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From traditional use to scientific scientific evidence: Medicinal potential of the amazonian plant *Hura crepitans* L

Do uso tradicional à evidência científica: Potencial medicinal da planta amazônica *Hura crepitans* L

Del uso tradicional a la evidencia científica: Potencial medicinal de la planta amazónica *Hura crepitans* L

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Abstract
This study aims to critically review the scientific literature on the medicinal use of *Hura crepitans* L. (assacu), focusing on its phytochemical composition, pharmacological activities, and toxicity. A narrative review was conducted in PubMed, Scopus, and LILACS, including 17 studies meeting the inclusion criteria. Plant parts—particularly latex, seeds, and bark—contain bioactive metabolites such as flavonoids, tannins, daphnane-type diterpenes, lectins, and ribosome-inactivating proteins, associated with antioxidant, anti-inflammatory, antitumor, antimicrobial, antidiabetic, and antiparasitic activities. In vitro and in vivo studies showed selective cytotoxicity against tumor cells, glycemic regulation, and inhibition of *Plasmodium falciparum* growth. However, the same compounds responsible for bioactivity also contribute to toxicity, as seen in latex-related poisoning cases. Despite its well-established traditional use, gaps remain regarding human safety, mechanisms of action, and clinical evaluation. *H. crepitans* demonstrates significant therapeutic potential, highlighting the need for a multidisciplinary approach integrating traditional knowledge and modern science for safe and effective use.
Keywords: Phytotherapy; Pharmacology; Toxicity Tests; Review.

Resumo
Este estudo tem como objetivo revisar criticamente a literatura científica sobre o uso medicinal de *Hura crepitans* L. (assacu), com foco em sua composição fitoquímica, atividades farmacológicas e toxicidade. Foi realizada uma revisão narrativa nas bases PubMed, Scopus e LILACS, incluindo 17 estudos que atenderam aos critérios de inclusão. As partes da planta — especialmente o látex, as sementes e a casca — contêm metabólitos bioativos, como flavonoides, taninos, diterpenos do tipo daphnane, lectinas e proteínas inativadoras de ribossomos, associados a atividades antioxidante, anti-inflamatória, antitumoral, antimicrobiana, antidiabética e antiparasitária. Estudos in vitro e in vivo

demonstraram citotoxicidade seletiva contra células tumorais, regulação glicêmica e inibição do crescimento de *Plasmodium falciparum*. Entretanto, os mesmos compostos responsáveis pela bioatividade também contribuem para a toxicidade, como observado em casos de intoxicação relacionada ao látex. Apesar do uso tradicional bem estabelecido, ainda persistem lacunas quanto à segurança em humanos, mecanismos de ação e avaliação clínica. *H. crepitans* demonstra expressivo potencial terapêutico, ressaltando a necessidade de uma abordagem multidisciplinar que integre o conhecimento tradicional e a ciência moderna para um uso seguro e eficaz.
Palavras-chave: Fitoterapia; Farmacologia; Testes de Toxicidade; Revisão.

Resumen
Este estudio tiene como objetivo revisar críticamente la literatura científica sobre el uso medicinal de *Hura crepitans* L. (assacu), con énfasis en su composición fitoquímica, actividades farmacológicas y toxicidad. Se realizó una revisión narrativa en las bases PubMed, Scopus y LILACS, que incluyó 17 estudios que cumplían con los criterios de inclusión. Las partes de la planta —en particular el látex, las semillas y la corteza— contienen metabolitos bioactivos como flavonoides, taninos, diterpenos tipo daphnane, lectinas y proteínas inactivadoras de ribosomas, asociados con actividades antioxidante, antiinflamatoria, antitumoral, antimicrobiana, antidiabética y antiparasitaria. Los estudios in vitro e in vivo demostraron citotoxicidad selectiva contra células tumorales, regulación glucémica e inhibición del crecimiento de *Plasmodium falciparum*. Sin embargo, los mismos compuestos responsables de la bioactividad también contribuyen a la toxicidad, como se observa en casos de intoxicación relacionada con el látex. A pesar de su uso tradicional bien establecido, persisten lagunas en cuanto a la seguridad en humanos, los mecanismos de acción y la evaluación clínica. *H. crepitans* demuestra un importante potencial terapéutico, lo que resalta la necesidad de un enfoque multidisciplinario que integre el conocimiento tradicional y la ciencia moderna para un uso seguro y eficaz.
Palabras clave: Fitoterapia; Farmacología; Pruebas de Toxicidad; Revisión.

