Journal of Chemical Health Risks

www.jchr.org

JCHR (2023) 13(4), 2370-2377 | ISSN :2251-6727

The Effect of Blueberry Consumption on Non-communicable Diseases

Rita Benya Adriani*[1], Artha Budi Susila Duarsa[2], Tri Yuniarti[3], Musyarrafah[2], Abdillah Adipatria Budi Azhar[2], Sabrina Intan Zoraya[2], Ayu Anulus[2], Hendra Dwi Kurniawan[4], Abd. Rohman[5], Santy Irene Putri[5]

1. Medical Polytechnic Surakarta, West Java, Indonesia
2. Faculty of Medicine, Universitas Islam Al-Azhar Mataram, Indonesia
3. School of Health Sciences Mamba'ul 'Ulum, Surakarta, Central Java, Indonesia
4. Sekolah Tinggi Ilmu Kesehatan Panti Kosala, Sukoharjo, Central Java, Indonesia
5. Universitas Tribhuwana Tunggadewi, Malang, East Java, Indonesia

(Received: 02 September 2023 Revised: 14 October Accepted: 07 November)

KEYWORDS

Non-communicable diseases (NCDs); Barberry; Hepatoprotective; Hypoglycemic; Diabetes

ABSTRACT:

Introduction: Non-communicable diseases are the illnesses that cannot transmit from person to another. Barberry has been reported as hepatoprotective, hypoglycemic, and an herbal remedy for the treatment of various complaints including diabetes, liver dysfunction, gallbladder pain, gallstone diarrhea, digestive disorders, and urinary tract diseases.

Objectives: this study aimed to estimate and analyze the effect of barberry consumption on non-communicable diseases.

Methods: it employed a prism diagram. The search for articles was carried out based on the eligibility criteria of the PICO Model: P= Patient; I= Consuming Barberry; C= Not consuming Barberry; O= Non-Communicable Disease. The articles used were derived from the Google Scholar database with the following keywords "barometer", "blood pressure", "cholesterol", "cardiovascular", and "randomized controlled trial".

Results: four articles in this study from Iran show that consuming barberry lowers the likelihood of non-communicable diseases. Patients with non-communicable diseases who consumed barberry decreased -0.08 times compared to the patients with non-communicable diseases who did not consume barberry (SMD= -0.08; CI 95%= -0.77 to 0.60; p<0.0001), and the results were statistically significant.

Conclusions: The meta-analysis of four articles with randomized controlled trial specialists concluded that taking barberry lowers the likelihood of non-communicable diseases.

1. Introduction

Non-communicable diseases, often referred to as NCDs, encompass a group of medical conditions that are not transmissible from one person to another and typically exhibit a slow and gradual onset characterized by their chronic nature. Among these NCDs, diabetes mellitus stands out as a metabolic disorder marked by the persistent elevation of glucose levels in the bloodstream over an extended period. The classification of diabetes broadly comprises four main types: Type I diabetes, Type II diabetes, gestational diabetes (occurring during pregnancy), and type-specific diabetes attributed to other underlying causes (Belwal et al., 2020). Diabetes causes hypertension in most diabetic patients. Hypertension accelerates cardiovascular disease, nephropathy, retinopathy, and neuropathy in diabetic patients (Lee & Lee, 2016).

The most prevalent cardiovascular affliction that predominantly affects the adult population is hypertension, which is characterized by abnormally high blood pressure levels. Hypertension, along with other conditions categorized as "vascular diseases," including stroke and kidney failure, collectively contributes to a substantial 43 percent of all annual recorded deaths (Aisha & Muhammad, 2014). Following the guidelines of the European Society of Cardiology (ESC) and the European Society of Hypertension (ESH), a diagnosis of hypertension (HT) is established when the systolic blood pressure (SBP) consistently measures at 140 mmHg or

Journal of Chemical Health Risks

www.jchr.org

JCHR (2023) 13(4), 2370-2377 | ISSN :2251-6727

higher, or when the diastolic blood pressure (DBP) consistently registers at 90 mmHg or higher, as emphasized in research by Lipert et al., (2022).

This information underscores the profound impact of hypertension on the adult population and its significant contribution to the overall burden of vascular diseases, including fatalities. The diagnostic criteria provided by the ESC and ESH are essential in identifying and managing hypertension, offering healthcare professionals clear parameters for making this crucial diagnosis and guiding treatment strategies to mitigate the risks associated with high blood pressure.

