The Biological Role of Toxic Secondary Metabolites of Different Origins on Insect and Humans

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ABSTRACT

Plant toxins are photochemical or secondary metabolites formed naturally by plants. They protect themselves against various threats like bacteria, Fungi, nematodes, insects, etc. Among secondary plant metabolites, one can find alkaloids, terpenoids, steroids, glycosides, phenolics, tannins, and others. Humans have used these secondary metabolites over thousands of years, both as drugs and agents to kill animals and humans. Some insects are food specialists and can feed on normally toxic plants to other herbivores. Many plant secondary metabolites interfere with the neuro receptors and neurotransmitters in vertebrates. Insects share many neuro receptors with vertebrates. PSM serves as olfactory cues for insects to identify their appropriate food plants. The behavior of insects towards such chemicals cues reminds us of drug addiction in humans and other vertebrates. This Chapter is incorporated the major aspects of plants' secondary metabolites and their impact on insect ecological adaptation.

Keywords: Phytochemical, secondary metabolites, bacteria, insects, phenolic, glycosides, steroid, terpenoids, alkaloids.

1. INTRODUCTION

1.1 EARLY HISTORY OF PLANT TOXIC SECONDARY METABOLITES

Plant toxins are produced as secondary metabolites that act as a defense mechanism for the plant. As a medicine and toxic use of plants cure disease and pain that are decided by the trial-and-error method. Early humans must have learned plants that relieve suffering and cure illnesses along with plant poisons and their antidotes through trial and error. From generation to generation, knowledge was passed by teaching observation, and experience, People of recent days, over 75% of the world's population depends on herbal medicines [1]. In the USA, only about 10% of the medical pharmacopeia comes directly from plants. However, many North American drugs are chemically synthesized from compounds found originally in plants [1]. In Sanskrit literature is full of records of the use plant In Chinese medicinal records also are available. The second Celestial Emperor (2000 BC), Shen Nung sampled more than 1000 herbs to determine their curative and poisonous properties. Shen Nung died perhaps from sampling one poison too

much [2]. Simoons (1998) [3] reviewed how poisoning showed up in various cultures, including the ancient Egyptians, the Greeks, and the Romans, continuing down to modern times. Around 400 BC, the Hippocratic Oath originated parameter values for many medical practitioners. Today, it is only administered in approximately 60% of U.S. medical tools at the granting of MD degrees [4]. Older versions of the Oath prohibit the use of poisons by physicians. This caution is not present in today's versions, although it may be covered by the caution to do no harm. Perhaps its omission relates to the treatment with many drugs that in higher concentrations could be deadly. In the mid-nineteenth and early twentieth centuries, the use, of plant-derived poison homicides became more common as the chemical detection of metallic poisons such as arsenic improved [5].

2. BIOLOGICAL ROLE OF PLANT TOXINS

Some plants produce toxins and can be used in treating many diseases. The action of plant toxins is based on their chemical constituent and their action by affecting specific mechanisms, There are a huge variety of plant poisons that are secondary metabolites and they can affect human and animal bodies so plant toxins my medicinal and poisonous.

3. PLANT POISONINGS AND SECONDARY METABOLITES

Homicides poisonings with heavy metals (e.g., antimony, arsenic, others) during medieval times, accidental and intentional were commonplace. These poisons were readily available to people as. active ingredients in a curative potion. In the transfer of property and wealth to heirs Arsenic was known as the nickname of "inheritance powder" as it was often used to hasten the postmortem but by the nineteenth century, chemists were developing procedures for detecting these poisons making them less attractive for nefarious purposes. Around the twentieth century, there was a transition from metallic poisons to alkaloids and other chemicals of plant origins that were more difficult to detect. Many of these plant poisons had been known for centuries and had made their way into many folk medicines All of these toxins were discovered as having some sort of curative property by ancient people, and many of them are still used today. General symptoms of poisoning caused by these compounds are summarized in Levine *et. al.* (2011) [6].

3.1. ALKALOIDS

Alkaloids naturally occurring organic chemicals that contain one nitrogen atom. This compound consists mostly of carbon, hydrogen, and nitrogen but may also contain sulfur and/or oxygen. Rarely, they will include elements such as chlorine, bromine, or phosphorus.

3.1.1 COLCHICINE

One plant poison first approved by FDA in 1961, it is an alkaloid drug favored by the Greeks and Romans and came from a species of crocus (Colchicum spp., family: Iridaceae). These plants are the source of the alkaloid drug colchicine (Figure 1) that sometimes is prescribed today for the treatment of gout, arthritis, and constipation-predominant irritable bowel syndrome. Colchicine is known to most biologists as an inhibitor of cell division. The drug comes from crocus corms and seeds. Colchicine can be deadly if misused as there is no known antidote for colchicine poisoning. Multiple system failures occur in 24-72h after consumption of a lethal dose. An unfortunate case of colchicine poisoning occurred in Colorado when a thief misread the label on a bottle he had stolen from a doctor's safe, and he died after ingesting the pills.

