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Cleopatra: from turpentine and juniper to ionone and irone

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Cleopatra VII (69–30 BC), the last Ptolemaic ruler of Egypt, is probably best known for her love affairs with Julius Caesar (100-44 BC) and Marcus Antonius (83-30 BC). Rightly or wrongly she became the epitome of shrewd seduction, leading brave Roman commanders on a path to debauchery and destruction. Among the seductive strategies attributed to her is the ingestion of small amounts of turpentine [the resin of the terebinth tree (*Pistacia terebinthus*)] or of derived oil (*Oleum terebinthinae*) with the purpose of conferring to her urine a more pleasant scent reminding of violets. Turpentine components are metabolized among other compounds to ionones and irones, which – renally excreted – are responsible for the flowery scent. Having obviously worked with great generals, the strategy is said to have been embraced for everyday use by many affluent Roman women. Complicating the issue somewhat is the fact that juniper berries (*Fructus juniperi*) and derived oil (*Oleum juniperi*) containing many of the same terpenoids as turpentine have a similar effect on urine. The purpose of this contribution is to briefly review the pharmacology of turpentine and juniper derived compounds assumed to be responsible for altering the scent of urine and to examine the origin and veracity of the mentioned habit. While the effect of ingested turpentine on the scent of urine is well documented our attempts at identifying Greek or Latin authors mentioning its intentional use for this explicit purpose (by Cleopatra or anybody else) failed.

1. Introduction

Cleopatra VII (69–30 BC, Fig. 1) was the last Ptolemaic ruler of Hellenistic Egypt (the Dynasty was started upon the death of Alexander the Great by Ptolemy the Savior, one of his generals or body guards, and ended with the death of Cleopatra and the Roman conquest in 30 BC). The Queen is probably best known for her love affairs with Julius Caesar (100-44 BC) and Marcus Antonius (83-30 BC). Rightly or wrongly she became the epitome of shrewd seduction, leading brave Roman commanders on a path to debauchery and destruction.

Among the customs of the time was the heavy use of perfumes (Donato and Seefried 1989). The sails of the ship on which Cleopatra received Marcus Antonius, we are told by Enobarbus (his friend and aide-de-camp) in Shakespeare's eponymous play, were soaked in fragrances: *Purple the sails and so perfumed that the winds were lovesick* (Shakespeare 2008). As her ship passed by, incense was burned along the banks of the Nile (Haskin 1907). The main ingredient of the sweet-smelling perfume is assumed to have been *Cyprinum* (O*leum cyprini; Hennablütenöl*), an oil derived from the flowers of the Henna tree (Egyptian privet; *Lawsonia inermis*), the same plant the leaves of which provide the renowned henna-red coloring (Miczak 2001).

Cleopatra's willingness to please went beyond the external use of perfumes; attributed to her is the ingestion of small amounts of turpentine [the resin of the terebinth tree (*Pistacia terebinthus*)] or of the derived oil (*Oleum terebinthinae*) with the purpose of conferring to her urine a more pleasing scent reminding of violets. In his textbook of pediatrics, John Apley (1908-1980) states "*I have sniffed a smell like violets in the urine of a child who drank turpentine, as Cleopatra of Egypt did for that effect"* (Apley 1973). The same is repeated by Wilfred Niels Arnold (1936-2014) in his book on the impressionist painter van Gogh, when detailing the uses of turpentine (Arnold 1992).

Mastic, the resin of the related *Pistacia lentiscus* (*lentescere* = to be or to become sticky), was chewed for *sweetening the breath and strengthening the gums* and (less frequently) used internally for a number of ailments. It is, however, not associated with any effect on the scent of urine, as it is *supposed to possess the virtues of turpentine in an inferior degree* (Stephenson and Churchill 1837). Apparently little O*leum lentisci* can be derived from the plant (Nicholson 1808).

