Al-Mustaqbal University College
Department of Pharmacy
5th stage
Clinical Toxicology
Lecture: 5

Herbal Products Toxicity

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Herbal Products

- ✓**Herbal products are medicine derived from plants.**
- ✓**They are used as supplements to improve health and well being, and may be used for other therapeutic purposes.**
- ✓**Herbal products are available as:**
  1. **Tablets**
  2. **Capsules**
  3. **Powders**
  4. **Extracts**
  5. **Teas & So On**

Is It Safe?

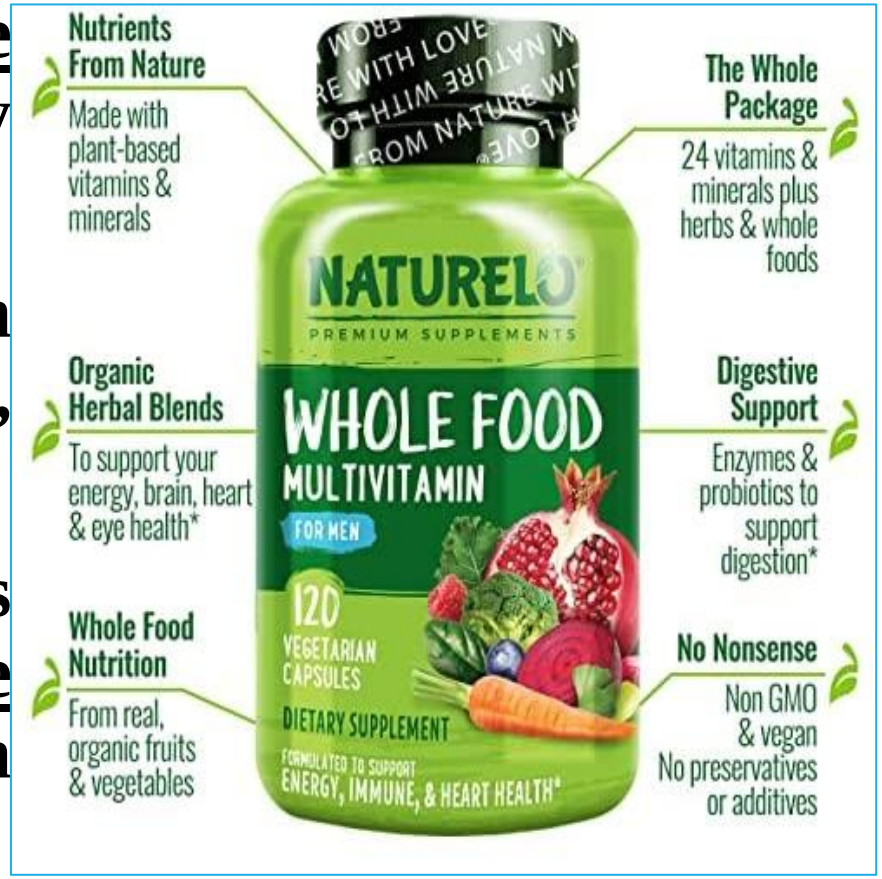
- ✓**Herbal medicines are thought to be safe as it is natural.**
- ✓**But in fact it can cause serious adverse effects and interaction with other drugs and supplements.**
- ✓**Less than 10% of herbal products in the world market are truly standardized to known active components.**

Herbal Products Hazards

- ✓For **majority** of these products in use, **very little** is known about their **active and/or toxic** constituents.
- ✓In many countries including the U.S, herbal medicines are **not subjected** to the same regulatory standards in terms of **efficacy & safety**.
- ✓In addition, many plants produce **toxic secondary metabolites**.

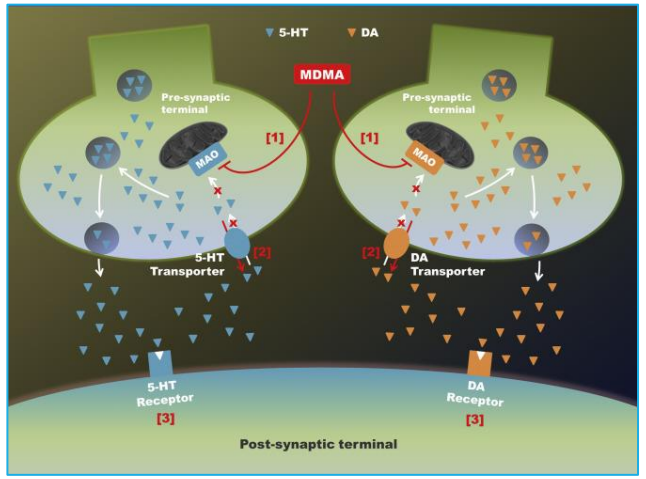
Excessive Use

- ✓Herbal products are **misused** in **excessive doses** or in **combinations** **without** any known **rationale**.
- ✓**Multi-ingredient** products may contain mixtures of **10 or more** different plants, vitamins, or minerals.
- ✓The **consumption** of many different herbs increases the risk of **toxicity** from **any one** of them or from their **interactions** with each other.

