A REVIEW ON THE NUTRITIVE VALUE AND TOXIC ASPECTS OF LEUCAENA LEUCOCEPHALA

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This review discusses the nutritive value of Leucaena leucocephala and its mimosine toxicity when used as a forage for livestock. Chemical analysis and feeding trial have indicated that Leucaena leaf-meal with its high protein, calcium, β-carotene and xanthophyll contents, is potentially a valuable feed for livestock in the tropics. The symptoms of mimosine toxicity in cattle, sheep, poultry, goats, horses, pigs and rats are discussed. The chemical value of mimosine and the possible mechanism of its toxicity are reviewed. Possible solutions to the toxicity problem are presented together with the suggestion that further studies be initiated to overcome this problem.

Key Words: Leucaena, mimosine toxicity, livestock, forage, feeding trials

The uses of the tropical legume Leucaena leucocephala are quite versatile. These uses include its function as a source of firewood and timber, its role in soil erosion control (Dijkman 1950), its ability to provide shade for other plants as well as its function in maintaining the fertility of the soil and of serving as a nutritious forage for animal feed (Ruskln 1977). Presently the greatest use of this plant in animal nutrition is its incorporation in cattle feed. Leucaena leaf-meal, with its rich protein, minerals and vitamin content, is also becoming a popular ingredient in poultry feeds in the tropics (D'Mello and Taplin 1978). However, the nutritive potential of this plant is still not fully realized, partly due to the presence of the alkaloid Mimosine in the plant. In livestock, as well as in experimental animals Mimosine is believed to induce alopecia, growth retardation, goitre, cataract, decreased fertility and mortality. Many investigations relating to the nutritive and toxic aspects of this tropical plant have been reported. It seems appropriate to review and discuss some of these latest findings concerning Leucaena leucocephala.

NUTRITIVE VALUE OF LEUCAENA’S FORAGE

The leaves of Leucaena leucocephala contain both nutrients and roughage and make an almost complete ruminant feed. Table I shows the crude protein, crude fibre and metabolizable energy of Malawi grown leucaena) Alfalfa (Medicago saliva) and extracted soybean meal. The N-corrected metabolizable energy (ME) for poultry was 2.83 ± 0.74 MJ/kg DM as found by D’mello and Thomas (1978). It is the only published data for the ME content of Leucaena. It is apparent that the ME content of this plant is very similar to that reported by Scott et al. (1969) for sun dried Alfalfa. It was suggested that the low ME of Leucaena results from the low digestibility of this legume (D'Mello and Thomas 1978).

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Table 1:
Crude protein, crude fibre and metabolizable energy of Leucaena leaf meal, sun dried alfalfa and extracted soybean meal

<table>
<thead>
<tr>
<th>Source of data:</th>
<th>D'Mello &amp; Taplin 1978</th>
<th>Scott et al 1969</th>
<th>D'Mello &amp; Taplin 1978</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crude Protein (% DM)</td>
<td>25.90</td>
<td>15.73</td>
<td>51.25</td>
</tr>
<tr>
<td>Fibre (%DM)</td>
<td>11.88&lt;sup&gt;1&lt;/sup&gt;</td>
<td>31.46&lt;sup&gt;2&lt;/sup&gt;</td>
<td>6.74&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>Metabolizable Energy (for poultry MJ/kg DM)</td>
<td>2.8&lt;sup&gt;3&lt;/sup&gt;</td>
<td>2.8</td>
<td>10.8</td>
</tr>
</tbody>
</table>

<sup>1</sup>TCA-fibre  <sup>2</sup> Crude fibre  <sup>3</sup> From D'Mello and Thomas, 1978

Leucaena leaves make a high protein feed because they can contain up to 34% crude protein in dry matter (table 2). Since the protein content is so high, leaflets of Leucaena are sun-dried in Malawi, Thailand and Philippines for use or for export to Japan and Singapore.

Leucaena protein is of high nutritional quality. Amino acids are present in well balanced proportions very similar to Alfalfa (Hegarty 1977). Leucaena's amino acid pattern is also comparable to that of Soyabean or fish-meal (table 3). The samples of Leucaena leaves and seeds analysed for their amino acids content, were obtained from Zaire.

