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## SENNA OCCIDENTALIS SEED: IS IT HEALTH RISK OR POTENTIAL MEDICINE?

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**ABSTRACT:** In resource-limited localities of developing countries, potentially manageable, if not useful, resources may present actual health and agricultural cost due to poor management and lack of awareness of health risk consequences. *Senna occidentalis* L. (Fabaceae) is a pan-tropical weed with a wide range of medicinal uses, and in some parts used as famine food. Despite possible use as alternative food or medicinal ingredient of this plant, many reports blame its seed as the cause of hidden intoxication to humans and various domestic animals, leading to considerable economic consequences. As has been described by experimentally reproduced natural cases of many animal studies and few human cases, intoxication by seeds of this plant presented varied and non-specific disease manifestations. Induction of mitochondrial damage has been suggested as the mechanism of toxicity, yet the exactly responsible toxin has not been identified. Thus, it seems that *Senna occidentalis* seed is presenting potentially manageable health risks to animal and human health, especially in resource limited localities of developing countries. In this review, the possible health risks of *Senna occidentalis* seeds are discussed based on reports from naturally or experimentally intoxicated animal studies, human case reports, and related records. Some scientific claims on its potential medicinal uses are also presented.

**INTRODUCTION:** *Senna* L. is one of the largest genera (300-350 spp.) in the legume family (Fabaceae) of subfamily Caesalpinioideae. It is a widespread and diverse genus, which was formerly included in the genus *Cassia* L. (~600 spp.)<sup>1, 2, 3</sup>. Distributed pantropical, *Senna* spp. are commonly used as shade plants, ornamentals, foods; and many have important medicinal properties and are used in both traditional and modern medicine<sup>3-6</sup>.

Potentially manageable or useful resources may present actual health and agricultural cost due to improper management or utilization. Despite numerous potential uses of plants from *Senna* species, there exist some safety concerns that need to be addressed.

Generally, it is suggested that all *Senna* spp. Should be considered toxic unless proven otherwise, but *S. occidentalis* (Fig. 1) and *S. obtusifolia* are regarded as more toxic than other species. *S. obtusifolia* is much more prevalent but somewhat less toxic than *S. occidentalis*. All parts of *Senna* spp. may contain the toxin, but the greatest concentration appears to be in the seeds. Several compounds that bind strongly to cell membranes occur in *Senna* spp.; however, the specific toxin responsible for toxicity



has not been identified<sup>5-12</sup>. The objective of the review is, therefore, to discuss the existing

scientific arguments on the health implications of *S. occidentalis* seeds.



FIG. 1: SENNA OCCIDENTALIS AND ITS SEEDS

### Toxicity of *S. occidentalis* Seed:

***S. occidentalis* Seed as Noxious Weed:** *Senna occidentalis* L. (Syn: *Cassia occidentalis* L.) (Fabaceae) is commonly known as Coffee senna. It is usually a weed of cultivation, pastures, roadsides and waste places, also in wooded grassland and near lakes and streams; pantropical, possibly originating in America. In some developing countries, roasted seeds of *S. occidentalis* may be used as a coffee substitute; hence the common name "coffee senna." Elsewhere all parts with a wide range of medicinal uses and in some parts used as famine food<sup>4, 13-18</sup>. *S. occidentalis* was recognized to be poisonous to livestock as early as 1911<sup>19</sup>. It has been found to be poisonous to many animal species, including cattle, pigs, horses, rabbits, goats, sheep, and poultry. It is a common contaminant weed of agricultural products, which grows in fields cultivated with soybean, corn, sorghum, wheat, and other crops.

Intoxication by this plant leads to considerable economic consequences<sup>13, 14</sup>. Its seeds are similar in size and density to the crop grains it contaminates, which could mean that it is almost impossible to prevent these seeds from coming with cultivated crops. Thus, a hidden intoxication may be present more frequently than thought, and its consequences must be evaluated<sup>20</sup>. Thus, it may be important to suggest that concerned personnel working in areas where *S. occidentalis* is prevalent, especially in limited-resource communities, are aware of the health risk consequences of this plant.

***Occidentalis* Seed Toxicity:** The toxic effects of *S. occidentalis* seed have been demonstrated using

several animal studies. Epidemiological studies and clinical observations on natural or experimental intoxications described varied and non-specific nature of toxicity. The clinical disease that results from experimentally induced poisoning differs in some aspects from that observed in the naturally occurring disease in cattle. Induction of mitochondrial damage has been the suggested mechanism by which *S. occidentalis* seeds produce toxic effects. However, the exact toxic substance and the exact intrinsic mechanism by which the toxin lead to mitochondrial impairment is still unknown<sup>19, 21-26</sup>. Because, there are few reports on human toxicity, most descriptions on the nature of *S. occidentalis* seeds caused toxicity have been based on animal studies as are presented below.

