



“Of all the sciences contributing to medicine, chemistry is the primary one, and, apart from the general light it throws on the entire art of healing, it will soon bestow on some of its branches a perfection such as one never could have anticipated.”

(Berzelius in his preface, addressed to King Gustav IV Adolf in the first Swedish edition of *Animal Chemistry* of 1806.)

CINCHONA SUCCIRUBRA

YELLOWBARK CINCHONA,  
PERUVIAN BARK

Rubiaceae

59

S Am  
Af



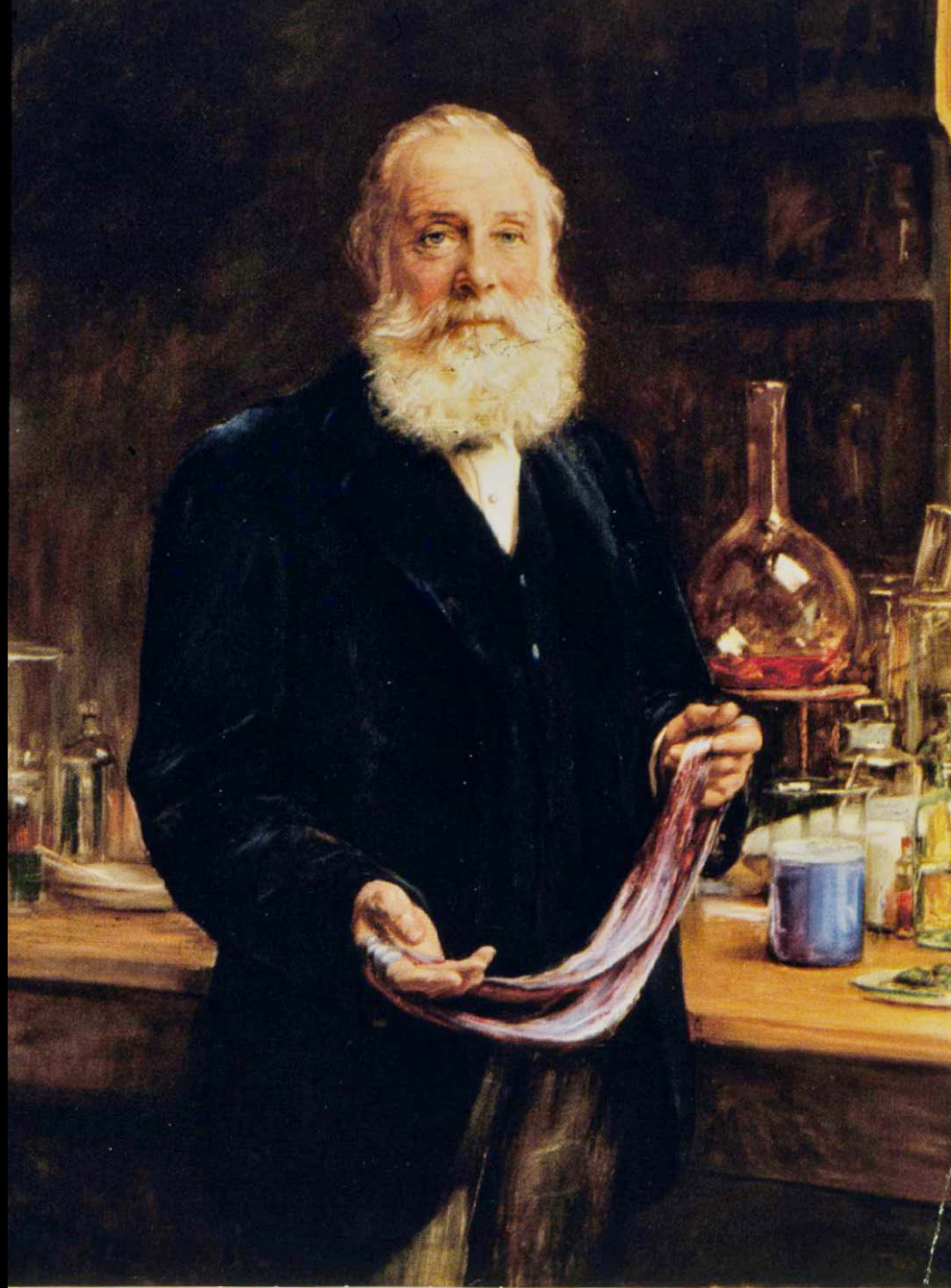
**CAVENTOU**



**PELLETIER**



Joseph B. Caventou (1795-1877), Joseph Pelletier (1788-1842). They isolated quinine from cinchona bark, for the first time, in a laboratory at Paris on September 11, 1820. Caventou was 25 years old and Pelletier 32.



WILLIAM HENRY PERKIN  
*Portrait by Sir Arthur Cope R.A.*



*Digitalis*



# DIGALEN

"Roche"

Name als Marke geschützt

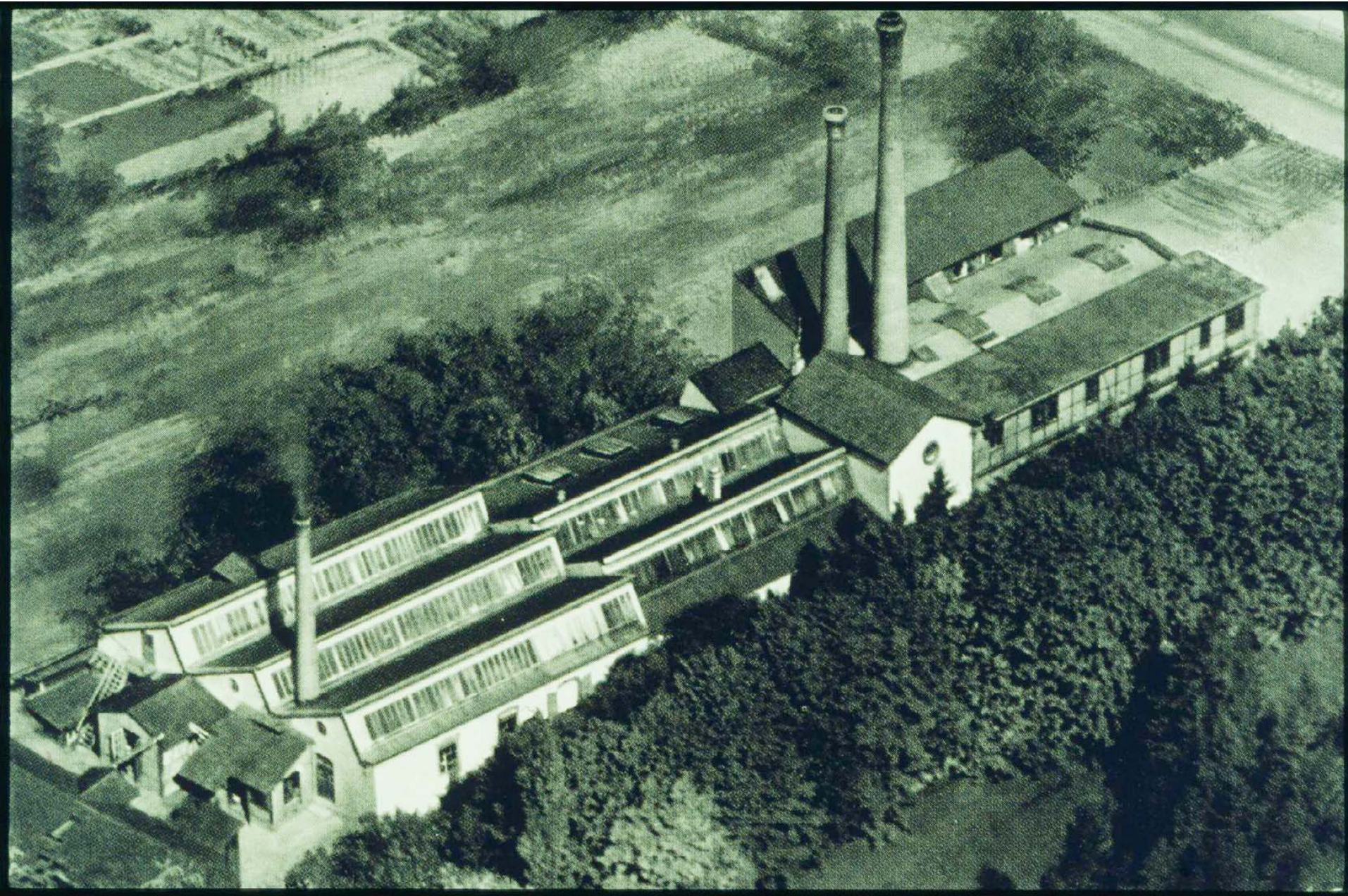
Digitoxin. solubile Cloetta

Sterile Lösung für Injektionen  
in zugeschmolzenen Glasphiolen.

