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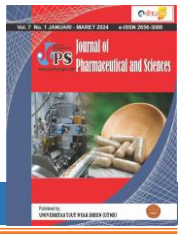

Article Review: Safety and Toxicity Testing of Herbal Medicines in the Development of Jamu, Standardized Herbal Medicines, and Phytopharmaceuticals

Artikel Review: Uji Keamanan dan Toksisitas Obat Herbal dalam Pengembangan Jamu, OHT, dan Fitofarmaka

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Abstract

Background: Safety and toxicity testing are essential stages in the development of herbal medicines to ensure therapeutic efficacy without causing adverse effects. In Indonesia, herbal products are classified into traditional herbal medicines (jamu), Standardized Herbal Medicines, and phytopharmaceuticals, each requiring different levels of scientific evidence for safety and efficacy. **Objective:** This study aims to review the results of safety and toxicity testing of herbal medicines in the development of jamu, Standardized Herbal Medicines, and phytopharmaceuticals in Indonesia over the last five years (2020–2025). **Methods:** This study employed a descriptive, qualitative literature review. Scientific articles were systematically retrieved from the Garuda, Neliti, Sinta, and Google Scholar databases using relevant keywords related to herbal medicine safety and toxicity testing. A total of twelve peer-reviewed research articles published between 2020 and 2025 met the inclusion criteria. The reviewed studies involved in vivo, in vitro, and in silico testing methods, with toxicity parameters including LD_{50}, LC_{50}, biochemical markers, and histopathological changes. **Results:** The findings indicate that in vivo testing is the most frequently applied method and generally demonstrates a high safety profile for most herbal preparations. Jamu products are considered safe based on empirical use and standardized raw materials. Standardized Herbal Medicines demonstrate safety through acute and subchronic toxicity evaluations. At the same time, phytopharmaceuticals exhibit the highest level of safety through comprehensive testing using combined in vivo, in vitro, and in silico approaches. Most herbal ingredients fall into the non-toxic to mildly toxic category at high doses. **Conclusion:** Overall, the reviewed evidence suggests that Indonesian herbal medicines, including jamu, Standardized Herbal Medicines, and phytopharmaceuticals, are generally safe when used appropriately. Strengthening multidisciplinary toxicological approaches and implementing pharmacovigilance principles are essential to ensure long-term safety and support the development of evidence-based national herbal medicines.

Keywords*: *Toxicity, Safety, Herbal Medicine, OHT, Phytopharmaceuticals

Abstrak

Latar Belakang: Pengujian keamanan dan toksisitas merupakan tahapan penting dalam pengembangan obat herbal untuk menjamin manfaat terapeutik tanpa menimbulkan efek merugikan. Di Indonesia, obat herbal diklasifikasikan menjadi jamu, Obat Herbal Terstandar (OHT), dan fitofarmaka, yang masing-masing memiliki tingkat pembuktian ilmiah yang berbeda terkait keamanan dan khasiat. **Tujuan:** Penelitian ini bertujuan untuk mengkaji hasil uji keamanan dan toksisitas obat herbal dalam pengembangan jamu, Obat Herbal Terstandar (OHT), dan fitofarmaka di Indonesia selama lima tahun terakhir (2020–2025). **Metode:** Penelitian ini menggunakan metode tinjauan literatur deskriptif-kualitatif. Penelusuran artikel ilmiah dilakukan secara sistematis melalui basis data Garuda, Neliti, Sinta, dan Google Scholar menggunakan kata kunci yang relevan. Sebanyak dua belas artikel penelitian yang dipublikasikan pada periode 2020–2025 memenuhi kriteria inklusi. Artikel yang direview mencakup metode uji in vivo, in vitro, dan in silico, dengan parameter toksisitas berupa LD_{50}, LC_{50}, parameter biokimia, serta perubahan histopatologi organ. **Hasil:** Hasil kajian menunjukkan bahwa metode in vivo merupakan pendekatan yang paling banyak digunakan dan

