Review

Potential significance of medicinal plants in forensic analysis: A review

Saqer S. Alotaibi [a,*], Doaa Alshoaibi [a], Hala Alamari [a,b], Sarah Albogami [a], Eman Khan [a], Areej Alshanbari [a], Hadeer Darwish [a], Bashaer Alshanqiti [a], Hanan Alghamdi [a], Wafa Almalki [a]

[a] Department of Biotechnology, College of Science, Taif University, P.O.BOX 11099, Taif 21944, Saudi Arabia
[b] Institute of Biology and Environmental Research, National Center for Biotechnology, King Abdulaziz City for Science and Technology, Riyadh, Saudi Arabia

A R T I C L E   I N F O

A B S T R A C T

Medicinal plants are a two-edged sword that might be exploited as a treatment specific dosage, and as deadly poisonous substances to commit murder or suicide when administered in high doses. Forensic experts can collect traces and residual materials from these toxic medicinal plants at a crime scene as forensic evidence. Further, more investigations need to be deeply implemented to in the future to understand the significance of medicinal plants in forensic investigations to detect these criminal offenses. Additionally, to provides a deep understanding of chemical substances that can impact human life positively or negatively with different doses as well as identifying the optimal or overdose concentrations for either treatments or poisonous effects using recent biotechnological approaches. This review aims to illustrate different contributions and the significance of medicinal plants in the field and further employment in the context of forensic science, especially in the Kingdom of Saudi Arabia.

© 2021 The Author(s). Published by Elsevier B.V. on behalf of King Saud University. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Contents

* Corresponding author.
  E-mail address: saqer@tu.edu.sa (S.S. Alotaibi).
Peer review under responsibility of King Saud University.

Production and hosting by Elsevier

1. Introduction

Plant contains enormous biochemical compounds that called Phytochemicals. They are classified as bioactive substrates in

which they offer many benefits for human health (Hasler et al., 1991; Quideau et al., 2011). These phytochemicals or substrates encompass several biological compounds such as terpenes, polyphenols, and alkaloids. Most of pharmacological activities are located in alkaloids; anti-asthma, anti-cancer (Kittakoop et al., 2014). Moreover, many toxic compounds could also be possessed into alkaloids such as tubocurarine and atropine (Awuchi, 2019).

For thousands of years, since about 2600 BCE, the healthcare system was dependent on herbal medicine (World Health Organization (WHO), 2013; Dar et al., 2017). Nowadays, medicinal plants are considered a typical ingredient for creating medications to treat people, especially in developing countries. Medicinal plants have been used for ages to cure diseases such as colds, coughs, inflammation, and parasitic infection. The plants listed include "oils of the *Commiphora* sp. (myrrh), *Cedrus* sp. (cedar), *Glycyrrhiza glabra* (liquorice), *Papaver somniferum* (poppy juice), and *Cupressus sempervirens* (cypress)" (Dar et al., 2017). However, several species of plants appear to have some side effects on human health. The concern over-using medicinal plants in the healthcare system is increasing abruptly regarding the adverse impact, which might be due to several influences, such as the plant's location, alterations in soil content and composition, and other environmental effects e.g. the harvesting process might play a role in changing the plant's chemical compounds (Saad et al., 2006).

It is recognised that medicinal plant is a double-edged sword that could be used not only for medical treatments, where it is called alternative medicine (AM), but also has been used for several adverse purposes, such as death, severe injury, and stupefying via controlling poisons substances concentration. Poisonous plants are one of several natural poisonous substances that can cause disturbances or even death (Pillay and Sasidharan, 2019). India has the highest incidence of the use of medicinal plants as a killer substance, in war as a war tactic (poisoned weapons), as well as for murder and suicide, using substantial doses in a singular instance or small doses for an extended period (Khajja et al., 2011; Pillay and Sasidharan, 2019). For example, Pillay and Sasidharan (2019) revealed that the *Nerium Oleander* is a medicinal plant that is grown in two attractive colours, pink and white. It is grown in gardens, schools, and all over India, and has been used as medicine to treat skin problems. However, it also appears to have some toxic effects attributable to its roots, leaves, seeds, and stems. Oleander plants contain cardiac glycosides, which predominantly cause cardiotoxicity, and in some cases, may lead to death. In contrast, some plants do not contain cardiac glycosides but still harm the human heart and oesophagus (Le Couteur & Fisher, 2002; Pillay and Sasidharan, 2019).

As another example, Peganum harmala (P. harmala) is a popular plant that grows in semi-arid rangeland regions such as the Middle East and North Africa. It is a toxic plant, poisoning humans and animals, which shows symptoms such as digestive and nerve syndromes accompanied by a narcotic state. It was confirmed that *P. harmala* is characterized by its constituent active chemical compounds, exhibiting high concentrations in the roots and seeds, especially when ripe. In the old days, the *P. harmala* plant was used to stimulate abortion. An experiment was performed on female rats by administering different doses of a methanolic extract from *P. harmala* for 30 days in small doses ranging from 2 to 3.5 g/day. It was observed that while the rats did not show any change in their physical and nutritional states, there was a uterine stimulatory effect (Mahmoudian et al., 2002).

