Topic 08

Secondary Metabolites

1) Hoefnagles p. 379 (Pacific Yew), 460-461 (Cash Crop; Candy, Herbs, and Drugs)
2) The relevant chapter on the Ethnobotany of Secondary Metabolism in lab manual

I. Plant Secondary Metabolites

A. Definitions

1) 1° vs. 2 ° Metabolism-

I. Plant Secondary Metabolites

B. Some 2 ° Metabolites

Compound	Example Source	Human Use
ALKALOIDS		
Codeine	Opium poppy	Narcotic pain relief; cough suppressant
Nicotine	Tobacco	Narcotic; stimulant
Quinine	Quinine tree	Used to treat malaria; tonic
Cocaine	Coca	Narcotic, tea, anesthetic, stimulant

I. Plant Secondary Metabolites

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PHENOLICS		
Tannin	Leaves, bark, acorns	Leather tanning, astringents
Salicin	Willows	Aspirin precursor
Tetrahydrocannabinol	Cannabis	Treatment for glaucoma & nausea

I. Plant Secondary Metabolites

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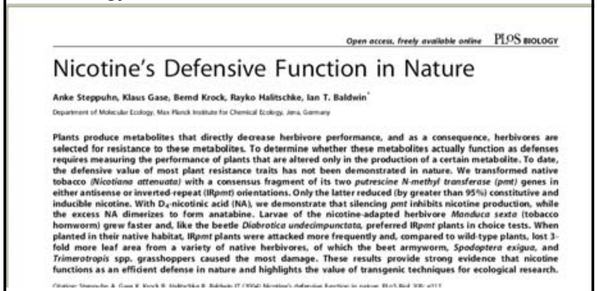
Tetrahydrocannabinol	Cannabis	Treatment for glaucoma & nausea
TERPENOIDS		
Camphor	Camphor tree	Component of medicinal oils, disinfectants
Menthol	Mints & eucalyptus	Strong aroma; cough medicines

I. Plant Secondary Metabolites

C. Ecology



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Nicotine's Defensive Function in Nature

Anke Steppuhn, Klaus Gase, Bernd Krock, Rayko Halitschke, Ian T. Baldwin*

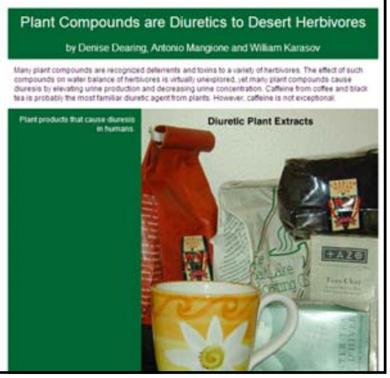
Department of Molecular Ecology, Max Planck Institute for Chemical Ecology, Jena, Germany

Plants produce metabolites that directly decrease herbivore performance, and as a consequence, herbivores are selected for resistance to these metabolites. To determine whether these metabolites actually function as defenses requires measuring the performance of plants that are altered only in the production of a certain metabolite. To date, the defensive value of most plant resistance traits has not been demonstrated in nature. We transformed native tobacco (*Nicotiana attenuata*) with a consensus fragment of its two *putrescine N-methyl transferase (pmt)* genes in either antisense or inverted-repeat (IR*pmt*) orientations. Only the latter reduced (by greater than 95%) constitutive and inducible nicotine. With D_4-nicotinic acid (NA), we demonstrate that silencing *pmt* inhibits nicotine production, while the excess NA dimerizes to form anatabine. Larvae of the nicotine-adapted herbivore *Manduca sexta* (tobacco hornworm) grew faster and, like the beetle *Diabrotica undecimpunctata*, preferred IR*pmt* plants in choice tests. When planted in their native habitat, IR*pmt* plants were attacked more frequently and, compared to wild-type plants, lost 3-fold more leaf area from a variety of native herbivores, of which the beet armyworm, *Spodoptera exigua*, and *Trimerotropis* spp. grasshoppers caused the most damage. These results provide strong evidence that nicotine functions as an efficient defense in nature and highlights the value of transgenic techniques for ecological research.

Steppuhn et al. 2004. *PLoS Biology* 2: 1074-1080.

