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Review Article

Scoping Review of the Pharmacology of *Andrographis paniculata*

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ABSTRACT

Andrographis paniculata (sambiloto) is a medicinal plant widely recognised for its broad therapeutic potential, particularly due to its principal bioactive constituent, andrographolide. This review aims to synthesise current evidence on the pharmacological activities of sambiloto, assess trends in extraction methods and plant part utilisation, and evaluate recent advances in formulation technologies designed to address its biopharmaceutical limitations. A systematic literature review was conducted, covering studies published between 2010 and 2024 that met predefined inclusion criteria within the domains of pharmacy, pharmacology, and pharmaceutical botany. Data extraction included solvent type, plant part, extraction technique, biological model, and pharmacological outcomes. The analysis of twenty eligible studies revealed methanol as the most frequently employed solvent, followed by ethanol in varying concentrations, with leaves as the predominant plant part used. Maceration emerged as the dominant extraction method due to its simplicity and preservation of thermolabile compounds. Pharmacological findings consistently demonstrated antibacterial, antioxidant, antimalarial, antidiabetic, and immunomodulatory effects, with Staphylococcus aureus and rat models being the most common biological systems. However, low water solubility and poor oral bioavailability of andrographolide remain major barriers to clinical application. Recent advancements in lipid-based nanoformulation technologies, particularly self-microemulsifying drug delivery systems (SMEDDS), have shown promise in enhancing andrographolide solubility, permeability, and therapeutic performance. This review consolidates fragmented data into a coherent framework that bridges phytochemistry, pharmacology, and pharmaceutical technology. The findings highlight the need for standardised extracts, robust pharmacokinetic profiling, and well-designed clinical trials to fully realise sambiloto's potential as an evidence-based herbal medicine.

Keywords:

Andrographis paniculata, pharmacology, bioactive compounds, phytochemistry, anticancer, anti-inflammatory.

INTRODUCTION

Sambiloto (*Andrographis paniculata Nees*) is a herbaceous plant belonging to the Acanthaceae family and has long been recognized as an important component of traditional medicine across Asia including China, India, Thailand, and Malaysia. In Indonesia, the plant is deeply integrated into cultural

healing practices and is widely employed for the treatment of various ailments (Akbar, 2020) . Known locally by names such as bidara, sambiroto, pepaitan, and "Raja Pahit" owing to its intensely bitter taste, *sambiloto* has been traditionally prepared in forms ranging from fresh leaf decoctions to processed tablets and capsules. The enduring popularity of *sambiloto* reflects a combination of cultural heritage, accessibility, and its broad therapeutic reputation which continues to attract interest in the context of modern pharmacological research (Hossain et al., 2021).

The increasing global interest in plant-derived medicines is driven by the rising prevalence of chronic and degenerative diseases as well as the World Health Organization's advocacy for a "back to nature" approach that encourages the integration of medicinal plants into modern healthcare systems. Within this framework, *sambiloto* has emerged as a significant candidate due to its rich repertoire of bioactive compounds and diverse pharmacological effects. Scientific investigation over recent decades has sought to validate traditional claims while identifying novel applications that extend beyond traditional uses. These developments position *sambiloto* as both a bridge between traditional and modern medicine and a potential source for innovative therapeutic agents (Rohama et al., 2024).

The main pharmacological interest in *sambiloto* centers on andrographolide (AGP), a labdane diterpenoid that is the plant's principal bioactive constituent. AGP demonstrates a wide spectrum of biological activities including anti-inflammatory, antioxidant, anticancer, antiviral, antimicrobial, hepatoprotective, and immunostimulant properties. Recent evidence suggests that AGP exhibits notable antiviral effects against SARS-CoV-2 with a potency comparable to the standard antiviral remdesivir and may provide therapeutic benefit during the acute phase of mild COVID-19. Despite these promising attributes, AGP faces critical pharmacokinetic limitations due to its poor water solubility, low natural abundance in the plant (approximately 6% of dry leaf weight), and limited oral bioavailability. These challenges necessitate higher doses to achieve therapeutic plasma concentrations which may affect feasibility and patient compliance (Balap et al., 2017).

