






RESEARCH ARTICLE

REVISED Pharmacy practitioners' practice, awareness and knowledge about herbal products and their potential interactions with cardiovascular drugs [version 2; peer review: 2 approved]

Previously titled: Pharmacy practitioners' attitudes and practice towards herbal products in Jordan: Exploring their knowledge about herbal products potential interactions with cardiovascular medications

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v2 First published: 08 Aug 2022, 11:912
<https://doi.org/10.12688/f1000research.121709.1>

Latest published: 22 Sep 2022, 11:912
<https://doi.org/10.12688/f1000research.121709.2>

Abstract


Background: Herbal medicine use is widespread among patients, as community pharmacies may provide such products. Therefore, pharmacy practitioners should be aware of potential herbal products' adverse effects and herb-drug interactions, particularly with medications for comorbid diseases, such as cardiovascular drugs, in which pharmacy practitioners need to have good knowledge to provide patients with relevant advice to get optimal and safe therapeutic outcomes. Accordingly, the study is designed to assess the knowledge and awareness of pharmacy practitioners regarding herbal product dispensing and cardiovascular drug interaction in Jordan and view their role in patients' counselling to set up safe and effective drug use.


Methods: A cross-sectional study was conducted in Jordan using an online formatted questionnaire distributed to pharmacy practitioners working in community pharmacies. Descriptive and analytical statistics were performed for the responses using the Statistical Package for the Social Sciences (SPSS) software, version 26.

Results: Out of 508 participants, 41.7% had medium knowledge of herbal products pertaining mainly to university education (68.1%); 55.1% of participants dispensed herbal products without prescriptions for obesity and weight reduction (72.8%) and gastrointestinal problems (70.9%); this is because respondents agreed that herbal

Open Peer Review

Approval Status  

	1	2
version 2		
(revision)		
22 Sep 2022		
version 1		
08 Aug 2022		

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remedies are safe (28.5%) and effective (38.4%). Whilst the knowledge level of respondents about herbal medicine interaction with cardiovascular medication was medium, with a mean of 1.94, as this interaction may result in potentially serious consequences, 40.7% of respondents strongly agreed to gain more knowledge about the side effects of herbal products and medicine interactions through educational courses.

Conclusions: The pharmacy practitioners had medium knowledge of herbal products; however, more attention should be paid to herb-drug interactions in the pharmacy educational curriculum. Additionally, pharmacy practitioners need to refresh their knowledge by attending periodic educational courses and by using reliable resources for information about herbal products in order to provide effective and competent pharmaceutical care.

Keywords

Herbal products, Pharmacy practitioner, Knowledge, Practice, Herb-cardiovascular drug interaction

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Competing interests: No competing interests were disclosed.

Grant information: The author(s) declared that no grants were involved in supporting this work.

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How to cite this article: Abudalo R, Abudalo R, Alqudah A *et al.* **Pharmacy practitioners' practice, awareness and knowledge about herbal products and their potential interactions with cardiovascular drugs [version 2; peer review: 2 approved]** F1000Research 2022, 11:912 <https://doi.org/10.12688/f1000research.121709.2>

First published: 08 Aug 2022, 11:912 <https://doi.org/10.12688/f1000research.121709.1>

REVISED Amendments from Version 1

The title was changed "Pharmacy practitioners" practice, awareness and knowledge about herbal products and their potential interactions with cardiovascular drugs.

In the end of introduction, a paragraph about Jordan's context that clarifies the research gap was added as follows:

Several studies have been conducted in Arab countrieshas been documented by other study conducted in Jordan⁶

In the introduction, line 42 and 49, two references were added.

In the study design and data collection section, a paragraph about study design was added as follows:

This survey was designed by the investigators based on previous studiespotential cardiovascular drug-herb interactions⁷⁻¹⁰

In the methods, line 14 and line 15, seven references were added.

In the methods, line 19, inclusion criteria were added as: We included the pharmacy practitioners in community pharmacies and excluded those who working in other places

In the methods, a paragraph about how the survey tool was developed and how the questionnaire is validated was added as follows:

A structured questionnaire was created for the purpose of this study, and was validated by a group of experts constituted of two pharmacologists, Phytochemist, cardiologist, and pharmacist.

Piloting of the questionnaire was performedThe CVI were ranged from 0.8-0.9 and it was deemed that the scale was valid.

In the methods, "the data normality was checked using Kolmogorov-Smirnov test" was added.

In the results, table 2 was amended.

In the results, figure 2 was amended.

In the 'Respondents' practice and knowledge of herbal products in community pharmacies section, majority was changed by more than third, and minority was changed to by lowest percent of respondents.

Any further responses from the reviewers can be found at the end of the article

Introduction

The consumption of herbal products has dramatically increased globally.¹ This is due to widespread self-drug administration among populations, as these products are safe, have minimum adverse effects, are inexpensive, and have better compatibility and cultural acceptability.^{2,3} Additionally, manufacturers use different methods for their marketing strategies, such as various forms of media, which has increased consumer awareness of herbal products.⁴ Nevertheless, the use of herbal products, either alone or in combination with other conventional products, without informing physicians or pharmacy practitioners may lead to detrimental clinical outcomes.

Herbal product use is common in Arab countries, including Jordan.⁵ They are available at community pharmacies as registered prepackaged products. Notably, patients use conventional drugs concurrently with herbal products for the treatment of various conditions,⁶ as they are easily purchased without a prescription. However, this has gained significant attention due to the potential risk of drug-herb interactions, as some herbs may mimic, increase, or decrease the action of conventional drugs, which is important to consider with drugs that have a narrow therapeutic index, such as warfarin or digoxin.⁷ Consequently, investigating the safe use of herbal products is considered a major priority.

