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A review of the uses of five dietary supplements in the management of hypertension and a composite survey

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Abstract

The goal of this study was two-fold. The first one was to conduct a literature review of five dietary supplements (L-arginine, coenzyme Q10, garlic, hawthorn, and pycnogenol) on their blood pressure lowering effects. The second goal was to survey first-year pharmacy students at Howard University College of Pharmacy on their knowledge of the various aspects of these DSs. The literature review showed that all the 5 DSs included in this study have beneficial effects in reducing high blood pressure, although their effects are mostly mild to moderate. However, their effects are more pronounced in patients with hypertension and have no or limited effects in normotensive patients. Despite these promising benefits, the survey from the students showed a lower-than-expected knowledge score. The average knowledge level was 57.5 % on all the questions related to the five selected dietary supplements. The knowledge levels ranged from 52.9% for L-arginine to 66.2% for garlic. When the knowledge scores were paired and further analyzed, no statistical differences were noted among the levels for each dietary supplement. Overall, the survey showed that there is a lack of adequate knowledge among the participants on the supplements included in this study. Thus, an additional effort must be made to incorporate key supplement topics in various therapeutics courses throughout the pharmacy education.

Keywords: L-arginine; Co-enzyme Q10; Garlic; hawthorn; Pycnogenol; Knowledge

1. Introduction

According to a survey, dietary supplement (DS) use among the US adult population has increased from 48.4% during 2007-2008 to 57.6% during 2017-2018 [1]. The global market of DS was estimated at USD 151.9 billion in 2021 and is projected to grow at a compound annual rate of 8.9% to 327.4 billion dollars in 2030 [2]. The number of DSs in the USA market grew from about 4,000 in 1994 to over 85,00 in 2014 [3]. The total sales of DSs in the USA for 2021 were estimated at 12.35 billion dollars, with garlic, pycnogenol, and hawthorn accounting for nearly $34 million, $23 million, and $3 million of the market share, respectively [4]. The market share of co-enzyme Q10 in North America is estimated at $316.73 million [5], while the amino acid L-arginine global market share was estimated at nearly $812 million [6].

A brief overview of selected clinical studies regarding the use of the DSs included in this study and their beneficial effects in lowering blood pressure are summarized below in alphabetical order.

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1.1. Coenzyme Q10 (CoQ10)

Coenzyme Q10 (CoQ10) is an antioxidant that the body produces naturally. It is found in all tissues and organs of the body, but in the highest concentration in the heart. Since the 1970's, many studies have reported on the potential of CoQ10 to lower blood pressure in hypertensive patients although findings are mixed. CoQ10 has also been shown to improve symptoms of congestive heart failure (CHF). Some research also suggests that when combined with other nutrients, CoQ10 might aid recovery in people who have had bypass and heart valve surgeries.

Rosenfeldt et al. reported a meta-analysis that included 12 clinical trials (362 patients) [7]. The study concluded that CoQ10 has the potential in hypertensive patients to lower systolic blood pressure (SBP) by up to 17 mm Hg and diastolic blood pressure (DBP) by up to 10 mm Hg without significant side effects.

1.2. Garlic

Garlic is a common household spice but also one of the most utilized DSs. Its widespread use is due to its antibacterial and antioxidant properties mainly produced by allicin in garlic. It is believed that allicin has angiotensin II–inhibiting and vasodilating effects [8]. Evidence from human trials suggests that garlic might be beneficial in the treatment of hypertension [9]. Ried and colleagues included 25 studies in a systematic review and found that garlic preparations were superior to placebo in reducing BP in individuals with hypertension [10]. During the past few years, several human trials have been carried out providing additional evidence. One such study by Wang et al. reported results of a meta-analysis by using Ovid Medline, Cochrane Library, and PubMed (1946 to 2013) to search for randomized controlled trials [11]. The study included 17 trials and the pooled analysis showed that garlic intake caused a 3.75-mm Hg reduction (P<0.001) in SBP and a 3.39-mm Hg reduction (P<0.001) in DBP compared with controls. The authors of the study concluded that based on their review, garlic supplements are superior to controls in reducing BP, especially in hypertensive patients.

