Review Article

Toxic treasures: A review of therapeutic compounds from poisonous plants

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Abstract

Humans have historically harnessed the inherent toxicity of living organisms for diverse applications, from hunting and warfare to traditional medicine. This ancient knowledge has significantly contributed to the development of numerous modern pharmaceuticals derived from natural compounds. While plants are essential for life, they also produce toxins as a defense mechanism, which can be detrimental upon ingestion. Paradoxically, these very compounds can offer therapeutic benefits when administered in controlled doses. The perceived "safety" of a plant is, therefore, not absolute; it is contingent upon individual factors such as sensitivity, genetic predisposition, health status, and hormonal balance. By integrating scientific research with traditional knowledge, we can better understand this dual nature of plant compounds, enabling us to both mitigate potential risks and leverage their benefits in medicinal and other fields. This underscores the intricate chemistry of the natural world and humanity's remarkable capacity for resilience and adaptation. This review further explores the toxic constituents found in sixteen common plants and their current therapeutic applications in modern medicine.

Keywords: *Abrus, Aconitum, Atropa,* atropine, *Cannabis, Catharanthus, Curarea, Datura, Digitalis, Gloriosa,* hyoscyamine, *Nicotiana, nux-vomica,* odollam, oleander, opium, reserpine, *Ricinus,* scopolamine, *Serpentine,* yohimbine.

Introduction

The inherent capacity of living organisms to produce toxins has been historically leveraged by ancient civilizations for diverse purposes, including hunting, tribal warfare, and traditional medicine. Indeed, a significant number of modern pharmaceuticals have been developed based on this ethno-medical knowledge and the applications of naturally occurring compounds.[1] The production of toxins is a natural phenomenon observed across eukaryotes, encompassing both plants and animals, often serving as a mechanism for defence and survival. A classic example of this is Alexander Fleming's observation of a fungal metabolite produced by *Penicillium notatum* that inhibited bacterial growth. This substance, which Fleming later named *penicillin* revolutionized the treatment of bacterial diseases in 1941.[2] The development of modern drugs and pharmacologically active compounds

derived from plants used in traditional medicine has been made possible through the collaborative efforts of scientists worldwide. Over the past 75 years of extensive research, modern medicine has isolated thousands of compounds and drugs that are now used to treat a wide range of diseases.

Plants serve as the primary source of food and energy for living organisms, providing essential nutrients, vitamins, and vital elements crucial for animal survival. However, as a defence mechanism against herbivores, insects, and parasites, certain plant species produce toxic substances that can exert adverse effects on humans and animals, if ingested. These plant toxins are diverse chemical compounds concentrated in various plant parts including roots, stems, leaves, flowers, and fruits. They present significant risks, ranging from mild gastrointestinal disturbances to severe organ damage and even mortality.[3] Chronic exposure to certain plant extracts, sometimes employed in traditional medicine, can also lead to cumulative toxicity and the development of conditions such as liver cirrhosis or kidney failure.[4] Conversely, the inherent toxicity of some plant compounds holds therapeutic and pharmacological significance when administered in controlled dosages, finding applications in patient treatment and drug discovery initiatives.[1] Common classes of toxic compounds present in plants include alkaloids, glycosides, saponins, cyanogenic compounds, oxalates, phenolics, and flavonoids. Understanding the dual role of these plants as both life-sustaining and potentially lethal, highlights the importance of careful study and respect for the complex chemistry of the natural world. Traditional knowledge of the effectiveness of toxic components, supported by animal studies, in vitro experiments, and carefully controlled clinical trials, is now being used in modern medicine to treat many diseases. Many modern drugs are of natural product origin and about 50% of them play an important role in drug development programs in the pharmaceutical industry. Even though some plants are known for their highly toxic components, certain plants considered safe for consumption can still cause adverse effects in some individuals. This phenomenon arises from the varying toxicity potential of plant substances, which can affect people differently due to many reasons. These substances can trigger immune responses that manifest as skin rashes, hives, swelling, or even anaphylaxis. Some fruits, nuts, and seeds trigger very severe allergic reactions, sometimes life-threatening. Certain fruits can adversely affect the body's physiology under the influence of elevated hormone levels and trigger abnormal effects in a presumably normal physiological situation such as pregnancy.[4] In essence, the "safety" of plant materials is not absolute but rather depends on the individual consuming or coming into contact with it. Factors such as genetic predisposition, pre-existing health conditions, the amount consumed, and even hormonal status can influence whether a plant substance elicits a beneficial, neutral, or adverse reaction.

