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Zoran Vacić\*

**Guidelines for the preparation and dosage of medicines, instructions for their use, and methods of application according to the *Hilandar Medical Codex No. 517***

Смернице за израду и дозирање лекова, упутства за употребу и средства за апликацију лека у *Хиландарском медицинском кодексу бр. 517*

<sup>1</sup>Serbian Medical Society, The Academy of Medical Sciences, Belgrade, Serbia

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**\*Correspondence to:**

Zoran VACIĆ

Serbian Medical Society, Džordža Vašingtona 19, 11000 Belgrade, Serbia

E-mail: [jeremija1955@gmail.com](mailto:jeremija1955@gmail.com)

## Guidelines for the preparation and dosage of medicines, instructions for their use, and methods of application according to the *Hilandar Medical Codex No. 517*

Смернице за израду и дозирање лекова, упутства за употребу и средства за апликацију лека у *Хиландарском медицинском кодексу бр. 517*

### SUMMARY

The Hilandar Medical Codex (HMC) is a medieval manuscript produced in the translation and copying workshop of the Hilandar Monastery (*scriptorium*). It is regarded as the most significant document for studying the history of Serbian medicine. The manuscript dates back to the mid-16th century. The aim of this paper is to identify and explain the measures for quantity outlined in HMC for medicine preparation, dosage, physician instructions, contraindications, and methods of application. The analyzed material includes the deciphered text of HMC and its translation into contemporary Serbian. To identify the scientific names of individual remedies, references were made to Dioscorides' *De Materia Medica*, *Antidotarium* of Nicholas of Salerno, as well as general and specialized dictionaries.

The prescribed weight and volume measures for the quantities of ingredients used in medicine preparation include the "aksag" (about 4.55 grams or 1/6 ounces), ounce, liter, cup, drop, and "handful". In the medication dosage instructions, the measurements, with the exception of ounces, are not precise but largely descriptive.

The warnings and instructions provided to the doctor regarding the use of certain drugs included the recommended duration of use and contraindications. The means of drug application included a quill (for instillation into the eye or nose), a balloon made from a pig's bladder (*vesica urinaria*) with a goose quill *calamus* (for flushing the ureter and administering enemas), a wick (*funiculus incendiarius*) for applying medicine into body cavities (such as the vagina, rectum, or nose), and a sponge (*litus*) for applying liquid medicines to the skin's surface.

**Keywords:** Hilandar Medical Codex; measurement for quantity; instructions; contraindications; means of drug application

### САЖЕТАК

*Хиландарски медицински кодекс* (ХМК) је средњовековни рукопис настао у преводилачкој и преписивачкој радионици (скрипторијум) манастира Хиландар и најзначајнији документ за проучавање историје српске медицине. Рукопис је датиран у средину XVI века.

Циљ рада је да се полишу и разјасне мере за количину које су коришћене приликом израде лекова, дозирање лекова, упутства лекару, контраиндикације и средства за апликацију лека описаних у ХМК.

Анализирани су рапчитани текст ХМК и његов превод на савремени српски језик. За утврђивање научног имена појединих симплиција (једноставних лекова) консултовани су Диоскоридова *De Materia Medica* и *Antidotarium* Николе из Салерна, општи и специјализовани речници.

Прописане мере за количине састојака који се користе у припреми лека укључују „аксаг“ (износио је око 4,55 грама или 1/6 унце), унцу, литар, шољу, кап и „шаку“. У упутствима за дозирање лекова, мере, са изузетком унци, нису прецизне, већ углавном описне. Упозорења и упутства лекару у вези са употребом одређених лекова укључивала су препоручено трајање употребе и контраиндикације.

Средства за апликацију лека су перо (за укапавање у око или нос), балон од свињског мехура (*vesica urinaria*) са каламусом гушчијег пера (за испирање уретера и за клистирање), стенило (фитиљ, *funiculus incendiarius*) за апликацију лекова у телесне шупљине (вагина, ректум, нос), сунђер за апликацију течних лекова (*litus*) на површину коже.

