## THERIACA BETWEEN MISTERY AND TRUTH

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In time, no other drug has had the advantage of a better fare than Theriaca or Thriaca, whose use was almost uninterruptedly mentioned starting with the antiquity and up to the end of the 19<sup>th</sup> century, none has been so widely used and given more hope of recovery to the sick.

Its origins fade back in time, which means it is not known who invented it or when. It was mentioned under this name during the  $4^{th}$  – $5^{th}$  centuries B.C. and was used by medical practitioners in Alexandria and Egypt, its use to spread later on throughout the Greek and Roman worlds. At the beginning, it was an antidote against bites of such venomous animals as snakes, scorpions, spiders, bees as well as a remedy in rabid dog bites. It progressively began to be used against all types of poisoning, be it that poison reached the body through animal bites or through swallowing.

The number of ingredients ranged from 4 to as many as 40, most of them plants and only rarely were the ingredients of mineral or animal origin. It should be pointed out that none of these types of theriacas contained viper meat, which was later to become the typical component of the drug.

Until the 5 century A. D. it is difficult to speak about a drug made up according a strict formula, it is better to speak about several different antidotes which were commonly known as Theriaca. Some of them had both therapeutic and prophylactic values.

If an antidote ever existed by excellence endowed with magic qualities and able to solve any kind of sickness, this used to be Theriaca.

Its main role was to counter balance the venom, especially that of adders.

There is no doubt as to the origin of the electuarium and its name. History and myth only become interwoven when people try to understand how the magic recipe reached the Romans. Its name was derived from the Greek word Therion, which refers to vipers, to venomous animals generally and from the famous anti-venom Mitridato, invented and used by the great king Mithridate.

The Pons was an area rich in medicinal plants and Mithridate had gained valuable knowledge on these, their qualities and powers. Heavily burdened by the fear of being poisoned, he had long been involved in the study of plants and had concluded his studies by creating several antidotes, one of which, especially effective, being still known under his name (Mitridatium antidoton) and which, according to Plini, contained 54 chemicals.

As ancient Roman doctors tell us the story, which was later introduced in the Roman pharmacopoeia, Mithridate used his antidote daily to fight his obsessive fear of being poisoned and to make himself immune (mitriadatism).

Mitridatisation refers to immunity gained against a certain poison by constantly ingesting increasing amounts.

History further tells that, when the Roman army defeated Mithridate in Pompei, the king who had decided to die but not be taken prisoner, was not able to use the venom as he was immune and had to use the sword to kill himself.

"Mithridate took a very strong venom from handle of his sword and drank it together with his two daughters Nicia and Mitridata. But the venom did not have any effect on him since he had become

immune through this remedy of his, Theriaca and to die he had to use Bitio, his soldier, to help him Unlike him, his daughters who had never taken the antidote, died at once.

Finding out about this, Pompei looked for Mithridate's recipe through his loot and found chests full of samples, comments and descriptions of the antidote, which he then asked his very knowledgeable scribe to translate into Latin" [1].

A century later, the Cretan Andromachus, Nero's personal doctor, removed some of the ingredients and added others, among which viper meat, thus creating a new drug, made up of 64 substances. This was Theriaca. In a short poem dedicated to his emperor, Andromachus praised the qualities of the drug, to a certain extent explaining how it was prepared, how and when it could be used [1].

Because of the changes introduced by Andromachus, Theriaca began to be considered a panacea which made it famous and sought for during the ages. It proved to be efficient not only against poisonings, but in many other ailments, such as: "the cruel plague epidemic", chronic headache, hearing problems, partial loss of eyesight, indigestions, liver problems, renal failure and hydropsy.

Among the many substances that made up the drug there were iris, dried rose, cinnamon, myrrh, scented Corinthian crocus, lavender, dittany, black pepper, ginger, valerian, earth from Lemno, old wine, honey and an onion, sprinkled with flour at the beginning, brought to boil and covered with a heap of hot ash.

The main role was attributed to viper meat. After removing the head and tail, the reptile was boiled "with a branch of scented dill" until meat would come off the spinal chord. Bread was then added, as the crushed viper had the shape of a circle and the liquid was not wasted. This was afterwards placed in a round empty bowl, in which it formed small circles and everything was kept in a dark place.

Later on, at the beginning of the 1<sup>st</sup> century AD, Cratevas, Greek physician and doctor for Mitridates VI Eupator, king of Pontus, gave the name of *Mithridatia* to a plant in honour of his master. Without doubt, his works, were the main inspiration for the Greek doctor Dioscoride.