1.3. Hawthorn (Crataegus spp.)

Hawthorn has been used to reduce blood pressure and for several cardiovascular illnesses in Europe since at least the 12th century [12]. The herb was an 'official medicine' in European pharmacopoeias for treating heart disease [13]. Most data on the efficacy of hawthorn have focused on leaf and flower extracts of the plant. These extracts are registered in Germany for treating minor coronary heart diseases and CHF [14].

Cloud et al. conducted a systematic review and identified 370 randomized controlled trials (RCTs) (254 participants) that assessed the effect of hawthorn mono-preparations on BP [15]. They used databases that included AMED (Ebsco), CINAHL, EMBASE (Ovid), and PubMed, and The Cochrane Central Register of Controlled Trials, and grey literature. The review was performed in 2016. Hawthorn administered as tablets or liquid drops reduced BP in patients with pre-hypertension or stage 1 hypertension. The authors reported significantly reduced BP in three trials of 12- and 16-week duration *(*P < 0.05). No serious adverse side effects were reported. The systematic review concluded that hawthorn can significantly lower BP in people with mild hypertension if administered for at least 12 weeks.

1.4. L-arginine

L-arginine is an amino acid produced in the body naturally. It is also obtained from dietary sources. L-arginine supplementation has been shown to exert several beneficial effects, including reducing BP [16]. One report indicated that a diet rich in L-arginine significantly reduces both SBP and DBP in healthy participants [17]. A meta-analysis of 11 RCTs has shown a decreased SBP and DBP in those who received a median dose of 9 g (4–24 g/d) for a median duration of 4 weeks (2–24 weeks). However, no significant correlation was reported in this study.

Shiraseb et al. conducted a meta-analysis of over 4,821 published articles through searches using PubMed, Scopus, and Embase from 1996-2021 to identify RCTs of oral L-arginine on SBP and DBP in adults [18]. Based on this report of pooled analysis, L-arginine demonstrated significant decreases in SBP (-6.40 mm Hg; P < 0.001) and DBP (-2.64 mm Hg; P < 0.001) after L-arginine supplementation. In addition, the study also reported a dose-effect relationship after subgroup meta-regression analysis for DBP (P = 0.020).

1.5. Pycnogenol

Pycnogenol is a DS believed to produce various potentially protective effects against chronic diseases, such as metabolic syndrome, obesity, dyslipidemia, diabetes, and hypertension [19]. The term pycnogenol was intended to serve as a scientific name for this class of polyphenols [20].

An early animal study found that SBP and DBP decreased in a dose-dependent manner after intravenous administration of pine bark extract to Sprague Dawley (SD) rats [21]. A randomized controlled trial showed that oral administration of pycnogenol reduced SBP to the normal value in hypertensive patients [22], although there were some inconsistencies in the results in normotensive patients.

Zhang and team conducted a meta-analysis through a literature search of PubMed, the Web of Science, and the Cochrane library in May 2016 [23]. They identified nine trials involving 549 participants who received pycnogenol supplementation ranging from 150 mg/d to 200 mg/d. The authors reported that the estimate of the change in SBP and DBP was −3.22 mm Hg (95% CI: −6.20, −0.24) and −3.11 mm Hg (95% CI: −4.60, −1.62), respectively compared with the control. They also reported a higher BP reduction among those who had a diagnosis of hypertension or in those who were treated for longer than 3 months.

Overall, all 5 DSs have shown to have some level of benefits in reducing BP although their effects are considered to be mild to moderate. One unique factor that was noted is that the BP-reducing effects of most of these DSs are only shown in patients with a diagnosis of hypertension and have no or limited effects in normotensive patients. This is important since it signifies the safety profile of the DSs if taken by people with no issues with their BP.

