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Endemic fluorosis in ruminants and its socioeconomic impact in Morocco

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Abstract

In Morocco, ruminant breeding is a sector with significant socio-economic value. It contributes to the red meat national production, and also provides jobs for a large rural population as well as being the main source of income for most livestock breeders. However, in phosphate areas, this sector is facing environmental poisoning due to an excess of fluoride. The chronic ingestion and/or inhalation of this element by ruminants exerts various toxic effects influencing the performance of the animal and thus leading to significant socio-economic consequences. Data of previous studies concerning geographic distribution of fluorosis in Morocco, metabolism of fluoride in ruminants as well as its harmful effects namely dental, skeletal and non-skeletal fluorosis in ruminants (sheep, goats, cattle) is clearly summarized in this review. Moreover, the socioeconomic impact and the updated progress in prevention or reducing fluorosis are reviewed. This review highlights the need to perform further investigations on endemic fluorosis in ruminants.

Keywords: Ruminants, hydrotelluric fluorosis, industrial fluorosis, socioeconomic impact, mitigation

La fluorose endémique chez les ruminants et son impact socio-économique au Maroc

Résumé

Au Maroc, l'élevage des ruminants est un secteur à une grande valeur socio-économique. Il contribue à la production nationale de viande rouge, fournit également des emplois à une importante population rurale et constitue la principale source de revenus pour la plupart des éleveurs. Pourtant, dans les zones phosphatées, cette filière est confrontée un défi environnemental due à un excès de fluor. L'ingestion et/ou l'inhalation chronique de cet élément par les ruminants exerce divers effets toxiques influençant les performances de l'animal et entraînant ainsi des conséquences socio-économiques importantes. Les données des études précédentes concernant la répartition géographique de la fluorose au Maroc, le métabolisme du fluor chez les ruminants ainsi que ses effets nocifs à savoir la fluorose dentaire, squelettique et non squelettique chez les ruminants (ovins, caprins, bovins) ont été clairement résumées dans cette revue. De plus, l'impact socio-économique, et les progrès actualisés en termes de prévention ou de réduction de la fluorose sont passés en revue. Cette revue mit également en évidence la nécessité de réaliser des investigations complémentaires sur la fluorose endémique chez les ruminants.

Mots clés : Ruminants, fluorose hydrotellurique, fluorose industrielle, impact socio-économique, atténuation.

التسمم بالفلور المستوطن عند المجترات وتأثيره الاجتماعي والاقتصادي في المغرب

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ملخص

تعتبر تربية الحيوانات المجترة في المغرب قطاعًا ذا قيمة اجتماعية واقتصادية كبيرة. إذ يساهم في الإنتاج الوطني للحوم الحمراء، كما يوفر فرص عمل لعدد كبير من سكان القرى وهو المصدر الرئيسي للدخل لمعظم مربي الماشية. لكن في بعض المناطق، يواجه هذا القطاع تحديًا بيئيًا بسبب وجود فائض من الفلور. ويؤدي الابتلاع و/أو الاستنشاق اليومي لهذا العنصر من قبل الحيوانات المجترة إلى عواقب وخيمة تؤثر سلبا على أداء الحيوان وبالتالي إلى مشاكل اجتماعية واقتصادية كبيرة. في خذا المنشور، تم تلخيص معطيات الدراسات السابقة المتعلقة بالتوزيع الجغرافي للتسمم بالفلور في المغرب، واستقلاب الفلورايد في المجترات وكذلك آثاره الضارة، والتي هي التسمم بالفلور في الأسنان والهيكل العظمي والتسمم بالفلور غير الهيكلي عند المجترات (الأغنام والماعز والأبقار) بوضوح في هذه الدراسة. بالإضافة إلى ذلك، تمت مراجعة التأثير الاجتماعي والاقتصادي، والتقدم المحدث فيما يتعلق بالوقاية أو الحد من التسمم بالفلور. سلط هذا العمل الضوء أيضًا على الحاجة إلى إجراء تحقيقات إضافية حول التسمم بالفلور عند المجترات في المغرب.

