(REVIEW ARTICLE)

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Review of berberine use for the treatment of type 2 diabetes mellitus & students' survey

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Abstract

Introduction: Berberine is a naturally occurring alkaloid substance that can be extracted from various plants and can be found in medicinal herbs. The goal of this study is to conduct a literature review of the clinical use of berberine and assess the knowledge and opinion of pharmacy students on its beneficial effect as a blood sugar-reducing supplement.

Methodology: An online survey was developed and sent to 42 students with a 100% response rate. The focal point of the remaining 15 questions was based on knowledge and perceptions regarding Berberine.

Results: A total of 42 individuals participated in the survey. The majority of the participants were female (64.29%); between 24- 26 years old age range (40.48%); live in the DMV area where the study was conducted (42.86%). When asked about work experience, 50% of those who took the survey answered full-time, and 16 (38.10%) worked part-time. The majority (61.9%) indicated high knowledge about feeling comfortable with the beneficial use of berberine in reducing blood sugar. However, their overall knowledge score was 59.5% which is much less than the passing score set at 70%. When looking at how comfortable participants were regarding dietary supplements, the majority (n=25; 59.5%) were positive in their comfort. But only a third of participants (n=14; 33.3%) had the opportunity to interact with patients to discuss dietary supplements. Interestingly, more than two-thirds (n=29; 69%) of participants had taken supplements in the past for various personal reasons and the majority (n=28; 66.7%) of participants responded that they are currently taking supplements including vitamins. However, because of the low number of participants as a limitation of this study, a larger study with students in the medical field is recommended as a future plan.

Conclusion: Overall, students showed a low level of knowledge despite their high opinion. The study shows the need to expose students more to dietary and herbal supplements during their pharmacy program. This would allow them to meet their patients' needs upon graduation particularly if they chose to practice in a community pharmacy setting.

Keywords: Berberine; Diabetes; Survey; Pharmacy Students; Knowledge; Opinion; Likert's score

1. Introduction

Berberine is a naturally occurring alkaloid substance that can be extracted from various plants and can be found in medicinal herbs. Previous pharmacological studies have shown berberine to be useful in treating diabetes, hypolipidemia, inflammation, and cancer.[1] It has also been shown the herb is useful as an immunosuppressive agent. Although it is extensively metabolized, it has the potential to regulate glucose and lipid metabolism in vitro and in vivo. [2] Therefore, it opens the possible option for treatment in diabetes. According to the Centers for Disease Control and Prevention (CDC), more than 37 million Americans have diabetes, and approximately 90-95% of them have type 2 diabetes.[3] Current pharmacological treatments for type 2 diabetes include metformin, sulfonylureas, meglitinides, insulins, etc. along with the addition of healthy eating, and regular exercise.

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1.1. Chemistry and chemical modifications

The structure of berberine ($C_{18}H_{20}NO_4^+$) is shown in Figure 1. It is an isoquinoline-derived alkaloid featuring a non-basic quaternary ammonium moiety. The modular structure of berberine is ideally suited for the development of focused Structure-activity relationship (SAR) libraries. A brief summary of the SAR studies is provided below.
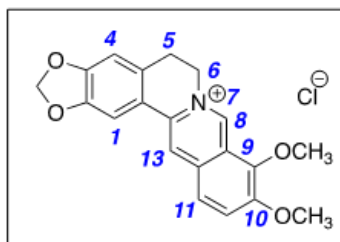

Figure 1 Chemical structure and numbering of berberine

Berberine analogs featuring the substitution of the methoxy moiety at C9 with hydrophobic, bulkier alkyl groups have shown good antitumor activity. Substituted cyclopropyl and adamantyl ethers at C9 are inhibitors of indoleamine-2,3-dioxygenase (IDO1). Derivatives of berberine containing 2-aminoalkyl group in the C9 side chain have been complexed with platinum and have exhibited good anticancer activity. Analogues that display aryl substitution at C12 of berberine are inhibitors of hypoxia-inducible factor-1. Berberine undergoes a chemoselective Mannich reaction at C11. Such analogs are reported to have antioxidant and anticancer activity. Finally, C13 substitution with electron-deficient vinyl groups led to analogs with antibacterial and antifungal activity.

