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Aluminum in food and potential role on Alzheimer's disease of aluminum

Günseli BOBUŞ ALKAYA*[1], Çağatay DEMİRCİ [2], Hüseyin ŞEVİK [3]

[1]Mersin University, Institute of Science, Food Engineer, Mersin, Turkey
[2]Mersin City Training and Research Hospital General Surgery Department, Mersin, Turkey
[3]Mersin University, Engineering Faculty, Metallurgy and Materials Engineering, Mersin, Turkey

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ABSTRACT

Several studies have shown the relationship between the aluminum exposure and the Alzheimer's disease. The gastrointestinal absorption of Aluminum (Al) is low. Also, If the renal filtering system works as needed, generally urine can be enough to eliminate overdose (rational over concentrations) of Al. But Al can be found in kinds of foods and drinks such as processed foods (because of additives, packaging materials, utensils…), fresh vegetables and fruits (because of soil) and even in drinking water therefore, in some cases, the Al level may pose a health risk. Chronic high concentration to Al exposure preferably intakes by oral, intravascular ways with also not having a good condition of Glomerular Filtering System of Kidneys (GFR). Nowadays, although mankind is having more Al by oral ways than past and many studies have been conducted to determine whether there is a relationship between aluminum and Alzheimer's disease(AD) or not. Therefore, this review is intended to provide a short summary of the works done in the past and it may warn people about Al intake in the next decade, therefore human can change their life to be more natural less industrial.

1. INTRODUCTION

Aluminum is the third most common element in the Earth's crust with about 8%. Pure aluminum has not been existing in nature, therefore it has mainly oxide, hydroxide and silicate compounds (Chappard 2016, EFSA 2011, Krewski et al. 2007, Stahl et al. 2017, Yokel 2016). Aluminum is used in many areas of the industry due to its advantages such as low density, good thermal conductivity, ductility and corrosion resistance. These areas can be listed as transportation (automobiles, aircraft, ships), construction (windows, doors, railing, profiles), packaging (cans, soft packaging, foils, cooking utensils), machine construction, electrical engineering (cable, distributing, dispensing bar), cosmetics, personal care industry and food additives (Chappard 2016, Krewski et al. 2007). Today, the fastest increase in the use of aluminum and its alloys is seen in the transportation industry. It is also used in forms of powders, dyes and pigments, gasoline and diesel additives, explosives, and propellant gases. The oxidized components of aluminum are often used as food additives, abrasive material, refractory, electrical insulators and ceramic (Krewski et al. 2007). Aluminum hydroxide is usually used in personal care products and pharmaceuticals. Also, various aluminum components are used in food such as preservatives, fillers, colorants, emulsifiers and baking powder; soy-based baby food. Furthermore, natural aluminum minerals, especially zeolite and bentonite are used in water treatment, sugar treatment, paper and beer industries (Becker et al. 2016, Krewski et al. 2007). As a result, we can say that aluminum is widely used in many industries. This study is compiled to compare the levels of aluminium content in different types of food then Al effects are viewed on human body. Finally, discussions on the relationship between Al and Alzheimer's are presented.

2. ALUMINUM CONTENT IN FOOD PRODUCTS

It is well-known that some metals such as magnesium, iron and zinc are necessary for body activities and they must intake via nutrition, while aluminum is unnecessary for body (Stahl et al. 2017). People can intake aluminum from two main sources; through food and dermal contact (Al-based

* **Corresponding Author**

*(gbobus@mersin.edu.tr) ORCID ID 0000 – 0003 – 1732 – 9163
(cagataydemirci@gmail.com) ORCID ID 0000 - 0002 – 6482 - 5007
(sevik@mersin.edu.tr) ORCID ID 0000 – 0002 – 2065 – 412X

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antiperspirant salts are widely used to reduce perspiration in the armpit area) (Chappard et al. 2016, Dabre 2016, Stahl et al. 2011). When considered Table 1, it is possible to classify these sources as "external sources" and "dietary sources". Humans exposure to aluminum more dietary then external contact (Chappard et al. 2016, Stahl et al. 2017).

