

EVALUATION OF HERBAL MEDICINES AND ANIMAL EXPERIMENTATION

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ABSTRACT

Over time, the use of herbal medicines has increased rapidly. This is influenced by several main factors, including the relatively cheap price and avoiding concerns about the side effects of chemical drugs. In practice, screening tests need to be carried out on a drug product that will be marketed, one of which is through a toxicity test. The use of animal models as experimental materials provides invaluable information in many aspects of pathophysiology, treatment, and diagnosis of human disease. Without exception, research on traditional ingredients also relies heavily on animals in in vivo, in situ, and in vitro experiments. This study uses a literature review with a descriptive approach based on secondary literature derived from Google Scholar, PubMed, and Science Direct. Research conducted on animals regarding herbal medicine can provide valuable insights into a herbal remedy. Selecting the appropriate animal for a study is crucial to obtain scientifically convincing results. Animals used for pharmacological studies should be standard species. Rodents, guinea pigs, rabbits, cats, and dogs are often used in traditional herbal medicine research. Moreover, herbal materials used for pharmacological research should be standardized to control quality and ensure the reproducibility of experimental outcomes. The standardization of herbal medicine should encompass species identification (name, origin, description, and purity), extraction procedures, chemical analysis of major and bioactive compounds, heavy metals, pesticides, and storage stability.

Keywords: Herbal Medicines, Animal Experimentation, In-Vitro, In-Vivo

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1. INTRODUCTION

Herbal medicine is defined as substances or preparations derived from plants with therapeutic or health benefits for humans, originating from one or more plants. The use of herbal remedies has rapidly increased worldwide, with many individuals now utilizing these products for treating various health issues within healthcare practices across different countries. According to the Indonesian Food and Drug Authority (BPOM), traditional medicines are categorized into several groups, namely herbal remedies, standardized herbal medicines, and phytopharmaceuticals. The distinction between these types of medicines lies in the testing they undergo. Traditional medicines that pass preclinical tests are known as standardized herbal medicines, while those based on clinical trials are referred to as phytopharmaceuticals. Based on the Basic Health Research of 2010, it was found that the prevalence of traditional medicine use among individuals aged over 15 was 59.12%, while in the 55-64 age group, it reached 67.69%, spread across various regions, including rural and urban areas. The utilization of traditional medicines in regions like Java, Sunda, Manado, Kalimantan, and other areas represents an inherited legacy that has further evolved through scientific testing.¹⁻³

The use of herbal medicines varies depending on the location, and its prevalence has recently increased. Around 80% of the population in Arab communities rely on herbal medicines for disease prevention and treatment. The most common reasons for using traditional herbal remedies include affordability, alignment with patient beliefs, avoidance of concerns about side effects from chemical (synthetic) drugs, meeting the need for more personalized healthcare, and enabling broader access to health information within communities. Many individuals report using herbal medicines to address various healthcare needs, including disease prevention and the management of chronic conditions such as dyslipidemia, hypertension, diabetes, cancer, and inflammatory bowel disease.⁴⁻⁷

The evaluation of herbal medicines is necessary to assess their safety and effectiveness. The validation of the effectiveness of new herbal combinations and the determination of their therapeutic doses are crucial aspects of herbal medicine evaluation. Additionally, evaluating herbal medicines can help in discovering new plant-based ingredients that are pharmacologically active. The field of pharmacological research plays a crucial role in modernizing traditional herbal medicine. Information about herbal remedies, not obtainable from humans, can be gathered through animal experiments. Animals are utilized as subjects in pharmacological studies. The utilization of animals in experimental medicine, pharmacology, pharmaceutical development, safety assessment, and toxicological evaluations has become a well-established and essential practice. Animals can serve as sources of organelles, cells, or isolated tissues; disease models; or predictors for drugs or other xenobiotic actions or transformations in humans. Therefore, animal-based research is essential, contributing significantly to the advancement of scientific knowledge in general and biomedical progress in particular.⁸

Pharmacological and toxicological studies of substances in animals provide information about their biological and physiological changes, which are highly relevant to humans. Animal models of human diseases or disorders offer valuable insights into various aspects of pathophysiology, treatment, and disease diagnosis in humans. Similarly, research on traditional remedies extensively relies on animal experimentation, including *in vivo*, *in situ*, and *in vitro* experiments.⁸ This study aims to explore the evaluation of herbal medicines and the application of animal experiments in traditional medicine.

