

DELTOS

Vol 33, No 51 (2023)

Deltos

DELTOS JOURNAL FOR THE HISTORY OF MEDICINE
Athens • June 2023 • Volume 33 • Issue 51 • ISSN 2945-1205



ΣΟΙΝΕΣ

Deltos ΠΕΡΙΟΔΙΚΟ ΤΗΣ ΙΣΤΟΡΙΑΣ ΤΗΣ ΙΑΤΡΙΚΗΣ
Αθήνα • Ιούνιος 2023 • Τόμος 33 • Τεύχος 51

Issues pertaining to posology in ancient Greek, Roman and Byzantine medical texts

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doi: [10.12681/dj.38108](https://doi.org/10.12681/dj.38108)

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To cite this article:

Valiakos, E., Marselos, M., & Diamandopoulos, A. (2024). Issues pertaining to posology in ancient Greek, Roman and Byzantine medical texts. *DELTOS*, 33(51), 31–43. <https://doi.org/10.12681/dj.38108>

Issues pertaining to posology in ancient Greek, Roman and Byzantine medical texts

Elias Valiakos¹, Marios Marselos², Athanasios Diamandopoulos³



Figure 1. Sir Christopher Wren's window at the Oxford University Museum of the History of Science, Oxford, England. It depicts Sir Isaak Newton's dictum "numero, pondero, et mesura Deus omnia condidit" (God created everything by number, weight and measure).

Abstract

Researching medical texts of the past reveals that the preparation of a therapeutic recipe usually involved the use of several active ingredients. There are many detailed reports on the ratio of the ingredients in a recipe, but also on the dosage administered to the patient. In this article, we recorded the use of units of weight and volume in therapeutic recipes from antiquity, the Hellenistic era, the Roman Empire, Byzantium, and also empirical medical texts of the 19th century. The changes emerging over time from the growing trade in the wider Mediterranean area, with the introduction of both new products and new units of measurement, did not affect the basic principles of the therapeutic methods. Through the centuries, the main concern of physicians was to fight the disease without burdening the patient with any unwanted effects. In this context, we observe even dosage modifications when it comes to special vulnerable population groups, such as children, the elderly and pregnant women. The period covered is very large, which means that the approach is impressionistic not aiming to the philologists. We hope that this does not pose a problem to the interested historians of medicine.

Key Words: *Ancient recipes, posology, weight and volume units, iatrosophia*

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Introduction

1st AD: “A little bit of opium poppy (a dose of orobos) is an analgesic, a hypnotic, and a digestive, soothes coughing and abdominal cavity afflictions. Taken as a drink too often it hurts (making people lethargic) and may be lethal” Dioscorides, 1st cent. AD¹.

13th cent AD: “The therapeutic agent (the medication) [...] must be given in analogues amount with the strength of the morbid agent. Because if it exceeds it will affect the neighbouring parts [of the body], exactly as when the fire burns out all the fuel, it ignites the neighbouring material, similarly the medicaments having dealt with the intruder, then affect the body parts” Bishop Apocaukos of Nafpaktos, 13th cent. AD².

These two extracts from Greek texts, twelve centuries and two Faiths (Paganism and Christianity) apart, prove authors’ continuous preoccupation with the precise dose of a prescribed drug and their fear over toxic side effects. To determine the “how much”, it was necessary to agree how this is weighted, that is the posology. In current scientific terminology, posology is a very important branch of modern pharmacology and therapeutics, being the science of dosage (from Greek *pósos*, how much, and *lógos*, study) concerned with “treatment dosage” and “dosage regimen”³. The earliest uniform systems of weights and measures that are currently known to us appear to have been formulated during the 4th and 3rd millennia BC among the ancient peoples of Egypt, Mesopotamia and the Indus Valley, and perhaps also Elam (in Iran). According to early Babylonian and Egyptian records and the Hebrew Bible, length was first measured with the forearm, hand, or finger and time was measured by the periods of the sun, moon, and other heavenly bodies. When it was necessary to compare the capacities of containers such as gourds or clay or metal vessels, they were filled with plant seeds which were then counted to measure the volumes. When weighing means were invented, seeds and stones served as standards. For instance, the carat, still used as a unit for gems, was derived from the carob seed⁴.

Accurately defining units of measurement, be it for weight or volume, is invariably a problematic issue due to their significant variability throughout different periods of history. In certain cases, a unit may even have varying values from one place to another within the same historical context, depending on the standards set by the authorities. For instance, even though the silver coin *ὀβολός* (obol) corresponded to the basic weight measurement in ancient Greece, in recipes of the Corpus Hippocraticum it is encountered with

three different values, as the obol of Athens (*Ἀττικός*), of the island of Aegina (*Αἰγινάϊος*), and of the island of Rhodes (*Ρόδιος*) (Table 1)⁵.

As expected, each historical period retained a traditional set of weight and volume units, whilst also introducing novel ones, tailored to the requirements of expanding commercial activities in new territories. Tables 2 and 3 demonstrate that the Roman and Byzantine measures include numerous units originating from antiquity, in addition to several newly established ones. It is noteworthy that a new weight unit, named the dram, which emerged during commercial transactions in the late Byzantine period, was in fact the Persian dirham, originating from the Greek drachma. Despite their similar names, the Greek drachma and Persian dirham represented different weight values (see Tables 1 and 3). Moreover, further difficulties are encountered when we try to transliterate the Greek name of a dose to other languages. Indicatively, the Syriac *qūqāyā* appears to come from the Greek *kókkion*, a diminutive of *kókkos* (“berry”), which is also used to denote “pills”. But there also is the word *qūqā* that may originate from *kaúkos* (a cup) or *kókkos* (berry). Furthermore, the Syriac *qūqāyā* can also mean ‘potter’⁶.