**Кључне речи:** Хиландарски медицински кодекс; мере за количину; упутства; контраиндикације; средства за апликацију лека

### INTRODUCTION

The Hilandar Medical Codex (HMC) is a medieval manuscript produced in the translation and copying workshop of the Hilandar Monastery (*scriptorium*). It is considered the most

significant document for studying the history of Serbian medicine. In 1952, while studying the collection at the Hilandar library, Đorđe Sp. Radojičić observed that "there are significant texts for the history of our medicine." (...) Among them was a larger manuscript, consisting of 204 pages, titled *Manuscript on the Recognition of Diseases by Palpation of Veins* [БЕЋЕДА ОТ(Ъ) ПОЗНАНИЈА БОЛѢСТИ ПО ПИПАНИЈУ ЖИЛАЪЪ] [1]. Paleographic analysis has dated the manuscript to the mid-16th century [2, 3].

His discovery demonstrated: (1) that the scientific medical advancements of Latin Europe were accessible to Serbian doctors during the Middle Ages, (2) that these achievements could be learned in their own language—an exception in a time when Latin and Greek were the dominant languages of all sciences, including medicine, and (3) the lexical richness of the Serbian language in terms of terminology related to anatomy, physiology, pathophysiology, and pharmacotherapy.

The pharmacological records, which serve as the most important source for our research, were created by translating documents such as *Practica IO. Serapionis dicta breviarium*, *Liber Serapionis de Simplicis Medicina*, *Liber de Simplicis Medicina dictus Circa Instans Practica Platearis* by Matthaeus Platearius (†1161) ("Book of Simple Medicines"), [4, 5] *Antidotarium Parvum* by Nicolaus Salernitanus (1140–?), ("Book of Compound Medicines") [6] and Avicenna's *Canon of Medicine* ("Book of Poisons") [7].

The translation of these documents into our vernacular, "with certain admixtures of Old Slavic" [8], provides a detailed insight into the development of medical terminology in the Serbian language during the Middle Ages.

The aim of this paper is to identify and clarify the measures for quantity outlined in HMC for the preparation of compound medications, the dosage of both simple and compound

medications, instructions for physicians, contraindications for specific medications, and the methods for administering these medications.

## METHODS

The deciphered and transcribed text of the Hilandar Medical Codex No. 517, along with its translation into contemporary Serbian, has been analyzed [9]. During the text analysis, significant inconsistencies between the deciphered text and the contemporary Serbian translation were addressed by consulting the photographed pages of the Codex manuscript preserved in the Serbian Academy of Sciences and Arts (SASA)' archive [10]. In addition to pharmacological manuscripts ("Book of Simple Medicines," "Book of Compound Medicines," and "Book of Poisons"), other manuscripts from the Hilandar Medical Codex were analyzed. These documents detail specific simple drugs, their effects, the methods for preparing compound drugs, and other instructions relevant to the topic of this paper.

To identify the scientific names of individual remedies and their equivalents in contemporary Serbian, classical manuscripts such as Dioscorides' *De Materia Medica* (Greek: Πεδάνιος Διοσκορίδης; Latin: *Pedanius Dioscorides*) [11] and the *Antidotarium* of Nicolaus Salernitanus [12] were consulted, along with general and specialized dictionaries [13–17].

## RESULTS AND DISCUSSION

### The measures for the preparation of medications

Specific measures are prescribed for the quantities of ingredients and the preparation method of medicines. For example: "Take one aksag (about 4.55 grams or 1/6 ounces) of Stinking gum

(*Ferula assa-foetida* L.) and boil it in one liter of water with an equal amount of honey." [18], "Take one ounce of *Agaricus* L., two ounces of honey, one ounce of barley flour yeast, two ounces of olive oil, one ounce of salt, and two cups of water. Boil everything together and strain." [19], "Take and mix one aksag of powdered Snake Root (*Polygonum bistorta* L.), ginger (*Zingiber officinale* Roscoe), clove (*Eugenia caryophyllata* Thunb.), cinnamon (*Cinnamomum ceylanicum* Breyn), mastic (*Pistacia lentiscus* L.), and nutmeg (*Myristica fragrans* Houtt)" [20], etc. In some prescriptions, the quantities of ingredients are not precisely specified: "Take a small amount of saltpeter powder (KNO<sub>3</sub>), a large quantity of salt water, honey, and olive oil. Mix everything together, cook, and use it for an enema." [21], etc. In some prescriptions, however, the ingredients are specified in equal parts: "Take coral powder (Coelenterate system) and mix it with an equal amount of juice from Bermuda grass (*Cynodon dactylon* L.)" [22], or in relative proportions to the main ingredient: "Take one part of *Senna alexandrina* powder (*Cassia acutifolia* Del.), three parts of wine, and rose water" [23], etc.

