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FLUORIDE AND DOMESTIC ANIMALS: A REVIEW

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***Abstract*:** It has been noticed that the literature on effects of fluoride on domestic animals is controversial on the basis that the amount of fluoride salts that can be tolerated by animal and its effect on the health of the domestic animals due to continuous ingestion above normal level. Lots of investigations and surveys had presented a data on the fluorosis in domestic animals, is surprising and alarming. Besides the skeletal and dental deformities, significant damage was observed in the reproductive physiology and growth of the domestic animals. Fluorosis became the severe health problem in domestic animals all over the world including India. Many states are under the effects of high fluoride content and its effect on the livestock. This is a brief review to grab the attention about the danger of fluoride to the livestock especially in domestic animals.

Keywords: Fluoride, toxicity of fluoride, dental fluorosis, Skeletal fluorosis, non- skeletal fluorosis.

1.Introduction

The quality of life and the health of the environment are directly dependent on each other. Variations in natural and anthropogenic activities leads to the contamination of ecosystem. The effect of fluoride on the health of domestic animals has been studied for over 100 years by researchers from wide variety of disciplines. Natural geological sources and increasing industrialization effectuates increasing incidence of fluoride-induced human and animal health issues. Toxic pollutants are released via abiotic factors which in due course accumulate in the food chain, affecting living population which shows deleterious effects for their survival. Unlike human beings, animals also respond to the toxic effects of F which ultimately shows deleterious effects. The reports indicating the chronic harmful effects of F on different organelles of domestic animals and various studies have been reviewed in this article.

2.Properties of fluoride

Latin term- "floure" means – to flow, giving fluoride its name. It is 13th more abundant trace element in the Earth's crust. It belongs to halogen family, represented as 'F' with atomic weight 19 and atomic number 9. It is most electronegative of all elements and can be rarely found in its elemental state. It is essential for human and animal health. According to WHO (1984) and Bureau of Indian standard drinking water specification (2003) the highest desirable limit is 1.0 ppm and maximum permissible limit of fluoride in drinking water is 1.5 ppm. It is an inevitable industrial toxicant of geological origin found in water Mishra *et al.,* (2009). Concentrations above 1.5 ppm causes fluorosis Kumar and Puri, (2012). Which is a resultant of excessive intake of fluoride. The permissible limit for fluorides in drinking water is 1.5 mg/l (WHO 2017).

Worldwide scenario of fluoride levels

Environmental pollution is a major global problem posing serious hazard to human and animals. Chronic fluoride intoxication (fluorosis) is a worldwide health problem and is endemic in those areas where fluoride content is high in drinking water. Billions of people are affected due to fluoride exposure. In India, twenty million people are severely affected by fluorosis and 40 million people are exposed to risk of endemic fluorosis Chinoy JN, (1991). In a study conducted above 50% of the groundwater sources were fluoride contaminated Nandan *et al.,* (2007). World-wide twenty-four nations are belonging to the critical region regarding the fluoride level. Among them, India is one where 19 states are contaminated due to high fluoride content varying from 2-20ppm in potable water sources. The ministry of health & family welfare has identified at least 132 districts in 19 states severely affected by high fluoride content in drinking water, a leading cause of fluorosis.

3. Sources of fluoride exposure in domestic animals

In recent years, alarming cases of fluoride exposure in domestic animals has been seen due to various sources of fluoride emission. Hydrofluorosis, industrial fluorosis and endemic fluorosis shows hazardous effects on majority of the population Swarup *et al.,* (2001) and Sahoo *et al.,* (2003).

a) Natural sources

Drinking water with high fluoride contents is the prime source of natural fluoride exposure to animals. The majority of fluoride toxicity occurs via oral intake as compared to air borne fluoride Swarup and Dwivedi (2002); Ranjan and Ranjan (2015). Contaminated soil and percolation of F into the ground water via leaching causes F toxicity. Geological factors, consistency of the soil, nature of rocks, pH and temperature of the soil, chelation of elements, leakage of shallow groundwater are the factors responsible for the presence of F in groundwater Li *et al.,* (2014).

b) Mineral Sources

Mineral and geochemical stores are prime sources of F whereas major part of discharge of F into subsoil water takes place through the degradation of rocks containing fluorine Jacks et al., (2005). Mineral forms of F are Cryolite (Na3AlF6), fluorite (CaF2) and Fluroapatite (Ca5(PO4)3F Edmunds and Smedley ;(2005) Tavener and Clark; (2006).