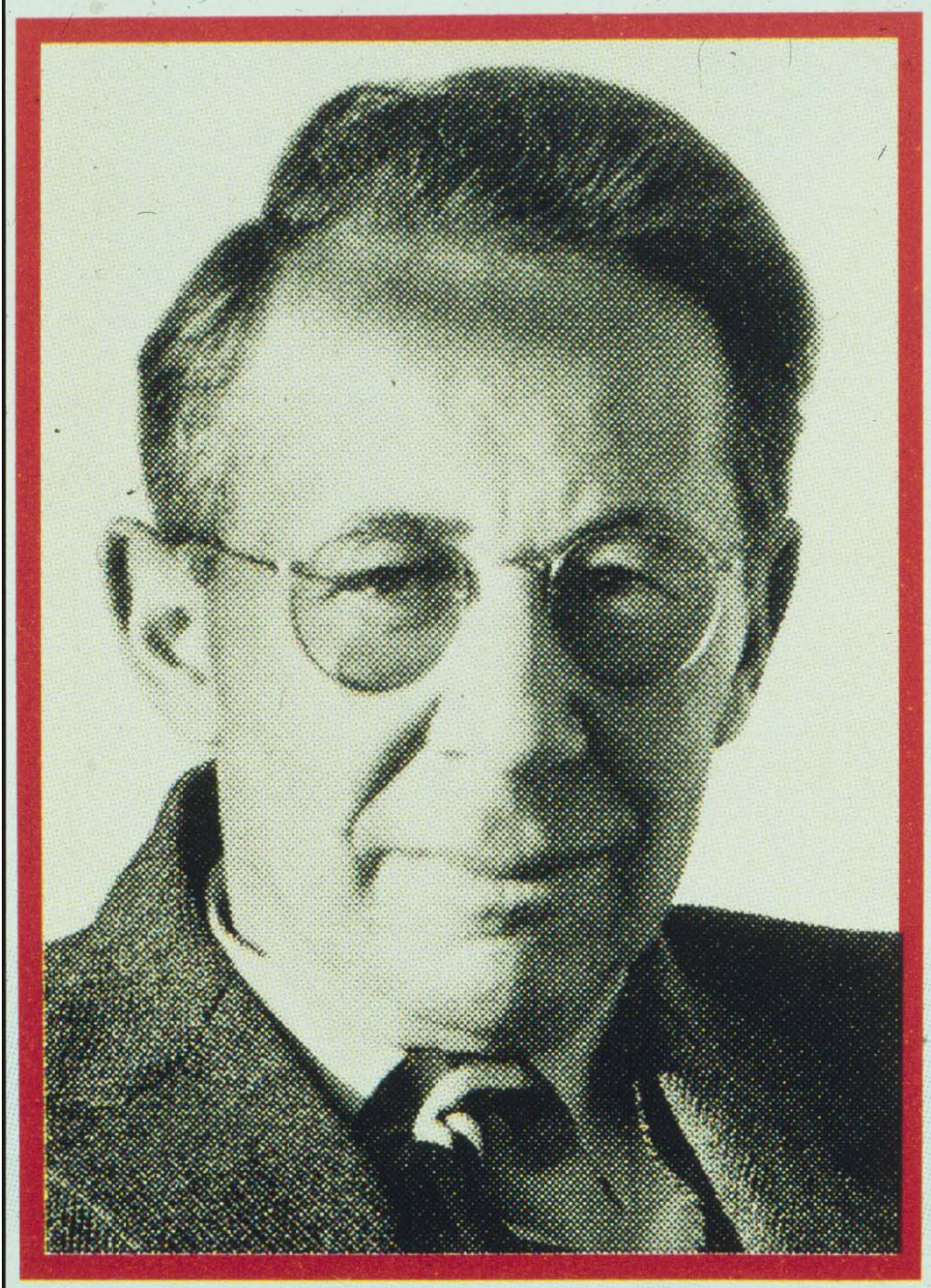
Jede Phiole enthält 1,1 ccm. Digalen

F. HOFFMANN-LA ROCHE & CO. AG.

— BASEL —









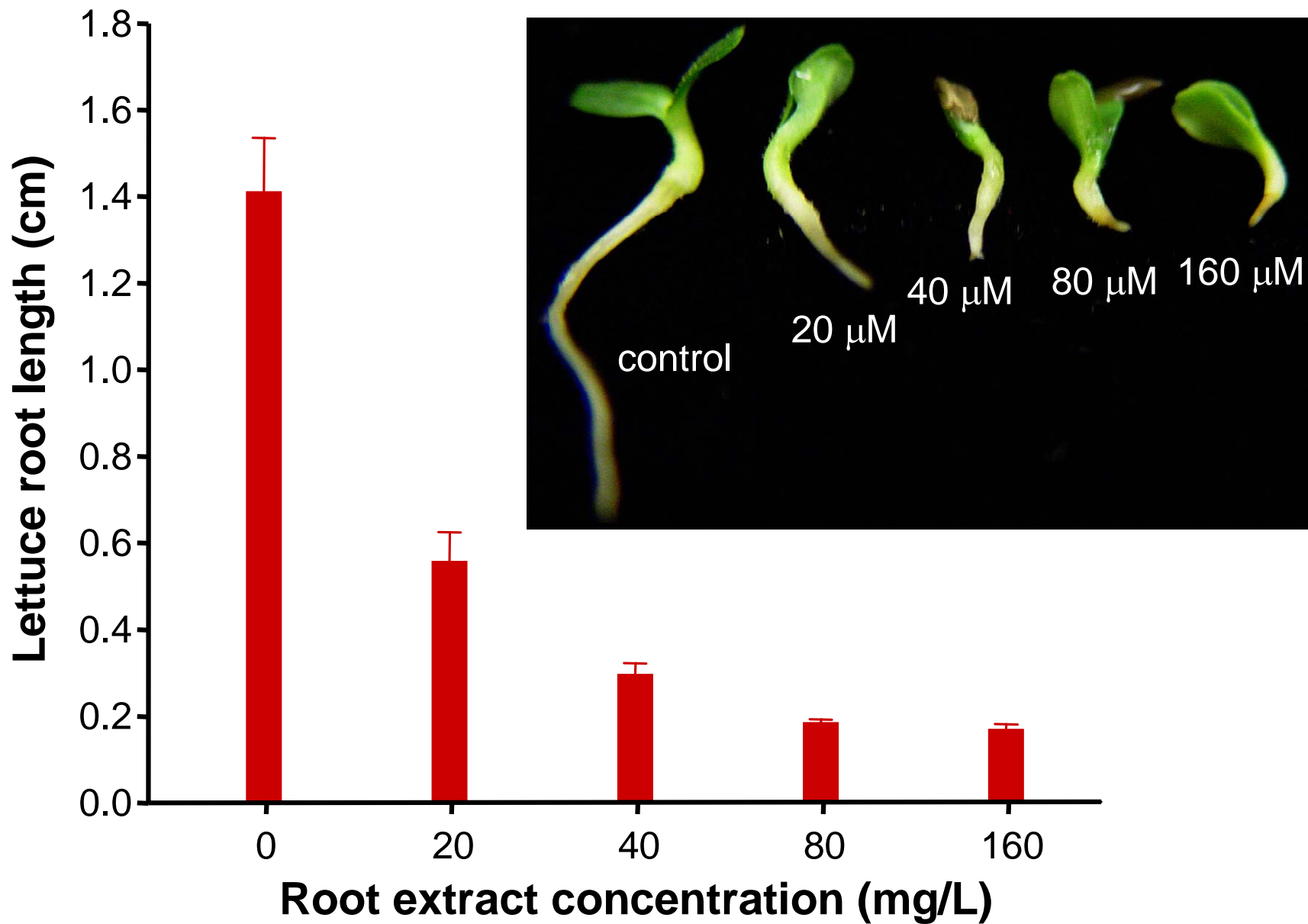




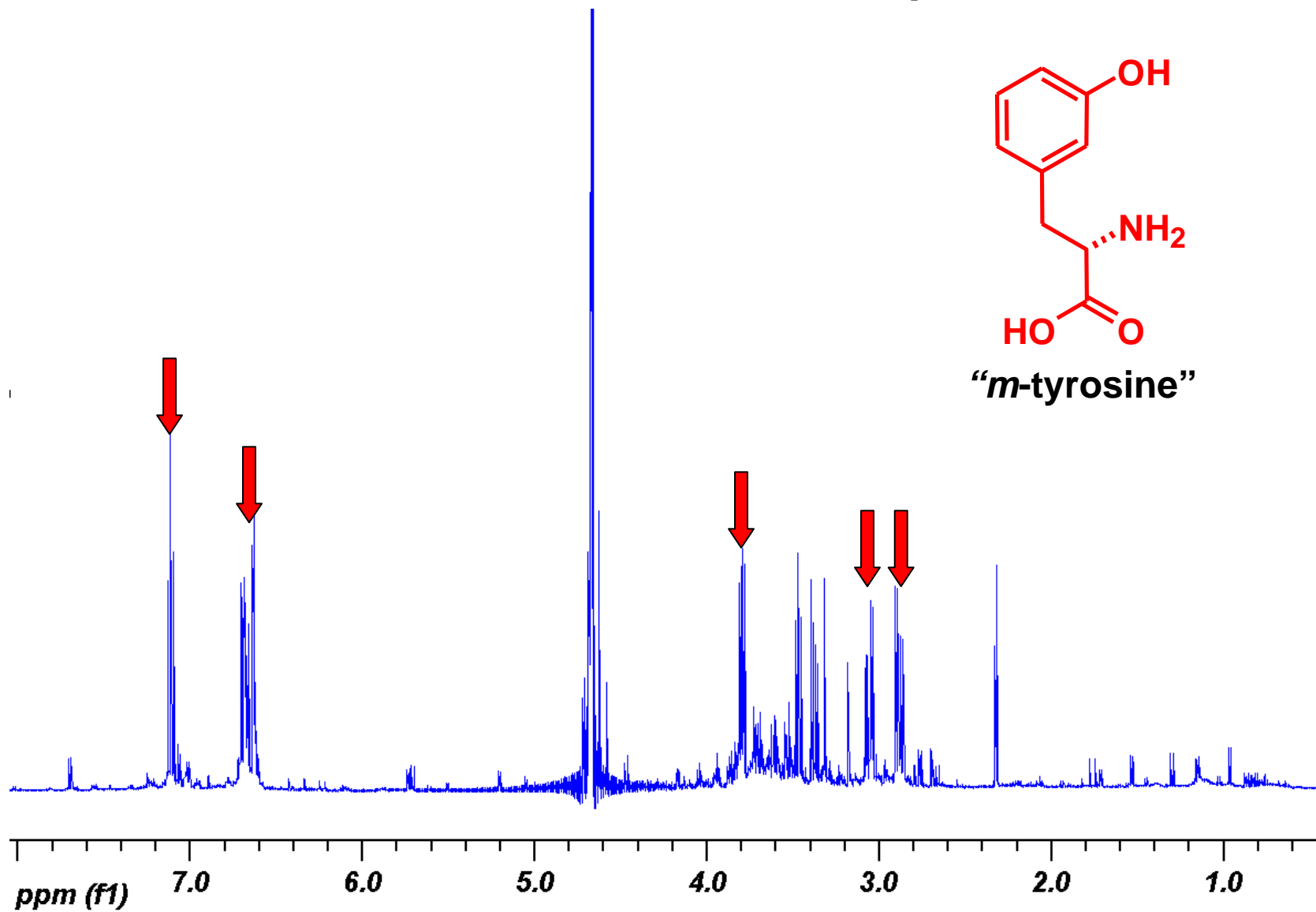
**Scottish Highlands**

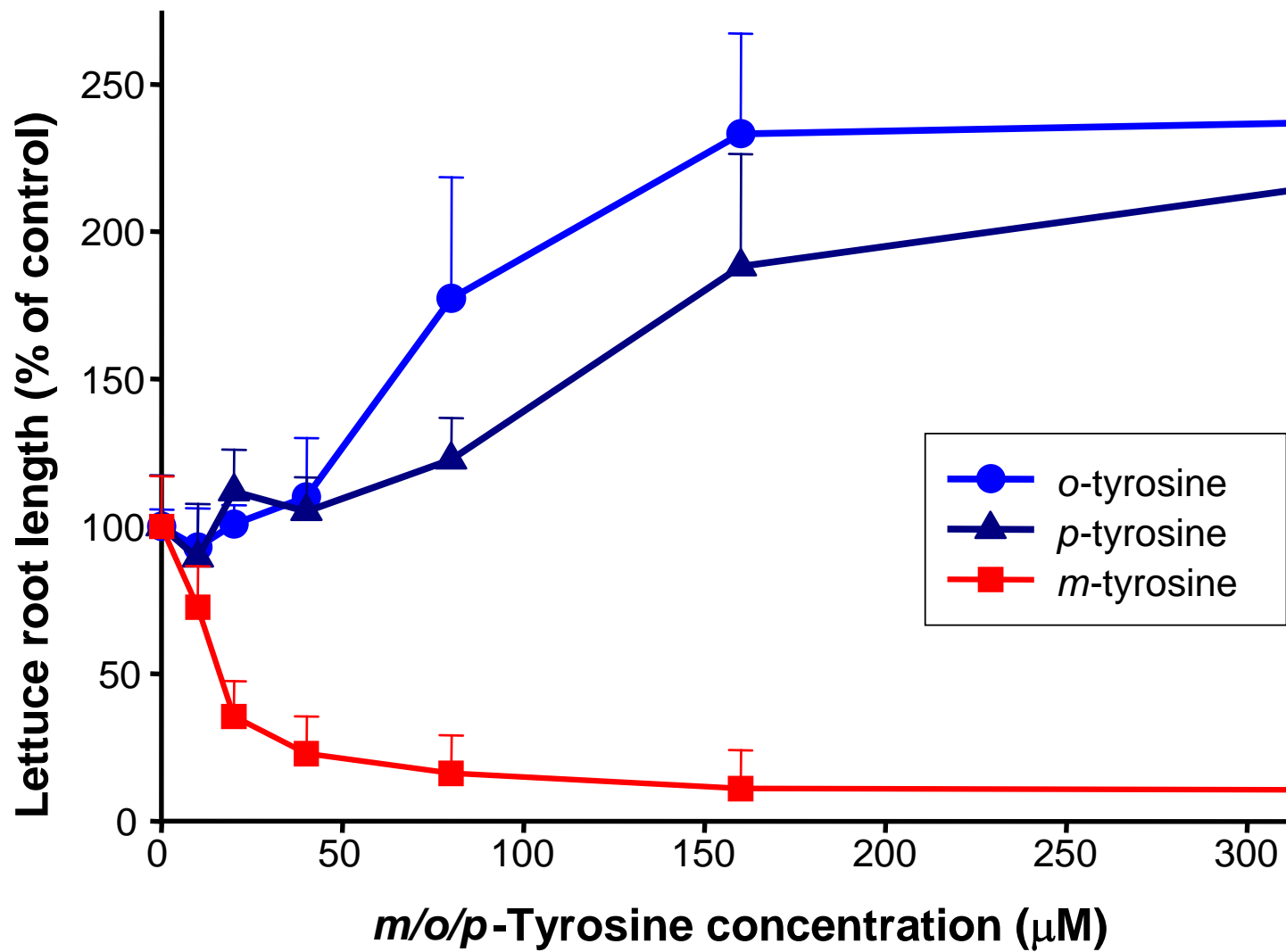


***Festuca rubra*, roots**

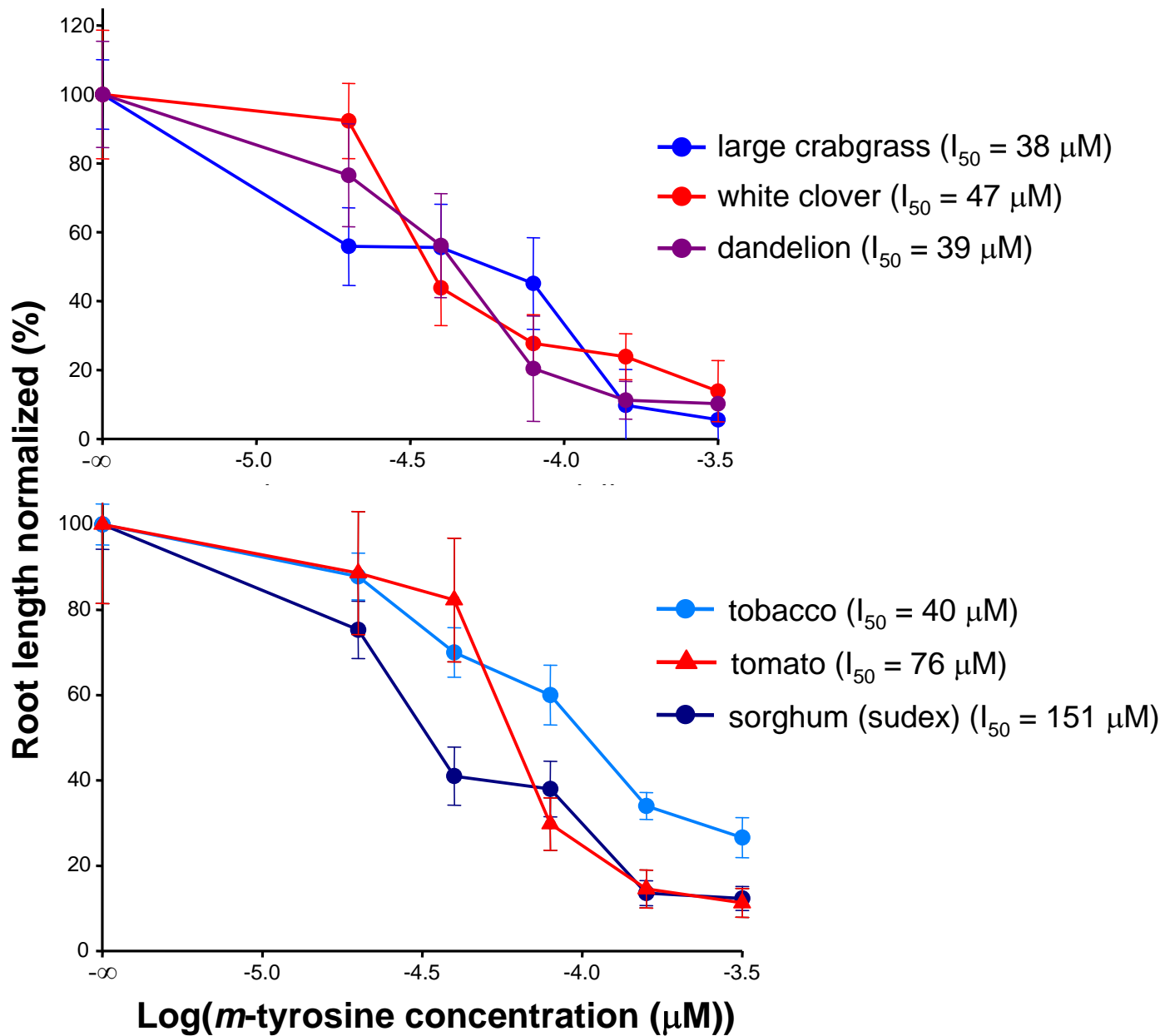


# *Festuca rubra*, root exudate, $^1\text{H}$ NMR spectrum



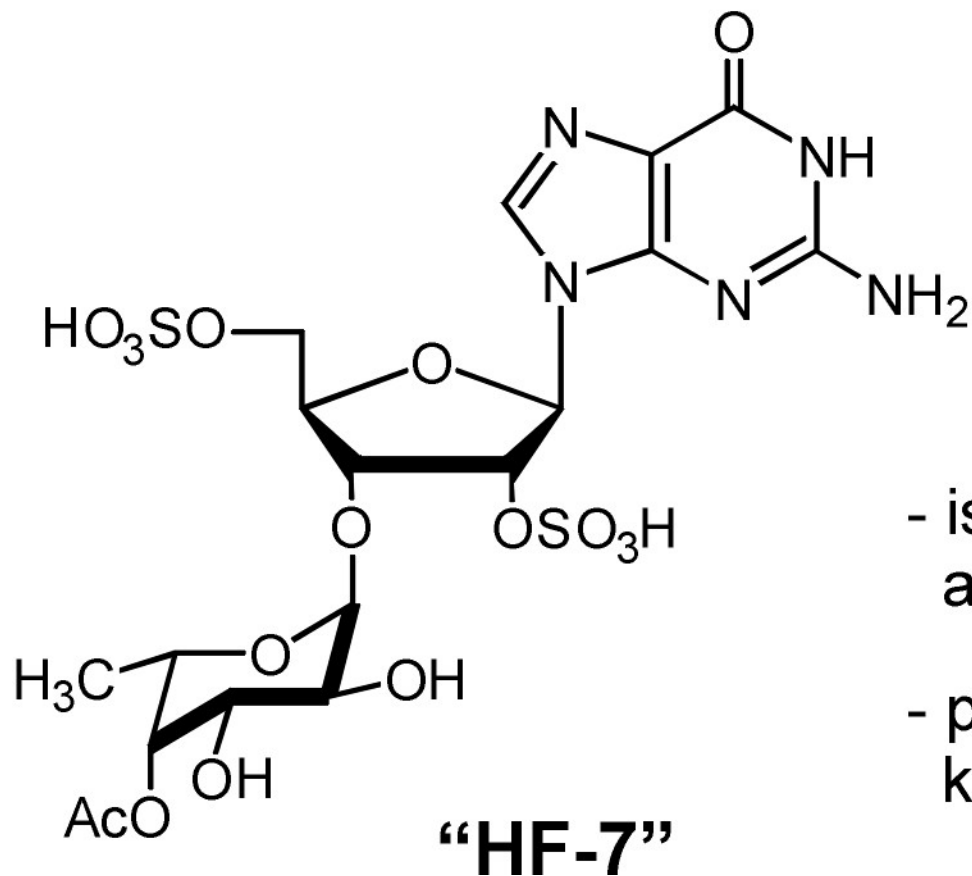






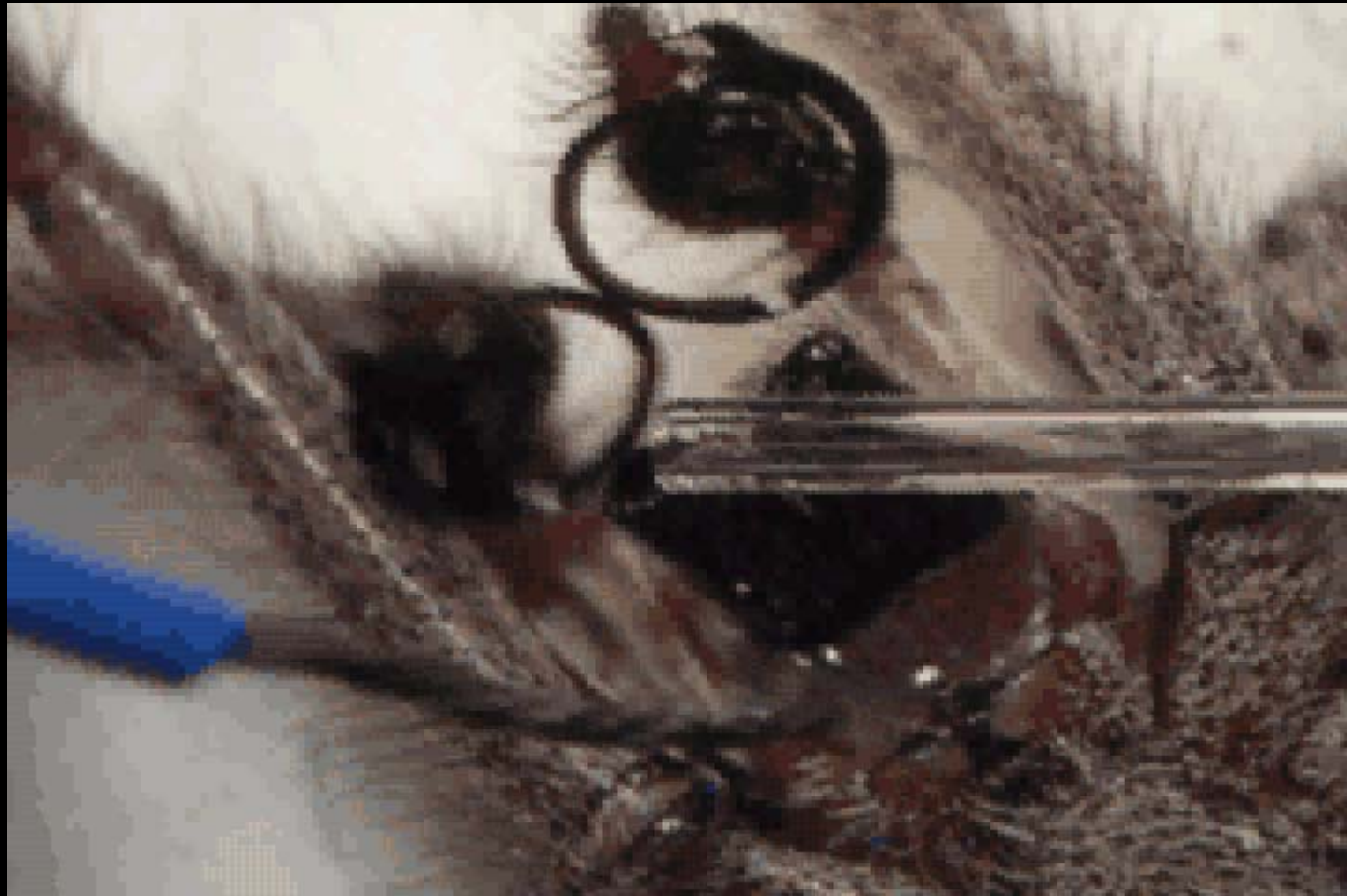
# A “one-of-a-kind” venom component

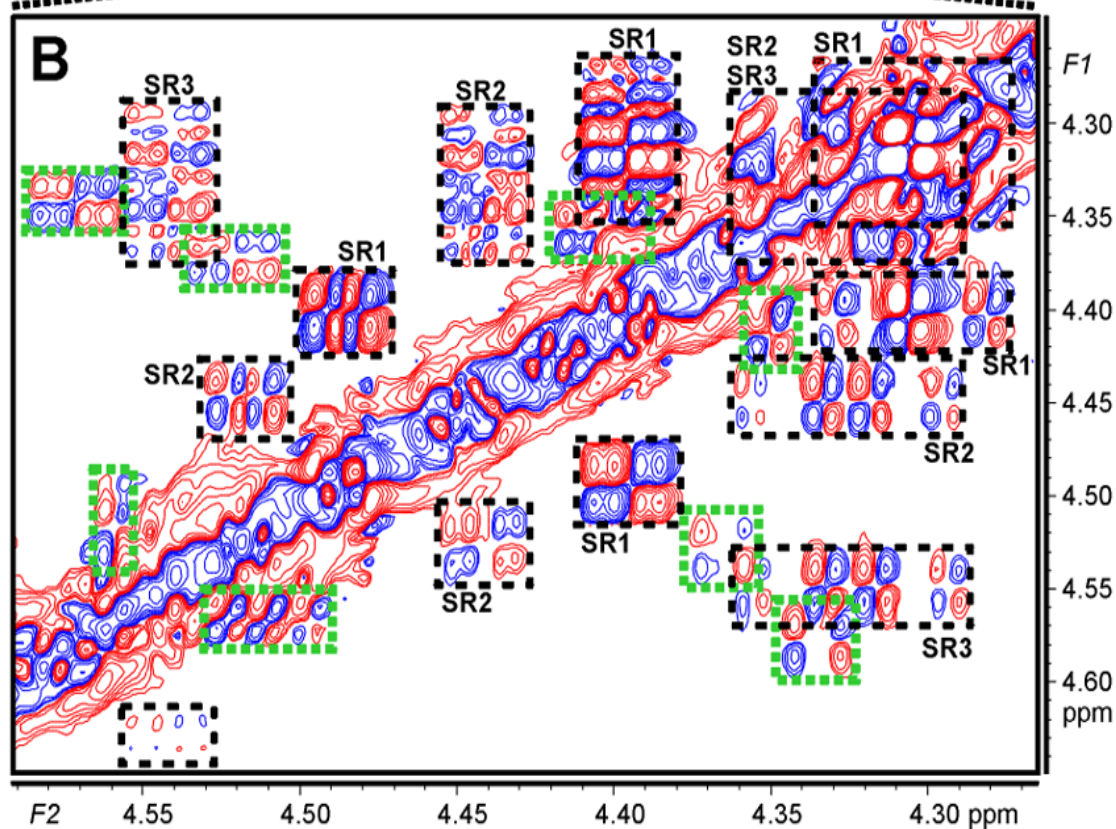
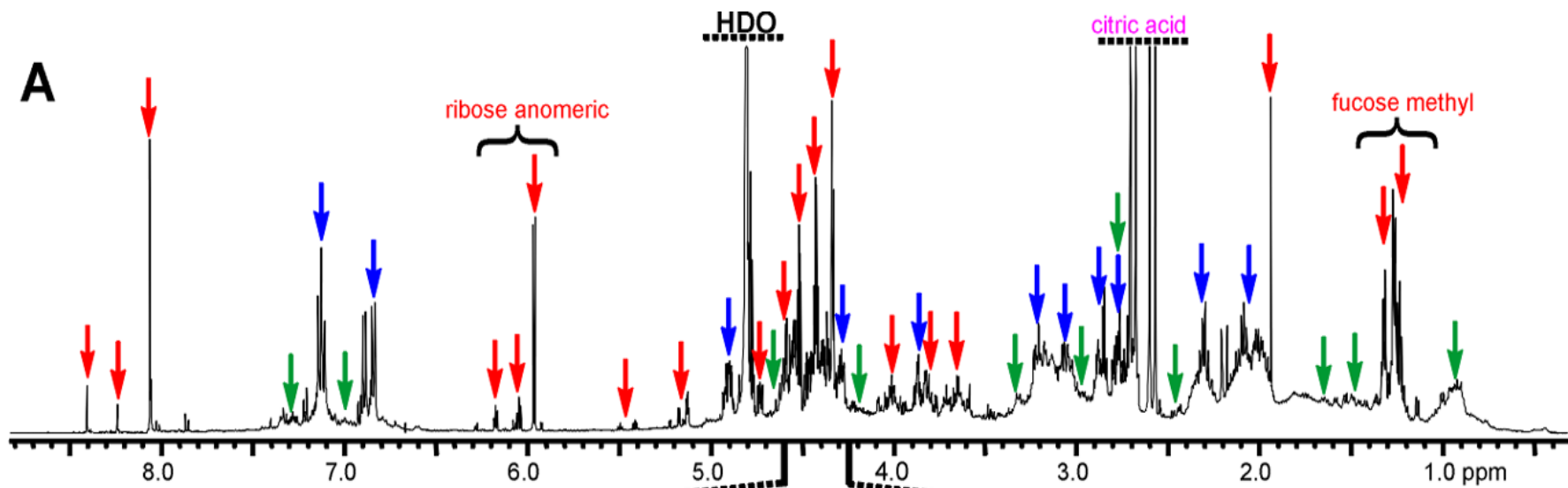