الكلمات المفتاحية: المجترات، التسمم بالفلور الهيدروليكي، التسمم الصناعي بالفلور، التأثير الاجتماعي والاقتصادي، التخفيف

Introduction

In Morocco, the animal production sector has a significant socioeconomic and nutritional influence. It contributes to 38% of the agricultural sector's turnover, 60% of agricultural jobs, and ensures the country's food security (MAPM, 2014; Lionboui *et al*., 2021). Moreover, sheep, goats, and cattle are the most ruminants raised in the country, with more than 20.5 million heads of sheep (MAPMDREF, 2018), 5.73 million heads of goats (FAOSTAT, 2020), and around 3.17 million heads of cattle. However, in several regions where ruminant breeding occupies a prominent place (El Amiri *et al*., 2022), an excess of fluoride in water, soil, and/or air has been reported (Abdennebi, 1982; Sadikaoui, 2014). Hence, the chronic ingestion of this halogen by ruminants can lead to irreversible toxic effects (Ranjan and Ranjan, 2015; Rahim *et al*., 2022a). Accurately, Chronic exposure to fluoride by ruminants, either through inhalation or consumption of contaminated water or plants grown in contaminated soil can lead to endemic fluorosis (locally called Daghmous) (Rahim *et al*., 2022a). Endemic fluorosis is a major public health concern, with the teeth mottling and skeletal osteosclerosis as the most popular negative effects in ruminants (Choubisa, 2022). Prolonged chronic ingestion of fluoride has been shown to affect the metabolism trough biochemical parameters disorder (Çetin *et al*., 2020), adverse effects on soft tissues (gastrointestinal tract, lungs, liver, kidneys, heart) (Efe *et al*., 2020) as well as a decrease in reproductive performance (Abdel-Rahman *et al*., 2018), growth performance (Milhaud *et al*., 1983) and genetic parameters (Perumal *et al*., 2013). Consequently, all these disturbances affect the general performance of the animal, leading to serious socio-economic problems for breeders (Zouarhi, 2009). In the present paper, the outcome of previous studies concerning the harmful effects of dental, skeletal and non-skeletal fluorosis in ruminants (sheep, goats, cattle), the socio-economic impact of endemic fluorosis, and the preventive measures of fluorosis in ruminants are reviewed. Moreover, this review highlights the need to perform further investigations on endemic fluorosis in ruminants.

Distribution and sources of fluoride in Morocco

In Morocco, the most famous type is the hydrotelluric fluorosis, and it concern mainly the phosphate zones (Abdennebi *et al*., 1995) that covers a large area ranging from Khouribga-Oued Zem and Tadla in the North East, Settat in the center, and BenguerirYoussoufia in the West (Abdennebi, 1982). Moreover, the hydrotelluric fluorosis was also reported in the provinces of Boujdour and Laayoune (Faye and Sinyavskiy, 2008). In these areas, fluoride is naturally present in phosphate rocks (Moufti, 2019), consequently, their weathering releases a large quantity of this element which contaminates the groundwater and soil (Rahim *et al*., 2022a). It is caused by a high level of fluoride in water and soil, which is particularly linked to phosphate rocks.

The consumption of fluoride-rich water and plants grown in contaminated soil, by animals grazed in these regions, leads to toxic effects in the form of hydrotelluric fluorosis (El Amiri *et al*., 2022; Sibaoueih et al, 2022). Normally, drinking water is considered contaminated when its fluoride levels is between 1.1 and 2.5 ppm and toxic when its fluoride levels is greater than 2.5 ppm (Susheela, 1999). On the other hand, soil, when its fluoride concentration is greater than 400 mg/kg, can be qualified as contaminated (Bharti *et al*., 2017). In hydrotelluric areas, previous investigations found high concentrations of fluoride in both water and soil (Belfakih, 1986; Diacono *et al*., 2008; El Jaoudi *et al*., 2014; Maadid *et al*., 2017). Whereas in Khouribga, high values in fluoride were reported just in soil (Haikel *et al*., 1986; Lebrahimi *et al*., 2017) suggesting that the soil is the main contributor to the toxic effects of fluoride in this region (El Amiri *et al*., 2022).