Table 1. Aluminum- external and dietary contact

Examples of external contact	Examples of dietary contact
Construction materials including aluminum alloys (e.g. facades, suitcases, tent construction)	Packaging and containers (beverage and food cans, coffee pots, outdoor cutlery and dishes, coffee capsules, household aluminum foil)
Vehicles, aerospace components including aluminum alloys (e.g. gearbox, seat frame, dashboard)	Nanoparticles in sunscreens
Electrotechnology, including alloys (e.g., electrical conductors)	Foodstuffs
Pigments for paints (e.g., "silver" bronze paints)	Toothpaste (e.g. Aluminum hydroxide, AlF_3)
Metal polish (Al_2O_3: paste, suspension in MeOH or H_2O)	Pharmaceuticals (e.g., heartburn medicines—pH-regulation; vaccine adjuvants)
Organic syntheses (e.g., $LiAlH_4$: reducing agent)	Cosmetics (e.g., deodorants–antitranspirants)
Jewelry and ornaments	Vaccine adjuvant (increases the immune reaction)
Fuel for solid-fuel rockets (up to 30% Al) and pyrotechnics	Food additives (e.g., as colorants or stabilizers)

Source: Chappard et al. 2016, Stahl et al. 2017

Aluminum is one of the most common elements in nature and therefore, it is a natural component of drinking water and foodstuffs (Stalh 2011). Natural puddles such as rivers, lakes, groundwater, coastal sea water and open ocean water (their aluminum concentration are approximately 0.15, 0.4, 0.1, 0.001–0.007, and 0.001 mg/l, respectively.) contain low aluminum concentration. However, the aluminum concentration can change based on acidic and organic matters. As a consequence, people can intake aluminum by having toxic effects via drinking water or foods (Barabasz et al. 2002, FIRA 2007, Flaten 2001, Yokel 2016, Wang et al. 2010, Wills and Savory 1985). The World Health Organization (WHO) has stated that several methods exist to minimize residual aluminum concentrations in filtered water. These involve the use of optimum pH in coagulation, avoiding extreme aluminum dosing, good mixing of the clumping agent (flocculants such as aluminum sulfate ($Al_2(SO_4)_3$) or poly-aluminum chloride (PACI) are commonly used in drinking water treatment to improve the removal of colloidal, particulate and dissolved substances via coagulation process), optimum paddle speeds for flocculation (water treatment process by precipitation), and the filtration of clumped aluminum (Bakar et al. 2010, Rondeau et al. 2008, Othman et al. 2010). In the case of good working circumstances, it can be obtained from those aluminum concentrations of 0.1 mg/l or less in large water treatment facilities. For small facilities (e.g. those serving fewer than 10 000 people), 0.2 mg/l or less is a practicable level for aluminum in finished water (they have some difficulty might experience in attaining this level, because the small size of the plant implements little buffering for fluctuation in operation). According to the U.S. Environmental Protection Agency (U.S. EPA), the European Union (EU) and the TC Ministry of Health have stated that the maximum Aluminum concentration in the drinking water should be lower than 0.2 ppm (Yokel 2016, Bakar et al. 2010, Rubinos et al. 2005).

Aluminum in foods is attributed to the two sources called primary and secondary causes. The primary cause is the natural content of foods taken from the geologic surrounding during growth. The secondary cause is intaking it in the additives, food processing, preparing and storage as well as from veterinary drugs, fertilizers and the air (Stalh 2011, Yokel 2016). Therefore, aluminum concentration in food is very changeable. Some of the negative consequences of rapid industrialization, such as acid rain, lead to an increase in the concentration of aluminum in natural waters and biological systems (Ranau et al. 2001). Ranau and friends had been researching the aluminum content of the edible part of sea food. Most of the fillets of fatty and lean fish species aluminum contents were found lower than 0.2 mg Al/kg wet weight. In the same research they indicated that the fish collected near the smelting plant had 1 mg Al/kg wet weight aluminum content. This was explained because of the aluminum content of the sea water (Ranau et al. 2001). Table 2 summarizes the allowable secondary aluminum sources that may lead to aluminum accumulation in food (Stalh 2011, WHO 1998).