from the Hobo spider, *Hololena curta*.



- isolated through activity-guided screening
- potent inhibitor of kainate receptors







# The **brown recluse**: *Loxosceles reclusa*

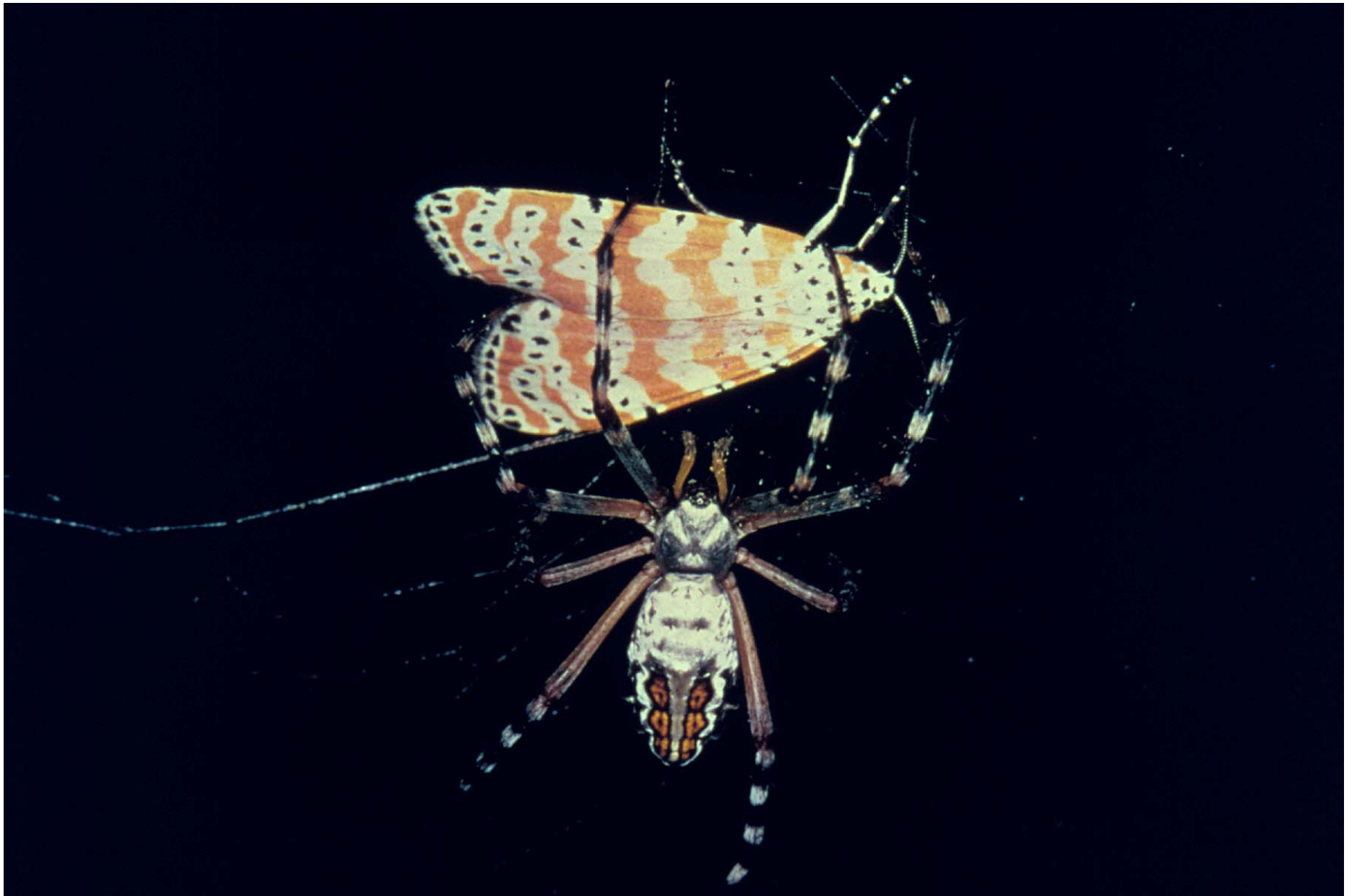


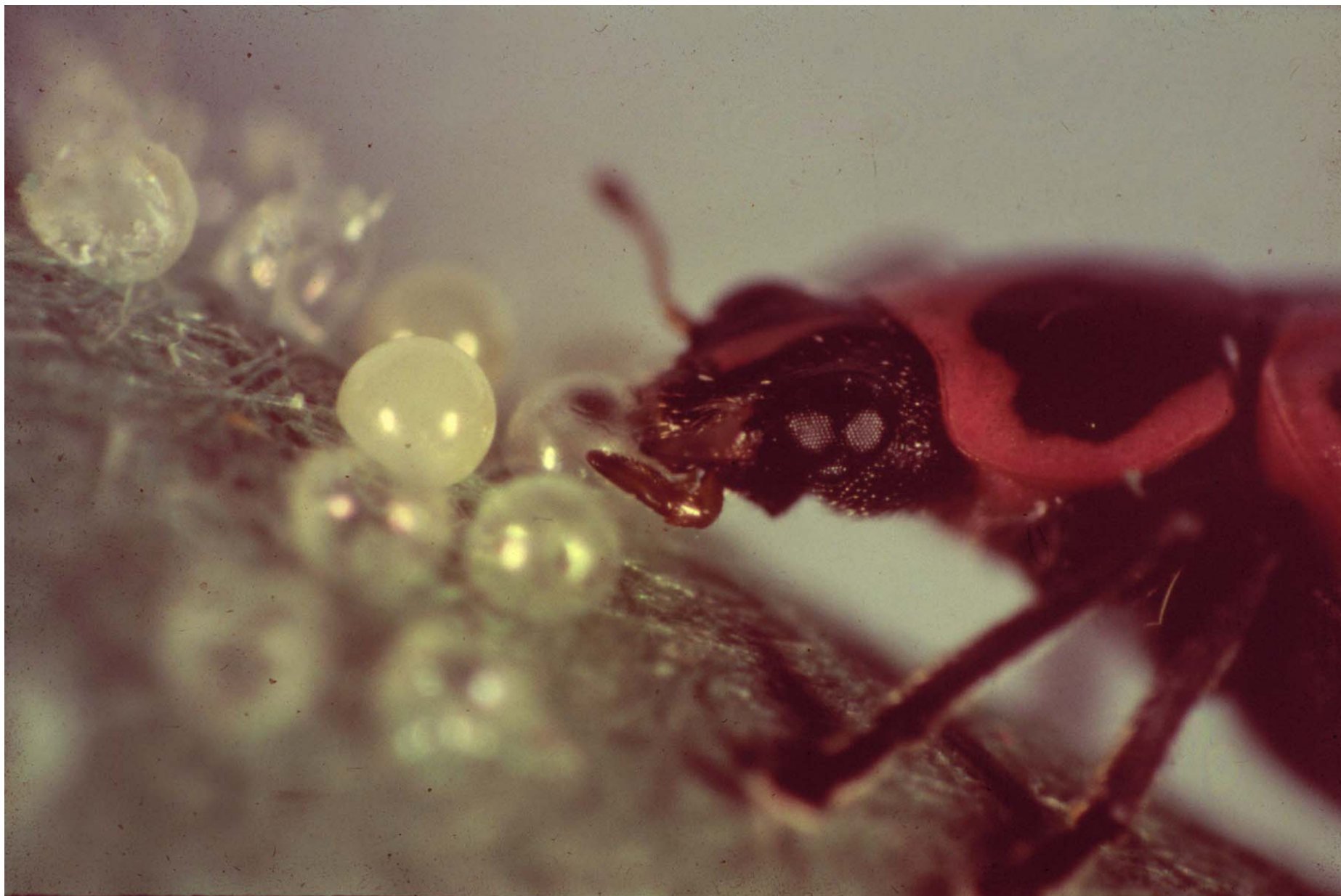
- Highly toxic to mammals
- Common in the U.S.
- Venom subject of > 500 papers
- Major reported components: *peptides*
- Major small-molecule components by direct NMR:  
*sulfated nucleosides* (> 80%)



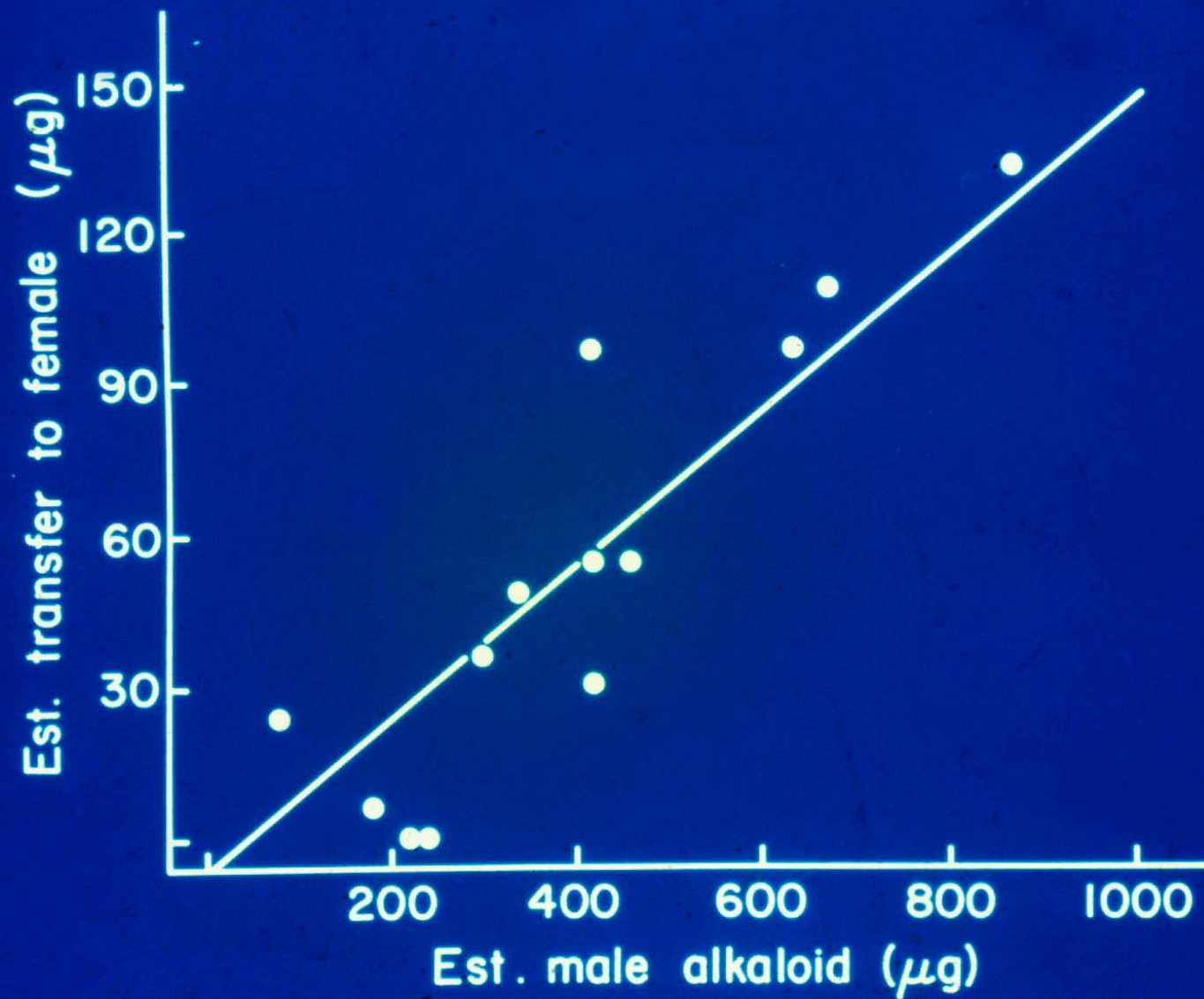




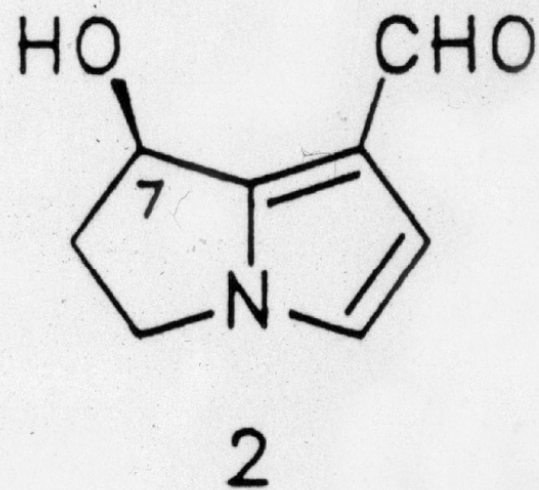
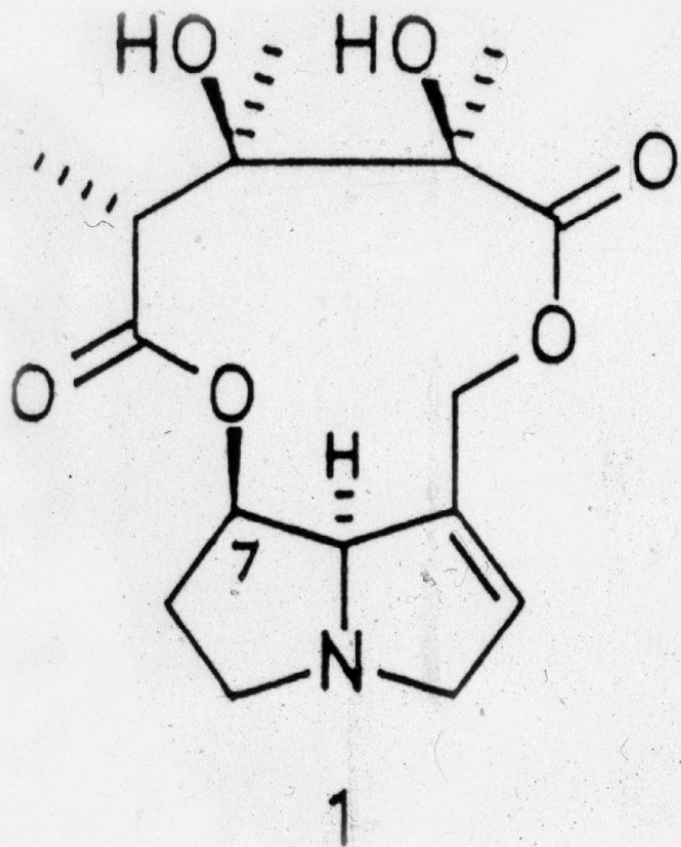












