

The seeds of croton species are not only rich in macronutrients but also the micronutrients. Bello et al. (2014a) reported that the seed of *C. zambesicus* are richer in strontium (869.27 mg/100g), potassium (2.2 g/100g) and iron (467.53 mg/100g) than its leaves. Another study by Adeyinka et al. (2013) on seeds of *C. penduliflorus* found that they are rich in magnesium and calcium which are important micronutrients. Removal of the seed coats significantly reduces the mineral content by 8.1% while increasing the fat content by 16.02% (Adeyinka et al., 2013).

Extraction of oil from the seeds leaves a protein rich seedcake, whose utilization in animal feeding is highly recommended. A study on *Jatropha curcus* seedcake, a tree from the same sub-family with croton with similar toxicity concerns, reported a protein content of 43.48% (Sánchez-Arreola et al., 2015). Oil extraction bears the benefit of reducing the phorbol esters, but concerns of toxicity still remain with the presence of toxic proteins (Rajput and Gaur, 2015). Evaluation of amino acid profile of croton seedcakes in comparison with common animal feed seedcakes by Peoples et al. (1994), showed that seedcakes of *C. capitatus* are richer in essential amino acids as compared to the others (Table 3).

Table 3-Essential amino acid profile of *Croton capitatus* seedcakes in comparison with other common animal feed seeds (% DM)

Essential amino acid	Sunflower	Croton (<i>C. capitatus</i>)	Redwood amaranth
Arginine	0.61	1.29	0.53
Glycine (plus Serine)	0.96	1.01	0.73
Histidine	0.11	0.24	0.12
Isoleucine	0.31	0.42	0.23
Leucine	0.51	0.63	0.38
Lysine	0.47	0.61	0.41
Methionine (plus cysteine)	0.11	0.16	0.08
Phenylalanine	0.36	0.50	0.25
Phenylalanine (plus tyrosine)	0.55	0.80	0.45
Threonine	0.31	0.40	0.22
Valine	0.36	0.57	0.29

Adapted from Peoples et al. (1994).

Phyto-chemicals and antinutrients in *Croton spp.* seeds

Phytochemicals in croton seeds range from health promoting to compounds with deleterious effects to health. The phytochemicals that have been found in the seeds of different croton *spp.* include diterpenes, phorbol ester, alkaloids, terpenoid, flavonoids, tannins, cardenolides and many others as shown in Table 4 (Parameswararao et al., 2016). The major phytochemical of concern in croton *spp.* seeds are the phorbol esters. This is majorly in the seed oil, with the most active phorbol ester being 12-O-tetradecanoylphorbol-13-acetate (TPA) (Nath et al., 2013). These compounds have tumour promoting properties. Seeds of similar species of croton from different regions also differ in their phyto-chemical composition. The proanthocyanodin and alkaloid property of croton induces a red sap property in croton seeds (Prassana and Karpaga, 2015).

Table 4 - Phyto-chemicals in different species of croton seeds

Croton <i>Spp</i>	Country of origin	Phyto-chemicals	Reference
<i>C. tiglium</i>	Far East	Alkaloids, flavonoids, terpenoids and phorbol esters	(Dey et al., 2014)
<i>Croton bonplandianum</i> Baill	India	Squalene, (9Z, 12Z)-octadeca-9, 12-dienoic acid, methyl 12-oxo-octadec-9-enoate, alkaloids, terpenoid, flavonoids, tannins, cardenolides and phytol.	(Parameswararao et al., 2016)
<i>C. tiglium</i> Linn.	India	Resin, resin, steroids, sugars, saponin	(Kishore et al., 2013)
<i>C. tiglium</i>	Pakistan	Alkaloids, steroids, terpenoids, glycosides and saponins.	(Abbas et al., 2011)
<i>C. bonplandianum</i>	India	Resins, alkaloids, saponins, phenols, flavonoids and steroids.	(Jeeshna et al., 2011)
<i>C. megalocarpus</i>	Kenya	Saponins, flavones, alkaloids, glycosides, terpenoids, steroids and flavonoids	(Waiganjo et al., 2013)

Safety of croton oil and seedcake

The croton oil is toxic to all living organisms, ranging from simple single cell organisms like bacteria to complex organisms such as the vertebrates (Pagani et al., 2017). The compounds that are known to be responsible for this toxic property include cardiac and cyanogenic glycosides, lectin, phorbol esters and alkaloids (Yumnamcha et al., 2014). Yumnamcha et al. (2014) in their study on *C. tiglium* found saponins and alkaloids in croton oils, which are known to possess DNA damaging property thus are genotoxic. Similar findings were reported by Aylate et al. (2017) in their study on the extracts from *C. macrostachycus*. Phorbol esters in the croton oil and seedcake has been associated with tumour-

enhancing property (Dey et al., 2014). Phorbol esters occur to the tune of 3-5% in the fatty acids in croton seeds (Jain, Mangal and Kushwaha, 2015). Sharma et al. (2016) reported a skin-cancer inducing property in the croton seed oil. The most studied mechanism by which phobol esters causes cancer is its role in binding and activating protein kinase C (PKC) that plays a role in signal transduction (Goel et al., 2007). They hyperactivate the PKC thus causes a proliferation of cells thereby amplifying the efficacy of carcinogens in the body of an animal. These phobol-12,13-diester are also responsible for the purgative and irritant property of ingested seeds. As it had been indicated earlier TPA is the most renowned toxic phobol-ester in croton seeds is the (EFSA CONTAM Panel, 2015).

