A Review of

Concentration of Fluoride In World and India:

Effects of Fluoride on Human Body

-K.R.Shanmugam,
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By

K.R.Shanmugam[a] M.Siva[a,b], S. Ravi [b], B.Shanmugam[b],

G.VenkataSubbaiah[b],Sathyavelu Reddy K[b],

a. Department of Zoology, T.R.R. Government Degree College, Kandukur, A.P

b. Division of Molecular Biology and Ethanopharmacology, Department of Zoology,Sri Venkateswara University, Tirupati – 517 502, India.

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427, Palhar Nagar, RAPTC, VIP-Road, Indore-452005 (MP) INDIA
Phone: +91-731-2616100, Mobile: +91-80570-83382
E-mail: **contact@isca.co.in** , Website: **www.isca.co.in**

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Author(s):	K.R.Shanmugam, M.Siva, S. Ravi , B.Shanmugam , G.VenkataSubbaiah, Sathyavelu Reddy K,
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Abstract

The objective of the present Research Review was to know the toxic effects of fluoride on human health in different parts of world and India. Data we used in our review were systematically searched and collected from web pages and documents published in journals and requested form the authors in relating to this topic. Fluoride occurs naturally but we consume it in small amounts. Exposure to fluoride can occur through food, water and fluoride supplements. Low quantity of fluoride is useful to humans but high quantity leads to several disorders and also it affects each and every part of the human being. The toxic effects of large doses of fluoride are predominantly confined to the teeth and skeletal system, with secondary involvement of the nervous system in advance and crippling fluorosis. The present review will give information regarding the fluoride contamination in different parts of world and India and also the effects of fluoride.

Keywords:Fluoride contamination, World, India, Fluoride diseases.

Introduction

Water is an essential natural resource for sustaining life and is among nature's most valuable gifts. Unfortunately, groundwater is either being increasingly depleted for irrigation of crops, industrial, or other uses, or is becoming contaminated by various pollutants. The presence of fluoride as a contaminant of groundwater has become a worldwide problem, because it is commonly found in groundwater sources. The problem of high fluoride content in groundwater resources is important, because of both toxicological and geo-environmental concerns. The chief source of fluoride in groundwater is fluoride-bearing minerals that exist in rocks and soil. In groundwater, the natural concentration of fluoride depends on the geologic, chemical and physical characteristics of the aquifers, porosity and the acidity of the soil and rocks, the temperature, the action chemical elements, and the depth of the wells.

Over all 200 million people worldwide rely on high fluoride contaminated water. The probability of occurrence of high fluoride concentration in ground and surface water was detected in varies countries like India, China, Argentina, Mexico, several African countries, Pakistan, Italy, Iran, Bangladesh, Newzeland, Ethiopia, UK. The dental fluorosis and skeletal fluorosis are endemic in South Africa, Australia, Japan, Thailand, Canada, Saudi Arabia, Persian Gulf, Srilanka and Syria. The above said countries are most prominent fluorosis affected countries in world. [1]. Fluoride is a halogen found in soil, water, air, plant and animals in different quantities.[2]. The major sources of internal exposure of individuals to fluorides are the diet, dental products, dermal absorption from chemicals or pharmaceuticals, ingestion of fluoride- containing drugs, tobacco consumption, exposure to industrial emissions and ingestion of fluoride-containing soil. [3]. It is now acknowledged that of the entire common foodstuff, tea has one of the highest potential for increasing the daily fluoride intake. [3], [4]. Tea trees

accumulate and store fluoride by absorbing it from the air and soil. Fluoride accumulates mostly in leaves of the tea plant. [3].

Table-1.Drinking water standards for fluoride ion has been prescribed by Various authorities.

S.NO	Authorities	Permissible limit of Fluoride S.NO concentration(mg/L)
1	WHO	0.5
2	US Public Health Standard	0.7-1.2
3	BIS(IS 10500)	1.0-1.5
4	Indian Council of Medical Research	1.0-2.0
5	CPHEEO	1.0-1.5

Fluoride distribution in World

Fluoride in groundwater shows both spatial and temporal variation. We have observed that in most countries, the fluoride-related health hazards are under control. Though, some dental fluorosis cases are reported in some countries like India, China, Ethiopia, Kenya and Argentina. Fluoride contamination in groundwater is a serious issue, while Mexico is moderately affected country .The details of worldwide distributions of fluoride in groundwater are discussed below.

South Asia: The South Asia can be considered as the epicenter of fluoride contamination in groundwater. All countries of South Asia such as India, Pakistan and Sri Lanka are highly

Sri Lanka: In Sri Lanka, high fluoride concentrations were observed mainly in eastern and southeastern part of the country. Most of the high concentrations of fluoride in groundwater

samples were observed in boreholes located on charnockitic gneiss, calc gneiss, biotite gneiss and granulite. Boreholes drilled in marble rarely reported values of fluoride in groundwater above 2.0 mg/L. Similarly, boreholes drilled in quartzite rarely reported fluoride in groundwater above1.5 mg/L. [5]. Dental fluorosis has been reported from WalaweRiver basin in southern Sri Lanka. Here, dry and hot climate is the major factor responsible for high fluoride concentrations in groundwater. [6] A recent study in Sri Lanka reports that weathering leading to dissolution of fluoride-bearing heavy minerals releases both immobile and mobile elements. The immobile elements are retained in the soils, while the mobile elements such as fluorine are released into the groundwater. [7]

East Asia: In East Asia, China is the most affected country. Here, the groundwater in areas of low rainfall and high temperature is highly contaminated compared with other regions. The details of contaminated regions of East Asia are discussed below.

China: In China there are three categories of water resources.

1. Shallow groundwater areas characterized by dry climate and evaporation exceeding precipitation. In this category, high fluoride level is found in areas such as western part of Songliao Plain, central part of north China Plain and Nemonguhigh Plain basin in central part of Shanxi Province. Besides, high fluoride levels are also found in inland basins and piedmont plains of Northwest China.

2. Deep groundwater areas characterized by semiarid conditions. High fluoride levels in this category include areas such as coastal plain of Bohaiwan, eastern part of Huang-Huai-Hai Plain and basins of the central part of Shanxi.