It may be easier to comprehend the ancient Greek medical texts on drugs, including their dosages and side effects, in this cultural context. However, the desire to establish precise drug dosages did not emerge suddenly in Greece, nor did it disappear abruptly after the fall of the Byzantine Empire. Everything in science – as in any other aspect of civilisation – took a considerable amount of time to develop and refine, or to be discarded entirely. Thus, the main body of this article is proceeded by a short reference to the ancestors of Greek medical texts on dosages and followed by a reference to their descendants. Our focus is solely on textual evidence from regions surrounding the Eastern Mediterranean.

i. The ancestors

The ancient Egyptians were very accurate in specifying each drug dose prescribed. Indicatively, incantations were recited when weighing a prescription’s ingredients. Moreover, the patient’s name in the Egyptian Medical papyri (1800 – 1300 BC) was always written in red ink while the ingredients were in black, with dosages in red⁷.

The Ebers Papyrus contains 850 recipes for various ailments where all the doses are written in red⁸. An indication of the observance by the Egyptians of the exact quantity of a drug’s ingredients:

Eb 5

Another (remedy) for an abdomen that has pain:

Cumin: 1/64 (dja), goose fat: 1/8 (dja), milk 1/16 (dja) (oipe=4 dja).

[2.15a] To be cooked; (then) squeezed out, (and) drunk.

Eb 6

Another remedy:

Figs: 1/8 (dja), Egyptian balsam fruit (?): 1/8 (dja), sweet beer: 1/16 (oipe=4 dja)

[2.20a] (To be treated in the same manner).

Later, we refer to a recipe inscribed on a clay Babylonian tablet of the 7th/6th cent. BC for treating menorrhagia

"If a woman's blood flows and does not stop, to stop

it: you prescribe (lit. "give her") alum, reddish kalgukku-mineral, [a mixture?] for 'soaking'; thereafter you give her the (mixture) for 'soaking' and 'damming up' (the flow); thereafter you give her thi[s] mixture [of alum?] and reddish kalgukku-mineral: You roast alum, kalgukku – [...], you make [a suppository?]. These drugs, as much as one has told you (to be appropriate), she applies one at a time, until? the wetness? Is [...]"⁹.

Moving several centuries later, we read at the Babylonian Talmud written between the 3rd and 6th century AD but incorporating many older recipes, the very comprehensive remedy for an anal "split" (fissure): "take 7 grains of worm(-coloured) alkali-plant, wrap them inside the neck (of a garment), wind it in thick cord, decoct it in white balm, roast it and spread it upon it (the anus)"¹⁰.

Table 1. Ancient Greek units in medical prescriptions.

Unit	Equivalent	Modern equivalent	Remarks
Weight units			
ὀβολός (obol)	Based on the barley grain: twelve grains to one obol.	0.72 g	A silver coin of the Attic standard. The Aegina obol was 1,05 g.
κεράτιον (keration) or δίχαλκον (dichalcon)	About ¼ of an obol (three barley grains).	0,19 g	A seed of the carob tree (<i>Ceratonia siliqua</i>). Dichalcon: a double chalcos (a copper coin).
δραχμή (drachma)	6 Attic obols.	4.31 g	As a weight unit, drachma is mentioned also as ὀλκή (holkē).
μνᾶ (mina)	100 drachmae.	431 g	
Liquid and dry volume units			
κοχλιάριον (kochliarion)		4,5 mL	A small spoonful.
χῆμη (chēmē)	2 kochliaria.	9,1 mL	A spoonful.
μύστρον (mystron)	2.5 kochliaria.	11,4 mL	A large spoonfull.
κόγχη (konchē)	5 kochliaria.	22.5 mL	A shell-full.
κύαθος (cyathos)	10 kochliaria.	45 mL	A small cup with a handle.
ὀξύβαφον (oxybaphon)	1,5 cyathoi.	67,5 mL	A shallow cup for vinegar.
κοτύλη (kotylē) or ἡμίνα (hēmīna).	6 cyathoi.	270 mL	A large cup with two handles (the Roman kotyla or hemina).
ξέστης (xéstēs)	12 cyathoi.	540 mL	A large vessel.
χοῖνιξ (choinix)	24 cyathoi.	1.08 L	
χοῦς (chous)	72 cyathoi.	3.24 L	A pitcher (the Roman congius).
Figurative description of size or dry volume			
ἄστρογάλος (astragalos)	A bone of the foot, in some instances specified, as e.g. astragalos of a deer.		
ὀροβός (orobos)	A small round seed (ervil) similar to a pea, from the plant <i>Vicia ervilia</i> ,		
κάρυον Ποντικόν (karyon of Pontus)	The hazelnut, nut of the shrub <i>Corylus colurna</i> .		
κάρυον Θάσιον (karyon of Thasos)	The almond, nut of the tree <i>Amygdalus communis</i> .		
κύαμος (kyamos)	The broad bean, the seed of the plant <i>Vicia faba</i> .		

Table 2. Roman units in medical prescriptions.