Table 3 shows the concentration range of aluminum in foodstuffs (it was obtained from the European food safety authority (EFSA) (Stalh et al. 2017). The concentration values of aluminum in unprocessed foods at Table 3 are below 5 mg/kg, the concentration values of Al in animal products (milk, sausage, seafood), bakery products and vegetables are between 5 and 10 mg/kg, the concentration values of Al in coffee, tea, spices and cocoa products is above 10 mg (Stalh et al. 2017). Table 4 contains more details about Al concentration values in some beverages and foodstuffs (Yokel 2016). As it can be seen from Table 4, the Al concentration values of most unprocessed foods are below 5 mg. Furthermore, Al concentration values in spices especially paprika and pepper, based on their wet weight, have much higher compared with other unprocessed foods, based on the dry weight.

Aluminum is not an easily absorbable element, but if vegetables such as spinach and lettuce grow in soil containing approximately 5-10% aluminum, they can have high aluminum content. Plant-eating animal products such as eggs and milk contain very little aluminum due to their low bioavailability and limited transport . However, some plants, such as black or green tea, concentrate aluminum in their leaves and accounting for the higher Aluminum concentration than other beverages by brewing method (Street et al. 2007, Yokel 2016).

Table 2. Allowable secondary aluminum sources. (Approved food additives are written with the ”E" prefix.)

Regulation	Designation	Permitted concentration	Admitted for
Feedstuffs Regulation	E 561 Vermiculi Mg Al Fe silicate		All feedstuffs
	E 554 Na-Al-silicate		All feedstuffs
	E 559 Kaolinite clay containing Al silicate		All feedstuffs
	E 599 Perlite Na Al silicate	50,000mg/kg	In mineral feedstuffs only
Drug colouring Regulation	E 173 Aluminum		
	Aluminum salts of all other colors		
Animal drug residues Regulation	Aluminum distereate		All animals for food production
	Aluminum hydroxyl acetate		
	Aluminum phosphate		
	Aluminum tristereate		
	Aluminum trisalicylate		
	Magnesium aluminum silicate		
	Aluminum hydroxide		
Cosmetics Regulation	Some particular aluminum compounds only are forbidden or subject to limited admission		
Ecology Regulation	Aluminum calcium phosphate		As fertilizer/soil improvement agent
Tobacco regulation	Aluminum hydroxide		White burning agent
	Aluminum oxide		Materials for filters
	Aluminium sulphate		Materials for filters
	Aluminum		Materials for filters
	Aluminum potassium sulphate		Chewing tobacco
Drinking water Regulation	Aluminum	0,2 mg/l	
Wine Regulation	Aluminum	8 mg/l	Wine and other products
Food additives admission	E 173 Aluminum		Covering of sugar confectionery for cake decoration, pastries
	E 520 Aluminum sulphate	30 mg/kg	Egg white
	E 521 Aluminum sodium sulphate		
	E 523 Aluminum ammonium sulphate	200 mg/kg expressed as aluminum	Candied, crystallized crystalized and glazed fruit and vegetables
	E 541 Sodium aluminum phosphate, acidic	1,000 mg/kg expressed as aluminum	Fine bakery wares (scones and sponge wares only
	E 554 Sodium aluminum silicate	10 g/kg	Sliced or grated hard, semi-hard and processed cheese
	E 556 Calcium aluminum silicate	30 g/kg	Spices
	E 556 Calcium aluminum silicate	30 g/kg	Products for the greasing of baking trays
	E 559 Aluminum silicate	As required	Confectionery excluding chocolate (surface treatment only)
	E 555 Aluminum potassium silicate	As required	Dye for coloring Easter eggs

