RESEARCH PROJECT ON **PRESENCE OF FLUORIDE IN TOOTHPASTE BY POTENTIOMETRIC DETERMINATION**

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The research opportunity I had with S.H.P.T College of Science was a great chance for learning and Knowledge enhancement. Therefore , I consider myself as a very individual as I was provided to be a part of it. I am also grateful for having chance to research on the topic thoroughly and applying it accordingly.

My special thanks to our **GUIDE** PROF. SULEKHA GOTMARE for helping me at each and every hurdle. She had always paved me a right way to conduct my research program by her effective guidance and good support. She has given me the solution that had our way of research as in spite of various short comings and failures she was always there to support and motivate me. After various per mutative & combination my research got successful just because of her.

I am using this opportunity to express my deepest gratitude to our Professors (Dr. SULEKHA GOTMARE & Dr. JAYA GADE) for guiding us.

I am also grateful to my friends and also my research partner for always motivating me and for always standing by my side. Also to all my friends for help and co-operation during our successful Research work.

CERTIFICATE

This is to certify that **Honey Dumralia** , a student of **M.Sc II Year** has successfully completed the research project in Analytical Chemistry on the topic "**PRESENCE OF FLUORIDE IN TOOTHPASTE BY POTENTIOMETRIC DETERMINATION"** under the guidance of **PROF. SULEKHA GOTMARE** in partial fulfillment for M.Sc Analytical Chemistry program during the year **2020 - 2021**.

This project is absolutely genuine and does not indulge in plagiarism of any kind.

Signature (GUIDE) **Signature (HOD)**

What is Toothpaste ?

Toothpaste is a paste or gel dentifrice used with a toothbrush to clean and maintain the aesthetics and health of teeth. Toothpaste is used to promote oral hygiene: it is an abrasive that aids in removing dental plaque and food from the teeth, assists in suppressing halitosis, and delivers active ingredients (most commonly fluoride) to help prevent tooth decay (dental caries) and gum disease (gingivitis). Salt and sodium bicarbonate (baking soda) are among materials that can be substituted for commercial toothpaste. Large amounts of swallowed toothpaste can be toxic.

Toothpaste is a key part of your daily oral hygiene routine. Along with your toothbrush and floss it helps to remove food debris and plaque from your teeth and gums.

Toothpastes can come in a gel, paste or powder form. While the ingredients differ slightly, all toothpastes contain the same general components:

- Mild abrasive. With some help from your toothbrush, these help to remove debris and surface stains.

- Humectants. This ingredient helps to prevent water loss, and keeps your toothpaste from drying out or getting gummy.
- Flavoring agents. This is what gives your toothpaste a little bit of sweetness, and that minty fresh scent. Since these do not contain sugar, they also do not promote tooth decay.
- Thickening agents. Also known as binders, these help to stabilize the toothpaste formula.
- Detergent. That foaming action comes from detergent. It also helps to spread the toothpaste through your whole mouth, and helps clean teeth.

They may have all the same basic ingredients, but all toothpastes are not the same. Depending on the toothpaste, other ingredients can also be added for other benefits. Here are some important things to keep in mind when choosing your toothpaste:

- Decay prevention. Fluoride is a natural cavity fighter that helps to strengthen tooth enamel and fight tooth decay. Not all toothpastes contain fluoride. Be sure to always use toothpaste containing this cavity-fighting mineral.

- Plaque and gingivitis. Several toothpaste contain active ingredients that can fight plaque and gingivitis, an early form of gum disease.
- Whitening. If you're looking for a little extra sparkle in your smile, "whitening" toothpastes have special chemical or polishing agents that help remove more surface stains than regular toothpastes.
- Desensitizing. If you have sensitive teeth, you may want to consider using a desensitizing toothpaste. These contain compounds which help to reduce tooth sensitivity.

Usefulness

Toothpastes are generally useful to maintain dental health and preventing dental disease like cavities. It also helps control and remove plaque buildup. It also helps in preventing and destroying the germ buildup in teeth and maintaining gum health. However, a 2016 systematic review indicates that using toothpaste when brushing the teeth does not impact the level of plaque removal.

Ingredients

In addition to 20%–42% water, toothpastes are derived from a variety of components, the three main ones being abrasives, fluoride, and detergents.

Abrasives :

Abrasives constitute at least 50% of a typical toothpaste. These insoluble particles are designed to help remove plaque from the teeth. The removal of plaque and calculus prevents the accumulation of tartar and is widely claimed to help minimize cavities and periodontal disease, although the clinical significance of this benefit is debated. Representative abrasives include particles of aluminum hydroxide ($Al(OH)_3$), calcium carbonate ($CaCO_3$), sodium bicarbonate, various calcium hydrogen phosphates, various silicas and zeolites, and hydroxyapatite ($Ca_5(PO_4)_3OH$).

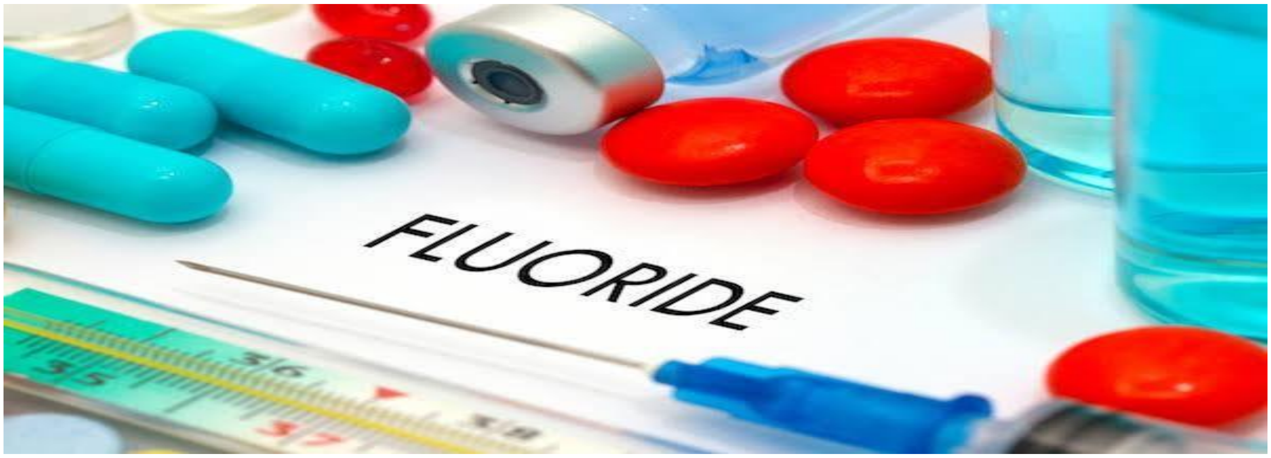
Abrasives, like the dental polishing agents used in dentists' offices, also cause a small amount of enamel erosion which is termed "polishing" action. Some brands contain powdered white mica, which acts as a mild abrasive, and also adds a cosmetically pleasing glittery shimmer to the paste. The polishing of teeth removes stains from tooth surfaces, but has not been shown to improve dental health over and above the effects of the removal of plaque and calculus.

