Plants toxicity

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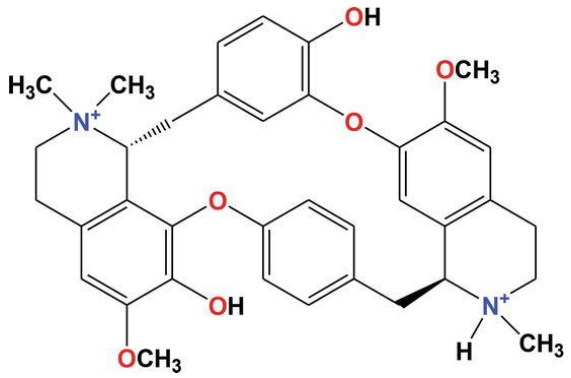
- Approximately 5% of all human exposures reported to poison control centers involve plants.

- The large number of exposures probably occur because plants are so accessible and attractive to youngsters.

- Approximately 80% of these cases involve individuals younger than 6 years.

- Many different plants contain pharmacologically active substances that cross the blood-brain barrier or could effect different organs

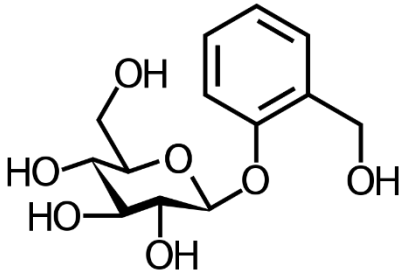
- **The major groups of concern in plants are as follows**:



1-Alkaloids: Molecules contain nitrogen, usually in a heterocyclic structure.

2-Glycosides: Organic compounds that yield a sugar derivative (the glycone) and a nonsugar moiety (the aglycone) upon hydrolysis.

- The aglycone is the basis of subclassification into saponin or steroidal glycosides and others such as salicin.



3-Terpenes and resins: Assemblages of 5-carbon units (isoprene unit) with many types of functional groups (eg, alcohols, phenols, ketones, and esters) attached. This is the largest group of secondary metabolites; approximately 20,000 are identified.

4-Proteins, peptides, and lectins:

- Lectins are glycoproteins like galactosamines, toxalbumins (eg, ricin).
- These components tend to be neurotoxins, hemagglutinins, or cathartics.

PLANTS CONTAINING ATROPINE AND RELATED ALKALOIDS

- Many members of the Solanaceae family contain the anticholinergic alkaloids.
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- Atropine is the primary alkaloid in *Atropa belladonna* . It acquired the name belladonna during the Italian Renaissance when women used it to beautify their eyes by enlarging their pupils.

- The foliage and berries are extremely toxic, containing tropane alkaloids. These include atropine, scopolamine and hyoscyamine,