2. METHOD

The research method employed was a literature review utilizing a descriptive approach. The search was conducted through Google Scholar, PubMed, and Science Direct using the keywords "herbal medicine" and "animal experimentation."

3. DISCUSSION

3.1 Evaluation of Herbal Medicine

Herbal medicines refer to substances or preparations derived from plants that offer therapeutic benefits or other health advantages to humans. These may contain raw materials or processed elements from one or more plants. Although inorganic and animal-based components treat illnesses in certain countries, herbal remedies consistently dominate traditional medicine. Experiments serve as a fundamental method in modern scientific inquiry, allowing for the acquisition of medicinal substances that cannot be obtained directly from humans, often achieved through animal experimentation¹

Following the confirmation of the therapeutic effects of herbal remedies through pharmacological experiments, there is a need to discover bioactive compounds that align with guided bioassay *in vitro* screenings. This process allows for further evaluation of mechanisms at the cellular or molecular level. Understanding bioactive compounds within the herbal mixtures enables more accurate standardization and quality control. It's acknowledged that combinations of herbal remedies or medications can lead to toxicities not evident with individual agents. Other pharmacological safety studies involving animal models are conducted to investigate the potential undesirable pharmacodynamic effects of individual substances on physiological functions.⁹

One of the most common types of herbal studies involving animals aims to uncover the mechanisms behind herbal actions. This information, once discovered, holds significant value in determining whether the herbal remedy warrants further investigation to enhance its benefits or for developing other medications with known effects. On the other hand, the World Health Organization (WHO) emphasizes that animal studies should be conducted with due regard to animal welfare, encouraging a reduction in whole-animal experiments by employing *in vitro* methods. *In vitro* experiments typically require fewer test samples than *in vivo* testing

and can provide information at the cellular or molecular level. The selection process between *in vivo*, *in vitro* experiments, or their combination should consider economic and ethical considerations and must align with the research project's objectives.¹

3.2 Animal Experimentation

In vivo and *in vitro* experiments complement each other in exploring the actions and mechanisms of traditional herbal medicine across various levels. However, compared to *in vitro* experiments, *in vivo* experiments sometimes cannot elucidate the working mechanisms of herbal remedies and explain the causes of all changes; their outcomes are easily influenced by various complex factors. To delve deeper into the mechanisms of herbal medicine, a combination with *in vitro* experiments is necessary, as their outcomes can be obtained accurately without the interference of the complex factors present in *in-vivo* experiments. However, *in vitro* experiments also have limitations and drawbacks. Results obtained from *in vitro* tests are far from clinical applications. The efficacy of test samples can be altered by various factors when introduced into the body. The impacts of absorption, distribution, and metabolism within the body cannot be reflected through *in vitro* testing. On the other hand, *in-vitro* experiments may not yield positive results if the herbal activity is only evident when its components are metabolized within the body.¹

Selecting the appropriate animal for a study is crucial to obtaining convincing scientific results. Animals used in pharmacological studies should be of standard species. Rats, guinea pigs, rabbits, cats, and dogs are often utilized in traditional herbal research. Detailed profiles for commonly used animals in pharmacological studies, including characteristics such as strain, gender, age, and housing conditions, are available in the literature.¹⁰⁻¹²

Animal models are essential in many pharmacological studies. These animal models may have pre-existing, congenital, or induced diseases or injuries to mimic human conditions. Sometimes, *in-situ* organs or tissues are also used, depending on the experimental objectives. Given the differences in observations between animals and clinical studies, it is essential to test a sample on several different animal species. The species, the number of animals in each test group, and the required number of groups mainly depend on the study's objectives and methodological indices. Typically, for small animals like rats and mice, the number of animals in each group is generally 8-12; for larger animals like rabbits or dogs, the minimum number in each group is 5-8.¹

There are numerous arguments against the use of animal studies in herbal plant or drug research, including the fact that animal studies do not always predict what will happen in humans. It is indeed true that significant interspecies variations in pharmacokinetic or pharmacodynamic components can lead to inappropriate extrapolation of animal doses to humans. Another concern is the lack of variability among subjects in animal research, as animals typically consist of healthy young adults with homogeneous genetic backgrounds, housed and fed uniformly.¹³