The abrasive effect of toothpaste is indicated by its RDA value. Too high RDA values are deleterious. Some dentists recommend toothpaste with an RDA value no higher than 50 for daily use.

Fluoride :

Fluoride in various forms is the most popular active ingredient in toothpaste to prevent cavities. Fluoride is present in small amounts in plants, animals, and some natural water sources. The additional fluoride in toothpaste has beneficial effects on the formation of dental enamel and bones. Sodium fluoride (NaF) is the most common source of fluoride, but stannous fluoride (SnF_2), olaflur (an organic salt of fluoride), and sodium monofluorophosphate (Na_2PO_3F) are also used. Stannous fluoride has been shown to be more effective than sodium fluoride in reducing the incidence of dental caries and controlling gingivitis, but causes somewhat more surface stains.

Much of the toothpaste sold in the United States has 1,000 to 1,100 parts per million fluoride. In European countries, such as the UK or Greece, the fluoride content is often higher; a NaF content of 0.312% w/w (1,450 ppm fluoride) is common. All of these concentrations are likely to prevent tooth decay, according to a 2019 Cochrane review. Concentrations below 1,000 ppm are not likely to be preventive, and the preventive effect increases with concentration. Clinical trials support the use of high fluoride dentifrices, as it was found to reduce the amount of plaque accumulated, decrease the number of mutans streptococci and lactobacilli and possibly promote calcium fluoride deposits to a higher degree than after the use of traditional fluoride containing dentifrices.However, these effects must be balanced with the increased risk of harm at higher concentrations.



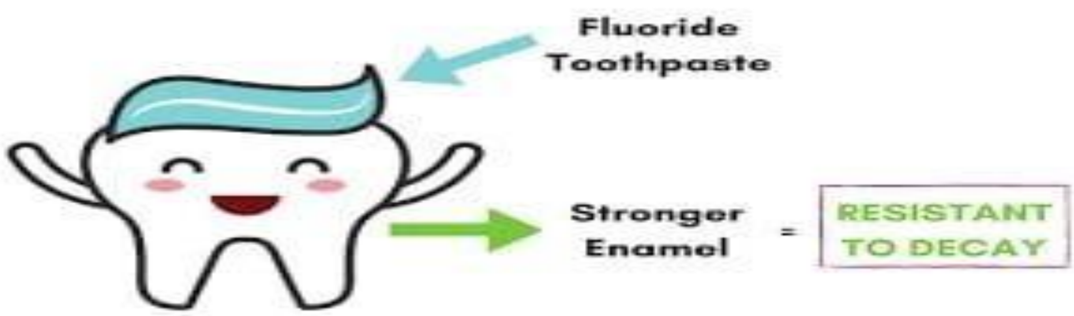
Surfactants :

Many, although not all, toothpastes contain sodium lauryl sulfate (SLS) or related surfactants (detergents). SLS is found in many other personal care products as well, such as shampoo, and is mainly a foaming agent, which enables uniform distribution of toothpaste, improving its cleansing power.

Other components :

Antibacterial agents :

Triclosan, an antibacterial agent, is a common toothpaste ingredient in the United Kingdom. Triclosan or zinc chloride prevent gingivitis and, according to the American Dental Association, helps reduce tartar and bad breath. A 2006 review of clinical research concluded there was evidence for the effectiveness of 0.30% triclosan in reducing plaque and gingivitis. Another Cochrane review in 2013 has found that triclosan achieved a 22% reduction in plaque, and in gingivitis, a 48% reduction in bleeding gums. However, there was insufficient evidence to show a difference in fighting periodontitis and there was no evidence either of any harmful effects associated with the use of triclosan toothpastes for more than 3 years. The evidence relating to plaque and gingivitis was considered to be of moderate quality while for periodontitis was low quality. Chlorhexidine is another antimicrobial agent used in toothpastes, however it is more commonly added in mouthwash products. Sodium laureth sulfate, a foaming agent, is a common toothpaste ingredient that also possesses some antimicrobial activities.There are also many commercial products available in the market containing different essential oils, herbal ingredients (e.g. chamomile, neem, chitosan, Aloe vera), and natural or plant extracts (e.g. hinokitiol). These ingredients are claimed by the manufacturers to fight plaque, bad breath and prevent gum disease. A 2020 systematic metareview found that herbal toothpastes are as effective as non-herbal toothpastes in reducing dental plaque at shorter period of follow-up (4 weeks). However, this evidence comes from low-quality studies.



Flavorants :

Toothpaste comes in a variety of colors and flavors, intended to encourage use of the product. The three most common flavorants are peppermint, spearmint, and wintergreen. Toothpaste flavored with peppermint-anise oil is popular in the Mediterranean region. These flavors are provided by the respective oils, e.g.

peppermint oil.More exotic flavors include Anethole anise, apricot, bubblegum, cinnamon, fennel, lavender, neem, ginger, vanilla, lemon, orange, and pine. Alternatively, unflavored toothpastes exist.

Remineralizers :

Hydroxyapatite nanocrystals and a variety of calcium phosphates are included in formulations for remineralization, i.e. the reformation of enamel.

Miscellaneous components :

Agents are added to suppress the tendency of toothpaste to dry into a powder. Included are various sugar alcohols, such as glycerol, sorbitol, or xylitol, or related derivatives, such as 1,2-propylene glycol and polyethyleneglycol. Strontium chloride or potassium nitrate is included in some toothpastes to reduce sensitivity. Two systemic meta-analysis reviews reported that arginine, and calcium sodium phosphosilicate CSPS containing toothpastes are also effective in alleviating dentinal hypersensitivity respectively.

Another randomized clinical trial found superior effects when both formulas were combined together.

Sodium polyphosphate is added to minimize the formation of tartar.[citation needed] Other example to components in toothpastes is the Biotene, which has proved its efficiency in relieving the symptoms of dry mouth in people who suffer from xerostomia according to the results of a randomized clinical trial.

Chlorohexidine mouthwash has been popular for its positive effect on controlling plaque and gingivitis,however, a systemic review studied the effects of chlorohexidine toothpastes and found insufficient evidence to support its use, tooth surface discoloration was observed as a side effect upon using it, which is considered a negative side effect that can affect patients' compliance.

Sodium hydroxide, also known as lye or caustic soda, is listed as an inactive ingredient in some toothpaste, for example Colgate Total.

Xylitol :

Some studies have demonstrated that toothpastes with xylitol as an ingredient are more effective at preventing dental caries in permanent teeth of children than toothpastes containing fluoride alone. Furthermore, xylitol has not been found to cause any harmful effects. Further investigation into the efficacy of toothpastes containing this product is however required as the currently available studies are of low quality and therefore the results of such studies must be applied carefully.

Safety

Fluoride :

Fluoride-containing toothpaste can be acutely toxic if swallowed in large amounts, but instances are exceedingly rare and result from prolonged and excessive use of toothpaste (i.e. several tubes per week). Approximately 15 mg/kg body weight is the acute lethal dose, even though as small amount as 5 mg/kg may be fatal to some children.