The chemistry of medicinal plants provides a deep understanding of chemical substances that can affect either positively or negatively human life. For example, Opium is an opiate sedate derived from the poppy plant that ties to particular opioid receptors within the nervous system framework to deliver pain relief. The structure of opioid compounds is categorised depending on on: (I) the 4, 5-epoxymorphinan ring, e.g., morphine, codeine, oxymorphone, oxycodone, buprenorphine, hydromorphone, and hydrocodone; (ii) the phenylpiperidines, e.g., alfentanil, fentanyl, and sufentanil; and (iii) the diphenyl heptyl amines, e.g., methadone. Morphine was the first isolated at the beginning of the nineteenth century, discovered by Friedrich Sertürner in Germany (Drewes et al., 2013). The word morphine is derived from the term morphism, for Morpheus, a Greek god of dreams. Within twenty years, morphine was accessible across Europe as a cure for pain and many different uses, including treats (Gilson et al., 2013). The unlawful use of opioids, including heroin is now more prevalent. Previous study shows that high health risk for individuals could be happened after hooking on opioids prescription in which it is induced by intravenous injection. This high level of opioids use increases diversion and abuse opportunities (Al-Tayyib et. al., 2017).

Hence, medicinal and toxic plants provide strong evidence for forensic investigations in criminal offenses such as suicide or burglary. Toxic substances extracted from plants have been used as botanical weapons for different purposes and can be used in self-defence or criminal intent. (Dubey and his colleague noticed that professional criminals prefer to use toxic plant substances due to their availability at no cost (Dubey et al., 2018). Consequently, the concentration of the poison is based on the criminal's purpose. Several ways can detect criminal offenses, for example, biotechnology and molecular tools can detect specific toxins, new technology as well can detect specific poisonous, which uses a probe binding with specific receptors molecules. A professional forensic scientist can determine the toxins present in the body and tissue fluids using both qualitative and quantitative analyses based on molecular analysis methods as forensic techniques (Dubey et al., 2018). This paper aims to review and deepen the understanding of how medicinal plants could be used in crime orensic investigation's effectiveness to detect these criminal offences.

2. Medical plants

Since ancient times, myrrh and opium have been recorded on clay tablets as medicinal plants. The ancient Egyptian Ebers Papyrus listed about 800 medicinal plants, including juniper, castor bean, garlic, mandrake, and cannabis. Since then, hundreds of these spices and herbs have been used. In the same period, the Chinese used herbal medicine, including ephedra and hemp, in the treatment of leprosy. Aristotle's pupil, Theophrastus, in the 4th century BCE, recorded the first systematic botany text titled Historia Plantarum. In the 60th century CE, a Greek physician named *Pedanius dioscrides* recommended over 1,000 herbal remedies prepared from over 600 medicinal plants in his De Material Medica. This precious book served as a reference for herbalists for more than 1,500 decades in the 17th century. Application of the chemical analysis of plants and the active compounds' extraction initiated a new mass scale science. When alkaloids such as morphine were extracted from poppy, and when *Strychnos ipecacuanha* quinine was extracted from the cinchona tree, new medicines were prepared. The history of morphine extraction began in 1826 and that of salicylic acid in 1853, ushering in the current era of drug discovery (Awuchi, 2019). Millions of people worldwide depend on local herbal remedies, plants, and animal products for the treatment of many ailments and wound care (WHO, 2013).

2.1. Uses and importance of medical plants

Medicinal plants are used in alternative medicine because they have several therapeutic effects. Using such natural preparations is steadily increasing because it is cheaper than a commercial synthetic drug. These preparations are typically taken as a drink with-

out a prescription. Furthermore, alternative medicine has limited some side effects than conventional treatment (So et al., 2018). Plants and some other organisms, such as fungi, are now considered important sources of potential medicines for several diseases, including cancer, heart disease, dementia, and malaria (Awuchi, 2019).

Developments in genetic engineering tools have enabled scientists to prepare several compounds used in medicine manufacture and facilitated advancements in using tissue culture to propagate and cultivate medicinal plants and the collection of desired bioactive compounds (Rao and Ravishankar, 2002). This advanced technology enables us to produce more significant quantities of active material via callus culture and micro-propagation (Baker et al., 2007). Recently, biotechnology has offered attractive opportunities for the production of plant-based in vitro systems (e.g., callus cultures, cell suspension cultures, and organ cultures) and genetic manipulation to facilitate the generation of desired plants and plant products. As an increasing number of natural habitats are rapidly being destroyed, biotechnological in vitro has been used to obtain secondary products in greater quantities than those found in vivo cultivated plants (Lata et al., 2008; Efferth, 2019).

2.2. Identifying the effectiveness of medicinal plants for human health

Plants have been used since time immemorial for diverse purposes by humankind, particularly as food for nutrition and as medicine for treating diseases in both humans and animals. Plants are used in all cultures worldwide and have been relied upon for several millennia to support, promote, and restore human health (Awuchi, 2019).

Medicinal plants have been the first-in-line treatment for trauma, infection, disease, and injury from prehistory. Over millennia, humans have learned to identify and transform botanical resources from the immediate environment, and with the development of trade, they have utilized these resources as food and medicine. Many of these ancient and traditional medicinal plants have been validated as having therapeutic benefits, albeit not always via controlled clinical trials. One unexpected outcome of these validation studies is how many medical plants synthesize equivalent or closely related compounds (Shedoeva et al., 2019).

The most critical drugs reported by the World Health Organization (WHO) as widely used and essential for health are 252 in number, 11% of which are derived from plants, e.g., digoxin is obtained from Digitalis spp., atropine is from Atropa belladonna, quinidine is from Cinchona spp., and codeine is from Papaver somniferum (So et al., 2018). Interestingly, of the new anticancer drugs developed between 1940 and 2002, approximately 54% were derived from natural products (Yuan et al., 2016). A study has determined that 73% of all current pharmaceutical products include ingredients derived from natural products (Wangchuk, 2018). (See some examples in table 1).