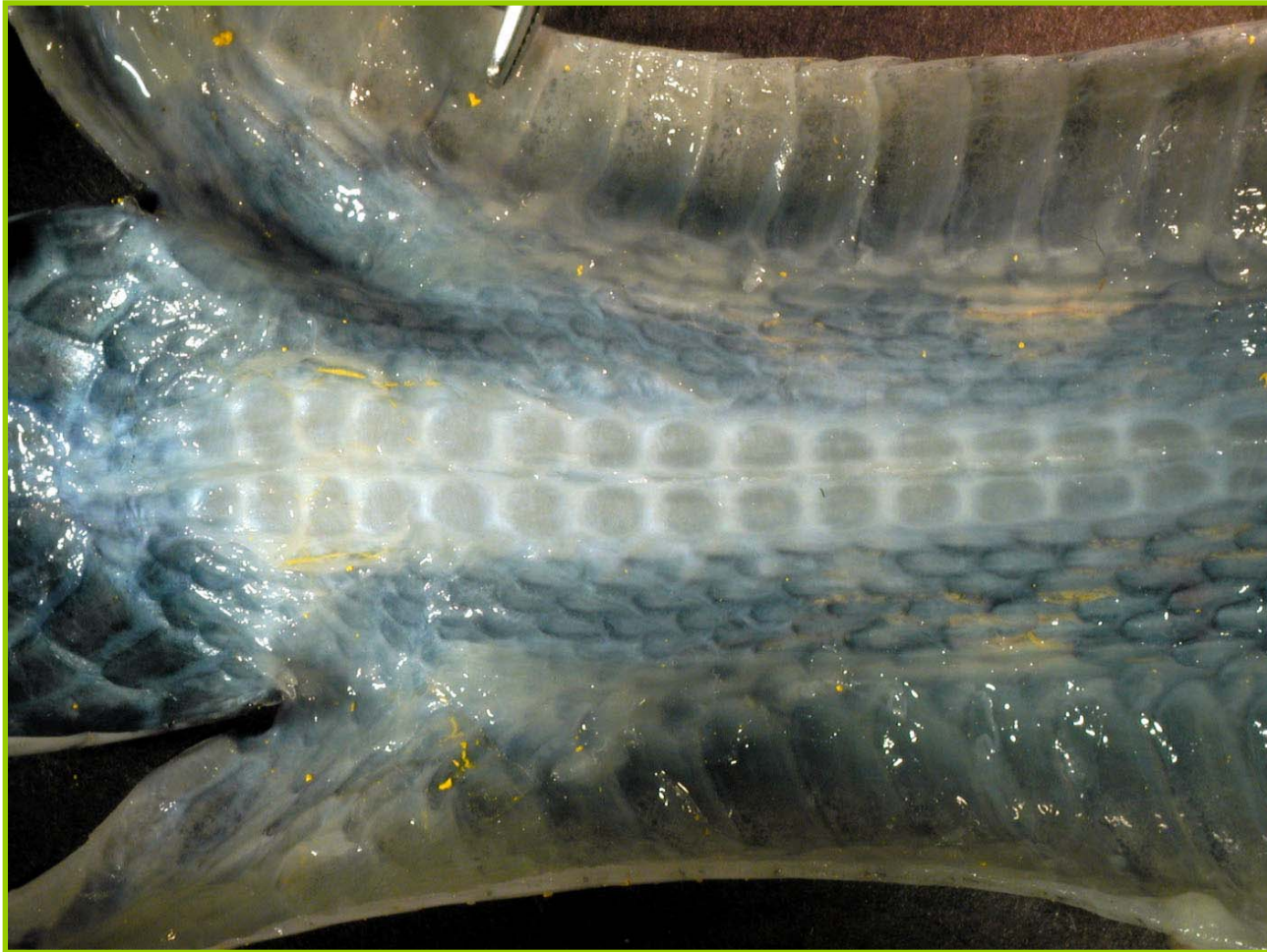
# *Rhabdophis tigrinus*



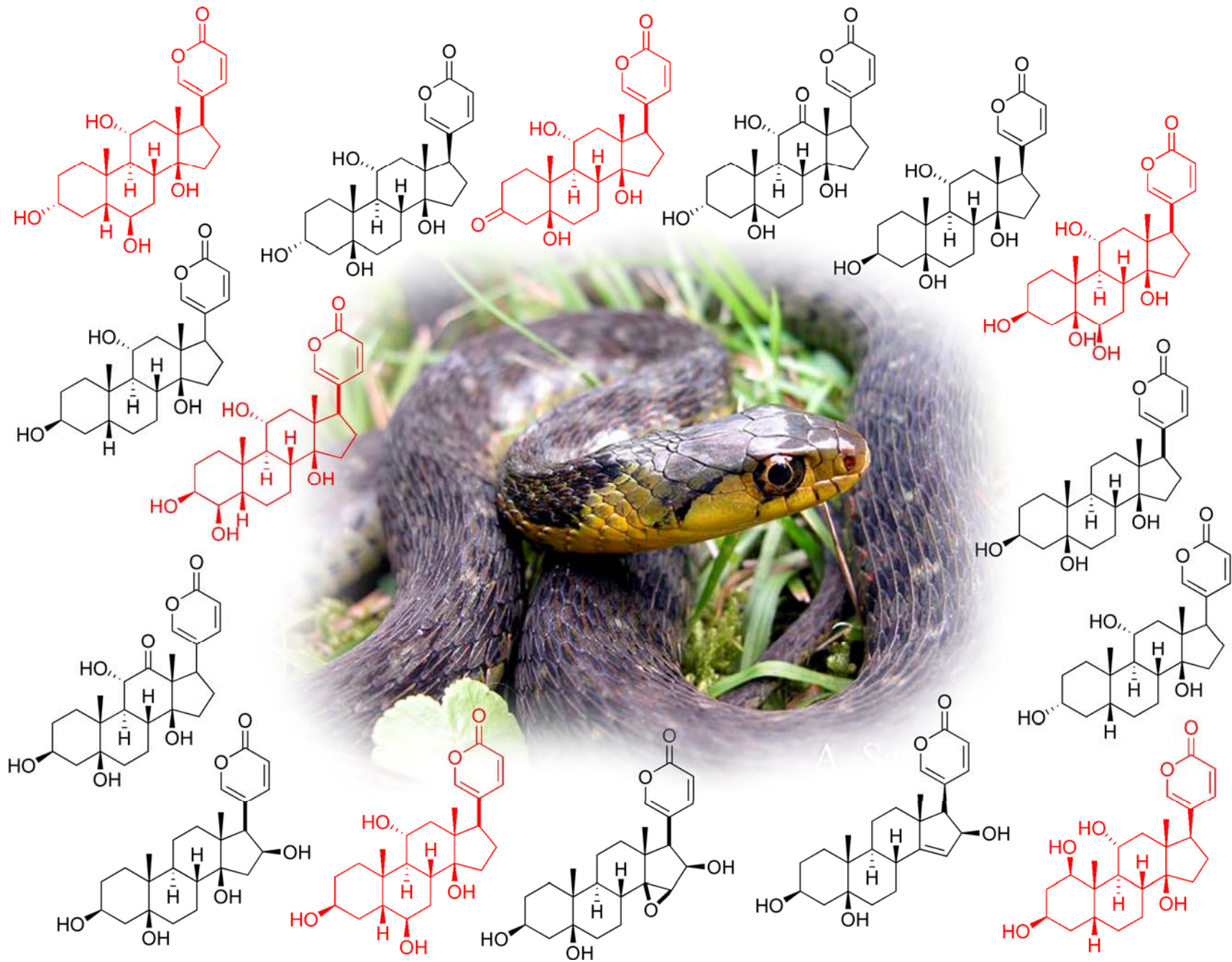
A. Savitzky

# Gross Morphology of the Nuchal Glands

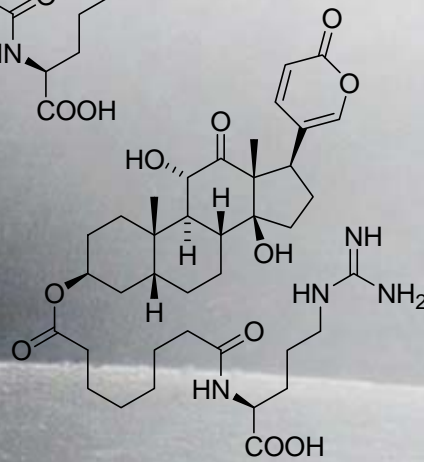
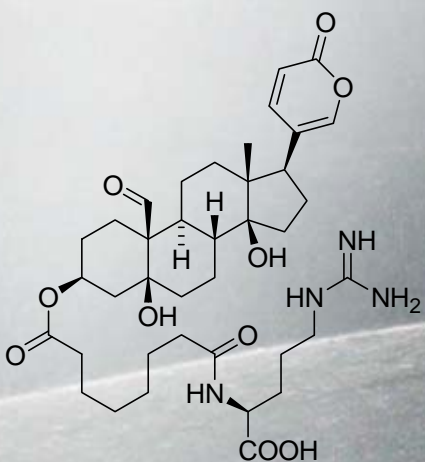
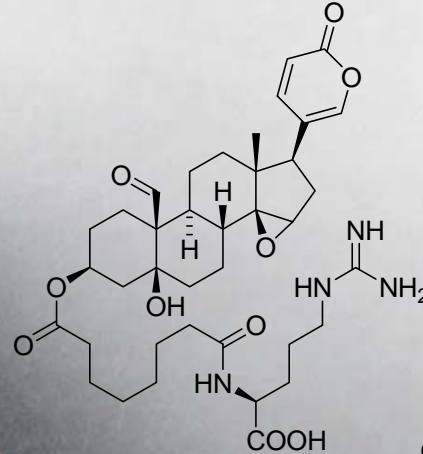
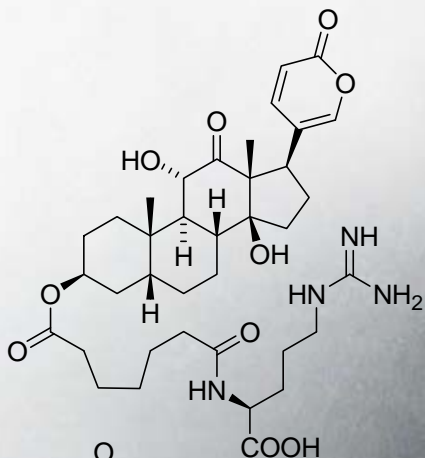
underside of skin, showing nuchal glands



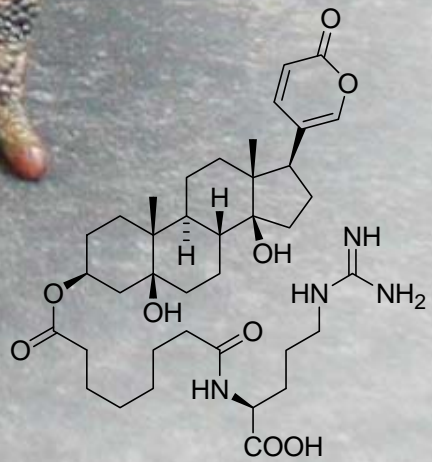
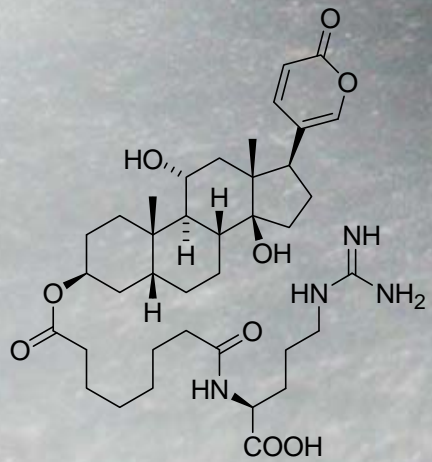




# *Bufo fowleri*



[www.turtleails.com](http://www.turtleails.com)

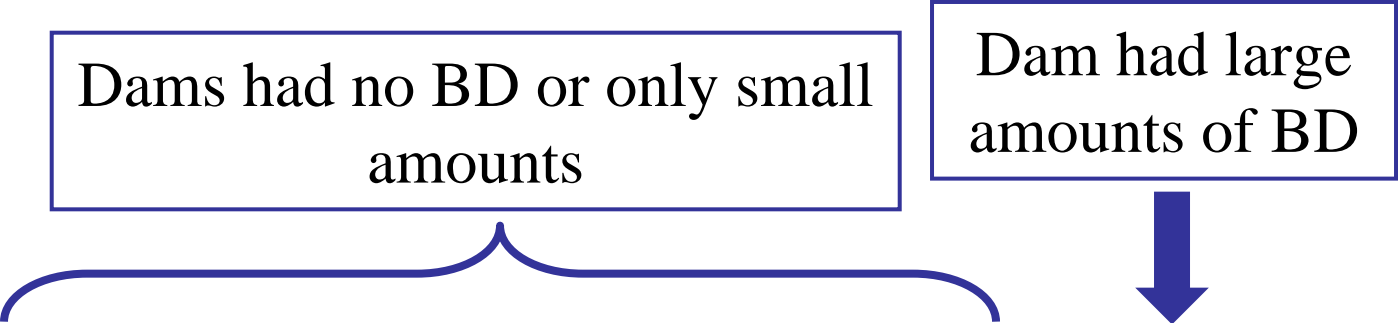




# Experiment #1: Summary of NMR findings

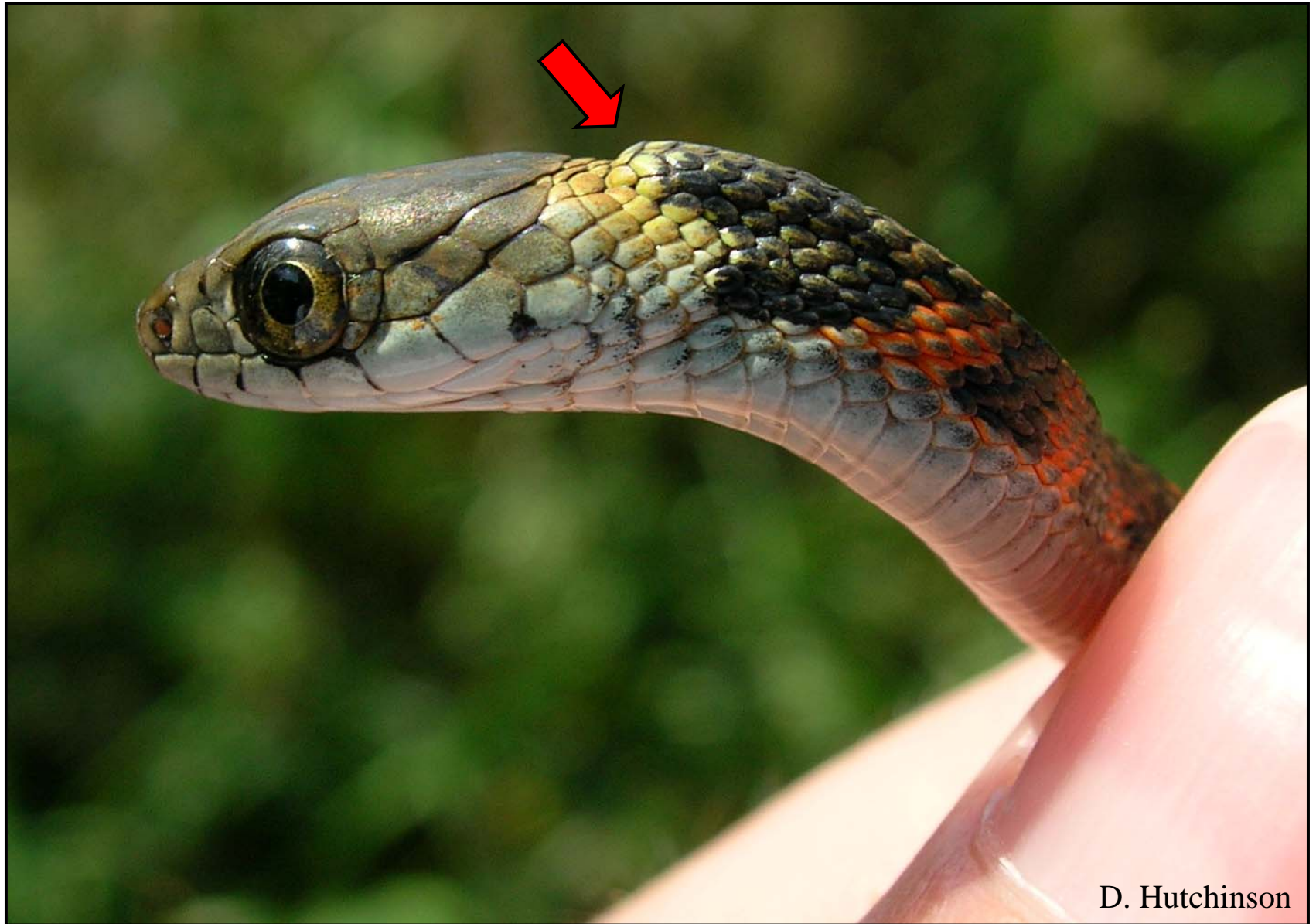
Dams had no BD or only small amounts

Dam had large amounts of BD



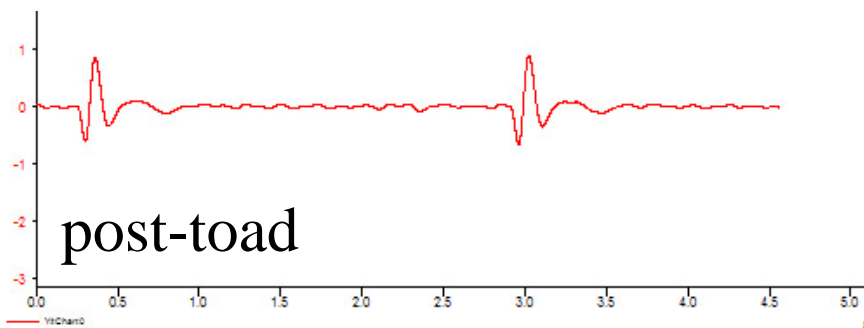
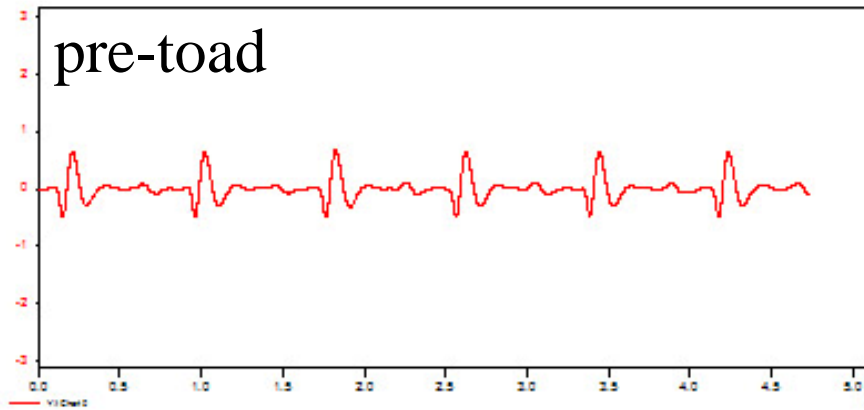
	<b>Clutch # 1</b>	<b>Clutch # 2</b>	<b>Clutch # 3</b>	<b>Clutch # 4</b>
<b>Unfed</b>	- (N = 3)	- (N = 4)	- (N = 3)	<b>+</b> (N = 3)
<b>Fed fish</b>	- (N = 8)	- (N = 1)	- (N = 6)	<b>+</b> (N = 5)
<b>Fed frogs</b>	- (N = 1)	- (N = 1)	- (N = 2)	<b>+</b> (N = 3)
<b>Fed toads</b>	<b>+</b> (N = 2)	<b>+</b> (N = 3)	<b>+</b> (N = 3)	<b>+</b> (N = 4)