The risk of using fluoride is low enough that the use of full-strength toothpaste (1350–1500 ppm fluoride) is advised for all ages. However, smaller volumes are used for young children, for example, a smear of toothpaste until three years old.A major concern of dental fluorosis is for children under 12 months ingesting excessive fluoride through toothpaste. Nausea and vomiting are also problems which might arise with topical fluoride ingestion.

Polyethylene glycol - PEG :

PEG is a common ingredient in some of the formulas of toothpastes; it is a hydrophilic polymer that acts as a dispersant in toothpastes. Also, it is used in many cosmetic and pharmaceutical formulas, for example: ointments, osmotic laxatives, some of the nonsteroidal anti-inflammatory drugs, other medications and household products.However, 37 cases of PEG hypersensitivity (delayed and immediate) to PEG-containing substances have been reported since 1977, suggesting that they have unrecognized allergenic potential.

Diethylene glycol

The inclusion of sweet-tasting but toxic diethylene glycol in Chinese-made toothpaste led to a recall in 2007 involving multiple toothpaste brands in several nations. The world outcry made Chinese officials ban the practice of using diethylene glycol in toothpaste.

Triclosan

Reports have suggested triclosan, an active ingredient in many kinds of toothpastes, can combine with chlorine in tap water to form chloroform, which the United States Environmental Protection Agency classifies as a probable human carcinogen. An animal study revealed the chemical might modify hormone regulation, and many other lab researches proved bacteria might be able to develop resistance to triclosan in a way which can help them to resist antibiotics also.

Miscellaneous issues and debates

With the exception of toothpaste intended to be used on pets such as dogs and cats, and toothpaste used by astronauts, most toothpaste is not intended to be swallowed, and doing so may cause nausea or diarrhea. Tartar fighting toothpastes have been debated. Sodium lauryl sulfate (SLS) has been proposed to increase the frequency of mouth ulcers in some people, as it can dry out the protective layer of oral tissues, causing the underlying tissues to become damaged. In studies conducted by the university of Oslo on recurrent aphthous ulcers, it was found that SLS has a denaturing effect on the oral mucin layer, with high affinity for proteins, thereby increasing epithelial permeability. In a double-blind cross-over study, a significantly higher frequency of aphthous ulcers was demonstrated when patients brushed with an SLS-containing versus a detergent-free toothpaste. Also patients with Oral Lichen Planus who avoided SLS-containing toothpaste benefited.

Alteration of taste perception

After using toothpaste, orange juice and other juices have an unpleasant taste. Sodium lauryl sulfate alters taste perception. It can break down phospholipids that inhibit taste receptors for sweetness, giving food a bitter taste. In contrast, apples are known to taste more pleasant after using toothpaste. Distinguishing between the hypotheses that the bitter taste of orange juice results from stannous fluoride or from sodium lauryl sulfate is still an unresolved issue and it is thought that the menthol added for flavor may also take part in the alteration of taste perception when binding to lingual cold receptors.

Whitening toothpastes

Many toothpastes make whitening claims. Some of these toothpastes contain peroxide, the same ingredient found in tooth bleaching gels. The abrasive in these toothpastes, not the peroxide, removes the stains. Whitening toothpaste cannot alter the natural color of teeth or reverse discoloration by penetrating surface stains or decay. To remove surface stains, whitening toothpaste may include abrasives to gently polish the teeth or additives such as sodium tripolyphosphate to break down or dissolve stains. When used twice a day, whitening toothpaste typically takes two to four weeks to make teeth appear whiter. Whitening toothpaste is generally safe for daily use, but excessive use might damage tooth enamel. Teeth whitening gels represent an alternative. A recent systematic review in 2017

concluded that nearly all dentifrices that are specifically formulated for tooth whitening were shown to have a beneficial effect in reducing extrinsic stains, irrespective of whether or not a chemical discoloration agent was added. However, the whitening process can permanently reduce the strength of the teeth, as the process scrapes away a protective outer layer of enamel.

Herbal and natural toothpastes

Companies such as Tom's of Maine, among others, manufacture natural and herbal toothpastes and market them to consumers who wish to avoid the artificial ingredients commonly found in regular toothpastes. Many herbal toothpastes do not contain fluoride or sodium lauryl sulfate. The ingredients found in natural toothpastes vary widely but often include baking soda, aloe, eucalyptus oil, myrrh, camomile, calendula, neem, toothbrush tree, plant extract (strawberry extract), and essential oils. A systemic review in 2014 found insufficient evidence to determine whether the aloe vera herbal dentifrice can reduce plaque or improve gingival health, as the randomized studies were found to be flawed with high risk of bias.

According to a study by the Delhi Institute of Pharmaceutical Sciences and Research, many of the herbal toothpastes being sold in India were adulterated with nicotine.

Charcoal has also been incorporated in toothpaste formulas; however, there is no evidence to determine its safety and effectiveness. A 2020 systematic metareview of 24 comparative Randomised controlled trials, involving 1,597 adults aged 18 to 65, showed herbal toothpaste was superior over non-herbal toothpaste, but not to fluoride toothpaste.

Fluoride in Toothpaste's :

What is fluoride?

Fluoride is a natural mineral that is found in many foods and in all drinking water. The amount of fluoride in water varies from area to area.

Fluoride is often called nature’s cavity fighter and for good reason. Fluoride, a naturally-occurring mineral, helps prevent cavities in children and adults by making the outer surface of your teeth (enamel) more resistant to the acid attacks that cause tooth decay.

Most toothpastes now contain fluoride, and most people get their fluoride this way. Fluoride toothpaste is very effective in preventing tooth decay. The amount of fluoride in toothpaste is usually enough to reduce decay. In areas where the water supply has fluoride added, fluoride toothpaste gives extra protection.

What are the benefits of fluoride?

Fluoride can greatly help dental health by strengthening the tooth enamel, making it more resistant to tooth decay. It also reduces the amount of acid that the bacteria on your teeth produce.

Children who have fluoride when their teeth are developing tend to have shallower grooves in their teeth, so plaque can be more easily removed. Plaque is a thin, sticky film of bacteria that constantly forms on your teeth.

The addition of fluoride to water has been researched for over 60 years, and water fluoridation has been proven to reduce decay by 40 to 60 percent.

Toothpaste with fluoride is used to assist in good dental hygiene and overall oral wellness. Research has shown that fluoride can reduce plaque, remove tartar, and clean and protect teeth.

The presence of fluoride in your mouth can attract other minerals (such as calcium) to the area. Calcium is good for our bones and helps maintain our teeth with a strong, healthy structure.

Where can we find fluoride?

Fluoride is found naturally in many foods and in water supplies, and is also added to some drinking water. Having 0.7 to 1.2 parts of fluoride for every million parts of water (0.7ppm to 1.2ppm) has been shown to have the best effect.

All water contains some fluoride. Your local water supplier can tell you how much fluoride is in your drinking water.

What about fluoride toothpaste?