Some of the toxic plants which produce a diverse range of bioactive molecules, making them precious sources for diverse medicinal applications, are mentioned below.

1. *Atropa belladonna*

Atropa belladonna, commonly known as deadly nightshade is a highly toxic perennial herbaceous plant belonging to family Solanaceae. Usually a native to temperate southern, central, and eastern Europe, North Africa, Turkey and Iran, this plant is also found in Simla and Kashmir in India. It has been introduced and

naturalized in some parts of Canada and the United States. All parts of the plant are highly poisonous, containing potent tropane alkaloids, including atropine, scopolamine, and hyoscyamine.[5]

Figure 1: *Atropa belladonna*

It is a shrub reaching up to 15 feet tall with dull green, oval-shaped leaves, bell-shaped, dull purple flowers with green tinges and a faint scent (Figure 1). The fruits are glossy black berries, about the size of cherries, which are sweet-tasting and particularly attractive to children, posing a significant danger. The plant extract was used by early tribes as arrow poison for hunting and tribal war, making it a lethal weapon. Despite its toxicity, *Atropa belladonna* has a long and varied history of use. Named "*bella donna*" meaning "*beautiful woman*", the plant extract was used by Italian women during renaissance time to dilate their pupils, considered a sign of beauty.[6]

Ingestion, especially of the berries, can lead to severe anticholinergic poisoning. Symptoms of poisoning can include tachycardia, dilated pupils, blurred vision, dry mouth, difficulty in swallowing, high fever, flushed skin, agitation, delirium, hallucinations, inability to urinate or sweat, spasms, mental confusion, convulsions, coma and death due to respiratory failure. It is also toxic to domestic animals, potentially causing paralysis and death. The antidote for belladonna poisoning is physostigmine or pilocarpine.[6,7]

The alkaloids atropine, scopolamine and hyoscyamine extracted from belladonna have important medicinal properties.[7] Atropine is a medication that has a variety of effects on the body due to its action as an anticholinergic agent. It primarily works by blocking the effects of acetylcholine, a neurotransmitter. It can treat bradycardia by blocking the vagal nerve's influence on the heart, thereby increasing the heart rate. In the eye, atropine dilates the pupils and hence is useful for eye examinations and treating certain eye conditions. It can relax the smooth muscles in the stomach, intestines, bladder, and other organs, which can help relieve spasms. Atropine is a crucial antidote for poisoning caused by organophosphate pesticides and nerve agents. These substances increase acetylcholine levels, and atropine blocks their effects at muscarinic receptors. Scopolamine is used to reduce body secretions and stomach acid, control heart rate, and relax muscles. It is also known for its use in treating motion sickness. Scopolamine acts as a nonselective competitive antagonist at muscarinic acetylcholine receptors. By blocking acetylcholine, it inhibits parasympathetic nervous system activity, causing various effects. In the central nervous system, it particularly affects M_1 receptors, contributing to its antiemetic, sedative, and amnestic properties. Its action on the vestibular system and the vomiting centre in the brainstem is key to preventing nausea and vomiting. Peripherally, it primarily affects M_3 receptors, reducing glandular secretions and relaxing smooth muscles. Hyoscyamine is used to relieve gastrointestinal disorders, like irritable bowel syndrome (IBS) and spasms.[8] It is an anticholinergic medication with effects similar to atropine and scopolamine, as it blocks the action of acetylcholine in the body. Hyoscyamine works by

competitively inhibiting the action of acetylcholine at muscarinic receptors in smooth muscle, secretory glands, and the central nervous system. This blockade leads to the relaxation of smooth muscle, reduced secretion of various fluids, and can have central nervous system effects, although generally less pronounced than scopolamine.[9]

Throughout history, *belladonna* has been used as a poison, both intentionally and accidentally. Due to its high toxicity and unpredictable effects, self-medication with the plant is extremely dangerous and should be avoided entirely. Any medicinal use should be done under strict medical supervision with isolated and purified compounds. In conclusion, *Atropa belladonna* is a plant with a captivating history, known for its poisonous properties and valuable medicinal alkaloids.

2. ***Digitalis purpurea*** (Fox Gloves)

Figure 2: *Digitalis purpurea*

Digitalis purpurea is native to temperate Western and Central Europe and northwest Africa. This plant is seen in India at the high altitudes of Jammu & Kashmir, Assam, West Bengal, Kerala, Uttarakhand and Himachal Pradesh (Figure 2). *Digitalis purpurea*, commonly known as foxglove is admired for the beauty of its flowers; typically, purple but pink, rose, yellow and white colours are also seen. This plant is highly toxic but has valuable medicinal properties.

