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Mandrakes: Phytochemistry, Toxicity and the Aphrodisiac Myth

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Abstract. The Greek goddess of sexuality, love, and beauty, Aphrodite, is the source of the word *"aphrodisiac."* Food or medication stimulating sexual desire is referred to as an aphrodisiac. Folk medicine and ethnobotany have long attributed an aphrodisiac, lust-inducing, or potency-boosting properties to a variety of plants and herbs. As a result, numerous edible and medicinal plant leaves, petals, or roots were utilized as ingredients in love potions that were intended to intensify amorous pleasures or serve as general sexually stimulating agents. However, in the past, such magic potions frequently contained narcotic and psychoactive plants in addition to love herbs or herbal aphrodisiacs. Although several drugs derived from plants have historically been used as sexual enhancers, their lack of defined dosages and propensity for toxicity can result in serious side effects and legal investigations. Tropane alkaloids (TA) (S-(-)-hyoscyamine and S-(-)-scopolamine) are biosynthesized from S-(-)-phenylalanine and are found in such plants that have historically been used as aphrodisiacs. During extraction of S-(-)-hyoscyamine from the plant material, its racemate atropine is formed. *Mandragora* species contain TA, primarily hyoscyamine and scopolamine, which make all portions of the plant dangerous. Mandrake is the common name for a variety of *Mandragora* species in the Solanaceae family. This herb has been used in medicine for thousands of years as a narcotic before surgery, as well as an emetic and an antidote to snakebites. Mandrake's root was also referred to as magic, aphrodisiac, psychedelic, and intimately associated with witchcraft under the term *"Devil's herb"* due to its "human body" shape and its narcotic and toxic effects. The concept of this strange plant is surrounded by a number of stories and legends that evoke feelings of something mysterious, sorrowful and even horrible – due to the belief that they would increase fertility. The plant's berries are also known as *"love apples."* All parts of the *Mandragora* species contain potent TA, making them extremely important in forensic research due to their strong toxic properties and potential for both accidental and intentional poisoning. In order to control the safety of herbal aphrodisiacs and to look into the health and legal ramifications of their abuse, forensic science plays a significant role. The main situations in which forensic science and aphrodisiac plants interact are poisoning, drug-facilitated crimes, illicit commerce, and product adulteration. In light of the forensic implications associated with *Mandragora* species, it is thought to be worthwhile to perform a comprehensive analysis of the studies conducted on these plants. The objective is to furnish forensic experts with extensive resources that focus on the phytochemical and toxicological aspects of *Mandragora* for better reference and understanding.

1. Introduction

Aphrodisiacs are substances, derived from plants, animals, or minerals, that enhance pleasure, increase sexual desire, and improve sexual performance. The term originates from “Aphrodite”, the Greek goddess of love [1]. Historically, aphrodisiacs have captured significant human interest. “Mandrake” – the Arabs call it “Satan's apple” – its narcotic and intoxicating properties, along with its use as a surgical anesthetic, made it highly valued in ancient Greece and Rome. The Bible mentions mandrake (*“love apples”*) (Gen. 30:14-16), and its use is frequently linked to its purported ability to increase fertility [2]. The historian Josephus Flavius wrote about the "dangerous" technique of gathering mandrake roots as early as AD 93. Uprooting a mandrake was seen extremely harmful in the Roman Empire. Because the mandrake's root resembles a human body or a phallus (Fig. 1), it was thought to possess occult abilities. During the Middle Ages, "the female" root was cut into the shape of a human. It was thought to bring prosperity and good fortune. The root was allegedly harvested by medieval witches under the gallows at night. It was said that the crushed root produced hallucinations, a death-like trance, and sleep. In addition, the root was thought to have been utilized in flying potions and to induce insanity.

The popularity of mandrake in Europe began to decline slowly in the sixteenth century [3]. Mandrake was once regarded as the most important plant in the Mediterranean, but its mytho-

logy and mystique have all but disappeared from modern usage. There are references to Mandrake's mythology in Middle Eastern cuneiform inscriptions from the fourteenth century B. C. Early Mesopotamian, Greek, Old Hebrew, Roman, Egyptian, Arabic, and various other cultures reference mandrake, which was also regarded as a crucial medicinal and magical plant throughout the Middle Ages in Europe. This plant was believed to have the ability to cure a wide range of ailments, such as insomnia and infertility and to have the capacity to predict the future and provide protection for soldiers in battle.

Additionally, the scent of mandrake's yellow fruits is highlighted in biblical texts, specifically Genesis and the Song of Solomon, where they are noted for their sexual connotations. So, it makes sense that mandrake became known as the middle-world equivalent of Viagra (!) [4]. Texts from the 12th to the 14th centuries (e. g. Rasaratna Samuchchaya) reference *Mandragora autumnalis* as "Vamshalochana". It was appreciated as a mild sedative for vata diseases and an occasional aphrodisiac to boost sexual energy (vata-pitta balance) – but only in extremely controlled formulations, mixed with black pepper, long pepper, and jaggery to promote safety and absorption [5]. Historically known as “Tufah Almajan” (“Satan’s Apple”), “love apples”, and “Beed Aljin” (“Eggs of the Jinn”), *M. autumnalis* has been used within the Islamic Empire for its therapeutic properties [6].

2. Mandrake in Myth and Magic: Historical Beliefs and Cultural Interpretations

Several authors have highlighted its historical significance, emphasizing its dual nature eliciting both fear and wonder. Notably, it has been remarked that no other medicinal herb from the ancient and medieval periods was as widely regarded for its mystical qualities as the mandrake. Scholar Silberman [7] underscores this view, noting that among all the plant representations in medieval herbals linked to mythological beliefs, superstition, and witchcraft, the mandrake is the most memorable and notable. The mandrake plant has such an unparalleled mythical legacy that it holds the unique distinction of being the subject of numerous works, including several books, solely dedicated to it [8]. This plants history illustrates the similarities between these two ostensibly unrelated areas at a time when the line between magic and medicine was less apparent than it is now.

Fig. 1. left: This medieval manuscript demonstrates the "Doctrine of Signatures" by depicting mandrake as either a man or a woman (illustration from https://commons.wikimedia.org/wiki/File:NaplesDioscuridesMandrake.jpg), right: Mandrake's magical power was considered to be so intense that it would scream and kill anyone within earshot when extracted from the ground (illustration from https://commons.wikimedia.org/wiki/File:Mandragora_Tacuinum_Sanitatis.jpg; both accessed March 3, 2026.

Historiography places the mandrake squarely into the contextual framework of a bygone era in which even medical doctors with university training frequently used charms and astrology as part of their daily practice [9]. Legends and tales from antiquity that related to the mandrake, plant Scripture and other sources from distant antiquity served as inspiration for the tales and

legends surrounding the mandrake plant. King Solomon's ring is one of the oldest instances of mandrake mythology. This ancient custom was transmitted through literature credited to Hermes Trismegistus. According to the legend, the King employed a ring containing mandrake root to ward off demons; this is why the plant is known as "The Tree of Solomon" in Arabic and Armenian [10]. J. A. Carter claims that the biblical story of Rachel seeking mandrake roots for conception in Genesis 30 is the source of the myth linking mandrake to fertility. John Gerard recorded this idea in his 1597 "Herball", which strengthened mandrake's standing as a fertility aid. Extensive harvesting rituals were part of the mythologies surrounding mandrake, which were based on the idea that the plant contained a ghost that could murder anyone who heard it cry when it was uprooted. It was customary to tie a dog to the root to ensure safe harvesting (Fig. 1), allowing the dog to perish rather than the human [11]. Translations of the Pseudo-Apuleius ("Herbarium Apulei"), a late antique medicinal literature from the fourth century CE, provide one of the earliest sources for this specific story [12].

Benítez et al. [13] also explore the historical significance of mandrake, particularly its purported aphrodisiac qualities, with references tracing back to the Old Testament and its prominence in ancient Greece, Rome, and Iran. The plant was linked to both Aphrodite, the Greek goddess of love, and Circe, as noted by Rahner [14] and Lee [15]. During the Renaissance, mandrake evolved into a symbol of love in Europe [16]. Unlike accounts in the Old Testament, medical texts such as "De Materia Medica" emphasized the roots of mandrake as the source of its aphrodisiac properties. Today, the fruits of mandrake are still harvested in Israel by Orthodox Jews and Arabs for uses related to enhancing fertility, as documented by Patai [17] and Dafni and Khatib [18]. The plant continues to hold cultural significance in countries like Spain, Turkey, Armenia, Iraq, Lebanon and Morocco, where it is recognized for similar purposes.

Numerous names exist for the mandrake plant across various languages, reflecting its unique qualities and rich mythology. Notable authors have explored the mandrake theme in their works. William Shakespeare alluded to mandrakes, e. g. in "Othello": *"And shrieks like mandrakes torn out of the earth."* Niccolo Machiavelli featured the plant in his comedic piece "La Mandragola". Its cultural significance is also highlighted in C. J. Celas "Diccionario del Erotismo" and J. K. Rowlings "Harry Potter and the Chamber of Secrets", showcasing the plants symbolic implications throughout diverse literary genres and historical contexts [10,11].