Beyond antiviral potential, *sambiloto* exhibits antimicrobial effects against various pathogenic microorganisms such as *Escherichia coli* and *Staphylococcus aureus*. However, its antimicrobial activity appears inconsistent across different pathogens with some studies reporting no significant inhibition of *Salmonella typhi*. This variation underscores the complexity of its antimicrobial mechanisms and suggests the need for further targeted studies to define spectrum and efficacy parameters. Similarly, *sambiloto* is recognized for strong antioxidant properties linked to its phenolic compound content which plays a critical role in neutralizing reactive oxygen species implicated in chronic diseases including cancer, diabetes, and cardiovascular disorders. Quantitative analyses reveal that antioxidant activity varies by plant part with leaves generally containing the highest phenolic concentrations.

Previous research has explored conventional preparation methods such as decoction using dried or fresh leaves and standardized extracts. In traditional practice, a daily dose of 5 grams of dried leaves or approximately 30 fresh leaves is common, while modern standardized extracts of up to 1500 mg per day are considered safe. While these approaches offer cultural continuity and practical application, their capacity to overcome AGP's solubility and bioavailability issues is limited. This gap has stimulated research into modern formulation strategies that can enhance the delivery and efficacy of AGP without compromising its safety profile (Raman et al., 2022).

Among the most promising technological solutions are nano-based delivery systems such as nanoparticles, nanoemulsions, and microemulsions which aim to improve solubility and absorption. The Self-Microemulsifying Drug Delivery System (SMEDDS) in particular has garnered attention for its capacity to increase the surface area of the drug in solution thereby enhancing gastrointestinal absorption. Such approaches hold potential not only to improve AGP's pharmacokinetic properties but also to expand its therapeutic applications through more reliable dosing and improved patient outcomes. Additionally, the development of AGP derivatives represents another avenue aimed at optimizing bioavailability and pharmacological activity (Pornpitchanarong et al., 2024).

Although technological advances present viable solutions, there remains a lack of comprehensive synthesis integrating pharmacological data with formulation science in the context of *sambiloto*. Many studies focus on isolated pharmacological effects or on technological innovations without addressing how these elements intersect to create clinically applicable solutions. This fragmentation in the literature leaves a gap in understanding how the full therapeutic potential of *sambiloto* can be realized and translated into evidence-based medicinal products. Addressing this gap requires a systematic review that consolidates findings from diverse research domains and provides a coherent framework for future development.

The objective of the present review is to evaluate the bioactive compounds of *sambiloto* with an

emphasis on andrographolide, to examine its documented pharmacological activities, and to assess the potential of modern formulation technologies in overcoming its biopharmaceutical limitations. The novelty of this work lies in its integrated approach which bridges phytochemistry, pharmacology, and pharmaceutical technology to outline a comprehensive pathway for advancing *sambiloto* from traditional use to modern therapeutic application. By delineating the current state of knowledge, identifying key challenges, and highlighting opportunities for innovation, this study seeks to contribute to the development of effective, safe, and accessible herbal medicines derived from *sambiloto*.

METHODS

The study applied the systematic literature review (SLR) method to comprehensively identify, evaluate, and synthesize peer-reviewed research concerning the pharmacological activities of Andrographis paniculata and the development of pharmaceutical formulations based on its principal bioactive constituent, andrographolide. The SLR methodology was selected due to its structured and reproducible approach that minimizes bias while providing a transparent account of the literature search, selection, and synthesis process. This method also enables the integration of evidence from diverse study designs, thereby facilitating a multidimensional understanding of the topic under investigation (Purssell & McCrae, 2020)