2.3. Poisonous medicinal plants

The biosafety of any material is the safety margin for the administration of such a compound. Plants are rich in chemical compounds that may interact with other chemical compounds to yield some toxic material. Furthermore, the administration of large quantities of such chemicals may interfere or disturb humans and animals' immune systems. Cytotoxicity or organotoxicity in living organisms may be acute, subacute, or chronic, depending on the dose and duration of exposure. Thus, a wise approach should be adopted, and administration should be under an herbalist's supervision. Investigation into the active components of the plant material should also be considered. Tropane alkaloids and cardiac glycosides are used in traditional medicine. However, these compounds may be toxic or exert side effects, even when taken in crude form or as plant material (Builders, 2019).

Moreover, some of these medicinal plants have toxic effects when taken in high doses, leading to death. An example is Peganum harmala, commonly known as Syrian rue, widely used as a medicinal plant (Khlifi et al., 2013). It belongs to the family Zygophyllaceae in the order Zygophyllales, which contains about 22 genera and more than 250 species (Asgarpanah and Ramezanloo, 2012). The primary origin of P. harmala is Central Asia. Still, it grows in Australia, North Africa, and Southwest America, and it is a part of the flora in the Kingdom of Saudi Arabia (Niroumand et al., 2015). Additionally, it is a highly branched perennial, herbaceous, and glabrous plant that grows from 30 cm to 60 cm in height, with short creeping roots and narrow leaves arranged alternately on fleshy, bright green stiff stems. The flowers are solitary, small, pale yellow or white, and five-petaled. The fruits are capsules with three chambers and are approximately 6–10 mm across. The unripe fruits are green, turning orange-brown when mature, and these capsules contain more than 50 tiny black-brown triangular seeds (Niroumand et al., 2015). The plant's main medicinal part is the seed, which contains approximately 2–6% pharmacologically active alkaloids, mostly b-carbolines (e.g., harmine, harmaline, harman, and harmalol), quinazoline subordinates, vasicine, and vasicinone (Khlifi et al., 2013). The best use of P. harmala is its utilization as a legendary pharmaceutical for the treatment of different conditions, including lumbago, asthma, colic, and jaundice, and as a stimulant emmenagogue. P. harmala is also notable for its anti-tumour impact, curing intestinal sickness, being antileishmanial, anti-spasmodic, anti-histaminic, and vasorelaxant. It is also useful for healing wounds, recuperation from leukaemia, pain relief, antioxidant movement, and hepatoprotection, as well as having immunomodulatory properties, anti-inflammatory properties, hypoglycaemic impact, and antinociceptive impact (Asgarpanah and Ramezanloo, 2012).

P. harmala contains β-carboline alkaloids, which have a distinctive cardiovascular impact, such as bradycardia, diminished systemic blood vessel function, and lower blood weight. It contributes to fringe vascular resistance, has been shown to have anti-platelet aggregation effects, and is used to treat some nervous

Table 1
Some examples of medicinal plants and their active components and utilizations:

No.	Plants	Active components	Utilization and toxic effects	Reference
1	**Glycyrrhiza glabra (liquorice)**	Glycyrrhizic acid 18β-glycyrrhetinic acid, glabrin A and B, isoflavones	Antibacterial, anti-inflammatory, antiviral, antioxidant, and anti-diabetic activities	(Pastorino et al., 2018)
2	**Nerium Oleande**	Oleandrin - cardenolide and pregnatriene compounds	Arrange heart beats disorder - toxic effect	(Bavunoğlu et al., 2016)
3	**Peganum harmala**	β-carboline alkaloids	Aistinctive cardiovascular impact, such as bradycardia, diminished systemic blood vessel function, - toxic effect	(Moloudizargari et al., 2013)
4	**Strychnos ipecacuanha**	Strychnos indole alkaloids	Anti-tumor alkaloids	(Knolker, 2017)

system diseases, e.g., Parkinson's disease (Khlifi et al., 2013). However, all parts of the plant are considered toxic. In other words, *P. harmala* has harmful effects on animals and humans (Asgarpanah and Ramezanloo, 2012). In animals, the common toxicity symptoms are accelerated breathing, accelerated pulse, clonic muscular spasms, anorexia, hypersalivation, vomiting, and diarrhea (Mahmoudian et al., 2002). Regarding toxicity in humans, women generally use *P. harmala* to treat amenorrhea, but it has toxic effects only when taken at high doses. The common symptoms are hallucinations, neurosensorial syndromes, bradycardia, and gastrointestinal disturbances such as nausea and vomiting (Asgarpanah and Ramezanloo, 2012). In other cases, the effects of an overdose come as gastrointestinal distress and vomiting blood. On physical examination, there is a slight elevation in body temperature, a high pulse rate, low blood pressure, convulsion, tremor (limbs and facial muscles), visual hallucination, and abdominal pain (Mahmoudian et al., 2002).

2.4. Medicinal plant overdose causing human death

Plants are full of different biologically active phytochemicals (alkaloids, glycosides, terpenoids) that affect living organisms and humans. Synergism, antagonism, or chemical reaction may occur between such compounds, leading to unknown effects that may be beneficial or harmful to health. Some of these phytochemicals have a wide safety margin. They do not affect biological function, while others should be taken cautiously as they may affect or damage the biological functioning of the individual. A toxic dose may be acute (exert its effect quickly) or chronic (take effect after a long period of exposure). However, most medicinal plants with toxic or harmful side effects are known and are used under the supervision of professionals or experienced individuals (Hasler et al., 1991; Awuchi, 2019).

