This Is A Hot, Sexy Topic

https://youtu.be/6z2HNCIsHzg

September 18, 2019
BUT The Conversation is Deep

- Detection of Pesticides
- Applying Tobacco Pesticide Research to Cannabis
- Setting The Research & Policy Trajectory
- Occupational Health
- Phytoremediation & Phytoextraction
We Know the Pests in Cannabis Cultivation

- Insects
  - Mites
  - Thrips
- Fungus
  - Powdery mildew
- Nuclear tactics…

What is a Pesticide?

- A pesticide is any substance intended to control, destroy, repel, or attract a pest.
- This includes insecticides, fungicides, herbicides, rodenticides and sanitizers.
Pesticide Regulation is Federal

• The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) is a United States federal law
  • The U.S. system of pesticide regulation is meant to protect applicators, consumers, and the environment

• The EPA is responsible for regulating pesticides under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and the Food Quality Protection Act (FQPA)
Standards For Quality Control Are Out There
Heavy Metal Limits Guideline For Elemental Impurities Already Exist

International Conference On Harmonisation Of Technical Requirements For Registration Of Pharmaceuticals For Human Use

Recommended For Adoption To The Regulatory Bodies Of The European Union, Switzerland, Japan, USA & Canada

ICH q3d (2014)
We Understand Safety Limiting Toxicity – Cadmium, for example

Cadmium has been shown to be genotoxic and has been acknowledged as a human carcinogen (Group 1; IARC, 2012).

Cadmium and cadmium compounds cause cancer of the lung.

An inhalation unit risk of 0.0018/µg/m³ has been derived by the US EPA (1992).
We Know The Cautionary Tale That Is Roundup “Weed-killer”

- endocrine disruptor
- “probably carcinogenic to humans”

Bayer, which bought Roundup maker Monsanto last year, has reportedly offered $8 billion to settle thousands of cancer claims.

Dose Response

“the dose makes the poison”

important concept in human health risk assessment & toxicology

Paracelsus (16th century)
Toxicity

Acute toxicity = the hazard associated with a single exposure

Chronic toxicity = the hazard associated with long term exposure to a chemical, such as repeated ingestion of low doses in food residues
Dose Response & Therapeutic Effect

Therapeutic effect is at the intersection of beneficial effects & adverse effects
Theoretically, We Have All The Tools We Need To Regulate Pesticides Used In Cannabis Cultivation
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Pesticides Have been Detected in Cannabis Smoke

- Chemical residues present on the cannabis flowers directly transfer into the mainstream smoke and ultimately... to the end user

Pesticides Have Been Detected in Edibles

- July 29, 2016
  - Denver Post reported a large-scale product recall due to pesticide contamination

- States are all regulating pesticides differently
  - There is no meaningful federal oversight

Baca and Migoya, 2015

Tobacco Can Teach Us (a Few) Things

- Multiple studies note the **distillation** behavior of pesticides in smoke
  - Cannabis has seen **10x concentration** of pesticides (Voelker & Holmes, 2015; Light, Orens, Lewandowski, 2014)
- The **raw flower** may be safest


Limits of What Tobacco Can Teach Us

• By virtue of Title 35, Article 9, C.R.S., Colorado is primarily using pesticides approved on tobacco
• BUT - Is this the right move?


Cannabis Needs Its Own Research Paradigm

• Tobacco Pesticide Studies generally have a 7.5 g carbon filter cartridge
  • Tobacco is Filtered – Cannabis Typically is Not
  • Data is falsely skewed in the direction of presumed safety

• When comparing “a bong” (filtered water pipe) to a glass pipe, the quantity of pesticide recovery was the highest in hand-held glass pipe
  • Route of ingestion is a major research consideration in cannabis

FDA concept of GRAS

"GRAS" is an acronym for the phrase Generally Recognized As Safe. Under sections 201(s) and 409 of the Federal Food, Drug, and Cosmetic Act

Have we adequately shown what is safe under the conditions of its intended use?
A medicine consists of 2 fundamental parts: the active pharmaceutical ingredient and the excipient.