1. Introduction

Hura crepitans L., commonly known as assacu, is a tropical tree belonging to the Euphorbiaceae family, widely distributed across Central and South America, including the Brazilian Amazon region. The species is easily recognized by its spiny trunk, explosively dehiscent fruits, and highly toxic white latex (EMPRESA BRASILEIRA DE PESQUISA AGROPECUÁRIA – EMBRAPA, 2018).

Various parts of the plant—such as the bark, leaves, roots, seeds, and especially the latex—are traditionally used in the treatment of infections, inflammation, gynecological disorders, and diseases such as leishmaniasis and cancer (Sarquis et al., 2019).

The growing scientific interest in the species stems from the presence of secondary metabolites with well-documented biological activity, including tannins, flavonoids, triterpenoids, lectins, and diterpenes. These compounds have been investigated for their antioxidant, antimicrobial, antiparasitic, and antiproliferative effects (Di Lorenzo et al., 2021; Shamsudin et al., 2022; Kovac et al., 2023).

Accordingly, this study aims to critically review the scientific literature on the medicinal use of *Hura crepitans* L. (assacu), focusing on its phytochemical composition, pharmacological activities, and toxicity, contextualizing its traditional applications and scientific findings.

2. Methodology

A qualitative research was conducted (Pereira et al., 2018) and of the specific type of literature review (Rother, 2007). A narrative literature review was conducted with the objective of compiling and analyzing scientific studies related to the plant *Hura crepitans* and its potential applications in human health. Data collection took place between February and July 2025. The bibliographic search was performed in the following electronic databases: PubMed, Scopus, and LILACS. The search strategy employed the descriptors "*Hura crepitans*" OR "assacu" OR "açacu," applied to the title, abstract, and keyword fields. Other terms or Boolean operators were deliberately omitted to avoid excessive filtering and to ensure the retrieval of all relevant studies available in the consulted databases.

The present review included articles with free full-text access, written in English, Portuguese, or Spanish, specifically addressing *Hura crepitans* in contexts related to human health. Considered studies comprised experimental research (in vitro, in vivo, or in silico), phytochemical and pharmacological investigations, as well as ethnopharmacological, ethnobotanical, and historical-documentary studies presenting evidence of the traditional or therapeutic use of assacu. Excluded were exclusively taxonomic works, literature reviews, studies focused on other species of the *Hura* genus, articles with only secondary mention of the plant without direct investigation, as well as studies with inadequate methodology or unclear results.

The screening process followed successive stages of title reading, abstract analysis, and full-text reading of articles that met the predefined criteria. The selected articles were critically and integratively analyzed, composing the body of the present review.

3. Results and Discussion

The overall research results were organized in the flowchart, illustrating the number of articles retrieved from the databases and their specifications. A total of 91 records were identified from three databases: PubMed (n = 33), Scopus (n = 47), and LILACS (n = 11). After removing 32 duplicate records, 59 articles remained for screening.

During screening, 10 records were excluded due to blocked access to the full text, leaving 49 publications to be assessed for eligibility. Of these, 32 were excluded for not meeting the inclusion criteria: 8 did not directly investigate *Hura crepitans*, 15 did not provide original experimental or observational data relevant to the objectives of this review (e.g., review articles, papers with insufficient methodological detail, or unrelated therapeutic contexts), and 9 contained only secondary or superficial mentions of the species without experimental analysis.

Based on the analysis, 17 studies were included in this narrative review (TABLE 1). Although the study selection process followed a structured flow for transparency, no formal methodological quality assessment or systematic synthesis was performed, which frames this work as a narrative review.

Among the 17 included studies, 59% were conducted in Brazil, with the remaining publications originating from other Latin American countries or Africa. In terms of experimental design, 59% consisted of in vitro investigations, 29% were in vivo studies, and 12% were ethnopharmacological surveys or studies using combined methodologies. Regarding plant parts studied, more than half (53%) focused on latex and seeds, reflecting their traditional medicinal importance. The remainder analyzed bark, roots, or leaves, while some studies explored nutritional and ethnobotanical aspects involving multiple plant parts.