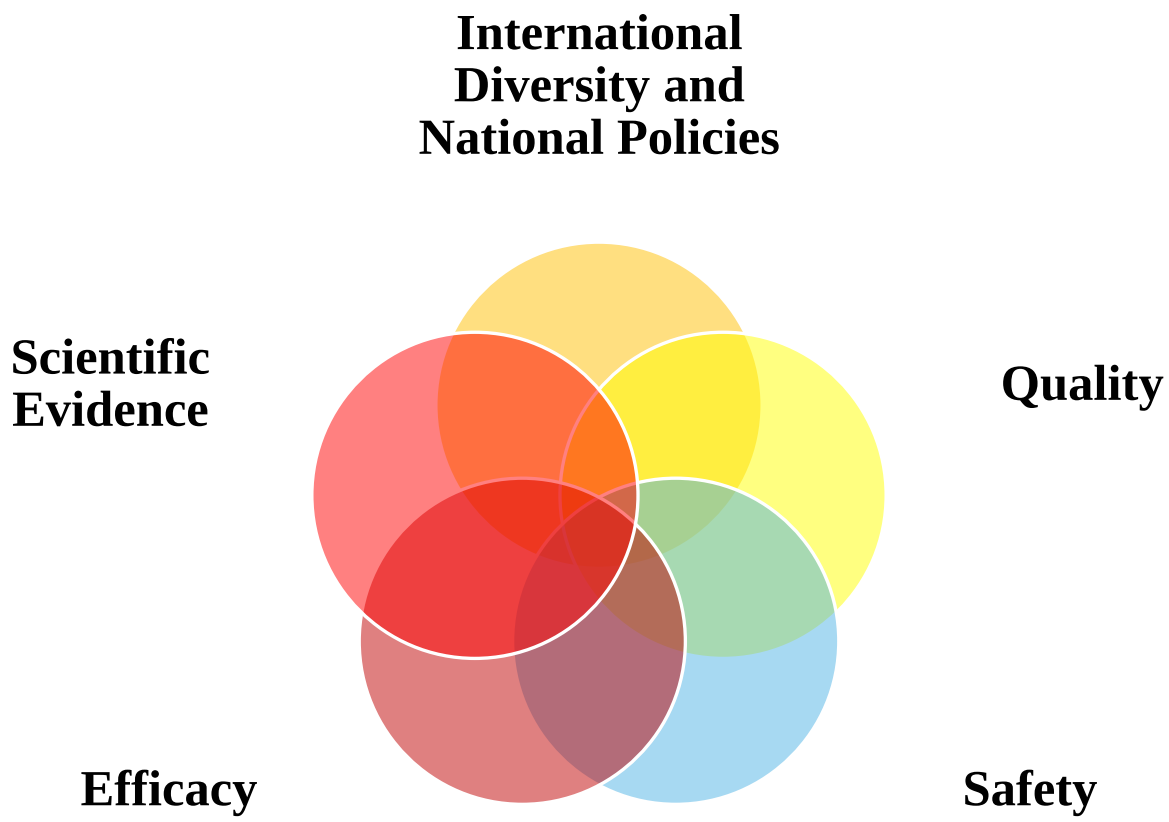


Inappropriate Use

- ✓Herbal products are marketed as “safe”
- ✓ecstasy (MDMA) alternatives(The popular nickname Molly), delivering a “natural” state of euphoria & alertness.
- ✓Caffeine, & ephedra are popular as nonprescription products promoted as dietary aides or as mild stimulants.
- ✓Adolescents & young adults may be more than willing to experiment with such herbs to improve their alertness before a test in school or their athletic performance.



Herbal Products Challenges



Contamination

- ✓Some herbal products contain high concentrations of heavy metals, such as lead, mercury, and arsenic.
- ✓Use of herbal medications should awaken suspicion of lead contamination.
- ✓Chinese herbal medications have been an incredible source of contamination.
- ✓One study showing that, out of 247 traditional Chinese medicines investigated, a proportion were contaminated with arsenic (5-15%), lead (5%), and mercury (approximately 65%).

Adulteration

- **Adulteration is the intentional introduction of extraneous ingredients into a product.**
- **The objects of such adulteration include drugs for clinical effectiveness, industrial dyes to modify appearance and substitution to enhance quantities.**
- **Some herbal preparations have been found to be adulterated with drug ingredients, For example, Caffeine, Acetaminophen, Hydrochlorothiazide, Ephedrine, & Chlorpheniramine.**

