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RE: Review of the Alkaloid Chemistry and Pharmacology of *Sceletium*

Gericke N, Viljoen AM. *Sceletium*–a review update. *J Ethnopharmacol.* 2008;119:653-663.

Plants of the genus *Sceletium* are among the most commercially promising plants indigenous to South Africa, with potential for use in dietary supplements, natural medicines, and veterinary and pharmacologic products. Since the first ethnopharmacological review of this genus by Smith et al. in 1966, several advances in *Sceletium* research have been made, and an increasing number of products containing *Sceletium* are becoming available. Commercial plantations have been established to produce a more consistent-quality crop for use in manufacturing such products. The purpose of this review was to provide a historical overview of the clinical applications of *Sceletium* and recent developments concerning the chemistry and pharmacology of this genus.

The genus name, *Sceletium*, is derived from the word *sceletus*, which means skeleton. This designation refers to the prominent lignified veins visible on the leaves of this plant. *Sceletium* species are distributed throughout the southwestern portion of South Africa in arid environments and are distinguishable on the basis of different vegetative, flower, fruit, and seed characteristics. The fruit capsule contains several kidney-shaped seeds that range in color from brown to black, and the flowers of this genus can be white, yellow, or pale pink.

Vernacular names for this genus include *kanna* (Khoi) and *kougoed* (Afrikaans). The earliest unambiguous illustration of a *Sceletium* plant was found in the journal of Cape of Good Hope Governor Simon van der Stel's from his expedition to Namaqualund in 1685. In 1738, Kolben noted that *kanna* was the "greatest Chearer [sic] of the Spirits, and the noblest Restorative in the World." Lewin noted in 1924 that Kolben, under the name *kanna* or *channa*, had been referring to the plant root used by the Hottentots as a means of enjoyment, which they "chewed, kept in their mouths for some time, thus becoming excited and intoxicated." The name *channa* refers to certain species of *Sceletium*, including *S. expansum* and *S. tortuosum*, both of which were illustrated in the 18th century. The Afrikaans vernacular *kougoed* was first recorded for *S. tortuosum* in approximately 1830. According to Meiring (1898), *S. tortuosum* was widely used for its soporific effect on young children; one

or two drops of fresh juice from the plant would be given to children, "who would enjoy a deep quiet rest for a few hours." It has also been reported that the leaves of *S. tortuosum* were chewed to relieve toothaches and abdominal pain. More recently (20^{th} century), extracts from the plant have been used to treat colic in infants.

Sceletium contains several alkaloids, which were categorized by Jeffs et al. (1982) into 4 categories: 1) 3a-aryl-*cis*-octahydroindoles (e.g., mesembrine), 2) C-secomesembrine alkaloids (e.g., joubertiamine), 3) alkaloids containing a 2,3-disubstituted pyridine moiety and two nitrogen atoms (e.g., *Sceletium* alkaloid A_4), and 4) a ring C-seco *Sceletium* alkaloid A4 group (e.g., tortuosamine). In 1966, Gerbaulet documented the existence of eight species of the genus *Sceletium. S. strictum, S. subvelutinum* (= *S. varians*), *S. tortuosum, S. joubertii*, and *S. namaquense* are the most well-studied. *S. joubertii* and *S. namaquense* are now considered to be synonymous with *S. tortuosum*. Most of the research on *Sceletium* alkaloids has involved isolation and structural elucidation. Little is known about the distribution and chemotaxonomic patterns. Furthermore, comparative analytical results between species are scarce. A concise summary of *Sceletium* alkaloids was recently compiled by Gaffney (2006).

Mesembrine and related compounds have potential use in pharmaceuticals for the management of psychiatric and psychological conditions, such as anxiety, depression, drug dependence, bulimia, and obsessive-compulsive disorder. This alkaloid has been confirmed to be a serotonin-uptake inhibitor. The inhibition of serotonin uptake is one of the possible mechanisms whereby intake of adequate doses of *Sceletium* can affect mood and the sleep state. Mesembrenone has also been shown to have cytotoxic activity against a murine non-tumoral fibroblast cell line and a human tumoral cell line.

Of the known *Sceletium* species, *S. tortuosum* has been researched the most and has been used most frequently commercially. Products containing *S. tortuosum* are increasingly becoming more available in the marketplace as natural supplements to combat stress, anxiety, and depression. The usual recommended dose of these supplements ranges from 50 to 200 mg, and no severe adverse effects have been reported at these doses. The authors note that the "pharmacologic study of *Sceletium* is in its infancy" and that "a great deal of work remains to be done." The focus of research for more than 100 years has been on the alkaloid constituents of this genus. However, the non-alkaloid constituents may provide a new avenue of research in the future. The authors suggest that placebo-controlled clinical trials be conducted to establish safety and efficacy parameters so that the health potential of this plant can be maximized.

—Brenda Milot, ELS

The American Botanical Council has chosen not to include the original article.