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Some aspects related to the presence of aluminium in waters

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Summary . - Aluminium is present in very small amounts in living organisms but it is abundant in the environment, where it exists in forms with low availability to man and most other biological species. Despite its abundance in the earth's crust only a small amount of aluminium is present in waters, with concentrations varying from a few tens to some hundreds of micrograms per liter. High levels of aluminium in drinking water are in most cases due either to acid precipitation or water treatment with aluminium salts. The presence of aluminium in dialysis fluids has been recognized as the major reason for development of aluminium toxicity in patients with renal failure. In subjects with normal renal function, high concentrations of this element in drinking water (> 80 µg/l) have been related to an elevated incidence of Alzheimer's disease, even though the real contribution of the element in the development of the disease has not yet been clarified.

Key words: aluminium toxicity, water.

Riassunto *(Alcuni aspetti associati alla presenza di alluminio nelle acque)*. - L'alluminio è un elemento ubiquitario ampiamente diffuso nell'ambiente in forme chimiche aventi scarsa biodisponibilità per l'uomo, mentre si ritrova in piccolissime quantità negli esseri viventi. Nonostante l'abbondante presenza nella crosta terrestre, nelle acque l'elemento è presente in bassissime concentrazioni che possono variare da poche decine ad alcune centinaia di microgrammi per litro. Elevati livelli di alluminio nelle acque naturali sono principalmente dovute all'effetto delle pioggie acide, mentre la sua eccessiva presenza nelle acque potabili è spesso legata a processi di trattamento di potabilizzazione con sali dell'elemento. La presenza di alluminio nei fluidi di dialisi è stata ampiamente riconosciuta come una delle principali cause di tossicità per i pazienti sottoposti al trattamento dialitico; inoltre, in soggetti con funzione renale normale, concentrazioni di alluminio nell'acqua potabile superiori a 80 µg/litro sono state poste in relazione con lo sviluppo di patologie neurodegenerative di tipo Alzheimer, sebbene il reale ruolo dell'elemento non sia stato definitivamente chiarito.

Parole chiave: tossicità dell'alluminio, acque.

Introduction

Over the last few years, an association has been made between the accumulation of aluminium in the body and several pathological events, with particular reference to uremic subjects undergoing long-term dialysis [1, 2]. The presence of this element in the haematic flow of these patients sometimes induces serious neurological [3, 4] and osteodystrophic complications [5, 6], forming a particularly unfavourable clinical picture. Epidemiological studies showed that these disorders occurred together in large numbers of patients undergoing dialysis with dialysate prepared from tap water containing large amounts of aluminium [7, 8]. Moreover, in subjects with normal renal function aluminium seems to be implicated as an aetiological factor in some diseases such as senile dementia of the Alzheimer's type, Parkinson's disease, and amyotic lateral sclerosis [9, 10].

Aluminium exists in the environment predominantly in forms with low availability to man and most other biological species. Concentrations in natural waters normally are low since the element tends to form stable structures with hydroxides that easily precipitate. However, in recent decades acid precipitation has caused the element to leach from soils, leading to high concentrations in natural waters. In addition, in order to remove suspended matter and highly coulored humic substances from raw waters used for drinking purpose, aluminium sulphate is used as a coagulant. This treatment may result in an increase of it concentration in drinking waters.

Occurrence and general properties

Aluminium is present in very small amount in living organisms but is abundant in the environment. Composing 8% of the earth's crust, the metal is the third most abundant element after oxygen and silicon. Despite its abundance in the crust, only little aluminium is present in the planet's waters. Concentrations in natural fresh waters vary from a few tens to some hundreds of micrograms per liter, whereas the concentration of aluminium in sea-water is generally lower than 1 $\mu g\,l^{-1}$ [11], possibly due to the siliceous remains of diatoms that bound Al^{+3}. Surface waters usually contain more aluminium than ground waters even though in some areas these latter may contain significant amounts of the element. Aluminium is present in air in the form of alumininosilicates associated with dust particles, as a result of the weathering of aluminosilicates rocks [12]. Concentrations of 50-500 ng/m^3 in rural areas and 100-500 ng/m^3 in urban environments have been reported [13]. Aluminium is widely used in industrial activities and its compounds play an important role in other applications such as in the pharmacological and domestic fields. As mentioned above, aluminium salts are also widely used in water treatment as flocculating agents.

