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RESEARCH ARTICLE

Bioactive non-sterol triterpenoid from *Streblus asper*: microwave-assisted extraction, HPTLC profiling, computational studies and neuro-pharmacological evaluation in BALB/c mice

Vandana Verma, Avinash C. Tripathi and Shailendra K. Saraf

Division of Pharmaceutical Chemistry, Faculty of Pharmacy, Babu Banarasi Das Northern India Institute of Technology, Lucknow, UP, India

ABSTRACT

Context: In folk medicine, the stem bark of *Streblus asper* Lour. (Moraceae) has been reported to possess anticonvulsant activity. However, no systematic/scientific validation is available.

Objective This study explores the constituents in the stem bark, their biosassy-guided isolation and their efficacy in neuro-pharmacological disorders, for validating the traditional claims.

Materials and methods: Microwave-assisted extraction (MAE) technique was employed to obtain the crude extract. The *n*-hexane, dichloromethane and aqueous fractions were prepared and phytoconstituents were ascertained by phytochemical tests. The isolated compound, betulin, was characterized by different physicochemical and spectral methods, including HPTLC. Finally, neuro-pharmacological evaluations were conducted at 100, 200, 400 mg/kg b.w., p.o. (25, 50, 100 mg/kg b.w. for betulin) doses in BALB/c mice.

Results: The *n*-hexane fraction (400 mg/kg), and isolated compound betulin (100 mg/kg), showed maximum anticonvulsant activity in maximal electroshock (87.84% and 85.14% seizure inhibition), and isoniazid induced convulsion models (88.85% and 83.18% seizure inhibition), respectively. A dose-dependent attenuation of epileptic seizures was observed, probably through GABArgic mechanism of anticonvulsant action. Moreover, the antidepressant study was also conducted using behavioural models and the results expound that *n*-hexane and dichloromethane fractions (400 mg/kg) significantly reduced the duration of immobility, as compared to the control.

Discussion and conclusion: This study reports some novel aspects like applying an environmentally benign/green approach of MAE, neuro-pharmacological screening and use of docking studies, for the first time, on the plant *S. asper*. The findings present a rational explanation for its use in traditional medicine, for the management of neuro-pharmacological disorders.

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Anticonvulsant; antidepressant; betulin; high-performance thin-layer chromatography; microwave-facilitated extraction; molecular docking; neurotoxicity

Introduction

The current anticonvulsant therapies are generally directed at the symptomatic treatment, by suppressing excitability within the brain. Consequently, they elicit unfavourable effects such as cognitive impairment, dependence and abuse. The need for more effective, and less toxic, anticonvulsants has generated renewed interest in natural products for the treatment of convulsions (Kim & Oh 2012). *Streblus asper* Lour. (Moraceae) is a well-known ethno-medicinal plant, distributed throughout the dry areas of India. Most parts of the plant have been used traditionally in the treatment of different ailments such as filariasis, leprosy, piles, diarrhea, dysentery and cancer (Warrier 1996; Wealth of India... 1998; Nadkarni 2002). Scientific investigations have revealed various activities of *S. asper* such as anti-hepatitis B, analgesic, anticancer, anti-inflammatory, antioxidant and antimicrobial (Wongkham et al. 2001; Phutdhawong et al. 2004; Sripanidkulchai et al. 2009; Basuri 2011; Chen et al. 2012; Kumar et al. 2012; Ibrahim et al. 2013; Rao et al. 2014). The literature also mentions that the stem bark of *S. asper* is a rich source of phyto-constituents, from which a number of compounds such as α-amyrin acetate, lupeol acetate, β-sitosterol, α-amyrin, lupeol and diol, strebloside and mansonin have been isolated (Prakesh et al. 1992; Warrier 1996; Khare 2004; Rastogi et al. 2006). A pregnane glycoside, sioraside (Mukherjee & Roy 1983), has also been isolated. *n*-Triacontane, tetraiacontan-3-one, β-sitosterol, stigmasterol, betulin and oleanolic acid have been identified in the aerial parts (Gaitonde et al. 1964; Saxena & Chaturvedi 1985). Chemically, pentacyclic triterpenes, viz., betulin, betulinic acid, lupeol, etc. share similar structural moieties, comprising of four 6-membered rings and one 5-membered ring, and are widely distributed throughout the plant kingdom. A number of non-sterol triterpenes have been reported from the plant *S. asper* (Figure 1), with betulin being most abundant followed by betulinic acid and lupeol, present mainly in the outer bark of the plant.

Muceniece et al. (2008) hypothesized that lipophilic molecules (betulin and lupeol) may also penetrate the blood–brain barrier to show central nervous system (CNS) activity, as has already been demonstrated for betulinic acid. They studied the influence of triterpenes on $GABA_A$-receptor antagonist bicuculline-induced seizures in mice and expressed distinct $GABA_A$-receptor related properties of lupane type triterpenes *in vivo* and *in vitro*. The findings of the study showed that betulin competed with GABA for binding to the corresponding sites on the $GABA_A$ receptor, through its central and peripheral administration, whereas betulinic acid and lupeol did not show any significant binding (Muceniece et al. 2008).

CONTACT Shailendra K. Saraf dirpharmniec@gmail.com Division of Pharmaceutical Chemistry, Faculty of Pharmacy, Babu Banarasi Das Northern India Institute of Technology, BBD City, Faizabad Road, Chinhut, Lucknow 226016, UP, India

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