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# Medical plants used for treatment of gynecological disorders in Ottomans in the 15th century

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#### **ABSTRACT**

**Aim:** The aim of the present study is to give a brief evaluation about plants used for the treatment of obstetric and gynecological conditions by using Cerrâhiyyetü'l-Hâniyye book which has been written by Serefeddin Sabuncuoğlu who was a famous surgeon in Anatolia in the 15th century.

Materials and Methods: Based on the Cerrâhiyyetü'l-Hâniyye book, we selected plants that are used for women health, and systematically arranged plants according to diseases. Plant species that detected in this book were compared with the plants of three works (Soranus' On Gynecology, Paulus Aeginata's The Seven Books, and Zahavi's At Tasrif)

**Results:** Cerrâhiyyetü'l-Hâniyye book contains 24 different medical plants for women health. Six plants found in Cerrâhiyyetü'l-Hâniyye were different from the other books compared. Sabuncuoğlu wrote about same 18 plants, which are typed by other authors for women health.

**Conclusion:** This study shade light on the Ottoman herbal remedy. Regard to plant treatment, difference between Cerrâhiyyetü'l-Hâniyye book and other books were submitted by the present study.

#### **ARTICLE HISTORY**

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Gynecology; obstetrics; medicinal plants; history of medicine

## Introduction

According to the literature on the history of medicine, humankind used plants for treatment of diseases. Ancient and folk medicine was incorporated plants, mineral, or animal products particularly in Anatolia located between Asia and Europe [1–5]. The way of using herbal medicine in obstetrics and gynecological conditions were similar to the treatment of other diseases [6–10]. Medicine men (monks, witch doctors, and shaman) maintained the health of people by herbal products and surgical procedures in prehistoric culture occurred before the invention of writing [5,10,11]. Then, special prescriptions for women's health are available in written medical literature in Anatolia, such as Ancient Greece and Roman medicine in

the fifth century BC and until the 11th century AC [6,11–14].

Islamic medicine began to improve in 12th century in Anatolia. Islamic medicine is not at limited to religious medicine, but also includes all the medicine of the rich and varied cultures of the Islamic community. The authors wrote many scientific books in this period. They have been dominant since about the 13th century and strongly influenced the Ottoman physician of Turkey [2,6,11,15,16]. Serefeddin Sabuncuoğlu is one of the famous surgeons in Ottoman State. Şerefeddin Sabuncuoğlu (Amasya, 1385–1468) translated the 30th chapter of Zahravi's At-Tasrif dedicated to surgery into Turkish and wrote his book named Cerrâhiyyetü'l-Hâniyye. He wrote his experiences in his book by drawing

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miniatures (pictures) concerning the first medical illustrations in Islamic medicine in the 15th century (Fig. 1). "Cerrâhiyyetü'l-Hâniyye" was divided into chapters in a way similar to that was done in At-Tasrif [11,14]. Three copies of Cerrâhiyyetü'l-Hâniyye book were present today in Istanbul (two copies) and Paris (one copy). Cerrâhiyyetü'l-Hâniyye book consists of three chapters of surgical procedures and incisions, interventions, and herbal remedy. Sabuncuoğlu also wrote three books namely Mürecebname, Müfid (Nazmü't-Teshil), and Akrabaddin for physicians [11,12,17]. In this study, books of Sabuncuoğlu which were written in classical period were investigated. The medical plants used for obstetrics and gynecological conditions were compared to find similarities and differences between the Cerrâhiyyetü'l-Hâniyye book and scientific literature of ancient medicine.

#### **Materials and Methods**

Plants that were used for women health in Şereffedin Sabuncuoğlu's Cerrâhiyyetü'l-Hâniyye book were systematically arranged according to diseases. Plant species that detected in this book compared with the three famous physicians books in the history of medicine such as Soranus, Paulus Aegineta, and Zahravi [10,11,14,16].