umumnya menunjukkan profil keamanan yang tinggi pada sebagian besar sediaan herbal. Produk jamu dinyatakan aman berdasarkan bukti empiris dan standardisasi bahan baku. Obat Herbal Terstandar (OHT) menunjukkan keamanan melalui uji toksisitas akut dan subkronis, sedangkan fitofarmaka memiliki tingkat keamanan terbaik karena telah diuji secara komprehensif menggunakan pendekatan in vivo, in vitro, dan in silico. Mayoritas bahan herbal berada pada kategori tidak toksik hingga toksik ringan pada dosis tinggi. **Kesimpulan:** Secara keseluruhan, obat herbal di Indonesia, baik jamu, Obat Herbal Terstandar (OHT), maupun fitofarmaka, memiliki tingkat keamanan yang tinggi apabila digunakan sesuai dosis yang dianjurkan. Penguatan metode toksikologi multidisipliner serta penerapan prinsip farmakovigilans sangat diperlukan untuk menjamin keamanan jangka panjang dan mendukung pengembangan obat herbal nasional berbasis bukti ilmiah.

Kata Kunci: Toksisitas, Keamanan, Jamu,OHT, Fitofarmaka.

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Introduction

Herbal medicines and traditional remedies have been used for generations in Indonesia as natural alternatives to synthetic drugs, believed to be safer. The public perception that natural ingredients do not cause side effects is often the main reason for their widespread use. However, not all herbal ingredients are proven to be safe, as some active compounds can be toxic if consumed in excess or over a long period of time without adequate scientific evidence. Therefore, safety and toxicity testing are crucial to ensure the benefits of herbal medicine for human health [1]. The use of herbal medicines continues to increase as public awareness grows of natural treatments considered safer and with minimal side effects. However, uncontrolled use without scientific data can increase the risk of toxic effects, especially in ingredients that contain potentially strong active compounds. Several publications emphasize that the safety of herbal medicines cannot be based solely on traditional use, but must be proven through standardized toxicity testing to avoid the risk of organ damage and long-term effects [2].

To regulate the safety of herbal medicines in Indonesia, the Food and Drug Administration (BPOM) has classified herbal products into three categories: Jamu, Standardized Herbal Medicine (OHT), and Phytopharmaceuticals. This classification distinguishes the level of scientific evidence for a product's safety, efficacy, and quality. Jamu is still based on empirical experience, while OHT and Phytopharmaceuticals must undergo preclinical and clinical testing, including acute, subchronic, and chronic toxicity tests. This classification emphasizes that toxicological testing is the main basis for assessing the safety of herbal medicines [3]. In addition, the development of the herbal industry in Indonesia requires standardization of quality, safety, and toxicological testing equivalent to pharmaceutical products. The diversity of secondary metabolites, such as alkaloids, flavonoids, terpenoids, and tannins, can provide pharmacological benefits but also pose the potential to cause side effects if they are not adequately screened for toxicity. Therefore, safety testing through in vivo, in vitro, and in silico approaches is crucial to determine the safe limits for the use of herbal ingredients before they are formulated into herbal medicines, OHTs, or phytopharmaceuticals [4].

In toxicology research, three general approaches are used to assess the safety of herbal ingredients: in vivo, in vitro, and in silico testing. In vivo testing is conducted on experimental animals, such as mice or rats, to observe effects on organ function and the body as a whole. In vitro testing uses cell cultures to assess specific toxic effects at the cellular level, while in silico testing utilizes computer modeling to predict the potential

toxicity of compounds based on their chemical structure. These three approaches complement each other in scientifically assessing the safety and toxicity of herbal medicines [5]. National regulations also emphasize the importance of safety testing as a key requirement for the commercialization of herbal medicines. Modern toxicological approaches enable early assessment of the risks of natural ingredients by monitoring biochemical changes and histopathology, and by predicting toxic activity based on chemical structure. The combination of these methods is necessary to produce more comprehensive data and support the implementation of pharmacovigilance for herbal products in Indonesia, thereby increasing public confidence and supporting the development of evidence-based phytopharmaceuticals [6].

