rendering the research invalid

Variation in the Method of Administering

A variety of options for cannabis administration are available, which makes research difficult.

- Patients often smoke cannabis or use a vaporizer as their preferred administration method

- Significant individual variations in inhalation techniques complicate the study of this delivery method

- Alternate dosage forms, including extracts, tinctures, candies, and lotions, add further complexity to this issue

Financial Limitations of Cannabis Research

- Without sufficient financial support, research will not be able to inform health care, public health practice, or keep pace with changes in cannabis policy and patterns of use

- In fiscal year 2015, studies supported by NIDA accounted for 59.3 percent ($66,078,314) of all NIH spending on cannabinoid research; however, only 16.5 percent ($10,923,472) of NIDA's spending on cannabinoid research supported studies investigating therapeutic properties of cannabinoids

Product Standardization

- The cannabis strains and types of products that patients receive from dispensaries are not the same as the federally approved product, making research using the University of Mississippi product potentially inapplicable
- To truly understand the short and long-term effects of cannabis, large controlled trials and observational studies are needed on the products that patients are actually using

Complications to Standardizing Cannabis Research

- Strains Selected - agree on what strain you're working on in order to get comparable data
- Consistent Culture Conditions
- Consistent Product Processing - getting constant medicine
- Analytic Analysis - same strategy for analyzing samples

Selecting Strains for Comparable Data

- Researchers have difficulty agreeing on the strain to study…

Consistent Culture Conditions

- **Growth Medium** - hydroponics, aeroponics, soil
- **Temperature** - affects potency and growth
- **Lighting** - outdoor growing and indoor growing
- **Water** - frequency and amount of water determines the temperature, light, age size and stage of growth
- **Humidity** - dry conditions slow the rate of photosynthesis
- **Nutrients** - nutrient soil amendments, chemical or organic fertilizers

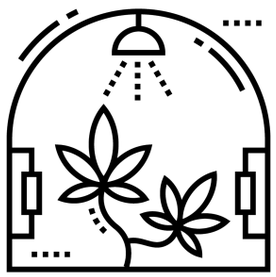
There is a strong need for SOPs to establish research cultivation.

Critical Capabilities for Developing the Ideal Cannabis Process

1. Cultivation
2. Analytics
3. Extraction
4. Biochemistry

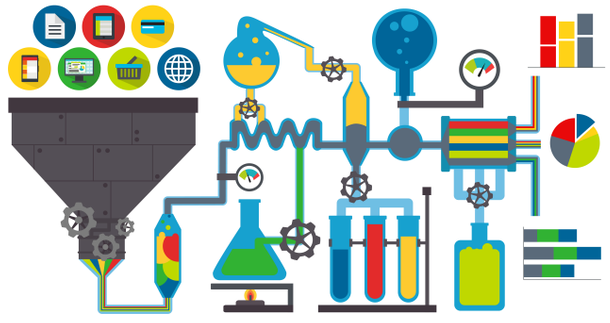
Cultivation Goals

- The natural process harnesses the cannabis flower
- Cultivation has requirements that start with mass yield
- Yield is expressed by mass and the cannabinoid content of the plant
- What is produced is a metric like CBD or THC which represents a successful grow
- Cultivators also focus on the unique ratios of cannabinoids and other bioactive compounds
- Because there is a synergistic affect of terpenes with cannabinoids, terpenes are another goal of cultivation
- Cultivation produces clean and safe cannabis flower free of microbial growth, heavy metals, pesticides or other contaminants



Analytics for Optimization

- Provide a feedback loop at every stage of production
- Liquid or Gas Chromatography method for terpene content
- Analytics must be precise, accurate and specific
- Goal is to identify the compounds in concentrates
- Ensures quality and reliability of results



Biochemistry

- **Plant Biochemistry** - focuses on cultivation to further understand the complex pathways that give rise to the ratios of bioactive molecules in the plant
- **Human Biochemistry** - focuses on how bioactive molecules interact with the human endocannabinoid system and how the different methods of administration impact the pharmacokinect delivery

Extraction

- Conversion of target molecules in raw material to usable form - this chemistry is not cooking
- Extract can be an isolated cannabinoid - CBD or 100 cannabinoids and terpenes or whole plant extract
- 550 chemicals in cannabis
- Require solid lab equipment and safety procedures
- Types of extraction:
  - Alcohol extraction
  - CO_2
  - Butane or Propane
  - Solvent-free

Constant Innovation

- Cultivation, Analytics, Extraction and Biochemistry are all connected and can be a constant source of innovation
- For example, when one applies analytics to determine terpene and cannabinoid content of incoming raw materials, this will ensure ongoing quality and consistency
- Analytics can provide feedback to tweak my extraction process
- Human biochemistry allows me to harness the complex polypharmacology associated with multidrug, multitarget plant cannabinoid therapies

Experimental Study Designs

- **Study Protocol** - patients are randomized, placebo-controlled, triple blind, crossover, multi-site to gather preliminary evidence of the safety and efficacy of 4 concentrates of cannabis with varying degrees of THC:CBD ratios
- **Dose Selection** - different effects between various strains of cannabis due to varying levels of cannabinoids
- **Study Timeline** - Familiarization, Stage 1, Stage 2, Stage 3
- **Outcome Measures**
- **Safety & Monitoring** - assess physiological effects, psychological distress, adverse events and suicidal ideation and behavior before/after the study, medical eligibility at screening uses comprehensive metabolic profile, thyroid panel, EKG, blood cannabinoid & HIV test, safety and monitoring
- **Recruitment** - print ads, internet ads, referrals from physicians, word of mouth

Take Away Key Points

- The barriers in cannabis research are complex and ultimately have an adverse affect on helping patients, health care professionals, and policy makers make sound decisions
- Standardizing cannabis research is complex because the interconnection of the key sectors for growing cannabis (cultivation, analytics, extraction and biochemistry) are constantly interacting and inspiring innovation

Agate Biosciences

www.agatebiosciences.com

800-346-4702

rkern@agatebiosciences.com