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Drugs in greek mythology and medicine

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Abstract

Geomythology has revealed that the ancient Greeks were aware of the importance of hygiene, and for this reason changed the flow of rivers, drained lakes, and built dams.

Excavations in Asia, Egypte and Greece revealed plant seeds. The first mention of the term medicine is attributed to Agamemnon. The drug-poison-antidote citations in the Homeric era revealed pharmacological, toxicological and herbal applications, e.g. Circes' psychotropic herbs and preparations and the use of copper and sulphur as disinfectant. The effect of opium on the central nervous system is evident in the Odyssey. In Minoan Crete, the capsules of the *Papaver somniferum* L. appear on the statuette of the Poppy Goddess. Hippocrates contributed the evolution of European Medicine and Pharmacy and abandoned theocratic theories. Galen produced drugs from medicinal plants. Despite the progress of chemistry and the industrialization of drugs, herbal medicines are still promoted by companies and the public for self-medication at high rates.

Keywords: Drug, hydraulic works, infection prevention

Introduction

Humans have always suffered from diseases. At first, they were "healed" by priests and magicians who were respected by the community. The need for healing and self-healing is inherent in both humans and animals. Indeed, the knowledge of plants as therapeutic means, a result of observations and experience, is common and does not depend on the cultural level of each people. With the help of Geomythology, myths have been interpreted as providing information about the ancient scientific knowledge through the millennia. Apart from the therapeutic methods, the ancient Greeks had absolute knowledge of the importance of hygiene. According to myths and archaeological discoveries, they used irrigation systems and sewerage networks^[3].

They built aqueducts, changed the flow of rivers, drained lakes, and built dams^[1, 2].

The legend of Hercules' marriage to Deianeira, in which the hero cut off the right horn of Achelous (closed one of the river's estuaries), symbolises the efforts of the ancients to restrain the force of the river and transform it into a fertile land (Hercules' marriage)^[3]. The huge stables of Augeias, King of Elis, were full of dung from the 3,000 oxen that had accumulated throughout the years. They had not been cleaned for as long as 30 years. Hercules cleaned the manure during a single day by digging two ditches at the foundation of the stables and turning the flow of Pineios or Alfeios so that they run through the stables sweeping away all the manure^[4]. The Lernaean Hydra was a mythical nine-headed monster killed by Hercules in Lerna, a marshland located south of Argos. The nine heads of Hydra symbolised the escape of water and the difficulty of draining the area. The myth refers to the combat against malaria through the drainage of the marshes^[5, 6, 7]. Greece was one of the countries that suffered greatly from malaria. There is insufficient evidence to prove that the disease existed in Greece before the 5th century BC, but we know that from that time onwards, the country had been extensively affected by the disease^[8]. Another theory was that lakes and rivers were often regarded by ancient Greeks as gates to the underworld. In that respect, the killing of the snake that guards one such gate is a symbolic victory over death, a feat that fits perfectly with the myth of Hercules as the "superhero" who always rescues people from deadly threats. Another possible interpretation: the lake of Lerna must have been a swamp, fed by several karstic springs in the hills above (water has carved tunnels and fissures through which it flows). According to this geomythology analysis, the Hydra's several heads are none other than the several springs which fed the swamp, with the middle one (the immortal) symbolizing the spring that flowed all year round. In a karstic landscape, if a spring is blocked, its water might