Confounding the issue somewhat is the fact that juniper berries (*Fructus juniperi*) and the oil derived from them (*Oleum juniperi*) have a similar effect on urine, as pointed out by John Hill (1714?-1775) in his *History of the Materia Medica*: "*The Germans are so fond of Juniper Berries that they use them in their Cookeries, and few of their common Dishes are without them; they are therefore called by Aroma Germanorum, German Spice. We use them only in Medicine .....The Berries chewed, or the essential Oil taken only in a few Drops, give the Urine the same sweet Violet Scent that it has after the taking of Turpentine..... They are in some Places esteemed a sort of universal Remedy, and called by the pompous Names of Panacea and Theriaca Pauperum"* (Hill 1751).

Andromachus' medicine was prohibitively expensive, a "theriac light"*, Theriaca diatessaron*, was introduced. This contained, as the name implies (diatessaron = made of four), at the origin, only four components. The *German Spice,* Juniperus, Aroma Germanorum, was added later on, becoming then a fifth component of the poor man's theriac, *Theriaca pauperum* (Horstius 1651; Corner 1916; Flahaut1998).

According to Jean-Louis Gimbert (1841-1905), ingested eucalyptus oil had a similar effect on urine (scent of violets and iris) with the added advantage of being better tolerated (Gimbert 1872). Gimbert was a practicing physician at Cannes where Prosper Mérimée (1803-1870) was one of his better-known patients. One can, however, confidently exclude Eucalyptus use by Cleopatra

Fig. 1: Cleopatra VII (69–30 BC) was the last Ptolemaic ruler of Hellenistic Egypt (the Dynasty was started upon the death of Alexander the Great (323 BC) and the break-up of his empire by Ptolemy the Savior, one of his generals and body guards, and ended after the battle of Actium with the death of Cleopatra and the Roman conquest). Tobacco card manufactured by John Player in 1912. Personal collection of the author [GP].

or anybody else around the Mediterranean Sea, as Eucalyptus was first observed 1792 by the naturalist Jacques Labillardière (1755-1834) during his voyage to Oceania on Van Diemen Land (Tasmania) (Papillion 1872).

Another contender is *Fragaria vesca*, the wild (forest) strawberry. No one lesser than William Withering (1741 –1799), the one who also recognized the therapeutic potential of the Foxglove, writes about *Fragaria: "They promote perspiration, impart a violet smell to the urine, and dissolve the tartarous incrustations upon the teeth"* (Withering 1776).

On this one, however, he was probably misguided; the original mention on fragaria's influence on urine scent is from pharmacist and physician Stephan Franz Geoffroy (Etienne François) (1672-1731). He writes in the French Edition of his *Materia Medica* in 1743: "*Il est certain que l'urine de ceux qui mangent beaucoup de Fraises, en a une odeur forte"* (it is certain that the urine of those who eat a lot of strawberries develops a strong smell from it) and in the revised German translation of 1761: *"In Wahrheit, der Urin ist bey denen, welche bestaendig Erdbeeren essen, mit dem starken Geruch der Erdbeeren angefuellt"* (truly, the urine of those who constantly eat strawberries is filled with a strong scent of strawberries) (Geoffroy 1743, 1776). While a strong fruity scent is acknowledged, there is no mention of violets. Even if the violet scent had been present, wild (forest) strawberries would probably not have been available in the quantities required at the time needed.

Nevertheless the strategy of altering one's urine scent, having obviously worked well with great generals, is said to have been embraced for a more mundane everyday use by many affluent Roman women, as alluded to by German poet Heinrich Heine (1797-1856): "*In unserem Vaterland herrschten jetzt nur römische Sprache und Sitten, ...Birch-Pfeifer söffe Terpentin, wie*

Fig. 2: Turpentine harvest at Ares (Gironde). Image from: Leçons De Chimie Élémentaire Appliquée Aux Arts Industriels (1880); Chimie Organique, Cinquante-Deuxième Leçon, page 348. Jean Girardin (1803-1884), Recteur De L'Académie De Clermont, Membre Correspondant De L'Institut, Membre Associé De L'Académte De Médecine. G. Masson, Éditeur, Libraire De L'Academie De Medecine, Paris.

einst die römischen Damen (Man sagt, daß sie dadurch den Urin besonders wohlriechend bekamen)", (nowadays, only the Roman language and customs reign in our native country,..... Birch-Pfeifer allegedly drinks turpentine as once the Roman ladies did (by doing so, she is said to obtain a particularly fragrant urine) (Heine 1844). Charlotte Karoline Birch-Pfeiffer (1800-1868) was a German actress and writer of whom Heine was obviously not particularly fond; his statement about *Roms galante Damen* (the Roman elegant ladies) making use of turpentine is apodictically dismissed however by Ruß and Krause (1870). Pharmacist Ernst Krause (1839-1903), also known as Carus Sterne, was a prolific but controversial German writer of books in general natural history and mythology; pharmacist Karl Ruß (1833 - 1899) is best known as a leading German ornithologist of the XIXth century.

