



# Asian Journal of Scientific Research

ISSN 1992-1454

**science**  
alert  
<http://www.scialert.net>

**ANSI***net*  
an open access publisher  
<http://ansinet.com>



## Research Article

# Pharmacists' and Patients' Knowledge and Perceptions Regarding the Use of Herbal Treatments for Memory Impairment: A Cross-sectional Study from Jordan

<sup>1</sup>Reem Issa, <sup>2</sup>Iman Bashiti, <sup>2</sup>Lubna Abu-Khadejeh and <sup>2</sup>RulaTayeh

<sup>1</sup>Department of Pharmaceutical Sciences, Faculty of Pharmacy, Yarmouk University, P.O. Box 566, 21163 Irbid, Jordan

<sup>2</sup>Department of Clinical Pharmacy, Faculty of Pharmacy, Applied Science Private University, Amman, Jordan

## Abstract

**Background and Objectives:** Herbal treatments commonly used for memory impairment can slow its progression but there is no cure. Pharmacists play a role in prescribing such treatments to patients in need. This study was conducted to investigate the current use of herbal treatments and conventional drugs commonly dispensed by pharmacists in Amman, Jordan, for the management of patients diagnosed with memory impairment and second, to assess pharmacists' knowledge and patients' perceptions regarding the use of these treatments. **Materials and Methods:** Validated questionnaires were used to collect data from pharmacists and patients diagnosed with memory impairment. The questionnaires investigated the current use of herbal treatments and conventional drugs dispensed by pharmacists for the treatment of patients with memory impairment. The interests of the patients/pharmacists in such treatments were also investigated, in addition to their reported knowledge on the topic. **Results:** A major proportion of pharmacists and patients (66.6 and 72.8%, respectively) showed interest in herbal treatments but they were not fully confident about their use due to poor knowledge. Four herbal products and another 4 conventional drugs were found to be commonly dispensed by pharmacists for the management of patients suffering from memory impairment. The herbal products commonly used included *Panax ginseng* and *Ginkgo biloba*, in addition to other herbs, nutraceuticals and vitamins with antioxidant, anti-inflammatory and vaso-relaxing effects. **Conclusion:** The pharmacists providing patients with herbal treatments and conventional drugs for their memory loss conditions lacked knowledge on the topic as did the patients. University education needs to focus on the local community needs regarding herbal treatments to provide pharmacy students with a suitable level of knowledge with regard to herbal treatment use.

**Key words:** Memory loss, pharmacy education, ethnomedicine, Jordan, pharmacology

**Citation:** Reem Issa, Iman Bashiti, Lubna Abu-Khadejeh and RulaTayeh, 2019. Pharmacists' and patients' knowledge and perceptions regarding the use of herbal treatments for memory impairment: A cross-sectional study from Jordan. Asian J. Sci. Res., 12: 524-534.

**Corresponding Author:** Reem Issa, Department of Pharmaceutical Sciences, Faculty of Pharmacy, Yarmouk University, P.O. Box 566, 21163 Irbid, Jordan  
Tel: + 962 2 7211111/ +962797510797 Fax: + 962 2 7274725

**Copyright:** © 2019 Reem Issa *et al.* This is an open access article distributed under the terms of the creative commons attribution License, which permits unrestricted use, distribution and reproduction in any medium, provided the original author and source are credited.

**Competing Interest:** The authors have declared that no competing interest exists.

**Data Availability:** All relevant data are within the paper and its supporting information files.

## **INTRODUCTION**

Memory can be defined as the registration, retention and recollection of experiences, thoughts, feelings, sensations, ideas and knowledge, while memory loss is defined as unusual forgetfulness<sup>1</sup>. Memory problems can affect some or all of these processes. Some memory problems develop slowly or suddenly, while some are reversible, others are permanent<sup>2</sup>. The loss of memory is considered to be the result of a shortage of the neurotransmitter acetylcholine, which can be treated with acetylcholinesterase inhibitors<sup>3</sup>. In addition, increased oxidative damage is also commonly observed during normal brain aging and therefore, antioxidants are considered one of the promising agents in the treatment of neurodegenerative processes that are usually observed during normal brain aging<sup>4</sup>.

Herbal treatments with anti-inflammatory and antioxidant activities, such as German chamomile, ginseng, licorice, turmeric and white willow bark, may be useful in the treatment of memory disorders<sup>5</sup>. Many studies investigating the effect of individual natural supplements on brain activity have been conducted in Europe and in the United States<sup>6,7</sup>. Certain advanced memory formulations embodied by crucial combinations of ingredients have been indicated to be very promising in maintaining healthy memory and in providing optimal neuroprotection<sup>8,9</sup>.

In Jordan, dietary supplements and herbal products are commonly used for the treatment of different health conditions<sup>10</sup>. Of special interest is vitamin B12, which has been used extensively as a result of the high prevalence of vitamin B12 deficiency detected among Jordanians in the last decade<sup>11</sup>. Different psychological disorders, including memory-related problems, have been reported in Jordan and may be related to B12 deficiency<sup>12</sup>.

The objective of this study was to investigate the current status of the commonly prescribed herbal treatments dispensed by pharmacists to patients with memory impairments in Amman, the capital of Jordan, where access to pharmacy services is public and provided to all patients<sup>13</sup>. The secondary objective involved investigating the knowledge, attitudes and behaviors of pharmacists and their patients regarding the use of herbal treatments for memory loss.

## **MATERIALS AND METHODS**

**Study design area and period:** This cross-sectional study was conducted in Amman city, which is the capital of Jordan, between April and August, 2018. The study included all

community pharmacies located in Amman based on a list provided by the Jordanian Pharmaceutical Association. Randomly selected community pharmacies distributed between Eastern Amman and Western Amman were visited and invited to participate in this study. In addition, all patients visiting these pharmacies during the period of the study were randomly approached and invited to participate in the study. All study participants (pharmacists and patients) who agreed to participate provided verbal consent before study entry. Patients who were common customers at the recruited pharmacy, aged 18 years or over and who had been living in Jordan for over 1 year were eligible for study inclusion. Ethical approval for the study was obtained from the Applied Science Private University ethics research committee.

**Study variables:** Data were collected using 2 structured questionnaires, one for the pharmacists (Appendix A) and one for the patients (Appendix B). Each questionnaire was composed of 2 parts (part I and part II). The questions in part I aimed at assessing the participants' sociodemographic profiles, including age, sex, educational level and location and the number of years of experience for the pharmacists.