Unit	Equivalent	Modern equivalent	Remarks
Weight units			
<i>uncia</i> (Roman ounce)	The units of weight were mostly based on factors of 12.	27.4 g	Derived from unus (one), as a "single unit" of weight.
<i>siliqua</i> (carat)	1/144 of an <i>uncia</i>	0.19 g	A carob seed, the Greek <i>keration</i> .
<i>obolus</i> (obol)	1/48 of an <i>uncia</i> .	0.57 g	From the Greek word <i>οβολός</i> (a metal stick). It differs as a weight from the Greek <i>obol</i> .
<i>scrupulum</i> (scruple)	1/24 of an <i>uncia</i> .	1.14 g	It means a "small pebble" and corresponds to the Byzantine <i>gramma</i> .
<i>libra</i> (Roman pound)	Twelve Roman ounces equal a <i>libra</i> .	328,8 g	A "balance".
Liquid and dry volume units			
<i>ligula</i>	1/288 <i>congius</i>	11.4 mL	A large spoonful.
<i>cyathus</i>	1/72 <i>congius</i>	45 mL	A small ceramic cup.
<i>acetabulum</i>	1/48 <i>congius</i>	68 mL	The Greek <i>oxybaphon</i> .
<i>quartarius</i>	1/24 <i>congius</i>	136 mL	"One fourth", from its relation to the <i>sextarius</i> .
<i>hemina</i> or <i>kotyla</i>	1/12 <i>congius</i>	273 mL	A large cup with two handles.
<i>sextarius</i>	1/6 <i>congius</i>	545 mL	The "Roman pint", with double the volume of <i>hemina</i> .
<i>congius</i>	1 <i>congius</i>	3.27 L	The Greek <i>chous</i> .

Table 3. Byzantine units in medical prescriptions.

Unit	Equivalent	Modern equivalent	Remarks
Weight units			
<i>οὐγγία</i> (ouggía)	Byzantine ounce.	27.3 g	Roman <i>uncia</i>
<i>γράμμα</i> (gramma), or <i>τρημίσις</i> (trēmísis)	1/24 of an ounce.	1.14 g	Roman <i>scrupulum</i>
<i>σημίσις</i> (sēmísis)	1/12 of an ounce.	2.27 g	semissis
<i>δράμι</i> (drámi)	1/8 of an ounce.	3.88 g	The Persian <i>dirham</i> , from the Greek <i>drachma</i> (approximately 3 <i>grammas</i>).
<i>νόμισμα</i> (nómisma)	1/6 of an ounce.	4.55 g	<i>nomisma</i> (coin).
Liquid and dry volume units			
<i>οὐγγία</i> (ouggía)	1/12 of a <i>litra</i> .	0.1824 Lt	Liquid Byzantine ounce.
<i>κοτύλη</i> (kotýlē) or <i>ἡμιξέστιον</i> (hēmíxéstion)	1/8 of a <i>litra</i> .	0.276 Lt	Roman <i>kotyla</i> or half- <i>sextarius</i> .
<i>ξέστης</i> (xéstēs)	1/4 of a <i>litra</i> .	0.548 Lt	Roman <i>sextarius</i> .
<i>λίτρα</i> (lítra)	1 <i>litra</i> .	2.1888 Lt	Roman <i>libra</i> .

These three extracts represent an embryonic form of the science of posology.

ii. Greek medical writings from the 5th cent. BC to the 15th cent. AD

Material

The following authors were selected for further analysis, because their treatises represent different

periods in medical history (Ancient Egypt, ancient Greece, Hellenistic era, Imperial Rome, Byzantium and its offspring): Egyptian Medical Papyri (2.000 BC – 4th cent. BC), Hippocratic Corpus (5th/4th cent. BC), Nicander^a (2nd cent. BC), Dioscorides (1st cent. AD),

a. Nicander (2nd cent. BC) was born in Colophon of Asia Minor, but spent most of his life in Alexandria. His text "Theriaca", in the hexameter verse, was a didactic work on the treatment of snakebites. He also wrote "Alexipharmaca", dedicated to the treatment of poisoning.



Figure 2. Fragment of the clay tablet K. 263.

Andromachus (1st cent. AD), Aelius Promotus (2nd cent. AD), Philumenus (2nd-3rd cent. AD?), Galen (2nd-3rd cent AD), Oribasius (4th cent. AD), Aëtius of Amida (6th cent. AD), Paulus of Aegina (7th cent. AD), Nikolaos Myrepsos (13th cent. AD), Nicephoros Vlemmydes (13th cent), Antonios Pyropoulos (15th cent.), Dimitrios Karakassis (18th cent.) and Hatzidimitris (19th cent.).

Method

A recipe description typically comprises the following parts: a. a title; b. clinical indications; c. a list of ingredients (herbal, animal, or mineral products) with the respective weight or volume units; d. instructions for the preparation of a homogenous mixture, with the appropriate formulation (oral solution, pill, lozenge, collyrium, pumice etc.); e. treatment instructions (dosage and frequency of administration). We have focused on remarks on the right dosage and duration of treatment and on descriptions of possible side effects as a result of therapy. Emphasis was placed on recipes containing details on posology, especially when prescriptions contained statements suggesting

specific concerns for particular groups of patients, such as children, the elderly, or pregnant women.

Results and Discussion

We accordingly classified our findings into the Classic Era, the Hellenistic and Roman Period and Byzantium and its descendants.

a. Classic Era

Several therapeutic recipes with information on the preparation and administration of remedies are encountered in books of the Hippocratic Collection. In general, recipes contain only a few references to weight units, which were *δραχμή* (drachma) or *ὀλκή* (holkē), *ὀβολός* (obolos), *στατήρ Αἰγινᾶιος* (stater of Aegina), *μνᾶ* (mina) (Table 1). There are also descriptions of rather vague dosages, with references to common utensils, such as *κύαθος* (cyathos, a small cup sometimes with a long handle), *κοτύλη* (kotylē, a large cup), και *ὀξύβαφον* (oxyvaphon, a saucer-like shallow cup). Additionally, the morphology of various natural products is used for the empirical description of units corresponding to weight or volume, such as *ἀστράγαλος* (astragalos, a bone of the foot), *ὄροβος* (orobos, ervil), *κύαμος* (kyamos, broad bean), *κάρυον Ποντικόν* (karyon of Pontus, hazelnut), *κάρυον Θάσιον* (karyon of Thasos, almond) (Table 1).