Table 2:
Crude protein and mimosine content of Zaire-grown Leucaena leucocephala (calculated on dry matter basis)<sup>1</sup>

<table>
<thead>
<tr>
<th>Source of data:</th>
<th>% crude protein</th>
<th>mimosine&lt;sup&gt;1&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leucaena leaves</td>
<td>34.4</td>
<td>7.19</td>
</tr>
<tr>
<td>Leucaena seeds</td>
<td>31.0</td>
<td>12.13</td>
</tr>
</tbody>
</table>

<sup>1</sup> Mimosine content was determined by the method of Hegarty et al (1964) and is expressed as a percentage from the crude protein content.

Leucaena leaves can also provide a rich source of carotene and vitamins. The β-carotene contents of 3 cultivars of Leucaena leaf-meal produced in Malawi were in the range 227-228 mg/kg DM (D'Mello and Taplin 1978). Besides being a good source of β-carotene, Leucaena leaf-meal is also rich in vitamin K. It was also found that it could be a richer source of this vitamin than dehydrated Alfalfa leaf-meal (Chou and Ross 1965).

Depending on the soil minerals available to the root system, Leucaena forage can be an excellent source of calcium, phosphorus and other dietary minerals (D'Mello and Taplin 1978). Table 4 shows the concentration of selected elements in a batch of leucaena grown in Malawi. The calcium level of 19 g/kg dry matter would appear to be the most significant feature of the mineral content of this plant, especially with regard to its use in poultry feeds.
LEUCAENA LEUCOCEPHALA AS A CATTLE FEED

Leucaena is highly palatable for cattle, although it may take a few days for cattle to get used to grazing this legume.

Similar to other legumes, the in vivo digestibility of Leucaena forage is estimated to be in the range 50-70%. The presence of mimosine tends to reduce the activity of cellulolytic bacteria, but in about a week the rumen bacteria adapt and digestion improves considerably (Ruskin 1977).

Table 3:
Comparative amino acids composition in soyabean, fish-meal, alfalfa and Leucaena leucocephala (values given are in mg/g N)

<table>
<thead>
<tr>
<th>Amino acid</th>
<th>Soybean</th>
<th>Fishmeal</th>
<th>Alfalfa</th>
<th>Leucaena Seeds</th>
<th>Leucaena Leaves</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cystine</td>
<td>106</td>
<td>69</td>
<td>77</td>
<td>79</td>
<td>67</td>
</tr>
<tr>
<td>Aspartic acid</td>
<td>756</td>
<td>625</td>
<td>-1</td>
<td>643</td>
<td>864</td>
</tr>
<tr>
<td>Methionine</td>
<td>88</td>
<td>175</td>
<td>96</td>
<td>64</td>
<td>98</td>
</tr>
<tr>
<td>Threonine</td>
<td>244</td>
<td>269</td>
<td>290</td>
<td>138</td>
<td>266</td>
</tr>
<tr>
<td>Serine</td>
<td>331</td>
<td>256</td>
<td>-</td>
<td>206</td>
<td>279</td>
</tr>
<tr>
<td>Glutamic acid</td>
<td>1138</td>
<td>813</td>
<td>-</td>
<td>911</td>
<td>640</td>
</tr>
<tr>
<td>Proline</td>
<td>300</td>
<td>244</td>
<td>-</td>
<td>222</td>
<td>305</td>
</tr>
<tr>
<td>Glycine</td>
<td>275</td>
<td>400</td>
<td>-</td>
<td>285</td>
<td>278</td>
</tr>
<tr>
<td>Alanine</td>
<td>275</td>
<td>394</td>
<td>-</td>
<td>205</td>
<td>311</td>
</tr>
<tr>
<td>Valine</td>
<td>300</td>
<td>325</td>
<td>356</td>
<td>204</td>
<td>311</td>
</tr>
<tr>
<td>Isoleucine</td>
<td>294</td>
<td>256</td>
<td>290</td>
<td>148</td>
<td>244</td>
</tr>
<tr>
<td>Leucine</td>
<td>488</td>
<td>475</td>
<td>494</td>
<td>283</td>
<td>444</td>
</tr>
<tr>
<td>Tyrosine</td>
<td>238</td>
<td>-</td>
<td>232</td>
<td>162</td>
<td>208</td>
</tr>
<tr>
<td>Mimosine</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>763</td>
<td>343</td>
</tr>
<tr>
<td>Phenylalanine</td>
<td>319</td>
<td>256</td>
<td>307</td>
<td>197</td>
<td>283</td>
</tr>
<tr>
<td>Lysine</td>
<td>388</td>
<td>500</td>
<td>368</td>
<td>324</td>
<td>339</td>
</tr>
<tr>
<td>Histidine</td>
<td>181</td>
<td>-</td>
<td>139</td>
<td>158</td>
<td>123</td>
</tr>
<tr>
<td>Arginine</td>
<td>463</td>
<td>375</td>
<td>357</td>
<td>493</td>
<td>277</td>
</tr>
</tbody>
</table>


