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Review

From arrow poison to herbal medicine – The ethnobotanical, phytochemical and pharmacological significance of *Cissampelos* (Menispermaceae)



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ABSTRACT

Ethnopharmacological relevance: *Cissampelos* species have a rich history of traditional use, being used for both therapeutic and toxic properties. It is traditionally applied therapeutically in a diverse range of conditions and diseases including asthma, cough, fever, arthritis, obesity, dysentery, snakebite, jaundice and heart, blood pressure and skin-related problems. Conversely, it was traditionally included in preparations of curare applied as arrow poison during hunting to cause death of animals by asphyxiation. This review unites the ethnobotanical knowledge on *Cissampelos* with the phytochemistry and pharmacological activity which has been explored thus far. In addition, it identifies knowledge gaps and suggests further research opportunities.

Methods: The available electronic literature on the genus *Cissampelos* was collected using database searches including Scopus, Google Scholar, Pubmed, Web of Science, etc. The searches were limited to peer-reviewed English journals with the exception of books and a few articles in foreign languages which were included.

Results: The literature revealed that pharmacological activity including analgesic and antipyretic, anti-inflammatory, anti-allergic, bronchodilator, immunomodulatory, memory-enhancing, antidepressant, neuroprotective, antimicrobial, antimalarial, antiparasitic, anti-ulcer, anticancer, anti-oxidant, cardiovascular, muscle-relaxant, hepatoprotective, antidiabetic, antidiarrhoeal, antifertility, and antivenom activity have been confirmed *in vitro* and/or *in vivo* for various *Cissampelos* species. *Cissampelos pareira* L. and *Cissampelos sympodialis* Eichl. are the most explored species of this genus and the smallest number of studies have been conducted on *Cissampelos laxiflora* Moldenke and *Cissampelos tenuipes* Engl. Many alkaloids isolated from *Cissampelos* such as warifteine, methylwarifteine, berberine, hayatin and hayatinid showed promising anti-allergic, immunosuppressive, antidepressant, anticancer, vasodilatory and muscle-relaxant activities.

Conclusion: The plants of this genus are used in traditional medicine for the treatment of various ailments. These plants are a rich source of bioactive bisbenzylisoquinoline and aporphine alkaloids together with other minor constituents. Although these plants are reputable and revered in various traditional medicine systems, many have not yet been screened chemically or pharmacologically and so there is a vast amount of research still to be conducted to validate their traditional use.

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Abbreviations: Ig, immunoglobulin; OVA, ovalbumin; PG, prostaglandin; PHF, polyherbal formulation; TGI, total growth inhibition; MIC, minimum inhibitory concentration; IZD, inhibition zone diameter; MLE, methanolic leaf extract; HLE, hydroalcoholic leaf extract; HRE, hydroalcoholic root extract; ELE, ethanolic leaf extract; ERE, ethanolic root extract; MRE, methanolic root extract; p.o., per oral; i.p., intra-peritoneal; i.v., intravenous

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1. Introduction

The genus *Cissampelos* (Menispermaceae) has diverse traditional uses, being applied for its therapeutic as well as toxic effects. In the rainforests of South America, *Cissampelos pareira* (called Abuta), commonly known as the midwives' herb, has a rich history of use to treat all types of women's ailments including menstrual cramps, menorrhagia, uterine haemorrhage etc. This is due to its profound relaxant effect on smooth muscle (Singh et al., 2010; Arora et al., 2012). At the same time however, it was traditionally included in the preparation of curares, the well-known South American arrow poison used in hunting to cause death by asphyxiation. Again, this effect is due to its muscle-relaxant and neuromuscular blocking effect (Maurya et al., 2013). The alkaloid isolated from *Cissampelos pareira*, hayatin methiodide, showed an equal amount of curariform activity as compared to the well known *d*-tubocurarine (Bhattacharji et al., 1952; Taylor, 1996). The members of this genus mostly contain alkaloids including bisbenzylisoquinolines, berberines, morphines, and aporphines, etc. along with a moderate quantity of other constituents (Thornber, 1970; Rocha et al., 1984; Blasko and Cordell, 1988).

Many alkaloids such as tropoloisoquinoline alkaloids isolated from the genus exhibited potent biological activities. Pareirubrines A and B (Morita et al., 1993a, 1993b) from *Cissampelos pareira* showed antileukemic activity, hayatin methiodide (Pradhan and De, 1953) and hayatinin methochloride (Basu, 1970) from *Cissampelos pareira*, and aporphine alkaloids (+)-cissaglaberrimine and (+)-trilobinine from *Cissampelos glaberrima* showed muscle-relaxant properties. Most of the plants including *Cissampelos capensis*, *Cissampelos pareira* and *Cissampelos sympodialis* have been recognised for their remarkable medicinal properties and these are being used in various indigenous medicine systems for antibacterial, anti-oxidant, anti-spasmodic, diuretic, hypotensive, muscle-relaxant, antiseptic, aphrodisiac, analgesic, anti-haemorrhagic and cardiotoxic properties (Kaur et al., 2012). Based on traditional knowledge, some species of the genus were also studied clinically for malaria (Wilcox et al., 2005),

dengue (Bhatnagar et al., 2011), diabetes (Jannu et al., 2011), the treatment of ulcers (Nwafor and Akah, 2003) and many other diseases and conditions (Roy et al., 1952; Hemraj et al., 2012).

The extremely diverse range of recorded traditional uses for *Cissampelos* species is in part due to its very wide geographical distribution. This review comprises of up-to-date information on the ethnobotany, phytochemistry and pharmacology of the genus *Cissampelos*.

2. Geographical distribution

The genus *Cissampelos* has a wide global distribution spanning five continents as well as several islands (Fig. 1). *Cissampelos pareira* is the only species that has a pantropical distribution – a geographical distribution which includes the tropical areas of the three major continents; Africa, Asia and the Americas. It occurs in Asia (Indo-China, Southern China, Malaysia, Thailand, India and Pakistan), Africa (Sierra Leone east to Congo, Rwanda, Tanzania, south to northern Angola, Zambia), America (Brazil, Argentina, Peru, Mexico, Colombia and Florida), Australia, the West Indies, Comores, Mauritius, Seychelles and Madagascar. *Cissampelos ovalifolia* is found only in North and South America and *Cissampelos sympodialis* only in South America (Brazil). *Cissampelos mucronata*, *Cissampelos owariensis* and *Cissampelos capensis* is restricted to the African continent: *Cissampelos mucronata* is distributed throughout tropical Africa from Senegal east to Ethiopia and south to southern Africa; *Cissampelos capensis* has a small natural distribution in Namibia and the Cape Provinces (Eastern Cape, Western Cape and Northern Cape) of South Africa; *Cissampelos owariensis* is found from Sierra Leone east to Uganda and south to Angola, Zambia and Mozambique. Based on various resources including flora of America, Africa, India, Pakistan, China and Australia, the distribution of selected ethnomedicinally important species,

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