We briefly review the pharmacology of turpentine and juniper derived compounds assumed to be responsible for altering the scent of urine and then examine the origin and veracity of the mentioned habit. While the effect of ingested turpentine on the scent of urine is well documented, our attempts at identifying Greek or Latin authors mentioning its intentional use for this explicit purpose (by Cleopatra or anybody else) failed. One can only hope that more erudite readers will be able to point – if existent at all – to such source.

2. Turpentine and juniper

Turpentine (*terebinth*) – in the strict sense of the word – is the resin (sap) of the terebinth tree (*Pistacia terebinthus)*. Sap harvesters injure the tree by removing the bark (Fig. 2). Debarked trees secrete oleoresin onto the surface of the wound as a protective measure in an attempt to seal the opening. In addition to the eponymous terebinth tree, many other species produce such protective resins; the chemical composition of the sap varies widely not only with the species but also with season and geographical distribution. Distillation of resin obtained from live trees yields *spirit of turpentine,* also called *oil of turpentine (Oleum terebinthinae*) or simply turpentine. Used as medicine for internal or external administration in the past, it is nowadays employed as a solvent and source of materials for organic synthesis. The distillation product is composed mainly of *terpenes* and some *terpenoids.*

Terpenes are cyclic molecules having the formula $C_{10}H_{16}$ resulting from the condensation of (two or more) isoprene units (C_5). The name is derived from *Terpentin*, the German word for turpentine. Terpenoids are modified terpenes, wherein methyl groups have been moved or removed, or oxygen atoms added. The name implies similarity to *turpentine*. In contrast to terpenes, the number of carbon atoms in terpenoids is not a multiple of five anymore.

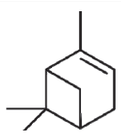
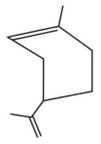
The most prevalent component of turpentine is the bicyclic mono-terpene pinene, with lesser amounts of carene, camphene and limonene, and trace amounts of many other compounds (Table).

The juniper tree is a species of conifer. Its so-called fruit or berry is not a berry or fruit at all but the female seed cone. The scales are fleshy and merged, which gives the cone a berry-like appearance. Cones need more than a year to ripen, so both ripe and unripe cones coexist on the same tree. Of the many species of juniper, a small number are poisonous and a majority have bitter fruits. Only a few yield edible berries and only one is routinely used for flavoring. The flavoring juniper, of world renown for its contribution to gin, is the common juniper (*Juniperus communis*). The word "gin" derives from the French word *genièvre* or the Dutch *jenever,* both meaning juniper.

In 1821, reviewing a book by surgeon Thomas Hare entitled *View of the Structure, Functions, and Disorders of the Stomach, and Alimentary Organs of the Human Body. With Physiological Observations and Remarks upon the Qualities and Effects of Food and Fermented Liquors,* the editor [Richard Reece (1775-1831)] notes that "*The urine of people who indulge in the use of gin, emits an odour resembling that of violets instead of gin"* (Reece 1821).

The chemical composition of juniper berry oil – as to be expected with natural products – also shows tremendous variation, with pinene, myrcene, sabinene, limonene and germacrene being most prevalent (Hoeferl et al. 2014; Salamon and Petruska 2017; Salamon et al. 2017).

