



## **Toxic Epidermal Necrolysis Induced by a Medicinal Plant: *Ziziphus mucronata***

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### **Authors' contributions**

*This work was carried out in collaboration between all authors. Author BAD designed the study, wrote the protocol and wrote the first draft of the manuscript. Authors MD, SON, MN, SD, NBS and MTD managed the analyses of the study. Author BAD managed the literature searches. All authors read and approved the final manuscript.*

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**Case Study**

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### **ABSTRACT**

**Introduction:** The fruits of the jujube tree of the genus *Ziziphus*, which are mostly edible, are used in traditional medicine for the treatment of certain infectious, urinary and metabolic diseases. Some studies have reported hypersensitivity reactions such as urticaria and angioedema following the consumption of jujube fruits. We report a case of toxic epidermal necrolysis caused by *Ziziphus mucronata*.

**Case Report:** A 17-year-old girl was hospitalized for a necrotic bullous rash to more than 80% of body surface with a mucosal involvement. These symptoms appeared 18 days after taking the powdered fruit of the jujube tree *Ziziphus mucronata* to treat enuresis. She did not take any modern medication three months before being admitted to the hospital. Healing of cutaneous and mucosal lesions was obtained after stopping the plant and symptomatic treatment.

**Conclusion:** Plant of the genus *Ziziphus* contains chemical compounds (alkaloid, tannins, flavonoids, terpene derivatives), which are known for being toxic and allergic to the skin. Their mechanisms of action may be pharmacological linked to overdosage or due to immunological reactions responsible for toxic epidermal necrolysis.

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## 1. INTRODUCTION

In Africa, medicinal plants are routinely and empirically used in traditional medicine. According to the WHO, traditional medicine is the primary medical care for up to 80% of the population [1,2]. Despite their beneficial health effects, cutaneous adverse events are being increasingly reported following the use of traditional therapies in Senegal [3]. Sometimes, they are severe forms such as erythroderma, urticaria, angio-edema, and bullous toxidermia [3,4,5]. We report a case of toxic epidermal necrolysis (TEN) or Lyell syndrome secondary to an oral consumption of a plant: *Ziziphus mucronata*.

## 2. CASE REPORT

A 17-year-old girl, with no previous history, was referred to our department for a generalized bullous eruption with mucosal involvement. Her symptoms began 10 days earlier with a generalized pruritus associated with fever. Eighteen days earlier she had been given a traditional therapy, “hyena jujube” to treat enuresis. The common local name of the medicinal plant used was “Siddem bouki” and scientific name “*Ziziphus mucronata*”. The fruits of the plant were ground into powder and consumed orally. The administered dose was 120 ml/day. Over the 28 days she consumed a total dose of 2.16 liters.

Physical examination revealed large flaccid blisters on the limbs and trunk, with a positive Nikolsky sign, giving a “wet dressing appearance” (Fig. 1). The involved body surface area was estimated to be 80%. We also noticed a desquamating, crusting rash of the lips, the vulva, and a conjunctival hyperaemia. She was conscious and had a fever at 37,9° C, a blood pressure at 130/80 mmHg, and a respiratory frequency at 17 cycles per minute.

The biological tests were normal with leukocytes measured at 6100/mm<sup>3</sup>, hemoglobin at 12 g/dl, and blood platelets at 240.103 /mm<sup>3</sup>. The fasting blood glucose was 1,04 g/l. The transaminases, serum electrolytes, urea, creatinemia, C-reactive protein, cytobacteriological examination of the urine, HIV serology and viral hepatitis were normal.

The plant was stopped and supportive therapy consisting of rehydration and nutritional support with protein supplementation and meticulous skin and mucous membrane care was undertaken. After 2 weeks of symptomatic treatment, she was afebrile and her skin had stopped blistering and superficial desquamated leaving behind striking post inflammatory hyperpigmentation (Fig. 2).



**Fig. 1. Necrotic bullous eruption over 80% of the body surface area**



**Fig. 2. Striking post inflammatory hyperpigmented macula on the trunk and limbs**

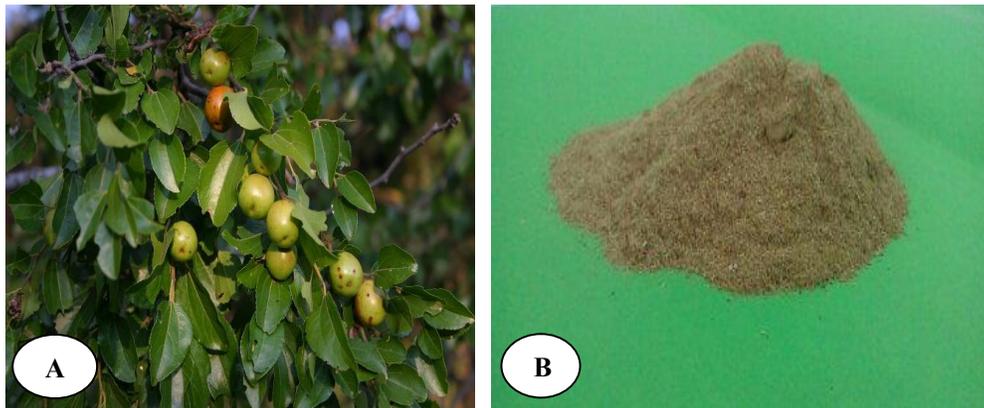


Fig. 3. The fruits (A) and powder (B) of *Ziziphus mucronata*

### 3. DISCUSSION

The toxic epidermal necrolysis in our patient was secondary to the intake of *Ziziphus mucronata*. In the absence of any other responsible drug in the preceding three months, the traditional plant was deemed responsible for this severe cutaneous drug reaction. This was further supported by the complete resolution following cessation of the plant medication. The diagnosis of toxic epidermal necrolysis fits best with the clinical features and pattern even in the absence of histology.

By applying these items to the french pharmacovigilance criteria [6], the imputability for the traditional drug was highly probable.

*Ziziphus mucronata* is a plant available in the desert regions of Senegal. It belongs to the family *Rhamnaceae*, to the genus *Ziziphus* of which two species are more frequent in Senegal, *Ziziphus mauritiana* and *Ziziphus mucronata*. The fruits and powder of *Ziziphus mucronata* are edible and bitter (Fig. 3). They are recommended in traditional medicine for the treatment of enuresis, dysuria and the roots for the treatment of gonococcal infections, diabetes and bacterial or fungal infections [7,8,9,10]. Plants of the genus *Zizyphus* contain alkaloids, tannins, flavonoids and terpene derivatives, which are substances known for being toxic and allergenic to the skin [7,11,12]. Cases of hypersensitivity reactions (urticaria, angio-edema) to the fruit of *Ziziphus jejuaba* have already been reported [5]. The mechanism of action of these plants may be immunoallergic as proven by the positivity of the epicutaneous tests of traditional plants conducted in Senegal [4].

### 4. CONCLUSION

Adverse cutaneous reactions following medicinal plants is increasingly reported due to its extensive use in traditional medicine. Plants of the genus *Ziziphus* are known in botanical and toxicological studies for their beneficial properties in the treatment of certain urinary, infectious and metabolic diseases. However, they may cause undesirable skin effects. We report to our knowledge the first case of toxic epidermal necrolysis induced by plants of the genus *Ziziphus*.

### CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

### ETHICAL APPROVAL

As per international standard or university standard, written approval of Ethics committee has been collected and preserved by the authors.

### COMPETING INTERESTS

Authors have declared that no competing interests exist.

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