Various in vivo studies on traditional herbal medicines show that most have a good safety profile. For example, a combination of tiwai onion, candlenut, basil leaves, lime, and honey has been shown to cause no toxic effects at doses up to 16 g/kgBW in mice, and turmeric herbal medicine has an LC_{50} value of more than 3000 ppm, which is considered non-toxic. These results indicate that most herbal medicines formulated with natural ingredients and used in reasonable doses are relatively safe for consumption [14]. Meskipun demikian, beberapa formulasi jamu masih menunjukkan potensi toksisitas ringan pada dosis tinggi. Penelitian terhadap jamu "Pegel Linu" menunjukkan adanya perubahan histopatologi hati dan peningkatan indeks relatif organ pada mencit, meskipun nilai LD_{50}-nya termasuk kategori toksik ringan. Hal ini menunjukkan bahwa tingkat keamanan jamu sangat bergantung pada dosis dan durasi penggunaannya, sehingga perlu dilakukan pengawasan terhadap takaran konsumsi dan bahan penyusunnya [7].

In the Standardized Herbal Medicine (OHT) category, the study results show that most ingredients have undergone toxicity testing, with no adverse effects at high test doses. Black onion ethanol extract and candlenut oil showed LD_{50} values above 2000 mg/kgBW without altering organ function. In contrast, princess vine extract caused a slight decrease in kidney function at high doses, still within normal limits. These results prove that most OHTs have a good safety profile and can be used rationally [8]. Research on phytopharmaceuticals has also shown positive results regarding medium-term safety. Subchronic testing of a propolis ethanol extract for 28 days did not alter glucose, cholesterol, or triglyceride levels in rats, while in silico research on flavonoid compounds showed potential to reduce toxicity through chemical structure modification. These findings support the notion that a combination of in vivo and in silico testing provides a more comprehensive picture of the safety of phytopharmaceutical ingredients [9].

Overall, research over the past five years shows that most herbal medicines, OHTs, and phytopharmaceuticals in Indonesia are considered safe and low-toxic. However, most studies are still limited to acute in vivo testing, and few have developed parallel in vitro and in silico methods. In fact, this multidisciplinary approach is important for obtaining a comprehensive picture of the safety profile of herbal medicines and supporting the application of pharmacovigilance principles to natural products [10]. Based on the above description, this study aims to examine the results of safety and toxicity tests of herbal medicines in the development of traditional herbal medicines, OHT, and phytopharmaceuticals in Indonesia over the past five years. This study is expected to provide a strong scientific basis for supporting the development of safe, effective, and evidence-based national herbal medicines.

Method

This study is a review article that analyzes and summarizes research on the safety and toxicity testing of herbal medicines in the development of traditional herbal medicines, standardized herbal medicines (OHT), and phytopharmaceuticals. The study used a descriptive-qualitative approach, involving systematic searches and reviews of scientific articles relevant to the research topic. This approach was chosen to obtain a comprehensive overview of the latest research trends, the testing methods used, and the safety levels of herbal ingredients tested on experimental animals via computer simulation [10]. The literature used in this study was sourced from national scientific journals published online through the Garuda, Neliti, Sinta, e-Journal Indonesia, and Google Scholar portals. Literature searches were conducted using the keywords herbal medicine toxicity testing, herbal medicine safety, standardized herbal medicines, phytopharmaceuticals, and in vivo herbal toxicity. The criteria for the literature used were original research articles published within the last five years (2020-2025), containing the results of toxicity or safety tests on herbal medicine preparations, OHT, or phytopharmaceuticals, and listing testing methods such as in vivo, in vitro, or in silico [9]