Current studies have tested the efficacy and usefulness of berberine in diabetes therapy. Yin et al., study findings showed a reduction of HBA1c levels and other glycemic parameters in diabetic patients[2]. Despite major advances achieved in drug therapy to lower blood sugar, diabetes is still a major health problem. As time progresses, the ability to explore alternative methods is necessary.

A decent amount of animal research suggests berberine may help lower blood sugar levels via various pathways, including by the following: increasing insulin sensitivity, promoting insulin production, regulating metabolism, increasing glycolysis, or the breakdown of glucose, reducing glucose production in the liver, increasing nitric oxide (NO) production, which helps widen arteries slowing carbohydrate absorption from the gut[4].

Several diabetic human studies have shown that taking 600–2,700 mg of berberine daily may lower fasting and long-term blood sugar levels by up to 20% and 12%, respectively, especially when taken alongside blood sugar medication[5,6].

Similarly, a review of 14 studies found that berberine lowered blood sugar levels and seemed to be as effective as common blood sugar medications, including metformin (Glucophage), rosiglitazone (Avandia), and glipizide (Glucotrol)[8]. Furthermore, research suggests berberine may help support the blood-sugar-lowering effects of other diabetes medications when taken alongside them[7].

It is thus important that students are taught and well-informed about the beneficial effects of dietary supplements including berberine during their therapeutic courses. A CDC study indicated that from 2007–2008 through 2017–2018, the prevalence of dietary supplement use increased in all age groups among U.S. adults[9]. A 2020 report showed that among U.S. adults aged 20 and over, 57.6% used any dietary supplement in the past 30 days, and use was higher among women (63.8%) than men (50.8%).

There are several studies published to assess students' knowledge of various herbal and dietary supplements[9-16]. However, no study was found specific to the use of berberine in the management of diabetes. Therefore, the goal of the present study was to assess the knowledge and opinion of students on the use of berberine as a supplement for the management of Type 2 diabetes mellitus.

2. Methods

A survey was developed and distributed to pharmacy students. The survey was sent to 42 students with a 100% response rate. The survey had a total of 24 questions. The first nine questions focused primarily on the demographics. The focal point of the remaining 15 questions was related to knowledge and perceptions regarding berberine. The data

utilized was collected based on a 4-scale Likert scale (strongly agree; somewhat agree; somewhat disagree; strongly disagree) and created using an online survey instrument. Questions were combined to compute an output based on knowledge. Answers were assigned 1 (high knowledge) if the answer was either agree or strongly agree. If the answer was disagree or strongly disagree with the question it was given a zero (low knowledge). A descriptive analysis was then done using SPSS software to compute the results.

3. Results

Table 1 Sociodemographic Characteristics of Participants at Baseline (N=42)

Baseline characteristics	N	%
Gender		
Female	27	64.29
Male	15	35.71
Age		
21-23	14	33.33
24-26	17	40.48
27-29	5	11.90
> 29	6	14.29
Highest Education Level		4
Some college or associate degree	2	.76
BA/BSC	34	80.95
MSC/MA or professional	6	14.28
Residence		
DMV	13	30.95
Other states	18	42.86
Work Experience		
Never worked or short term	5	11.90
Part-time	16	38.10
Full-time	21	50.00
Type of Jobs Worked		
RX related	16	38.10
Other healthcare	12	28.57
Non-healthcare or not applicable	14	33.33
Annual Income		
< $10,000	13	30.95
$10,001-20,000	7	16.67
$20,001-30,000	6	14.29
$30,001-40,000	5	11.90
> $40,000	11	26.19

Years Worked		
Never worked	1	2.38
1-2 years	19	45.24
3-4 years	11	26.19
> 4 years	11	26.19
Currently Working		
Yes	9	21.43
No, but plan soon	18	42.86
No, but plan on working	15	35.71

A total of 42 individuals participated in the survey. Female participants made up the majority (64.29%) of those who completed the survey. When asked their age, most were under the age of 26 with the majority ranging between the ages of 24-26 (40.48%). When asked about their current residence, most participants came from outside the DMV area where the study was conducted (42.86%). While roughly one-third (30.95%) were residents of Maryland, 16.67% were from Virginia and 9.52% were from Washington, DC. Current income was asked, which indicated that 13 participants had an income less than 10, 000 dollars while 11 participants had an income greater than 40, 000 dollars. When asked about work experience, 50% of those who took the survey answered full-time, and 16 (38.10%) worked part-time. Over one-third (38.1%) have pharmacy-related jobs. Also, more than half have either a different healthcare job or a non-healthcare-related job.