3. Groundwater system associated with hot spring and mines. High fluoride here is mostly found in the areas such as Liaodong Mountains, Liaoning Peninsula, hills of south-eastern China and mountains in southern Xizang. [8]

Indonesia: In Asembagus, the coastal area of East Java, wells found in the vicinity of riverbed were characterized by highest fluoride concentrations. Moreover, the river water, which is used for irrigation, has fluoride concentration as high as 14.2 mg/L. On the other hand, the range of fluoride in well water is found to be in the range of less than 0.1–4.2 mg/L. [9]

Africa: Groundwater is the main source of fresh water supply for most of the rural communities in Africa. This groundwater in east African rift valley area has high level of fluoride concentration. This rift valley is a part of Great Rift Valley of Africa extending from Jordan valley down through Sudan, Ethiopia, Uganda, and Kenya to Tanzania. It seems that high fluoride concentration in groundwater is somehow linked to geology of rift valley. It may be the anomalous concentration of fluoride in groundwater could be found in other areas along the Great Rift Valley.

Tanzania: In Tanzania, weathering associated with rock–water interaction is a significant factor for fluoride contamination. Nanyaro et al. [10] studied the lowland rivers of Tanzania and observed that fluoride is derived from soil and weathering of fluorine rich nephelinite and carbonatiticrocks. However, in regions around Mt. Meru crater, gaseous emanations through mineral springs are responsible for increased fluoride concentrations. High concentrations of fluoride in Mt. Meru area in northern Tanzania are attributed to weathering of villiaumite (NaF) triggered by high temperatures coupled with high precipitation. [10]

Pakistan: In East Punjab area of Pakistan, around 75 % of groundwater samples were reported to exceed WHO standard of fluoride. [11]In this area, groundwater exhibits a positive correlation

between fluoride and sodium as well as bicarbonate ions, while fluoride shows a negative correlation with calcium and magnesium ions. Further, the concentration of fluoride is higher in shallower aquifer than deeper one. [12]Groundwater near Nagar Parkar Town (South East Pakistan) has also been reported to have fluoride concentrations up to 7.85 mg/L (Table 6). Dental and skeleton fluorosis cases are commonly reported from people living in Thar region. [13]

South Africa: In the Republic of South Africa, researchers have reported that around 803 sites are affected by endemic fluorosis. These include locations in Western and Karoo Regions of Cape Province, north western, northern, eastern and western areas of transvaal, western and central free state. Fluoride levels as high as 6 mg/L were reported in groundwater of Madibeng local municipality in northwest Province of South Africa. [14]

Germany: In Germany, Queste et al. [15] have reported fluoride in Muenster region. Up to 8.8 mg/L of fluoride is reported from private wells (Table 6). Geological processes are responsible for high fluoride in the Muenster region. [15]

Mexico: In Northern Mexico, fluoride is found to be in the range of 0.5–3.7 mg/L. [16]They also reported a positive correlation of fluoride with arsenic.Vasquez et al. (2006) observed fluoride concentration in groundwater up to 7.59 mg/L in La Victoria area, Hermosillo City (Table 6). [17]Here, higher values of fluoride are observed in deeper aquifers compared with shallower ones. 5.6 mg/L of fluoride is reported in the drinking water of Durango. [18]

USA: In the USA, fluoride in groundwater ranges from less than 0.2 to 3.58 mg/L in Ohio. [19] Robertson (1984) observed up to 13 mg/L of fluoride in groundwater of Arizona. [20]Up to 7.60 mg/L of fluoride was also reported from crystalline bedrock aquifers of Marathon County,

Wisconsin. [21] In Wisconsin, felsic igneous and equivalent rocks are considered to be the source rock for fluoride in groundwater.

Canada: In Canada, up to 15.1 mg/L of fluoride (Table 6) was reported in Lake St. Martin region of Manitoba. [22]In the Gaspe region (Quebec), some skeletal fluorosis cases are also reported. [23]

Argentina: Argentina is the most affected country as observed by various researchers. Smedley et al. (2002) studied La Pampa area of Argentina and found fluoride in the range of 2.9–25.7 mg/L in shallow aquifer (9–10 mbgl), while they reported higher concentration of fluoride in deeper aquifer beyond depth of 17 m in TalleresNorte borehole. [24]Nicolli et al. [25] studied Chaco- Pampean area and also reported fluoride up to 3.7 mg/L in the shallow aquifer and 7.34 mg/L in deeper aquifers. Kruse and Ainchil[26] studied Buenos Aires Province and found fluoride content in the range of 0.2–5 mg/L.[26] Further, Paoloni et al. [27] observed fluoride concentrations in the range of 0.9–18.2 mg/L in south east subhumid region of Pampa. [27] Cabrera et al. (2001) also observed fluoride in the range of 1.4–10.6 mg/L in Pampian plain,[28] whereas Cid et al. [29]reported fluoride content in the range of 0.15–0.56 mg/L in Midwest of Argentina (Table 6).[29]

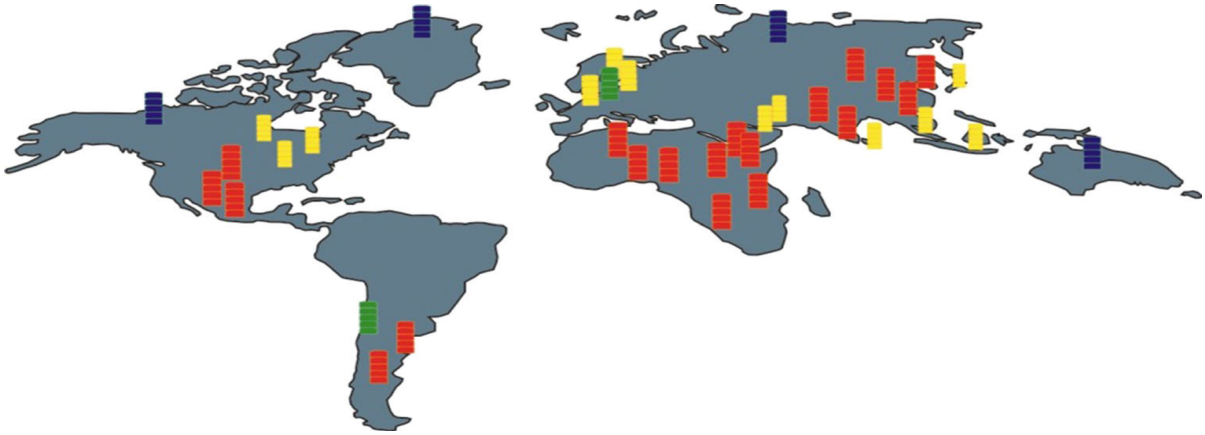


Figure. 1 Worldwide distribution of fluoride; red bars highly affected areas; yellow bars moderately affected areas; green bars least affected areas; blue bars insufficient data (based on worldwide dataset). Note: the highly affected areas are in general arid and semiarid regions

Table 2.Dietary fluoride supplements schedule

	Fluoride ion level in drinking water (in ppm)*		
Age	<0.3	0.3-0.6	>0.6
Birth to 6 months	None	None	None
6 months to -3 years	0.25 mg/day	None	None
3-6 years	0.50 mg/day	0.25 mg/day	None
6-16 years	1.0 mg/day	0.50 mg/day	None

Fluoride contamination in India

The occurrence of fluoride contamination were observed in groundwater's in several states of Andhra Pradesh, Rajasthan, Haryana, Uttarpradesh, Madhya Pradesh, Maharashtra, Tamilnaduand Karnataka in India was well documented. [30] In India, it was first detected in Nellore District in Andhra Pradesh in 1937. Approximately 62 million people including 6 million children suffer from fluorosis because of consumption of water with high fluoride contaminations.[31],[32] (Table 5.)