**Toxicity in Animals:** A variety of natural intoxications due to *S. occidentalis* seeds have been reported at different times. Discussions of this topic start from briefly describing two recent case reports of an outbreak in cattle and horses that occurred in Brazil. A review of sixteen outbreaks blamed *S. occidentalis* poisoning as an important cause of death in cattle in southern Brazil. The main gross changes in poisoned cattle were degenerative myopathy in skeletal muscles of the hind limbs. Other organs affected were the heart, liver, kidney, and the spleen as myocardial, hepatic, renal, and splenic microscopic lesions were observed occasionally<sup>25</sup>.

Similarly, epidemiological data and history of an outbreak of sudden death due to *S. occidentalis* seed ingestion have been reported in a large number of horses, in Brazil. Poisoned horses

demonstrated clinical signs associated with hepato-encephalopathy and frequently die suddenly. Lesions primarily involve the liver and secondarily, the central nervous system. Hepatocellular pericentriolobular necrosis and cerebral edema were the main histological findings<sup>27</sup>. An outbreak of poisoning by *S. occidentalis* is also reported in wild boars (male swine)<sup>28</sup>. A similar outbreak of natural poisoning by *S. obtusifolia* has also been reported in Brazil. The plant showed myotoxic and hepatotoxic effects on the poisoned animals, and the disease was almost always lethal<sup>12</sup>.

Most studies on natural or experimental intoxications of *S. occidentalis* seeds reported lesions to the skeletal muscle, the heart, and the liver. Other affected organ systems include the nervous system, vascular system, lymphoid organs, and the immune system, lungs, kidney, electrolyte balance, and impact on pregnancy. However, the type and extent of severity of organ damage demonstrated wide variation in different animal species, dosage, and preparation conditions<sup>15, 29</sup>.

Toxic response and clinical signs indicated variation in different animal species and even within the same species. Rabbits dosed at similar levels showed a wide range of survival times indicating variation in toxicity response. Multiple doses of up to 2% body weight produced fatal intoxication in rabbits, whereas single doses more than 0.7% body weight were consistently lethal for calves indicating that rabbits were less susceptible to poisoning than calves. Also unlike cattle, the involvement of skeletal muscle in poisoned rabbits was minimal<sup>19, 21</sup>. In cattle, pigs, and poultry, predominant degenerative changes in skeletal muscle have been reported.

In rabbits and rats, the heart and liver have been the main organs affected, whereas skeletal muscle lesions were of mild intensity<sup>5, 13, 14, 19, 21, 23, 25, 29</sup>. No brain damage has been observed in cattle<sup>25</sup>, whereas hepato-encephalopathy has been demonstrated in horses<sup>27</sup>. Other reported toxic effects to include neurotoxic effect<sup>30</sup>, lymphoid organs and immunotoxic effects in chickens<sup>20, 31</sup>; multi-organ damage<sup>32</sup>, impact on fetal and post-birth body development during pregnancy at a larger dose<sup>33</sup>, damage to vascular system and lungs in goats<sup>34</sup>; disturbance in acid-base balance

<sup>35</sup>, decreased oxidative enzyme activity in smooth muscle cells and in myenteric neurons of the large bowel of rats<sup>36</sup>.

The nature and severity of toxicity may also be influenced by dosage and by the type of preparation conditions. At a low dose, animals develop features of mild liver damage and myodegeneration; whereas, at higher doses, hepatic degeneration may be rapidly fatal before myodegeneration has time to develop. Histopathological changes of the liver of intoxicated rabbits showed concentration-dependent severities of lesions, and the animals that received higher doses presented ascites. Cardiomyopathy was also more severe in animals that received higher doses<sup>15, 23</sup>.

Several studies have demonstrated the toxicity of the fresh, dried, roasted or unroasted beans (seeds) of *S. occidentalis*. Freshly ground seeds produced consistent lethality to rabbits in a period of 5-8 days, but ground material stored up to 6 weeks required longer periods to produce its effect or produced no visible effects at all. Heat may reduce but not eliminate toxicity. Toxic activity was reduced, but not eliminated when heated (90 °C, 40 minutes) seed extract was administered to chickens. Both roasted and unroasted seeds intoxicated goats in varying degrees but roasting partially reduced the toxic effects<sup>15, 19, 34, 37</sup>. Recent work reported that roasting of seeds at 200 °C for 10 min eliminated the toxicity<sup>38</sup>.