Animals cannot communicate symptoms, and research involving them is often criticized for their inability to detect adverse drug reactions, the most common of which include headaches, anorexia, dizziness, drowsiness, edema, and redness. However, some studies indicate a correlation between drug side effects in humans and their manifestation in experimental animals. For instance, if a drug induces dizziness as a side effect, spontaneous motor activity would be observed in experimental animals. Similarly, if a drug leads to edema in humans, the sign in animals would be urinary sodium excretion, and so on. These signs observed in animals, as described above, have increased their relevance to human outcomes.^{7,9}

4 CONCLUSION

Research on animals regarding herbal plants can provide valuable information about an herbal remedy. Selecting the appropriate animal for the study is crucial in obtaining scientifically convincing results. Animals used in pharmacological studies should be standardized species. Rats, mice, guinea pigs, rabbits, cats, and dogs are commonly used in traditional herbal medicine research. Furthermore, herbal materials used in pharmacological research must be standardized to ensure quality control, ensuring the reproducibility of experimental results. The standardization of herbal medicine should encompass species identification (name, origin, description, and purity), extraction procedures, analysis of major and bioactive chemical compounds, heavy metals, pesticides, and storage stability.

REFERENCES

1. Wu C fu, Wang F, Li C li. Functional Evaluation of Herbal Medicines by Animal Experiments. In: Liu WJ., editor. *Traditional Herbal Medicine Research Methods*. John Wiley & Sons, Inc; 2011. p. 271–301.
2. Vickers A, Zollman C, Lee R. Herbal medicine. *West J Med*. 2001;175(2):125–8.
3. Adiyasa MR, Meiyanti M. Pemanfaatan obat tradisional di Indonesia: distribusi dan faktor demografis yang berpengaruh. *J Biomedika dan Kesehat*. 2021;4(3):130–8.
4. James PB, Taidy-Leigh L, Bah AJ, Kanu JS, Kangbai JB, Sevalie S. Prevalence and Correlates of Herbal Medicine Use among Women Seeking Care for Infertility in Freetown, Sierra Leone. *Hindawi*. 2018;2018:1–11.
5. Awad A, Al-Shaye D. Public awareness, patterns of use and attitudes toward natural health products in Kuwait: A cross-sectional survey. *BMC Complement Altern Med* [Internet]. 2014;14(1):1–11. Available from: BMC Complementary and Alternative Medicine
6. Cecilia NC, Washali A.Y A, Abuaisha AA, Albishty MM, I S, M RA. The Use of Herbal Medicine in Arab Countries : A Review. *Int J Public Heal Clin Sci*. 2017;4(February 2018):1–14.
7. Wachtel-Galor S, Benzie IF. *Herbal Medicine: Biomolecular and Clinical Aspects*. Boca

- Raton, FL: CRC Press/Taylor & Francis. 2nd ed. Taylor & Francis; 2011.
8. Liu WJ. Traditional Herbal Medicine Research Methods. Traditional Herbal Medicine Research Methods. Canada: Wiley; 2011.
 9. Valentin JP, Bialecki R, Ewart L, Hammond T, Leishmann D, Lindgren S, et al. A framework to assess the translation of safety pharmacology data to humans. *J Pharmacol Toxicol Methods* [Internet]. 2009;60(2):152–8. Available from: <http://dx.doi.org/10.1016/j.vascn.2009.05.011>
 10. Wojcikowski K, Wohlmuth H, Johnson DW, Gobe G. Effect of Astragalus membranaceus and Angelica sinensis combined with enalapril in rats with obstructive uropathy. *Phyther Res* [Internet]. 2008;22(4):544–549. Available from: <http://www3.interscience.wiley.com/journal/117934759/abstract>
 11. Gad SC. *Animal Models in Toxicology*. 3rd ed. CRC Press; 2016. 1–1152 p.
 12. Hau J, Van Hoosier G. *Handbook of laboratory animal science, second edition: Essential principles and practices*. Vol. 1, *Handbook of Laboratory Animal Science, Second Edition: Essential Principles and Practices*. 2002. 1–569 p.
 13. Olson H, Betton G, Robinson D, Thomas K, Monro A, Kolaja G, et al. Concordance of the toxicity of pharmaceuticals in humans and animals. *Regul Toxicol Pharmacol*. 2000;32(1):56–67.