In nature aluminium exists only in the oxidation state Al^{+3} ($1s^2\,2s^2\,2p^6$). Large amounts of the element are in alumino-silicates (mica, feldespars), hydrate oxides (particularly bauxite), criolyte; moreover, many aluminium salts are characterized by high insolubility, particularly the phosphates. Its electric charge and the small ionic radius (0.51 Å) give Al^{+3} a strong polarizing effect on adjacent atoms; therefore, the element is too reactive to be found free in nature [14].

Despite its abundance it is usually excluded from normal biochemical and metabolic processes because of its chemical nature. This is due to the low availability of its chiefly occurring chemical forms [15]. The only accessible oxidation state in biological systems is +3 since the standard reduction potential for the reaction $Al^{+3} + 3e^- \rightleftarrows Al^\circ$ is highly negative (-1.67 V) [16]. In organisms aluminium is easily bound to many substances and structures, but its ligands are often non-specific and can bind other ions which have similar properties. For this reason some elements that are chemically similar to aluminium can have a similar metabolism. In its complexes Al^{+3} is usually bound to oxygen but, sometimes, nitrogen binding also occurs [14]. The ion has a strong affinity to phosphate, both inorganic free phosphate ions and various organic phosphate compounds. As a strongly hydrolyzing element, aluminium is practically insoluble in the pH range of 6.0-8.0; the solubility is enhanced under acidic (pH < 6.0) or alkaline (pH > 8.0) conditions, and/or in the presence of complexing ligands. Acidification of soil by appliying acid-generating fertilizers is one of the main causes which releases aluminium from Al-bearing minerals through the action of protons [17]. In addition, acid rain containing natural acids (HNO_3, H_2CO_3) or acids from hydrocarbon combustion plays a primary role in these processes.

The concentration of aluminium in food varies widely depending both on the nature of foodstuffs and the procedures utilized in preparing and transforming foods. Aluminium that is present naturally in foods of animal origin reflects the aluminium content of the food and drinking water of the animals, together with the capacity of tissues to concentrate the element. Aluminium that is present naturally in foods of plant origin reflects the content of the soil and water in contact with the plants and the ability of the plants to absorb and retain the element [18]. The dietary intake of aluminium can vary from 3 to 30 mg/day, but a reasonable average dietary intake is probably about 5-10 mg/day [18, 19].

Aluminium chemistry in aqueous solutions

In aqueous solution, Al^{+3} protolyzes part of the water envelope and forms hydroxocomplexes. When the pH value is less than 5, the ion shows an octahedral hexahydrate form, $[Al(H_2O)_6]^{+3}$, usually abbreviated as Al^{+3}. As the acidity decreases, a series of deprotonations occur:

$$Al^{+3} + H_2O \rightleftarrows [Al(OH)]^{2+} + H^+ \qquad Ka_I = 10^{-5.5}$$

$$[Al(OH)]^{2+} + H_2O \rightleftarrows [Al(OH)_2]^+ + H^+ \qquad Ka_{II} = 10^{-5.6}$$

$$[Al(OH)_2]^+ + 2H_2O \rightleftarrows [Al(OH)_4]^- + 2H^+ \qquad Ka_{III} = 10^{-12}$$