Table 1 – Included and analyzed articles.

Author/Year/ Database	Title	Study Objective	Outcome
Owojuyigbe et al., 2022, PUBMED	*Hura crepitans* stem bark extract: a potential remedy to sub-acute liver damage	To evaluate the effect of stem bark on carbon tetrachloride (CCl_4)-induced subacute liver damage in rats.	*Hura crepitans* showed antioxidant, anti-inflammatory, and antifibrotic effects in rats with liver injury.
Vassallo et al., 2020, PUBMED	*Hura crepitans* l. Extract: phytochemical characterization, antioxidant activity, and nanoformulation	To assess the impact of green extraction methods on the phytochemical profile and biological activity of *Hura crepitans* extracts.	Aqueous extracts of assacu exhibited high antioxidant activity and cytoprotective effect influenced by extraction parameters. Liposomal incorporation enhanced this activity, indicating therapeutic potential when properly formulated.

Crossay et al., 2023, PUBMED	Daphnanes diterpenes from the latex of *hura crepitans* l. And their pkcζ-dependent anti-proliferative activity on colorectal cancer cells	To evaluate daphnane diterpenes from assacu latex in colorectal cancer cell lines.	Five new daphnane diterpenes and two known analogues, including huratoxin, were isolated, showing significant and selective inhibition of colorectal cancer cell growth. Cytostatic activity was linked to modulation of protein kinase C zeta (PKCζ), indicating therapeutic potential in colorectal cancer.
Lukman, et al., 2024, PUBMED	Evaluation of terpenes rich *hura crepitans* extract on glucose regulation and diabetic complications in stz-induced diabetic rats	To assess the antidiabetic potential of assacu methanolic extract using *in vitro, in vivo*, and *in silico* approaches.	The methanolic extract exhibited dose-dependent antidiabetic effects, improving biomarkers of oxidative stress, inflammation, and liver and kidney function in diabetic rats. Bioactive compounds showed strong affinity for relevant pharmacological targets, supporting therapeutic potential for diabetes and its complications.
Trinel, et al., 2018, PUBMED	Profiling of *hura crepitans* l. Latex by ultra-high-performance liquid chromatography/atmospheric pressure chemical ionisation linear ion trap orbitrap mass spectrometry	To identify daphnane diterpenes and cerebrosides in assacu latex.	The latex contained 34 chemical compounds, including 24 daphnane esters—17 of which were new—and 10 cerebrosides, the latter described for the first time in the *Hura* genus. The abundant presence of daphnane diterpenes highlights the pharmacological potential and chemical uniqueness of the plant latex.
Trinel, . et al., 2020, PUBMED	Daphnanes diterpenes from the latex of *hura crepitans* l. And activity against human colorectal cancer cells caco-2	To isolate and characterize diterpenes from assacu latex and evaluate their cytotoxicity on Caco-2 cells and mechanisms of action.	Five diterpenes, including huratoxin, were isolated, showing selective cytotoxic effects in Caco-2 cells. Huratoxin induced morphological changes suggestive of cell differentiation. The compounds exhibited distinct mechanisms of action, indicating anticancer potential.
fowomola, & akindahunsi. 2007, PUBMED	Nutritional quality of sandbox tree (*hura crepitans* linn.)	To evaluate the nutritional profile of assacu seeds with emphasis on bioactive compounds and minerals.	Assacu seeds have high protein, oil, and essential amino acid content. Despite antinutrients, they show potential for food and industrial use.
uchiyama, chiyoko ET AL. 2012, PUBMED	Effects of *hura crepitans* and its active ingredient, daphne factor f3, on dihydrotestosterone-induced neurotrophin-4 activation and hair retardation	To investigate the relationship between NT-4 and androgens in androgenetic alopecia and evaluate the effect of assacu on hair growth.	NT-4 transcription is increased by androgens, contributing to androgenetic alopecia. Extract of assacu and its active component daphne factor F3 inhibit this activation and improve delayed hair growth in mice, suggesting therapeutic potential for androgenetic alopecia.
Crossay et al., 2025, PUBMED	Integrated untargeted metabolomics and bioactivity studies as new insights into the chemotaxonomy of hura crepitans specimens from peru and sub-saharan africa	To compare the chemical composition of assacu latex from different regions and evaluate its cytotoxic activity.	Geographic variations in assacu latex influenced cytotoxicity. Daphnanes acted on Caco-2 cells, while elasterol and cerebrosides acted on HeLa cells. Data indicate promising new bioactive compounds.
Barbieri et al., 1983, PUBMED	Purification and properties of two lectins from the latex of the euphorbiaceous plantS *Hura crepitans* L. (sand-box tree) and euphorbia characias l. (mediterranean spurge)	To purify and characterize lectins present in the plant, including analysis of their biochemical and biological properties.	Assacu lectin has three isoforms with hemagglutinating activity inhibited by D-galactose. It is mitogenic for human T lymphocytes and inhibits protein synthesis, differing from *E. characias* lectin.
Falasca et al., 1980, PUBMED	Mitogenic and haemagglutinating properties of a lectinpurified from hura crepitans seeds	To isolate and characterize assacu seed lectin, analyzing its hemagglutination and mitogenic activity.	Assacu lectin is a glycoprotein that agglutinates erythrocytes from various species and exhibits strong mitogenic activity for human T lymphocytes even at low concentrations