Source: Stalh 2011, WHO 1998

Table 3. Concentration range of aluminum in foodstuffs

Concentration range (aluminum in mg/kg foodstuff)	Foodstuff
≤ 5.00	Most unprocessed foods
5.00 – 10.0	Bread, cake, pastries, baking mixes, flour, vegetables: mushrooms, spinach, radishes, chard, lettuce
	Candied fruits
	Animal products: milk products, sausage, offal, sea foods
> 10.0	Tea leaves
	Cocoa and cocoa products
	Spices, herbs
	Coffee

Source: Stalh et al. 2017

Table 4. Median Al concentration in some representative beverages and foodstuffs

Beverage or foodstuff	Median Al concentration (mg/l or mg/kg)
Cow milk	0.070
Human milk	0.043
Apple	0.72
Banana	0.55
Grape	0.82
Orange	1.5
Peach	2.6
Pear	0.64
Plum	1.1
Raisin (sultana)	10
Strawberry	1.0
Watermelon	0.28
Apple juice	0.44
Orange juice	0.18
Pineapple juice	0.35
Tomato juice	0.67
Bean	4.0
Broccoli	1.3
Cabbage	0.31
Carrot	0.57
Cauliflower	0.80
Celery	0.90
Corn	1.5
Cucumber	2.2
Lettuce	5.5
Mushroom	2.9
Onion	0.30
Pea	2.1
Pepper (green)	0.94
Potato	2.5
Soybean	7.8
Spinach	24
Tomato	0.74
Corn flour	5.3
Oats	4.0
Rice	3.3
Wheat flour	5.6
Eggs	0.27
Beef	1.2
Chicken	1.2
Pork	2.2
Fish	0.15
Almonds	3.0
Cashews	4.6
Chestnuts	3.8
Peanuts	2.0
Pine nuts	38
Walnuts	2.3
Paprika	92
Pepper	31

Source: Yokel 2016

Table 5 exhibits the aluminum concentration in some processed foods and beverages (Stahl et al. 2017, Yokel 2016). When we compare Tables 4 and 5, it can be seen that the aluminum concentration in the soy-based infant formula is higher than cow milk-based infant formula. Predictably, the main source for this is the use of soybeans with higher aluminum content. Among the food additives, the sodium aluminum phosphate (SALP), American Food and Drug Administration (FDA) approved, is the most widely used as a food additive (FAO/WHO 2011, Paiva et al. 2020, Stahl et al. 2011, Yokel et al. 2009, Yokel 2012).

Table 5. The aluminum concentration in some processed foods and beverages

Beverage or food	Median Al concentration (mg/l or mg/kg)
Tap water	0.04
Mineral water	0.016
Cow milk – based infant formula	0.19
Soy - based infant formula	3.9
Infant foods (>50 foods, many commercial, from 15 reports)	10
Infant foods (strained) (>30 commercially purchased foods from 2 reports)	0.41
Cola	0.25
Noncola soft drinks	0.40
Beer	0.16
Wine	0.90
Butter	1.4
Cheese (non goat)	3.8
Cheese (processed)	15
Cheese (goat)	15
Cheese (on restaurant pizza)	2.9
Cheese (on frozen pizza)	415
Yogurt	0.28
Yogurt (goat)	2.8
Margarine	1.7
Olive oil	0.043
Vinegar	0.21
Peanut butter	1.9
Bacon	2.4
Luncheon meat	3.2
Sausage	6.2
Soup	1.2
Chocolate	9.4
Honey	0.050
Sugar	1.7
Jelly and jam	4.1
Biscuit	22
Bread (white)	3.6
Bread (wheat)	4.5
Cake mix	445
Cake (not stated to contain SALP)	6.3
Cake (containing acidic SALP)	190
Cereal	1.0
Cookie	6.9
Baking power	69
Pancake mix	100
Pancake	85
Pasta	5.5
Nondairy creamer powder (multiple-serving container)	38
Nondairy creamer (single-serving packet)	170
Salt (single-serving packet)	180
Fine pastries in aluminum trays	3.0
Salt pretzels and similar savory biscuits	4.0
Evaporated milk	0.205
Soft cheese	1.37
Harz cheese	0.438
Milk curd	0.109
Ready-cooked meals in aluminum trays	1.0
Pork (canned)	1.08
Beef (canned)	0.669
Herring (canned)	1.60
Crustaceans	2.54