1. Fluoride contamination in Andhra Pradesh: Andhra Pradesh is most prominent fluoride contaminated state in India. In Andhra Pradesh, Nellore district, in the region of UdayagiriTaluk villages having high fluoride concentration in drinking water. They are Turakapali 4.01 ppm, and pakeerpalem 4.00 ppm, Varikuntapadu 6.74 ppm, Gangireddypalli4.43 ppm, Basinepalli 3.12 ppm. [33] The fluoride contamination in the South-eastern part of Rangareddy district (present in Telengana State), in Andhra Pradesh. The endemic district of Andhra Pradesh has indicated that fluoride rich ground water present in the wells located downstream water samples were determined in eight villages of Andhra Pradesh in India. Among these villages thirty-eight samples were collected and analyses for fluoride content along with PH, electrical conductivity, total dissolved solid(TDS), total hardness, total alkalinity, chlorides, sulfates and nitrate. Fluoride concentration in surface and ground water samples varied from 0.5 and 9.0 mg/l. [34]

Fluoride concentrations in groundwater samples were determined in Uravakonda, Anantapur district of Andhra Pradesh. Fluoride concentrations in groundwater samples of these villages varied between 0.5 to 7.2 mg/l. Fluoride contaminations in groundwater in parts of Kudupa district, Andhra Pradesh. The fluoride concentrations in groundwater of this region ranged from 0.226 to 3.52 mg/l. [35] In Kandukur the range of fluoride ion in all drinking water has varied from 1.22 to 3.09 mg/l and 1.4 to 4.6 mg/l. [36] In Guntakal area of Anantapur district drinking water has fluoride level in the range of 0.18 to 2.00 mg/l. [37]Range between 1.1 to 5.8 ,mg/l fluoride concentration was determined in drinking water of Kommala area, Warangal district in (present in Telengana state) Andhra Pradesh. [38]

2. Fluoride contamination in Tamilnadu:

Tamilnadu state has severe problem with fluoride contamination. In to be In Dharmapuri, and Krishnagiri, Salem, thegroundwaterhashigh concentration of fluoride.

Ambattur industrial area in Chennai was the highly contaminated by fluoride. Ten different habitations were selected for the study and compared. Fluoride concentration in the range of 0.8 to 1.4 mg/l was finding in 10different location of Ampatture industrial area. [39]

3. Fluoride contamination in Maharashtra:

The Occurrence of fluoride was observed in ground water of Pandharkawada area in Yavatmal district of Maharashtra. The following villages having high fluoride concentration in groundwater's viz, Chikhaldara 0.48 mg/l, Mohadari 0.34 mg/l, Runjha 0.61 mg/l, Khatara 4.81 mg/l,Sonurli 3.03 mg/l, Karanji (phul pod) 2.45 mg/l, Wadhona (Bk) 5.76 mg/l, Wadhona(Kh) 5.75 mg/l, Dharna 13.41 mg/l, Skhra 11.9 mg/l, Nilgiri 3.50 mg/l, Ganeshpur 2.84 mg/l, Wai 3.02 mg/l, Datpari 2.91 mg/l, Pimpri 0.90 mg/l, Gevrai munch 4.81 mg/l,Karegaon 0.30 mg/l. [40]

4. Fluoride contamination in Gujarat:

The fluoride concentration in the groundwater varies in the district of north Gujarat region. It varies from 0.99 to 5.48 ppm in Sabarkantha district, 1.96 to 10.85 ppm in Patan district, 3.82 to 10.08 ppm in Mehsana district and 2.77 to 6.64 ppm in Banaskan district. Around 80% of the groundwater samples from Sabarkanth district contain fluoride above the maximum permissible limit, in Mehsana district also 95% of groundwater samples having higher fluoride level, in Banaskan district 92% samples having fluoride above maximum permissible level. [41]

5. Fluoride contamination in Rajasthan:

In Northern Rajasthan many parts were contaminated by excess fluoride contamination in drinking water. The following areas are having high fluoride contamination in drinking water, Fluoride range between 4.78 to 1.01 mg/l. Some parts of Rajasthan risk in endemic fluorosis, where as above 1.5 ppm of fluoride concentration in drinking water. [42]Astudy on distribution

and health hazards by fluoride contaminate in ground water was performed in 1,030 habitations of bhilwara district of central Rajasthan. 1030 samples were collected and analyzed for fluoride concentration Fluoride content in these villages varies from 02 to 13.0 mg/l. [43]

6. Fluoride contamination in West Bengal:

The assessment of potential hazards of Fluoride contamination in drinking water was reported in West Bengal of India. The following villages have fluoride contamination in groundwater viz, Moga having fluoride contamination in the range of 0.11 to0.96μg/ml, Chanditala-2 is 0.03-1.12 μg/ml, Haripal is 0.07-1.05 μg/ml, Tarakeswar is 0.07 to 1.00 μg/ml, and Dhaniakhali is 0.02 to 1.00 μg/ml. In West Bengal fluoride rich groundwater was reported in Birbhum district. Bankara district of West Bengal peoples affected by dental and skeletal fluorosis due to the high concentration of fluoride in drinking water. [44]

7. Fluoride contamination in Uttar Pradesh:

In Uttar Pradesh Makur and Tumkur district having high fluoride concentration in drinking water. In Makur block, the fluoride concentration in the groundwater was found to vary between 1.05 to 13.9 mg/l. Which exceeded the maximum desirable limits of 1.0 mg/l of fluoride in the drinking water as lay down by bureau of Indian standards (BIS). [45]

8.Fluoride contamination in Karnataka:

In Karnataka Kolar and Tumkur districts, have high fluoride concentration in drinking water. The fluoride concentration in Kolar district, in the range of 0.36 to 3.34 mg/l and fluoride concentration in Tumkur district in the range of 0.78 to 5.35 mg/l. Hathiguddur in Gulbarga district has a fluoride level of 704 mg/l, while 5.75 mg/l was observed in Farthtabad. [46]

9.Fluoride contamination in Kerala:

Kerala is the one of the states which has,low fluoride contamination compared to other Indian states. In Palakkad, the fluoride levels varied from the detection limit to 1.8 mg/l and concentration in Alappuzha varied from 0.3 to 1.6 mg/l. [47]

10.Fluoride contamination in Assam:

Fluoride concentration was reported in groundwater of small Tea gardens in Sonitpur district, Assam in India. The fluoride concentration in Tea garden water samples varied from 0.6 to 5.602 ppm. [48] In Assam Nalbari district drinking water fluoride concentrations in the range of 0.02 to 1.56 mg/l. [49]

11.Fluoride contamination in Chhattisgarh:

Fluoride contamination was reported in groundwater of Tammar area, Raigarh district in the state of Chhattisgarh, Hence this district peoples are risk in dental fluorosis. [50]

12.Fluoride contamination in Haryana:

Haryana is one of the fluorosis affected states in India. The spent wash samples were collected from distilleries areas of Haryana. The samples were having fluoride concentration in the range of 1.95 to 2.32 mg/l.35. [51] Fluoride concentration was found to be more than permissible limit at seven locations. Highest value of 19.36 mg/l was observed at Korawal. [52] The fluoride concentration in Hodal blocks area in the range of 1.0 to 40.0 mg/l. [53]

13.Fluoride contamination in Orissa:

In India Orissa is one of the fluoride contaminated state. In Orissa, Nayagarh district was have high fluoride contamination in drinking water. In Nayagarh district many villages having fluoride contamination in the range of 0.3 to 10.1 mg/l in groundwater. [54]Delineation of fluoride contaminated groundwater around a hot spring in Nayagarh district of Orissa.

Balasore district of Odisha is one of the fluoriderich state contamination are in India. The data show that many peoples in this region of Odisha have either dental or skeletal fluorosis. [55]

14.Fluoride contamination in Himachala Pradesh:

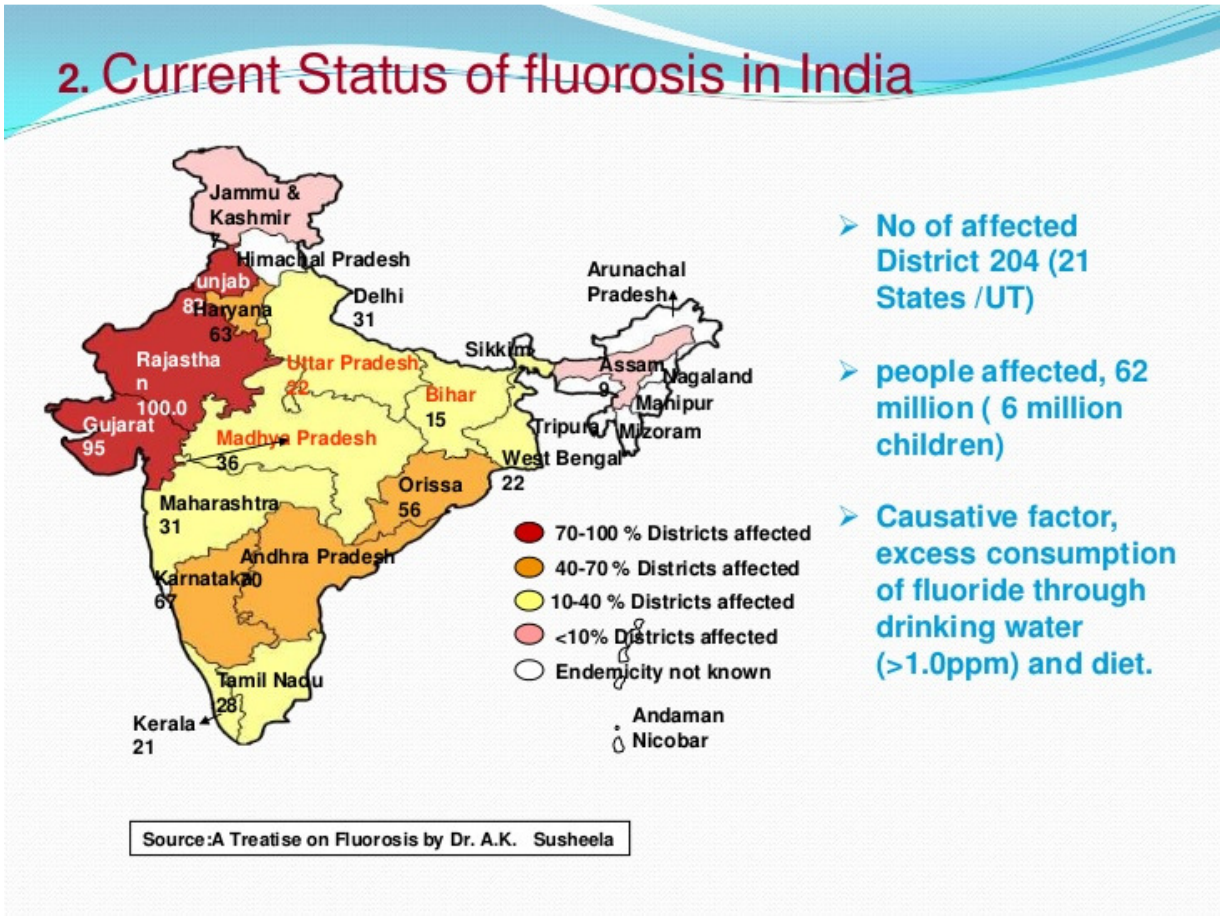
Himachalapradesh is one of the Fluoride contamination states in India. Quality of water from hot springs in Mandi district of Tattapani habitation has brackish water with EC ranging from 1480 to 9700 μs/cm and fluoride concentration ranging from 1.03 to 1.66 mg/l. [56]

15.Fluoride contamination in Jharkhand:

Fluoride contamination in groundwater sources in Palmu district, Jharkhand. Groundwater samples were collected from different parts of Palmu district. The maximum fluoride concentration (4.2 mg/l) was observed in daltongani block. [57]Fluoride concentration in drinking water in the range of 0.018 to 5.92 mg/L. Kharaundhi and untari blocks has high fluoride concentration. [58]

16.Fluoride contamination in Punjab:

According to a survey conducted by Ministry of water resources, Government of India, thirteen states in India have been identified as fluorosis affected places. Punjab (Bhatinda and Sangrur), is one of them. The maximum value fluoride 22.6 mg/l has been reported in Kachikhanuri in Sangur district. [59] Fluoride contamination was observed in groundwater of Kalalanwala village in east Punjab. The maximum fluoride concentration was 22.8 mg/l. [60] In Punjab many Blocks has fluoride contamination above permissible limit (1.5 mg/l) viz, Amiritsar, Bhatinda, Faridkot, Firozepur and Gurdaspur. [61]



Fluorine Chemistry

Fluorine (F) is element number 9 on the periodic table of elements and has a atomic weight of 18.998 g/mol. Fluorine gas(F2) is yellow but does not exist in nature as it is too reactive. Fluorine is also the most electro-negative element.