Thus, the measured aluminium concentration is the sum of all the species present in solution:

$$[Al]_{TOT} = [Al^{+3}] + [Al(OH)]^{2+} + [Al(OH)_2]^+ + [Al(OH)_4]^-$$

The species $[Al(OH)_4]^-$ prevails at pH > 6.2, whereas a mixture of species occurs in the pH range of 5.0 - 6.2. The chemical thermodynamic properties of the possible species of aluminium ions which coexist at equilibrium with the solid phase may be determined from the solubility curve of gibbsite which represents the stable crystalline phase of $Al(OH)_3$. The solubility of aluminium in equilibrium with the solid phase $Al(OH)_3$ is highly pH-dependent and may be represented by the reaction:

$$Al(OH)_{3\,(gibbsite)} + 3H^+ \rightleftarrows Al^+ + 3H_2O \qquad [16]$$

In natural waters, aluminium can be variously bound to sulfate, fluoride, hydroxide and to naturally occurring anions of complex structure [20-22]. The sizes of F^- and OH^- are similar and, therefore, fluorine readily displaces the OH^- ions in the metallic complexes. The process is still pH-dependent and the formation of various species is correlated with the total F^- concentration in the solution. At low pH values, reactions of the type:

$$[Al(H_2O)_6]^{+3} + F^- \rightleftarrows [Al(H_2O)_6F]^{+2}$$

are to be expected, while at higher pH a reaction of the type:

$$Al(OH)_3 + F^- \rightleftarrows AlOH_2F + OH^-$$

probably prevails. As F^- concentration increases, OH^- or H_2O ligands are displaced until all octahedral positions of Al are occupied by F^- (AlF_6^{-3}). The F^- concentration in fresh waters is normally low ($x \approx 0.18$ mg/l) and the concentration of the element sometimes added in drinking water do not exceed 1 mg/l [23]. When the pH is less than

5.5, the molar concentration of dissolved aluminium usually is greater than that of F^- and the formation of species such as AlF^{2+} and AlF_2^+ occurs. Under alkaline conditions, the concentration of OH^- ions is high and becomes difficult for F^- to compete with OH^- for aqueous aluminium; in this situation, OH^- complexes predominate [22]. In acidic solutions, aluminium forms complexes also with SO_4^{-2} even though they are not as strong as F^- complexes. When the SO_4^{-2} concentration is quite low, the $AlSO_4^+$ species is predominant; at higher SO_4^{-2} concentrations the form $Al(SO_4)_2^-$ is to be expected. In fresh waters, despite the fact that SO_4^- concentrations ($x \approx 38.4$ mg/l) are normally higher than F^- concentrations, complex formations become significant only at low pH values. Some evidence reported in the literature suggests that aluminium may also form strong complexes with other inorganic ligands, like phosphate and silica. The insoluble species $AlPO_4$ is well- known, but complexes that are probably soluble, such as $AlHPO_4^+$ and $AlH_2PO_4^{2+}$, have also been hypothesized in solution [16, 22, 23]. However, it seems that only a small fraction of dissolved aluminium in natural waters could be involved in the formation of complexes. Owing to the abundance of aluminosilicate minerals in the natural environment, the interactions between aluminium and H_4SiO_4 are of particular interest since this compound has been demonstrated to affect the various steps of aluminium hydrolysis processes. Taking into account the mean concentration of Si dissolved in fresh waters ($x \approx 8.4$ mg/l), it is reasonable to hypothesize that Al-Si complexes may be significant. Other inorganic ions present in natural waters, such as HCO_3^-, Cl^-, NO_3^- do not seem to form significant complexes with aluminium.

Aluminium content and toxicity in water

Although the toxicity of aluminium in the presence of normal renal function still remains to be defined clearly, some evidence indicates a possible geographical association between aluminium in drinking water and registered cases of dementia [24, 25]. This finding is surprising, given the small amount of the total aluminium intake attributable to drinking water. Assuming for example, a quota of 10 mg/day from food, an adult drinking two litres of water per day at 50 μg/l Al would receive approximately 1% of the total intake from water. However, urinary excretion of aluminium is only 0.02 to 0.05 mg per day [14] which represents less than 1% of the 5-10 mg ingested daily, so most dietary sources of the element are presumably not absorbed. Thus, it is possible that aluminium in drinking water is more bioavailable than aluminium from other sources [26]. The concentrations of the element in raw waters are usually low and depend on either geological or seasonal factors, and the effects of acid rain [27]. Aluminium may also be transported with HCO_3^-, organic and acidic counteranions from soil to surface waters. Stumm and Morgan [28] reported a median concentration of 10 μg/l for terrestrial waters, while Bowen [29] gave a mean value of 243 μg/l for fresh waters including bogs. Concentrations of 200-300 μg/l were associated with low pH levels and those of 400-600 μg/l with afforested catchments [30].