Foxglove has a long history in medicine for treating heart conditions. In 1775 William Withering described its use for oedema from heart failure noting that extracts of the leaves increased urine output and strengthened the pulse.[10] Later researchers found out that the plant leaves, flowers and seeds contain potent cardiac glycosides, principally digitoxin and digoxin. These glycosides inhibit the Na^+/K^+-ATPase pump in cardiac cells, leading to increased intracellular sodium which, in turn, increases the calcium influx via the sodium-calcium exchanger, strongly affecting heart function. The net effect is a stronger (positive inotropic) heartbeat. Digoxin also stimulates the vagus nerve, slowing conduction through the AV node and reducing heart rate (negative chronotropic effect).[11] Thus, digitalis drugs increase cardiac contractility and help control ventricular rate in atrial fibrillation. In modern cardiology, digoxin (brand name Lanoxin) is prescribed for selected patients with heart failure or atrial fibrillation who continue to experience symptoms despite other medical therapy. Although considered safe, digoxin has a narrow therapeutic window, and clinicians are taking utmost care in treating patients to avoid its toxicity.[12,13]

3. ***Curarea toxicofera***

Figure 3: *Curarea toxicofera*

Curarea toxicofera is a vigorous climbing vine growing up to 20 metres, found in the humid rainforests of tropical America, mostly at low elevations (Figure 3). It is abundant in Amazon rainforest and in countries like Colombia, Ecuador, Peru, Brazil, Venezuela, and Bolivia. This plant is a well-known arrow poison used by indigenous people for hunting. The poisonous substance is an alkaloid called curare present in the plant, particularly in the root. Curare acts as a neuromuscular blocking agent. [14]

In an experimental frog nerve-muscle preparation, stimulation of the nerve can lead to the release of neurotransmitters, primarily acetylcholine (ACh), which then binds to receptors on the postsynaptic muscle, causing contraction. Curare blocks the action of ACh by binding to the receptors, preventing muscle contraction. It binds to nicotinic acetylcholine receptors at the neuromuscular junction causing muscle paralysis. This paralysis typically progresses in live animals, eventually affecting the respiratory muscles, leading to death by respiratory arrest. Importantly, curare is only toxic when it enters the bloodstream parenterally. It is not active when ingested orally and hunters can safely consume animals killed with curare toxin.[14]

While historically known for its poisonous properties, tubocurarine also has uses in modern medicine. Curare derivatives are primarily used as muscle relaxants, often administered alongside general anaesthesia during surgeries, especially of the chest and abdomen, to achieve profound muscle relaxation. They can be used to relax the throat muscles, making it easier to insert a breathing tube. This effect of curare can be reversed using anticholinesterase drugs like neostigmine.

4. *Cerbera odollam* (Othallam)

Figure 4: *Cerebra odollam*

Cerebra odollam (local name *Othallam*) is a tree belonging to the family Apocynaceae that include several poisonous species of plants (Figure 4). Its seeds are excessively toxic containing a cardenolide called cerebrin. The odollam tree is responsible for about 50% of the plant poisoning cases and 10% of the total poisoning cases in Kerala. There are numerous instances in which it is misused for both suicide and homicide. Odollam tree grows to a height of 50ft and has large white flowers with a faint smell of jasmine. While highly toxic, some research explores its potential medical uses. Studies suggest that the seeds have anticancer properties through apoptotic activity. Fruit extracts exhibit enhanced anticancer properties when used in combination with other treatments in certain cancer cell lines. Leaf extracts have been screened for antioxidant properties. In traditional medicine the wood has been used in paralysis treatment. The latex has been used as an emetic and purgative. The plant has been investigated for use as a bio-insecticide, insect repellent, and rat poison. The potential use of *Cerbera odollam* for medical applications are still under investigation. It is worth mentioning that ingestion of any part of this plant, especially the seeds, is extremely dangerous and should be avoided.[15]

5. ***Gloriosa superb*** **(Flame Lily)**

Figure 5: *Gloriosa superba*

Gloriosa superba, also known as *Flame Lily* is native of Africa, China and Asia including the Indian subcontinent (Figure 5) and has been used in traditional Ayurvedic medicine for many diseases. This is a poisonous plant due to the presence of alkaloids like colchicine and gloriosine. Discovered more than 3,000 years ago, colchicine is one of the oldest drugs still in use today. It was mentioned in the oldest Egyptian medical text, Ebers Papyrus (1550 B.C.), where it was described for relieving pain and treating swellings. In traditional medicine it has been used in small doses for gout and rheumatism, bruises, sprains, arthritic pain, skin problems, ulcers, colic and indigestion, leprosy, piles, fever, and as a general tonic.[16]