Part II was aimed at assessing participants' (pharmacists and patients) knowledge and perceptions of the use of herbal treatments for memory improvement. In addition, information regarding the source of knowledge about herbal treatments and the pharmacists' role in counseling patients suffering from memory impairment on the use of prescribed and non prescribed herbal treatments. The pharmacists' knowledge regarding the effectiveness and safety of the herbal treatments used by patients suffering from memory impairment was also explored.

**Data collection and management:** The 2 questionnaires were developed by the principal researchers, validated and used in this study. Both questionnaires included closed questions (using a 5-point Likert scale) and open-ended questions, the latter were used for reporting the treatments most frequently recommended/used by pharmacists/patients for the treatment of memory loss.

Each questionnaire underwent face validation following its review by expert researchers in the field. The questionnaire was also distributed to pharmacists (n = 10) and pharmacy students (n = 10) to assess its clarity. Based on the results of this pretest, necessary corrections were conducted before the final versions of the questionnaires were prepared.

Pharmacy students enrolled in the phytotherapy course at the Applied Science Private University for the year

2017/2018 (n = 60) were trained to assist in carrying out the data collection part of the study. Students attended a specialized workshop on herbal treatment use by patients suffering from memory impairment and on how to utilize the 2 questionnaires for data collection. Each student was requested to approach 10-15 pharmacists or patients.

**Data interpretation:** Following data collection, the herbal treatments and conventional medicines most frequently recommended/used by pharmacists/patients for the treatment of memory loss were reviewed, they were then evaluated in terms of their effectiveness and safety for improving poor memory conditions.

To complete this part of the study, peer-reviewed published clinical, *in vitro* and *in vivo* studies were reviewed.

**Sample size:** Based on the number of licensed pharmacies (2250) and the size of the population (2.600.000) in Amman, the sample size was calculated using a margin of error of 5%, a confidence level of 95% and a response distribution of 50%, a minimum of 327 pharmacies and 400 patients were needed.

**Statistical analysis:** The statistical analysis was performed using Statistical Package for Social Sciences (SPSS version 21, Chicago, IL, US). A descriptive analysis was carried out to determine the frequencies, means and SDs for the categorical variables. Statistical tests including one-way analysis of variance were conducted to determine the associations between sociodemographic variables and the knowledge/perception of the study participants regarding herbal treatments. In performing the statistical analyses, a p-value of 0.05 and a confidence interval of 95% were employed.

## RESULTS AND DISCUSSION

**Sociodemographic characteristics of the pharmacists:** Of the approached pharmacists in the study, 327 agreed to participate and complete the questionnaire (a response rate of 100%). Table 1 shows that the majority of respondents were males, with less than 5 years of working experience, living in Western Amman (higher socioeconomic areas of Amman) and mainly accessed single pharmacies that did not belong to any of the chain pharmacies currently found in Jordan. All pharmacists had a Bachelor of Pharmacy degree or higher and all were licensed as trained pharmacists.

**Sociodemographic characteristics of the patients:** A total of 239 out of the 400 patients who were approached agreed to

Table 1: Demographic characteristics of the pharmacists

Independent variables	Frequency (n = 440)	Percentage
<b>Age (years)</b>		
<25 (22-24)	65	14.8
25-34	225	51.1
35-44	89	20.2
45-54	40	9.1
<b>Sex</b>		
Male	227	51.6
Female	213	48.4
<b>Level of education</b>		
BSc. Pharmacy	382	86.8
BSc. Pharm-D	34	7.7
Higher education level	22	5.0
<b>Work experience</b>		
≤1 year	72	16.4
1≤5 years	153	34.8
5≤10 years	105	23.9
<b>Residential area</b>		
Western Amman	294	66.8
Eastern Amman	143	32.5
<b>Type of pharmacy</b>		
Single pharmacy	331	75.2
Chain pharmacy	109	24.8

participate and complete the questionnaire (a response rate of 59.7%). The majority of the patients were males (53.1%), Jordanians (62.3%) and residents of Western Amman (higher socioeconomic areas of Amman) (75.7%).

### Pharmacists' knowledge and practices toward the use of herbal remedies for memory loss:

Pharmacists were asked to assess their knowledge and practices about using herbal products for memory improvement (Table 2). The majority (66.6%) of the pharmacists evaluated their knowledge as average or good. Significant ( $p < 0.05$ ) effects for the duration of their study experience, their location and the type of pharmacy were found to influence their knowledge score.

Pharmacists were also asked about their preferences for using herbal products and conventional medicines. A higher proportion of pharmacists said they always or usually prefer conventional medicine (39.7%) over herbal products (17.1%) or the combination of conventional and herbal treatments (35.0%). They explained that their choices were based on their confidence and strong beliefs about the effectiveness of these treatments over herbal products. Nevertheless, pharmacists who chose herbal products as their preferred choice showed stronger beliefs in terms of the safety of these treatments at the expenses of their effectiveness. The cost of the treatment appeared to not influence their treatment choice.

When they were asked to assess their knowledge about potential herb-drug interactions, the majority (60.9%) of the pharmacists said that they had average or good knowledge,

Table 2: Cross tabulation of pharmacists' knowledge and practices toward herbal remedies used for memory loss based on the length of their work experience, residential area and type of pharmacy (n = 327)

