

CASE REPORT

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# Case series: star anise toxicity presenting to the emergency department in Eastern Regional Referral Hospital in Bhutan

Sherab Wangdi<sup>1\*</sup>, Jurmi Wangdi<sup>1</sup> and Nima Wangchuk<sup>1</sup>

## Abstract

**Background** Star anise fruit has been used in spice in Asian cuisine, ingredient for traditional medicines, component for antiviral drugs and as parts of tea and beverage across the globe. Toxicity from these plants has been reported due to adulteration with similar toxic species and from consumption with high toxic dose. Most physician and public are unaware of these adverse effects.

**Cases** We present two cases of star anise toxicity. Both of the patients presented with gastrointestinal and neurological symptoms after consumption of the said fruit. All of the labs and imaging test was negative for other causes and star anise toxicity diagnosis was made after detailed history, events and related symptoms. They were managed supportively and discharged after 24 h of observation.

**Conclusion** Emergency department doctors should be vigilant about possible star anise toxicity in patient presenting with suggestive symptoms, negative investigation for other possible cause and in area where these plant species is available. A detailed drug and ingestion history is essential.

**Keywords** Star anise, Toxicity, Emergency Department, Bhutan

## Background

Star anise is a plant native to Asia that has been widely used since ancient times for its antioxidant, antimicrobial and analgesic properties [1, 2]. Star anise (*Illicium verum*) better known as Chinese star anise, belongs to the Magnoliaceae family and its fruit is a very important element as a spice in the Asian cuisine. It is also highly regarded medicinal plant with a number of medicinal properties [2]. Several biologically important phytochemicals have been reported and possesses antimicrobial, antiviral, and

antioxidant properties [2, 3]. Star anise is the industrial source of shikimic acid, a primary ingredient used to create the antiviral drug, Tamiflu (oseltamivir phosphate) [2, 4]. Chinese star anise has been commonly regarded as being safe and nontoxic [2, 5].

A closely related species, Japanese star anise (*Illicium anisatum*) has been well documented to cause both neurologic and gastrointestinal toxicities [5]. All *Illicium* species contain sesquiterpene compounds (anisatin, neoanisatin, and pseudoanisatin), the potent neurotoxins found in Japanese star anise [5]. Anisatin compounds act as potent noncompetitive gamma-aminobutyric acid antagonists [1, 5]. Although Chinese star anise is considered safe for consumption, this species also contains toxic compounds named veranisatins A, B, and C. These veranisatins, though not as potent as anisatin itself,

\*Correspondence:

Sherab Wangdi  
sherabw1989@gmail.com

<sup>1</sup>Department of Emergency Medicine, Eastern Regional Referral Hospital, Mongar, Bhutan



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neurologic symptoms are observed at higher doses [1, 2, 5]. Several case studies reported to star anise toxicity has been due to adulteration of *I verum* with *I anisatum* [3, 5, 11, 12].

Another related species (also known as star anise), *Illicium griffithii* (Fig. 1) is distributed sporadically in Bhutan, Hongkong, India and Vietnam [6, 7]. In Bhutan, it is found in Chhukha, Mongar, Thimphu, Trashigang, Trashigang, and Samdrup Jongkhar districts [6, 8]. Traditionally, the fruits are used as incense, tea leaves, to improve the strength of local alcohol and medicine for sinusitis [6, 7]. Farmers in these rural places have been harvesting and selling these plants helping them generate income and government agencies have been helping to maximize the harvest and finding markets for these plants [6, 8, 9]. Oil extract from *Illicium griffithii* seeds and fruit have isolated hexane, methanol and ethyl acetate compounds where some are sesquiterpene in nature [7, 10]. These compounds are tested for its antimicrobial activity but are also found to be toxic in high doses [7, 10].

We present two cases of star anise toxicity who presented to our emergency department.

