Undergraduate Certificate in Toxicology of Plants

Toxic Plant Metabolites

Alkaloids – nitrogen-containing secondary metabolites that often act on the nervous system. Related terms: pyrrolizidine alkaloids, indole alkaloids, quinolizidine alkaloids. Alkaloids are synthesized via amino-acid precursors such as tryptophan, tyrosine, or lysine and are stored in vacuoles or specialized cells. Classic examples include nicotine from Nicotiana tabacum, morphine from Papaver somniferum, and caffeine from Coffea arabica. In toxicology, alkaloids serve as model compounds for studying receptor binding, dose-response relationships, and metabolic activation. Practical applications involve using alkaloid profiles for species identification, developing pest-resistant crops, and exploring pharmacological leads. Challenges include complex stereochemistry, variable extraction efficiencies, and the need to distinguish toxic from therapeutic doses in human exposure assessments.

Anthraquinones – aromatic polyketide pigments derived from the shikimate pathway. Related terms: emodin, chrysophanol, alizarin. These compounds are produced by many Rubiaceae and Polygonaceae species and confer red, orange, or yellow coloration to roots, bark, and leaves. Anthraquinones such as senna glycosides are used as laxatives, while others like alizarin have historic textile-dye applications. Toxicologically, certain anthraquinones exhibit genotoxicity and hepatotoxicity after metabolic activation to quinone-imines. Their practical relevance includes monitoring herbal supplements for contaminant levels and evaluating environmental persistence of plant-derived dyes. Analytical challenges arise from strong UV absorbance that interferes with chromatographic detection and the need to differentiate closely related isomers.

Aflatoxins – a group of difuranocoumarin mycotoxins produced primarily by Aspergillus flavus and A. parasiticus that colonize crops such as maize, peanuts, and tree nuts. Related terms: B1, B2, G1, G2, M1. Although not a plant metabolite per se, aflatoxins are integral to plant toxicology because they result from fungal infection of plant tissues. Aflatoxin B1 is the most potent carcinogen, forming DNA adducts after metabolic activation by cytochrome P450 enzymes. Practical applications involve using rapid immunoassays for field screening, establishing regulatory limits, and developing resistant plant varieties through breeding or gene editing. Challenges include the high variability of contamination levels, climate-driven increases in fungal growth, and the need for sensitive multi-mycotoxin detection platforms.

Betalains – nitrogen-derived pigments that replace anthocyanins in the order Caryophyllales. Related terms: betacyanins, betaxanthins. Betalains are responsible for the vivid red-purple hues of beetroot (Beta vulgaris) and the yellow-orange colors of cactus fruits. They possess antioxidant activity and are marketed as natural food colorants. Toxicologically, betalains are generally regarded as safe, yet high concentrations can cause gastrointestinal irritation. Practical uses include employing betalain content as a chemotaxonomic marker and exploring their health-promoting properties in functional foods. Analytical challenges involve their

susceptibility to pH-dependent degradation and the need for stable extraction protocols that preserve both betacyanins and betaxanthins.

Cardiac Glycosides – steroidal metabolites that inhibit the Na^+/K^+-ATPase pump, leading to increased intracellular calcium and positive inotropic effects. Related terms: digitoxin, ouabain, bufadienolides. Classic sources include Digitalis purpurea (foxglove) and Strophanthus gratus. In toxicology, these compounds are studied for their narrow therapeutic index, arrhythmogenic potential, and mechanisms of acute poisoning. Practical applications encompass the development of digoxin-based heart medications, using plant extracts for wildlife management, and employing cardiac glycoside assays to assess environmental contamination. Challenges include the difficulty of quantifying low-level exposures, inter-individual variability in metabolism, and the risk of accidental ingestion of ornamental plants containing potent glycosides.