Concerns have been raised with regard to the safety of the croton oil and seedcake as animal feed. Apart from croton oil inducing gastrointestinal discomfort, the proteins in the seedcake have been shown to possess proinflammatory effects on the gastrointestinal system in clinical trials (Liu et al., 2017). EFSA has raised concerns on the safety of *C. tiglium* or its seed cake as an animal feed as it contains crotonin I which is a ribosome inactivating protein (RIP II) thus causes acute death of animal (Alexander et al., 2008). The compound has a LD₅₀ of 20mg/kg body weight in mice.

Other health concerns have also been raised on oils from some species of croton. Ojokuku, et al. (2011) posits that in as much as *C. penduliflorus* seed oil has the positive hypocholesteremic health effect, it also poses the risk of inducing anemia. Crotonic acid, a compound in croton spp. seed oil, induces hemagglutination and hemolytic activity in animals (El-Kamali et al., 2015). *Croton tiglium* L. seed oils also possess piscicidal properties that some communities have exploited in fishing especially in India (Rajput and Gaur, 2015; Saha et al., 2015). Acute toxicity studies on the *C. penduliflorus* seed oils also showed deleterious effects on some internal organs at doses of 200, 600 and 800 mg/kg of feed in mice (Ashafa et al., 2012). *C. penduliflorus* seed oils have been shown to cause adverse effects on the kidney and nervous systems of animals (Ojokuku et al., 2011). Extracting oil is not an automatic procedure for removal of toxins from the seedcake in as much as the most toxic compounds, phorbol esters, are in the oil (Sadubthummarak et al., 2013).

CROTON SEEDCAKE AS ANIMAL FEED

There are only few documented studies of the exploitation of croton seeds and seedcakes as animal feed. Most documented feeding trials have exploited whole seeds of croton spp with varied efficacy as shown in Table 5. However, care is advised as these seeds have toxins that have deleterious effects on the health of the animal. Feeding trials by Gadir et al. (2003) on goats using *C. macrostachycus* whole seeds at 1g/kg and 0.25g/kg showed 100% mortality for all animals and weight loss of 21.6% and 26.3% respectively within 21 days. On the other hand, Thijssen (1998) reported satisfactory feeding efficiency, weight gain, feed intake and growth rate of the chicks fed on feeds with *C. megalocarpus* seedcake incorporated at the proportions of 10-25%. *C. macrostachycus* based feeds were found to be some of the high proteins feeds suitable for use in aquaculture (Kassahun et al., 2012). Feeding trials for croton have also been done on fishes. Dada and Adeparusi (2012) reported an increased fecundity index of 21,987.16 for catfish that were fed on 200g/kg body weight of *C. zambesiscus* seeds. A study by El-Kamali et al. (2015) established that croton seeds incorporated into feed for rats in experimental diets induced no deleterious hematological effects.

Table 5 - Performance of animals in feeding trials utilizing croton seeds

Croton spp.	Test animal	Type of seed	Amount incorporated	Performance of the animal
<i>C. macrostachys</i>	7 month-old Nubian kids	Whole	1 g/kg body weight	Mortality within 7-21 days
<i>C. macrostachys</i>	6 month-old Nubian kids	Whole	0.25 g/kg body weight	Mortality within 7-21 days
<i>C. zambesiscus</i>	Catfish (<i>Clarias gariepinus</i>)	Powdered seed	50 g/kg body weight	Increased fish weight and increased fecundity
<i>C. zambesiscus</i>	Catfish (<i>Clarias gariepinus</i>)	Powdered seed	100 g/kg body weight	Increased fish weight and increased fecundity
<i>C. zambesiscus</i>	Catfish (<i>Clarias gariepinus</i>)	Powdered seed	200 g/kg body weight	Increased fish weight and increased fecundity
<i>C. zambesiscus</i>	Wistar rats	Aqueous extract of powdered seed	75 mg/kg body weight	0.07 g/day weight gain
<i>C. zambesiscus</i>	Wistar rats	Aqueous extract of powdered seed	300 mg/kg body weight	0.68 g/day weight loss
<i>C. zambesiscus</i>	Wistar rats	Methanol extract of powdered seed	75 mg/kg body weight	0.71 g/day weight loss
<i>C. zambesiscus</i>	Wistar rats	Methanol extract of powdered seed	300 mg/kg body weight	0.28 g/day weight loss
<i>C. tiglium</i>	One-week old Chicks	Seedcake	10-25 % incorporated in commercial chick mash	Increased growth rate of up to 117.5 g

There are other plants that are similar to *Croton spp.* that have had their seedcakes exploited as animal feeds. *Jatropha curcas* (belongs to the same sub-Family with croton) seedcake were incorporated into soybean meal at 25% both as raw *Jatropha* seedcake and detoxified *Jatropha* seedcake, where 33.3% mortalities was noted in each case

(Elangovan et al., 2013). Detoxification in this study employed addition of 3% sodium bicarbonate as similar to croton *spp.* seeds, toxicity concerns have been raised for *Jatropha* seeds. Another study by Barros et al. (2015) noted more deleterious effects as increasing the *Jatropha* seedcake in the diet of broiler chicken, resulted into decreased body weight and diminishing size of spleen and kidneys; chicken fed on 100g *jatropha* seedcake per kg of diet lost up to 21.6g/day. This was attributed to the phorbol esters in the seedcake. Thus, detoxification of these seedcakes is necessary before their utilization as feeds.