From the search results, 12 research articles met the study criteria. Each article was thoroughly reviewed to extract key information, including the research title, year of publication, type of herbal preparation, testing

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method, toxicity parameters used, safety results, and the strengths and limitations of the study. The data obtained were then categorized by herbal medicine development level (traditional medicine, OHT, and phytopharmaceuticals) and by testing method (in vivo, in vitro, and in silico). The analysis used a descriptive-comparative approach, comparing results across studies to identify common patterns, differences, and general trends in the safety and toxicity of herbal medicines in Indonesia [8]. Because this study is a secondary literature review that only uses scientific publication data, it does not directly involve human subjects or test animals. Therefore, this study does not require research ethics approval, but data validity is maintained by only selecting articles that have undergone peer review and been published in accredited national journals [7]

Result and Discussion

Research on the safety and toxicity testing of herbal medicines in Indonesia has shown significant progress in the last five years. Based on a review of 12 journals, the most widely used method is in vivo testing, particularly using mice (Mus musculus) and rats (Rattus norvegicus) as test animals. Several studies also utilized alternative methods, such as the Brine Shrimp Lethality Test (BSLT) and zebrafish embryos, as well as in silico approaches to predict the toxicity of herbal compound molecules. The overall results show that most of the herbal medicines, OHTs, and phytopharmaceuticals studied have high safety profiles with low or insignificant toxicity.

In general, the differences in results between herbal medicine, OHT, and phytopharmaceuticals lie in the level of scientific evidence and the testing methods. Traditional herbal medicine is generally tested to ensure its empirical safety. At the same time, OHT and phytopharmaceuticals undergo a more complex laboratory approach, including blood biochemistry tests, organ histopathology, and chronic toxicity analysis. The results of these studies reinforce the importance of toxicological testing in validating the safety of herbal medicines and providing a scientific basis for the standardization process of herbal products in Indonesia.

Table 1. Data on the Results of Safety and Toxicity Tests of Various Herbal Preparations at the Development Stage of Traditional Medicines, Over-the-Counter Medicines, and Phytopharmaceuticals in Indonesia.

No	Preparation	Method	Parameters observed	Results	Discussion	Source
1	Red gedi leaf herbal medicine (*Abelmoschus manihot*)	In vivo	Parameters: clinical symptoms, mortality, LD_{50} Doses 2.8; 4.2; 5.6; 7 g/kgBW	Red Gedi Leaf was tested on mice and found to be safe at doses up to 7 g/kgBW, with no deaths and only minor changes, making it practically non-toxic.	All doses are safe; $LD_{50} > 7$ g/kg indicates very low toxicity.	[11]
2	Combination of herbs (tiwai onion, candlenut, basil, lime, honey).	In vivo	Parameters: body weight, organ weight, clinical symptoms, mortality Dosage: 2; 4; 8; 16 g/kg	A combination herbal medicine containing tiwaikemirikemangijeruk nipismadu was tested in mice and found to be safe at doses up to 16 g/kgBW, with no organ changes or toxic symptoms.	A combination herbal medicine containing tiwaikemirikemangijeruk nipismadu was tested in mice and found to be safe at doses up to 16 g/kg BW, with no organ changes or toxic symptoms.	[1]
3	Jamu Pegel Linu	in vivo	toxic symptoms, relative organ index (ROI), liver histopathology, LD_{50} Doses: 1.3; 2.6; 5.2; 10.4 mg/kgBW	Jamu Pegel Linu showed mild toxicity, with an LD_{50} value of 1.479 mg/kgBW and the presence of liver necrosis at high doses.	Liver necrosis was observed at high doses, classified as mild toxicity (LD_{50} = 1.479 mg/kg).	[7]
4	Turmeric and Tamarind Herbal Medicine	BSLT	Parameters: larval mortality rate, LC_{50}, Artemia survival rate Dosage: varying concentrations (ppm, BSLT)	Turmeric and Tamarind Herbal Medicine has an LC_{50} value of 3366 ppm, indicating it is non-toxic based on a BSLT test conducted on larvae (Artemia salina).	LC_{50} = 3366 ppm → non-toxic category according to BSLT criteria.	[14]
5	Standardized Herbal Medicine Soursop Leaf	In vivo	Parameters: Liver function (SGOT, SGPT)	No significant increase in SGOT/SGPT. Urea and creatinine levels remain	Soursop leaf extract at doses of 400–1200 mg/kg body weight is safe and	[15]