c) Anthropogenic sources

The main anthropogenic sources of F occur due to industrialization, motorization, fluoride containing pesticides, fluoridation of drinking water supplies, dental products, fire extinguishers and refrigerators WHO, (2002) and Paul *et al., (*2011). These sources releases fluoride in the environment in the form of gaseous like HF, F2, SiF2 and particulate like CaF2, NaF, and Na2SiF6. Industrial emission contaminates the rainfall with fluoride and responsible for fluorosis in nearby farm animals Fuge and Andrews, (1988)

d) Forage and grasses

Forages and grasses around industrial area are highly contaminated due to F rich dust, ash, fluorine from industrial effluents, splashing on soil particles, on fodder by rain. This F contaminated food is also a source for F toxicity. Some studies stated that the plants contamination depends on various factors like the distance from the F source, types of vegetation, F released in to the atmosphere, atmospheric condition, height of the plants and the seasons etc. NRC 1960 and Mascola *et al.,* (1974)

e) Volcanic sources

From the volcanic eruption, F has been released in the form of hydrogen fluoride. Erupted F may cover several places and exists for long time. After decaying and leaching, F caused severe effects on domestic and wild animals**.** Weinstein and Davison;(2004, Araya *et al.*, (1993) and Bellomo *et al.*, (2007). The common sources of excess fluorine for animals have been reported by many workers as follows:

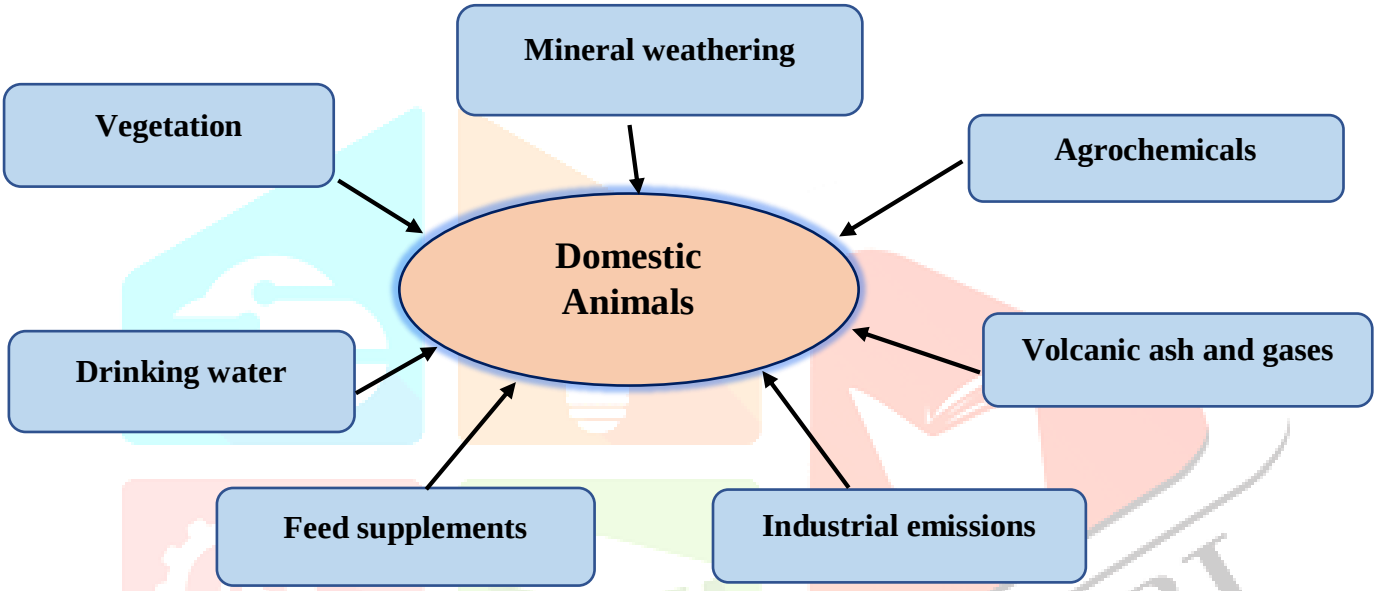

Figure 1. Sources of Fluoride in Animals

4. Bioavailability and absorption

Fluorides are ubiquitous in nature. The three main routes of absorption of fluoride are ingestion, inhalation, and percutaneous absorption. Only ingestion is significant in a farm context as well as in polluted environments Weinstein and Davidson, (2004). Absorbed fluoride is rapidly distributed in the circulation to the intracellular and extracellular fluid irrespective of route of intake. It is retained only in calcified tissues of bone and teeth. Ninety-nine percent of the total fluoride content of the body is concentrated in calcified tissue and the remainder is excreted in the urine EFSA (2005); ATSDR, (2003).

