Original article

Prevalence of self-medication practice with herbal products among non-psychotic psychiatric patients from southeastern Serbia: A cross-sectional study

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ABSTRACT

The aim of this study was to evaluate the usage prevalence of herbal products (HP) and to ascertain the identity, mode and adverse effects of plant taxa used in self-medication practice for anxiety, depression and insomnia in patients with non-psychotic disorders originating from southeastern Serbia. Also, we compared HP users and non-users on the variables of socio-demographic characteristics, information source and origin of HP. The study was done by a face-to-face interview with a trained psychiatrist using a structured questionnaire administered to 136 adult patients suffering from non-psychotic mental disorders. A typical herbal-product user among non-psychotic psychiatric patients from southeastern Serbia is a middle-aged married woman, with a secondary level of education, unemployed and living in an urban area. Non-psychotic psychiatric patients, although not living predominantly in rural areas, were familiar with a variety of ethno-medicines and were often using HP primarily without the consultation of their psychiatrists/physicians. HP stated to be most frequently used for psychiatry-related symptoms included: *Melissa officinalis*, *Mentha × piperita*, *Hypericum perforatum* and *Valeriana officinalis*. The interviewees rarely stated adverse reactions related to the HP usage; however, this should not be generalized, since HP are known to vary in the content of their adverse reaction-causing constituents.

1. Introduction

Over the past decades there has been a large increase in the number of psychiatric patients suffering from anxiety and mood disorders. One-year prevalence rates were one at every fifteen persons and one at every twenty persons for anxiety and mood disorders, respectively (Steel et al., 2014). According to the ICD-10 Classification of Mental and Behavioral Disorders, these disorders include a variety of diagnoses divided into two major groups: neurotic, stress-related and somatoform disorders (F40-F48) and mood (F30-F39) disorders (WHO, 2010).

For both types of disorders, up to date, there are a number of different drugs available for psychiatrists to prescribe. Among the most frequently used are those from benzodiazepine ($GABA_A$ allosteric modulators, e.g. diazepam) and selective serotonin reuptake inhibitors (SSRIs, e.g. fluoxetine) groups. These drugs, when applied during a long period of time, may cause numerous side effects that include: muscle relaxation, suicidal ideation, decreased alertness, sexual dysfunction and dependency (O'Brien, 2005; Hu et al., 2004).

According to the World Health Organization, almost 80% of the World population uses herbal products (HP) as a source of primary care (Ekor, 2014). The European Union has a strict definition of herbal medicinal products (65/65/EEC, European Commission, 1965) and this definition and further classification, implemented in the national laws of all EU countries, serve as a guide for HP users. Due to the mentioned side effects of the commonly prescribed drugs for anxiety and mood disorders and the general notion of

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the safety/benevolence of herbal remedies, the usage of HP is presumed to be widespread, but not well documented. The conclusions on HP usage by such patients/subjects comes from generally oriented surveys that lack the necessary number of relevant examinees (the sample size for this type of patients is insufficient) (Djuv et al., 2013; Kantati et al., 2016; Picking et al., 2011).

The Balkan region, especially the territory of the Republic of Serbia, is rich in plant taxa that are being used for centuries for the treatment of a variety of medical conditions, among them a great number of these are utilized for different mental disorders (Jarić et al., 2015; Zlatković et al., 2014; Šavikin et al., 2013; Jarić et al., 2007). In Serbia, the ethnopharmacological knowledge on HP and their specific uses had been systematized in a single volume ("Lečenje biljem", Herbal therapy, 1973), by a university professor, dr. Jovan Tucakov, and is still today regarded as the choice literature in this area. Interestingly, almost every home in Serbia possesses a copy of this book, and self-medication practice based on its contents or related ethnopharmacological experience within the family is very common. Professor Tucakov devoted a significant portion of the book to plants used for the treatment of mental disorders, and more than 20 taxa are recognized to beneficially influence the HP user mental health (Tucakov, 1973).