3.1.2. POISON HEMLOCK

Poison hemlock, is a well-known toxin plant of the carrot family, known, since ancient Greece, is poison hemlock (*Conium maculatum L*), a member of the carrot family (*Apiaceae*). In ancient Greece, Important people who received death sentences were allowed to choose their method of death. Socrates selected poisoning with a tea made from poison hemlock. Plato witnessed his death and described in detail the stages of the poison's action [7]. Plato's description fits the symptoms of contemporary poisoning by poison hemlock [8]. The active toxic ingredient is the alkaloid coniine (Figure 1), which causes paralysis of the respiratory muscles leading to death. As little as 100 mg (1.6mg/kg body weight for a 60kg adult) is a lethal dose (e.g., six to eight leaves of *C. maculatum*). Poison hemlock is widespread in the northern hemisphere and a few cases of poisoning occur each year.

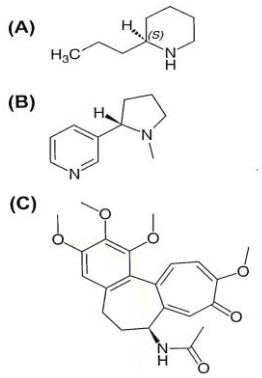

Figure 1: Structure of Alkaloid toxins. (A) Coniine; (B) Nicotine; (C) Colchicine.

3.1.3 THE TROPANE ALKALOIDS is a valuable secondary metabolite found in high concentrations in the family Solanaceae that include potato, and tomato. Deadly nightshade, *Atropa belladonna*; jimson weed or "loco weed" (*Datura spp.);* angel's trumpet (*Brugmansia spp*.); and henbane (*Hyoscyanus niger)* are the

sources of several hallucinogenic and potentially lethal tropane alkaloids scopolamine, atropine, and hyoscyamine (Figure 2).

3.1.4 SCOPOLAMINE is used as an antidepressant and antinausea drug. It is anticholinergic and antimuscarinic. Paradoxically, overdoses can produce depression. It is hallucinogenic but the experiences are generally extremely unpleasant. Scopolamine at one time was administered to pregnant women in labor as "twilight sleep."

3.1.5 ATROPINE is also an anticholinergic, ant-muscarinic drug that causes pupil dilation, increases heart rate, and increases secretion of saliva. A fatal dose of atropine is greater than 10mg, whereas scopolamine is toxic at 2-4mg. The name "belladonna" comes from Italy where it was once used to dilate the eyes of women to make them more attractive ("bella") to men.

3.1.6 HYOSCYAMINE is the levorotatory 1somer of atropine and is also the precursor for the synthesis of scopolamine. Its actions are similar to scopolamine and atropine. Hyoscyamine is named for the genus of henbane which concentrates tropane alkaloids in the leaves and seeds (Figure 3). Perhaps a leader in poisonings among these plants is jimson weed. This plant is featured in the many controversial books by Carlos Castenada (http://en.wikipedia.org/wiki/Carlos_Castaneda) [9] that first came to prominence in the 1960s. Jimson weeds are very hallucinogenic and can be fatal.

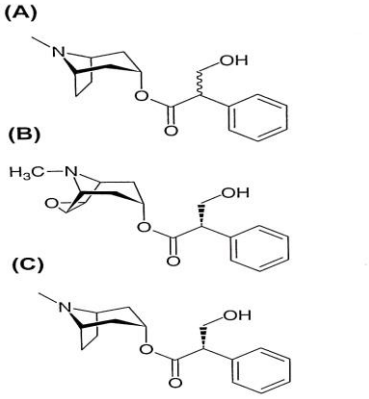

Figure 2: Structures of tropane alkaloids. (A) Atropine; (B) Scopolamine; (C) Hyoscyamine.

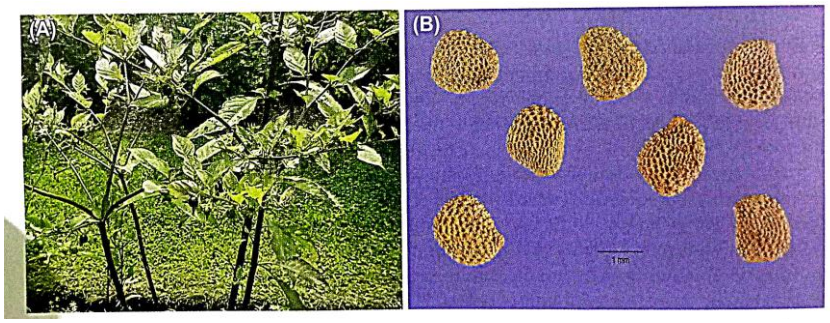

Figure 3: (A) Deadly nightshade, Atropa Belladonna. (Courtesy of Kurta Stiiber, available at Caliban.mpiz-koeln.mpg.de/mavica/index.html part of www.biolib.de) [10] (B) Seeds of henbane, Hyoscyanusnigar. (Courtesy of Steve Hurst, USDA.)