3. Botanical description

Monadi et al. [19] conducted a comprehensive review of the Mandragora genus, detailing its taxonomy, phylogeny, morphology, geographical distribution, habitat, and phenology. The study indicates that *Mandragora turcomanica* is closely related to *Mandragora autumnalis*, with both species being sister taxa based on genetic, molecular, and morphological evidence. Mandragora species belong to the Kingdom Plantae, Subkingdom Viridiplantae, Infrakingdom Streptophyta, Superdivision Embryophyta, Division Tracheophyta, Subdivision Spermatophytina, Class Magnoliopsida, Superorder Asteranae, Order Solanales, Family Solanaceae, Genus Mandragora [20]. The number of recognized Mandragora species has varied over time, with three species identified by Ungricht et al. [21]: *M. officinarum* L., *M. turcomanica* MIZGIR., *M. caulescens* C. B. CLARKE. Clarke combined *M. autumnalis* and *M. officinarum* based on their morphological characteristics, while *M. chinghaiensis* was recognized as a synonym of *M. caulescens*. Currently, phylogenetic and morphological studies classify the genus Mandragora to include five species: *M. officinarum* L., *M. autumnalis* BERTOL., *M. turcomanica* MIZGIR., *M. caulescens* C. B. CLARKE and *M. chinghaiensis* [22].

Morphology of the Mandragora species is detailed in various texts [21-25]. Each species has unique features in terms of root structure, leaf formation, and flower morphology, which are

essential for classification and understanding their ecological significance. Furthermore, comparative studies between these species can provide insights into their adaptations and evolutionary relationships within the genus Mandragora (Fig. 2 and 3).

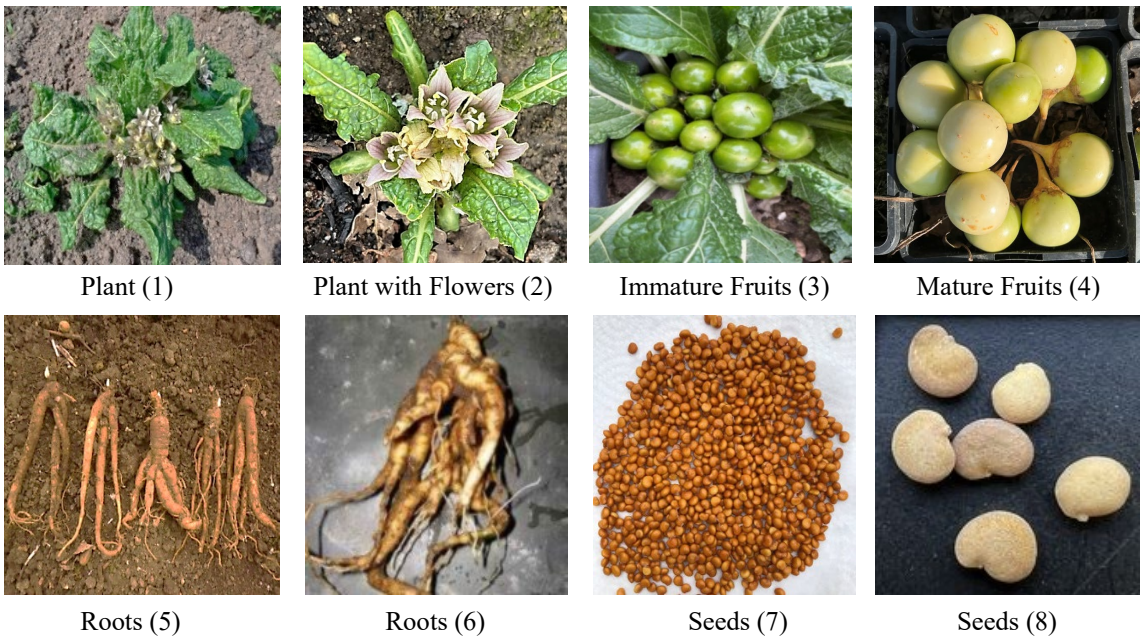


Fig. 2. Plant, flowers, fruits, roots and seeds of *Mandragora officinarum* L. 1-5,7: Courtesy of Yves Coconnier, Conservatoire National de la Mandragore, France; https://la-mandragore.eu/, 6,8: Sander Onsman, Onszaden, Wageningen, Netherlands, https://onszaden.com/mandragora-officinarum, accessed April 27, 2026.

Fig. 3. *Mandragora autumnalis* with flowers and with fruits. Courtesy of Yves Coconnier, Conservatoire National de la Mandragore (France); https://la-mandragore.eu/, acc. April 27, 2026.

The present article provides a comprehensive review of the phytoconstituents found in Mandragora species, documenting various investigations that have identified numerous compounds, including alkaloids, coumarins, lipids, flavonoids, withanolides, calystegines, essential oils and carotenoids. By analysing the literature that has been gathered from significant academic databases such as PubMed, Scopus, Google Scholar, Web of Science and Science Direct, it synthesizes current data about *Mandragora spp*. The research employs keywords such as Mandragora, mandrake, ethnobotany, phytochemistry, ethnopharmacology and toxicity to investigate multiple aspects of Mandragora. The review emphasizes not only the phytochemical profile but also explores historical context, botanical characteristics, folkloric significance, pharmacological uses, and toxicological implications. It includes case histories pertaining to Mandragora poisoning, thereby shedding light on the potential dangers and consequences associated with its use.

4. Phytochemical studies

Mandragora spp. contain a diverse range of phytoconstituents, including alkaloids, calystegines, terpenoids, withanolides, coumarins, steroids and fatty acids, some of which exhibit various bioactivities both *in vivo* and *in vitro*.

4.1 Alkaloids

The pioneering works of the German authors Hesse [26] and Thomas and Wetzel [27,28] at the turn of the 19th to the 20th century detailed the alkaloid content in mandragora. They isolated scopolamine and hyoscyamine alongside atropine, though not in pure form. The tropane alkaloids (TA) (S-(-)-hyoscyamine and S-(-)-scopolamine) are biosynthesized in such plants starting form S-(-)-phenylalanine. During extraction of S-(-)-hyoscyamine from the plant material, its racemate atropine is formed.

In 1992, Carr and Reynolds identified norhyoscyamine (pseudohyoscyamine) in mandragora and other Solanaceae. Staub [29] published one of the first chemical studies on *M. officinarum* L., employing paper chromatography and the preparation of crystalline picrates to determine the presence of atropine, scopolamine, cuscohygrine, scopine and hyoscyamine in Mandragora roots (Fig. 4). Furthermore, he identified Apoatropine and its cyclized dimer belladonnine through paper chromatography. He also detected norhyoscyamine in the roots [3].