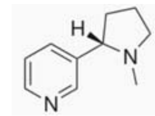
I. Plant Secondary Metabolites

C. Ecology



I. Plant Secondary Metabolites

C. Ecology
1. Defense
e.g., Nicotine



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I. Plant Secondary Metabolites

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1. Defense
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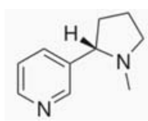
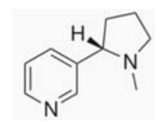
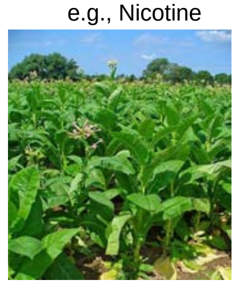


- Source: *Nicotiana tabacum*
- Neurotoxic to most herbivores

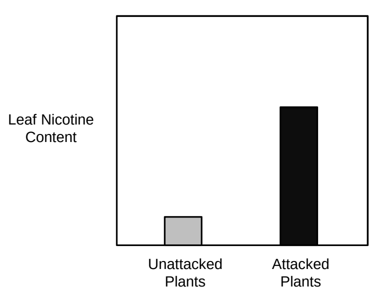
I. Plant Secondary Metabolites

C. Ecology
1. Defense
e.g., Nicotine





- Source: *Nicotiana tabacum*
- Neurotoxic to most herbivores
- But tobacco hornworm (a moth larva) can sequester & secrete it.



Baldwin, IT. 2001. *Plant Physiology* 127: 1449-1458.

Mechanism

1. Herbivory induces jasmonic acid (JA) production.
2. JA to roots, stimulates nicotine synthesis.
3. Nicotine to shoots via xylem

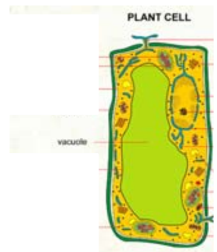
I. Plant Secondary Metabolites

C. Ecology
1. Defense
2. Attraction
e.g., colors & floral fragrances

Jasminum

I. Plant Secondary Metabolites

D. Storage



II. Caffeine case study

A. Caffeine

-Alkaloid

-*Coffea, Theobroma, Camellia, Cola,* etc.

-Psychoactive stimulant, diuretic

II. Caffeine case study

A. Caffeine

-syn. w/ guarinine

Species: *Paullinia cupana* (guarana' vine)
Family: Sapindaceae
Nativity: S. America

II. Caffeine case study

A. Caffeine

-syn. w/ theine

Species: *Camellia sinensis* (tea bush)
Family: Theaceae
Nativity: S. Asia

II. Caffeine case study

A. Caffeine

-syn. w/ mateine

Species: *Ilex paraguariensis*
(yerba mate)
Family: Aquifoliaceae
Nativity: S. America.

II. Caffeine case study

A. Caffeine

-First IDed in *Coffea arabica.*

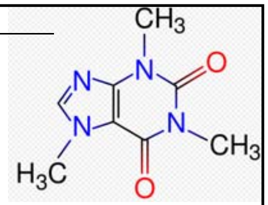
Species: *Coffea arabica* (arabica coffee)
Family: Rubiaceae.
Nativity: NE Africa.

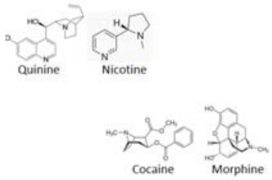
II. Caffeine case study

B. Alkaloids in general

•Secondary metabolites

•Nitrogenous, cyclic





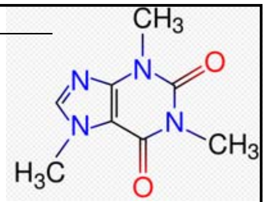
II. Caffeine case study

B. Alkaloids in general

•Secondary metabolites

•Nitrogenous, cyclic

•Psychoactive (act on CNS): herbivory defense



II. Caffeine case study

C. Ecological role of caffeine in nature

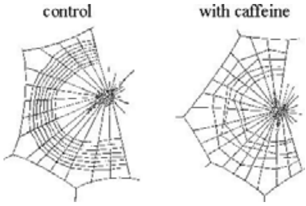
1. Excess can over stimulate CNS

II. Caffeine case study

C. Ecological role of caffeine in nature

1. Excess can over stimulate CNS

Spider web manufacture when influenced by caffeine.



II. Caffeine case study

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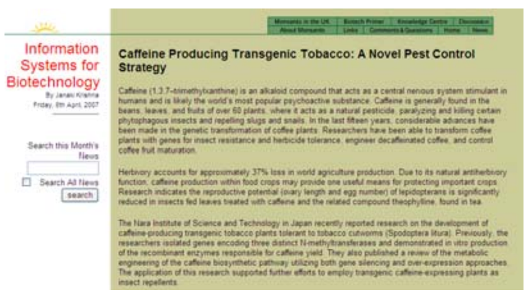
1. Excess can over stimulate CNS
   Caffeine's natural role noticed by Monsanto.