# Hatchling from toad-rich island

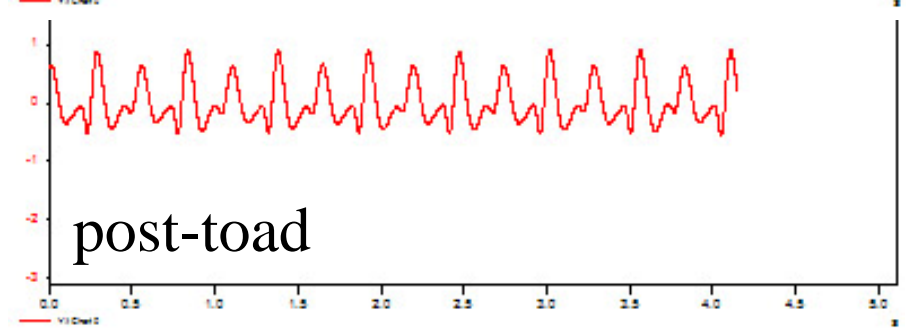
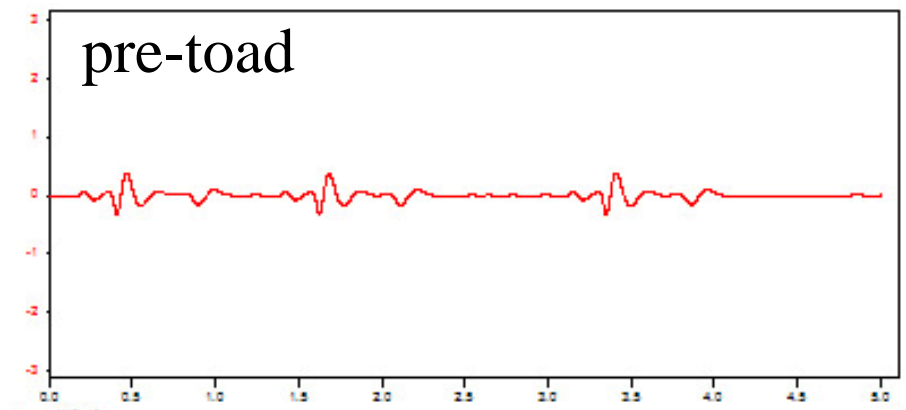


# Ongoing Studies of *Rhabdophis*

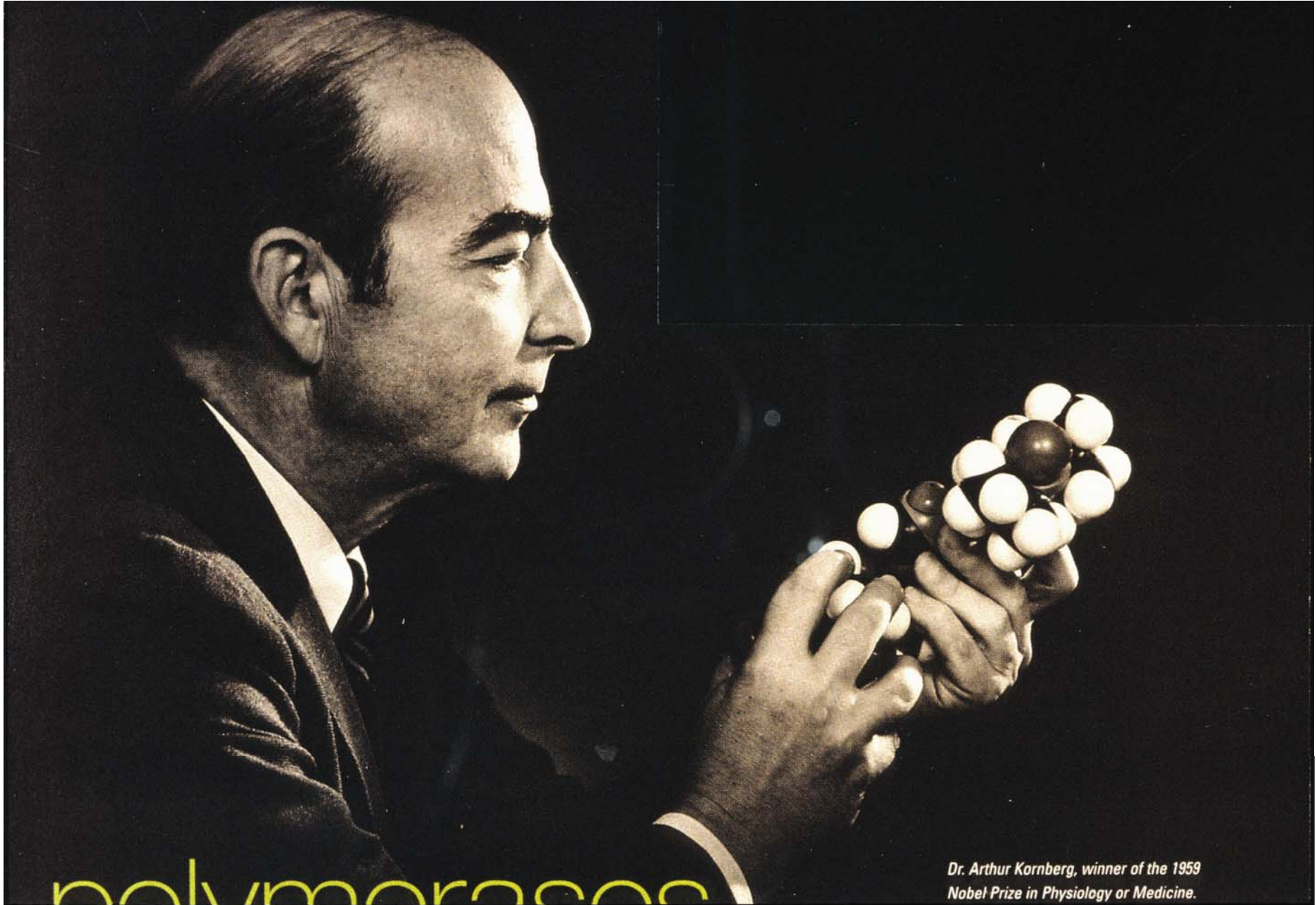
- Resistance to cardiovascular effects of bufadienolides



*Elaphe quadrivirgata*  
preys on frogs  
bradycardia after *Bufo*



*Rhabdophis tigrinus*  
preys on toads  
tachycardia after *Bufo*



polymers

*Dr. Arthur Kornberg, winner of the 1959  
Nobel Prize in Physiology or Medicine.*

"Among scientists, both physicists and biologists have had a low regard for chemistry, and little patience for it. Biologists need to be aware that life processes, their evolution and variety, can be and ultimately must be described in molecular terms. They must resort to chemical techniques to refine and broaden the scope of their explorations of how plant, animal, and microbial forms compete and cooperate on earth.

Arthur Kornberg (1989) *For The Love of Enzymes*, Harvard University Press, Cambridge, MA.





*"Sometimes I wonder if there's more to life than  
unlocking the mysteries of the universe."*

## **An Expression of Urgency: The Göteborg Resolution (August, 1989)**

Natural products constitute a treasury of immense value to humankind. The current alarming rate of species extinction is rapidly depleting this treasury, with potentially disastrous consequences. The International Society of Chemical Ecology urges that conservation measures be mounted worldwide to stem the tide of species extinction, and that vastly increased biorational studies be undertaken aimed at discovering new chemicals of use to medicine, agriculture, and industry. *These exploratory efforts should be pursued by a partnership of developing and developed nations in such fashion that the financial benefits flow in fair measure to all participants.*

T. Eisner and J. Meinwald  
*J. Chem. Ecol.* **16**, 643 (1990)

“Advances in medicine, including treatments for currently untreatable diseases, would not be possible without the powerful pharmaceuticals derived from plants, animals, and microbes or without the knowledge gained from other species in biomedical research. We must conserve and sustainably use this pillar of human life. Yet biodiversity is declining at an unprecedented rate and is woefully underappreciated as a resource and as an issue meriting high-level attention.”

Kofi Annan  
former Secretary-General of the U.N.

“For many reasons, not least our own well-being, we need to take better care of the rest of life. Biodiversity . . . will pay off in every sphere of human life, from medical to economic, from our collective security to our spiritual fulfillment.”

Edward O. Wilson  
*Sustaining Life, 2008*

“The library of life is burning and we do not even know the titles of the books.”

Gro Harlem Brundtland  
former Director General of the WHO, and  
former Prime Minister of Norway



W. Steig

*Rare Specimen*

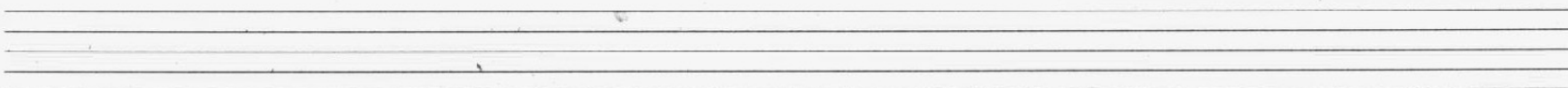
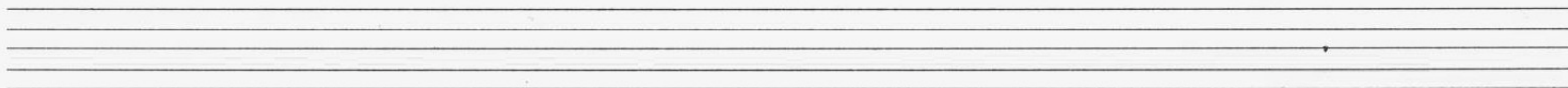
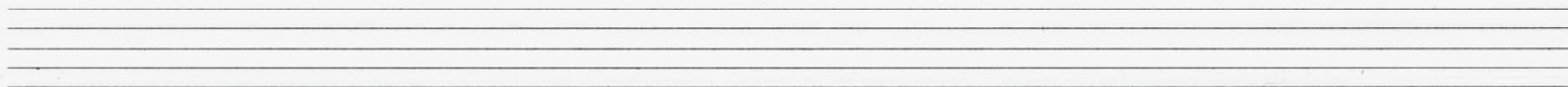
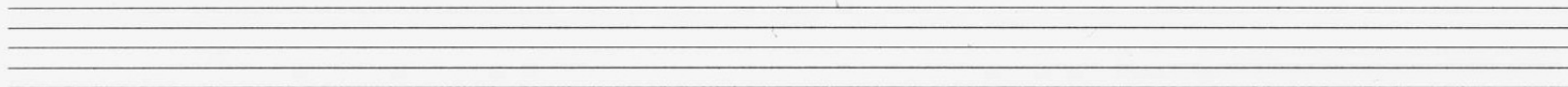
# BIOPIRACY



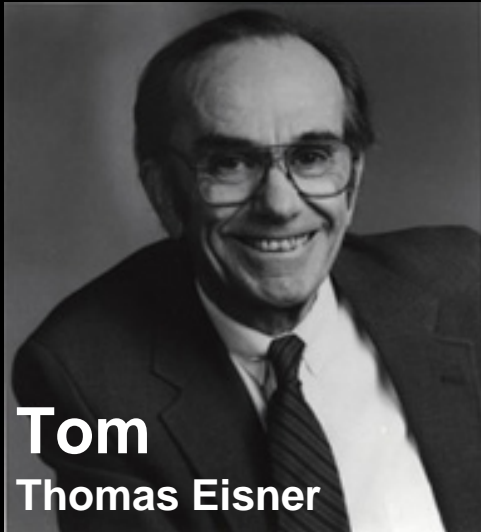
# OHNE GELD KEINE MUSIK

Text: R. Klein

Musik: R. Klein







**Tom**  
Thomas Eisner



**Drew**  
Andrew Taggi



**Frank**  
Frank Schroeder



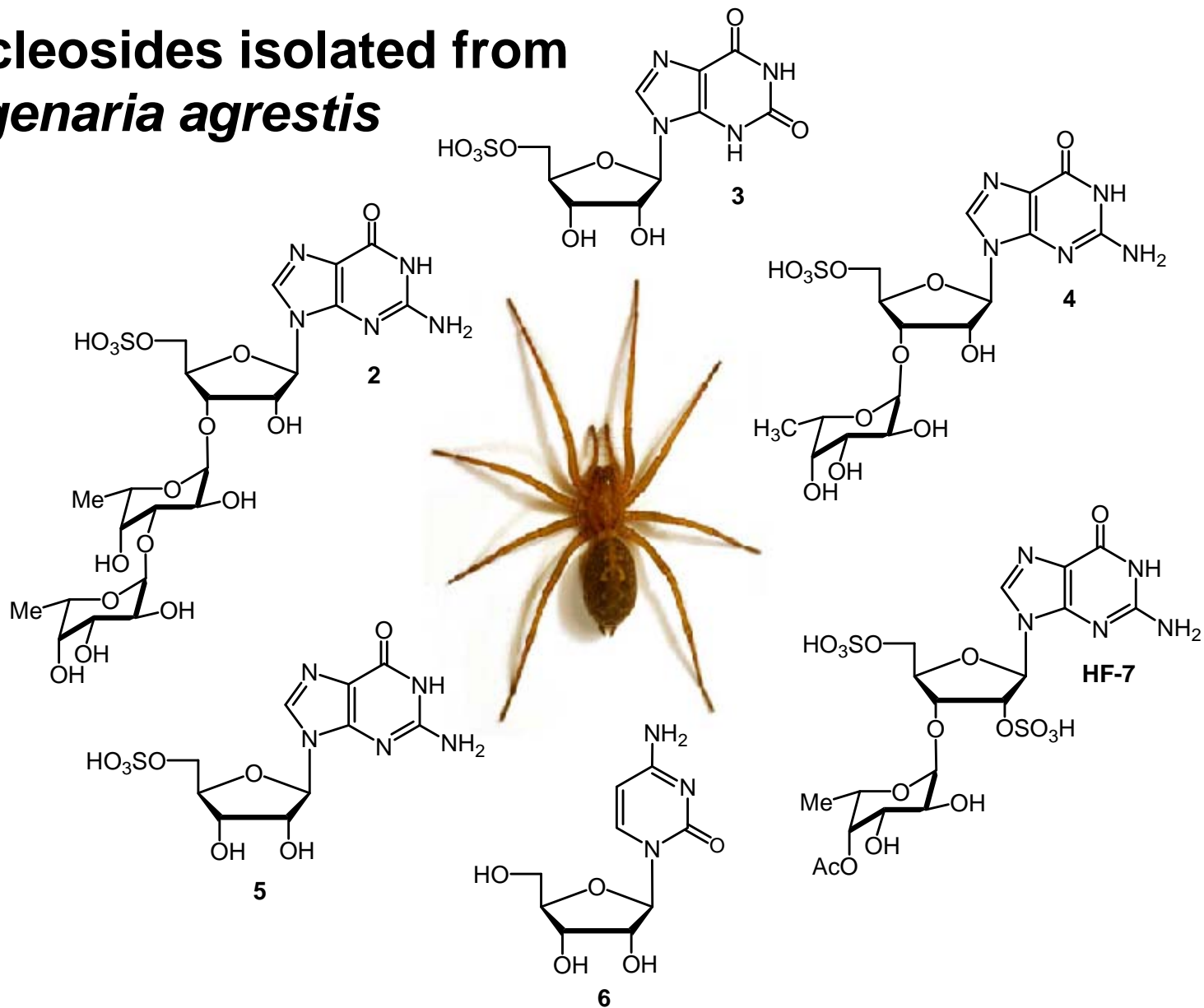
**Matt**  
Matthew Gronquist

**\$ NIH \$**

"Biodiversity is our most valuable but least appreciated resource... a rare beetle sitting on an orchid in a remote valley of the Andes might secrete a substance that cures pancreatic cancer."

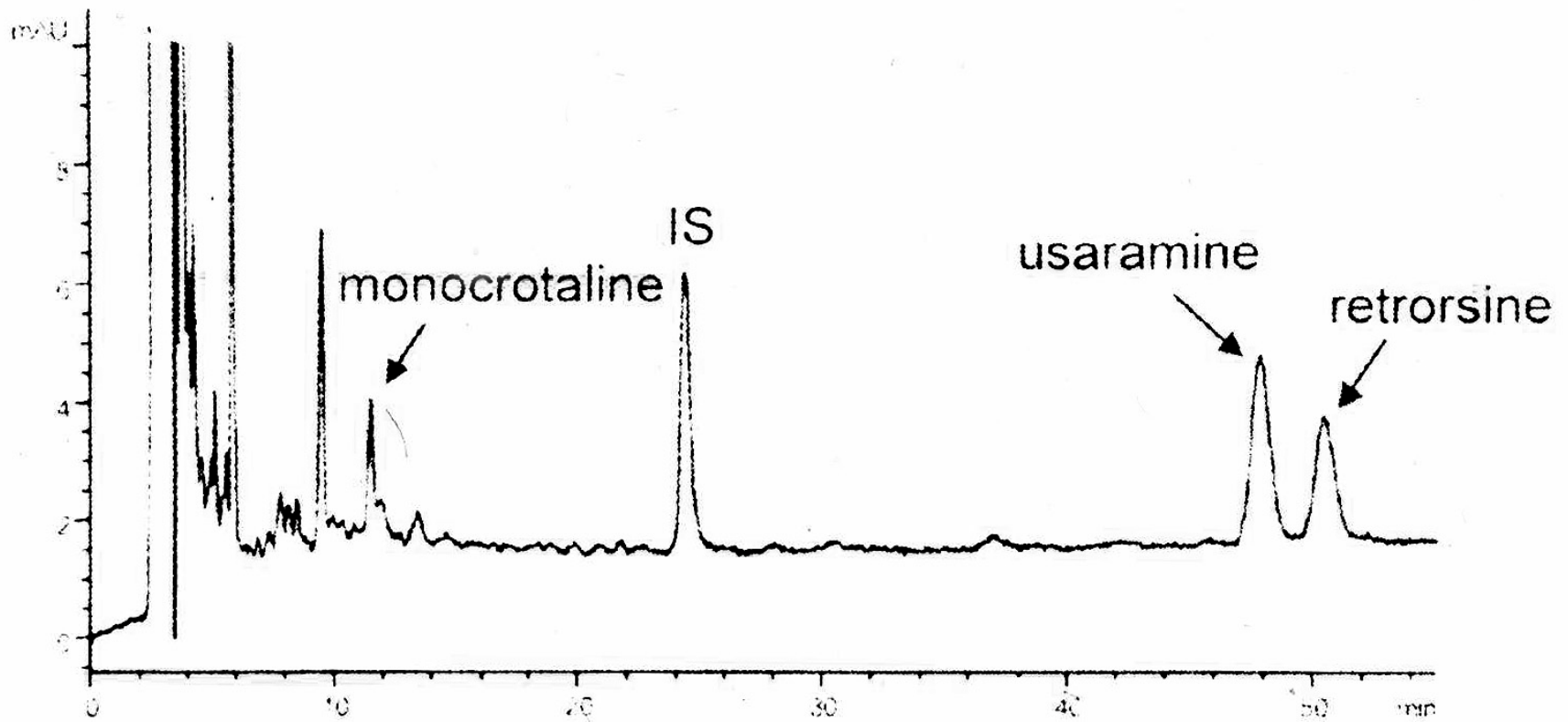
E.O. Wilson cited in *An Inordinate Fondness for Beetles*,  
A.V. Evans and C.L. Bellamy (1996)

# Nucleosides isolated from *Tegenaria agrestis*









**Fig. 5** High pressure liquid chromatogram of the extract of the one egg (asterisk, Fig. 6, female 1, 9-day time slot), shown to contain all three PAs of male origin. The internal standard (ridelline) is also shown

# SEXUALLY TRANSMITTED DEFENSES IN *UTETHEISA ORNATRIX*

Fate of "pinto bean" females in spider bioassay following mating with chemically protected (*Crotalaria* - fed; alkaloid - containing) *versus* chemically unprotected (pinto bean - fed; alkaloid - free) males.