Table 4:
Concentration of certain minerals in Leucaena leaf meal (D’Mello & Taplin, 1978)

<table>
<thead>
<tr>
<th>Major elements (g/kg DM):</th>
<th>Calcium</th>
<th>19.00</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Phosphorus</td>
<td>2.16</td>
</tr>
<tr>
<td></td>
<td>Magnesium</td>
<td>3.35</td>
</tr>
<tr>
<td></td>
<td>Sodium</td>
<td>0.16</td>
</tr>
<tr>
<td></td>
<td>Potassium</td>
<td>17.0</td>
</tr>
</tbody>
</table>

Trace elements (mg/kg DM):

<table>
<thead>
<tr>
<th>Copper</th>
<th>11.4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iron</td>
<td>907.4</td>
</tr>
<tr>
<td>Zinc</td>
<td>19.2</td>
</tr>
<tr>
<td>Manganese</td>
<td>50.9</td>
</tr>
</tbody>
</table>


Dried Leucaena leaf-meal was equivalent to cottonseed cake, when used in rations for fattening cattle (Thomas and Addy 1977). Very high live weight gains have been recorded in Queensland, Australia. Young calves fed on Leucaena gained up to 1 kg per day during the main summer season, whereas calves fed on sugar cane supplemented with Leucaena gained 0.6 kg per day. Dairy cattle also produced well when fed on Leucaena (Ruskin 1977). Fresh milk from Leucaena fed cows has an attractive yellow colour, but may have an objectionable odour which disappears on boiling or pasteurising.

However, the use of Leucaena for cattle feeding is not without its problems, due to the presence of mimosine in the plant. Whyte and co-workers (1953) reported that Leucaena could be responsible for causing some sterility in cows.

An earlier report in 1948 from the University Agricultural Station in Hawaii stated that the reproductive efficiency of cows fed Leucaena averaged 92% and was little different from those fed a diet free from this legume (Ruskin 1977).

Heifers grazing Leucaena for more than six months showed loss of hair and developed goitres. Out of fourteen mated heifers, six were not detectably pregnant (Holmes 1976). Although Holmes concluded that Leucaena reduced fertility of cows, he admitted that the experimental variations were too great to permit a proper assessment of the fertility of these cows.

Hamilton et al (1968) found that four out of five calves born from heifers fed on a diet comprising about 80% Leucaena, had grossly enlarged thyroid glands at birth. The control heifers gave birth to significantly heavier calves (25.8 kg as opposed to 19.6 kg) with no detectable abnormalities. A suggestion was made by those workers that either mimosine and/or some other goitrogenic compound in Leucaena leucocephala may be interfering with the metabolism of the thyroid gland. Hegarty and co-workers (1976) reported that mimosine itself is not goitrogenic, but rather the compound 3,4-dihydroxypyridine (3,4-DHP). It was found that mimosine is hydrolysed by the gut microflora of ruminants to 3,4-DHP (Figure 1). Mice fed on diets containing 3,4-DHP developed hyperplastic goitres with enlarged vesicles deficient in colloids and lined by enlarged epithelial cells. The hyperplastic changes in the thyroid of goitrous cattle were similar to those produced in mice. The evidence strongly suggested that the goitres in cattle were associated with absorption of 3,4-DHP (Hegarty et al 1976).