In addition to conducting a relevant review of clinical studies, the goal of this study was to determine the knowledge level of pharmacy students in the use of DSs in the management of hypertension.

Although DSs are taken to maintain good health, they also have health risks. The FDA advises pharmacists to counsel consumers by sharing their knowledge about the benefits, risks, and adverse effects of supplements [24]. The question remains: are pharmacists well equipped with evidence-based knowledge to offer consumers the best counseling services? In a survey conducted in Italy among 232 pharmacists, it was noted that only about a third of respondents provided correct answers to 20 questions. However, a positive association was observed between professional experience and better knowledge levels, whereas the gender of the respondents did not play a significant role [25]. In a comprehensive review by Kwan et al [26], it was reported that in the United States and Canada pharmacists' herbal medication knowledge test scores were low, averaging less than 50%. Overall, pharmacists were more likely to give correct answers on the uses of herbal medications than about adverse effects and precautions [26]. In one study, 98% of community pharmacists and 58% of hospital pharmacists reported fielding questions from patients about herbal and other natural products, while in a Canadian study, 57% of community pharmacists reported being asked about herbal products [26]. In a previous study, we reported a-59.5% DS knowledge satisfaction rate among first-year pharmacy students at Howard University, USA [27]. In the current study, we report the knowledge levels of first-year pharmacy students at the same institution, based on five common DS: L-arginine, co-enzyme Q10, garlic, hawthorn, and pycnogenol.

2. Methods

The survey enrolled 45 first-professional-year pharmacy students at Howard University College of Pharmacy. The Qualtrics tool was employed to collect and evaluate data. A survey questionnaire was developed for each of the five supplements. Five questions were formulated for each DS. Demographic data such as age, gender, prior education, residence, working status, and work details were collected.

A 4-point Likert score was used to record responses to knowledge statements: 1=strongly agree; 2=agree; 3=disagree and 4=strongly disagree. The strongly agree and agree responses were pooled to get total agree responses, while disagree and strongly disagree were aggregated to total disagree responses. Forty-two students completed the survey, with a-93% response rate. The questionnaires were distributed to the students during a drug information course.

3. Results and Discussion

There were more female (*n*=27; 64.3%) than male students (*n*=15; 35.7%) who completed the survey. Most of the respondents (*n*=34; 81%) had a bachelor's degree before joining the pharmacy program. Thirty-three students (78.6%) reported not working while they were in the first year of pharmacy education. Most (*n*=24; 57.1%) lived in the Washington, D.C. metropolitan area. Thirty-seven respondents (88.1%) had prior work experience, with 28 (66.7%) reporting to have worked in pharmacies or other healthcare-related services. Twenty-two respondents (52.4%) had over three years of work experience. The demographic data are given in Table 1.

Responses to survey statements are shown in Tables 2-6. Five commonly used DSs were used to measure the knowledge levels of the survey participants. When all the responses were combined, the mean knowledge level was found to be 57.54% (standard deviation=4.971358), with a median of 54.3%. As can be seen from Tables 2-6, nearly all the responses scored less than a mean of 2.5 on a 4-point Likert scale, showing that the respondents responded in a similar way to nearly all the survey statements.

As shown in a review by Kwan et al [26], pharmacists with prior continuing education on DS, or with access to information resources, perform much better. Many pharmacists in the U.S. and Canada receive questions about DS from patients and healthcare practitioners as well [26]. The authors of the review also noted that the low knowledge levels may be related to inadequacy of DS education early on, in pharmacy schools [26]. A survey of 64 pharmacy schools in the USA revealed that 13 schools did not offer any kind of course on natural products, while only 11 schools provided some courses embedded in other courses [28]. This situation calls for the need for pharmacy schools to offer more nuanced and well-structured courses of DSs in pharmacy schools. In the past, several studies were published on the knowledge and opinion of pharmacy studies on various herbal and DSs [29- 34].