3.2 OTHER ALKALOIDS

3.2.1 STRYCHNINE

Strychnine (Figure 4) is a plant product taken by mouth, inhaled or mixed in a solution, or injected in the vein is a potent alkaloid neurotoxin that blocks cholinergic receptors in skeletal muscles. If taken in excess doses can lead to paralysis of respiratory muscles causing asphyxia and death. The lethal dose for humans is 32 mg/kg body weight. Strychnine is

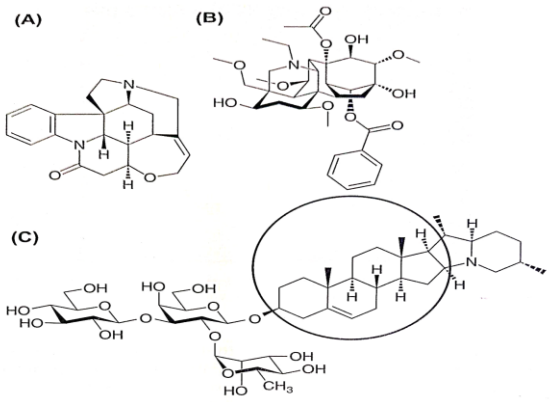

Figure 4: Structure of Some other alkaloid toxins. (A) Strychnine; (B) Aconitine; (C) Solanine. Note the inclusion of a steroid nucleus (circle).

most commonly derived from the seeds of Strychnic nux-vomica, a native tree of South India, and a related climbing shrub, *Strychnos ignatii*, native to the Philippines called St. Ignatius'bean. It was used as a rodent poison in Europe beginning in the seventeenth century until the present time. Accidental poisonings were not uncommon. It is suggested that the death of Jane Stanford in 1905, a cofounder of Leland Stanford University was a result of strychnine poisoning although it is not clear how this came about [11]. Once strychnine became readily available, it made its way into use for homicides. It has been suggested that it was the poison given to Alexander the Great in 323 BC [12]. However, because of the overt symptoms of strychnine poisoning and its easy chemical detection, it is not the poison of choice today. Nevertheless, it

did appear in the San Diego death of Sue Morency who died under unusual circumstances in 1990. She had a body concentration of strychnine that as4 times the lethal level. Her husband was arrested and charged with homicide [13].

3.2.2 ACONITINE

Aconitine is also an alkaloid toxin, (Figure 5) and is produced by the 250 species of Aconitum 90 family *Ranunculaceae* commonly called Wolf's bane and monkshood (Figure 5). All parts of these plants are extremely toxic, especially the roots. In addition to its use in ancient medicines, it was used to make poisoned arrows for hunting (Chinese, Japanese Ainu, Aleuts) and warfare (Chinese).

Figure 5: Monkshood, *Aconitum variegatum* Härtsfela, Germany, courtesy of Bern Haynold, available at http: //commons.wikimedia.org/wiki/ File: Aconitum_variegatum_ 110807f.jpg [14]

Aconitine effectively opens sodium channels so that muscles and neurons cannot be repolarized. Thus, aconitine can produce ventricular dysrhythmia of the heart leading to death. It can also cross the blood-brain barrier and produce neural effects. One of the early uses of Aconitum extracts in Europe was to kill wolves, hence another of the plants' many common names is wolf's bane. The lethal dose for humans is 32 mg/kg body weight. Surprisingly, the caterpillars of numerous moth species feed on this plant despite its toxicity to many other animals. The lowest oral dose reported to kill a human is only 29 ug/kg body weight (100x more lethal than strychnine). Reportedly, Cleopatra used aconitine to poison her brother (and husband) Ptolemy XIV so she could replace him with her son(http://en.wikipedia.org/wiki/Aconitum) [15]. A promising young Canadian TV and film actor, Andre Noble, died after consuming monks hood while on a hike in Newfoundland [16]. In 2009, the British "Curry Killer," Lakhbir Singh, murdered her lover by feeding him a curry dish laced with aconitine [17].