Most toothpastes now contain fluoride, and most people get their fluoride this way. Fluoride toothpaste is very effective in preventing tooth decay. The amount of fluoride in toothpaste is usually enough to reduce decay.
In areas where the water supply has fluoride added, fluoride toothpaste gives extra protection.

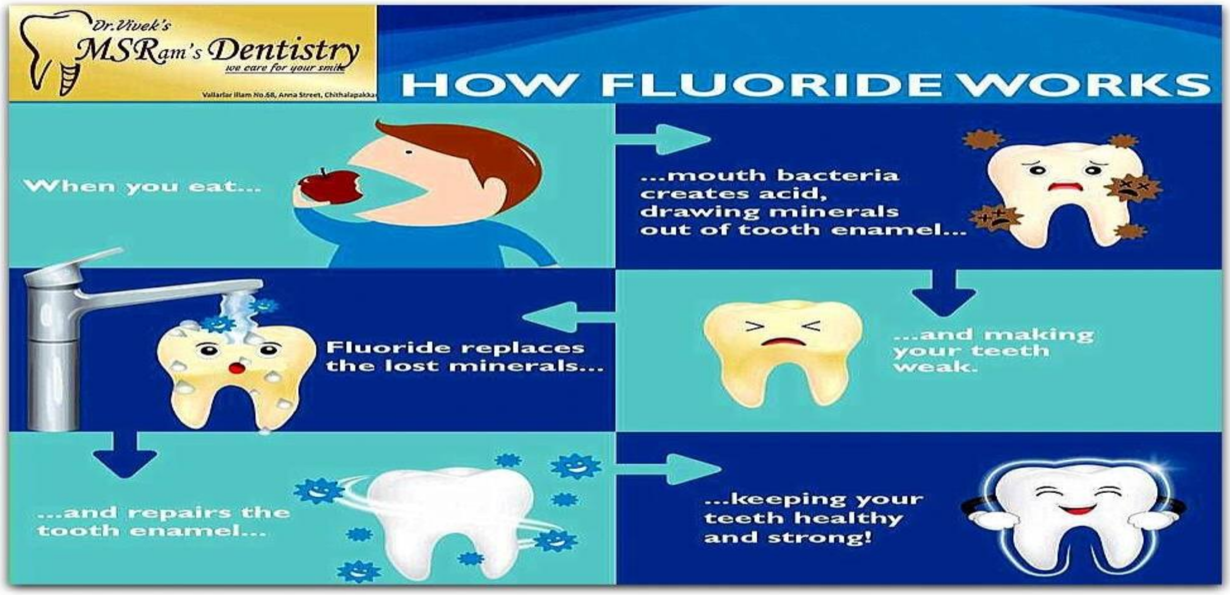
All children up to three years old should use a toothpaste with a fluoride level of at least 1000ppm (parts per million). After three years old they should use a toothpaste that contains 1350ppm to 1500ppm.

Parents should supervise their children's brushing, and use only a pea-sized smear of fluoride toothpaste until they are about 7 years old.

Spit out after brushing and do not rinse, so that the fluoride stays on your teeth longer.

Should people have extra fluoride?

Children living in poorer areas where the water supplies are not fluoridated can have 5 times more decay than children living in more affluent or fluoridated areas. Research suggests that adding fluoride to the water is the best way of reducing these ‘dental inequalities'.



Your dental team can apply fluorides to your teeth. These come as varnishes or gels and are more concentrated than ones you can apply yourself, so you do not need them as often. Some adults can benefit from these applications. Fluoride varnishes can help to reduce tooth decay - especially for people with dry mouth.

Some people are more likely to have tooth decay, and the dental team may also advise using a higher-strength fluoride toothpaste for extra protection.

Are there any side effects of fluoride?

‘Dental fluorosis' is caused by having too much fluoride when the teeth are developing. This can happen when fluoride supplements are taken by children under 7 who live in areas where the water supply is fluoridated. It can also happen when children swallow toothpaste.

Sources of Fluoride :

Fluoride can be ingested or applied topically to your teeth.
Here are some of the major sources of fluoride:

- **Fluoridated water:** Countries like the US, the UK and Australia add fluoride to their public water supplies. In the US, fluoridated water generally contains 0.7 parts per million (ppm).

- **Groundwater:** Groundwater naturally contains fluoride, but the concentration varies. Typically, it’s between 0.01 to 0.3 ppm, but in some areas dangerously high levels are present. This may cause serious health problems.

- **Fluoride supplements:** These are available as drops or tablets. Fluoride supplements are recommended for children over 6 months of age who have a high risk of developing cavities and live in non-fluoridated areas.

- **Some foods:** Certain foods may be processed using fluoridated water or may absorb fluoride from the soil. Tea leaves, especially old ones, may contain fluoride in higher amounts than other foods.

- **Dental care products:** Fluoride is added to a number of dental care products on the market, such as toothpaste and mouth rinses.

Literature Survey :

Abstract :

Fluorides are common ingredients in pharmaceutical products for oral hygiene due to their recognized effect in the prevention of tooth decay. In dental products, fluorides can be added in several different forms, such as sodium fluoride,

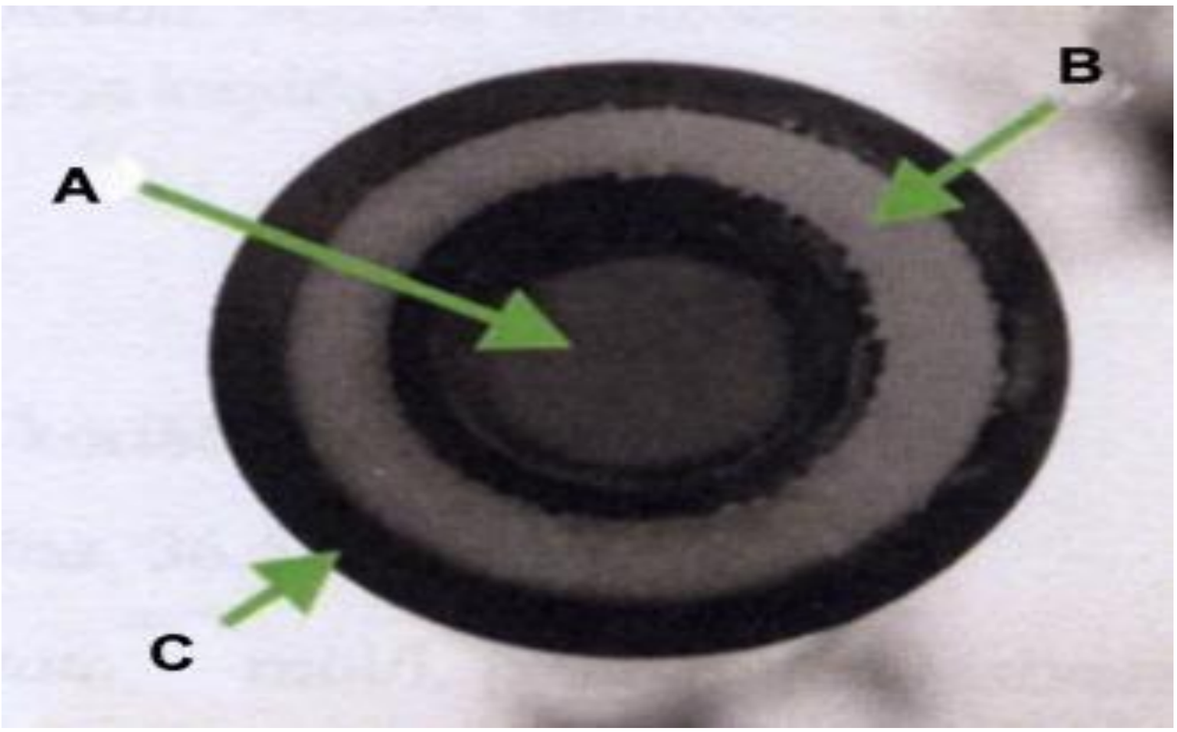
sodium monofluorophosphate, tin fluoride, or in the form of different amines. This work describes potentiometric determination of fluorides in the samples of toothpastes and mouthwash. The method was optimized for the particular analytical purpose; namely, for the analysis of toothpastes and mouthwash by applying different sample preparation protocols depending on the fluoride source. Good recovery (93–103%) confirmed the correctness of the sample preparation procedures. Calculated limit of detection and limit of quantification for the optimized method were 1×10^{-3} mg/L and 2.8×10^{-3} mg/L fluoride, respectively. In the minority of the analyzed samples, calculated contents agreed well with the certified values, whereas the samples of mouthwash demonstrated better agreement.

