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Scientific Studies of The Activity and Acute Toxicity of Ld50 Rattan As A Natural Ingredient Drug in Suku Anak Dalam (Sad) Bukit Dua Belas Jambi, Indonesia: Review Articles

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Abstract:

Scientific review of articles based on Indonesian local wisdom has been carried out, especially on the potential of 11 types of rattan in Suku Anak Dalam (SAD) jambi province, Indonesia. Scientific studies are carried out with reference to the same type of species, related to the study of their potential activity pharmacologically and toxicity studies on values LD_{50}. The article review study was conducted using the PRISMA method. Retrieval of article sources from science direct, springer and pubmed databases is performed. Limitations are carried out related to data collection, that only take original research articles and review articles with article sources in English. Interesting data have been obtained here, no study of the pharmacological effect on 11 types of rattan has been carried out in this article review study. Rattan by species *Daemonorops draco*, *Calamus scipionum*, *Calamus manan*, *Calamus ornatus*, *Calamus axillaris* and *Calamus caesius* studies of pharmacological effects have been carried out. Only on *Daemonorops draco* obtained data that is quite capable and gets attention by world researchers because it is known to have the potential for anti-cancer activities. However, in other types of rattan, the data obtained is not so much and it is still very feasible to conduct a study search on drug discovery based on natural product sources as drug candidates. Rattan by species *Calamus fabellatus*, *Calamus javensis*, *Korthalsia echinometra* and *Daemonorops geniculate* no scientific studies have been found related to its potential activities pharmacologically. In the study of acute toxicity LD_{50}, has not been done at all on the 11 types of rattan. In conclusion, the "Gap of Science" of the topic of rattan available on the environment Suku Anak Dalam (SAD) Bukit Dua Belas Jambi Province still has great potential for scientific and in-depth studies related to the potential and study of drug discovery by utilizing natural product sources that can be done by all researchers with an interest in natural products as a source of treatment.

Keywords: Rattan Species, Suku Anak Dalam (SAD), Jambi Indonesia, Natural Product, Pharmacological Effect, Toxicity

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1. Introduction

Geographically, Indonesia is located in the equatorial area as well as also located in an archipelago area rich in spices which are international market commodities (1). In Indonesia, there is also ethnic and tribal diversity. Each tribe has its own uniqueness both culturally, where it will also not be spared also in terms of traditions, each of which often consumes medicinal plants as a source of treatment and certain rituals (2,3). Suku-anak-dalam (SAD) is a native of Indonesia who comes from the province of Jambi, rattan is an interesting topic for further research. This tribe is a tribe that lives isolated from the surrounding area, so the cultural influence is still very strong on this tribe (4,5).

Rattan is an interesting thing to do further studies because the use of rattan in this area is still quite widely used in daily life in this tribe. The 11 types of rattan that are the focus of the study are Jernang - Daemonoropsdraco (Willd.) Blume; Semambu - Calamus scipionum (Lour.); SenamoKekecik/Pledais - Calamus fabellatus (Becc.); Manau - Calamus manan (Miq.); Cacing - Calamus javensis (Blume); Tetebu - Calamus ornatus (Blume); Gelang - Daemonorops verticiliaris (Grifft.) Mart; Sego Air - Calamus axillaris (Becc.); Sego Putih - Calamus caesius (Blume); Siuh/Udang - Korthalsia echinometra (Becc.); Cikoi - Daemonorops geniculate (Griff.) Mart (6).

The study and tracing of scientific evidence of a medicinal product from natural sources of ingredients certainly needs to be carried out carefully and absolutely has a clear degree of measurability. This also proves the activity claims of natural medicines that have been used by the community empirically. Studies of drug activity from natural ingredients also confirm that it is related to the dose that patients need to consume to get the expected therapeutic effect. Where the right dose can certainly increase the success of the therapy (7–10).

In toxicity studies, it is clearly described what the level of safety of a drug is. Medicinal products sourced from natural ingredients consumed at high enough doses will trigger an influence on organs in the body. In the toxicity value of natural ingredient medicinal products, there are quite a lot of combinations of forms that can be tested, including the results of the extraction process, fractionation and isolation of single compounds that have been isolated from these natural ingredient products, this also applies to studies on their pharmacological activities (11–15).

2. RESEARCH METHODS

Prisma method was used (16–18) in the creation of this article review which was done in August 2022 to September 2022. According to these guidelines, there are several steps in the study: 1) determining eligibility criteria; 2) determine the source of information; 3) study selection; 4) the data collection process; and 5) selection of data items (24). Figure 1 describes the steps of our work in conducting a systematic review.