Four physicians, who practiced in the classical medicine era, were selected as resources according to chronological order. In this study, Soranus's Gynekiea, which was translated by Temkin into English and was published in 1991 under the name



**Figure 1.** Miniature shows fumigations for gynecological conditions. Fumigation instrument had been used instead for medical plants to open delivery of the placenta. Şerefeddin Sabuncuoğlu drew a miniature painting of the procedure.

of "On Gynecology"; Zahravi's At Tasrif 's English version translated by Spink and Lewis; two volumes of Şereffedin Sabuncuoğlu's Cerrâhiyyetü'l-Hâniyye, prepared by İlter Uzel in a comparative way; and Paulus Aegineta's book, translated into English by Adams were used [10,11,14,16]. In addition, Mücerebbname and Acrabaddin written by Sabuncuoğlu referenced as additional resources [12,17]. Plants prescribed in the books that are not specific to women's diseases were not included in our study.

#### Results

Sabuncuoğlu's Cerrâhiyyetü'l-Hâniyye has been written in two volumes. The first volume of the book consists of 57 sections, drawings of operations scene and surgical procedures (54), instruments (7), and four incisions, one of them was about cauterization of the uterus. Eight of 98 issues in the second volume of this book has been written about women health. Sabuncuoğlu recommended surgical, dietetic, and pharmacologic treatment for obstetrics and gynecological conditions [11]. Commonly used Sabuncuoğlu's herbal formulas include decoctions, powders, pills, washes, fumigants, suppositories, and enemas. Decoctions and fumigation were dominant forms of pharmacologic therapy treatment of Sabuncuoğlu's works [11,12].

Descriptions of diseases, information on their treatment, and the names of plants are present in all the works investigated. Sabuncuoğlu used the terms of Greek physicians and discussed the subjects under the same titles. The plants present in his prescriptions were either a single or a combination of plants [10,11,14,16]. Cerrâhiyyetü'l-Hâniyye is a translation of Zahravî's *At-Tasrîf* that is devoted to surgery [11,14].

Sabuncuoğlu's books for providing information for physicians contain nine chapters focused specifically on gynecology and obstetrics [11]. Şerefeddin Sabuncuoğlu described nine obstetrics and gynecological conditions in the Cerrâhiyyetü'l-Hâniyye. Title of these conditions are hermaphroditism (70th Section), clitoridectomy (71st Section), the treatment of the children with vaginal occlusion or atresia (72nd Section), the treatment of the vaginal and vulval lesions (genital warts and pustules) (73rd Section), extirpation of fibrous tissue in vagina (74th Section), about abnormal delivery (75th Section), about the removal of the dead fetus (76th Section), about the removal of the fetus that died in the maternal uterus (77th Section), and

about the removal of the placenta (78th Section) (11) (Table 1).

Regard to gynecological conditions, Soranus, Paulus Aeginata, Zahravi, and Sabuncuoğlu used 19, 12, 26, and 24 of 51 different plants, respectively (Tables 1–3).

Zahravi and Sabuncuoğlu similarly used acacia and Dragon's blood for vaginal occlusion or atresia. Paulus Aeginata, Zahravi, and Sabuncuoğlu similarly used pomegranate, also Zahravi, Serefeddin Sabuncuoğlu similarly used oak galls, sumac, and barley for genital warts and pustules. Paulus Aeginata, Zahravi, and Şerefeddin Sabuncuoğlu similarly used mallow and rose for the extirpation of fibrous tissue in the vagina. Paulus Aeginata and Sabuncuoğlu used birthwort for the extirpation of fibrous tissue in the vagina. Zahravi and Sabuncuoğlu similarly used liquorices extirpation of fibrous tissue in vagina. Paulus Aeginata and Zahravi similarly used fenugreek used for abnormal delivery. Zahravi and Şerefeddin Sabuncuoğlu similarly used sesame, marsh mallow, and myrrh for abnormal

delivery. Paulus Aeginata and Sabuncuoğlu similarly used figs for removal of the placenta. Soranus, Zahravi, and Sabuncuoğlu similarly used cassia for removal of placenta. Soranus and Zahravi similarly used artemisia for removal of the placenta. Zahravi and Şerefeddin Sabuncuoğlu similarly used cassia, chamomile, rue, and pennyroyal for removal of the placenta (Table 2).

In Cerrâhiyyetü'l-Hâniyye, 24 different plants are present for gynecological conditions. On the other hand, Sabuncuoglu used same plants for different gynecological conditions in Cerrâhiyyetü'l-Hâniyye.