Figure 1:
Transformation of mimosine into dihydroxypyridine by the rumen micro-organisms

![Figure 1](image-url)
In cattle the rumen micro-organisms hydrolyse mimosine into 3,4-DHP so efficiently and rapidly that even when the animals are fed on a diet rich in Leucaena, their blood, meat and milk are quite free of mimosine.

Generally when diets contain less than 30% Leucaena meal, cattle can thrive on them for long periods without signs of ill health, but when Leucaena comprises more than 50% of the animal’s feed intake, and feeding is continued for more than 6 months, the result may be general ill-health, loss of hair, production of goitres, reduced fertility and poor growth of the goitrous cows. However, cattle with goitres resulting from feeding on Leucaena forage do not die. The effects are mostly reversible, and can be seen early enough that the legume can be withdrawn from the cattle feed to allow them to recover (Ruskin 1977).

Leucaena contains almost negligible amounts of cyanide, selenium or bloat causing agents that kill cattle feeding mainly on pastures such as white clover. The mimosine content of Leucaena has no effect on the milk or meat of cattle feeding on the plant, that can cause a health hazard to humans consuming these animal products.

LEUCAENA AS A SHEEP FEED

Like cattle, sheep find Leucaena forage very palatable, although they are less able to tolerate mimosine in their diet. It seems that the rumen bacteria of sheep do not hydrolyse mimosine into 3,4-DHP as efficiently as those of cattle. Consequently some mimosine is absorbed and enters the blood stream (Ruskin, 1977). High intakes of Leucaena by sheep have been shown to cause remarkable shedding of fleece within 7-10 days (Hegarty et al 1964). Nonetheless, if sheep are slowly introduced to Leucaena feeds, the rumen bacteria adjust and the animals can feed on the plant (especially the low mimosine types) with the minimum depilatory effect (Ruskin 1977).

In sheep, the depilatory effect of Leucaena was influenced by the level and method of feeding. Small amounts of mimosine were excreted by sheep consuming Leucaena, but the major metabolise in the urine was identified as 3,4 DHP (Hegarty et al 1964). The same workers established from the results of intravenous, intraabomasal and intraruminal administration of mimosine that sheep, like cattle, cannot detoxicate mimosine after absorption, but rather, extensive degradation of mimosine to 3,4-DHP takes places in the rumen. Hence, absence of toxic symptoms in sheep conditioned to Leucaena is due to an increased detoxification in the rumen, rather than to an adaptive tolerance.

Reis et al (1975) found that defleecing in sheep was associated with hair follicle retrogression and an abrupt cessation of wool growth within 7-14 days of the start of intravenous infusion of mimosine.

Pregnant ewes, fed ad libitum on Leucaena, from one to three months postcoitus, produced lambs of low birth weight and viability. These lambs and lambs of ewes fed Leucaena from the time of parturition gained less weight than lambs from ewes fed Alfalfa hay (Bindon and Lamond 1966).
LEUCAENA IN POULTRY DIETS

The use of Leucaena leucocephala leaf-meal in poultry diets in the tropics was recently thoroughly reviewed (D'Mello and Taplin 1978). Apart from the rich protein and minerals (especially calcium) content of Leucaena leaf meal, the high ~carotene content alone can justify the use of this leaf-meal in poultry diets. Many research workers have noticed that incorporation of Leucaena leaf meal at a 4-6% dietary level, in poultry diets restored health to chicks suffering from vitamin A deficiency (Ruskin, 1977). Leucaena leaf-meal is also very rich in xanthophyll pigments, estimated to be in the range of 741-766 mg/kg DM (DMello and Taplin, 1978). This pigment colours the egg yolks and the skin of broilers, and it seems that the pigmenting power of Leucaena leaf-meal is double that of Alfalfa.

