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(REVIEW ARTICLE)

Intoxication of the immature fruit of the ackee (*Blighia sapida* Koenig): Summary and development

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Abstract

Deaths linked to the consumption of plants are sometimes overlooked by health personnel in tropical environments. Parts of several plants are recognized as potentially toxic, including the fruit of the ackee.

This review paper aimed to synthesize data on the toxicity of the fruit of the ackee (*Blighia sapida*) and a brief overview on the measures of management of its acute intoxication.

This was a documentary and analytical study. We made an analysis/synthesis of the articles relating to the poisoning with the immature fruit of the ackee. The PubMed, AJOL and Google scholar databases were used.

The ackee is a plant native to West-Africa. Known by several names, *lissètin* in Fon in Benin, *atsia* in Evé in Togo, *Finzan* in Bambara in Mali, its aril contains lipids, proteins, carbohydrates, vitamins and trace elements. Hypoglycin is present in two forms A (2-methylene-cyclopropane-alanine) and B found in immature fruit, a very toxic compound which disrupts β-oxidation of fatty acids. Acute immature fruit poisoning, manifests as an acute hypoglycemic encephalopathy, gastrointestinal signs, hydro-electrolyte disturbances, metabolic acidosis and liver damage. The detection of urinary dicarboxylic acids is pathognomonic. Its treatment is symptomatic. A crude gastrointestinal and hepatic symptomatology characterizes chronic intoxication.

The ackee is a tree whose unripe fruit is of acute lethal toxicity. Treatment of acute intoxication is symptomatic.

Keywords: Ackee; Hypoglycin; Hypoglycemia; Urinary dicarboxylic acid; Poisoning.

1. Introduction

In the health context that is ours today, where any infant death must be a source of questioning, it becomes indisputable to wonder especially about the causes of those who are preventable. In addition to the causes which are classically incriminated (malaria, infections, etc.), there are many others, such as poisoning, especially in our rural areas, which kill children, outside of the radar of official statistics. In the Republic of Benin and as in the West African sub-region, several plants and fruits constitute an essential food resource [1, 2]. Given their physicochemical properties, some constitute edible poisons that cause sometimes collective infant deaths [3, 4].

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The ackee (*Blighia sapida*), is a tree whose fruit is highly prized by people in certain regions of Benin and the world [1]. The history of this plant relates to cases of death linked to the consumption of its fruit [4]. The first poisoning in Africa dates back to 1984 in Côte d'Ivoire, where mysteriously more than 70 deaths have been recorded [3, 5]. Investigations were needed later to clear the pesticides that were initially implicated. This fruit is said to contain a substance called hypoglycin, responsible for these deaths [6]. Several other cases of morbidity due to the consumption of the aril of *Blighia sapida* have been recorded worldwide [7]. Cases continue in our countries and deserve a closer look.

This synthesis aimed to take stock of the toxicity of the unripe fruit of the apple tree and the measures for managing its acute intoxication.

2. Botanical aspects of *Blighia sapida*

The ackee (*Blighia sapida*) is a medium-sized tree in the *Sapindaceae* family native to West Africa. The plant is said to have been introduced from Guinea to the Antilles, and to Jamaica in 1789, thanks to the slave trade [2, 5, 7, 8]. It is a species close to the "lychee" (*Litchi chinensis*). The ackee belongs to the reign of the *plantae*, to the division of *magnoliaphyta* and to the order of *sapindales* [2]. It is a beech tree, with prominent roots at the base of the trunk. Its foliage is massive, with a dense crown of spreading branches and carried by a robust trunk (Figure 1) [2, 7, 9]. The leaves are fifteen centimeters long. They are oval in shape, ending in a point; dark green in color and shiny at the upper base. The flowers are small, greenish or white in color. They measure less than a centimeter and are arranged in axillary clusters. The fruits, the size of a small pear, are pink to red in color, oval in shape, marked by three protruding ribs five to six centimeters long, sometimes longer (Figure 2). They contain one to three kernels the size of a nutmeg, black in color and shiny [9]. These stones are topped with a mass of ivory, white or cream-colored flesh, which has a nutty or avocado flavor. The black seed has a detestable taste (Figure 3) [7]. *Blighia sapida* is cultivated in tropical regions for its fruit which is widely consumed [10]. It is found in the countries of West Africa [2, 9, 11]. The different parts of the tree are used for several purposes: consumption, manufacture of soaps, pharmacopoeia [1, 12, 13]. He is very well known among the Malinkés, who call him *finzan*, from which comes the name which is sometimes given to him in French, "fisanier". Several other names are used to designate it: finsan fig, sweetbread, fricassee tree. It has various vernacular names (Table 1).