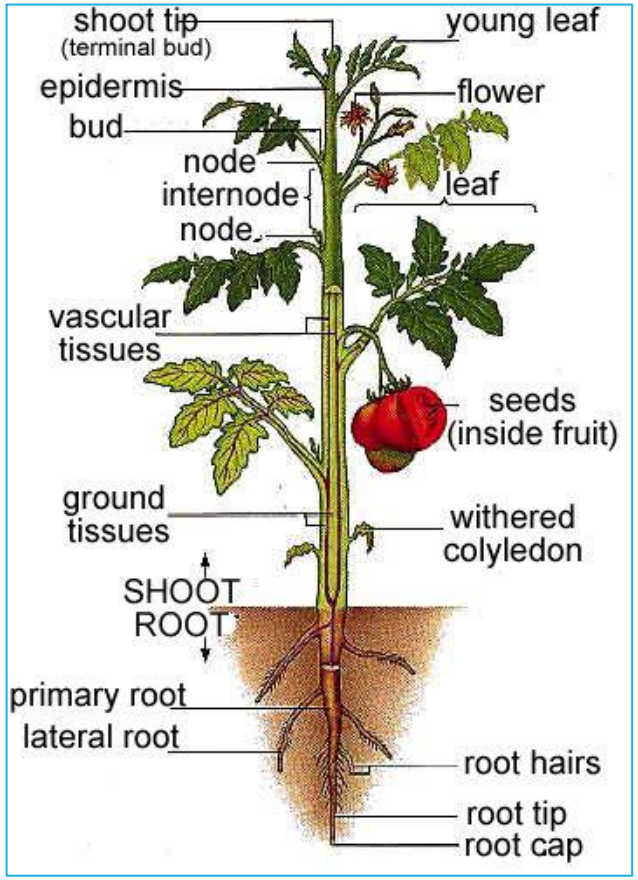
Herbal Toxicity
Etiology

Toxicity effects from herbal preparations can be classified into the following 4 types:

1. **Type A: Pharmacologically predictable, dose dependent, and preventable by dose reduction**
2. **Type B: Idiosyncratic, pharmacologically unpredictable, toxicity not correlated with dose, often immunologically mediated, often serious and potentially fatal.**
3. **Type C: Developed over long-term therapy, well-described, and may be anticipated.**
4. **Type D: Delayed effects (eg, carcinogenicity, teratogenicity).**

Herbal Sources

- ✓**Herbal product is constituted in general from leafy green or flowering parts of a plant (either fresh or dried).**
- ✓**Also seeds, bark, roots and fruits are another sources.**
- ✓**While many herbal products are harmless or possess minimal toxicity, some contain toxic ingredients that may not be identified on the label.**



HERBAL TOXICITY

✓**These unidentified ingredients may be unintentionally included in the product for example:**

1. **Misidentification of a toxic plant as a desired non-toxic plant**
2. **Or contamination with pesticide residues or heavy metals**
3. **Or introduced for increased effect (e.g addition of a pharmaceutical agent to the herbal preparation).**

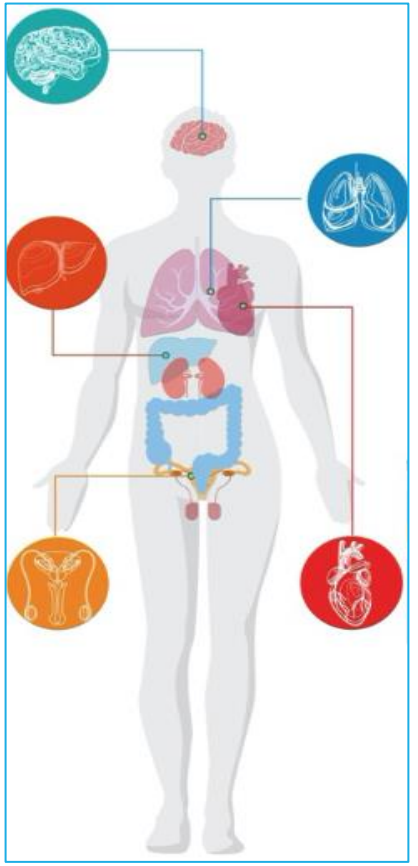
Herbal Toxicity

- ✓**Dietary supplements, including herbal products, are regulated as a food product, thus does not require to be effective or safe prior to marketing.**
- ✓**The US Food and Drug Administration (FDA) has little control over the marketing of herbal products, but may prohibit sales of herbal products containing pharmaceutical agents.**
- ✓**The FDA also may prohibit sale of an herbal product proven to have serious or unreasonable risk under conditions of use on the label or as commonly consumed.**

HERBAL TOXICITY PHATHOPHYSIOLOGY

✓**Herbal products are generally heterogeneous, may produce multiple effects, and may affect multiple organ systems, including:**