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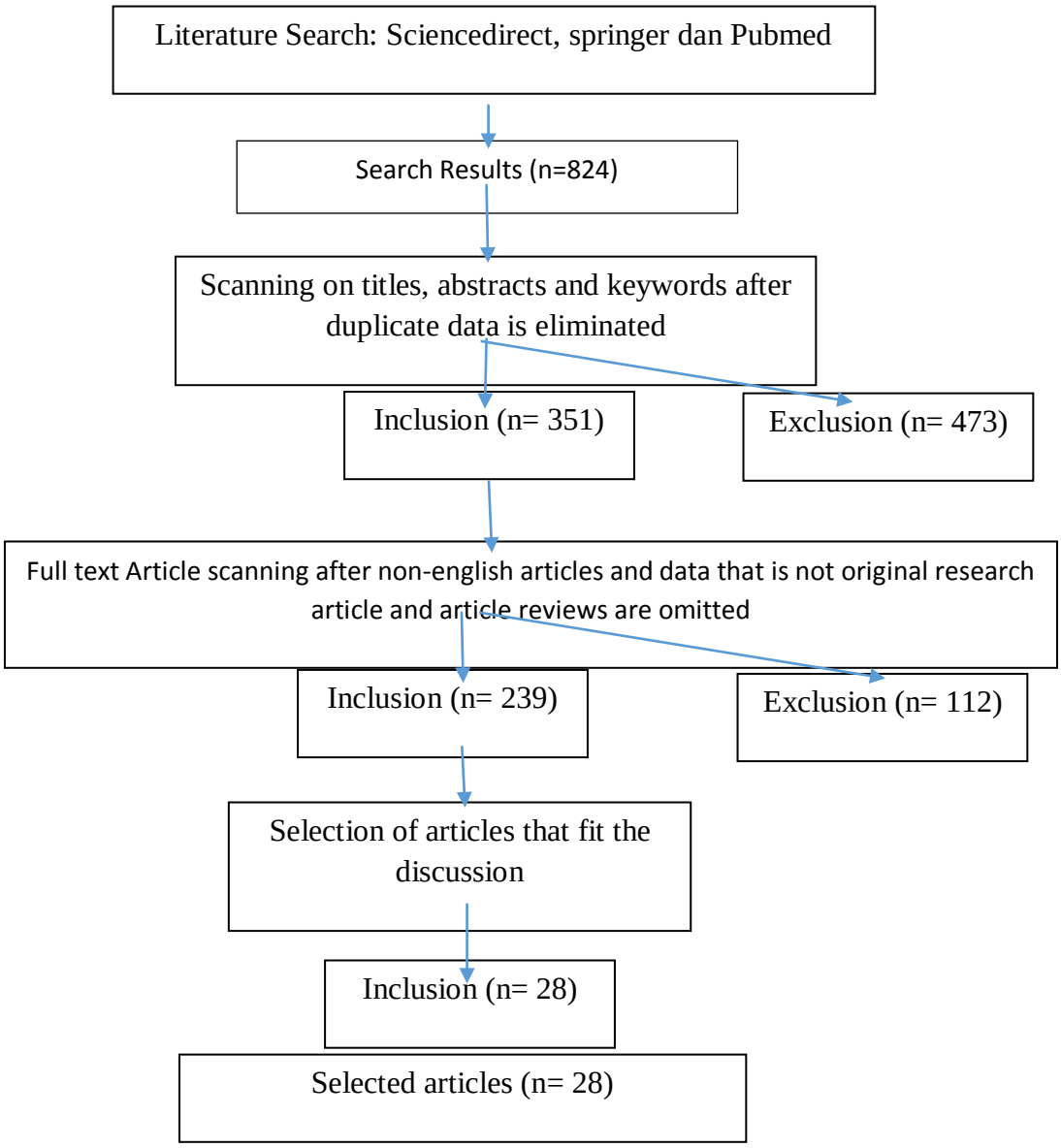

Figure 1. PRISMA Flowchart

Eligibility Criteria

The following inclusion criteria are established for the review guidelines:

IC_1: Research journal, peer-reviewed written in English, with a publication year range of 2012 to 2022 in PDF format;

IC_2: Journal of medicinal plant activities derived from natural ingredients with the target of natural ingredients medicinal plants, 11 types of rattan located in Bukit-Dua-Belas Jambi Province, Indonesia; and

IC_3: Journal of drug toxicity activities derived from natural ingredients with the target of natural ingredients medicinal plants, 11 types of rattan located in Bukit-Dua-Belas Jambi Province, Indonesia.