Parameters	Frequencies (%)							
	Work experience (years)			Residential area		Type of pharmacy		Total
	>5	5-10	<10	EA	WA	Single	Chain	
<b>How do you rate your knowledge of using herbal products to improve poor memory?</b>								
Very good	13.0	16.0	23.0	15.4	14.3	13.6	17.4	14.5
Good	35.0	30.0	31.0	29.4	32.0	27.8	40.4	30.9
Average	29.0	42.0	30.0	37.8	34.7	37.2	31.2	35.7
Little	19.0	11.0	8.5	13.3	13.6	16.0	5.5	13.4
Few	4.0	1.0	7.5	4.2	5.4	5.4	5.5	5.5
p-value	0.003			0.020		0.009		
<b>Do you recommend that your patients use herbal products to treat poor memory instead of conventional medicines?</b>								
Always	15.7	16.2	12.0	16.1	11.9	4.2	3.7	4.1
Usually	33.3	25.7	33.3	28.7	32.7	13.9	10.1	13.0
Often	36.6	43.8	38.9	39.2	38.1	39.9	33.9	38.4
Seldom	11.1	12.4	10.2	12.6	13.3	29.3	37.6	31.4
Rarely	3.3	1.9	5.6	3.5	4.1	12.7	14.7	13.2
p-value	0.080			0.39		0.120		
<b>If your answer is usually to always, what is the reason?</b>								
More effective	24.2	27.6	37.0	28.7	25.5	25.7	30.3	26.8
Fewer side effects	67.3	61.0	59.3	65.0	66.3	66.2	64.2	65.7
Lower cost	8.5	11.4	3.7	6.5	8.2	8.2	5.5	7.0
<b>Do you recommend that your patients use conventional medicines to treat poor memory instead of herbal products?</b>								
Always	13.1	11.4	12.0	14.7	10.5	13.0	9.2	12.0
Usually	25.5	28.6	22.2	30.3	22.4	28.1	26.6	27.7
Often	32.0	29.5	35.2	35.0	28.6	29.0	35.8	30.7
Seldom	24.2	22.9	25.9	19.6	25.9	32.9	22.9	23.6
Rarely	5.2	7.6	4.6	8.4	4.8	6.0	5.5	5.9
p-value	0.730			0.417		0.558		
<b>If your answer is usually to always, what is the reason?</b>								
More effective	61.4	55.2	60.2	55.9	59.9	60.1	54.1	58.6
Fewer side effects	32.0	33.3	32.4	32.9	34.0	33.2	34.9	33.6
Lower cost	6.5	11.4	7.4	11.2	6.1	6.6	11.0	7.7
<b>Do you recommend that your patients use herbal products to treat poor memory in combination with conventional medicine?</b>								
Always	9.8	16.2	11.1	11.9	10.2	10.3	11.9	10.7
Usually	22.9	21.9	24.1	23.1	25.2	24.8	22.9	24.3
Often	36.6	27.6	26.9	29.4	30.3	29.3	31.2	29.8
Seldom	23.5	22.9	22.2	23.8	22.8	22.7	25.7	23.4
Rarely	7.2	9.5	15.7	11.9	10.9	12.7	7.3	11.4
p-value	0.526			0.457		0.578		
<b>If your answer is usually to always, what is the reason?</b>								
More effective	57.5	59.0	58.3	58.7	57.1	56.8	60.6	57.7
Fewer side effect	38.6	40.0	40.7	39.2	40.5	40.8	37.6	40.0
Lower cost	3.9	1.0	0.9	2.1	2.4	2.4	1.8	2.3
<b>How do you rate your level of knowledge about the potential herb-drug interactions?</b>								
Very good	7.2	6.7	10.2	4.9	8.5	6.0	11.0	7.3
Good	19.0	28.5	27.8	23.8	23.5	23.6	22.9	23.4
Average	39.2	39.0	35.2	42.7	35.0	35.3	44.0	37.5
Little	24.8	21.0	13.8	22.4	21.4	23.9	14.7	21.6
Few	9.8	4.8	13.0	6.3	11.6	11.2	7.3	10.2
p-value	0.071			0.108		0.027		
<b>If your answer is above average, what are the sources of your information?</b>								
Books	59.5	57.1	61.6	58.0	60.2	59.2	61.5	59.8
TV and radio	3.9	8.6	5.6	8.4	4.8	6.3	4.6	5.9
Medical rep	8.5	10.5	13.0	10.5	8.8	9.7	8.3	9.3
Internet	11.1	8.6	6.5	8.4	10.2	8.8	11.9	9.5
Medical colleagues	8.5	10.5	8.3	7.7	8.8	9.1	6.4	8.4
Social media	3.3	0.0	2.8	2.1	2.0	2.1	1.8	2.0
University requirement	5.2	4.8	2.8	4.9	5.1	4.8	5.5	5.0

Table 3: Cross tabulation of the patients' beliefs and behaviors toward the use of herbal treatments for memory loss based on their age and sex (n = 239)

Parameters	Frequencies (%)							
	Age groups (years)					Sex		Total
	18-24	25-34	35-44	45-54	<55	Male	Female	
<b>Do you suffer from poor memory?</b>								
Yes	36.4	23.0	22.4	47.2	68.0	33.9	34.8	34.3
p-value	0.000					0.876		
<b>Would herbal products be your first choice of treatment?</b>								
Yes	63.6	79.7	71.4	72.2	76.0	74.0	71.4	72.8
p-value	0.370					0.655		
<b>Do you believe that the method of preparation or use of herbal products may affect the effectiveness of the treatments?</b>								
Yes	76.4	70.3	67.3	69.4	52.0	70.1	67.9	69.0
p-value	0.301					0.712		
<b>From where would you buy the herbal product?</b>								
Pharmacy	81.8	79.7	81.6	69.4	72.0	74.8	82.1	78.2
Herbal shop	18.2	20.3	18.4	30.6	28.0	25.2	17.9	21.8
p-value	0.555					0.171		
<b>What is your main source of information for the use of herbal products?</b>								
Books	18.2	24.3	24.5	22.2	20.0	21.3	23.2	22.2
Internet	52.7	41.9	40.8	36.1	32.0	40.2	44.6	42.3
Pharmacists	23.6	28.4	26.5	30.6	32.0	29.1	25.9	27.6
Herbalists	5.5	5.4	8.2	11.1	16.0	9.4	6.3	7.9
p-value	0.615					0.310		
<b>If you do not prefer to use herbal products, what is the reason?</b>								
Weak effectiveness	70.9	67.6	77.6	66.7	72.0	70.0	70.5	70.8
High cost	7.3	23.0	20.4	27.8	16.0	19.7	17.9	18.8
Other	21.8	9.5	2.0	5.6	12.0	9.4	11.6	10.5
<b>Do you suffer from any chronic diseases?</b>								
Hypertension	3.6	8.1	26.5	38.9	48.0	26.0	12.5	19.7
Diabetes	1.8	5.4	10.2	16.7	28.0	10.2	8.9	9.6
Heart disease	1.8	1.4	10.2	11.1	12.0	5.5	6.3	5.9
Other	7.3	0.0	4.1	0.0	4.0	1.6	4.5	2.9
p-value	0.000					0.866		
<b>Did you inform your doctor/ pharmacist about your use of herbal products before they prescribed any medicines for you?</b>								
Yes	65.5	62.2	57.1	58.3	56.0	54.3	67.9	60.7
p-value	0.887					0.033		
<b>Have you suffered from any side effects that can be attributed to your use of herbal products?</b>								
Yes	20.0	23.0	24.5	25.0	20.0	16.5	29.5	22.6
p-value	0.971					0.017		

unfortunately, only a few (7.3%) said they had a very good amount of knowledge about the potential herb-drug interactions, with a significant effect between single and chain pharmacies. As such, these pharmacists were not capable of advising their patients on the use of herbal remedies with full confidence.

