



REVIEW

Ground Flaxseed – How Safe is it for Companion Animals and for us?

Michael Lindinger*

The Nutraceutical Alliance, Torrevieja, Spain

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ABSTRACT

EFSA released the 89-page Scientific Opinion “Evaluation of the health risks related to the presence of cyanogenic glycosides in foods other than raw apricot kernels”. This opinion, and the ensuing media coverage, has left uncertainty in the minds of consumers, feed and supplement manufacturers and flaxseed producers of how much ground flaxseed can safely be consumed without crossing the threshold of cyanide toxicity. This editorial updates the science and tries to bring clarity to the question “how much flaxseed can I safely feed my dog, cat, horse on a daily basis?” and “how much can I safely eat?” The great majority of ground flaxseed products have a cyanogenic glycoside content of less than 200 mg / kg seed. For people, consuming 30 grams of such flaxseed the average peak blood cyanide concentration will be about 5 µmole / L, much less than the toxic threshold value of 20 to 40 µmole / L favoured by EFSA. Thus, as much as 120 grams of crushed / ground flaxseed can be consumed by a 70 kg adult person before a toxic threshold of 40 µmole / L is reached (up to 1.7 grams ground flaxseed / kg body weight). The toxic threshold of cyanide for dogs is 2 to 4-fold greater than for humans, and unknown for cats and horses. The daily serving amounts for dogs and cats are about 0.23 grams / kg body mass per day, which will result in blood cyanide well below the toxic threshold. The highest recommended daily serving amount for horses is 454 grams per day, or 0.8 to 2 grams per kg / body mass depending on mass of the horse. This amount for horses should not be exceeded.

1. Introduction

The feed ingredient and food supplement industries for both humans and animals are reacting to the release of the 89-page EFSA “Scientific Opinion” entitled **Evaluation of the health risks related to the presence of cyanogenic glycosides in foods other than raw apricot kernels** <https://www.efsa.europa.eu/sites/default/files/consultation/consultation/181127-ag.pdf>. Statements at the heart of the issue include:

“Estimated acute {and chronic} exposures to cyanide originating from foods containing CNGs [cyanogenic glycosides] across 43 different dietary surveys and all age groups ranged from 0.0 to 13.5 µg/kg bw per day”

and

“At the 95th percentile, the ARfD was exceeded by up to about 2.5-fold in some consumption surveys for ‘Infants’, ‘Toddlers’, ‘Other children’ and the adolescent age groups.”

Note: ARfD is the acute reference dose, above which

*Corresponding Author:

Michael Lindinger,

The Nutraceutical Alliance, Torrevieja, Spain;

Email: michael@nutraceuticalalliance.ca

cyanide is more likely to have toxic effects; the ARfD for humans is 20 µg cyanide / kg bw per day for chronic consumption, and 80 µg CN / kg bw per day for acute consumption. Read below for how much ground flaxseed this equates to.

The reporting of this document by the press, in particular that in Britain (<https://www.dailymail.co.uk/sciencetech/article-7367955/Scientists-warn-superfood-porridge-topping-flaxseed-cause-cyanide-poisoning.html>), is generating justifiable concerns by both manufacturers and consumers of flaxseed products. The basis for the concerns arises from the following two statements:

(1) *“Depending on the body weight, consumption of 1.3 g – 14.7 g ground linseed containing a high concentration of 407 mg CN/kg could reach the ARfD”.*

(2) *“The highest acute and chronic exposures were estimated for ‘Infants’, ‘Toddlers’, and ‘Other children’”.*

Granted, the EFSA Scientific Opinion admits that this is a worst-case scenario if consuming a product with a very high content of cyanogenic precursors.

Most people are aware that cyanide is a poison, and they would be correct in saying that there is really no safe amount of cyanide, i.e. there is no known concentration of cyanide in the body that exerts a beneficial effect in normal, healthy individuals. The concern, therefore, is that ingestion of flaxseed in foods and supplements will result in the production of cyanide in the body and produce toxic effects. The threshold for cyanide toxicity in the human body is a daily ingestion in the range 0.5 to 3.5 µg / kg bw, so concentrations lower than 0.5 µg / kg bw should not result in any observable toxic effect in over 97% of the population. Some people (~3% of the population) may be more sensitive.