Figure 1 *Blighia sapida* shrub. (Photo Kakpo, 2017)

Figure 2 Not fully ripe fruit of *Blighia sapida* (Photo Kakpo, 2017)

Figure 3 Fully ripe fruit of *Blighia sapida* [6]

Figure 4 Fully ripe fruit of *Blighia sapida*. (Photo Kakpo, 2020)

Table 1 Vernacular names of the ackee [3, 7]

Language	**Vernacular name**
Tagwana	Kou, kohou, koum
Djimini	Kokougo
Baoulé	Kaa
Shien	Pagwé
Attie	Baza
Agni	Founzan, Foufoué, Baza
Koulango	Songo
Wobé	Goihien
Bobo	Finsan
Bambara	Finzan
Haoussa	Fisa, Gwanja Kousa
Ashanti	Achin, akyen, akye
Twi	Ankye, akye, fufuo
Fanti	Twitakwada
Losso	Peso
Ga	Hatschi, Ayigbeatia
Basari	Bugpom
Konkomba	Bugpob
Malinké	Finzan
Ebrié	Atuanbi
Gouro	Tia
Gagou	Sen
Onitscha	Okwocha
Yorouba	Ishin, ishinjife, ishinoka
Bété	Newgouei
Dioula	Finzan
Mooré	Finzan
Kabure	Peso
Tschandjo	Peso
Chumbulu	Kake
Awuna	Adza, atsia
Ewe	Adza, atsia
Kuatchi	Keka
Krobo	Kngatscho
Ibo	Okpu
Boki	Otusi-shet
Kukuruku	Awai
Jekri	Abikotor
Ijaw	Ilipa
Owerri	Okpuocha
Nupe	Ila, ella
Sobo	Ukperehren

Fulani	Feso
Adja	Atjan
Ditamari, somba	Nufugodom, Moufodom
Batombu	Diremou
Natemba	Foulama
Kabyé	Kposso
Koto	KoléKpezo
Moba	Gbeng
Portuguese	castanheiro da África
Fon	Lissètin, Sissitin
English	ackee, akee, akeeapple, achee, vegetable brain

3. Phytochemical composition of *Blighia sapida* aril

The main components of the aril of this fruit are lipids, which constitute more than 40%, an oil level comparable to that of peanuts [7, 11, 13]. Proteins are also well represented with 20% while carbohydrates are low, representing less than 10% [14]. Aril is also rich in vitamin C and contains various other vitamins and minerals, mainly magnesium, sodium, calcium and phosphorus [7, 8, 10, 15, 16]. However, the aril contains, when the fruit is not ripe, a toxic compound, hypoglycin, which exists in two forms A (Figure 5) and B (Figure 6) [2, 8, 17]. It is an amino acid not included in the composition of proteins, isolated (as well as its gamma-glutamyl derivative, hypoglycin B) for the first time in 1955 by Hassal and Reyle [7]. Hypoglycin A is a water-soluble and thermostable compound, therefore not denatured by cooking. Fruit cooking water is more toxic than the fruit itself [7]. It is formed from an alanine residue linked to a methylene-cyclopropane group and whose systematic name is 2-methylene-cyclopropane-alanine. Hypoglycin A is very high (1000 ppm) in the unripe fruit, and its concentration decreases with ripening, until it drops below 100 ppm in the ripe fruit.