Herb-drug interactions are based on either pharmacokinetic or pharmacodynamic mechanisms.⁸ Herbal products may alter drug absorption (e.g., pectin reduces lovastatin absorption),⁹ drug metabolism (e.g., St. John's wort might increase warfarin metabolism, thus decrease its efficacy),¹⁰ or drug renal excretion (e.g., digoxin renal excretion is increased by St. John's wort).¹¹ Furthermore, such interactions may have an additive or synergistic effect. For example, aspirin's antiplatelet effect is enhanced by ginkgo biloba.¹² On the other hand, some herbal products may antagonize the action of some drugs. For example, green tea can antagonize the anticoagulant effect of warfarin as green tea contains small amounts of vitamin K, which may alter warfarin's action.¹³

The prevalence of cardiovascular diseases has increased worldwide.¹⁴ Most affected patients have been prescribed anticoagulants, antiplatelets, digoxin, antihypertensives, and antihyperlipidemic agents, which may have a synergistic or antagonistic interaction with herbal products, consequently raising patients' morbidity and mortality risks.^{10,15} Therefore, the use of herbal products should not be initiated without careful consideration of possible drug-herb interactions.

Since pharmacists are the connection between the patient and effective drug utilization, they are the primary attainable health care practitioners¹⁶ and they receive a greater number of queries about drugs.¹⁷ Therefore, they play a pivotal role in advising patients and fostering an awareness of the safe, proper, and rational use of herbal products.¹⁸ Nevertheless, to advise patients properly, pharmacists must have considerable knowledge about herbal products' therapeutic indications, doses, side effects, and potential interactions with conventional products. Inadequate knowledge about herbal products may result in potentially severe adverse events.

Several studies have been conducted in Arab countries to assess pharmacists' knowledge and attitudes towards herbal products.^{19–22} In Jordan, the prevalence and awareness of herbal products used among pharmacy staff have been measured, revealing that pharmacists' awareness about herbal products was good. However, their knowledge of the adverse effects of herbal products and drug interactions were inadequate²³ which is concerning. Additionally, no studies have focused on Jordanian pharmacy practitioners' knowledge and awareness towards herb-drug interactions particularly with cardiovascular drugs, which are commonly used in Jordan. Therefore, the present study's investigators strive to increase attention to pharmacy practitioners regarding herb-drug interaction, especially where it may lead to toxic manifestations. Likewise, the investigators seek to reinforce the need for periodic education programs for pharmacy practitioners that are focused on herbal product indications, side effects, and drug interactions, with a view to refresh their knowledge so that they can provide competent and holistic and health care, since this has been documented by other studies conducted in Jordan.²⁴

The present study was therefore conducted to assess the attitudes, awareness, and dispensing practices of pharmacy practitioners regarding the safe use of herbal drugs, as well as assess their knowledge of potential herbs interactions with cardiovascular drugs.

Methods

Ethical considerations

The study was approved by the Institutional Review Board (IRB) of The Hashemite University, Jordan, with IRB approval code 4/10/2020/2021 that was granted on the 9th of May 2021.

Sample size

According to the [Raosoft online calculator](#) (Raosoft),^{25,26} and as mentioned by Taherdoost,²⁷ the minimum recommended sample size would be 384 respondents at a 95% confidence interval and a 5% margin of error. However, to increase the sample generalizability, a sample size of 508 was collected.

Study design and data collection

This survey was designed by the investigators based on previous studies related to pharmacists' knowledge about herbal products,^{19,21,22} along with extensive literature reviews of the existing clinical data of potential cardiovascular drug-herb interactions.^{11,15,28,29}

The study was a cross-sectional survey carried out via an anonymous online questionnaire created with Google Forms to obtain the study's objectives. The web-based questionnaire was distributed across multiple locations in Jordan through Facebook and WhatsApp applications by the study panel members. We included pharmacy practitioners in community pharmacies and excluded those who working in other areas.

Respondents provided written informed consent statement at the beginning of the questionnaire to decide whether they were willing to participate in the study or not. They were informed that their participation was voluntary and anonymized for research purposes and that the data was kept confidential to overcome any self-report bias. Moreover, no specified group was targeted and no leading questions were included in the questionnaire. The sample's diversity might add validity and rigor to the obtained results in this study. Eligible respondents are pharmacy practitioners aged 20 years and older, with either a diploma, bachelor or postgraduates' education level in pharmacy. Data collection was performed between 11th June 2021 till 9th September 2021.

A structured questionnaire was created for the purpose of this study, and was validated by a group of experts constituting two pharmacologists, Phytochemist, cardiologist, and pharmacist.

Piloting of the questionnaire was performed to assess the accuracy and comprehension of the questions in relation to the research topic, and to identify possible redundancy. The knowledge scale, as well as the opinions and beliefs towards herbal products scale were calculated and showed an excellent reliability with a Cronbach's alpha coefficient of 0.791, and 0.788 respectively, indicating a high internal consistency among the items. However, responses completed during the piloting phase were excluded from the final analysis.

The knowledge scale was assessed for validity by examining the content validity index (CVI). Five experts were consulted for their opinion on each scale item including clarity, simplicity and relevancy, which were scored from 1 (strongly disagreed), 2 (disagreed), 3 (agreed) and 4 (strongly agreed). Questions were tested/re-tested for their clarity and simplicity by interviewing 20 participants. The CVI ranged from 0.8-0.9 and it was deemed that the scale was valid.

The questionnaire was designed to have four domains. The first part consisted of demographic information, such as gender, age (minimum of 20 years old), level of education (with at least diploma education), and practicing years. The second part was concerned with pharmacy practitioners' practice and attitudes towards herbal remedies in pharmacies, which were determined via participants choosing any of these responses: always, usually, frequently, and rarely. The third part assessed pharmacy practitioners' knowledge of the interactions between herbal products, such as ginseng, ginger, ginkgo biloba, cranberry, and St John's wort, with cardiovascular drugs. Respondents' level of knowledge was assessed by 3-point Likert scale options: 'correct', 'incorrect', or 'I don't know'.