Source: Stahl et al. 2017, Yokel 2016

When acidic SALP, which acts as acidifying and leavening agent, is used as a food additive, processed food will contain high amounts of aluminum. For example, SALP added to processed cheeses or cream cheeses, easy melting and soft texture give the property. The use of acidic SALP in foodstuffs such as biscuits, cake mix, pan cakes, baking powder causes these foods to contain high aluminum. Table 5 can be evaluated and many examples can be given like this.

2.1. Migration of Aluminum and Alloys Used in Storage and Packaging

Metal packaging provides advantages as high mechanical and thermal stability for food industry. Metals used are generally tin, aluminium, certain steel grades (Bott et al. 2018). Pure aluminum and its alloys have low density, low melting temperature, excellent formability because of surface-centered cubic crystal, good corrosion resistance good thermal conductivity and recyclable, therefore they are intensively used for food processing, packaging and storage operations by many countries without any restrictions (Aguilar at el. 2008, Carrasco et al. 2014, Chappard 2016, Filippini et al. 2019, Jabeen et al. 2016, NSCFE 2013, Seruga et al. 1994, Seruga et al. 1997, Soares et al. 2019, Verissimo and Gomes 2008, Yokel 2016,). While pure or near-pure aluminum is widely used for foil production, 3xxx (usually 3104) and 5xxx (usually 5182) series aluminum alloys are used for food and beverages packaging (Soares et al. 2019). In beverage industry over 95% of carbonated drinks and beer are preferred to be packaged in aluminium cans due to their lightness and recyclability (Krewski et al. 2007). When pure aluminum or its alloys contact with oxygen in the air, a very thin aluminum oxide (Al_2O_3) layer forms on the aluminum surface, this has provided excellent corrosion resistance between pH 4.5 to 8.5 medium. The layer is colorless, tough and non-flaking and few chemicals are able to dissolve it. Especially in cases where the pH is below 4.5, it occurs very quickly on the surface of the aluminum to a layer of corrosion. For this reason, lacquer (polymeric) coating is applied to the contact surface of the alloy to prevent food contact with aluminum alloys. Food content (acidity, high salt concentration…) can cause to increase the migration. (Chappard 2016, Krewski et al. 2007, Mannheim and Passy 2009, Yokel 2016). Different variations of lacquer are applied due to the food in the cans. So that the coating protects the food from free metal ions which may cause sensory deterioration or even health related concerns (Bott et al. 2018). Table 6 displays examples of food contact materials made of aluminum (Stahl et al. 2017).

Many studies have shown that the migration of aluminum into food occurs over time as a result of food contact with aluminum and the values for each food vary (Yokel 2016, Seruga et al. 1994, Seruga et al.1997, Verissimo and Gomes 2008). For instance, it was determined that when tap water (pH 8.2) was kept in a new aluminum bottle for 32 hours, the amount of aluminum increased from 0.053 to 0.16 mg/l. It was

Table 6. Examples of food contact materials made of Al

Food packaging	Aerosol cans (e.g., canned whipped cream) Aluminum foil Containers for convenience foods Lids for yogurt containers Beverage cans Coffee capsules Tubes for mustard, mayonnaise Packaging for candy Composite materials for beverage cartons and packaged coffee
Food manufacturing	Aluminum tanks for wine, juices, oil, milk Baking trays Meat and sausage hooks Machine parts
Cooking and kitchen utensils	Baking sheets Bread boxes Lids Coffee pots Cooking utensils (cooking spoons, ladles) Pans Pots
Household equipment	Ice cream makers Juicers Moka pots Coffee percolators

Source: Stahl et al. 2017

observed that the amount of aluminum increased by 31 times as a result of keeping the tomato puree in the aluminum pan for 72 hours, and it was determined that this value increased by 10% with the addition of salt. The concentration of aluminum was observed to increase 14-fold by coke and lemonade at the end of 12 weeks. At the end of 12 months, there was a 26-fold increase in orange soda and a 9-fold increase in lime (lime) soda (Yokel 2016).