However, a linear depression of growth was observed when chicks were fed 10, 20 or 40% Leucaena leaf-meal diets (Labadan 1969). Mortality was high amongst the hens fed on the 40% Leucaena meal diet. Addition to these diets of structural analogs of mimosine, such as tyrosine, pyridoxine and niacin, counteracted the growth depression caused by the Leucaena diets even at the highest dietary level of 40%. There was a significant improvement in growth and feed conversion efficiency when these Leucaena diets were supplemented with 0.15% and 0.30% ferrous sulphate. In an earlier report, rations containing 10 and 20% Leucaena leaf-meal resulted in depressed growth of chicks (Ross and Springhall 1963). The additions of dry ferrous sulphate to rations containing the 20% Leucaena meal diet failed to alleviate this growth depression. Those authors suggested that the phosphorus salts in the rations may interfere with the iron mimosine complex formation, by forming insoluble phosphates with iron.

Using sun-dried Malawi grown Leucaena leaf meal. D'Mello and Thomas (1978) demonstrated marked depressions in growth and feed intake of chickens fed on a 5% Leucaena leaf-meal diet. Higher dietary levels of Leucaena ( 10% and 15% ) leaf meal caused further decreases in growth and feed intake, the effects being particularly severe at a dietary level of 15%. Efficiency of food conversion however, was markedly reduced only at the highest dietary level(15%) of Leucaena leaf meal.

Pullets fed on diets containing 30% Leucaena leaf-meal had immature ovaries at 22 weeks of age. After administering mammalian follicle stimulating hormone (FSH) to half of this group of hens they were found to have fully developed ova after 3 weeks, whereas the untreated pullets showed virtually no ovarian development (Scott et al 1969). It was concluded that a factor in Leucaena leaves possibly mimosine, has an inhibitory action upon production and/or release of F.S.H. by the anterior pituitary of the hen.

PERFORMANCE OF PIGS, HORSES AND GOATS FED ON LEUCAENA LEUCOCEPHALA FORAGE:

Pigs are sensitive to mimosine. Owen (1958) reported that pigs raised on Leucaena leaf-meal diets lost their hair, without stating the level at which the Leucaena meal was used. In Papua New Guinea and the Philippines Leucaena leaf-meal has been used satisfactorily to supplement rations, up to 10%, for growing pigs (Ruskin 1977).
Horses fed on Leucaena lost hair, mainly the long hair of the mane and tail, Ring formation occasionally occurred on the hooves of these horses (Owen 1958). There is a variety of reports concerning the feeding of Leucaena to horses, and it is possible that loss of hair is the main ill-effect suffered by horses grazing this legume.

Leucaena leucocephala is a plant favoured by goats on small farms in parts of the tropics without reported ill-health effects (Ruskin, 1977).

MIMOSINE IN LEUCAENA LEUCOCEPHALA

The alkaloid mimosine was first isolated from Mimosa pudica and named "mimosine" by Renz (1936). Later mimosine was again isolated from Mimosa pudica by Bickel and Wibaut (1946) and was named leucaenol. Wibaut and Klipool (1950) isolated mimosine from Leucaena leucocephala and gave it the name "leucaenine", and proved that the three differently named substances are the same. The chemical structure of mimosine was determined by Bickel et al. (1947a,b; 1948a,b) as \(\beta\)-N-(3-hydroxy-4pyridone)\(\alpha\)Oaminopropionic acid. Figure 2 shows the chemical structures of mimosine and L-tyrosine.

The concentration of mimosine in the leaves and seeds of Leucaena leucocephala varies with the different types and strains of the plant. In samples of the plant grown in Zaire, we found that the concentration of mimosine was 7.19% and 12.13% of the total protein (dry weight basis) in the leaves and seeds respectively (table 2). Although few determinations of mimosine have been performed, one can generally say that in most varieties of the plant mimosine comprises about 5% of the total protein.

Data for the mimosine content in the different types and strains of Leucaena leucocephala, and for the effect of storage on the mimosine content are much needed at the present time.