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	Extract (*Annona muricata* L.)		Kidney function (urea, creatinine), Organ weight, Toxic symptoms, Mortality Dosage: 400 mg, 800 mg, 1200 mg	within normal limits. No significant changes in organ weight were observed. No test animals died. No toxic symptoms were observed at any of the three doses.	does not affect liver or kidney function, nor does it cause systemic toxicity. It is classified as non-toxic.	
6	Standardized Herbal Medicine Candlenut Oil (*Aleurites molucanna* L.)	In vivo	Parameters: mortality, clinical symptoms, temperature, respiration, heart rate, body weight, organ weight Dosage: 5; 10; 15; 20 g/kgBW	Candlenut oil is safe up to 20 g/kg BW, with an LD_{50} greater than 20 g/kg BW, indicating it is non-toxic. No toxic symptoms; LD_{50} > 20 g/kg → very safe.	Tidak ada gejala toksik; LD_{50} > 20 g/kg → sangat aman.	[8]
7	Standardized Herbal Medicine Black Garlic Extract (*Allium sativum L.*)	In vivo	Parameters: motor activity, tremors, convulsions, respiration, behavior, mortality Dose: 5; 50; 300; 2000 mg/kgBW	Black Garlic Extract is safe up to 2000 mg/kg BW without significant toxic effects.	Shows no significant toxicity; safe up to a dose of 2000 mg/kg.	[13]
8	Standardized Herbal Medicine Lemongrass Syrup	In vivo	Parameters: signs of toxicity, mortality, body activity Dosage: 2000; 5000 mg/kgBW	Lemongrass Basil Syrup is safe up to 5000 mg/kgBW and is categorized as practically non-toxic.	No animals died at the highest dose; it is classified as practically non-toxic.	[13]
9	Fitofarmaka Lemongrass Basil Tea	In vivo	Parameters: signs of toxicity, mortality, body activity Dosage: 2000; 5000 mg/kgBW	Lemongrass Basil Tea is safe up to 2000 mg/kgBW, causing only mild tremors at very high doses.	Safe; only mild tremors at a dose of 2000 mg/kg.	[10]
10	Phytopharmaceutical Karonda Fruit (*Carissa carandas* L.)	embryo zebrafish (OECD 236)	Parameters: embryo mortality, malformations (tail, yolksac, pericardium), LC_{50} Doses: 546; 571; 608 µg/mL	Karonda fruit is non-toxic with an LC_{50} value of 546–608 µg/mL in zebrafish embryos.	Non-toxic (LC_{50} > 500 µg/mL); malformations only appear at extreme exposures.	[12]
11	Fitofarmaka Derivat Flavonoid	In silico	Parameters: mutagenicity, carcinogenicity, Cramer test, Ames test (software prediction) Dose: (in silico, no direct dose)	Flavonoid derivatives (in silico) show that some natural compounds are mutagenic, but structural modifications can reduce toxicity to class II.	Some natural flavonoids are potentially toxic, but structural modifications reduce their toxicity.	[5]
12	Phytopharmaceutical Propolis extract	In vivo	Parameters: blood glucose, cholesterol, triglycerides Dosage: 0.3–720.3 mg/kgBW (28 days)	Propolis is safe at doses up to 720.3 mg/kg BW for 28 days without changes in glucose, cholesterol, or triglycerides.	No significant changes → safe for repeated consumption (28 days).	[9]

