Ocular toxicity by seeds of *Annona squamosa* (custard apple)

Harsha Nagaraja, Thungappa Kugar, Yathish Shivanna, Archita Agrawal, Rohit Shetty

Custard apple seeds have been used in native medicine from time immemorial for the management of head lice and skin exfoliation. We report six consecutive patients who developed toxic keratoconjunctivitis within 6–12 h of ocular exposure to custard apple seeds. The use of topical steroid worsens the toxicity and predisposes to the development of microbial keratitis in such cases. Patients showed a good response to primary treatment with topical fortified antibiotics and lubricants. This case series highlights the need to educate the patients regarding the potential toxic effects of the custard seeds and the treating physicians about possible deleterious effects on using topical steroid.

Key words: *Annona squamosa*, custard seeds, toxic keratitis

Custard apple is the fruit of *Annona squamosa* or *Annona asiatica*, which belongs to the genus *Annona* and family *Annonaceae* [Fig. 1].[1] Custard apple is cultivated throughout India and is commonly known as "sitaphal" or "sugar apple" due to the sweet taste of the fruit (tastes like custard).[1,2] Different parts of this plant are used in folklore medicine for the treatment of various diseases such as boils, ulcers, maggot infested sores, head lice, and skin exfoliation.[3] Their accidental contact with the eyes, especially when used for head lice or as a facial skin exfoliant, is not uncommon in some parts of South India. We present a series of cases wherein the patients developed severe symptoms of toxic keratitis following accidental ocular exposure to the custard apple seeds.

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Case Reports

Six female patients presenting to our tertiary care center with a history of ocular exposure to custard seed powder were included in the case series. Five patients had used the custard seed powder as a treatment for the management of hair lice and hair loss while one patient had applied custard seed powder mixed with water to her face to prevent acne. All patients presented with severe pain, redness, watering, and photophobia within 6–24 h of using the custard seed powder.

Case 1

A 26-year-old female presented to us with the above-mentioned symptoms after using oil mixed with custard seed powder over her scalp. On examination, the patient had severe blepharospasm, conjunctival congestion, and coarse punctate epithelial diffuse erosions, with central epithelial defect measuring 4 mm × 5 mm, stroma was compact, and no anterior chamber reaction was noticed in both eyes [Fig. 2]. A silicone hydrogel bandage contact lens (PureVision, Bausch and Lomb, USA) was applied in both eyes, and she was advised to use moxifloxacin hydrochloride 0.5% eye drops four times a day, topical lubricants, and oral nonsteroidal anti-inflammatory

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Figure 1: Custard apple fruit from *Annona squamosa* tree

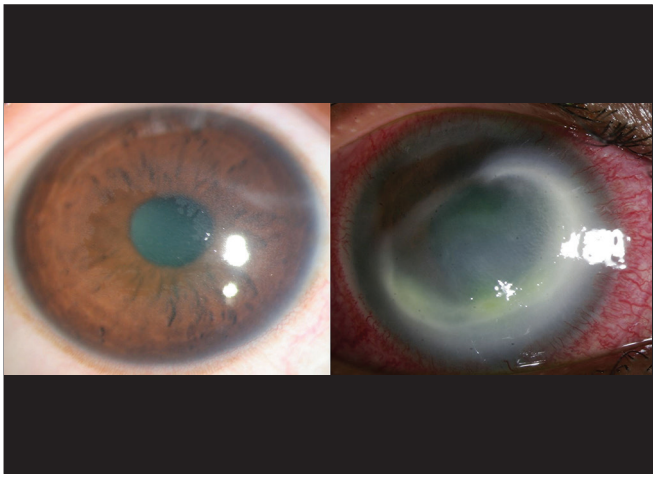

Figure 2: Slit-lamp photo of a patient after ocular exposure to custard apple seed powder. Left image shows coarse corneal punctate epithelial erosion with central epithelial defect 12 h after exposure, and right image shows the development of subepithelial and midstromal infiltrate 7 days after the use of topical steroids

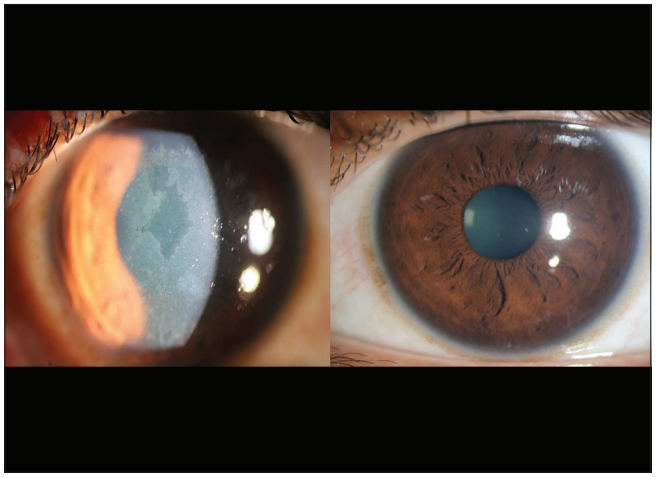

Figure 3: Slit-lamp photo of a patient after ocular exposure to custard apple seed powder. Left image shows coarse corneal punctate epithelial erosion with central epithelial defect after exposure, and right image shows complete healing of the corneal epithelium at 2 weeks after treatment with topical antibiotics and lubricants

