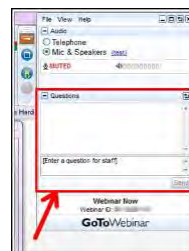


Have Questions?



Type them into questions box!

“Why am I muted?”

Don't worry. Everyone is muted except the presenter and host. Thank you and enjoy the show.

Contact ACS Webinars[®] at acswebinars@acs.org

1



@AmericanChemicalSociety



@AmerChemSociety



@AmerChemSociety



<https://www.linkedin.com/company/american-chemical-society>

Contact ACS Webinars[®] at acswebinars@acs.org

2

Check out the Archive!

An ACS member exclusive benefit



Hundreds of presentations from the best and brightest minds that chemistry has to offer are available to you on-demand. The Archive is divided into 6 different sections to help you more easily find what you are searching.

Professional Development

▶ View the Collection

Learn how to write better abstracts, deliver more engaging presentations, and network to your next dream job. Brush up on your soft skills and set a new career path by mastering what can not be taught in the lab.

Technology & Innovation

▶ View the Collection

From renewable fuels to creating the materials for the technology of tomorrow, chemistry plays a pivotal role in advancing our world. Meet the chemists that are building a better world and see how their science is making it happen.

Drug Design and Delivery

▶ View the Collection

The Drug Design Delivery Series has built a collection of the top minds in the field to explain the mechanics of drug discovery. Discover the latest research, receive an overview on different fields of study, and gain insight on how to possibly overcome your own med chem roadblocks.

Culinary Chemistry

▶ View the Collection

Why does food taste better when it is grilled or what molecular compounds make a great wine? Discover the delectable science of your favorite food and drink and don't forget to come back for a second helping.

Popular Chemistry

▶ View the Collection

Feeling burdened by all that molecular weight? Listen to experts expound on the amazing side of current hot science topics. Discover the chemistry of rockets, how viruses have affected human history, or the molecular breakdown of a hangover.

Business & Entrepreneurship

▶ View the Collection

How do ideas make it from the lab to the real world? Discover the ins and outs of the chemical industry whether you are looking to start a business or desire a priceless industry-wide perspective.

<https://www.acs.org/content/acs/en/acs-webinars/videos.html>

3



ACS Webinars®

CLICK • WATCH • LEARN • DISCUSS



Learn from the best and brightest minds in chemistry! Hundreds of webinars on diverse topics presented by experts in the chemical sciences and enterprise.

Edited Recordings are an exclusive ACS member benefit and are made available once the recording has been edited and posted.

Live Broadcasts of ACS Webinars® continue to be available to the general public several times a week generally from 2-3pm ET!

A **collection of the best recordings** from the ACS Webinars Archive will be broadcast on Fridays from 2-3pm ET!

www.acs.org/acswebinars

4

What is ACS on Campus?



ACS visits campuses across the world offering FREE seminars on how to be published, find a job, network and use essential tools like SciFinder. ACS on Campus presents seminars and workshops focused on how to:



- Publish in top journals
- Find a job
- Effectively use research tools like SciFinder® and ACS ChemWorx
- Communicate your science
- Write grant proposals
- Build industry partnerships
- Prepare for a changing employment landscape

<http://acsoncampus.acs.org>

5

Advance YOUR CAREER

ChemIDP™

ChemIDP.org

Discover ACS PUBLICATIONS

Publishing Resources

publish.acs.org

Connect WITH CHEMISTS AND OTHER SCIENCE PROFESSIONALS

CAS SciFinder Future Leaders

171 alumni, 35 countries
and over 120 institutions

acsoncampus.acs.org/resources



From ACS Industry Member Programs

◆ Industry Matters Newsletter

Exclusive interviews with industry leaders and insights to advance your career

Preview & Subscribe: acs.org/indnews



Connect, collaborate, and stay informed about the trends leading chemical innovation

Join: bit.ly/ACSinnovationhub

ACS Efforts and Resources on COVID-19



Browse [ACS Resources](#) and [Initiatives!](#)

- **YOU MAY RECEIVE A ONE-YEAR WAIVER ON YOUR NATIONAL DUES** If your membership is up for renewal, but you're experiencing a special hardship, such as unemployment, furlough, reduced wages or illness.
- **RECEIVE ACCESS TO LINKEDIN LEARNING THROUGH THE END OF THIS YEAR** This powerful resource includes over 15,000 on-demand courses to support your continued learning and career advancement for active ACS members.
- **INOVA EAP/WORK-LIFE ASSISTANCE PROGRAM** 24/7 assistance on a wide range of issues, such as emotional, relationship, major life, health, wellness, educational and more for ACS members based in the United States. Confidential services are provided via telephone or comprehensive online resources.

www.acs.org/covid-19

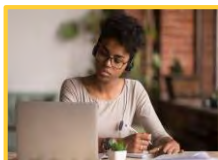
8

ACS Career Navigator: Your Home for Career Services



Whether you are just starting your journey, transitioning jobs, or looking to brush up or learn new skills, the **ACS Career Navigator** has the resources to point you in the right direction.

We have a collection of career resources to support you during this global pandemic:



Professional Education



Virtual Career Consultants



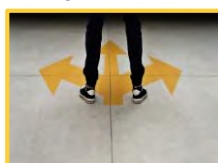
ACS Leadership Development System



Career Navigator LIVE!



ChemIDP



College to Career



ACS Webinars



Virtual Classrooms

Visit www.ACS.org/COVID19-Network to learn more!

9

Free ACS Webinars Every Weekday! *Upcoming Broadcasts*



Friday, September 25, 2020 at 10-11am ET

Speaker: Pamela Tadross, Organic Process Research & Development
Moderator: Kali Miller, ACS Publications

[Register for Free!](#)

What You Will Learn

- What editors look for when reviewing submissions
- Tips for responding to reviewer reports
- Qualifications to become a reviewer and strategies to evaluate a manuscript

Co-produced with: ACS Publications



Wednesday, September 30, 2020 at 2-3pm ET

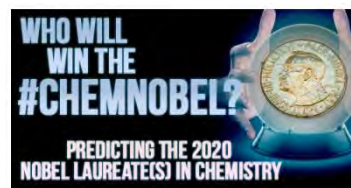
Speaker: Steve Mohyla, Woodbury Financial Services
Moderator: Mary Bet Dobson, American Chemical Society

[Register for Free!](#)

What You Will Learn

- What to consider when creating or updating a will
- How tax law changes may impact your current plans
- How philanthropy may factor into your plans

Co-produced with: ACS Office of Philanthropy



Thursday, October 1, 2020 at 2-3pm ET

Speakers: Kit Chapman, Science Historian and Writer / Wendy Queen, Materials Chemist, EPFL (École Polytechnique Fédérale de Lausanne) / Darryl Boyd, U.S. Naval Research Laboratory and Science Made Simple
Moderator: Laura Howes, *Chemical & Engineering News*

[Register for Free!](#)

What You Will Learn

- Who are our front-runners for this year's Nobel Prize in Chemistry and why
- Big ideas in chemistry that we think should someday win the prize
- Nobel trivia, including how the celebrations will work this year

Co-produced with: *Chemical & Engineering News*

www.acs.org/acswebinars

10

2021 National Biotechnology Conference

AAPS seeks experienced scientists to lead the 2021 NBC Scientific Programming Committee!