- The seeds and unripe fruits contain hyoscyamine.
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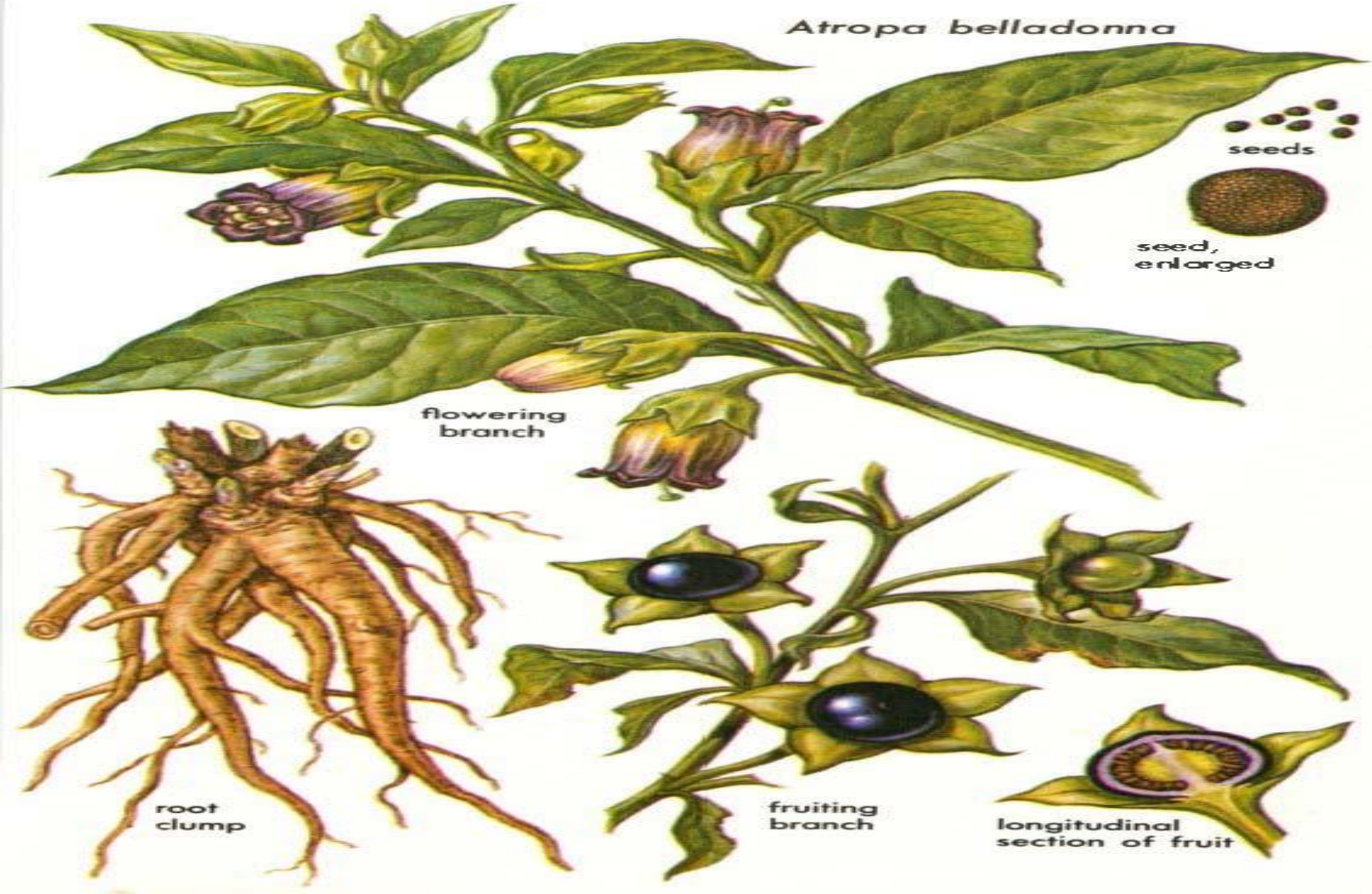
- **Anticholinergic: Belladonna Alkaloids**
- The belladonna alkaloids have potent antimuscarinic effects, manifested by tachycardia, hyperthermia, dry skin and mucous membranes, skin flushing, diminished bowel sounds, urinary retention, agitation, disorientation, and hallucinations

FIGURE 118–1. Jimsonweed (*Datura stramonium*) initially has a showy


Atropa belladonna
seeds
seed, enlarged
flowering branch
root clump
fruiting branch
longitudinal section of fruit

- Ingestion of ripe berries from ***Cestrum diurnum*** **and** ***Cestrum nocturnum*** has resulted in poisonings

- Solanine, an alkaloid with gastrointestinal (GI) toxicity, is the predominant alkaloid in unripe berries, while atropine predominates in ripe berries.

- The major alkaloid in *Hyoscyamus niger* is l-hyoscyamine.

- Scopolamine is the predominant alkaloid in *Mandragora officinarum*

- Atropine and its related alkaloids are muscarinic receptor antagonists that block the binding of acetylcholine to muscarinic cholinergic receptors in smooth muscle, cardiac tissue, gland cells, autonomic ganglia, and the CNS.

- Scopolamine penetrates more readily into the CNS, resulting in drowsiness, euphoria, disorientation, hallucinations, delirium, and amnesia at lower doses.

- Atropine is less likely to produce CNS effects with therapeutic doses.

Treatment

- Treatment consists of supportive care, GI decontamination with activated charcoal

- benzodiazepines therapy with physostigmine (Physostigmine, an acetylcholinesterase inhibitor, causes acetylcholine to accumulate at the cholinergic receptor.

- Physostigmine reverses both peripheral and central anticholinergic effects

- **Cholinergic Alkaloids: Arecoline, Physostigmine, and Pilocarpine**
- **Betel nut chewing**, also called **betel quid chewing** or **areca nut chewing** has been a habitual practice in the tropical Pacific, Asia and East Africa.