Another study done by Seruga et al. was stated that analyzed seven soft drink aluminum cans (two arms, two oranges, two lemons, one tonic) had found that the aluminum content increased throughout the storage period of 12 months. The obtained result was attributed to the low pH value of these drinks by the authors (pH = 2.80 to 3.20) (Seruga et al. 1994). Another study conducted by Seruga et al. related to beer drinks belonging to different brands, found that the amount of aluminum in expired cans was higher than in bottles of beer. In contrast, they found the amount of aluminum in both cans and bottles below 1 mg/l (Seruga et al. 1997).

A study performed by Verrisimo and Gomes on aluminum cans of beer and tea, measured the aluminum migration values at the end of seven months. According to the measurements, they calculated an increase of 0.14 mg/l in beer and 0.6 mg/l in tea drink compared with their initial values. Also, in this study included dented cans and found that there was a significant increase by measuring the aluminum value of 9.6 mg/l, especially in tea. Also, they observed an increase of 0.17 mg/l in beer. The reason for the higher amount of aluminum in tea than in beer is due to the difference in pH values (tea pH 3.0, beer pH 4.2) (Verrisimo and Gomes 2008).

2.2. Tolerable Weekly Intake of Aluminum

People are exposed to a considerable amount of aluminum because they consume foods, water, drugs, the air they breathe (flying powders), the anti-perspiration deodorants. Food and drink are the most effective ones. Food additives used especially in food and beverages make up a significant proportion of the percentage of aluminum taken daily (Aguilar et al. 2008, NSCFE 2013, Stahl et al. 2017, Yokel 2016). In 1990, depending on the results obtained from animal experiments studying the toxicology of aluminum in dogs, mice and rats, The World Health Organization (WHO), The Food and Agriculture Organization (FAO), and The Scientific Food Committee (SCF) announced a provisional tolerable weekly intake (PTWI) for aluminum of 7.00 mg/kg body weight (BW) per week (Aguilar et al. 2008, NSCFE 2013, Stahl et al. 2017). The same committee revised this value to 1 mg/kg body weight as a result of several meetings held in 2008 (new data are taken into account), which is 7 times lower than the first (Aguilar et al. 2008). According to the obtained data, an adult weighing an average of 70 kg may be allowed to take 70 mg of aluminum per week, while a child weighing an average of 30 kg has 30 mg (Stahl et al. 2017, Stahl et al. 2011).

People's weekly intake of aluminum from foods varies according to the food consumption habits of countries. For example, studies in America have shown that men intake more aluminum than women. The average daily intake of aluminum was 4.8 mg/day in adults, 8.6 in teens, 6 in children and 0.7 mg/day in infants under two years of age. The highest values were determined for people living in China, Japan and Taiwan (approximately 9 mg/day). Besides, adults in the United States and Canada have been reported to intake more aluminum than adults in Europe, which is mainly since they have placed more restrictions on the use of aluminum additives. Also, the main reason for the higher daily intake of aluminum in young people is the higher consumption of prepared meals (Yokel 2016).

3. ALUMINUM IN THE BODY AND ALZHEIMER'S DISEASE (AD)

Aluminum taken either way (external or nutritional sources) can be eliminated by excretion via intestines and normal, healthy kidneys (Krewski et al. 2007, Stahl et al. 2011). However, various studies have shown that the daily amount of aluminum increases in the kidneys of dialysis patients having kidney failure (Krueger et al. 1984, Krewski et al. 2007, Stahl et al. 2011). Aluminum has not been considered in the healthcare field up to 1965 because of its low bioavailability. But in 1965 a study related to aluminum salts injected directly into the rabbit brain was carried out and it was observed that these salts caused tissue alterations. Obtained results from this study suggested a possible connection between aluminum and Alzheimer's disease (Stahl et al. 2011). However, recent studies have shown that there is no conclusive evidence to support or disprove the existence of a relationship between Alzheimer's disease and aluminum (Campbell 2002, Gupta et al. 2005, Rogers and Simon 1999, Tomljenovic 2011, Wang et al. 2016).