[READ MORE!](#)

AAPS Happenings:

PharmSci 360

Check out the program today!

[Read More](#)

PharmSci 360

Registration is now open!

[Read More](#)

PharmSci 360 Workshops

View full list today!

[Read More](#)

AAPS Member Demographics

Sector	
Industry	72%
Academia	23%
Other Non-Faculty	6%
Government	6%
Education	
Ph. D.	61%
Pharm. D.	5%
Master's	18%
Bachelor's	15%

Member Testimonial

"Over time, I've built up this network of people I can ask about anything work-related."

Rita Hegmann, Ph.D.
AAPS Member since 2008

AAPS Live Webinars Are Free and Open Access

Webinars offer a great opportunity to receive the latest information on pharmaceutical science topics without the need for travel or time away from home and office. Plan to participate in our upcoming live events, replay a past session in our archives, or submit a proposal for organizing your own webinar!

[Register for Upcoming Webinars](#)

[Replay Archived Webinars](#)

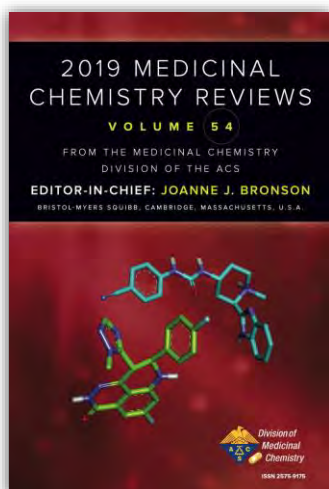
Archived webinars are a member benefit—join today!



<https://www.aaps.org>

11

Join the Division Today!



For \$25 membership (\$10 for students), You Will Receive:

- A free digital copy of our annual medicinal chemistry review volume (over 680 pages, \$160 retail price)
- Abstracts of MEDI programming at national meetings
- Access to student travel grants and fellowships

Find out more about the ACS MEDI Division! www.acsmedchem.org

12

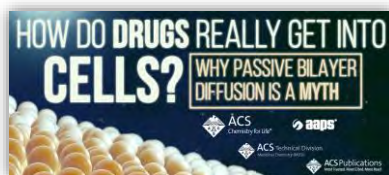
Catch up on 2020's Free Open Access Recordings!



Join Angela Zhou, an Information Scientist at CAS, as she provides an overview of published scientific information relevant to COVID-19 research with an emphasis on patents in the CAS content collection. <https://www.acs.org/content/acs/en/acs-webinars/drug-discovery/covid-19.html>



Join Research Fellow Li Di of Pfizer as she discusses why design principles that increase passive permeability are effective approaches to increase oral bioavailability, enhance brain penetration, and reduce renal clearance. <https://www.acs.org/content/acs/en/acs-webinars/drug-discovery/passive-permeability.html>



Join Douglas Kell, Research Chair in Systems Biology at the University of Liverpool to discover how drugs pass through cell membrane solely by hitchhiking on membrane transporters and why so-called "passive diffusion" through any bilayer in real cells is negligible. <https://www.acs.org/content/acs/en/acs-webinars/drug-discovery/so-lute-carriers.html>

13

ACS Publications
aaps
ACS Technical Division
ACS
Chemistry for Life

MITRAGYNA SPECIOSA

WHAT SCIENCE IS TELLING US ABOUT KRATOM

THIS ACS WEBINAR WILL BEGIN SHORTLY...

14

Mitragyna Speciosa: What Science is Telling Us about Kratom



Christopher McCurdy
Professor of Medicinal Chemistry and Director, UF Translational Drug Development Core, Department of Medicinal Chemistry, College of Pharmacy, University of Florida



Amy Newman
Acting Scientific Director, National Institute on Drug Abuse IRP
Chief, Molecular Targets and Medications Discovery Branch
Chief, Medicinal Chemistry Section
Director, Medication Development Program

Presentation slides are available now! Edited recordings are an exclusive ACS member benefit.

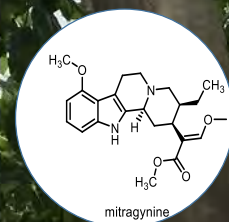
www.acs.org/acswebinars

This ACS Webinar is co-produced with ACS Division of Medicinal Chemistry, American Association of Pharmaceutical Scientists, and ACS Publications.

15

Mitragyna speciosa: What Science is Telling us About Kratom

Christopher R. McCurdy, PhD, FAAPS
Professor of Medicinal Chemistry
College of Pharmacy
University of Florida



16

Mitragyna Speciosa



- **FAMILY:** Rubiaceae
- **GENIUS:** Mitragyna
- **SPECIES:** speciosa
- Tree found in tropical Southeast Asia, particularly Thailand and Malaysia
- Referred to as “**Kratom**” in Thailand and “**Biak Biak**” or “**Ketum**” in Malaysia
- Contains over 40 alkaloids that have been isolated to date¹



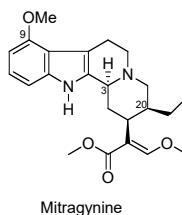
¹ Adkins, J.E.; Boyer, E.W.; McCurdy, C.R. *Curr. Topics Med. Chem.*, **11**, 1165-75 (2011)

UF College of Pharmacy
UNIVERSITY OF FLORIDA

17

Kratom and Mitragynine

- Kratom tea is used by field workers to relieve **pain**, as a **stimulant** to improve work capacity, and **to reduce opioid withdrawal**¹
- Recently, polydrug users (**METH**) are using kratom to reduce use²
- The predominant active agent in Kratom is **mitragynine (MG)**



¹ Jansen K.L.R., Prast C.J. *J. Ethnopharmacology*, **23**, 115-119 (1988)

² Singh, D. et al. *J. Ethnopharmacology*, **249**, 112462 (2020)

UF College of Pharmacy
UNIVERSITY OF FLORIDA

18

Audience Survey Question

ANSWER THE QUESTION ON BLUE SCREEN IN ONE MOMENT



According to the American Kratom Association, how many people does this suggest that use Kratom in the U.S.?

