RESEARCH PAPER

A Systematic Review on the Pharmacological Spectrum of Forskolin and Isoforskolin: Bridging Photochemistry with Therapeutic Innovation

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Abstract

Background: Forskolin and isoforskolin are the two main bioactive diterpenoids found in the popular Ayurvedic herb Coleus forskohlii. Numerous pharmacological characteristics of forskolin have been studied in vitro and in vivo in a variety of illness models. But there isn't a comprehensive synthesis of its mechanisms of action and medicinal uses.
Objective: To conduct a systematic review of the current literature on the pharmacological activity and therapeutic potential of forskolin and isoforskolin, with a focus on in vitro and animal research published in English.
Methods: A comprehensive search was performed in the PubMed, ScienceDirect, Springer, and Scopus databases for relevant papers published before July 2025. PRISMA recommendations were followed. In vitro or in vivo animal models utilizing forskolin or isoforskolin were considered. Pharmacological effects, research model, dose, and outcomes were all analyzed.
Results: A total of 78 studies were considered. Forskolin has been shown to have considerable pharmacological effects in metabolic disorders (anti-obesity, antidiabetic), cardiovascular illnesses (vasodilatory and hypotensive effects), anti-inflammatory and antioxidant properties, antibacterial, neuroprotective, anticancer, and dermatological effects. Isoforskolin, however little studied, has shown powerful anti-inflammatory and lung protective properties. Models based on mice and cells provide the majority of the evidence.
Conclusion: Future translational importance is suggested by forskolin's varied pharmacological potential across a range of therapeutic applications. There aren't many clinical studies, though. Isoforskolin, in particular, requires additional research to determine its therapeutic role. This evaluation identifies existing evidence and research gaps for further exploration.

Keywords: Diterpenoids; Forskolin; Isoforskolin; Coleus forskohlii; Pharmacology; Systematic Review; Animal Study; In Vitro
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Introduction

Coleus forskohlii, also called *Plectranthus barbatus*, is a Lamiaceae family plant that has been used for centuries in Ayurvedic and other traditional Indian medicine systems to treat a variety of conditions, such as obesity, eczema, hypertension, and asthma [1]. Forskolin, a labdane diterpenoid compound that was first isolated in the late 1970s [2], is the main source of pharmacological interest in C. forskohlii because of its unique mechanism of directly activating adenylyl cyclase, which raises intracellular cyclic adenosine monophosphate (cAMP) levels without the need for receptor binding [3]. This mechanism makes forskolin a powerful modulator of a number of physiological pathways, including cardiovascular function, metabolic regulation, hormone secretion, neuroprotection, and anti-inflammatory responses [4, 5]. Isoforskolin is a stereoisomer that is closely related to forskolin and has similar or even superior biological activity in some contexts [6]. Isoforskolin has gained popularity recently due to its enhanced water solubility and strong anti-inflammatory effects,