Paulus Aeginata and Sabuncuoğlu used same seven plants (birthwort, figs, iris, mallow, pomegranate, and rose oil); Soranus and Sabuncuoğlu used same three plants (myrrh, rose, and cassia); Zahravi and Sabuncuoğlu used same 14 plants (acacia, dragon's blood, barley flour, cassia, liquorices root, mallow, marshmallow, oak galls, pennyroyal, pomegranate rind, rose oil, sesame, sumac, chamomile, and rue) for same or different gynecological conditions (Table 2).

**Table 1.** Titles of gynecological conditions and preferred plants by authors.

	Soranus*	Paulus Aeginata**	Zahravi***	Şerefeddin Sabuncuoğlu
Hermaphroditism (70th Section)		None	None	None
Clitoridectomy (71st Section)	-	None	None	None
The treatment of the children		Fenugreek Rosin	Acacia Dragon's blood	Acacia Dragon's blood
with vaginal occlusion or atresia (72nd Section)		Turpentine pp 640	Dry linen (linseed) Olibanum	Date Olive oil
The treatment of the vaginal		Rose oil Illyrian	Acacia Dragon's blood	Oak galls Barley
and vulval lesions (genital warts		iris Pomegranate	Olibanum Sumac	flour Bramble Sumac
and pustules) (73rd Section)		Turpentine	Pomegranate rind Thyme Oak galls Barley flour Plantain Eglantine	Pomegranate rind
Extirpation of fibrous tissue in		Birthwort Iris Mallow	Green oil Liquorices	Liquorices Mallow Rose
vagina (74th Section)		Rose oil	Mallow Rose oil	oil Olive oil Birthwort
About abnormal delivery(75th	Anise Cedar resin Dittany	Fenugreek Mallow	Fenugreek Gum Marsh	Ferula Sesame
Section)	Olive oil Southernwood	Linseed Camphor	Mallow Myrrh Ptarmica	Pomegranate
	Sweetbay Wild cucumber		(green oil) Sesame	Marshmallow Myrrh St John's wort
About the removal of the dead			74th Fenugreek	74th
fetus (76th Section)			Marshmallow Linseed	
About the removal of the Fetus that died in the maternal uterus (77th Section)			None	None
About the removal of the	Black cumin Cassia	Cardamum Figs	Anise Artemisia	Cassia Chamomile
placenta (78th Section)	Celery Dittany Galbanum		Cassia Chamomile	Figs Pennyroyal Rue
	Illyrian iris Lilies oil Myrrh		Marshmallow	Speedwell St John's
	Rose Salvia Soap wort Spikenard Wormwood (Artemisia)		Pennyroyal Rue Sesame	wort
Common title	19	12	26	24

<sup>\*</sup>Sabuncuoğlu and Soranus wrote same two titles for gynecological situations.

www.jocmr.com 173

<sup>\*\*</sup>Sabuncuoğlu and Paulus Aeginata wrote same five titles.

<sup>\*\*\*</sup>Sabuncuoğlu and Zahravi wrote same eight titles.

**Table 2.** Titles of gynecological conditions and the number of plants used by the authors.

S	oranus	Paulus Aeginata	Zahravi	Sabuncuoğlu	
The treatment of the children		3	4	4	*2
with vaginal occlusion or atresia					
(72nd Section),					
*Zahravi and Sabuncuoğlu similarly us	ed Acacia,	Dragon's blood.			
The treatment of the vaginal		4	10	5	*1 **3
and vulval lesions (genital warts					
and pustules) (73rd Section)					
*Paulus Aeginata, Zahravi, and Sabund	uoğlu simi	larly used Pomegranate.			
**Zahravi, Şerefeddin Sabuncuoğlu sir	-	-	arlev.		
Extirpation of fibrous tissue in	,	4	4	5	*2 **1 ***1
vagina (74th Section)					
*Paulus Aeginata, Zahravi, and Şerefeo	din Sabun	cuoğlu: Mallow and Rose.			
**Paulus Aeginata, Sabuncuoğlu simil					
***Zahravi, Sabuncuoğlu similarly use	•				
About abnormal delivery (75th	7	4	6	6	*1 **3
Section)					
*Paulus Aeginata and Zahravi similarly	used Fenu	greek.			
**Zahravi and Şerefeddin Sabuncuoğlı		•	and Sesame		
About the removal of the dead	-	-	3	_	_
fetus (76th Section)			3		
About the removal of the	13	2	8	6	*1 **1 ***1 **** <i>1</i>
placenta (78th Section)	13	<b>~</b>	U	U	1 1 1 4

<sup>\*</sup>Paulus Aeginata and Sabuncuoğlu similarly used figs.