- ~500,000
- ~1 million
- ~5 million
- ~15 million
- ~50 million

19

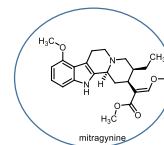
Kratom Use in USA

- Widely available across the internet and smoke/vape shops
- June 2019*: American Kratom Association reported **1950 metric tons** exported to US **every month**
- Typical dose 3-5g[#] suggesting **>15 million users**





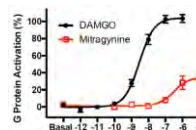
Kratom and Mitragynine



Case Reports: Few deaths are attributable to kratom alone

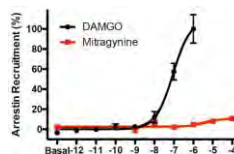
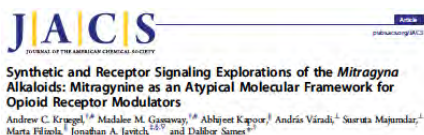
- Mitragynine is a **partial mu opioid agonist**

- 40% maximal effect in G Protein activation



- Mitragynine is a “biased agonist” with **no β -arrestin recruitment**

- such molecules are under investigation and development as opioids with **low respiratory depressive and constipation effects.**



21

Therapeutic Potential of Kratom

- **Opioid Detoxification:** Kratom has potential to replace several medications used during detoxification (**opioid, adrenergic, analgesic and anxiolytic**). This would improve medication adherence and chances of completing detoxification.
- **Lack of opioid-like overdoses:** Possibly due to MOA and multiple targets that kratom alkaloids interact with.
- **Medication Assisted Therapy:** Kratom is informally used to reduce opioid use. Kratom withdrawal is mild (<9 on SOWS scale). **Polydrug users report Kratom also reduces methamphetamine use.**
- **THE LACK OF A STANDARDIZED PRODUCT HAS PREVENTED RIGOROUS CLINICAL TRIALS TO EVALUATE THESE CLAIMS**



22

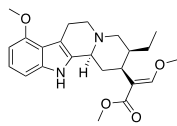


11/06/2019

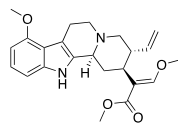
UF College of Pharmacy
UNIVERSITY OF FLORIDA

23

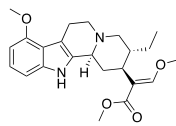
Isolation of kratom alkaloids



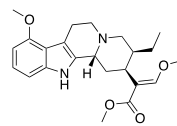
Mitragynine
66%



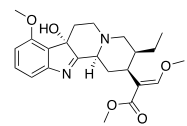
Paynantheine
9%



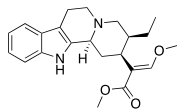
Speciogynine
7%



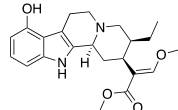
Speciociliatine
~1%



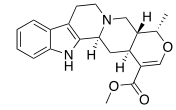
7(-)-hydroxymitragynine
~2%



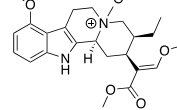
Corynantheidine
<1%



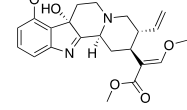
9-Hydroxycorynantheidine
<1%



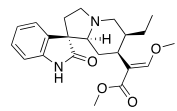
Ajmalicine
<1%



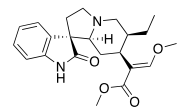
Mitragynine N-oxide
<1%



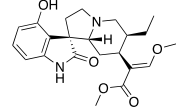
7α-hydroxypaynantheine



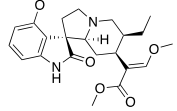
Corynoxine A
<1%



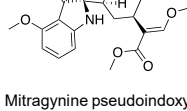
Corynoxine B
<1%



Isospeciofoline
<1%



Mitragynine oxindole B
<1%



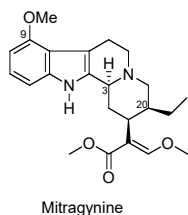
Mitragynine pseudoindoxyl

UF College of Pharmacy
UNIVERSITY OF FLORIDA

24

Mitragynine Eurofins screen at 82 CNS drug targets

Assay	100 nM (1.0E-07 M)	10000 nM (1.0E-05 M)
5-HT _{1A} (h) (agonist radioligand)		x
5-HT _{2B} (h) (agonist radioligand)		x
α _{1A} (h) (antagonist radioligand)		x
α _{1D} (h) (antagonist radioligand)		x
β ₂ (h) (antagonist radioligand)		x
D ₁ (h) (antagonist radioligand)		x
D _{2S} (h) (agonist radioligand)		x
D ₃ (h) (antagonist radioligand)		x
κ (KOP) (agonist radioligand)		x
μ (MOP) (h) (agonist radioligand)		x
Na ⁺ channel (site 2) (antagonist radioligand)		x
Potassium Channel hERG (human)- [3H] Dofetilide		x

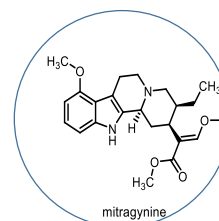


25

Binding and functional effects of mitragynine

- Mitragynine has **partial agonist effects** at the μ opioid, α_{1A} and α_{1D} adrenergic receptors
- Poison Control Centers:** Kratom overdoses resemble **stimulants** (not opioids)

Target	Ki (nM)	Agonist/ Antagonist
μ	136.0	Partial agonist
κ	157	Antagonist
δ		Antagonist
α _{1A}	1,660	Partial agonist
α _{1B}	2,490	Antagonist
α _{1D}	4,610	Partial agonist
α _{2A}	3,590	ND
α _{2B}	9,190	ND
α _{2C}	1,400	ND



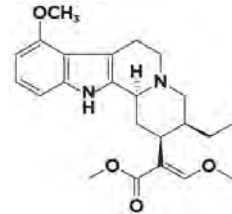
Obeng, Samuel, et al. *J Med Chem.* 63 (2019). 433-439.

26

Macko et al. (1972) SK&F 12711 (mitragynine)

Antinociceptive }
Antitussive } Similar to codeine

Effects on gastric motility }
Respiratory depressant activity } Less than codeine



More effective after p.o. and i.p. than s.c., but low potency overall

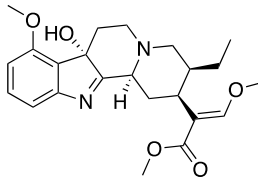
Antinociception blocked by naloxone (Matsumoto et al., 1996)

Macko et al. *Arch. Int. Pharmacodyn.* **198**, 145-161 (1972).