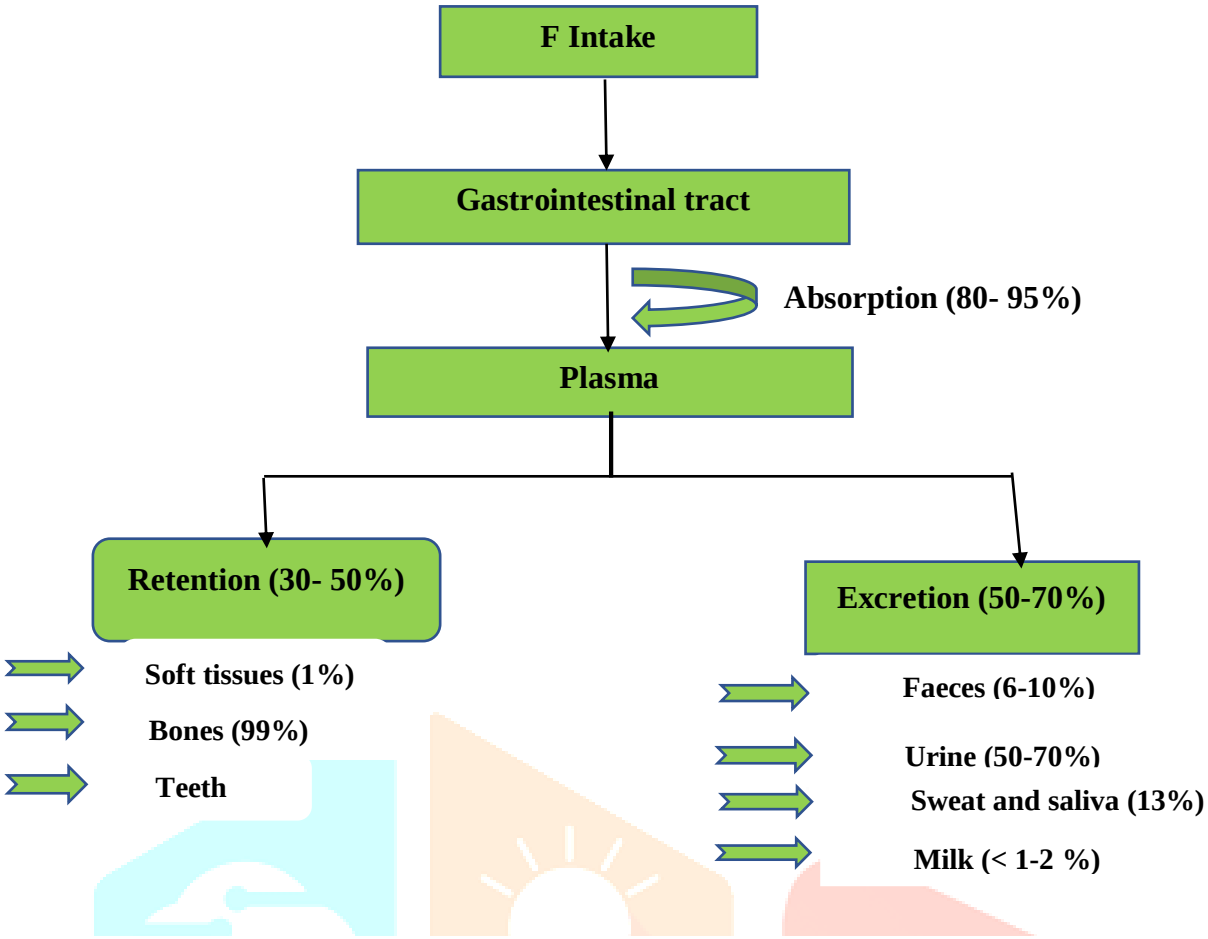

Figure 2. Summary of metabolism and excretion of Fluoride

Excess intake of fluoride for lengthened period results in its accumulation predominantly in hard tissues, teeth and bones and causes adverse effects which appear in the form of dental and skeletal fluorosis. Prolonged ingestion of fluoride also affects other organs and alters their architecture and physiology. It has been observed that, dental, skeletal and non-skeletal fluorosis have been described in different species of domestic animal due overexposure of fluoride in their drinking water, however maximum permissible limit for these animals has not been well studied yet.