Cyanogenic Glycosides – plant-derived glucosides that release hydrogen cyanide (HCN) upon enzymatic hydrolysis. Related terms: amygdalin, linamarin, dhurrin. These compounds are widespread in legumes, rosaceous fruits, and certain grasses. When plant tissue is damaged, β-glucosidases cleave the glycoside, liberating HCN, which inhibits cytochrome c oxidase in mitochondria. Practical considerations include processing methods such as soaking, fermentation, or heat treatment to reduce cyanide content in food crops like cassava and almond kernels. Toxicological studies focus on acute cyanide poisoning, chronic exposure effects, and the role of endogenous detoxification pathways (e.g., rhodanese). Analytical challenges involve rapid volatilization of HCN, matrix interferences, and the need for simultaneous detection of both glycoside and free cyanide.

Diterpenes – a diverse class of C_{20} terpenoids synthesized via the methyl-erythritol phosphate (MEP) pathway. Related terms: resin acids, phorbol esters, forskolin. Diterpenes serve as defensive chemicals, growth regulators, and pharmaceutical leads. Notable toxic examples include phorbol esters from Jatropha curcas, which activate protein kinase C and act as tumor promoters. In contrast, forskolin from Coleus forskohlii is used therapeutically to raise intracellular cAMP. Practical applications involve using diterpene profiles for chemotaxonomy, developing bio-herbicides, and screening for novel anticancer agents. Challenges arise from structural complexity, low natural abundance, and the necessity of advanced spectroscopic techniques to resolve stereochemistry.

Ellagitannins – hydrolyzable tannins formed by the esterification of hexahydroxydiphenic acid to a glucose core, which upon hydrolysis yield ellagic acid. Related terms: punicalagin, castalagin, vescalagin. These compounds are abundant in pomegranates, oak woods, and certain berries. Ellagitannins exhibit antioxidant, anti-inflammatory, and antimicrobial properties, yet they can also bind dietary proteins and reduce nutrient digestibility. Toxicological interest centers on their ability to form urolithin metabolites after gut microbiota processing, some of which have been linked to hepatotoxicity in high-dose animal studies. Practical uses include employing ellagitannin content as a quality marker for fruit juices and investigating their role in plant-insect interactions. Analytical challenges involve the propensity of ellagitannins to undergo oxidation and the need for high-resolution mass spectrometry to distinguish isomeric forms.

Flavonoids – a large family of polyphenolic compounds derived from the phenylpropanoid pathway, characterized by a C_6-C_3-C_6 skeleton. Related terms: flavonols, flavones, anthocyanins. Flavonoids such as quercetin, kaempferol, and catechin contribute to UV protection, pigmentation, and defense against herbivores. In toxicology, flavonoids are studied for their capacity to modulate enzyme activity, act as antioxidants, and occasionally interfere with drug metabolism (e.g., inhibition of CYP3A4). Practical applications include using flavonoid fingerprints for cultivar authentication, developing nutraceuticals, and assessing plant stress responses. Challenges consist of extensive glycosylation patterns that complicate quantification, matrix effects in complex plant extracts, and the need to differentiate between beneficial and potentially pro-oxidant activities at high concentrations.

Fusarium Toxins – a group of mycotoxins produced by Fusarium species that infect cereals, legumes, and other crops. Related terms: deoxynivalenol (DON), fumonisins, zearalenone. These toxins can cause vomiting, immunosuppression, and endocrine disruption in humans and livestock. Although fungal in origin, Fusarium toxins are integral to plant toxicology because infection dynamics are influenced by plant defense metabolites. Practical approaches involve breeding Fusarium-resistant varieties, applying fungicides, and implementing post-harvest sorting based on toxin levels. Toxicological investigations focus on the synergistic effects of multiple Fusarium toxins and the role of plant-derived detoxifying enzymes (e.g., UDP-glucosyltransferases). Analytical hurdles include co-occurrence of several toxins, matrix complexity, and the need for multi-mycotoxin LC-MS methods with low detection limits.

