

ETHNOBOTANY AND ETHNOPHARMACOLOGY OF *ARUM MACULATUM* L. (ARACEAE) IN BULGARIA WITH AN EMPHASIS ON ITS EFFECT AGAINST HAEMORRHOIDS

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ABSTRACT

The objective of the present study was the contemporary folk medicine application of snakehead, *Arum maculatum* L. (Araceae) with an emphasis on its effect against haemorrhoids. Therefore we set ourselves the following tasks: 1) to collect the contemporary traditional knowledge about the therapeutic effects of snakehead; 2) to collect anecdotal reports from persons who are known to have used the snakehead for treating haemorrhoids; 3) to analyze the data obtained about the effectiveness of this herb against haemorrhoids and other medicinal conditions in order to determine the mechanism of its activity; 4) to investigate how popular snakehead is nowadays in Bulgaria as a medicinal plant.

All randomly selected informants basically recognized the plant but only 16% knew about its medicinal properties. With regard to the medicinal application, its properties as a cure for haemorrhoids was most frequently cited. Less frequently mentioned was the use of *A. maculatum* for chronic traumatic pain, purulent infections, and for "melting of adipose formations". Informants who had used snakeshead for haemorrhoids categorically reported improvement of the condition.

The analysis of the therapeutic effect of *A. maculatum* tuber both directly in the treatment of various haemorrhoids and indirectly in cases of chronic traumatic pain and purulent infections allows us to hypothesise that the plant substance: 1) contracts the blood vessel walls; 2) has an anti-inflammatory effect and 3) has a painkiller effect. The knowledge about these empirically established activities will be used to design *in vitro* pharmacological tests to better study the therapeutic effect in the treatment of haemorrhoids. Even though the definitive treatment of haemorrhoids is basically considered surgery it has sometimes side effects that make the possible application of the herb preferable.

Keywords: folk medicine, ethnomedicine, haemorrhoids, *Arum*.

INTRODUCTION

Snakehead *Arum maculatum* L. (Araceae, sect *Arum*, with rhizomatous tuber) has been known as a medicinal plant for centuries. It is mentioned in "The pharmacopeia of Pedanius Dioscorides" (20-70 AD), entitled Περί ύλης ιατρικής (Latinized as *De Materia Medica*, On Medical Matters), originally written in Greek about the year 65 AD. The plant was then believed to cure snake bites.¹ It is among the

plants found in renaissance herbals, e. g. Zwinger, XVII century, to treat malaria.² Culpeper³ reports that "it is a present and sure remedy for poison and the plague.... and riddeth away phlegm from the stomach, chest, and lungs".

In Bulgaria, *A. maculatum* is an officially acknowledged medicinal plant⁴, even though it is not often used.^{5,6} In Bulgarian traditional and folk medicine, *A. maculatum* tuber has been

shown to be widely used in cases of kidney stone, colitis, liver disease or hyperacidity. The plant has been also reported as a remedy for haemorrhoid.⁵⁻¹⁰ Moreover, *A. maculatum* tuber extract has been clinically tested for its anti-inflammatory activity in the intestinal and respiratory tract.⁵ According to the herbalist Georgy Nedev " *A. maculatum*", known in Bulgarian language as "zmiiska hurka", "zmiiski lapad", "zmiisko grozde", "ustrelche", is used in traditional folk medicine for haemorrhoid.¹¹ It is important to note that *A. orientale* (sect. *Dioscoridea*, with discoid tuber) should not be confused with *A. maculatum*.⁶

In the western part of the Balkans (Peshkopia, eastern Albania), *A. maculatum* has a ritual use in spring festivals.¹² To the west of the Balkans, e.g. in south Italy, *A. italicum* Mill. is used in traditional and folk medicine in the treatment of warts^{13,14}. Leaves and tubers of *A. italicum* are macerated in oil and applied in cases of rheumatic pains in Sicily^{15,16}

