UNIVERSITY OF CALGARY

UNIVERSITY OF CALGARY
FACULTY OF SCIENCE
DEPARTMENT OF BIOLOGICAL SCIENCES
COURSE OUTLINE

1. **Course: BIOL 505, Medicinal Plant Biochemistry – Fall 2019**
Lecture 01: MWF 14:00-14:50 in ST 057

Instructor	Email	Phone	Office	Hours
Dr. Dae-Kyun Ro	daekyun.ro@ucalgary.ca	**220-7099**	**BI 393**	**TBA**
Dr. Peter Facchini	pfacchin@ucalgary.ca	**220-7651**	**BI 396**	**TBA**

Course Site: D2L: BIOL 505 L01-Fall 2019)-Medicinal Plant Biochemistry

Note: Students must use their U of C account for all course correspondence.

Department of Biological Sciences BI 186 220-3140 biosci@ucalgary.ca

2. **Requisites:**

See section 3.5.c in the Faculty of Science section of the online Calendar.

Prerequisite(s): **Biology 331 and Biochemistry 393**

Antirequisite(s): **Credit for Biology 505 and Botany 503 will not be allowed**

3. **Grading:**

The University policy on grading and related matters is described in F.1 and F.2 of the online University Calendar. In determining the overall grade in the course the following weights will be used:

Component(s)	Weighting %	Date
Midterm Exam	30%	October 21 (In-Class)
Seminar	20%	
Term Paper	20%	
Final Exam*	30%	Scheduled by the Registrar

*This course has a registrar scheduled final exam.

Each piece of work (Seminar, term paper, midterm exam(s) or final examination) submitted by the student will be assigned a grade. The student's grade for each component listed above will be combined with the indicated weights to produce an overall percentage for the course, which will be used to determine the course letter grade.

The conversion between a percentage grade and letter grade is as follows.

Letter Grade	A+	A	A-	B+	B	B-	C+	C	C-	D+	D
Min. Percent Required	90%	85%	80%	77%	73%	70%	67%	63%	60%	55%	50%

Department Approval: Heather Addy Date: 29 August /19
Biol 505 co F19; 2019-08-29 3:16 PM

4. **Missed Components Of Term Work:**

In the event that a student misses the midterm or any course work due to illness, supporting documentation, such as a medical note or a statutory declaration will be required (see Section M.1; for more information regarding the use of statuary declaration/medical notes, see FAQ). Absences must be reported within 48 hours.

The regulations of the Faculty of Science pertaining to this matter are found in the Faculty of Science area of the Calendar in Section 3.6. It is the student's responsibility to familiarize themselves with these regulations. See also Section E.3 of the University Calendar.

5. **Scheduled Out-of-Class Activities:**

There are no scheduled out of class activities for this course.

6. **Course Materials:** Text: Recommended: Plant Biochemistry and Molecular Biology. Hans-Walter Heldt., Oxford University Press, 1997; Biochemistry & Molecular Biology of Plants. Buchanan, B., W. Gruissem & R. Jones, American Society of Plant Physiologists, 2000.

7. **Examination Policy:**

No aids are allowed on tests or examinations.

Students should also read the Calendar, Section G, on Examinations.

8. **Approved Mandatory And Optional Course Supplemental Fees:**

There are no mandatory or optional course supplemental fees for this course.

9. **Writing Across the Curriculum Statement:**

For all components of the course, in any written work, the quality of the student's writing (language, spelling, grammar, presentation etc.) can be a factor in the evaluation of the work. See also Section E.2 of the University Calendar.

10. **Human & Living Organism Studies Statements:**

Students will not participate as subjects or researchers in human studies.

See also Section E.5 of the University Calendar.

STUDIES IN THE BIOLOGICAL SCIENCES INVOLVE THE USE OF LIVING AND DEAD ORGANISMS. Students taking laboratory and field based courses in these disciplines can expect involvement with the experimentation on such materials. Students perform dissections on dead or preserved organisms in some courses. In particular courses, students experiment on living organisms, their tissues, cells or molecules. Sometimes field work requires students to collect a variety of living materials by many methods, including humane trapping.

All work on humans and other animals conforms to the Helsinki Declaration and to the regulations of the Canadian Council on Animal Care. The Department strives for the highest ethical standards consistent with stewardship of the environment for organisms whose use is not governed by statutory authority. Individuals contemplating taking courses or majoring in one of the fields of study offered by the Department of Biological Sciences should ensure that they have fully considered these issues before enrolling. Students are advised to discuss any concerns they might have with the Undergraduate Program Director of the Department.

Students are expected to be familiar with Section SC.4.1 of the University Calendar.