Determination of fluorides in pharmaceutical products for oral hygiene :

Fluorides are common ingredients in pharmaceutical products for oral hygiene due to their recognized effect in the prevention of tooth decay. In dental products, fluorides can be added in several different forms, such as sodium fluoride, sodium monofluorophosphate, tin fluoride, or in the form of different amines. This work describes potentiometric determination of fluorides in the samples of toothpastes and mouthwash. The method was optimized for the particular analytical purpose; namely, for the analysis of toothpastes and mouthwash by applying different sample preparation protocols depending on the fluoride source. Good recovery (93–103%) confirmed the correctness of the sample preparation procedures. Calculated limit of detection and limit of quantification for the optimized method were 1×10^{-3} mg/L and 2.8×10^{-3} mg/L fluoride, respectively. In the minority of the analyzed samples, calculated contents agreed well with the certified values, whereas the samples of mouthwash demonstrated better agreement.

Materials and methods :

The combined fluoride-selective electrode "Jenway" was used as a sensor for fluoride determination.



In fluoride-selective electrodes, the active membrane was made of a LaF3 monocrystal, doped with a small amount of europium(II) fluoride to lower its electrical resistance and to facilitate ionic charge transport. Fluoride ions bound to this crystalline surface according to:

$$\mathbf{LaF_3(s) + F^-(aq) \leftrightarrow LaF_4^-(s)}$$

The LaF_3 crystal, sealed into the end of a plastic tube, was in contact with the measuring solution. Internal electrolyte contained 0.1 M NaCl and 0.1 M NaF. The activity of fluoride ions in the inner solution controlled the potential on the inner surface of the crystal.

The electrode was connected to a read-out device HANNA potentiometer (USA). A magnetic stirrer (MM-510; Tehtnica, Železniki, Slovenia) was used to agitate solutions during the measurements. The usual laboratory glassware was used in the experiments. In the potentiometric measurements, polyethylene process vessels were used. All laboratory accessories were washed with nitric acid–water mixture (1:1, v/v), distilled, and triply distilled water.

Standards and reagent solutions :

For all measurements, triply distilled water was used in order to reduce fluoride content to a minimum. A 1 g/L fluoride stock solution was prepared by dissolving an appropriate amount of

NaF (Merck, Darmstadt, Germany, pro-analysis) in triply distilled water. Prior to dissolution, NaF was dried at 110°C for 2 hours.

TISAB was used in potentiometric measurements. There are several different formulations to make TISAB solutions. The preparation procedure of TISAB solution used in the present study was as follows: 58 g NaCl (Merck, Darmstadt, Germany, pro-analysis), 0.3 g sodium citrate (Merck, Darmstadt, Germany, pro-analysis), and 57 mL acetic acid (Merck, Darmstadt, Germany, pro-analysis) were dissolved in 500 mL triply distilled water. After dissolution, the pH was adjusted to 5.0–5.5 with 5 M NaOH (Merck, Darmstadt, Germany, pro-analysis) and the volume was adjusted to 1 L with triply distilled water. TISAB solution was stored in a plastic bottle until use. Recommended volume ratio between TISAB and test solutions was 1:1 (v/v). TISAB was used for the preparation of samples and standard free fluoride solutions. Fluoride calibration solutions in the range of 0.5–100 mg/L were prepared by serial dilution of the stock solution in triply distilled water. Finally, equal volumes (15 mL) of each calibration solution and TISAB solution were mixed and used in potentiometric measurements.

Samples :

Fluorides were determined in six samples of commercial toothpastes and five samples of commercial mouthwash. The samples were collected randomly from retail outlets in Guwahati , Assam. Collected samples encompassed domestic and foreign products including the most readily available and common ones. The intention of sampling strategy was to cover different products with different fluoride sources. Available products were fortified with one of two distinct fluoride sources as shown in Table.

Sample no.	Sample	Fluoride source
1	Toothpaste	NaF
2	Toothpaste	NaF
3	Toothpaste	Na_2FPO_3
4	Toothpaste	Na_2FPO_3
5	Toothpaste	Na_2FPO_3
6	Toothpaste	NaF
7	Mouthwash	NaF
8	Mouthwash	NaF
9	Mouthwash	NaF
10	Mouthwash	NaF
11	Mouthwash	NaF

Sample preparation :

Sample preparation depended on the sample type, sample matrix, and the form of the fluoride ion, that is, in its free or complexed form.

Samples of toothpastes (1 g) were dissolved in triply distilled water and were quantitatively transferred to a 100-mL volumetric flask that was filled to the mark. To speed up the dissolution, the sample was heated for 10 minutes in a water bath prior to filling to the mark. Upon cooling, 10 drops of propanol (Kemika, Zagreb, Croatia) were added to reduce foaming. For samples in which Na2FPO3 was specified as the fluoride source, prior to filling to the mark, 4 mL 6 M HCl was added to release fluoride ions completely.

Samples of mouthwash were prepared by transferring 10 mL of a liquid sample to a 100-mL volumetric flask, adding 10 drops of propanol, and filling to the mark with triply distilled water.

Potentiometric measurements :

Prior to analysis, 15 mL of standards or prepared samples were transferred to polyethylene process vessels and 15 mL TISAB solution was added. A magnetic stirrer was used to facilitate the convective mass transfer during measurements, and the potentiometer was set to read the voltage. After thorough rinsing and drying with a paper tissue, the electrode was immersed in the solutions. Solutions were stirred mechanically for 2 minutes and then the potential was read. Measurements were repeated three times.