3. Opioids

In 3400 BCE, the opium poppy was planted in Mesopotamia. Opium is a combination of poppy seed alkaloids. Opiates include alkaloids such as morphine or codeine that exist naturally, and opioid is the word commonly used to refer to several compounds that bind to opioid receptors. Initially, the concept of narcotics (derived from the Greek word stupor) was used to denote sleep medication and describe opioids. Still, today it is the legal concept for abused drugs (Trescot et al., 2008).

Furthermore, opioids have been used for several years to relieve pain. The use of opium for pain relief is recorded in ancient Egyptian papyrus records (Trescot et al., 2008). In 1973, Candace Pert, a graduate student, used radioactive morphine to determine the location of morphine's target site and discovered, unexpectedly, that the drug bonded to particular regions of the brain now called morphine receptors (Trescot et al., 2008).

Opioids have been classified as a family of related pain-relieving medications. Most opioids (sometimes called narcotics) are chemically linked to opium, a substance harvested from poppy plants. Opioid drugs primarily include heroin, opium, hydrocodone, morphine, codeine, sufentanil, fentanyl methadone, oxycodone, and paregoric. Furthermore, the pain-relieving effects of opioids have been employed before and during surgical operations, e.g., to mitigate childbirth pain , injuries, and other pain-inducing conditions, as administered by a doctor. While opioid prescriptions have benefited millions of patients afflicted with pain, it is possible to misuse these medicines (Torpy et al., 2004).

3.1. Structure

Prototypical opioids are called phenanthrenes. The presence of a 6-hydroxyl group is associated with an increased incidence of hallucinations and nausea. For instance, codeine and morphine, combined with 6-hydroxyl groups, are correlated with sickness and show a stronger association than hydromorphone and oxycodone, free of 6-hydroxyl groups. In this appropriate case, the opioids comprise codeine, morphine, levorphanol, hydromorphone, hydrocodone, oxycodone, buprenorphine, oxymorphone, butorphanol, and nalbuphine. Benzomorphans, which have only pentazocine as a member of this group, is considered an agonist or antagonist associated with a high likelihood of dysphoria. Phenylpiperidines comprise alfentanil, fentanyl, meperidine, and sufentanil. Fentanyl possesses the highest affinity for the mu receptor. Diphenylheptanes include methadone and propoxyphene (Trescot et al., 2008).

3.2. Ingredients of prescribed opioids and their mode of action

Feelings of pleasure that relieve pain: some health care providers prescribe opioids for patients in severe or persistent pain. Legally prescribed opioids include fentanyl, oxycodone, codeine, buprenorphine, methadone, morphine, oxymorphone, and hydrocodone. Other opioids are illegal, e.g., heroin. The mode of action of opioids is to bind to receptors within the CNS and in peripheral tissues. Typically, naturally secreted endogenous peptides bind to these receptors, triggering stimulation. Specific natural compounds, including enkephalins, endorphins, and dynorphins, are synthesized and effect after noxious stimulation. Greek letters express the names of opioid receptors based on their prototype agonists (Rosenblum et al., 2008).

Mu (μ) receptors (agonist: morphine) are present primarily in the medial thalamus and the brainstem. Mu receptors are specifically implicated in down-regulation of the respiratory core and gastrointestinal motility, supraspinal analgesia, activation or euphoria, analgesia, or sedation. Subtypes include mu1 and mu2. Mu1 is related to analgesia, activation, and luminosity, while mu2 is related to dyspnoea or respiratory function, hypersensitivity, prolactin secretion, reliance, and appetite loss. These are also called OP3 morphine opioid receptors (MORs). Kappa (κ) receptors (agonist: ketocyclazocine) are also called OP2 or kappa opioid receptors (KORs). Kappa receptors are found in the brain stem, the diencephalic and limbic areas, and the spinal cord. They are responsible for spinal sedation, analgesia, dyspnoea, reliance, and dysphoria. Delta (δ) receptors (agonist: delta-alanine-enkephalin-delta-leucine) are found primarily in the brain, and to date, their effects have not been well investigated. They may be responsible for psychomimetic euphoric effects. They are also called OP1 or delta-opioid receptors (DORs) (Jaffe and Martin, 1990; Rosenblum et al., 2008; Drewes et al., 2013).

Sigma (σ) receptors (agonist: N-allylnormetazocine) regulate psychomimetic effects, speech, dysphoria, and depression resulting from stress. They are no longer treated as opioid receptors but as the target sites for phencyclidine (PCP) and its analogs. These three opioid receptors are under the control of specific genes. Each receptor consists of an extracellular N-terminus, an intracellular C-terminus, seven *trans*-membrane helical twists, and three extracellular and intracellular loops (Hanner et al., 1996; Rousseaux and Greene, 2016).

After the receptor is stimulated, it secretes a specific G protein, diffuses through the membrane, and binds to its target (either an enzyme or an ion channel). These targets inhibit cyclic adenosine monophosphate (cAMP) and modify the phosphorylation of the protein. The cAMP acts as the second messenger inside the cell and induces the activation of enzymes such as protein kinases

(short-term effect) and gene transcription proteins (long-term impact) (Jain et al., 2020). While these compounds differ in chemical structure, physicochemical properties, and pharmacokinetics, they are characterized by their interaction with the mu opioid receptor as the primary target. However, significant differences have been reported regarding the clinical responses (efficacy, toxicity, and safety) to the different opioid classes. Furthermore, substantial pharmaceutical inter-individual variations exist between these opioid classes (Drewes et al., 2013).