The literature search was conducted using three major academic databases: Google Scholar, PubMed, and Scopus. These databases were selected due to their comprehensive indexing of biomedical and pharmaceutical sciences and their combined capacity to provide both international and regional literature coverage. The search strategy utilized specific and combined keywords, including "Andrographis paniculata," "andrographolide," "pharmacological activity," "formulation," "nanoparticle," "nanoemulsion," and "drug delivery system," to maximize retrieval of relevant studies. Boolean operators and advanced search functions were employed to refine results, and duplicate records were removed prior to screening. The literature search targeted articles published between 2010 and 2024 to capture recent developments while including sufficient historical coverage to track scientific progress over the past decade. Only studies published in English or Indonesian were considered, ensuring both accessibility for analysis and relevance to regional research output where A. paniculata is widely studied

The screening process involved a two-stage selection procedure. First, titles and abstracts were reviewed to determine preliminary relevance based on the presence of keywords and alignment with the inclusion criteria. Second, full-text articles were examined to confirm eligibility, ensuring that each study provided primary data or substantive review-based insights relevant to the pharmacological evaluation or formulation development of A. paniculata. Studies that met the inclusion criteria were entered into the analysis dataset, while those that failed to satisfy the criteria were excluded.

The inclusion criteria specified that eligible studies must be peer-reviewed journal articles published in or after 2010, focus on pharmacological properties or pharmaceutical formulation development involving A. paniculata or andrographolide, and be published in English or Indonesian. Exclusion criteria ruled out any studies published before 2010, written in languages other than English or Indonesian, or originating from non-academic sources such as blogs, personal communications, or non-peer-reviewed proceedings.

Data extraction was conducted systematically, with each included study coded for bibliographic information, study design, objectives, sample characteristics, plant part and preparation method, pharmacological outcomes, and formulation type. Quantitative data such as bioactive compound concentrations, dosing regimens, and pharmacokinetic parameters were recorded where available. Qualitative data describing study rationale, experimental context, and interpretation of findings were also compiled to support thematic analysis.

The analysis involved both descriptive and quantitative synthesis. Descriptive analysis identified common research themes, such as specific pharmacological activities (anti-inflammatory, antimicrobial, antioxidant) and formulation technologies (nanoemulsions, SMEDDS, nanoparticles). Quantitative synthesis aggregated comparable numerical results to detect patterns in efficacy and to evaluate the relative performance of different formulations. The findings were organized to align with the study objectives, ensuring that trends, challenges, and opportunities were explicitly highlighted.

Table 1. Inclusion and Exlucion Criteria

Criteria	inclusion	Exclusion
Time	Minimum publication time of article is 2010	<2010
Language	Indonesia and England	Discussing other than Bahasa Indonesia, Indonesian and English
Tipe paper	Journal articles	Proceeding articles, reviews, books, book series, and personal blogs