The analyte concentration was measured against a calibration curve that was prepared as described earlier. The recovery assays were performed by adding a known amount of the same salt, as specified by the manufacturer, to the sample prior to its preparation. Thus, for Samples 3–5, Na2FPO3 was added, whereas NaF was used for the rest of the samples. The percentage recovery values were calculated by comparing concentrations obtained from the spiked samples with actual added concentrations of fluoride, as follows:

$$\mathrm{Recovery}\,(\%) = \left(\mathrm{C_{Spiked\ \ Sample}} - \mathrm{C_{Sample}}\right)/\mathrm{C_{Add}} \times 100$$

CSpiked Sample represents mg/kg of determined fluoride content in spiked sample, CSample represents mg/kg of fluoride actually present in the sample, and CAdd represents mg/kg of fluoride added to the sample. Recovery test was performed for each toothpaste and mouthwash sample in three replicates.

Results :

Determination of the equilibration time : In potentiometric measurements, the error is highest at the pre-equilibrium phase, that is, in the first moments of the electrode/solution contact. Over time the error diminishes and reaches a constant value. When the system is equilibrated, that is, when the equilibrium between the particular ion and a membrane potential is reached, the error is minimal. Equilibration time differs among the systems and depends on numerous factors. Prior to defining optimal experimental parameters, it was necessary to define the equilibrium time for the systems used in this particular investigation. Equilibration time was defined for different fluoride concentrations, 0.05 mg/L, 0.25 mg/L, 1 mg/L, 2.50 mg/L, and 5 mg/L. Potential was monitored in regular time intervals of 1 minute, 2 minutes, 3 minutes, and 5 minutes for each fluoride concentration and each measurement was repeated three times. It took longer in a solution of lower fluoride concentrations to reach potential equilibration, so in solutions containing 1 mg/L fluoride it needed 3 minutes for the potential to reach a standstill value. Furthermore, the reproducibility was markedly better.The intervals around the values represent 2 standard deviations

(SD) of the signal. In solutions containing >1 mg/L fluoride, the potential could be read after 1 minute when it reached a stable value. An equilibration time of 2 minutes was chosen for further experiments because it provided a relatively accurate determination over a wide concentration range. For general application, an equilibration time of 2 minutes allows time-efficient and accurate measurement of a broad concentration range, and it was thus adopted for practical measurements. Namely, according to specified contents in real samples of toothpastes and mouthwash, <0.05 mg/L fluoride could not be expected. Furthermore, the accepted equilibration time provided an acceptable duration of analysis.

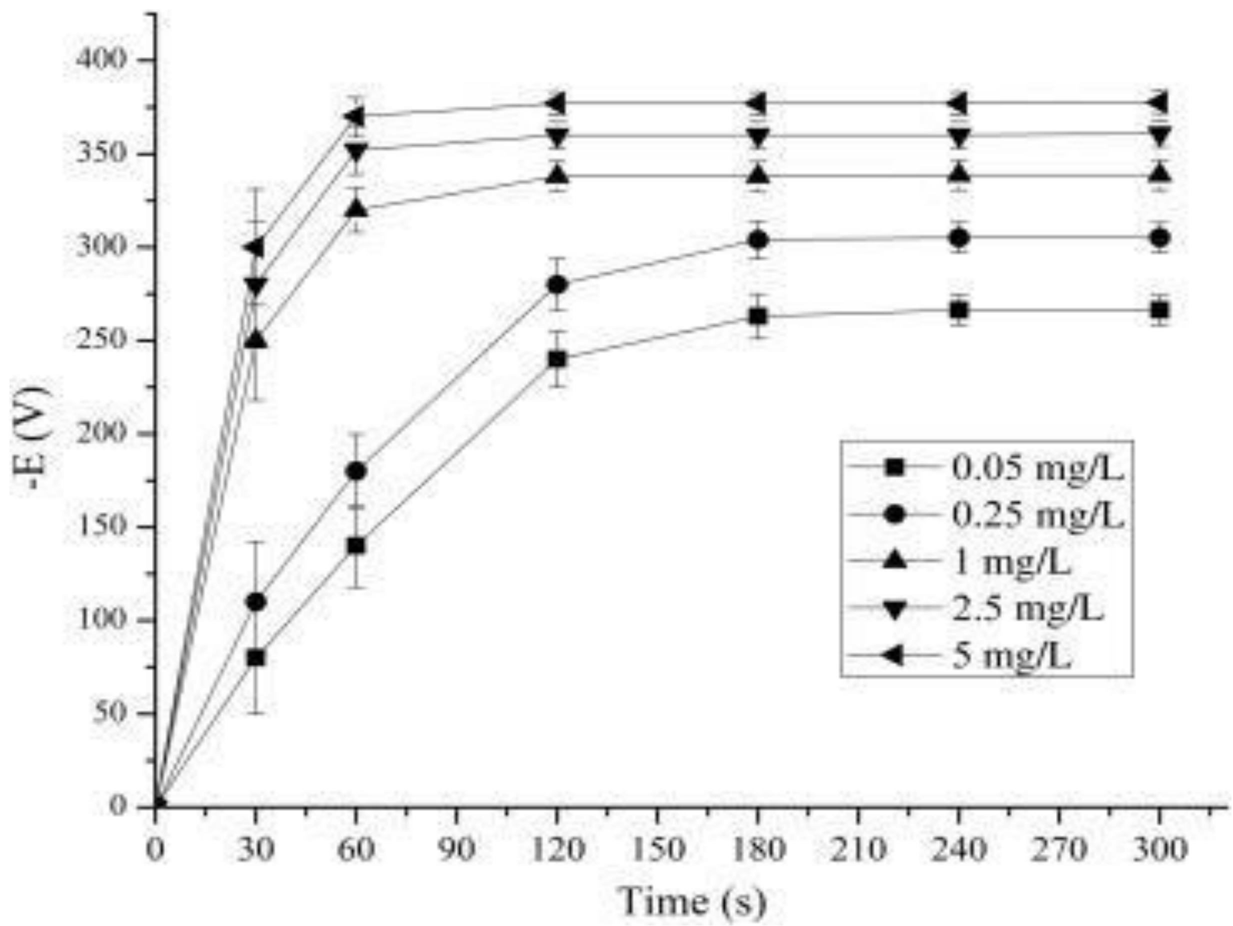


Fig. Equilibration times for different fluoride concentrations.

Linearity :

When quantification is in question, it is of utmost importance to define the linear range. For the system used, the linearity was verified for a wide concentration range from 1 mg/L to 1000 mg/L of fluoride. Experimental results demonstrated that the dependence of the potential versus logC was correlated well with the assumed linear dependence ($-E = 338.7 + 55.6 \log C$; $r = 0.9996$) over the whole examined concentration range. Furthermore, the slope of 55.6 mV/logC was in good agreement with the theoretical Nerstian slope for monovalent cations. A similar value of intercept (343.8 V) was reported in the literature , but the proposed method offered better agreement with the theoretical Nerstian slope.