Information Systems for Biotechnology

By Janani Krishna
Friday, 6th April, 2007

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Caffeine Producing Transgenic Tobacco: A Novel Pest Control Strategy

Caffeine (1,3,7-trimethylxanthine) is an alkaloid compound that acts as a central nervous system stimulant in humans and is likely the world's most popular psychoactive substance. Caffeine is generally found in the beans, leaves, and fruits of over 60 plants, where it acts as a natural pesticide, paralyzing and killing certain phytophagous insects and repelling slugs and snails. In the last fifteen years, considerable advances have been made in the genetic transformation of coffee plants. Researchers have been able to transform coffee plants with genes for insect resistance and herbicide tolerance, engineer decaffeinated coffee, and control coffee fruit maturation.

Herbivory accounts for approximately 37% loss in world agriculture production. Due to its natural antiherbivory function, caffeine production within food crops may provide one useful means for protecting important crops. Research indicates the reproductive potential (ovary length and egg number) of lepidopterans is significantly reduced in insects fed leaves treated with caffeine and the related compound theophylline, found in tea.

The Nara Institute of Science and Technology in Japan recently reported research on the development of caffeine-producing transgenic tobacco plants tolerant to tobacco cutworms (Spodoptera litura). Previously, the researchers isolated genes encoding three distinct N-methyltransferases and demonstrated in vitro production of the recombinant enzymes responsible for caffeine yield. They also published a review of the metabolic engineering of the caffeine biosynthetic pathway utilizing both gene silencing and over-expression approaches. The application of this research supported further efforts to employ transgenic caffeine-expressing plants as insect repellents.

www.monsanto.co.uk

II. Caffeine case study

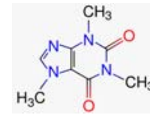
C. Ecological role of caffeine in nature

1. Excess can over stimulate CNS
2. Vertebrate diuretic

D. Caffeine's effects on CNS

•Caffeine from coffee in blood w/in 5 min
•Stimulates heart
•Increases stomach acidity
•Increases urine output
•10% rise in metabolic rate

•Mimics feelings assoc. w/ adrenaline



caffeine

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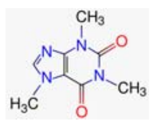

caffeine

•Excess (1 g; 10 cups) can cause anxiety, headache, dizziness, insomnia, heart palpitations, delirium, 4% lower birth weights.

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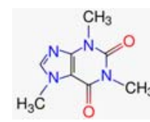


caffeine

•Excess (1 g; 10 cups) can cause anxiety, headache, dizziness, insomnia, heart palpitations, delirium, 4% lower birth weights.

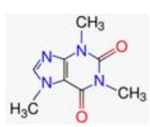
•Ranks as most widely used psychoactive drug worldwide (coffee, tea, additives to soft drinks)

D. Caffeine's effects on CNS

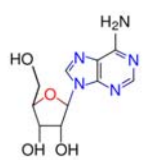
How?

Antagonist of adenosine.

Adenosine:
- Attaches to brain cell adenosine receptors.
- Neurotransmitter inhibitor.
- Promotes sleep
  (accumulates in brain each waking hour).
- Suppresses arousal.



caffeine



adenosine

E. Caffeine and Parkinson's prevention?

What is Parkinson's Disease?

•no cure, just treatments
•Symptoms: trembling arms and legs, trouble speaking, and poor coordination
•Associated with loss of dopamine-transmitting neurons in midbrain

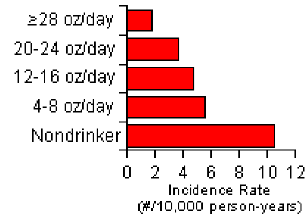
E. Caffeine and Parkinson's prevention?

What is Parkinson's Disease?

•no cure, just treatments
•Symptoms: trembling arms and legs, trouble speaking, and poor coordination
•Associated with loss of dopamine-secreting neurons in the midbrain.
•Dopamine levels fall, and the balance between dopamine and other neurotransmitters disrupted, affecting muscular control
•Blocking of adenosine receptors elevates levels of dopamine in brain.

E. Caffeine and Parkinson's prevention?

Honolulu Heart Program study of 8,000+ men over 30?

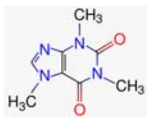


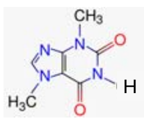
- Blocking of adenosine receptors by caffeine elevates levels of dopamine in brain.

F. Caffeine and Theobromine are similar in structure and action

Table 1. Stimulant alkaloids in world's major stimulating beverages (Simpson 1986). Given in % weight. Amt. in particular beverage depends on how it is made.

Plant, part	Caffeine	Theobromine
Coffee, unroasted, dried seeds	1-1.5	--
tea, dried lvs.	2.5-4.5	--
Cacao, dried or fresh seeds	0.6-0.8	1.7-2.4
Kola, fresh seeds	2.0	--
Guarana, dried fruit	3.0-4.5	--

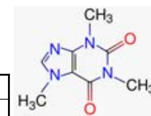

caffeine


theobromine

G. Caffeine in some beverages

Table 2. Caffeine quantities in select beverages.