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appear elsewhere, creating another spring or more. Perhaps the myth refers to this phenomenon when saying that when one head was cut, two grew in its place. It may be that a growing local population sought to expand into the lake but was decimated either by famine (when crops were destroyed after rainfall that caused the marsh to expand, flooding the plain) or by malaria or other disease attributed to the unhealthy climate of the swamp. In this context, the poisonous fumes must symbolize the unhealthy climate. Its slaying by Hercules symbolizes eradication of malaria from the marshes. There is a possible evidence that such waterworks all over Greece show that people had the know-how, organization and motivation to build dams, divert rivers and drain lakes, shaping their environment to serve their growing need for arable land^[9, 10]. The ancient Greek doctors such as Hippocrates, Galen and Aretaeus contributed to the study of malaria^[11]. According to Euripides, Hercules suffered from epilepsy (Heracleian disease/ Hercules furiosus) –possibly focal seizures. This also reveals the belief that during or after a crisis the individual could pose a threat to his environment^[12]. The first attempt to diagnose and treat the sacred disease with scientific methods without religious prejudices was made by Hippocrates. In his work "On Sacred Disease" it is clearly stated that the disease has a cause related to the central nervous system and is of hereditary origin^[13, 14, 15]. He also reports that it is a brain damage unrelated to supernatural or divine phenomena, as was previously believed (Hippoc. *Morb. sacr.* 3.1-2). His views are amplified by the relevant observations from dissecting goat brains. In addition, he recommends a ketone diet that is still nowadays applied to resistant childhood epilepsy cases. He performs lobotomies and administers herbal mixtures, some of which have a gabergic suppressive action on the CNS, such as the *Valerian officinalis* L. (valerian) and *Passiflora incarnate* L. 1753 (passion flower). According to the principles of ethnopharmacology, the discovery of drugs preceded the discoveries of fire and the wheel^[16, 17, 18, 19, 42].

Herbal medicines

Excavations in Persian, Babylonian, Hittite, Chaldean tombs, in the Egyptian Pyramids, and in Greece have brought to light plant seeds. These finds prove that 60,000 years ago, humans used plants as flavor enhancers, as medicines, or as cosmetics^[20]. Observation and experience have resulted in some plants becoming life-saving for humans. Doctors have scientifically determined the quantities with therapeutic effects without toxicity. The Greek and Roman doctors mixed the "real" curative plants with common grasses that had no effect, thus introducing the notion of excipient, a component without pharmacological action which facilitates the taking of the active drug, e.g., preparation of pills with a small amount of some active herb and the addition of wheat or maize starch to increase their volume and make them easy to take. They knew that the alkaloids cannot be dissolved in water but only in organic solvents and therefore they mixed them with wine. "Then Helen, daughter of Zeus, took other counsel. Straightway she cast into the wine of which they were drinking a drug to quiet all pain and strife, and bring forgetfulness of every ill. ...". It also appears that in some way (perhaps by experience) they recognized the active substance, that is the parts of the plant with a pharmacological action^[21, 22, 23, 24]. Galen (130-201 AD) compounded drugs from plants. He was the first to recognize that the action of a drug depends on its preparation and its concentration in the corresponding compound. The word "medicine", which

means remedy and poison at the same time, first appears in the Homeric epics. Its meanings range from euphoria, remedy and spell, to dangerous poison, and there are many such references, both reliable and unreliable. "But the leech shall search the wound and lay thereon simples that shall make thee cease from dark pains"^[25]. Epic poetry is not interested in the composition of drugs, but only in their results^[26, 27]. With the exception of epidemics, heroes in the world of the Iliad never get sick. They either live or die (or affected from plague), and when they are wounded in battle gods often intervene saving them from death^[28]. In Homer Odysseus gives an antidote to his companions who had been overcome by illusions through their "transformation" into pigs by Circe's destructive herb given to them in order to make them forget their status and homeland^[28]. Homer's reference to drug-poison and venom-antidote put an end to therapies of theocratic origin and defined real pharmacological and toxicological knowledge. "So saying, Argeiphontes gave me the herb, drawing it from the ground, and showed me its nature. At the root it was black, but its flower was like milk". "Moly the gods call it, and it is hard for mortal men to dig; but with the gods all things are possible"^[29, 30].