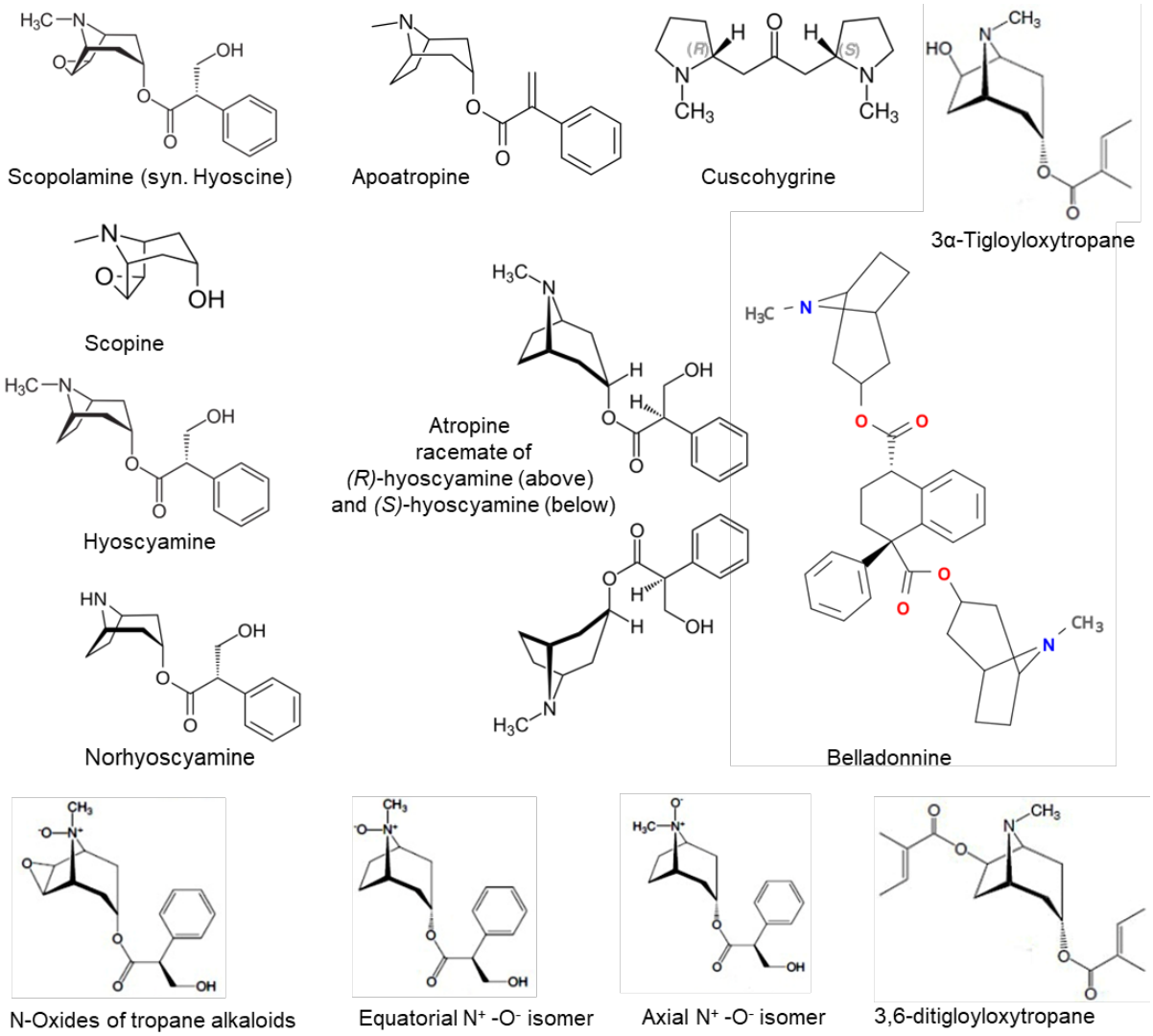


Fig. 4. Structures of Mandragora alkaloids (apoatropine, atropine, cuscohygrine, hyoscyamine, scopolamine: wikipedia.de, belladonnine: https://de.wikipedia.org/wiki/Schwarze_Tollkirsche, norhyoscyamine: https://www.wikidata.org/wiki/Q27107545, scopine: https://en.wikipedia.org/wiki/Scopine, 3α-Tigloyloxytropane, 3,6-ditigloyloxytropane, N-Oxides of tropane alkaloids, equatorial N^+ -O^- isomer Axial and N+ -O- isomer with kind permission from the corresponding authors of [3].

In 1973, Jackson and Berry [30] conducted an analysis of total alkaloids extracted from fresh and dried roots of *M. autumnalis* BERTOL and *M. vernalis* BERTOL (identical to *M. officinarum*)[1]. Using thin-layer chromatography (TLC) and gas chromatography (GC), they compared the alkaloid profiles to authentic standards to ascertain potential differentiation between the species based on alkaloid content. The study confirmed the presence of several alkaloids including hyoscyamine, hyoscine, cuscohygrine and apoatropine, with the latter previously suggested by Staub [29] via paper chromatography. Belladonnine was found in dried roots but not in fresh roots, potentially masked by high cuscohygrine levels due to similar retention (Rf) values. GC-results were inconclusive for belladonnine as it decomposed to apoatropine during analysis. The species *M. autumnalis* and *M. vernalis* contained two tigloyl esters of hydroxytropane: 3α-tigloyloxytropane and 3,6-ditigloyloxytropane, along with a minor unidentified alkaloid. Analysis indicated no significant concentration differences in alkaloid compositions, falling within normal biological variations. Cuscohygrine, scopolamine, apoatropine and hyoscyamine were found in the dried roots, with tigloyl esters being a novel discovery in this research. N-oxide derivatives of the tropane alkaloids hyoscyamine and hyoscine were prepared and identified and their occurrence in several members of the Solanaceae was investigated. Two hyoscyamine N-oxides and one hyoscine N-oxide were detected in genera including Atropa, Datura, Hyoscyamus, Scopolia and Mandragora. The study demonstrated that N-oxide forms of these alkaloids occur naturally in Solanaceous plants and may serve as metabolic or storage forms of the parent alkaloids [31].

4.2 Calystegines – Polyhydroxy alkaloids with a nortropane skeleton

Calystegines are polyhydroxylated nortropane alkaloids. Dragger et al. [32] investigated the extracts from various parts of *M. officinarum*, including roots, leaves, spring leaves, flowers, and fruits, specifically analysing calystegine A3 and calystegines B1 and B2 (Fig. 5).

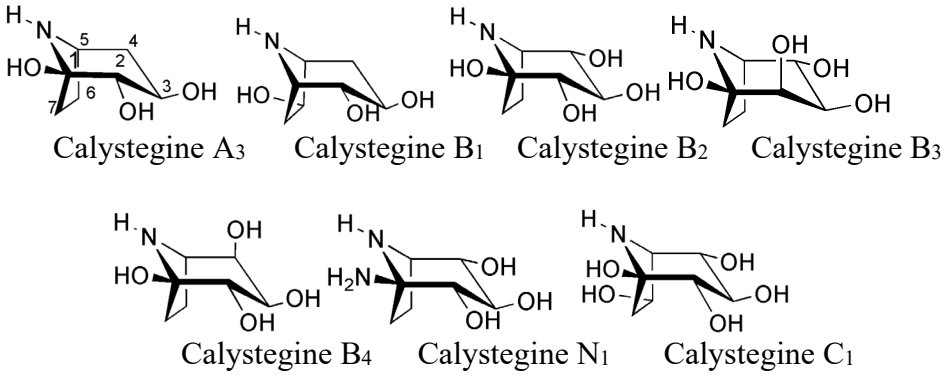


Fig. 5. Calystegine structures (with kind permission from the corresponding author of [3]).

Their findings indicated that the aerial parts of the plant contained a higher concentration of calystegines compared to the root. Among the examined parts, spring leaves exhibited the highest concentration, while fruits had the lowest. Bekkouche et al. [33] employed GC coupled with mass spectrometry (GC-MS) to analyze the distribution and content of eight calystegines (A3, A5, B1, B2, B3, B4, C1, and N1) across several plant species, including *Datura metel*, *Atropa belladonna*, *Hyoscyamus albus*, *Mandragora autumnalis*, *Solanum sodomaeum*, *Withania somnifera*, *Withania frutescens* and *Brunfelsia nitida*.

[1]*Mandragora autumnalis* and *Mandragora vernalis* are not currently recognized as subspecies of *Mandragora officinarum* L. in modern taxonomy. Instead, their status varies among authorities: *M. autumnalis* is treated either as a distinct species or a synonym of *M. officinarum*, while *M. vernalis* is generally regarded as a synonym of *M. officinarum*. Overall, the genus Mandragora remains taxonomically complex, with differing interpretations reflecting an ongoing taxonomic debate.

The study revealed a more restricted distribution for calystegines N1 and C1, while calystegines A3, B1, B2, and B3 were the most frequently detected. Notably, A5 and B4 were not found in any of the samples investigated. This research marks the first examination of calystegines in the genera Withania and Brunfelsia, as well as in *Solanum sodomaeum* and *M. autumnalis*. Additionally, chemical structures of some of these calystegines were reported.

Al-Khalil and Alkofahi [34] identified several compounds, including scopolin, herniarin, scopoletin, umbelliferon, chlorogenic acid, and angelicin in the roots, leaves, unripe fruits, and seeds of *M. autumnalis*, a plant that grows wildly in the Jordan valley. Additionally, Staub [35] conducted an examination of the roots of *M. autumnalis*, focusing on the identification of non-alkaloidal constituents. In this study, tropic acid and scopoletin were identified as key compounds present in the roots. Razzakov et al. [36] conducted a comprehensive study of surface parts of M. turcomanica MIZGER, including leaves, roots, rhizomes, fruits and seeds during different vegetation periods. They successfully isolated several alkaloids: scopolamine, hyoscyamine and apohyoscine. Furthermore, their analysis using TLC and MS techniques identified norhyoscyamine, apoatropine, α- or β-belladonnine, (±)-3α-tigloyloxytropan-6β-ol, tigloidine, and three unidentified alkaloids with molecular weights of 209, 219 g/mol, and 333 g/mol. Using LC-MS, Albahri et al**.** [37] examined the ethanolic leaf extract of *M. autumnalis* and identified 34 chemical components. In positive ionization, key compounds included bioactive alkaloids such as hyoscyamine and tropine, along with phenolic compounds such as chlorogenic acid and flavonoids such as quercetin. Significant findings also included fatty acid derivatives, various esters and a novel quinoline alkaloid, simulanoquinoline. In negative ionization, high levels of polyphenolic acids and linolenic acid were found, suggesting that *M. autumnalis* has a diverse phytochemical profile with potential pharmacological applications.