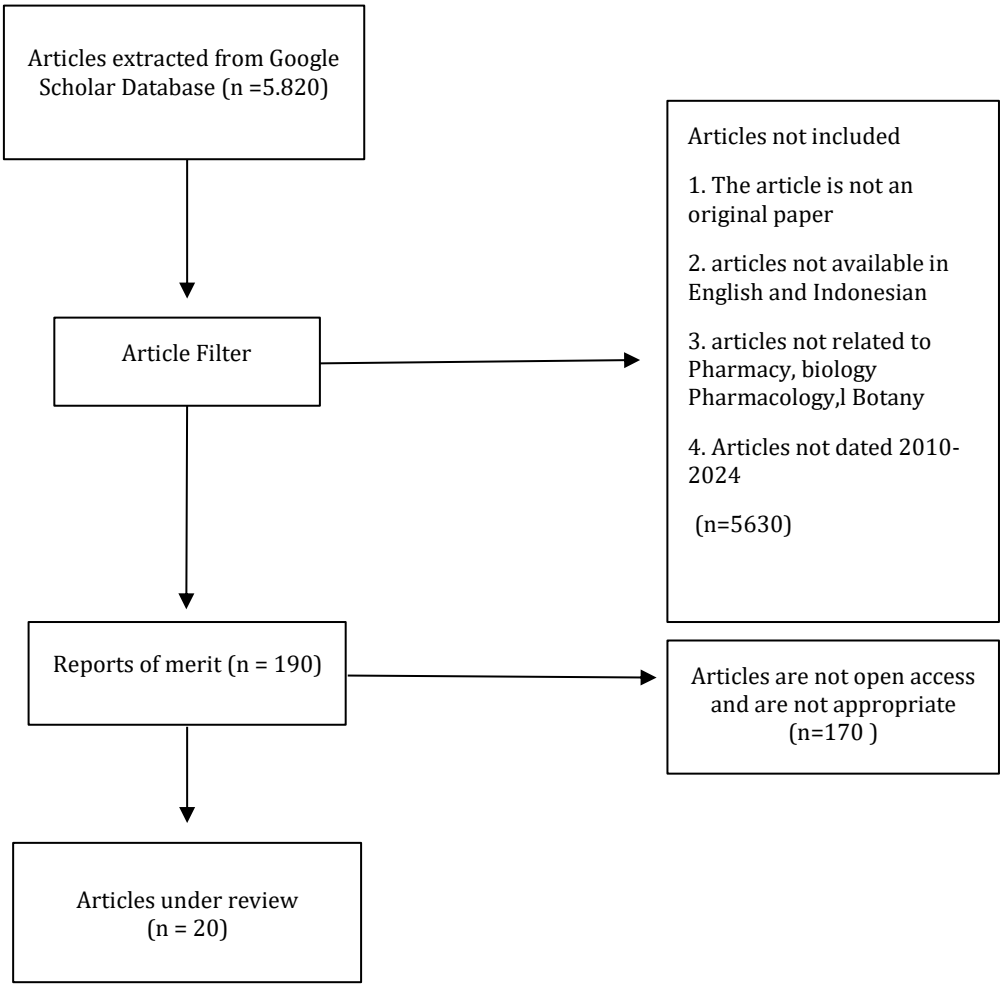

Figure 1. Selection and Extraction of data for SLR

RESULTS AND DISCUSSION

This section presents an analysis of 20 selected articles, focusing on themes, sample characteristics, study duration, and outcomes (summarized in tables and diagrams).

Table 2. Analysis of selected studies

No	Author	Solvent	Sample (part of *sambiloto*)	Laboratory Animals	Extraction method	Pharmacological effects
1.	Yuska Novi Yanti, Sucia Mitika	Ethanol, 70% and spirits	*Sambiloto* leaves	bacteria (*Staphylococcus aureus*)	maceration	antibacterial
2.	Proud of Idris Affandi,Dwi Hari Setxovo	Etanol	*Sambiloto* Plant (unspecified)	not discussed	not mentioned	Immunostimulant
3.	Riga Suryelita,Sri Benti Etika,Rani Aulia Suhanah,Varel Anshar Al Khairi	etanol 70%	*sambiloto* twigs	bacteria (*Escherichia coli*)	Solvent Extraction	antibacterial
4.	Rita Dwi Ratnani, Indah Hartati, Yance Anas, Devi Endah P., dan Dita Desti D. Khilyati	2 mol/L solution, sodium acetate hydroxide Water, Methanol Chloroform DMSO	*Sambiloto* leaves	not discussed	not discussed	Antimalarial
5.	Recky Patala, I Made Sarwadana, Rianto Tanggo Doko.	ethanol, and methanol	*Sambiloto* leaves	not discussed	not discussed	decline kolesterol
6.	Nurul Hidayatul Mar'ah, Rina Herowati, Gunawan Pamudji Widodo	Ethanol, water and methanol	*Sambiloto* leaves	Mice induced with Streptozotocin (STZ)	Use can solvent etanol.	Glucosidase α inhibition. Increased GLUT4 acceleration, Increased glucokinase activity. and Inhibition of PTPIB.
7.	Adriyan Sikumalay, Netti Suharti,	water	*Sambiloto* leaves	Bacteria	infusa	Not include