Discussion

In vivo testing of red gedi leaf ethanol extract showed that there was no mortality or toxic symptoms in mice up to a dose of 7 g/kgBW. This indicates that the substance is classified as safe with a category of practically non-toxic. The flavonoid, polysaccharide, and anthocyanin content in red gedi leaves is thought to play a role in protecting tissues, reducing oxidative stress, and preventing damage to the liver and kidneys, thus supporting its use as a safe herbal medicine ingredient [11]. This combination herbal medicine formulation showed excellent safety test results in experimental animals. No deaths were observed up to 16 g/kg BW, and no significant physiological changes occurred. Synergistic effects between ingredients such as flavonoids in basil, vitamin C in lime, and the antimicrobial activity of honey contribute to metabolic stability and high antioxidant effects, thereby preventing organic toxicity at high test doses [2]

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Acute toxicity testing results for Pegel Linu herbal medicine showed an LD_{50} value of 1,479 mg/kgBW, which is classified as mildly toxic. Histopathological examination revealed mild necrosis in the liver, indicating that excessive consumption can cause hepatotoxic effects. However, at traditional doses, this herbal medicine is still considered safe. These findings emphasize the importance of standardizing doses and monitoring the long-term safety of herbal preparations containing ingredients with strong pharmacological effects [7]. Toxicity testing using the Brine Shrimp Lethality Test (BSLT) yielded an LC_{50} of 3366 ppm, indicating non-toxicity. The curcumin content of turmeric and the ascorbic acid in tamarind have high antioxidant activity, can stabilize cell membranes, and help protect the body from the effects of oxidative stress. The BSLT test using Artemia salina larvae is effective for initial screening of the toxicity of liquid herbal medicine extracts, and the results reinforce the safety of turmeric and tamarind herbal medicine as a traditional herbal drink [14]

Research on soursop leaf extract shows no toxic effects in rats at doses up to 5000 mg/kgBW. Liver and kidney function tests showed normal results, with no increase in liver enzymes or histological abnormalities. The acetogenin compounds in soursop leaves are cytotoxic to cancer cells but harmless to normal tissue, making them a safe OHT candidate with natural anticancer potential [9]. Candlenut oil has an LD_{50}> 20 g/kg BW, indicating it is non-toxic in mice. Although liver weight decreased slightly at the highest dose, this effect remained within normal physiological limits. The unsaturated fatty acid content, such as oleic and linoleic acids, in candlenut oil has a protective effect on the cardiovascular system, thus causing no systemic toxicity. These results indicate that candlenut oil can be used as an OHT ingredient with a safe dose limit [8]. Acute toxicity testing of black onion extract showed an LD_{50} value > 2000 mg/kgBW without causing toxic symptoms. Fermentation of garlic produces S-allyl cysteine, a powerful antioxidant that can help suppress gastrointestinal irritation. The hepatoprotective effects found indicate that fermentation increases the safety of garlic consumption, making it a candidate for OHT ingredients that are safe for long-term use [13]

Acute toxicity test results showed no deaths in mice at doses up to 5000 mg/kgBW. This preparation is classified as practically non-toxic. The citronellal content in lemongrass and eugenol in basil provides natural antitussive, antiseptic, and anti-inflammatory effects without affecting vital organ function. This proves that this herbal combination is safe for consumption as an OHT syrup preparation [9]. This phytopharmaceutical exhibits an LD_{50}> 2000 mg/kgBW without pathological changes in organs, although mild tremors may occur at very high doses. The essential oils of lemongrass and basil eugenol may cause mild stimulation of the central nervous system at high doses, but these effects are not harmful. These findings support the long-term safety of consuming lemongrass and basil herbal tea at reasonable doses [10]