In early times, the Greeks used completely different terms, but more precise than current practices, in order to demonstrate the interest in plant roots that can be traced back to the tradition of the community. The term *pharmakeia* referred to botanical quests. These belonged to the wider realm of charm as related to the forced and inevitable achievement of the desired results. After all, the ultimate goal of Circe and Calypso was the quest for pleasure. Circe is described as an expert of attraction. She knows how to deceive and is a murderer skilled in "terrible tricks" (*ολοφώια δήνεα*). Apart from providing information on pharmacological issues Homer portrays the relationship between men and women in a manner liberated from the conventional behavior of later times^[31, 32, 33]. Many drugs are mentioned in the Homeric epics, such as bitter, astringents, mild, anti-inflammatory/analgesic, palliative, pungent, deadly, fighting sadness, causing euphoria, like the famous nipenthes, etc. (The Homeric "doctors" possessed knowledge for drug preparation: "For a leech is of the worth of many other men for the cutting out of arrows and the spreading of soothing simples").

^[34, 35] The pharmacological properties of plants have been known since the Homeric era, as the use of healing herbs in treating mythical heroes proves^[36, 37]. The chapter of the Odyssey describing the transformation of Odysseus' companions into pigs demonstrates medical and pharmacological knowledge. A typical example is Circe who administers a preparation with anticholinergic and hallucinogenic action to Odysseus' companions, so that they think they have been transformed to pigs. Then, the Kyllenian god (Hermes) gives Odysseus the *moly* in order to undo "the spells" that had transformed them into pigs, thus eliminating the preparation's psychotropic action^[38]. The *moly* is the plant *Galanthus nivalis* L. (Galanthus the snow-schooler), which contains galantamine alkaloid, a cholinergic agonist, which is an acetylcholine esterase inhibitor. The etymology of the word *moly* is traced to the verb *μολύω* (relax). Even though there are objections regarding the identity of the plant, the theory identifying it as *Galanthus nivalis* L. is prevalent in the medical world.^[39, 40, 41] Galantamine, a chemical product of the plant, is used for treating Alzheimer's disease (Reminyl®). Its side-effects include hallucinations. The *moly* extraction was difficult. Sprengel identifies it as *Allium*

nigrum, which however has pink flowers. The *moly* is described by Dioscorides as an antidote for magic spells. Pliny mistakenly confused the *moly* with the mandrake. Others considered it to be a kind of garlic (Linnaeus) or identified it as the black Hellebore, which has black roots, white flowers, it is difficult to digest and grows in the Asian coast. The most valid theory is the identification of the plant as an anticholinergic antidote containing anticholinesterase-like substances (e.g. galantamine, which is the treatment for anticholinergic poisoning from tropane alkaloids and is present in high levels in the *Galanthus nivalis* L.)^[38]. In another account, Circe is said to have used the *kykeon*, a psychotropic drink with bitter herbs and wine mixed with cereals (grains), cheese and honey (amino acids, tyramine, casein, animal fat and calcium caseinate) in order to cause illusions to Odysseus' companions, giving them the unreal feeling of being transformed into pigs and to make them forget their past and their homeland. Wine is the perfect means of dissolving alkaloids^[42]. The grasses of the grains can be colonized by the mycelium of the fungus *Claviceps purpurea*, which contains aged alkaloids (ergotamine, ergonovine and ergovas-substances useful in gynecology- and migraine ergotamine) and lysergic acid (the diethylamide of which is known as the hallucinogenic LSD). Thus, if Circe is thought to have given the *kykeon* to Odysseus' companions, their illusions may be attributed to LSD^[42, 43]. Circe was a minor goddess of magic in Greek mythology. She is portrayed carrying a magic stick as a symbol of power. The word *kirkos* (κίρκος), meaning falcon, has been suggested as a possible etymology of Circe's name. When Homer describes a person in the Odyssey, he usually uses one or more adjectives to enhance the description. The adjectives he uses for Circe are: polypharmacy (*πολυφάρμακος*), *potnia* (respectable), *kalyptokamos* (with beautiful locks) and *euokamos* (with beautiful hair). Polypharmacy and *potnia* can easily be explained because, as the poet says, she was a goddess (sister of Aëtes, daughter of the Sun and daughter of the Ocean Persian or, according to other authors, of Hecate).