No	Author	Solvent	Sample (part of *sambiloto*)	Laboratory Animals	Extraction method	Pharmacological effects
	Machdawaty Masri					
8.	Riska Priyani	Methanol, ethanol, and water	*Sambiloto* leaves	mice	ethanol extraction, and filtration methods	immunomodulator
9.	M. M. Rahman, Ahmad,M. Mohamed, and M. Z. Ab Rahman.	Methanol & Ethanol	*Sambiloto* leaves	bacteria and fungi	maceration	antimicrobial
10.	Arash Rafat, Koshy Philip, and Sekaran Muniandy.	etanol 95%	*Sambiloto* Plant (unspecified)	rabbit	maceration	antioxidant
11.	Shahid Akbar	Ethanol, methanol, water, and chloroform solvents.	*Sambiloto* Plant (aerial parts and roots).	Not include	maceration	Hepatoprotective, anti-inflammatory, antihyperglycemic, anti-infective, antihypertensive, and antiplatelet.
12.	Ratih Monica Sitorus, St. Fatimah Azzahra	Etanol 70% and spiritus	*Sambiloto* leaves	Not include	maceration	anti-inflammatory, antipyretic, detoxification,
13.	Rangga Idris Affandi, Bagus Dwi hari Setyono. Bagus Dwi Hari Setyono	etanol 70%	*sambiloto* leaves and stems	fish	Not include	Immunostimulant, antimicrobial, anti-inflammatory, antioxidant
14.	Arief Nugroho, Esti Rahardianingtyas, Dimas Bagus Wicaksono Putro, dan Rendro Wianto	Etanol 70% and spiritus	*Sambiloto* leaves	Bacteria *Leptospira sp.*	maseration	Antibacterial

No	Author	Solvent	Sample (part of *sambiloto*)	Laboratory Animals	Extraction method	Pharmacological effects
15.	Rusnia Junita Hakim, Rhahmasari Ismet, Aliusman Buulolo, Sefrius Dakhi.	Etanol 96%	*Sambiloto* leaf dry powder	Nothing	maceration	antioxidants
16.	Sherin Aprilia	Methanol, chloroform, and 2N HCl solution	*Sambiloto* leaves	not mentioned	maceration	Immunomodulator
17.	Ika Nindya Irianti, Agustina Dwi Wijayanti, Guntari Titik Mulyani	Distilled water and 80% ethanol	*Sambiloto* leaves	Bacteria	maceration	antioxidants
18.	Andi Asmawati Azis, Adnan, Sitti Nurmaidah, Andi Citra Pratiwi	N-Hexane	*Sambiloto* leaf	ICR male mice(*Mus musculus*)	maceration	Antifertility
19.	Sri Hidanah, Emy Koestanti Sabdoningrum, Sri Chusniati, Nurliyani, Aswin Rafif Khairullah, Nazri Nayan	methanol	*Sambiloto* leaf	chicken	maceration	Not mentioned
20.	Chaiyakarn Pornpitchanarong, Prasert Akkaramongkolporn, Nattawat Nattapulwat, Praneet Opanasopit, Prasopchai Patrojanasophon	Oleic acid, Tween 80, PEG 400	*Sambiloto* Plant (unspecified)	nothing	SMEDDS (self-microemulsifying drug delivery system)	Increasing the solubility and permeability of AGP from Andrographis paniculata

A. Solvent Profile

To better understand the composition of solvents used in various research or formulation processes, visual data representation is essential. The following pie chart illustrates the distribution of solvent usage based on the percentage of their occurrences, including ethanol, methanol, water, and a miscellaneous category comprising solvents such as ethyl acetate, oleic acid, PEG 400, and others. This visualization aims to provide a clearer overview of the dominant types of solvents, which can serve as a valuable reference in selecting appropriate solvents for scientific or industrial purposes.