Ingestion of any of its parts can lead to severe symptoms, including nausea, vomiting, diarrhoea, burning sensation, numbness, and potentially life-threatening complications like respiratory depression, cardiovascular issues, and multi-organ failure. The toxic alkaloid, colchicine, interferes with cell division. In modern medicine colchicine is used primarily for the treatment of gout, an inflammation in a joint.[17] Colchicine does not cure gout, but it prevents gout attacks. Colchicine is also used to reduce the risk of heart attack, stroke, certain types of heart procedures, and cardiovascular death in patients with atherosclerosis or with multiple cardiovascular risk factors. However, it is a potent drug with a narrow therapeutic window and used under strict medical supervision. [18]

6. ***Ricinus Communis***
(Castor Oil Plant, Avanaku)

Figure 6: *Ricinus communis*

Ricinus communis (Avanaku), the castor oil plant, belonging to the family Euphorbiaceae, has a history of various medicinal applications, primarily through its oil (castor oil) extracted from its seeds (Figure 6). It has naturalized throughout tropical and subtropical regions worldwide. It can also be found in some temperate countries, where it is being cultivated. Castor oil is well-known for its potent laxative properties. It contains ricinoleic acid which interact with the prostanoid receptors on the intestinal smooth muscle causing influx of calcium causing contraction. By the same mechanism it can cause uterine smooth muscle contraction, suggesting its potential usage in the induction of labour.[19] Topical application of castor oil has been used for dry skin warts, fungal infections, inflammation and joint pains.[20]

While castor oil itself is generally considered safe for its intended uses, the seeds are highly toxic as it contains ricin, a potent toxin. Ingestion of the seeds can cause severe poisoning, with symptoms

including nausea, vomiting, abdominal pain, and in severe cases, dehydration, organ damage, and even death. The primary medicinal usage of this plant is through castor oil, mainly as a laxative and for some topical applications.[20]

7. ***Strychnos nux-vomica*** (Kanjiram)

Figure 7: *Strychnos nux-vomica*

Strychnos nux-vomica is a deciduous tree native to India and south east Asia. It is a medium-sized tree coming under the family Loganiaceae that grows in open habitats (Figure 7). It is known for being the natural source of the extremely poisonous alkaloids strychnine and brucine which affect the nervous system.[21] It has a long history of use in traditional medicine systems like Ayurveda, Unani, and Traditional Chinese Medicine. Its usage in modern medicine is very limited and highly cautious due to its potent toxicity.[22]

Strychnine poisoning can lead to muscle spasms, convulsions, respiratory failure, and death. Experiments are going on to find out the effects of various compounds isolated from this tree for anti-inflammatory, antioxidant, and even anticancer effects.[23] However, these are preliminary findings and far from clinical applications due to the toxicity concerns. *Nux vomica* is a well-known remedy in homeopathy, used for a wide range of conditions, particularly digestive issues, irritability, and hangovers. However, it's important to note that homeopathic preparations use highly diluted substances. Due to its toxicity, the use of *Strychnos nux-vomica* parts and strychnine is heavily regulated in many countries. It is a well-known rodenticide and known for killing stray pests. *Strychnos nux-vomica* is not used in modern allopathic medicine due to its high toxicity. While traditional systems value it in carefully processed forms and minute doses, modern medicine generally relies on safer and more effective alternatives.[23]

8. ***Cannabis sativa***

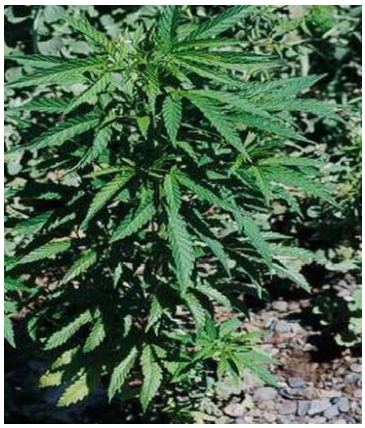

Figure 8: *Cannabis sativa*

Cannabis (Figure 8) is a genus of flowering plants in the family Cannabaceae that is widely accepted as an intoxicating plant grown in Indian subcontinent and has been in use since 1000 BCE. *Cannabis sativa,* has gained significant attention for its modern medicinal uses. This is largely attributed to its diverse chemical compounds, collectively known as cannabinoids, with the most well-known being tetrahydrocannabinol (THC) and cannabidiol (CBD).[24]