Metabolism of fluoride in ruminants

The basic characteristics of fluoride metabolism are similar in both humans and all animals (Ranjan and Ranjan, 2015; Martínez-Mier, 2012). The accumulation of fluoride is under control of many factors such as the exposure route, the dietary habits, the pH of the digestive tract, and the occurrence of calcified tissues (Kabir *et al*., 2020). The metabolism of fluoride includes absorption and/or inhalation, distribution, and excretion (Figure 1). In monogastric animals, fluoride is absorbed in the stomach whereas in ruminants it is absorbed in the rumen and abomasum (Ranjan and Ranjan, 2015). It was highlighted that 80-90% of ingested fluoride enters the body through the gastrointestinal tract in the form of hydrogen fluoride (HF). However, since the pH of the gastrointestinal tract of ruminants is around 5 to 6, the ingested fluoride does not exceed 50% (Messer *et al*., 1989; Nopakun *et al*., 1989). The remaining fluoride is then absorbed by the proximal small intestine in a pH-independent mechanism (Messer *et al*., 1989; Nopakun *et al*., 1989)**.** Coming back to the gastrointestinal tract, since HF is a weak acid, half of it is in the dissociated or ionic form (F^-) at pH 3.4. When the pH decreases (pH<3.4), the non-dissociated form prevails, while at high pH, the ionized form dominates (Martínez-Mier, 2012; Buzalaf *et al*., 2015).