To determine the minimum and maximum length of a 3-point Likert scale, the range is calculated by $(3-1 = 2)$, then divided by three, which is the greatest value of the scale $(2 \div 3 = 0.66)$; one is the least value in the scale. Therefore, the scale length is as follows:

- (2.34–3.00) is a high score on the Likert scale, indicating a high level of respondents' knowledge and experience regarding herb-drug interaction.
- (1.67–2.33) is a medium score on the Likert scale, indicating a medium level of respondents' knowledge and experience regarding herb-drug interaction.
- (1.00–1.66) is a low score on the Likert scale, indicating a low level of respondents' knowledge and experience regarding herb-drug interaction.
- Finally, the fourth part of the questionnaire assessed pharmacy practitioners' opinions and beliefs towards herbal products dispensed in community pharmacies using a five-point Likert scale³⁰ with responding options: (1) strongly disagree; (2) disagree; (3) neutral; (4) agree; (5) strongly agree. The minimum and maximum length of the 5-point Likert scale is calculated by $(5 - 1 = 4)$, then divided by five, which is the greatest value of the scale $(4 \div 5 = 0.80)$; one is the least value in the scale. Therefore, the scale length is as follows:
 - (4.20–5.00) represents a very high score on the Likert scale, indicating a very high level of respondents' attitudes and perceptions.
 - (3.40–4.19) represents a high score on the Likert scale, indicating a high level of respondents' attitudes and perceptions.
 - (2.60–3.39) represents a medium score on the Likert scale, indicating a medium level of respondents' attitudes and perceptions.
 - (1.80–2.59) represents a low score on the Likert scale, indicating a low level of respondents' attitudes and perceptions.
 - (1–1.79) represents a very low score on the Likert scale, indicating a very low level of respondents' attitudes and perceptions.

The final question in part four was concerned with respondents' attitudes regarding ending conventional drug use while using herbal products. Since the questionnaire was simple, it was completed by the respondents without loss of any reading items.

Statistical analysis

The data were analyzed using the **Statistical Package for Social Sciences** version 26 (SPSS 26). Percentages and frequencies of responses were calculated for each question. Moreover, mean and standard deviation were calculated for respondents' practice towards herbal products as well as respondents' opinions on the use and dispensing of herbal products in pharmacies in order to allow for the objective measure of opinion and provide a basis for comparison. Notably, one-way ANOVA F-test analysis was used to identify the variables' relation and dependency by testing the equality of means. A P-value of <0.05 was considered statistically significant. Data normality was checked using a Kolmogorov–Smirnov test.

Results

Pharmacy practitioners' characteristics

A total of 508 pharmacy practitioners from various regions in Jordan responded to the study.⁷⁷ The demographic responses are shown in **Table 1**. Females responded to the questionnaire more than males (72.2% versus 27.8%). Respondents aged between 20 and 29 years old accounted for the highest frequency at 89.8% (456 out of 508). The respondents had varying degrees of education, with the majority having a bachelor's degree in pharmacy, at 90.1% (458 out of 508). Further, they had varying years of experience in practice with 259 of the respondents (51%) having 1 to 5 years of experience, while 1.8% of respondents had more than 20 years of experience. The demographic data are illustrated in **Table 1**.

Respondents' practice and knowledge of herbal products in community pharmacies

According to pharmacy practitioners' practice towards herbal products, the respondents reported that there is a medium demand for customers to buy herbal products (36.2%), and 55.1% of respondents said that herbal products are mainly dispensed without prescription due to consumers' preferences towards self-drug administration (**Table 2**). Notably, the most common herbal products were dispensed for obesity and weight reduction (72.8%) and gastrointestinal disorders (70.9%), whilst 3.7% and 3.1% of herbal products were dispensed for hyperlipidemia and central nervous system disorders respectively, as shown in **Table 2**.

When respondents were asked about their knowledge pertaining to herbal products, more than a third (41.7%) reported that they had medium knowledge about herbal products in their pharmacies, while only 2% reported that they had very good knowledge (**Figure 1**). Regarding medical and pharmaceutical information they had available about herbal products, more than two-thirds of the respondents (68.1%) relied on university education during their pharmacy study

Table 1. Socio-demographic characteristics of respondents.

Variable	Categorization	Frequency	Percent
Gender	Male	141	27.8
	Female	367	72.2
Age	From 20 – 29 Years	456	89.8
	From 30 – 39 Years	36	7.1
	From 40 – 49 Years	2	0.4
	From 50 – 59 Years	14	2.8
	60 Years and above	-	-
Education level	Diploma	20	3.9
	Bachelor of Pharmacy	458	90.2
	Bachelor's Pharm. D	15	3
	Postgraduate	15	3
Years of experience	Less than 1 Year	15	3
	From 1 – 5 Years	259	51
	From 6 – 10 Years	216	42.5
	From 11 – 15 Years	7	1.4
	From 16 – 20 Years	2	0.4
	Above than 20 Years	9	1.8

Table 2. Pharmacy practitioners’ practice towards herbal remedies in community pharmacies.

Variable	Categorization	Percent
Herbal preparations sold more	Prescription	44.9
	Without a prescription	55.1
Is there a demand for herbal products	Weak	30.1
	Medium	36.2
	High	32.3
For which of these chronic diseases does the consumer ask to buy herbal products	Obesity	72.80%
	Digestive problems	70.90%
	Diabetes	41.50%
	Kidney and urinary system diseases	32.30%
	Other diseases	26.20%
	Respiratory problems	7.90%
	Hypertension	6.10%
	Hyperlipidemia	3.70%
	Central nervous system problems	3.10%

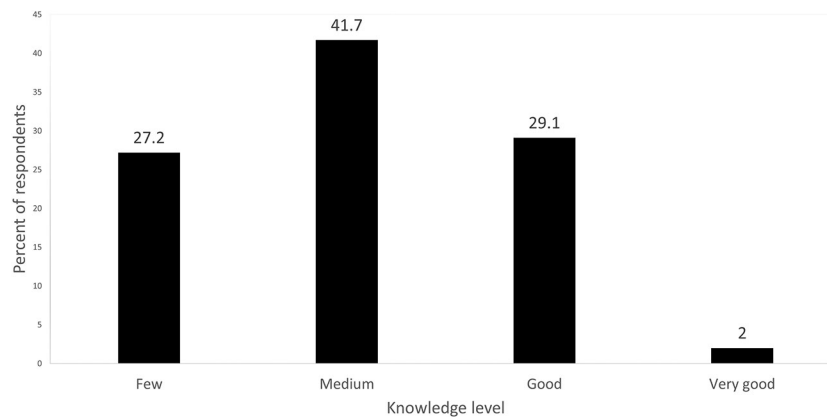


Figure 1. Respondents’ knowledge level regarding herbal products sold in pharmacies.

years as their source of knowledge. Other findings showed that 66.1% and 65.9% of pharmacy practitioners relied on websites and their colleagues (pharmacists and physicians) to find the required information about herbal products, respectively. Meanwhile, others mentioned that they obtained their knowledge from herbal products’ package instructions (63.4%) or from pharmaceutical firms’ medical representatives (6.7%), whilst the lowest percent of respondents (3.7%) obtained their information from books. The data are shown in [Figure 2](#).

