

Berberine Use for the Treatment type 2 Diabetes Mellitus & Students' Survey

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Received date: **May 15, 2023**; Accepted date: **June 02, 2023**; Published date: **June 06, 2023**

Citation: Bisrat Hailemeskel, K. Ndidi Theme, Anywise, Pierre, (2023), Berberine Use for the Treatment type 2 Diabetes Mellitus & Students' Survey, *J. General Medicine and Clinical Practice*. 6(4); DOI:10.31579/2639-4162/084

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Abstract

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

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

Results: A total of 42 individuals participated in the survey. Majority of the participants were female (64.29%); between 24- 26 years old age range (40.48%); live in 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%) work part-time. Majority (61.9%) indicted high knowledge about feeling comfortable of 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, majority (n=25; 59.5%) are positive in their comfort. But only a third of participants (n=14; 33.3%) had the opportunity interacting with patients to discuss dietary supplements. Interestingly, more than two-third (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 a 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 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 need upon graduation particularly if they chose to practice in a community pharmacy setting.

Key Words: berberine; diabetes; survey; pharmacy students; knowledge; opinion; likert's scor

Introduction

Berberine is a naturally occurring alkaloid substance that can be extracted for 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 to be 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.

Chemistry and chemical modifications: The structure of berberine (C₁₈H₂₀NO₄⁺) is shown in Figure 1. It is an isoquinoline-derived alkaloid featuring a non-basic quaternary ammonium moiety. 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.

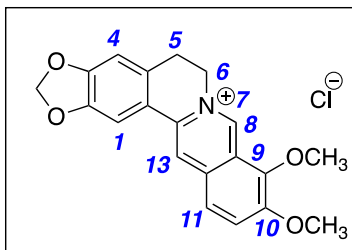


Figure 1: Chemical structure and numbering of berberine

Berberine analogues 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 analogues are reported to have antioxidant and anticancer activity. Finally, C13 substitution with electron-deficient vinyl groups led to analogues 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 patients². 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 gut⁴.

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]. It is 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 studied published to assess students' knowledge of various herbal and dietary supplements⁹⁻¹⁶. However, no study was found specific to the use of berberine in management of diabetes. Therefore, the goal of the present study was to assess the knowledge and opinion of students on the use of the berberine as a supplement for the management of Type 2 diabetes mellitus.

Methods

A survey was developed and distributed to pharmacy students. The survey was sent to 42 students with 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 were 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 the question it was given a zero (low knowledge). A descriptive analysis was then done using SPSS software to compute the results.

Results

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		
Some college or associate degree	2	4.76
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

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

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 residence 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%) work part-time. Over one-third (38.1%) have pharmacy-related jobs. Also, more than half have either a different health care job or a non-healthcare related job.

Participant Questions	Somewhat or Strongly Disagree N (%)	Somewhat or Strongly Agree N (%)
1. How comfortable are in your knowledge of dietary supplement	17 (40.5)	25 (59.5)
2. I am or have been involved in counseling or interacting with patients discussing dietary supplements	28 (66.7)	14 (33.3)
3. I have taken dietary supplements personally in the past for various reasons	13 (31.0)	29 (69.0)
4. I am currently on some type of dietary supplements including vitamins.	14 (33.3)	28 (66.7)
5. I am familiar with berberine's blood sugar levels reducing effect.	21 (50)	21 (50)

6. 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)
7. I do not believe in plant-based drugs especially in chronic diseases such as diabetes.	21 (50)	21 (50)
8. 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)
9. I believe in taking Berberine for prediabetes before patients qualify for prescription drugs.	16 (38.1)	26 (61.9)

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

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

third (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.

Participant Questions	Somewhat or Strongly Disagree N (%)	Somewhat or Strongly Agree N (%)
1. I am familiar with berberine's blood sugar levels reducing effect.	21 (50)	21 (50)
2. 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)
3. I do not believe in plant-based drugs especially in chronic diseases such as diabetes.	21 (50)	21 (50)
4. 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)
5. I believe in taking Berberine for prediabetes before patients qualify for prescription drugs.	16 (38.1)	26 (61.9)

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

Participants were also asked of their opinion specific to the beneficial effect of berberine in 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 use 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 in using the herb as a supplement to FDA-approved prescription drugs or during early stage of diabetes (prediabetes) respectively.

Participant Questions	Low Knowledge (incorrectly answered) N (%)	High Knowledge (correctly answered) N (%)
Berberine can reduce blood sugar level 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 risk of heart disease in diabetic patients when used to reduce blood sugar.	14 (33.3)	28 (66.7)
Berberine have an additive effect if used with other blood sugar lowering prescription medications.	18 (42.9)	24 (57.1)
Berberine not only reduce blood sugar, but it 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.

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

Table 5: Berberine Relationships.

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 felt more comfortable in using dietary supplement and also feel more knowledgeable ($p=0.03$ vs. 0.042 respectively) Additionally, a significant difference between years worked and taking dietary supplements in the past for various reasons (52.4 vs 47.6, $P=0.02$). The same association could be made for years worked versus participants comfortability in their knowledge of dietary supplements.

Discussion

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

In this study, a survey was administered to students to get their opinions and level of their knowledge on the beneficial effects of berberine for diabetic patients. It was interesting to see students were split (50% and 50%) on their beliefs in using a plant-based herb for treat of a chronic disease such as diabetes. Although majority (61.9%) indicted high in their knowledge of dietary supplement, their score is much lower than expected on the knowledge score. Two of the demographic characteristics shows 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 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 patients need upon graduation particularly if they chose to practice in a community pharmacy setting. However, because of a 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.

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DOI:10.31579/2693-7247/084

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