Table 1 Demographic characteristics of respondents

Characteristics	**Respondents (*n*, %)**	**95% CI (% range)[1]**
Age (years)		
21-23	14 (33.3)	19.1-47.6
24-26	17 (40.5)	25.6-55.3
27-29	5 (11.9)	2.1-21.7
>29	6 (14.3)	3.7-24.9
Gender		
Male	15 (35.7)	21.2-50.2
Female	27 (64.3)	49.8-78.8
Education		
Some college	1 (2.4)	0.0-7.0
Associate Degree	1 (2.4)	0.0-7.0
BA/BSc	34 (81)	69.1-92.8
MSc	4 (9.5)	2.7-22.6
PhD/Professional	2 (4.8)	0.0-11.2
Residence		
Washington, D.C.	4 (9.5)	0.7-18.4
Maryland	13 (31)	16.9-44.9
Virginia	7 (16.7)	5.4-27.9
Other States	18 (42.9)	27.9-57.2
Working now		
Yes	9 (21.4)	9.0-33.8
No	33 (78.6)	66.2-90.9
Work experience		
Never worked.	2 (4.8)	0.0-11.2
Short-term	3 (7.1)	0.0-14.9
Part-time	16 (38.1)	23.4-52.8

Full-time	21 (50)	34.9-65.1
Type of job		
Pharmacy related.	16 (38.1)	23.4-52.8
Other healthcare	12 (28.6)	14.9-42.2
Non-health related.	13 (31)	16.9-44.9
Not applicable	1 (2.4)	0.0-7.0
Annual income		
< USD 10,000	13 (31)	16.9-44.9
10,001-20,000	7 (16.7)	5.4-27.9
20,001-30,000	6 (14.3)	3.7-24.9
30,001-40,000	5 (11.9)	2.1-21.7
>40,000	11 (26.2)	12-9-39.5
Years Worked		
None	1 (2.4)	0.0-7.0
1-2	19 (45.2)	30.2-60.3
3-4	11 (26.2)	12.9-39.5
>4	11 (26.2)	12.9-39.6

[1]CI = Confidence Interval; normal approximations of binomial exact values.

Table 2 shows the results of the knowledge-based survey questions related to L-arginine. There was a total of 5 statements: 2 of them were true and the other 3 were false. The statement that had a higher percentage of correct answers is item 2. It is known that L-arginine is an amino acid that helps the body build protein. Although the body usually makes all the L-arginine it needs, it is also found in most protein-rich foods, including fish, red meat, poultry, soy, whole grains, beans, and dairy products. However, only about half of the survey participants answered the questions referring to the source (statements 1 and 3) correctly.

Table 2 Responses to knowledge-based survey statements on L-arginine[1]

	Survey statement	**SA/A**	**DA/SDA**	**Correct responses[2] [*n*, (%)]**	**Mean LKS± S.D.**
1	L-arginine is found naturally in red meat, poultry, and fish	25	17	25 (59.5)	2.26±0.94
2	It is used to lower blood pressure in patients with hypertension	28	14	28 (66.7)	2.33±0.90
3	It is not always produced naturally in the body and should be taken as a supplement if its blood pressure-reducing effect is needed	25	17	17 (40.5)	2.36±0.85
4	L-arginine is shown in studies to lower blood pressure effectively. It can be taken by mouth or used as a cream for the management of hypertension	26	26	26 (61.9)	2.38±0.96
5	Dietary supplements, such as arginine, can be harmful to the body and have long-lasting effects even if they are known to reduce high blood pressure effectively	27	15	15 (35.7)	2.14±0.93

[1]Abbreviations: SA=strongly agree; A=agree; DA=disagree; SDA=strongly disagree; LKS=Likert Score; S.D.= standard deviation; [2]The average correct response rate is 52.9%.

Table 3 represents the results of responses related to statements about Coenzyme Q10. The statement related to the role of Coenzyme Q10 in the body (item 3) received the highest correct score. Coenzyme Q10 supports cellular energy production in the mitochondria. Thus, a high plasma level is directly related to lower cardiovascular risk. However, participants were equally split in their response statement 4.