The lack of specific and reliable information on the preparation of remedies and dosages for patients contradicts the well-established ethical principles of the Hippocratic physicians, who pursued the well-being of their patients through accuracy in posology, to ensure effective treatment without adverse effects¹¹. It is believed that such information was depicted in one or more books with the title *Pharmakitis*, as stated in the paragraphs 9, 15, 18 and 23 of the book *Internal Affections*^{5,12}. Exceptionally, the treatises *Diseases of Women* contain several recipes with full instructions on the weights for preparing and administering a medicament. For example: “Another: one *obolos* of castoreum or sagapenum, one *drachma* of bitumen, two of soda; crush all these in sweet wine and oil, in the amount of half a *kotylē*. Give two *oboloi* to drink whilst fasting”¹³, or “Purgative enemas for the womb if it is ulcerated after birth or if there is inflammation: winter wild figs; cover with water, boil, sieve and leave to rest. Then add lukewarm oil and mix; inject two *kotylai* at the most. No enema should exceed this amount”¹⁴. For a detailed discussion on weights in Hippocratic texts, see Totelin¹⁵.

b. Hellenistic and Roman Period.

Dioscorides (circa 40 AD-90 AD) includes almost 360 weight or volume measures for ingredients in his treatise *Materia Medica* (teaspoonful: 144 times, grains: 60, ounces: 56, gallons: 39, cupful: 38, litre: 14, kilo: 6)¹⁶. In some instances, the instructions show a clear concern for the adjustment of dosages, when needed, as is the case of a recipe containing squirting cucumber (*Echallium elaterium*), advocated in patients with dyspnoea, when necessary to clear excess phlegm and bile. Posology, is modified, as follows: "...the ideal dose is an obolos and it should not be less than half an obolos; to children use only a dichalcon [1/4 of an obol]; when given at larger doses, it is harmful"¹⁷.

Hyoscyamus niger, "[...] and the seed doth perform the same things [...] as much as an obolos is drank [...]"¹⁸.

As mentioned already, Dioscorides seems well-informed on the possible risks of overdosing, when he describes the properties of opium poppy: "A little of it (a dose of orovos) is an analgesic, a hypnotic, and a digestive, soothes coughing and abdominal cavity afflictions; taken as a drink too often it hurts (making men lethargic) and may be lethal"¹⁹.

Krataiogonon, "[...] It is said that drinking of the seed doth cause a woman to bring forth a male. If [...] do drink fasting, 3 times a day the quantity of 3 oboloi with 2 cyathoi of water for 40 days"¹⁹. *Apsinthion* (*Artemisia absinthium*), "[...] is good also for inflations and the pains of the belly and the stomach [...] being taken every day to the quantity of 3 cyathoi"^{20,21}.

Aelius Promotus of Alexandria (1st/2nd cent. AD), in his therapeutic compendium *Dynameron*²², recommends modifying the dosage or duration of treatment to prevent toxicity. In a recipe for a plaster for patients with spleen ailments, we read: "Wonderful for the spleen; 2 drachmas of quicklime; 16 drachmas of caper root; chop them up and, after having softened them with vinegar, apply for 1 hour; no more, so that the spleen does not liquefy completely"²³. Furthermore, for patients with spleen ailments, there is another recipe for a solution to be administered internally: "Take willow bark and boil it, and for three days [give the patient to] drink the third left of the boil; do not administer more; otherwise, you will deprive him of spleen"²⁴.

Some recipes also contain recommendations for dose adaptations in special groups of patients: "Against pains in the urethra, urine retention, difficulty in urinating, for those who urinate blood and suffer from stones; it is called 'of Hippocrates' or 'herbal'; equal parts of *asarum*, *meum* [baldmoney], *celtic spikenard*; mix with

Attic honey; administer a dose the size of a hazelnut to robust people, but to children and the elderly less..."²⁵. A similar recipe exists for patients with dyspnoea: "Give one or half a spoonful of sodium carbonate to lick with honey or tempered wine; for children, give half the dose"²⁶. Interestingly, for highly toxic substances, such as antimony, lead or mercury, medical applications were restricted to topical use only. These examples demonstrate that Aelius Promotus' recipes reflect a certain degree of accumulated experience, through successful and failed trials, which he used for the benefit of his patients. It was during his era and in his region that lead cosmetics were overused^{27,28}, although lead powder had been documented as a cosmetic ingredient since Bronze Age²⁹.

As previously mentioned, the accurate reproduction of a recipe was crucial, not only in terms of the ingredients used but also in their proportions. This ensured that treatments were effective and safe, without any side effects or toxicity. We know that Nicander, Andromachus the Elder^a and Damocrates^b were three physicians who used versed recipes in order to facilitate memorization. *Theriaca* is the longest surviving poem by Nicander³⁰; it deals with the bites and stings of venomous animals, and describes antidotes for them. Bellow there is a fragment of *Theriaca*³¹:

[...] If however you can cast snakes coupled at a crossroads, alive and just mating, into a pot, and the following medicaments besides, you have a preventive against deadly disasters. Throw in thirty drachmas' weight of the marrow of a freshly killed stag and one-third of a chous of rose-oil, - essence which perfumers style 'prime' and 'medium' and 'well-ground' - and pour on an equal measure of raw, gleaming oil and one-quarter of wax. These you must quickly heat in a round, bellying pot until the fleshy portions are softened and come in pieces about the spine. Next take a shaped, well-made pestle and pound up these many ingredients in a mixture with the snakes; but cast aside the vertebrae, for in them a venom no less deadly is engendered. Then anoint all your limbs, be it for a journey or for a sleep or when you gird yourself after work at the threshing-floor in summer's drought and

a. Andromachus the Elder (1st cent. AD), a Greek who lived in Rome, was the personal physician to Emperors Nero, Claudius, and Augustus. He is credited with the creation of several recipes written in verses, including *mithridatium*, a variation of an antidote similar to *thēriakē*, attributed to Mithridates VI, the king of Pontus. The original recipe was allegedly brought to Rome as a trophy, after the Mithridatic wars (88-63 BC).

b. Damocrates (mid to late 1st cent. AD) was a Greek physician at Rome. His medical treatises in the iambic verse are lost, but some extracts have been preserved by Galen.

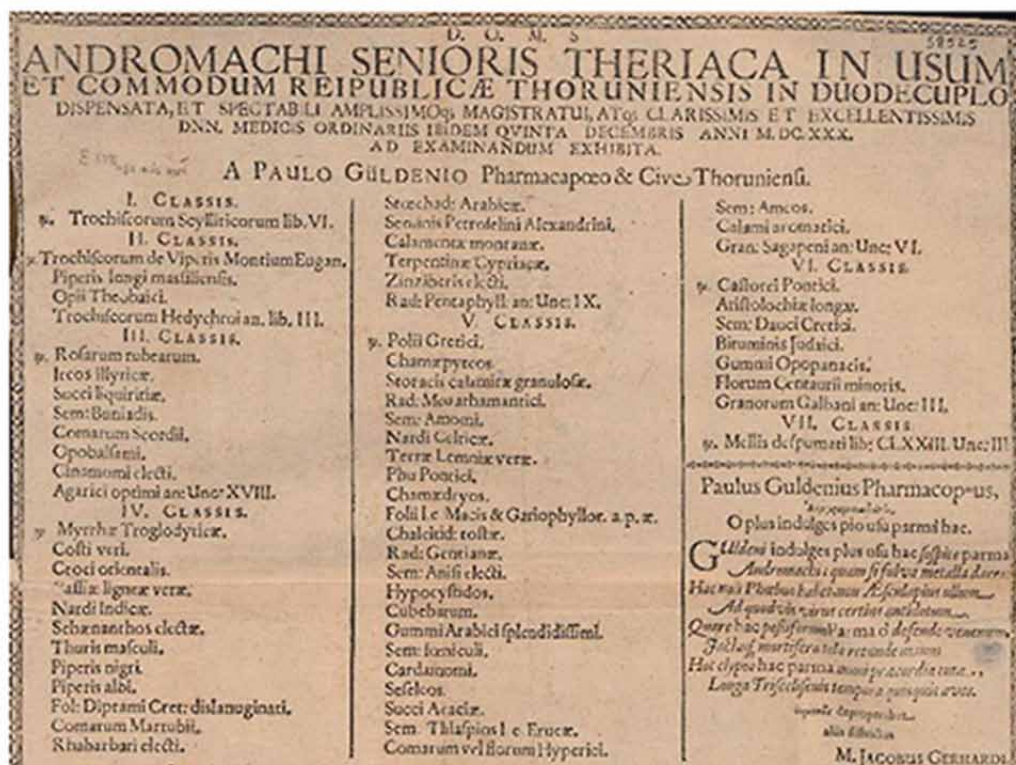


Figure 3. The printed Paul Guldenius Theriac recipe (Gdansk Library of the Polish Academy of Sciences).

with pronged forks winnow the high pile of grain [...]

Andromachus the Elder developed a recipe with the name *galēnē*, a variation of *thēriakē* against snakebites, which was written as an eighty-seven elegiac distich poem. It continued to be used for many centuries after³². A recipe of the famous Venetian *thēriakē*, c. 1630, is shown in Figure 2³³.

The English translation of its beginning reads: “Hear the vigorous power of the antidote of many virtues Caesar, giver of the peaceful freedom. Listen, Nero; it is called Galene, cheerful and serene, which does not worry about the dark ports, neither is it defeated if one would drink avidly from a hateful cup in which has been squeezed bundles of poppy”.

Galen (2nd/3rd cent. AD) was pedantic on the accuracy of the weights for herbal ingredients and doses. He expresses his anger on the variations of weight in various terms used in pharmacopoeia: “But among those who have written about weights and measures there has been disagreement on how much the weight of the *mna* is [...] some say that the *mna* consists of sixteen *unciae*, others of twenty, and still others draw a distinction, saying that the Alexandrian *mna* consists of twenty *unciae*, whereas the other consists of sixteen, and this is smaller. But among those who convert the *mna* into *drachmai* some say the *mna* consists of a hundred

drachmai, others say of more, since most people also say that the *uncia* consists of seven and a half *drachmai*, while others say only seven and others again eight. This being so, it is difficult to discover how many *drachmai* one should calculate the *mna* recorded by Crito in his prescription”³⁴.

Indicatively, in the treatise “On Theriac to Piso”, which is arguably attributed to him, Galen gives accurate instructions for preparing *thēriakē*: “Weigh out rose petals equal to 12 drachmas and add Illyrian iris and mix in an equal amount of sweet-boughed black liquorice and the seeds of sweet French turnip. Add the juice of fragrant garlic germander, taking Assyrian balsam from within. Put in the same amount of cinnamon by weight and do not forget to add an equal amount of agaric and myrrh and sweet scented *Saussurea Lappa* and crocus grown in the Corycian cave and [...] Take the weight of one bean which the well-shaded water has nourished in the water, hidden by many petals of the Nile bean, mixing it with three tablespoonfuls of warm water [...]”³⁵.