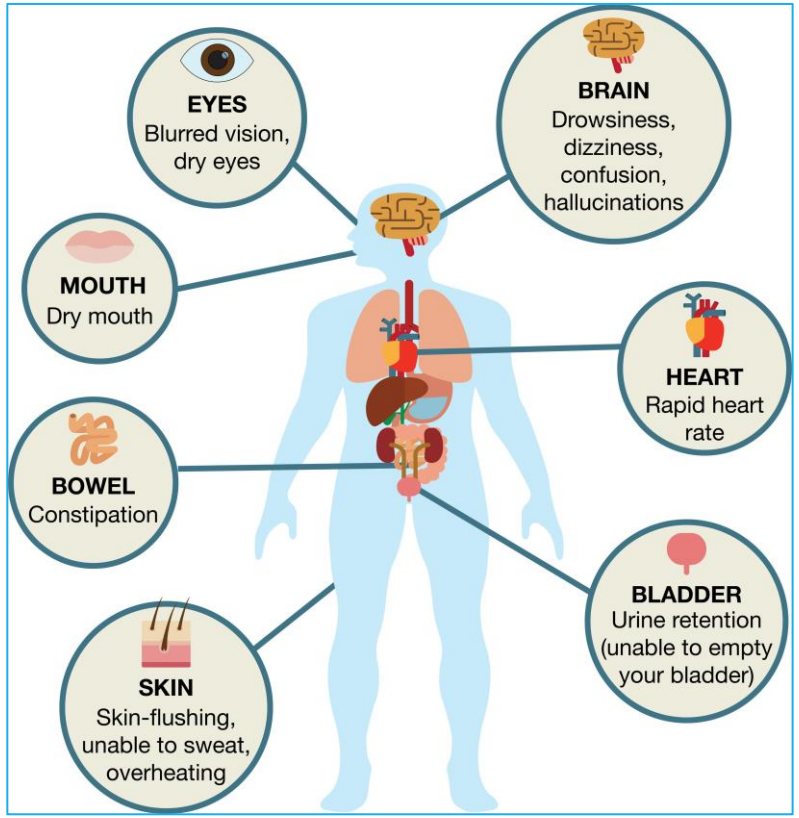
- ❖ **Nervous system**
- ❖ **Cardiovascular system**
- ❖ **Gastrointestinal tract**
- ❖ **Hepatic and renal systems**
- ❖ **Hematologic system**



CNS TOXICITY

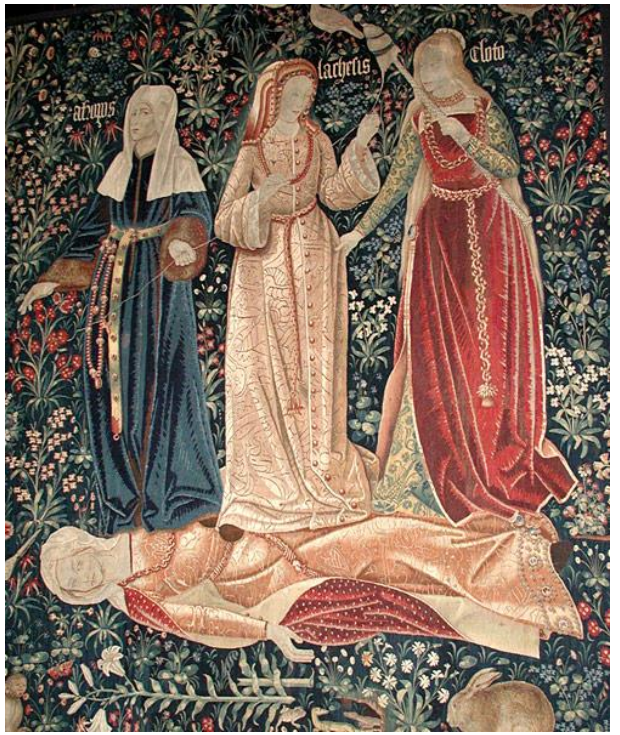
Several herbal products can produce anticholinergic symptoms as

- ***Atropa belladonna***
- ***Datura stramonium***
- ***Hyoscyamus niger***



Atropa belladonna

- ✓**The name of the plant comes from the Greek word "Atropos" and refers to one of the three Fates in Greek mythology, who cut the thread of life. "Bella-donna" is an Italian phrase meaning "beautiful lady."**
- ✓**This name was given to the plant because the ladies of Venice used Atropa Belladonna as a cosmetic (due to the mydriasis caused by its use).**



Atropa belladonna

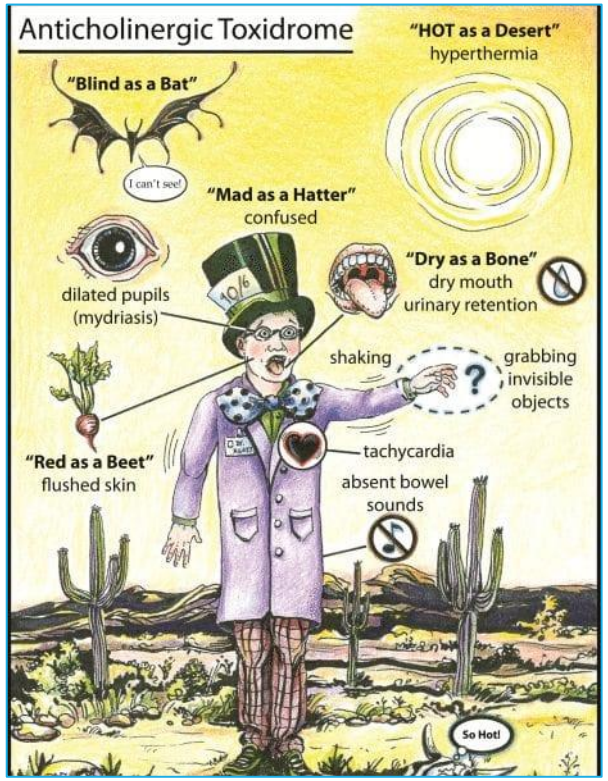
- ✓ **The alkaloids present in *Atropa belladonna* have toxic anti-cholinergic effects on the body.**
- ✓ **The anti-cholinergic toxidrome affects both central and peripheral nervous system, causing acute delirium, hallucination, tachycardia, dry mouth, flushed skin, vomiting and blurry vision.**