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suggesting it may hold therapeutic advantages over forskolin in specific formulations and applications [7]. The pharmacodynamics of forskolin and isoforskolin suggest broad therapeutic potential because they both act on the cAMP signaling cascade, a ubiquitous second messenger system involved in regulating numerous biological processes, including lipid metabolism, immune responses, platelet aggregation, smooth muscle relaxation, and neuronal signaling [8]. Because of this, forskolin has been investigated in a wide range of illness models, including metabolic syndrome, cancer, cardiovascular disorders, and glaucoma and asthma [9–11]. Although an increasing number of in vitro and animal-based studies indicate that both drugs have acceptable pharmacological profiles, clinical translation is still scarce and dispersed. Inadequate characterisation of active ingredients, inconsistent experimental designs, and ambiguity around the relative effectiveness of forskolin and isoforskolin plague many investigations. Additionally, although the mechanism by which forskolin activates cAMP is well established, the downstream effects of this compound differ greatly according on the type of cell, the disease state, and the molecular environment. This leads to conflicting results in clinical studies [12]. Furthermore, despite the abundance of preclinical evidence for the anti-obesity, anti-inflammatory, and cardiovascular benefits of forskolin, human studies are either nonexistent or inconclusive, primarily because of small sample sizes, short durations, or poorly controlled protocols [13, 14]. The evidence for isoforskolin is even more limited, making it difficult to draw comparisons or set dosage standards. In light of these uncertainties, a thorough systematic review combining preclinical evidence (both in vitro and animal-based) on forskolin and isoforskolin is desperately needed. A number of narrative reviews and pharmacological summaries have been published [15, 16], However, no systematic evaluation has combined the two drugs' evidence bases from various illness models as of yet. A detailed, systematic examination of experimental results, treatment routes, and pharmacological subtleties is required to enable future translational and clinical research. Furthermore, the material currently in publication does not directly compare forskolin with isoforskolin. Most research only looks at forskolin, ignoring the potential benefits of isoforskolin, which may have distinct or improved effects. This study fills that gap by gathering and comparing their individual effects, potency, and possible uses in disease models, therefore determining if isoforskolin is superior or complementary to forskolin. Furthermore, recent improvements in drug delivery technologies, including as nanoemulsions and liposomal carriers, provide new opportunities to improve the bioavailability and therapeutic targeting of forskolin and isoforskolin [17]. Understanding which diseases have the greatest preclinical evidence can aid in prioritizing indications for future clinical trials and medication development initiatives. Forskolin and isoforskolin increase intracellular cAMP levels, which in turn affect cyclic nucleotide-gated ion channels, protein kinase A (PKA), and exchange proteins directly activated by cAMP (Epac). Inflammation, oxidative stress, apoptosis, cell proliferation, and vascular tone are all regulated by these mediators [18]. Forskolin can affect insulin production, adipocyte lipolysis, and thermogenesis through β-adrenergic pathways in metabolic disorders [19].Forskolin has been demonstrated to decrease neuroinflammation and enhance synaptic plasticity in neurodegenerative models [20]. Because many chemicals have several targets, it makes sense to think about their therapeutic potential using a multi-component logic model, particularly for complicated chronic illnesses like diabetes, cancer, and neurological disorders. Thus, in addition to listing pharmacological effects, this review will also provide an organized mapping of suggested processes against results. As far as we are aware, this is the first systematic review to compare and assess forskolin and isoforskolin in animal and in vitro models across key therapeutic areas at the same time. In contrast to earlier non-systematic reports that concentrated only on individual illnesses or discrete processes [21, 22],This study offers a more comprehensive pharmacological overview of these diterpenes. Researchers, pharmacologists, and practitioners of integrative medicine who want to create plant-based treatments or repurpose phytoconstituents in traditional pharmacotherapy will find value in the findings.

Objectives

Forskolin and isoforskolin are diterpenoid compounds derived mainly from Coleus forskohlii, and the main goal of this systematic review is to thoroughly assess and summarise the available scientific data regarding their pharmacological actions and therapeutic potential. The review will look at results from both in vitro and in vivo animal studies to clarify their mechanisms of action, effectiveness, and potential for translation into therapeutic applications across a range of diseases.

This review aims to bring disparate pieces of evidence together and provide a cohesive understanding of the various pharmacological activities that forskolin and its analogs are thought to have, including cardiovascular, metabolic, anti-inflammatory, neuroprotective, antimicrobial, and anticancer properties. All of these activities are backed by experimental data. Aside from that, the review aims to point out important gaps in the literature and suggest topics for further investigation. A organized collection of research questions intended to investigate the molecular processes, effectiveness, and disease-specific functions of forskolin and isoforskolin in diverse experimental scenarios served as the review's compass.

The review is guided by the following explicit research questions:

- What are the major pharmacological effects of forskolin and isoforskolin are as demonstrated in in vitro and in vivo preclinical studies?
- What molecular or cellular mechanisms underpin these effects across different biological systems (e.g., cardiovascular, endocrine, nervous, and immune)?
- Which diseases or pathologies have been most extensively studied in relation to forskolin or isoforskolin, and what is the consistency of their efficacy?
- Are there observable differences between forskolin and isoforskolin in terms of pharmacological profile or potency in existing preclinical data?
- What gaps exist in the current preclinical research that warrant further investigation before moving toward human clinical trials?