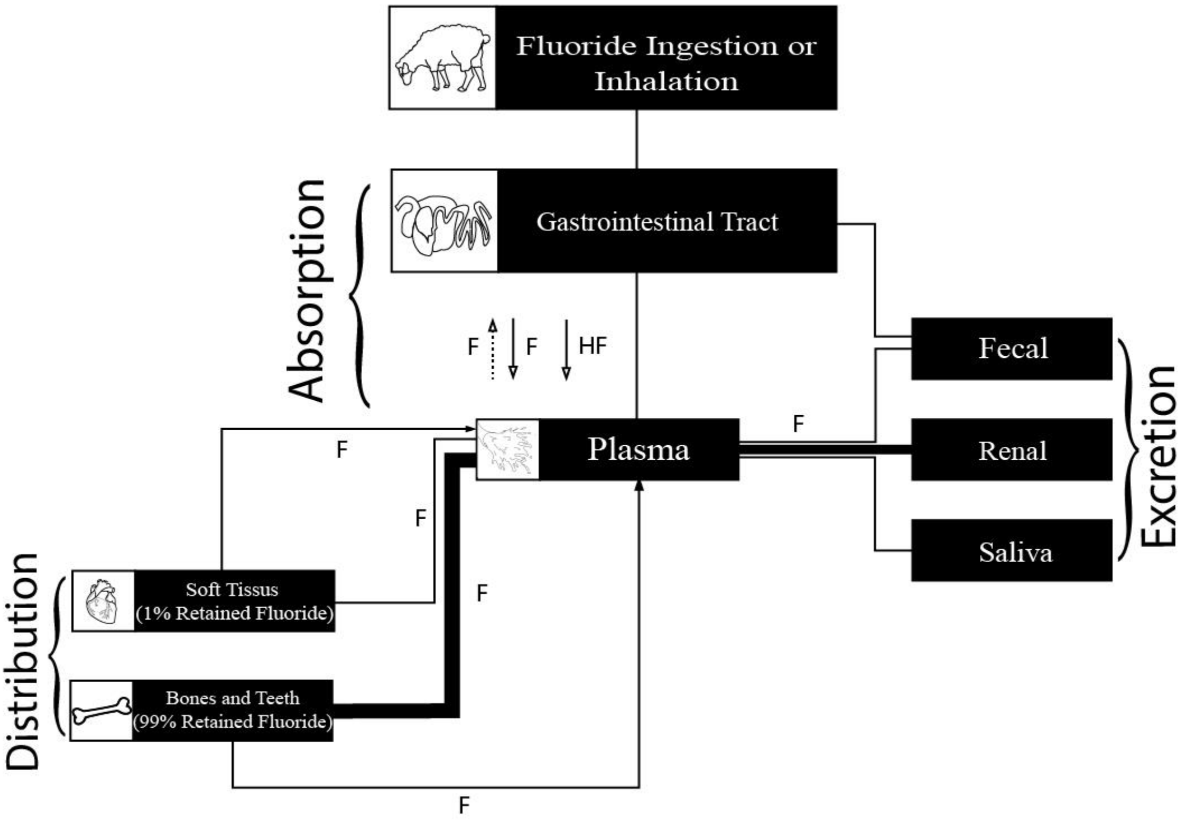

Figure 1. The main steps of the fluoride metabolism in the animal's body.

After absorption, fluoride enters the bloodstream, which can act as a mean of transport and allows its distribution throughout the body. About 75% is found as a free form in plasma, 5% is bound to plasma proteins, and the rest is present in erythrocytes (Singer and Armstrong, 1964). Ten minutes after the fluoride enter the body, its plasma levels start to increase. Depending on the ingested amount, basic plasma fluoride levels are reached within 3 to 11 hours after ingestion (Whitford, 1996). Afterwards, the blood allows the distribution of fluoride to hard and soft tissues. About 99% of the total fluoride is retained in bones as well as enamel and dentin. The remaining fluoride (about 1%) is retained by the soft tissues (Buzalaf and Whitford, 2011).

Finally, the main route of excretion of absorbed fluoride is urination, in which the kidneys play an important role (Zheng *et al*., 2002). Another part was excreted by feces and others specialized body fluids like saliva (Kanduti *et al*., 2016); (Kabir *et al*., 2020).

Fluoride toxicity in ruminants

In Morocco, toxic effects of fluoride were first reported in 1917 in Ben Ahmed region (Velu, 1932). It took decades to figure out that the underlying cause of these poisonings is an excess of fluoride (Velu, 1932). From 1978, studies have focused on the epidemiological, clinical, and biochemical aspects. Hence, it was highlighted that the daily ingestion or inhalation of toxic doses of fluoride in Moroccan endemic areas causes dental, skeletal, and tissue damage, metabolic disturbances, and negatively influences growth performance(Rahim *et al*., 2022b).

Hard tissue: teeth and bones

Calcified tissues such as teeth and bone are the main sites of fluoride accumulation(Perumal *et al*., 2013). It exerts effects during the renewal of the dental and bone formation. Due to its high affinity with calcium, fluoride can reduce its absorption and cause hypocalcemia, it also replaces the hydroxyl group in hydroxyapatite forming fluorapatite (Idini *et al*., 2019). Moreover, it was highlighted that fluoride can disrupt protein synthesis affecting endoplasmic reticulum function in ameloblasts(Sharma *et al*., 2008).In all animals including ruminants, the first clinical signs that appear after chronic fluoride poisoning are dental lesions, followed by osteosclerosis as a major clinical sign of skeletal fluorosis (Rahim *et al*., 2022a).