Directive 2002/32/EC16 provides a maximum content of hydrocyanic acid (essentially cyanide) in feed materials and complete feeding stuffs of 50 mg/kg of food (relative to a moisture content of 12%). Exceptions are linseed, linseed cakes, and manioc products/almond cakes for which maximum contents are 250, 350 and 100 mg of cyanide / kg, respectively and complete feeding stuffs for chicks which can contain a maximum of only 10 mg/kg (EFSA, 2018).

But before getting into how much is safe of us or our companion animals to eat, we need to have a better picture of what type of flaxseed (or linseed) product is being consumed. The main concern is with fresh, crushed or ground flaxseed. Not whole flaxseed from which little cyanide is formed and released when consumed, nor flax oil which is extracted from the seed and does not contain appreciable amounts of cyanogenic glycosides or the enzymes needed to produce cyanide from cyanogenic glycosides. It is also

not with some types of treated ground flaxseed.

Scientists have developed ways of treating flaxseed to prevent cyanide production, with the ability to conserve all of the nutritive and nutraceutical benefits. Using fresh, crushed flaxseed Yamashita et al. [24] developed a commercial-scale method to enzymatically release cyanide and effectively remove the cyanide by steam-evaporation. Steam-evaporation was more effective than heating or lyophilisation to evaporate the cyanide. This method lowered the residual cyanide content below the detection limit without affecting the protein, fat, fibre and lignan content of the linseed. More recently, Wu et al. [23] developed a fermentation technique that can be performed on a commercial scale with the benefit of lower energy consumption and no environmental pollution compared to steam evaporation. Importantly, “the detoxified flaxseed retained the beneficial nutrients, lignans and fatty acids at the same level as untreated flaxseed”.

Other forms of heat-treatment to detoxify crushed flaxseed (boiling, roasting, autoclaving, microwave) may not result in appreciable cyanide production in the body because the heat destroys the enzymes responsible for cyanide production. Some people may not want buy such heat-treated products because they are of lower nutrient value, particularly for the beneficial unsaturated fatty acids and because removal of cyanogenic precursors is incomplete [2,7]. Such heat-treated products would, however, certainly be safer as far as the cyanide issue is concerned.

2. Fresh, Crushed or Ground and Untreated Flaxseed – How Much is Safe to Eat?

So how much fresh crushed or ground flaxseed can one safely eat? Particularly in view of the fact that many product labels and websites are advising people to consume 30 grams / day and sometimes more. How much is safe depends on the content of the cyanogenic precursors present in the product.

Table 23 of the EFSA Scientific Opinion provides for how much ground flaxseed can be consumed without exceeding the ARfD. For toddlers (infants) the amount should not exceed 1.7 grams per eating occasion, and this value becomes 10.9 grams for adults. Therefore a daily maximum amount for adults with 3 eating occasions would be 32.7 grams.

In flaxseed the two main cyanogenic precursors are the glycosides linustatin and neolinustatin [4] and there may be small amounts of linamarin [3]. Enzymes (β-glycosidase enzymes) naturally present in the cell walls of flaxseed hulls catalyze the conversion of the glycoside precursors to cyanide. Cyanide binds to proteins in the mitochondria

of all cells and this results in the inhibition of oxidative phosphorylation, the primary process by which cells generate ATP (cellular energy). Oxidative phosphorylation is required for life.

The EFSA Scientific Opinion provides the following information:

“The acute lethal oral dose of cyanide in humans is between 0.5 and 3.5 mg/kg body mass^[9]. The toxic threshold value for cyanide in blood is considered to be between 0.5 (~20 µM) and 1.0 mg/L (~40 µM), the lethal threshold value ranges between 2.5 (~100 µM) and 3.0 mg/L (~120 µM). Signs of acute cyanide poisoning in humans include headache, vertigo, agitation, respiratory depression, metabolic acidosis, confusion, coma, convulsions, and death. Poisoning cases, some fatal, have resulted from ingestion of amygdalin preparations, bitter almonds and cassava. Several neurological disorders and other diseases have been associated with chronic exposure to cyanide in populations where cassava constitutes the main source of calories.”

Based on the limited data available, the EFSA recommends an acute reference dose (ARfD) of 0.020 mg CN / kg body mass, also established by FAO/WHO^[6] for chronic consumption. For acute consumption an ARfD of 0.080 mg CN / kg is used. In an Australian assessment^[8] it was determined that a “high consumption of linseed containing bread led to exposure estimates of up to 511 µg HCN/kg bw per day thereby exceeding the ARfD of 80 µg HCN/kg bw per day (EFSA, 2018).