3.3. Medicinal chemical components

Morphine is well known as the opioid of choice for sedation for cancer pain (Drewes et al., 2013). It is widely recommended because of its availability, familiarity, and price. Recently, potent alternative opioids have become available as buprenorphine, oxycodone, methadone, hydromorphone, alfentanil, and fentanyl. The choice of a powerful opioid in severe pain treatments is incredibly varied (Drewes et al., 2013). Morphine and codeine are the most widely used opium alkaloids. In humans, they act on the CNS to promote analgesia, euphoria, sedation, respiratory depression, and cough sedation, and they have peripheral effects such as constipation (Tok and Gowder, 2019).

Morphine has a benzene ring bound to a phenolic hydroxyl group at the 3-carbon atom, an alcoholic hydroxyl group at the 6-carbon atom, and its nitrogen atom. When both hydroxyl groups change to ether, codeine is formed as a morphine derivative. The nitrogen group attached to the benzene ring plays a vital analgesic role in morphine. Because morphine cannot pass into the CNS. Nalorphine is a morphinane alkaloid, N-allylnormorphine, synthesized from morphine by its complete acetylation, i.e. by transformation into heroin to temporarily protect the hydroxyl groups, and then by undergoing demethylation (Trescot et al., 2008). Morphine is optically active, and only its laevorotatory isomer has an analgesic effect. Oral administration of morphine has not been recommended because it has been accompanied by immediate metabolic changes in the liver, decreasing analgesia duration, except when administered as sustained-release tablets (Tok and Gowder, 2019).

4. Forensic diagnosis

Forensic science involves the application of different scientific fields to the legal system. Forensic toxicology is a hybridization of contemporary analytical chemistry and fundamental toxicology and their implementation within the legal framework to answer questions that arise during judicial proceedings linked to intoxication.

Forensic toxicology is primarily concerned with the medicolegal features of the of xenobiotics' damaging effects on human beings and animals. The analysis and the empathy of medicines and the conservation of agricultural, industrial, and public health law to safeguard clean air, pure water, and provisions of safe food are also fields of forensic toxicology, though more relevant to civil courts than criminal courts. Storage steadiness is also a significant issue to be measured during the pre-analytic phase. Its deliberation would reduce the valuation of sample quality and the systematic result obtained from that sample. Information mechanisms and means to raise storage faithfulness may enable forensic toxicologists to avoid likely difficulties. Therefore, the benefits and limitations of specimen preservation events are thoroughly deliberated in this review. Presently, matched protocols for sampling in supposed intoxications should have direct utility (Dinis-Oliveira et al., 2010).

Plants can be witnesses that offer evidence of suicide, theft, and other criminal offenses . Parts of plants may have lodged in the clothing or properties of the perpetrator of a crime. They may later serve as evidence in a court of law when those trained in taxonomy, molecular taxonomy, anatomy, and ecology perceive their significance. The first incident happened in 1935 when Bruno Hauptmann was tried for kidnapping. The son of Charles and Anne Lindbergh, and Arthur Koehler, a wood technologist (scientist), used his knowledge of wood anatomy to detect the origin of one of the parts of a wooden ladder used in the crime to reach the baby son. Botanical information had never before been admitted as evidence in the history of the American judicial system. Later, Koehler's work and testimony served as a precedent for the addition of botanical evidence in subsequent court cases. Plants that produce toxic substances in the form of secondary metabolites for self-defence can also be used as forensic investigation indicators. Plants are used as tools and weapons for killing and various crimes in recent times. Some poisonous plant species, such as Conium, Cicuta, Nerium, Aconitum, Datura, and Ricinus, which are very toxic and are used for homicidal and suicidal purposes, are particularly useful in forensics for the apprehension of criminals (Dinis-Oliveira et al., 2010).

Plants that are allergens and only slightly poisonous are commonly used in the robbery. These plants choose of professional criminals because they are easily obtainable at no cost and have played a significant role, both in romance and crime. Poisoned weapons were used in ancient war tactics. Numerous poisoning methods were illustrated, explaining how poisons were mixed with food, drink, honey, and snuff or scattered over bedclothes, couches, shoes, jewelry, garlands, and horse saddles. Currently, there are numerous cases where criminals have applied these toxicants to food material or a target's body during bus and train rides. Much research has informed plants' toxicology, but nothing has been done on poisonous plants in a forensic framework. The toxicological materials of these plants offer a database for forensic toxicologists. Forensic specialists can save evidence connected to deliberate or accidental poisoning at crime scene using poisonous plants. Related to parts of plants, crime scenes such as forests/gardens and poisoning indications might lead investigations in the right direction (Dinis-Oliveira et al., 2010).

4.1. A dose of a poisonous plant may be a panacea or a lethal poison

The poisonous plant is an ancient system that has been used for treating illness from most diseases, even chronic diseases. The WHO confirmed that 80% of the Indian population relies on plant drugs, with 25% relying on modern drugs derived from isolated plants (Tamilselvan et al., 2014). The Siddha system is a technique in Indian traditional medicine that uses toxic plants to treat chronic disease people.