3.2.3 SOLANINE, A GLYCOALKALOID

Genus Potatoes (Solanum tuberosum, Solanaceae) that show signs of greening, sprouting, rotting, or physical damage have high concentrations of solanine and should not be eaten (Figure 4C). If one observes green material beneath the skin of a potato, one should not eat the potato because solanine is concentrated in this green layer and there may also be elevated levels in the rest of the potato. Greening in a potato is

evidence of excessive exposure to light. Solanine, like other cyanide compounds, is produced as a deterrent to insects and other animals that might feed on the plants. It is found in lower amounts in other food plants such as eggplant and green peppers. In the USA, each adult human consumes about 65 kg of potatoes/year. Ingestion of potatoes high in solanine and a closely related glycoalkaloid, chaconine, has been associated with numerous poisonings and some fatalities [18]. The compounds can cause neurological impairments, vomiting, and diarrhea. Most varieties of potatoes contain less than 5mg/kg. Concentrations of 14 mg/kg potato cause a bitter taste and 20 mg/kg causes a burning sensation in the mouth and throat.

4. GLYCOSIDES

Glycosides, in chemistry molecules in which sugar (saccharide) is associated with another functional chemical group via a glycosidic bond. Joining these components is usually formed through an oxygen, sulfur, or nitrogen atom. A glycoside with a sulfur bond would be a thioglycoside, for example, given below:

4.1 DIGOXIN, A CARDIAC GLYCOSIDE

Digoxin is a drug, used in medication to treat cardiac failure and certain arrhythmias and abortion, The family Solanaceae does not have a corner on poisonous/medicinal plants. Although its use is declining its overuse result in death, there are about 20 species of foxglove (Digitalis spp.: figwort family, Scrophulariaceae). Digoxin (Figure 6) is a cardiac glycoside extracted from foxglove. It often goes under the name of digitalis. Some cardiac patients under treatment for congestive heart failure and atrial arrhythmia carry a supply of Digitalis pills for self-medication if they feel symptomatic and

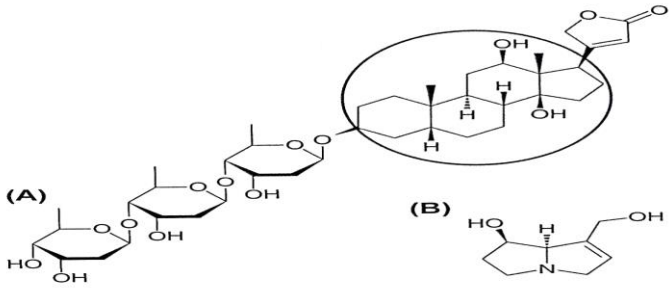

Figure 6: Structure of Comfrey contains the pyrrolizidine alkaloid retronecine

Figure: 7 Flower of a toxic "comfrey tea"

are away from professional help, although its use is declining. Overdosing of digitalis can result in death. People have sometimes confused foxglove with comfrey (*Symphytum* spp) and brewed a toxic "comfrey tea" (Figure 6). However, comfrey contains the pyrrolizidine alkaloid retronecine (Figure 7) that is hepatotoxic and linked to liver cancer and probably should not be ingested. Treatments for accidental and purposefully overdoses of these drugs remain a major field of research [6].

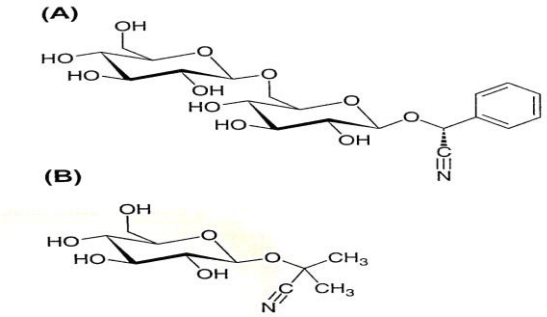

Figure 8: Cyanogenic glycosides. (A) Amygdalin; (B) Linamarin. CN=cyanide grouping.

4.2 CYANOGENIC GLYCOSIDES

Cyanide has been a popular poison for homicides and mass murders. It inhibits the mitochondrial enzyme cytochrome c oxidase and stops cellular respiration leading to death in minutes. It can be administered as a gas (hydrogen cyanide or prussic acid) or taken orally in compound form (e.g., potassium cyanide, sodium thiocyanate). In 2013, Urooj Khan of Chicago cashed in his lottery ticket for $600,000 only to fall ill the next day and die. It was considered a natural death until a relative pressed the authorities to exhume his body and do a toxicology scan. The results indicated that he had been poisoned with cyanide. Although the common sources for cyanide are artificial, more than 1500 species, mostly angiosperms, produce cyanogenic glycosides as predator deterrents. Although these compounds may produce unpleasant effects in humans, the concentrations are not likely to be lethal. During droughts, the lack of water increases the concentrations of cyanogenic glycosides, and they prove more toxic to insects and other predators that attempt to feed on the leaves, stems, or roots.