Alzheimer's disease (AD) was first defined by German neurologist Alois Alzheimer in 1906 as language problems, short-term memory loss, slow memory loss and unpredictable behavior (Yang et al. 2019). Many studies extensively were carried out related to the absorption, elimination and distribution properties of aluminum and its compounds in humans and experimental animals. Previous biochemical and toxicological studies in animals related to Food additives, flavorings, processing aids and food contact materials (AFC) did not measure the "normal" aluminum content of the main diet fed to the animals, and thus the stated dose in such studies is likely to be an underestimate of the total aluminum exposure (EFSA 2011). However, it is well-known that aluminum has long been toxic (Crepeaux et al. 2017, Domingo 1995, Exley 1998, Mailloux et al. 2011, Meyer-Baron et al. 2007, Rensburg et al. 2001, Stahl et al. 2017, Walton 2006, Walton 2007). In a study conducted by Crapper et al. in both human and animal subjects in 1973, they identified neurofibrillary degeneration of aluminum concentration in the brain and considered its possible role in the etiology of AD (Meyer-Baron et al. 2007). Although morphological changes are not defined as those seen in AD, great efforts are being made to decipher the relationship between aluminum exposure and neurodegenerative sequels (Gupta et al. 2005, Mailloux et al. 2011). Aluminum toxicity, depending on the amount of intake of food sources (such as food, cooking utensils, aluminum content storage and packaging products, drinking water) into the body, has been related to various pathological conditions such as Alzheimer's, Parkinson's disease, osteomalacia, anemia and obesity (Mailloux et al. 2011).

The amount of aluminum in the brain increases from birth to old age, even in patients without dementia. Aluminum has irregular distribution in the brain (Walton 2006), it is known to accumulate higher concentrations in brain regions including the entorhinal cortex, hippocampus, lower lateral lobe (inferior parietal lobule) and amygdala region (a region that shows the earliest pathological changes in ad) (Campbell 2002, Kasbe et al. 2005, Tair et al. 2016, Tomljenovic 2011, Walton 2007, Walton 2009). Pyramidal cells in the Cortex and hippocampus, basal forebrain cholinergic neurons, and upper brainstem Catecholaminergic neurons associated with higher cognitive functions are the neuronal populations most susceptible to aluminum-induced neurofibrillary degeneration and also most affected in AD (Tomljenovic 2011). Around 50 million people worldwide (about 60% of that number are in low-and middle-income countries) have Alzheimer's and other dementia patients, according to 2019 World Health Organization data. This number is expected to increase by about 10 million each year. The incidence of Alzheimer's disease is highest in Latin American and Asian countries (Bostancıklıoğlu 2019). In 2019, the number of Alzheimer's patients in America (AAR 2019) and Germany (AA 2020) were approximately 5.8 and 1.5 million, respectively while this number is around 600 thousand in Turkey (Özbabalık and Hussein 2017).