drugs. Epithelial defect had healed the next day and topical 1% prednisolone acetate was added to reduce the inflammation. On the 3rd day, the patient presented with worsening of symptoms. Slit-lamp examination showed a larger epithelial defect with subepithelial and anterior stromal infiltrate in both eyes. Corneal scraping for Gram's stain, potassium hydroxide wet mount and culture using blood agar, chocolate agar, and Sabouraud dextrose agar revealed Gram-positive cocci - coagulase negative *Staphylococcus aureus* to be the causative agent. The patient was started on topical fortified cefazolin 5% hourly, fortified aminogen 5% every 2 h, and homatropine 2% eye drops. Topical steroids were stopped. At 6 weeks after presentation, epithelial defect had healed and corneal infiltrates had resolved with scarring. The patient had an uncorrected visual acuity of 20/400 in the right eye and 20/60 in the left eye while the corrected distance visual acuity showed no improvement in the right eye and the left eye improved to 20/30. Optical penetrating keratoplasty was performed in the right eye to restore vision.

Case 2

A 32-year-old female with a history of ocular exposure to custard seed powder for which she was prescribed topical ciprofloxacin and dexamethasone, and as her symptoms worsened with the treatment, she was referred to us for further management. Slit-lamp examination showed typical signs of toxic keratoconjunctivitis with an epithelial defect in both eyes and peripheral anterior stromal infiltrate. Topical steroids were stopped and she was advised to use topical cefazolin 5%, homatropine 2%, and lubricants. She responded well to treatment and the keratoconjunctivitis resolved in 3 weeks with complete restoration of vision (20/20) in both eyes.

Case 3, 4, 5, and 6

These patients had a similar course of presentation after 8–12 h of exposure to custard seeds. Slit-lamp examination showed coarse punctate epithelial diffuse erosions in both eyes. All patients were prescribed topical cefazolin 5%, homatropine 2%, and lubricants. Case 3, 5, and 6 responded well to treatment and ocular signs resolved completely in 2 weeks while Case 4 developed an epithelial defect on the 2nd day with no infiltrate which needed 2 weeks to resolve completely. All patients regained best-corrected visual acuity of 20/20 after the condition completely resolved [Fig. 3].

Discussion

The reports of toxic keratoconjunctivitis following exposure to plant extracts are sparse.[4] Seeds of *A. squamosa* contain active compounds such as alkaloids, cyclohexapeptides, and acetogenins.[5] Numerous annonaceous acetogenins have been shown to be responsible for the medicinal effects such as anti-HIV activity, antidiabetic properties, antioxidant property, antitumor activity, wound healing properties, insecticidal, antifungal, anti-lice, and mosquitocidal properties.[5-7]

Allen, an American Botanist, mentions personal knowledge of a case of blindness resulting from "the juice of the crushed custard apple seeds" coming in contact with the eyes.[8] Others have mentioned that the crushed seeds on contact with the eye can cause conjunctival irritation and ulcers in the eye.[9] Testing of toxic extracts of *Annona* seeds on rabbit eyes caused conjunctival inflammation and corneal epithelial delayed damage.[10]

We observed a similar effect on human eyes, with epithelial irregularity developing within hours of contact, corneal epithelial defect usually developing 1–2 days following exposure and a high incidence of vision-threatening secondary bacterial infections, especially on the use of topical steroids. Symptoms suggestive of toxic keratoconjunctivitis were common to all patients. This shows that *A. squamosa* seed extract is toxic to ocular structures, especially corneal epithelium probably due to the various chemicals it contains leading to chemical toxicity. The high incidence of secondary bacterial infections despite prophylactic antibiotic therapy may be either due to preexisting contamination of seeds of *Annona* or due to alteration in the pathogenicity of the normal commensals due to the compromised ocular surface or use of topical steroids. A high degree of suspicion and a detailed history of the use of custard seeds need to be elicited (since most patients do not consider these seeds to be toxic) to make an accurate diagnosis.

To the best of our knowledge, there has been no previous publication of this sort and this is the first case series describing the symptoms, clinical features, management, and prognosis of ocular toxicity due to custard seeds.

We conclude that the seeds of *A. squamosa* are highly irritant and toxic to human corneal epithelium and conjunctiva with a high incidence of secondary infection, and these patients should be treated aggressively with topical fortified antibiotics while avoiding topical steroids. Furthermore, the patients need to be educated about the toxic nature of *Annona* seeds and their potential to cause blindness.

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Conflicts of interest

There are no conflicts of interest.

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