Amygdalin is present in the almond fruits of Prunus dulcis. Its name is derived from the ancient Greek word for"almond." There are two varieties of almonds, one that tastes sweet (variety dulcis) and one that is bitter (variety amara, also called bitter almond). In the bitter almond, amygdalin is enzymatically converted to the toxic prussic acid and benzaldehyde, the chemical that gives the almond a bitter taste. The edible almonds consumed in the USA are sweet almonds, but bitter almonds can be found in specialty stores.

Cyanogenic glycosides may be found throughout many edible fruits, including, apples, peaches, pears, raspberries, cherries, apricots, and plums, but they are especially concentrated in the seeds. If these seeds are swallowed, they generally pass through the digestive system untouched. It is strongly recommended, however, that elderberries not be eaten raw as cooking releases a considerable amount of cyanide from the pulp of the fruits that diffuses harmlessly into the air. Bamboo shoots have high concentrations of cyanogenic glycosides as

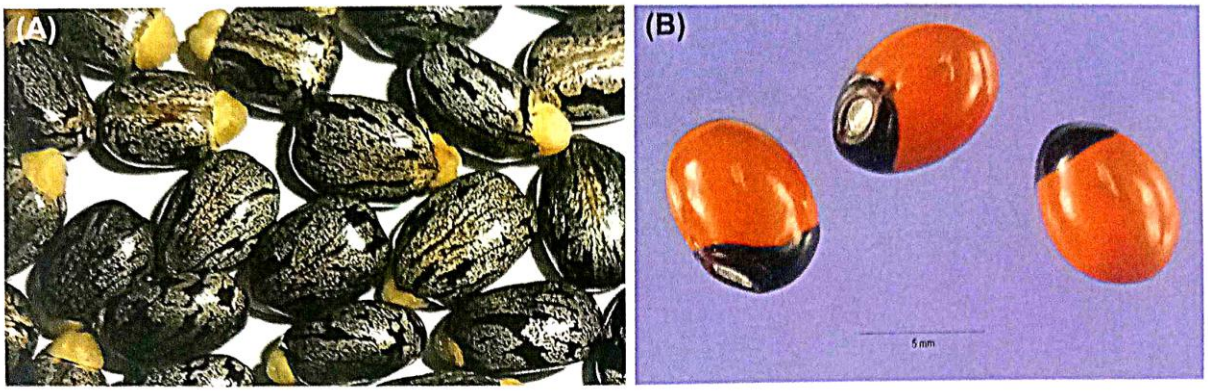

FIGURE 9: Sources of lectin toxins. (A) Seeds of castor beans, *Ricinus annus*, source of ricin. (B) Seeds ofjequirity, Abrus precatorius, source of abrin. Castor bens, courtesy of Hedi Bousghanmi 2014, available at http://en.wikipedia.org/wiki/Ricin#/media/File:Castor_beans1.jpg **[19]**. Abrus precatorius Nutt. Ex Hook, courtesy of Steve Hurst, USDA.

do cassava roots. The processing of cassava roots (the source of tapioca) requires the release of cyanide from the glycoside linamarin (Figure 8, 9) (also present in lower amounts in lima beans and flax). Otherwise, the cassava roots are very poisonous. Considerable amounts of cyanide are also released from burning tobacco although the amounts of cyanide inhaled are well below the lethal range.

5. TOXIC PLANT LECTINS

Proteins chiefly of plant origin bind to certain sugars and so cause agglutination of particular cell types. People eating even small amounts of raw or undercooked kidney beans cause a reaction and can cause red blood cells to clump together producing nausea, vomiting stomach upset, and diarrhea. Two very toxic plant lectins (carbohydrate-rich proteins or toxalbumins) are ricin and abrin. Ricin is made in the endosperm tissue of castor beans (*Ricinium* spp.). It is very toxic if inhaled or ingested (lethal dose=22 µg/kg body weight) but considerably less toxic orally (lethal dose 1mg/kg). Ricin inhibits protein synthesis but is often not fatal if treated. Castor beans (Figure 8 are compressed into "castor cakes" that are high in protein (43%) and are used for organic fertilizer. These cakes are not appropriate for animal feed due to their high ricin content. Ricin has been used in assassinations, has been a candidate for a chemical weapon, and has been used to contaminate letters sent to political figures in the USA.

A major source of **abrin** is the jequirity, *Arbus preceptories*, an invasive pan-tropical plant originating in India. Abrin also inhibits protein synthesis but is much more toxic than ricin. The median adult human toxic dose orally is 10-1000 g/kg, whereas the inhalation toxic dose is 3.3 μg/kg. Seeds (Figure: 8B) of A. preceptors are often used as beads in jewelry.