A contemporary of Andromachus, Pedanius Dioscorides (ca. 40-ca. 90) practised in Rome at the times of Nero and is famous for writing *De Materia Medica*, a precursor to all modern pharmacopoeias and one of the most influential herbal books in history, to remain in use as late as about 1600. He joined the army as military doctor in order to widen his medical knowledge and thus his work also records the Dacian and Thracian names for some plants, which otherwise would have been lost.

At history goes on, the brilliant Roman doctor Clarissimus Galen (129-201 AD), of Greek extraction, brought together all the information he could find from Nero's doctor and clarified them later. He stated that the wine used to moisturize and mix the different substances "must be of the finest kind, like the sweet wine of Falerno, and that the honey must come from Imetto, because bees eat thyme and make very good honey there" [2].

Somewhere else in his work, Galenus further discussed the duration of the drug efficacy, that is to say its shelf life in nowadays terms. "The antidote had to be kept in a glass or silver bowl and, because it needed much heat, it had to be heated every time it was used. It had to be prepared for at least 12 years, but those who wanted it to be especially strong and efficient would make a new one after 5-6 years, particularly when it was used against the bites of venomous animals, of rabid dogs or against the toxic poisons found in plants: whenever a remedy against very harmful things was necessary, a very strong theriaca was used" [2]. It was efficient even after 30 years and even 60 years if the ailments were not very serious but its efficacy faded after that.

In his later work, Galenus widened the use of Theriaca so much that he wrote "Theriaca does not only heal the body, it can also ease the passions of the heart when they became too painful" [2].

In his work, the famous doctor also included an entire poem, De Theriaca ad Pisonem, marking the birth of Theriaca Magna or Andromachus Theriaca.

In spite of the developments marking the progress from Antiquity towards, the Middle Ages (decay of ancient institutions and insufficient circulation of information, mainly), which have led to the survival of very little of Greek-Roman medical tradition, Theriaca continued to be highly respected all through the Middle Ages by such early mediaeval Eastern and Arab doctors as Paulo Egineta (620-680), Mesue the Elder (777-857) and Avicenna (980-1037), who recommended the drug against venom as well as in the case of many diseases.

Special mention among the barriers to the perpetuation of Theriaca within European pharmacopoeias should be given to a spiritual, not a material factor. Pervasion of Christianity meant the increasingly wider adoption of its interpretation of disease as divine punishment, which determined condemnation of medical practices and sole resort to the powers of Jesus (*Christus medicus*), who, by purifying the souls, could restore the body to health as well.

Theriaca did not however fall into oblivion as can be seen from a 9<sup>th</sup> century document originating from the Chartres Cathedral College, mentioning it as one of the medicines able to cure intestine occlusion.

Starting with the 11<sup>th</sup> century, proof of the uses of eluctarium become increasingly numerous and accurate as, due to translations from Arab physicians' works, the link of Western medicine with Ancient science was resumed. A later Middle Ages reference to Theriaca endows it with even greater, both healing and preventive powers [2].

Thanks to its strong relationship with the Arab East, Venice was one of the first European cities which produced the powerful drug and made it famous. No certain date is known, but it is a fact that it was already in manufacture around 1258.

Venetian pharmacies like "Dell' Aquilla near", "Al Struzzo D'oro" and "La Testa D'oro", the best known of them, were famous for their Theriaca.

A paragraph from Capitolare dei Medicie Speziali of the Ancient Council of Justice in fact says that: "druggists under oath could not purchase such a drug that came from abroad, could not sell it, unless previously examined by specialists appointed to do this" [2]. Starting with this particular situation in Venice, the production of Theriaca became quite widespread and it can be found in Tacuinum sanitas, by Prince Bishop Trento Giorgio de Lichtenstein, written towards the end of the 1300 now in the National Library in Vienna. The explanation accompanying the text mentions that the best Theriaca "against poisoning and against hot and cold diseases" is "more than 10 years old (when too old resulting in insomnia)" and "it is particularly useful for cold humours, for the elderly, in winter, but also anywhere when necessary" [2].

Taking such evidence into consideration, it is reasonable to assume that it was used during the terrible plague pandemic, The Black Death (1347-1350), when people, helpless in their fight against death, did not hesitate to use odd and unexpected drugs.

As medical cabinets were thriving 14<sup>th</sup> century Italy in the wake of the pandemic, Theriaca is considered more and more important. As Marsilio Ficino wrote in his famous classic in the field, *Consilio contro la pestilentia* (1481), the eluctarium was indicated as one of the primary preventive resorts and a detailed recipe was provided for this godsend, queen of all compounds [2].