Fluorotoxicosis is both beneficial and harmful to the living population, and is also required for various physiological functions: calcification of teeth and bones, fertility, haematopoiesis, and certain enzyme activation systems hence, it has been considered as one of the 14 essential elements for animal life Anonymous (1973). But as per Wheeler and Fell (1983), the necessity of fluoride in biological functions is still doubted, as the amount required is so negligible that deficiency cannot be produced under even the most careful laboratory conditions. Swarup and Dwivedi, (2002) observed that the readily soluble inorganic fluoride compounds are relatively more toxic and are easily absorbed by digestive tract of animals. Due to accumulation of fluoride in biological systems, constant and increasing intake of F results in pathognomonic signs of intoxication and is referred to as fluorotoxicity Wheeler and Fell, (1983). Overall, these signs appear in teeth, bones and soft tissues or organs of body and are known as dental, skeletal and non-skeletal fluorosis, respectively.

It has been observed in many studies that young animals are more prone to fluoride deposition in body tissues. It is reported to be dependent on various factors as species, age, food, nutrients, fluoride exposure, intake frequency, ambient factors, etc. Choubisa (1999) and Choubisa (2007). In a study conducted by Kaminsky *et al.,* (2011) it was reported that fluoremia increases with the age of the animals.

Domestic animals have a threshold level of fluoride tolerance, above which fluorotoxicosis develops.