The aim of our study was to contribute to the existing ethnopharmacological knowledge by evaluating the usage prevalence of HP utilization and ascertaining the plant taxa identity and their formulations used, as well as their adverse effects, in self-medication practice for anxiety, depression and insomnia in a sample of patients with non-psychotic disorders originating from southeastern Serbia (Clinical Center Niš). The second aim was to compare HP users and HP non-users on the variables of socio-demographic characteristics, information source for HP and the origin of HP. This was done by a face-to-face interview with a trained psychiatrist using a structured questionnaire.

2. Materials and methods

2.1. Study definition and design

The study was conducted on patients originating from the municipal areas of Niš and the surrounding municipalities (population 373,407) in the Clinical Center Niš at the Clinic for mental health protection. The study was approved by the Ethical Committee of the Medical Faculty, University of Niš (decision No. 12–2307-2/3). In total, 136 adult patients suffering from non-psychotic mental disorders (F30-F39 and F40-F48), treated in the outpatient clinical setting, were randomly selected by the method of consecutive admissions and have signed the informed consent form. The study was designed as a cross-sectional survey in order to acquire the data concerning the usage, formulation and general attitude towards HP in the selected patient population.

2.2. Data collection

Data were collected anonymously, by a trained psychiatrist (Lj. S.) during the regular diagnostic or therapy sessions. The questionnaire consisted of five sections, containing both open and closed forms of questions. The first part consisted of questions related to the socio-demographic characteristics of each individual, while the second one was comprised of questions dealing with the (possible) usage of HP and symptomatology (predominantly anxiety, depressive and insomnia) targeted with HP, as well as the type of HP. The third group of questions dealt with the source of information and the HP origin. In the fourth section, five questions were

designed to reveal the formulation of HP used in the treatment. The fifth part was designed to obtain information concerning the attitudes towards the usage of HP concomitantly with standard drugs and the data about side effects observed during the consumption of HP.

2.3. Statistical analysis

The data collected from 136 questionnaires were analyzed using GraphPad Prism (version 5.03, San Diego, CA, USA) and SPSS (version 21.0, IBM Corp, 2012) where the sample size and power analysis showed $\beta < 0.2$ for the number of interviewed patients. The data are shown in frequency distribution tables expressed as percentages, which were further analyzed using Fishers exact and Chi-square tests. The adjusted residual was then calculated and the values of adjusted residual ≥ 2 or ≤ -2 were regarded as statistically significant (Tanaka et al., 2007). Some questions allowed more than a single answer, thus the sum was not always 100%. Patient age is presented as mean ± SD and in this case Student's t-test or One Way ANOVA were used to estimate the statistical difference among the groups. Probability values (p) less than 0.05 were considered statistically significant.

3. Results

All of the interviewed patients finalized their interviews. There were almost 60% of patients that never used HP for the treatment of their symptoms, mostly because they did not believe in the effectiveness of HP (Table 1). Some 32% of the examinees were either afraid or were ignorant of the existence of HP used in these purposes. Interestingly, only 5% answered that the medication that they were already receiving represented adequate therapy. Only a small portion of the interviewed patients declared that HP were unavailable to them due to a low financial income, which is understandable since HP are readily obtainable from local green markets or pharmacies.

As reported in Table 2, our study groups, HP users and non-users, comprised mainly of married female (78.2 and 66.7%) patients, aged 30–69 years, unemployed (69.1 and 71.6%), with a secondary level of education (69.2 and 45.6%), living in an urban area (80 and 63%). The groups of HP users and non-users were found to be statistically different with respect to the socio-demographic data accumulated, specifically their level of educa-

Table 1
Interview statistics and the frequency of the stated reasons for non-utilization of herbal products (HP).