According to Tamilselvan et al. (2014), 'the dose makes the poisons' (p. 1), i.e., substances from a toxic plant can be harmful when used in a particular concentration. Forensic specialists can detect the side effects of using toxic plants on physiology and behaviour via tests on the blood, hair, liver, and kidney of an infected person (Beyer et al., 2009). Tamilselvan et al. (2014) clarified the method by which poisonous plants infect people or animals, in some cases causing death. Precatory pea or bean, or Indian licorice, is an example of a toxic plant that is toxic because it contains abrin. Abrin is a toxic substance derived from seeds that have two types of protein subunits: A and B. The subunit B binds to a specific protein that simplifies the access on host cell membranes. In contrast, protein A inactivates 26 subunits of a mammal's cell ribosomes, such that one molecule of abrin can lock 1,500 ribosomes (Tamilselvan et al., 2014).

A brain affected by the seeds of precatory pea shows adverse effects when imbibed via inhalation, which causes some breathing difficulties that can turn the skin blue. In contrast, oral ingestion can cause digestion difficulties such as vomiting, liver spleen, low blood pressure, and blood in urine, diarrhea, hallucination, and the kidneys may stop working. It also causes death (Tamilselvan et al., 2014). Consequently, Tamilselvan et al. (2014) classified abrin as an illegal substance that can kill the victim with an amount as little as 0.1 μg/kg to 1 μg/kg. However, the precatory pea's seed does not show any clinical effects when swallowed because it has a hard shell. Furthermore, some plants have side effects on an individual's mental health by inducing hallucinogenic behaviours (Sam Houston State University, 2016). For example, the stem and bark of *Banisteriopsis caapi* contain β-carbolines, such as harmine or harmaline, and is known to be an ingredient in a psychoactive drink called *ayahuasca*, which is a famous drink in South America (Beyer et al., 2009). Beyer et al. (2009) demonstrated preparing ayahuasca by mixing and boiling *Banisteriopsis caapi* stems and bark with some specific plants that containing the alkaloid N, N-dimethyltryptamine (DMT). DMT does not affect the human body when imbibed via oral ingestion, even at amounts as high as 1000 mg. Still, it becomes active with only 25 mg assimilated via a parenteral route. The alkaloid is metabolised through monoamine oxidase (MAO), in which it comes from the β-carbolines, due to inhibitors, the enzyme MAO (Riba et al., 2003).

According to Callaway et al. (1996), forensic and clinical samples can detect DMT and β-carbolines in the host blood. Each substance has a specific detection mechanism: for instance, DMT has been detected via gas chromatography with selective nitrogen–phosphorus detection (GC-NPD), followed by liquid–liquid extraction (LLE) with butyl chloride, while β-carbolines are detected via high-performance liquid chromatography (HPLC) combined with fluorescence detection of the sedimentation of the protein (Callaway et al., 1996).

Hayashida et al. (2003) shed light on a liquid chromatography-mass spectrometry (LC-MS) technique involving a "liquid chromatography-mass spectrometry–electrospray ionization (LC/MS/ESI) method coupled with a column-switching technique. This process develops the determination of tetrodotoxin (TTX), and Aconitum alkaloids and their metabolites" (p. 1). The technique can determine the metabolizes of β-carbolines in blood serum. The LC-MC technique was used on a dead 25-year-old white male to determine the cause of death, and the evidence proved that the concerned man had the ayahuasca drink (herbal extracts) in his blood (Sklerov et al., 2005).

4.2. What can forensic research tell us about crimes involving poisonous medicinal plants?

The botanical knowledge deficiency among most people exploited in criminal investigations is the primary cause of insufficient use of botanical forensic analysis information as a source of evidence. Nevertheless, resourceful investigators and experts are now taking steps to change this. Whether anatomy or plant ecology, various botanical sciences are essential as pieces of evidence for forensic medicine. In toxicity from poisonous plants, a fast and relaxed screening test is necessary for precise forensic or medical examination (Dubey et al., 2018). Molecular and biotechnological tools are used in detecting specific toxins associated with particular organs of animals or humans (Byard, 2010). Techniques regularly used for forensic purposes are enzyme-linked immunosorbent assay, High-performance liquid chromatography (HPLC), radioimmunoassay, reverse transcription-polymerase chain reaction (RT-PCR), liquid chromatography-tandem mass spectrometry, and gas chromatography-mass spectrometry. In recent times, scientists have used modern technology, such as

the probe binding methodology, which effortlessly binds to specific receptor molecules. Occasionally, to make a comparison between particular proteins or genetic samples, such as the victim's DNA or RNA, RT-PCR is typically used for multi-fold amplification, especially in solving cases of rape or sexual harassment (Dinis-Oliveira et al., 2010).

5. Conclusion

Medicinal plants are a source of life and death, though this depends on the dosage., and can also be exploited as lethal poisonous substances to commit murder or suicide when administered in high doses. Furthermore, forensic experts can collect traces and residual materials from these toxic medicinal plants at a crime scene and use them as forensic evidence to decipher the mysteries behind the crime and resolve the cases through several molecular analyses and applications used in the field of forensics. More investigations and studies need to effectively be implemented in the future to speed up utilizing new biotechnological tools for determining the optimum and appropriate concentrations used of plants and their relations diagnostic forensic analyses.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

Al-Tayyib, A.A., Koester, S., Riggs, P., 2017. Prescription opioids prior to injection drug use: Comparisons and public health implications. Addict. behav. 65, 224–228.

Asgarpanah, J., Ramezanloo, F., 2012. Chemistry, pharmacology and medicinal properties of Peganum harmala L. Afr. J. of Pharm. Pharmacol. 6 (22), 1573–1580.

Awuchi, C.G., 2019. Medicinal Plants: the Medical, Food, and Nutritional Biochemistry and Uses. Int. J. Adv. Acad. Res. 5 (11), 220–241.