Since aluminium salts are widely used as flocculating agents in water purification processes, some domestic waters could contain high concentrations of the element. Some factors influence the concentration of residual aluminium in finished waters, namely the aluminium levels in raw water, the concentrations of HCO_3^- SO_4^{-2} and natural organic matter and the pH. Moreover, the amount of the Al coagulant added and the efficiency of the filtration process of the Al-floc undoubtedly represent other critical points [31]. The element added to water is usually filtered as a precipitate by carefully adjusting the pH. Nevertheless, this process can easily be perturbed and, as a consequence, the amount of aluminium remaining in solution in colloidal and/or ionic form can be significant. The solubility of Al at pH 7 is limited to 2.5 mg/l, even though solubility increases considerably as the pH diverges from 7 [26]. In this situation, the amount of aluminium in waters can be higher than the natural levels.

The current European Community directive specifies a maximun acceptable concentration of 0.2 mg/l in tap water, with a recommended value of 0.05 mg/l. Miller *et al.* [32] reported that in a recent monitoring program carried out in the US, the aluminium levels in finished waters were always above 14 μg/l which also represented the limit of his analytical method, at median levels between 31 and 112 μg/l, and with a maximum aluminium concentration of about 2.7 mg/l. Data also indicated that when "alum" is used as coagulating agent, there is a 40-50% possibility that the original content of aluminium in raw water increases. Parkinson *et al.* [33] reported that in England, the aluminium concentration in tap water can vary day-to-day depending on the changes in weather conditions which affect the organic content of the water. An important consequence of the acidification of lakes and streams by acid rain is the mobilization of aluminium from the edaphic to the aquatic environment; these elevated aluminium levels in acidic waters may be toxic to aquatic biota [22, 34]. The total effect on fish life is due to the combination of two factors: acidification of their environment, and increased of aluminium concentration (as well as other metals) in solution. Aluminium appears to be toxic for fish at levels of 100-200 μg/l; this range of concentrations has been reported to be typical for acidic surface waters. The extent of Al toxicity to fish is also dependent on the forms of aqueous aluminium in the aquatic environment. Driscoll *et al.* [22] reported that aluminium toxicity to fish was heavily reduced when the element was complexed to organic matter, while the inorganic forms were lethal. Baker and Schofield [34] found that in the range of pH 4.2-4.8 the presence of aluminium improved egg survival but reduced the growth of young fish. In a study carried out by the same authors on acidified lakes in the Adirondack region (US), aluminium species were found to be highly variable; thus, a variation in Al toxicity was continuously observed. A loss of ions such as Na^+ and Cl^- from the blood of brown trout was observed by Muniz and Leivestad [35] in solutions having an aluminium concentration of 189 µg/l at pH 5.0. Gill damage to the same species was also observed by Schofield and Trojnar [36] in acidic solution at an aluminium concentration ranging from 486 to 972 µg/l. The concentrations of the element are generally lower in ground waters than in surface waters. Two possible explanations are suggested for this: ground waters are generally less acidified than the others, and have a higher buffer capacity.

In plants aluminium toxicity seems to act at the growth level and accumulation is a function of the acidity of the soil which influences its bioavailability. Most plants seem to contain aluminium but excess is toxic. Experiments on excised roots have shown that Al^{+3} ions can both increase and decrease the uptake of other metal ions, depending on the external experimental conditions. The uptake of aluminium itself is dependent mainly on the pH of the soil and is best in slightly acid soils but less so under alkaline conditions, owing to the formation of insoluble aluminium hydroxide polymers. The few studies carried out in this specific field of application suggest that plant tolerance to aluminium is due to the combination of two factors (exclusion mechanisms and internal tolerance) through the formation of a pH barrier induced in the rizosphere, and also the action of radical exudates which have chelating properties [37].