Table 3 Responses to knowledge-based survey statements on co-enzyme Q10[1]

	Survey statement	**SA/A**	**DA/SDA**	**Correct responses [*n*, (%)][2]**	**Mean LKS±S.D.**
1	Coenzyme Q10 is a fat-soluble compound synthesized in the body	24	18	24 (57.1)	2.33± 0.72
2	Coenzyme Q10 concentration in the plasma is maintained by a well-balanced diet, including meat, fish, and nuts to prevent high blood pressure	27	15	27 (64.3)	2.29± 0.97
3	It is used by the body for cell growth and maintenance and to lower blood pressure	29	13	29 (69.1)	2.24± 0.96
4	A low plasma concentration of coenzyme Q10 is a good biomarker to determine hypertension	21	21	21 (50)	2.48±0.99
5	It is not recommended to take coenzyme Q10 with anticoagulants, because it decreases the effectiveness of the latter	25	17	25 (59.2)	2.29±0.97

[1]Abbreviations: SA=strongly agree; A=agree; DA=disagree; SDA=strongly disagree; LKS=Likert Score; S.D.= standard deviation; [2]The average correct response rate is 60.0%.

As shown in Table 4, most of the statements related to garlic were answered wrongly by about one-third of the participants. This level of knowledge is found to be interesting since garlic is one of the most common household spices in many cultures around the world.

Table 4 Responses to knowledge-based survey statements on garlic[1]

	Survey statement	**SA/A**	**DA/SDA**	**Correct responses [n, (%)]2**	**Mean LKS±S.D.**
1	Garlic can be used to reduce high blood pressure	27	15	27 (64.3)	2.26±0.83
2	It increases the body's production of nitric oxide	28	14	28 (66.7)	2.33±0.90
3	Allicin is the main component of garlic that helps to lower blood pressure	29	13	29 (69.1)	2.34±0.79
4	Garlic supplements cause garlic breath, body odor, garlic taste, and unpleasant sensory perceptions	28	14	28 (66.7)	2.14±0.95
5	High doses of garlic may thin the blood and cause bleeding when taken with anticoagulant medications	27	15	27 (64.3)	2.21±0.87

[1]Abbreviations: SA=strongly agree; A=agree; DA=disagree; SDA=strongly disagree; LKS=Likert Score; S.D.= standard deviation; [2]The average correct response rate is 66.2%.

Table 5 shows the response to questions related to hawthorn. Item 3 states the effect of the herb on the gastrointestinal system and it received the lowest score. Only one-third of them answered it correctly. The berries contain fiber, which has been proven to aid digestion by reducing constipation and acting as a probiotic. Hawthorn is also one of the DSs that has been shown to slow blood clotting and increases the risk of bruising and bleeding. However, only half of the students answered item 3 correctly.

Table 5 Responses to knowledge-based survey statements on hawthorn[1]

	Survey statement	SA/A	DA/SDA	Correct responses [n, (%)]2	Mean LKS±S.D.
1	Hawthorn is known to lower the risk of high blood pressure	29	13	29 (69.0)	2.24±0.85
2	It is safe to be taken by children/adolescents	19	23	23 (54.8)	2.55±1.02
3	It has no risk of bleeding if taken during and after surgery	21	21	21 (50.0)	2.38±0.09
4	Hawthorn has anti-inflammatory properties that can improve health in hypertensive patients	25	17	25 (59.5)	2.29±0.92
5	Besides its blood pressure-lowering effects, hawthorn cannot aid in digestion	26	16	16 (38.1)	2.31±0.81

[1]Abbreviations: SA=strongly agree; A=agree; DA=disagree; SDA=strongly disagree; LKS=Likert Score; S.D.= standard deviation; [2]The average correct response rate is 54.3%.