4.3 Odoriferous principles

Fleisher and Fleisher [38] studied the odoriferous elements of mandrake fruits (*M. officinarum*) and identified fifty-one chemicals using capillary GC-MS. Major compounds included ethyl butyrate (21.6 %), butyl acetate (9.1 %), hexanal (0.25 %), butanol (4.1 %), hexyl acetate (6.1 %), hexanol (14 %), ethyl 3-hydroxybutyrate (4.1 %), linalool (0.38 %), 3-methyl thiolpropanol (4.4 %), 3-phenylpropanol (2.1 %) and eugenol (2.3 %), along with several minor compounds. Hanus et al. [39] conducted a comprehensive analysis of the extracts from the fruit of *M. autumnalis* (mandrake) using GC-MS. Their study successfully identified a total of 135 distinct compounds present in the extracts after the seeds had been removed. The identified compounds included a diverse range of chemical classes: twenty-three n-alkanes, one branched-chain alkane, two cyclohexanes, eight alkenes, two branched-chain alkenes, three alcohols, three aldehydes, six ketones, eight heterocyclic compounds, four thio compounds, six benzene hydrocarbons, three phenols, eighteen carboxylic acids and a significant presence of forty-eight esters of carboxylic acids. Arbia et al [40] examined the essential oils (EOs) and aromatic volatiles from *M. autumnalis* in Central Tunisia. Essential oils were extracted via hydro distillation from fresh leaves, roots and fruits, while volatile emissions were sampled using headspace solid phase micro extraction (HS-SPME) and analyzed with GC/MS. The analysis revealed 51 substances, including esters, alcohols and hydrocarbons, ketones, aldehydes and acids comprising 96.2 - 98.6 % of the oil content, with pentadecanoic acid (34.2 %) and hexadecanol (26.3 %) as predominant components. Additionally, 78 volatile compounds were identified, largely consisting of esters and alcohols, with 1,3-butanediol and ethyl hexanoate both at 12.3 %.

Baser et al. [41] investigated the essential oil of fresh, ripe *M. autumnalis* fruits, by headspace GC-MS, identifying over 100 compounds, predominantly ethyl esters of medium-chain acids. The study analyzed ripe and unripe Mandragora fruits from the Jerusalem region, revealing more than 130 compounds. The main constituents were 34.6 % ethyl hexanoate, 25.5 % ethyl

butyrate, 14.2 % ethyl decanoate, 13.1 % ethyl dodecanoate and 10.7 % decyl acetate. Additional compounds were present in varying percentages such as ethyl caprate 6.15 %, ethyl caproate 4.40 %, ethyl caprylate 8.70 %, ethyl cinnamate 0.60 %, ethyl laurate 3.19 % and various ethyl esters and fatty acids at minor concentrations. Karakaş and Dörtbudak [42] investigated the essential oil components of *M. autumnalis* using GC-MS with a capillary column. The study identified several major volatile components, including phytol (17.91 %), citronellyl propionate (19.15 %) and farnesol (cis-17.05 %). Other notable components included heptadecane (6.31 %), pentacosane (5.305 %), octadecane (3.98 %), pelargonaldehyde (3.37 %), docosane (8.3 %), geranyl propanoate (2.96 %), dodecane (2.54 %), 3,7-Dimethyloct-7-en-1-ol (listed as *"Oct-7-enol < 3,7-dimethyl- >"* in [42], 2.44 %), nerylisovalerate (2.2 %), hexadecane (2.0 %) and 2-methyl butyraldehyde *(listed as "Butyraldehyde < 2-methyl- >"* in [42], 1.22 %).

4.4 Carotenoid composition

Pakhlavouni et al [43] analysed carotenoid composition and chloroplast ultrastructure in two cell lines of *M. turcomanica*. High total chlorophyll and carotenoid levels were present in both lines, with grana formation linked to increased chlorophyll b and epoxy-carotenoids, specifically antheraxanthin and violaxanthin (Fig. 6).

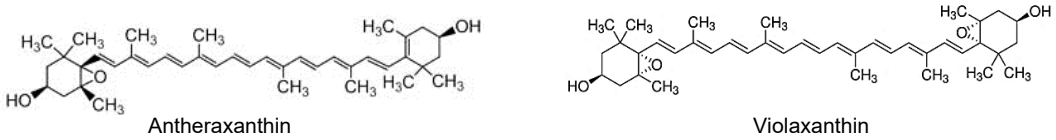


Fig. 6. Structures of antheraxanthin and violaxanthin (with kind permission from the corresponding author of [3]).

Observations indicated chloroplast degradation with disorganized lamellae and large osmiophilic globules. Furanoid xanthophylls may indicate chloroplast degradation, and thylakoid grana formation correlates with specific chlorophyll and carotenoid ratios.

4.5 Polyphenolic compounds and Flavonoids of *Mandragora autumnalis*

Mahmod and Talib [44] conducted a phytochemical analysis and reported that crude extract of *M. autumnalis* leaves are rich in polyphenolic compounds. Nawaf Al-Maharik et al. [45] studied the flavonoids fraction in *M. autumnalis* mature fruit, identifying four compounds: luteolin, myricetin, kaempferol and (+)-taxifolin, using 1H and 13C NMR spectral approaches.

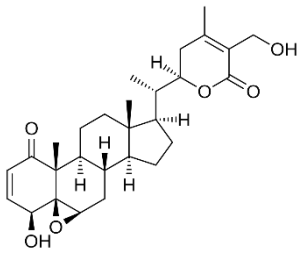
4.6 Lipids in Mandragora species

Studies on the lipids, present in the tuberous roots, fruits seeds and plant flesh of *M. turcomanica* MIZGER are presented in [46-49]. These aimed to explore and characterize the lipid composition of this particular species, contributing to the understanding of its biochemical properties. The studies revealed for the first time the identification of lipids in this plant. Hanus et al. [3] thoroughly reviewed the findings on *M. species* in these reports. Mahmod and Talib [50] investigated the ethanol extract of *M. autumnalis* through GC-MS technique, identifying several compounds, including palmitic acid, lauric acid, caprylic acid, capric acid, stearic acid, margaric acid, methylcaprate, vianol, eicosane, squalene, linoleic acid, cinnamic acid, methyl stearate, β-belladonnine, apoatropine, borneol, 3α-tigloyloxytropan and ethyl butanoate.

4.7 Withanolides

Withanolides are a category of naturally occurring C28 steroids, characterized by an ergostane skeleton modified at carbons 1, 22 and 26, referred to as the withanolide skeleton. Between

August 1996 and March 2010, a total of 360 new naturally occurring withanolides were isolated and characterized. An overview by Chen et al. [51] offers a detailed summary of the structural classification and distribution of these newly identified compounds.



The review also addresses the various biological and pharmacological properties of natural withanolides in relation to their structural characteristics, and it includes 211 references to substantiate the findings.

Fig. 7. Structure of withaferine A, the first withanolide that has been isolated, https://en.wikipedia.org/wiki/Withanolide#/media/File:Withaferin_A.svg, accessed April 27, 2026.

Suleiman et al. [52] conducted a study in which they isolated two new withanolides, namely mandragorolide A and mandragorolide B, alongside five known withanolides: larnaxolide A, withanolide B, withanicandrin, salpichrolide C and datura lactone 2. These compounds were extracted from a methanol extract of the whole plant of *M. officinarum*, which was sourced from Jordan. Compound 3 from *Larnax glabra* leaves has only been recorded once. According to the authors, withanolides of various biogenetic kinds from the genus Mandragora have never been reported before. This investigation also succeeded in isolating known fatty compounds, coumarins, sterols and TA.

5. Identification of tropane alkaloids (TA) in biological samples

Atropine, scopolamine and hyoscyamine are deliriant hallucinogenic TA found in mandrakes that produce delirium and hallucinations [53]. According to Faro et al. [54], several approaches have been documented for the examination of mandrake active ingredients in biological fluids of eventual customers. GC-MS techniques for identifying the active principles (e. g. hyoscyamine and scopolamine) in blood, urine, serum and plant material have been described. The last two decades have seen advancements in drug and poison assays in biological fluids, improving result reliability, especially for medico-legal cases. Some significant investigations have been reported concerning the analysis of TA [55].