Table 2 Opinion Questions Regarding Overall Dietary Supplements (N=42)

Participant Questions	Somewhat or Strongly Disagree N (%)	Somewhat or Strongly Agree N (%)
How comfortable are you in your knowledge of dietary supplement	17 (40.5)	25 (59.5)
I am or have been involved in counseling or interacting with patients discussing dietary supplements	28 (66.7)	14 (33.3)
I have taken dietary supplements personally in the past for various reasons	13 (31.0)	29 (69.0)
I am currently on some type of dietary supplements including vitamins.	14 (33.3)	28 (66.7)
I am familiar with Berberine's blood sugar levels reducing effect.	21 (50)	21 (50)
I feel comfortable using herbs such as berberine to help manage diabetes even if there are approved medications on the market.	16 (38.1)	26 (61.9)
I do not believe in plant-based drugs, especially in chronic diseases such as diabetes.	21 (50)	21 (50)
I may consider recommending Berberine in addition to prescription diabetic drugs if it also helps patients to lose weight.	17 (40.5)	25 (59.5)
I believe in taking Berberine for prediabetes before patients qualify for prescription drugs.	16 (38.1)	26 (61.9)

When looking at how comfortable participants were regarding dietary supplements, the majority (n=25; 59.5%) are positive in their knowledge. But only a third of participants (n=14; 33.3%) had the opportunity to interact with patients to discuss dietary supplements. Interestingly, more than two-thirds (n=29; 69%) of participants had taken supplements

in the past for various reasons. Lastly, the majority (n=28; 66.7%) of participants responded that they are currently taking supplements including vitamins.

Participants were also asked for their opinion specific to the beneficial effect of berberine on diabetes. The data showed that the participants are equally divided in their knowledge comfort of berberine's blood sugar-reducing effect. They are also equally split regarding their opinion in the use of dietary or plant-based supplements for managing chronic illnesses such as diabetes. However, about two-thirds (25; 59.5%) and over half (n=26; 61.9%) of participants are comfortable using the herb as a supplement to FDA-approved prescription drugs or during the early stage of diabetes (prediabetes) respectively.

Table 3 Opinion Questions Regarding Overall Dietary Supplements (N=42)

Participant Questions	Somewhat or Strongly Disagree N (%)	Somewhat or Strongly Agree N (%)
I am familiar with berberine's blood sugar levels reducing effect.	21 (50)	21 (50)
I feel comfortable using herbs such as berberine to help manage diabetes even if there are approved medications on the market.	16 (38.1)	26 (61.9)
I do not believe in plant-based drugs especially in chronic diseases such as diabetes.	21 (50)	21 (50)
I may consider recommending Berberine in addition to prescription diabetic drugs if it also helps patients to lose weight.	17 (40.5)	25 (59.5)
I believe in taking Berberine for prediabetes before patients qualify for prescription drugs.	16 (38.1)	26 (61.9)

Table 4 Berberine Knowledge Questions (N=42)

Participant Questions	Low Knowledge (incorrectly answered) N (%)	High Knowledge (correctly answered) N (%)
Berberine can reduce blood sugar levels in individuals with type 2 diabetes just as much as metformin does	6 (38.1)	26 (61.8)
Besides its blood sugar-reducing effect, berberine also decreases symptoms of hypotension, bradycardia, and vasodilation.	15 (35.7)	27 (64.3)
Berberine reduces the risk of heart disease in diabetic patients when used to reduce blood sugar.	14 (33.3)	28 (66.7)
Berberine has an additive effect if used with other blood sugar-lowering prescription medications.	18 (42.9)	24 (57.1)
Berberine not only reduces blood sugar but also helps with weight loss.	13 (31.0)	29 (69)

Survey participants were also given questions to determine their actual knowledge and their answers were scored. In all the questions, none of their responses received a passing score (70%) showing that although they believe they are knowledgeable, this is found to be not supported. The question that received the highest correct response is the benefit of berberine in both diabetes and weight loss. The question that received the lowest score is berberine's additive effect along with approved prescription drugs. The overall score for all the questions was 67% which is lower than the seventy percent mark.