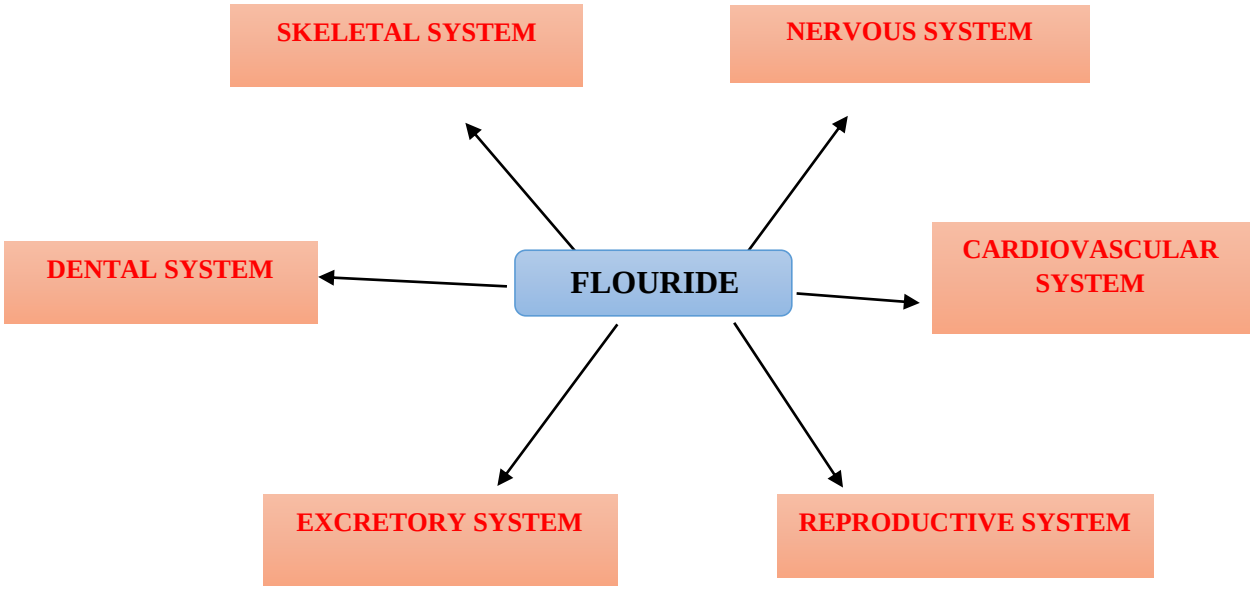

Figure 3. Toxicity of Fluoride On Organ System

5.1. Dental fluorosis

Dental fluorosis is a well-known developmental enamel defect due to excessive intake of fluoride which interferes with amelogenesis and dentinogenesis resulting in defective enamel and dentin formation Swarup and Dwivedi (2002). Mascarenhas (2000) reviewed that fluorosis was correlated with excessive fluoride intake especially during teeth development. According to Shearer *et al.*, (1978) dental lesions in animals include hypomineralized outer enamel, coronal cementum hyperplasia, disrupted subsurface pigment band, hypoplastic pits, puckered incremental lines, periodic radiolucent regions, and decreased microhardness of the outer enamel. Pitches and fine dots on the enamel surface of teeth causing loss of natural shine and early loss of the teeth Shupe (1980). In Goats living in an industrial F polluted areas saw teeth, excessive abrasion or wearing of enamel, and loss of teeth were more frequently seen Wang (1987). Damage to all of the enamel surface of the fluorosed teeth has been also observed. Wang (1992) and Wang (2003). Singh *et al.*, (2002) observed clinico-pathological signs of fluorosis. In dogs with chronic fluorosis, Kilicalp *et al.*, (2004) reported that teeth were abnormal in shape, size, color, orientation, and structure. The incisors and the molars were pitted and abraded respectively. Petrone *et al.* (2013) studied that long-term exposure of high levels of fluorides revealed hypomineralization and mottling in teeth. Choubisa (1997) and Choubisa (2000) mentioned the prevalence of dental fluorosis in calves is relatively higher than the prevalence in adult bovines rearing in the same F endemic areas. Also, Choubisa (1998) reported highest prevalence (100%) of dental mottling in bovine calves at 4.7 ppm of F concentration in drinking water. It indicates that Cows which are affected with fluorosis often shown a gingivitis. An adult cow might show indications of fluorosis without any remarkable effect on the teeth.

Choubisa, (2010) conducted a study in Bikaner district of Rajasthan where, calves (33.3%) and cows (40.0%) exhibited the signs of dental fluorosis. Pati, (2014) studied fluorosis in calves and observed that the prevalence of dental fluorosis was 79.5% and also brownish-yellow staining was seen. But in some cases, deep blackish colour instead of brownish-yellow was reported. Affected camels (*Camelus dromedarius*) showing varying degrees of dental fluorosis were recorded. Also enamel of mandibular and maxillary teeth were bilaterally and vertically stained from brown to deep yellow Choubisa, (2008). It is the most noticeable, irreparable, sensitive and indexive sign of chronic fluoride poisoning. Choubisa, (2010) conducted a survey in F endemic areas of Rajasthan on 18 domesticated dromedary camels of which 15 were mature and 3 were immature. It was reported eight of these camels showed mild to severe dental fluorosis.

Table 1: Showing classification in dental lesions in fluorosis Shupe *et al.*, (1979)

Score	Type	Description
0	Normal	Translucent, smooth, glossy white enamel, teeth are normal in shape.
1	Questionable effect	Slight deviation from the usual translucency of normal enamel. Cause is no precise. May have enamel flecks; cavities, if present may be unilateral or bilateral, but no mottling is evident.
2	Slight effect	Slight mottling of enamel; may have some discolouration, but no abrasion. Teeth have normal shape.
3	Mild effect	Moderate mottling (large patches of chalky enamel), discolouration of enamel; teeth may have slight abrasion.
4	Marked effect	Definite mottling, discolouration, hypoplasia and hypocalcification; may have pitting of enamel; enamel maybe cream coloured; definite abrasion of teeth.
5	Excessive effect	Definite mottling, discolouration, hypocalcification, may have pitting of enamel; enamel may be cream coloured, excessive abrasion of teeth.

The animals reared within 0.5 km of the aluminium smelter Odisha had more dental fluorosis (91.02%). However, the percentage of animals with severe dental fluorosis decreased with increasing distance from the smelter plant. A rough body coat, stunted growth, emaciation, decrease in milk yield, unthriftiness, and chronic wasting were the prominent clinical findings in the fluorotic cattle. Ray *et al.*, (1993); Patra *et al.*, (2000); Maiti *et al.*, (2004) Horses and donkeys were also afflicted with mild to severe dental fluorosis.