Pharmacists who indicated average, good or very good knowledge were asked about the source of their knowledge regarding herbal product use and their potential interactions with drugs. Unfortunately, only a few (5.0%) said they were educated at their universities (during their BSc. for pharmacy) as part of their phytochemistry, pharmacognosy and phytotherapy courses. The majority (59.8%) of pharmacists were seeking information using different textbooks. The rest of the pharmacists reported that they gained their knowledge

via different sources, including medical colleagues, medical representatives, searching on the internet and commercial advertisements on social media, TV and radio.

**Patients' beliefs and behaviors toward the use of herbal remedies for memory loss:**

Table 3 shows the patients' beliefs and behaviors toward the use of herbal treatments for memory impairment. As expected, many patients (34.3%) visiting their community pharmacies reported suffering from memory impairment, with significantly ( $p \leq 0.05$ ) higher percentages among older patients and no significant differences between the 2 sexes. The majority (72.8%) of these patients reported that they would prefer to use herbal treatments that are useful for their medical condition, with higher preferences shown among older and male patients.

A high proportion of patients (69.0%) were found to believe that the method of preparation or use of herbal treatments would influence the effectiveness of the treatment, which was especially true among the younger patients. Therefore, 78.2% of these patients would prefer to buy their herbal treatments from their community pharmacies rather than from the herbal shops. This was especially apparent among female patients.

Regarding the patients' source of knowledge on using herbal treatments, 42.3% of them declared that they depend on the internet, this was followed by the pharmacist and specialized textbooks and a minority of patients depended on the herbalist. By comparing both sexes, females and younger patients were found to depend more on the internet, while older and male patients were found to depend more on the pharmacist.

Nevertheless, 70.8% of the patients who reported a low preference for using herbal treatments revealed concerns about the effectiveness of the herbal products in treating their conditions, with only 18.8% reporting that the high cost of herbal treatments was the main limitation for their use.

Only 38.1% of the patients were previously diagnosed with chronic diseases, mainly hypertension, with a significant ( $p \leq 0.05$ ) difference shown among the age groups, chronic conditions were more prominent among older and male patients.

In answering the question of whether patients informed their pharmacists/doctors of their use of herbal treatments before requesting treatment for their chronic conditions, the majority of patients (60.7%) reported informing their healthcare provider, with significant variations ( $p \leq 0.05$ ) among the two sexes, this was specifically true among younger female patients.

A small proportion of patients (22.6%) reported experiencing side effects that could be attributed to their use of herbal treatments along with their conventional medications, all age groups showed similar experiences. Comparing the 2 sexes, 29.5% and 16.5% of the female and male patients, respectively, reported a low frequency of these interactions, with significant variations ( $p \leq 0.05$ ) among the 2 sexes.

**Evaluation of the available treatments commonly used for memory loss:** Pharmacists and patients were asked to report the most commonly used/prescribed herbal products and conventional medicine for the treatment of poor memory, the claimed effectiveness of these treatments was evaluated based on the available scientific evidence. A comprehensive list (Table 4) of these treatments was prepared, showing the

Table 4: Frequencies of commonly prescribed or recommended herbal treatments for memory improvement reported by study pharmacists and patients

Treatments	Use (%)	Scientific-based evidence	References
<b>Herbal products</b>			
<i>Ginkgo biloba</i>	75.70	Animal studies indicate beneficial effects Clinical studies reveal beneficial effects on healthy young people but not on elderly patients	Alimoradian <i>et al.</i> <sup>23</sup> , Chen <i>et al.</i> <sup>24</sup> Van Dongen <i>et al.</i> <sup>16</sup> , Van Dongen <i>et al.</i> <sup>15</sup> , Snitz <i>et al.</i> <sup>25</sup> Zhu <i>et al.</i> <sup>27</sup>
<i>Panax ginseng</i>	14.30	Animal studies show improvement in enhanced long-term memory	Ossoukhova <i>et al.</i> <sup>26</sup> , Scholey <i>et al.</i> <sup>29</sup>
Huperzine A	7.00	Clinical studies indicate a significant benefit on working memory and extending the age range of this effect to middle aged individuals Animal studies show a protective effect of huperzine A against memory deficits	Ohba <i>et al.</i> <sup>30</sup>
Olive oil	7.00	Preclinical studies show that huperzine A is a potentially safe AChE inhibitor Animal studies show a beneficial effect of olive oil on learning and memory deficits Cross-sectional studies find that moderate or intensive use of olive oil lowers the odds of cognitive deficits for verbal fluency and visual memory	Damar <i>et al.</i> <sup>41</sup> Pitozzi <i>et al.</i> <sup>24</sup> , Benton <i>et al.</i> <sup>25</sup> Berr <i>et al.</i> <sup>42</sup>
<b>Conventional medicine</b>			
Omega-3 and vitamin B12	62.00	A randomized clinical trial conducted in people with mild cognitive impairment finds that, when omega-3 levels are in the upper normal range, B12 vitamins interact to slow cognitive decline	Oulhaj <i>et al.</i> <sup>43</sup>
Omega-3	15.90	Animal studies reveal that omega-3 supplementation plays an important role in the central nervous system, preventing the progression of neuro inflammation and cognitive impairment linked to obesity or aging A double-blind placebo-controlled study provides clinical experimental evidence that supplementation with omega-3 fatty acids exert positive effects on memory functions in healthy older adults	De Andrade <i>et al.</i> <sup>44</sup> , Labrousse <i>et al.</i> <sup>45</sup> Külzow <i>et al.</i> <sup>46</sup>
Vitamin B12	13.60	Animal studies show that intrahippocampal microinjection of vitamin B12 improves memory impairments induced by scopolamine and orofacial pain in rats Short-term clinical trials only show B12 supplementation to be effective in improving cognition in those with preexisting deficiency	Erfanparast <i>et al.</i> <sup>47</sup> Denis <i>et al.</i> <sup>28</sup>
Acetyl-L-carnitine	5.00	Animal studies show that memory impairment is prevented by treatment with L-carnitine through antioxidant normalizing mechanisms in the hippocampus, neurodegeneration and cognitive deficits are ameliorated Meta-analysis of double-blind randomized controlled clinical trials of acetyl-L-carnitine versus placebo shows improvement in the treatment of mild cognitive impairment	Alzoubi <i>et al.</i> <sup>48</sup> , Singh <i>et al.</i> <sup>49</sup> Montgomery <i>et al.</i> <sup>50</sup>
Vitamin E	3.40	Animal studies show maximum learning ability and memory functions of vitamin E A randomized, double-blind, placebo-controlled trial concludes that long-term use of vitamin E supplements is not beneficial to cognitive and memory functions among generally healthy older women	Takatsu <i>et al.</i> <sup>51</sup> Kang <i>et al.</i> <sup>52</sup>

prevalence of their use (% frequency) and the reported evidence in the literature, if any was found (published *in vivo*, *in vitro* and clinical studies). These treatments were reported to exert different mechanisms of action and possess preventive or curing agents. The findings are summarized below:

- **Ginkgo biloba:** *Ginkgo* is known to exert vaso relaxing and antioxidant activities, in addition to many other different mechanisms that are still under investigation<sup>14,15</sup>. Clinical trials do not support the results from the *in vivo* studies, which showed that *Ginkgo biloba* had benefits for patients with dementia or age-associated memory impairment<sup>16</sup>. More recently, a systematic review and meta-analysis of the randomized controlled trials studying *Ginkgo biloba* concluded that it is potentially beneficial for the improvement of cognitive function and activities of daily living but the results need to be further confirmed by further clinical and pharmacological studies<sup>17</sup>
  - **Panax ginseng:** The clinical trials support the results from the *in vivo* studies, various animal and human studies have suggested that the active compounds obtained from *ginseng*, "ginsenosides" are neuroprotective and are an effective treatment for cognitive and memory performance enhancement through homeostasis-maintaining, anti-inflammatory, antioxidant, anti-apoptotic and immune-stimulatory activities<sup>18,19</sup>. In addition, *Panax ginseng*, which contains saponins, is reported to have memory-enhancing activity that is beneficial in patients with a learning impairment<sup>4</sup>
  - **Huperzine A:** Huperzine A improved learning and memory and was approved for treatment in Alzheimer's disease in China in 1996. Although *in vivo* studies have confirmed that Huperzine A is a highly effective and selective reversible inhibitor of acetylcholine esterase<sup>20</sup>, more clinical studies are still necessary to confirm the effectiveness and safety of the treatment
  - **Olive oil:** Despite the beneficial effects of olive oil on memory performance shown by *in vivo* studies and the traditional use of olive oil as a potential agent in preventing and treating neurodegenerative disorders<sup>21,22</sup>, a gap in the clinical research still needs to be filled by further research. Farr *et al.*<sup>23</sup> and Pitozzi *et al.*<sup>24</sup> suggested that olive oil has beneficial effects on the learning and memory deficits found in aging by reversing oxidative damage in the brain, the effects of olive oil are associated with its high content of polyphenols
  - **Vitamin B12:** B vitamins, especially B12 are known as memory vitamins that help the brain make and use neurotransmitters if given in combination with folic acid<sup>25,26</sup>. Both *in vivo* and clinical studies agree with the proposed beneficial effects of this vitamin on memory function deficiency. To date, short-term clinical trials have shown that B12 intake by better food selection, fortified foods or supplements may play a role in maintaining cognitive function in those who are at risk of developing B12 deficiency<sup>27</sup>
  - **Omega-3:** Experimental data in the literature indicate that omega-3 is involved in vital processes, such as neurotransmission, neuroprotection and neurogenesis that prevent brain aging<sup>28</sup>. While *in vivo* and clinical studies agree with the proposed beneficial effects of this vitamin on memory functions, a systematic review and meta-analysis<sup>29</sup> showed that there was only marginal evidence regarding the effects of omega-3 supplementation on cognition in those who are omega-3 deficient. The study showed no positive effects on healthy patients or patients with neuro developmental disorders
  - **L-acetylcarnitine:** L-acetylcarnitine is used to improve memory and studies have shown that it can facilitate the regeneration of nerves and can function as a cholinergic neurotransmitter, providing significant improvements in cognitive function, long- and short-term memory, mood and the response to stress<sup>26</sup>. While *in vivo* and clinical studies have shown the preventive effect of this nutraceutical on memory function, a well designed, randomized, placebo controlled trial of L-carnitine for cognition enhancement in cognitively healthy people, with large samples and relatively long term follow up, is still needed<sup>30</sup>
  - **Vitamin E:** Vitamin E has a neuroprotective effect caused by its antioxidant activity that can reverse aging complications in the brain of the healthy aging population<sup>31</sup>. Clinical investigations on the effect of vitamin E on memory do not completely agree with the *in vivo* studies. Supplementation with vitamin E and nutraceuticals (folic acid, B12, S-adenosylmethionine, N-acetyl cysteine and acetyl-L-carnitine) has been shown to improve memory and cognitive performance in community-dwelling adults without dementia<sup>32</sup>
- In this study, memory impairment conditions associated with the aging progress were usually treated with commonly used herbal treatments in Amman, Jordan. Despite the proven effectiveness of the herbal treatments used in this study, the



effects were limited to only 4 plant species. Most important were the *ginkgo* and *ginseng*-containing treatments as they were widely highlighted as promising herbal remedies that can be successfully used by patients suffering from memory impairment.

Despite the wide range of herbal treatments available for the treatment of memory loss, pharmacists could not provide their patients with herbal products suitable for the treatment of their memory loss as they were more confident about the effectiveness of conventional treatments. In addition, pharmacists showed moderate knowledge regarding the effective and safe use of the available herbal treatments, reporting the internet as their main source of information. In agreement with other previous similar studies, this study showed that most patients in Amman also depend on the internet to obtain their knowledge about herbal treatments, their second most used source of information was community pharmacists. In addition, the pharmacists rarely noticed any side effects that were correlated with the use of herbal treatments along with medications used for chronic conditions, which was also similar to the findings reported in previous studies<sup>10</sup>. These findings shed light on the need for improving the role of community pharmacists in providing their patients with trusted information rather than having them depend on the internet, which may be contaminated with inaccurate information as a source of knowledge. In this regard, pharmacy schools in the country can help resolve this issue by integrating more courses and educational strategies to increase the pharmacy students' knowledge of the herbal treatments available in the country. In addition, increasing patient awareness regarding the respected source of information in terms of herbal treatment use is urgently needed and may enhance patient confidence in using these treatments.

Pharmacists showed an interest in the use of herbs and other nutraceuticals directed at memory loss. Of special interest were *Ginkgo biloba* and *Panax ginseng*, both herbs were among the most commonly used herbs by the participating pharmacists. Similarly, these herbs are often featured in the lists of the most commonly purchased over the counter extracts in some Western countries (e.g., Germany, Sweden)<sup>53,54</sup>. A recent review showed that there was evidence in the literature that a single dose of Gincosan® (a combination between *Panax ginseng* and *Ginkgo biloba*) improved aspects of cognitive functioning beyond memory processes, indicating a synergistic relationship between its constituent parts<sup>55</sup>.