 Table 3. Plants used for gynecological conditions in this study.

Common name	Local name	Name of the plant	Genus (Family)	
Olive (oil)	Zeytin ağacı Akdeniz Zeytini Şifalı Zeytin	Olea europaea L.	Olea (Oleaceae)	
Rose (oil)	Gül (Isparta gülü, yağ gülü, and fındık gülü)	Rosa ×damascena Herrm.	Rosa (Rosaceae)	
Rue	Sedefotu	Ruta chalepensis L.	Ruta (Rutaceae)	
Barley	Arpa	Hordeum vulgare L.	Hordeum (Poaceae)	
Cucumber	Salatalık	Cucumis sativus	Cucumis (Cucurbitaceae)	
Date Palm Tree	Hurma, Şeker Ağacı	Phoenix dactylifera	Phoenix (Arecaceae)	
Fenugreek	Çemenotu Boyotu Buyotu Hulebe	Trigonella foenum-graecum	Trigonella (Leguminosae)	
Camphor	Kafurun, kafur	Cinnamomum camphora (L.) J. Presl	Cinnamomum (Lauraceae)	
Fig	İncir	Ficus carica L.	Ficus (Moraceae)	
Linseed (linen) Linseed, Flax seed	Keten tohumu, zeyerek, bızıktan, zeylek, zerek	Linum usitatissimum L.	Linum (Linaceae)	
Myrrh	Sarı Sakız, Mür, Mirra Mirrisafi Mürrüsafi Hakiki Mirra	Commiphora myrrha (Nees) Engl.	Commiphora (Burseraceae)	
Pomegranate Rind	(Nar Kabuğu), Cülnar-I Mısri	Punica granatum L.	Punica (Lythraceae)	
Turpentin	Çam Terebentin Kızılçam	Pinus brutia Ten.	Pinus (Pinaceae)	
İris	Nevruz Çiçeği	Iris persica L.	Iris (Iridaceae)	
Anise	Anason (Büyük) Tekeotu Akanason	Pimpinella anisum L.	Pimpinella (Apiaceae)	
Cassia	Çin Tarçını	Cinnamomum cassia (L.) J. Presl	Cinnamomum (Lauraceae)	
Cumin	Kimyon Şifalı Kimyon	Carum carvi L.	Carum (Apiaceae)	
Mugwort, Wormwood, Artemis	Pelin Acı Pelin Pelinotu Mideotu Ak Pelinotu	Artemisia absinthium L.	Artemisia (Co mpositae)	
Pennyroyal	Yaban Fesleğeni Yarpuz Fesleğen Reyhan Fütenec	Mentha pulegium L.	Mentha (Lamiaceae)	

(Continued)

<sup>\*\*</sup>Soranus, Zahravi, and Sabuncuoğlu similarly used cassia.

<sup>\*\*\*</sup>Soranus and Zahravi similarly used Artemisia.

<sup>\*\*\*\*</sup>Zahravi, Şerefeddin Sabuncuoğlu similarly used cassia, chamomile, pennyroyal, and rue.

Table 3. Plants used for gynecological conditions in this study. (Continued)