Table: The most prevalent component of turpentine is the bicyclic mono-terpene pinene, with lesser amounts of carene, camphene and limonene, and trace amounts of many other compounds

Pinene	
Carene	
Camphene	
Limonene	

3. What smells like violets?

The scent of violets is due to various mono-cyclical terpenoids, mainly ionones (C_{13}) and irones (C_{14}). Ionone synthesis was first achieved – with some help from serendipity – in 1893 by Ferdinand Tiemann (1848-1899) and Paul Krueger (1859-1916), the latter working for the Haarmann & Reimer fragrance company in Holzminden, Germany, of which Tiemann was a silent partner (Tiemann and Krüger 1893). They condensed citral (Fig. 3A) with di-methyl-ketone (acetone) thus generating an intermediate which upon exposure to an acidic environment cyclizes to ionone (Fig. 3B). The name is obtained from merging *ion*a (Greek for violet) and ket*one* (EK 1894).

Using different ketones, related compounds can be obtained; the ring methylated ionone is known as irone (Fig. 3C). The name *irone* is a combination of *ir*is and ket*one*, irone being the chief odorous constituent of dried *Iris rhizome* (creeping rootstalks). A superb and detailed history of ionone synthesis was published by Gautschi et al. (2001).

For crossword puzzle fans it might be useful to remember that *odor of violets* in six letters is *ionone* while *odor of iris* in five letters is *irone*.

The complex stereochemistry of ionones and irones was elucidated about half a century later thanks to contributions by various groups such as those of Ruzicka, Naves and Ohloff. Leopold Ruzicka (1887-1976) was a Croatian-Swiss scientist, Professor of Organic Chemistry at the ETH in Zurich; in 1939 he was a joint winner of the Nobel Prize in Chemistry. Yves-René Naves (1902-1981) was a French chemist working for perfume manufacturers, later Professor in Neuchâtel. Günther Ohloff (1924-2005) was a distinguished German chemist, researcher and book author.

The ability not only of ingested, but also of topically applied or inhaled turpentine essence to confer a violet-like scent to urine was experimentally confirmed by Sloane and later by Stehberger (Sloane 1743; Stehberger 1827). Sir Hans Sloane (1660-1735) was an Irish physician, naturalist and collector. The large naturalist collection he amassed provided the foundation of the British Museum after his passing away. Georg Adam Stehberger (1799-1866) was a German physician practicing at Mannheim, in the Grand Duchy of Baden. He was married to Carolina Huebsch, sister of the architect Heinrich Hübsch (1795-1863).

The fate of about fifty substances in the human body (among them turpentine and juniper oil components) was examined by Friedrich

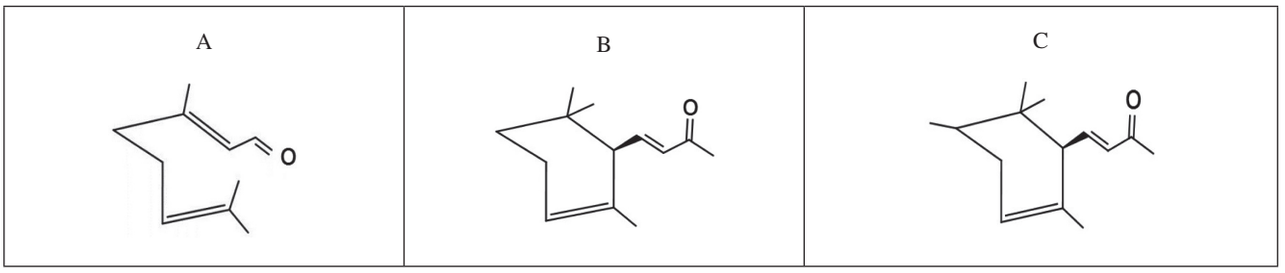


Fig. 3: Ferdinand Tieman (1848-1899) and Paul Krüger (1859-1916) condensed citral [A] with di-methyl-ketone (acetone) thus generating an intermediate which upon exposure to an acidic environment cyclizes to ionone [B]. The name is obtained from merging *ion*a (Greek for violet) and ket*one*]. Using different ketones, related compounds can be obtained; the ring methylated ionone is known as irone [C]. The name *irone* is a combination of *ir*is and ket*one*, irone being the chief odorous constituent of dried Iris *rhizome* (creeping rootstalks).

Wöhler (1800-1882), who was the first to synthesize an organic molecule from inorganic educts, i.e. urea. He won a prize whilst a medical student for his studies on the passage of metabolic products into the urine; many of the investigations were carried out on either himself or a dog.