Oertel et al. [56] developed a sensitive and selective method for determining scopolamine in serum using capillary column GC coupled with ion trap tandem MS, achieving a detection limit of 50 pg/mL. Deutsch et al. [57] developed a GC-MS method for detecting scopolamine, a muscarinic receptor antagonist, in rat plasma and brain. This technique can identify scopolamine concentrations as low as 2 ng/mL in plasma and 20 ng/g in brain tissue. Florou et al. [58] developed a broad-spectrum LC-MS/MS method, capable of screening and quantifying 100 analytes in clinical and autopsy blood samples, including three deuterated internal standards. This sensitive method exhibited low limits of detection (LOD) and quantification (LOQ) between 0.01 to 5 ng/mL and 0.05 to 20 ng/mL. It demonstrated linearity from 0.05 to 500 ng/mL and inter- and intra-day precision of 3-15 % and 7-18 %. Christen et al. (53) conducted a review focused on the analytical methods used to analyze TA within biological matrices. Namera et al (59) reported quantitative analysis of TA in biological materials by GC-MS. The method demonstrated excellent linearity for tropane alkaloids within a concentration range of 10-5000 ng/mL, with a detection limit of 5.0 ng/mL applicable to biological materials. This approach finds practical utility in the investigation of poisoning cases involving tropane alkaloids. Dong et al (60) developed and validated a sensitive LC-MS/MS method for the simultaneous analysis of three-tropane alkaloids in blood and urine. The TA showed strong linearity from 0.05 to 100 ng/mL in blood and from 0.2 to 100 ng/mL in urine, with detection limits between 0.02 and 0.05 ng/mL for biological samples. Azaryan et al. [61] developed a method using HPLC coup-

led with ESI-MS/MS to detect TA and cathinones in urine. Sample preparation included acid hydrolysis or dilution. The lower limit of quantification was 200 pg/mL, with a detection limit of 100 pg/mL (linear calibration from 0.2 to 50 ng/mL). The procedure was validated with real samples for forensic applications.

6. Toxicological profile of *Mandragora spp.*

The toxicological profile of *Mandragora spp.* is shaped by its TA. In this genus, scopolamine and hyoscyamine are regarded as the main compounds responsible for producing adverse effects, presenting in the peripheral and central nervous systems [62]. TA act as competitive antagonists at muscarinic acetylcholine receptors, producing a characteristic anticholinergic toxidrome with mydriasis, tachycardia, xerostomia, hyperthermia and neuropsychiatric manifestations such as agitation, delirium and hallucinations. Scopolamine exhibits more pronounced central effects due to its greater penetration of the blood-brain barrier, whereas atropine and hyoscyamine predominantly produce peripheral toxicity [63,64].

Scopolamine, recognized in non-scientific contexts as “Devil’s breath” or “Burundanga” is a muscarinic antagonist noted for its cognitive inhibition effects, particularly when misused for criminal activities. [65]**.** All parts of the Mandragora plant contain scopolamine and hyoscyamine, making it teratogenic, especially due to hyoscyamine, which can result in malformations in foals [66].

The variability in the dose-response relationship can be attributed to environmental, seasonal and genetic factors, affecting alkaloid production, heightening the risk of accidental poisoning and restricting therapeutic use [67]. Additionally, recent studies indicate that other constituents like calystegines may play a minor role in toxicity through glycosidase inhibition, although this contribution is secondary [68].

Mandragora intoxication exhibits similarities with poisoning from other members of the Solanaceae family, like *Atropa belladonna* and *Datura stramonium*, requiring comparable management approaches, including supportive care and the use of physostigmine in severe cases. Polyhydroxylated nortropane alkaloids, such as calystegine, do not pass the blood-brain barrier due to their hydrophilicity. Thus, psychoactive effects are missing and pharmacological activity is weak, which has limited their use in ancient medicines. Though recent studies have suggested these compounds may inhibit glucosidases in mammals and plants, they lack pharmacological applications and have received little research focus [69].

Mandrake (*M. officinarum*) is recognized as toxic across various cultures; for instance, people of Delos Island (Greece), avoided it, citing toxicity, while Jordanian folk medicine identifies the whole plant as poisonous, associated with conditions like mania, epilepsy and hysteria [70]. Its unripe fruits are considered toxic, whereas ripe ones are deemed edible by local people [71]. An ethanoic extract of *M. officinarum* fruits has shown no cytotoxicity in a brine shrimp bioassay at concentrations up to 10 mg/mL after 24 hours and no mutagenic activity was observed at 5 mg/mL through a plate incorporation assay [72].

Despite its historical significance in ethno pharmacology, evidence highlights that *Mandragora spp*. have a narrow therapeutic index and pose significant toxicological risks, necessitating careful evaluation in medicinal and forensic settings. Documented cases of poisoning underscore the importance of controlled dosages and medical oversight. Toxicological studies indicate that the LD 50 of atropine in rodents is between 453 to 620 mg/kg, reflecting a narrow therapeutic index. The development of standardized extracts with defined alkaloid content is crucial for risk mitigation and safety enhancement. To facilitate the therapeutic use of Mandragora-based products, it is necessary to establish regulatory frameworks. [13].

7. Reported cases of Mandrake poisoning

Mandrake (*Mandragora spp.*) poisoning is a severe toxicological condition, resulting from the presence of TA. This poisoning leads to a specific anticholinergic syndrome characterized by various physiological disturbances due to the inhibitory effects of these alkaloids on the neurotransmitter acetylcholine. The clinical symptoms of mandrake poisoning include mydriasis (dilated pupils), tachycardia (increased heart rate), xerostomia (dry mouth), urinary retention and various disturbances in the central nervous system, which can manifest as agitation, hallucinations, delirium and, in severe instances, acute psychosis. This type of poisoning primarily occurs when individuals accidentally ingest mandrake, often mistaking it for edible plants or use it for its ethno medicinal properties, particularly as an aphrodisiac.

One of the earliest **fatal cases of Mandragora poisoning** was documented in 1902 by A. W. Buck [73], involving mandrake ingestion. The patient exhibited acute anticholinergic toxicity leading to delirium and systemic deterioration, resulting in death. This case highlighted mandrakes lethal potential and narrow therapeutic index, offering early insights into the toxicodynamics of tropane alkaloids through muscarinic acetylcholine receptor inhibition. Bucks report is a key reference in toxicological literature, underscoring risks of unregulated Mandragora use.

Jiménez-Mejías et al (74) evaluated 15 patients, from two family groups, with anticholinergic symptoms (AS) due to poisoning by Mandragora autumnalis. The onset of symptoms occurred 1-4 hours post-ingestion, with an average latency of 2.7 ± 0.9 hours. Common clinical manifestations included blurred vision, xerostomia (dryness of mouth), dysuria (difficult micturition) in 60 % of patients, dizziness, headache, vomiting (53 %), dysphagia (difficult swallowing) and abdominal pain. Symptoms varied in severity and there was no link between latency and clinical severity. Universal signs included flushing, mydriasis and tachycardia, with 93 % showing dry skin and mucosae and 14 patients experiencing hyperactivity/hallucinations. Nine patients had agitation/delirium, while one suffered from a severe psychotic episode. Treatment involved prostigmine (2-6 mg) for 11 patients and physostigmine (0.5-2 mg) for six. The response time varied between 3-36 hours, with physostigmine users reporting better improvement in psychoneurological symptoms. The Mandragora was found mixed with *Beta vulgaris* and *Spinacia oleracea* leaves, alongside the detection of atropine and hyoscyamine.

Tsiligianni et al. [75] documented two severe cases in Greece, involving mistaken consumption, leading to supraventricular tachycardia and prolonged hospitalization. Similarly, Giovita A et al. [76] reported multiple case of *M. autumnalis* poisoning, a solanaceous plant found in the Sicilian countryside. This plant contains varying concentrations of solanum alkaloids, which can cause gastrointestinal irritation, and tropane alkaloids, that exhibit anticholinergic properties, leading to typical and sometimes severe atropine-like symptoms. The authors noted that patients inadvertently consumed the leaves of *M. autumnalis*, mistakenly identifying it as the edible *Borago officinalis* due to their similar appearance, including comparable leaves and small blue-violet flowers with five petals. The authors recommend supporting vital functions, decontamination and symptomatic treatment for affected individuals. In severe cases of poisoning, administration of the antidote physostigmine may be necessary to manage acute symptoms.

Earlier case documentation further confirms that clinical severity varies depending on the concentration and dose of alkaloids. De Salvo et al. [77] provide a comprehensive overview of mandragora, detailing its botanical characteristics, geographical distribution, morphological traits and the toxicological effects of its alkaloids. The document includes a clinical case of accidental mandragora poisoning, which was effectively treated using atropinic block antagonists, specifically cholinesterase inhibitors. The poisoning is noted for its severe symptoms and significant metabolic impact on the liver and kidneys, which display clear signs of disruption. The authors emphasize the importance of disseminating information about such toxic plants to

prevent rare cases of poisoning, underscoring the seriousness of these incidents due to their infrequency in clinical settings.

Bildik et al. [78] documented two instances of herbal poisoning in Turkey linked to the improper use of toxic plants. The first case involved *Datura stramonium*, which was used by a patient to alleviate haemorrhoidal pain, while the second case pertained to *M. officinarum,* ingested for its alleged aphrodisiac properties.