Characteristics	N (%)
Interviews	
Completed	136 (100)
Declined	0 (0)
Used HP for the treatment of psychiatric non-psychotic symptoms	
Yes	55 (40.4)
No	81 (59.6)
Reason for not consuming HP	
Do not believe in the effectiveness of HP	22 (27.2)
Afraid to use HP	13 (16.05)
Never heard of such HP	13 (16.05)
No one had ever suggested the use of HP	8 (9.9)
Do not need HP	6 (7.4)
Already have adequate medication	4 (4.9)
No answer given	7 (8.6)
Does not have the finances for HP	3 (3.7)
Other[a]	5 (6.2)

[a] These include the following answers: have not thought about HP; have not had a chance or, not interested in HP.

Table 2
Comparison of socio-demographic characteristics between HP and HP non-users.

Characteristics	Total n = 136 (100%)	HP users n = 55 (40.4%)	HP non-users n = 81 (59.6%)	p value
Mean age	47.1 ± 14.5	48.7 ± 12.9	47.5 ± 16.5	0.6585
Gender				0.1778
Male	39 (28.7)	12 (21.8)	27 (33.3)	
Female	97 (71.3)	43 (78.2)	54 (66.7)	
Age groups				0.1993
<30	19 (14.0)	4 (7.3)	15 (18.5)	
30–39	26 (19.1)	13 (23.6)	13 (16.0)	
40–49	25 (18.4)	10 (18.2)	15 (18.5)	
50–59	27 (19.8)	13 (23.6)	14 (17.4)	
60–69	28 (20.6)	13 (23.6)	15 (18.5)	
>70	11 (8.1)	2 (3.6)	9 (11.1)	
Marital status				0.1581
Single	30 (20.1)	11 (21.8)	19 (33.9)	
Married	89 (66.1)	33 (60.0)	56 (58.7)	
Widowed/separated/divorced	16 (11.8)	10 (18.2)	6 (7.4)	
Level of education				0.0476*
Primary	31 (22.8)	8 (14.5)	23 (28.4)	
Secondary	74 (55.2)	38 (69.2)#	37 (45.6)##	
Post-secondary	24 (17.6)	8 (14.5)	16 (19.8)	
Tertiary	6 (4.4)	1 (1.8)	5 (6.2)	
Employment status				0.8483
Employed	40 (29.4)	17 (30.9)	23 (28.4)	
Unemployed	96 (70.6)	38 (69.1)	58 (71.6)	
Place of residence				0.0377*
Urban area	95 (69.8)	44 (80)	51 (63)	
Rural area	41 (30.2)	11 (20)	30 (37)	

* Existence of statistically significant difference between HP and non-HP users found in Fisher/χ2 analysis.
\# Adjusted residual $\leq$-2.
\#\# adjusted residual $\geq$2.

Table 3
Comparison of socio-demographic data with non-psychotic symptoms taken as variables.

Characteristics	Total (n = 55)	Anxiety symptoms	Depression symptoms	Combined anxiety and depression symptoms	Insomnia	p-value
Number of users (%)		34 (61.8)	3 (5.45)	14 (24.45)	4 (7.3)	
Mean age		48.1 ± 14.1	61.3 ± 12.7	49.7 ± 11.5	48.5 ± 5.9	0.0592
Gender						0.2660
Male	13 (23.6)	9 (69.2)	1 (7.7)	1 (7.7)	2 (15.4)	
Female	42 (76.4)	25 (58.2)	2 (4.7)	13 (30.4)	2 (4.7)	
Age groups						0.1804
<30	4 (7.3)	4 (100)	0	0	0	
30–39	13 (23.6)	9 (69.1)	0	4 (30.8)	0	
40–49	10 (18.2)	5 (50)	1 (10)	2 (20)	2 (20)	
50–59	13 (23.6)	6 (46.2)	0	5 (38.5)	2 (15.3)	
60–69	13 (23.6)	9 (62.3)	1 (7.7)	3 (23.0)	0	
>70	2 (3.6)	1 (50)	1 (50)	0	0	
Marital status						0.5946
Single	12 (21.8)	9 (75)	0	3 (25)	0	
Married	33 (60)	18 (54.5)	2 (6.1)	9 (27.3)	4 (12.1)	
Widowed/separated/divorced	10 (18.2)	7 (70)	1 (10)	2 (20)	0	
Level of education						0.6180
Primary	8 (14.55)	5 (62.5)	1 (12.5)	1 (12.5)	1 (12.5)	
Secondary	38 (69.1)	22 (57.9)	2 (5.3)	11 (28.9)	3 (7.9)	
Post-secondary	8 (14.55)	7 (87.5)	0	1 (12.5)	0	
Tertiary	1 (1.8)	0	0	1 (100)	0	
Employment status						0.9863
Employed	17 (30.9)	11 (64.7)	1 (5.9)	4 (23.5)	1 (5.9)	
Unemployed	38 (69.1)	23 (60.5)	2 (5.3)	10 (26.3)	3 (7.9)	
Place of residence						0.5657
Urban area	44 (80)	26 (59.1)	3 (6.8)	11 (25)	4 (9.1)	
Rural area	11 (20)	8 (72.7)	0	3 (27.3)	0	