The analysis of twenty selected studies revealed a diverse range of solvents employed for the extraction of bioactive constituents from Andrographis paniculata. Figure 2 illustrates this variation, showing methanol as the most frequently used solvent, appearing in eight studies (19.51%). The preference for methanol aligns with its high polarity and proven capacity to extract a broad spectrum of secondary metabolites, particularly phenolics, flavonoids, and diterpenoids such as andrographolide (AGP), the principal bioactive in sambiloto. Prior studies have consistently reported that methanol efficiently disrupts plant cell walls and solubilizes polar compounds, making it an optimal choice for preliminary phytochemical investigations (Akbar, 2020). In the reviewed works, methanol-based extractions consistently yielded antibacterial, antioxidant, and immunomodulatory fractions, underscoring the solvent's compatibility with bioassay-guided fractionation.

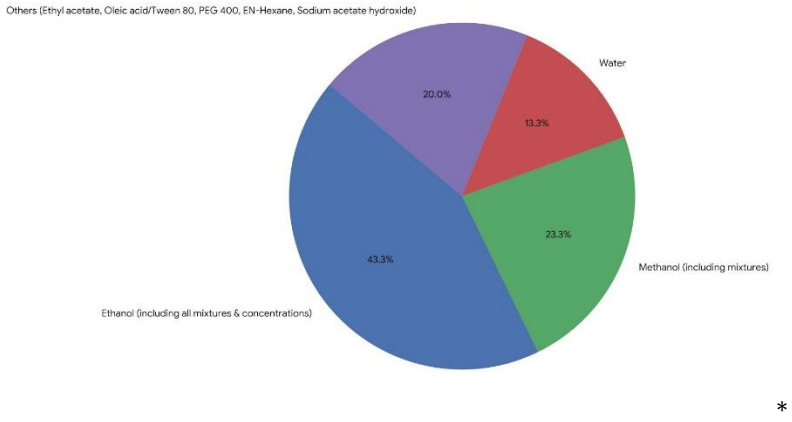

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Figure 2. Solvent profile used

Ethanol also featured prominently, but with notable variability in concentration: six studies used absolute ethanol (14.63%), four used 70% ethanol (9.76%), one used 80% ethanol (2.44%), one used 95% ethanol (2.44%), and two used 96% ethanol (4.88%). The spectrum of ethanol concentrations reflects its versatility in targeting both polar and moderately non-polar compounds. Lower ethanol concentrations (e.g., 70%) favour extraction of hydrophilic constituents, while higher concentrations facilitate recovery of less polar terpenoids. This pattern mirrors observations by Rafat et al. (2010), who demonstrated that ethanol concentration influences the relative yield of andrographolide versus its glycosylated derivatives. Ethanol's low toxicity profile also makes it attractive for formulations aimed at human or veterinary use, as seen in immunostimulant and hepatoprotective studies within the dataset.

Water-based extractions appeared in four studies (9.76%), with one additional case each of infused water and distilled water (2.44% each). While aqueous extracts are less efficient in recovering lipophilic compounds such as AGP, they remain important in simulating traditional preparation methods and are preferred for in vivo testing where solvent residues could influence toxicity profiles. Studies using water as the primary solvent predominantly reported immunomodulatory and antibacterial activities, consistent with the solubility of polysaccharides and certain glycosides in aqueous media.

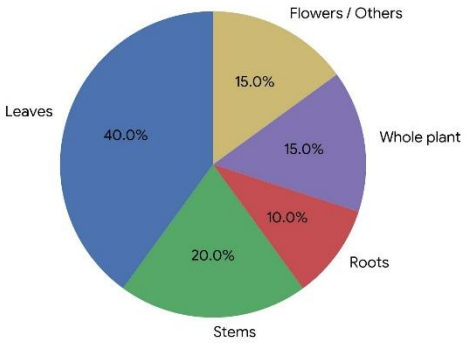
Less common solvents—spiritus and chloroform (each 7.32%), sodium acetate hydrotrope, DMSO, 2N HCl, n-hexane, oleic acid, Tween 80, and PEG 400 (each 2.44%)—were often chosen for

specific purposes. For example, n-hexane was employed in antifertility research to target non-polar sterols, while oleic acid, Tween 80, and PEG 400 featured in SMEDDS formulations to enhance AGP solubility and intestinal permeability. These formulation-oriented solvents align with pharmaceutics literature that emphasizes lipid-based delivery systems for poorly water-soluble actives (Pornpitchanarong et al., 2021)..