The data showed that there was a statistically significant relationship between income and the usage of berberine supplements in diabetes treatment. Those with an income less than $25,000 fell more comfortable in using dietary supplements and also feel more knowledgeable (p=003 vs. 0.042 respectively) Additionally, a significant difference between years worked and taking dietary supplements in the past for various reasons (52.4 vs47.6, P=0.02). The same association could be made for years worked versus participants' comfortability in their knowledge of dietary supplements.

Table 5 Berberine Relationships

Participant Questions	Income	P value < 0.05 (CI = 95%)
Income vs. I feel comfortable using herbs such as berberine to help manage diabetes even if there are approved medications on the market	< $25K vs. >$25K (47.6% vs. 26.2%)	0.030
Income vs. How comfortable are you in your knowledge of dietary supplements	< $25K vs. >$25K (47.6% vs. 26.3%)	0.042
Years worked vs. I have taken dietary supplements in the past for various reasons.	<2 years vs >2 years work experience (52.4% vs. 47.6%)	0.002
Years worked vs I am comfortable are you in your knowledge of dietary supplements	<2 years vs >2 years work experience (52.4% vs. 47.6%)	0.042
Working now vs. I have taken dietary supplements in the past for various reasons.	Currently working vs. no current job (35.7% vs. 64.3%)	0.024

4. Discussion

Diabetes is a field of medicine that is often discussed and taught to pharmacy students during their didactic courses. Diabetes continues to be a leading cause of various health outcomes including death in the older population. Although, the prevalence of diabetes continues to rise in younger populations. This is why continued research efforts are needed to discover more treatment options that can cater to different populations.

In this study, a survey was administered to students to get their opinions and level of knowledge on the beneficial effects of berberine for diabetic patients. It was interesting to see students split (50% and 50%) on their beliefs in using a plant-based herb to treat a chronic disease such as diabetes. Although the majority (61.9%) indicated high in their knowledge of dietary supplements, their score is much lower than expected on the knowledge score. Two of the demographic characteristics shown as predictors of participants' knowledge or belief in the use of berberine as a blood sugar-lowering herb are low income and less work experience. The salary they earned was significant to how comfortable the participants were with using supplements. It also seems that those with no job or those working part-time have been shown to have taken dietary more dietary supplements previously.

Overall, students need to be exposed more to dietary and herbal supplements during their pharmacy program to be able to meet their patient's needs upon graduation particularly if they chose to practice in a community pharmacy setting. However, because of a small number of participants as a limitation of this study, a larger study with students in the medical field is recommended as a future plan.

Compliance with ethical standards

Disclosure of conflict of interest

The study was approved by the Howard University IRB and done as a part of a course. Therefore, there was no need to obtain informed consent from all individual participants included in the study.

References

[1] Kun Wang, Xinchi Feng, Liwei Chai, Shijie Cao & Feng Qiu (2017) The metabolism of berberine and its contribution to the pharmacological effects, Drug Metabolism Reviews, 49:2, 139-157, DOI: 10.1080/03602532.2017.1306544

[2] Yin, Jun et al. "Efficacy of berberine in patients with type 2 diabetes mellitus." Metabolism: clinical and experimental vol. 57,5 (2008): 712-7. doi:10.1016/j.metabol.2008.01.013

[3] "Diabetes Symptoms." Centers for Disease Control and Prevention, Centers for Disease Control and Prevention, 27Apr2021. https://www.cdc.gov/diabetes/basics/symptoms.html.

[4] Yun J, JianpingY, and Weiping J. Effects and mechanisms of berberine in diabetes treatment. Acta Pharmaceutica Sinica B. Volume 2, Issue 4, August 2012, Pages 327-334

[5] Pang B, Zhao LH, Zhou Q, Zhao TY, Wang H, Gu CJ, Tong XL. Application of berberine on treating type 2 diabetes mellitus. Int J Endocrinol. 2015;2015:905749. doi: 10.1155/2015/905749. Epub 2015 Mar 11. PMID: 25861268; PMCID: PMC4377488.