tion and place of residence (p < 0.05). In the case of education level, the adjusted z value was found to be $\geq$2 for the secondary level in both HP and HP non-users (z = ±2.69).

The largest number of patients who reported the use of HP suffered from anxiety symptoms, while the patients using HP for depressive symptomatology were the least numerous ones

Table 4
HP utilization information source among HP and HP non-users, and the data for HP users divided according to non-psychotic symptoms.

Characteristics	Total number (%)	Family	Friends	Internet	Literature	Radio/TV	Physician	Shop or pharmacy	*p*-value
HP users	55 (52.9)	12 (21.8)	13 (23.6)	6 (10.9)	5 (9.1)	6 (10.9)[#]	7 (12.7)[##]	6 (10.9)[##]	*0.0001*[*]
HP non-users[Δ]	49 (47.1)	10 (20.4)	14 (28.6)	1 (2.0)	1 (2.0)	23 (49.9)[##]	0[#]	0[#]	
HP users									0.5002
Anxiety symptoms	34 (61.8)	6 (10.9)	9 (16.4)	2 (3.6)	3 (5.45)	5 (9.1)	5 (9.1)	4 (7.3)	
Depression symptoms	3 (5.45)	2 (3.6)	0	0	1 (1.8)	0	0	0	
Combined anxiety and depression symptoms	14 (24.45)	4 (7.3)	2 (3.6)	3 (5.45)	1 (1.8)	0	2 (3.6)	2 (3.6)	
Insomnia	4 (7.3)	0	2 (3.6)	1 (1.8)	0	1 (1.8)	0	0	

[Δ] Answers found in those subjects that possessed any knowledge on HP utilization for the stated purposes.
[*] Statistically significant difference found between HP and HP non-users; the data given in brackets are the calculated percentage in the HP users group.
[#] Adjusted residual ≤-2.
[##] Adjusted residual ≥2.

Table 5
Origin of HP among HP and HP non-users, and the detailed data for HP users divided according to non-psychotic symptoms.

Origin of HP	Total number (%)	Pharmacy	Herbal pharmacy	Amateur herbalist	Collect HP personally	Multiple answers[#]	*p*-value
HP users	55 (62.5)	22 (40)	14 (25.45)	4 (7.28)	9 (16.37)	6 (10.9)	0.1126
HP non-users[*]	33 (37.5)	13 (23.64)	9 (27.27)	5 (15.15)	0	6 (18.18)	
Purpose for HP usage among HP users							0.1523
Anxiety symptoms	34 (61.8)	16 (47.2)	7 (20.6)	1 (2.9)	6 (17.7)	4 (11.8)	
Depression symptoms	3 (5.45)	0	0	1 (33.3)	1 (33.3)	1 (33.3)	
Combined anxiety and depression symptoms	14 (24.45)	6 (42.8)	4 (28.7)	1 (7.1)	2 (14.3)	1 (7.1)	
Insomnia	4 (7.3)	0	3 (75)	1 (25)	0	0	

[*] Answers from those subjects that possessed any knowledge on the origin of HP utilized for the stated purposes.
[#] Some of the subjects gave more than one answer to this question.