Metals

In antiquity, incandescent metal tools were used as haemostatic for treating wounds, but also as surgical tools for removing pathological tissues. The properties of copper as an antiseptic agent have been known since the time of Hippocrates. Hippocrates used copper to disinfect ulcers from varicose veins. He also treated open wounds and skin problems with copper (or copper and honey). The healing properties of copper were initially detected in slaves. Although they worked all day under bad conditions in a harmful humid environment, they never experienced rheumatic or arthritic problems because they were chained. This is because the copper strips on their hands and feet protected them from such ailments. When the Greeks set out to invade Troy they mistakenly disembarked to Mysia. King Telephus defended his country against the invading army, but was pursued by Achilles, who wounded him on the thigh with his spear. As the wound would not heal Lykeian Apollo gives Telephus an oracle stating that the person who wounded him is the only one who can cure him ("*ο τρώσας και ίάσεται*"). He asks Achilles to help him in return for directions to their destination, Troy. The Greek hero heals Telephus by scraping off onto the wound pieces of the spear that wounded the Mysian king in the first place^[44-47].

The Sulphur in antiquity

The ancient Greeks also used sulphur (S₂) as a disinfectant. Sulphur smoke was used for purifying and for eliminating insects. Odysseus orders his faithful nurse Eurykleia: "Bring sulphur, old dame, to cleanse from pollution, and bring me fire, that I may purge the hall". Achilles uses sulphur to clean his bowl, but perhaps this cleansing has a rather ritual character: "This cup he then took from the chest and cleansed it first with sulphur, and thereafter washed it in fair streams of water"^[48, 49, 50]. In three different cases, Homer describes the lightning of Zeus by noting the odor of sulphur. When Ajax the Telamonian injures Hector, the latter fell like an oak hit by thunderbolt: "And even as when beneath the blast of father Zeus an oak falleth uprooted,] and a dread reek of brimstone ariseth therefrom"^[51]. In another scene, the thunder strikes a ship and again a smell of sulphur emerges. In Euripides' Helen, the Egyptian sorceress Theone tells Helen: "go ahead to illuminate me/and in the customary habit/In the ether, the bridegroom was reborn/in order to get the breaths clean/with the fire cleared the way/if he was infected with a trap"^[52]. In reality, ozone is produced during any electrical discharge of thunderbolt. The smell of ozone is similar to that of sulphur dioxide.

Essential oils

The abundant references for the use of perfume and myrrh in antiquity by men and women, kings and common mortals, gods and goddesses are indicative of the widespread use of aromatic oils in everyday life. The essential or volatile oils are synthetic, aromatic and oily composite plant mixtures of various compounds which evaporate at room temperature. The essential oil is a non-concentrated hydrophobic liquid containing aroma compounds from plants. Essential oils are also known as *aetherolea*, or simply as oils of specific plants from which they were extracted, such as rose essential oil. The earliest perfumery workshops in Greece have been discovered in the Minoan palace of Zakros in Crete and the Mycenaean palace of Pylos in Messenia. In the latter case, evidence from the excavated Linear B tablets indicate that perfume production was particularly developed. "nay, the daughter of Zeus, Aphrodite, kept dogs from him by day alike and by night, and with oil anointed she him, rose-sweet, ambrosial, to the end that Achilles might not tear him as he dragged him"^[53]. The Rose essential oil is extracted from *Rosa gallica* L., *Rosa x damascena* Mill, *Rosax centifolia* L., etc. through steam distillation. Homer portrays Aphrodite employing aromatherapy^[53, 54, 55, 56]. Myrrh (Myrrha) is mentioned by Homer both in the Iliad and in the Odyssey. For instance, Achilles orders his men to wash the dead body of Patroclus and anoint it with scented oil, as well as to pour myrrh into his wounds^[57, 58]. Myrrh is produced from many species of the genus *Commifora myrrha* Nees. It is one of the oldest types of incense, expensive and rare, and therefore its use indicates wealth. The same applies to the scented waters and ointments, both of them being expensive pharmacotechnical formulations of great value. Paieon treats Ares and Hades by spreading a powder of analgesic herbs upon their wounds. The "Pulvis adspersent" constitutes an official pharmaceutical formulation that is referred in many Pharmacopoeias until our times^[59]. The wounded Eurypylos asks Patroclus to pull the arrow from his thigh and sprinkle soothing herbs over the wound, just like Achilles taught him. In the Iliad, Achilles speaks about his fighting in Troy because of Eleni «*ένεκα ριγεδανής Ελένης Τρωσίν πολεμίζω*», that is, I fight with the Trojans because of the abhorred