Due to its toxicity, mimosine has been a great concern to livestock nutritionists. Searches have been made for new low mimosine varieties (Hutton and Gray 1959). Most Leucaena leucocephala strains and other related species such as Leucaena pulverulenta have much less mimosine content. A low-mimosine Leucaena hybrid was
recently bred by back-crossing Leucaena leucocephala with Leucaena pulverulenta in Queensland, Australia (Ruskin 1977). This hybrid was a well branched forage plant, whose leaves contained about half the mimosine of the original Leucaena leucocephala.

The original colorimetric method for the quantitative determination of mimosine (Matsumoto and Sherman, 1951) was further developed (Hegarty et al, 1964) by improving the techniques of extraction and purification of mimosine in the sample. The developed method is a good one for determining quantitatively mimosine and 3,4-DHP in biological (plant and animal) materials. Isolation of mimosine from the plant (seeds or leaves) can be performed by a simple dialysis technique and recrystallised from aqueous alcohol (Spencer and Notation, 1962).

THE MECHANISM OF MIMOSINE TOXICITY

Many reports relating to the biochemical effects of mimosine have been reviewed (Hylin 1969; Thompson et al 1969; Fowden et al 1967). However many aspects of mimosine's toxic mechanism or mechanisms still remain unrevealed. We have already mentioned that mimosine in experimental animals as well as in livestock can cause hair-loss, growth retardation, cataract, goitre, decreased fertility and mortality.

Amongst the earliest reports on mimosine's toxicity was that of Yoshida (1944), in which rats were reported to have suffered from alopecia, cataract, paralysis, reduced growth and mortality, when they were fed diets containing mimosine isolated from Leucaena leucocephala.

The fact that mimosine bears a structural resemblance to L-tyrosine (figure 2), led Lin and co-workers (1964) to put forward the hypothesis that mimosine probably acts as a tyrosine analogue or tyrosine antagonist which inhibits protein biosynthesis in the living body and causes toxic symptoms including retardations of growth. In rats, Lin and co-workers (1964) found that addition of phenylanaline (1%) to diets containing mimosine (0.5%) could antagonise 3% of the growth inhibition caused by mimosine. Addition of glutamic acid (5%) showed only a slight recovery (8%), while pyridoxine hydrochloride (0.025%) did not affect the growth retardation caused by mimosine.

On the other hand, the metal chelating power of mimosine (Tsai and Ling 1973), could possibly disturb the action of metal containing enzymes, especially those containing iron cations (Tsai 1961).

In a similar manner to other L-neutral amino acids, mimosine was found to be appreciably absorbed from the gastrointestinal tract in rats, and was later excreted rapidly in the urine. There was a small but significant accumulation of mimosine in the skin, eyes and serum of the rat when mimosine was administered for several weeks (Tsai and Ling 1974).

Hegarty et al (1976) found that mimosine caused a small depression of iodine uptake by the thyroids of rats, while 3,4-DHP depressed this uptake by 50%. 3,4-DHP produced goitre in mice, even when they were fed on a high iodine diet. Hegarty and co-workers suggested that 3,4-DHP may interfere with the organic binding of iodine, rather than with the trapping mechanism of iodine by the thyroid gland.
In vitro studies with H.Ep-2 cell cultures (Tsai and Ling 1971) revealed that cell growth, mitotic frequency and thymidine incorporation, or DNA synthesis was less inhibited than DNA synthesis. No inhibition of protein synthesis was observed in the presence of mimosine or 3,4-DHP. The antimitotic activity of mimosine was also reported by other workers (Montagna and Yum 1963; Hegarty et al 1964). A reduction of mitotic index in lens epithelial cells of rats suffering from mimosine induced cataract was reported by Sallmann and co-workers (1959).

The in vitro activity of the enzyme alkaline phosphatase, obtained from mouse kidney was inhibited by mimosine (Chang 1960). Similarly, the in vitro activity of glutamate oxaloacetate transaminase was inhibited in the presence of mimosine (tin et al 1962).