In terms of the pharmacy practitioners’ current practicing attitudes towards herbal product dispensing, the results showed that 38.6% of respondents usually informed the patient about the condition or medical conditions in which the herbal preparations were used. A total of 35.4% and 35.8% of the respondents usually informed the customer about medical conditions that may make herbal preparations unsafe and drugs that may interact adversely with herbal preparation, respectively ([Table 3](#)). However, when the respondents were asked about the perceived obstacles in discussing the use of herbal remedies with patients in community pharmacies, the majority (89.4%) answered that there was a lack of sufficient or reliable sources supporting the proper and safe use of herbal products, while 82.9% of respondents acknowledged that they had limited interest in herbal product therapy. Likewise, 65% of respondents confessed they had inadequate knowledge about herbal products, which may hinder their herbal products counselling ([Table 4](#)). Therefore, pharmacy practitioners need to be vigilant and knowledgeable about herbal products. This is achieved by providing resources

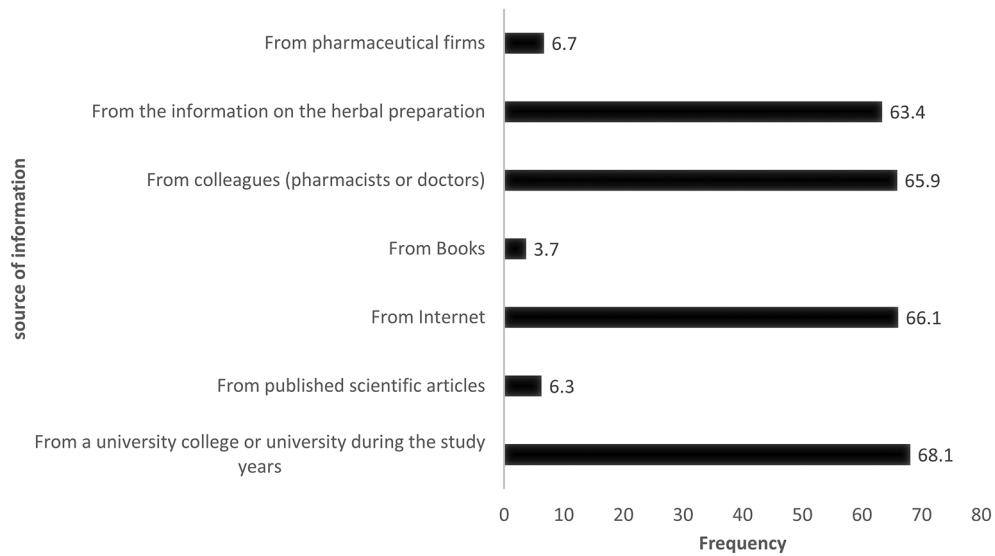


Figure 2. Source of information about herbal products.

Table 3. Pharmacy practitioners’ practicing attitudes towards herbal product dispensing in community pharmacies.

Practicing attitudes towards herbal products dispensing	Answer alternatives								Mean	Standard Deviation
	Always		Usually		often		Rarely			
	Freq	%	Freq	%	Freq	%	Freq	%		
The patient has been informed about medical conditions for which the herbal preparations can be used	146	28.7	196	38.6	155	30.5	11	2.2	2.939	0.826
The patient has been informed about medical conditions that may make herbal preparations unsafe	172	33.9	180	35.4	133	26.2	23	4.5	2.986	0.885
The patient has been asked about any other products he or she uses to avoid drug interactions with herbal preparation	171	33.7	182	35.8	130	25.6	25	4.9	2.982	0.889

Table 4. Factors impeding the discussion of herbal products use with patients.

Variable	Frequency	Percent
Does not care about the topic	421	82.9
Lack of knowledge about herbal products	330	65
Lack of sufficient or reliable resources about herbal products, their side effects and/or drug interaction	454	89.4
Others	19	3.7

Table 5. Pharmacy practitioners' knowledge about herbs and cardiovascular drugs interaction.

Herb and cardiovascular drug interaction	Answer alternatives				Mean	Standard Deviation	Level	References		
	Correct		Incorrect						I don't know	
	Freq	%	Freq	%					Freq	%
Ginkgo biloba can increase the bleeding tendency of warfarin or aspirin	204	40.2	153	30.1	151	29.7	1.90	0.833	Medium	31,32
Ginkgo biloba can decrease the antihypertensive effects of thiazide diuretics	147	28.9	200	39.4	161	31.7	2.10	0.821	Medium	33
Ginkgo biloba can increase the effectiveness of calcium channel blockers	149	29.3	200	39.4	159	31.3	2.02	0.824	Medium	10
Garlic can increase the anticoagulant effect of warfarin	205	40.4	137	27	166	31	1.92	0.810	Medium	34
Ginger can increase the risk of bleeding when combined with warfarin	203	40	169	33.3	136	26.8	1.87	0.854	Medium	35
Green tea can decrease the anticoagulant action of warfarin	177	34.8	175	34.4	156	30.7	1.96	0.833	Medium	36,37
Evening primrose can increase the risk of bleeding tendency of warfarin, aspirin or clopidogrel	185	36.4	198	39	125	24.6	1.88	0.869	Medium	38
St John's wort may increase blood digoxin level	194	38.2	177	34.8	137	27.0	1.88	0.855	Medium	39
Cranberry may increase warfarin's anticoagulant effect	168	33.1	186	36.6	154	28.5	1.97	0.835	Medium	40
Turmeric can increase the blood level of warfarin and clopidogrel	183	36	180	35.4	145	35.4	1.93	0.846	Medium	41
Senna may increase digoxin toxicity	188	37	171	33.7	149	29.3	1.97	0.841	Medium	15
Ginseng may decrease warfarin anticoagulant effect	186	36.6	176	34.6	146	28.7	1.92	0.845	Medium	42
Coenzyme Q-10 can decrease the effectiveness of warfarin	179	35.2	127	33.9	157	30.9	1.92	0.832	Medium	43
Total							1.94	-	Medium	

Table 6. Sociodemographic variables' association with pharmacy practitioners' overall knowledge on herbal product-cardiovascular drugs interaction.