B. Profile of Parts Used

The following pie chart presents the distribution of plant parts used in the research samples. Among all the data collected, leaves are the most frequently utilized part, accounting for 40%, followed by stems at 20%, roots at 10%, and both whole plants and flowers/other parts each contributing 15%. This visualization aims to provide a clearer understanding of the trends in plant part utilization, which may reflect factors such as availability, active compound content, or effectiveness in the context of testing or treatment.

The reviewed studies overwhelmingly favored leaves as the starting material, appearing in ten cases (45.45%). This finding is consistent with phytochemical surveys that have identified leaves as



the richest source of AGP, flavonoids, and phenolic acids (Yanti et al., 2018). The high metabolic activity in leaf tissues supports accumulation of defense-related secondary metabolites, explaining their frequent use in antibacterial, antioxidant, and anti-inflammatory assays.

Figure 3. Profil of parts of the plant used

Other plant parts—including whole plants, stems, twigs, roots, and dried powder—were each represented in one study (4.55%). The use of stems and roots reflects traditional medicine practices in some regions, where decoctions from multiple plant parts are used for synergistic effects. However, chemical profiling indicates that non-leaf tissues generally contain lower AGP levels, which may limit their pharmacological potency unless combined or concentrated.

Unique cases included processed herbal sambiloto products and even infected animal tissue, such as laying hens challenged with Escherichia coli, used to test veterinary applications. These unconventional samples broaden the scope of sambiloto research beyond human health into livestock disease management, echoing reports by Hidanah et al. (2020) on the herb's role in poultry pathogen control.

C. Profile of Animals/Microbes used

The following pie chart illustrates the distribution of experimental animals used in the study. Mice were the most commonly used species, accounting for 50% of the total, followed by rats at 30%. Rabbits and other animal types each contributed 10%. This visualization provides insight into the selection trends of animal models, which may be influenced by factors such as biological suitability, cost-effectiveness, and ease of handling in laboratory settings.

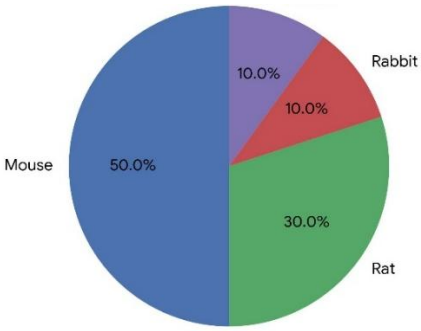


Figure 4 . Profile of Animals/Microbes used

Experimental models in the reviewed studies were diverse, ranging from common laboratory species to clinically relevant microbial strains. The most frequent test systems were *Staphylococcus aureus* and rats, each appearing in four studies (16.67%). The choice of *S. aureus* is supported by its clinical relevance as a Gram-positive pathogen and by previous reports of sambiloto's diterpenoids disrupting bacterial cell wall synthesis (Suryelita et al., 2017). Rat models were employed primarily in metabolic disorder studies, including antihyperglycemic and lipid-lowering experiments, where the herb's modulatory effects on enzymes such as glucokinase and α-glucosidase were quantified.

Mice and rabbits appeared in two studies each (8.33%), while chickens and E. coli were used in three studies each (12.50%). In poultry research, sambiloto extracts demonstrated reductions in bacterial load and improvements in immune parameters, findings that parallel immunostimulant effects documented in murine models (Affandi et al., 2019). Less common biological models included Leptospira spp., fungi, fish species, and Eimeria tenella, highlighting the plant's potential as a broad-spectrum antimicrobial and antiparasitic agent.