Recently it was found that the decarboxylation of L-tyrosine, catalysed by the bacterial enzyme tyrosine decarboxylase, was inhibited if mimosine was preincubated with the enzyme (Grove et al, 1978). In contrast, when mimosine and tyrosine were preincubated, the subsequent decarboxylation reaction was stimulated indicating the possibility of complex formation between tyrosine and mimosine. However, tyrosine catabolism in rats (in vivo) was not apparently altered by the inclusion of mimosine in the diet. Rats fed mimosine developed characteristic symptoms of mimosine toxicity, and cystathionine was abundant in the urine indicating a possible functional lack of pyridoxal-5-phosphate (Grove et al 1978). However other research results were not in agreement with the deduction claiming that the deficiency of vitamin B6 may be caused by mimosine.

While mimosine was shown to inhibit the in vitro activity of alkaline phosphates (Chang, 1960) as well as that of glutamate oxaloacetate transaminase (Lin et al 1962), mimosine was proved to have insignificant effects on the in vivo activities of pyridoxal-5-phosphate requiring enzymes, such as glutamate decarboxylase, dopamine decarboxylase and glutamate oxaloacetate transaminase (Lin et al 1967).

In an earlier report Lin and co-workers (1965) demonstrated the interactions of mimosine and pyridoxal-5-phosphate (in vitro) by paper chromatography and electrophoretic techniques. It was observed that the mechanism of the interaction of mimosine and pyridoxal-5-phosphate was quite different from that of glutamic acid, phenylalanine and L-tyrosine with pyridoxal-5-phosphate (Lin et al 1965).

Yang and Ling (1968) confirmed that mimosine can form a Schiff's base (in vitro) with pyridoxal-5-phosphate. They found that mimosine intoxicated rats excreted in their urine a lower amount of xanthurenic and kynurenic acids than vitamin B6 deficient rats did after tryptophan loading. The tryptophan tolerance test has been considered as a good test for the assessment of vitamin B6 activity (Kang and Davanzo 1966; Koerner and Nowak, 1966); therefore increased excretion of xanthurenic and kynurenic acids after tryptophan loading can be used as an index for vitamin B6 deficiency. In contradiction to the conclusion reached by Grove and co-workers (1978), Yang and Ling's (1968) results following the tryptophan loading test indicated that mimosine intoxicated rats did not suffer from vitamin B6 deficiency.

Since vitamin B6-dependent-enzymes did not decrease in the livers of mimosine intoxicated rats (Lin et al 1967), and because addition of pyridoxine, to the diets of those rats, failed to stop or influence cataract formation in those animals (Yang and Ling 1968), it seems highly improbable that the toxicity of mimosine can be derived from the antivitamin mechanism through the formation of a complex between mimosine and vitamin B6.
The adverse effect of mimosine on the biosynthesis of collagen in embryonic cartilage from chick's embryos was studied by Tang and Ling (1975). They observed that the synthesis of hydroxyproline was markedly inhibited in the presence of mimosine. Consequently, "protocollagen", deficient in hydroxyproline, accumulated within the cells synthesising collagen. This "protocollagen" is more susceptible to the action of callagenase and other tissue proteases than to normal collagen (Hurych et al. 1967). It follows then that the reduction in collagen content, or the more fragile character of the collagen in various organs might induce such symptoms as capillary haemorrhage, proteinuria and uterine perforations in mimosine-fed animals. An example of such symptoms were noticed by Dewreede and Waymann (1970) in mimosine-fed female pregnant rats.

In our laboratory (El-Harith et al 1979), we noticed that young rats fed on 25% Leucaena meal (equivalent to 0.7% mimosine) developed distinct paralysis of the hind limbs, and that this effect was reversible when the animals were fed on the normal control diet. This effect was noticed before in Yoshida's animal's (1944), when she fed them with mimosine. Apart from this reference, almost no mention was made earlier in regard to this important pharmacological effect of mimosine. In our view, more studies on the neurotoxicity of mimosine are warranted.

Like many other legumes, the seeds and leaves of Leucaena leucocephala contain a haemaglutinin, (a substance which can aglutinate red blood cells; Liener, 1969) which was isolated and identified by Lesniak(1977). It is not improbable that the presence of a haemaglutinin in Leucaena is an additional factor to the toxicity of this plant, although direct evidence is needed to verify this. Haemaglutinins are normally rendered harmless by heat treatment (Liener 1969). Furthermore, Hathcock and Labadan (1975) found from their work with chicken embryos that Leucaena contains one or more toxic factors besides mimosine.