Common name	Local name	Name of the plant	Genus (Family)
Rosin weed	Reçine bitkisi	Silphium integrifolium Michx.	Silphium (Compositae)
Birthwort	Lohusa Otu Ziravend-İ Tavilin	Aristolochia clematitis L.	Aristolochia
			(Aristolochiaceae)
Mallow	Ebegümeci	Malva sylvestris L.	Malva (Malvaceae)
Liquorice (licorice) Root	Meyan Kökü	Glycyrrhiza glabra L.	Glycyrrhiza
			(Leguminosae)
Acacia	Akasya	Acacia arabica (Lam.) Willd.	Acacia (Leguminosae)
Dragon's Blood	Kardeş Kanı	Daemonorops draco (Willd.) Blume	Daemonorops
			(Arecaceae)
Olibanum (frankincense)	Günlük, buhur, tütsü	Boswellia ameero Balf. f.	Boswellia (Burseraceae)
Sumac	Sumak Sumak (Zehirli)	Toxicodendron pubescens Mill.	Toxicodendron
	Huzurotu Siyatikotu		(Anacardiaceae)
Thyme	Kekik	Thymus vulgaris L.	Thymus (Lamiaceae)
Oak Galls	Mazı Meşesi	Quercus infectoria G. Olivier	Quercus (Fagaceae)
St. John's Wort	Sarı Kantaron Kılıçotu	Hypericum perforatum L.	Hypericum
	Binbirdelilikotu Mayasıl Otu		(Hypericaceae)
	Koyunkıran Yara Otu		
Plantain	Sinir otu, Damar Otu	Plantago Major L.	Plantago
			(Plantaginaceae)
Eglantine, Sweet Bier	Yaban Gülü (Kokulu)	Rosa rubiginosa L.	Rosa (Rosaceae)
Bramble (Blackberry)	Böğürtlen	Rubus ulmifolius Schott*	Rubus (Rosecease)
Cedar Resin	Sedir Reçinesi	Cedrus libani A. Rich	Cedrus (Pinaceae)
Sweet Bay, Trunk Bark, Magnolia Bark	Manolya	Magnolia virginiana L.	Magnolia
Extract			(Magnoliaceae)
Dittany Winter Savory, Herb	Geyik Otu	Satureja Montana L.	Satureja (Lamiaceae)
Southernwood	Miskotu	Artemisia abrotanum L.	Artemisia (Compositae)
Ferula	Çakşır Cavşir (Oğlan Aşı)	Ferula elaeochytris corovin	Ferula (Apiaceae)
Marshmallow	Tıbbi Hatmi Hatmi İbiskökü Şifalikök Tıbbikök Devegülü	Althaea officinalis L.	Althaea (Malvaceae)
Gum	Çadır Uşağı, Uşşak, Keleh	Dorema ammoniacum D. Don	Dorema (Apiaceae)
	El-Kanaveşak		. , ,
Mastic (Gum)	Sakız Ağacı	Pistacia lentiscus	Pistacia
	-		(Anacardiaceae)
Ptarmica sneezewort, Yarrow (green oil)	Civanperçemi	Achillea ptarmica L.	Achillea (Compositae)
Sesame	Susam Sırık Sırlan Şırlagan	Sesamum İndicum L.	Sesamum (Pedaliaceae)
	Süsen		·
Celery	Kereviz	Apium graveolens L.	Apium (Apiaceae)
Galbanum	Kasnı otu Kasnısı	Ferula szowitziana DC.	Ferula (Apiaceae)
Lili	Ak Zambak (Misk zambağı)	Lilium candidum	Lilium (Liliaceae)
Salvia Sage Clary Sage Trilobed Sage	Yünlü Adaçayı	Salvia aethiopis L.	Salvia (Labiatae)
Soap Wort	Sabunotu Çöğen Otu	Saponaria Officinalis	Saponaria
•	Çövenotu, Çoğanotu	, 33	(Caryophyllaceae)
	Üşnan,Tahdik Otu, Köpürgen,		
	Kargasabunu		
Spikenard	Hint Sümbülü	Nardostachys Jatamansi (D. Don)	Nardostachys
•		DC	(Caprifoliaceae)
Chamomile	Papatya	Chamaemelum nobile (L.) All.	Chamaemelum
	• •	` '	(Compositae)
Speedwell	Şıh (Yavşan)	Artemisia spicigera K. Koch	Artemisia (Compasitae)
Cardamom	Kakule Malabar Kahvesi	Elettaria Cardamomum (L.) Maton	Elettaria
			(Zingiberaceae)

Sabuncuoğlu wrote same 19 plants which typed by other authors for gynecological conditions in Cerrâhiyyetü'l-Hâniyye book. These plants are acacia, barley flour, birthwort, cassia, chamomile, dragon's blood, figs, liquorices, mallow, marshmallow, myrrh, olive oil, oak galls, pennyroyal, pomegranate rind, rose oil, rue, sesame, and sumac (Table 2). Sabuncuoğlu used different five plants (St

John's wort, date, bramble, ferula, and speedwell) similarly for medicinal purpose in Cerrâhiyyetü'l-Hâniyye (Table 2).

## **Discussion**

In the present study, plants used to treat the gynecological conditions in Sabuncuoğlu's

www.jocmr.com 175

Cerrâhiyyetü'l-Hâniyye book were systematically determined. Sabuncuoğlu's book had an effect on physicians in Islamic medicine literature [11,18–20].