In a study conducted by (Shupe 1980) few mature buffaloes also showed deep black dental fluorosis instead of yellowish, striated, horizontal lines. A survey was conducted among domestic ruminants in the Dungarpur district of Rajasthan, included cattle (*Bos taurus*), buffaloes (*Bubalus bubalis*), camels (*Camelus dromedarius*), sheep (*Ovis aries*), and goats (*Capra hircus*) showed signs of dental fluorosis among mature and immature animals. It was reported that 55.9% buffaloes, 48.0% cattle, 10.7% goats, 7.3% sheep and 5.3% camels were prevalently affected among the mature ruminants. Among 43 immature cattle and 37 buffalo calves, the prevalence rate was 51.1% and 62.2% respectively Choubisa, (2011). Choubisa, (2013) conducted another study on buffaloes in which, adult ones were found to be affected with varying degrees of dental mottling.

In advanced condition of dental fluorosis, pronounced loss of teeth supporting alveolar bone with recession and swelling of gingival and excessive wearing of teeth giving a wavy appearance are also due to chronic fluoride exposure/intoxication.

From the above reviewed it can be concluded that dental fluorosis is directly proportional to the concentration of F present and is variable from place to place and species to species. Discoloured, mottled enamel, uneven wearing of teeth were common symptoms in cattle. The maximum susceptibility to fluoride toxicosis was found in bovines (buffaloes and cattle) followed by equines (donkeys and horses), flocks (goats and sheep) and camelids (camels). The maximum prevalence to F toxicosis was shown by bovine. The severity of F toxicity in camels was found less in comparison with other domestic animals Overall, fluoride is slow toxicant and causes chronic health hazards in domestic animals.

5.2. Skeletal fluorosis

Bone is the principal site of F accumulation, which stimulates the proliferation of (osteoblasts) and gradually builds up the bones by increasing the uptake of calcium by bones Farley *et al.*, (1983). Common symptoms of skeletal fluorosis are poor body condition, muscle wasting, locked up joints, diffidence to move, painful and rigid joints, bony outgrowths and osseous lesions in animals. In calves during developmental condition, over exposure of fluoride in cows causes skeletal fluorosis in calves and it was also reported that fluoride could pass through placenta during gestational period Krook and Maylin, (1979). Maylin *et al.*, (1987**)** also reported that calves born from fluoride intoxicated cows had severe symptoms of osteo fluorosis such as severe malfunctioning in cartilage cell differentiation, osteoblasts bone marrow atrophies and stunted growth. Changes appear clinically in the form of vague aches and pains in the body and joints associated with

rigidity or stiffness and lameness, stunted growth, palpable bony lesions and snapping sound in feet during walking, lesions in the mandibles, ribs, metacarpus and metatarsus regions.

Progressive and unrepairable osteal changes become more severe with advancing of age Choubisa (1999). Swarup and Dwivedi, (2002) noticed mild to moderate intermittent lameness in hind legs, stiffness of leg tendons, and wasting of main mass of hind quarters in camels. Industrial skeletal fluorosis was observed near aluminium smelter Odisha, it was reported that skeletal lesions in the fluorotic cattle were found as exostoses of ribs, mandible, metacarpal, metatarsal and pelvic vertebrae, swelling of joints, lameness, bending of limbs, and deformed over growth of hooves. Such pathognomic signs of chronic industrial F intoxication in cattle were also observed and reported earlier. Ray *et al.,* (1993); Patra *et al.,* (2000); Maiti *et al.,* (2004). Kilicalp *et al.,* (2004) conducted a study on dog and observed pulp cavities were exposed to fracture. Also, osseous lesions included exostoses of the jaw and long bones, usually accompanied by thickening and change of the bones. The dogs were lame and showed pain and difficulty when moving. In goats, physical weakness, indolence, and reluctancy to move was seen. They also showed mild to severe intermittent lameness, especially in the hind legs, stiffness of the leg tendons, and wasting of the main mass of the hind quarters were noticed. They also showed a lowering of the neck while walking. Kant *et al (*2009) also experimented with goats of Jammu and Kashmir. Sodium fluoride without and with aluminium sulphate was supplied in their diet. Goats exhibited decreased movement with muscle wasting, thickened and dense bones.