With respect to flaxseed, there have been only two human studies that have examined the pharmacokinetic aspects of cyanide after ingestion of linseed (flaxseed)^[1,25]. Also, the Schultz et al. study appears to have used whole flaxseed, not crushed or ground flaxseed, so therefore the bioavailability of cyanide will be much lower than if a ground product had been used^[1].

Schultz et al.^[25] reported 3 main trials:

In the acute trial, 20 normal subjects and 5 patients consumed 30 grams of flaxseed (capable of producing ~9 mg of cyanide in the body). The dosage of cyanide, for a 70 kg person, is thus 0.13 mg / kg body mass, which is 1.6 times higher than the EFSA-recommended acute ARfD of 0.080 mg / kg body mass. Now one can appreciate the concern. A peak increase in plasma cyanide occurred at 15 – 30 minutes and concentration returned to baseline by 2 hours. No adverse effects were reported.

In the second chronic trial, 25 normal subjects consumed 15 grams of flaxseed, three times daily, for up to 5 weeks. The daily dose of cyanide equivalents was 13.5 mg, or 0.19 mg / kg body mass, which is 10 times higher than EFSA-recommended chronic ARfD of 0.020 mg / kg

body mass. There were increases in thiocyanate (cyanide breakdown metabolite) in plasma and urine throughout the trials.

One subject consumed 100 grams of flaxseed in a single dose, and for this subject plasma cyanide did not increase above baseline. In contrast, when this subject ingested 3, 6 or 12 mg of potassium cyanide the concentration of plasma cyanide peaked 20 to 30 minutes later and returned to baseline by 3 hours.

Abraham et al.^[1] used fresh, ground flaxseed with a serving amount of 30.9 grams and a cyanide-equivalent dose of 6.8 mg (0.08 to 0.1 mg / kg body mass), consumed by 12 healthy subjects. This was approximately the EFSA chronic ARfD of 0.08 mg / kg body mass). It is also known that the concentration of cyanide inside red blood cells is about 10-fold greater than in plasma^[9], and Abraham et al.^[1] measured total blood (not just plasma) concentration of cyanide. Peak blood cyanide occurred 30 – 60 minutes after ingestion, and varied widely from 1.7 to 13.9 µmoles / L with a mean (\pm SD) of 6.4 ± 3.3 µmoles / L. In one subject that consumed 100 grams, a sustained peak cyanide of 42 µmoles / L occurred between 2 and 3 hours after ingestion and rapidly returned towards baseline over the next 3 hours. No adverse events were reported.

Abraham et al.^[1] also reported that there are “no reports on cyanide poisoning after consumption of linseed [were] found in the literature”. And I also could find no reports.

The highest daily dose reported in the literature is 80 g of ground linseed given as “fiber shock” in a private spa setting^[20]. The typical high dose recommendation by health practitioners is 15 grams three times daily (EMA 2006) with Abraham et al.^[1] stating this “this dose is safe with respect to possible acute toxicity of cyanide”.

The normal content of cyanogenic precursors present in flaxseed from many sources in different continents ranges from less than 80 up to about 300 mg cyanide-equivalents / kg seed^[1]. Using data from Abraham et al.^[1] one can arrive at the following generalizations for fresh, ground flaxseed: Consuming 30 grams of flaxseed with a cyanogenic precursor content of 200 mg / kg seed will result in an average peak blood cyanide concentration of 5 µmole / L. This is less than the toxic threshold value of 20 to 40 µmole / L favoured by EFSA. Using these scientific data as a guide, as much as 120 grams of crushed / ground flaxseed can be consumed before a toxic threshold of 40 µmole / L is reached. For the ‘average’ 70 kg person this equates to 1.7 grams ground flaxseed / kg body mass.

3. Translating This for Our Dogs, Cats, Horses

Ground flaxseed is widely used in pet foods, as well as in veterinary health products and various types of supplements. Evidence-based research in the target species is very low, with the majority of studies supporting product claims coming from studies performed on mice and rats. Research performed using dogs suggests that it can be added to the diet to support g.i. health ^[12,21] blood lipid profile ^[5], skin health ^[14,15,19] and reproductive health ^[13]. Studies using cats also support a role for reproductive health ^[13] and modulation of immune health and inflammatory responses ^[17]. While flaxseed, as well as flaxseed oil, is widely used to supplement the diet of horses there are few published research studies. Research using flaxseed (not the oil) in horses supports an improved blood and tissue lipid profile and hematology ^[10,18,22], immune function ^[22] and skin health and immune response ^[16].