- The “quid” consists of betel nut (*Areca catechu) and other ingredients.*

- *The effects of acute exposure to arecoline, the major alkaloid, include sweating, salivation, hyperthermia, and rarely death.*
- *Prolonged use is linked to dental decay and oral cancer.*

- *Physostigmine is an alkaloid derived from the Calabar bean (Physostigma venenosum), where it is present in concentrations of 0.15%*

- *Pilocarpine is derived from Pilocarpus jaborandi from South America.*

- *Its stimulatory effects on muscarinic receptors have proven valuable in the treatment of glaucoma.*

- *Reversal of toxicity can be achieved by atropine.*

- **Nicotine and Nicotinelike Alkaloids: Nicotine, Anabasine, Lobeline, Sparteine, *N-Methylcytisine, Cytisine, and Coniine***
- Nicotine toxicity occurs via ingestion of leaves of *Nicotiana tabacum, cigarettes and their remains,*

- Overstimulation of the nicotinic receptors by high doses of the alkaloid produces nicotinism, a toxidrome that progresses from gastrointestinal symptoms to diaphoresis, tachycardia, hypertension, hyperthermia, seizures, respiratory depression, and death

STIMULANT PLANTS

- Plants with stimulant properties cause symptoms ranging from anxiety and insomnia to seizures followed by CNS depression.

- The *Cicuta* species Common names include water hemlock.

- The toxic alkaloid cicutoxin is present in all parts of the plant but is concentrated in the roots.

- Death has occurred following ingestion of a small piece of the root. The overall mortality rate in the reported cases of water hemlock poisoning is close to 30 per cent.

- The toxic constituent of water hemlock, cicutoxin, is an unsaturated aliphatic alcohol that produces toxicity by

✓ central cholinergic stimulation.

✓ Seizures are the most serious manifestation.

- *Strychnos nux vomica* contains strychnine and brucine, which cause tetanic muscle contractions, which may be mistaken for seizures.
- Plants used as stimulants in herbal medicine often contain either ephedrine, caffeine, or similar ingredients.

- Catha edulis (khat), which contains norpseudoephedrine

- and Ephedra nevadensis (Mormon tea), which contains ephedrine, can cause euphoria, insomnia, anorexia, tachycardia, hypertension, and mydriasis.

- Similar clinical effects are produced by the caffeine and theobromine in Cola nitida (kola nut, botu cola).

- **Emetine/Cephaline, Strychnine/Curare**

- Emetine and cephaline are derived from Cephaelis ipecacuanha, a tropical plant native to the forests of Bolivia and Brazil.

- They are the principal active constituents in syrup of ipecac, which produces emesis.

- Chronic use of syrup of ipecac, typically by patients with eating disorders has caused cardiomyopathy, smooth muscle dysfunction, myopathies, electrolyte, and acid–base disturbances related to excessive vomiting, and death.

- Curare was used as an arrow poison derived from plants of the genus *Strychnos*

- The convulsant strychnine and brucine are major alkaloids.

- The seeds of Strychnos nux-vomica are especially rich in strychnine, which causes muscular spasms and rigidity by antagonizing glycine receptors in the spinal cord and brain stem.

- Strychnine interferes with the postsynaptic binding of glycine result is a loss of motor inhibition in parts of the brainstem and spinal cord.

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- Hypoxia results from diaphragmatic or respiratory muscle paralysis.
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Treatment

- Treatment consists of supportive care, seizure control, and GI decontamination.

Plants: Cardiovascular Toxicity

- The five most common classes of plants causing cardiovascular toxicity contain

(1) cardiac glycosides
(2) cardioactive steroids or alkaloids
(3) cholinergic toxins
(4) anticholinergic toxins, and
(5) adrenergic substances.

- *Coca* (cocaine) and *Ephedra* (ephedrine) exert their actions through α- and β-adrenergic receptors,

- *Digitalis* (digoxin) affects the myocardial sodium-potassium ATPase pump,

- plants with anticholinergic alkaloids produce vagolytic tachycardia and hypertension, as well as the familiar anticholinergic syndrome.

- Plants with cardioactive steroids or alkaloids represent a diverse group of plants from various families that share toxic effects on cardiac conduction.