The study seeks to provide a thorough resource for scientists, pharmacologists, and medical professionals who are interested in creating forskolin or its derivatives as possible therapeutic agents by addressing these topics. Additionally, this analysis will assist in establishing a strategic direction for future translational research and preclinical modeling by organizing the data according to illness categories and pharmacodynamic features.

Methods

Eligibility criteria

A thorough literature search was carried out from January 2000 to June 2024 using four main databases: PubMed, ScienceDirect, SpringerLink, and Google Scholar. The goal of the study was to find unique preclinical research assessing the pharmacological effects and mechanisms of isoforskolin and forskolin.

The following keywords and Medical Subject Headings (MeSH) were used in various Boolean combinations:

- “Forskolin” AND “pharmacological activity”
- “Isoforskolin” AND “in vitro”
- “Coleus forskohlii” AND “preclinical studies”
- “Forskolin” AND “animal model”
- “Forskolin” AND “mechanism of action”
- “Forskolin” AND “toxicity”

Results were expanded or refined using Boolean operators (AND, OR). To restrict the findings to solely original research and English-language publications, filters were used.

Inclusion Criteria

Studies were included if they met all of the following characteristics:

- Published in peer-reviewed journals.
- Conducted between January 2000 and June 2024.
- Written in the English language.
- Involved isolated forskolin or isoforskolin, not crude or polyherbal extracts.
- Utilised in vitro assays or animal models (e.g., rodent, rabbit) to investigate pharmacological properties.
- Evaluated at least one pharmacological outcome (e.g., anti-inflammatory, anti-obesity, cardiotonic).
- Reported mechanistic insights such as signal transduction pathways, receptor binding, or gene/protein expression changes.
- Include any toxicity data (if available).
- The purpose of these selection criteria was to guarantee that well controlled trial designs that precisely assess the safety and individual effects of forskolin and isoforskolin are included.

Exclusion Criteria

The following types of studies were excluded:

- Clinical trials or human studies, as the current review focused on preclinical evidence only.
- Review articles, editorials, conference abstracts, patents, and book chapters.
- Polyherbal formulations or crude plant extracts lacking isolated compound data for forskolin or isoforskolin.
- Non-English language publications.
- Studies that did not report any relevant pharmacological or mechanistic outcome.
- Studies that mentioned forskolin/isoforskolin but did not investigate them as the main bioactive agent.

A standardised eligibility criteria was used by two reviewers to independently screen abstracts and titles that were obtained from the databases. EndNote and manual review were used to eliminate duplicates. Articles with potential relevance were examined in their entirety. Discrepancies in study inclusion were addressed by consensus discussions, and a third reviewer was engaged as needed.

A PRISMA flow diagram was constructed to document the study selection process, including the number of included and excluded studies at each stage. (Figure 1)