11. **Reappraisal Of Grades:**

A student wishing a reappraisal, should first attempt to review the graded work with the Course Coordinator/ Instructor or department offering the course. Students with sufficient academic grounds may request a reappraisal. Non-academic grounds are not relevant for grade reappraisals. Students should be aware that the grade being reappraised may be raised, lowered or remain the same. See Section I.3 of the University Calendar.

a. **Term Work:** The student should present their rationale as effectively and as fully as possible to the Course coordinator/instructor within 15 days of either being notified about the mark, or of the item's return to the class. If the student is not satisfied with the outcome, the student shall immediately submit the Reappraisal of Graded Term work form to the department in which the course is offered. The department will arrange for a re-assessment of the work if, and only if, the student has sufficient academic grounds. See sections I.1 and I.2 of the University Calendar.

b. **Final Exams:** The student shall submit the request to Enrolment Services. See Section I.3 of the University Calendar.

12. **Other Important Information For Students:**

a. **Mental Health:** The University of Calgary recognizes the pivotal role that student mental health plays in physical health, social connectedness and academic success, and aspires to create a caring and supportive campus community where individuals can freely talk about mental health resources available throughout the university community, such as counselling, self-help resources, peer support or skills-building available through the SU Wellness Centre (Room 30, MacEwan Student Centre, Mental Health Services Website) and the Campus Mental Health Strategy website (Mental Health).

b. **SU Wellness Center:** The Students Union Wellness Centre provides health and wellness support for students including information and counselling on physical health, mental health and nutrition. For more information, see www.ucalgary.ca/wellnesscentre or call 403-210-9355.

c. Sexual Violence: The University of Calgary is committed to fostering a safe, productive learning environment. The Sexual Violence Policy ttps://www.ucalgary.ca/policies/files/policies/sexual-violence-policy.pdf) is a fundamental element in creating and sustaining a safer campus environment for all community members. We understand that sexual violence can undermine students' academic success and we encourage students who have experienced some form of sexual misconduct to talk to someone about their experience, so they can get the support they need. The Sexual Violence Support Advocate, Carla Bertsch, can provide confidential support and information regarding sexual violence to all members of the university community. Carla can be reached by email (svsa@ucalgary.ca) or phone at 403-220-2208 .

d. Misconduct: Academic misconduct (cheating, plagiarism, or any other form) is a very serious offence that will be dealt with rigorously in all cases. A single offence may lead to disciplinary probation or suspension or expulsion. The Faculty of Science follows a zero tolerance policy regarding dishonesty. Please read the sections of the University Calendar under Section K. Student Misconduct to inform yourself of definitions, processes and penalties. Examples of academic misconduct may include: submitting or presenting work as if it were the student's own work when it is not; submitting or presenting work in one course which has also been submitted in another course without the instructor's permission; collaborating in whole or in part without prior agreement of the instructor; borrowing experimental values from others without the instructor's approval; falsification/ fabrication of experimental values in a report. These are only examples.

e. Assembly Points: In case of emergency during class time, be sure to FAMILIARIZE YOURSELF with the information on assembly points.

f. Academic Accommodation Policy: Students needing an accommodation because of a disability or medical condition should contact Student Accessibility Services in accordance with the procedure for accommodations for students with disabilities available at procedure-for-accommodations-for-students-with- disabilities.pdf.

Students needing an accommodation in relation to their coursework or to fulfill requirements for a graduate degree, based on a protected ground other than disability, should communicate this need, preferably in writing, to the Associate Head, Undergraduate of the Department of Biological Sciences, Heather Addy by email addy@ucalgary.ca or phone 403 220-6979. Religious accommodation requests relating to class, test or exam scheduling or absences must be submitted no later than 14 days prior to the date in question. See Section E.4 of the University Calendar.

g. Safewalk: Campus Security will escort individuals day or night (See the Campus Safewalk website). Call 403-220-5333 for assistance. Use any campus phone, emergency phone or the yellow phones located at most parking lot pay booths.

h. Freedom of Information and Privacy: This course is conducted in accordance with the Freedom of Information and Protection of Privacy Act (FOIPP). Students should identify themselves on all written work by placing their name on the front page and their ID number on each subsequent page. For more information, see Legal Services website.

i. Student Union Information: VP Academic, Phone: 403-220-3911 Email: suvpaca@ucalgary.ca. SU Faculty Rep., Phone: 403-220-3913 Email: sciencerep@su.ucalgary.ca. Student Ombudsman, Email: ombuds@ucalgary.ca.

j. Internet and Electronic Device Information: Unless instructed otherwise, cell phones should be turned off during class. All communication with other individuals via laptop, tablet, smart phone or other device is prohibited during class unless specifically permitted by the instructor. Students that violate this policy may be asked to leave the classroom. Repeated violations may result in a charge of misconduct.

k. Surveys: At the University of Calgary, feedback through the Universal Student Ratings of Instruction (USRI) survey and the Faculty of Science Teaching Feedback form provides valuable information to help with evaluating instruction, enhancing learning and teaching, and selecting courses. Your responses make a difference - please participate in these surveys.

l. Copyright of Course Materials: All course materials (including those posted on the course D2L site, a course website, or used in any teaching activity such as (but not limited to) examinations, quizzes, assignments, laboratory manuals, lecture slides or lecture materials and other course notes) are protected by law. These materials are for the sole use of students registered in this course and must not be redistributed. Sharing these materials with anyone else would be a breach of the terms and conditions governing student access to D2L, as well as a violation of the copyright in these materials, and may be pursued as a case of student academic or non-academic misconduct, in addition to any other remedies available at law.