Even though many other herbal products are widely used in the country for the treatment of other ailments or as food

materials, they are currently highlighted for their effectiveness and safety in treating memory loss, unfortunately, they were not preferred by the pharmacists. These treatments, including *Matricaria recutita*, *Melissa officinalis*, *Curcuma longa*, *Salvia officinalis* and *Rosmarinus officinalis*, all have antioxidant, anti-inflammatory, anti-anxiety and anti-insomnia effects or they have inhibitory acetylcholinesterase effects<sup>56-60</sup>. Similarly, in a recent double-blind, randomized, placebo-controlled pilot study performed with subjects randomized into active and placebo groups, an oral preparation of sage, rosemary and melissa at a selected dose was found to be more effective than a placebo in treating verbal episodic memory in healthy subjects under 63 years of age during the period of administration<sup>61</sup>.

The main factor associated with the observed lack of knowledge and awareness regarding the available varieties of effective and safe herbal treatments that can be used for the treatment of memory impairment is that the majority of the pharmacists evaluated their knowledge about herbal treatments and herb-drug interactions as average or good. In addition, a high proportion of pharmacists said that they always or usually prefer conventional medicines based on their confidence in and strong beliefs about the effectiveness of these treatments over herbal products. Unfortunately, only a few of the pharmacists said that they were educated about their role in herbal medicine uses and practices during their university courses.

**Limitations and strengths of the study:** To the best of our knowledge, this is the first national study evaluating the community pharmacists' and patients' knowledge and perceptions regarding the available herbal treatments used for memory impairment.

One of the limitations of this study is that it was performed by pharmacy students who were not fully aware of the available herbal treatments at the community pharmacies. In addition, patients who participated in this study were suffering from memory loss and therefore, they were not fully confident about their abilities to recall the information needed to answer the study questions, suffering from memory impairment was one of the inclusion criteria in this study.

## CONCLUSION

This study provides evidence for a substantial interest in using herbal treatments for memory impairment among patients living in Amman, Jordan. In spite of the wide range of herbs available for the treatment of memory loss, pharmacists, unfortunately are able to provide their patients with only a few

herbal products for the treatment of memory loss as they revealed concerns about their effectiveness and reported only a moderate level of knowledge regarding the use of these herbal treatments. Therefore, pharmacy schools in the country are called to expand the content of their phytochemistry, phytotherapy and complementary medicine courses, in addition to their training strategies that target pharmacy students' knowledge of the herbal treatments available in the country. Moreover, academics at pharmacy schools need to play an essential role in revealing critical issues, which may turn into action plans that would largely influence patients' perceptions on the role of the community pharmacists as a trusted source of information and aim to increase patient awareness of the need to depend only on validated sources of information to obtain their knowledge regarding the use of herbal treatments.

### SIGNIFICANCE STATEMENT

This study revealed that a high proportion of patients suffering from memory impairment in Amman, Jordan are using herbal treatments. Unfortunately, the recommended herbal treatments are not all clinically proven. Such findings highlight the vital role of community pharmacists in increasing their patients' awareness of the possible health risks associated with the random use of these treatments. Therefore, health care sectors can increase such knowledge by conducting regular scientific lectures and providing workshops to the interested pharmacists'. The results from this study also emphasize the need for stronger regulations for the use and supply of the herbal medicine used to improve memory impairments in addition to increasing the knowledge and practice of herbalists for the safe and efficacious use of these treatments.

### ACKNOWLEDGMENT

The authors would like to thank the pharmacists, the patients and the students, who agreed to participate in this study and were very kind to give us their time. Special thanks go to Dr. Fayez Bassam Shriedeh for his aid in the statistical analysis performed on our data.

### REFERENCES

1. Worcman, K. and J. Garde-Hansen, 2016. Introduction: Human Memory as Intangible Heritage. In: Social Memory Technology: Theory, Practice, Action, Worcman, K. and J. Garde-Hansen (Eds.). Routledge, London, UK., ISBN-13: 9781315774732, pp: 13-32.
2. Small, G.W., 2002. What we need to know about age related memory loss. Br. Med. J., 324: 1502-1505.
3. Jayaprakasam, B., K. Padmanabhan and M.G. Nair, 2010. Withanamides in *Withania somnifera* fruit protect PC-12 cells from  $\beta$ -amyloid responsible for Alzheimer's disease. Phytother. Res., 24: 859-863.
4. Jivad, N. and Z. Rabiei, 2014. A review study on medicinal plants used in the treatment of learning and memory impairments. Asian Pac. J. Trop. Biomed., 4: 780-789.
5. Singhal, A.K., V. Naithani and O.P. Bangar, 2012. Medicinal plants with a potential to treat Alzheimer and associated symptoms. Int. J. Nutr. Pharmacol. Neurol. Dis., 2: 84-91.
6. Essa, M.M., M. Akbar and G. Guillemin, 2016. The Benefits of Natural Products for Neurodegenerative Diseases. 1st Edn., Springer International Publishing, Cham, Switzerland, ISBN: 978-3-319-28383-8, Pages: 496.
7. Ward, L. and G.M. Pasinetti, 2016. Recommendations for development of botanical polyphenols as "natural drugs" for promotion of resilience against stress-induced depression and cognitive impairment. NeuroMolecular Med., 18: 487-495.
8. Gorsek, W.F., 2003. Memory loss treatment formulation. U.S. Patent No. 6,572,899. U.S. Patent and Trademark Office, Washington, DC., USA. <https://patents.google.com/patent/US6572899B1/en>
9. Macpherson, H., K.A. Ellis, A. Sali and A. Pipingas, 2012. Memory improvements in elderly women following 16 weeks treatment with a combined multivitamin, mineral and herbal supplement. Psychopharmacology, 220: 351-365.
10. Issa, R.A. and I.A. Basheti, 2017. Herbal products use among chronic patients and its impact on treatments safety and efficacy: A clinical survey in the Jordanian field. Trends Med. Res., 12: 32-44.
11. Al-Amoush, A., Q. Abu Shaqra and R. Al-Groom, 2016. Evaluation of vitamin B<sub>12</sub> serum level in a group of Jordanian patients with type 2 diabetes mellitus. Pak. J. Nutr., 15: 561-564.
12. Al-Fararjeh, M.A., N. Jaradat and A. Aljamal, 2011. Deficiency of vitamin B12 among Jordanian people with psychological and biological activity. Afr. J. Biochem. Res., 5: 298-302.
13. Mukattash, T.L., N.H. Bazzi, K.Q. Nuseir, A.S. Jarab, R.K. Abu-Farha and M.R. Khmour, 2018. Pharmaceutical care in community pharmacies in Jordan: A public survey. Pharm. Pract., Vol. 16, No. 2. 10.18549/PharmPract.2018.02.1126
14. Gaiardo, R.B., T.F. Abreu, A.K. Tashima, M.M. Telles and S.M. Cerutti, 2018. Target proteins in the dorsal hippocampal formation sustain the memory-enhancing and neuroprotective effects of *Ginkgo biloba*. Front. Pharmacol., Vol. 9. 10.3389/fphar.2018.01533.