In the early times, the safety of excipients was overlooked and no specific safety tests were generally conducted…

**Today, an excipient's toxicity is not negligible** = \frac{\text{risk}}{\text{benefit}}
What Is The Ideal Pesticide?

• As with medications, the ideal pesticide is safe in terms of human and ecosystem health & effective at controlling the target species

• Definition of Certified Organic Products
  • must demonstrate protecting natural resources, conserving biodiversity using only approved pesticides

• The EU has implemented Integrated Pest Management
  • low-pesticide-input as part of sustainable food production


EU Integrated Pest Management Regulation (EC) No 396/2005 (Seventh Framework Programme)
Integrated Pest Management

- The **EPA defines** Integrated Pest Management (IPM) as **an environmentally sensitive approach to pest management**
- How nature does it
- **Fight bugs with bugs** (ex. predator release)
  - Lifecycles of pests are used to interrupt and control infestations
- Co-locate beneficial species (ex. marigold)


E. B. Radcliffe, W. D. Hutchison & R. E. Cancelado Radcliffe's IPM World Textbook, University of Minnesota, St. Paul, MN.
LIFE CYCLE of a cannabis plant

1. Germination/Seed
   1-2 weeks
   Seeds ready for germination are dark brown, hard, and dry. Encourage sprouting by watering seeds in a paper towel.

2. Seedling
   2-3 weeks
   Move seeds into growing medium. Plants need the maximum light at this stage, and appropriate water levels. Cotyledon (seed leaves) and iconic fan leaves will grow.

3. Vegetative
   2-8 weeks
   Plants need flowing dry air, fresh warm water, and increased nutrients — especially nitrogen.

4. Flowering
   6-8 weeks
   Gradually reduce light exposure to produce medicinal qualities. Increase phosphorus levels and decrease nitrogen. Fertilizers can help stimulate bud formation.

5. Harvesting
   Trim and dry the buds — plant is ripe when buds turn from milky white to reddish orange. Harvest once 70-90% of pistils are browned for maximized taste and effect.
Timing of Pesticides within the Cultivation Lifecycle

- Spraying at different points in the lifecycle has different implications
- Spraying during the flowering phase ends up on the finished product
Setting the Research & Policy Trajectory

- **Regulate for inclusion/expectation** for the industry
  - Rather than exclusion style regulation
  - Not one molecule away from being on/off the regulated list

- Regulate for environmental priorities
  - Air quality, zoning, water, waste disposal
- Regulate for patient safety
- Regulate for worker safety


Massachusetts - Sept 2018 – Case Study

• Code of Massachusetts Regulations explicitly stated that “application of any non-organic pesticide in the cultivation of marijuana is prohibited”

• MA Dept of PH ruled that “an immediate or serious threat to the public’s health, safety, or welfare” and issued a cease-and-desist and quarantine
New Mexico – Case Study

• Product labeling shall identify “pesticide(s) used in the production of the cannabis or cannabis-derived products.”
  • No additional specification of best practices or forbidden chemical compounds has been made

• Laboratory validation is expensive
  • Confirmatory tests for pesticide are expensive - even for NM Scientific Laboratories
The Role of Mass Spec in Cannabis Regulation


Pyrolysis

• decomposition brought about by high temperatures

• We have no data on the combustion of cannabis pesticides. (only as a food – sprayed on a fruit – not on fire)
EPA can help us understand the Effect of Temperature

<table>
<thead>
<tr>
<th>Insecticide/Species</th>
<th>Rate</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emamectin Benzoate</td>
<td>90</td>
<td>100-150</td>
</tr>
<tr>
<td><em>Dylyphus isaea</em></td>
<td>0</td>
<td>500-1,000</td>
</tr>
<tr>
<td>Spinosad</td>
<td>90</td>
<td>0.1%</td>
</tr>
<tr>
<td>Spinetoram</td>
<td>90</td>
<td>0.1%</td>
</tr>
<tr>
<td>Abamectin</td>
<td>80</td>
<td>0.1%</td>
</tr>
<tr>
<td>Buprofezin</td>
<td>90</td>
<td>0.5%</td>
</tr>
<tr>
<td>Aphidius colemani</td>
<td>0</td>
<td>1,000</td>
</tr>
<tr>
<td>Soap Nut</td>
<td>21</td>
<td>0.8%</td>
</tr>
<tr>
<td>Azadirachtin</td>
<td>21</td>
<td>0.2%</td>
</tr>
<tr>
<td>Melaleuca alternifolia + Sophora sp. + Natural Pyrethr</td>
<td>21</td>
<td>0.5%</td>
</tr>
<tr>
<td>Melaleuca alternifolia + Natural Pyrethr</td>
<td>21</td>
<td>0.5%</td>
</tr>
<tr>
<td>Pyrethrins + Neem Oil + Vegetable Oil</td>
<td>21</td>
<td>0.2%</td>
</tr>
<tr>
<td>Potassium Salt of Fatty Acids</td>
<td>21</td>
<td>0.8%</td>
</tr>
<tr>
<td>Amblyseius swirskii</td>
<td>0</td>
<td>50,000-100,000</td>
</tr>
<tr>
<td>Fatty Acid Potassium Salt</td>
<td>21</td>
<td>3%</td>
</tr>
</tbody>
</table>
Canada will require producers to have an independent lab test all products for 100 different pesticides before they can be sold.