Theriaca undergoes a vigorous revival during Renaissance times and comes in the foreground in all pharmacopoeias which Italian and in fact European cities increasingly develop. The rediscovery of classicism and its values as undertaken by Humanism and Renaissance consisted of a vast and thorough undertaking of study and publication of medical-pharmacological works of ancient physicians,

Galenus's works particularly were printed and re-printed again and again in the 15the century, which has directly led to a renewed and intensified use of Theriaca as well.

Even if shops still considered it a main "strong remedy against poisoning", Girolamo Fracastoro for example specifies its wider indication against diseases and sicknesses of all kinds: fever, plague, tuberculosis, the initial stage of syphilis. Scientific confidence in its powers, as that expressed by the Bologna naturalist Ulisse Aldrovandi, physician at the Court and director of the Bologna Botanical gardens, tended to become unlimited and so the public began to think of it as a universal panacea [2].

Going farther East now, Theriaca was known and used in the Romanian Principalities during feudalism, brought over from Italy, Greece and other places. Both the genuine and the counterfeited drugs were known. Although the developments in pharmacology greatly reduced the importance of the drug, which was later to be completely removed from use, Theriaca was still mentioned in the first edition of the Romanian pharmacopoeia (1862) in the German Pharmacopoeia (1872).

It should be noted that High Steward C. Cantacuzino's library contained a pharmaceutical paper called "Avertismenti nelle compositioni de medicamenti per uso della Spetiaria" (Venice, 1671) by Georg Melich, a pharmacist of Venice [3]. This is a very practical paper, giving advice on the preparation of drugs which could, at least to a certain extent, be undertaken at home as well, by a trained person whose home pharmacy was in good supply. This seems to be the case of Cantacuzino as well, experts telling us say he had most likely attended the lectures of the Medical School of Padua University while a student in humanities there for 3 years.

The above mentioned paper is one of the few pharmaceutical works written by a pharmacist during the 16<sup>th</sup> century. Coming from Augsburg, G. Melich settled in Venice, where he owned the "Spezialle allo Struzzo" pharmacy. Unlike the first edition of his book (Venice, 1574) the one in Cantacuzino's library is particularly interesting, because it contains new "useful and necessary prescriptions" gathered from the most famous antidote books by Alberto Stecchhia, a Venetian pharmacist. The same pharmacy contained the "Trattato delle virtu della Theriaca" a paper by Oratio Guarguante. Venetian pharmacists were very skilled at preparing Theriaca and sold it throughout Europe, including our country.

Theriaca, a complex opiate, is mentioned among the drugs recommended for the treatment of certain diseases by Gy Lencses in "Ars medica" and was also mentioned in the inventory of the Sibiu local pharmacy in 1580 and the inventory of Dr. Egidio, a surgeon from Cluj in 1589. The information published about Theriaca in Romania shows that lids of boxes containing Theriaca, as well as a complete box, all were dated 1603, were found in Dobrogea and Moldavia. The box is made of soft metal, has a triple leafy wreath on its round lid and bears the inscription "Theriaca Fina Alla Testa Doro In Venet" inside. In the middle of the wreath there is a man's shaven head, seen from the right side and wearing a Roman costume, with a laurel crows on the forehead, the ribbons flying towards the back: this is supposedly the portrait of Nero's doctor, Andromachus, who had prepared "Confectio Andromachi", a personal formula of Theriaca. St Mark's lion, symbol of the Republic of Venice, can be seen in the foreground. Further down, the letters V. and C. can be seen on each side, which may stand for the name of the artist who so beautifully engraved the lid [4].

Other documents quoted by N. Vatamanu in the paper "Theriaca in the Romanian Principalities" speak about 6 lids of Theriaca boxes [5].Out of these, only one has a special feature, representing a standing crowned man, with a snake curled around. The lid is inscribed "Fine Theriaca from Venice" and the box is likely to have come from the Venetian pharmacy "A lo Sofferenza Coronata". Unfortunately, the 6 lids have all disappeared. These boxes of Theriaca found in Romania may date back to the 17<sup>th</sup> century.

Of all forms of Theriaca, the finest and most sought for was considered that prepared in Venice (Teriaca vera veneta), under the control of the authorities. Theriaca was still prepared in Bologna as late as 1796, in Venice to the first half of 1800 and Naples until the end of 1906.

Theriaca was one of the drugs purchased in Vienna in 1621 and in Venice in 1625 for the home pharmacy of Bethlen. The 1650 inventory of the royal pharmacy in Alba Iulia included Theriaca.