Variable	Source of variance	Df	Mean square	F	Sig (p value)
Age	Between Groups	3	14.853	3.161	0.024
	Within Groups	504	4.699		
	Total	507			
Education level	Between Groups	3	30.728	6.674	0.000
	Within Groups	504	4.604		
	Total	507			
Years of experience	Between Groups	5	12.152	2.594	0.025
	Within Groups	502	4.685		
	Total	507			

DF, degrees of freedom, *p*, significant value ($p < 0.05$).

regarding available herbal products, as well as by continuing education programs focused on safety and potential herb-drug interactions.

Pharmacy practitioners' knowledge about herbal products and cardiovascular drug interaction

Regarding pharmacists' experiences with interactions of herbal products and cardiovascular drugs, the participants were asked 13 questions to evaluate their knowledge level (Table 5). It was observed that they had a medium level of knowledge (mean = 1.94), with an average of 35.4% correct answers where they recognized the possible herb and cardiovascular drug interaction, as reported in the literature. The results shown in Table 5 exhibit that an average of 35% of pharmacy practitioners were unaware of the selected herb and cardiovascular drug interaction, and 29.6% didn't know about the herb-drug interaction.

Regarding the association between pharmacy practitioners' overall knowledge on herbal product-cardiovascular drug interaction and sociodemographic variables, one way ANOVA results established a significant relationship of age ($F [3, 504] = 3.161, p = 0.024$), years of experience ($F [5, 502] = 2.594, p = 0.025$), and educational level ($F [3, 504] = 6.674, p = 0.000$) on pharmacy practitioners' overall knowledge levels (Table 6). Respondents aged between 50 to 59 had a higher level of knowledge about herb and cardiovascular drug interactions than respondents aged between 20 to 29 and those aged between 30 to 39 (LSD post hoc, $p = 0.003, 0.045$, respectively). Meanwhile, postgraduate respondents scored a higher knowledge level compared to respondents with a bachelor's degree (LSD post hoc, $p = 0.000$). According to work years of experience, pharmacy practitioners who had greater than 20 years of experience had a significantly higher overall knowledge score about herb-drug interactions than those who had 1 to 5 and those who had 6 to 10 years of work experience (LSD post hoc, $p = 0.02, 0.012$, respectively). Unexpectedly, respondents who had less than one year of experience showed a higher overall knowledge in comparison to those with 6 to 10 years of experience (LSD post hoc, $p = 0.03$).

Pharmacy practitioners' opinions and beliefs regarding the use and dispensing of herbal products in community pharmacies

When respondents were asked about their opinions on herbal product use and dispensing, the level of the use and dispensing of herbal products in pharmacies was high, with mean ranges of 3.69–4.15 and a general mean of 3.92. Exactly 38.4% of respondents agreed that herbs are effective, with a mean of 3.90 and a standard deviation of 0.804, while 28.5% and 32.3% agreed that herbal products are safe, with fewer adverse effects and with limited drug interactions, respectively. Additionally, 43% of respondents in this study strongly agreed they need to gain more knowledge about herbal products, their side effects and drug interactions, through educational courses and training programs in order to be more highly qualified for better pharmaceutical care services. The results are displayed in Table 7.

Regarding respondents' attitudes regarding stopping the use of conventional products when using herbal products, 36.6% found that it depends on whether there are any drug interactions, 25% believed conventional drugs should not be stopped, and 17.5% answered that patients should stop using traditional products. All opinions are summarized in Figure 3.

Discussion

Herbal product use has increased tremendously, both globally as well as in Arab countries,^{19,44} including Jordan.^{5,45,46} It has been reported that 80.2% of the general population use herbal products in Jordan⁴⁷; herbal remedies are favored by

Table 7. Pharmacy practitioners' opinions on the use and dispensing of herbal products in pharmacies.

Use and dispensing of herbal products in pharmacies	Answer alternatives										Mean	Standard deviation	Level
	Strongly agree		Agree		Neutral		Disagree		Strongly disagree				
	Freq	%	Freq	%	Freq	%	Freq	%	Freq	%			
Herbal products are effective and able to improve the health of patients	133	26.2	195	38.4	175	34.4	4	0.8	1	0.2	3.90	0.804	High
Herbal products are safe and have fewer side effects as they are natural	158	31.1	145	28.5	171	33.7	27	5.3	7	1.4	3.83	0.978	High
Herbal products are safe and have limited drug interactions	143	28.0	164	32.3	156	30.7	38	7.5	7	1.4	3.78	0.983	High
Herbal products are always available at reasonable prices	124	24.4	156	30.7	182	35.8	40	7.9	6	1.2	3.69	0.965	High
The need for medical personnel to gain more knowledge about herbal products	219	43.1	151	29.7	136	26.8	-	-	2	0.4	4.15	0.844	High
The importance of providing courses to workers on the use of herbal products, their side effects and product interactions	207	40.7	163	32.1	136	26.8	-	-	2	0.4	4.13	0.834	High
Total											3.92	-	High