TENTATIVE LECTURE SCHEDULE

Date	Topic	Instructor
September 6	Introduction	DKR
September 9	Bioactive natural products	DKR
September 11	Terpenoid principles and history	DKR
September 13	Terpenoid mechanism	DKR
September 16	Terpenoid synthase gene family	DKR
September 18	Terpenoid precursor biosynthesis I	DKR
September 20	Terpenoid precursor biosynthesis II	DKR
September 23	Terpenoid biotechnology	DKR
September 25	Research tools to study plant metabolism	DKR
September 27	Carotenoid principles	DKR
September 30	Carotenoid metabolism	DKR
October 2	Introduction to phenylpropanoids	DKR
October 4	Phenylpropanoid metabolism I	DKR
October 7	Phenylpropanoid metabolism II	DKR
October 9	Antibiotics	DKR
October 11	Polyketide I	DKR
October 14	Holiday - Thanksgiving	No lecture
October 16	Polyketide II	DKR
October 18	Review	DKR
October 21	**Mid-term exam (In-class)**	**DKR**
October 23	Terpenophenolics	PJF
October 25	Benzylisoquinoline alkaloids I	PJF
October 28	Benzylisoquinoline alkaloids II	PJF
October 30	Benzylisoquinoline alkaloids III	PJF
November 1	Benzylisoquinoline alkaloids IV	PJF
November 4	Monoterpenoid indole alkaloids I	PJF
November 6	Monoterpenoid indole alkaloids II	PJF
November 8	Monoterpenoid indole alkaloids III	PJF
November 10 – November 16		Reading Break
November 18	Tropane alkaloids I	PJF
November 20	Purine alkaloids I	PJF
November 22	Purine alkaloids II	PJF
November 25	Pyrrolizidine alkaloids	PJF
November 27	Cellular compartmentalization of alkaloid metabolism I	PJF
November 29	Cellular compartmentalization of alkaloid metabolism II	PJF
December 2	Glucosinolates I	PJF
December 4	Glucosinolates II	PJF
December 6	Cyanogenic glucosides	PJF

Course Outcomes Biol 505

Terpenoids

- To know the definition and history of terpenoids
- To understand the chemical mechanism of prenyl diphosphates (e.g., GPP, FPP) and terpene formations –
- how the carbocations can be formed, how the carbon backbones are rearranged, and how the carbocation
- cascade reactions can be terminated.
- To know the definitions of different subclasses of terpenoids (monoterpene, sesquiterpene, diterpene,
- carotenoid etc)
- To understand how the terpene synthase (TPS) was first isolated and their gene sequences were determined.
- What insights can we obtain from the sequence information?
- To conceptually understand how TPS enzyme mediated the biosynthesis of specific terpene.
- To know the evolutionary origin of TPS
- To know the mevalonate (MVA) and methylerythritol phosphate (MEP) pathway for IPP formation – starting
- precursors, linkage to primary metabolism, rearrangement of carbon backbone formation, key features in
- energetics, and key rate-limiting enzymes
- To know the lineage-specific occurrences of MVA and MEP pathway
- To know the subcellular compartmentalization of MVA and MEP pathway, and uses of the
- compartmentalization in biological engineering
- Be familiarized with the structural elucidation of terpenoids
- To know several terpene hydrocarbon-modifying enzymes
- To understand biochemical roles of key enzymes in carotenoid biosynthesis
- To understand approaches to develop nutrition-enhanced crops (bio-fortified crops)
- Bio-engineering principles of microbial synthesis of artemisinin

Phenylpropanoids

- To know the definition of phenylpropanoid
- To know precursors of shikimate pathway
- To know three key enzymes and reactions in the core PP pathway
- To know the evolutionary origin of PAL
- To understand key structural features of several different subclasses of PP products and the key enzyme(s)
- for each subclass
- To understand the lignin biosynthesis
- To know how the floral colors are determined and how the floral colors can be altered
- To know the history and rationale for the discoveries of transposable elements and RNA interference
- To understand the importance of Myb transcription factors in PP metabolism