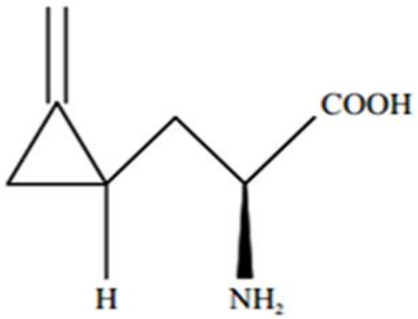

Figure 5 Structure of hypoglycin A [17, 18]

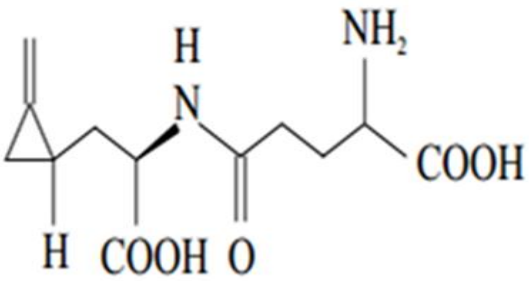

Figure 6 Structure of hypoglycin B [17, 18]

Table 2 presents the quantified composition of the fruit seed of *Blighia sapida*.

Table 2 Phyto-chemical composition of the aril of the *Blighia sapida* fruit [6, 12]

	Quantity/100 g	**Composition of 1 kg of dried aril**
Humidity (water)	57,60 g	6,84±1,13%
Lipids	18,78 g	45,32±2,90%
Carbohydrates	9,55 g	24,43±2,24%
Protein	8,75 g	11,99±1,12%
Fibers	3,45 g	3,21±0,34%
Phosphate	0,098 g	-
Calcium	0,083 g	139,67±0,85 (mg/100 g)
Ascorbic acid	0,065 g	-
Iron	0,00552 g	17,33±0,24 (mg/100 g)
Niacin	0,00374 g	-
Riboflavin	0,00018 g	-
Thiamine	0,00010 g	-
Potassium	-	1503,3±1,89 (mg/100 g)
Magnesium	-	215,33±1,03 (mg/100 g)
Sodium	-	53,17±1,03 (mg/100 g)
Zinc	-	± 0 (mg/100 g)

4. *Blighia sapida* fruit poisoning

4.1. Pathophysiology

Hypoglycin A is found in seeds and arils, while hypoglycin B is only found in seeds. This difference explains the fact that intoxications related to hypoglycin B are rare because the seed is not also consumed. Once ingested, hypoglycin A is metabolized in the liver to methylene-cyclopropyl-Acetyl-Coenzyme A (MCPA-CoA) [5]. This compound disrupts the catabolism of fatty acids in the mitochondria, preventing their oxidation (by inhibiting β-oxidation) and the resulting energy production [10]. MCPA-CoA binds in particular irreversibly to coenzyme A, carnitine and carnitine acyltransferases, reducing their bioavailability and consequently inhibiting β-oxidation of fatty acids [10]. The site where hypoglycine toxicity manifests has been identified as acyl-CoA dehydrogenases which catalyze the first stage of fatty acid oxidation [7]. The process of inhibiting acyl-CoA dehydrogenases by MCPA-CoA is initiated by a deprotonation, followed by a break in bond, leading to the formation of a conjugated carbanion. This carbanion binds covalently to the coenzyme Flavin Adenine Dinucleotide (FAD), which causes enzyme inactivation. The energy that the body needs can then only be produced from carbohydrates [3, 12]. The hypoglycemic coma observed is therefore due to an abnormally exaggerated catabolism of carbohydrates since lipids are almost no longer a source of energy [5].