Baker, D.D., Chu, M., Oza, U., Rajgarhia, V., 2007. The value of natural products to future pharmaceutical discovery. Nat. Prod. Rep. 24 (6), 1225–1244.

Bavunoğlu, I., Balta, M., Türkmen, Z., 2016. Oleander Poisoning as an Example of Self-Medication Attempt. Balkan med. J. 33, 559–562.

Beyer, J., Drummer, O.H., Maurer, H.H., 2009. Analysis of toxic alkaloids in body samples. Forensic Sci Int. 185 (1–3), 1–9. https://doi.org/10.1016/j.forsciint.2008.12.006.

Builders, P., 2019. Herbal Medicine. BoD–Books on Demand. DOI: 10.5772/intechopen.69412.

Byard, R.W., 2010. A review of the potential forensic significance of traditional herbal medicines. J. Forensic Sci. 55 (1), 89–92.

Callaway, J.C., Raymon, L.P., Hearn, W.L., Mckenna, D.J., Grob, C.S., Brito, G.S., Mash, D.C., Da, D.E.M., Postal, C., 1996. Quantitation of N, N-Dimethyltryptamine and Harmala Alkaloids in Human Plasma after Oral Dosing with Ayahuasca. J. Anal. Toxicol. 20 (6), 492–497.

Dar, R.A., Shahnawaz, M., Qazi, P.H., 2017. General overview of medicinal plants : A review. J. Phytopharmacol. 6 (6), 349–351.

Dinis-Oliveira, R.J., Carvalho, F., Duarte, J.A., Remião, F., Marques, A., Santos, A., Magalhães, T., 2010. Collection of biological samples in forensic toxicology. Toxicol. Mech. Methods. 20 (7), 363–414.

Drewes, A.M., Jensen, R.D., Nielsen, L.M., Droney, J., Christrup, L.L., Arendt-Nielsen, L., Riley, J., Dahan, A., 2013. Differences between opioids: pharmacological, experimental, clinical and economical perspectives. Br. J. Clin. Pharmacol. 75 (1), 60–78.

Dubey, N. K., Dwivedy, A.K., Chaudhari, A.K., Das, S., 2018. Common Toxic Plants and Their Forensic Significance. In Natural Products and Drug Discovery: An Integrated Approach, pp. 349–374. https://doi.org/10.1016/B978-0-08-102081-4.00013-7.

Efferth, T., 2019. Biotechnology Applications of Plant Callus Cultures. Engineering. 5 (1), 50–59.

Gilson, A.M., Maurer, M.A., Ryan, K.M., Rathouz, P.J., Cleary, J.F., 2013. Using a morphine equivalence metric to quantify opioid consumption: examining the capacity to provide effective treatment of debilitating pain at the global, regional, and country levels. J Pain Symptom Manage. 45 (4), 681–700.

Hanner, M., Moebius, F.F., Flandorfer, A., Knaus, H.G., Striessnig, J., Kempner, E., Glossmann, H., 1996. Purification, molecular cloning, and expression of the mammalian sigma1-binding site. Proceedings of the National Academy of Sciences of the United States of America. 93 (15), 8072–8077. https://doi.org/10.1073/pnas.93.15.8072.

Hasler, C.M., Blumberg, J.B., 1991. Symposium on Phytochemicals: Biochemistry and Physiology. J. Nutri. 129, 756S–757S.

Hayashida, M., Hayakawa, H., Wada, K., Yamada, T., Nihira, M., Ohno, Y., 2003. A column-switching LC/MS/ESI method for detecting tetrodotoxin and Aconitum alkaloids in serum. Leg. Med (Tokyo) 5, S101–S104.

Jaffe, J.H., Martin, W.R., 1990. Narcotic analgesics and antagonists. In: Goodman, LS., Gilman, A. (Eds.), The Pharmacological Basis of Therapeutics. Macmillan, New York, pp. 485–521.

Jain, V., Yuan, J.M., 2020. Predictive symptoms and comorbidities for severe COVID-19 and intensive care unit admission: a systematic review and meta-analysis. Int. J. Public Health. 65, 533–546.

Khajja, B., Sharma, M., Singh, R., 2011. Forensic Study of Indian Toxicological Plants as Botanical Weapon (BW). A Review. J. Environment Analytic. Toxicol. 01 (04), 1:112.

Khlifi, D., Sghaier, R.M., Amouri, S., Laouini, D., Hamdi, M., Bouajila, J., 2013. Composition and anti-oxidant, anti-cancer and anti-inflammatory activities of Artemisia herba-alba, Ruta chalpensis L. and Peganum harmala L. Food Chem. Toxicol. 55, 202–208.

Kittakoop, P., Mahidol, C., Ruchirawat, S., 2014. Alkaloids as important scaffolds in therapeutic drugs for the treatments of cancer, tuberculosis, and smoking cessation. Curr. Top Med. Chem. 14 (2), 239–252. https://doi.org/10.2174/1568026613666131216105049.

KNOLKER, H.J., 2017. The Alkaloids. Academic Press, PP 246. Volum 77 1st Edition.

Lata, H., Chandra, S., Khan, I.A., Elsohly, M.A., 2008. Propagation of Cannabis sativa L. using synthetic seed technology. Planta Medica 74 (03), P-18. https://doi.org/10.1007/s12298-009-0008-8.

Le Couteur, D.G., Fisher, A.A., 2002. Chronic and criminal administration of Nerium oleander. J. Toxicol. Clin. Toxicol. 40 (4), 523–524.