The measures (weight and volume) mentioned in the prescriptions of HMC include "aksag", ounce, liter, cup, drop, and "handful".

Aksag (Greek: ἐξάγιον, Latin: *exagium*) is a unit of weight used for valuables. It was widely employed during the Middle Ages. The earliest mention of aksags in our region comes from Dubrovnik, where, in a 1305 treatment contract, four gold rings, each weighing four "aksadjes," were pledged to a wound-healer as collateral for the payment of treatment costs. In the fourth century, when the gold coin known as the solidus was introduced, its weight was standardized to the Roman sextula, or the Greek ἐκάγιον, as 72 parts of a liter. As a result, one aksag of a fine scale weighed 4.55 grams. Valuables such as gold, silver, and pearls were measured using a fine scale, as were medicinal substances that were considered precious due to their limited quantities in nature or the great distance from their country of origin [24].

The ounce (Latin: *uncia*), a unit of weight used since Roman times, was widely used in the Serbian lands during the Middle Ages. From the mid-16th century, the ounce became a standard measure for medicines in the region. The Roman ounce weighed 27.288 grams, the Byzantine ounce 27.30 grams, and the Dubrovnik fine ounce 27.328 grams in the 14th century, increasing to 27.427 grams in the 16th century. A fine ounce was equivalent to six aksags [25].

The liter (Greek: λίτρα, Latin: *libra*) is one of the oldest publicly recognized units of weight. In the *Karyes Typikon* of St. Sava (1199), it was stipulated that the Hilandar Monastery was obliged to provide "60 liters of oil" for Sava's cell [26]. The Roman and Byzantine liters both weighed 327.45 grams, while the fine Venetian liter (*libra*) weighed 302 grams, and the Serbian medieval liter weighed approximately 316 grams [27]. In the HMC drug prescriptions, the liter, as a unit of weight, is equivalent to 72 aksags and corresponds to the Roman or Byzantine liter.

The liter was also used as a unit of volume. The volume of one liter is determined by a container calibrated to hold one liter by weight, typically referring to water, although it can also be applied to other liquids.

The cup (Latin: *cuppa*) was primarily used as a measure for wine, but also for other substances. It is difficult to determine the exact volume of the cup, as various descriptions in the literature refer to cups of differing capacities.

The drop was also used as a unit to measure the quantity of a medicinal ingredient in a preparation. For example: "Mix one drop of balm [ЕДНУ КАПЮ БАЛ'ШАДЛА] with a small amount of warm water" [28].

The handful is mentioned as a unit of measure in the prescription for bitter electuary [ΛΕΤΥΑΡΙΩ ΓΟΡΚΩ]. "Take Dutchman's pipe (*Aristolochia* (L.) *Tourn.*) and the great yellow gentian (*Gentiana lutea* L.), each in one *handful*." [ωΤЪ СКАКОГА .А. РҮҢИЦҮ]. The "handful" refers to a

bundle that is "just the right size to be easily held by hand" [29]. A common Serbian term for this measure is *rukovet*.

In some prescriptions, instructions specify using ingredients in quantities sufficient for preparing the medicine, such as "add as much honey as needed" [и меда колико потребује] [30].

### Medication dosing

In the "Book of Simple Medicines," the dosage measures for medicines are provided. These measures, with the exception of ounces, are not precise, as is often the case with prescriptions, but are mostly descriptive. For example, the medicine was given in amounts corresponding to the size of a hen's egg [јанце] or a goose egg [гус'ѣе јанце]. Other measures used for the medicine included a spoon, a teaspoon, a cup, or a small cup. Solid forms of medicines are defined by the size of various fruits, such as a hazelnut, a walnut, a kidney bean, or a pinch of pepper. The size of a suppository was intended to correspond to the length of a finger [дуго и дебел окакo прѣстѣ], a middle finger [дуго и дебел окакo срѣднѣи прѣстѣ], or the shape and size of a date [какo фѣнѣкѣ].

Doses of medications were adjusted based on age, with different amounts prescribed for children and adults. For example, when using aloe (*Aloë sp.*) as an anthelmintic, the adult dose is half an aksag of aloe powder [ако бѣде великѣ љовѣкѣ дан љѣ полѣ азакаы], while the children's dose is an amount that fits in half a hazelnut shell [ако бѣде мало дѣтѣ дан љѣ алоѣ колико полѣ лѣшнѣнка] [31].