To the east of the Balkans, *Arum* spp. is mentioned more often in the ethnobotanical studies. In Turkey *A. maculatum* is applied for colitis.¹⁷ In ethnopharmacological records from western Turkey, *A. maculatum* is a cure for haemorrhoid.¹⁸⁻²⁰ Further east (Asia Minor part of Turkey), other *Arum* spp. (belonging to sect. *Dioscoridea*, with discoid tuber) are mentioned to have the same application as a treatment for haemorrhoid. According to Gürhan and Ezer²¹, *A. elongatum* Steven, *A. balansanum* R. Mill., and *A. detruncatum* C.A. Meyer ex Schott together with *Dracunculus vulgaris* Schott are among the plants (84 plant genera belonging to 46 families) that are used for the treatment of haemorrhoid in Turkey. In the Asiatic part of Turkey, *A. maculatum* is also applied in cases of rheumatism.²² Local people of Solhan District located in the eastern Anatolia Region of Turkey apply *A. elongatum* Steven subsp. *detruncatum* (C.A. Meyer ex Schott) H. Riedl as a compress or else "drink a decoction of of the plant on an empty stomach in the morning" to treat abdominal pain, arterial hypertension, diabetes mellitus, goitre and rheumatism.²³

Haemorrhoids are vascular structures in the anal canal. They become pathological (extreme in a way that is not normal or that shows an illness) or piles when swollen or inflamed. Haemorrhoids often break and hardly heal. They can be very painful and occasionally cause serious anemia.^{24,25} Haemorrhoids are a very common anorectal condition defined as the symptomatic enlargement and distal displacement of the normal anal cushions.²⁶ Orthodox medicine usually treats haemorrhoids through surgery combined with medication

containing the flavonoid diosmin. Open haemorrhoidectomy described by Milligan and Morgan has been one of the common procedures carried out for haemorrhoids up to the present time, but lately an easier procedure known as anal stretching and ligation has been suggested.²⁷ For more than 30 years, diosmin has been used as phlebotonic (phlebotonics are a class of drugs that are often used to treat chronic venous insufficiency).²⁸

The objective of the present study was to examine the contemporary folk medicine application of snakehead, *Arum maculatum* L. (Araceae) with an emphasis on its effect in the treatment of haemorrhoids. Therefore we set ourselves the following tasks: 1) to collect the contemporary traditional knowledge about the therapeutic effects of snakehead; 2) to collect anecdotal reports from persons who are known to have used the snakehead for treating haemorrhoids; 3) to analyze the data obtained about the effectiveness of this herb in the treatment of haemorrhoids and other medicinal conditions in order to determine how it works;; 4) to assess the popularity of snakehead nowadays in Bulgaria as a medicinal plant.

MATERIAL AND METHODS

During the March – November 2013 and June – August 2014 periods, semi-structured interviews were conducted with Bulgarian people in order to investigate the traditional ethnobotanical knowledge of the remedial properties of *Arum maculatum*.

Study sites

The interviews were performed in 11 districts of Bulgaria (Fig. 1), in the vicinity of native populations of *Arum* spp. We applied this approach, as the informants would be potentially familiar with snakehead plants in the vicinity of their settlements and they possibly might have traditional information about them. These study sites were also part of our field research on the autecology and horology of *Arum* spp. distributed in Bulgaria.^{29,30}

Informants

We aimed to collect as much information as possible about the medicinal properties of snakehead. Therefore we addressed people with different attitudes to the plant. The informants fell into the following groups.

Firstly, we interviewed herb sellers ($n = 3$), at two markets in Sofia (two women at the market Zhenski Pazar, and a man at the Market Ivan Vazov), because they offered snakehead tubers together with other herbs. This was an

indication that they possessed traditional knowledge of the remedial properties of *A. maculatum* and we needed to obtain details about which applications they were aware of. Herb sellers are seldom found in Bulgarian markets and these were all we located during the period of investigation.

Secondly, we interviewed a random sample of local people (n = 50 of age between 18 and 88 years). We tried to interview as many local people as possible in the vicinity of the snakehead's populations (Fig. 1). The number of informants in each district corresponded to the size of the settlements/number of inhabitants. All interviews were conducted *ex situ* (in the settlements, without the presence of the live plants in their native populations) – the snakehead is a distinctive plant and describing the specific features of the plant (leaves, inflorescence and infrutescence) worked very well. Additionally we double-checked the recognition by using colour prints of photographs. A total of 23 men and 27 women were interviewed. People often decoded the question about their education and profession as an intrusion into their private space; therefore these data are scarce. In this random group of informants we aimed to test 1) whether the people know/recognize the snakehead, *A. maculatum*; 2) whether they possess traditional knowledge of the remedial properties of the snakehead; 3) their level of awareness of the medicinal properties of snakehead.