Research has delved further into making croton seeds safe for use as animal feeds. Solvent extraction accompanied with heat treatment of the seed cakes has successfully been employed as a way of producing feeds free of toxic levels of phorbol esters (Goel et al., 2007). Phorbol esters are mainly in the croton oil rather than the seedcake (Pagani et al., 2017). However, oil extraction is not an assurance of total removal of the phorbol esters from the seedcake (Sadubthummarak et al., 2013), thus other efficient detoxification methods are necessary.

In India, milk is employed as a detoxicant of croton seeds but this has only been evaluated in its medicinal use but not as a feed (Maurya et al., 2015). A study by Pal et al. (2014) found that the use of milk in detoxifying *C. tiglium* seeds reduced the phorbol esters and crotonic acids by 65.4% and to undetectable levels respectively. Kishore et al. (2013) reported that the method has no significant impact on the phytochemical components such as alkaloids, saponins, resin and saponins. However, it reduces the fat content thus would reduce the phorbol esters (Jain et al., 2015). The effect of such treatment on the nutritional composition of these seedcakes has also not been studied. Phorbol esters that have been traced in seedcakes in plants with the same toxicity as croton have been shown to degrade after 21 days of storage at moisture content of 130g/kg (Fujiki et al., 2017). This, points to a possible way of detoxification of the seedcakes to free them of these tumour-enhancing compounds thus making them safe as feeds. In the detoxification procedure, it is necessary not to induce any deleterious effects in the nutritional composition. Another study on *Jatropha* seedcake found that thermal treatment at 120°C and 220°C, followed by addition of 10% adsorbing bentonites (nanoparticle of zinc oxide) and 4% NaHCO₃ and incubation for four weeks, reduced phorbol esters to non-toxic levels of 0.04-0.05 mg/g with no cytotoxicity while on other hand not affecting the proximate composition (Sadubthummarak et al., 2013). Absence of cytotoxicity is an indication of absence of the toxic lectin proteins.

In croton *spp.* seedcakes, the most injurious proteinous compounds are the crotons, a lectin class of proteins (Vasconcelos and Oliveira, 2004). Crotons are hemolytic proteins that exhibit hematological adverse effects in animals. Croton I and II exhibited toxicity in mice at acute LD₅₀ of 1.33 and 4.38 mg/mouse respectively (at 72 hours), and delayed LD₅₀ of 0.92 and 1.68 mg/mouse respectively (at 7 days) (Stirpe et al., 1976). The *C. tiglium* seeds have an acute LD₅₀ of 2000mg/kg body weight (Harshavardhan et al., 2016). For these seedcakes to be exploited for feeds, it would be necessary to detoxify them of these proteins. In the detoxification of *jatropha* seeds, it was found that samples that were deshelled followed by defatting, enzyme hydrolysis (pectinase and cellulase) and treatment with 60% methanol and 65% ethanol; lowered toxic lectin proteins by 52.8% and other antinutrients such as saponins, phytic acid, total phenolics and trypsin inhibitor activity by 65.1%, 31.8%, 71.9% and 21.5% respectively (Xiao et al., 2011). The treatment also improved the protein digestibility corrected amino acid scores by 47.1% and crude protein content by to 15.22%.

CONCLUSION

There is increasing utilization of seeds croton *spp.* for oil extraction expanding the use of croton, but the possibility of extending the value chain by using the seedcake as a feed remains less explored. The nutritional composition of the croton seedcakes make them viable for possible exploitation as poultry feed. However, the toxicity of these seeds induced by various phytochemicals still remains the greatest challenge to this venture. Croton has been shown to pose various toxic effects to various animals ranging from simple organisms to complex ones including poultry. A possible way for detoxification of these seeds serves to ameliorate their quality as feeds. Practical ways for detoxification have been tried but not possibly for its utilization for feed for poultry or any other animal. The effect of such technique to the nutritional composition has also not been explained. For its possible use as a feed, it would be important for the safety of croton seedcakes to be evaluated to provide scientific justification for its use. Future research should evaluate the use of these identified detoxification technique and their influence on nutritional composition of the croton seeds.

DECLARATION

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Authors' contribution
All the three authors reviewed the paper and contributed in developing the content.

Availability of data
The data can be availed to the journal upon request.

Consent to publish
Not applicable

Conflict of Interest

The authors declare they have no competing of interests.

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