## Male Type

*Crotalaria* - fed

Pinto bean - fed

## Spider Bioassay Result

Females uneaten

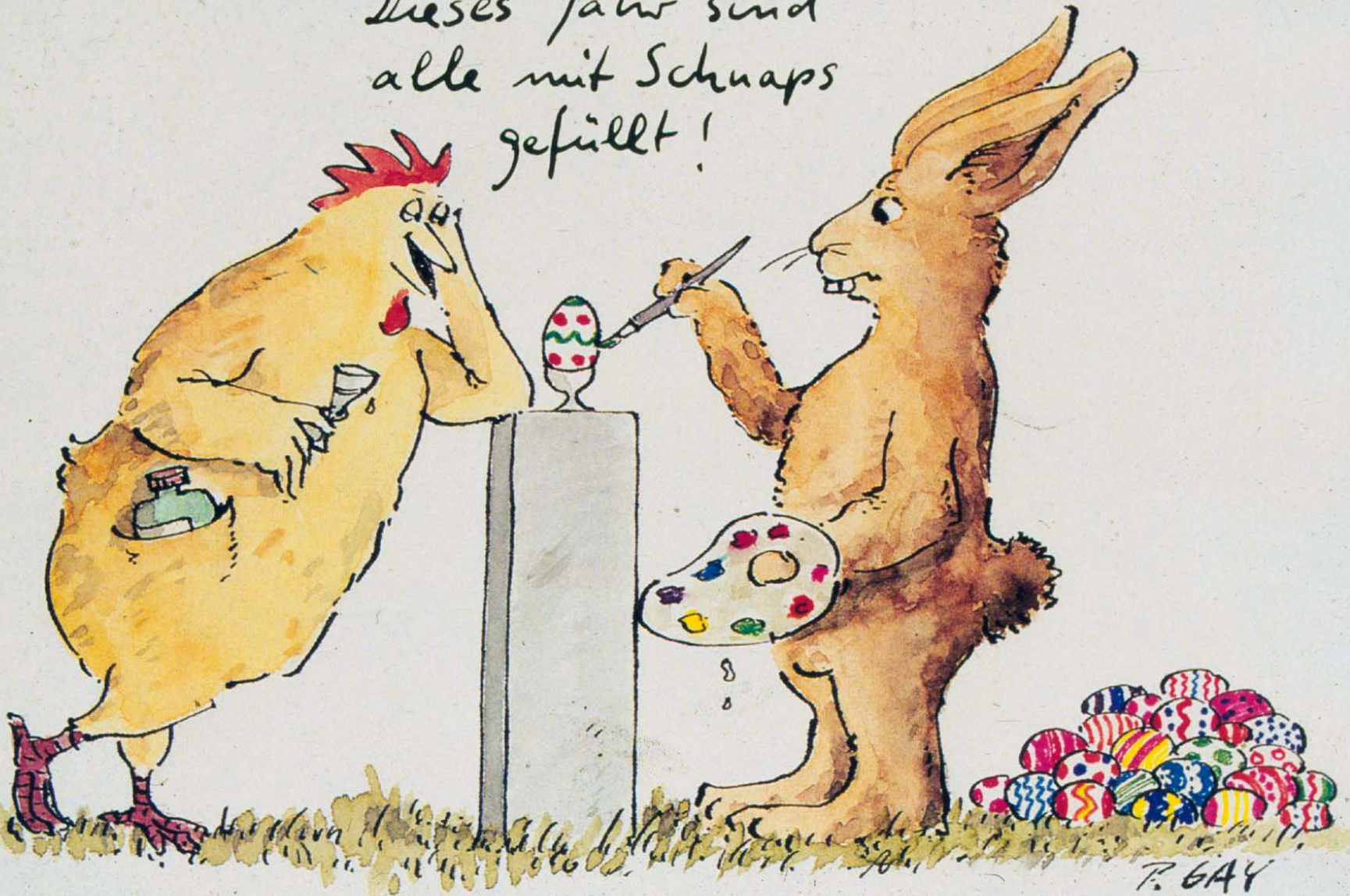
Females eaten



**Fine fescue (*Festuca rubra*)**



Dieses Jahr sind  
alle mit Schnaps  
gefüllt!



T. GAY



# One Indicator of Scientific Effort

Membership in the *American Chemical Society*: ~160,000

Membership in the *International Society of Chemical Ecology*: ~500

# WHAT MONEY CAN BUY

U.S. Submarines + missiles (currently \$2-4 B/boat)	\$417.5 B (Cold War period)
New European Fighter Aircraft (development to date) (unit cost recently reduced from \$81M to 57M)	9.0 B
Stanford University Annual Budget (2007-2008)	3.5 B/year
Recently Built Sports Facilities (12 USA cities)	>2.4 B
Rush Limbaugh (radio show host, 8 year contract)	0.048 B/year
Brazilian Biodiversity Initiative (12 Ph.D.s @\$200,000/year)	0.0024 B/year