Fluorine is the most abundant element in nature, and about 96% of fluoride in the human body is found in bones and teeth. Fluorine is essential for the normal mineralization of bones and formation of dental enamel. [62]Theprincipal sources of fluorine were drinking water and food such as sea fish, cheese and tea. [63]

The behavior of fluoride ions in the human organism is a classic example of double-edged sword. [64] Like many other nutrients and substances, fluoride is beneficial in small amounts but

toxic in large amounts. Daily supplementation with fluoride within optimum limits is an important factor in preventing dental caries and an important mitogenic stimulus for osteoblasts as it may enhance mineral deposition in bone, but on the other hand, fluoride, above a threshold concentration, has been demonstrated to be toxic. [65]

Toxic/Lethal Level of Fluoride: Chronic toxic doses of fluoride can accumulate over a long period of time. It is difficult to prove chronic fluoride toxicity because this depends on the length of exposure, which may stretch many decades. Acute lethal doses can result from one significant exposure. A lethal dose for children is 5-15 mg/kg fluoride. Thus, as little as 35mg can kill a 7kg infant while 5-10 g (32-64 mg/kg) can kill a 70 kg adult. [66]More than this amount per day would put a person at risk for developing chronic fluoride toxicity over time.

Fluoride is a cumulative toxin. [67] Along with urinary excretion, uptake by bone removes excess fluoride from circulation, thus effectively removing fluoride from the fluids bathing the soft tissues. [68]

Fluorosis is an important public health problem in 24 countries, including India, which lies the geographical fluoride belt that extends from Turkey to China and Japan through Iraq and Afghanistan .[69]85 million tons of fluoride deposits on the earth's crust, of which 12 millions are found in India. [70]

Metabolism of Fluoride

After ingestion of fluoride, such as drinking a glass of optimally fluoridated water, the majority of the fluoride is absorbed from the stomach and small intestine into the blood stream. [71]This causes a short- term increase of fluoride levels in the blood. The fluoride levels increase quickly and reach a peak concentration within 20-60 min. [72]The concentration declines rapidly, usually

within 3-6 hrs following the peak levels, due to the uptake of fluoride by hard tissue and efficient removal of fluoride by the kidneys. [73] Approximately, 50% of the fluoride absorbed each day by young or middle-aged adults becomes associated with hard tissues within 24 hrs while virtually of the remainder is excreted in the urine. Approximately, 99% of the fluoride present in the body is associated with hard tissues. [71]

*1.0ppm=1mg/l; **2.2 mg sodium fluoride contains 1 mg fluoride ion

According to generally accepted scientific knowledge, the ingestion of optimally fluoridated water does not have an adverse effect on bones. [74]

Fluoride Toxicity

It is well established that prolonged use of fluoride at recommended levels does not produce any harmful physiological effects in the human. However, there are safe limits for fluoride beyond which harmful effects can occur. These effects can be classified as acute and chronic toxicity.

Acute toxicity: This can occur due to a single ingestion of a large amount of fluoride. Ingestion of an acute fatal dose of fluoride is very rare. The amount of fluoride considered lethal when taken orally is 35-70 mg per kg body weight. This is equivalent to 5-10 g sodium fluoride for a 70-kg adult and 1-2 g sodium fluoride for a 15-kg child. [75]

Symptoms of acute toxicity occur rapidly. There is diffuse abdominal pain, diarrhea, vomiting, excess salivation, and thirst. Rapid measures to reduce fluoride absorption should be started by inducing vomiting and administrating large volume of calcium as in lime water or milk. [73]

Chronic toxicity: This is caused due to long- term ingestion of smaller amounts of fluoride in drinking water. Excessive fluoride more than 8ppm in drinking water daily for many years can lead to skeletal fluorosis. Severe cases are normally found only in warm climates where contains

very high levels of fluoride. Due to chronic toxicity, bone density slowly increases the joint stiffen and becomes painful.

At higher levels of ingestion from 2 to 8 mg daily, skeletal fluorosis may arise. Whereas dental fluorosis is easily recognized, the skeletal involvement is not clinically obvious until the advanced stage and early cases may be misdiagnosed as rheumatoid or osteoarthritis. [75]

Fluoride increases the stability of the crystal lattice in bone, but makes bone more brittle. The total quantity of fluoride ingested in the single most important factor in determining the clinical course of skeletal fluorosis; the severity of symptoms correlates directly with the level and duration of exposure.

Effects of Fluoride on Various Tissues, Cells and Organ Systems:

Fluoride affects each and every part of the humans and animals. They are:

Skeletal Muscle involvement in Fluorosis: During the 1970s, many scientists reported that fluoride toxicity destroys skeletal muscle. The muscle proteins actin and myosin are not laid down as fluoride inhibits the enzymes leading to derangement in protein biosynthesis. Therefore generalized atrophy of skeletal muscle is observed. The muscle mitochondrion is destroyed. The muscle membranes become highly permeable. These events lead to generalized muscle weakness.

Red Blood Cell (Erythrocyte) involvement in Fluorosis: As red blood cell membrane is an entity which lodges the chemical factor(s) responsible for blood group substances. Considerable enquiry into the membrane structure and function has been carried out. These studies have led to certain vital information on fluoride action on red blood cell membrane and the cell as a whole. It is now know that when fluoride is ingested it will also accumulate on the erythrocyte membrane, besides other cells, tissues and organs. The erythrocyte membrane in turn loses its calcium

content. The membrane which is deficient in calcium content is pliable and is chrown into folds. The RBCs are termed as echinocytes. It has also been observed among workers exposed to fluoride pollution in aluminum smelters, that the number of echinocytes increases depending upon the duration of exposure to the fluoride polluted environment. Echinocytes have also been observed in newborn infants having physiological jaundice as bile salts are also know to induce echinocyte formation.

Gastro-Intestinal Mucosa in Fluorosis: It is now well established that fluoride in drinking water can cause 'non-ulcer dyspeptic' complaints in human subjects. The main complaints are Nausea, Loss of appetite, Pain in the stomach, Gas formation and bloated feeling. Constipation followed by intermittent diarrhea and Headache. It is a fact that for non-ulcer dyspeptic complaints, drugs are not required for treating, if the causative factor is fluoride. Safe drinking water with fluoride as low as possible is good enough to reverse the adverse health complaints within a fortnight.