Henrique, 2020, PUBMED	From passos the indian to doctor chernoviz: experiments to cure leprosy in nineteenth-century pará	To analyze the use of the plant for leprosy treatment in 1847, investigating relations between Indigenous and official Brazilian medicine of the time.	Indigenous knowledge of medicinal plants, such as assacu for leprosy, was recognized and incorporated by official physicians, reflecting dialogue between traditional and official medical practices in 19th-century Brazil.
Stirpe et al., 1983, PUBMED	Ribosome-inactivating proteins from the seeds from the latex of hura crepitans l. (sandbox tree)	To isolate and characterize ribosome-inactivating proteins from assacu latex and evaluate their biological activity.	Proteins isolated from assacu (~30 kDa) inhibit protein synthesis and showed relevant activity against HeLa cells. They vary in sugar content.
Sarquis, et al., 2019, PUBMED	The use of medicinal plants in the riverside community of the mazagão river in the brazilian amazon, amapá, brazil: ethnobotanical and ethnopharmacological studies	To conduct an ethnopharmacological survey of medicinal plants used by a riverside community of the Mazagão River (AP).	130 medicinal species were identified, mostly from the floodplain forest, including assacu. Most are used against infections, inflammation, and gastrointestinal disorders. Traditional knowledge is widely distributed, indicating potential for pharmacological studies.
AJANI et al., 2019, SCOPUS	Phytochemical screening and nutraceutical potential of sandbox tree (*hura crepitans* l.) Seed oil	To evaluate the nutraceutical potential of assacu seed oil through compositional characterization.	The seed oil had high yield and contains bioactive compounds and essential minerals. Results indicate nutraceutical potential and applications in functional foods and industry.
Igiri et al., 2018, SCOPUS	Phytochemical and antimicrobial studies of root, stem bark and leaf extracts of hura crepitans l. (sand box tree)	To quantify phytochemicals in assacu extracts and evaluate their antimicrobial activity.	Leaf and bark extracts of assacu presented rich phytochemical composition and significant antimicrobial activity. Variation in effects suggests potential for phytotherapeutic and pesticide use.
Aymé et al., 2011, SCOPUS	Antimalarial activity and cytotoxicity of hydroalcoholic extracts from six plant species used in cuban traditional medicine	To evaluate the antimalarial activity and selectivity of assacu extracts *in vitro.*	Hydroalcoholic extract of assacu showed potent antiplasmodial activity and high selectivity. Action was attributed to phenolic compounds, alkaloids, and flavonoids, indicating potential as a source of new antimalarials.

Source: Research data (2025).

The analysis of the available studies reveals a broad range of applications for *Hura crepitans*, underscoring its pharmacological versatility. Nonetheless, significant limitations persist regarding the scope and methodological depth of investigations. Research has predominantly focused on seeds and latex—plant parts rich in bioactive compounds but also associated with considerable toxicity. In contrast, leaves, bark, and roots, despite being widely used in traditional medicine, remain underexplored, representing an important knowledge gap and potential sources of novel bioactives with lower toxicity profiles.