In addition to the decrease in blood sugar, hypoglycin causes a digestive syndrome made of uncontrollable vomiting, without diarrhea. It also causes convulsions, especially in young children. It is also a riboflavin or vitamin B2 antagonist. Consumption of high level of ackee fruit arils can cause vitamin deficiency, [5]. Figure 7 shows schematic summary of the different mechanisms that lead to this hypoglycemia.

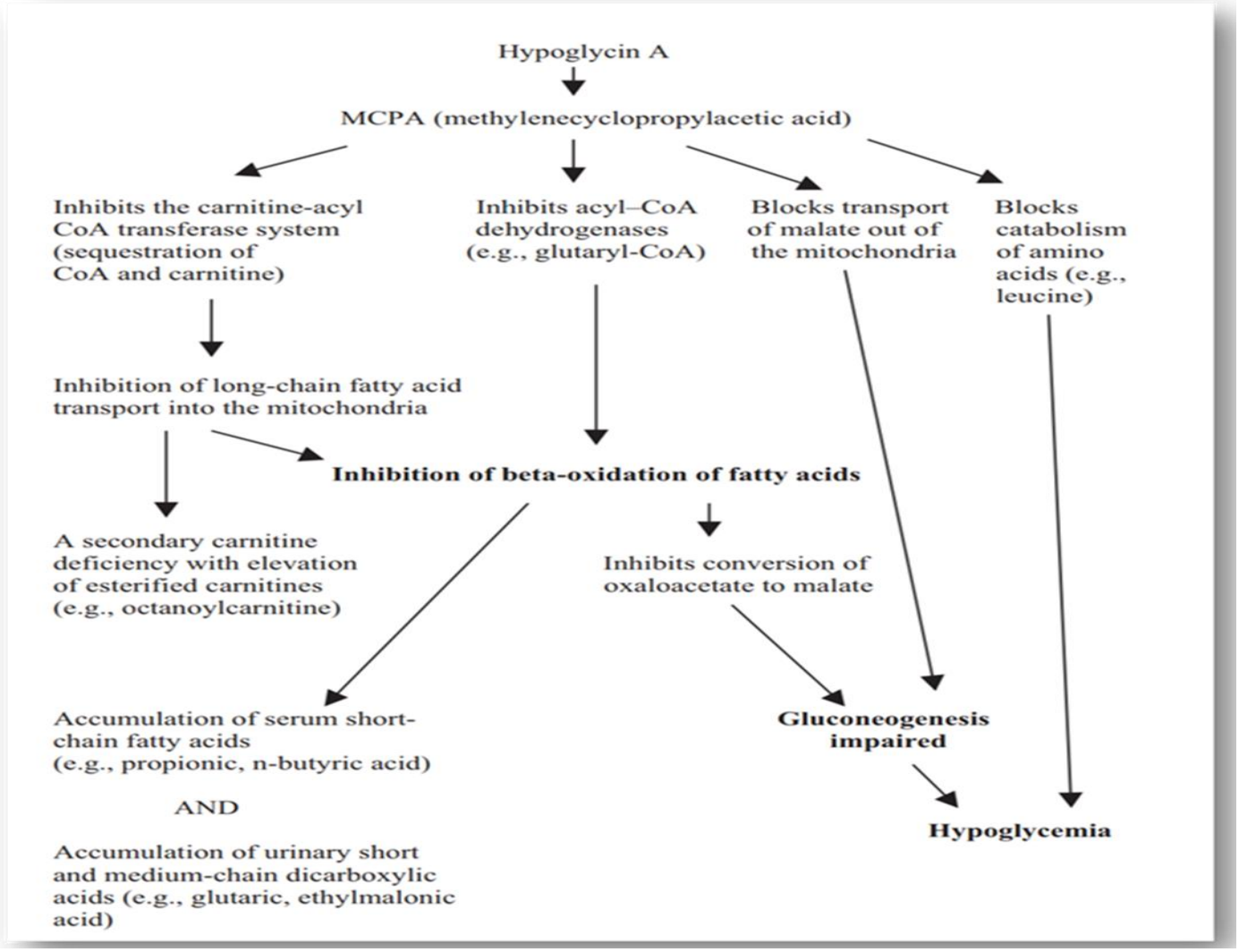

Figure 7 Metabolism and metabolic effects of the ackee fruit toxin, hypoglycin [19]