Various indices have been developed to classify dental lesions according to their severity. The Dean's Index (DI) is the most recognized by the World Health Organization as the basic method for its use in oral health surveys (Mohd Nor, 2017). It is based on scores (ranging from 0 to 5) assigned to the severity of dental damage caused by fluorosis (Rahim *et al*., 2022a). In hydrotelluric fluorosis areas (Kouribga, Fkih ben Salah, Settat, Bengurir, and Youssoufia), it was reported that the teeth of the affected animals became hypoplastic and decalcified, with the presence of abnormalities in structure, shape and orientation. Additionally, it was shown that the appearance of dental lesions in animals also varies according to the type of incisor and the stage of formation of its bud (Abdennebi, 1982). Furthermore, maxillary exostosis which is considered as one of the clinical signs of skeletal fluorosis is much more pronounced in cattle than in sheep and goats, whereas exostosis of the limbs is present only in cattle (Abdennebi, 1982). In another study realized in South Safi, signs of dental fluorosis were observed in cattle, sheep and goats, with a higher severity of lesions in the villages closest to the industrial zone (Kessabi *et al*., 1983). Moreover, 65% of sheep reared in El Broujarea had dental fluorosis with severity ranging from moderate to severe according to the dean's index (Benassila, 2014). In the 10 rural areas belonging to the Sidi Abed and Moulay Abdellah communes, located in the JorfLasfar, it was observed that 82% of cattle, 79% of sheep and 75% of goats aged 2 years show dental lesions. On the other hand, 30% of cattle, 17% of sheep, and 16% of goats present skeletal exostosis (Sadikaoui, 2004). Furthermore, the severity of the dental lesions varies according to the geographical location of the rural area in relation to the factory (Sadikaoui, 2004). According to these studies, it should be noted that in both hydrotelluric and industrial areas, cattle species are the most susceptible to osteodental fluorosis, followed by sheep and goats. Similar results are obtained in Tanzania, Kenya and India (Choubisa, 1999). This high prevalence of osteodental fluorosis in cattle species can be explained by the feeding practices. Previous study revealed that fluoride is accumulated mostly in plants' roots and least on their fruits, which means that fluoride is exposed less to browsing animals, opposite to grazers. Which may explain why goats and sheep showed less signs of osteo-dental fluorosis.

Soft tissue and biochemical parameters

In Moroccan endemic areas, ruminants such as cattle, sheep, and goats suffer from non-skeletal fluorosis (Zouarhi, 2009). In those areas, previous studies reported that chronic fluoride toxicity is harmful to the soft tissues such as kidneys, liver, lungs, heart, and gastrointestinal tract and disturbs the biochemical parameters (Rahim *et al*., 2022a). In order to highlight the blood, biochemical and urinary modifications in ruminants reared in Morocco, several studies concerning experimental and endemic fluorosis were carried out (Aajouj, 1982; Bennis *et al*., 1993; Zouarhi, 2009). Aajouj (1982) reported that the administration of 0.25 mmol/kg (BW)/day of Sodium fluoride (NaF) significantly increased potassium level and blood Glutamate dehydrogenase, succinate dehydrogenase, gamma-glutamyl transferase, alkaline phosphatase and lactate dehydrogenase activities in fluorotic sheep compared to control. This dose of NaF also decreased the urea level and the activity of urinary gamma-glutamyl transferase (Aajouj, 1982). In addition, chronic fluoride toxicity caused hypoglycemia, decreased plasma protein levels, and increased serum urea and serum creatinine in sheep (Hamliri, 1981). In a study conducted on cattle species reared in endemic areas, an increase in aspartate amino-transferase, alanine amino-transferase, and lactate dehydrogenase which come mainly from the liver and secondarily from the muscle has been reported by Khouzaimi (1980). Moreover, an increase in potassium, urea, gamma globulins, lactate dehydrogenase, alkaline phosphatase and aspartate aminotransferase blood and decreases in calcium, total protein and albumin blood have been reported in cattle reared in the hydrotelluric area (Kouribga and Oued Zem) compared to cattle reared in free fluoride area (KasbaTadla) (Kessabi *et al*., 1983). Furthermore, these toxic effects have also been reported in sheep (Kessabi *et al*., 1983) and goats (Bennis *et al*., 1993) reared in the same hydrotelluric area. Additionally, a comparative study between hydrotelluric (Krakra-Settat) and industrial (khatazzakane-Safi and Sebtgzoula-Safi) fluorosis areas was carried out on sheep, it showed a high level of plasma fluoride and an excessive accumulation of fluoride in the bone with no significant differences between the two regions studied (Belfaqih, 1986). On the other hand, according to previous studies, it is clear that fluoride exerts toxic effects on reproduction and growth performance in animals(Said *et al*., 1977; Krook and Justus, 2006; Dhurvey *et al*., 2017; Abdel-Rahman *et al*., 2018). In Morocco, there are no studies on the effect of fluorosis on these two parameters in ruminants, except two studies on sheep which reporting a negatively influences of the fluorosis on the growth of young lambs (Dahri, 1990; Zouarhi, 2009).