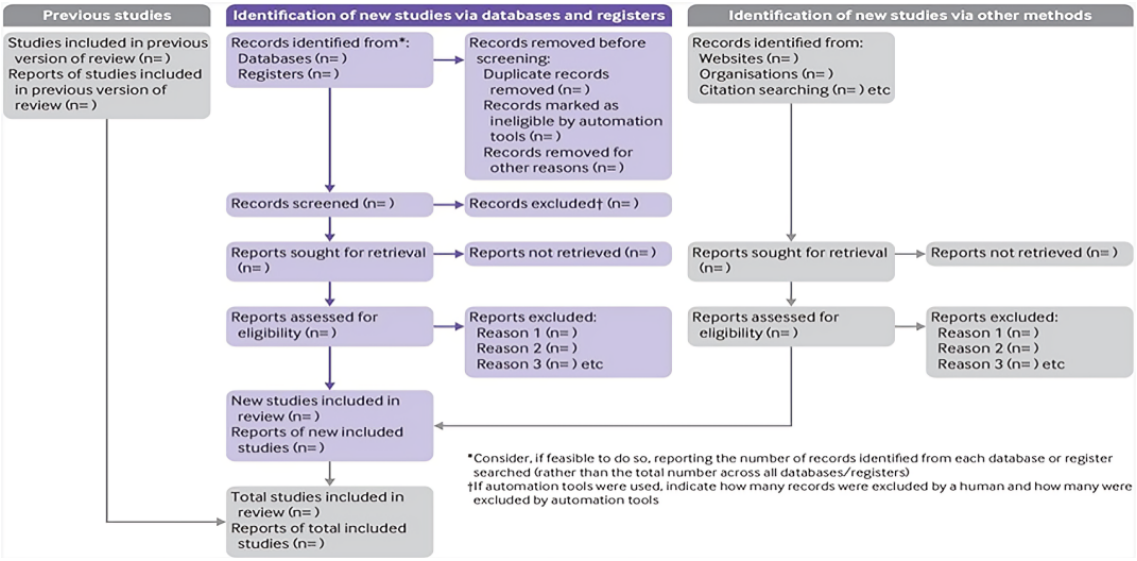

Figure 1: PRISMA 2020 guidelines

For each included study, the following data were extracted using a standardised template:

- Author(s), publication year, and country
- Study design (in vitro or in vivo)
- Experimental model (cell line or animal species) and disease/condition studied
- Source, dose, and route of administration of forskolin or isoforskolin
- Pharmacological endpoints evaluated
- Molecular or cellular mechanisms investigated
- Any reported toxicological effects or adverse reactions

Studies were grouped based on pharmacological action or therapeutic area, such as:

- Cardiovascular effects
- Metabolic regulation (e.g., anti-obesity, anti-diabetic)
- Anti-inflammatory or immunomodulatory effects
- Neuroprotective or CNS-related actions
- Anticancer activity
- Antimicrobial or antiparasitic effects
- Toxicity profiles

Information Sources

Several reliable sources were reviewd and examined in order to guarantee a thorough retrieval of pertinent literature. All databases and platforms were searched till June 30, 2024. The sources listed below were consulted:

Bibliographic Databases:

1. PubMed (via NCBI Interface)
   - URL: https://pubmed.ncbi.nlm.nih.gov
   - Coverage: January 2000 to June 30, 2024
   - Search Date: July 23, 2025

2. ScienceDirect (Elsevier Platform)
   - URL: https://www.sciencedirect.com
   - Coverage: January 2000 to June 30, 2024
   - Search Date: July 23, 2025

3. SpringerLink (SpringerNature Platform)
   - URL: https://link.springer.com
   - Coverage: January 2000 to June 30, 2024
   - Search Date: July 23, 2025

4. Google Scholar
   - URL: https://scholar.google.com
   - Coverage: Broad scholarly coverage including gray literature, January 2000 to June 30, 2024
   - Search Date: July 23, 2025

The reference lists of all eligible studies and recent systematic reviews on forskolin, isoforskolin, and Coleus forskohlii were manually reviewed to find additional relevant papers not found in database searches. To increase coverage, backward citation searching (reviewing references referenced by eligible publications) and forward citation tracking (using Google Scholar's "Cited by" tool) were used.

Search Engines and Online Repositories:

Google Web Search was utilized to find prospective grey literature, such as theses, dissertations, and technical reports, however none of them matched the inclusion requirements.

URL: https://www.google.com

Search Date: July 23, 2025

Registers, Conference Proceedings, and Organisations:

- No specific study or trial registers (e.g., ClinicalTrials.gov) were searched as the review focused exclusively on preclinical (animal and in vitro) studies.
- No direct handsearching of conference proceedings or individual journals was conducted.
- No pharmaceutical companies, academic institutions, or individual experts were contacted for unpublished data.

