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Review

A review of the medicinal uses, phytochemistry and pharmacology of the genus *Sapium*

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ABSTRACT

Q 2 Q5 *Ethnopharmacological relevance:* Several species from the genus *Sapium* possess a broad range of medicinal properties and they have been used as traditional medicines by indigenous groups in several regions such as Malaysia, Africa, Southern China and Bolivia. Most of the species reported to possess therapeutic effects which are used for the treatment of skin-related diseases such as eczema and dermatitis, but they may also be used for overstrain, lumbago, constipation and hernia. Species of this genus are also used to treat wounds and snake bites. In addition, the saps/latex of *Sapium glandulosum*, *Sapium indicum* and *Sapium sebiferum* have/has toxic effects and are used as bird and fish poisons. This review discusses the current knowledge of the medicinal uses, phytochemistry, biological activities and toxicities of species from the genus *Sapium* to reveal their therapeutic potentials and gaps offering opportunities for future research.

Materials and methods: This review is based on a literature study of scientific journals and books from libraries and electronic sources, such as ScienceDirect, PubMed and ACS.

Results: As many as 65 compounds are included in this review. They belong to different classes of compounds including flavonoids, terpenoids and several other types of compounds, such as alkaloids, phenolic acids and amides. The pharmacological studies revealed that various types of preparations, extracts and single compounds of species from this genus exhibited a broad spectrum of biological activities including antioxidant, antimicrobial, anti-inflammatory and cytotoxic activities. However, *Sapium glandulosum*, *Sapium indicum* and *Sapium sebiferum* were reported to possess toxic effects and *Sapium sebiferum* was found to contain phorbol esters acting as a tumor-promoting agent.

Conclusion: The genus *Sapium* consists of 23 accepted (high confidence) species. However, only very few of species have been phytochemically and pharmacologically studied. There is great potential to discover new chemical constituents from this genus because only a few species have been phytochemically investigated thus far. Only 27 compounds of 65 identified compounds have been studied for their biological activities. Several extracts and single compounds from this genus were reported to exhibit interesting biological activities such as antimicrobial, antioxidant and cytotoxic effects. Furthermore, the toxicity studies of some phorbol esters suggested that the compounds acted as potential tumor-promoting agents by stimulating protein kinase C. This is an interesting fact in which a plant with medicinal properties also possesses toxic effects as well. Therefore, more clinical studies on the toxicity of the extracts of the plants and the compounds isolated from this genus are also crucial to ensure their safety and to assess their eligibility for use as sources for modern medicines.

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1. Introduction

Sapium is a genus in the family Euphorbiaceae. Members of this genus are distributed in India, Vietnam, China, throughout Malaysia, parts of New Guinea and Africa (Esser and Welzen, 2005; Mwine and Damme, 2011). In addition, some species of this genus are also distributed in Mexico, Central America, Caribbean, tropical South America, southern Brazil and temperate South America (Richter and Dallwitz, 2000-onwards). This genus consists of 23 accepted (high confidence) species with 254 names of synonym species according to http://www.theplantlist.org. This review describes the medicinal uses and the phytochemical and pharmacological properties of species from the genus *Sapium*. The phytochemical studies resulted in the isolation of 65 compounds consisting of several classes of compounds dominated by flavonoids and terpenoids. The pharmacology of this genus has not been widely investigated. Although many species of this genus have been discovered, only a handful of species have been studied for their biological activities.

This is an important review describing the current progress in research regarding the pharmacology and phytochemistry of the genus *Sapium* including the conducted studies and areas requiring more research. If we consider the important medicinal uses of this genus in the treatment of many types of ailments, it is clear that a broader range of biological activity studies are required to explore their pharmacological properties. These gaps create an important research opportunity to study more about the phytochemistry and pharmacology of genus *Sapium* considering the interesting medicinal properties possessed by the species and the chemical constituents of this genus. As a vast number of species in this genus have not yet been explored, significant opportunities are available to find novel and bioactive compounds as well as promising medicinal and pharmacological properties from various extracts of the species. This research can also lead to possibilities of finding new sources of drugs for future applications, such as drugs to treat cancer, hernia and acute skin diseases.