Datura stramonium

- ✓ ***Datura stramonium*** **is one of the widely well known folklore medicinal herbs.**
- ✓ **The troublesome weed, *D. stramonium* is a plant with both poisonous and medicinal properties.**
- ✓ ***D. stramonium*** **has been scientifically proven to contain alkaloids, tannins, carbohydrates and proteins.**
- ✓ **This plant has contributed various pharmacological actions like analgesic and anti-asthmatic activities.**

Datura stramonium

- ***Datura stramonium*** **is a widespread annual plant, containing atropine, hyoscyamine, and scopolamine.**
- **It can produce poisoning with a severe anticholinergic syndrome.**
- **Teenagers ingest the roots, seeds or the entire plant to obtain its hallucinogenic and euphoric effects.**



Hyoscyamus niger

- ✓**Black henbane** (BH) or ***Hyoscyamus niger***, has been described in all traditional medicines.
- ✓It applies as a **herbal medicine**, but may induce **intoxication** <u>accidentally</u> or <u>intentionally</u>.
- ✓**All** part of BH including <u>leaves</u>, <u>seeds</u> and <u>roots</u> contain some **alkaloids** such as Hyoscyamine, Atropine, Tropane and Scopolamine.

Hyoscyamus niger

✓**Clinical manifestations of acute BH poisoning are very wide which include but not limited to:**

- **Mydriasis, tachycardia, arrhythmia, agitation, convulsion and coma.**
- **Drowsiness, hyperreflexia, auditory, visual or tactile hallucinations, confusion, disorientation, delirium, and aggressiveness.**

Piper methysticum

- ✓**Kava-kava (*Piper methysticum*) is a herbal preparation that may be fermented into a beverage.**
- ✓**Methysticine and kawain (a local anesthetic) are its main constituents.**
- ✓**However, primary effects of kava-kava are anxiolytic, myorelaxant, and sedation.**

Piper methysticum

✓**Milder adverse effects are more common, including:**

- ❖ **Changes in vision, mydriasis, and disturbances in eye tracking.**
- ❖ **As well as impaired motor reflexes and rare difficulties in motor coordination, including choreoathetosis.**
- ❖ **This herbal preparation has also been associated with hepatotoxicity.**

Lobelia inflata

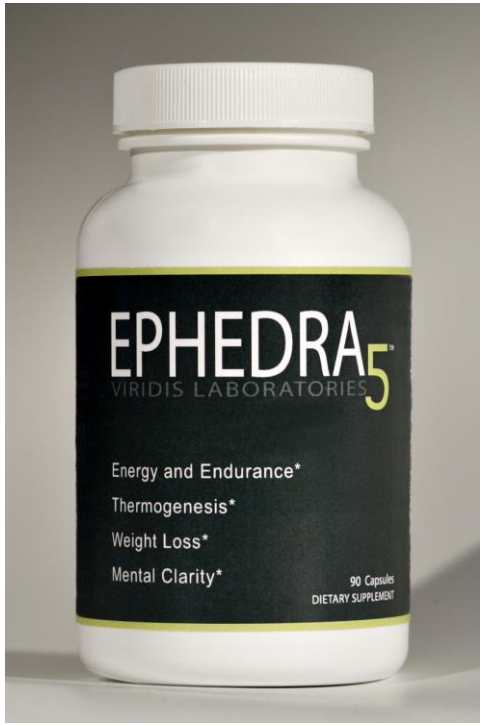
- ✓ ***Lobelia inflata*** **(Indian tobacco) contains lobeline and other pyridine alkaloids.**
- ✓ **It has been used as an emetic, antidepressant, respiratory stimulant.**
- ✓ **Also it aids to smoking cessation, and a treatment for methamphetamine abuse.**

Lobelia inflata

- ✓ ***Lobelia inflata*** **products can cause toxicity with and CNS excitation.**
- ✓ **Severe cases may progress to neuromuscular paralysis.**