POSSIBLE SOLUTIONS TO THE PROBLEM OF MIMOSINE TOXICITY

Addition of Iron salts: Addition of ferrous sulphate at a 1–2% dietary level, to rats rations containing Leucaena leaf-meal or mimosine, reduced or completely counteracted the toxic effects of mimosine (Yoshida 1944; El-Harith et al 1979). There was a significant improvement in the growth and feed conversion efficiency of chicks when the basal Leucaena leaf-meal diets were supplemented with ferrous sulphate (Labadan 1969). Ross and Springhall (1963) found that additions of dry ferrous sulphate to rations containing Leucaena leaf-meal (20%) failed to counteract the growth depression of the chicks receiving those rations. They demonstrated that addition of ferrous sulphate solution to the Leucaena leaf-meal prior to mixing with the balance of the ration was effective in reducing the toxic symptoms due to mimosine. Additional improvement was obtained when the iron treated Leucaena leaf-meal was allowed to stand at least for one week prior to mixing with the other ingredients in the ration. Ross and Springhall (1963) suggested that the high level of phosphorus in the ration may interfere with the iron-mimosine complex formation by forming insoluble phosphates with the iron.

The stability constants of chelates between mimosine and various metal ions were found to be in this order $Fe^{2+} > Al^{3+} > Cu^{2+} > Pb^{2+} > Ca^{2+} > Mg^{2+}$ (Tsai and Ling 1973). The
ferrous chelate of mimosine was found to be unstable. The property of the reduction of mimosine toxicity by ferrous ions may be due to the formation of a ferric chelate of mimosine after oxidation of ferrous ions to ferric ions. Figure 3 illustrates a possible structure of the ferric mimosine complex compound as proposed by Tsai and Ling (1973).

Figure 3:
A possible structure of Fe (III) - mimosine chelate complex

(proposed by Tsai and Ling, 1973)

Heat treatment of leucaena meal: Matsumoto and co-workers (1951) found that heat treatment of Leucaena meal improves its nutritional value through destruction of mimosine. They reported that the mimosine content of leaves and seeds of Leucaena stored at elevated temperatures was decreased. This effect was most pronounced and rapid when the temperature was over 70°C in the presence of moisture, but did not occur when dry leaves were heated. Similarly, in our laboratory we observed that dry heating (at 90°C for 24 furs) of a Leucaena meal (seeds and leaves 1:1), did not protect young rats from the characteristic symptoms of mimosine toxicity i.e. retarded growth, paralysis of the hind-limb, cataract, alopecia and mortality. Hence, it is apparent that moist heating is important to reduce or counteract the toxicity due to mimosine in Leucaena meal.

Water washing or soaking of leucaena leaves: Washing with water significantly reduced the mimosine content of Leucaena leaf-meal. Chicks receiving this "washed" leaf -meal showed better growth rates (Labadan 1969). Samples of Leucaena leucocephala (grown in Zaire) leaves were soaked in water for 36 furs, and were found to contain 5.96% mimosine of the total protein, as opposed to the value of 7.19% (table 2) before water treatment (El-Harith et al unpublished).
Rotation of cattle and sheep between leucaena pastures and other grass pastures can be a very effective method of protecting those animals from the ill-effects of mimosine (Ruskin 1977).

Development of new Leucaena hybrids with low mimosine content, but still with high protein content (Hutton and Gray 1959) can be a possible solution to the problem of mimosine toxicity. Although the solution of the problem via this line of research is rather difficult, some good results have already been achieved (Ruskin 1977).

Supplementation of Leucaena diets with ferrous sulphate and moist heat treatment of Leucaena leaf-meal can be practical in the case of poultry feeding. These two methods could be very expensive if applied to cattle or sheep feeding. Water washing on the other hand requires more attention, particularly with regard to the nutrient composition in Leucaena leaf-meal after water treatment.

More studies are needed to elucidate the mechanisms of mimosine toxicity. Evaluation of the dietary treatments of Leucaena meal, which would protect livestock from its toxic effect is also needed.

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