In a case involving a 69-year-old man who presented to the emergency department in a state of confusion and agitation, clinical signs indicated anticholinergic syndrome. Upon admission, he exhibited tachycardia (130 beats/min), dry skin, widely dilated pupils unresponsive to light, elevated body temperature (38.3 °C) and high blood pressure (160/100 mmHg). Abdominal examination revealed a distended bladder due to urinary retention. A detailed history from his wife revealed that he consumed a plant, *M. autumnalis*, before the symptoms began, intended to boost sexual desire. Initial treatment involved cardiac monitoring, intravenous fluids, urinary catheter insertion and diazepam to manage his agitation, though the latter proved ineffective in controlling his symptoms. Consequently, a slow intravenous infusion of physostigmine (2 mg) was administered. Following 36 hours of clinical observation, he was symptom-free and subsequently discharged in good health.

In a case study by Nikolaou et al. [79], a 35-year-old male suffered unintentional poisoning from *M. officinarum* berries, presenting with anticholinergic syndrome upon hospital admission. Toxicological urine analysis confirmed hyoscyamine and scopolamine presence, with concentrations of 539.8 mg/L and 32.7 mg/L, respectively. Blood analysis was negative for tropane alkaloids. The analysis involved biological samples from the patient and the berries consumed, leading to the identification of the berries as Mandragora through GC/MS analysis, which indicated TA at concentrations of 25.6 mg/g for hyoscyamine and 0.7 mg/g for scopolamine. The limit of detection of the method (recovery ≥ 85%) used for blood and urine analysis, for both hyoscyamine and scopolamine in blood, was 5.0 mg/L.

Gönüls and Çakmak [80] reported a case of allergic contact dermatitis in a 32-year-old male patient caused by *Mandragora radix*. Three days before his clinic visit, he developed erythema and pruritus on his forearm after contact with the plants sap. His sister, who used the sap for joint pain, did not experience any adverse effects. The patient had immediate lesions upon exposure, which resolved within 2-3 days after treatment. Although he had no prior exposure to the plant, the lesions reappeared 10 days later without further contact. A dermatological examination confirmed the diagnosis of allergic contact dermatitis linked to *M. radix*.

Baysak et al. [81] documented a case involving an 82-year-old male who developed a rash, burning sensation and itching on his knees four days after repeatedly applying *M. radix* sap for three consecutive days. Upon dermatological examination, erythematous, edematous and scaly plaque lesions were observed on his knees. An open application test confirmed the diagnosis of allergic contact dermatitis attributed to *M. radix*. This plant, belonging to the Solanaceae family, is known for its diverse properties, including sedative, aphrodisiac, emetic, analgesic and anesthetic effects. Remarkably, this case is one of the scarce documented instances of allergic contact dermatitis linked to *M. radix*, with only one other case reported in prior literature.

Vlachos and Poulos [82] detailed a case involving a 55-year-old male tourist who ingested 10 mandrake fruits while on the island of Dilos. Approximately 30 minutes post-ingestion, he exhibited symptoms including visual abnormalities and heightened anxiety. Upon examination one hour later, the patient was found to have tachycardia with a heart rate of 160 bpm, pupil dilatation and facial flushing. An intramuscular injection of apomorphine (5 mg) was administered, which induced repeated vomiting. Three hours after consuming the mandrake fruits, the patient exhibited confusion and central nervous system (CNS) depression. At this stage, 1 mg

of prostigmine was injected intramuscularly in an effort to alleviate the symptoms. After administering three doses of protamine at half-hour intervals, the patients pulse rate decreased to 100 bpm; however, he continued to show signs of confusion and depression. Over the following three hours, the patient began to improve gradually and 20 hours after the ingestion, he experienced a complete resolution of symptoms.

Despite the potential for severe symptoms associated with anticholinergic effects, the overall prognosis remains favourable when supportive care is administered promptly. One of the most effective treatments is the use of cholinesterase inhibitors, particularly physostigmine, which has shown significant efficacy in reversing the central anticholinergic effects. Physostigmine is identified by Dawson and Buckley [83] as an effective and relatively safe treatment option for anticholinergic delirium. However, its use should be cautioned in individuals at a high risk of seizures or those showing signs of cardiac toxicity. The recommended titrated dosage ranges from 0.5 to 1 mg (or 0.01 - 0.02 mg/kg for children), with a suggested minimum delay of 10 - 15 minutes before any additional doses. This dosing strategy is believed to have comparable response rates to many existing approaches while providing enhanced safety. Furthermore, the consideration of other sedative medications and non-pharmacological interventions is emphasized, particularly for patients where non-cholinergic factors may also play a role in the presence of toxicity or delirium

Although Mandragora species contain potent TA, capable of inducing severe anticholinergic toxicity, documented fatalities in modern clinical literature are rare. Reported cases – primarily accidental ingestions – typically present with pronounced but reversible symptoms when managed with supportive care and, where necessary, physostigmine therapy. The apparent low mortality likely reflects effective clinical management rather than reduced intrinsic toxicity of the plant [73-76].

8. Unveiling Mandragora *spp.*: Scientific evidence behind its aphrodisiac reputation

M. officinarum roots contain varying levels of TA, mainly hyoscyamine and scopolamine, ranging from 0.2 % to 0.4 % [84-86]. As the dosage increases, the pharmacological profile quickly transforms from modest central nervous system (CNS) modulation to strong muscarinic receptor blockage, resulting in delirium, hallucinations and possibly life-threatening complications [59,87]. This strong dose-response relationship demonstrates the lack of a safe or therapeutically significant range for aphrodisiac usage.

Furthermore, from a mechanistic aspect, anticholinergic drugs are more typically related with sexual dysfunction, such as decreased lubrication and erectile impairment, than with enhancement [88,89]. This contradicts the traditional assertions on libido enhancement. Thus, rather than being a pharmacologically supported characteristic, *M. officinarums* longstanding reputation as an aphrodisiac is better understood as the result of cultural interpretations of its psychoactive effects [11,86].

Clinical case reports by F. Bildik et al. [78] show that the ingestion of Mandragora, which is often consumed for its presumed aphrodisiac effects, leads to toxicity instead of improving sexual performance. The belief that Mandragora has aphrodisiac properties lacks support from contemporary pharmacological evidence. Mandragora TA are better known to produce central and peripheral anticholinergic effects rather than any genuine enhancement of libido [90,91].

At low doses, certain compounds may produce effects such as mild euphoria, sedation, altered perception or disinhibition. Historically, these effects might have been misinterpreted as aphrodisiac properties [11]. These responses reflect non-specific neuropsychiatric effects instead of directly targeting the modulation of sexual function.

9. Conclusion

In summary, the combination of pharmacological and clinical data clearly demonstrate that the Mandrake plant is a powerful representation of how nature, mythology and science interact. It was an important tool in early medicine for sedation and healing due to its strong alkaloids. But the plants distinctive humanoid look and psychotropic qualities also sparked a multitude of superstitious and mystical customs. Examining the mandrake from a variety of perspectives – botanical, medicinal, and cultural – offers insightful information on how people view nature, revealing a nuanced relationship marked by awe, terror and curiosity. The story of the mandrake emphasizes a universal truth: nature serves as both a source of inspiration for human creativity and a source of concrete solutions [92].

Herbal drugs are gaining popularity across both developed and developing nations due to their proposed safety and better tolerance compared to allopathic medications. This trend reflects a growing preference for natural remedies among consumers seeking alternatives to conventional pharmaceuticals. Yet unchecked dosage can be hazardous. Further research is required to even better understand the pharmacological effects and toxicological profile of such preparations to assure the safety of persons who may be tempted to use it recreationally. Our report is intended as a comprehensive and easily accessible information for e. g. medical doctors and (forensic) toxicologists.

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11. References

[1] Yakubu MT, Akanji MA, Oladiji AT. Aphrodisiac potentials of the aqueous extract of Fadogia agrestis (Schweinf. Ex Hiern) stem in male albino rats. Asian J Androl 2005;7:399-404.
[2] Fleisher A, Fleisher Z. The fragrance of Biblical mandrake. Economic Botany 1994;48:243-251.
[3] Hanuš LO, Řezanka T, Spížek J, Dembitsky VM. Substances isolated from Mandragora species. Phytochemistry 2005;66(20):2408- 2417. doi:10.1016/j.phytochem.2005.07.016.
[4] Forest Service, United States Department of Agriculture. The powerful Solanaceae: Mandrake. www.fs.usda.gov/wildflowers/ethnobotany/Mind_and_Spirit/mandrake.shtml, last accessed Mai 4, 2026.
[5] Ask Ayurveda. Mandragora autumnalis. https://ask-ayurveda.com/wiki/article/5022-mandragora-autumnalis, accessed April 10, 2026.
[6] Casini E. Rethinking the multifaceted aspects of Mandrake in ancient Egypt. Pisa University Press, Pisa, Italy, 2017.
[7] Silberman HC. Superstition and medical knowledge in an Italian herbal. Pharm Hist 1996;38(2):87-94.
[8] Hill D. The magic of the mandrake. Praxis-Knowledge. 2025, 4, https://doi.org/10.61149/WQZG9627, accessed April 10, 2026.
[9] Wright SH, Klassen F. Everyday Magicians. Penn State University Press. 2002.
[10] Dafni A, Blanché C, Khatib SA, Petanidou T, Aytaç et al. In search of traces of the mandrake myth: the historical, and ethnobotanical roots of its vernacular names. Journal of Ethnobiology and Ethnomedicine 2021;17(1):68. https://doi.org/10.1186/s13002-021-00494-5, last accessedMay 05, 2026.
[11] Carter AJ. Myths and mandrakes. Journal of the Royal Society of Medicine 2003;96:144-147.