UF College of Pharmacy
UNIVERSITY of FLORIDA

27

Binding and function of 7-hydroxymitragynine



Target	Ki (nM)	Potency (nM)	Efficacy (% agonist response)	Agonist/ Antagonist
μ	6.2	7.6	96.8%	Agonist
κ	52.7	No agonist effect	98.4% inhibition of agonist response	Antagonist
δ	228.2	No agonist effect	81.5% inhibition of agonist response	Antagonist

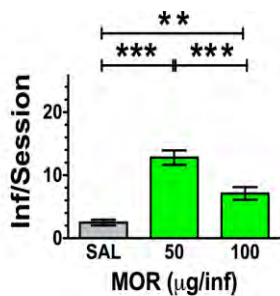
7-Hydroxymitragynine has agonist effects at the MOP

Obeng, Samuel, et al. *J Med Chem.* 63 (2019). 433-439.

UF College of Pharmacy
UNIVERSITY of FLORIDA

28

Substitution of MG and 7-HMG for morphine

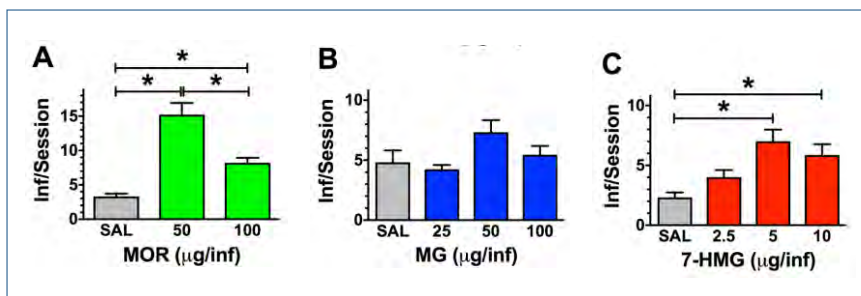


Hemby SE, et al. *Addict Biol.* 2018 June 27.

UF College of Pharmacy
UNIVERSITY of FLORIDA

29

Drug naïve rats acquire IVSA of 7-HMG but not MG

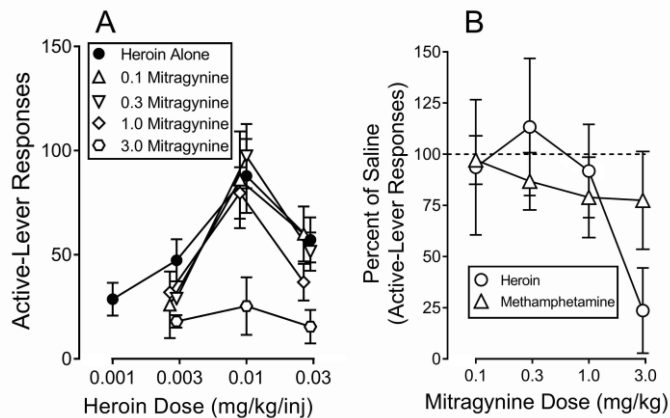


Hemby SE, et al. *Addict Biol.* 2018 June 27.

UF College of Pharmacy
UNIVERSITY of FLORIDA

30

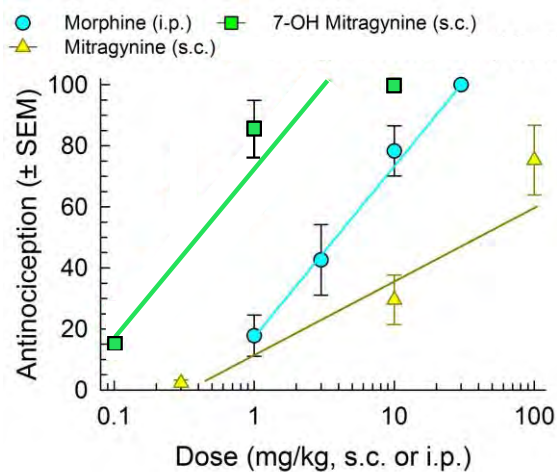
MG administration *reduced* heroin self-administration



Yue K, Kopajtic TA, Katz JL. *Psychopharmacology* (Berl) 2018 Oct; 235(10):2823-2829

31

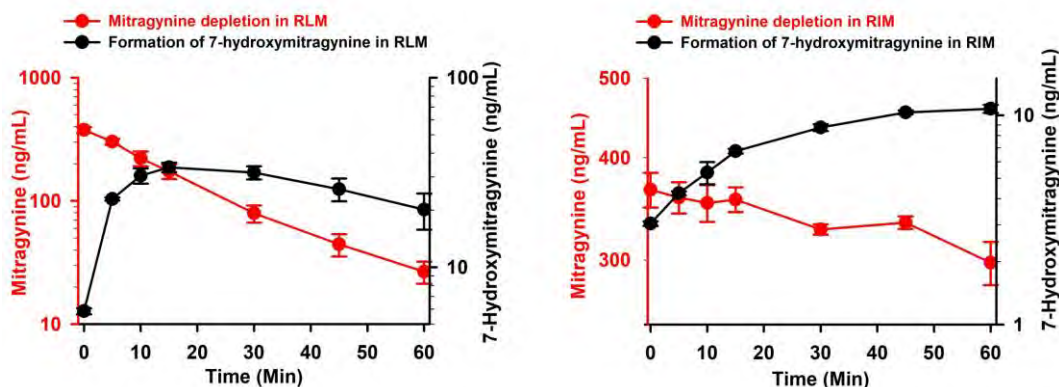
55°C mouse warm water tail-withdrawal test



McLaughlin et al. (unpublished data)

32

Metabolism of mitragynine in rat liver (RLM) and intestinal microsomes (RIM)



33

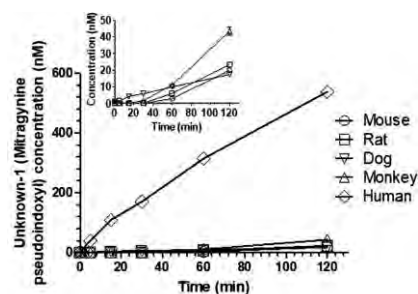
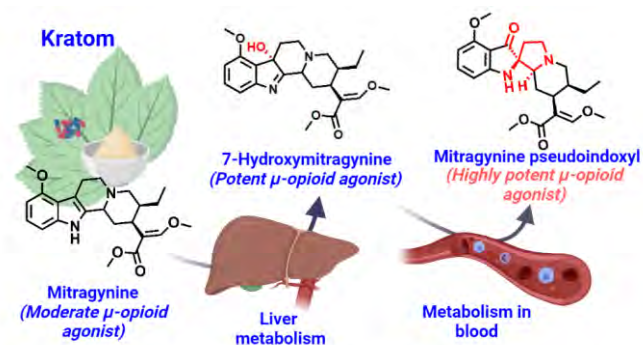
Pharmacokinetic parameters of mitragynine and 7-hydroxy mitragynine after single oral (20 mg/kg) and intravenous (5 mg/kg) administration of mitragynine in female *Sprague Dawley* rats (N=6)