The work of Sabuncuoğlu contains detailed information about the treatment of women diseases and obstetrics. Sabuncuoğlu presented the medical applications without focusing on the underlying mechanism of disease and the results of treatments [3,5,11,13,15].

The treatment modalities in Cerrâhivyetü'l-Hâniyye consists of three groups: dietetic, surgery, and pharmacology. Three groups of treatment, which also used for difficult delivery, were used to cure diseases of women. Sabuncuoğlu written difficult delivery and placenta retention sections under the same title like other authors such as Soranus. Paulus Aeginata, and Zahravi [10,11,14,16]. Sabuncuoğlu repeats the procedures of these physicians about the diagnosis and treatment of gynecological conditions [10,11,14,16]. However, there are differences between other books and Cerrâhiyyetü'l-Hâniyye in term of the names and numbers of plants used for obstetrics and gynecological conditions. Submitted difference in the present study was about prescriptions written by Sabuncuoğlu and the lack of occurrence of same plant names is remarkable for the history of medicine [10,11,14,16]. Half of the plants used for obstetrics and gynecological conditions in the Cerrâhiyyetü'l-Hâniyye were different from the other books compared. Physicians in the present study lived in different regions and different periods.

In accordance with the period which the physicians lived, it is obvious in the works that there exists a lack of knowledge among the physicians with regard to anatomy, microbiology, and pathology and it is obvious that the physicians were not able to evaluate the etiopathogenesis of the diseases [10,11,14,16]. Therefore, selection criterions of plants for a disease were different compared to nowadays. Gynecology and obstetrics conditions diagnosed according to symptoms and observations by the physicians without determining the relationship of reason-result [4,9]. The chosen treatment performed according to the experience of the physician.

In addition, the relationship between the "active ingredient" in the plant and the expected effect had not been known by physician of that period. Therefore, the plants were either used alone or in mixtures, without knowing the active ingredients. The treatments were not changed according to the response to the treatment [10,11,14,16]. Sabuncuoğlu recommended the necessity of

continuing to the treatment in the case of even if the disease was not cured. Nevertheless, Sabuncuoğlu used a considerable number of different plants for gynecological conditions. For that reason, it is difficult to reach a conclusion about the efficacy of the plants on the treatment of the diseases [10,11,14,16]. In the Sabuncuoğlu's Mücerebname work, it mentioned that he performed medical drug experiments [12]. Nevertheless, it was different from our current understanding of drug tests.

The historical period and its environment affected the attainability of the plant used to treat the illness. On the other hand, plants used by the physicians either grow in that area or it depends on the conduction of trade of the plants [4,13,15,21]. Anatolia is one of the richest regions on this subject.

Medical applications and recipes in the work of Sabuncuoğlu are same with the other works examined, but some of the plants used to prepare drugs are different. The difference that we detected could depend on the effect of the period that physician lived in or the environment that physician worked. One of the writers examined in the present study Soranus lived in the first century in Bergama and Alexandria city. Paulus Aeginata and Zahravi were the most important physicians in the sixth and nineth century, respectively. Paulus Aeginata lived in Aeginata, a city in Greece; Zahravi was a surgeon in Cordova, Spain; and Sabuncuoğlu had spent most of his life practicing medicine in Amasya and Bolu cities in Anatolia [10,11,14,16]. Therefore, physicians could have used the plants likening the appearance, shape, smell, or a property of the plant [4].

According to the modern modality of medicine, a relationship is established between the active ingredient used in drugs for the treatment of disease and the effect which the drug has [22,23]. Some of the plants used in the folk and traditional medicine continued to be used in Anatolia [5,20,24]. Experimental studies to uncover the benefits of this kind of plants are available [23,25,26].

## Conclusion

Plants used as treatments for conditions related to gynecology and obstetrics in Cerrâhiyyetü'l-Hâniyye book have some differences from the other works compared. One of classic medicine representative Sabuncuoğlu who lived in 15th century in Anatolia did not copy the use of plant methods of preceding physicians but instead used his knowledge and experiences according to his conditions. Differences and similarities in the use of the plants we determined

in our study may contribute to the existing knowledge of medical history. In addition, botanists, geographers, and archeologists could examine these findings from their aspects and comparison of more works in a similar way will strengthen the result of our study.

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