Thirdly, we interviewed a random sample of local people (n = 58 of age between 40 and 80 years) in the Rhodopes (Fig. 1), consisting of 13 men and 45 women. In this random group of informants we aimed to test how the local people treat haemorrhoids ("majasul") traditionally. This investigation on the folk medicine treatment of haemorrhoids was a part of general ethnopharmacological research in the Rhodopes. Finally we knew, based on our previous experience, some people who had used *A. maculatum* to treat haemorrhoids. We interviewed these informants (n=4) and they provided data about persons (n=34, men and women) who had experienced the therapeutic effect of the plant substance *Ari Tubera* as a treatment for haemorrhoids. We developed a questionnaire to obtain feedback about the effectiveness of the plant substance in this medicinal condition based on their empiric experience. The following questions were asked: details of the medicinal condition; plant part used; method and time of collection, method of application; conventional medications used to treat the medical condition;

therapeutic effect of the plant substance *Ari Tubera* and longevity of the positive effect; side effects, awareness of plant toxicity; attitude to traditional versus conventional medicine, etc.

The following analyses and interpretations of the data were carried out

- 1) We calculated the ratio of people (percent), who i) are familiar with snakeshead versus those who never heard of it; ii) are ignorant versus knowledgeable about its medicinal properties. Considering the data sample we used descriptive statistics.
- 2) We classified and sorted the reports about the usage of this herb.
- 3) We analyzed the feedback from the informants who have used the snakeshead to cure haemorrhoids in order to test the positive effect of the plant substance. Comparatively analyzing the medical conditions where plant substance *Ari Tubera* had positive effect, we formulated a hypothesis about the functional mechanism of the plant.

RESULTS AND DISCUSSION

Results from our interview of random sample of local people (n = 50, men and women; age between 18 and 88 years) in different regions of Bulgaria demonstrated that the informants basically knew/recognized the plant due to its very specific inflorescence and fruits and only few people had never heard of it (Fig. 2).

In this group of informants (random sample of local people) only 8 persons (16%) reported knowledge of the medicinal properties of the plant (Fig. 2).

We presented in Table 1 a compilation of data for particular medicinal applications received from 8 informants from the random sample of local people and 3 herb sellers (11 informants totally). Among all informants whose response concerned the medicinal application of the snakeshead, most acknowledged its application against haemorrhoids (72% - all of the herb sellers and some of the random sample of local people). It is less popular as a cure against chronic traumatic pain (9%), purulent infections (9%), and for "melting of adipose formations" (9%). Interestingly the Bulgarian folk medicine tradition of applying rizhomes macerated in oil as a cure for joint pains is related with the folk medicine tradition of local people in Sicily, where a rather similar type of application against rheumatic pains is recorded¹⁵

Less than a quarter (21%) of the informants in the Rhodopes reported traditional treatment of haemorrhoids, (12 persons – 9 of them females and 3 males). They listed for internal use *Arum*

maculatum, Araceae, *Juniperus communis* L., Cupressaceae (galbulae), *Pulmonaria officinalis* L., Boraginaceae *Achillea millefolium* L., Asteraceae, *Viscum album* L., Viscaceae *Onopordum acanthium* L., Asteraceae, *Tanacetum balsamita* L., Asteraceae, *Teucrium polium* L., Lamiaceae. For external use were listed (sit baths) *Cotinus coggygria* (Scop.), Anacardiaceae *Consolida* spp. Ranunculaceae, *Persicaria hydropiper* (L.) Delabre, Polygonaceae *Teucrium polium* L., Lamiaceae *Tanacetum balsamita* L., Asteraceae or unguents *Calendula officinalis* L., Asteraceae. Most often reported were the snakehead *Arum maculatum* and *Cotinus coggygria* (twice each). Interestingly in the area of the Rhodopes (East Rhodopes) it was reported that the fruits of *Arum maculatum* were applied, while most of the other reports referred to usage of the rhizome.