Parameter		Oral		Intravenous	
		Mitragynine	7-Hydroxymitragynine	Mitragynine	7-Hydroxymitragynine
C_{max} ($\mu\text{g/L}$)	1	794.1 \pm 83.0	77.5 \pm 11.5	-	22.6 \pm 5.8
	2	955.4 \pm 110.5	-	-	-
T_{max} (h)	1	0.6 \pm 0.1	0.8 \pm 0.1	-	0.4 \pm 0.1
	2	2.0 \pm 0.0	-	-	-
AUC ($\text{h} \cdot \mu\text{g/L}$)		8202.7 \pm 889.9	737.5 \pm 130.7	2132 \pm 146.9	72.1 \pm 10.7
CL (L/h/kg)		2.7 (18.5%)	-	2.4 (7.7%)	-
V_d (L/kg)		18.3 (8.2%)	-	3.1 (7.1%)	-
K_{met} (1/h)		-	-	0.02 (9.8%)	-
$\%AUC_{7OHmitra} / AUC_{Mitra}$		-	9.1 \pm 0.3	-	3.3 \pm 0.3

Each value is mean \pm SEM or fixed effect parameters, (%Relative standard error provided by NLME)
Abbreviations: AUC = area under the plasma concentration-time curve, C_{max} = peak plasma concentration, T_{max} = time to reach C_{max} , K_{met} = conversion coefficient of parent to metabolite, CL = clearance and V_d = volume of distribution

34

Metabolism of 7-hydroxymitragynine in human plasma

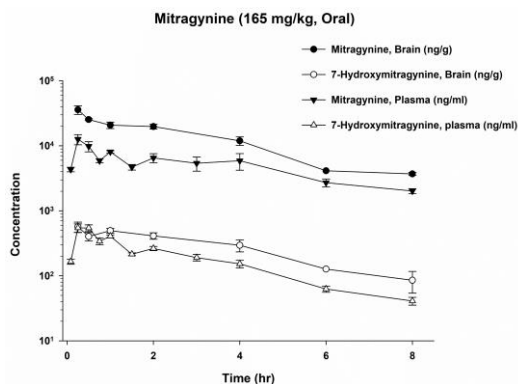


Formation of unknown-1 (mitragynine pseudoindoxyl) upon 7-hydroxymitragynine incubation with the mouse, rat, dog, cynomolgus monkey, and human plasma. All values are plotted as mean \pm SD ($n = 3$)

Kamble, Shyam, et al. *ACS Pharmacology & Translational Science* (2020). DOI: 10.1021/acspsci.0c00075



35



Mean plasma and brain concentration-time profile after oral dose of mitragynine in male *C57BL/6J* mice

$$\frac{AUC_{\text{BrainMitragynine}}}{AUC_{\text{PlasmaMitragynine}}} = 2.44$$

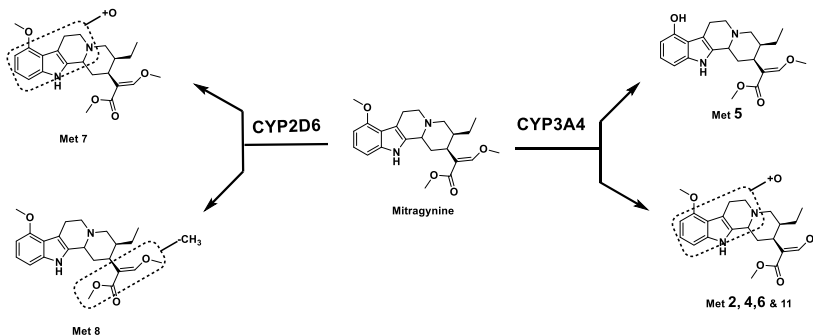
$$\frac{AUC_{\text{Brain}_{7\text{-OH-mitragynine}}}}{AUC_{\text{Plasma}_{7\text{-OH-mitragynine}}} = 1.65$$

Sharma et al, unpublished data



36

Cytochrome P450 reaction phenotyping of mitragynine



- **CYP3A4 plays predominant role in mitragynine metabolism** with minor contributions by CYP2D6 and CYP2C19
- The metabolic clearance of mitragynine was found to be mediated by CYP3A4
- **Met 2 = 7-hydroxymitragynine**
- Total of 12 metabolites identified in microsomes and 31 in hepatocytes

CYP P450 inhibition mediated drug-drug interaction potential



CYP450s	IC ₅₀ (μM)					
	Mitragynine	7-OH-mitragynine				
CYP1A2	>45	>45				
CYP2C8	33.5	>45				
CYP2C9	>45	>45				
CYP2C19	10.5	27.7				
CYP2D6	2.2	>45				
CYP3A4/5	11.4	>45				
CYP3A4/5	>45	>45	>45	>45	>45	>45

Data are expressed as the mean of triplicate determinations. The IC₅₀ values obtained for positive control inhibitors used for CYP450 inhibition were as follows: CYP1A2, α-naphthoflavone (0.016 μM); CYP2C8, montelukast (0.083 μM); CYP2C9, sulfaphenazole (0.431 μM); CYP2C19, (+)-N-3-Benzylirivanol (0.217 μM); CYP2D6, quinidine (0.056 μM); CYP3A4/5 midazolam and testosterone, ketoconazole (0.022 and 0.036 μM)

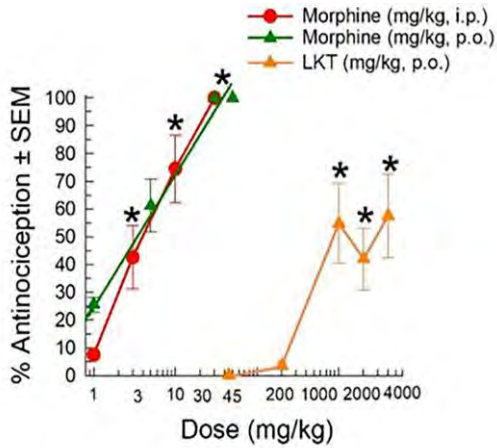
Take home message about mitragynine

- Atypical opioid with additional non-opioid pharmacology
- Shares some but not all effects with μ opioid agonists
- Low potency, with low μ efficacy
- Less tolerance than morphine (at equianalgesic doses)
- Less dependence than morphine (at equianalgesic doses)
- Discriminative stimulus effects different from morphine
- Less tolerance, abuse, and dependence liability than other opioid analgesics
- Does not appear to have abuse or addiction potential and reduces morphine intake in rats – **desired characteristics of candidate pharmacotherapies for opiate addiction and withdrawal**