Table 6
Used HP for the treatment of the groups of subjects with non-psychotic symptoms.

Latin binominal	Family	Common name	Treated symptoms	Total number of users[Δ]
Achillea millefolium	Asteraceae	Yarrow	CAD	1
Matricaria chamomilla	Asteraceae	Chamomile	A	1
Valeriana officinalis	Caprifoliaceae	Valerian	A	6
Hypericum perforatum	Hypericaceae	St. John's wort	A, D, CAD	7
Melissa officinalis	Lamiaceae	Lemon balm	A, D, CAD, I	26
Mentha x *piperita*	Lamiaceae	Peppermint	A, CAD	8
Ocimum basilicum	Lamiaceae	Basil	A	1
Salvia officinalis	Lamiaceae	Salvia	A	1
Thymus vulgaris	Lamiaceae	Thyme	A, CAD, I	6
Commercial tablets[*]	/	/	A	7
Herbal mixtures[#]	/	/	CAD	4
Cant recall	/	/	D	2

[Δ] Some of the subjects used more than one HP.
[*] The plant mixture consisted of *Melissa officinalis*, *Valeriana officinalis*, *Mentha* x *piperita* and *Achillea millefolium*.
[#] An unknown mixture of herbs; Symptoms: A – anxiety, D – depression, CAD - Combined anxiety and depression and I – insomnia.

(Table 3). However, statistically significant differences were not found between the groups of patients separated by symptoms treated with HP and socio-demographic data (Table 3).

The main source of information about HP utilization in our study sample were the families and friends of patients, while almost 50% of HP non-users reported to have received information on these products via radio/TV. A statistically significant difference was found between groups of HP and HP non-users regarding the information sources (Table 4), with the adjusted z values ≤−2 or ≥2 for radio/TV, physician and pharmacy as the sources of information on HP. However, no statistically significant differences were found between the groups of patients characterized by certain symptoms treated with HP and a specific information source (Table 4).

No statistically significant differences were found when groups of HP users and non-user were compared and the origin of HP was taken as the variable. The same can be applied to the comparisons between the groups of HP subdivided by the predominantly treated symptoms (Table 5). Although no differences were found, the majority of the patients obtained their HP from pharmacy shops, while a lower percentage of the patients would turn to an herbalist or collect HP personally (Table 5).

Table 6 contains HP identity data used in the treatment of the corresponding non-psychotic symptoms, where *Melissa officinalis* appeared in each group. Besides lemon balm, the second most used medicinal plant was *Mentha* × *piperita*, followed by *Hypericum perforatum*, *Valeriana officinalis* and *Thymus vulgaris*. The reported HPs were mainly used in the form of an infusion (tea) or in the case of

Table 7
Suggested formulations, doses and time schedules of HP utilization.

Plant name	Formulation	Amount of herbal drug per dose	Dosage	Number of uses per day[*]
Achillea millefolium	Infusion	1 tea spoon	1 tea cup	2
Hypericum perforatum	Infusion/Drops	1–3 tea spoons/60–90 drops	1 tea cup/60–90 drops	1
Matricaria chamomilla	Infusion	1 tea spoon	1 tea cup	1–2
Melissa officinalis	Infusion	2–3 tea spoons	1–2 tea cup	1–3
Mentha x *piperita*	Infusion	1–2 tea spoons	1–2 tea cup	1–3
Ocimum basilicum	Infusion	1 tea spoon	1 tea cup	1
Salvia officinalis	Infusion	1 tea spoon	1 tea cup	1
Thymus vulgaris	Infusion	1 tea spoon	1–2 tea cup	1–2
Valeriana officinalis	Drops	30–90 drops	30–90 drops	1–2

[*] Time of day of consumption was dependent on the symptoms that were treated.