Polyketides

- To know the mechanism of the first synthetic sulfa drug
- To understand the biosynthesis and development of different variants of penicillin
- To understand the sharing and different features of penicillin and cepharosporin
- To be familiarized with structures of penicillin, cepharosporin, chloramphenicol, tetracycline, aminoglycoside,
- macrolide (or macrolactone) quinolone
- To understand the strategies to develop new antibiotics that can kill drug-resistant bacteria
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- To know the definition and central precursor of polyketide products.
- To understand several key reactions in fatty acid and polyketide biosynthesis (AT, acyl transferase; KS, keto
- synthase; KR, keto reductase; DH, dehydratase; ER, enoyl reductase, TE, thioesterase)

- To understand the role of ACP (acyl carrier protein) and the essential co-factor in ACP
- To know the history and key findings in the creation of Canola
- What makes the polyketide synthases produce far more diverse natural products than fatty acid synthase
- does?
- To know differences between Type I modular and Type I iterative PKS
- To understand why the lovastatin biosynthesis challenges scientists
- To know the differences among Type I, Type II, and Type II PKS

Terpenophenolics

- Know the family Cannacabeae and the two included genera of plants that produce terpenophenolics
- Be able to recognize the basic structure of a terpenophenolic
- Know the basic morphological, anatomical and functional features of glandular trichomes
- Understand the meaning of 'homologous' as opposed to 'analogous'
- Know the similarities and differences between hemp and marijuana
- Be able to recognize the basic structure of a cannabinoid
- Be able to recognize the basic structure of a hops bitter acid
- Be able to recognize the basic structure of a xanthohumol
- Know the three basic steps involved in the biosynthesis of a prototype terpenophenolic
- Understand the roles of polyketide synthases, aromatic prenyltransferases and various 'tailoring' enzymes in the biosynthesis of □9-tetrahydrocannabinol, humulone and xanthohumol
- Know the general type of precursor (i.e. a CoA ester of various origin) used to generate the phenolic component of a terpenoidphenolic
- Know the precursor pathway leading to the terpene moiety of a terpenophenolic
- Understand the general role of cyclization and 'decoration' reactions in the creation of terpenophenolic diversity in plants
- Know the meaning of 'malt', 'wort' and 'fermentation' in the process of brewing beer
- Know why and when hops are used to brew beer, and understand what happens to the relevant terpenophenolics in the process

Benzylisoquinoline alkaloids

- Know the general definition of an alkaloid
- Be able to recognize the canonical structures of (i) benzylisoquinoline, (ii) monoterpenoid indole, (iii) tropane and pyrrolidine, and (iv) pyrrolizidine alkaloids
- Know the major order (Ranunculales), a principal family (Papaveraceae), and some of the important species (Papaver somniferum, Hydrastis canadensis, Sanguinaria canadensis, etc) that produce BIAs
- Know the main essential medicines produced by opium poppy, which are natural and which are semi-synthetic
- Know the name of the German pharmacist's assistant that discovered morphine in 1804
- Know the major geographical locations for the licit production of opium poppy crops that starts the supply chain for the availability of morphine and codeine in Canada
- Understand the relationship between heroin, morphine and opium
- Be able to recognize and draw the canonical 1-benzylisoquinoline structure
- Understand the structural relationship between 1-benzylisoquinoline (e.g. (S)-reticuline), protoberberine (e.g. scoulerine), phthalideisoquinoline (e.g. noscapine), promorphinan (e.g. salutaridine) and morphinan (e.g. morphine) alkaloids
- Understand the concept that all known BIA (and other alkaloid) biosynthetic enzymes belong to a limited number of protein families
- Understand the basic metabolic functions of (i) "Pictet-Spenglerases", (ii) cytochromes P450, (iii) reductases, (iv) O- and N-methyltransferases, (v) acyltransferases
- Know the primary metabolite from which all BIAs are derived
- Know the tyrosine-derived precursors used as substrates to produce the central alkaloid intermediate in BIA metabolism
- Be able to describe the basic features of a Pictet-Spengler condensation
- Be able to draw (S)-norcoclaurine

- Know the four reactions that convert (S)-norcoclaurine to (S)-reticuline
- Be able to draw (S)-reticuline
- Know the carbon atoms in (S)-reticuline that undergo carbon-carbon coupling yielding the promorphinan salutaridine
- Understand the meaning of "stereoisomer"
- Understand what is meant by "stereochemical inversion" or "epimerization" and be able to define to key features of how it happens in opium poppy
- Understand the basic and unique features of reticuline epimerase
- If shown the structure of thebaine, be able to describe the three enzymatic events that yield morphine
- Know the carbon atoms in (S)-reticuline that undergo carbon-carbon coupling yielding the protoberberine scoulerine
- Know that scoulerine is a common intermediate in the biosynthesis of the antimicrobial sanguinarine and the potential anticancer drug noscapine
- Understand the role of the two key oxidation reactions that lead to the conversion of the protoberbeine structure to the seco-berbine structure, and the importance of O-acetylation in the process, in the biosynthesis of noscapine
- Understand how O-deacetylation results in the conversion of the seco-berbine structure to the phthalideisoquinoline structure in the biosynthesis of noscapine
- Understand the basic underlying concepts involved in the reconstitution of morphine and noscapine pathways in engineered yeast
- Be able to suggest some of the fundamental biochemical, metabolic and biological reasons for the low yield of BIAs in engineering yeast, compared with the host plant