Take home message about 7-hydroxymitragynine

- Should be considered a kratom constituent with high abuse potential that may also increase the intake of other opiates
- Very selective opioid ligand (doesn't bind any other targets at 10 micromolar concentration)
- ***The extent that MG is converted to 7-HMG in vivo remains to be understood in terms of the pharmacological ramifications***

Antinociception with LKT

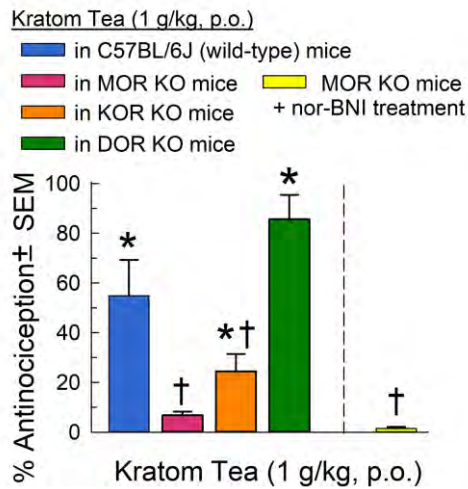


Wilson, L.L. et al, Drug and Alcohol Dependence, 2020 (Accepted)



41

LKT analgesia is mediated through MOR & KOR

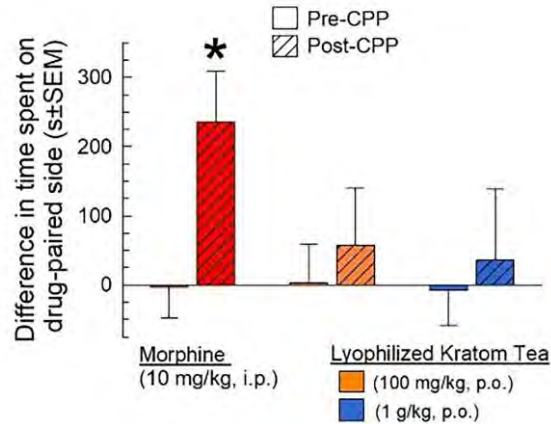


Wilson, L.L. et al, Drug and Alcohol Dependence, 2020 (Accepted)



42

LKT lacks a Conditioned Place Preference

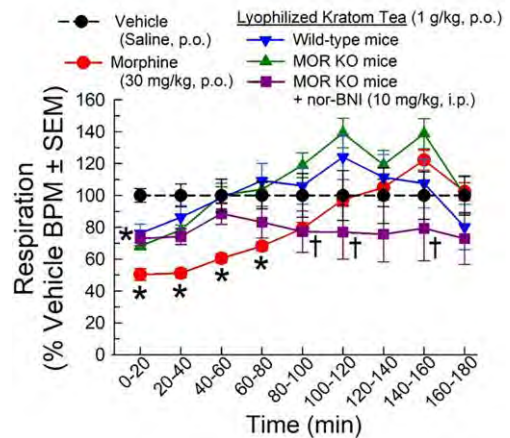
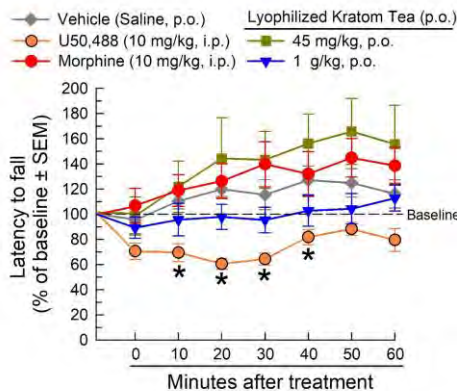


Wilson, L.L. et al, Drug and Alcohol Dependence, 2020 (Accepted)



43

Measured Liabilities with LKT

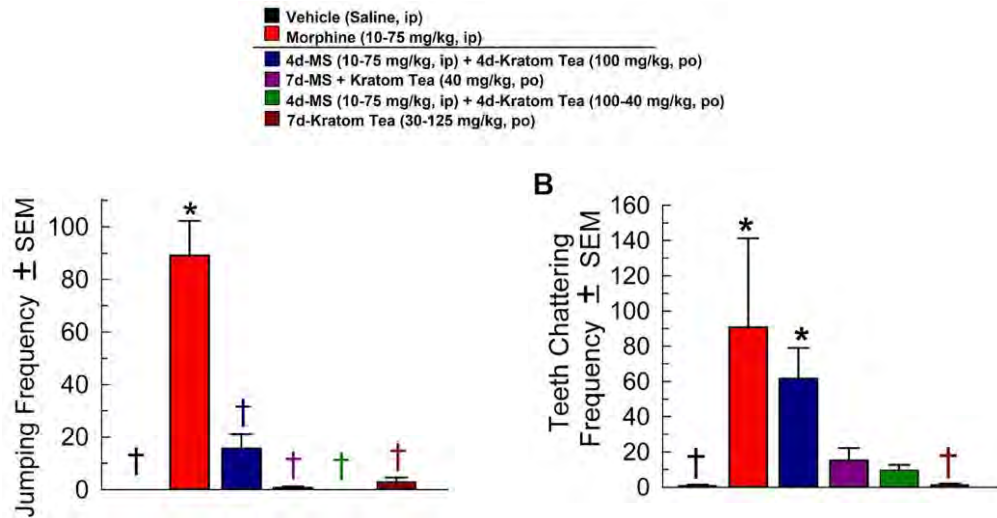


Wilson, L.L. et al, Drug and Alcohol Dependence, 2020 (Accepted)



44

Reduction of Naloxone PPT Withdrawal



Wilson, L.L. et al, Drug and Alcohol Dependence, 2020 (Accepted)