As mentioned before, the one of ways of intaking aluminum into the body is oral. In general, people are exposed to aluminum during the day from drinking water, unprocessed or processed foods, beverages, foods that come in contact with aluminum (packaging, storage). The sources of intaking aluminum vary in each country. For instance, the main source in the United States is foods and beverages (unprocessed meat, fruit, fish, coffee, wine, black tea, green tea, and tap water) (Mathiyazahan et al. 2015, Paolo et al. 2014, Yokel and Florence 2008, Walton 2009). Most adult Americans intake between 1-10 mg Al/day of aluminum, especially from fruit, fish and unprocessed meat foods. In addition to this, it is estimated that 50% of Americans are exposed to less than 0.34 mg/kg (body weight-Day), 45% to 0.34-1.36 mg/kg, and the rest to more than 1.36 mg/kg of aluminum (Walton 2009). In another study conducted in France, it was reported that adults who are living in the country exposure hot beverages except of coffee (13%) and vegetables containing potatoes (11%). The French adults and children exposure to aluminum are estimated at 40.3 μg/kg bw/day and 62.2 μg/kg bw/day, respectively (Arnich et al. 2012). In Italy, the amount of exposure to aluminum for adults has been reported as 4.1 mg/day. (Most of the aluminum is taken from legumes, sweets and cereals) (Filippini et al. 2019). In Germany, Stahl et al. estimated Al consumption by German adults (70 kg) and children (30 kg). It was informed within all German foods used in this study, that cocoa powders had the highest mean Al (165 mg/kg) and chocolate had a mean 48 mg Al/kg. According to average annual cocoa consumption, the German adult and child received 2% and 4% of the PTWI, respectively; chocolate provided up to 12% of the adult and 30% of the child's PTWI (Stahl et al. 2011). In 2008, EFSA declared that the daily intake of aluminum in adults living in European countries was between 28.6-214 μg/kg body weight-per day (Bostancıklıoğlu 2019). Finally, a study conducted in Japan in 2019 found that adults were exposed to 41.1 μg/kg of aluminum daily (Hayashi et al. 2019).

Another source of aluminum is drinking water (Kramer and Heath 2014, Krewski et al. 2007, Panhwar et al. 2016). Many people consume water between meals. When water is not taken with food, it reaches directly from the esophagus to the stomach, where it comes into contact with the digestive juice (pH is between 2-3.5 and, as mentioned earlier, Aluminum dissolves more quickly in acidic medium) (Rogers and Simon 1999, Rondeau et al. 2000, Samir and Rashed 2018, Walton 2012). In such cases the free Al^{+3} in the water is more absorbed by the body (Gardner et al. 2003, Klotz et al. 2017, Mendecki et al. 2020, Yang et al. 2019, Zhang et al. 2016, Willhite et al. 2014).

Studies have shown that Alzheimer's patients accumulate 2-3 times more aluminum in their hippocampus and cortices than those who do not have dementia (Samir and Rashed 2018, Yang et al. 2019). Data from another study declared that individuals who consumed foods with high aluminum content had twice the risk of developing Alzheimer's disease (Rogers and Simon 1999). The concentration of aluminum in the brain of deceased Alzheimer's patients has been observed to increase, however, other studies have found no definitive indicators supporting the hypothesis that aluminum plays a causal role in Alzheimer's disease or causes pathological changes in the species studied. Many studies have been performed in the literature, such as the examples given above.

4. CONCLUSION

Even the mechanisms of aluminum on humans are not totally understood, it is certain that exposure to Al at high values or at low values for a long time causes health problems. Also many studies indicate the aluminum content of various foods. The most important effect of Al is on the nervous system. Beside this many studies have been conducted to determine the relationship between aluminum and Alzheimer's disease. Some authorities mention a significant correlation, some authorities declare that there is no meaningful relation between aluminum and Alzheimer's disease. In this review we have tried to mention about all these studies in a wide range, but the conclusion has not yet been reached that there is no definite evidence supporting or refuting the association between aluminum and Alzheimer's disease. As a consequence, the uncertainties in the literature regarding aluminum can be overcome by conducting interdisciplinary studies. As future work, it could be necessary to develop new materials for the food industry to consume healthy foods (no health risks) as an alternative material to aluminum.

Author contributions

Günseli Bobuş Alkaya: Investigation, writing, methodology. **Çağatay Demirci:** Investigation, methodology, writing, reviewing and editing. **Hüseyin Şevik:** Conceptualization, reviewing and editing, supervision.

Conflicts of interest

The authors declare no conflicts of interest.

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