4.2. Signs

4.2.1. Acute poisoning

Still called emetising disease of Jamaica, acute hypoglycin A poisoning usually appears late in the meal. The affected subjects are very often young children who cannot identify the ripe fruits of the unripe. The weight/amount of toxin ratio also influences the severity of this disease in children. The clinical picture is that of an acute hypoglycemic often fatal encephalopathy. Depending on the extent of intoxication, the time for onset of symptoms may be delayed by several hours. Once started, the progression of symptoms is quite rapid and often of uncertain outcome. The clinical signs observed are diverse and sometimes inconsistent. There is often a deceptive lull before the fatal development. This period of calm must be known to the nursing staff so as not to lower their guard. Death occurs on average in 12 to 24 hours after the onset of signs [2, 3, 7]. The clinical signs observed are of three groups: general signs, gastrointestinal signs and neurological signs.

General signs

They are represented by impairment of the general condition with weakness, hypotonia, pallor and often intense thirst. Body temperature is normal or hypothermia can occur. Tachycardia and tachypnea are also observed in some cases [7].

Gastrointestinal signs

These signs boil down to persistent nausea and vomiting [20]. They are the first alarming symptoms of poisoning. They can be followed by a period of very deceptive lull. Cramps, abdominal pain and diarrhea are often absent [3].

Neurological signs

Neurological signs often start with headache. Above all, generalized convulsions are observed, sometimes preceded by clonic spasms or localized contractions of the limbs, then coma occurs.

From a biological point of view, the manifestations are of several orders [7, 20, 21]:

- A biological sign characteristic of intoxication with ackee fruit, hypoglycemia generally occurs a few hours after the onset of symptoms. Often very severe, it can reach values lower than 0.2 g/L;
- Metabolic acidosis following the accumulation of dicarboxylic acids;
- A hydro-electrolyte imbalance, a consequence of intense vomiting;
- The accumulation of lipids following the inhibition of β-oxidation in the liver cells will cause hepatotoxicity, manifested by: an increase in total and conjugated bilirubin as well as alkaline phosphatases, a syndrome of hepatic cytolysis (increased aminotransferases);
- Excessive elimination of dicarboxylic acids in the urine is a pathognomonic sign of poisoning in the ackee fruit; in particular, ethylmalonic, glutaric and adipic acids. Their detection and dosage makes it possible to establish the diagnosis of certainty;
- Some post-mortem liver biopsies revealed massive micro-vesicular steatosis, surrounded by macro-vesicular steatosis affecting more than 90% of hepatocytes, without necrosis or associated inflammatory lesions. Cases of fulminant hepatitis have been described as linked to the consumption of the ackee fruit [22]

4.2.2. Chronic poisoning

Chronic poisoning by the ackee fruit is poorly documented. The literature mentions the possibility of cholestatic jaundice, observed following the repeated consumption of the ackee fruit. It is clinically characterized by pruritus, intermittent diarrhea, and localized abdominal pain in the hepatic region [23]. Liver tests show increased levels of total and conjugated bilirubin, alkaline phosphatases, and aminotransferases [14]. At liver biopsy, central lobular necrosis is observed [23]. A typical equine myopathy, a relatively rare disease touching horses consuming the seeds or seedlings of some maples, is known to be caused by hypoglycin A [21].

4.3. Supported

It often comes down to symptomatic treatment, depending on the clinical and biological manifestations observed. This care begins at the place of intoxication and must continue in a hospital environment.