Monoterpenoid indole alkaloids

- Be able to recognize and draw the canonical monoterpenoid indole alkaloid structure
- Know the primary metabolites from which all MIAs are derived
- Know the tryptophan-derived precursor of MIAs
- Know the isoprenoid-derived precursor of MIAs
- Understand how the coupling of tryptamine and secologanin is a Pictet-Spengler condensation
- Know the central MIA intermediate from which all MIAs are produced
- Understand the similarities and differences between (S)-norcoclaurine and strictosidine with respect to their role in BIA and MIA metabolism, the mechanism of their formation, and the nature of the enzymes responsible for their formation
- Understand the relationship between strictosidine and various structural types of MIAs, including those that retain an indole moiety and those with a modified indole moiety
- Be able to recognize the structures of tabersonine (and it's derivative vindoline), catharanthine, vinblastine, and camptothecin
- Know the importance of the following plants as sources of valuable MIAs: Catharanthus roseus, Camptotheca acuminate, Chincona officinalis, Rauwolfia serpentine, Strychnos nux-vomica
- Know the pharmacological importance of the MIAs: vinblastine, camptothecin, quinine, strychnine, ajmalicine
- Understand the role of tryptophan decarboxylase in MIA metabolism
- Understand the role of strictosidine synthase in MIA metabolism
- Understand how we know that the Pictet-Spengler condensations resulting in the formation of (S)-norcoclaurine and strictosidine have independent evolutionary origins
- Be able to explain, in general terms, what is meant by a Pistet-Spengler condensation
- Understand what part of the MIA structure in strictosidine is modified to yield the corynanthe, iboga and aspidosperma MIA structures
- Know that the primary metabolic origin of the monoterpenoid component in MIAs produced in plants is the non-mevalonate (MEP) pathway
- Now the differences in the primary metabolic origin of the mevalonate pathway (i.e. acetyl-CoA) and the MEP pathway (i.e. pyruvate and glyceraldehyde 3-phosphate)
- Understand why the origin of IPP used to produce MIAs is important for engineering the pathway in microorganisms

- Be able to recognize the major steps involved in the formation of secologanin from IPP [i.e. (i) IPP to GPP, (ii) GPP to 10-oxogeranial, (iii) 10-oxogeranial to a bicyclic iridoid intermediate, (iv) final glycosylation, ring hydroxylation, carboxy methylation, and ring opening
- Understand that secologanin is glycosylated and an aldehyde, and why these features are important for downstream MIA metabolism
- Understand the basic biosynthetic relationship between tabersonine and catharanthine in Catharanthus roseus (i.e. they are derived from a common pathway proceeding from (i) strictosidine to geissoschizine via deglycosylation [SGD] and reduction [GS], (ii) ring rearrangement of a geissoschizine derivative to O-acetylstemmadinine via oxidation [GO], two successive reductions [Redox1 and Redox2], and O-acetyltransfer [SAT] (iii) further ring rearrangement of O-acetylstemmadinine to catharanthine and tabersonine involving two related hydrolases
- Know that vindoline is a seven-step derivative of tabersonine and that, in particular, the final two steps catalyzed by D4H and DAT result in the addition of an O-acetyl group
- Understand the relationship between vinblastine, vindoline and catharanthine
- Understand the fundamental similarities and differences in the proposed biosynthetic pathways for the anticancer drugs vinblastine and camptothecin [e.g. role and origin of strictosidine, timing of the deglycosylation step, general location of ring rearrangement in the MIA structure
- Conceptually understand the basic experimental strategies and methods used to elucidate (e.g. determine the chemical steps, and isolate enzymes and genes) specialized metabolic pathways (e.g. use of transcriptomes, metabolite profiling, in vitro enzyme assays, in plant a gene silencing, and the in vivo reassembly of known pathways in yeast)
- Be able to recognize lysergic acid, and that this plant metabole contains an indole moiety
- Understand how the synthetic compound LSD is related to the natural plant metabolite lysergic acid
- Know that morning glories produce lysergic acid, but not LSD