Precision :

Precision of fluoride determination was defined in terms of repeatability (intra-day assay) and reproducibility (inter-day assay). Repeatability was defined on the basis of seven replicate analyses of solutions containing 1 mg/L, 5 mg/L, and 50 mg/L fluoride under optimal experimental conditions in a single day. Reproducibility was defined by analyzing fluoride solutions every day in triplicate for three consecutive days. The results are summarized in Table below. For all fluoride contents, calculated relative standard deviation (RSD) was <1% for both intra- and inter-day precision assays, indicating high precision of the method.

Fluoride content (mg/L)	Repeatability (intra-day precision)	Reproducibility (inter-day precision)
	RSD (%)	RSD (%)
1	0.46	0.75
5	0.02	0.04
50	0.0001	0.0002

RSD = relative standard deviation.

Table: Intra- and inter-day precision of determination for different fluoride concentrations.

LOD :

In defining LOD, multiple criteria can be applied. The sensitivity of a certain analytical method is determined by the lowest analyte concentration that can be reliably determined in statistically acceptable limits. This practically means that a signal detected in blank tests should be increased by its reproducibility in order to take into account the variation in the measurement results. This reproducibility component is normally expressed via 3 SD.

In this work the criterion ± 3 SD was used to calculate the LOD, where represented the mean of five blank measurements. The signal in the blanks increased by 3 SD was interpolated in the dependence −E versus logC, defined for low content range, in order to transform potential units into content units. Using such a statistical approach, a remarkable LOD of $1 \times 10-3$ mg/L of fluoride was calculated. In comparison to other previously reported potentiometric methods, which reported LOD of $10 \times 10-3$ mg/L and $6.5 \times 10-3$ mg/L , there was evidently better sensitivity of the proposed method. In terms of sensitivity, the defined method demonstrated superiority with respect to flow injection analysis, which is able reliably to detect $38 \times 10-3$ mg/L [18], as well as over capillary electrophoresis (LOD = 0.17 mg/L).

Limit of quantification was calculated on the basis of $x \pm 10$ SD and was $2.8 \times 10-3$ mg/L fluoride.

Fluoride determination in samples :

Taking into account fluoride content in samples specified by the manufacturers, calibration curves were defined for a broad concentration range, from 0.5 mg/L to 100 mg/L fluoride. Calibration was repeated three times, yielding a linear dependence ($r = 0.9999$) with good reproducibility, expressed via RSD for the intercept and the slope, 0.04% and 0.019%, respectively. Calculated contents, on the basis of three replicates, are presented in Table below. According to the determined contents, an equilibration time of 2 minutes was sufficient, because the lowest content of fluoride in the working solution contained 5.95 mg/L fluoride (Sample 10; taking into consideration twofold dilution with TISAB), for which even 1 minute would allow measurement at the equilibration point.

Sample	Certified fluoride content	Calculated fluoride content
Toothpaste samples	(mg/kg)	(mg/kg)
1	1450[a]	1479 ± 20[b] (101)[c]
2	1450	987 ± 17 (96)
3	1450	896 ± 9 (98)
4	1450	1100 ± 17 (94)
5	1450	906 ± 10 (98)
6	1450	1345 ± 13 (103)
Mouthwash samples	(mg/L)	(mg/L)
7	1450	1305 ± 11 (99)
8	226	246 ± 5 (97)
9	226	226 ± 4 (101)
10	112	119 ± 3 (99)
11	450	443 ± 5 (103)

a

The manufacturer did not specify the measurement uncertainty.

b

Data are presented as mean ± 2 SD, $n = 3$.

c

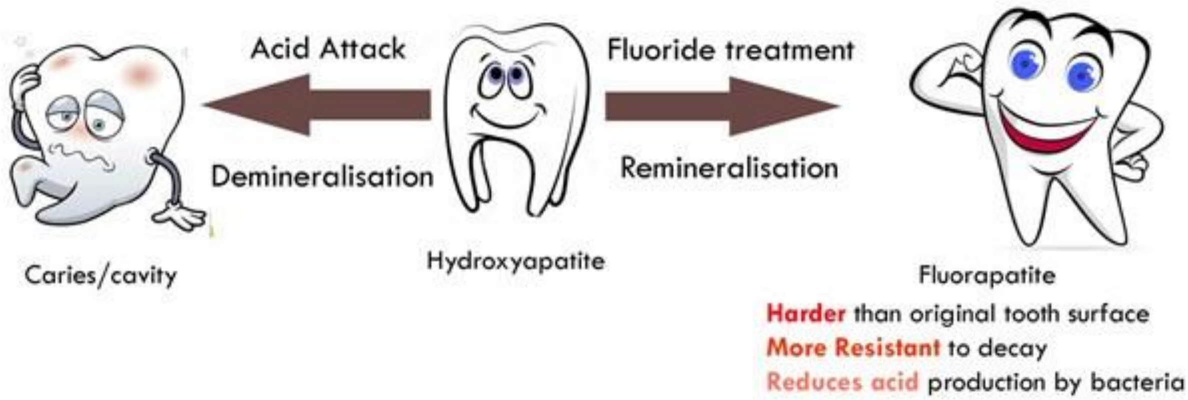
Results of the recovery test (%).

In the present work, a potentiometric method for fluoride determination in pharmaceutical products for oral hygiene was developed, particularly focusing on sample preparation due to different possible sources of fluoride. Analyzed samples encompassed toothpastes and mouthwash. In addition to differences in sample matrix, different fluoride salts were added to the samples as a source of fluoride, namely Na2FPO3 or NaF. For both types of sample, the procedure for sample preparation was rapid and simple, but for the samples with Na2FPO3, an additional step of acid hydrolysis should have been applied. In aqueous solutions, Na2FPO3 dissociates to FPO32− ions, which does not produce a signal at the ion-selective membrane, so acid hydrolysis was necessary to liberate fluoride ions from FPO32− ions. Calculated sensitivity of the developed method for fluoride determination was 1 × 10−3 mg/L of fluoride. The defined procedures for sample preparation were shown to be reliable, which was indicated by good recovery of the spiked non-fluoride samples (96–98%) as well as analyzed fluoride-containing samples (94–103%). Among 11 analyzed samples, in general, the samples of mouthwash exhibited better agreement with the specified fluoride contents. In a minority of the analyzed samples, calculated contents agreed well with the specified values. Taking into consideration the toxicity and the specified benefits of fluorides, more strict control of fluoride content in pharmaceutical products for oral hygiene is proposed.

How Does Fluoride Protect Teeth?

Fluoride benefits both children and adults.

Before teeth break through the gums, the fluoride taken in from foods, beverages and dietary supplements makes tooth enamel (the hard surface of the tooth) stronger, making it easier to resist tooth decay. This provides what is called a "systemic" benefit.



After teeth erupt, fluoride helps rebuild (remineralize) weakened tooth enamel and reverses early signs of tooth decay. When you brush your teeth with fluoride toothpaste, or use other fluoride dental products, the fluoride is applied to the surface of your teeth. This provides what is called a "topical" benefit.

In addition, the fluoride you take in from foods and beverages continues to provide a topical benefit because it becomes part of your saliva, constantly bathing the teeth with tiny amounts of fluoride that help rebuild weakened tooth enamel.