Drink	Caffeine (mg)
Coffee (Starbucks)	
12 oz drip	240
1 oz espresso	?
12 oz drip decaf	19


caffeine

G. Caffeine in some beverages

Table 2. Caffeine quantities in select beverages.

Drink	Caffeine (mg)
Coffee (Starbucks)	
12 oz drip	240
1 oz espresso	75
12 oz drip decaf	19

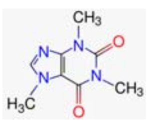
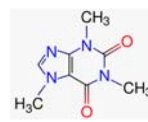

caffeine

Table 6. Average caffeine content in products (most amounts from the Center for Science in the Public Interest, 2007; chocolate amounts from Simpson and Orzogoly 1995).

Product	Caffeine (to the nearest mg)
Coffee (Starbucks)	
12 oz drip coffee	240
1 oz espresso	75
12 oz drip decaf coffee	19
Tea (various)	
12 oz brewed tea	80 (60-180)
12 oz Nestea	26
12 oz Snapple	14-32
Cocoa and chocolate (various)	
12 oz, from powder	14 (4.5-20)
1 oz baking choc	35
1 oz dark choc	20
1 oz milk choc	6
Soda (various)	
8.3 oz Red Bull	80
12 oz Jolt Cola	72
12 oz Mountain Dew	54
12 oz Dr. Pepper	42
12 oz Pepsi	38
12 oz Coca-Cola Classic	35


caffeine

III. *Coffea*

A. Sysematics

1. Genus *Coffea*
2. *Coffea* contains nearly 100 spp., tropical Africa & Asia
3. Commercial spp:
   - *C. arabica,*
   - *C. canephora,*
   - *C. liberica*

III. *Coffea*

B. *Coffea* berries and flowers

III. *Coffea*

C. *Coffea* seeds

III. *Coffea*

C. *Coffea* seeds

III. *Coffea*

D. Coffee is a major commodity globally.

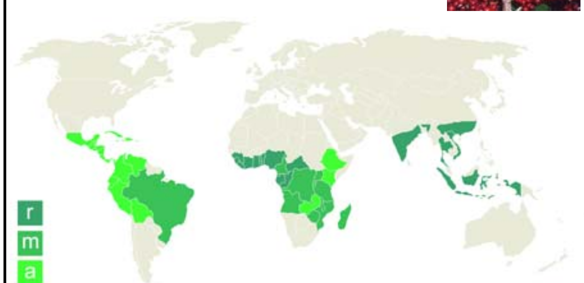
Coffea arabica (arabica coffee)

Table 3. Production of top 3 stimulant beverages.

Top 3 continents	Total (MT)
Coffee	5,919
1. S Amer	
2. Africa	
3. N & C Amer	
Tea	2,473
1. Asia	
2. Africa	
3. S Amer	
Cocoa	2,329
1. Africa	
2. S Amer	
3. Asia	

III. *Coffea*

D. Coffee is a major commodity globally.



III. *Coffea*

Coffee Biotech Group (Campinas, Brazil)

III. *Coffea*

E. Coffee origins

Coffea arabica, Ethiopian highlands

•Relatively few Africans drink it.

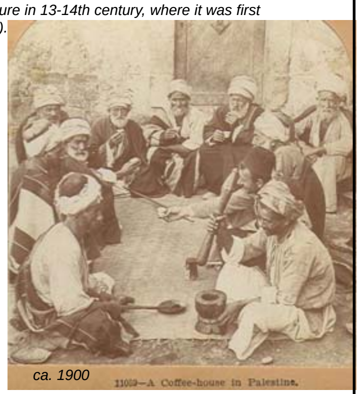
•Traditionally chewed leaves & fruits.

•Relief of fatigue, hunger on hunts.

Farmer in Ethiopia

E. Coffee (the drink) developed in Yemen

Arrival in Yemen and Arab culture in 13-14th century, where it was first brewed (hence, Coffea arabica).



ca. 1900

F. Coffee timeline

1. *Yemen 13-14th century.*
2. Arabia to Egypt by 1510.
3. To Italy & Europe by 1616.
4. Vienna priests threatened by “coffee culture”, but Pope Clement VIII would not ban coffee.
5. To England by 1650 and coffee houses became important socio-politico institutions.
6. Europe looked to break Arabian monopoly on production.

   (*Arabs killed embryos in seeds before export*).

7. Spread of Coffee production

•*Dutch obtained live seeds from Mocha (Red Sea Coast, Yemen, 1706)*

•*Throughout Dutch colonies in Indonesia (e.g., Java) and to S America by 1717.*

•*Today, Brazil is world's leading producer.*