6. DICOUMAROL AND ANTICOAGULANTS

Strychnine was replaced as a rat poison by the very effective warfarin in 1948. In the 1920s, some cattle developed a disease that caused them to bleed to death. It was discovered that the disease resulted from feeding cattle spoiled silage made from sweet clover hay. Sweet clover produces a nontoxic sweet-smelling compound called coumarin that certain fungi in the silage can metabolize into dicoumarol (Figure 9 B), a potent anticoagulant that was responsible for cattle bleeding to death. In the presence of dicoumarol, their blood would not clot. Researchers at the University of Wisconsin modified dicoumarol to produce warfarin (Figure 9C), which was an even more potent anticoagulant. Because after years of use, many rat populations became resistant to warfarin, chemists developed a highly lethal anticoagulant

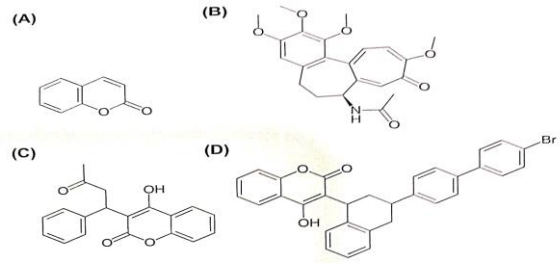

Figure 10: Structure of Anticoagulants derived from sweet clover. (A) Coumarin, the parent compound; (B) Dicoumarol, synthesized from coumarin by fungi; (C) Warfarin, a synthetic anticoagulant made from dicumarol in the laboratory;(D) Brodifacoum or "super warfarin."

called brodifacoum, which is currently being used to poison rats as well as other pest mammal such as possums. The new drug, brodifacoum (Figure 9D), is sometimes called "super warfarin." The 96-h LC_{50} for brodifacoum in rainbow trout (lethal concentration to kill 50%o after exposure for 96h) is a concentration of only 40 μg/L. The lethal dose for a 60-kg human male is 15 mg (250 μg/kg). Warfarin is sometimes administered today to humans as an anticoagulant.

7. MUSHROOM TOXINS

A fruiting body of the fungus is a mushroom. Its community spans the glove. People collect wild mushrooms and mistake poisonous mushrooms for edible species 6 because of most cases of mushroom poisoning [5]. Occasionally, they are involved in homicides. Best known are the amatoxins found in several genera including Amanita. Amatoxins (Figure 10A) disrupt protein synthesis by inhibiting the enzyme RNA

polymerase II. When ingested, the liver is the organ usually affected first and survivors may require a liver transplant. The estimated lethal dose for an adult human is about 100 µg/kg body weight.

Muscimol (Figure 10B) is a psychotic alkaloid found in some species of Amanita but is much less toxic than amatoxins. It is a potent agonist of GABA receptors and causes visual perception problems and auditory hallucinations. The LD_{50} (lethal dose to kill 50% of the test animals) for muscimol in mice is 3.8 mg/kg body weight.

Oreleanine (Figure 10 C)) is a nephrotoxic bipyridine dioxide isolated from Cortinarius spp. The LD_{50} for mice is quite high (12-20mg/kg body weight) but humans are believed to be more sensitive to oreleanine than mice. There is no known antidote.

Methylhydrazine (MMH) is a toxic substance in false morels (Gyromitra spp.). NASA used MMH as a rocket propellant in the Apollo lunar modules. Although it causes gastrointestinal upsets and is a potential carcinogen, it is usually not fatal.

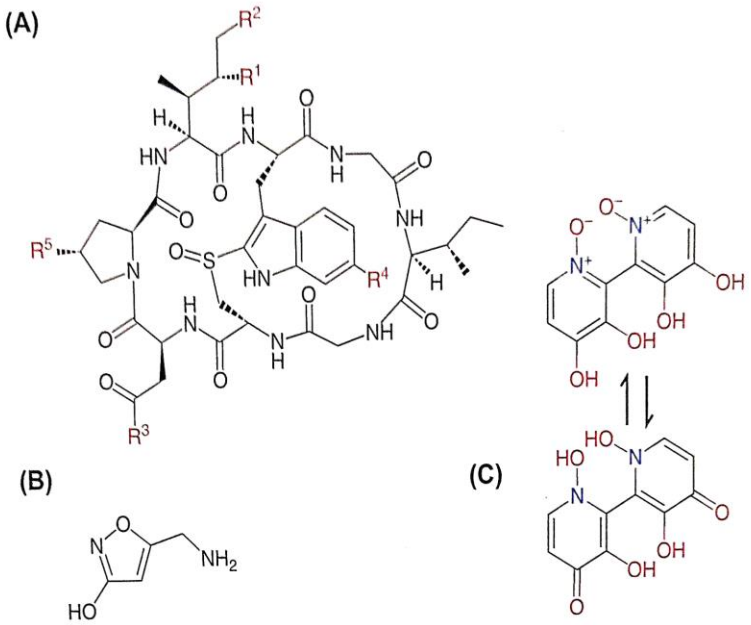

Figure 10: Structure of Some mushroom toxins. (A) Amatoxins, 10 are known with different substitutions at the "R" positions; (B) Muscimol; (C) Oreleanine.