Tropane alkaloids, calystegines and nicotine

- Be able to recognize and distinguish between a tropane alkaloid, a calystegine and the pyrrolidine alkaloid nicotine
- Know the occurrence of atropine in Atropa belladonna, scopolamine in Hyoscyamus spp., hyoscyamine in Datura stramonium, and cocaine in Erythroxylon coca
- Know some of the pharmacological properties of atropine (pupil dilation, anti-nerve gas agent, heart attack treatment), scopolamine (motion sickness treatment) and cocaine (topical anesthetic, central nervous system stimulant)
- Know that nicotine occurs at high levels almost exclusively in members of the genus Nicotiana
- Know the primary metabolites from which tropane alkaloids, calystegines and nicotine are derived
- Know the common first three steps (i.e. decarboxylation, N-methylation, oxidative deamination) in the formation of tropane alkaloids, calystegines and nicotine
- Know the three enzymes ornithine decarboxylase (ODC), putrescine N-methyltransferase (PMT) and N-methylputrescine oxidase (MPO) and what they do to convert ornithine to N-methyl-□1-pyrrolium cation
- Understand the central role of N-methyl-□1-pyrrolium cation in the formation of tropane alkaloids, calystegines and nicotine
- Recognize that the final step in the formation of N-methyl-□1-pyrrolium cation is a spontaneous cyclization of 4-methylaminobutanal, which contains reactive aldehyde and amine groups
- Know that N-methyl-□1-pyrrolium cation condenses with nicotinic acid derived from NAD metabolism, and that the resulting dihydronicotine undergoes further oxidation to nicotine (and that the enzymes responsible for these reactions are not known)
- Know that nicotine can be further oxidized to nornicotine by a cytochrome P450 the catalyzes N-demethylation
- Know that nornicotine is converted to a highly carcinogenic compound during the curing, aging, processing and smoking of tobacco
- Understand the basic pharmacology of nicotine (e.g. how it functions as an insecticide, and as a stimulant and toxin in mammals)
- Understand the relationship between N-methyl-□1-pyrrolium cation and tropinone involving the addition and subsequent decarboxylation of an acetoacetate moiety
- Understand the roles in members of the Solanaceae of tropinone reductase I (TR-I) and tropinone reductase II (TR-II) in the formation of tropine and pseudotropine, respectively
- Know that tropine and pseudotropine are stereoisomers, and understand what this means

- Know the relationship between tropine and pseudotropine, and tropane alkaloids and calystegines, respectively
- Understand that TR-I and TR-II are closely related enzymes with similar structures that belonging to the short-chain dehydrogenase/reductase (SDR) family, and that differences in the amino acids in their active sites affect the binding position of the substrate tropinone
- Know that in members of the Solanaceae, tropine condenses with phenyllacetate yielding and intermediate (littorine) that undergoes subsequent (i) oxidative "chain-shortening" and (ii) reduction yielding hyoscyamine
- Know that hyoscyamine can be oxidized to scopolamine by a dioxygenase (hyoscyamine 6-hydroxylase, H6H), which contains an epoxide on the tropane ring
- Know that pseudotropine is converted to a number of calystegines via oxidation (addition of hydroxyl groups) and N-demethylation
- Know that in addition to the Solanaceae , calystegines are produced in other plant families, especially the Convolvulaceae
- Know that cocaine is a tropane alkaloid produced in Erythroxylum spp., and that the main species used for the commercial / illicit production of cocaine in Erythroxylum coca
- Understand the evidence available to know that the occurrence of tropane alkaloids in members of the Erythroxylaceae and Solanaceae (e.g. cocaine and atropine, respectively) is an example of convergent evolution
- Know that enzymes in the Erythroxylaceae and Solanaceae involved in the formation of N-methyl-□1-pyrrolium cation are highly conserved, but the corresponding genes were likely independently recruited
- Know that the N-methyl-□1-pyrrolium cation is converted to ecgonine-CoA ester in the Erythroxylaceae, rather than to tropine as occurs in the Solanaceae
- Know that methylecgonone derived from ecgonine-CoA ester is the substrate from reduction of the keto group in the Erythroxylaceae
- Know that the enzyme methylecgonone reductase (MecgoR) converts methylecgonone to methylecgonine, which is the equivalent step catalyzed by TR-II in the Solanaceae
- Know that MecgoR is an aldo-keto reductase (AKR) and not an SDR, and that this is strong evidence for convergent evolution
- Understand the role of cocaine synthase in the biosynthesis of cocaine
- Know that cocaine synthase is an acyl-CoA dependent BAHD acyltransferase that uses benzoyl-CoA as a substrate
- Be able to identify the corresponding acylation step in the formation of tropane alkaloids in the Solanaceae
- Know that the acylation steps in the formation of tropane alkaloids in the Erythroxylaceae and Solanaceae is further evidence of convergent evolution
- Understand the basic role of cocaine as a central nervous system stimulant via the blocking of dopamine transport
- Understand the difference between cocaine hydrochlorine and cocaine free base, and why for recreational purposes the former can be smoked whereas the latter is snorted or injected