The presence of aluminium in dialysis fluids has been recognized as the major reason for development of aluminium toxicity in patients with renal failure. Indeed, persons receiving chronic dialysis treatment through an "artificial kidney" are normally exposed to 150-200 litres of dialysis fluid 2-3 times every week. Epidemiological studies have demonstrated geographical distributions of osteomalacic dialysis osteodystrophy and dialysis dementia correlated to aluminium concentrations in tap water used to prepare the dialysate [7, 8]. The latter appears to be the major source of this type of metal contamination. The driving force for aluminium transfer during hemodialysis seems to be the effective concentration gradient between the element in the dialysis bath and the fraction of diffusible aluminium in serum. Moreover, transfer of the element from the solution across the dialyzing membrane occurs despite low aluminium concentrations. Studies carried out on aluminium kinetics in hemodialysis [38] have demonstrated that Al concentration in the dialysis fluid should be less than 10 µg/l in order to prevent the development of toxicity in patients. In a study performed on 202 patients who where on home hemodialysis for chronic renal failure and who presented clear signs of toxicity, Platts *et al.* [39] reported that aluminium concentrations in tap water turned out to be higher than those found in the water used by patients without complications. In addition, patients with multiple fractures had been dialysed against water that had higher aluminium and manganese content than those with a single fracture. Although the authors did not definitively incriminate aluminium as toxic contaminant, they emphasized the need to treat tap water adequately. Numerous investigations have been performed on the different procedures for tap water treatment before dialysis, namely softening, deionisation and reverse osmosis. Results indicate that the last two are the best procedures, while softening is not suitable. Using this method, the aluminium extracted is only partially removed during resin rigeneration, and consequently, the element is subsequently transferred to the water. In a study carried out on patients maintained on regular haemodialysis in Newcastle upon Tyne (UK), Ward *et al.* [40] reported that after one to four years of dialysis treatment, osteomalacia was observed only in 15% of patients using deionized water compared with 70% of patients using non-treated or softened water from the same source. They also showed that both osteomalacia and dialysis dementia occured in centers which had a high aluminium content in the tap water; moreover, patients using softened water had serum aluminium concentrations higher than those using deionised water. In light of these results, they concluded that this content is enough to justify the expense of treating water by deionisation, reverse osmosis, or both, prior to use in the preparation of dialysate. Nowadays, reverse osmosis is the recommended method of water treatment since it produces water with an aluminium concentration which is less than 10 µg/l and also a low content of other ions and organic contaminants [41, 42]. This water treatment seems to be effective in altering the natural history of dialysis dementia and in preventing the appearance of this syndrome.

The results of an investigation performed by Costantini *et al.* [43] in 1988 on Italian dialysis centers (Table 1) showed improved water treatment in comparison with the situation previously observed in a similar study done in 1981. In Tables 2 and 3, the aluminium concentrations determined in tap waters are reported before and after treatment, respectively. However, the investigation was not representative of the entire Italian situation because the data covered only 31% (1988) of the dialysis centers (9371 patients, 44.3%), and of these, only 41.4% provided the aluminium content in waters.

Table 1. - Water treatment for dialysis in Italy

Type of treatment	Treatment (%) 1981	Treatment (%) 1988
Hospital dialysis		
Untreated	0	0
Softening	6.4	0
Deionization	80.3	54.0
Reverse osmosis	9.0	13.1
Dionization + Reverse osmosis	4.3	32.9
Home dialysis		
Untreated	6.6	3.5
Softening	17.7	5.3
Deionization	64.6	59.6
Reverse osmosis	8.9	15.8
Dionization + Reverse osmosis	2.2	15.8

Table 2. - Aluminium concentrations in tap water (µg/l)

	Mean	Range (1988)
Hospital dialysis	17	3-195
Home dialysis	18	4-181

Table 3. - Aluminium concentrations in treated tap water for dialysis (µg/l)

	Minimum	Mean	Maximum
Softening	6	8	12
Deionization	5	6	8
Reverse osmosis	3	6	7
Deionization + Reverse osmosis	2	4	6