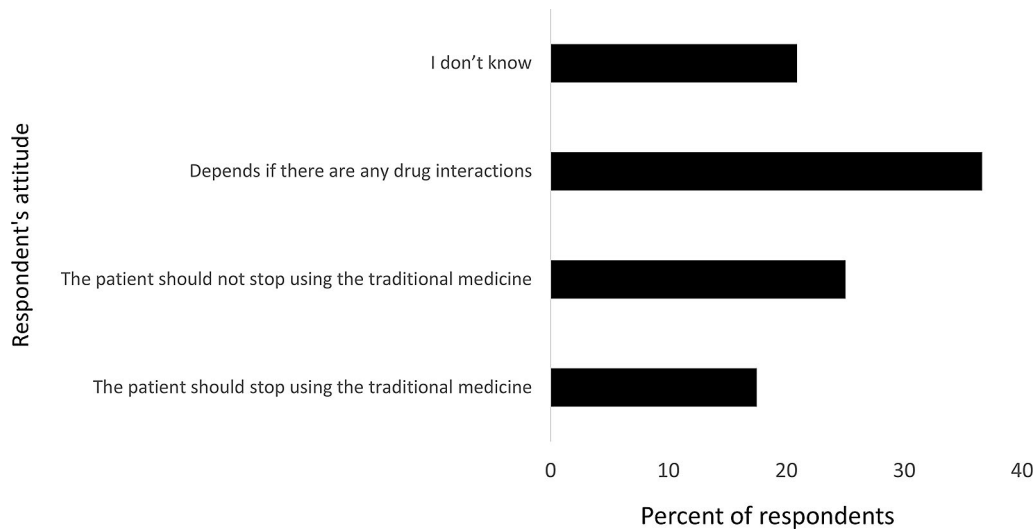


Figure 3. Pharmacy practitioners' attitudes toward stopping the use of conventional drugs while using herbal products.

individuals, as evidenced by previous studies, because they are natural and, consequently, safe. Meanwhile, herbal products have good efficacy and low cost.^{48,49}

Knowledge and awareness of drug-herb interactions are substantial for delivering safe and effective drug therapy. Although herbal products are natural and, therefore, safe,⁵⁰ some herbal products can affect P-glycoprotein drug transporters, cytochrome P450 enzymes, and other metabolic enzymes⁵¹; this may result in potential drug interactions, particularly with narrow window drugs, if they are taken simultaneously,⁵² which can result in life-threatening consequences and can increase health care costs. Recent studies have demonstrated serious interactions between herbal remedies and drugs used in cardiovascular diseases.^{11,29,53} Therefore, this study was the first conducted in Jordan to assess the knowledge and awareness of pharmacy practitioners concerning the interaction of herbal products and cardiovascular drugs.

This study revealed that more than half of respondents dispensed herbal remedies without a prescription,⁵⁴ specifically for the treatment and control of different illnesses, mainly gastrointestinal problems,^{23,55} obesity,⁵⁶ and diabetes.²³ Notably, respondents had medium knowledge about herbal products, which was mainly gained from university during their years of study, where they were exposed to herb-related academic courses in the pharmacy curriculum.⁵⁷ Other respondents chose websites, product leaflets and took advice from other colleagues or medical representatives as sources of information about herbal products.⁵⁸ A large proportion of respondents also relied on the internet to gain knowledge about herbal products; however, media and internet information are not often supervised by a medical or pharmaceutical institution to ensure the accuracy of the information. It has been reported that the knowledge of Missouri pharmacists regarding herbal products was determined by the familiarity of the pharmacists with resource accessibility rather than resource quality.⁵⁹ Thereby, providing access to authenticated resources, in addition to offering educational programs for pharmacy practitioners about herbal products, is strongly needed.

Despite pharmacy practitioners' knowledge about herbal products, they usually informed patients about herbal products indications, interactions with conventional drugs, and conditions that make herbal products unsafe.⁵¹ Nevertheless, not caring about herbal products being available in community pharmacies impedes pharmacy practitioners from discussing the use of herbal products with consumers when they purchase or ask about them.⁶⁰ This suggests that pharmacy practitioners should be aware about their role in guiding the safe and effective use of herbal products via better communication with patients.⁶¹ Additionally, other barriers that could impede pharmacy practitioners and have a considerable influence on discussing herbal remedies are having a lack of knowledge or lack of authoritative resources about herbal products.^{62,63} To facilitate patients' acquisition of adequate herbal product counselling, pharmacy practitioners' education programs and training should be implemented to ascertain the awareness of herbal product counselling and consolidate the provided professional pharmaceutical care services.^{24,64} Because the prevalence of cardiovascular diseases has increased dramatically in Jordan,⁶⁵ this may expand the number of patients' taking multiple cardiovascular drugs in addition to herbal remedies. Some herbal products may have adverse cardiovascular effects, whilst others may interact with cardiovascular drugs, such as ginseng, ginkgo biloba, St. John's wort, garlic, and induce serious

consequences. For example, patients taking anticoagulants, such as warfarin, should avoid the use of ginseng and ginkgo biloba, as they can increase warfarin's anticoagulant effect, thereby increasing the risk of bleeding.⁶⁶ Green tea may antagonize warfarin's anticoagulant effect,⁶⁷ therefore reducing warfarin's effectiveness.

St. John's wort may induce the activity of cytochrome P450 isoenzymes CYP1A2, CYP3A4, and CYP2C9⁶⁸; thus, it may reduce the plasma concentration of co-drugs like digoxin,³⁹ simvastatin,⁶⁹ and warfarin,⁷⁰ which may reduce their therapeutic efficacies. It has been reported that a patient who had used aspirin for five years experienced eye bleeding after the addition of ginkgo biloba self-drug administration for one week.⁷¹ Therefore, pharmacy practitioners should be vigilant regarding patient counselling on herbal-drug interactions if they are used concurrently with cardiovascular drugs to achieve the intended therapeutic outcomes and minimize health complications.

This study has revealed that pharmacy practitioners' overall knowledge score about herbal product interactions with cardiovascular drugs significantly differs based on their age, education level, and years of experience. It was expected that older pharmacy practitioners with more years of work experience and a higher educational level attained would demonstrate a higher overall knowledge score. Unexpectedly, respondents with less than one year of work experience had a significantly higher knowledge score compared to respondents who had 6 to 10 years' experience. One possible explanation is that they are newly graduated and have taken courses related to herbal products recently in their studies, as shown in [Figure 2](#), given 68.1% of the respondents relied on their university study courses to gain information about herbal products.