Data received by the informants who have used the snakeshead for haemorrhoids is summarized in Table 2. The results of the analysis of the therapeutic effect in cases of haemorrhoids demonstrate categorically improvement of the condition. Most informants insisted that a prolonged process of treatment was not necessary even though it depended on the level of suffering. The positive effect remained for a long time and further treatment was not necessary in many cases. Consequently, according to the informants' feedback, there is a stable and positive effect of the plant substance. It was noted that *A. maculatum* was more efficient as a cure for haemorrhoids as compared to medications with diosmin active compound (Table 2). Due to the specific activity of the flavonoids (reducing the venous stasis and permeability of the capillaries), medications with diosmin active compound are used to treat symptoms associated with venous-lymphatic insufficiency characterized by weight and pain in lower limbs, the feeling of having "tired legs" in the morning. Medications with diosmin active compound are recommended in the symptoms associated with acute haemorrhoidal attacks. It has been applied lately for other therapeutic purposes, such as cancer, PMS, colitis, and diabetes. Its vascular protective, anti-inflammatory and anti-mutagenic effects have been proved.²⁸

Notably, one of the informants warned that during the treatment alcohol should be avoided while one of the herb sellers preserved the tubers in alcohol. However in most cases the opinion is that the effect is stronger if the tuber is fresh when applied even though the dried tuber and even the pulp of the fruits posses the above mentioned therapeutic effect.

Despite the fact that the plant is considered toxic no adverse reactions were reported for the doses applied, except one case of irritation when trying to swallow the piece without water, but after drinking water, the irritation disappeared (Table 2). The toxicity is due to the presence of raphides.²⁹ Also *Arum maculatum* is known to storage lectins. Araceae lectins are a family of closely related proteins, the sequence of which contains the highly conserved domains of the Amarylidaceae, Alliaceae, and Orchidaceae lectins. With respect to their specificity the Araceae lectins resemble the previously isolated Man-binding lectins from Amarylidaceae, Alliaceae, and Orchidaceae species, except that they interact more strongly with glycoproteins.³⁰ At the same time lectins are considered toxic.³¹ However we do not exclude the possibility that it is actually the lectins that are responsible for the therapeutic effect of the snakehead in the treatment of haemorrhoids.

CONCLUSION

The analysis of the therapeutic effect of *Arum maculatum* tuber both directly in various haemorrhoids and indirectly in cases of festers and old traumas suggests that the plant operates in the following manner: 1. it contracts the blood vessel walls; 2. it has a demonstrable anti-inflammatory effect; 3. it acts as a painkiller. Experimental tests of *Arum maculatum* leaf extract demonstrated antibacterial properties³² in particular against some of the tested gram negative bacteria.³³

There are a number of implications for further research. The knowledge about these empirically established activities will be used to design *in vitro* pharmacological tests to undertake improved studies of the therapeutic effect with regard to haemorrhoids. The fact that in one case the effect of *Arum maculatum* plant substance in the treatment of haemorrhoids was compared to the effect of medication based on diosmin available in the pharmacy store and the result was positive for the herb (Table 2) increases the necessity of such tests. Additionally even though the definitive treatment of haemorrhoids is basically considered to be surgery, it sometimes has negative side effects. This makes the possible application of the herb preferable.

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Table 1: Informants (N=11) who reported medicinal properties for the snakehead, *Arum maculatum*. Informants were divided into 2 categories – i) persons from the random excerpt who possessed knowledge about snakehead therapeutic effect (N=8) and ii) persons who are known for having experience in traditional herbal medicine (N=3). Information is organized in columns according to the medical conditions

Medical condition	Haemorrhoids	Haemorrhoids and other diseases	Furuncle	"Adipose formations"	Arthralgia and chronic traumatic pain
Number of reports for the particular medical condition treatment	7	1	1	1	1
Informant details	Two women above 60 years old herb sellers at the market Five women above 60 years old from rural areas	A man above 60 years old, herb seller at the market	A man about 50 years old, biologist	A woman about 60 years, teacher	A man about 50 years old, mountain guide
Way of application	Fresh tubers (or dried if no fresh are available) are cut into pieces approximately the size of a maize grain and applied per os.	Tuber pieces preserved in spirit.	Small piece of the <i>Arum maculatum</i> tuber is cut and the top of the furuncle is touched with it.	The tubers (grated) are applied on the targeted area.	The tubers are ground and mixed with salad oil. Applied as formentation.
Precautions!	Poisonous		Even the hand holding the piece might be scalded. Use glove.		
Adverse reactions					
Effectiveness	The only effective cure with no need for additional treatment.		The best cure for furuncles	"They melt after 2-3 applications."	The only effective remedy.