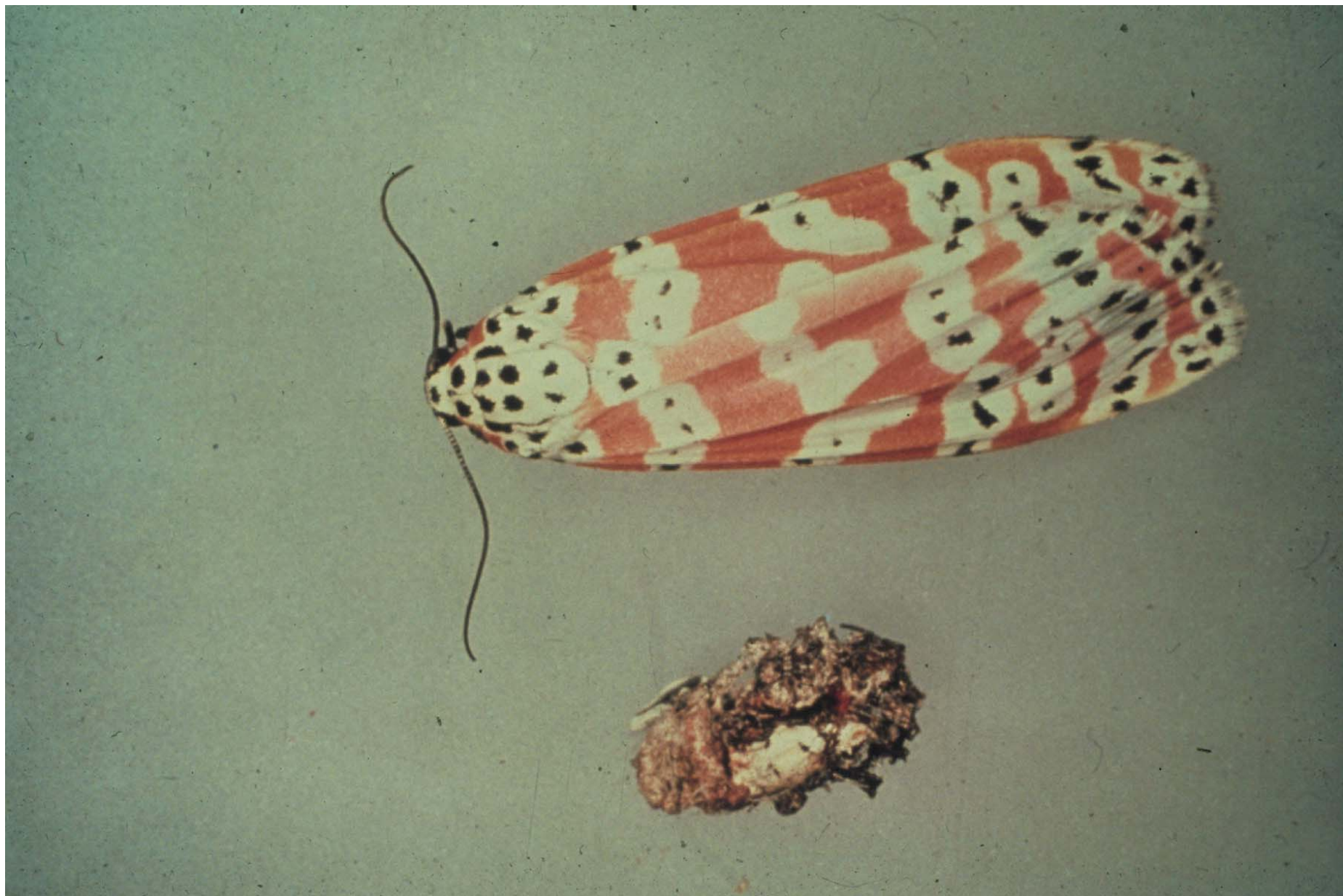


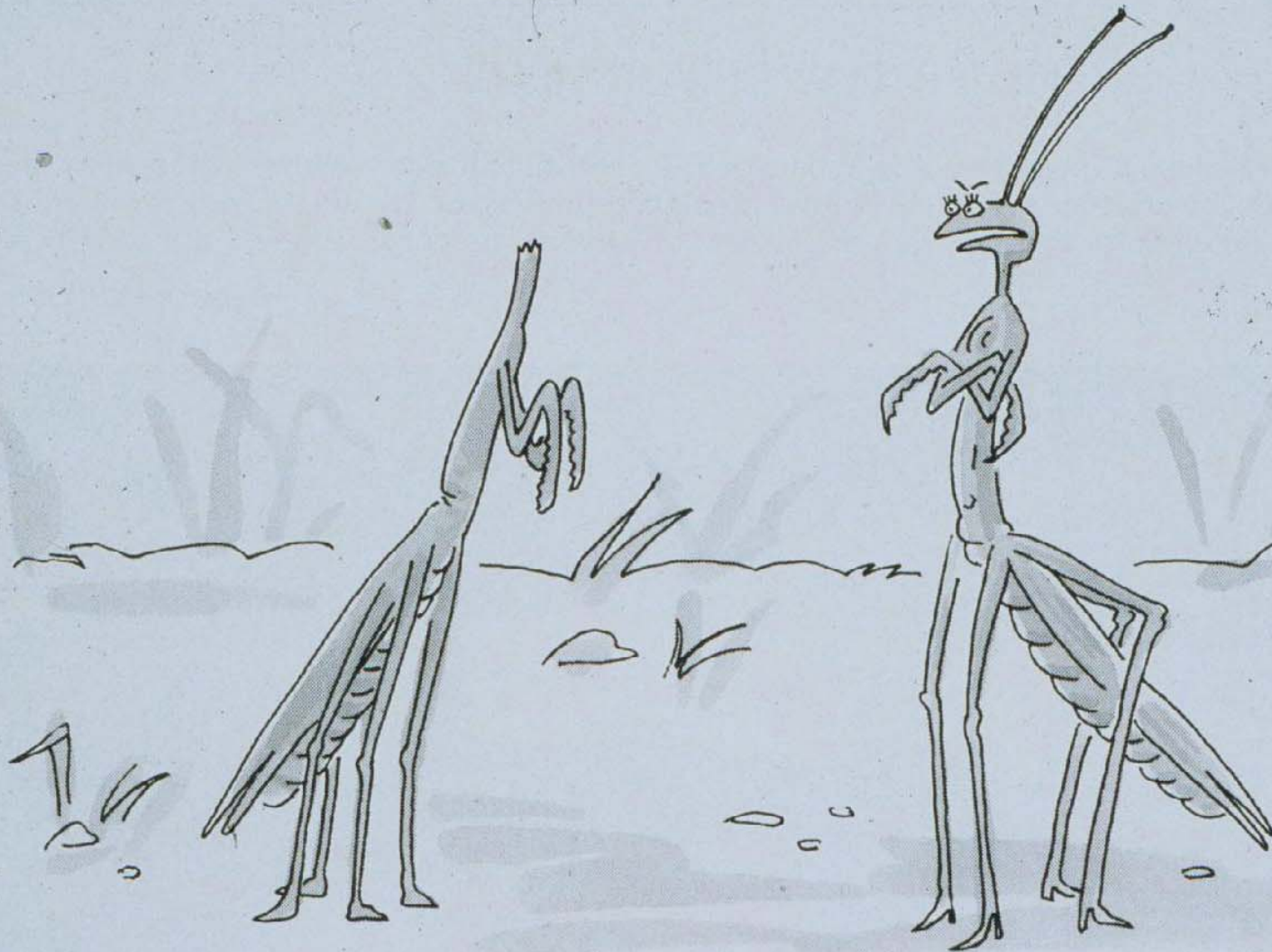
**Kinkazan**

**Ishima**

# Hatchling from toad-rich island





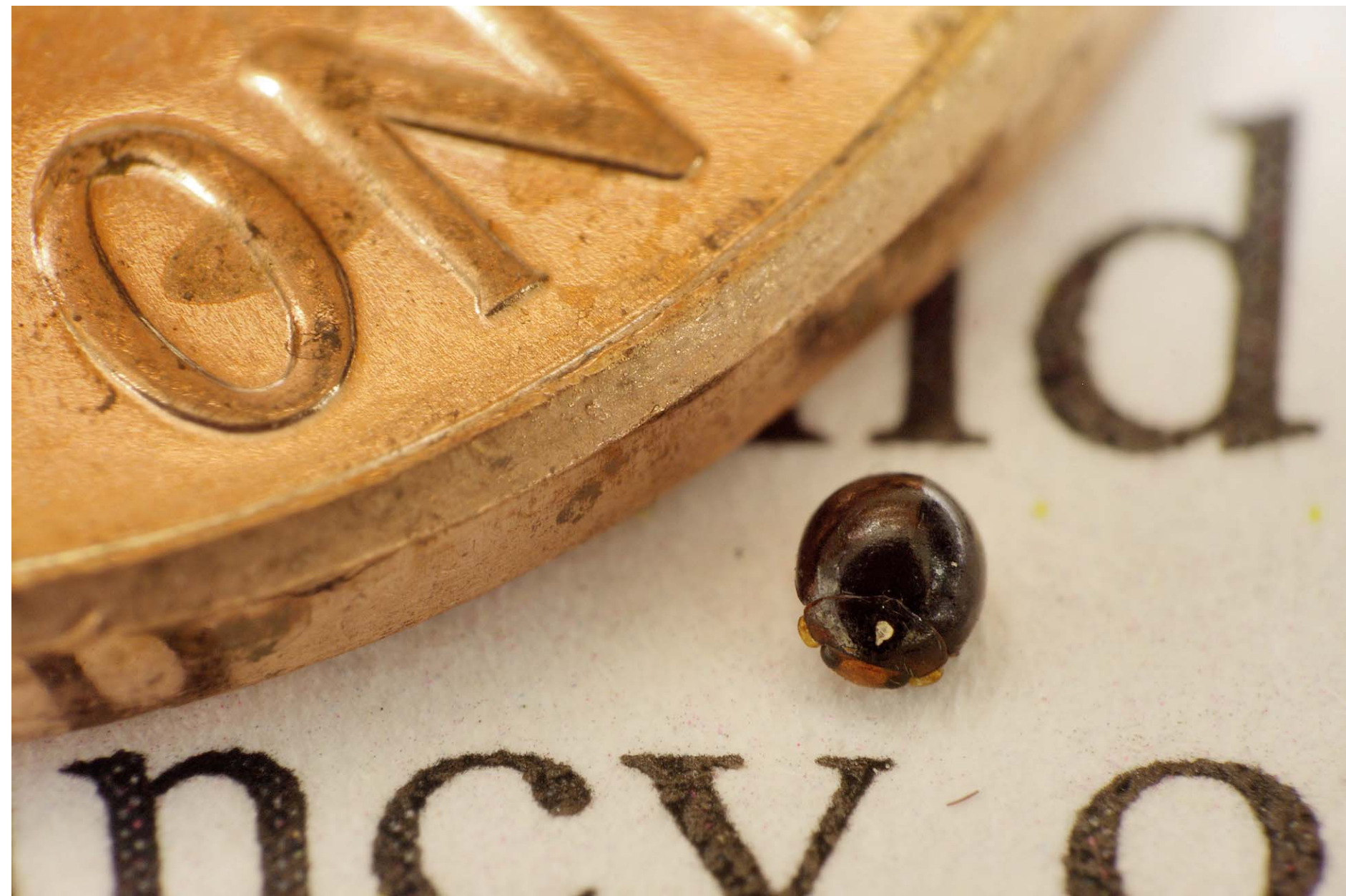


Shanahar

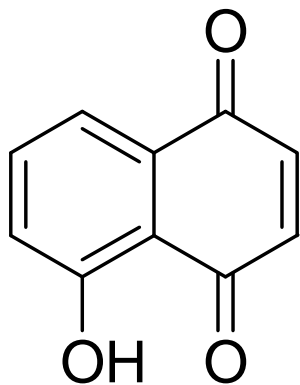
*"You slept with her, didn't you?"*



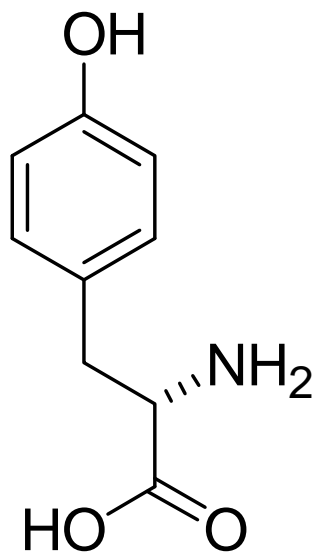
*Delphastus* sp. Polypropanoids



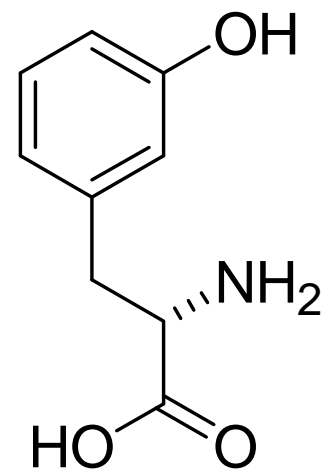




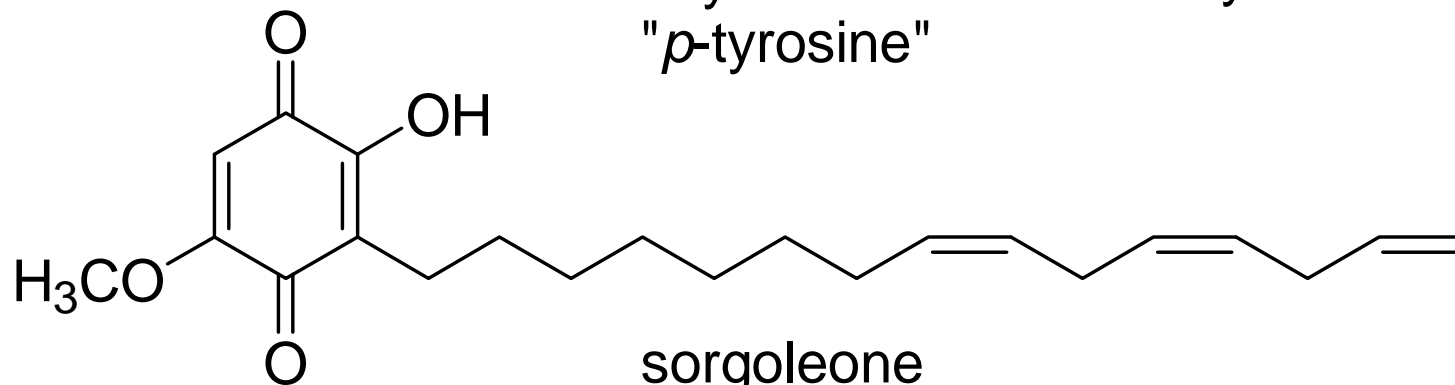
juglone



tyrosine  
"*p*-tyrosine"

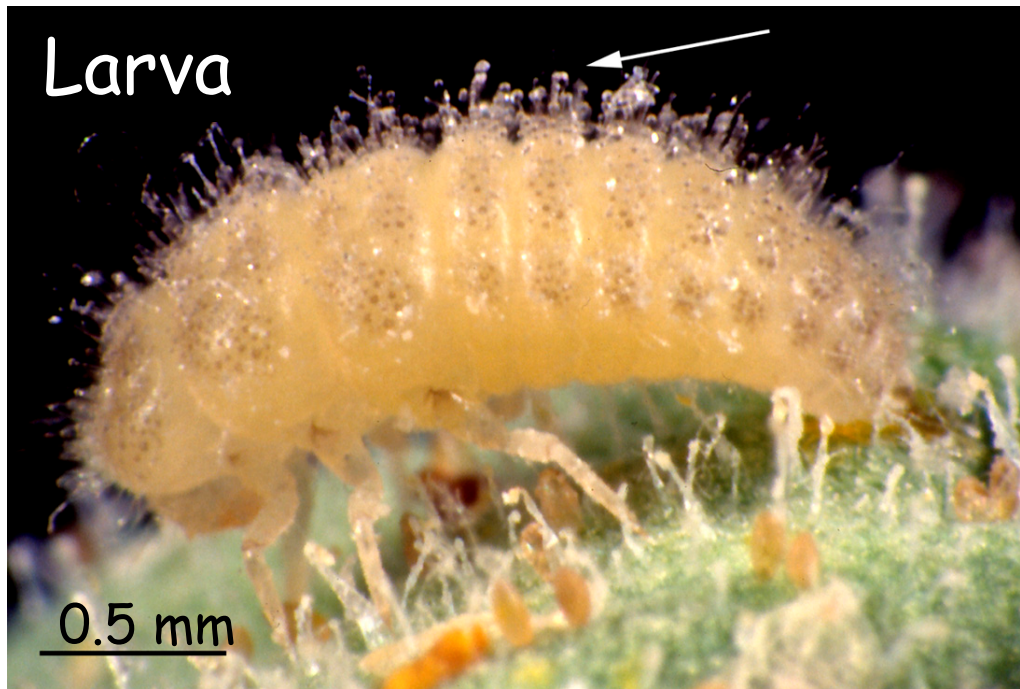


*m*-tyrosine



sorgoleone

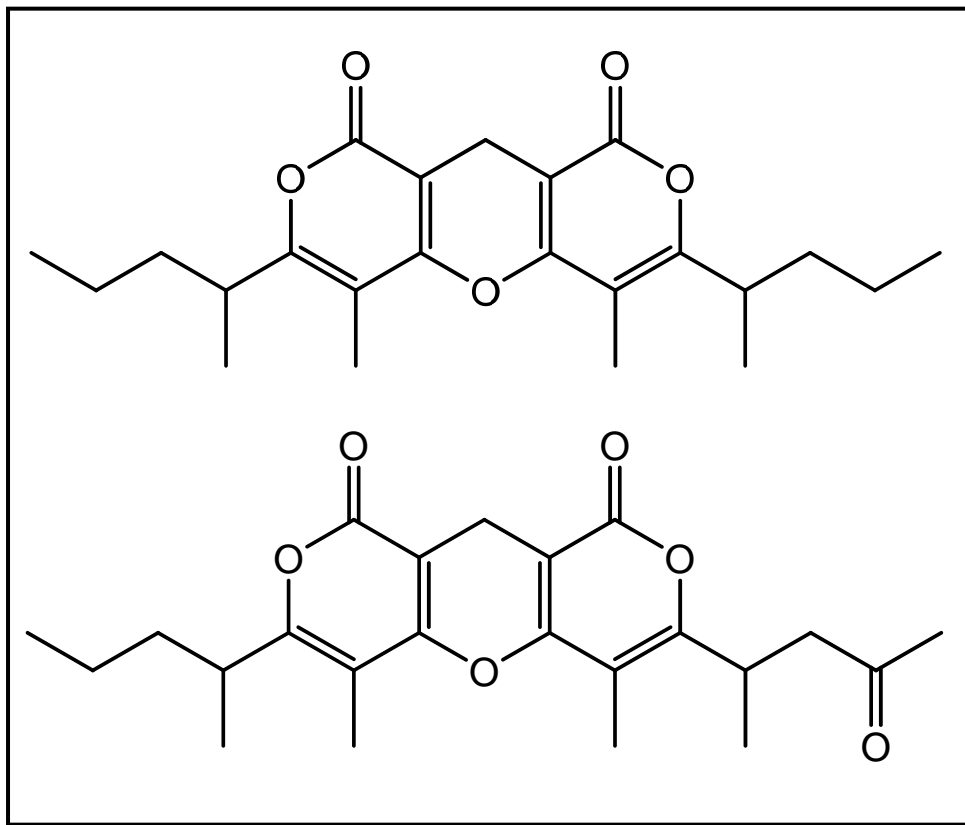
Larva



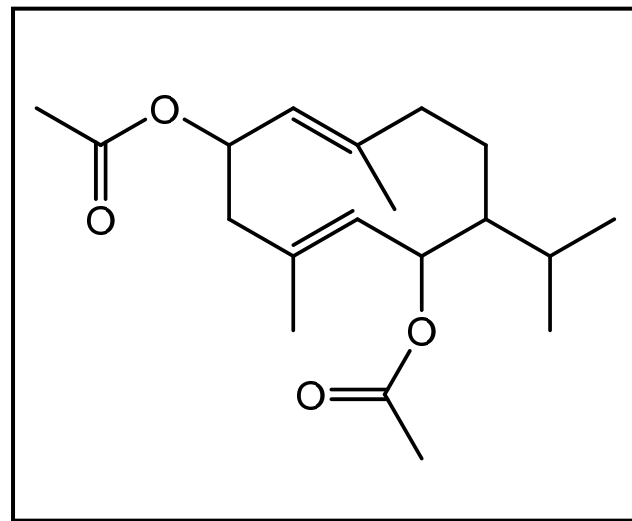
Pupa



# *Delphastus* pupal secretion



+

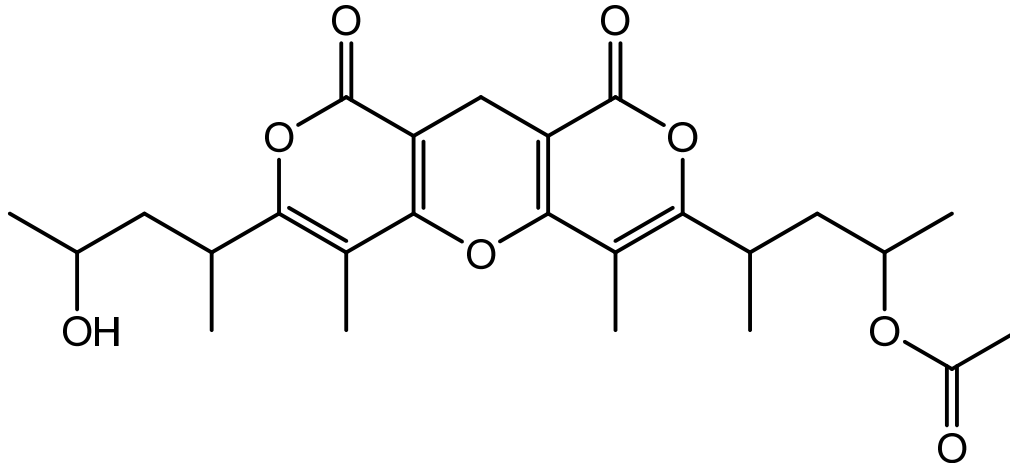
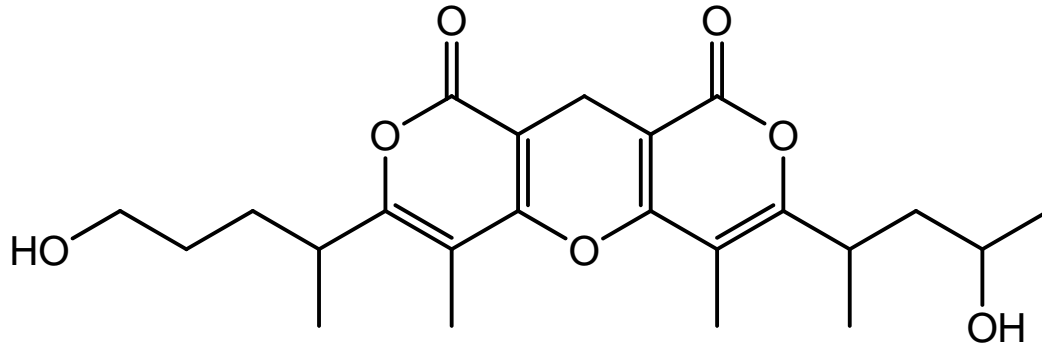
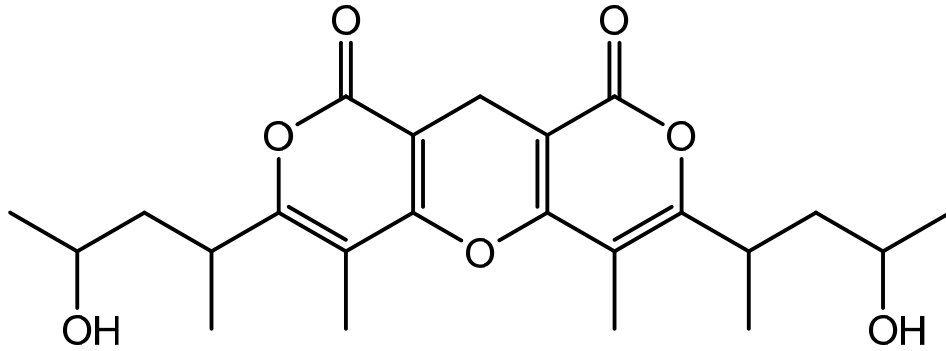