Barberry is recognized as a rich source of polyphenols that can be harnessed for the promotion of health and the prevention and management of various diseases (Emamat et al., 2020). Several studies have explored the potential benefits of barberry and have unveiled its promising and selective attributes, including its capacity to combat cancer, regulate blood pressure, ameliorate atherosclerosis, and enhance the immune system, particularly in the context of coronary heart disease. Additionally, it exhibits preventative effects against insulin resistance and related ailments, alongside hypolipidemic and antioxidant properties (Kermani et al., 2020). Barberry holds a longstanding reputation for its hepatoprotective qualities, aiding in liver health, and its hypoglycemic effects, making it a valuable herbal remedy for an array of health issues. These include but are not limited to diabetes management, relief from liver dysfunction, gallbladder pain, gallstone-related symptoms, diarrhea, digestive disorders, and urinary tract conditions (Aisha & Muhammad, 2014). The multifaceted potential of barberry underscores its significance in traditional and contemporary medicinal practices, which offers a wide range of health benefits for those who incorporate it into their wellness regimens.

2. Objectives

Given the context provided above and drawing upon previous research that shares common themes regarding the impact of barberry consumption on non-communicable diseases, the present study sought to conduct a systematic review of primary research findings. The objective of this research was to meticulously examine the outcomes of these primary studies for deriving more accurate estimates and ultimately formulating novel conclusions. It aimed to assess and analyze the influence of barberry consumption on non-communicable diseases, which further shed light on its effects and implications in this domain.

3. Methods

The present study constitutes a systematic review and meta-analysis. It used a PRISMA diagram to guide the research process. The initial step in gathering relevant articles involved adhering to the eligibility criteria outlined in the PICO Model, where P signifies the patient group, I represents individuals who consume barberry, C designates those who do not consume barberry, and O pertains to the impact on non-communicable diseases. The search for pertinent articles was conducted utilizing the Google Scholar database with a combination of specific keywords, such as "barberry," "blood pressure," "cholesterol," "cardiovascular," and "randomized controlled trial." This approach was adopted to ensure the comprehensive inclusion of studies relevant to the research focus.

Articles were analyzed using diagram PRISMA and Application Review Manager 5.3.

Meta analysis was done with 5 steps as follows:

1) formulating PICO format research questions (Population, Intervention, Comparison, and Outcome).

2) searching for primary study articles from various electronic and non-electronic databases, such as PubMed and Google Scholar.

3) conducting screening to determine the inclusion and exclusion criteria and a critical assessment.

4) extracting primary study data and synthesizing effect estimation using the Revman application.

5) interpreting the results and drawing conclusions.

4. Results

The articles in this study were accessed from two databases, PubMed and Google Scholar, with the following keywords, *" barometer "AND" blood pressure "and" cholesterol "and" cardiovascular "and" randomized controlled trial".* Figure 1 shows the Prisma flow diagram for the process of reviewing corresponding articles. There were 628 items discovered during the first search. 100 of the 150 papers that were gathered after being filtered to include exclusively journal publications met the qualifying requirements.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2023) 13(4), 2370-2377 | ISSN :2251-6727

Only four publications were found to have satisfied the quality evaluation after undergoing a full-text review. These articles were then included into a quantitative synthesis by meta-analysis. The study article was initially published in Iran, as Figure 2 demonstrates.

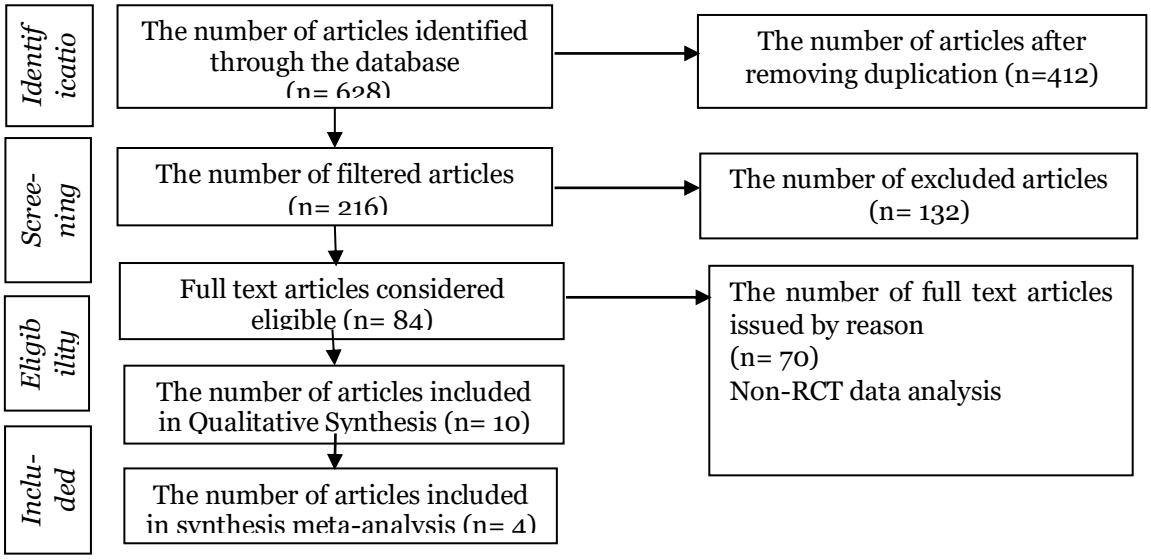

Figure 1. PRISMA Flow Diagram

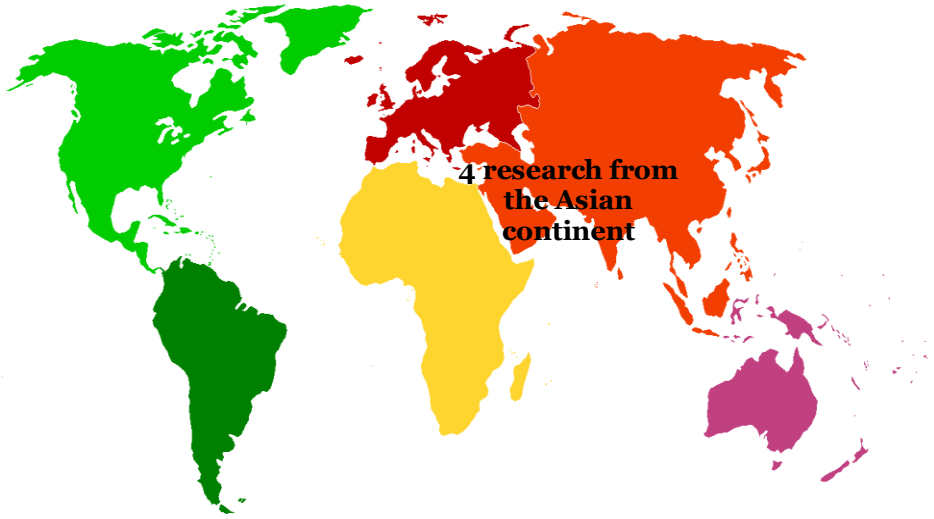

Figure 2. The map of research area

Journal of Chemical Health Risks

www.jchr.org

JCHR (2023) 13(4), 2370-2377 | ISSN :2251-6727

Table 2. RCT study Quality Assessment results

Author (Year)	Question Criteria							Total
	1	2	3	4	5	6	7	
Emamat et al. 2022	7	4	4	4	4	4	2	29
Lazavi et al. 2018	8	3	4	4	4	4	2	29
Kermani et al. 2020	8	4	4	4	4	4	2	30
Emamat1 et al. 2022	7	4	4	4	4	4	2	29

Description of score for each type of answer:

1. "0" for a conflict of interest
2. "2" for no conflict of interest
3. "1" for doubtful answer

The criteria for assessing research quality encompass several key aspects:

1. Formulation of Research Questions in the PICO Acronym:
   a. The first consideration is whether the population in the primary study aligns with the population intended for the PICO meta-analysis.
   b. It's essential to verify if the operational definition of exposure/intervention in the primary study corresponds to the expected definition in the meta-analysis.
   c. For randomized controlled trials (RCTs), an important aspect is ensuring that the comparison used in the primary studies matches the planned comparison in the meta-analysis, such as placebo or standard therapy.
   d. Another crucial factor is determining if the outcome variables in the primary study are similar to those planned for the meta-analysis.

2. Methods for Choosing Research Subjects:
   a. The method of sample selection is examined to determine if it effectively represents the target population.
   b. The allocation of subjects into experimental and control groups is assessed to ascertain whether randomization was employed.

3. Methods for Measuring the Comparison (Intervention) and Variable Results (Outcome):
   a. Consistency in measuring exposure/intervention and outcome variables across primary studies is crucial.
   b. For variables measured on a categorical scale, it's important to verify if the cutoff or category used is consistent among the primary studies.

4. Design-Related Bias:
   a. The use of double-blinding and whether research subjects and assistants measuring outcome variables were kept unaware of the intervention status is considered.
   b. The potential for "Loss-to Follow-up Bias" is assessed, and any strategies adopted by primary studies to mitigate this bias are examined.

5. Methods for Controlling Confounding:
   a. The presence of confounding in the results/conclusions of the primary study is evaluated.
   b. The appropriateness of methods employed by primary study researchers to control the influence of confounding is scrutinized.

6. Statistical Analysis Methods:
   a. The analysis of outcome data between experimental and control groups post-intervention is reviewed.
   b. The evaluation extends to whether data analysis was conducted in accordance with the results of randomization or only data from subjects adhering to the research protocol.

7. Conflict of Interest:
   a. The presence of any conflict of interest with the research sponsor is considered.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2023) 13(4), 2370-2377 | ISSN :2251-6727

Following the assessment of research quality, four articles meeting the criteria for randomized controlled trials were selected. These articles will serve as primary sources for a meta-analysis exploring the effects of barberry consumption on non-communicable diseases. The data from these articles were then extracted and summarized in alignment with the PICO research framework.

Table 4. The description of the primary study of relaxation aromatherapy

Author (Year)	Country	Sample	P	I	C	O
Emamat et al. 2022	Iran	39	Hypertensive patients	Consuming barberry	Not consuming barberry	Blood pressure
Lazavi et al. 2018	Iran	23	Diabetic patients	Consuming barberry	Not consuming barberry	Blood pressure
Kermani et al. 2020	Iran	26	Metabolic syndrome patients	Consuming barberry	Not consuming barberry	Blood pressure
Emamat1 et al. 2022	Iran	42	Cardiometabolic patients	Consuming barberry	Not consuming barberry	Cholesterol

In Table 2, four publications with different research sites (Iraq, Egypt, Indonesia, and Iran) are meta-analyzed to show the overall primary research on the effects of barberry consumption on non-communicable illnesses. The similarities in the study were in terms of research design which employed randomized controlled trials, the subjects of the study which were patients with non-communicable diseases, and interventions which were given to those who consume barberry and those who do not. There were variations in the quantity of samples in this investigation as well; the smallest sample size was 23 and the greatest sample size was 130.

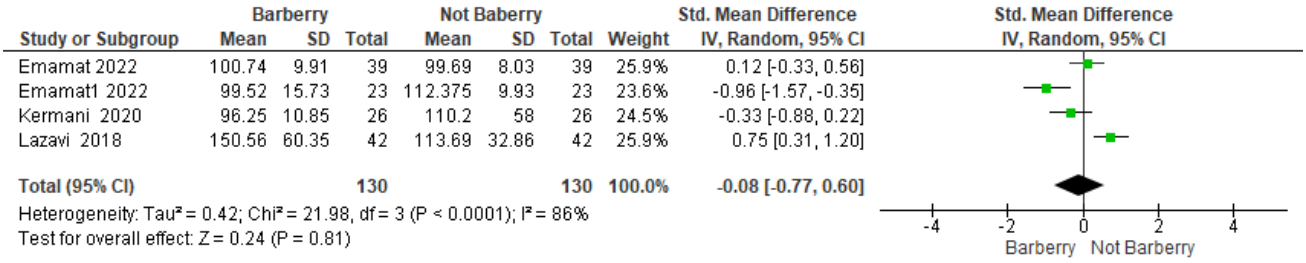

Figure 3. ***Forest plot***

Fores plot in Figure 3 shows that the consumption of barberry can lower the likelihood of non-communicable diseases. Patients with non-communicable diseases who consumed barberry decreased -0.08 times compared to the patients with non-communicable diseases who do not consume barberry (SMD= -0.08; CI 95%= -0.77 to 0.60; p<0.0001), and the results were statistically significant.

Journal of Chemical Health Risks
www.jchr.org
JCHR (2023) 13(4), 2370-2377 | ISSN :2251-6727

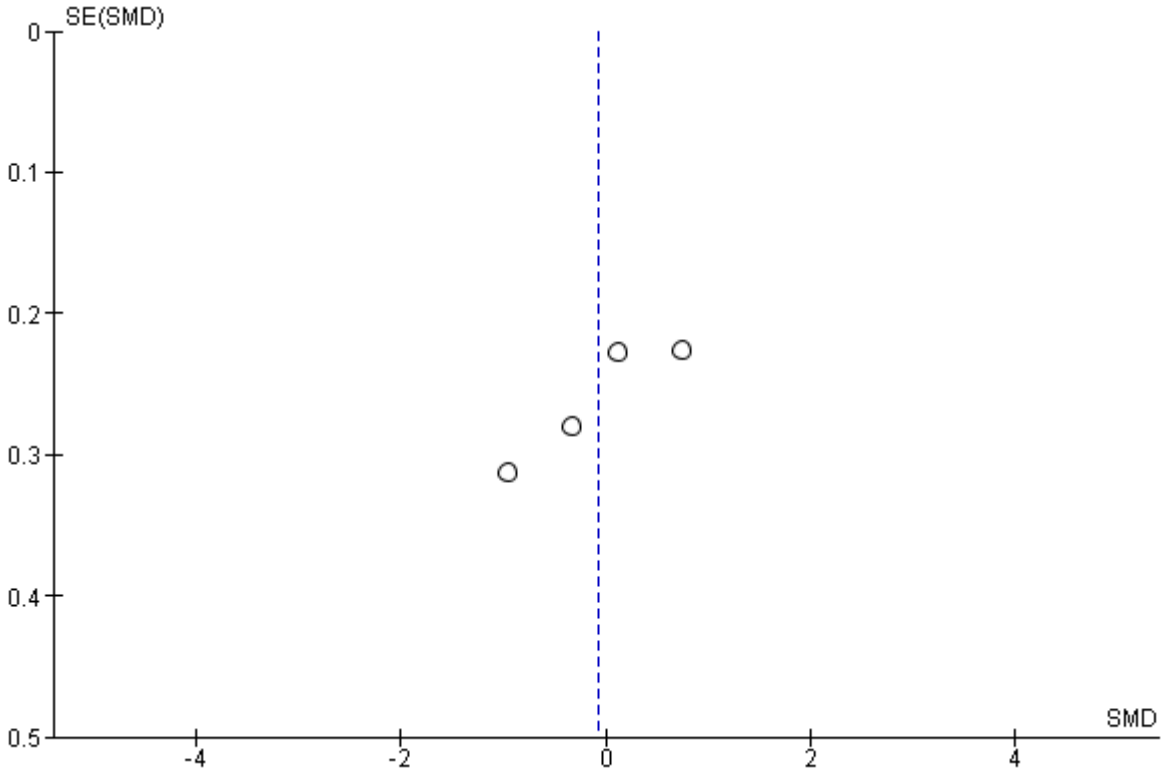

Figure 4. ***Funnel plot***

Funnel plot in Figure 4 shows the distribution of effect estimates among studies to the right and left of the average vertical line of estimates. The above figure shows no publication bias. The left-hand side of the plot amounts to two with a default error between 0 and 0.25. Meanwhile, the right-hand side plot amounts to two with a standard error between 0 and 0.35.

5. Discussion

The consumption of barberry appears to have a potential impact on lowering blood pressure, although the statistical significance of this effect remains inconclusive. However, it's important to note that there is a considerable level of heterogeneity among the studies, indicating variations in their findings. A more detailed examination through subgroup analysis reveals that the effectiveness of barberry supplementation is more pronounced when the duration of supplementation exceeds 8 weeks compared to shorter-term interventions and the overall effects (Atefi et al., 2021). Furthermore, barberry exhibits several potential health benefits in humans, including the control of hypertension, management of hyperlipidemia, and mitigation of chronic inflammation, which collectively contribute to the prevention of cardiovascular diseases. Additionally, barberry has been attributed with potential cardioprotective effects, as indicated in the research conducted by Emamat et al., (2020).

Barberry is rich in vasodilator factors, including aqueous components and berberine, which can effectively reduce blood pressure by modulating the central nervous system (Ma et al., 2021). Furthermore, the vasodilatory properties of barberry, attributed to substances like water and berberine, play a role in blood pressure regulation by affecting the central nervous system, promoting the release of endothelial relaxation factors, and blocking calcium channels, as revealed in research conducted by Emamat et al., (2022b). Emamat et al. go further with the effects of barberry consumption on individuals at risk of cardiovascular issues. Their study found that daily ingestion of 10 grams of barberry led to a significant reduction in average systolic and arterial blood pressure, assessed using ambulatory blood pressure monitoring (ABPM). Importantly, there were no appreciable

Journal of Chemical Health Risks

www.jchr.org

JCHR (2023) 13(4), 2370-2377 | ISSN :2251-6727

variations in the research participants' 24-hour urine excretion of potassium and salt. It is noteworthy that urine NOx levels rose in the barberry group relative to the control group, even though there were no discernible variations in plasma ACE activity or NOx concentration between the groups. Moreover, there was an inverse relationship found between variations in systolic blood pressure and variations in urine NOx, suggesting a possible connection between eating barberries and controlling blood pressure.

Berberine, a bioactive compound found in barberry, exhibits the capacity to reduce total cholesterol and low-density lipoprotein cholesterol (LDL-C). Its mechanism of action differs from that of statin drugs and involves influencing the expression of low-density lipoprotein receptors through a post-transcriptional mechanism. This unique mechanism stabilizes mRNA, thus enhancing the uptake of LDL-C (Lazavi et al., 2018). The distinctive mechanism through which berberine influences cholesterol levels sets it apart from conventional statin drugs. While statins primarily function by inhibiting an enzyme involved in cholesterol synthesis, berberine takes a different route. Berberine's approach targets the post-transcriptional regulation of LDL receptors. Specifically, it stabilizes the mRNA responsible for encoding these receptors, ultimately leading to an increase in their production. This upregulation of LDL receptors plays a pivotal role in the body's ability to remove LDL-C from the bloodstream, thus contributing to reduced total cholesterol and LDL-C levels. This novel mechanism of action has garnered significant attention within the realm of cardiovascular health, offering a potential alternative for individuals with cholesterol-related concerns.

Moreover, berberine's influence on lipid profiles holds promise not only in terms of its cholesterol-lowering effects but also its potential impact on overall cardiovascular health. Elevated levels of LDL-C are recognized as a risk factor for atherosclerosis and coronary artery disease, making the modulation of cholesterol levels a key target in preventive cardiology. The unique ability of berberine to enhance the expression of LDL receptors without directly interfering with cholesterol synthesis provides a fresh perspective in the pursuit of healthier cholesterol profiles. As research continues to explore the full scope of berberine's effects on cardiovascular health, it may emerge as a valuable component of therapeutic strategies aimed at reducing cardiovascular risk and improving lipid profiles.

The findings from a separate study by Emamat et al. (2022a). shed further light on the potential health benefits of barberry. This study demonstrated that the consumption of seedless barberry led to a reduction in plasma C-reactive protein (CRP) levels and improvements in lipid profiles among individuals with cardiovascular risk factors. Importantly, these beneficial effects were observed independently of variables such as participants' weight, physical activity levels, and dietary intake. This suggests that the incorporation of dried black barberry into one's daily regimen may be recommended for individuals with cardiovascular disease (CVD) risk factors, with the aim of enhancing lipid profiles and ameliorating inflammatory status. Nevertheless, it is prudent to underscore that while these results are promising, further validation through additional studies with larger sample sizes and varying quantities of barberry intake is strongly advised. These future investigations can provide a more comprehensive understanding of barberry's potential role in cardiovascular health.

6. Conclusion

In summary, barberry promises potentials in improving cardiovascular health. Its vasodilatory properties, fueled by ingredients like berberine, support its historic usage in cardiovascular therapies. It may also help lower blood pressure, especially when used over extended periods of time. By promoting the synthesis of low-density lipoprotein receptors, berberine, a main bioactive component in barberry, offers a novel method for decreasing cholesterol. Furthermore, research indicated that barberries—particularly the seedless kinds—may improve lipid profiles and reduce inflammation in those who are at risk for cardiovascular disease without requiring the involvement of other variables. Barberry has great potential as a safe and natural way to reduce cardiovascular risk factors and support heart health; however, more studies with bigger sample sizes and different doses are required.

References

Aisha, A., & Muhammad, A. (2014). Hypotensive activity, toxicology and histopathology of different

Journal of Chemical Health Risks

www.jchr.org

JCHR (2023) 13(4), 2370-2377 | ISSN :2251-6727

extracts of Berberis vulgaris. *Journal of Medicinal Plants Research*, *8*(8), 378–385. https://doi.org/10.5897/jmpr2013.5310

Atefi, M., Ghavami, A., Hadi, A., & Askari, G. (2021). The effect of barberry (Berberis vulgaris L.) supplementation on blood pressure: A systematic review and meta-analysis of the randomized controlled trials. *Complementary Therapies in Medicine*, *56*, 102608. https://doi.org/10.1016/j.ctim.2020.102608

Belwal, T., Bisht, A., Devkota, H. P., Ullah, H., Khan, H., Pandey, A., Bhatt, I. D., & Echeverría, J. (2020). Phytopharmacology and Clinical Updates of Berberis Species Against Diabetes and Other Metabolic Diseases. *Frontiers in Pharmacology*, *11*(February), 1–27. https://doi.org/10.3389/fphar.2020.00041

Emamat, H., Zahedmehr, A., Asadian, S., & Nasrollahzadeh, J. (2022a). The effect of barberry (Berberis integerrima) on lipid profile and systemic inflammation in subjects with cardiovascular risk factors: a randomized controlled trial. *BMC Complementary Medicine and Therapies*, *22*(1), 1–9. https://doi.org/10.1186/s12906-022-03539-8

Emamat, H., Zahedmehr, A., Asadian, S., & Nasrollahzadeh, J. (2022b). The effect of purple-black barberry (Berberis integerrima) on blood pressure in subjects with cardiovascular risk factors: a randomized controlled trial. *Journal of Ethnopharmacology*, *289*(December 2021), 115097. https://doi.org/10.1016/j.jep.2022.115097

Emamat, H., Zahedmehr, A., Asadian, S., Tangestani, H., & Nasrollahzadeh, J. (2020). Effect of barberry (Berberis vulgaris) consumption on blood pressure, plasma lipids, and inflammation in patients with hypertension and other cardiovascular risk factors: study protocol for a randomized clinical trial. *Trials*, *21*(1), 1–9. https://doi.org/10.1186/s13063-020-04918-7

Kermani, T., Kazemi, T., Molki, S., Ilkhani, K., & Sharifzadeh, G. R. (2020). The Effect of Berberis vulgaris (Barberry Fruit) on a Component of Metabolic Syndrome: A Randomized Clinical Trial. *Modern Care Journal*, *17*(2). https://doi.org/10.5812/modernc.93955

Kesehatan Masyarakat UNS. (2023). *Penilaian Kualitas Studi Primer untuk*. *36*, 3–4.

Lazavi, F., Mirmiran, P., Sohrab, G., Nikpayam, O., Angoorani, P., & Hedayati, M. (2018). The barberry juice effects on metabolic factors and oxidative stress in patients with type 2 diabetes: A randomized clinical trial. *Complementary Therapies in Clinical Practice*, *31*, 170–174. https://doi.org/10.1016/j.ctcp.2018.01.009

Lee, K. J., & Lee, Y. J. (2016). Effects of Vitamin D on blood pressure in patients with type 2 diabetes mellitus. *International Journal of Clinical Pharmacology and Therapeutics*, *54*(4), 233–242. https://doi.org/10.5414/CP202493

Lipert, A., Szadkowska, I., Matusiak-Wieczorek, E., & Kochan, E. (2022). The Effect of Herbal Supplements on Blood Pressure: Systematic Review and Meta-Analysis. *Antioxidants*, *11*(8). https://doi.org/10.3390/antiox11081419

Ma, C., Zheng, X., Yang, Y., & Bu, P. (2021). The effect of black tea supplementation on blood pressure: A systematic review and dose-response meta-analysis of randomized controlled trials. *Food and Function*, *12*(1), 41–56. https://doi.org/10.1039/d0fo02122a