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In this study we will only focus on the study of the activities and tosisity of LD_{50} from 11 medicinal plants including the: Jernang - Daemonoropsdraco (Willd.) Blume; Semambu - Calamus scipionum (Lour.); SenamoKekecik/Pledais - Calamus fabellatus (Becc.); Manau - Calamus manan (Miq.); Cacing - Calamus javensis (Blume); Tetebu - Calamus ornatus (Blume); Gelang - Daemonorops verticiliaris (Grifft.) Mart; Sego Air - Calamus axillaris (Becc.); Sego Putih - Calamus caesius (Blume); Siuh/Udang - Korthalsia echinometra (Becc.); Cikoi - Daemonorops geniculate (Griff.) Mart.
This will be specified again with research studies from various countries in the world with database sources. The source articles that are used as a study, of course, all articles that have been comprehensively studied by experts in their respective fields by considering the inclusion criteria in this review.

Sources of Information
The selection of each article is focused on an online database indexed on sciencedirect, springer and pubmed. We eliminate articles that are not fully accessible to the author, articles written not in English and other articles other than original research articles and review articles. In addition, we also scan the list of references included in the article to find studies related to the object of study of the study.

Study Selection
(1) Keyword searches, selected according to our research interests in reviewing the studies to be adopted; thus, it is related to the topic of research. The search keywords used are : activity+Daemonorops+Draco; activity+Calamus+scipionum; activity+Calamus+fabellatus; activity+Calamus+manan; activity+Calamus+javensis; activity+Calamus+ornatus; activity+Daemonorops+verticiliaris; activity+Calamus+axillaris; activity+Calamus+caesius; activity+Korthalsia+echinometra; activity+Daemonorops+geniculate; toxicity+Daemonorops+Draco; toxicity+Calamus+scipionum; toxicity+Calamus+fabellatus; toxicity+Calamus+manan; toxicity+Calamus+javensis; toxicity+Calamus+ornatus; toxicity+Daemonorops+verticiliaris; toxicity+Calamus+axillaris; toxicity+Calamus+caesius; toxicity+Korthalsia+echinometra; toxicity+Daemonorops+geniculate.
(2) Exploration and selection of the titles, abstracts, and keywords of the identified articles is carried out based on notability criteria.
(3) Each article that will be included in the review discussion, is part of the article that is included in the review discussion that will be made by the author, and this is limited by the eligibility criteria.
(4) The reference list of articles is scanned to find related studies and begin this phase.

Data Collection Process
Data collection is carried out manually using data extraction consisting of the following content: database, keywords, meta data search results, file search and file selection.

Data Information
The studies drawn from each article consist of: (i) Studies of medicinal plant activities of natural ingredients specific to 11 types of rattan. (ii) Study of toxicity of medicinal plants specific to 11 types of rattan.

The purpose of the search related to the study of the activity and toxicity of medicinal plants of natural ingredients that are specific to the 11 types of rattan that are the topic of research is to dig deeper into the "gap of science" and explain that the potential of medicinal plants in Indonesia. This study also proved that dose is a relefan size factor as a reference so that patients get optimal therapeutic goals and avoid the effects of poisoning due to consuming medicinal plants with uncontrolled amounts.

Study selection
Search results were obtained in the online database as many as 824 article data that can be searched. The article was written from 2012 to 2022, obtained 434 article data after eliminating articles with duplication. Furthermore, a search of article files was carried out in each database in PDF format, 351 articles were obtained.

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Next, articles with non-English language and scientific studies other than the original research article and review article were eliminated, a total of 239 articles were obtained in this process. In the final stage, a study of the article related to the object of research was carried out until a total of 28 articles were obtained that were relevant to the object of this study.

Characteristics of the study
This section describes the demogradi data from the articles selected for discussion. The results showed that out of a total of 824 article data obtained from database search results. This data identifies search results related to the data obtained which refers to the activity and toxicity of 11 types of rattan plants with the same species as rattan types that have been studied by researchers throughout the country.

3. RESULT AND DISCUSSION

Studies on the potential pharmacological effects of these 11 types of rattan have not been fully carried out by researchers and this could be caused by various matters. On rattan by species *Daemonorops draco*, *Calamus scipionum*, *Calamus manan*, *Calamus ornatus*, *Calamus axillaris* dan *Calamus caesius* studies of pharmacological effects have been carried out. Only in Daemonorops draco obtained data that is quite capable and gets attention by world researchers because it is known to have the potential for anti-cancer activities, especially leukemia (19). However, in other types of rattan, the data obtained is not so much and is still very feasible to search for studies on drug discovery based on natural product sources as drug candidates.