Cannabis sativa, including varieties like *indica* can be toxic, particularly in high doses or for certain individuals. While not typically fatal, cannabis intoxication can cause temporary adverse effects like anxiety, confusion, respiratory distress, and gastrointestinal problems. Chronic use can lead to more serious issues like cannabinoid hyperemesis characterized by nausea, vomiting, and abdominal pain and potential

cardiovascular effects. Overconsumption of cannabis can lead to symptoms like difficulty in coordinating movements, decreased muscle strength, lethargy, and delayed responses. In some cases, higher doses can cause confusion, amnesia, delusions, or hallucinations.[24]

Cannabis and cannabinoids may be effective in relieving chronic pain, particularly neuropathic pain. Certain cannabinoid medications, dronabinol and nabilone, which are synthetic forms of THC are approved to treat nausea and vomiting caused by chemotherapy.[25] Oral cannabinoids may help improve spasticity symptoms in some people with multiple sclerosis. CBD-based medications like epidiolex are approved for treating specific severe forms of epilepsy. Dronabinol is also approved for medical use to stimulate appetite in individuals with AIDS-related weight loss. Cannabinoids might play a role in treating sleep issues. There is some evidence suggesting cannabis may help relieve symptoms of post-traumatic stress disorder. It also has analgesic, antiemetic and appetite-stimulating properties. A non-psychoactive cannabinoid such as CBD has shown potential therapeutic effects, with anti-inflammatory, analgesic, anti-anxiety, and anti-seizure properties.[26]

9. ***Papaver somniferum*** (Opium poppy)

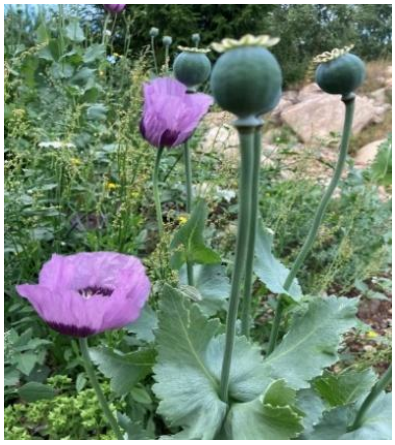

Figure 9: *Papaver somniferum*

Papaver somniferum, commonly known as the opium poppy (Family Papaveraceae) is an annual flowering herb growing to about 40 inches (Figure 9). Originally a native of eastern Mediterranean regions, it was propagated throughout the world by different rulers, traders and races. Opium poppy is an incredibly significant plant and historically been used from the third century B.C. for the treatment of dysenteries. The term opioid refers to all compounds related to opium. It is used in modern medicine as it contains numerous alkaloids such as morphine, codeine, thebaine, papaverine and noscapine that are classified as narcotic drugs. Their use is strictly regulated due to the risk of abuse and dependency.[27] Australia, Turkey and India are the major producers of poppy for medicinal purposes and poppy-based drugs, such as morphine or codeine.

Morphine is a highly effective narcotic analgesic commonly used to manage severe pain, including post-surgical pain, cancer-related pain, and pain associated with heart attacks. It can be administered orally, intravenously, or epidurally. Codeine is a mild analgesic and antitussive, commonly used to treat mild to moderate pain. It is included in some cough syrups to suppress coughing. Thebaine is not directly used as an analgesic; it is a precursor in the synthesis of other opioids like oxycodone, a semi-synthetic opioid analgesic used for moderate to severe pain and naloxone which is an opioid antagonist. Hydrocodone is another semi-synthetic opioid analgesic, often combined with other pain relievers like acetaminophen. Papaverine is primarily used as a vasodilator, to relax smooth muscles and improve blood flow. It has applications in treating erectile dysfunction and some vascular conditions. Noscapine has been studied for its potential anticancer and antitussive properties, although it is not as

widely used as morphine or codeine. Morphine and thebaine extracted from *Papaver somniferum* are chemically modified to produce other important opioid medications, including heroin and diacetylmorphine. While having potent analgesic effects, its high addictive potential restricts its medical use in many countries.[25]

In summary, *Papaver somniferum* is fundamental to modern medicine as the natural source of vital opioid analgesics like morphine and codeine, as well as precursors for other synthetic and semi-synthetic opioids used to manage pain and other conditions. The cultivation and processing of opium poppies for medicinal purposes are strictly regulated globally due to the addictive nature of these substances.[28]