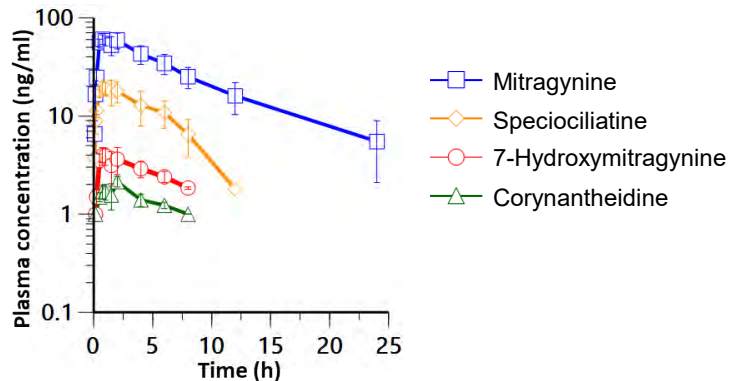


45

The pharmacokinetic profiles of kratom alkaloids

Following oral administration of 366 mg/kg (containing 5.7 mg/kg mitragynine, human dose equivalent) LKT

The data represent mean plasma concentration-time profiles and the error bar represents SEM (n=4)



	Content of Individual Alkaloids							
	Mitragynine	7-Hydroxymitragynine	Corynantheidine	Speciogynine	Speciocillatine	Paynantheine	Corynoxine	Corynoxine-B
LKT (% w/w)	1.57	BLQ	0.04	0.22	0.56	0.30	BLQ	0.04

BLQ: below the lower limit of quantification (0.02% w/w for LKT)

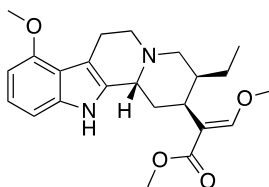
Kamble, S.H. et al, 2020 (Submitted)



46

Binding and function of speciociliatine at opioid receptors

Target	Ki (nM)	Potency (nM)	Efficacy (% agonist response)	Agonist/ Antagonist
μ	39.8	39.2	73.6	Agonist
κ	98.1	No agonist effect	No agonist effect	No agonist or antagonist effects



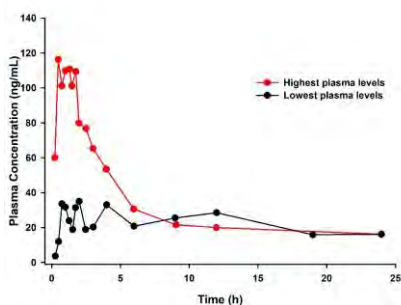
Speciociliatine has a partial agonist effect at the MOP

Obeng, Samuel, et al. *J Med Chem.* 63 (2019). 433-439.

UF College of Pharmacy
UNIVERSITY of FLORIDA

47

Clinical Pharmacokinetics of Mitragynine (Thailand Study)



Parameters	Mean \pm SD
T_{max} (h)	0.8 ± 0.4
Terminal $t_{1/2}$ (h)	23.2 ± 16.1
V_d/F (L/kg)	38.0 ± 24.3
CL/F (L/h kg)	98.1 ± 51.3

Forensic Analysis in the United States

Case I: The measured mitragynine plasma concentration in a deceased individual from Florida was found to be **1,800 ng/mL**

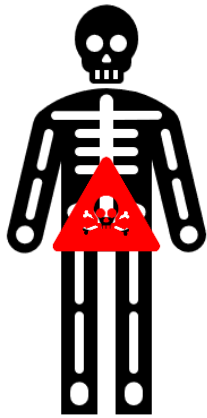
Case II: The measured mitragynine plasma concentration in a deceased Tupper Lake police Sgt was found to be **3,500 ng/mL**

Satariya Trakulsrichai *et al.*, *Drug Des Devel Ther.* 2015; **9**: 2421.

Chrostowski L. Report of diagnosis and autopsy of Christopher Waldron. Medical Examiner Department. Hillsborough County, FL, USA [22 August 2017] <http://speciosa.org/analysis-of-two-deaths-reportedly-associated-with-kratom/>

UF College of Pharmacy
UNIVERSITY of FLORIDA

48



Measured mitragynine plasma concentration in the deceased Americans were found to be **17.1- to 189-times higher** than the peak plasma concentrations (C_{max}) (18.5 – 105.0 ng/mL) measured in regular kratom users.

Men'sHealth SEX HEALTH WEIGHT LOSS STYLE GET SUMMER BODY READY SUBSCRIBE NEWSLETTER

This Healthy 27-Year-Old Bodybuilder Died After Using a Common Supplement

Matthew Dana was taking kratom, and now people are calling for a total ban on the substance

UF College of Pharmacy
UNIVERSITY of FLORIDA

49

Take Home – The Two Faces of Kratom

- Long history of safe use in the traditional manner from SE Asia
- Associated with a range of adverse events in the Western World
- Alkaloids are structurally different from opiates, and therefore may have different pharmacokinetic and pharmacodynamic properties
- Products in the USA are not the same, as the traditionally utilized “fresh leaf” tea preparations
- Gaps in the science around this plant exist
- A possible solution to the opioid epidemic could be from nature

UF College of Pharmacy
UNIVERSITY of FLORIDA

50

Acknowledgements

• Chemistry

- Francisco Leon, PhD
- Marco Mottinelli, PhD
- Grant Zwolinski
- John Fortner
- Nelson Chear

• Receptor Binding and Function

- Samuel Obeng, PhD
- Takato Hiranita, PhD

• DMPK

- Bonnie A. Avery, PhD
- Abhisheak Sharma, PhD
- Shyam Kamble, PhD
- Raju Kanumuri, PhD
- Tamara King, PhD
- Erin Berthold

• Behavioral Pharmacology

- Lance McMahon, PhD
- Takato Hiranita, PhD
- Jay McLaughlin, PhD
- Lisa Wilson
- Scott Hemby, PhD (Highpoint Univ)
- Jonathan Katz, PhD (NIDA IRP)

• Horticultural Science

- Brian Pearson, PhD (UF/IFAS)

• UG3 DA048353

• R01 DA047855

• Urban Ice Organics and Kelly Dunn

• University of Florida Foundation

• Multiple UF student workers!

51

UF College of Pharmacy
UNIVERSITY OF FLORIDA

Free ACS Webinars Every Weekday!