Glycoalkaloids – steroidal alkaloids conjugated to sugar moieties, primarily found in Solanaceae species. Related terms: solanine, chaconine, tomatine. Glycoalkaloids protect plants against insects and pathogens but can be toxic to mammals, causing gastrointestinal distress, neurological symptoms, and cardiac arrhythmias at high doses. Practical relevance includes monitoring glycoalkaloid levels in potatoes, tomatoes, and eggplants to ensure food safety, and exploiting their antifungal properties for natural preservative development. Challenges involve variability of glycoalkaloid content due to cultivar, storage conditions, and processing methods, as well as the difficulty of distinguishing between the aglycone and glycosylated forms in analytical protocols.

Hormesis – a biphasic dose-response phenomenon where low concentrations of a toxic plant metabolite stimulate beneficial effects, while higher concentrations are inhibitory or lethal. Related terms: adaptive response, low-dose stimulation. Hormetic effects have been documented for compounds such as curcumin, resveratrol, and certain alkaloids. In toxicology education, hormesis illustrates the importance of dose in risk assessment and the potential for using sub-toxic levels of plant metabolites as therapeutic agents or growth promoters. Practical applications include designing low-dose dietary supplements and employing hormetic stressors to enhance plant resilience. Challenges lie in reproducibly defining the hormetic window, accounting for species-specific sensitivity, and avoiding misinterpretation of low-dose effects as universally beneficial.

Indole Alkaloids – a subclass of alkaloids derived from the indole precursor tryptophan, featuring a bicyclic indole core fused to various ring systems. Related terms: vincristine, strychnine, reserpine. These metabolites

are abundant in families such as Apocynaceae and Rubiaceae and display a wide range of pharmacological activities, including antineoplastic, anticholinergic, and adrenergic effects. Toxicologically, indole alkaloids provide valuable case studies for receptor binding specificity, metabolic activation (e.g., N-oxidation), and the management of narrow therapeutic indices. Practical uses encompass the extraction of vincristine from Catharanthus roseus for cancer therapy and the utilization of strychnine as a rodenticide. Challenges include the complex semi-synthetic pathways required for large-scale production, the risk of accidental exposure in laboratory settings, and the need for precise analytical standards to monitor trace levels in plant material.

Jatropha curcas Toxins – a collection of bioactive diterpenes, primarily phorbol esters, present in the seeds and other tissues of the biofuel plant Jatropha curcas. Related terms: curcins, jatrophine. These toxins inhibit protein kinase C, leading to inflammation, tumor promotion, and acute gastrointestinal toxicity when ingested. In toxicology curricula, Jatropha toxins illustrate the trade-off between renewable energy crops and food safety concerns. Practical applications involve detoxification strategies such as seed roasting, solvent extraction, or genetic engineering to suppress phorbol ester biosynthesis. Challenges comprise the high variability of toxin concentration among cultivars, the difficulty of completely removing phorbol esters from oilseed meals, and the potential environmental impact of residual toxins on non-target organisms.

Kava Lactones – kavalactones are lactone-containing phenylpropanoids found in the roots of Piper methysticum (kava). Related terms: kavain, methysticin, yangonin. Kavalactones exert anxiolytic and sedative effects by modulating GABAergic neurotransmission, yet high-dose or prolonged use has been linked to hepatotoxicity, possibly due to reactive metabolites or co-contaminants. Toxicological investigations focus on the metabolic pathways involving CYP2D6 and the role of oxidative stress. Practical considerations include standardizing kava extracts for safe consumption, developing analytical methods to detect adulterants, and assessing the risk of drug-herb interactions. Challenges involve the variability of kavalactone profiles across cultivars, the influence of extraction solvents on toxicity, and the need for clear regulatory guidelines distinguishing safe from hazardous preparations.