Table 2: Data, obtained from informants who are known to have used the snakehead for treating haemorrhoid

	Informants			
	1 st Informant	2 nd Informant	3 rd Informant	4 th Informant
gender	female	male	male	male
age	70	33	34	51
education	university	university	university	university
profession	botanist	medical doctor	medical doctor	pharmacist
indications - medical condition	Haemorrhoids – bleeding, inflamed and painful	Haemorrhoids and their complications.	Haemorrhoids – bleeding, inflamed and painful (multiple use in all of the above mentioned conditions)	Internal haemorrhoids – bleeding
Way of application	1 piece approximately the size of maize grain is swallowed (without chewing) 3 times a day after meals, in 3 subsequent days. The same procedure is repeated after 10 days.	The tubers are cut in pieces approximately the size of maize grain. No more than 5 pieces are swallowed without chewing with some water. It must be done once per year.	The tuber: 2-3 pieces of the fresh (or fresh frozen) tuber, piece approximately the size of large maize grain are put inside a piece of bread and swallowed every day in 3 subsequent days. Berries: 4-5 fresh berries are eaten every day in 3 subsequent days without swallowing the seed.	The tubers are cut in pieces approximately the size of maize grain.
	Fresh tubers have stronger effect, but dried are also usable.	Fresh tubers are stronger.	Fresh tubers are stronger.	
Precautions!	The tubers are poisonous and they shouldn't be taken in greater dose. Optionally, they may be put in a piece of bread. No alcohol during the treatment.	The tubers are very pungent. The sensation it rather painful. This is the reason why they should be taken inside a piece of bread and directly swallowed.	The tubers are poisonous .	
Adverse reactions	Not known when the correct dose is applied, but some care should be taken. Only one person had irritation when trying to swallow the piece without water, but after drinking water, the irritation disappeared.			
Effectiveness	The effect in unbelievable – the bleeding stops, the pain is relieved, the nodes shrink. It is especially obvious in the more severe cases. Even if the problem is not entirely cured, it is alleviated and if necessary, the treatment may be repeated next year.	* Anyway, the definitive treatment of the haemorrhoids is surgical. * Note – the informer is a neurologist	The improvement of the symptoms is dramatic – after the second day of applications. The symptom free period lasted for months. Recently I haven had any symptoms at all. * Generally, I prefer the orthodox medicine, but in this case, the surgery often gives relapses of the condition. * Note – the informant is a surgeon	The only effective remedy, no relapses have been observed.
Data from further recommendation	I have recommended this to 29 people, all of them with good effect.	Do not have information from other people – personal positive experience	I have recommended this to 1 more person, who also cured.	I have recommended this to 2 people, both of them with positive outcome.
Total feedback positive effect neutral or negative effect	29 0	1 0	2 0	2 0

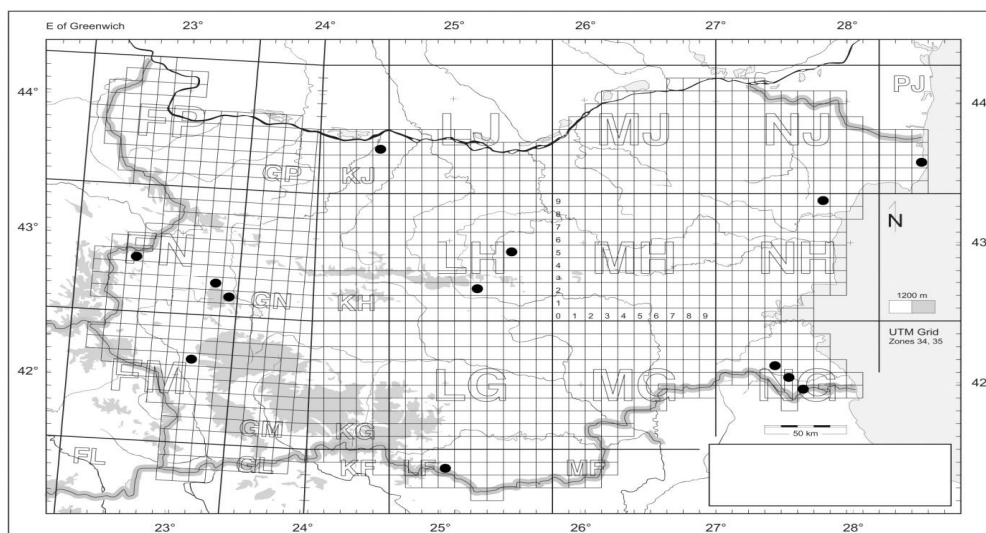


Fig. 1: Study sites. Legend: ● random sample of local people in the vicinity of the snakehead's populations ▲ random sample of local people (n = 58) from the Rhodopes about the traditional treatment of haemorrhoid ("majasul"). This investigation on the folk medicine treatment of haemorrhoid was a part of general ethnopharmacological research in the Rhodopes