Rattan by species Daemonorops draco, is indeed the type of rattan species with the most research data. It is well known that *Daemonorops draco*, has potential pharmacological effects such as efficacious and selective killing of cancer cells induce apoptotic cell death in cancer cells (20), inhibition of a-toxin production, decreasing a-toxin production without inhibiting bacterial growth, anti-virulence agent combating Staphylacocus aureus infection (21), Anti-inflammatory, pro-proliferative and antimicrobial effect (22), pro-angiogenic (23), skin wound healing (24), Anticancer, Acute myeloid leukemia (AML) (19), Osteogenic, osteoblastic (25), Type II diabetes (26), Osteoclastogenesis (27), Hyperglycaemia, Vascular disorders (28), in traumatic injuries (TCM), anti-platelet aggregation antithrombotic (29), Antiplatelet, Atherothrombosis (30), diarrhoea and haemorrhage (31), α-glucosidase inhibitor for diabetes type II (32), Alzheimer's disease in to inhibitors of amyloid-β (Aβ) aggregation (33), Diabetes (Sheng-ji Hua-yu (SJHY) formula) (34), treat inflammatory factors and tissue damage in an experimental model of Hemorrhoidal disease (HD) in rats (35), analgesic, anti-inflammatory, antibacterial, hypolipidemic, hypoglycemic (36), pain, Hemorrhage (37), wound healing armamentarium (38), healing (39) and Candida albicans as antifungal activity (40).

Other types of rattan apart from the species *Daemonorops draco*, indeed, the data can be found. However, the data obtained is still very little and this opens up opportunities for other researchers with an interest in the theme of natural product sources, it is still very possible to conduct drug discovery studies as drug candidates in the future. Obtained 2 studies on rattan with species *Calamus scipionum*. Because in rattan with species *Calamus scipionum* has been known to detect quercetin, then it has the potential to show effects anti-allergy, anti-inflammatory, anticancer, cardiovascular protection, anti-tumor, anti-viral, anti-diabetic, immunemodulatory, anti-hypertensive, and gastroprotective effects (41). In other articles, information was obtained that rattan with the species Calamus scipionum can be used as a source of traditional treatment, but it is not explained the intended pharmacological effect (42).

On rattan by species *Calamus axillaris*, obtained information that this type of rattan is known to have potential pharmacological effects as antimalarial activity (43). Only this activity has been gained so far. Because its potential as an antimalarial has been known, therefore there is an opportunity for further studies to be carried out related to pharmacological activity and toxicity studies on rattan types. There is no research data on the isolation

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of a single compound in *Calamus axillaris*, this will also give rise to hypotheses as well as in the findings of the *Cinchona sp*, yang lebih dahulu diketahui sebagai anti malaria. Namun setelah dilakukan isolasi senyawa tunggal diketahui bahwa *Cinchona sp*, juga memiliki potensi aktifitas pada anticancer, antioxidant, antidiabetic, antifungal, muscle cramps, hair growth stimulant, antimicrobial, antiobesity, antiplatelet, antiviral, anesthetic, and antipyretic (44).

On rattan by species *Calamus manan*, also obtained 2 articles that add to his activities. It is known that *Calamus manan* has the potential for somatic embryogenesis (45), however, in other articles it is only explained that rattan with this species can be used as a traditional medicine (42). On rattan by species *Calamus caesius*, obtained 3 research data. Known *Calamus caesius* has potential Antibacterial, anti-inflammatory and antioxidant activities (46). However, in the other 2 articles, it is not explained exactly the study of the pharmacological effects of rattan with species *Calamus caesius* (42,47). Referring to *Calamus caesius* can show anti-bacterial effects, especially on *Streptococcus pyogenes*, and has good anti-inflammatory data (46). This will certainly be relevant to the study of diseases with pathogenesis such as pharyngitis and other diseases that trigger excessive inflammation. On rattan by species *Calamus ornatus*, obtained information that can be categorized as information that is far from perfect. Because only 1 article was found that discusses its traditional use, but it is not explained in detail related to the activities that appear in rattan with this species (42).