Traditional and Ethnobotanical Uses

Traditional knowledge indicates a long-standing medicinal use of *H. crepitans*, particularly among Indigenous and riverside populations. Historical accounts (Henrique, 2020) and recent ethnopharmacological surveys (Sarquis et al., 2019) highlight practices such as latex-based decoctions for cancer treatment and the use of bark and seeds in the management of infections and gynecological disorders. However, these practices lack systematic scientific validation, especially concerning preparation methods, dosage, and toxicity. Bridging this gap requires research that respects cultural knowledge while providing evidence-based parameters for safe use.

Phytochemical Composition and Bioactive Properties

Phytochemical analyses describe *H. crepitans* as chemically complex, containing flavonoids, phenolic compounds, diterpenes, alkaloids, and quinones. Studies report antioxidant and cytoprotective effects of aqueous extracts (Vassallo et al., 2020), antimicrobial properties of bark and leaf preparations (Igiri et al., 2018), and antimalarial activity in seed-derived fractions (Aymé et al., 2011). Despite these findings, heterogeneity in extraction protocols and analytical techniques complicates cross-study comparisons. Standardization of methods is crucial to validate bioactivity and enable reproducibility across different laboratories.

Pharmacological Activities and Therapeutic Applications

Reported pharmacological activities include antioxidant, anti-inflammatory, antifibrotic, antidiabetic, and antitumor effects. Particularly promising are experimental oncology studies identifying cytotoxic diterpenes that act via PKCζ-dependent pathways (Trinel et al., 2020; Crossay et al., 2023), suggesting potential molecular targets for drug discovery. However, these results remain restricted to preclinical models, reinforcing the need for translational studies and clinical validation. Moreover, recent evidence that phytochemical composition varies by geographic origin (Crossay et al., 2025) highlights the importance of integrating ecological and genetic considerations when developing standardized therapeutic formulations.

Toxicological Potential

The toxicity of *H. crepitans*, especially from latex preparations, poses a central challenge to its therapeutic development. Compounds such as huratoxin and hexahydrohuratoxin lectins demonstrate strong hemagglutinating and protein synthesis inhibition properties, explaining both their pharmacological potential and toxic risks. Documented poisoning cases underscore the urgency of dose–response studies and detailed toxicological assessments. Future research should also explore whether less toxic plant parts (e.g., bark or leaves) or modified extraction methods can preserve bioactivity while minimizing adverse effects.

Gaps and Future Perspectives

Despite encouraging pharmacological findings, substantial gaps remain. Clinical studies are virtually absent, hindering the establishment of safe and effective therapeutic protocols. Furthermore, research has disproportionately emphasized latex and seeds, neglecting ethnobotanically relevant plant parts that could offer safer bioactive profiles. Integrating ethnopharmacological data with modern approaches such as metabolomics, molecular docking, and systems pharmacology may accelerate the discovery of active compounds and their mechanisms of action. Collaborative research with knowledge holders is also essential to align scientific exploration with cultural practices. Moving forward, priorities should include comprehensive toxicological profiling, clinical validation, and sustainable resource management to enable the safe incorporation of *H. crepitans* into evidence-based therapeutic frameworks.

4. Conclusion

Assacu stands out as a species of significant ethnobotanical and pharmacological relevance. Its diverse phytochemical composition, rich in tannins, flavonoids, diterpenes, and lectins, has garnered growing scientific interest due to multiple described biological activities, including antioxidant, anti-inflammatory, antitumor, and antimicrobial effects. Although the plant's latex is known to be toxic, experimental evidence points to potential therapeutic applications of other plant parts, such

as bark, leaves, seeds, and roots. Studies demonstrate promising effects in models of neglected tropical diseases, such as leishmaniasis, as well as potential for metabolic diseases and colorectal cancer.

Despite its widespread traditional use among Amazonian communities, significant gaps persist in the literature, particularly concerning human toxicity, mechanisms of action, and clinical studies. Therefore, there is a reinforced need for multidisciplinary approaches that integrate traditional knowledge and modern science, enabling the safe and sustainable utilization of the resources offered by assacu.

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