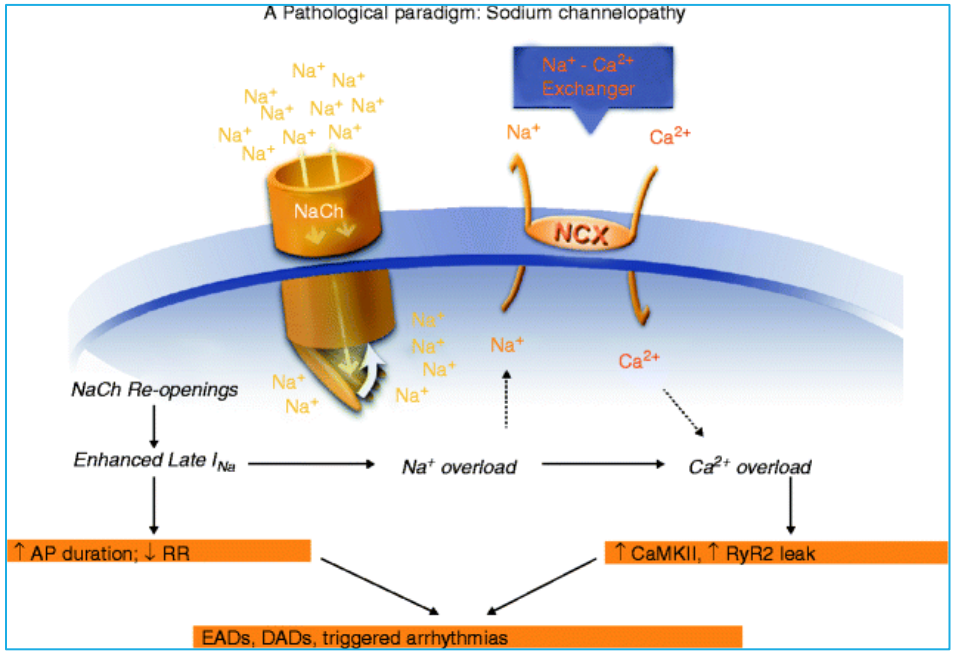
CVS TOXICITY

- ✓**Cardiac glycosides** and other cardioactive steroid contaminants may cause toxicity e.g. ***Digitalis lanata*.**
- ✓**Ephedra** and **ephedrine-containing** products may produce cardiac stimulation, hypertension, peripheral vasoconstriction, chest pain, myocardial infarctions, and intracerebral hemorrhage.



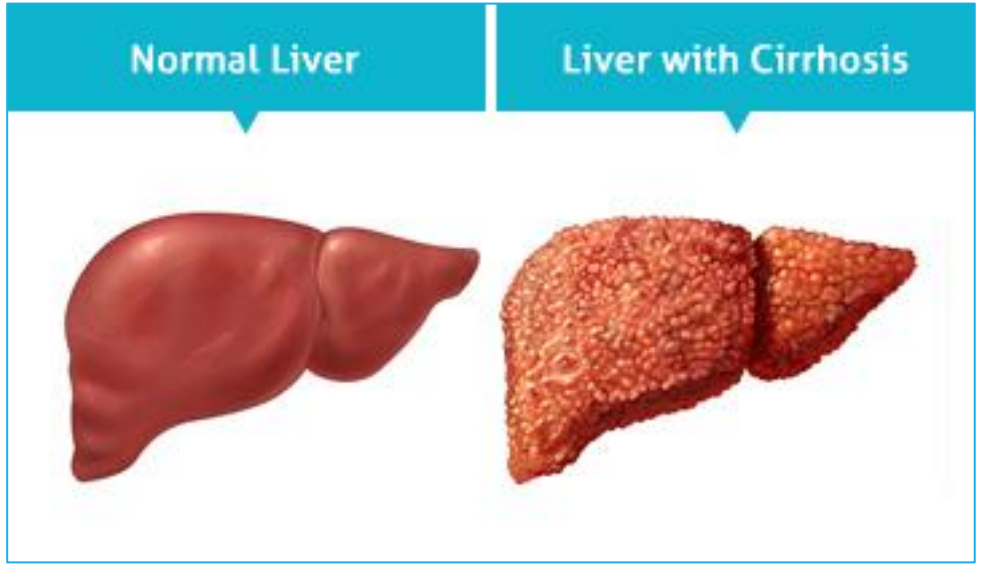
CVS TOXICITY

- ✓ ***Aconitum species*** **(contain aconitine) and *Veratrum species* (contain veratrum alkaloids).**
- ✓ **These toxins open sodium channels in cardiac myocytes, resulting in conduction blockade, bradycardia, ventricular dysrhythmias and cardiovascular collapse.**