Treatment Essentials for Cardiotoxic Plant Poisoning

- ✓ **Activated charcoal**
- ✓ **Fluid replacement Electrolyte correction**
- ✓ **Antiemetic (ondansetron)**
- ✓ **Atropine 0.5 mg IV (0.02 mg/kg for children)**
- ✓ **Digoxin-specific Fab fragments**

Plants: Gastrointestinal Toxicity

- Much more serious exposures occur in plant gatherers who mistake a morphologically similar yet highly toxic plant for an edible variety.

- For example, a number of fatalities have resulted when the root of water hemlock was mistaken for wild carrot. Herbal remedies are becoming increasingly popularity and misidentification or overzealous use has also lead to significant toxicity.

- Accurate identification of the ingested plant may be difficult even when a common name is known.

- For example *Atropa belladonna* is **often confused** with common nightshade, a member of the Solanaceae family that produces severe gastroenteritis.

- **Often no remnant** of the ingested plant is available for identification. Descriptions such as “a small houseplant with green leaves” or “a small, red berry” leave much to be desired.

- In addition, **most physicians lack the botanical training** to identify specimens or even to describe them accurately to a phone consultant.

- The actual toxicity of a plant depends upon several factors

1. Season,

2. the plant's age and sex,

3. and the plant structure(s) ingested.

- The common tomato plant, a member of the Solanaceae family, has obviously edible fruit but its leaves and stalks contain toxic solanaceous alkaloids.

- Foxglove *(Digitalis purpurea)* and oleander *(Nerium oleander)* have higher concentrations of cardiac glycosides (digoxin-like substances) within their flowers. Their toxicity also increases with age.

- Some exposures to highly toxic plants have limited clinical effects due to limited availability of the toxin. The hard seeds of the castor bean and rosary pea prevent release of the potent toxalbumins contained inside.

plant affecting gastrointestinal divided into three groups:

(1) those with isolated oral irritant effects;

(2) those with gastrointestinal irritative effects; and

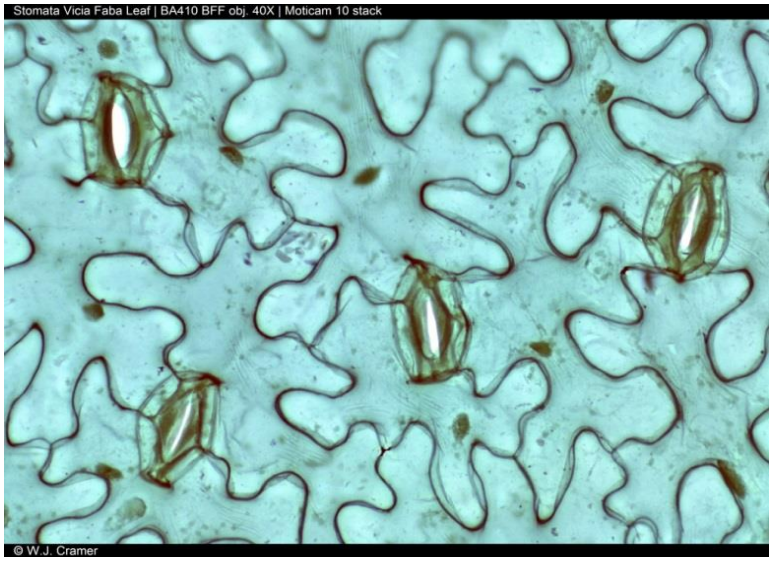
(3) those in which gastrointestinal manifestations predominate but systemic toxicity can occur.

Oral Irritants

- Calcium Oxalate Crystals
- Classic examples of plants that cause oral mucosal irritation are found in the Arum family.

- These are attractive indoor plants with smooth, broad green leaves that are often streaked or mottled with white.

- Plant members of this family contain insoluble calcium oxalate crystals that are arranged in bundles within pressure-sensitive, cigar-shaped structures called idioblasts.



Oral Irritants

- When mechanically deformed they fire calcium oxalate needles into the mucosa, producing immediate local pain.
- They also precipitate the release of bradykinin and histamine, which cause vasodilation and vascular permeability, resulting in edema.
- Patients describe a sensation akin to chewing on pins or glass.
- Symptoms are usually self-limited and resolve over a few hours.
- In severe exposures symptoms can last days and mucosal ulcerations or airway obstruction may occur.

Oral Irritants

- Arum family also includes well-known plants as jack-in-the-pulpit *(Arisaema triphyllum)* and elephant ear.