In phosphate areas where fluorosis is hydrotelluric, a relationship between selenium deficiency and worsening toxic effects of fluoride has been observed in sheep (Dahri, 1990). Normally, plants take up selenium from the groundwater and the soil as an anion (SeO_3^{2-}). Consequently, due to the high affinity between phosphate (PO_4^{3-}) and selenite (SeO_3^{2-}), plants consumed by animals raised in phosphate area have low selenium levels (Lopes *et al*., 2017; Liu *et al*., 2018; Eliopoulos *et al*., 2020). Additionally, because of its great affinity with selenium, high of fluoride levels in an animal's body can decrease the antioxidant activity of GPx that uses selenium as cofactor, leading to oxidative stress which can aggravate the toxic effects of fluorosis. Therefore, it is important to further investigate the relationship between selenium deficiency and chronic fluoride toxicity in ruminants in Moroccan phosphate areas. Further studies to evaluate the application of Selenium-rich fertilizers to enhance its uptake by plants growing in the soil in these regions are also needed.

Socioeconomic impact of fluorosis

Because of its wide geographical distribution, its great diverse species that it affects, and considering the large number of ruminants in the regions concerned by fluoride excess, fluorosis is considered the first toxicological problem in Morocco (Zouarhi, 2009). It is well documented that the bioaccumulation of fluoride in the body of animals reared in endemic areas, exerts various toxic effects influencing their production and reproduction performances (El Amiri *et al*., 2022; Rahim *et al*., 2022a). Additionally, the prevalence and severity of fluoride toxicity in animals depend on many factors such as age, sex, individual biological response, and stress. Also, the environmental conditions (temperature and humidity), as well as fluoride concentration, duration of exposure, frequency of fluoride intake and nature of conducted work may also influence the prevalence and severity of fluoride toxicity (Shupe, 1971; Choubisa, 2000; Choubisa *et al*., 2010).

In hydrotelluric and industrial Moroccan areas, chronic ingestion and/or inhalation of fluoride by ruminants has caused different lesions in the form of dental fluorosis after the eruption of their first two teeth. Thus, in rural markets the examination of the teeth to look for lesions caused by fluorosis is a systematic act that the consumer performs before assessing the other criteria such as animal weight. In this regard, breeders report that the price undergoes a significant reduction (Maadid *et al*., 2017)while the teeth showed that the animal come from fluorosis region. Moreover, if the animal is not sold and remains exposed to fluoride for an extended period, it will be affected bypain and damage to bones and joints. Increasingly, it has been proven that with age fluoride also reduces the appetite, reduce the animal weight and reduced milk and wool production(Suttie and Kolstad, 1977; Ammerman *et al*., 1980; Ranjan and Ranjan, 2015). These damages are also reported by Maadid *et al*. (2016) in Beni Meskin areas. In this case, it has been reported that animals affected by dental and skeletal fluorosis tend to eat less because lesions of the jaw and teeth make food mastication difficult. Furthermore, locomotive syndromes hinder the animal from moving during grazing (Rahim *et al*., 2022a). As a result, animals incompletely grind their food, which will be poorly assimilated in the digestive tract. Thus, to compensate for their energy deficit, they catabolize their lipid and protein reserves, resulting in weight loss (Suttie and Faltin, 1973; Suttie, 1980).