[12] Kinney SC. The origins of the Herbarium of Pseudo-Apuleius (Doctoral dissertation, University of Toronto (Canada) 2022, https://utoronto.scholaris.ca/server/api/core/bitstreams/7abbda09-67fb-4fd7-9220-66212d7c9710/content, last accessed May 05, 2026.
[13] Benítez G, Leonti M, Böck B, Vulfsons S, Dafni A. The rise and fall of mandrake in medicine. J Ethnopharmacol. 2023;303:115874, doi: 10.1016/j.jep.2022.115874.
[14] Rahner H. Greek myths and Christian mystery. Biblo & Tannen Publishers, New York. 1971.
[15] Lee MR. The Solanaceae II: The mandrake (Mandragora officinarum); in league with the Devil. Jornal of the Royal College of Physicians of Edinburgh 2006;36:278-285.
[16] Griffiths JG (Ed.). Amarna Studies and Other Selected Papers, University Press, Vandenhoeck Ruprecht, Fribourg, Göttingen. 2001.
[17] Patai R. Jewish folk cures for barrenness. Folklore 1944;55:117-124.
[18] Dafni A, Khatib SA. Plants, Demons and Wonders: Folklore of Plants of the Bible Lands. Olam Hadash. Tel Aviv. 270. 2017.
[19] Monadi T, Azadbakht M, Ahmadi A, Chabra A. A comprehensive review on the ethno pharmacology, phytochemistry, pharmacology, and toxicology of the Mandragora genus: From folk medicine to modern medicine. Current Pharmaceutical Design 2021;27(34):3609-3637.
[20] Integrated Taxonomic Information System (ITIS). Mandragora L. Taxonomic serial no.: 500625.
[21] Ungricht S, Knapp S, Press J. A revision of the genus Mandragora (Solanaceae). Bulletin of the Natural History Museum, London (Botany) 1998;28(1):17-40.
[22] Volis S, Fogel K, Tu T, Sun H, Zaretsky M. Evolutionary history and biogeography of Mandragora L. (Solanaceae). Molecular Phylogenetics and Evolution 2018;129:85-95.
[23] Akhani H, Ghorbani AB. Mandragora turcomanica (Solanaceae) in Iran: a new distribution record for an endangered species. Systematics and Biodiversity 2003;1(2):177-180.
[24] Tu T, Volis S, Dillon MO, Sun H, Wen J. Dispersals of Hyoscyameae and Mandragoreae (Solanaceae) from the New World to Eurasia in the early Miocene and their biogeographic diversification within Eurasia. Molecular Phylogenetics and Evolution 2010;57(3):1226-1237. https://doi.org/10.1016/j.ympev.2010.09.007
[25] Fakir H, Özçelik H. Mandragora officinarum L. (Solanaceae): A new record for the flora of Turkey. African Journal of Biotechnology 2009;8(15):3560-3564.
[26] Hesse O. Über die Alkaloide der Mandragorawurzel. Journal für Praktische Chemie 1901;64:274-286.
[27] Thoms H, Wentzel M. Ueber mandragorin. Berichte der deutschen chemischen Gesellschaft 1898;31(2):2031-2037.
[28] Thoms H, Wentzel M. Ueber die Basen der Mandragorawurzel. Berichte der deutschen chemischen Gesellschaft 1901;34(1):1023-1026.
[29] Staub H. Über die chemischen Bestandteile der Mandragorawurzel 2. Die Alkaloide. Helvetica Chimica Acta 1962;45(7):2297-2305.
[30] Jackson BP, Berry MI. Hydroxytropane tiglates in the roots of Mandragora species. Phytochemistry 1973;12(5):1165-1166.
[31] Phillipson JD, Handa SS. N-oxides of hyoscyamine and hyoscine in the Solanaceae. Phytochemistry 1975;14(4):999-1003.
[32] Dräger B, van Almsick A, Mrachatz G. Distribution of calystegines in several Solanaceae. Planta Medica 1995;61(06):577-579.
[33] Bekkouche K, Daali Y, Cherkaoui S, Veuthey JL, Christen P. Calystegine distribution in some solanaceous species. Phytochemistry 2001;58(3):455-462.
[34] Al-Khalil S, Alkofahi A. The chemical constituents of Mandragora autumnalis. Alexandria Journal of Pharmaceutical Sciences 1996;10:135-138.
[35] Staub H. Über nichtalkaloidische Inhaltsstoffe der Mandragorawurzel. Helvetica Chimica Acta 1942;25(4):649-683.
[36] Razzakov NA, Aripova SF, Akhmedova E, Karimov A. Alkaloids of Mandragora turcomanica. Chemistry of Natural Compounds 1998;34(6):741-742.
[37] Albahri G, Badran A, Hellany H, Baydoun S et al. Mandragora autumnalis: Phytochemical composition, antioxidant and anti-cancerous bioactivities on triple-negative breast cancer cells. International Journal of Molecular Sciences 2025;26(17):8506.
[38] Fleisher Z, Fleisher A. The odoriferous principles of mandrake, Mandragora officinarum L. Aromatic plants of the Holy Land and the Sinai. Part IX. Journal of Essential Oil Research 1992;4(2):187-188.
[39] Hanuš LO, Dembitsky VM, Moussaieff A. Comparative study of volatile compounds in the fresh fruits of Mandragora autumnalis. Acta Chromatogr 2006;17:151-160.
[40] Arbia F, Ayari-Gribaa O, Souilem F, Chiboub W et al. Profiles of the essential oils and headspace analysis of volatiles from Mandragora autumnalis growing wild in Tunisia. Chemistry & Biodiversity 2019;16(10):e1900345.