Medicines were administered according to specific instructions: "take the medicine for three days, every morning," "take it every morning and evening," "drink warm every morning," "take the pills five times a day," etc. In some cases, the duration of treatment was based on the

patient's improvement: "give him this until you see that he is better," or "repeat this several times until his condition improves." Some medicines intended for the treatment of chronic conditions or bodily dysfunctions (such as stomach weakness, meteorism, flatulence, etc.) could be taken by the patient "whenever he/she wished" and "as much as he/she desired." Pills and powders for oral administration were taken with water, wine, or the juice of a specific plant, with the wine and juice serving a therapeutic role.

### Warnings and instructions

The "Book of Simple Medicines" also includes warnings for the physician regarding the use of certain medicines, such as the recommended duration of use, contraindications, and the appropriate time of year for administering the medicine.

The application time is specified when using ointments for the treatment of ringworm, old wounds, and for hair removal in cases of hirsutism and hypertrichosis. The ointment for ringworm and old wounds is made from cashew (*Anacardium occidentale* L.) and orpiment ( $\text{As}_2\text{S}_3$ ), while the hair removal ointment is composed of orpiment and quicklime [варе несквашена] [32]. In the contemporary Serbian translation of the HMC, it is stated that the ingredients of the ringworm ointment are cashew and asphaltite. However, the correct component of this ointment is not asphaltite, but orpiment, as indicated in the deciphered text of the Codex [и ст҃҃ци толнкожде д҃҃р҃нимен'та] [33]. Both prescriptions include instructions to apply the ointment for no longer than one hour. After this time, the treated area should be promptly washed with warm water. If the ointment is left on longer, "his skin will peel off." [да дрѣжн он҃҃н масть лнхо .а. часъ ер ако внекѣ ұзѣдрѣжн хокѣ м҃҃ се кожа ог҃҃лн҃҃тн] [32, 33]. Orpiment is the active ingredient in these ointments and can cause the aforementioned complication if left on the skin for too long.



In the section of the text referring to cashew, there is a warning that "anyone who eats cashew or drinks it without other medicines may develop morphea." [кто ѿст анакарди или пие безъ другого бѣлѣа може му ѿтннѣт мор'фна] [33].

The author of the "Book of Simple Medicines" cautions doctors never to use white coral as a medicine unless explicitly instructed to "take white coral!" [нѣ никѣда немоу поставити бѣлѣ коралѣн ѿ бѣлѣа докле не рече възми бѣлѣ коралѣн]. In recommendations regarding the use of corals in medicine, they almost always refer specifically to red corals [къдѣ говорѣ възми коралѣн тои зна да говорѣ възми црѣвенѣ коралѣнѣ] [22].

Rockcap fern (*Polypodium vulgare* L.) is not used in the preparation of medicines that do not contain anise (*Pimpinella anisum* L.) or fennel (*Foeniculum vulgare* Mill.) [34]. Additionally, kerosene should not be administered orally in summer, but only in winter [35].

A medicine made from saffron crocus powder (*Crocus sativus* L.) and wine, used for a weak stomach or palpitations, should not be given to individuals with an excess of black bile, as it may irritate the stomach and induce vomiting [36]. Coral pills with barley water should not be used by individuals with bloody diarrhea [ако бѣде нѣмалѣ здола течеѣа ѿтъ крѣвѣн]. Instead, the pills should be prepared with buckhorn (*Plantago lanceolata* L.) juice [22]. An enema containing saffron crocus (*Crocus sativus* L.) should not be given to individuals with general weakness or dizziness, particularly those suffering from rheumatism or gout. In such cases, instead of saffron crocus, a bigroot geranium (*Geranium macrorrhizum* L.) should be used in the enema [37].

According to the HMC, Dioscorides writes that medicines containing honey are contraindicated for those with acute fever [кои нѣма острѣ ѿгнѣцѣ], as honey is considered hot and unsuitable for treating this condition [38]. For the same reasons, honey should not be given to individuals who are excessively thirsty [39].

Pregnant women should not be allowed to eat celery [која жена нѣс(тъ) празна не трѣбѹе дати и селни(тъ) да грнзѣ] [40].