### Case 1

56 years old woman is brought to the emergency department with complaints of persistent vomiting with abdominal cramps for one day. She also gave history of loose stools and headache. She denied having fever, anorexia or any urinary symptoms. No other family members were having similar symptoms. On examination, she looked pale and dehydrated. Abdomen was soft and non-tender. Other than tachycardia of 112/min, rest of her initial vitals were normal. She was managed as acute gastroenteritis with IV hydration and anti-emetics. Her blood report did not show signs of infection, electrolytes studies were normal and urine for pregnancy was also negative. After few hours of observation, she was feeling better and her vitals were stable. Soon after, patient complaint of giddiness and had an episode of tonic clonic seizure; lasting about 30–45 s with minimum post ictal events. Her RBS was normal. CT brain was



**Fig. 1** Star anise (*Illicium griffithii*) fruit. Taken on the way to Aja Valley, Monggar. (Picture courtesy: Jurmi Wangdi)

done which was negative for any lesion or meningitis. ECG has normal sinus rhythm.

She denied previous history of seizures. On further inquiring about any drug history, she gave account of drinking tea brewed from star anise fruit a day prior to having the symptoms. She had taken 3 cups of tea (450 ml) for “dyspeptic” symptoms she was having.

Following the history and the associated symptoms, likely diagnosis of star anise toxicity was made considering all the negative test and investigation. She was kept under observation for 24 h and discharged the following day. One week follow up was unremarkable with no residual neurological and gastrointestinal symptoms.

## Case 2

48 years old male referred from local basic health unit after alleged history of star anise poisoning. He was a patient of diabetes mellitus on lifestyle modification and not on any oral hypoglycemic drugs. He allegedly has drank 4 large cups of tea (200 ml per cup) brewed from 5 piece of star anise fruit for his diabetes. He developed symptoms about 2 h after drinking the tea. He said that he has collected the fruit from the Aja region of Mongar. The symptoms included abdominal cramps, continuous vomiting, giddiness and chest tightness. He also complained of loose stools and tingling sensation around the mouth and paresthesia in lower limbs. He denied seizure like activity or palpitation. His vital signs were normal with BP 127/79 mmHg, pulse 102/min and normal temperature. ECG showed sinus rhythms and electrolytes were not deranged. He was managed conservatively with antispasmodic, anti-emetics and IV fluid. He was kept under observation for 24 h and discharged the next day with normal repeated labs, sinus rhythm ECG and improved symptoms.

Following history of ingestion and symptoms, and negative test and investigations, diagnosis of star anise toxicity was made during his discharge. He was followed up in a week with no residual symptoms and was referred to diabetic clinic.

## Discussion

Star anise toxicity has been reported despite its long history of use especially in pediatric population [1, 11–14]. Few cases has been reported in adult population [15, 16]. All these cases has been associated with Japanese star anise (*Illicium anisatum*) which are found to be mixed with Chinese variety (*Illicium verum*) [1, 4, 5]. *Illicium griffithii* is found in Bhutan specifically around the region where our cases are residing [6]. Though there are no documented case reports, *Illicium griffithii* is stated to be toxic in higher dose [8, 17]. There were few cases of star anise toxicity presented in our hospital but no records were available. Main toxic compound found in Japanese

star anise is anistatin which is a potent neurotoxic causing seizures [1, 2, 5]. Although anistatin is not isolated from *Illicium griffithii*, other related compound like anethole, estragole and safrole are isolated from the plant which has been found toxic in high doses [1, 7, 10].

Farmers harvesting these plants in Aja region of Monggar, Bhutan have described that only seedless fruit and carpel are safe for consumption and used as medical herbs. They have reported of severe vomiting and gastrointestinal symptoms if over consumed or if “even single seed is consumed.” [8] Casanova CM et al., have specified that *Illicium verum* cause neurotoxicity above the maximum recommended dose or if it is boiled for long periods, resulting in higher concentrations [1, 4]. A case report has documented maximum safe dose to be 1 star per 200 ml of water [1]. Our cases has had 5–6 stars in brewed in 500 ml of water going above the recommended dose and had also brewed it over the longer period of time. George C.K has described in his book *Illicium griffithii* as partly poisonous species [17].