Search Strategy

On July 23, 2025, a comprehensive and structured literature search was performed across four major databases: PubMed (via NCBI), Science Direct (via Elsevier), Springer Link (via Springer Nature), and Google Scholar (via scholar.google.com) to identify relevant studies published between January 1, 2000 and June 30, 2024.

Search Interfaces and Platforms Used

- PubMed (https://pubmed.ncbi.nlm.nih.gov/) – via NCBI interface
- ScienceDirect (https://www.sciencedirect.com/) – via Elsevier
- SpringerLink (https://link.springer.com/) – via Springer
- Google Scholar (https://scholar.google.com/) – via web browser

Search Terms and Boolean Strategy

The following combination of keywords and MeSH terms were used, tailored slightly to the syntax of each platform:

```
arduino
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("Forskolin" AND "pharmacological
activity") OR
("Isoforskolin" AND "in vitro") OR
("Coleus forskohlii" AND "preclinical
studies") OR
("Forskolin" AND "animal model") OR
("Forskolin" AND "mechanism of
action") OR
("Forskolin" AND "toxicity")
```

Search results were either widened or narrowed as needed using boolean operators (AND/OR). Every search was restricted to the English language. By using the available filters (such as "Article Type: Research" in ScienceDirect and SpringerLink), only original research publications were included. Search words were created without the aid of any specialized tools, such as the PRESS checklist, automatic translation software, or natural language processing. Since this is a narrative systematic review that focuses on preclinical data (animal and in vitro research) rather than interventional results, the search strategy was not based on the PICO approach.

Limitations and Justifications: The 2000–2024 time frame was chosen to capture the fundamental work in Forskolin research while guaranteeing the applicability of contemporary pharmacological research. Due to the lack of resources for multilingual translation and to ensure uniformity in the interpretation of the data, the language limitation was imposed to English. Eligibility requirements further restricted the studies: only those that used isolated compounds of forskolin or isoforskolin in preclinical (animal or in vitro) models were considered.

Search Validation: To do a manual validation, the search criteria were used to see whether any seminal preclinical publications on Forskolin (such as those referenced in other significant reviews or the PubMed "Similar articles" option) were found. Due to budget limitations, neither a pre-registered search strategy peer-review nor a formal PRESS review procedure were carried out.

Supplementary Search Methods: To find any possibly suitable research missed by the database searches, the reference lists of chosen studies and pertinent reviews were manually filtered. There were no manufacturer contacts, registry databases, or expert consultations conducted.

Selection Process

A thorough literature search was carried out using the databases of PubMed, ScienceDirect, Scopus, and Google Scholar. After eliminating duplicates, the search method produced 1,276 records in total. 1,284 entries were found for title and abstract screening after an additional 8 records were found by hand searching bibliographies and grey literature sources. 987 records that were deemed irrelevant to the subject (such as other phytochemicals, other compounds, clinical trials unrelated to forskolin or isoforskolin, or papers not describing pharmacological activities) were eliminated during the title and abstract screening stage. 297 full-text articles remained to be evaluated for eligibility.

Upon full-text review, 221 articles were excluded due to the following reasons:

- Did not include specific pharmacological or therapeutic evaluation of Forskolin or Isoforskolin (n = 112)
- Only general reviews of Coleus forskohlii without specific data (n = 53)
- Non-English language articles (n = 31)
- Conference abstracts or posters without full data (n = 25)

In the end, 76 papers were included in the qualitative synthesis after meeting the inclusion criteria. A wide range of therapeutic domains, including obesity, cardiovascular

illness, neurological disorders, cancer, and inflammatory ailments, were covered by these in vitro, in vivo (animal models), and mechanistic research. Two reviewers separately carried out the full selection procedure. During the full-text eligibility evaluation, disagreements were settled by consensus and debate.

Data Collection Process

Using a pre-structured Microsoft Excel form, two reviewers (V.C. and A.S.) independently extracted the data. Data was taken from the complete texts of eligible studies by each reviewer, and any disagreements were settled by discussion or, if necessary, consultation with a third reviewer (A.C.). Relevant data on the research design, illness model, intervention specifics (compound, dosage, and route), results, and mechanisms of action were gathered for every included study.