Calcification of Ligaments in Fluorosis: Ligaments are soft connective tissue providing a protective sheath to bones. Under normal circumstance one is unlikely to appreciate the sheath as it appears as a fine 'muslin' cloth covering the bone. However, in Fluorosis the ligaments tend to calcify and shall be visible in radiographs. Detection of calcified ligaments through radiograph of the forearm is very useful for diagnosing Skeletal Fluorosis during early stages.

Sperm Abnormality in Fluorosis: It is also a fact that infertility with abnormality in sperm morphology. Oligospermia (deficiency of spermatozoa in the semen) azoospermia (absence of spermatozoa in semen) and low testosterone levels are common in those residing in endemic areas for Fluorosis and consuming fluoride contaminated water.

Polyurea and Polydisia in Fluorosis: Fluoride ingestion in excess can also lead to polyurea (tendency to urinate more frequently though urine volume may be less) and polydipsia (excessive thirst) which are associated with fluoride toxicity.

Skeletal Fluorosis:

Exposure to very high fluoride over a prolonged period of time results in acute to chronic skeletal fluorosis. It was stated in 1993 that crippling skeletal fluorosis might occur in people who have ingested 10 to 20 mg of fluoride per day for over 10 to 20 Years. [76]Early stages of skeletal fluorosis start with pain in bones and joints, muscle weakness, sporadic pain, stiffness of joints and chronic fatigue. During later stages calcification of the bones takes place, osteoporosis in long bones, and symptoms of osteoclerosis where the bones become denser and develop abnormal crystalline structure. In the advanced stage the bones and joints become completely weak and moving them is difficult.

The vertebrate in the spine fuse together and the patient is left crippled which is the final stage. Skeletal fluorosis is usually not recognized until the disease reaches an advanced stage.[77] General skeletal fluorosis directly affects the economy of villagers (mostly tribal population) as it causes illness and debilitation not only in humans but, also in their domestic animals, on which they depend for their basic income. Skeletal fluorosis leads to impairment, disability and subsequently makes the affected subject handicap. Therefore, they are unable to get employment or labor for their daily livelihood, lead their life as dependents on others. Similarly, the skeletal fluorosis affected youth were at extremely difficult situation, where they were unable to find alliance from non-fluoride affected villages, thus, they are forced to marry the youth the same or fluoride affected villages. The prevalence of skeletal fluorosis in various geographical regions of India is presented in (Table 3).

Table 3.Prevalence (%) of skeletal fluorosis in different parts of India by age groups

S.No	State/Area	Age group	Prevalence (%)
1.	Nalgonda, Andhra Pradesh	All ages	24.9
2.	Durg, Chhattisgarh	Adults	6.3-38.1
3.	Dungapur& Udaipur, Rajasthan	All ages	12-27.6
4.	Bihar, India	1-5 years	20
5.	Palamau, Jharkhand	Adults	47.4
6.	Assam	Adults	1.74
7.	Uttar Pradesh	All ages	14.2
8.	Kareka&Shivpuri, Madhya Pradesh	13-50	39.2

Dental Fluorosis:

Fluorosis of dental enamel occurs when excess fluoride is ingested during the years of tooth calcification-essentially during the first 7years of life. It is characterized by molting of dental enamel, which has been reported at levels above 1.5 mg/L intake. [4]On prolonged continuation of this process the teeth become hard and brittle. This is called dental fluorosis. Dental fluorosis in the initial stages results in the tooth becoming coloured from yellow to brown to black. Depending upon the severity, it may be only discolouration of the teeth may be in the form of spots or as streaks. Dean's classification of dental fluorosis is presented in below table.

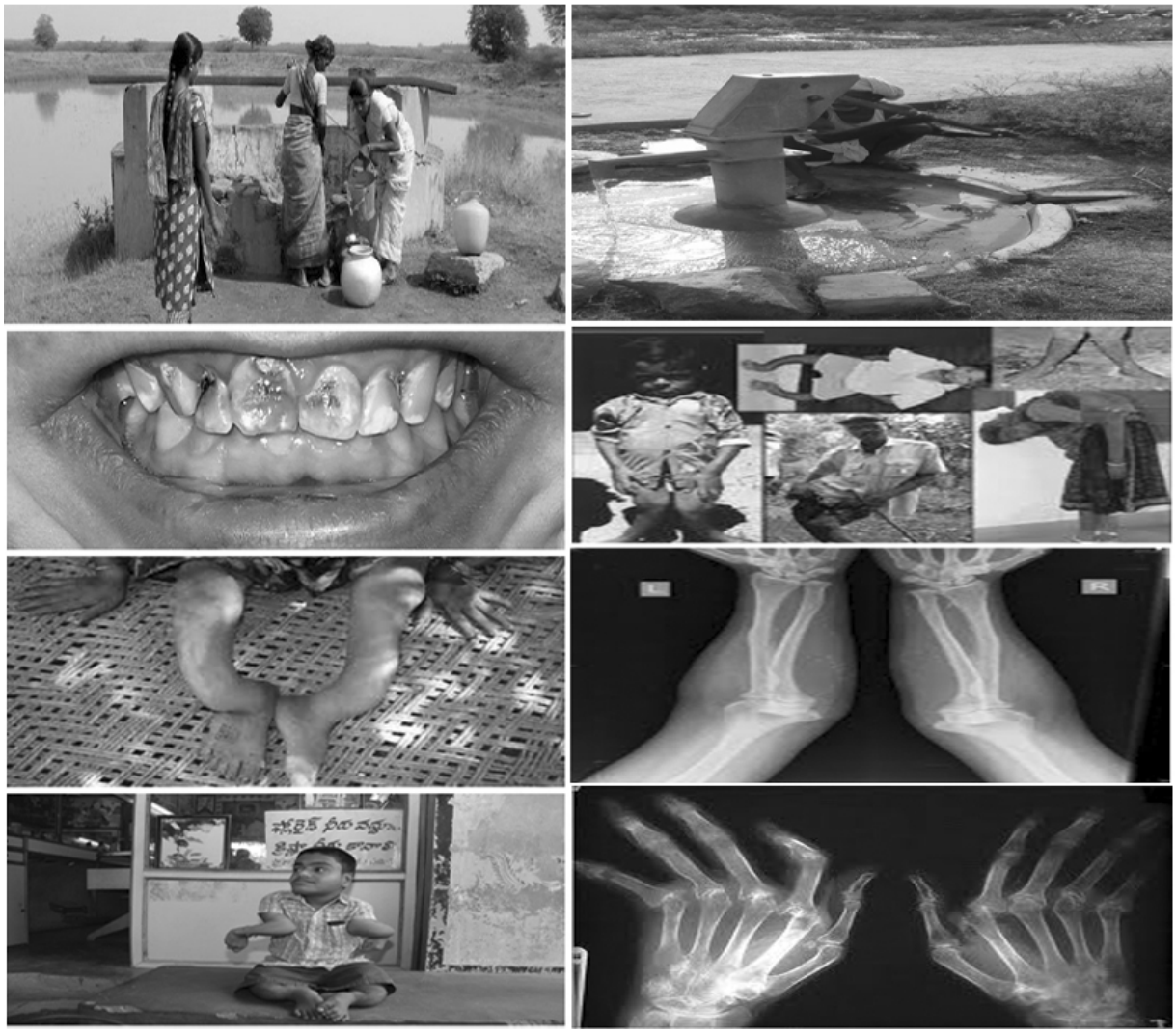


Figure 2 : The effects of fluoride on teeth and skeleton

Genotoxicity of fluoride:

Many studies have examined the possible effects of fluoride on chromosome damage. While there are no published studies on the genotoxic (damage to DNA) effect of fluoride in humans, but numerous studies have been done on mice. [76,77]

Table 4. Criteria for Dean's Fluorosis Index (Dean. 1993)[78]

Score	Criteria
Normal	The enamel represents the usual translucent semivitri form type of structure. The surface is smooth, glossy, and usually of a pale creamy white colour.
Questionable	The enamel discloses slight aberrations from the translucency of normal enamel, ranging from a few white flecks to occasional white spots. This classification is utilized in those instances where a definite diagnosis of the mildest form of fluorosis is not warranted and a classification of "normal" is not justified
Very Mild	Small opaque, paper white areas scattered irregularly over the tooth but not involving as much as 25% of the tooth surface. Frequently included in this classification are teeth showing no more than about 1 – 2 mm of white opacity at the tip of the summit of the cups of the bicuspids or second molars.
Mild	The white opaque areas in the enamel of the teeth are more extensive but do not involve as much as 50% of the teeth.
Moderate	All enamel surfaces of the teeth are affected, and the surfaces subject to attrition show wear. Brown stain is frequently a disfiguring feature.
Severe	Includes teeth formerly classified as "moderately sever and severe."All enamel surfaces are affected and hypoplasia is so marked that the general form of the tooth may be affected. The major diagnostic sign of this classification in discrete or confluent pitting. Brown stains are widespread and teeth often present a corroded-like appearance.

These studies have shown no evidence of effect of fluoride on chromosomes in bone marrow or sperm cells even at fluoride levels 100 times higher than that in fluoridated water. [79] Another independent group of researchers reported a similar lack of fluoride-induced chromosomal damage to human white blood cells, which are especially sensitive to agents that cause genetic mutations. The genotoxic effects of fluoride were also studied in hamster bone

marrow cells and cultured hamster ovarian cells. Again, the results supported the conclusion that fluoride does not cause chromosomal damage, and therefore, was not a genetic hazard. [80] In further tests, fluoride has not caused genetic mutations in the most widely used bacterial mutagenesis assay (the Ames test) over a wide range of fluoride levels. [81]

Defluoridationof Water

Defluoridation is the conventional and widely tested method for supplying safe water to the fluorosis affected communities. It is defined as the "the downward adjustment of level of fluoride in drinking water to the optimal level".

Defluoridation can be achievedthrough: **a)** the treatment of water at the source (central treatment); **b)** the treatment of water at the household level (point of use treatment). Treatment at the source is the preferred method in most of the developed countries as it can be carried out on a large scale under direct supervision of skilled personals. [82]

Defluoridation techniques can be broadly classified into following categories: [83]

1. Adsorption technique
2. Ion –exchange technique
3. Precipitation technique
4. Other techniques, which include electro chemical defluoridation and Reverse Osmosis.

1. Adsorption:

This technique functions on the adsorption of fluoride ions onto the surface of an active agent. In the adsorption method, raw water is passed through a bed containing defluoridating material. The material retains fluoride either by physical, chemical or ion exchange mechanisms. The adsorbent gets saturated after a period of operation and requires regeneration.

A). Activated Alumina:

Activated alumina (Al_2O_3), which has been in use for defluoridation since 1934, is prepared by low temperature dehydration (300-600^{0}C) of aluminum hydroxides. The ligand exchange reaction at the surface of activated alumina is thought to be the probable mechanism of fluoride removal. [82]

Handpump attached Defluoridation Units and Domestic Defluoridation Units, [82]have been developed in India by IIT Kanpur in collaboration with UNICEF using indigenously manufactured activated alumina. The advantages of this approach domestic defluoridation unit are: a lower cost for treatment as only a limited volume of water is required (for cooking and drinking) to be treated and the lower requirement of treated water correspondingly lowers the need of chemicals and generates lower volume of sludge.

B) Bone Char:

Bone char is ground animal bones, charred optimum temperature (500^{0}C) to remove organics. The fluoride removal mechanism involves the replacement of carbonate of bone char by fluoride ion. Exhausted bone char is regenerated using caustic soda. Bone char has been used for defluoridation unit of drinking water, primarily using bone char, was developed by the inter-country Centre for Oral Health (ICOH), Chiangmai, Dental Faculty of Chulalongkoran University, Bangkok, and the WHO in 1988. [84]

C) CalcinedClay :

Aluminum oxide (Al_2O_3) present in the brick soil gets activated during burning and adsorbs excess amount of fluoride present in the raw drinking water. Filter media need to be replaced every three months if the fluoride content of raw water is 2.5 ppm. [83]Freshly fired brick pieces were used in Sri Lanka for the removal of fluoride in domestic defluoridation units.

D) Mud Pots :

Collection and storing of water in mud pots is an ancient method. Red soil and clay are used to prepare the mud pots. The raw pots are subjected to heat treatment as in the case of brick production. Hence, the mud pots also acts as an adsorbent media. The major advantages of mud pots are they are economic and readily acceptable for the rural communities.

E) Natural Adsorbents :

A relatively less know approach of potential utility, particularly in third world rural communities, that has attracted the attention of researchers in recent years is plant-based (natural) defluoridation technique. The plants can be grown locally as needed and the costs for production and transportation can be relatively low. The use of plants for defluoridation might also achieve widespread acceptance and application by local communities more easily. Many natural adsorbents from various trees and animal sources have been tried as defluoridation agents. Seeds of the Drumstick, [85] Tamarind seeds, [86] tea ash, [87] egg shell powder [88]are few among them.

2. Ion Exchange [89]

The different ion exchange materials studied include bone, bone char, anion and cation exchange resins such as carbon, defluoron-1, defluoron-2, etc.