The symptoms of star anise toxicity has been reported in 3–4 h after consumption in most cases and in few cases by 24 h [11, 12, 15]. The symptoms described in cases can broadly classified into neurological and gastrointestinal symptoms [1, 5]. Neurological symptoms includes seizures, abnormal movements of limbs, nystagmus, spasticity, irritability and lethargy [1, 5, 11, 12, 14, 15]. Gastrointestinal symptoms like vomiting, diarrhea and abdominal cramps has been reported [5, 11, 12]. Other described symptoms are hepatotoxic damage and hypersensitivity reaction [12, 14]. The compounds found in the plant act as GABA receptor antagonist, increasing nerve excitability and causing the neurological symptoms [1, 12]. Other mechanism described are direct neurotoxin and hepatotoxic effects [1, 12].

The diagnosis is clinical as there is no labs in Bhutan to check the content and amount of toxin. Even in developed countries, there is no regular lab investigation done for diagnosis and the toxin compound analysis in cases was only done for studies and research purposes [5]. Good and detailed history of symptoms and ingestion history are crucial for diagnosis and by excluding other more common causes of symptoms [1, 11]. The patients in case series both clearly provided a history of recent use of star anise tea prepared in higher dose and presented with symptoms commonly seen with toxicity. Both patients had gastrointestinal and neurological symptoms with case 1 also developing tonic clonic seizures. Both underwent series of investigations which was not significant for other cause. By next 24 h, both patients were symptoms free and 1 week follow up was unremarkable.

The prognosis of star anise are favorable and patients improve after supportive care and treatment. There are no reported cases on mortality after star anise toxicity.

According to Ludlow et al., all seven infants became asymptomatic after 48 h of supportive care for star anise toxicity [5]. There are report of 63 adults who experienced symptoms of toxicity after consuming herbal tea from star anise requiring hospitalization and their symptoms improved after 24 h and no reported case of mortality [5, 16].

There are several cases reported about star anise toxicity in pediatric population [5, 11–14]. The toxicity is commonly seen in infant less than 2 months of age as star anise “tea” is used as remedy and antispasmodic for infantile colic [5, 11, 12]. Madrigal A. et al. reports 47 cases of infant toxicity of which average age was 34.4 days old [18]. Though the use of star anise tea is widespread and cases are reported from Spain, South America, France, Netherland and Asian countries, reports from the USA are specifically seen in Hispanic and Latino populations [5, 11, 14, 15]. A study showed that one third of population surveyed in South Florida uses star anise in their diet [11]. The ingestion of star anise should be considered in differential diagnosis in pediatric population especially infants who presents with unexplained irritability and seizures in specific population group.

There are no recorded long term effect of toxicity and to our knowledge, there are no known long term sequelae of star anise poisoning.

The management is primarily supportive and symptomatic as there is no specific antidote [1, 11, 12]. Patient require close monitoring for any seizure activity. Seizure and convulsion are treated with diazepam. Antiemetic and IV fluid are given as supportive treatment.

## Conclusion

This case series illustrates the risk of star anise toxicity with its use as spice and as local treatment for ailment in Bhutan. We hope to create awareness about toxic effect of star anise and to include star anise use in our history taking if patient presents with neurological and gastroenteritis symptoms with no definite cause and especially in the area where these plants are widely available and used for minor ailments.

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## Author contributions

S.W, J.W and N.W was involved in recruitment of patients, collecting data and obtaining consent from the patients. J.W took the image in the content while visiting the Aja region. S.W obtained site clearance from the hospital and administration for case report. S.W wrote the manuscript with contribution from N.W. All authors read, reviewed and approved the manuscript.

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## Data availability

No datasets were generated or analysed during the current study.

## Declarations

### Ethical approval

The site clearance for the study was sought from the hospital. Since the study is a case report, the need for ethical clearance is waived off. The study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

### Consent to participate

Written informed consent was taken from all participants of the study. They expressed his/her will to allow the use of clinical data and the publication of this information for academic purposes. It is specified in this consent that all information that can identify or correlate to the person will be anonymized to guarantee their confidentiality.

### Consent for publication

Written informed consent was obtained from the patient for publication of this study and accompanying images.

### Competing interests

The authors declare no competing interests.

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