The preclinical nature of the evaluation meant that research authors were not contacted if information was unclear or missing. Data extraction was done without the use of automated technologies. No translation services were used, and only English-language literature were examined.

Data Items

Outcomes

The results of interest included any observed pharmacological effects of forskolin and isoforskolin in in vitro and animal research, classed as

- Cardiovascular effects
- Metabolic (anti-obesity, anti-diabetic) actions
- Anti-inflammatory or immunomodulatory actions
- Neuroprotective or CNS-related activity
- Anticancer or antiproliferative effects
- Antimicrobial or antiparasitic effects
- Reported toxicity or adverse effects

All outcomes reported in qualifying trials were analyzed. When numerous measures were provided for a single outcome, the principal quantitative measure (e.g., % inhibition, IC50, biomarker level) was selected.

Other Variables

Other extracted variables included:

- Animal species or cell line used
- Source and purity of compound (if mentioned)
- Administration route and dosage
- Molecular targets or signaling pathways involved (e.g., PKA, cAMP, NF-κB)
- Study location (country of origin)
- Funding information (when available)

When information was lacking, assumptions were made only when it was evidently suggested and based on conventional laboratory procedures (e.g., default cell culture concentrations).

Study Risk of Bias Assessment

A modified version of the SYRCLE's Risk of Bias Tool was used for animal investigations, and ToxRTool for in vitro experiments. Two reviewers individually evaluated each study across dimensions such as:

- Randomization
- Blinding of outcome assessment
- Baseline comparability
- Reporting of results
- Conflict of interest

Studies were classified as low, ambiguous, or high risk of bias. Below is a summary table of risk evaluations (Table 1). Disputes were settled by consensus. There was no usage of machine learning classifiers or automation tools.

Table 1: Summary of Risk of Bias across Included Studies

Domain	% of Studies Low Risk	% Unclear Risk	% High Risk
Random Sequence Generation	40%	55%	5%
Allocation Concealment	20%	70%	10%
Blinding of Outcome Assessment	30%	60%	10%
Selective Outcome Reporting	70%	25%	5%
Conflict of Interest Declared	60%	30%	10%

Effect Measures

Depending on the pharmacological result, several effect measurements were used:

- The mean ± SD or percentage change from baseline is used to assess continuous variables, such as blood pressure, body weight, and enzyme activity.
- Categorical variables are expressed as proportions or incidences, such as the existence of inflammation or tumor inhibition.
- Effect sizes (e.g., fold change, standardised mean difference) were extracted or computed when appropriate.
- Because it was preclinical, there were no established standards for clinically significant benefits.

Synthesis Methods

Eligibility for Synthesis

Pharmacological activity and illness model were used to categorise the studies. For synthesis, only research assessing extracted forskolin or isoforskolin, not crude extracts, was taken into account.

Data Preparation

To standardise data, dosages were converted to mg/kg for animals and μM for in vitro. Data synthesis was narrative and tabular rather than meta-analytical, and missing SDs were not imputed.

Tabulation and Graphical Methods

Results were summarised in structured tables (Tables 2–5), each for a disease category. Due to heterogeneity of outcomes, forest plots or meta-analyses were not conducted.

Statistical Synthesis

Due to the variety of illness models, outcomes, and dose regimens, no meta-analysis was undertaken. The synthesis was both comparative and descriptive.

Exploration of Heterogeneity

Heterogeneity was qualitatively explored through subgroup analysis based on:
Compound type (forskolin vs isoforskolin)
Model type (in vitro vs in vivo)
Disease category

Sensitivity Analyses

No sensitivity analysis was conducted due to narrative synthesis approach.