Purine alkaloids

- Know at least six different and unrelated plants of commercial importance that produce caffeine
- Recognize the canonical structure of a purine alkaloid
- Know the similarity and difference between caffeine and theobromine in terms of structure and pharmacological properties
- Understand purine alkaloid biosynthesis from xanthosine
- Now the primary metabolic origins of xanthosine in plants
- Understand the relationships among the N-methyltransferases involved in caffeine biosynthesis
- Be able to explain the evidence and the proposed mechanism for the convergent evolution of caffeine in several different plants
- Understand what happens to caffeine in your body

Pyrrolizidine alkaloids

- Be able to recognize a pyrrolizidine alkaloid
- Be able to identify and draw a necine base moiety

- Know at least two genera in which pyrrolizidine alkaloids are found (e.g. Myosotis [comfrey], Senecio, Eupatorium, Crotalaria)
- Know the major plant families in which pyrrolizidine alkaloids are found (i.e. Boraginaceae, Asteraceae, Fabaceae, Orchidaceae)
- Understand that the plant families containing pyrrolizidine alkaloids are taxonomically distant indicating convergent evolution
- Know that the primary metabolic origins of pyrrolizidine alkaloids involve the polyamines spermidine and putrescine
- Know that spermidine and putrescine are coupled by the enzyme homospermidine synthase (HSS) yielding homospermidine, which is a committed intermediate leading to the necine base
- Know that homospermidine undergoes two oxidative deaminations the result in cyclyzation and, thus, formation of the necine base
- Know that HSS was recruited from deoxyhypusine synthase (DHS), wich is found is all plants
- Know that DHS uses spemidine as a substrate, from which it transfers an aminobutyl moiety to the lysine residue of theeukaryotic transcription factor elF5A
- Know that both HSS and DHS can produce homospermidine, but only DHS activates elF5A
- Understand that the duplicated HSS gene lost the ability to activate elF5A, but retained the ability to produce homospermidine
- Understand that the duplication of the DHS to the HSS gene, the lost ability to activate elF5A, and the retained the ability to produce homospermidine evolved independently in several plant lineages
- Understand that pyrrolizidine alkaloids are extremely poisonous (i.e. liver, lung and blood vessel toxicity) to humans and livestock
- Understand that the toxic derivatives of pyrrolizidine alkaloids a produced metabolically in the liver by release of necine base derivatives and subsequent oxidation to harmful metabolites
- Know that pyrrolizidine alkaloids play an important demonstrated role in plant chemical ecology
- Know that the larvae of certain insects such as some moths feed on pyrrolizidine alkaloid-containing plants and store the toxic alkaloids as defense compounds
- Know that other moths select mates based on their content of pyrrolizidine alkaloids, which are transferred during mating
- Know that other insects use plant-produced pyrrolizidine alkaloids as to produce pheromones that serve as aphrodisiacs

Compartmentalization

- Know the anatomical location and general physiological roles for the following cell and/or tissue types: root endodermis, root pericycle, root cortex, leaf epidermis, palisade mesophyll, spongy mesophyll, laticifer, internal phloem associated parenchyma (IPAP) cells, phloem sieve element, phloem companion cell
- Know that PMT and H6H in tropane alkaloid biosynthesis are localized to root pericycle
- Know that TR-I is localized to root endodermis
- Know that TR-II is localized to root endodermis and inner root cortex
- Know that tropane alkaloids, calystegines and nicotine are produced in roots, but accumulate in shoots (especially leaves)
- Understand the implications of enzyme localization on the intercellular transport of pathway intermediates in tropane alkaloid biosynthesis
- Know that TDC, SLS, and STR (and other downstream enzymes involved in catharanthine and tabersonine biosynthesis) are localized to leaf epidermis
- Know that D4H and DAT, which catalyze the final two steps in the conversion of tabersonine to vindoline) are localized to leaf mesophyll idioblasts and laticifers
- Know that enzymes of the non-mevalonate pathway supplying the IPP used to make secologanin, and G10H and other iridoid biosynthetic enzymes, are localized to internal phloem associated parenchyma (IPAP) cells
- Understand the implications of enzyme localization on the intercellular transport of pathway intermediates in monoterpenoid indole alkaloid biosynthesis
- Know that HSS in pyrrolizidine alkaloid biosynthesis is differentially localized in different plant taxa, which is further evidence of the convergent evolution of pyrrolizidine alkaloids
- Know that HSS is localized to root epidermis and root cortex adjacent to the phloem in Senecio spp.