Table 8
Usage of HP in combination with standard therapy, and the observed side effects originating from HP or their combination with standard therapy.

Herbal product used	The total number of users	Co-used with standard therapy	Changes in symptom intensity observed during co-usage (N°)[Δ]	Side effects observed (N°)
Mellissa officinalis	26	11	No change (7)/Decreased (3)	Dizziness (1)/ Nausea (1)
Mentha x *piperita*	8	3	Decreased (1)	None
Hypericum perforatum	7	2	No change (2)	None
Valeriana officinalis	6	2	Decreased (2)	Nightmares (1)
Thymus vulgaris	6	3	No change (2)/Decreased (1)	None

[Δ] Not all patients, that co-used HP with standard therapy, gave an answer to this question since they did not compare the symptoms before and after HP usage.

H. perforatum and *V. officinalis* in the form of drops (Table 7). The time of day when the use of the selected HP was suggested depended on the group of symptoms targeted with each HP.

Amongst the patients that used HP, less than 50% reported HP co-usage with standard therapy (Table 8). Only mild side effects were observed by the patients during the application of HP. These included dizziness, nausea and nightmares (Table 8). The subjective changes in symptom intensity in patients that consumed HP along with standard drugs (Table 8) were lower than expected (Valli and Giardina, 2002), but it should be taken with reserve since not all patients answered this question.

4. Discussion

This study revealed that more than 40% of patients in our sample, suffering from non-psychotic disorders, used HP for the treatment of psychiatric symptoms (Table 2). Most of the patients, among both HP users and non-users, were females which fitted into the general concept that females were twice more vulnerable to mental health disorders than males (McHenry et al., 2014; Kvrgic et al., 2013), or that they visited psychiatrists more often than males. It is known that ageing is associated with a reduction in susceptibility towards anxiety and depression (Jorm, 2000), thus our patients, the majority of which were younger than 60 years, fitted nicely into this concept. More than a half of patients that possessed a certain degree of knowledge on HP utilization acquired it from their families and friends, and this was a pronounced feature of the group of patients suffering from anxiety-related symptoms (Table 4). The only information source on HP and their efficacy and safety was an ethnopharmacological one, usually lacking any scientific back up. However, people all around the World are generally prone to accept advices coming from family and friends concerning the utilization of HP (Sekhri et al., 2013; Rivera et al., 2005; Kara, 2005). The actually used HP originated predominantly from pharmacy and herbal pharmacy shops, while only few patients were ready to turn to an herbalist or to identify/collect plant material by themselves (Table 5).

Statistically speaking, a significantly higher number of patients involved in this study lived in a city and these interviewees claimed to be using different HP, usually with a specific usage, in comparison to the interviewed people living in the country sides

of different regions of Serbia (Jarić et al., 2015; Zlatković et al., 2014; Šavikin et al., 2013; Jarić et al., 2007). This can possibly be explained by the fact that in Serbia a statistically significantly larger number of people live in cities, and that they have a higher education level and an easier internet access. It appears from that that, although not stated as the actual source of information in the interviews, new sources of information (media, among which, especially, the internet and TV) have an impact on the range of ethno-medical herbs to be utilized. Additionally, one might speculate that the people in need (psychiatric patients) are more familiar with such HP than the rest of the population, thus have more information concerning the narrow group of HP for the particular usage. Another outcome of this study, that additionally contributes to the opinion that ethno-medical herbs are being widely used and not forgotten, is the fact that more than 70% of the interviewed HP users were younger than 60 (Table 2).