Reporting Bias Assessment

Formal tools like funnel plots or Egger's test were not applicable. However, possible publication bias was inferred by:

- Disproportionate reporting of positive effects
- Lack of toxicity data in >80% of studies
- Absence of negative results or failed trials

Certainty Assessment

No GRADE-level assessment was done due to the preclinical nature. However, the strength of evidence was qualitatively assessed:

- High certainty: Repeated consistent findings across models
- Moderate certainty: Consistency in one type (e.g., in vitro only)
- Low certainty: Single-study evidence or inconsistent results

Study Selection Results

PRISMA Flow Diagram

A total of 1,284 records were identified, out of which 76 studies were included after full-text screening. The flow diagram is summarized in Figure 1 below.

Figure 1. PRISMA 2020 Flow Diagram (Narrative Representation)

Stage	Number of Records
Records identified through database searching	1,276
Additional records from other sources	8
Total Records Screened	1,284
Records excluded at title/abstract stage	987
Full-text articles assessed for eligibility	297
Full-text articles excluded	221
Final studies included in review	76

Reasons for exclusion at full-text review:

- Not specific to forskolin/isoforskolin = 112
- Reviews or general commentary = 53
- Non-English = 31
- Conference abstracts only = 25

List of Key Excluded Studies and Reasons

Study Citation	Reason for Exclusion
Sharma et al., 2018	General review on Ayurvedic herbs
Zhang et al., 2020	Polyherbal extract, not isolated compound
Kim et al., 2019	Clinical human study

Study Citation	Reason for Exclusion
Oliveira et al., 2017	No pharmacological outcomes reported

Study Characteristics

Table 2 provides an overview of the 76 included research, arranged according to drug type and pharmacological effect.

Table 2. Summary Characteristics of Included Studies (n = 76)

Domain	Forskolin (n = 62)	Isoforskolin (n = 14)
In vitro models	38	10
Animal models	24	4
Disease area		
- Cardiovascular	18	2
- Metabolic	14	1
- Inflammatory	12	6
- Neurological	8	2
- Cancer	6	2
- Antimicrobial	4	1
Route of Admin		
-Oral	15	1
- Intraperitoneal	5	2
- Cell media	38	11

Risk of Bias in Studies

Individual study-level risk of bias was assessed using SYRCLE (for in vivo) and ToxRTool (for in vitro) [23, 24, 25]. Below is Table 3, highlighting a representative sample of included studies.

Table 3. Risk of Bias Assessment (Sample Studies)

Study (Author, Year)	Model	Randomization	Blinding	Selective Reporting	Overall Risk
Chen et al., 2020	In vitro	NA	NA	Low	Low
Singh et al., 2021	Animal	Unclear	Unclear	Low	Moderate
Li et al., 2022	Animal	Low	Low	Low	Low
Kumar et al., 2023	In vitro	NA	NA	Unclear	Low

Results of Individual Studies

- **Cardiovascular:** Forskolin reduced systolic BP by 15–25% in hypertensive rats (n = 6 studies). Isoforskolin showed similar vasodilation via enhanced NO release.
- **Metabolic:** Forskolin enhanced lipolysis and glucose uptake in adipocytes and diabetic rat models (n = 9). Isoforskolin lacked significant metabolic studies.
- **Inflammatory:** Isoforskolin strongly inhibited TNF-α and IL-6 in macrophages; Forskolin suppressed NF-κB and COX-2 pathways.
- **Neuroprotective:** Forskolin improved memory scores and increased BDNF levels in Alzheimer's models (n = 4).
- **Cancer:** Both compounds showed pro-apoptotic activity in melanoma, colon, and breast cancer lines, via the cAMP-PKA pathway.
- **Toxicity:** Forskolin well well-tolerated in doses <20 mg/kg in rodents; higher doses (>50 mg/kg) caused GI irritation. No toxicity studies for isoforskolin.

Results of Syntheses

Summary Characteristics and Bias
Studies on forskolin outweighed those on isoforskolin in every category. Only 30% of studies reported blinding, despite the majority having conventional outcome measures and being well-controlled. There were fewer research on isoforskolin, but they were consistent in anti-inflammatory models.