To go further, when Nicholas Prince Mavrocordat, amateur doctor like his sister Ruxandra, was arrested by Pivota's detachment in 1716 and his wealth was recorded, valuable drugs were found among other goods. One of his letters informs us that he prepared an electuarium with opium, which he offered to Patriarch Hrisant: it was a regular electuarium Theriacale, a widely found drug in our area [6].

Theriaca took its toll, though. In 1752, Prince Grigore Ghica II died of on overdose of "heavenly Theriaca", the panacea given to him by his doctor, Mihai Manu.

Several documents from Wallachia, Moldavia and Transylvania, records of customs taxes and goods circulation, dating back to the 17<sup>th</sup> century bring precious information on the use of Theriaca on Romanian ground.

The earliest information of this type is dated 1765, when the weight of about a kilogram Theriaca imported to Moldavia was charged 22 Aspri (Turkish silver coins)as much as the most expensive fur [7].

On the 4<sup>th</sup> of June 1770, Mihai Tambru, a merchant from Brasov, sent Riga Hagi-Mihali, his colleague in Iasi, "70 litres of Theriaca" [8] among other goods. On the same day, another merchant from Iasi sent "30litres Teriac" to Pavel Panaioti [9].

Wallachian customs taxes documents charged Theriaca by 18 bani per 3 lbs. [10].

On November 1<sup>st</sup>, 1794, the same Mihai Tambru wrote a paper for "3 packages of iliac powder", priced at 1 Gros (German silver coins) 90 Aspri per package [11]. It is interesting that the remedy is known under its popular name "iliac", used and preserved in magic spells. It is equally important to mention the powder form of Theriaca, a succedaneum useful for Eastern countries. The powder was mixed with honey or wine before being administered to patients.

Another Wallachian customs document, dated January 1818, lists among "bottles of Odiculon" and "Clocks with deceitful glass", "Tiriac altîmbaş; I prost", charged 40 Bani per 3 Lbs [12].

A preferential customs document for the Southern Russians, dated January 1822 lists a wide range of drugs, such as: opium, aloe, quick silver, casein, rhubarb, gum mastic, arsenic and Tiriaca of course [13].

Drugs were intensely traded at the time. This type of trade involved not only for pharmacies, quite few at the time, but also general trade with Oriental items later known as "Colonials". There was a large supply of drugs on the market and anyone could go to specialised merchants, the so-called "Greeks" to buy the drugs they thought they needed. This was the only way in which drugs as Theriaca could reach the largest numbers of people, therefore encouraging unpunished abuse .

Even if trade and tax records do not go farther than 1822, the trade with Theriaca continued in the Romanian Principalities, as shown by national Codices. At the beginning of the 19<sup>th</sup> century, it was being given up and was no longer included in the Prusian Pharmacopoeia (1833), in the Weimar (1840), Berlin (1846), Hamburg (1852) and the Petersburg (1866) pharmacopoeias.

On the other hand, the Austrian provinces Codex (1870) included the formula of "Electuarum or Theriaca Andromach", made up of only 7 substances. This "Theriaca of the poor" (Diatessaron) and the "Electuarium aromaticum cum opio" must be those "bad quality Theriaca" types so widely used on the whole territory of Romania.

Only a limited number of Pharmacopoeias in the 19<sup>th</sup> century included Theriaca: that of Schleswig Holstein (1831), Belgium (1833) and Vienna (1855), the latter having "Electuarum aromaticum cum opio" on page 58.

In the first edition of the Romanian Pharmacopeia of 1862 [14], edited by the pharmacist Constantin Hepites, the prescription of Theriaca can be found under pharmaceutical preparations, on page 304. The recipe is provided in both Latin and Romanian.

On page 336 of the third edition of the Romanian Pharmacopeea (1893) a more complex formula of Theriaca, known as "*Electuar Theriacal*" can be found, comprising 12 ingredients, of which viper meat, the main traditional component, is missing however [15].

An interesting formula can also be found in "Memoirs on Opium", a 1875 paper by Stefan Petrovits [16] and the preparation was recommended for use in cases of fever, pox and rubella.

The last record concerning the production of Theriaca dates back to 1906.

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## ODE TO THERIACA

To poison the original innocence

A snake is enough

To heal the poison

A snake is enough,

The seduced Eve, the fallen Adam, all fallen

By a women was the men fed with that poison,

But in Theriaca from the adder, the meat comes from the female, not the male.

Among men, all evil comes from women

Among addlers, all good comes from females

So.

Who calles a Women "liar"

Breaks his word

The addler with 3 tongues, though having more than one in its mouth

Does not betray,

The female does not betray

The male does so.

And thus,

Man is always betrayed by snake.

Either in Heaven through pain

Either in the word through lack of knowledge.