10. ***Nicotiana tabacum***

Figure 10: *Nicotiana tabacum*

Nicotiana tabacum (tobacco) is a toxic plant which, belongs to the family Solanaceae (Figure 10). Historically and in some traditional medicine systems, tobacco has been used for various medicinal purposes. Native Americans traditionally used it for conditions like bronchitis, toothache, healing wounds and skin issues. Traditional Chinese Medicine also documented its use for pain relief and detoxification. Tobacco is mainly used in cigarettes and other tobacco products. The plant contains an alkaloid called nicotine which gives a sense of pleasure through its effects on the brain. Smoking of tobacco is an addiction as nicotine stimulates the brain to release dopamine, a neurotransmitter associated with pleasure and relaxation. Nicotine, along with other alkaloids like anabasine, acts on nicotinic receptors, causing various physiological effects that can be toxic. Nicotine is a highly toxic alkaloid and it acts on nicotinic acetylcholine receptors, causing a chain of events that can lead to various toxic effects. Nicotine's action on nicotinic receptors leads to increased sodium ion influx, membrane depolarization, and enhanced action potential propagation. This affects the central and autonomic nervous systems, neuromuscular junctions, and the adrenal medulla, leading to a range of symptoms. Exposure to nicotine can cause symptoms like abdominal pain, hypertension, tachycardia, tremors, and even respiratory failure in severe cases. Poisoning can occur through ingestion, skin contact, or occupational exposure.[29]

Nicotiana tabacum and its components are used in modern medicine for Nicotine Replacement Therapy (NRT). It is available as patches, gums, lozenges, inhalers and nasal sprays. It contains various other phytochemicals. Much emphasis is placed in modern medical and pharmaceutical research on these metabolites, excluding the harmful components of smoke, to elucidate their potential therapeutic value in neurodegenerative diseases such as Alzheimer's and Parkinson's, inflammatory conditions like colitis, arthritis, and multiple sclerosis, as well as metabolic disorders including obesity and fatty liver.[30] However, this research is still in its early stages, and many of these components have yet to be fully explored or integrated into mainstream medical practice as anticipated.

11. ***Abrus precatorius*** **(Kunnikuru)**

While *Abrus precatorius* (Kunnikuru) has a long history of use in traditional medicine,

its usage in modern medicine is extremely limited due to its high toxicity (Figure 11). The seeds contain abrin, a potent toxin that

Figure 11: *Abrus precatorius*

can be fatal if ingested, especially if the seeds are chewed or broken. In traditional systems of medicine like Ayurveda, after careful detoxification processes, various parts of *Abrus precatorius* have been used for premature greying and hair fall. Paste made from purified seeds is used for joint pain, swelling, and sciatica; root powder mixed with honey is used for cough; leaf decoction for cough and flu; and leaf paste for leucoderma and other skin conditions. Seed powder is used for treating worms. The plant also holds significance in traditional medicine, where it is used as an aphrodisiac, abortifacient, and in the treatment of jaundice and snakebites. Due to the potent toxicity of abrin, *Abrus precatorius* is not generally used in mainstream modern medicine. The risks associated with its internal use without proper detoxification are very high. However, there is some modern research exploring the potential of certain compounds found in *Abrus precatorius*. Studies are underway on the potential use of seed extracts in protecting against oxidative damage in the eye lens, antimicrobial, anti-diabetic, anti-tumor, and anti-inflammatory properties.[31] Researches are investigating the potential use of the plant with various extracts of the plant parts.

12. ***Nerium oleander*** **(Arali)**

Figure 12: *Nerium oleander*

Nerium oleander popularly known as 'oleander' or 'arali' is an ornamental plant coming under the family Apocynaceae. It is grown in gardens for its beautiful pink, red, yellow and white flowers (Figure 12). The plant is widely seen in the tropical and subtropical regions and is commonly recognized as a toxic plant to animals. Toxicity in humans is rarely reported. Animal deaths are common as they may eat the leaves and flowers of this plant in large quantity, which causes acute poisoning. Many incidents of deaths of domestic animals due to eating oleander flowers and leaves have been reported in Kerala. It has been shown in animal studies that the toxicity of oleandrin is about 40-50mg/kg body weight.[32] That means a person of 60 kg body weight needs at least 3 grams of toxin to show an effect. It is known that oleander leaves are more poisonous than the flowers and has been estimated that 12-15 oleander leaves can produce a fatal quantity of the toxin in the human blood.