Lathyrism Toxins – neurotoxic β-N-oxalyl-L-α,β-diaminopropionic acid (β-ODAP) produced in certain Lathyrus species, notably the grass pea (Lathyrus sativus). Related terms: excitatory amino acid, glutamate agonist. β-ODAP mimics glutamate, overstimulating NMDA receptors and causing irreversible motor neuron damage, leading to spastic paralysis known as lathyrism. Toxicology studies use β-ODAP as a model for excitotoxic neurodegeneration and to evaluate dietary risk in regions where grass pea is a staple. Practical interventions include breeding low-β-ODAP varieties, implementing dietary diversification, and applying post-harvest processing (e.g., soaking) to reduce toxin levels. Challenges consist of maintaining agronomic performance while lowering β-ODAP, detecting low concentrations in mixed grain samples, and providing culturally acceptable alternatives in vulnerable populations.

Mycotoxins – a broad term encompassing toxic secondary metabolites produced by fungi that colonize plants. Related terms: aflatoxins, ochratoxin A, patulin. Mycotoxins can be hepatotoxic, nephrotoxic, immunosuppressive, or carcinogenic, and they often accumulate in stored grains, fruits, and nuts. In plant toxicology, mycotoxin studies intersect with plant defense chemistry, as host resistance genes can limit

fungal growth and toxin production. Practical applications include developing rapid field test kits, employing biological control agents (e.g., non-toxic strains of Trichoderma), and setting regulatory maximum residue limits. Analytical challenges arise from the coexistence of multiple mycotoxins, matrix interferences, and the need for high-throughput, multi-analyte detection platforms with low limits of quantification.

Naphthoquinones – aromatic quinone compounds derived from the shikimate pathway, characterized by a naphthalene core with two carbonyl groups. Related terms: juglone, plumbagin, lapachol. Naphthoquinones serve as allelopathic agents, antimicrobial compounds, and pigments. Juglone from black walnut (Juglans nigra) inhibits the growth of many neighboring plants, exemplifying chemical competition. Toxicologically, naphthoquinones can undergo redox cycling, generating reactive oxygen species that cause oxidative stress and cytotoxicity. Practical uses include employing juglone as a natural herbicide and exploring plumbagin derivatives for anticancer drug development. Challenges involve controlling environmental persistence, ensuring selective toxicity toward target species, and overcoming solubility limitations in formulation design.

Oxalates – inorganic salts of oxalic acid that accumulate in many plant tissues as calcium oxalate crystals. Related terms: raphides, soluble oxalate, crystal idioblasts. Oxalates are common in spinach, rhubarb, and members of the Araceae family. Ingestion of high oxalate loads can lead to renal stone formation, hypocalcemia, and gastrointestinal irritation. Toxicology curricula address oxalate metabolism, the role of gut microbiota in degrading oxalate, and the interaction between dietary calcium and oxalate absorption. Practical applications involve breeding low-oxalate cultivars, processing methods such as blanching to reduce soluble oxalates, and using calcium oxalate crystals as a defense mechanism against herbivory. Analytical challenges include distinguishing soluble from insoluble oxalate fractions and accurately quantifying low concentrations in complex plant matrices.

Pyrrolizidine Alkaloids – hepatotoxic alkaloids formed by the condensation of necine bases with necic acids. Related terms: senecionine, lycopsamine, riddelliine. These compounds are widespread in families such as Asteraceae, Boraginaceae, and Fabaceae. After metabolic activation by hepatic cytochrome P450 enzymes, pyrrolizidine alkaloids generate reactive pyrrolic intermediates that alkylate DNA and proteins, leading to veno-occlusive disease and carcinogenesis. Toxicological investigations focus on biomarker development (e.g., pyrrole–protein adducts), risk assessment for herbal medicines, and the impact of chronic low-dose exposure. Practical measures include screening honey, herbal teas, and dietary supplements for pyrrolizidine alkaloid content, and implementing good agricultural practices to minimize contamination. Challenges involve the structural diversity of necic acids, the requirement for high-resolution mass spectrometry to differentiate isomers, and the limited availability of reference standards.