Canada Sets Acceptable Limits on Oil, Fresh, & Dried Cannabis *Individually*

<table>
<thead>
<tr>
<th>Active ingredient</th>
<th>Limits of Quantification in parts per million</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Fresh cannabis and plants</td>
</tr>
<tr>
<td>Abamectin</td>
<td>0.25</td>
</tr>
<tr>
<td>Acephate</td>
<td>*</td>
</tr>
<tr>
<td>Acetamiprid</td>
<td>0.050</td>
</tr>
<tr>
<td>Acequinocyl</td>
<td>*</td>
</tr>
<tr>
<td>Aldicarb</td>
<td>0.50</td>
</tr>
<tr>
<td>Allethrin</td>
<td>0.10</td>
</tr>
</tbody>
</table>

* Limit of quantification under development.

Cannabis Act (S.C. 2018, c. 16)
California

California Restricted Materials

DPR designates certain pesticides as California restricted materials (3 CCR section 6400). A pesticide can be considered a restricted material for many reasons including designation as a federal Restricted Use Pesticide. Many of these products have product labels that clearly state "Restricted Use Pesticide." Consult your local CAC to determine whether a product is a restricted material. Examples of California restricted materials include:

- Abamectin
- Bifenthrin
- Brodifacoum
- Bromodiolone
- Cyfluthrin
- Difenacoum
- Difethialone
- Fipronil
- Naled
## Approved Pesticide Count by State

<table>
<thead>
<tr>
<th>State/Region</th>
<th>Number of permitted pesticides registered (approved)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorado</td>
<td>12,000 (200)</td>
</tr>
<tr>
<td>OR</td>
<td>(362) – test 59</td>
</tr>
<tr>
<td>Canada</td>
<td>Test 100</td>
</tr>
<tr>
<td>Washington</td>
<td>(330)</td>
</tr>
</tbody>
</table>
Legal Cannabis Growing Operations Hazards & Health Risks

Personal Protective Equipment


Occupational Health & WPS

• Federal Worker Protection Standards (WPS) offer guidelines to reduce risk in occupational settings

• WPS measures include restricted-entry intervals, use of personal protective equipment, and postings that notify workers of pesticide applications and re-entry times

Stone D., Cannabis, pesticides and conflicting laws: The dilemma for legalized States and implications for public health, Regulatory Toxicology and Pharmacology, Volume 69, Issue 3, 2014, Pages 284-288, ISSN 0273-2300,
Heavy Metals & Regulation

• Occupational exposure is no bueno
• Metals accumulate over time & frequent, extended exposure is a major concern
• Resulting health issues from heavy metals may include cardiovascular disorders, neuronal damage, renal injuries, and risk of cancer and diabetes.

• All cannabis harvested or products manufactured in the state of California on or after December 31st, 2018 must be tested for Class 1 heavy metals.
  • arsenic (As), cadmium (Cd), mercury (Hg), and lead (Pb)


Phytoextraction & Phytoremediation

• Phytoextraction = when plants remove dangerous elements or compounds from soil or water

• **Phytoremediation properties make cannabis subject to heavy loads of heavy metals** = when your strength is your weakness
  - Cannabis is known to act efficiently in the uptake of heavy metals from soil.
  - favorable for industrial hemp - could be problematic for producers, and ultimately consumers.


PyGanic®
Crop Protection EC 1.4

Specimen Label

- Contains pyrethrum—a botanical insecticide derived from chrysanthemums
- Provides rapid knockdown and kill of plant pests
- For use on growing crops and ornamentals
- Can be used on day of harvest
- Kills key livestock pests
- Controls more than 100 insects

For Organic Production
OMRI Listed

KEEP OUT OF REACH OF CHILDREN
CAUTION PRECAUCIÓN
Si usted no entiende la etiqueta, busque a alguien para que se la explique a usted en detalle.
Take Home Messages

- Route of ingestion - matters (flower vs. vape)
- Temperature - matters (pyrolysis...)
- When you spray – matters (don’t spray during flower cycle)
- Let’s not retrofit our regulations – as we’ve done for alcohol & tobacco

Richter, 2014
THANK YOU

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