



Review

Ethnopharmacological uses, phytochemistry, biological activities, and therapeutic applications of *Clinacanthus nutans* (Burm. f.) Lindau: A comprehensive review



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ABSTRACT

Ethnopharmacological relevance: *Clinacanthus nutans* (Burm. f.) Lindau, a widely used medicinal plant, is extensively grown in tropical Asia and Southeast Asian countries. *C. nutans*, with its broad spectrum of pharmacological activities, has been traditionally used to treat cancer, inflammatory disorders, diabetes, insect bites, and skin problems, consumed as a vegetable, mixed with fresh juices, in concoctions, and as a whole plant. The present review analyzes the advances in the ethnopharmacology, phytochemistry, pharmacology, and toxicology of *C. nutans*. In addition, the needs and perspectives for future investigation of this plant are addressed.

Aim of the review: This review aims to provide a comprehensive report on the ethnomedicinal use, phytochemistry, pharmacological activities, molecular mechanisms, and nutritional values of *C. nutans*. The present review will open new avenues for further in-depth pharmacological studies of *C. nutans* for it to be developed as a potential nutraceutical and to improve the available products in the market.

Material and methods: All the available information on *C. nutans* was collected using the key words “*Clinacanthus nutans*” and/or “ethnomedicine” and/or “phytochemicals” and/or “anticancer” and/or “anti-inflammatory” and/or “antiviral” through an electronic search of the following databases: PubMed, Web of Science, EMBASE, Cochrane Library, Clinical Trials.org, SciFinder Scholar, Scopus, and Google Scholar. In addition, unpublished materials, Ph.D. and M.Sc. dissertations, conference papers, and ethnobotanical textbooks were used. The Plant List (www.theplantlist.org) and International Plant Name Index databases were used to validate the scientific name of the plant.

Results: The literature supported the ethnomedicinal uses of *C. nutans* as recorded in Thailand, Indonesia, and Malaysia for various purposes. Bioactivities experimentally proven for *C. nutans* include cytotoxic, anticancer, antiviral, anti-inflammatory, immunomodulatory, antidiabetic, antioxidant, antihyperlipidemic, antimicrobial, and chemotherapeutic (in aquaculture) activities. Most of these activities have so far only been investigated in chemical, cell-based, and animal assays. Various groups of phytochemicals including five sulfur-containing glycosides, eight chlorophyll derivatives, nine cerebrosides, and a monoacylmonogalactosyl glycerol are present in *C. nutans*. The presence of two glycerolipids, four sulfur-containing compounds, six known flavones, a flavanol, four flavonols, two phytosterols, one polypeptide, and various phenolics and fatty acids largely influences its diverse bioactivities. Numerous reports justify the ethnomedicinal use of *C. nutans* as an antiviral agent in treating herpes simplex virus and varicella-zoster virus infections and as part of a traditional anticancer anti-inflammatory concoction agent for various inflammatory diseases. *C. nutans* tea was reported to have a good percentage of carbohydrate, crude protein, minerals, essential amino acids, nonessential amino acids, and essential fatty acids. Acute, subacute, and subchronic toxicity studies demonstrated that oral administration of

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ethanol and methanol extracts of *C. nutans* to male Swiss albino mice and male Sprague–Dawley (SD) rats, respectively, did not lead to any toxicity or adverse effects on the animal behavior and organs when used in amounts as high as 2 g/kg.

Conclusion: The collected literatures demonstrated that, as an important traditional medicine, *C. nutans* is a promising ethnomedicinal plant with various extracts and bioactive compounds exhibiting multifarious bioactivities. However, it is important for future studies to conduct further *in vitro* and *in vivo* bioactivity evaluations systematically, following the standard pharmacology guidelines. It is crucial to elucidate in-depth molecular mechanisms, structure-activity relationships, and potential synergistic and antagonistic effects of multi-component extracts and bioactive constituents derived from *C. nutans*. Further studies should also focus on comprehensive toxicity that includes long-term effects and adverse effects on target organs of *C. nutans* and bioactive compounds in correlation with the specific pharmacological effects.