15. Zamberlam, C.R., N.C. Vendrasco, D.R. Oliveira, R.B. Gaiardo and S.M. Cerutti, 2016. Effects of standardized *Ginkgo biloba* extract on the acquisition, retrieval and extinction of conditioned suppression: Evidence that short-term memory and long-term memory are differentially modulated. *Physiol. Behav.*, 165: 55-68.
16. Van Dongen, M., E. van Rossum, A. Kessels, H. Sielhorst and P. Knipschild, 2003. Ginkgo for elderly people with dementia and age-associated memory impairment: A randomized clinical trial. *J. Clin. Epidemiol.*, 56: 367-376.
17. Yang, G., Y. Wang, J. Sun, K. Zhang and J. Liu, 2016. *Ginkgo biloba* for mild cognitive impairment and Alzheimer's disease: A systematic review and meta-analysis of randomized controlled trials. *Curr. Top. Med. Chem.*, 16: 520-528.
18. Cho, I.H., 2012. Effects of *Panax ginseng* in neurodegenerative diseases. *J. Ginseng Res.*, 36: 342-353.
19. Rokot, N.T., T.S. Kairupan, K.C. Cheng, J. Runtuwene and N.H. Kapantow *et al.*, 2016. A role of ginseng and its constituents in the treatment of central nervous system disorders. *Evidence-Based Complement. Altern. Med.*, Vol. 2016. 10.1155/2016/2614742.
20. Lian, W.W., A.L. Liu and G.H. Du, 2018. Huperzine A. In: *Natural Small Molecule Drugs from Plants*, Du, G.H. (Ed.). Springer, Singapore, ISBN: 978-981-10-8022-7, pp: 271-275.
21. Khalatbary, A.R., 2013. Olive oil phenols and neuroprotection. *Nutr. Neurosci.*, 16: 243-249.
22. Piroddi, M., A. Albini, R. Fabiani, L. Giovannelli and C. Luceri *et al.*, 2016. Nutrigenomics of extra-virgin olive oil: A review. *BioFactors*, 43: 17-41.
23. Farr, S.A., T.O. Price, L.J. Dominguez, A. Motisi and F. Saiano *et al.*, 2012. Extra virgin olive oil improves learning and memory in SAMP8 mice. *J. Alzheimers Dis.*, 28: 81-92.
24. Pitozzi, V., M. Jacomelli, D. Catelan, M. Servili and A. Taticchi *et al.*, 2012. Long-term dietary extra-virgin olive oil rich in polyphenols reverses age-related dysfunctions in motor coordination and contextual memory in mice: Role of oxidative stress. *Rejuvenation Res.*, 15: 601-612.
25. Benton, D., J. Fordy and J. Haller 1995. The impact of long-term vitamin supplementation on cognitive functioning. *Psychopharmacology*, 117: 298-305.
26. Smith, P.W., 2015. How to Maintain Memory at Any Age. In: *Anti-Aging Therapeutics*, Klatz, R. and R. Goldman, (Eds.). A4M American Academy of Anti-Aging Medicine ISBN 978-1-934715-19-2, United States, Pages: 574.
27. Moore, E.M., D.A.K. Watters, D. Ames and A.G. Mander 2015. Vitamin B12 and Cognitive Impairment. In: *Diet and Nutrition in Dementia and Cognitive Decline*, Colin R. Martin and Victor R. Preedy, (Eds.). Elsevier, pp: 637-648.
28. Denis, I., B. Potier, C. Heberden and S. Vancasse, 2015. Omega-3 polyunsaturated fatty acids and brain aging. *Curr. Opin. Clin. Nutr. Metab. Care*, 18: 139-146.
29. Cooper, R.E., C. Tye, J. Kuntsi, E. Vassos and P. Asherson, 2015. Omega-3 polyunsaturated fatty acid supplementation and cognition: A systematic review and meta-analysis. *J. Psychopharmacol.*, 29: 753-763.
30. Chen, N., M. Yang, M. Zhou, J. Xiao, J. Guo and L. He, 2017. L carnitine for cognitive enhancement in people without cognitive impairment. *Cochrane Database Syst. Rev.*, Vol. 3. 10.1002/14651858.CD009374.pub3.
31. Ulatowski, L.M. and D. Manor, 2015. Vitamin E and neurodegeneration. *Neurobiol. Disease*, 84: 78-83.
32. Chan, A., R. Remington, E. Kotyla, A. Lepore, J. Zemianek and T.B. Shea, 2010. A vitamin/nutraceutical formulation improves memory and cognitive performance in community-dwelling adults without dementia. *J. Nutr. Health Aging*, 14: 224-230.
33. Alimoradian, A., S. Ghasemi, M. Zahiri, A.H. Saeedi, H. Miladi and M. Sadegh, 2018. Investigation of the effect of Ginkgo biloba leaf extract on spatial memory impairment and hippocampal neuronal loss caused by diabetes induced by streptozotocin in rats. *Sci. J. Kurdistan Univ. Med. Sci.*, 23: 114-124.
34. Chen, L.E., F. Wu, A. Zhao, H. Ge and H. Zhan, 2016. Protection efficacy of the extract of *Ginkgo biloba* against the learning and memory damage of rats under repeated high sustained +Gz exposure. *Evidence-Based Complementary Altern. Med.*, Vol. 2016. 10.1155/2016/6320586.
35. Kennedy, D.O., A.B. Scholey and K.A. Wesnes, 2000. The dose-dependent cognitive effects of acute administration of *Ginkgo biloba* to healthy young volunteers. *Psychopharmacology*, 151: 416-423.
36. Snitz, B.E., E.S. O'Meara, M.C. Carlson, A.M. Arnold and D.G. Ives *et al.*, 2009. *Ginkgo biloba* for preventing cognitive decline in older adults: A randomized trial. *JAMA.*, 302: 2663-2670.
37. Zhu, G., Y. Wang, J. Li and J. Wang, 2015. Chronic treatment with ginsenoside Rg1 promotes memory and hippocampal long-term potentiation in middle-aged mice. *Neuroscience*, 292: 81-89.
38. Ossoukhova, A., L. Owen, K. Savage, M. Meyer and A. Ibarra *et al.*, 2015. Improved working memory performance following administration of a single dose of American ginseng (*Panax quinquefolius* L.) to healthy middle-age adults. *Hum. Psychopharmacol.: Clin. Exp.*, 30: 108-122.
39. Scholey, A., A. Ossoukhova, L. Owen, A. Ibarra and A. Pipingas *et al.*, 2010. Effects of American ginseng (*Panax quinquefolius*) on neurocognitive function: An acute, randomised, double-blind, placebo-controlled, crossover study. *Psychopharmacology*, 212: 345-356.
40. Ohba, T., Y. Yoshino, M. Ishisaka, N. Abe and K. Tsuruma *et al.*, 2015. Japanese *Huperzia serrata* extract and the constituent, huperzine A, ameliorate the scopolamine-induced cognitive impairment in mice. *Biosci. Biotechnol. Biochem.*, 79: 1838-1844.