A search for potential pharmacological effects of rattan with species has been carried out *Daemonorops draco*, *Calamus scipionum*, *Calamus manan*, *Calamus ornatus*, *Calamus axillaris* and *Calamus caesius*. The most capable data was obtained on rattan with species *Daemonorops draco*. In other types of rattan species, some data were obtained as well, but the data obtained was still very small and even only illustrated that the type of rattan can be used traditionally (42,47). Another type of rattan that has the potential for further studies is that *Calamus manan* has the potential for somatic embryogenesis (45), *Calamus axillaris* which has been known to exhibit anti-malarial effects (43) and *Calamus caesius* shows anti-bacterial and anti-inflammatory power (46).

However, in other types of rattan such as *Calamus fabellatus*, *Calamus javensis*, *Korthalsia echinometra* and *Daemonorops geniculate*, no data have been found related to scientific research that has been carried out and it is still very feasible to conduct studies on drug discovery based on natural product sources as drug candidates. It has been known in advance that differences in sampling locations and differences in the geographical location of the source of the growth of the sample will display different potential effects as well (48). Triggered by this factor, the potential for the "Gap of Science" of these 11 types of rattan species, especially in pharmacological studies, will be even wider. Moreover, rattan is a commodity with a high value in the international market at an expensive price (42,47). Rattan is also a source of commodities for regional residents for a source of income, especially Indonesia (49).

In the study of acute toxicity LD_{50}, no data was obtained from these 11 types of rattan species. However, cytotoxicity data were obtained in rattans with the species *Daemonorops draco*. This is very natural because from the review of pharmacological effects, it is only rattan with the species *Daemonorops draco* which has qualified research data. Cytotoxicity against $HepG_2$ cell line, among them, compounds 1, 9 and 10 exhibited modest cytotoxic activity with IC_{50} value in the range of 12.0–13.2 μM (50). the cytotoxicity of the D. draco extracts, the results showed that the aqueous (CC_{50} = 91.20–96.60 μg/mL), dichloromethane (CC_{50} = 87.30–85.40 μg/mL) and alkaloid-rich dichloromethane (CC_{50} = 84.70–85.80 μg/mL) extracts did not show relevant cytotoxicity ($p = 0.074$) when compared to the positive control (Actinomycin D, CC_{50} = 7.95 nM) in any of the cell lines (THP-1, NIH-3T3 and HaCaT) (22). The high lethality of the embryos from Medan, Indonesia, particularly caught our attention as this indicates the presence of unidentified substances that are toxic to the zebrafish embryos (23). An MTT assay and propidium iodide exclusion detected using flow cytometry were used to detect cell viability of HaCaT cells (24). No cytotoxic effect was observed on the osteoblastic MC3T3-

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E1 cells (25). Low IC_{50} (12 µM) against a-amylase (26). No cytotoxicity at 10 µM (27). Interestingly, cells simultaneously incubated with glucose (25 and 50mM) increased cell viability in a concentration dependent manner (28).

There is a huge potential for research that can be unearthed from the rattan species that are the focus of this article's review. The characterization of each species of natural materials is very important in determining the prediction of the bioactivity of a compound. Various types of instruments are needed to support the characterization of the isolation of natural materials. The insilico test can be carried out if natural material compounds have been obtained that have been separated from other compounds. The insilico test can be used to predict the bioactivity test of compounds that have been obtained singly. For subsequent testing, in-vitro and in-vivo preclinical tests can be carried out. After a series of processes, valid results are obtained, it can be continued to clinical trials which are the final trials of each candidate compound as a drug.

4. CONCLUSION

It turns out that there is still great research potential that can be extracted from rattan with these species. Some previous research, only discussed the potential for pharmacological activities. Found several articles related to toxicity tests, however that's all mostly discussed related to rattan with the species *Daemonorops draco*. On rattan by species *Daemonorops draco*, *Calamus scipionum*, *Calamus manan*, *Calamus ornatus*, *Calamus axillaris* and *Calamus caesius* studies of pharmacological effects have been carried out. Only in Daemonorops draco obtained data that is quite capable and gets attention by world researchers because it is known to have the potential for anti-cancer activities. However, in other types of rattan, the data obtained is not so much and is still very feasible to search for studies on drug discovery based on natural product sources as drug candidates.

On rattan by species *Calamus fabellatus*, *Calamus javensis*, *Korthalsia echinometra* and *Daemonorops geniculate* no scientific studies have been found related to its potential activities pharmacologically. In the study of acute toxicity LD_{50}, has not been done at all on the 11 types of rattan. In conclusion, the "Gap of Science" of the topic of rattan available on the environment Suku Anak Dalam (SAD) Bukit Dua BelasJambi Province still has great potential for scientific and in-depth studies related to the potential and study of drug discovery by utilizing natural product sources that can be done by all researchers with an interest in natural products as a source of treatment.

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