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Phenylpropanoid from Alpinia Species and Their Antibacterial Activity: A Comprehensive Systematic Review and Meta-Analysis

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ADMINISTRATIVE INFORMATION

Support - UMREG021-2023.

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Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 9 June 2025 and was last updated on 9 June 2025.

INTRODUCTION

eview question / Objective Extensive phytochemical studies on Alpinia genus have identified numerous phenylpropanoid (PP) derivatives, which exhibit a wide range of biological activities, particularly, antibacterial properties. Systematic review on the antibacterial efficacy of phenylpropanoids derived from Alpinia species remains limited. This systematic review and meta-analysis aim to evaluate the antibacterial activity of phenylpropanoids extracted from Alpinia species and compare their effectiveness against various bacterial strains, and assess their performance relative to positive controls.

Condition being studied The use of metals as antibacterial agents has raised concerns due to their disadvantages, particularly their impact on the environment. As a result, the search for natural antibacterial alternatives has intensified. Phenylpropanoids, a diverse class of secondary metabolites commonly found in plants, have emerged as promising candidates. This study systematically analyzes and evaluates phenylpropanoid compounds derived from Alpinia species and their effectiveness against various bacterial strains. This meta-analysis aims to identify consistent patterns, highlight knowledge gaps, and inform future drug development and natural product-based therapeutic strategies.

METHODS

Search strategy A comprehensive literature search will be conducted using databases such as SciFinder, Scopus and Web of Science were searched up to (4 March 2025). Publication language was limited to English-language studies only. Publication type was limited to article, and research area was excluded the topics irrelevant to chemistry on each database automatically. All of the results were imported to Endnote and conducted deduplication.

Participant or population Original research articles that provide quantitative data on

antibacterial activities of phenylpropanoid derived from Alpinia species.

Intervention Phenylpropanoid compounds derived from Alpinia species, which were tested for their antibacterial effects against the selected bacterial strains.

Comparator Antibiotic positive control.

Study designs to be included A comprehensive literature search will be conducted using databases such as SciFinder, Scopus and Web of Science. Publication language was limited to English-language studies only. Publication type was limited to article, and research area was excluded the topics irrelevant to chemistry on each database automatically. All of the results were imported to Endnote and conducted deduplication.

Eligibility criteria Studies were included if they met the following criteria: (1) peer-reviewed publications between the years 2000 and 2025, (2) reporting of minimum inhibitory concentration (MIC) or minimum bactericidal concentration (MBC) values, (3) specific investigation of phenylpropanoids derived from Alpinia species, and (4) evaluation of the antibacterial properties of pure compounds rather than crude extracts.

Studies were excluded if they (1) lacked quantitative antibacterial data, (2) were review articles, commentaries, or editorials, (3) focused exclusively on non-bacterial pathogens such as fungi or viruses, or (4) focused solely on the antibacterial properties of crude extracts.

Information sources A comprehensive literature search will be conducted using databases such as SciFinder, Scopus and Web of Science were searched up to (4 March 2025) using the following k e y w o r d s :- (((phenylpropanoid OR "phenylpropanoid derivative" OR chavicol OR hydroxychavicol OR "1-acetoxychavicol acetate") AND (antibacterial OR antimicrobial OR (anti AND bacterial) OR (anti AND microbial)) AND (isolation OR purification OR identification OR (pure AND compound) OR (isolated AND compound)))).

Main outcome(s) Minimum Inhibitory Concentration (MIC)

Minimum Bactericidal Concentration (MBC) These outcomes will be extracted as continuous data, expressed in mg/mL. If values are reported in other units, they will be converted to mg/mL for consistency. MIC and MBC values will be recorded separately for:

(1) Extract

(2) Isolated phenylpropanoid compound (PP)

(3) Control (e.g., standard antibiotics).

Additional outcome(s) Title, author(s), and year of publication.

Plant species: Scientific name of the Alpinia species or other plant sources of phenylpropanoids.

Solution extract: Type of solvent used for extraction (e.g., ethanol, methanol, aqueous).

Type of phenylpropanoid: Specific compound identified

Bacteria tested: Bacterial strains used for antibacterial testing (e.g., E. coli, S. aureus).

Controls used: Type of positive or negative control reported in the study.

Data management For each outcome measure (Minimum Inhibitory Concentration [MIC], Minimum Bactericidal Concentration [MBC]), a quantitative synthesis (meta-analysis) is planned when sufficient data are available (i.e., when at least two studies report the same outcome using comparable methods and measurement scales). The decision between quantitative and narrative synthesis will be guided by: The number of studies reporting a given outcome, the consistency of reported outcome measures, the statistical heterogeneity (l² values), and the availability of necessary summary data (means, standard deviations, sample sizes, etc.).

Quality assessment / Risk of bias analysis ToxRTool consists of two parts, one to evaluate in vivo and one to evaluate in vitro data. Two researchers independently assessed the risk of bias using the ToxRTool evaluation. If there was any ambiguity, it can be resolved through discussion and third-party negotiation. The assessment results were grouped into three categories: reliable without restrictions (for in vitro studies with 15–18 points), reliable with restrictions (for in vitro studies with 11–14 points), and not reliable (for in vitro studies less than 11 points).

Strategy of data synthesis Key data from the selected studies will be extracted and organized into a structured table. The data to be recorded includes the compound name and plant extract, the bacterial strains tested, the MIC and MBC values, positive control and its MIC or MBC values and the type of study (in vitro, in vivo, or in silico). The activity values were extracted from the studies for each compound and positive controls if reported, and the meta-analysis was conducted by RevMan 5.4 software, including effect size calculation, pooling effect sizes and heterogeneity analysis. Meta-analyses will be performed using a random-effects model, especially when

heterogeneity is substantial ($I^2 > 50\%$). Standardized Mean Differences (SMD) with 95% Confidence Intervals will be used for continuous outcomes measured with different scales (e.g., MIC expressed in µg/mL or mm inhibition zone). Subgroup and sensitivity analyses, as well as publication bias assessment, will be carried out where feasible to ensure robustness and transparency of the findings.

Subgroup analysis Type of phenylpropanoid compound (e.g., ACA, TPCA)

Type of bacterial strain (e.g., S. aureus, MRSA, M. smegmatis, P. acnes, S. epidermidis)

Type of test compound (e.g., crude extract vs. pure compound)

Type of positive control used (e.g., tetracycline, CCCP, oxacillin).

Sensitivity analysis A leave-one-out sensitivity analysis was performed to evaluate the robustness of the meta-analysis results concerning the antibacterial activity of phenylpropanoid compounds.

Language restriction English.

Country(ies) involved Malaysia.

Keywords Alpinia; phenylpropanoid; antibacterial; gram- positive bacteria; systematic review; meta-analysis.

Contributions of each author

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