The toxin oleandrin can cause both gastrointestinal and cardiac effect. The central nervous system manifestations of oleandrin toxicity are confusion, dizziness, drowsiness, weakness, visual disturbances and mydriasis. The most serious side effects

of oleander poisoning are cardiac abnormalities, including various ventricular dysrhythmias, tachyarrhythmias, bradycardia, and heart block. The poison oleandrin can produce burning sensation in oral cavity, headache, vomiting, gastric colic, hyperkalaemia and diarrhoea. It can cause cardiac arrhythmias possibly through electrolyte imbalances by disturbing the homeostasis mechanism of the body. Even if the toxicity is not dangerous, prolonged vomiting and diarrhoea can cause the loss of electrolytes leading to death if no proper medical attention is given. In traditional medicines, oleander parts have been used and tried for its presumed therapeutic purposes. Nevertheless, there is no clinical evidence that oleander or its constituents, including oleandrin, are safe or effective in any disease.[33] During Covid-19 pandemic, the Trump administration in US was considering oleandrin as a phytochemical to treat the disease; however, it was not approved by FDA. *Oleander* plant tissues contain cardenolide glycosides, a phytotoxin, that are capable of exerting positive inotropic (force of contraction) and negative chronotropic effects (decreased heart rate) on the heart muscles of animals and humans. Pharmacological action of oleander cardenolides is similar to that of the classic digitalis glycosides by inhibiting Na^+ K^+ ATPase enzyme but there are differences in toxicity and extra cardiac effects. Toxic exposures of humans and wildlife to oleander cardenolides occur throughout geographic regions where these plants are grown. The human mortality associated with oleander ingestion is generally very low, even in cases of intentional consumption. Experimental animal models have been successfully utilized to evaluate various treatment protocols designed to manage toxic oleander exposures.[34]

13. *Aconitum heterophyllum*

Aconitum heterophyllum is a perennial herb native to the Western Himalayas, found in Jammu & Kashmir, Himachal Pradesh,

Figure 13: *Aconitum heterophyllum*

Uttarakhand, Sikkim, Nepal and Pakistan (figure 13). It typically grows at high altitudes in the sub-alpine and alpine zones, ranging from 2500 to 4000 metres above sea level. It prefers grassy slopes in the alpine Himalayan region and sometimes grows in forests with humus-rich soils. Aconitum contains diterpenoid alkaloids, including benzoyecasonine, mesaconitine, aconitine, hypaconitine, heteratisine, atidine, isotisine, hetidine, and hetsinone. Aconitine, found in many *Aconitum* species, is a highly toxic cardiotoxin and neurotoxin. Symptoms of Aconitum poisoning generally include neurological, cardiovascular, and gastrointestinal issues.[35] However, some reports suggest that *Aconitum heterophyllum* may not contain or have very low levels of aconitine compared to other *Aconitum* species. But it does contain other intensely bitter alkaloids. Traditional preparation methods, such as boiling and purification, are employed to reduce potential toxicity. [36]

Aconitum heterophyllum has significant use in traditional medicine systems like Ayurveda and Chinese Medicine. It is used to reduce fever, especially in paediatric

medicine, indigestion, flatulence, abdominal pain, and diarrhoea. It is also used in alternative medicine as an expectorant for treating coughs, bronchitis, and asthma.[36] It is used to relieve pain and inflammation. Anthelmintic, antiemetic, hepatoprotective, antioxidant, and immunomodulatory effects also have been reported. Modern research is exploring its antimicrobial, anti-inflammatory, analgesic, antioxidant, and nephroprotective activities.

14. ***Datura stramonium***
(Thorn Apple, Ummum)

Figure 14: *Datura stramonium*

Datura stramonium is an annual, erect, herbaceous plant that typically grows to a height of 0.5 to 1.5 meters (Figure 14). It is believed to be native to Central America but has naturalized widely throughout the world in temperate and tropical regions. It thrives in disturbed sites, such as wastelands, roadsides, cultivated fields, and gardens. It prefers rich, well-drained soil and sunny locations. In India, including Kerala, it can be found as a common weed, particularly in wastelands and along roadsides. It tends to flourish during the warmer months.[8]

All parts of *Datura stramonium* are highly toxic. The concentration of toxic alkaloids can vary depending on the plant's age and the specific part. The primary toxic compounds are tropane alkaloids, including scopolamine (hyoscine), hyoscyamine, atropine.[37] These alkaloids have anticholinergic effects, blocking the action of acetylcholine in the central and peripheral nervous systems. Symptoms of Datura poisoning can appear rapidly and may include, dilated pupils (mydriasis), blurred vision, dry mouth and skin, rapid heartbeat (tachycardia), increased body temperature, flushed face, restlessness, agitation, confusion, hallucinations, delirium, seizures and coma. Accidental poisoning can happen through ingestion of seeds or other plant parts. There are also documented cases of intentional misuse for hallucinogenic effects, which is extremely dangerous due to the unpredictable and severe toxicity.[38]