In a study conducted in endemic areas of the Dungarpur district, Rajasthan 16.7% mature camels showed periosteal exostoses, moderate intermittent lameness, and hardening of tendons in the legs as pathognomonic signs of skeletal fluorosis abortions Choubisa, (2010). In Horses and donkeys slight to severe intermittent lameness in their hind legs, stiffness of tendons in the legs, wasting of main mass of hind quarter and shoulder muscles, deformed hooves, snapping sounds, and lowering of neck and head during walking was observed Choubisa, (2010**).** Choubisa, (2011) reported prevalence of skeletal fluorosis in mature ruminants. 48.3% in buffaloes, 39.8% in cattle, 8.4% in goats, 5.6% in sheep, and 5.3% in camels. In another study, it was reported that goats were physically weak, indolent, and reluctant to move, mild to severe intermittent lameness, especially in the hind legs, stiffness of the leg tendons, and wasting of the main mass of the hind quarters were also observed Choubisa, (2013) The seasonal variation in the F intake in the goat may also contribute to the lower prevalence and severity of osteo fluorosis Choubisa (2013).

Highest frequency of exostosis was recorded in metacarpal and metatarsal (20% in buffalo, 15% in cattle and 10% in goat) followed by in ribs (15% in buffalo and 15% in cattle and 5% in goats) and frontal bones (10% in buffalo 10% in cattle and 5% in goat Swarup and Dwivedi (2002) and Modasiya *et al.,* (2014). In fluorotic bovines, snapping sound was heard from legs during walking. In addition to these, poor body condition, stunted growth, decreased draught power were observed. The present findings are in correspondence with Modasiya *et al.,* (2014).

Kumar *et al. (*2015) conducted a study and stated that excessive intake of fluoride causes abnormalities or damage in skeleton and immature cattle are highly liable and more susceptible and less tolerant to fluoride Kumar *et al.,* (2015).

Painful walking due to periosteal exostoses at ligament & tendons, osteomalacia and osteoporosis has been reported in fluorotic animals by Samel *et al.,* (2016). Sheikh and Panchal (2018) reported skeletal fluorosis in cows, goats and buffaloes of Udaipur, Rajasthan.

From the various available reports, it can be reviewed that animals showing severe skeletal fluorosis were bodily weak, indolent and more reluctant to stand. High fluoridated groundwater, fodder, soil, emission from various factories and mining of rock phosphate were responsible for the severity of skeletal fluorosis.

Prevalence of skeletal fluorosis was severe among immature animals as compared to the matured ones.

5.3. Non-skeletal fluorosis

Non skeletal forms of fluorosis are earlier manifestations which develop long before the onset of typical changes in teeth and skeletal bones these are seen as gastro-intestinal symptoms and may overlap with other diseases. Toxic effects of F in various organ systems are referred to as non-skeletal fluorosis. Singh and Swarup (1999) observed biochemical changes in serum and urine in fluorotic cow and buffaloes and higher levels of F in urine and serum were noticed. Industrial fluoride toxicity in cattle was studied by Patra *et al. (*2000) in Udaipur. Toxic effects of NaF has been found to produce deleterious effects in soft tissues such as gastrointestinal tract, lungs, heart, kidneys and liver of domestic animals. Shinde and Shinde (2006) also stated that fluorosis is caused by ingestion of excess fluoride over a long period. It affected multiple systems

of the body and resulted in several clinical deformities. Kumar and Choudhary, (2015) reported about the other signs of chronic F intoxication as colic, intermittent diarrhoea, polydypsia, and polyuria, Sheep were reported to be less susceptible to fluorosis as compared to cattle.

a. Hepatotoxicity of fluoride- An increase in activities of serum transaminases, sorbitol dehydrogenase, and decreased levels of serum total protein and albumin reflecting altered liver function were reported in fluorotic cattle Araya *et al.*, (1990) and goats Tsunoda *et al.*, (1985). Liver is an important organ for metabolism and detoxification of foreign substances WHO, (2002). Evidences of changes in liver may relate to that the liver has a central role as a detoxifying organ towards xenobiotics and chemicals. Thus, fluoride shows adverse effect by altering the regular hepatic functioning in domestic animals.