Moreover, postgraduate education is correlated with more educational courses being studied, which might be relevant to herbal products. Whilst previous studies have not specifically demonstrated the impact of demographic factors on pharmacy practitioners' knowledge about herbal product interactions with traditional drugs, they have established that age, education level, and experience (year) influence their general knowledge related to herbal products.⁶⁴ Regarding the findings of pharmacy practitioners' practice on the use and dispensing of herbal products, 38.4% agreed that herbal products are effective in improving patient's health,⁷² 32.3% agreed they are safe and have limited drug interactions,⁵¹ whilst 43.1% strongly agreed they need more knowledge about herbal products, which could be achieved by providing courses to workers on the use of herbal products, their side effects, and product interactions. Therefore, educational courses on herbal products are mandatory.⁷³ However, their attitudes about stopping conventional drug while using herbal products were positive if there were any drug interactions (36.6%), whilst others said patients should not stop using conventional products (25%).⁷⁴ Patients with chronic diseases who use herbal remedies without informing their physicians, or even physicians who do not guide patients about using these products, may increase potential drug-herb interactions, particularly cardiovascular drugs, which induce detrimental health complications.⁷⁵ Therefore, a lack of counselling that warns patients about the risk of inappropriate consumption of herbal products will aggravate the condition. Pharmacy practitioners thus play a pivotal role in ensuring patients adhere to the safe use of herbal remedies.

In summary, pharmacy practitioners having good knowledge is compulsory for good practice.⁷⁶ It is essential for pharmacy practitioners to broaden their knowledge pertaining to the adverse effects of herbal products and drug-herb interactions to provide the desired pharmaceutical care to patients, which can be achieved by identifying reliable information resources about herbal products, attending mandatory educational courses on herbal product dispensing in community pharmacies, and advising patients when they are seeking herbal products. All of these recommendations will equip them for good practice, thus, implementing pharmaceutical care services to ascertain the rational and appropriate use of drugs.

Conclusion

The interaction between cardiovascular drugs and herbal products is potentially significant, particularly with narrow therapeutic index drugs. Because herbal products are more often dispensed as over-the-counter drugs, and since pharmacy practitioners in this study have shown medium knowledge about herb-drug interactions, it is crucial to increase their awareness and knowledge regarding herbal products via educational programs focused on herb indications, drug interactions, and adverse effects. Additionally, it is important for the Jordan Pharmacists Association to provide reliable resources. The association plays an important role in collaboration with pharmacy colleges at all Jordanian universities, as pharmacy practitioners in community pharmacies are the main accessible health care providers.

Consent

Respondents provided written informed consent.

Data availability

Underlying data

Open Science Framework: Pharmacy Practitioners' attitudes and practice towards herbal products in Jordan: Exploring their knowledge about herbal products potential interactions with cardiovascular drugs. <https://doi.org/10.17605/OSF.IO/752DA>.⁷⁷

The project contains the following underlying data:

- Knowledge and awareness of Herbal Products and dietary supplements xlsx (respondents' responses were coded for SPSS software)
- questionnaire.docx (pharmacy practitioners' attitude and practice towards herbal products as English version)
- Raw data.sav (respondents' responses to the questionnaire)

Data are available under the terms of the [Creative Commons Attribution 4.0 International license](https://creativecommons.org/licenses/by/4.0/) (CC-BY 4.0).

Acknowledgements

The authors would like to thank all the respondents for their participation and support in this study.

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Current Peer Review Status:  

Version 2

Reviewer Report 28 September 2022

<https://doi.org/10.5256/f1000research.138508.r151163>

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Banaz Jalil 

Pharmacognosy and Phytotherapy, UCL School of Pharmacy, London, UK

Thanks for the revised manuscript! The authors have addressed the reviewer's comments in their response and manuscript revisions. Therefore, I have no further comments.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Social and Pharmaceutical Sciences, Medicinal Plants Research, Pharmacy Practice and Research Policy.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 23 September 2022

<https://doi.org/10.5256/f1000research.138508.r151162>

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Muna Barakat 

Faculty of Pharmacy, Applied Science Private University, Amman, Jordan

Thank you for addressing the comments. From my side, it looks better and is suitable for indexing in its current form.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Pharmacy Practice and clinical pharmacy

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 01 September 2022

<https://doi.org/10.5256/f1000research.133604.r146934>

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Banaz Jalil 

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Thanks for the review invitation. The authors surveyed pharmacists' knowledge of herbal products and their awareness of potential interactions with conventional medicines in Jordan (e.g., cardiovascular medications). An online questionnaire was used in this study. In total, 508 participants have completed the study. The overall knowledge scores about herbal product interactions with cardiovascular medications differed based on the participant's age, education level, and years of experience. I believe the following areas could be strengthened before indexing:

1. The title is wordy, so it would be good to revise it.
2. Please use consistent terms to refer to herbal medicines, herbal products and/or herbs throughout the manuscript, preferably reflecting the terms used in the survey. The same goes for the terms 'medications and drugs'. Also, 'Participants and Respondents'.
3. Instead of using the term 'herbal product-drug interaction', please use 'herb-drug interactions throughout the manuscript.
4. Please add a paragraph on how the survey tool was developed, was it based on previous studies or developed by the authors? Please cite other studies if pre-validated questionnaires were used. If developed by the authors, then how was it validated?
5. Table 2, it will be better if you list the results (either by frequency or %) from high to low.
6. In the 'Respondents' practice and knowledge of herbal products in community pharmacies' section, it's better to use two-thirds, a quarter, half etc., to refer to the participants' responses rather than the majority and/or minority.
7. Finally, although the manuscript is clear and well written, editing is needed, especially for the introduction, method, and results sections. There is also some repetition in these areas.

So, I would suggest proofreading the manuscript.

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Social and Pharmaceutical Sciences, Medicinal Plants Research and Pharmacy Practice.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 10 Sep 2022

Abdelrahim qudhah, The Hashemite University, Zarqa, Jordan

We would like to thank you for the invested time and effort in carefully reviewing our manuscript. We are grateful for giving us the opportunity to revise our manuscript. Your comments were very useful and helped us in improving our manuscript. After careful consideration of the comments, the revision included many positive changes as suggested.

C1: The title is wordy, so it would be good to revise it.

R1: Thank you for your comment. Title was amended as follows: "Pharmacy practitioners' Practice, awareness and knowledge about herbal products and their potential interactions with cardiovascular drugs."