- Know that HSS is localized throughout the root cortex in Eupatorium spp.
- Know that Senecio and Eupatorium are related genera in the Asteraceae family
- Know that pyrrolizidine alkaloids are produced in roots, but accumulate in shoots (especially leaves)
- Understand the implications of enzyme localization on the intercellular transport of pathway intermediates in pyrrolizidine alkaloid biosynthesis
- Know that all BIA biosynthetic enzymes involved in the biosynthesis of thebaine are localized to phloem sieve elements in opium poppy
- Know that BIAs are transported to and accumulate in laticifers adjacent to sieve elements in opium poppy
- Know that the biosynthetic enzymes involved in the conversion of thebaine to morphine are localized in laticifers in opium poppy
- Understand the implications of enzyme localization on the intercellular transport of pathway intermediates in benzylisoquinoline alkaloid biosynthesis in opium poppy
- Know that benzylisoquinoline alkaloids in plant families related to opium poppy are produced in root endodermis and (apparently) shoot apical meristems and shoot cortex, rather than in phloem sieve elements and laticifers
- Understand that differential localization of biosynthetic enzymes and corresponding metabolites does not necessarily indicate convergent evolution

Glucosinolates

- Know the plant family (Brassicaceae) in which glucosinolates are primarily found
- Know the basic molecular components (aldoxime, thiol, glucose, sulfate) and general structure of a glucosinolate
- Be able to recognize the glucosinolate structure
- Know the primary metabolites that serve as precursors [amino acids methionine, phenylalanine, and tryptophan (R-group); (UDP)-glucose, glutathione (thiol); 3`-phosphoadenosine-5`-phosphosulphate (PAPS; sulfate group)] for the biosynthesis of glucosinolates
- Know the difference between aliphatic, aromatic and indole glucosinolates and their primary metabolic origins
- Know how an amino acid is converted to an aldoxime, and the general type of enzyme (cytochrome P450; CYP79 family) involved
- Know how a thiol sulfur is added to the aldoxime and the primary metabolic origin of the thiol sulfur (glutathione)
- Know that aldoxime is initially further oxidized to a nitrile oxide by a second cytochrome P450 from the CYP83 family
- Know that sulfur is donated to the nitrile oxide produced by a CYP83 from the aldoxime by glutathione S-transferase (GST) and that most of the glutathione is cleaved off by a C-S lyase
- Know that the final two steps in glucosinolate biosynthesis involve S-glycosylation and O-sulfation by specific glucosyltransferase and sulfotransferase enzymes
- Know that glucosinolates are stable and biologically inactive until the glucose moiety is cleaved by the enzyme myrosinase
- Know that myosinase is stored in specific cells of the Brassicaceae separate from the cells that store glucosinolates
- Know that tissue damage exposes the stored glucosinolates to myrosinase
- Know that the deglycosylation of glucosinolates results in the spontaneous conversion of the aglycone to a variety of biologically active compounds (isothiocyanates, thiocyanates, nitriles, epithionitriles oxazolidine-2-thiones) toxic to insects
- Know the glucosinolate (glucoraphanin) and the breakdown product of the corresponding aglycone (sulphoraphane) in broccoli and other vegetables that have been linked to cancer prevention
- Understand what is meant by the 'mustard oil bomb'
- Know the difference between S cells and M cells in glucosinolate-producing plants, where they are generally located, and their corresponding functions

Cyanogenic glycosides

- Know some of the major crop plants (cassava, sorghum, bitter almond, lima bean) that accumulate cyanogenic glucosides

- Know the basic molecular components (oxime, cyanogenic moiety, sugar) and general structure of a cyanogenic glucoside
- Be able to recognize the cyanogenic glucoside structure
- Know that hydrolysis of the sugar moiety destabilizes a cyanogenic glucoside and results in the release of cyanide
- Know that cyanide is a respiratory poison that inhibits cytochrome c reductase from passing electrons to molecular oxygen, which ultimately prevents the formation of ATP
- Know that cyanogenic glucoside biosynthesis involves the conversion of an amino acid to an aldoxime bu the same general type of enzyme (cytochrome P450; CYP79 family) involved in the first step of glucosinolate biosynthesis
- Know that dhurrin is the cyanogenic glucoside produced by sorghum
- Know that the amino acid precursor to dhurrin is tyrosine
- Know that the aldoxime in cyanogenic glucoside biosynthesis is further oxidized to a nitrile oxide by a second cytochrome P450 from the CYP71 family (and that this is different from the second cytochrome P450 family (CYP83) involved in glucosinolate biosynthesis
- Know that the final step in cyanogenic glucoside biosynthesis involved glucosylation by a glucosyltransferase
- Know that the CYP79, CYP71 and UGT enzymes have been shown to form a metabolon in sorghum
- Understand what structure and function of a metabolon
- Know that linamarin is the cyanogenic glucoside produced by cassava
- Know that the amino acid precursor to linamarin is valine

General

- Be able to recognize paradigms in plant specialized metabolism
- Recognize common enzyme types in different plant secondary metabolic pathways
- Understand the meaning of 'convergent evolution'