Historically, *Datura stramonium* has been used in traditional medicine in various cultures. But due to its high toxicity,its use in modern medicine is very limited and highly controlled. Traditonal practices include smoking the leaves to relieve symptoms of asthma and topical application for pain and muscle spasms. The isolated tropane alkaloids, scopolamine, hyoscyamine, atropine are used in modern pharmacology allowing for precise dosing and safer application. Scopolamine is used to prevent motion sickness and sometimes as a pre-anaesthetic to reduce secretions. Atropine is used as a mydriatic, to treat bradycardia, and as an antidote for certain types of poisoning. Hyoscyamine is used to treat gastrointestinal disorders such as irritable bowel syndrome.[37]

15. ***Catharanthus roseus***

Figure 15: *Catharanthus roseus*

Catharanthus roseus is formerly known as *Vinca rosea* is widely cultivated as an ornamental plant in almost all tropical and subtropical countries worldwide (Figure 15). It has been grown as a garden plant for its colourful flowers. All parts of *Catharanthus roseus* are considered poisonous if consumed orally by humans and animals. The toxicity is due to the presence of various alkaloids, including vincristine and vinblastine. If ingested it can produce stomach cramps, nausea and vomiting, and diarrhoea as immediate sign of poisoning. It also produces hypotension, cardiac complications, and neuropathy and in severe cases systemic paralysis leading to death.[39]

Despite its toxicity, *Catharanthus roseus* is a significant medicinal plant, primarily known as a source of vinca alkaloids used in cancer chemotherapy. The plant contains alkaloids like vincristine, vinblastine, vinflunine, and vindesine, which are used to treat various cancers, including leukaemia, Hodgkin's lymphoma, breast cancer, lung cancer, neuroblastoma Wilms' tumour, testicular carcinoma and urothelial carcinoma.[40]

16. ***Rauvolfia serpentina***
(Local name Sarpagandha)

Figure 16: *Rauvolfia serpentina*

Rauvolfia serpentina belonging to the family Apocynaceae is a native of Indian subcontinent and Southeast Asia usually well adapted to hot and humid climates (Figure 16). *Rauvolfia serpentina* contains several alkaloids, including ajmaline, ajmalicine, reserpine, and serpentine and yohimbine, which are potent toxins and can cause side effects.[41] In folk medicine, it has been used for snake and insect bites, fever, malaria, abdominal pain, dysentery, and to stimulate uterine contractions during childbirth. The plant was mentioned in Hindu manuscripts as long ago as 1000 BC.

The alkaloid reserpine lowers blood pressure by depleting neurotransmitters in the sympathetic nervous system, leading to vasodilation and a reduced heart rate. In the past, it was widely used to treat hypertension.[42] Traditionally, it has been used to manage anxiety, insomnia, and psychosis. Although reserpine has sedative and tranquilizing effects, its use for severe mental disorders has largely been replaced by safer alternatives. Ajmaline is effective as an antiarrhythmic, particularly in treating Brugada syndrome and acute atrial or ventricular tachycardia. Ajmalicine is also used in the management of circulatory disorders and possesses potential neuroprotective and anti-inflammatory effects. Serpentine exhibits antihistaminic activity and has been used in traditional medicine for treating snakebites, along with its known anti-inflammatory properties. Yohimbine, an α2-adrenergic receptor antagonist, works by blocking the action of norepinephrine at the receptor level. It has been explored in various research contexts, particularly for its effects on cardiovascular and neurological functions.[43]

Conclusion

In conclusion, the term "poisonous" when applied to plants is fundamentally a relative concept, contingent upon dosage, individual sensitivity, and the specific context of human interaction. Far from being inherently malicious, the compounds

we perceive as toxic are, in fact, vital biochemical tools that have evolved over millennia to serve crucial roles in the plant's survival acting as deterrents against herbivores, defences against pathogens, or even as facilitators in reproductive strategies. Toxic plants and their therapeutic use underscore that the plant-derived substances are not arbitrary threats but rather sophisticated products of natural selection, integral to the ecological balance and a need for the plant's survival. As intelligent beings, humans have consistently demonstrated a remarkable ability to adapt, learn, and innovate, often transforming adversity into opportunity. Through the integration of scientific research, traditional knowledge, and technological advancement, the complexities of plant biochemistry can be progressively unravelled. This growing understanding enables us not only to mitigate the potential dangers of certain plant compounds but also to harness their benefits for medicinal, agricultural, and industrial applications. In doing so, we move beyond a simplistic notion of "toxins" towards a more nuanced appreciation of nature's intricate chemistry and our own adaptive ingenuity.

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