Mahmoudian, M., Jalilpour, H., Salehian, P., Ward, E., Hospital, F., 2002. Toxicity of Peganum harmala : Review and a Case Report. Iran. J. Pharmacol. Ther. 1 (1), 1–4.

Moloudizargari, M., Mikaili, P., Aghajanshakeri, S., Asghari, M.H., Shayegh, J., 2013. Pharmacological and therapeutic effects of Peganum harmala and its main alkaloids. Pharmacogn. rev. 7, 199–212.

Niroumand, M.C., Farzaei, M.H., Amin, G., 2015. Medicinal properties of Peganum harmala L. in traditional Iranian medicine and modern phytotherapy: A review. J Tradit. Chin Med. 35 (1), 104–109. https://doi.org/10.1016/s0254-6272(15)30016-9.

Pastorino, G., Cornara, L., Soares, S., Rodrigues, F., Oliveira, M.B.P.P., 2018. Liquorice (Glycyrrhiza glabra): A phytochemical and pharmacological review. Phytother. res. 32 (12), 2323–2339.

Pillay, V.V., Sasidharan, A., 2019. Oleander and Datura poisoning: An update. Indian J. Crit. Care Med. 23, S250–S255.

Quideau, S.P., Deffieux, D., Douat-Casassus, C.L., Pouységu, L., 2011. Plant Polyphenols: Chemical Properties, Biological Activities, and Synthesis. Angew. Chem. Int. Ed. 50 (3), 586–621. https://doi.org/10.1002/anie.201000044.

Rao, S.R., Ravishankar, G.A., 2002. Plant cell cultures: Chemical factories of secondary metabolites. Biotechnol. Adv. 20 (2), 101–153.

Riba, J., Valle, M., Urbano, G., Yritia, M., Morte, A., Barbanoj, M.J., 2003. Human Pharmacology of Ayahuasca : Subjective and Cardiovascular Effects, Monoamine Metabolite Excretion, and Pharmacokinetics. J. Pharmacol. Exp. Ther. 306 (1), 73–83.

Rosenblum, A., Marsch, L.A., Joseph, H., Portenoy, R.K., 2008. Opioids and the treatment of chronic pain: controversies, current status, and future directions. Exp Clin Psychopharmacol. 16 (5), 405–416. https://doi.org/10.1037/a0013628.

Rousseaux, C.G., Greene, S.F., 2016. Sigma receptors [σRs]: biology in normal and diseased states. J Recept Signal Transduct Res. 36 (4), 327–388. https://doi.org/10.3109/10799893.2015.1015737.

Saad, B., Azaizeh, H., Abu-Hijleh, G., Said, O., 2006. Safety of traditional Arab herbal medicine. Evid. Based Complement. Alternat. Med. 3 (4), 433–439.

Shedoeva, A., Leavesley, D., Upton, Z., Fan, C., 2019. Wound healing and the use of medicinal plants. Evid. Based Complement Alternat. Med. 2684108. https://doi.org/10.1155/2019/2684108.

Sklerov, J., Moore, K.A., King, T., Fowler, D., 2005. A Fatal Intoxication Following the Ingestion of 5-Methoxy-N, N-Dimethyltryptamine in an Ayahuasca Preparation. J. Anal. Toxicol. 29 (8), 838–841. https://doi.org/10.1093/jat/29.8.838.

So, O., Oyewole, S.O., Jimoh, K.A., 2018. Medicinal plants and sustainable human health: a review. Horticult Int J. 2 (4), 8–10. https://doi.org/10.15406/hij.2018.02.00051.

Tamilselvan, N., Thirumalai, T., Shyamala, P., David, E., 2014. A review on some poisonous plants and their medicinal values. J. Acute Dis. 3 (2), 85–89. https://doi.org/10.1016/s2221-6189(14)60022-6.

Tok, T.T., Gowder, S.J.T., 2019. Structural and Pharmacological Properties of Alkaloids with Special Reference to Thebaine Type Alkaloids. Biomed. J. Sci. & Tech. Res. 17 (3), 12767–12780.

Torpy, J.M., Lynm, C., Glass, R.M., 2004. Opioid abuse. JAMA. 292 (11), 1394. https://doi.org/10.1001/jama.292.11.1394.

Trescot, A.M., Datta, S., Lee, M., Hans, H., 2008. Opioid pharmacology. Pain Physician. 11 (2 Suppl), S133–S153.

Wangchuk, P., 2018. Therapeutic applications of natural products in herbal medicines, biodiscovery programs, and biomedicine. JBAPN. 8 (1), 1–20.

World Health Organization (WHO)., (2013). WHO Traditional Medicine Strategy: 2014-2023. World Health Organization (WHO), 1–76. https://doi.org/2013.

Yuan, H., Ma, Q., Ye, L., Piao, G., 2016. The traditional medicine and modern medicine from natural products. Molecules. 21 (5), 559. https://doi.org/10.3390/molecules21050559.

Sam Houston State University. 2016. "Forensic botany uses plant DNA to trace crimes." ScienceDaily. https://www.sciencedaily.com/releases/2016/02/160229140134.htm (accessed April 12, 2021).

Further Reading

Akinyemi, O., Oyewole, S.O., Jimoh, K.A., 2018. Medicinal plants and sustainable human health: a review. Hortic. Int. J. 2 (4), 8–10.

Mina, C.N., Farzaei, M.H., Gholamreza, A., 2015. Medicinal properties of Peganum harmala L. in traditional Iranian medicine and modern phytotherapy: A review. J. Tradit. Chin. Med. 35 (1), 104–109.