8. ILLEGAL DRUGS OF PLANT ORIGINS

For centuries there has been cultivation of cannabias, coca and the opium poppy. The illegal drug that can readily be cultivated, extracted, and purified with minimal expenditures. The drugs are capable of producing euphoria and hallucinations and are lethal in high dosages. Law enforcement may ask The forensic plant scientist to identify plants grown for this illegal trade.

The major drug trade has traditionally been focused on the products of the opium poppy Papaver somniferous (Figure 11A). Knowledge of the pain-relieving capacity of this plant apparently extends from

the Stone Age. The latex collected from the opium poppy contains three main addictive pain relievers: morphine, codeine, thebaine (Figure12). Morphine and codeine are used medically as analgesics. Additionally, morphine is treated chemically to produce heroin, which has twice the potency of morphine. Cannabis spp. are sources of marijuana. The principal psychoactive constituent in Cannabis is tetrahydrocannabinol (THC) (Figure 13A). Marijuana is used both recreationally for its psychoactive properties and medically for its analgesic properties. The use of psychoactive alkaloids obtainable from cacti is generally illegal as well. However, the use of the cactus known as peyote (*Lophophora williamsii*) (Figure 11 B) that contains the alkaloid mescaline (Figure 13B) has historically been used ritualistically.

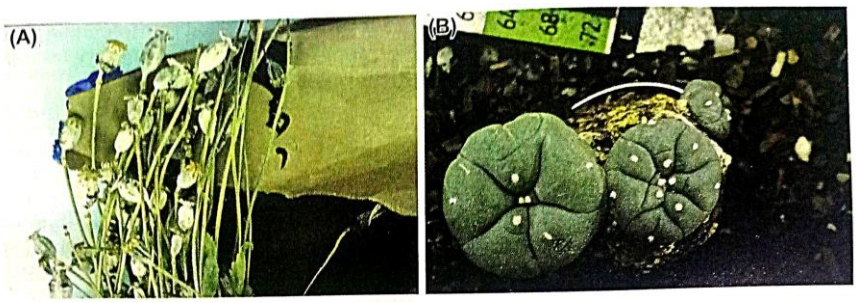

Figure 11: (A) Fruits of the opium poppy, *Papaver somniferunm*; (B) Fruits of Peyote, *Lophophora williamsii*, source of mescaline.

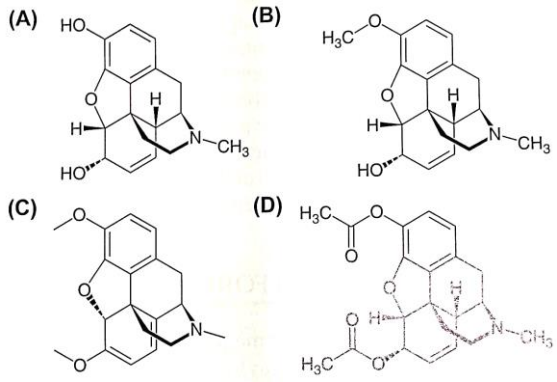

Figure 12: Structure of Natural opiates and heroin. (A) Morphine; (B) Codeine; (C) Thebaine: (D) Heroin.

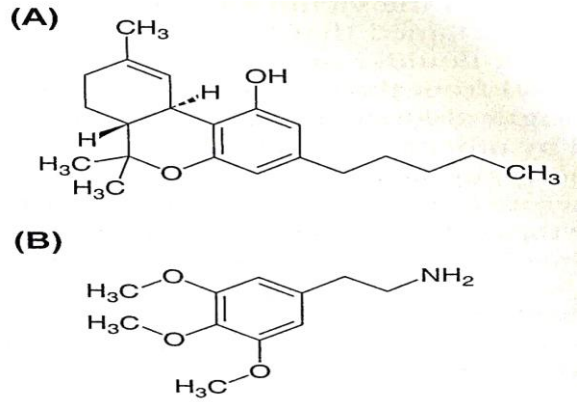

Figure 13: (A) Tetrahydrocannabinol from *Cannabis spp*.; (B) Mescaline from Peyote, *Loplhophora williamsii*.

Other psychoactive compounds are found in many cactus species, some of which are very toxic as unfortunately discovered by people who have experimented on themselves.