[41] Baser KHC, Kürkçüoglu M, Demirci B, Erdogmus H. Composition of the essential oil and the headspace sample of Mandragora autumnalis Bertol. Fruits. Journal of Essential Oil Research 1998;10(6):632-634. https://doi.org/10.1080/10412905.1998.9700991
[42] Karakaş HH, Dörtbudak MY. Investigation of the toxic effect of Mandragora autumnalis (mandrake) extracts on daphnia magna. Applied Ecology and Environmental Research 2023;21(6):5495-5504.
[43] Pakhlavouni I, Khaibullina L, Serebryakova V. Carotenoid composition and chloroplast ultrastructure in two cell lines of Mandragora turcomanica (Solanaceae). Russ J Plant Physiol 2000;47(1): 38-47.
[44] Mahmod AI, Talib WH. Chemical composition, antioxidant, antimicrobial, and immunomodulatory activity of Mandragora autumnalis grown in Jordan. The Natural Products Journal 2023;13(3):72-83.
[45] Al-Maharik N, Jaradat N, Bassalat N, Hawash M, Zaid H. Isolation, identification and pharmacological effects of Mandragora autumnalis fruit flavonoids fraction. Molecules 2022;27(3):1046.
[46] Asilbekova DT, Gusakova SD, Murdakhaev YM, Glushenkova AI. Lipids of the tuberous roots of Mandragora turcomanica. Chemistry of Natural Compounds 1994;30(5):566-572.
[47] Gusakova SD, Asilbekova DT. Structure and composition of the triacyl-glycerols of the tuberous roots of Mandragora turcomanica. Chemistry of Natural Compounds 1997;33(4):441-444.
[48] Asilbekova DT, Glushenkova AI. Lipids of the seeds and flesh of the fruit of Mandragora turcomanica. Chemistry of Natural Compounds 1998;34(6):664-667.
[49] Asilbekova DT, Glushenkova AI. Triacylglycerols of the seeds and fruit flesh of Mandragora turcomanica. Chemistry of Natural Compounds 1999;35(3):291-294.
[50] Mahmod AI, Talib WH. Anticancer activity of Mandragora autumnalis: an in vitro and in vivo study. Pharmacia 2021;68(4):827-83.
[51] Chen LX, He H, Qiu F. Natural withanolides: an overview. Nat Prod Rep. 2011;28(4):705-40. doi: 10.1039/c0np00045k.
[52] Suleiman RK, Zarga MA, Sabri SS. New withanolides from Mandragora officinarum: first report of withanolides from the Genus Mandragora. Fitoterapia 2010;81(7):864-868. doi: 10.1016/j.fitote.2010.05.013
[53] Kennedy David O. The Deliriants - The Nightshade (Solanaceae) Family. Plants and the Human Brain. New York: Oxford University Press. 2014, 131-137.
[54] Faro AFL, Di Trana A, La Maida N, Tagliabracci A et al. Biomedical analysis of New Psychoactive Substances (NPS) of natural origin. Journal of Pharmaceutical and Biomedical Analysis 2020;179:112945. https://doi.org/10.1016/j.jpba.2019.112945.
[55] Flanagan RJ. The poisoned patient: the role of the laboratory. Br J Biomed Sci. 1995;52(3),202-13.
[56] Oertel R, Richter K, Ebert U, Kirch W. Determination of scopolamine in human serum by gas chromatography-ion trap tandem mass spectrometry. J Chromatogr B Biomed Appl. 1996;682(2):259-64. doi: 10.1016/0378-4347(96)00095-3.
[57] Deutsch J, Soncrant TT, Greig NH, Rapoport SI. Electron-impact ionization detection of scopolamine by gas chromatography-mass spectrometry in rat plasma and brain. J Chromatogr. 1990 ,528(2),325-31. doi: 10.1016/s0378-4347(00)82391-9)
[58] Florou D, Di Rago M, Orfanidis A, Gerostamoulos D, Boumba VA. A broad-spectrum LC-MS/MS method for screening and quantification of 100 analytes in clinical and autopsy blood samples. Journal of Chromatography B, 2024;1247:124323.
[59] Namera A, Yashiki M, Hirose Y, Yamaji S, Tani T et al. Quantitative analysis of tropane alkaloids in biological materials by gas chromatography-mass spectrometry. Forensic Sci Int. 2002;130(1):34-43. doi: 10.1016/s0379-0738(02)00302-x
[60] Dong X, Liu W, Shen M. Development and validation of a sensitive LC-MS/MS method for the simultaneous analysis of three-tropane alkaloids in blood and urine. Analytical Letters 2013;6(1):18-28.
[61] Azaryan AA, Temerdashev AZ, Svetlichnaya EV et al. Determination of some cathinones, tropane alkaloids, and “pharmaceutical narcotics” in urine. J Anal Chem 2016;71:955–964. https://doi.org/10.1134/S1061934816090021.
[62] Vlachos P, Poulos L. A case of mandrake poisoning. J Toxicol Clin Toxicol 1982;19(5):521-522. http://dx.doi.org/10.3109/15563658208992510.
[63] Shim KH, Kang MJ, Sharma N, An SSA. Beauty of the beast: anticholinergic tropane alkaloids in therapeutics. Natural Products and Bioprospecting 2022;12:33. https://doi.org/10.1007/s13659-022-00357-w
[64] Duan L, Guo L, Dou LL, Chen XY, Jiang L, Li P. Tropane alkaloids: chemistry, pharmacology, biosynthesis and production. Molecules 2019;24(4):796. https://doi.org/10.3390/molecules24040796
[65] Ignacio SS, Jorge RV, Javier PA, Trino BT. Treating ‘Devil’s Breath’ intoxication: use of rivastigmine in six patients with toxic psychoses due to non-pharmaceutical scopolamine. J Pharmacol Clin Toxicol 2018;6(4):1115.
[66] Katırcı Y, Demirel B, Coşkun F. Contact dermatitis associated with Mandragora plant. Acta Medica Anatolia 2014;2(1):27-8.)

[67] Zhang Y, Li X, Chen L, Wang Z. Advances in biosynthesis, pharmacology, and toxicology of tropane alkaloids in Solanaceae. Frontiers in Plant Science 2023;14:1187654. https://doi.org/10.3389/fpls.2023.1187654
[68] European Food Safety Authority (EFSA). Binaglia M, Baert K, Schutte M, Serafimova R. Overview of available toxicity data for calystegines. EFSA Journal 2019;17(1):e05574. doi: 10.2903/j.efsa.2019.5574.
[69] Jocković N, Fischer W, Brandsch M, Brandt W, Dräger B. Inhibition of human intestinal b-glucosidases by calystegines. J Agric Food Chem 2013;61:5550-5557. doi: 10.1021/jf4010737).
[70] Al-Qura'n S. Ethnobotanical survey of folk toxic plants in southern part of Jordan. Toxicon 2005;46(2):119-29. http://dx.doi.org/10.1016/j.toxicon.2005.04.010
[71] Sinev IE. The history of Mandragora turkomanica (Solanaceae). Israel Journal of Plant Sciences 2016;63(3):176-181. http://dx.doi.org/10.1080/07929978.2016.1177956
[72] Alkofahi AS, Abdelaziz A, Mahmoud I, Abuirjie M et al. Cytotoxicity, mutagenicity and antimicrobial activity of forty Jordanian medicinal plants. Int J Crude Drug Res 2008;28(2):139-44. http://dx.doi.org/10.3109/13880209009082798].
[73] Buck AW. A fatal case of Mandrake poisoning. Boston Medical and Surgical Journal 1902;147:543.
[74] Jiménez-Mejías ME, Montaño-Díaz M, López Pardo F, Campos Jiménez E et al. Atropine poisoning due to Mandragora autumnalis**:** Description of fifteen cases. Medicina Clínica (Barcelona). 1990;95(18):689-692. (Article in Spanish).
[75] Tsiligianni IG, Vasilopoulos TK, Papadokostakis PK, Arseni GK, Eleni A, Lionis CD. A two cases clinical report of mandragora poisoning in primary care in Crete, Greece: two case report. Cases J 2009;2:9331. doi: 10.1186/1757-1626-2-9331
[76] Piccillo GA, Mondati EG, Moro PA. Six clinical cases of Mandragora autumnalis poisoning: diagnosis and treatment. Eur J Emerg Med. 2002;9(4):342-7. doi: 10.1097/00063110-200212000-00010.
[77] De Salvo R, Sinardi AU, Santamaria LB, Carfì VM et al. A rare case of acute mandragora poisoning. Diagnostic and therapeutic criteria]. Minerva anestesiologica, 1980;46(12):1265-72.
[78] Bildik et al. Two herbal poisoning cases from Turkey; Datura for Haemorrhoidal Pain Relief, Mandragora for Aphrodisiac Effect. Journal of Academic Emergency Medicine Case Reports 2011;2(2):18-21.
[79] Nikolaou P, Papoutsis I, Stefanidou M, Dona A et al. Accidental poisoning after ingestion of "aphrodisiac" berries: diagnosis by analytical toxicology. J Emerg Med 2012;42(6):662-665. doi: 10.1016/j.jemermed.2011.03.023.
[80] Gönül M, Çakmak SK. Case of allergic skin reaction to Mandragora radix, J Clin Exp Dermatol Res 2013;S6. DOI: 10.4172/2155-9554.S6-008.
[81] Baysak S, Gönül M, Atacan D, Ergin C. A case report of allergic contact dermatitis due to Mandragora radix. Case Reports Immunol 2015;591438. doi: 10.1155/2015/591438)
[82] Poulos L, Vlachos P. A mandrake poisoning case. Clinical Toxicology1982;19(5):521-522. https://doi.org/10.3109/15563658208992510
[83] Dawson AH, Buckley NA. Pharmacological management of anticholinergic delirium - theory, evidence and practice. Br J Clin Pharmacol 2016;81(3):516-24. doi: 10.1111/bcp.12839
[84] Bekkouche K, Lazrek HB, Jana M, El Amri H. Tropane alkaloids from Mandragora autumnalis. Fitoterapia 1993;64:49-52.
[85] Jackson BP, Berry MI. Hydroxytropane tiglates in the roots of Mandragora species. Phytochemistry 1973;12(5):1165-1166. doi:10.1016/S0031-9422(00)85025-5.
[86] Heinrich M, Appendino G, Efferth T, Fürst R et al. Best practice in research – overcoming common challenges in phytopharmacological research. Journal of Ethnopharmacology 2022;292:115053. https://doi.org/10.1016/j.jep.2022.115053
[87] Dräger B. Tropane alkaloids in the genus Mandragora. In: Alkaloids: Chemistry and Biology, Academic Press. 2020, 83. https://doi.org/10.1016/bs.alkal.2019.12.003.
[88] Andersson K-E. Mechanisms of penile erection and basis for pharmacological treatment of erectile dysfunction. Pharmacological Reviews 2011;63(4):811–859. https://doi.org/10.1124/pr.111.004515.
[89] Giuliano F, Rampin O. Neural control of erection. Physiology & Behavior 2004;83(2):189-201. https://doi.org/10.1016/j.physbeh.2004.08.014.
[90] Bruneton J. Pharmacognosy, Phytochemistry, Medicinal Plants (2nd ed.). Paris: Lavoisier Publishing, 1999.
[91] Heinrich M, Barnes J, Gibbons S, Williamson EM. Fundamentals of Pharmacognosy and Phytotherapy (2nd ed.). Edinburgh: Elsevier Churchill Livingstone, 2012.
[92] https://ethnoleaflets.com/mandrake-whispers-between-magic-medicine-and-myth/, last accessed May 05, 2026.