**Aluminum in Antiperspirants: A Genuine Concern or Just a Hype?**

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**Abstract**

Aluminum is the third abundant element after oxygen and silicon, and the most abundant metal in the earth’s crust. Aluminum has been widely used in many industrial, food, cosmetic and household applications and thus, the human exposure to aluminum and its health effects has been a matter of concern for more than six decades. In the last decade or so, the use of aluminum in antiperspirants and its potential adverse effects have gained traction in the consumer space (just like the use of parabens in cosmetics). Some of the key questions concerning antiperspirants in today’s digital space are - (a) Does aluminum in antiperspirants cause Breast cancer and Alzheimer’s disease? (b) Do antiperspirants cause a buildup of toxins due to blockage of sweat glands? (c) Is aluminum a pro-oxidant? (d) Does aluminum penetrate the skin? (e) What’s the link between antiperspirants, mammogram, and radiation therapy? This review article gives a scientific perspective on answering these questions by analyzing the scientific data available to date on the safety and transdermal penetration of aluminum-containing antiperspirants. This review concludes that the scientific evidence to support the adverse effect claims are scant and most of the concerns stem from the hypothesis, theories, and questionable interpretations.

**Keywords:** Aluminum, Human Skin, Antiperspirants, Aluminum Chlorohydrate, Alzheimer’s Disease, Breast Cancer

**Introduction**

Aluminum, a ubiquitous metal, is the third most common element found on earth, after oxygen and silicon. The safety and toxicity of Aluminum have been a topic of intense debate in the scientific community for many decades without a conclusive resolution. The two most debated topics are Breast cancer [1-4] and Alzheimer’s disease [5]. The objective of this review is to analyze the research available to date on transdermal penetration and toxicity of aluminum to form a scientific perspective on the following questions: (a) Does aluminum in antiperspirants cause Breast cancer and Alzheimer’s disease? (b) Do antiperspirants cause a buildup of toxins due to blockage of sweat glands? (c) Is aluminum a Pro-oxidant? (d) Does aluminum penetrate the skin? (e) What’s the link between antiperspirants, mammogram, and radiation therapy? The scope of this review article is limited to the transdermal route of exposure for Aluminum and will refrain from deep-diving into an analysis of all other modes of Aluminum exposure.

**What are antiperspirants and how do they work?**

The primary function of antiperspirants is to inhibit the production of sweat. Food and Drug Administration (FDA) classifies antiperspirants as Over-The-Counter (OTC) drugs that “prevent” sweat production, which is a biological function. In contrast, deodorants are considered as cosmetic products as their main function is odor-masking and does not interfere with any of the biological functions. US FDA [6] and EU cosmetic directive [7] gives a very in-depth understanding of the regulations associated with the use of antiperspirants. Aluminum and its salts are the only actives approved by FDA for antiperspirant products. Table 1 gives a list of antiperspirants currently approved by US FDA. The current understanding of the mechanism of action of antiperspirants (aluminum and aluminum zirconium salts) focuses on the formation of an occlusive metal hydroxide plug in the sweat ducts which hinders sweat excretion [8-11]. This is supported by the studies performed by Quatrale et al. [10] in which eccrine sweat glands treated with aluminum chlorohydrate (ACH) followed by tape-stripping and transmission electron micrographs, showed the presence of occlusive amorphous material in the sweat glands. Although less known, few other theories on sweat reduction by aluminum based salts are detailed by Laden [12].

**Table 1: List of antiperspirant actives currently approved by US FDA [1].**

|  |  |  |
| --- | --- | --- |
| No. | Compound | Maximum allowed concentration |
| 1 | Aluminum chloride | 15% a |
| 2 | Aluminum chlorohydrate | 25%. |
| 3 | Aluminum chlorohydrex polyethylene glycol | 25% |
| 4 | Aluminum chlorohydrex propylene glycol | 25% |
| 5 | Aluminum dichlorohydrate | 25% |
| 6 | Aluminum dichlorohydrex polyethylene glycol | 25% |
| 7 | Aluminum dichlorohydrex propylene glycol | 25% |
| 8 | Aluminum sesquichlorohydrate | 25% |
| 9 | Aluminum sesquichlorohydrex polyethylene glycol. | 25% |
| 10 | Aluminum sesquichlorohydrex propylene glycol. | 25% |
| 11 | Aluminum zirconium octachlorohydrate | 20% |
| 12 | Aluminum zirconium octachlorohydrex gly | 20% |
| 13 | Aluminum zirconium pentachlorohydrate | 20% |
| 14 | Aluminum zirconium pentachlorohydrex gly | 20% |
| 15 | Aluminum zirconium tetrachlorohydrate | 20% |
| 16 | Aluminum zirconium tetrachlorohydrex gly | 20% |
| 17 | Aluminum zirconium trichlorohydrate | 20% |
| 18 | Aluminum zirconium trichlorohydrex gly | 20% |

a calculated on the hexahydrate form, in an aqueous solution non-aerosol dosage form.

**Does Aluminum in antiperspirants cause Breast cancer and Alzheimer’s disease?**

This question has been the center of controversy for decades. In 1960’s and 70’s, aluminum was hypothesized as a possible suspect for the cause of the Alzheimer’s disease. This lead to a consumer suspicion that everyday exposure to aluminum from food, cookware, antiperspirants, beverage cans and antacid would be harmful. Since then, several studies failed to confirm the role of aluminum in causing Alzheimer’s disease, and FDA has concluded that there is insufficient evidence to link aluminum to Alzheimer’s disease [1,13] or other neurological conditions [46-48].

In 2004, Guillard et al. [14] reported a case study on a single woman with bone pain and fatigue symptoms, who was using antiperspirants for four years. Hyperaluminemia was reported to be the contributing factor, with levels of aluminum reaching 3.88 µmol/L (Al normal range 0.1-0.3 µmol/L). In 2005, