

INPLASY PROTOCOL

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**Review Stage at time of this
submission:** Data extraction.

Conflicts of interest:
None declared.

Effects of Piper sarmentosum on Diabetes Mellitus and Hypertension: A Systematic Review

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Review question / Objective: This study will provide a comprehensive information on the effects of Piper sarmentosum on diabetes mellitus and hypertension.

Condition being studied: Diabetes mellitus and hypertension are two non-communicable diseases that frequently co-exist. Both diabetes and hypertension are the risk factors for cardiovascular diseases. Hypertension and diabetes mellitus not only share common pathophysiologic pathways but also common complications involving the macrovascular and microvascular disorders. Hence, a therapy or supplement that can help in both glycemic and blood pressure control will be of significant clinical value.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 05 April 2022 and was last updated on 05 April 2022 (registration number INPLASY202240020).

INTRODUCTION

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exist. Both diabetes and hypertension are the risk factors for cardiovascular diseases. Hypertension and diabetes mellitus not only share common pathophysiologic pathways but also common complications involving the macrovascular and microvascular disorders. Hence, a therapy or supplement that can help in both glycemic and blood

pressure control will be of significant clinical value.

METHODS

Search strategy: A computerized database search will be performed on Scopus, Medline and Web of Science databases with the following set of keywords: Piper sarmentosum AND (diabetes mellitus OR diabetic OR diabetes OR hyperglycemia OR blood glucose OR HbA1c OR glycated h*emoglobin OR h*emoglobin A1c OR hyperten* OR blood pressure). Reference of the included studies will also be manually screened for eligible studies. No restrictions on date of publication will be applied. Only studies published in English will be included. No geographical restriction will be applied.

Participant or population: Adult patients with established hypertension and/or diabetes as well as preclinical models of hypertension and diabetes, regardless of animal species, will be included.

Intervention: Studies that used *P. sarmentosum* as an intervention in the experimental group will be included, regardless of route of administration, formulation, dose and duration of intervention.

Comparator: The comparator groups received either no intervention or were treated with relevant conventional drug.

Study designs to be included: Clinical (randomised controlled trial) and preclinical (in vitro, in vivo, ex vivo) studies will be included. Observational studies, editorial, review, abstract/ conference proceedings will be excluded.

Eligibility criteria: Any clinical and preclinical studies that reported the effect of *P. sarmentosum* on diabetes and hypertension models.

Information sources: Scopus, Medline and Web of Science databases will be searched with the following set of keywords: Piper sarmentosum AND (diabetes mellitus OR

diabetic OR diabetes OR hyperglycemia OR blood glucose OR HbA1c OR glycated h*emoglobin OR h*emoglobin A1c OR hyperten* OR blood pressure). Reference of the included studies will also be manually screened for eligible studies.

Main outcome(s): 1. Changes in blood pressure, including systolic and diastolic blood pressure, and mean arterial pressure observed as mean with accompanied standard deviation (SD), or present or absent. 2. Changes in fasting blood glucose and glycosylated hemoglobin (HbA1c) observed as mean with accompanied standard deviation (SD), or present or absent.

Additional outcome(s): Additional outcomes will be the levels of nitric oxide, asymmetric dimethylarginine, endothelin-1 level and malondialdehyde, α -glucosidase activity and histopathological changes related to the target organ damage.

Data management: Two reviewers (N.S.O. and A.U.) will independently extract the data from the included studies based on the predefined, standardized form of data collection. Any disagreement will be resolved through discussion with the third reviewer (N.A.C.R.). A data spreadsheet will be created using Microsoft Excel to collect relevant information and data. The following data will be extracted: author, publication time, article title, country where the study is conducted, study design, intervention, time and dose of treatment, comparators, plant source, plant part, type of extract, phytochemicals, and the outcomes.

Quality assessment / Risk of bias analysis: The risk of bias will be analyzed independently by two reviewers (N.S.O and A.U.). Any disagreement will be resolved through discussion with the third reviewer (N.A.C.R.). Cochrane risk of bias (RoB) tool will be used to assess the risk of bias in randomized clinical trials. Meanwhile, animal studies will be assessed using Systematic Review Center for Laboratory Animal Experimentation (SYRCLE) risk of bias tool. The main components of this

item are as follows: (1) Selection bias: random sequence generation, baseline characteristics, allocation concealment; (2) Detection bias: random housing, blinding, random outcome assessment; (3) Attrition bias: incomplete outcome data; (4) Reporting bias: selective reporting; and (5) Other bias. For in vitro studies, a customized risk of bias tool based on the Joanna Briggs Institute (JBI) checklist for non-randomized experimental studies (2020) will be used. The customized RoB tool comprises three domains as follows: (1) Reporting quality: source of plant, amount of plant/extract/sample used; (2) Performance bias: reliable tools and /or reagents used to measure outcome; and (3) Detection bias: standard/appropriate control used, multiple measurement of outcome performed. Each domain will be evaluated as being a high, moderate, low or unclear risk of bias. Nevertheless, the ratings used in the respective RoB tool will not be used as a criterion for study eligibility.

Strategy of data synthesis: Both study characteristics and outcome data will be tabulated and described narratively. A meta-analysis will be conducted if the data permits. The risk of bias will be summarized and reported narratively.

Subgroup analysis: Where possible, we plan to evaluate the effect of *P. sarmentosum* based on different part of plants, various solvents and extracts of *P. sarmentosum*, and pre-clinical model used.

Sensitivity analysis: A sensitivity analysis will only be conducted if a meta-analysis was performed.

Language: English.

Country(ies) involved: Malaysia.

Keywords: Antidiabetic; antihypertensive; diabetes mellitus; hypertension; Piper sarmentosum.

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