4.3.1. First steps at the scene of intoxication

If the poisoning is recent and the patient is still conscious, he should be vomited immediately. This gesture can reduce the digestive absorption of the toxic and therefore limit its effects. It should be given to bite into pieces of sugar or to drink any glucose-containing substance to prevent hypoglycemia.

The transfer of unconscious patients must be done urgently and in a lateral safety position. The circumstances of discovery (notion of ingestion of unripe ackee fruit or the presence of unripe ackee fruit in or near the family concession) are very important for diagnosis and management.

4.3.2. In a hospital environment

Symptomatic treatment must be implemented upon admission to the hospital. It consists of taking charge of hypoglycemia, convulsions, hydro-electrolyte imbalances and possible coma.

Hypoglycemia

The correction of hypoglycemia is the first emergency of this therapy. It is done by the infusion of glucose serum (SG): 1cc/kg of SG 30% or 3 to 5cc/kg of SG 10% [7, 21, 24-28]. Glucagon can be used from 0.5 to 1 mg intramuscularly or subcutaneously. A relay to the 10% glucose serum in vein guard or an oral intake of slow sugar depending on the patient's condition must be systematic. Other authors suggest the use of cortisone [3]. When the venous route is impossible, a glucose solution must be provided by oral route or by a nasogastric tube. The response to treatment should be checked after 30 minutes. Highly concentrated solutions should be avoided as much as possible as they can lead to a state of hyper-osmolarity as well as reaction hypoglycemia in reaction to an increased secretion of insulin.

The glucose intake usually required to maintain acceptable blood sugar is 3 to 5 mg/kg/min [7, 24-28].

Convulsions

Intravenous or intra-rectal administration of diazepam at a dose of 0.5 mg/kg allows the convulsions to subside, possibly repeated after half an hour if the attacks do not subside. If convulsions persist, the use of phenobarbital and then clonazepam (RIVOTRIL®) is indicated [7, 24-28].

Maintenance of vital functions

Clearance of the airways, ventilation, vascular filling, oxygenation and if necessary intubation to provide assisted ventilation are measures to be taken. These gestures are very important and are done according to the child's weight and age [24-28].

Gastric lavage

Gastric lavage is never the emergency for which priority should be given, since it is an evacuating treatment aimed at reducing the digestive absorption of the toxic. In all cases, vital failures must be corrected before practicing gastric lavage. The earliness and effectiveness of initial symptomatic treatment are more important than gastric lavage.

Gastric lavage requires certain conditions, in particular the good mastery of the technique by the nursing staff, the commitment or not of the vital prognosis, the duration of the ingestion which must not exceed three hours and the absence of ingestion of corrosive substances or derivatives of the associated oil. Make sure that a vacuum cleaner is available in case the child vomits. From a practical point of view, put the child on the left side, head down; measure the length of the probe to be inserted. The introduction of the probe is done by mouth. You just have to make sure it's in the stomach. The actual washing is carried out with saline serum at the rate of 10 cc/kg which is sent by the probe and which is removed immediately. The volume of liquid discharged should be approximately equal to that administered. Washing is stopped as soon as the liquid without gastric residue is obtained [24].

Care-nursing

They boil down to the prevention of bedsores, phlebitis and the administration of eye drops.

Monitoring sheet

It must include the following points: general information concerning the patient, vital signs (indicated by the score obtained on the coma scale or degree of consciousness, temperature, respiratory rate, pulse and weight), water balance, presence of clinical signs, presence of signs of complication, results of examinations, treatments administered, new signs or new complications.

5. Conclusion

The ackee is a tree whose unripe fruit is deadly toxic. Hypoglycin, a non-standard amino acid found abundantly in its unripe fruit, is responsible for the main manifestations of acute intoxication, by blocking the fatty acid oxidation. The dangerous nature of its immature fruit is not known. The management of acute intoxication is essentially focused on the correction of hypoglycemia and the maintenance of vital functions.

Compliance with ethical standards

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Disclosure of conflict of interest

No conflict financial authors declared

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