3. Precipitation

In this method, chemicals added to raw water cause precipitation of the fluoride salt as insoluble fluorapatite, which is separated from the water. Commonly used materials in precipitation technique are Aluminium salts (e.g.Alum), lime, Poly Aluminium Chloride, Poly AluminiumHydroxysulphate and Brushite. [83]

A). Nalgonda Technique:

The first community defluoridation plant for removal of fluoride from drinking water was constructed in nalgonda in telangana state, in the town of Kathri. The technology was developed by National Environmental Engineering Research Institute (NEERI), Nagpur in 1961. [89]Nalgonda Technique involves addition of Aluminium salts, lime and bleaching powder followed by rapid mixing, flocculation, sedimentation, filtration and disinfection.Aluminium salt may be added as aluminiumsulphate (alum) or aluminium chloride or combination of these two. It is responsible for removal of fluoride from water.[89] The technique is highly versatile and has the applications like; for large communities, fill and draw technique for small communities, fill-and-Draw defluoridation plant for rural water supply for domestic defluoridation units, etc.

B). Contact Precipitation:[90]

Contact precipitation is a recently reported technique in which fluoride is removed from water through the addition of calcium and phosphate compounds which leads to precipitation of fluoride. The water is then filtered through bone char that has been pre-saturated with fluoride. The presence of saturated bone charcoal medium acts as a catalyst for the precipitation of fluoride either as CaF_2, and /or fluorapatite. The process uses buckets, column filters or a combination of both. [91]

C). IISc Method (Eswar , 2011):[89]

The Indian Institute of Science (IISc), Bangalore developed this simple defluoridation technique. The method uses magnesium oxide, calcium hydroxide and sodium bisulphate. Magnesium oxide removes dissolved fluoride ions from water samples by precipitating fluoride as insoluble magnesium fluoride;

$$MgO + H_2O \rightarrow Mg(OH)_2$$

$$2NaF + Mg(OH)_2 \rightarrow MgF_2 + 2NaOH$$

A simple to use domestic defluoridation unit was developed for fluoride removal based on IISc Method at Kolar, Karnataka to treat 15 litres of fluoride contaminated water.

4. Other techniques of defluoridation of water

Reverse Osmosis, electrolysis & electro dialysis and distillation are physical methods that are tested for defluoridation of water.[92]Though they are effective in removing fluoride salts from water, but there are certain procedural disadvantages that limit their usage on a large scale.

Table 5.The Range of fluoride levels in the groundwater of India(Shakir Ali et al; 2016).[93]

S.No	Fluoride range (mg/L)	State/locality/area/country
1.	20	Nalgonda water, AP
2	5.80	Anantapur district, AP
3	0.5–4.5	Ranga Reddy district, AP
4	0.38–4	Maheshwaram area, AP
5	2.8	Sarada River basin, AP
6	0.1–8.8	Nalgonda district, AP
7	0.18–6.88	Guwahati, Assam
8	0.1–2.5	Rohtas district, Bihar
9	8.8	Raigarh district, Chhattisgarh
10	0.10–16.5	Delhi
11	0.02–4.13	Delhi
12	1–5.12	Delhi
13	0.94–2.81	Kadi Tehsil, Mehsana, Gujarat
14	0.56–0.72	Ahmadabad, Gujarat
15	0.3–6.9	Gind district, Haryana
16	0.95–2.42	Pataudi, Haryana
17	1.90–5.20	Hailymandi, Haryana
18	1.65–1.90	Harsaru, Haryana
19	0.1–6	Damodar River basin, Jharkhand
20	7.80	Bellary, Karnataka
21	2.60–7.40	Gulbarga, Karnataka
22	2.02–5.15	Raichur, Karnataka
23	0.80–7.40	Bellary, Karnataka
24	1.55–3.40	Kolar, Karnataka
25	0.97–3.20	Tumkur and Chitradurga, Karnataka
26	0.3–6.5	Bagalkot district, Karnataka
27	5.75	Palghat, Kerala
28	1.5–4	Chandidongri, MP

29	0.06–4.74	Chhindwara, MP
30	0.30–13.41	Yavatmal, Maharashtra
31	0.27–5.3	Chandrapur, Maharashtra
32	0.21–1.78	Imphal, Manipur
33	0.16–0.80	Thoubal, Manipur
34	2.4–3.4	Balasore, Orissa
35	1.6–8.3	Sundergarh, Orissa
36	0.3–5.4	Ajmer, Rajasthan
37	1.01–4.78	Hunumangarh, Rajasthan
38	0.12–16.9	Ajmer, Rajasthan
39	0.2–13	Bhilwara district, Rajasthan
40	0.11–2.5	Chennai, TN
41	0.07–3.13	Neyveli, TN
42	0.18–3.24	Dindigul, TN
43	0.4–6.7	Sonbhadra, UP
44	0.07–2.8	Varuna River basin, UP
45	0.8–13.9	Unnao, UP
46	0.1–14.8	Agra, UP
47	2.4	Chhatarpur, UP

CONCLUSION

This research review will give information about the fluoride toxicity in different parts of India and world. The present review has focused the details regarding the effects of fluoride in humans and also the diseases.

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Most developed nations, including all of Japan and 97% of western Europe DO NOT Fluoridate

Fluoride

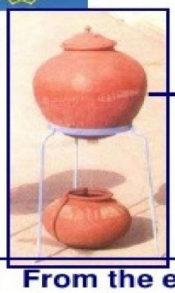
BIOLOGICAL EFFECTS OF SODIUM FLUORIDE:

Causes Cancer
Impairs Bone Strength
Impairs IQ
Impairs Kidneys
Impairs Thyroid
Recedes Gums
Depresses Heart
Depresses Cell Growth
Increases Infertility
Increases Fluorosis

- Toothpaste Containing Fluoride
- Fluoridated Municipal Water Supplies
- Food/Drinks Processed With Fluoridated Water
- Mouthwash Containing Fluoride

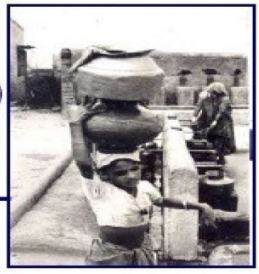
Defluoridation of Water

1. A Terracotta domestic filter for removal of fluoride (Activated Alumina System)



2. Nalgonda – Bucket treatment

3.
- From the existing safe water sources in the village, the water can also be stored in an overhead reservoir.
- From the reservoir water can be supplied through a central stand post with multiple taps.



4. Reverse Osmosis though expensive is available as Domestic Filters

5. Reverse Osmosis Technology (RO Filter) is the only technology which would remove fluoride and other chemical contaminants