Quinolizidine Alkaloids – a subclass of alkaloids featuring a quinolizidine ring system, predominantly found in the legume subfamily Papilionoideae. Related terms: lupanine, sparteine, cytisine. These alkaloids protect plants against insect herbivores but can cause neurotoxicity, respiratory depression, and cardiotoxicity in mammals at high doses. Toxicology case studies often cite lupin (Lupinus spp.) poisoning in livestock, where

lupanine accumulation leads to paralysis and death. Practical applications involve breeding low-alkaloid lupin varieties for human consumption, using quinolizidine alkaloids as lead compounds for nicotine-replacement therapies, and assessing environmental exposure risks. Analytical challenges encompass the detection of multiple alkaloid analogues within a single plant matrix and the need for chiral separation to distinguish active from inactive enantiomers.

Ricin – a type I ribosome-inactivating protein (RIP) found in the seeds of the castor bean plant (Ricinus communis). Related terms: ricin A-chain, ricin B-chain, castor oil. Ricin depurinates a specific adenine residue in the 28S rRNA, halting protein synthesis and causing cell death. In toxicology, ricin serves as a model for studying protein toxins, intracellular trafficking, and the development of antitoxin therapies. Practical considerations include strict handling protocols for ricin research, the use of castor oil as a non-toxic industrial product after thorough seed processing, and the potential for ricin as a bioterrorism agent. Challenges involve the high potency of ricin ($LD_{50} \approx 0.02\,mg\,kg^{-1}$ in humans), the difficulty of detecting low levels in complex matrices, and the need for rapid decontamination methods.

Saponins – amphiphilic glycosides composed of a hydrophobic aglycone (sapogenin) linked to one or more sugar chains. Related terms: triterpenoid saponins, steroidal saponins, hemolytic activity. Saponins can form complexes with cholesterol, leading to membrane disruption and hemolysis, which underlies their toxic properties. They are abundant in species such as Quillaja saponaria, Saponaria officinalis, and many legumes. Toxicological relevance includes their use as natural surfactants in vaccine adjuvants, their role in plant-insect interactions, and concerns over gastrointestinal irritation in high-dose dietary supplements. Practical applications involve exploiting saponin foaming properties in food formulations and employing them as eco-friendly pesticides. Analytical challenges stem from the diversity of sugar moieties, the need for both hydrophilic and lipophilic extraction steps, and the interference of saponins with protein-based assays.

Sesquiterpene Lactones – a class of C_{15} terpenoids featuring a lactone ring, commonly found in the Asteraceae family. Related terms: parthenolide, helenalin, guaianolides. These metabolites exhibit anti-inflammatory, cytotoxic, and allelopathic activities, often acting by alkylating cysteine residues in proteins (e.g., NF-κB inhibition). Toxicologically, sesquiterpene lactones can cause allergic contact dermatitis and, at high doses, gastrointestinal upset. Practical uses include developing anti-cancer leads from parthenolide, using helenalin as a natural herbicide, and applying these compounds as markers for chemotaxonomic classification. Challenges include their rapid oxidation upon exposure to air, the need for careful handling to prevent skin sensitization, and the difficulty of quantifying low-level constituents within complex plant extracts.

Tannins – polyphenolic polymers that can be classified as hydrolyzable (gallotannins, ellagitannins) or condensed (proanthocyanidins). Related terms: astringency, protein precipitation, antinutritional factors. Tannins protect plants by deterring herbivory and inhibiting microbial growth, yet they also reduce protein digestibility and interfere with mineral absorption in animals. In toxicology, tannins are examined for their dose-dependent effects, ranging from beneficial antioxidant activity to potential hepatotoxicity at excessive intake. Practical applications involve using tannin-rich extracts as natural preservatives, employing tannin

profiles for wine quality assessment, and breeding low-tannin varieties for improved feed quality. Analytical challenges include the polymeric nature of condensed tannins, which complicates accurate quantification, and the need for standardized assays to compare tannin activity across different plant sources.