2. Medicinal uses

Some species from this genus have been used traditionally in several countries as therapeutic remedies (Table 1). In southern China, skin-related diseases such as eczema, dermatitis, scabies and herpes zoster can be treated using the leaf part of *Sapium chihsianum, Sapium discolor, Sapium rotundifolium* and *Sapium sebiferum*. The root bark and leaf of *Sapium japonicum* were found to be effective for treating overstrain, lumbago and pain in the knees. *Sapium sebiferum* root bark and seed have been reported to have medicinal potential for digestive and excretory ailments, such as constipation, ascites, dysuria and turbid urine (Lai et al., 2004; Shimizu et al., 2007). The resin of *Sapium glandulosum* has been used to treat hernia in Bolivia (Hajdu and Hohmann, 2012). The bark juice of *Sapium insigne* is used traditionally in Nepal to help with wound healing by dispelling worms and killing germs (Manandhar and Manandhar, 2002). *Sapium ellipticum* is widely used as an ethnomedicine in different parts of Africa. The root decoction of *Sapium ellipticum* is used for treating coughs in Kenya. In Tanzania, the dried stem is powdered and crushed with water and applied on wounds, pain in the chest and head, among others. The leaves are used for abdominal swelling and eye diseases. The root decoction is used for malaria. The traditional healers in Zambia and Burundi prescribe the stem bark decoction for anemia, fever, guinea worms, elephantiasis and rheumatic problems. The leaves of this plant are traditionally used for the treatment of mumps in Ethiopia by the Kaffa people of the Bonga zone (Neuwinger, 1994; Mwine and Damme, 2011). The diverse, important ethnomedicinal properties possessed by this genus can be the basis for further research to investigate the phytochemical and pharmacological aspects of this genus.

3. Phytochemistry

According to the authors' literature search, there is a great chance of discovering new chemical constituents from this genus, as only six of 23 species of the genus *Sapium* have been phytochemically investigated thus far. This genus has been reported to contain several types of compounds from classes including flavonoids, terpenoids and a few compounds from other classes. However, within these compounds, diterpenoids are the most dominant constituent to be found in the currently studied species in this genus.

3.1. Flavonoids

Six flavonoid compounds have been reported from the genus *Sapium* (Table 2). Devkota et al. (2009) isolated four known flavones including rutin, quercetin, guaijaverin and nicotiflorin (**1–4**, respectively) from the water-soluble fraction of the methanolic extract of *Sapium insigne* leaf. In 2004, Woldemichael et al. reported a new highly oxygenated chalcone named α,β,3,4,5, 2′,4′,6′-octahydroxydihydrochalcone (**5**) from *Sapium haematospermum*. In another study conducted three years later, a new chalcone glycoside, chalcononaringenin 2′-*O*-β- -glucoside (**6**), was successfully obtained from the flower of *Sapium sebiferum* (Huang et al., 2007). All structures of the flavonoids are presented in Fig. 1.

3.2. Terpenoids

Diterpenoid compounds of the genus *Sapium* are divided into three major types based on their basic skeletons, i.e. phorbol ester, labdane and kaurane (Table 3). All the diterpenes were isolated from the aerial parts of the plants. No such compounds were obtained from the stem or root parts. Chumkaew et al. (2003) successfully isolated nine methylaminobenzoate-containing phorbol esters (**10**–**14**, **19**–**22**) from the fruit of *Sapium indicum*. However, some of those compounds are also found in *Sapium sebiferum* (Brooks et al., 1987). *Sapium insigne* was also found to be rich in phorbol esters. Devkota et al. reported the occurrence of two phorbol esters (**7** and **8**) in the leaf part in 2009. Three years

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