Galen wrote a thorough treatise on weights and measures, although its authenticity is questioned. An excellent collection of all his references on the subject in this treatise as well as similar others scattered into his various writings was published with comments in

Latin and Greek in 1888³⁶. To avoid errors caused by the inconsistent use of terms with varying actual weights, Galen advocated for the use of verses in recipe writing. When cites remedies of Damocrates, he praises his verse-form recipes, because they “are more useful than prose recipes, not only for the sake of memory, but also for the precision in the proportions of the various ingredients”^{37,38}. He repeats the same when he mentions the recipes of Andromachus for *thēriakē*³⁹ and *mithridatium*⁴⁰, but he prefers the version written by Damocrates, as more precise⁴¹. On two occasions, Galen gives a recipe of a golden remedy taken from Asclepiades, and cast in the first person plural: “Straight after [the previous recipe], Asclepiades wrote another thus. Emollient which we call (*kaloumen*) golden: golden arsenic and asbestos, of each 2 ounces; moist alum, 2 ounces; split alum, 2 ounces; we chop (*koptomen*) the dry ingredients, we sieve (*sēthomen*) them, putting them in a mortar; to these we add (*epibalomen*) 8 cyathoi of vinegar, grinding carefully as we mix with (*analambanomen*) the melted ingredients. These are wax, torch and pine resin, of each 2 litrai; common oil, 8 cyathoi. Melting these, we leave them (*eōmen*) to cool down, and scraping them we add (*epiballomen*) them to the ground ingredient”^{42,43}.

During Galen’s time, poetic recipes were prevalent, particularly those written in elegiac meter as opposed to Nicander’s hexameter. The resurgence of elegiac poetry occurred alongside the flourishing of the Second Sophistic movement. The creators of “elegiac pharmacology” were not only interested in conveying precise prescriptions but also in showcasing their overall education, or “paideia”. Characteristically, Aglaïas of Byzantium, a Hellenistic poet from the 1st century AD, composed a riddle poem for the treatment of cataracts, including various drug weights, which he addressed to a scholarly acquaintance:

“[...] Five obols of the flower of copper, and the same weight of the lovely mother of him that was slain by a boar. Add too one obol less than these of the fiery grain which grows in the Callatitan fields; and also twice the weight of two drachmas, one from the tawny-haired flower, and take the other from the genitals of the tamer of horses, of which let half the weight be of the pseudonymous father who gave his daughter in marriage to the son of a female slave”.

There is an abundance of allegories to Homer and other myths which only an equal learned addressee like Aglaïas could understand. A number of points of interest reveal the poet’s shot at originality. The first is found in line 10, which contains the enigmatic “lovely mother of him that was slain by a boar”. It alludes to Adonis who was killed by a boar. His mother’s name

was Smyrna, who after her death was turned to a homonymous tree. Thus, the poem refers to *smyrna*, alias *myrrh*, from which five obols should be used. Several other similar mythological allusions are used to decipher the whole recipe^{44,45}.

c. Byzantium

Early Byzantine medical writers were also meticulous in specifying precise weights for the medicaments they prescribed. This is evident in the numerous Greek medical papyri discovered in Antinoopolis, Egypt. In terms of therapeutics, they usually comprise extensive descriptions of medicinal preparations, rather than mere ingredient lists. Instead, the recipes usually provide ranges of application, ingredients with doses, and precise directions for administration, which have not been entirely omitted even when prescriptions are copied concisely⁴⁶.

Referring to the dosage of a medicine for the treatment of malaria (then known as “tertian” or “quartan” fever), Philumenus (3rd cent. AD) recommends the administration of three drachmas for adults and half the amount for children⁴⁷.

St. Epiphanius of Salamis (315-403 AD) wrote an extensive treatise “On Weights and Measures” in Greek preserved mainly through Syriac translations. Using his able knowledge of five languages he elaborated on the weights and measures referred in the Bible and their variable equivalents to the then used weights in the Greco-Roman world⁴⁸.

Oribasius, in the 4th cent. AD, personal physician to Emperor Julian the Apostate, describes a lozenge as a recipe of Andromachus, with a recommended dosage of 3 to 4 drachmas for adults, which should be reduced to 2 drachmas for paediatric patients⁴⁹. Similar recommendations for dosage reductions are also found in the treatise *Βιβλία ἱατρικὰ ἐκκαίδεκα* (Eleven Medical Books) of Aëtius of Amida (6th cent. AD). One worth mentioning dates back to the Ptolemaic era in ancient Egypt. It cites a recipe of Nechepso^{a,50}, with instructions for administering one twelfth of a drachma (*holkē*) to melancholic patients and to children with respiratory problems⁵¹.

a. The author with the pseudonym Nechepso(s) and Petosiris is thought to have been Greek because the preserved fragments were written at least partially in Greek verse, presuppose good knowledge of the major Greek dramatic authors from the classical period, and drew upon elements of Greek physics, mathematics and astronomy. The recently discovered demotic texts indicate that the fragmentarily preserved Greek texts originated from a pre-existing Egyptian tradition and Nechepsos can be identified with Necho II who ruled 610-595 BC as successor to Psammetichus I.



Figure 4. German postage stamp from 1991, commemorating 750 years of the apothecary profession.