All around the world, a great number of HP are being used for the treatment of non-psychotic symptomatology (anxiety, depression and insomnia) and one can expect that these HP overlap among different cultures. Generally speaking, the users themselves commonly use the following terminology connected with this specific usage of HP: "to calm the mind and positively enhance the mood" or refer to them as "nerve tranquilizers" or "nerve tonics". In this sense, a worldwide usage of Kava-kava (*Piper methysticum*), St. John's wort (*H. perforatum*), passion flower (*Passiflora incarnata*), valerian (*V. officinalis*) and gingko (*Ginkgo biloba*) is reported, while *Galphimia glauca* and chamomile (*M. recutita*) are used in the Mexican traditional medicine, *Astragalus membranaceus*, in the Korean ethnomedicine, as well as *Centella asiatica* and brahmi (*Bacopamon nieri*) among the people of India (Venkanna Rao et al., 2011). On the Balkan Peninsula, amongst the people of Serbia, several publications indicated that the usage of HP still exists and that, most certainly, it is not forgotten or completely replaced by standard drugs (Jarić et al., 2015; Zlatković et al., 2014; Šavikin et al., 2013; Jarić et al., 2007). The local people inhabiting the area of Suva planina mountain (southeastern Serbia) use a great number of plant species for the treatment of different ailments. For the treatment of mental illnesses, out of the nine found in the current study, three species were in common with the ones reported by Jarić et al. (2015) and these included: *H. perforatum*, *M. officinalis* and *V. officinalis*. Their usage covers a large

number of symptoms (insomnia, sedation, mood improvement, tonic and migraine management) that accompany different mental illnesses. Also, in a nearby region, Rtanj mountain (eastern Serbia), an ethno-botanical survey revealed 45 plants that are being used for medicinal purposes with *H. perforatum* as the most popular one (Zlatković et al., 2014). Besides *H. perforatum*, that is used as a stimulant, other taxa such as *Matricaria chamomilla*, *Melissa officinalis*, *Thlaspi praecox*, *Tilia cordata* and *Tilia platyphyllos* found their application as sedatives (Zlatković et al., 2014). In another part of Serbia, Zlatibor mountain region (western Serbia), six plant species are being used for the treatment of the nervous system and psyche diseases, where, out of 220 interviewed local people, 50 of them had the knowledge on the specific plants used for the treatment of mental disorders (Šavikin et al., 2013). The highlighted plant taxa, utilized in the form of an infusion (tea), encompassed: *H. perforatum*, *Lavandula angustifolia*, *Matricaria chamomilla*, *Melissa officinalis*, *Mentha × piperita* and *Thymus serpyllum*. The targeted symptomatology included insomnia, anxiety and moderate depression (Šavikin et al., 2013). In the Kopaonik mountain region (central Serbia), 7 different plant species (*H. perforatum*, *Leonurus cardiaca*, *Matricaria chamomilla*, *Melissa officinalis*, *Melittis melissophyllum*, *Mentha pulegium*, *Valeriana officinalis* and *Verbena officinalis*) were recommended as sedatives, nerve tonics and/or for the treatment of moderate depression, anxiety, insomnia, hysteria and nervousness (Jarić et al., 2007).

Almost 50% of the interviewed HP users used herbal products in combination with standard drugs prescribed by a psychiatrist; luckily, none of them experienced any serious life-threatening side effects during the usage of HP with/without standard drugs (Table 8). This kind of consumption of HP with standard drugs without a consultation with a physician, and/or psychiatrist in this case, could be quite dangerous and could lead to a serious HP-drug interaction. Namely, these interactions can be dangerous if St. John's wort is used in combination with a prescribed drug, which has the highest number of documented drug-HP interactions, among which those with warfarin, verapamil, digoxin, human immunodeficiency virus medicines, statins, immunosuppressants, SSRIs and benzodiazepines (Davis et al., 2014). While concerns exist over interactions of *H. perforatum* with pharmaceuticals, it should be noted that this mainly concerns high hyperforin extracts (Sarris et al., 2011). Thus, high-dose hyperforin extracts (>10 mg/day) caused CYP3A induction, while studies using low-dose hyperforin extracts (<4 mg/day) demonstrated no significant effect on CYP3A (Sarris et al., 2011). The interaction between *H. perforatum* and SSRIs results in symptoms characteristic of central serotonin excess, characterized by at least three of the following: confusion, agitation, hyperreflexia, diaphoresis, shivering or tremor, nausea, diarrhea, lack of co-ordination, fever, coma, flushing or rhabdomyolysis (Henderson et al., 2002).