C2: Please use consistent terms to refer to herbal medicines, herbal products and/or herbs throughout the manuscript, preferably reflecting the terms used in the survey. The same goes for the terms 'medications and drugs'. Also, 'Participants and Respondents

R 2: Thank you for your comment. Terms were amended as:

- Herbal medicines term was replaced by herbal products.
- Medications term was replaced by drugs.
- Participants term was replaced by Respondents

C 3: Instead of using the term 'herbal product-drug interaction', please use 'herb-drug interactions throughout the manuscript.

R 3: Thank you for your comment. 'herbal product-drug interaction' was amended as 'herb-drug interactions.

C 4: Please add a paragraph on how the survey tool was developed, was it based on previous studies or developed by the authors? Please cite other studies if pre-validated questionnaires were used. If developed by the authors, then how was it validated?

R4: Thank you for your comment Kindly find this paragraph. A structured questionnaire was created for the purpose of this study, and was validated by a group of experts constituted of two pharmacologists, Phytochemist, cardiologist, and pharmacist.

Piloting of the questionnaire was performed to assess the accuracy and comprehension of the questions in relation to the research topic, and to identify possible redundancy. The knowledge scale as well as opinions and beliefs towards herbal products scale were calculated and showed an excellent reliability with a Cronbach's alpha coefficient of 0.791, and 0.788 respectively indicating a high internal consistency among the items. However, responses completed during the piloting phase were excluded from the final analysis.

The knowledge scale was assessed for validity by examining the content validity index (CVI). Five experts were consulted for their opinion for each scale item including clarity, simplicity and relevancy and scores from 1 (strongly disagreed), 2 (disagreed), 3 (agreed) and 4 (strongly agreed). Questions were tested/re-tested for their clarity and simplicity by interviewing 20 participants. The CVI were ranged from 0.8-0.9 and it was deemed that the scale was valid.

C5: Table 2, it will be better if you list the results (either by frequency or %) from high to low.

R5: Thank you for your comment, table 2 has been amended.

C6: In the 'Respondents' practice and knowledge of herbal products in community pharmacies' section, it's better to use two-thirds, a quarter, half etc., to refer to the participants' responses rather than the majority and/or minority.

R6: Thank you for your comment, Words have been amended as: 'Majority is replaced by more than third, minority is replaced by lowest percent of respondents.

C7: Finally, although the manuscript is clear and well written, editing is needed, especially for the introduction, method, and results sections. There is also some repetition in these areas. So, I would suggest proofreading the manuscript.

R7: Thank you for your comment. The manuscript is now proofread by Ryan Gibson Proofreading Services in UK.

Competing Interests: No competing interests were disclosed.

Reviewer Report 18 August 2022

<https://doi.org/10.5256/f1000research.133604.r146933>

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Muna Barakat 

Faculty of Pharmacy, Applied Science Private University, Amman, Jordan

Thank you for inviting me to review this work, "Pharmacy practitioners' attitudes and practice towards herbal products in Jordan: Exploring their knowledge about herbal products potential interactions with cardiovascular medications". This manuscript discusses a very important research area; hence, Jordanians believe herbal medicine is a safe replacement for chemical medications. So, it is worth it to investigate the KAP of the practitioners towards herbs.

I believe this work is suitable for indexing after addressing the comments:

Title:

- In my opinion, the title could be rephrased comprehensively, for example, "Pharmacists' Knowledge, Practice and awareness about herbal products and their potential interactions with cardiovascular medications"

Introduction:

- I believe you need to add a small paragraph about Jordan's context, and clarify the research gap.

Methods:

- Add the inclusion criteria, please.

Statistical analysis:

- You need to add if you have checked the data normality and the used test.

Results:

- Figure 2, no need to add "From" before each source of information and reorder them according to percentages.
- Table 3. I believe it is important to calculate the overall mean of attitude, to express the level

of attitude concisely.

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Pharmacy Practice and clinical pharmacy

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response 10 Sep 2022

Abdelrahim qudhah, The Hashemite University, Zarqa, Jordan

We would like to thank you for the invested time and effort in carefully reviewing our manuscript. We are grateful for giving us the opportunity to revise our manuscript. Your comments were very useful and helped us in improving our manuscript. After careful consideration of the comments, the revision included many positive changes as suggested.

C1: In my opinion, the title could be rephrased comprehensively, for example, "Pharmacists' Knowledge, Practice and awareness about herbal products and their potential interactions with cardiovascular medications"

R1: Thank you for your comment. Title was amended as follows: "Pharmacy practitioners' Practice, awareness and knowledge about herbal products and their potential interactions with cardiovascular drugs."

C2: Introduction: I believe you need to add a small paragraph about Jordan's context, and clarify the research gap.

R2: Thank you for your comment. Kindly find this paragraph:

Several studies have been conducted in Arab countries assess pharmacists' knowledge and attitudes towards herbal products[1-4]. In Jordan, the prevalence and awareness of herbal products used among pharmacy staff have been measured which revealed that pharmacists' awareness about herbal products indication was good. However, their knowledge of herb's adverse effects, and drug interactions were inadequate[5] which sounded alarm. Additionally, no studies focused on Jordanian pharmacy practitioners' knowledge and awareness towards herb-drug interactions particularly with cardiovascular drugs as they are commonly used in Jordan. Thereby, the study's investigators strive to increase the attention of pharmacy practitioners regarding herb-drug interaction that may lead to toxic manifestations. Likewise, investigators seek to reinforce the need of periodic education programs for pharmacy practitioners focused on herbal products indications, side effects and drug interactions to refresh their knowledge for competent and holistic and health care as this has been documented by other study conducted in Jordan [6].

C3: Methods-Add the inclusion criteria, please.

R3: Thank you for your comment, we included the pharmacy practitioners in community pharmacies and excluded those who working in other places.

C4: Statistical analysis: You need to add if you have checked the data normality and the used test?

R4: Thank you for your comment, the data normality was checked using the Kolmogorov-Smirnov test.

C5: Results: Figure 2, no need to add "From" before each source of information and reorder them according to percentages.

R5: Thank you for your comment, figure 2 has been amended.

C6: Table 3. I believe it is important to calculate the overall mean of attitude, to express the level of attitude concisely.

R6: Thank you for your comment, you are right. However, the mean values of the measured variables are very close, thereby it is incapable to setup a range and to express the overall level of attitude is high, medium or low.

Competing Interests: No competing interests were disclosed.

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