Adult



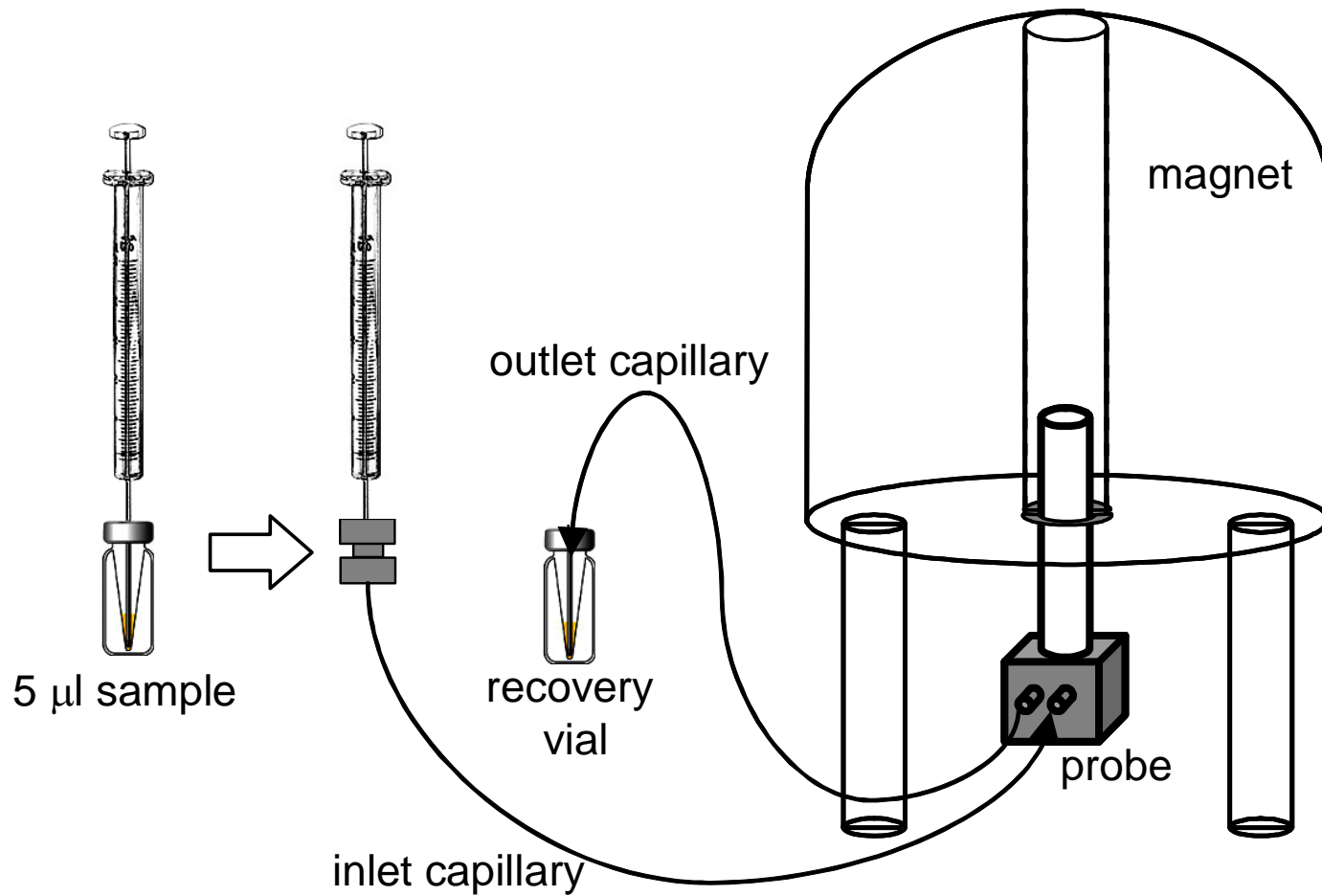
0.5 mm

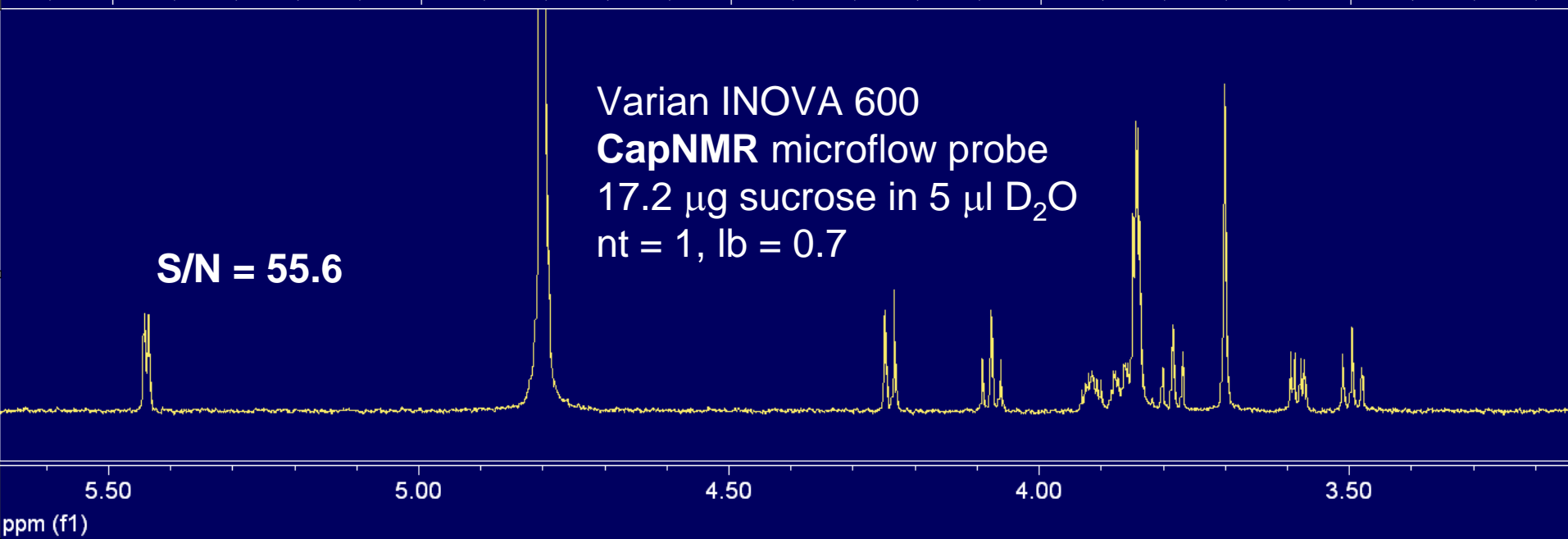
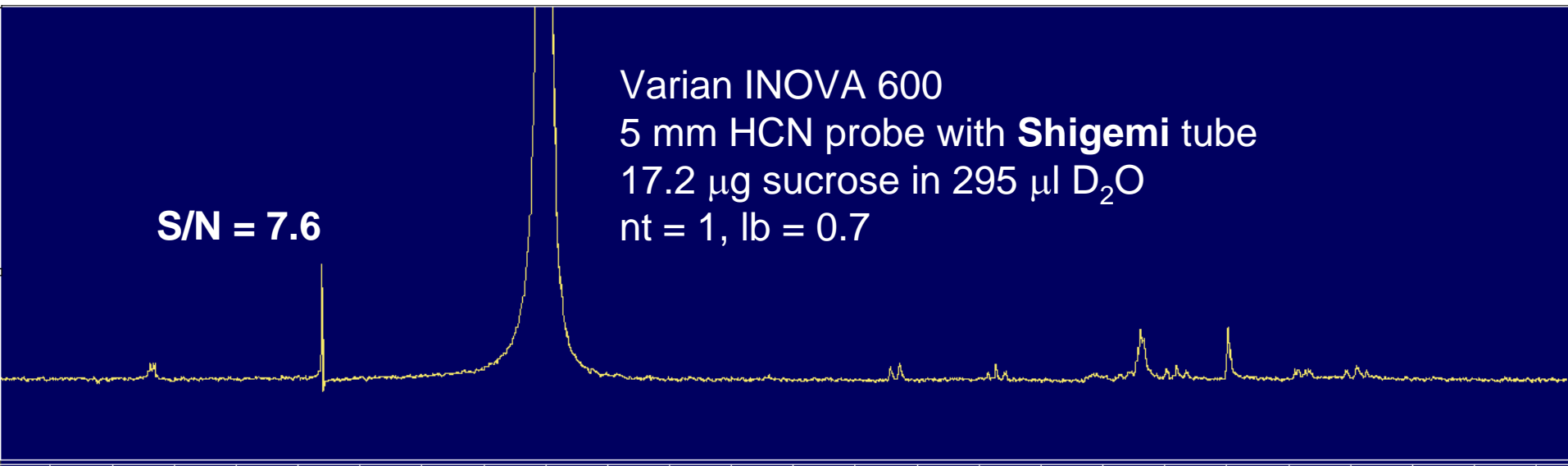
# *Delphastus* adult hemolymph

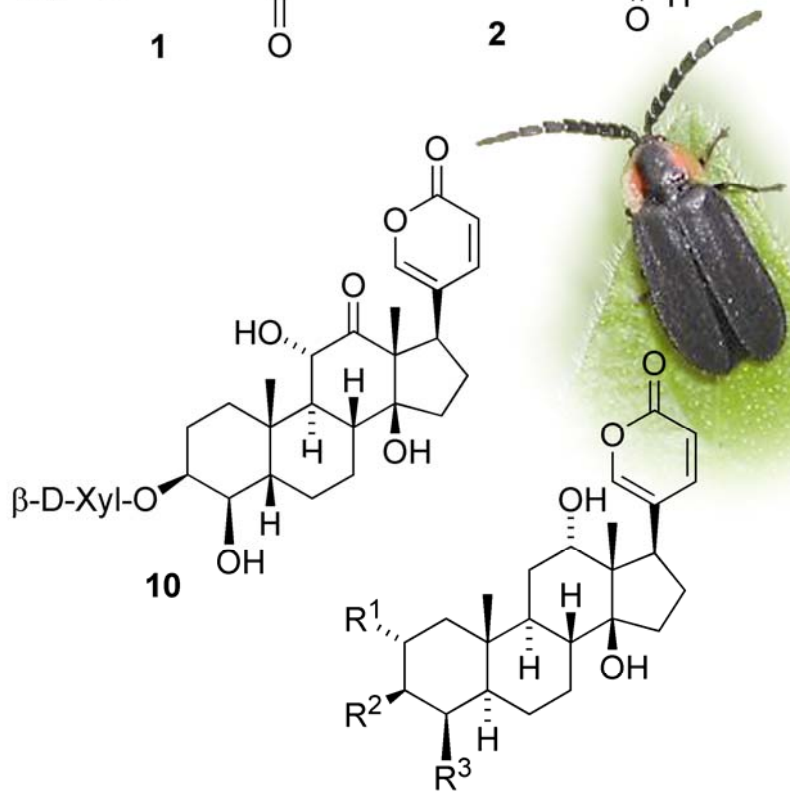
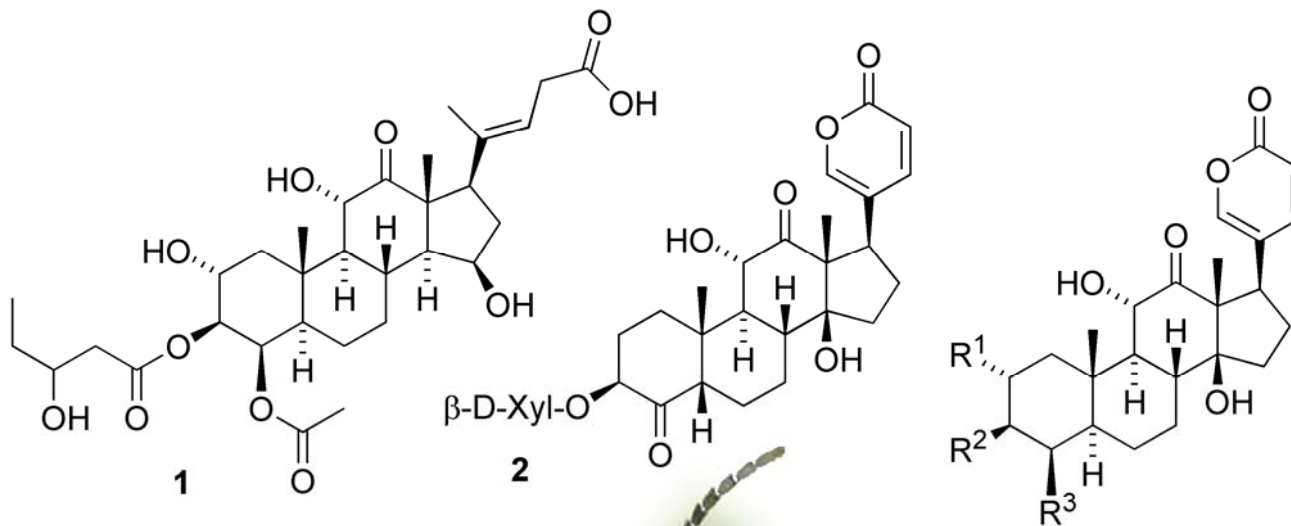




# Sample injection with CapNMR

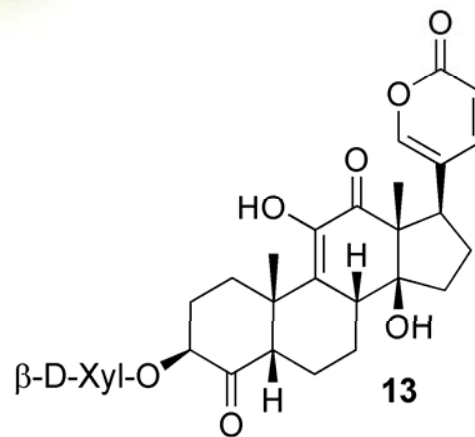






- 3 - R<sup>1</sup>= OH, R<sup>2</sup>= OH, R<sup>3</sup>= OH  
 4 - R<sup>1</sup>= OH, R<sup>2</sup>= OH, R<sup>3</sup>= OAc  
 5 - R<sup>1</sup>= OH, R<sup>2</sup>= OAc, R<sup>3</sup>= OH  
 6 - R<sup>1</sup>= H, R<sup>2</sup>= O-β-D-Xyl, R<sup>3</sup>= OH  
 7 - R<sup>1</sup>= H, R<sup>2</sup>= OH, R<sup>3</sup>= OH  
 8 - R<sup>1</sup>= OAc, R<sup>2</sup>= OH, R<sup>3</sup>= OH  
 9 - R<sup>1</sup>= OAc, R<sup>2</sup>= OH, R<sup>3</sup>= OAc

- 11 - R<sup>1</sup>= OH, R<sup>2</sup>= OH, R<sup>3</sup>= OH  
 12 - R<sup>1</sup>= OAc, R<sup>2</sup>= OH, R<sup>3</sup>= OH



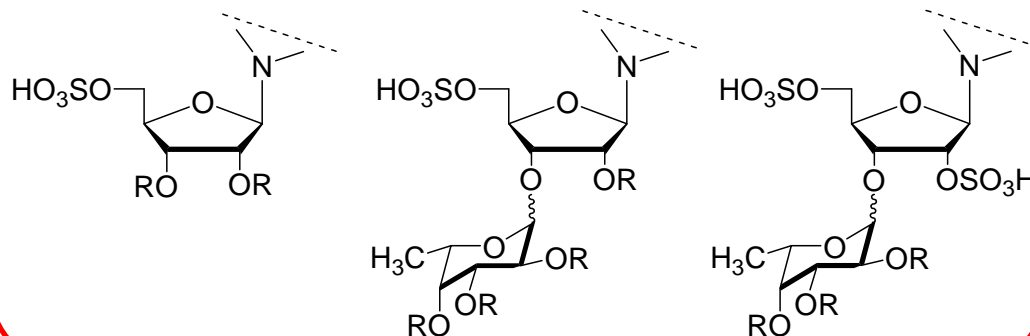
# WHAT MONEY CAN BUY

<u>Activity</u>	<u>Cost in billions (<math>10^9</math>) of U.S. dollars</u>
National Institutes of Health (NIH), annual budget (2009)	\$30
U.S. Submarines + missiles, annual cost during Cold War period (currently \$2-4 B/boat)	10
Stanford University, annual budget (2007-2008)	3.5
Metropolitan Opera, annual budget	0.200
Rush Limbaugh (radio show host, annual cost of 8 year contract)	0.048
Chemical Ecology Research Surge (200 P.I.s @ \$200,000/year)	0.040

# SPIDER VENOM

**NMR Analysis**  
dqf-COSY  
HMBC

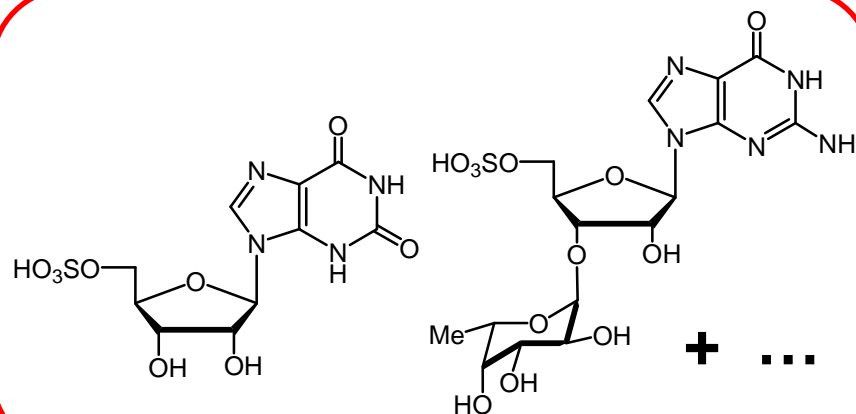
## Eight **Sulfated** Nucleoside Derivatives



## Re-Designed Fractionation Scheme

**A**   **B**   **C**   **D**   **E...**

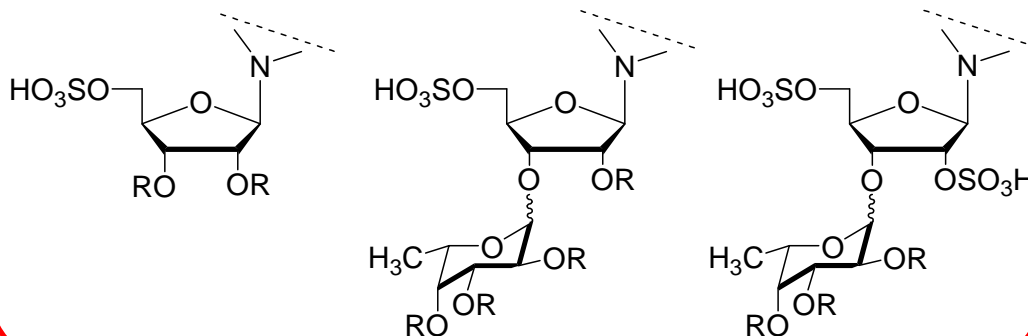
**Detailed Characterization**  
(NMR, MS, IR etc.)



# SPIDER VENOM

**NMR Analysis**  
dqf-COSY  
HMBC

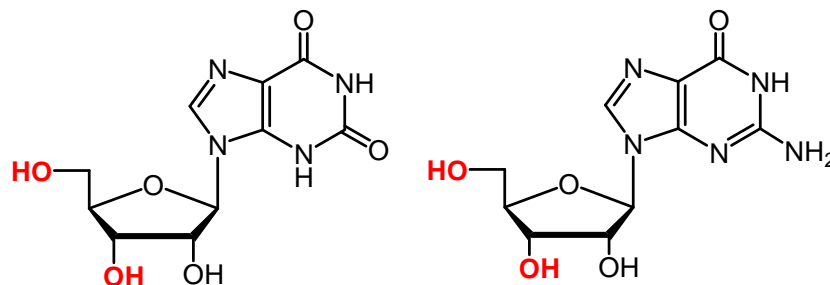
## Eight **Sulfated** Nucleoside Derivatives

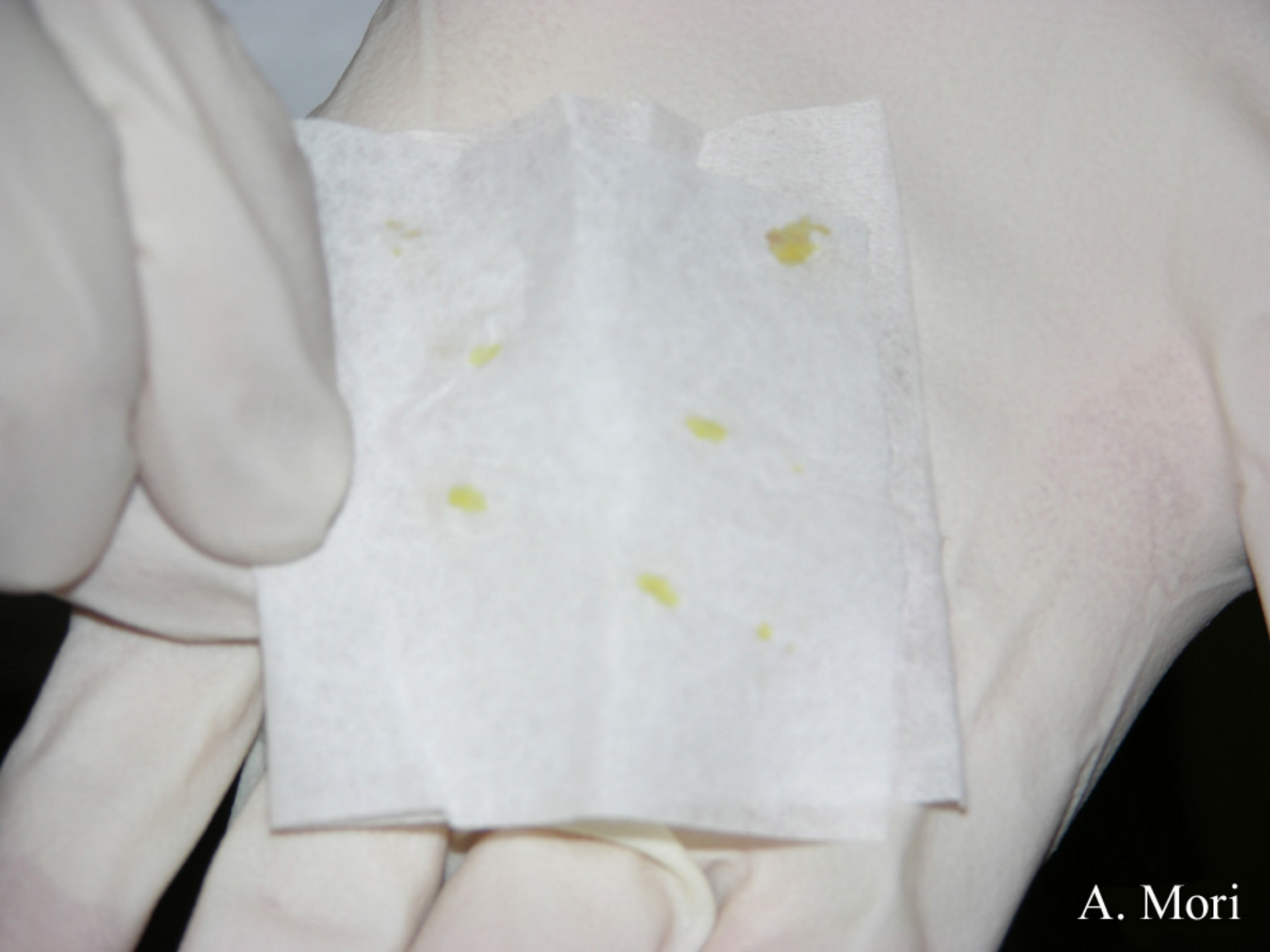


**Fractionation**  
(HPLC etc.)

**A** **B** **C** **D** **E...**

**Detailed Characterization**  
(NMR, MS, IR etc.)





A. Mori