Paulus of Aegina (7th cent.) presents a Galen's medicine for epilepsy, with pulp from the bulb of squill (*Scilla maritima*) mixed with honey. The daily dose for adult patients is a large spoonful, while children should be given a small spoonful⁵².

The monk, philosopher, poet and astronomer Nicephoros Vlemmydes (13th cent.) wrote two books on medical themes. One was the “Περὶ Ἰατρικῆς” (On Medicine) and the «τοῦ σοφωτάτου καὶ λογιωτάτου κυροῦ Νικηφόρου τοῦ Βλεμίδου εἰδησις τῶν ἱατρικῶν μέτρων» (A report on medical weights by the wisest and erudite Nicephoros Vlemmydes). In the latter, he describes several units for measuring ingredients for the preparation of drugs and their proper doses. The units were named after their container⁵³. There is a detailed explanation of the correspondence of various weights and their subdivisions (Fol. 28^r)⁵⁴. The *myrep-soi* were spice [and drugs] merchants who traded by weight. They operated from the Portico of Achilles, situated between the Million and the Chalke Gate⁵⁵. They, and their counterparts in the Latin West, used scales for weighting their goods (Figure 4).

In his book *Dynameron*⁵⁶, Nikolaos Myrepsos (13th century) provides numerous prescriptions, with dosages based on the patient's gender, age, and pathological condition. For instance, one medication is recommended for men at a dose of one ounce, reduced for women to half an ounce⁵⁷. The *Dynameron* also includes a recipe with the *thēriakē* of Andromachus, which should be administered to patients on an empty stomach, provided that they are not very old or feverish⁵⁸. Additionally, a remedy with the pharmaceutical

formulation of a *trochiscus* (lozenge) is given to adults as a single dose, whereas children receive a minimal dose (στάθμιον, stathmion)⁵⁹. Myrepsos seems deeply concerned about medicines potentially harmful to pregnant women, such as those including ingredients that may provoke miscarriage, be they of plant origin (euphorbium, hyoscyamus, opopanax, sagapenum), or natural inorganic compounds (cadmia, salmiac)⁶⁰⁻⁶². He also describes a recipe bearing the name of Mithridates, to be administered with wine to healthy individuals, but with water in smaller doses to the sick, depending on their condition⁶³. This is a medicine with more than fifty ingredients, most probably originating from *mithridatium*, but no reference is made to Andromachus.

d. Later periods

The cultural legacy of historical periods does not simply end with their conventional conclusion. In fact, it often endures for many centuries thereafter. For example, in the case of Byzantium, its legacy, referred to as *Byzance après Byzance*, persisted long after its Fall in 1453. A prominent figure during the transitional 15th century was Antonios Pyropoulos, who received his education in Constantinople from the renowned medico-philosopher Ioannis Argyropoulos. A depiction of Argyropoulos as a wise teacher can be found in a miniature illustration in Codex Oxoniensis Barocc. gr. 87, which features an epigram in the upper margin identifying some of his students: (Figure 5).

“Argyropoulos teaching the physician Antonios Pyropoullos and Marcos Pyropoullos, along with the physician John Panaretos, and Demetrios Angelos, and Aggalona, the son of Moschos, the physician Vranas of the first master at the Xenon of the Kral”. It also identifies the teaching institution, a very rare characteristic in Byzantine medical illustrations⁶⁴.

There is a treatise by Pyropoulos in the Iberian Monastery at Mount Athos titled “Εξήγησις του Πυρόπουλου περί των σταθμών / των νυν διαγόντων επί τας χώρας και πόλεις τας ημετέρας” (Explanation on weights used nowadays in our counties and towns). It names many weights used in medicine and trade and introduces new ones like “tsoflion” i.e. the amount contained in a nut shell, and the percentage (ἐξάγιον, *exagium* in Latin) the one who processes it is due to receive⁶⁵. In a catalogue titled «De antiquitatibus et libris manuscriptis constantinopolitanis» («Περὶ ἀρχαιοτήτων και χειρογράφων βιβλίων εκ Κωνσταντινουπόλεως»), B. Foerster (1877)⁶⁶ lists an *iatrosophion* by Pyropoulos. According to Kouzis, this was the source for all “*iatrosophia*”, that is manuals



Figure 5. Antonios Argyropoulos as depicted in Codex Oxoniensis Barocc. gr. 87.

used by empirical healers in Greece up to the 19th century⁶⁵.

Dimitrios Karakassis (Siatista, Northwestern Greece, 1734 - Bucharest, Romania, 1804) was a medico-philosopher, writer and poet⁶⁷. Following a turbulent career with studies in central Europe and teaching at local communities in Greece and the Western Balkans, he became Chief Physician at the Court of Michael Drakou Soutsou, Voivode (Prince) of Vlachia, the heir *par excellence* of the Byzantine Heritage. There, he wrote five books on medicine. He continued the tradition in using verse for his medical topics: (Fig. 6) as practiced by Andromachus, Nicander, Aglaïas, Psellus, Vlemmydes and other Greeks and enriched in the Latin West with the famous medical poem *Regimen sanitatis Salernitanum*⁶⁸ and in the Islamic East with Avicenna's *Canon of Medicine*⁶⁹. The second of his poetic books, written in Ancient Greek and Latin was titled "*Medical poems B! the apologetic, or the Hippocratic method invalidating the excess use of drugs*". It was inspired by the Hippocratic dictum "quite often the best medicine is no medicine".