[6] Zhang Y, Li X, Zou D, Liu W, Yang J, Zhu N, Huo L, Wang M, Hong J, Wu P, Ren G, Ning G. Treatment of type 2 diabetes and dyslipidemia with the natural plant alkaloid berberine. J Clin Endocrinol Metab. 2008 Jul;93(7):2559-65. doi: 10.1210/jc.2007-2404. Epub 2008 Apr 8. PMID: 18397984.

[7] Lan J, Zhao Y, Dong F, Yan Z, Zheng W, Fan J, Sun G. Meta-analysis of the effect and safety of berberine in the treatment of type 2 diabetes mellitus, hyperlipemia and hypertension. J Ethnopharmacol. 2015 Feb 23;161:69-81. doi: 10.1016/j.jep.2014.09.049. Epub 2014 Dec 10. PMID: 25498346.

[8] Dong H, Wang N, Zhao L, Lu F. Berberine in the treatment of type 2 diabetes mellitus: a systemic review and meta-analysis. Evid Based Complement Alternat Med. 2012;2012:591654. doi: 10.1155/2012/591654. Epub 2012 Oct 15. PMID: 23118793; PMCID: PMC3478874.

[9] Mishra S, Stierman B, Gahche JJ, and Potschman P. Dietary Supplement Use Among Adults: United States, 2017–2018. NCHS Data Brief No. 399, February 2021.

[10] Nelson T, Hailemeskel B, Fullas F. Review of melatonin and results of students' survey. Palliat Med Hosp Care Open J. 2022; 8(1): 20-24. doi: 10.17140/PMHCOJ-8-147. Obtained from: https://openventio.org/wp-content/uploads/Review-of-Melatonin-and-Results-of-Students-Survey-PMHCOJ-8-147.pdf. Accessed 4/22/2022.

[11] Hailemeskel B, Fullas F. Dietary supplements: A survey of the opinion of first-year professional pharmacy students. Diabetes Res Open J. 2022; 8(1): 18-22. doi:10.17140/DROJ-8-155. Accessed from: https://openventio.org/wp-content/uploads/Dietary-Supplements-A-Survey-of-the-Opinion-of-First-Year-Professional-Pharmacy-Students-DROJ-8-155.pdf. 3/25/2022.

[12] Hailemeskel B, Mohamed B, Mbami I. Lycopene for hypertension and factors affecting its use: A survey of pharmacy students. Diabetes Res Open J. 2022; 8(1): 6-10. doi: 10.17140/DROJ-8-153. Obtained from: https://openventio.org/wp-content/uploads/Lycopene-for-Hypertension-and-Factors-Affecting-Its-Use-A-Survey-of-Pharmacy-Students-DROJ-8-153.pdf. Accessed date: 3/5/2022.

[13] Hennessee M, Hailemeskel B, and Fullas F. Flaxseed: Knowledge and opinion of first-year pharmacy students. International Journal of Science and Research Archive, 2022, 06(01), 107–112. Accessed from: https://ijsra.net/sites/default/files/IJSRA-2022-0097.pdf. Accessed on 5/24/2022.

[14] Nwabuoku J, Boateng MG, Jajua M, and Hailemeskel B. Pharmacy students' knowledge in the use of glutathione for multiple sclerosis. International Journal of Science and Research Archive, 2022, 06(01), 159–166. Available at: https://ijsra.net/sites/default/files/IJSRA-2022-0109.pdf. Access date 5/31/2022.

[15] Boateng MG, Nwabuoku J, Jajua M, and Hailemeskel B. Glutathione use in multiple sclerosis and student's opinion. International Journal of Science and Research Archive, 2022, 06(01), 139–149. Available at: https://ijsra.net/sites/default/files/IJSRA-2022-0110.pdf. Access date 5/31/2022.

[16] Harris M, N'Dea Johnson, Hailemeskel B. Assessment of awareness and opinion: grape seed extract's health benefits. Adv Food Technol Nutr Sci Open J. 2022; 8(1):20-28. doi: 10.17140/AFTNSOJ-8-176. Obtained from: https://openventio.org/wp-content/uploads/Assessment-of-Awareness-and-Opinion-Grape-Seed-Extracts-Health-Benefits-AFTNSOJ-8-176.pdf. Accessed on 10/17/2022.