Mitigation of fluoride toxicity in ruminants: outcome of previous studies

Mitigation based on farmers knowledge

Since fluoride excess causes irreversible toxic effects, prevention remains the best way to reduce its toxicity in animals. To prevent the damages cited above, several strategies have been adopted by breeders (Table 1). As reported by Abdennebi (1982), they used to sell young animals before their first teeth appear and buy adult animals from areas free of fluoride. However, this results in a loss of profits for the herd due to the low selling prices of young animals in the local markets in fluorosis regions. Even when breeders try to sell these young animals on far from the fluorosis region, the owner's teeth give an idea of the origin of the animal (Abdennebi, 1982) and cause a drastic drop in prices (El Amiri *et al*., 2022). Besides, transhumance is an old strategy adopted by breeders in endemic areas, which consists of transporting young animals from endemic areas to free fluorosis areas during the period of tooth formation (Maadid *et al*., 2017). However, this strategy it not practiced nowadays because of the reduction of grazing routes and the deterioration of social relationship between breeders (El Amiri *et al*., 2022). In hydrotelluric areas, breeders have tried to deepen wells to exceed underground fluoride depths (Abdennebi, 1982), but this strategy can lead to groundwater depletion (Rahim *et al*., 2022a). Nowadays, the majority of breeders use water of ONEE (the National Office for Electricity and Drinking Water) instead of well water (El Amiri *et al*., 2022), but in any case, it is still expensive. Other breeders recommended avoiding animal grazing during the winter (*Liali*: December 25 to February 05) and summer (Smaim: July 25 to September 5) seasons, and provide them with food purchased from unaffected areas, and water purchased from ONEE, but it's still expensive. Other strategies have been adopted by some breeders such as *faytour* (replacing the soil of the sheepfolds with cement or with soil from a fluoride-free region, or with a layer of feces). Besides, some farmers use an aluminum drinker to chelate the fluoride but these strategies are not always effective.

Table 1. Strategies for mitigating of fluoride toxicity in ruminants in Morocco.

The different mitigation strategies of fluoride toxicity		References
Farmers knowledge	Young animals' sale and the purchase of adults.	Abdennebi, 1982
	Transhumance of young animals.	Maadid *et al*. (2017)
	Deepening wells to exceed underground fluoride depths.	El Amiri *et al*. (2022)
	Avoid animal grazing during winter and summer seasons.	Abdennebi (1982)
	Use of *faytour* (a layer of feces) or replacement of the soil of the sheepfolds with cement, with soil from a fluoride-free region.	El Amiri *et al*. (2022)
	Use of an aluminum plateto chelate the fluoride from drinking water.	Zouarhi (2009)
Scientific research	Oral administration of sheep by 0.25 mmol of aluminum sulfate kg (BW)/day.	Aajouj (1982)
	Oral administration of sheep by 0.5 mmol of aluminum sulfate kg (BW)/day.	Kessabi *et al*. (1988)
	Injection of pregnant ewes with 0.056 mg Selenium (BW)/day (1 month before lambing), then the incorporation of aluminum sulphate in the diet of their lambs.	Dahri (1990)
	Daily consumption of 500 g of food enriched with 300 mg of aluminum sulphate per animal per day until the eruption of their first two teeth.	Zouarhi (2009)