Reviewing Wöhler's work in the 1928 North American Medical & Surgical Journal, the reviewer states that "*No fact is better determined, than that the internal and external use of this oil (Oil of Turpentine), as well as the inhalation of its vapour, very quickly communicates a violet odour to the urine. The peculiar character of the odour is not explained; for, on mixing oil of turpentine with ordinary urine, the violet smell is not developed. Juniper berries communicate a similar odour to the urine* (Woehler 1824; Anonymus 1928).

This indicates the need for metabolic conversion of turpentine and juniper oil components in order to obtain the violet-like scent. Most likely is hepatic metabolism via cytochrome P450 enzymes to more water soluble *ionones-like* and *irones-like* substances and subsequent renal elimination. While the exact metabolic pathway (in humans or otherwise) has (to our knowledge) not yet been described, pinene, the main component of both turpentine and juniper oil, is an important intermediate in the industrial synthesis of many products, also of ionone (Vespermann et al. 2017).

4. Turpentine and juniper in history

Ernest Monin (1856-1928) in his publication titled *Odeurs du Corps Humain* states *Rarement l'odeur cutanée est agréable. Cependant, on cite (d'après Plutarque) Alexandre-le-Grand, don't la sueur odorait la violette* (The smell of skin is rarely pleasant. However, the sweat of Alexander-the-Great is cited (according to Plutarch) to have smelt of violets) (Monin 1886). When something or somebody smells of violets, at least in the context of this contribution, that is (for this author) very exciting and most likely related to the ingestion of turpentine and/or juniper.

Unfortunately, Plutarch (46-120) does not make the statement attributed to him by Monin; Plutarch cites commentaries by Aristoxenus of Tarentum (375-335 BCE) where reference is made to the fact that *his skin* (Alexander's) *had a marvelous good savour, and his breath was very sweet, insomuch that his body had so sweet a smell of itself, that all the apparel he wore...took thereof a passing delightful savour, as if it had been perfumed* (Plutarch 1895). Not only that violets are not mentioned, but most historians agree that this is in fact not about Alexander's smell: the ancients believed that a man's character was created by the balance of the four elements and the four bodily fluids (blood, phlegm, yellow and black bile). If a man had a really strong character, this would be "*smellable*", and Plutarch implies that a sweet smell meant a sweet character (Nawotka 2010).

The manipulation of the scent of urine, intentional or otherwise, by drugs starts with the *kyphi* of ancient Egypt: the compound was used both for religious (as incense) and therapeutic purposes (as drug). While the number of ingredients in and composition of the mixture varies from source to source, it contains in most of its iterations both turpentine (resin) and juniper berries (Loret 1887). Victor Loret (1859-1946) was the Chair of Egyptology at the University of Lyon; he is credited with the discovery of a number of tombs in the Valley of Kings. Since *kyphi a boire, a la dose d'une drachme* (≈ 3-4 grams) was used for internal cleansing, it is almost certain that the effect on the urine scent was noticed, even if the association of the scent with a particular ingredient was not likely.

A more direct approach to changing the scent of the genitals was also the direct vaginal insertion of kyphi pellets; this habit – as mentioned by some authors – would have had the consequence of affecting the urine as well (Baas 1896; Hagen 1901).

Theriac(a), the concoction formulated by Andromachus the Elder, was based on Mithridatum, an earlier Greek/Persian version of this universal remedy (*panacea*) which was in turn influenced by the even earlier Egyptian kyphi (Norton 2006; Mayor 2011).

Galen (129-210) devoted whole books to theriaca whereby *terebinth* was a (key?) ingredient (Norton 2006). A cheaper later version *Theriaca Pauperum* (poor man's theriac) contained juniper berries (Horstius 1651; Flahaut 1998). Johann Daniel Horstius (1616-1685) was a German physician, Professor in Marburg and Gießen, and member of the Leopoldina Academy.