Capsaicin Alkaloids

- Local irritation also occurs after exposures to members of the Capsicum, or hot pepper, family.

- The toxins involved are capsaicin and other related alkaloids that deplete substance P and serotonin from efferent and sensory nerve terminals.

- When ingested, these plants cause an immediate sensation of warmth and burning, which can progress to severe pain following large exposures.

- Simply handling the peppers causes adherence of capsaicin to the skin, which may then be transferred to the eyes and other sensitive mucous membranes.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Gastrointestinal Irritants

- Many plants produce isolated gastrointestinal symptoms which include nausea, vomiting, and diarrhea.

- Common examples include Pokeweed also known as ink berry.

- Young, tender leaves of poke are frequently eaten as cooked greens or in salad. Parboiling may render them harmless, but poisoning is still possible.

Gastrointestinal Irritants

- All parts of the pokeweed plant contain the toxins phytolaccine and pokeweed mitogen
- greatest concentrations in the roots and the least in the ripe berries.
- Phytolaccine is a potent gastrointestinal mucosal irritant.
- Pokeweed mitogen typically produces clinically insignificant lymphocytosis 2–3 days postingestion and resolves spontaneously within 10 days.
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- Symptoms begin within 2–4 hours after ingestion. These include a burning or bitter sensation in the mouth followed shortly by nausea, vomiting, crampy abdominal pain, and foamy, sometimes bloody diarrhea.

Prominent Gastrointestinal Symptoms with Potential Systemic Toxicity

- This group includes plants that contain potent toxins that produce profound gastrointestinal symptoms.
- Systemic poisoning may also occur in large ingestions.
- Toxins include toxalbumins found in the castor bean and the rosary pea;
- Solanaceous alkaloids found in parts of the common potato , the tomato, and the jerusalem cherry *(Solanum pseudocapsicum)*
- mitotic inhibitors such as colchicine and podophyllotoxin found respectively in the *(Colchinum autumnale)* and the *(Podophyllum peltatum)*.

Mushrooms

- Poisonous M. account for 50-100 of 5000 species in USA.
- Poisoning unpredictable
- some are poisonous only if eaten raw and other only if eaten at certain stage of growth.
- The problem is compounding further because poisonous M may grow next to non poisonous variety.
- In general most of cases in M poisoning due to Amanita genus especially A.muscaria and A. phalloides and this responsible for 90% of M. poisoning.
- Amanita M contain a mixture of thermostable cyclopeptides including phalloidin, phalloin and amanitin congeners.

A

B

FIGURE 117–1. Group I: Cyclopeptide-containing mushrooms. (**A**) *Amanita phalloides* and (**B**) *Amanita virosa*. *(Used with permission from John Plischke III.)*

Characteristics of M poisoning

- Phase I of cyclopeptide poisoning resembles severe gastroenteritis, with profuse watery diarrhea that is delayed until 5 to 24 hours after ingestion.
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- Early onset of gastrointestinal distress before 5 hours is strong support for another non-*Amanita species or an etiology other than mushroom ingestion.*

- Transient improvement occurs during phase II from 12 and 36 hours after ingestion although hepatic injury begins during this phase

- Acute liver injury steatosis, central zonal necrosis, and centrilobular hemorrhage,

- Gastrointestinal manifestations including nausea, vomiting, abdominal pain and diarrhea may persist during the entirety of the clinical course

- phase III, manifested by hepatic and renal toxicity and death, may ensue 2 to 6 days after ingestion.

- Cyclopeptide toxicity also alters the hormones that regulate glucose, calcium, and thyroid homeostasis, resulting in widespread endocrine abnormalities.

- Insulin and C-peptide concentrations are elevated at a stage of poisoning prior to hepatic and renal compromise.

- These findings are suggestive of direct toxicity to pancreatic *b cells, resulting in release of preformed hormone or induction of hormone synthesis.*

Management of M poisoning

- Supportive care including fluid replacement and correction of metabolic disturbances including hypoglycemia.
- For A.muscaria, if ingestion is suspected, administered ipecac and observe for signs and symptoms for at least 3 hours.
- For A.phalloides if the time since ingestion is less than 4hr. ipecac induced emesis may be beneficial.
- Since signs and symptoms delayed it is unlikely to detect poisoning before 4 hr.
- activated charcoal and cathartics have been recommended.