In dogs and rats, LD50s (lethal dose for 50% of the animals) were equivalent to 2.13 and 4.0–6.03 mg CN / kg bw, respectively. The lowest lethal dose identified in humans was 0.56 mg cyanide/kg body mass. These values have not been determined for cats and horses, and it will be assumed that the LD50 would be in the range of 1 mg CN / kg body mass.

(For a typical ground flaxseed product containing 200 mg cyanide-equivalents / kg, a mammal would need to consume 10 grams of flaxseed per kg body mass to reach the lowest LD50 of 0.56 mg cyanide / kg body mass. A safe limit would be 10-fold lower, or 1 gram of flaxseed / kg body mass, which is about 2-fold greater than for humans, as described above).

The serving amounts for dogs and cats are typically provided using teaspoons and tablespoons. One teaspoon of ground flaxseed weighs about 2 grams, and a tablespoon weighs about 7 grams. The body mass range for adult cats is from 2 to 10 kg, and serving amounts are scaled to body mass. The lowest serving amounts for very small dogs (~2 kg body mass) is 1/8 teaspoon / day, thus the daily serving dosage works out to 0.125 grams / kg body mass per day. In the largest breeds (~60 kg body mass) a recommendation is to start with up to 2 tablespoons (14 grams), thus the daily serving dosage is 0.23 grams / kg body mass per day. These dosages are 5 to 10 times lower than what could be considered a safe maximum limit. It is likely that all known commercial dog and cat foods or supplements containing ground flaxseed should not be of any concern to the pet owner or veterinarian.

For horses, a recent recommendation in a trade blog is that up to 1 pound (454 grams) of fresh, ground flaxseed can be fed to horses per day ⁽¹¹⁾ <https://thehorse.com/148473/5-facts-about-flax/>. No research has been

cited to support the statements. Therefore the 1 pound per day recommendation would be ‘safe’ as the cyanide dose would be about 10-fold lower than the assumed LD50. Most recommendations are in the 100 gram per day range, with some short-term recommendations approaching 800 grams per day for adult horses. Short-term use of fresh, ground flaxseed at more than 500 grams per day should be used under close veterinary supervision because, based on rodent studies, signs of toxicity may occur in sensitive animals at this dose.

4. What do Consumers Need to do?

Consumers are right to ask questions. They should ask questions like: Is this product safe, and how much can I safely eat? What is the level of cyanogenic precursors present in these products? How do I know if this product has been processed to destroy the enzymes responsible for producing cyanide? Are you able to show me something on paper that certifies these levels for this product?

Consumers should not take just the word of their retailer. Retailers are not scientists they do not fully understand the science or health concerns and may not be able to properly understand product specification sheets. If you can, obtain the information and take it to your physician or pharmacist.

5. What do Manufacturers Need to do?

Manufacturers of ingredients, foods and supplements are for the most part very responsible and want to produce safe products that work the way they are supposed to.

Manufacturers need to ask their flaxseed suppliers for product specification sheets that detail the amount of cyanogenic precursor, state if the product is processed to destroy the cyanide-producing enzymes, among many other things. If their supplier is not willing to provide this information, then they should not purchase that product.

Manufacturers should be proactive in allaying the concerns of companies and people purchasing their products, and freely supply supporting documentation and information.

6. What do Flaxseed Producers Need to do?

Aside from the consumer, the flaxseed producer remains in a high-risk situation with the classification of flaxseed as having a high potential for cyanide production. The current media coverage may translate to a moderate potential for lost revenue resulting from decreased sales. Now, we have known for decades that crushed / ground flaxseed results in cyanide production, but it has not really been an issue because the amounts produced do not cause

toxic levels of cyanide in people or animals when consumed in the amounts that most people and animals are having.

Producers need to know the levels of cyanogenic precursors in their products. This means that for each field of flaxseed that is harvested, they need to obtain a triplicate analysis of a number of representative samples of flaxseed for the cyanogenic glycosides. The average and range of these values needs to be reported on the specification sheet of each 'batch' of flaxseed or flaxseed product, and this information provided to their customers.

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