b. Reproductive toxicity of fluoride- Adverse effects on sperm motility, sperm morphology, and semen hyaluronidase activity was also recorded invitro studies on bovine semen Schoff and Lardy (1987); Tanyildizi and Bozkurt (2002). In fluoride endemic areas calves of fluorosed cattle and buffaloes showed abnormal morphology which indicates placental transfer of fluoride Choubisa (2011). In female goats, repeated abortions, still births, and irregular estrous cycles were also prevalent in Rajasthan due to industrial fluorosis Choubisa, (2015). Chronic fluoride intoxication can impair reproductive function. High prevalence of sterility, still birth, repeated oestrus cycle, and birth of weak offspring have been reported in domestic animals in the areas with high fluoride contents in water. Since fluoride has the ability to cross the placental barrier, it can alter reproductive processes in animal species in diverse ways which leads to reproductive toxicity.

c. Renal toxicity of fluoride- Kidneys are primary organs concerned with excretion and retention of fluoride and thus are generally involved in chronic fluoride intoxication. High levels of serum urea and creatinine in the affected cows, buffaloes and goats are therefore indicative of degenerative changes in the kidney Singh and Swarup (1994). Elevated serum urea, nitrogen and creatinine are reported in cows and buffaloes afflicted with fluorosis Suttie (1957) and Singh and Swarup (1999). Enhanced fluoride levels have also been reported in the serum of camels Zhang *et al.*, (2015). In short it is observed that intoxication of fluoride in domestic animals causes degenerative effects on kidney.

d. Gastrointestinal toxicity of fluoride- Readily soluble fluoride compounds are relatively more toxic and are easily absorbed by digestive tract of animals Swarup and Dwivedi (2002). Being a highly electronegative element, fluoride has strong affinity towards electropositive elements. In the gastrointestinal tract, fluoride binds with calcium, thereby reduces its absorption. Significant decrease in serum calcium in fluorotic animals such as cattles and buffalo was recorded Maiti *et al.*, (2004) and Bharti *et al.*, (2007). Discomforts such as decreased appetite, abdominal pain, constipation, excess gas production or formation and loose watery faecal matter were seen, body muscles of calves were found to be weakened. Such health problems have also been reported in the immature equine animals Choubisa (2010). Thus, it is observed that due to higher dissolution rate of fluoride in the gastrointestinal tract of animals, it decreases the rate of absorption and causes discomfort in the other body parts.

e. Cardiovascular toxicity of fluoride- The vascular wall is rich in collagen fibres and are one of the major sites of action of fluoride. Cardiac changes and cardiac arrest can occur due to hypocalcemia and/or hyperkalemia that develop following exposure to high doses of fluoride Cummings and McIvor (1988). Electrocardiogram changes along with a decrease in heartbeat were also reported in dogs Kilicalp *et al.*, (2004) and sheep Donmez and Cinar, (2003). It can be seen that diffusion of fluoride into the vascular wall increases the risk of cardiovascular changes in the affected animals.

f. Neurotoxicity of fluoride- Cattle, buffaloes and other domestic animals living in hyper-endemic areas for long time developed para and quadriplegia, polyurea and neurological disorders Choubisa (1999) and Choubisa (2007). Hence the toxicity of fluoride gives rise to various neurological disorders in the animals.

g. Endocrine toxicity of fluoride- According to Wheeler (1983) and Swarup Dwivedi (2002) extremely high intake of fluoride influences function of thyroid, parathyroid and adrenal gland causing subsequent changes in humoral profile. Fluoride-induced effects on reproductive organs, gametogenesis, embryogenesis and brain are also not well studied in domestic animals. Thus, it is observed that excessive intake of fluoride leads to malfunctioning of the endocrine organs in the animals, which further causes changes in their humoral profile.

Conclusion:

This review encapsulates the F toxicity in animals. High F intake leads to acute and chronic health problems in livestock. Anthropogenic sources of F causes health issues but majority of the problem arises from natural sources via ingestion. Since animals are economically important, more epidemiological studies are needed on natural fluorotoxicosis or hydrofluorosis in relation to different fluoride concentrations in drinking water and biological and non-biological determinants in diverse species of domestic animals to determine safe limit of fluoride in drinking water. Fluorosis is also responsible for a decline in zootechnical performance which explains the economic losses. In addition to this more studies are also required on molecular, histochemical, histoenzymological, biochemical and radiological aspects so as to assure the mechanism involved in fluoride toxicosis. Also, ameliorative measures are important to prevent their endemicity of fluorosis.

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