**Toxicity in Humans:** Despite few reports from India, there is no definitive study on human toxicity of *Senna occidentalis* seeds. In western Uttar Pradesh of India, an acute brain disease in children was recurring every year, with very high (70-80%) fatality for over two decades. Initially, it was considered as acute viral encephalitis of unknown origin. Later, it was found to be not encephalitis, but a multi-system disease affecting liver, muscle, and brain which was re-named as acute hepatic-my encephalopathy (HME) syndrome caused by phytotoxins. Currently, the source of toxicity was found to be the consumption of beans of *Senna occidentalis* by unsupervised young children of low-income families. Massive campaign of two year educational and agricultural measures resulted in drastic reduction in the number of cases of most affected district.

HME syndrome in Children is a fatal disease, in the majority, in spite of intensive care and supportive therapy. The clinical spectrum and histopathology of *S. occidentalis* poisoning in children resemble those of animal toxicity, affecting mainly hepatic, skeletal muscle and brain tissues. Like in many animal species, the clinical features depend upon the number of seeds eaten. Massive hepatic damage predominates the clinical presentation with concurrent brain edema without inflammation. Involvement of the brain appears to be secondary to massive hepatic necrosis. The characteristic histopathology, especially the liver histology resembled that of toxicity caused by plants like *Senecio* spp, *Crotalaria* spp. and *Heliotropium* groups of weeds producing pyrrolizidine alkaloids, which are known hepatotoxic agents<sup>15, 39, 40</sup>.

One important lesson that can be learned from the Indian reports is that in some resource-limited localities of developing countries where *S. occidentalis* is prevalent, it may be causing hidden intoxications and subsequently presenting a risk to both animal and human health. Especially in such areas, where diagnosis is empirical and diagnostic facilities are limited, it is less likely for health professionals to notice the possibility of such environmental toxin caused disease condition while they do their diagnosis. Instead, they tend to associate it with other disease conditions that are most prevalent to the specific localities. Such cases usually remain hidden and neglected causes of morbidities and mortalities in the victim areas. Furthermore, since the disease manifestations of *S. occidentalis* caused toxicity is varied and non-specific, it can be easily associated with other disease conditions. These quests health professionals and concerned staffs in limited resource areas where *S. occidentalis* is widespread to be aware of the toxic potential of this plant.

**Chemical Nature of Phytotoxins:** The phytochemical groups identified in *S. occidentalis* seeds include alkaloids, tannins, saponins, carbohydrates, glycosides, phytosterols, oils and fats, phenols, flavonoids, proteins, and amino acids as well as other miscellaneous constituents such as N-methyl morpholine<sup>41-43</sup>. The nature and amount of phytochemicals vary according to climate. For example stems, leaves and the root bark of the plant from Ivory Coast, Africa contain a small number of

saponins, no alkaloids, sterols, triterpenes, quinones, tannins, and flavonoids. However, a large number of alkaloids were found in the stem, leaves, and fruits from Ethiopia<sup>24</sup>. The specific toxin responsible for *S. occidentalis* seed caused toxicity has not been identified. However, reported candidates to include N-methyl morpholine, toxic alkaloids, anthraquinone derivatives and toxalbumins<sup>5, 13, 15, 23-25, 41-45</sup>. Toxic albumin, which can be partially or entirely detoxified through the action of formalin, has been reported to behave as an allergen<sup>46</sup>. Dianthrone, an anthraquinone-derived compound which caused mitochondrial injury, was identified in *S. occidentalis* seeds<sup>25, 47</sup>. It has also been hypothesized that highly reactive anthrones, derived from anthraquinones in the colon, could be absorbed and transported to the liver where they induce cellular damage<sup>48</sup>.

Whether the toxin resides in the endosperm or external tegument (seed coat or hulls) of the seed has not been resolved. Some reports claim the toxin resides in the external tegmen. Severe clinical signals and reduced body weight in birds that received the external tegument of the seed has been demonstrated, whereas no adverse effects were observed in birds that received the whole seed or other parts of the seed, which indicate that the active principle is more concentrated on the external tegument fraction<sup>13,14,20</sup>. On the hand, the ground endosperm, after seed hulls were removed, of *S. occidentalis* seed administered to rabbits, orally, 0.25-3.0% body weight produced a fatal cardiomyopathy<sup>19, 21</sup>.