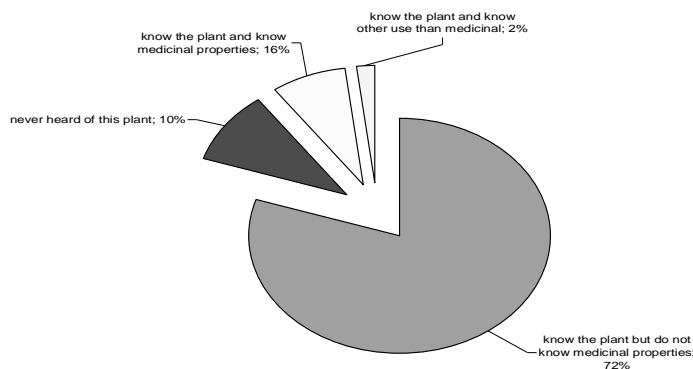


Fig. 2: Ratio of the informants [%] and their knowledge about the snakehead and its application

REFERENCES

1. Janick J and Stolarczyk J. Ancient Greek Illustrated Dioscoridean Herbals: Origins and Impact of the Juliana Anicia Codex and the Codex Neopolitanus. *Notulae Botanicae Horti Agrobotanici Cluj-Napoca*. 2012;(40):1.
2. Adams M, Alther W, Kessler M, Kluge and Hamburger M. Malaria in the Renaissance: remedies from European herbals from the 16th and 17th century. *J Ethnopharmacol.* 2011; 133(2):278-288.
3. Culpeper N. *The English Physitian: or an Astrologo-physical Discourse of the Vulgar Herbs of This Nation*. Printed for the benefit of the Commonwealth of England, London, 1652.
4. Medicinal plant act. State gazette vol. 29, 07.04.2000. <http://lex.bg/laws/ldoc/21349160> 96 12.11.2013.

5. Petkov V. Contemporary phytotherapy. Medicine and physculture, Sofia, 1982. (Bulgarian language).
6. Nikolov S (ed.), Specialized Encyclopedia of medicinal plants in Bulgaria. Bulgarian encyclopedia – Bulgarian Academy of Sciences, Faculty of Pharmacy MU, Publishing House Trud, Sofia, 2006.
7. Pamukov D and H Ahtardjiev. Pharmacy from the nature. Zemizdat, Sofia, 1989. (Bulgarian language)
8. Pamukov D. Home pharmacy. Gea-Libris, Sofia, 1995 (Bulgarian language).
9. Dimkov P. Natural healing methods and living with nature; Bulgarian traditional medicine Vol. 1-3. Astrala, 2001. (Bulgarian language)
10. Ivancheva S and Stantcheva B. Ethnobotanical inventory of medicinal plants in Bulgaria. Journal of Ethnopharmacology. 2000;69(2):165-172.
11. Grozeva J. Haemorrhoid are cured with the herb snakeshead, <http://www.blitz.bg/article/34466> 2013 (Bulgarian language).
12. Pieroni A, Nedelcheva A, Hajdari A, Mustafa B, Scaltriti B, Cianfaglione K and CL Quave. Local knowledge on plants and domestic remedies in the mountain villages of Peshkopia (Eastern Albania). Journal of Mountain Science. 2014;11(1):180-193.
13. Pieroni A and Quave CL. Traditional pharmacopoeias and medicines among Albanians and Italians in southern Italy: A comparison. Journal of Ethnopharmacology. 2005;101:258–270.
14. Pieroni A and Quave CL. Traditional pharmacopoeias and medicines among Albanians and Italians in southern Italy: A comparison. Journal of Ethnopharmacology. 2005;101(1):258-270.
15. Pieroni A and Quave CL. Traditional health care and food and medicinal plant use among historic Albanian migrants and Italians in Lucania, Southern Italy. Traveling Cultures and Plants the Ethnobiology and Ethnopharmacy of Human Migrations. 2007;204-227.
16. Leto C, Tuttolomondo T, La Bella S and Licata M. Ethnobotanical study in the Madonie Regional Park (Central Sicily, Italy)—Medicinal use of wild shrub and herbaceous plant species. Journal of ethnopharmacology. 2013;146(1):90-112.
17. Tuttolomondo T, Licata M, Leto C, Savo V, Bonsangue G, Gargano LM, Venturella G and La Bella S. Ethnobotanical investigation on wild medicinal plants in the Monti Sicani Regional Park (Sicily, Italy). Journal of Ethnopharmacology. (in press)
18. Everest A and Ozturk E. Focusing on the ethnobotanical uses of plants in Mersin and Adana provinces (Turkey). Journal of Ethnobiology and Ethnomedicine. 2005;1:1-6.
19. Uzun E, Sariyar G, Adersen A, Karakoc B, Ötük G, Oktayoglu E and Pirildar S. Traditional medicine in Sakarya province (Turkey) and antimicrobial activities of selected species. Journal of Ethnopharmacology. 2004;95(2–3):287–296.
20. Kültür S. Medicinal plants used in Kırklareli province (Turkey). Journal of Ethnopharmacology. 2007;111(2):341-364.
21. Demirci S and Özhatay N. An ethnobotanical study in Kahramanmaraş (Turkey); wild plants used for medicinal purpose in Andirin, Kahramanmaraş. Turk. J Pharm Sci. 2012;9(1):75-92.
22. Gürhan G and Ezer Halk Arasında Hemoroit Tedavisinde Kullanılan Bitkiler IN. Hacettepe Üniversitesi Eczacılık Fakültesi Dergisi. 2004;24(1):37-55 (Turkish language).
23. Tetik F, Civelek S and Cakilcioglu U. Traditional uses of some medicinal plants in Malatya (Turkey). Journal of Ethnopharmacology. 2013;146(1):331-346.
24. Polat R, Selvi S, Cakilcioglu U and Acar M. Investigations of ethnobotanical aspect of wild plants sold in Bingöl(Turkey) local markets. Biological Diversity and Conservation. 2012;5(3):155-161.
25. Schubert MC, Sridhar, Schadeb S and RRWexner SD. What every gastroenterologist needs to know