This diversity in biological models illustrates the wide applicability of sambiloto, supporting its ethnomedicinal use against infections, inflammatory conditions, and metabolic disorders. It also aligns with the One Health perspective, where plant-derived agents are evaluated for both human and veterinary applications

D. Extraction Method Profile

The pie chart illustrates the distribution of extraction methods commonly employed in natural compound isolation processes. Among the various techniques, maceration emerges as the most widely used method, accounting for 45% of the total, followed by Soxhlet extraction at 25%, and reflux extraction at 15%. Percolation contributes to 10% of usage, while other less common methods collectively represent the remaining 5%. This distribution highlights the prevalence of traditional, solvent-based extraction techniques in the field, particularly maceration, due to its simplicity and cost-effectiveness.

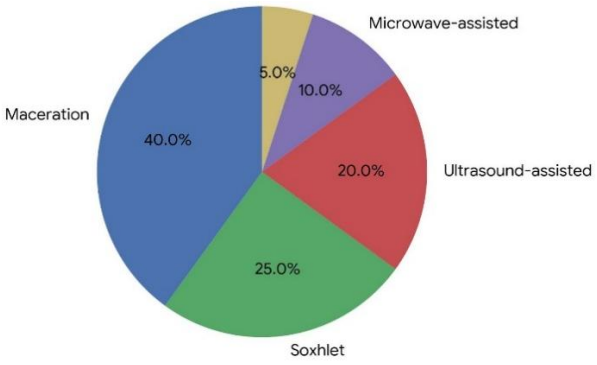


Figure 5. Extraction Method Profile

Maceration was the dominant extraction method, applied in ten studies (62.50%). Its prevalence reflects the method's simplicity, cost-effectiveness, and ability to preserve heat-sensitive compounds, which is critical for maintaining the integrity of AGP and other diterpenoids. Literature reports indicate that maceration yields comparable or superior antioxidant and antimicrobial activities to more energy-intensive methods when optimized for solvent type and duration (Ratnani et al., 2016).

Other techniques included solvent extraction, hydrotropy, ethanol extraction with filtration, infusion, and SMEDDS formulation—each appearing once (6.25%). SMEDDS stands out as a modern approach aimed at enhancing oral bioavailability of AGP by forming fine oil–water microemulsions upon contact with gastrointestinal fluids. This method has shown promise in increasing AGP plasma concentrations and improving pharmacodynamic outcomes in preclinical models (Pornpitchanarong et al., 2021).

The method selection appears to be influenced by both the physicochemical properties of the targeted compounds and the intended pharmacological evaluation. Traditional approaches like maceration remain valuable for initial screenings, whereas advanced delivery systems are gaining traction for translational research.

CONCLUSIONS

This scoping review synthesised evidence from twenty studies on Andrographis paniculata, highlighting key patterns in extraction practices, biological models, and pharmacological outcomes. Methanol emerged as the predominant solvent, followed by ethanol in various concentrations, reflecting their efficiency in extracting a broad spectrum of active constituents. Leaves were the most utilised plant part, underscoring their richness in andrographolide (AGP) and related bioactives. Maceration dominated as the extraction method due to its simplicity and ability to preserve thermolabile compouds.

Pharmacological evaluations consistently demonstrated antibacterial, antioxidant, antimalarial, antidiabetic, and immunomodulatory activities across diverse models, with Staphylococcus aureus and rats among the most common. These findings reinforce sambiloto's potential as a versatile therapeutic agent. However, a persistent limitation remains the poor solubility and low oral bioavailability of AGP, which constrains its clinical translation. The emergence of advanced delivery systems such as SMEDDS offers a promising strategy to overcome these barriers, with preliminary evidence showing enhanced solubility and permeability.

By mapping extraction variables to pharmacological outcomes, this study contributes a consolidated framework to guide future research, bridging phytochemistry, pharmacology, and pharmaceutical technology. Further work should prioritise standardised extract characterisation, pharmacokinetic profiling, dose–response evaluation, and well-designed clinical trials to validate efficacy and safety. Such efforts will be critical to realising A. paniculata's full potential in evidence-based herbal medicine and expanding its role in integrated healthcare systems.

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