41. Damar, U., R. Gersner, J. T. Johnstone, S. Schachter and A. Rotenberg, 2017. Huperzine A: A promising anticonvulsant, disease modifying and memory enhancing treatment option in Alzheimer's disease. *Med. Hypotheses*, 99: 57-62.
42. Berr, C., F. Portet, I. Carriere, T.N. Akbaraly and C. Fearnt *et al*, 2009. Olive oil and cognition: Results from the three-city study. *Dement. Geriat. Cogn. Disord.*, 28: 357-364.
43. Oulhaj, A., F. Jernerén, H. Refsum, A.D. Smith and C.A. de Jager, 2016. Omega-3 fatty acid status enhances the prevention of cognitive decline by B vitamins in mild cognitive impairment. *J. Alzheimers Dis.*, 50: 547-557.
44. De Andrade, A.M., M. da Cruz Fernandes, L.S. de Fraga, M. Porawski, M. Giovenardi and R.P. Guedes, 2017. Omega-3 fatty acids revert high-fat diet-induced neuroinflammation but not recognition memory impairment in rats. *Metab. Brain Dis.*, 32: 1871-1881.
45. Labrousse, V. F., A. Nadjar, C. Joffre, L. Costes and A. Aubert *et al*, 2012. Short-term long chain omega3 diet protects from neuroinflammatory processes and memory impairment in aged mice. *Plos One*, Vol. 2012.10.1371/journal.pone.0036861.
46. Külzow, N., A.V. Witte, L. Kerti, U. Grittner, J. P. Schuchardt, A. Hahn and A. Flöel, 2016. Impact of omega-3 fatty acid supplementation on memory functions in healthy older adults. *J. Alzheimers Dis.*, 51: 713-725.
47. Erfanparast, A., E. Tamaddonfard and S. Nematj, 2017. Effects of intra-hippocampal microinjection of vitamin B12 on the orofacial pain and memory impairments induced by scopolamine and orofacial pain in rats. *Physiol. Behav.*, 170: 68-77.
48. Alzoubi, K.H., A.M. Rababa'h, A. Owaisi and O.F. Khabour, 2017. L-carnitine prevents memory impairment induced by chronic REM-sleep deprivation. *Brain Res. Bull.*, 131: 176-182.
49. Singh, S., A. Mishra, N. Srivastava, R. Shukla and S. Shukla, 2018. Acetyl-L-carnitine via upregulating dopamine D1 receptor and attenuating microglial activation prevents neuronal loss and improves memory functions in parkinsonian rats. *Mol. Neurobiol.*, 55: 583-602.
50. Montgomery, S.A., L.J. Thal and R. Amrein, 2003. Meta-analysis of double blind randomized controlled clinical trials of acetyl-L-carnitine versus placebo in the treatment of mild cognitive impairment and mild Alzheimer's disease. *Int. Clin. Psychopharmacol.*, 18: 61-71.
51. Takatsu, H., K. Owada, K. Abe, M. Nakano and S. Urano, 2009. Effect of vitamin E on learning and memory deficit in aged rats. *J. nutr. sci. vitaminology*, 55: 389-393.
52. Kang, J.H., N. Cook, J. Manson, J.E. Buring and F. Grodstein, 2006. A randomized trial of vitamin E supplementation and cognitive function in women. *Arch. Internal Med.*, 166: 2462-2468.
53. Isah, T., 2015. Rethinking *Ginkgo biloba* L.: Medicinal uses and conservation. *Pharmacogn. Rev.*, 9: 140-148.
54. Patel, S. and A. Rauf, 2017. Adaptogenic herb ginseng (*Panax*) as medical food: Status quo and future prospects. *Biomed. Pharmacother.*, 85: 120-127.
55. Reay, J.L., P. van Schaik and C.J. Wilson, 2019. A systematic review of research investigating the physiological and psychological effects of combining *Ginkgo biloba* and *Panax ginseng* into a single treatment in humans: Implications for research design and analysis. *Brain Behav.*, Vol. 9, No. 3. 10.1002/brb3.1217.
56. Antikolinesteraz, A.H.T.P. and B.K.O.L.F. Bitkileri, 2014. Lamiaceae family plants as a potential anticholinesterase source in the treatment of Alzheimer's disease. *Bezmialem Sci.*, 1: 1-25.
57. Duke, J.A., 2007. The garden pharmacy: Rosemary, the herb of remembrance for Alzheimer's disease. *Altern. Complementary Ther.*, 13: 287-290.
58. Patel, K.C., S. Pramanik and V.C. Patil, 2014. Ayurvedic approach with a prospective to treat and prevent alzheimers and other cognitive diseases. *World J. Pharm. Pharm. Sci.*, 3: 234-252.
59. Pengelly, A., J. Snow, S.Y. Mills, A. Scholey, K. Wesnes and L.R. Butler, 2012. Short-term study on the effects of rosemary on cognitive function in an elderly population. *J. Med. Food*, 15: 10-17.
60. Tang, S.W., W.H. Tang and B.E. Leonard, 2017. Herbal medicine for psychiatric disorders: Psychopharmacology and neuroscience-based nomenclature. *World J. Biol. Psychiatry*. 10.1080/15622975.2017.1346279
61. Perry, N.S.L., R. Menzies, F. Hodgson, P. Wedgewood and M.J.R. Howes *et al*, 2018. A randomised double-blind placebo-controlled pilot trial of a combined extract of sage, rosemary and melissa, traditional herbal medicines, on the enhancement of memory in normal healthy subjects, including influence of age. *Phytomedicine*, 39: 42-48.