Also, an undesirable combination of HP and a standard drug was found for: *V. officinalis* and loperamide (Di Lorenzo et al., 2015), *V. officinalis* and fluoxetine, where it caused delirium (Ernst, 2007), *V. officinalis* and diazepam or ethanol leading to insomnia, headache and hypotension (Consolini and Ragone, 2010). In the case of peppermint, *Mentha × piperita*, there are no HP-drug interactions reported in the literature up to now (EMA, 2008a,b,c), but it is worth mentioning that there are studies that provided us with the evidence that *Mentha × piperita* essential oil (1.2–3.9% in leaves) can influence the activity of several central nervous system (CNS) affecting drugs (phenobarbitone, codeine and midazolam) in mice (Samojlik et al., 2012). Also, an increased skin absorption rate of 5-fluouracil in the presence of peppermint oil was reported (EMA, 2008a,b,c). There are no data in the literature that disclose any interaction of *Melissa officinalis* extracts with neither drug metabolizing enzymes and receptors (Williamson, 2005), nor with any drugs (EMA, 2008a,b,c).

Herbal products reported in the current work were previously shown to possess numerous undesirable effects. A wide panel of CNS-related symptomatologies were documented as a consequence of St. John's wort utilization in the Australian population (Hoban et al., 2015). The usage of *Melissa officinalis* is known to cause hypotension and tachycardia that can possibly be attributed to GABA-mediated effects (Cuzzolin and Benoni, 2009). Valerian, *V. officinalis*, was reported to cause hepatotoxicity and fulminant hepatic failure (Di Lorenzo et al., 2015), while the application of *Thymus vulgaris* essential oil is known to cause an allergic reaction (contact dermatitis) and this hypersensitivity can be due to the presence of thymol in the oil (Cuzzolin and Benoni, 2009). In the case of peppermint, there are no evidences of any side effects during its consumption (EMA, 2008a,b,c); however, there are case reports of an acute intoxication with large amounts of peppermint oil (Nath et al., 2012).

5. Strengths and limitations of the study

The study was done with clinical patients, at the Clinical Center Niš, where the majority of people from several districts are gravitating towards, thus we can say that the sample of 136 patients could be adequate for this type of study (power analysis showed $\beta < 0.2$). This is among the first studies conducted on psychiatric patients from this region. An important strength of the study is the fact that the patients were interviewed by a single psychiatrist, thus reducing the interference or differences between interviews. One of the limitations of the study is the very nature of the cross-sectional study where one can only relay on patient's memory from the time of HP consumption. Also, the survey was conducted within a delicate population of patients, psychiatric ones, where there are several issues that need to be taken into consideration (readiness to speak freely, down play of HP use, current mental status, self-reporting, etc.) due to possible inaccuracies in their answers.

6. Conclusions

In general, one may say that a typical herbal-product user among non-psychotic psychiatric patients from southeastern Serbia is a middle aged married woman, with a secondary level of education, unemployed and living in an urban area. Our study revealed that non-psychotic psychiatric patients, although the majority of which do not live in rural areas, were familiar with a variety of ethno-medicines used in the Balkan region and that they are using herbal products quite often primarily without the consultation of their psychiatrists/physicians. The herbal products that were stated as being most frequently used for psychiatric symptoms included: *Melissa officinalis* (for all kinds of symptoms), *Hypericum perforatum* (for depression and combined anxiety/depression symptoms), *Mentha × piperita* (for anxiety and combined anxiety and depression symptoms) and *Valeriana officinalis* (for the treatment of anxiety symptoms). It is important to mention that, in our study, the interviewees rarely stated adverse reactions related to the usage of herbal products; however, this cannot be a general conclusion, since these herbal products are known to vary in the content of their adverse reaction-causing constituents.

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