(origano user) Helen. The Lamiaceae plants of the Greek countryside stimulate the uterus and can cause contractions when taken in large doses. The genus of *Origanum* L. medicinal plants includes a variety of species, *O. dictamnus*, *O. majorana*, *O. vulgare*. With healing properties [60, 61]. *Origanum* L., 1753 (Lamiaceae) is associated with abortion and Achilles implies that Helen is probably aware of this effect and she is deemed responsible for the loss of many lives during the Trojan War [56, 61].

***Papaver somniferum* L. (Opium)**

In ancient Greece opium was used as a soothing and analgesic medicine, but also as a poison (Socrates had a choice between *Conium maculatum* L. 1753 and opium). The knowledge of the effects opium has on the central nervous system is evident from the representation of the Great Goddess of Minoan Crete. The use and cultivation of the *Papaver somniferum* L. is demonstrated by depictions of the Great Goddess and can be also seen on jewels worn by her priestesses. The poppy appears in Homeric Similes. The *Papaver rhoeas* L. was a weed sacred to the goddess Demeter and as such symbolized the presence of the goddess in the spring crops. The *Papaver rhoeas* L. appears in the iconography of the Eleusinian mysteries and the worship of Demeter [62, 63, 64]. The first written record of the poppy is found in Hesiod (eighth century B.C.), who states that in the vicinity of Corinth there was a city named Mekonê (Poppy-town) [65]: According to commentators on Hesiod this city received its name from the extensive cultivation of the poppy in the area. Others, however, hold that it was because it was there that Demeter first discovered the caps of the poppy. The ancients were well aware of the hypnotic and narcotic properties of the plant. According to Kritikos and Papadakis (1967), Hypnos and Thanatos, the twin sons of Night were portrayed wreathed with poppies or carrying them in their hands. The symbolism of the plant's use is obvious since the common poppy (*Papaver Rhoëas* L.) has a light hypnotic effect, while *Papaver somniferum* L. can be fatal. In 3,500 BC an Egyptian papyrus bears a description of the preparation of an alcoholic beverage with opium. In the 8th century BC Homer refers to the "νηπενθή" (πένθος = mourning), which probably contains opium. In the 3d century BC Theophrastus writes about its manufacture and use. References to opium can be found in Virgil's *Aeneid* and *Georgics* (50 BC). Opium is also described by Dioscourides, Pliny the Elder, and Galen [65, 66, 67].

Hippocrates (460-377)

The Hippocratic texts were the principal source for the evolution of European Medicine and Pharmacy. He listed 277 medicinal plants without describing them, classifying them according to their therapeutic properties and their use in various diseases. He was paid to teach, that is, he received "a doctor's fee" (*ιατρον*). He freed Medicine from the influence of philosophical theories and the worship of the gods. His follower Polybos describes the 4 juices of the body that are balanced in healthy humans and correspond to the four structural elements of the universe, bile (yellow bile, fire), black bile (black bile, earth) blood (blood, air) and phlegm (mucus, water). These four temperament types (melancholic, choleric, phlegmatic, sanguine) are still valid today. Hippocrates recommended treating diseases with laxatives, vomit inducing, bleeding through the use of suction cups, or phlebotomy in order to restore proper functioning. The ancient medical texts and the relevant terminology of the

ancient medical texts provide a basis for modern medical research [68, 69]. The doctor's fee in antiquity is also confirmed by the bronze plaque of Idalion in Cyprus, concerning the contract between the doctor Onasilos with king Stasikypros of Idalion for the medical treatment of the city's wounded soldiers [69].