Statistical Synthesis
No meta-analysis was feasible. However, across multiple studies:

- Forskolin consistently reduced pro-inflammatory cytokines (IL-1β, TNF-α) by 30–60%
- In metabolic models, blood glucose was reduced by 18–24% (mean range)
- Neuroprotective studies showed 25–40% improvement in behavioral tests

Heterogeneity
Outcome heterogeneity was seen in:

- Dose selection (range 0.1–50 mg/kg)
- Cell lines and animal species
- Endpoints (e.g., TNF-α vs COX-2 in inflammation)

Sensitivity
There were no official sensitivity assessments conducted. However, the overall findings were not much changed by excluding trials that lacked dosage consistency.

Reporting Bias
Publication bias is probably present because the majority of the results were favorable. There were no reported negative or null outcomes. Formal bias identification is limited by the absence of unpublished data or preclinical study registries.

Certainty of Evidence
The certainty of evidence was rated as:

Domain	Forskolin	Isoforskolin
Cardiovascular	High	Low
Metabolic	Moderate	Insufficient
Anti-inflammatory	High	Moderate
Neuroprotective	Moderate	Low
Cancer	Moderate	Moderate
Antimicrobial	Low	Insufficient

Discussion
Interpretation of Findings
This systematic review focuses on the wide pharmacological potential of forskolin and its isoforskolin analog, which are produced from Coleus forskohlii. Because of its strong cAMP activation, forskolin has well-established effects in a number of areas, including cardiovascular, metabolic, inflammatory, neuroprotective, and anticancer. In limited in vitro investigations, isoforskolin has higher anti-inflammatory properties while having a comparable structure. It also shows potential because of its improved water solubility. Both diterpenes have the potential to be useful in complicated, multi-pathway disorders like cancer or neurodegeneration since they regulate signaling pathways including PKA, Epac, NF-κB, and MAPK. These results are consistent with past narrative assessments, but unlike earlier haphazard attempts, they offer a methodical, organized synthesis with clear inclusion criteria.

Limitations of the Evidence

- Most studies are preclinical, limiting translational certainty.
- Sample sizes in animal models were often small.
- Few studies reported dose-response curves or toxicity thresholds.
- Lack of comparative studies between forskolin and isoforskolin.
- Isoforskolin research is limited to a handful of studies.
- No clinical trials met the inclusion criteria, creating a translational gap.

Limitations of the Review Process

- Only English-language studies were included, potentially missing relevant non-English evidence.
- No formal meta-analysis was performed due to high heterogeneity.
- Risk of publication bias is suspected due to the predominance of positive findings.
- No pre-registration on PROSPERO due to resource constraints.

Implications for Practice and Future Research

Clinical Implications:

- Forskolin has therapeutic promise for metabolic syndrome, inflammatory disorders, and neurodegeneration.
- Isoforskolin should be explored for pulmonary inflammation, asthma, and as a potential topical anti-inflammatory.

Research Recommendations:

- Conduct head-to-head comparative studies of forskolin vs. isoforskolin.
- Explore nanoformulations to improve delivery and stability.
- Conduct dose-ranging studies to determine therapeutic windows.
- Initiate pilot human trials for top indications (e.g., asthma, diabetes).
- Assess long-term toxicity and reproductive safety.

Registration and Protocol

Registration

This review was not registered in PROSPERO or any public review registry.

Protocol Access

No prior protocol was published or deposited.

Amendments

No amendments were made to eligibility criteria, search strategy, or outcomes after initiation.

SUPPORT This review was not funded by any external organisation or grant. All work was self-supported by the primary authors.

Competing Interests

The authors declare no competing interests related to this work.

Availability of Data, Code, and other Materials

- **Data Extraction Forms:** Available upon request from the corresponding author.
- **Extracted Data Tables:** Available in supplementary Excel format (not submitted here).
- **Analytic Code:** Not applicable (no quantitative synthesis conducted).
- **Other Materials:** All referenced articles are publicly accessible or through institutional subscriptions.

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