A more specific use of *terebinth*, the treatment of vaginal discharge, is mentioned by Armand Trousseau (1801-1867) (of eponymous sign) and his student Hermann Pidoux (1808-1882) and attributed to Hippocrates (460 – c. 370 BC): "*Is etiam (fructus terebinthi) in vino et aqua dilutus et potus, fluorem muliebrem sistit"* (diluted in wine and water and drunk, it (the fruit of terebinth) also stops the female flow) (Trousseau and Pidoux 1839; Hippocrates 1900; Haller 1984). Again, an effect on the urine scent was highly likely to be noticed by prescriber and/or user.

The first direct association (we have been able to identify) between turpentine or juniper and the scent of urine is from Theophrast (ca. 371-ca. 287 BC), the father of botany: in his book *De odoribus* (Of aromas) he mentions that juniper berries make the urine pleasantly scented (Theophrast 1993). Similarity to the scent of violets is, however, not mentioned.

The earliest specific reference to the scent of violets (we have been able to identify) is from Michel de Montaigne (1533-1592) describing his voyages: in Rome (November 1580), affected by renal colic, he was treated by the personal physician of the French ambassador to the Holy See, Charles d'Angennes (Cardinal Rambouillet) (1530-1587) with (among other things) terebenthine de Venise. Montaigne notes somewhat sarcastically that he observed no other effect than a smell of violets (*urine a la violette de mars*) in his urine (Montaigne 1967). Dating around the same time (1595) is a case history published originally in Latin by the Swiss physician Felix Plater (1536-1614), Professor in Basel: he prescribes terebenthine and *l'urine prendra l'odeur de la violette* (the urine will take the smell of the violet) (Plater 1669).

Both Montaigne and Plater describe the occurrence of the flowery scent of urine in a very *matter-of-fact way,* clearly giving the impression that the phenomenon was common knowledge and not a surprising or novel observation.

In the same year (1669), the most elaborate (not necessarily correct) early description of the fate of *terebentine* in the body is

provided by Nicaise Le Fevbre (1610-1669), pharmacist of French origin appointed Professor of Chemistry to Charles II of England*: "Mais ce qui est encore plus admirable, c'est que la terebentine qui est dissoute dans un lavement penetre par la vertu de son huile aetherée au travers de toutes les parties membraneuses & nerveuses, où elle imprime le caractere de son efficacite, & de la prouve cette verité par l'agreable odeur de violette que l'urine en recoit"* (but what is even more admirable, is that terebentine, which is diluted in an enema, thanks to its ether oil, penetrates all membranous and nervous parts, leaving traces of its efficacy, thereby proving this to be true by the pleasant smell of violet, which the urine obtains from it) (Le Febvre 1669).

By the end of the *XV*th century, the association between turpentine and the violet scent of urine is solidly established and mentioned in works of reference: in his *Dictionnaire Universel contenant generalement tous les mots Français tant vieux que modernes* Antoine Furetière (1619-1688) under the entry *Violette* states that *l'urine de ceux qui ont mangé de la terebenthine sent la violette* (the urine of those who have eaten terebentine smells of the violet) (Furetiere 1690).

Benjamin Franklin (1706-1790), one of the Founding Fathers of the United States, suggesting new areas of applied research, writes 1781 to the Royal Academy of Brussels: "A *Pill of Turpentine no bigger than a Pea, shall bestow on it (our Urine) the pleasing Smell of Violets. And why should it be thought more impossible in Nature, to find Means of making a Perfume of our Wind than of our Water?"* (Oberg 1996).

5. Conclusion

Both turpentine and juniper were widely used in Antiquity both for ritual and medicinal purposes; it appears almost certain that the effect of their ingestion on the scent of urine could not have gone unnoticed. Considering the importance placed on *smelling good* by Egyptians, Greeks and then Romans, it appears likely that such attempts at manipulation would have been popular. It is thus surprising that we have been unable to identify any ancient source making reference to such practices. The *oldest* reference (we have been able to identify) to Roman women ingesting turpentine for boosting their attractiveness by means of changing the odor of urine is written two millennia *post facto* by the German poet Heinrich Heine. As to the role of Cleopatra's urine in her love affairs, the source we identified is even less likely: a text of pediatrics authored by John Apley in the mid-seventies of the last century. One can only hope that more erudite readers will be able to point – if existent at all – to such source.

Conflicts of interest: None declared.

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