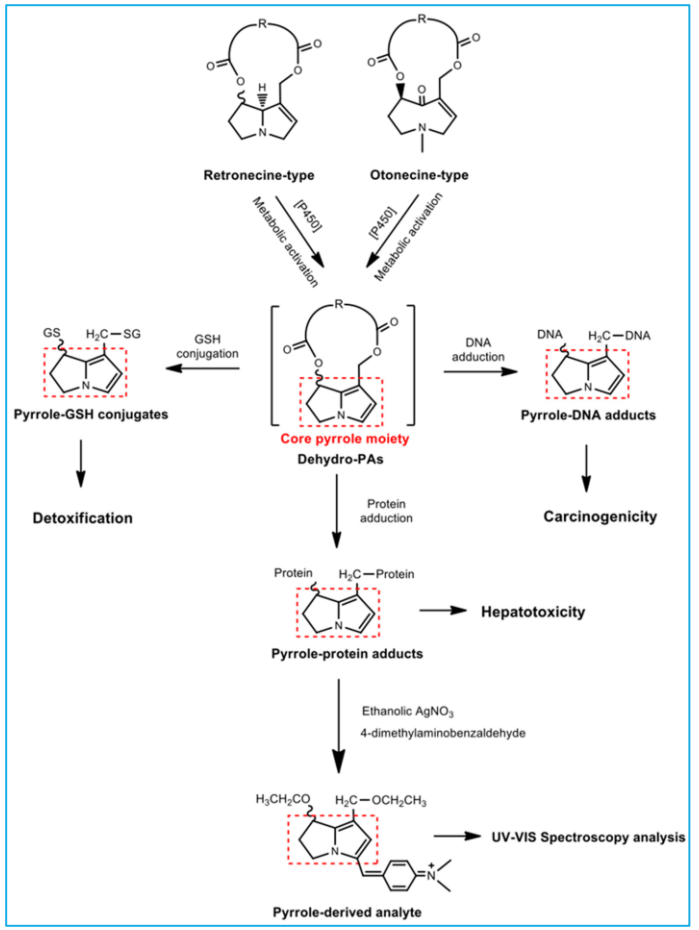
HEPATIC TOXICITY

- ✓**Hepatic toxicity has been reported with pyrrolizidine alkaloids, which are metabolized to alkylating agents that produce hepatomegaly and cirrhosis.**
- ✓**Plants that contain these substances include *Heliotropium, Senecio*, and *Symphytum*.**
- ✓**Some preparations have caused fatal hepatic injury.**



HEPATIC TOXICITY

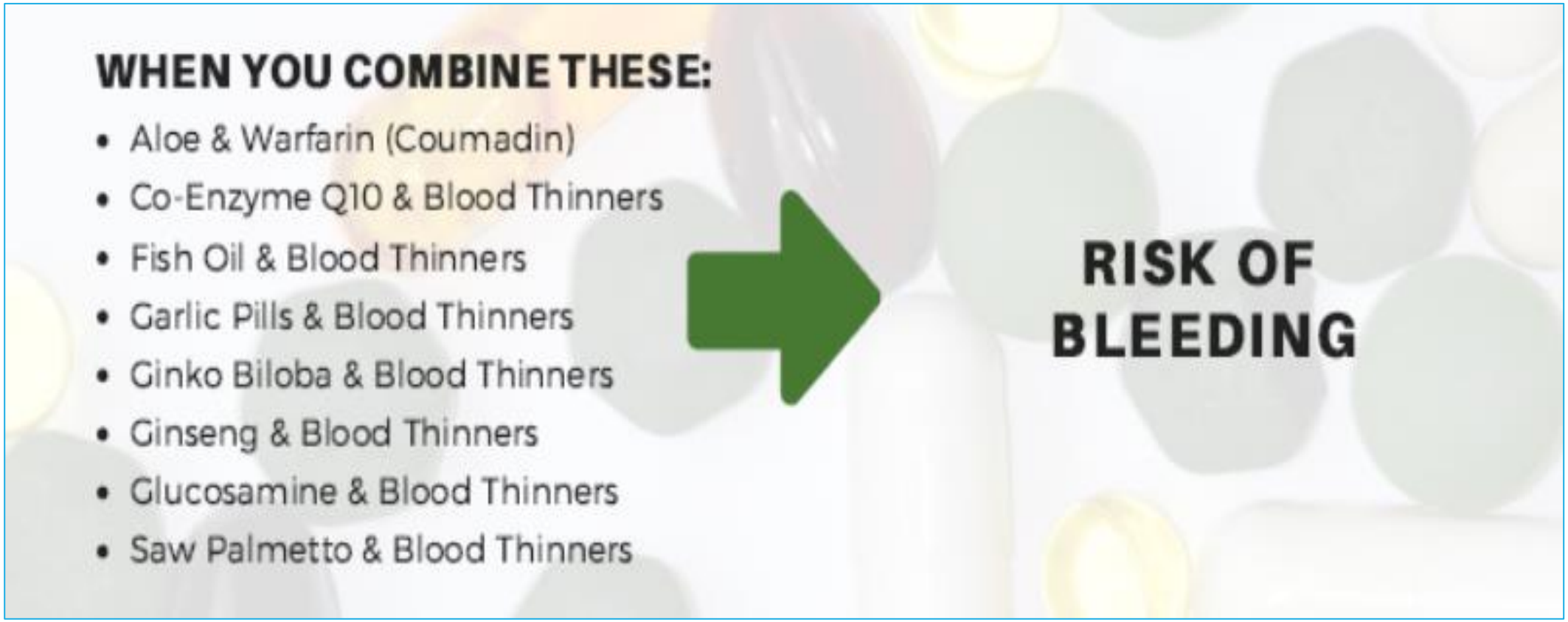
- ✓**Toxic PAs require metabolic activation, catalyzed by cytochrome P450 isozymes in the liver, to form dehydropyrrolizidine alkaloids (dehydro-PAs).**
- ✓**Dehydro-PAs are biologically reactive and rapidly bind to cellular proteins and DNA to form pyrrole–protein adducts and pyrrole–DNA adducts, leading to hepatotoxicity and carcinogenicity.**
- ✓**Besides, dehydro-PAs can also react with the reduced form of glutathione (GSH) to generate pyrrole–GSH conjugates, which are rapidly excreted out of the body.**