The response to questions related to pycnogenol is shown below in Table 6. The dose of the herb varies widely from 50 mg to 450 mg per day. However, only one-fourth of the participants answered the dosing question correctly (item 5). The question with the highest correct response was related to the side effects of the DS (item 2).

Table 6 Responses to knowledge-based survey statements on pycnogenol[1]

	Survey statement	SA/A	DA/SDA	Correct responses [n, (%)]2	Mean LKS±S.D.
1	Pycnogenol can be effective in reducing high blood pressure	26	16	26 (61.9)	2.33±0.85
2	Its side effects are dizziness, gut problems, headache, and mouth ulcers	28	24	27 (64.2)	2.17±0.93
3	Besides its beneficial effects, pyconogenol may also help with ADHD, edema, heart failure, and muscle soreness	26	16	26 (61.9)	2.40±0.94
4	When taking pyncogenol, caution should be used with the co-administration of anticoagulants and antiplatelets	25	17	25 (59.5)	2.31±0.95
5	If you have mild high blood pressure and are taking pycnogenol, you should not exceed 200 mg daily	32	10	10 (23.8)	2.07±0.89

[1]Abbreviations: SA=strongly agree; A=agree; DA=disagree; SDA=strongly disagree; LKS=Likert Score; S.D.= standard deviation; [2]The average correct response rate is 54.3%.

When the statements are further categorized by type, the ones that are associated with indications or use of the DS constitute the highest number, followed by drug interactions as shown in Table 7.

Table 7 The top category of questions by type

Category of Questions	Number of Questions n (%)	
Indications/Use	9	37.5
Drug Interactions	4	16.7
Side Effects	3	12.5
Dose and Dosage Regimen	2	8.3
Support in the use of the herb	2	8.3

Among the DSs included in this study, statements related to garlic had the highest percentage of correct answers at 66.2% as shown in Table 8. However, compared to others, this difference did not reach a statistical difference.

Table 8 List of DSs and average respective correct answers

Name of the DS	Participants with correct answers (%)
Garlic	66.2
Coenzyme Q10	60.0
Hawthorn	54.3
Pycnogenol	54.3
L-arginine	52.9

The individual questions that have the highest scores are listed in Table 9. Only one question out of a total of over 30 individual questions received a passing score (above 70%).

Table 9 Questions with the highest respective correct responses

Survey Questions	Correct responses
Allicin is the main component of garlic that helps to lower blood pressure	69.1
Hawthorn is known to lower the risk of high blood pressure	69.0
Coenzyme Q10 is used by the body for cell growth and maintenance and to lower blood pressure	69.0
If you have mild high blood pressure and are taking pycnogenol, you should not exceed 200 mg daily	28.3

The mechanism of action-related questions was answered correctly by most, followed by interaction (drug-drug; drug disease, etc.). Dosage-related questions were answered correctly by less than half the participants.

Table 10 The top category of questions with the corresponding correct responses

Category of Questions	Correct Responses (%)
Mechanisms of action	66.70
Interaction	60.42
Indications	60.01
Side Effects	56.00
Support in the use	55.35
Dosage	46.10

4. Conclusion

All the DSs included in this study have shown some level of benefits in reducing BP in hypertensive patients with less or no effect in normotensive patients. Despite these proven beneficial effects, the results of the knowledge survey among the participants show a lower score of knowledge. The overall percentage knowledge levels in decreasing order were: 66.2 (garlic), 60.0 (co-enzyme Q10), 52.9 (L-arginine), and 54.3% each (hawthorn and pycnogenol). This survey shows that there is a knowledge gap among the participants in dietary supplements included in this study. There were no statistical differences between the composite data.

Compliance with ethical standards

Acknowledgments

The authors thank all participants of the survey.

Disclosure of conflict of interest

The authors declare no conflict of interest.

Statement of ethical approval

The survey was approved by Howard University IRB as part of a Drug Information course given by one of us (BH).

Statement of informed consent

The survey was conducted as part of HU College of Pharmacy drug information course; therefore it didn't require the informed consent of survey participants.

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