The medicine applied to the ear should be warm, while the medicine applied to the eye should be cold [и да знаш(тъ) ерѣ svaky сътвар(тъ) трѣбѹе топло поставити у ухо а хладно у око] [41]. The enema fluid should be warmed to lukewarm temperature before use [и съгрѣти да бѹдетъ млатно] [42].

### Means of drug application

For the application of non-oral drugs, the following methods were used:

- (1) To apply drops to the eye or nose, a quill was dipped into the prepared medicine (solution) [и ѿмакѹи перо] and then the liquid was dripped from the quill into the eye [стави у оѣи] or nose [стави у носѣ] [43, 44].
- (2) A pig's bladder [мѣхѹрь свински, *vesica urinaria*] was used for flushing the ureter [чини мѹ ганстирѣ водопустомѣ], and likely also for enemas. A liquid for rinsing or an enema was poured into the bladder, and then a hollow goose quill was inserted into it [кран ѿтъ гѹшчѣга пера, *calamus*]. The quill was securely tied to prevent any leakage at the connection with the bladder. Under pressure, the rinsing solution (or enema) was then introduced into the ureter or rectum [35].
- (3) A wick [сѣѣниѹ] was used to apply medication into body cavities (such as the vagina, rectum, or nose) or wounds. It appears that "wick" was a general term for the tool used to administer medicine. Relja Katić referred to it as *funiculus incendiarius* [10, 45]. A wick was used for the application of ointments, salves, and powders "Take one aksag of musk

(*Muscus*) and three aksags of Frisco clover (*Trifolium fibrinum*), mix them together, and soak a paper towel with the mixture. Place the towel in the woman's vagina." [үзми москось .а. ажаж н трнфериана .г. ажак(а) і смѣшан заєдно н смочи стѣннао бѹбакєрнѡ н постави женѣ въ плодѣхъ] [46]. Paper and cloth were used to make a wick. "Create a dressing from cloth, coat it with honey, sprinkle birthwort powder on top, and apply it to the raw wound." [шчинны стѣннао ѡт(ъ) крѣпѣ, н помажи га медом(ъ) н поспани згора прахѡм(ъ) ѡт(ъ) арцѡлогіе н постави ү живннү] [47]. Unfortunately, the other dictionaries we consulted do not provide a definition for this term. However, based on how the use of a wick is described in the deciphered text of the HMC, we believe that, in addition to Katić's interpretation, it should be noted that a wick could also take the form of a funnel (such as paper fiche) or another shape.

- (4) A sponge (*litus*) was used to apply liquid medicines to the skin's surface [ѡт(ъ) бяуванїа] скваси гѹбѹ морскѹ въ ѡцѣ н постави на стомах(ъ) [48].

## CONCLUSION

The Hilandar Medical Codex is a manuscript created by translating and compiling key texts from European and Arabic medieval scientific medicine. It was written as a practical manual for physicians.

The analysis of the HMC text identified the measurements of weight and volume mentioned in the prescriptions for preparing compound medicines (aksag, ounce, liter, cup, drop, and handful), as well as the measurements for dosing both simple and compound medicines. It also outlined the methods of administering the medicines, provided instructions for the doctor

regarding contraindications, and described the means of applying drugs that are not taken orally.

We found that the measures for quantity and instructions for preparing medicines were clearly defined, with careful attention given to the dosage, duration of therapy, and age-appropriate dosing. Additionally, the prescriptions included explicit guidelines on contraindications for certain drugs. This reflects the advanced understanding that physicians of the time had regarding the benefits and potential risks of specific remedies.

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34. „O slatkoj paprati (Polypodium vulgare) [ωт(ъ) полѣподѣм(ъ) сѣрѣч(ъ) ωт(ъ) папратно мѣлѣ коренѣ нѣже растѣ по камени]“, Hilandarski medicinski kodeks № 517, 147, 346.
35. „O petroleju ili nafti (Petroleum) [ωт(ъ) петролеум(ъ) сѣрѣч(ъ) нафта]“, Hilandarski medicinski kodeks № 517, 147, 346.

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37. „Ovde počinja o mlečici (*Euphorbia officinarum*) [зде почнѣ ωт(ъ) еѳωρβιω]“, Hilendarski medicinski kodeks № 517, 145, 344.
38. „Ovde počinja o tome kako se priprema đulap ili sirup [ωвде почнѣ како се тинн(н) гюлап(ъ) і шнрωп(ъ)]“, Hilendarski medicinski kodeks № 517, 168, 369.
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