Association between aluminium in drinking waters and some neurodegenerative disorders

The neurotoxic effects of aluminium on patients with renal failure does not necessarily imply that the element is harmful for persons with normal renal function who appear to have a formidable barrier toward aluminium absorption [14]. However, some evidence has demonstrated that aluminium may be toxic to the central nervous system for persons with normal kidney function. The element is present in neurofibrillary tangle-bearing neurons [44] and in the cores of senile plaques [45] which represent the neuropathological hallmarks of Alzheimer's disease. Moreover, it seems to be implicated in some forms of amyotrophic lateral sclerosis and parkinsonism-dementia. Although knowledge of aluminium bioavailability is very poor, it is well known that sometimes very small quantities of the element deposited in the brain suffice to induce clear neurological effects [46]. In general, absorption of aluminium from the gastrointestinal tract is poor [47] but the pharmacokinetics of various species of the element in humans may be different. For this reason, it is very important to characterize the forms of aluminium found in drinking waters. Although aluminium from this source represents only a small part of the total daily intake, it may comprize a significant amount of the total quantity absorbed from the gastrointestinal tract since its bioavailability may be higher than aluminium from other sources [25], such as foodstuffs or medicines. Slanina *et al.* [48] reported that Al-citrate is much more readily absorbed than Al-hydroxide both in rats and in humans. Finnegan *et al.* [49] described a neutral water-soluble complex between aluminium and maltol; in aqueous solution this complex presents a neutral charge, it is very stable to hydrolysis, and it appears to be a very potent neurotoxin. In general, the electroneutrality and a molecular weight of about 400 dalton, or less, are the necessary requisites for possible passage of the blood-brain barrier, while both solubility and stability in water are required to deliver the complex to the barrier.

In the last few years, great interest has been aroused by some epidemiological studies which implicate aluminium in water supplies as a significant risk factor in the aetiopathogenesis of Alzheimer's disease. Two Norwegian investigations of the chemical composition of drinking water and its possible relationship with the epidemiology of some diseases were carried out by Flaten [24] and Vogt [50], respectively. Although some evidence suggested a link between the concentration of aluminium in water and dementia, some aspects of these studies were criticized, [51] owing to the lack of data showing a clear relationship between cases of dementia and incidence of Alzheimer's disease. In a survey of 88 country districts within England and Wales, Martyn *et al.* [25] found that the risk factor of Alzheimer's dementia development in people under the age of 70 years increased about 50% in areas where the levels of aluminium in drinking water exceeded 110 μg/l vs areas with concentrations below 10 μg/l. They identified a total of 1203 patients with dementia, 445 of whom were classified as having Alzheimer's disease, and 2936 patients were identified for epilepsy. Although the authors found a positive correlation between the rates of Alzheimer's disease and the concentration of aluminium in drinking water (no correlation was found for other causes of dementia or for epilepsy), they also emphasized the possibility of wrong interpretations caused by some unknown counfounding variables. Neri and Hewitt [52] confirmed the findings of Martyn *et al.* and Flaten in a Canadian study (Province of Ontario) from which they obtained data on 2344 patients aged 55 or over who had been diagnosed with Alzheimer's disease. On the contrary, a recent investigation carried out by Wettstein *et al.* [53] on Swiss districts with high (98 μg/l) or low (4μg/l) aluminium concentrations in drinking water did not find any significant correlation between aluminium content in waters and rates of the disease. The explanation for the discrepancy between these studies may be attributed to some critical variables, such as the accuracy of the method used in ascertaining the frequency of Alzheimer's disease, the possible movement of patients between areas having different aluminium content in waters, and the reliability of the data for aluminium concentrations.

Conclusions

After all, even though much evidence indicates aluminium as being responsible for some neurological disorders, the real effect that the element in drinking water may have on the pathogenesis of Alzheimer's dementia is still to be clarified. In the meantime, it would be prudent to maintain the aluminium concentration in drinking water at the lowest possible levels and, in any case, not higher than the "guideline value" of 50 μg/l proposed by the EEC directive.

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