- about common anorectal disorders. *World J Gastroenterol.* 2009;15(26):3201–3209.
26. Lorenzo-Rivero S. Haemorrhoid: diagnosis and current management. *Am Surg.* 2009;75(8): 635–642.
27. Lohsiriwat V. Haemorrhoid: From basic pathophysiology to clinical management. *World J Gastroenterol.* 2012;18(17):2009-2017.
28. Dubey V and Choudhary SK. Anal stretching and ligation technique for treatment of haemorrhoid. *International Journal of Pharma and Bio Sciences.* 2012;3(4):485-492.
29. Dimitrov S and Zahariev T. Application of Detralextm for patients suffering from chronic arterial insufficiency of lower limbs. *Angiology and Vascular Surgery.* 2012;2:24-27 (in Bulgarian).
30. Boyce PC. The genus *Arum*. HMSO/Kew. 1993.196 pages.
31. Kozuharova E, Kochmarov V, Kachaunova E, Espindola A, Aleksandrov B and I Mincheva. Distribution of *Arum* (Araceae) in Bulgaria. — *Fl. Medit.* 2014;24:51-62.
32. Kozuharova E, Kochmarov V and Kachaunova E. On the autecology of Bulgarian *Arum* (Araceae) species. *Comptes rendus de l'Académie bulgare des sciences.* 2014;67(6):789-802.
33. Van Damme EIS JM, Coossens K, Smeets K, Van Leuven F, Verhaert P and Peumans WJ. The major tuber storage protein of araceae species is a lectin (characterization and molecular cloning of the lectin from *Arum maculatum* L.). *Plant Physiology.* 1995;107(4):1147-1158.
34. Kumari PS, Maduri Latha T, Harika D and Nagaraju P. Herbal toxicities – an over view. *International Journal of Pharmaceutical Chemical and Biological Sciences.* 2011;1(1):17-25.
35. Safari E, Amiri M, Bahador A, Amiri M and Esmaeili D. The study of antibacterial effects of alcoholic extracts of *Arum maculatum*, *Allium hirtifolium* and *Teucrium polium* against nosocomial resistance bacteria. *Int J Curr Microbiol App Sci.* 2014;3(2):301-605.
36. Çolak F, Savaroğlu F and İlhan S. Antibacterial and antifungal activities of *Arum maculatum* L. Leaves Extracts. *Journal of Applied Biological Sciences.* 2009;3(3):13-16.