How Do we Get Fluoride?

Drink Water with Fluoride

Fluoride is naturally found in most all water sources, rivers, lakes, wells and even the oceans. For the past 70 years, fluoride has been added to public water supplies to bring fluoride levels up to the amount necessary to help prevent tooth decay. Community water fluoridation is like drinking milk fortified with Vitamin D or eating bread and cereals enriched with folic acid. Before water fluoridation, children had about three times as many cavities. Because of the important role it has played in the reduction of tooth decay, the Centers for Disease Control and Prevention has proclaimed community water fluoridation one of ten great public health achievements of the 20th century. Studies prove water fluoridation continues to help prevent tooth decay by at least 25% in children and adults, even with fluoride available from other sources, such as toothpaste. Today, almost 75 percent of the U.S. population is served by fluoridated community water systems.

Use Toothpaste and Mouthrinse with Fluoride
Toothpaste with fluoride has been responsible for a significant drop in cavities since 1960. Look for one with the ADA Seal of Acceptance to make sure it contains fluoride.

- Brush twice a day (morning and night) or as directed by your dentist and physician.

- For children younger than 3 years, start brushing their teeth as soon as they start to appear in the mouth by using fluoride toothpaste in an amount no more than a smear or the size of a grain of rice.
- For children 3 to 6 years old, use no more than a pea-sized amount of fluoride toothpaste.

- Always supervise your child's brushing to make sure they use the right amount and try to get your child to spit out most of the toothpaste.
- Mouthwash with fluoride can help make your teeth more resistant to decay, but children six years or younger should not use it unless it's been recommended by a dentist. Many children younger than 6 are more likely to swallow it than spit it out because their swallowing reflexes aren't fully developed.

Application of Fluoride :

Fluoride salts and hydrofluoric acid are the main fluorides of industrial value. Compounds with C-F bonds fall into the realm of organofluorine chemistry. The main uses of fluoride, in terms of volume, are in the production of cryolite, Na_3AlF_6. It is used in aluminium smelting. Formerly, it was mined, but now it is derived from hydrogen fluoride. Fluorite is used on a large scale to separate slag in steel-making. Mined fluorite (CaF_2) is a commodity chemical used in steel-making.

Hydrofluoric acid and its anhydrous form, hydrogen fluoride, is also used in the production of fluorocarbons. Hydrofluoric acid has a variety of specialized applications, including its ability to dissolve glass.

Cavity prevention :

Fluoride-containing compounds, such as sodium fluoride or sodium monofluorophosphate are used in topical and systemic fluoride therapy for preventing tooth decay. They are used for water fluoridation and in many products associated with oral hygiene. Originally, sodium fluoride was used to fluoridate water; hexafluorosilicic acid (H_2SiF_6) and its salt sodium hexafluorosilicate (Na_2SiF_6) are more commonly used additives, especially in the United States. The fluoridation of water is known to prevent tooth decay and is considered by the U.S. Centers for Disease Control and Prevention to be "one of 10 great public health achievements of the 20th century".In some countries where large, centralized water systems are uncommon, fluoride is delivered to the populace by fluoridating table salt. For the method of action for cavity prevention, see Fluoride therapy. Fluoridation of water has its critics (see Water fluoridation controversy). Fluoridated toothpaste is in common use. Meta-analysis show the efficacy of 500 ppm fluoride in toothpastes. However, no beneficial effect can be detected when more than one fluoride source is used for daily oral care.

Biochemical reagent :

Fluoride salts are commonly used in biological assay processing to inhibit the activity of phosphatases, such as serine/threonine phosphatases. Fluoride mimics the nucleophilic hydroxide ion in these enzymes' active sites. Beryllium fluoride and aluminium fluoride are also used as phosphatase inhibitors, since these compounds are structural mimics of the phosphate group and can act as analogues of the transition state of the reaction.

Fluoride-ion Battery :

In 2018, a team of researchers including Simon C. Jones of California Institute of Technology and

Christopher J. Brooks of the Honda Research Institute created a Fluoride-Ion Battery (FIB). They used a liquid electrolyte to shuttle fluoride ions in the battery and demonstrated its use in a room-temperature, rechargeable FIB.

Safety

Ingestion

According to the U.S. Department of Agriculture, the Dietary Reference Intakes, which is the "highest level of daily nutrient intake that is likely to pose no risk of adverse health effects" specify 10 mg/day for most people, corresponding to 10 L of fluoridated water with no risk. For young children the values are smaller, ranging from 0.7 mg/d to 2.2 mg/d for infants. Water and food sources of fluoride include community water fluoridation, seafood, tea, and gelatin.

Soluble fluoride salts, of which sodium fluoride is the most common, are toxic, and have resulted in both accidental and self-inflicted deaths from acute poisoning. The lethal dose for most adult humans is estimated at 5 to 10 g (which is equivalent to 32 to 64 mg/kg elemental fluoride/kg body weight). A case of a fatal poisoning of an adult with 4 grams of sodium fluoride is documented, and a dose of 120 g sodium fluoride has been survived. For sodium fluorosilicate (Na2SiF6), the median lethal dose (LD50) orally in rats is 0.125 g/kg, corresponding to 12.5 g for a 100 kg adult.

Treatment may involve oral administration of dilute calcium hydroxide or calcium chloride to prevent further absorption, and injection of calcium gluconate to increase the calcium levels in the blood. Hydrogen fluoride is more dangerous than salts such as NaF because it is corrosive and volatile, and can result in fatal exposure through inhalation or upon contact with the skin; calcium gluconate gel is the usual antidote.

In the higher doses used to treat osteoporosis, sodium fluoride can cause pain in the legs and incomplete stress fractures when the doses are too high; it also irritates the stomach, sometimes so severely as to cause ulcers. Slow-release and enteric-coated versions of sodium fluoride do not have gastric side effects in any significant way, and have milder and less frequent complications in the bones. In the lower doses used for water fluoridation, the only clear adverse effect is dental fluorosis, which can alter the appearance of children's teeth during tooth development; this is mostly mild and is unlikely to represent any real effect on aesthetic appearance or on public health. Fluoride was known to enhance the measurement of bone mineral density at the lumbar spine, but it was not effective for vertebral fractures and provoked more non vertebral fractures.

A popular urban myth claims that the Nazis used fluoride in concentration camps, but there is no historical evidence to prove this claim.

In areas that have naturally occurring high levels of fluoride in groundwater which is used for drinking water, both dental and skeletal fluorosis can be prevalent and severe.

Hazard maps for fluoride in groundwater

Around one-third of the human population drinks water from groundwater resources. Of this, about 10%, approximately three hundred million people, obtains water from groundwater resources that are heavily contaminated with arsenic or fluoride.These trace elements derive mainly from minerals.Maps are available of locations of potential problematic wells.

Topical

Concentrated fluoride solutions are corrosive.Gloves made of nitrile rubber are worn when handling fluoride compounds. The hazards of solutions of fluoride salts depend on the concentration. In the presence of strong acids, fluoride salts release hydrogen fluoride, which is corrosive, especially toward glass.

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