Upcoming Broadcasts



Friday, September 25, 2020 at 10-11am ET

Speaker: Pamela Tadross, Organic Process Research & Development
Moderator: Kali Miller, ACS Publications

[Register for Free!](#)

What You Will Learn

- What editors look for when reviewing submissions
- Tips for responding to reviewer reports
- Qualifications to become a reviewer and strategies to evaluate a manuscript

Co-produced with: ACS Publications



Wednesday, September 30, 2020 at 2-3pm ET

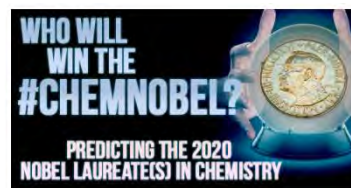
Speaker: Steve Mohyla, Woodbury Financial Services
Moderator: Mary Bet Dobson, American Chemical Society

[Register for Free!](#)

What You Will Learn

- What to consider when creating or updating a will
- How tax law changes may impact your current plans
- How philanthropy may factor into your plans

Co-produced with: ACS Office of Philanthropy



Thursday, October 1, 2020 at 2-3pm ET

Speakers: Kit Chapman, Science Historian and Writer / Wendy Queen, Materials Chemist, EPFL (École Polytechnique Fédérale de Lausanne) / Darryl Boyd, U.S. Naval Research Laboratory and Science Made Simple
Moderator: Laura Howes, Chemical & Engineering News

[Register for Free!](#)

What You Will Learn

- Who are our front-runners for this year's Nobel Prize in Chemistry and why
- Big ideas in chemistry that we think should someday win the prize
- Nobel trivia, including how the celebrations will work this year

Co-produced with: Chemical & Engineering News

www.acs.org/acswebinars

52

Mitragyna Speciosa: What Science is Telling Us about Kratom



Christopher McCurdy
Professor of Medicinal Chemistry and Director, UF Translational Drug Development Core, Department of Medicinal Chemistry, College of Pharmacy, University of Florida



Amy Newman
Acting Scientific Director, National Institute on Drug Abuse IRP Chief, Molecular Targets and Medications Discovery Branch Chief, Medicinal Chemistry Section Director, Medication Development Program

Presentation slides are available now! Edited recordings are an exclusive ACS member benefit.

www.acs.org/acswebinars

This ACS Webinar is co-produced with ACS Division of Medicinal Chemistry, American Association of Pharmaceutical Scientists, and ACS Publications.

53

AAPS American Association of Pharmaceutical Scientists

Contact Us:
2107 Wilson Blvd
#700
Arlington, VA 22201

(703)243-2800
aaps@aaps.org

AAPS Membership
membership@aaps.org
(877)998-2277 (AAPS)

2021 National Biotechnology Conference

AAPS seeks experienced scientists to lead the 2021 NBC Scientific Programming Committee!

[READ MORE!](#)

AAPS Happenings:

PharmSci 360

Check out the program today!

[Read More](#)

PharmSci 360

Registration is now open!

[Read More](#)

PharmSci 360 Workshops

View full list today!

[Read More](#)

AAPS Member Demographics

Sector	
Industry	72%
Academia	23%
Other Non-Academy	6%
Government	6%
Education	
Ph. D.	61%
Pharm. D.	5%
Master's	18%
Bachelors	15%

Member Testimonial

"Over time, I've built up this network of people I can ask about anything work-related."

Ruth Hightower, Ph.D.
AAPS Member Since 2008

AAPS Live Webinars Are Free and Open Access

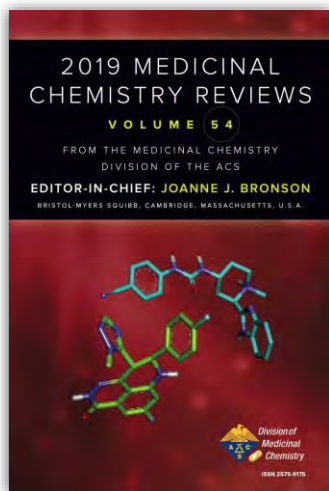
Webinars offer a great opportunity to receive the latest information on pharmaceutical science topics without the need for travel or time away from home and office. Plan to participate in our upcoming live events, replay a past session in our archives, or submit a proposal for organizing your own webinar!

- Register for Upcoming Webinars
- Replay Archived Webinars
- Archived webinars are a member benefit: join today!

<https://www.aaps.org>

54

Join the Division Today!



For \$25 membership (\$10 for students), You Will Receive:

- A free digital copy of our annual medicinal chemistry review volume (over 680 pages, \$160 retail price)
- Abstracts of MEDI programming at national meetings
- Access to student travel grants and fellowships

Find out more about the ACS MEDI Division! www.acsmedchem.org

55



ACS Webinars®

CLICK • WATCH • LEARN • DISCUSS



Learn from the best and brightest minds in chemistry! Hundreds of webinars on diverse topics presented by experts in the chemical sciences and enterprise.

Edited Recordings are an exclusive ACS member benefit and are made available to once the recording has been edited and posted.

Live Broadcasts of ACS Webinars® continue to be available to the general public on Tuesdays, Wednesdays, and Thursdays from 2-3pm ET!

A **collection of the best recordings** from the ACS Webinars Archive will be broadcast on Mondays and Fridays from 2-3pm ET!

www.acs.org/acswebinars

56

ACS Webinars® does not endorse any products or services. The views expressed in this presentation are those of the presenter and do not necessarily reflect the views or policies of the American Chemical Society.



Contact ACS Webinars® at acswebinars@acs.org

57

Free ACS Webinars Every Weekday!

Upcoming Broadcasts



Friday, September 25, 2020 at 10-11am ET

Speaker: Pamela Tadross, Organic Process Research & Development
Moderator: Kali Miller, ACS Publications

Register for Free!

What You Will Learn

- What editors look for when reviewing submissions
- Tips for responding to reviewer reports
- Qualifications to become a reviewer and strategies to evaluate a manuscript

Co-produced with: ACS Publications



Wednesday, September 30, 2020 at 2-3pm ET

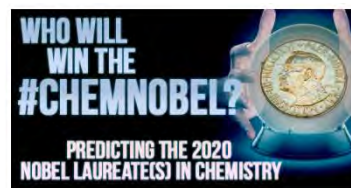
Speaker: Steve Mohyla, Woodbury Financial Services
Moderator: Mary Bet Dobson, American Chemical Society

Register for Free!

What You Will Learn

- What to consider when creating or updating a will
- How tax law changes may impact your current plans
- How philanthropy may factor into your plans

Co-produced with: ACS Office of Philanthropy



Thursday, October 1, 2020 at 2-3pm ET

Speakers: Kit Chapman, Science Historian and Writer / Wendy Queen, Materials Chemist, EPFL (École Polytechnique Fédérale de Lausanne) / Darryl Boyd, U.S. Naval Research Laboratory and Science Made Simple
Moderator: Laura Howes, Chemical & Engineering News

Register for Free!

What You Will Learn

- Who are our front-runners for this year's Nobel Prize in Chemistry and why
- Big ideas in chemistry that we think should someday win the prize
- Nobel trivia, including how the celebrations will work this year

Co-produced with: Chemical & Engineering News

www.acs.org/acswebinars

58