9. TWENTIETH CENTURY FORENSIC PLANT SCIENCE

Today, forensic plant science covers many discipline anatomy, taxonomy, ecology, palynology and diabology. The specific identification of poisonous plants as well as plants that were sources of illegal drugs became important when attempting to obtain convictions for possession and/or cultivation of the plants. However, it was the 1932 kidnapping and murder of the 20-month-old son of Charles and Anne Lindbergh that brought forensic plant science to the attention of the American public. Charles was a famous aviator and a national hero for being the first person to fly solo from the US to France. The Lindbergh child was abducted from a second-floor nursery by the use of a crudely constructed wooden ladder that was left at the scene. Two years later, Bruno Hauptmann was arrested for the kidnapping after a portion of the ransom money was discovered in his possession. Hauptman claimed that the money was left with him by a former associate and that he had no idea it was connected to the kidnapping. However, a wood expert, Arthur Koehler, matched the grain in wood samples from Hauptmann's attic to the wood of the ladder used in the abduction. Kohler's analysis confirmed the wood from the ladder was from Hauptmann's attic and that tool marks found on the wood pieces matched marks left on test wood by Hauptmann's tools. Replicas of the crude ladder were sold to attendees of Hauptmann's trial. He was convicted and sentenced to death.

10. USES IN FORENSIC PLANT SCIENCE

Our first experience with forensic science came in 1982 when one of us (Bock) was contacted by Ben Galloway (Dr. William B. Galloway) who at that time was a medical examiner for Jefferson County in Colorado and a professor of Pathology at the University of Colorado Health Sciences Center in Denver [22]. Ben had a collection of materials from the stomach of a homicide victim that did not match the victim's last known meal, but he was unsure as to how to identify it. Galloway ascertained that Bock taught a course titled "Plant Anatomy" at the University of Colorado at Boulder and sent her slides to examine in order to positively identify the plant material from the stomach contents (for case details, see Chapter 5, PP 85-86). Bock asked a colleague (Norris) to collaborate with her on this work. Soon, Bock and Norris were being asked by other agencies to provide similar information. This led them to develop procedures for the examination and identification of plant cells and tissues from common food plants. They wrote a manual including a microscopic atlas of numerous food plants that was published by the National Institutes of Justice (NIJ) in 1988. The N distributed copies free of charge to forensic laboratories throughout the USA. Dr Meredith Lane participated in this project by providing scanning electron micrographs of some of the

plant foods and helped with the construction of a key for identifying food plants from their microscopic structure.

REFERENCES

1. Simpson, B.B., Ogorzaly, M.C., 1995. *Plants in Our World*. McGraw Hill, New York.
2. Magner, LN., 1992. *A History of Medicine*. Marcel Dekker Inc., New York.
3. Simoons, FJ, 1998. *Plants of Life, Plants of Death*. University of Wisconsin Press, Madison, Wl.
4. Jnala,, Jhala, K.N., 2012. The Hippocratic oath: a critical analysis of the ancient text's relevance to American and Indian modern medicine. *Indian Journal of Pathology and Microbiology.* 53, 2/- Levine,
5. Blum, D., 2011. *The Poisoner's Handbook*. Penguin Books, New York.
6. Levine, M., Ruha, A., Graeme, K., Brooks, D, Canning, I, Curry, S., 2011. Toxicity in the ICU part 3: natural toxins. Chest 140, 1357-1370.
7. Gallop, D., 2009. *Plato's Phaedo*. Oxford University Press, Oxford.
8. LCwis, W.H., Ehwin-Lewis, M.PE, 2003. *Medical Botany: Plants Affecting Human Health*. John Wiley & Sons, New York.
9. http://en.wikipedia.org/wiki/Carlos_Castaneda
10. www.biolib.de
11. Cutler, R., 2003. *The Mysterious Death of Jane Stanford*. Stanford General Books.
12. Phillips, G., 2004. *Alexander the Great. Murder in Babylon*. Virgin Books.
13. Bellandi, D., August 25, 1990. Husband Arrested in Woman's Poisoning Death. Los Angeles Times. http://articles.latimes.com/1990-08-25/local/me-818-1strychnine-poisoning.
14. http: //commons.wikimedia.org/wiki/ File: Aconitum_variegatum_ 110807f.jpg
15. Gallagher, S., August 10, 2004. *Andre Noble*. Filmmaker Blog.
16. BBC, February 10, 2010. *Poisoning in West London in 2009*. BBC TV News.
17. Morris, S.C., Lee, T.H., 1984. The toxicity and teratogenicity of Solanaceae glycoalkaloids particularly those of the potato (Solanum tuberosum): a review. *Food Technology in Australia* 36, 118-124.
18. Bock, JH., Lane, M., Norris, D.O, 198. The Use of Plant Cells in Forensic Investigation. U. S. Department of Justice, USA
19. http://en.wikipedia.org/wiki/Ricin#/media/File:Castor_beans1.jpg