## Sceletium Tortuosum: A review on its Phytochemistry, Pharmacokinetics, Biological and Clinical Activities

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Abstract: Ethnopharmacological relevance: Sceletium tortuosum (L.) N.E.Br, the most sought after and widely researched species in the genus Sceletium is a succulent forb endemic to South Africa. Traditionally, this medicinal plant is mainly masticated or smoked and used for the relief of toothache, abdominal pain, and as a mood-elevator, analgesic, hypnotic, anxiolytic, thirst and hunger suppressant, and for its intoxicating/euphoric effects. Sceletium tortuosum is currently of widespread scientific interest due to its clinical potential in treating anxiety and depression, relieving stress in healthy individuals, and enhancing cognitive functions. These pharmacological actions are attributed to its phytochemical constituents referred to as mesembrine-type alkaloids. Aim of the review: The aim of this review was to comprehensively summarize and critically evaluate recent research advances on the phytochemistry, pharmacokinetics, biological and clinical activities of the medicinal plant S. tortuosum. Additionally, current ongoing research and future perspectives are also discussed. Methods: All relevant scientific articles, books, MSc and Ph.D. dissertations on botany, behavioral pharmacology, traditional uses, and phytochemistry of S. tortuosum were retrieved from different databases (including Science Direct, PubMed, Google Scholar, Scopus and Web of Science). For pharmacokinetics and pharmacological effects of S. tortuosum, the focus fell on relevant publications published between 2009 and 2021. Results: Twenty-five alkaloids belonging to four structural classes viz: mesembrine, Sceletium A4, joubertiamine, and tortuosamine, have been identified from S. tortuosum, of which the mesembrine class is predominant. The crude extracts and commercially available standardized extracts of S. tortuosum have displayed a wide spectrum of biological activities (e.g. antimalarial, anti-oxidant, immunomodulatory, anti-HIV, neuroprotection, enhancement of cognitive function) in in vitro or in vivo studies. This plant has not yet been studied in a clinical population, but has potential for enhancing cognitive function, and managing anxiety and depression. Conclusion: As an important South African medicinal plant, S. tortuosum has garnered many research advances on its phytochemistry and biological activities over the last decade. These scientific studies have shown that S. tortuosum has various bioactivities. The findings have further established the link between the phytochemistry and pharmacological application, and support the traditional use of S. tortuosum in the indigenous medicine of South Africa.

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