It has been indicated that the toxin is more soluble in water than organic solvents. Organic extracts with methanol, ethanol, chloroform, ethyl acetate, and benzene were ineffective in removing the toxin from the seeds. Aqueous extractions, using 25 mM sodium bicarbonate or 250 mM sodium citrate, effectively removed the toxin from the seeds; but left the toxin bound to the particulate matter in the extract. *i.e.* centrifugation of these extracts gives supernatant solution and a pellet of particulate matter. The pellet is the concentrated toxin although its identity is still unknown. Addition of Triton X-100 to the aqueous buffers effectively solubilized the toxin from the particulate matter<sup>24, 37, 49</sup>.



**S. occidentalis Seed as Medicinal or Food**

**Ingredient:** Despite substantial toxicity reports, some scientific claims support the potential use of *S. occidentalis* seed as alternative food and feed or as herbal medicine. Most reports neglect to mention any caution of adverse effect, and even others claim it is safe. Below are presented a few recent reports of such kind.

It has been suggested that *S. occidentalis* seed can serve as a cheap source of protein, energy, as well as antioxidant micronutrient supplements in both man and animal<sup>50</sup>. Similarly, the potential use of an aqueous extract of *S. occidentalis* seed as an effective agent to prevent oxidative stress-mediated epilepsy has been suggested based on its effects on male Sprague Dawley rats<sup>51</sup>. Also, aqueous extract of the seed exhibited potent hepatoprotective activity against paracetamol-induced liver damage in rats<sup>18</sup>. Ethanolic extract of the seeds possesses anti-inflammatory effects in both acute and sub-acute inflammatory conditions in rats<sup>52</sup>, activated antioxidant enzymes and protected CCl<sub>4</sub> induced liver damage in Wistar albino rats<sup>53</sup>, and showed pronounced antibacterial<sup>54</sup> and antifungal<sup>55</sup> activities.

As presented in these reports, the seed of this plant may have potential use as alternative food or medicinal ingredient. However, the potential adverse effects need to be addressed because in herbal medicine safety is more important than efficacy; and if possible detoxification options have to be suggested to encourage safe usage. Midala *et al.*, (2013) recommended the use of *S. occidentalis* seed as a potentially economical source of the meal to rabbits but stressed the need of appropriate processing method that eliminates or reduce the anti-nutritional factors<sup>56</sup>.

**SUMMARY:** *Senna* spp. are potentially useful resources of herbal products for use as medicinal or food ingredients. Effective medicines can be expected from these species; yet, addressing some safety concerns is important because in herbal medicine safety is more important than efficacy. Generally, there are few reports on toxicity of *Senna* spp.; however, substantial reports exist on the toxicity of *S. obtusifolia* and *S. occidentalis*, the later being most toxic. *S. occidentalis*, commonly known as Coffee senna, is a pan-tropical weed with

a wide range of medicinal uses and in some parts used as famine food. It is usually a common contaminant weed of agricultural products, which grows in cultivation fields, pastures, roadsides and waste places, wooded grassland and near lakes and streams. Many reports blame its seed as the cause of intoxication to various domestic animals, leading to considerable economic consequences as it results in death, impaired health, and reduced productivity to animals.

Similarly, few reports blame it as a health risk to humans. As has been described by experimentally reproduced natural cases of many animal studies and few human cases, the nature of *S. occidentalis* seed toxicity is characterized by varied and non-specific disease manifestations. Cattle, sheep, goats, horses, pigs, rabbits, chickens and humans have been shown to be susceptible. It affected multiple organs and systems; yet most studies reported lesions to the skeletal muscle, the heart, and the liver. Hepatomyoencephalopathy has been manifested in humans and horses. The type and extent of severity of toxic response and clinical signs varied depending on species, dosage, and preparation conditions. Induction of mitochondrial damage has been suggested as the mechanism by which the seeds produce toxic effects. The specific toxin responsible for *S. occidentalis* seed caused toxicity has not been identified; yet, N-methyl morpholine, toxic alkaloids, anthraquinone derivatives, and toxalbumins are reported, candidates. Toxicity by both the endosperm and external tegument (seed coat or hulls) has been reported, and the toxin tends to be soluble in water than organic solvents.

There are also some reports that support the potential use of *S. occidentalis* seed as alternative food or medicinal ingredient. However, although it may have the claimed use, the potential adverse effects need to be addressed and if possible detoxification options have to be suggested to encourage safe usage. To sum up, *S. occidentalis* seed could be a potentially useful resource and its health risks can be manageable; but it seems that currently, it is presenting actual health and agricultural cost due to improper management or utilization, especially in resource limited localities of developing countries.

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