1. Introduction

Since ancient times, natural products have been used in different parts of the world as traditional medicine depending on their high therapeutic efficacy in treating various diseases. To date, the use of natural products offers high biocompatibility with marginal side effects, and thus, they have contributed to the development of up to 50% of the approved drugs in the market (Newman and Cragg, 2016). In Africa and Asia, particularly Southeast Asia, primary health care needs are still greatly met through the consumption of traditional medicines, such as the use of herbal tea, among the majority of the population due to the lack of modern health facilities and high cost of medical expenses (de Boer and Cotingting, 2014; Mahomoodally, 2013). Among these traditional medicines, *Clinacanthus nutans* has been used as a folk medicine in Asia, particularly in Thailand and Malaysia, for various ailments (Alam et al., 2016; Pratoomsot et al., 2015). Various communities in Indonesia, Malaysia, and Thailand use the leaves of *C. nutans* for diverse medicinal purposes such as antiviral, anticancer, and anti-inflammatory activities and to treat fever and diabetes. Despite its long history of use as traditional medicine, the ethnopharmacological reports of *C. nutans* are only partly established, and therefore, extensive scientific investigations are required to justify its therapeutic potential. We have collected all the available and relevant information on *C. nutans* from the following databases using electronic

search engines: PubMed, Web of Science, EMBASE, Cochrane Library, Clinical Trials.org, SciFinder Scholar, Scopus, and Google Scholar. We used the following key words: “*Clinacanthus nutans*” and/or “ethnomedicine” and/or “phytochemicals” and/or “anticancer” and/or “anti-inflammatory” and/or “antiviral.” Scientific literature from unpublished materials, Ph.D. and M.Sc. dissertations, conference papers, and ethnobotanical textbooks were carefully selected and included. The scientific names of the plants were validated using The Plant List (www.theplantlist.org) and International Plant Name Index databases.

This review provides a comprehensive summary of *C. nutans*’ ethnopharmacology, phytochemistry, biological activities, nutritional value, and possible molecular mechanisms for bioactivities. Therefore, the current review may provide the scientific basis for future in-depth studies of *C. nutans*. Moreover, this present review may provide necessary information for improving the readily available therapeutic agents and health products of *C. nutans*.

1.1. Botanical description and taxonomy

C. nutans is known as “Sabah snake grass” or “belalai gajah” in Malaysia; “dandang gendis” in Indonesia; “phaya yo” or “phaya plong-tong” in Thailand; “Bim Bip,” “Xuong Khi,” or “Manh Cong” in some regions of Vietnam; and “e zui hua” or “you dun cao” among the Chinese community (Committee, 1994; Panyakom, 2006; Roosita et al., 2008;

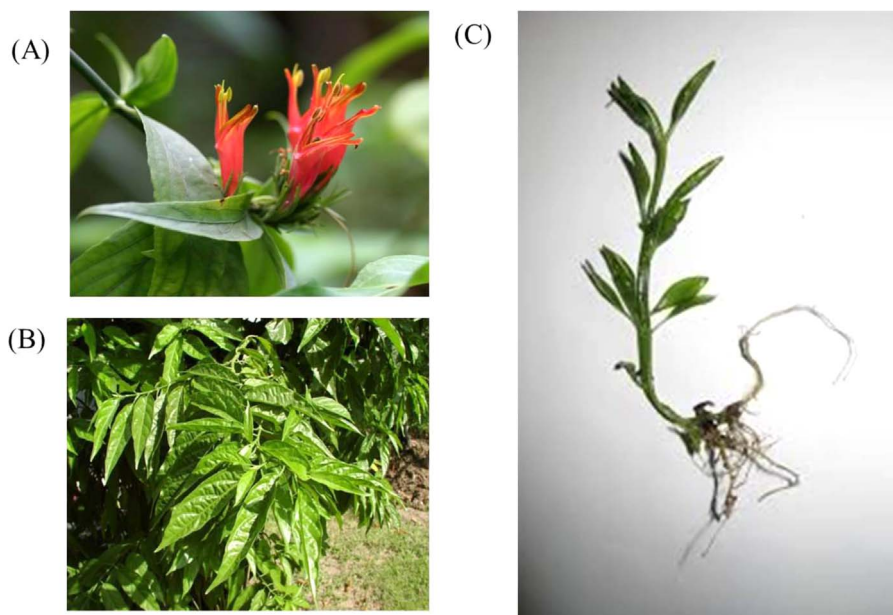


Fig. 1. (A) The flowers of *C. nutans* (B) The leaves of *C. nutans* (C) The whole plant structure of *C. nutans*, including the roots.

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