For his poems he used a difficult form of the Greek language, imitating the writers of the 5th-4th century BC, the "attikizousa". The apologetic second poem with its 1120 verses was a vitriolic attack against the prescrip-

tion of multiple drugs and excessive doses. In essence, he argued, in the usual Byzantine metaphorical lore, that each disease, like a plant, had one reason, the root, and many branches, the symptoms. An inexperienced doctor prunes the branches with many drugs and leaves the root intact to spring new branches. An experienced doctor, understanding the cause, prescribes one correct drug in the correct amount and counterattacks the cause, destroying the root⁷⁰.

We end with an iatrosophion of the 19th century. The origin and contents of iatrosophia have been described earlier in this article in the section on Pyropoulos. We read: "After our good author Dimitris Xatzi-Apostolis completed the first two entities, he ended his work with four additions, from which the first two are necessary for the correct use of his book and the safe application of the recipes. The first (fol 12r-v) is a very useful record on weights and measures and symbols of chemical substances [...] The list was composed by the author himself in the year 1807"⁷¹.

Conclusions

Studying historical medical texts can be a cumbersome undertaking due to challenges in identifying the implied nosological entities and the pharmaceutical ingredients used. Equally arduous are matters pertaining to the ingredient ratios in each recipe and the patient dosages prescribed. Notably, weight and volume units have undergone inevitable fluctuations

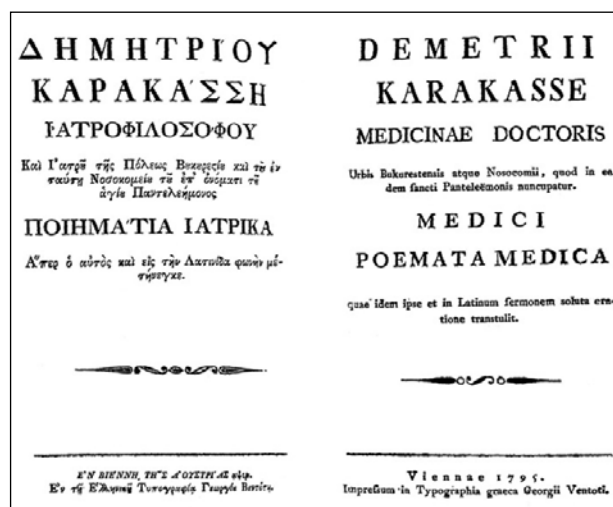


Figure 6. Front page of Karakassis' Book with Medical Poems: "Demetrii Karakasse Medicinae Doctoris Urbis Bukurestensis atque Nosocomii, quod in eadem sancti Panteleemonis nuncupatur. Medici Poemata Medica quae idem ipse et in Latinum sermonem soluta oratione transtulit. Viennae 1795, Impressum in Typographia graeca Georgii Ventoti".

over time and varied between regions during the same era. Nevertheless, despite all these changes through time, posology remained a subject of significant concern for almost all physicians of the past. The safety of patients has always been a key focus, as evidenced in the precise instructions for recipe preparation and dosage administration. As a result of accumulated clinical experience, certain groups, such as children,

the elderly and pregnant women, who are assumed to be more sensitive to particular active ingredients, were typically given a lower dosage. In conclusion, the pharmacological treatises of the past adhered to the long-standing principle exemplified later by Newton's dictum "*numero, pondero, et misura Deus omnia condidit*" (God created everything by number, weight and measure).

ΠΕΡΙΛΗΨΗ

Θέματα αφορώντα την ποσολογία σε αρχαία Ελληνικά, Ρωμαϊκά και Βυζαντινά ιατρικά κείμενα

Ηλίας Βαλιάκος, Μάριος Μαρσέλος και Διαμαντόπουλος Αθανάσιος

Η αναδίφηση ιατρικών κειμένων του παρελθόντος αποκαλύπτει ότι η προετοιμασία μιας θεραπευτικής συνταγής περιλάμβανε συνήθως τη χρήση ποικίλων δραστικών συστατικών. Υπάρχουν πολλές λεπτομερείς αναφορές για την αναλογία των συστατικών μιας συνταγής, αλλά και για τη δοσολογία στον ασθενή. Στο παρόν άρθρο, καταγράφηκε η διαχρονική χρήση μονάδων βάρους και όγκου σε θεραπευτικές συνταγές της αρχαιότητας, της ελληνιστικής εποχής, της ρωμαϊοκρατίας, του Βυζαντίου, αλλά και πρόσφατων ιατροσοφικών κειμένων. Οι μεταβολές που προέκυψαν με την πάροδο του χρόνου από το αναπτυσσόμενο εμπόριο στην ευρύτερη περιοχή της Μεσογείου, τόσο με την εισαγωγή νέων προϊόντων όσο και με την αλλαγή των μονάδων μέτρησης, δεν επηρέασαν τις βασικές αρχές των θεραπευτικών μεθόδων. Κύριο μέλημα των γιατρών ήταν να καταπολεμηθεί η νόσος χωρίς να επιβαρυνθεί ο ασθενής από τυχόν ανεπιθύμητες ενέργειες. Στο πλαίσιο αυτό, παρατηρούμε ακόμη και τροποποιήσεις της δοσολογίας, όταν πρόκειται για ειδικές ευπαθείς ομάδες του πληθυσμού, όπως τα παιδιά, οι ηλικιωμένοι και οι έγκυες γυναίκες. Τα κείμενα που επιλέξαμε καλύπτουν ένα χρονικό εύρος πολλών αιώνων, με αποτέλεσμα η μελέτη μας να είναι δειγματοληπτική, με ιστορικό και ιατροφαρμακολογικό χαρακτήρα, και όχι μία φιλολογική ανάλυση των πηγών.

Λέξεις Κλειδιά: Αρχαίες συνταγές, ποσολογία, μονάδες βάρους και όγκου, ιατροσόφια

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