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New cases of star anise poisoning: are we providing enough information?[☆]



Persisten las intoxicaciones por anís estrellado, ¿estamos dando la suficiente información?

Dear Editor,

Star anise (*Illicium verum* [I. verum] Hook. F.) is a plant native to Asia that has been widely used since ancient times for its antioxidant, antimicrobial, expectorant, analgesic, and sedative properties.¹ Since its introduction in Spain, it has been used as carminative, especially for treating baby colic. Despite its long history of use, there continue to be cases of poisoning with neurological and gastrointestinal manifestations, especially in infants younger than 3 months.

We present the case of a 2-month-old patient with no relevant history. He presented episodes of jitteriness in the lower limbs, with increasing frequency over the previous week, displaying startle movements during sleep followed by crying; this had prevented sleeping for more than an hour in the previous 2 days. The patient partially rejected food (baby formula) and presented isolated vomiting with normal bowel movements. He lived in a non-infectious environment and was not taking any medication. Baseline general physical and neurological examinations yielded normal results. We requested a blood analysis including ion concentration, hepatic marker enzymes, and acute-phase reactant levels; results were normal for these parameters and for urine toxicology testing. He was admitted for observation and assessment with other complementary tests.

During admission, we discovered that the mother was giving the patient a star anise tea, which she reported having administered for one week; it was prepared with 1-2 stars in 400-500 cc of boiling water for several minutes.



Figure 1 Resemblance between the fruits of *I. verum* and *I. anisatum*.⁵

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Table 1 Plant species known as anise.

Scientific names and synonyms	Common names	Uses	Origin/introduction to Europe	Cultivation	Potentially toxic compounds	Toxicity
<i>Pimpinella anisum</i> Linné (Umbeliferae family)	Anise, anis vert, aniseed	Carminative, antispasmodic, expectorant, insecticide, bactericide, aromatic; manufacture of preserves, liquors, and confectionery	Middle East/introduced by the Moors	Mediterranean	Anethole	Relatively safe
<i>Illicium verum</i> Hooker filius; <i>Illicium anisatum</i> Lour (Magnoliaceae family)	Star anise, Chinese star anise, badiane	Antioxidant, antimicrobial, expectorant, analgesic, and sedative	Asia/17th century	Southeast Asia	Anethole, estragole, veranisatin A, B, and C	Toxic at high doses
<i>Illicium anisatum</i> Linné, <i>Illicium japonicum</i> , <i>Illicium religiosum</i>	Japanese star anise, shikimmi, skimmi	No clear medicinal effects	Asia	Southeast Asia	Anethole Anisatins	Highly toxic (not authorised use)

Without questioning the efficacy of medicinal plants, we should highlight the false perception of safety and lack of adverse effects associated with their use, with families even forgetting to mention their use during clinical history taking. This false perception of innocuity has resulted in repeated cases of poisoning due to the intake of some of these plants.

There are several plants known as anise, with different uses and toxicities; this may lead to confusion due to the lack of awareness of the population and professionals (Table 1). Aniseed is the fruit of *Pimpinella anisum* L, one of the oldest medicinal plants, which is widely used both for culinary and for medicinal purposes. Star anise, the fruit of *I. verum*, has a characteristic star-shaped form comprising 6 to 8 carpels. Both species contain anethole; the antispasmodic effect of this compound confers these plants with carminative and expectorant properties. However, it may be toxic at high concentrations, particularly to the nervous system. Furthermore, *I. verum* contains neurotoxic sesquiterpenes named veranisatin A, B, and C.² A third variety of anise may be confused with star anise due to their visual resemblance: the fruit of *Illicium anisatum* L. (*I. Anisatum*), known as Japanese star anise, is practically undistinguishable from that of star anise (Fig. 1) but contains anisatins, which are much more toxic than the veranisatins found in *I. verum*. Anisatins act as non-competitive GABA_A receptor antagonists, inhibiting the function of the inhibitory neurotransmitter and therefore increasing nerve excitability, even causing seizures.³

In Spain, *I. anisatum* is included on the list of plants whose sale is forbidden or restricted due to their toxicity (Law 29/2006 of 26 July, on guarantees and rational use of medicines and medical devices).

Star anise (*I. verum*) is considered safe due to its low veranisatin content, although it may cause neurotoxicity above the maximum recommended dose (one star per 200 cc of water)² or if it is boiled for long periods, resulting in higher concentrations. However, most cases of poisoning are due to contamination with the fruit of *I. anisatum*.⁴ Given the difficulty of distinguishing between these species, star anise should not be administered to children.

In all infants with acute neurological or digestive symptoms with no known cause, we should inquire about the use of star anise in tea or as gripe water. Furthermore, paediatricians play an essential part in recognising, asking about, and informing of the possible adverse effects of anise and other natural products.

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