Urushiol – a mixture of catechol derivatives with long, unsaturated alkyl side chains found in the sap of Toxicodendron species (e.g., poison oak, poison ivy). Related terms: allergic contact dermatitis, catechol lipids, sensitization. Upon skin contact, urushiol oxidizes to quinones that covalently modify epidermal proteins, triggering a delayed hypersensitivity reaction. Toxicological education emphasizes the molecular basis of sensitization, the role of oxidative stress, and the importance of early decontamination. Practical measures include public education on plant identification, development of barrier creams, and testing for urushiol content in commercial lacquer products derived from the same species. Challenges involve the variability of side-chain length that influences potency, the difficulty of removing urushiol from contaminated clothing, and the potential for cross-reactivity with other phenolic compounds.

Viscum album Toxins – a suite of bioactive compounds, chiefly viscotoxins (small cysteine-rich proteins) and lectins, produced by European mistletoe (Viscum album). Related terms: mistletoe extract, immunomodulation, cardio-inhibitory peptides. Viscotoxins exhibit cytotoxic and antiviral activities, while mistletoe lectins bind to cell-surface carbohydrates, stimulating immune responses. In toxicology, these proteins are studied for their dual role as potential anticancer agents and as sources of adverse reactions (e.g., anaphylaxis) when used in complementary therapies. Practical applications include standardized mistletoe extracts for adjunct cancer treatment and the use of viscotoxins as molecular tools to probe cell-surface glycosylation. Challenges involve batch-to-batch variability in natural extracts, the risk of unintended immunogenicity, and the need for rigorous clinical evaluation to substantiate therapeutic claims.

Xanthotoxin – also known as 8-methoxypsoralen, a furanocoumarin produced by several Apiaceae and Rutaceae species. Related terms: phototoxicity, PUVA therapy, psoralen. Xanthotoxin intercalates into DNA and, upon UVA exposure, forms covalent cross-links that inhibit DNA replication, a property exploited in photochemotherapy for skin disorders such as psoriasis. Toxicologically, accidental ingestion followed by sun exposure can cause severe skin burns (phytophotodermatitis). Practical considerations include the controlled use of xanthotoxin in PUVA treatment, monitoring of natural plant sources to prevent accidental poisoning, and the development of topical formulations with precise dosing. Challenges consist of balancing therapeutic efficacy with the risk of mutagenesis, ensuring uniform UVA exposure, and mitigating variability in xanthotoxin content among wild plant populations.

Yew (Taxus) Taxines – a group of diterpenoid alkaloids responsible for the cardiotoxicity of yew species (Taxus baccata, T. brevifolia). Related terms: taxine A, taxine B, arrhythmogenic compounds. Taxines block voltage-gated calcium channels and disrupt cardiac conduction, leading to ventricular arrhythmias and sudden death. In toxicology, yew poisoning serves as a classic example of plant-derived cardiac toxins and illustrates the importance of rapid identification and supportive care. Practical applications include the extraction of paclitaxel (taxol) from yew bark for anticancer therapy, while ensuring safe handling to prevent

accidental exposure to taxines. Challenges involve the low concentration of taxines in foliage, the potential for cross-contamination during horticultural work, and the need for reliable analytical methods capable of detecting trace amounts in biological samples.

Zearalenone – a resorcylic acid lactone mycotoxin produced by several Fusarium species, commonly contaminating corn, wheat, and barley. Related terms: estrogenic activity, reproductive toxicity, zearalenone metabolites. Zearalenone mimics estrogen, binding to estrogen receptors and disrupting endocrine function, which can lead to infertility, reduced litter size, and feminization of male livestock. Toxicological studies focus on its metabolic conversion to α-zearalenol (more potent) and β-zearalenol (less potent), as well as the interaction with other mycotoxins. Practical measures include routine screening of feed, use of adsorbent feed additives to reduce bioavailability, and breeding for Fusarium-resistant crop varieties. Analytical challenges stem from the presence of multiple stereoisomers, matrix interferences in grain samples, and the need for sensitive LC-MS/MS methods to comply with stringent regulatory limits.