HEMATOLOGICAL TOXICITY

- ✓**Ginkgo biloba** has been reported to **increase bleeding times** and may have contributed to **intracranial hemorrhages**.
- ✓**Yohimbine** use has been associated with **agranulocytosis**.
- ✓Other herbal medication, has been associated with **thrombocytopenia**.

HEMATOLOGICAL TOXICITY



PHYSICAL EXAMINATION

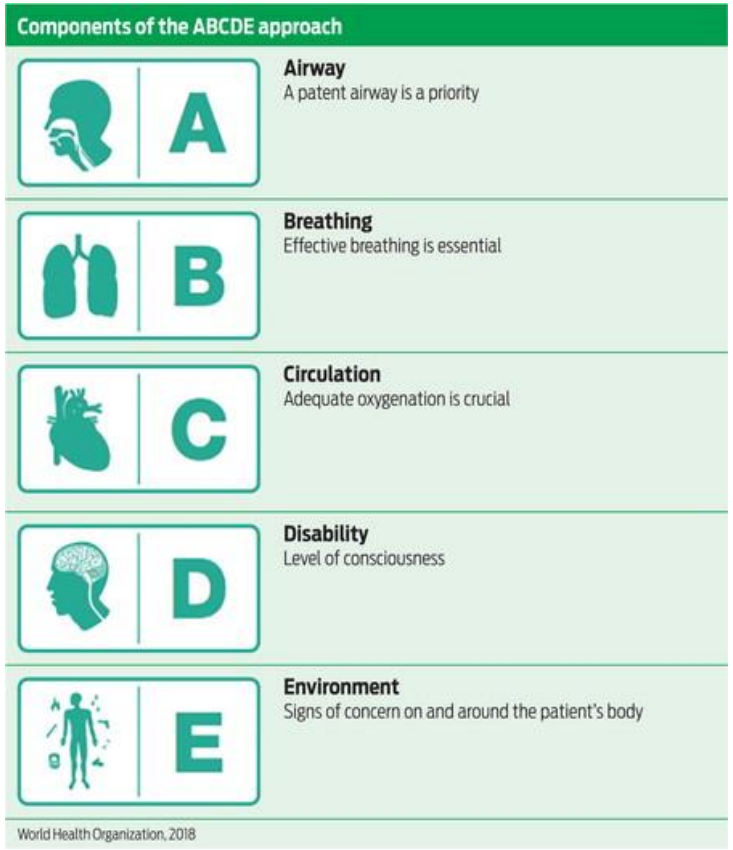
✓**Evaluate the patient for the following:**

1. **Anticholinergic syndromes (ie, mydriasis, dry mucous membranes and axilla, urinary retention, tachycardia, disorientation, hallucinations).**
2. **Cardiac dysrhythmias (suspect cardiac glycoside or aconitine toxicity)**
3. **Hepatomegaly and jaundice (suspect pyrrolizidine alkaloids and herbal teas)**

HERBAL TOXICITY TREATMENT

✓**As with any poisoned case the following steps are essential:**

1. **Supportive care including stabilization of the airway, assess respiration, and initiate respiratory assistance**
2. **Assess blood pressure and pulse; initiate advanced cardiac life support (ACLS) resuscitation.**



HERBAL TOXICITY TREATMENT

3. **Decontamination with activated charcoal may be considered in patients who present shortly after (within 1 hour) a potentially toxic herbal preparation ingestion.**

✓ **However, it carries the risk of vomiting and charcoal aspiration pneumonitis and should not be used for non-toxic ingestions.**

HERBAL TOXICITY TREATMENT

4. **Antidotal therapy may be indicated following ingestion of specific herbal preparations, including:**

- ✓ **Consider anti-digoxin antibodies in patients with severe cardiac glycoside toxicity from an herbal preparation.**
- ✓ **N-acetylcysteine should be administered for hepatotoxicity from pennyroyal oil**
- ✓ **Physostigmine may be used both diagnostically and therapeutically for anticholinergic toxicity from belladonna alkaloid preparations**
- ✓ **Chelation may be indicated for heavy metal poisonings**

THANK YOU
FOR YOUR ATTENTION