Test results using zebrafish embryos showed LC_{50} values above 500 µg/mL, indicating low toxicity levels. No significant morphological abnormalities were found in the fish embryos, either in the n-hexane, ethyl acetate, or water fractions. Non-mammalian models, such as zebrafish, are considered effective for assessing the initial toxicity of phytopharmaceuticals because they are sensitive to toxic compounds and are ethically and economically efficient [12]. Computational simulations of flavonoid derivatives using Toxtree software show that molecular structure modifications can reduce toxicity potential to class II. This in silico prediction is useful for initial safety screening of active compounds before biological testing. This approach is efficient and complies with the 3R principle (Replace, Reduce, Refine) in toxicology research ethics [5]

Subchronic testing of propolis ethanol extract for 28 days showed no significant changes in glucose, cholesterol, or triglyceride levels in rats. These results indicate that propolis consumption is safe for medium-term use. The flavonoids and phenolic acids in propolis have antioxidant and immunomodulatory effects, which contribute to physiological stability without toxic effects [9]. Based on the overall research results, most of the herbal medicines, OHTs, and phytopharmaceuticals tested exhibit high safety and low toxicity. Variations in results between products are mainly due to differences in the composition of active ingredients and dosage. The combination of in vivo, in vitro, and in silico approaches has been proven to provide a more comprehensive picture of the safety of herbal ingredients in Indonesia.

Implications and Future Research Directions

Based on this review's results, strengthening a multidisciplinary toxicological approach is necessary for the development of herbal medicines in Indonesia. The integration of **in silico**, **in vitro**, and **in vivo** methods should be applied in a sequential and complementary manner. In silico approaches can be used at the initial stage to screen the potential toxicity of thousands of herbal bioactive compounds based on their chemical structures, allowing only candidates with favorable safety profiles to proceed to biological testing. This

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strategy not only improves research efficiency but also aligns with the 3R principles (Replace, Reduce, Refine) in toxicological research.

Furthermore, the development of organ-specific in vitro models should be enhanced, particularly for detecting subchronic and chronic toxicity. The use of primary hepatocytes or liver cell cultures is highly relevant for hepatotoxicity screening, as the liver is the primary organ responsible for metabolizing herbal compounds. This approach can provide early mechanistic insights before conducting more complex in vivo studies.

In addition to pre-marketing testing, the implementation of a pharmacovigilance system should be expanded to include Standardized Herbal Medicines and phytopharmaceuticals already available on the market. An integrated post-marketing adverse event reporting system for herbal products, aligned with the national pharmacovigilance framework, would enable long-term safety monitoring and early detection of rare or delayed adverse effects. Thus, the combination of multidisciplinary toxicological approaches and continuous pharmacovigilance can provide a strong foundation for the development of safe, evidence-based national herbal medicines.

Conclusion

This review examined the results of safety and toxicity testing of herbal medicines in the development of traditional herbal medicines (jamu), Standardized Herbal Medicines, and phytopharmaceuticals in Indonesia during the period 2020–2025, based on twelve relevant research articles. The findings indicate that most herbal ingredients and formulations exhibit good safety profiles, with low to mild toxicity observed only at high doses. In vivo testing remains the primary approach for toxicity evaluation, particularly through the assessment of clinical signs, biochemical parameters, and histopathological examination of target organs.

At the product development level, jamu is generally considered safe based on empirical evidence and standardized raw materials. In contrast, Standardized Herbal Medicines demonstrate more measurable safety profiles through acute and subchronic toxicity testing. Phytopharmaceuticals show the most comprehensive safety profiles, as they have been evaluated using a combination of in vivo, in vitro, and in silico methods. Nevertheless, this review also reveals that most studies are still focused on acute toxicity testing, while the parallel application of multidisciplinary approaches has not yet been optimally implemented.

Based on these findings, strengthening the integration of multidisciplinary toxicological methods and implementing herbal product pharmacovigilance are the main recommendations to ensure long-term safety. These approaches are essential to support the development of safe, high-quality, and evidence-based national herbal medicines.

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