Mitigation based on scientific research

From 1982, researchers in Morocco were oriented towards the search for preventive solutions against fluorosis in ruminants, mainly by supplementing sheep and cattle with aluminum sulphate ($Al_2(SO_4)_3$). In this regard, oral administration of 0.25 mmol NaF/kg (BW)/day plus 0.25 mmol of $Al_2(SO_4)_3$/kg (BW)/day attenuated disturbances in biochemical parameters, bone fluoride, and osteodental manifestations, compared to rams administered NaF only (Aajouj, 1982). Moreover, it was shown that oral administration of 0.25 mmol NaF/kg (BW)/day plus 0.5 mmol of $Al_2(SO_4)_3$/kg (BW)/day decreased digestive absorption of fluoride (approximately 33% to 45%) and reduced serum, urine, bones and teeth fluoride compared to sheep administered NaF only (Kessabi *et al*., 1988). This enhancing effect was subsequently confirmed in sheep and cattle reared in endemic fluorosis areas (Dahri, 1990; Zouarhi, 2009). In the El Brouj area, it has been documented that the injection of pregnant ewes with 0.056 mg of Selenium (BW)/day (1 month before lambing), then the incorporation of aluminum sulphate in the diet of their lambs, allowed live weight gain of 11.4 kg per animal for 1 year and a 20% decrease in blood fluoride levels (Dahri, 1990). Furthermore, in some communes belonging to the province of Settat (Beni Khloug, Lakrakra, Meskoura, and Ouled Ammer), a study carried out on lambs aged 6 months showed that the daily consumption of 500 g of food enriched with 300 mg of aluminum sulphate per animal per day until the eruption of their first two teeth protected them against dental lesions. Also, it significantly reduced (30%) the level of plasma fluoride and improved serum calcium compared to animals with endemic fluorosis not supplemented with the enriched food (Zouarhi, 2009). However, till recently and due to the lack of awareness and motivation of breeders, this solution is not applied in endemic areas (Benasila, 2014). The effect of aluminum sulphate has not been assessed on other ruminants, although toxicological studies have shown that cattle are the most susceptible to chronic fluoride poisoning. Generally, all research has focused on the application of aluminum sulphate as chelator to mitigate chronic fluoride toxicity in animals reared in Moroccan endemic areas. Moreover, other divalent chelator has been tested in other countries such as aluminum hydroxide (Spencer *et al*., 1980), Aluminum chloride (Said *et al*. 1977), Calcium carbonate (Ekambaram and Paul, 2002) with an encouraging degree of success. This is due to fluoride being a highly electronegative element that has a strong affinity with electropositive elements. Hence, this phenomenon of affinity and similarity between divalent elements and fluoride significantly reduces their absorption by the animal's body and mitigates the toxic effects of this halogen (Rahim *et al*., 2022b). However, recent studies indicated that chronic ingestion of synthetic metal chelators can lead to other chronic toxicities in animals (Samal et al., 2016). For instance, aluminum has been shown to induce oxidative stress (Exley, 2013), immunological perturbations (Mujika *et al*., 2018), genotoxicity (Nam *et al*., 2014), and metabolic dysregulation. Moreover, it had shown pathological conditions associated with aluminum such as pulmonary alveolar proteinosis (Iijima *et al*., 2017), granulomatosis and fibrosis (Igbokwe *et al*., 2019), toxicmyocarditis (El Hangouche *et al*., 2017), infertility (Malekshah *et al*., 2005), neurodegenerative, and hepatorenal disease in animals (Igbokwe *et al*., 2019). Therefore, recent studies have been oriented towards the supplementation of animals with medicinal plants and microalgae rich in divalent minerals as chelating agents (Banji *et al*., 2013; Samal *et al*., 2016). Moreover, these natural products are rich in antioxidants that can scavenge free radicals generated by chronic fluoride toxicity in animals (Rahim *et al*., 2022b). Since then, several researches have achieved remarkable results in reducing fluoride toxicity in cattle (Dey *et al*., 2013; Samal *et al*., 2016).

Conclusion

In Moroccan areas where fluorosis is hydrotelluric or industrial, the chronic ingestion and/or inhalation of fluoride leads to toxic effects which influence production, reproduction and growth performance in animals, leading to serious socio-economic problems for the breeders. Despite breeders own remedies and the research investigation of preventive methods, fluorosis remains a major handicap for ruminant breeding in these areas. More investigations are needed to update the status of fluorosis in ruminants in Morocco, to understand the mechanisms of toxicity in each animal species, and to pinpoint the exact source of intoxication in each endemic area. Moreover, the supplementation of animals by natural products instead of synthetic metals to prevent fluorosis in ruminants is new research niche.

Declaration of Competing Interest

The authors report no declarations of interest.

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