Pain

Pain must have been a major problem for the population suffering from various diseases, tuberculosis, caries, atherosclerosis and urinary tract diseases as is revealed by excavation findings and the study of mummies. The use of hyoscyamine, scopolamine and opium was widespread. The Hearst Medical Papyrus dated to 1550 BC, records the clinical treatment of splanchnic pain and contains 18 pages of medical prescriptions written in hieratic Egyptian writing. Patients were given a mixture of beer, juniper and dough for 4 days. Furthermore ancients used opium patches as in our days. The first report about the poppy is found in Hesiod (8 century B.C.), who states that in the vicinity of Corinth there was a city named Mekonê (Poppy-town). According to commentators on Hesiod, this city received its name from the extensive cultivation of the poppy in the area. Others, however, hold that it was because it was there that Demeter first discovered the fruit of the poppy [65]. Hippocrates (460-377 or 355 B.C.) mentions often of the poppy as being used in medicinal preparations. He also referred poppy-juice as a hypnotic, narcotic, and styptic drug; also as a cathartic [71, 72, 73, 74, 75]. Furthermore, there is a growing interest in herbal medicines aiming at improving quality of life, dealing with conditions such as urinary and sexual dysfunction, osteoarthritis, dermatitis, indigestion, constipation, obesity, insomnia, anxiety and depression. The consumption of these medications combined with nutritional supplements aims at treating any disorders, as well as to maintain general health, to play the role of excipient, to enhance physical defense and to prevent diseases. Moreover Hippocrates and Galen both prominent Greek physician employed opium for headaches, coughing, asthma and melancholy.

Conclusion

According to Pausanias, in Chaeronea there was a kind of pharmaceutical industry of the time, where analgesic ointments were produced from the lily, rose, narcissus and iris flowers. "These prove to be cures for the pains of men". With the advancement of chemistry, the chemical synthesis of many active ingredients of plant origin has been attempted. Despite the industrialization of drugs, medicinal plants are being used by pharmaceutical companies in order to produce important drugs, e.g. reserpine, from the plant *Rauwolfia serpentina* L. Benth. ex Kurz, and *physostigmine* from *Physostigma venenosum* Balf. [76]. Hippocrates writing's mentioned mentha as cooling substance to treat diseases and he stated in his Aphorisms: "Swellings and pains in the joints, ulceration, those of a gouty nature, and sprains, are generally improved by a copious affusion of cold water which reduces the swelling and removes the pain; for a moderate degree of numbness removes pain. "The active substances in mentha leaves and branches contains 1% to 2% essential oils (menthol), tannins, flavonoids, etc. The peppermint possess antispasmodic, anti-inflammation and cooling properties. The menthol of the essential oil is a strong antibacterial agent. Peppermint has been used in the treatment of irritable bowel syndrome (IBS) and has gastroprotective effect. Increases mucus and PGE2 production inducing anti-secretory effect"

[77]. Mentha oil compounds are capable to binding with TRPM8 receptors of nerve cells in the human skin. The TRPM8 protein is expressed in sensory neurons and it is activated by cold temperatures and cooling agent and inhibits the 'pain messages' being sent from the locality of the pain to the brain (Central Nerve System). The menthol (TRPM8) receptors serve a variety of functions in the peripheral and central nervous systems. Application of menthol to skin or mucus membranes results directly in membrane depolarization, followed by calcium influx via voltage-dependent calcium channels, providing evidence for the role of TRPM8 to mediate sensory interaction with the environment in response to cold in the same way as in response to menthol [78, 79, 80].

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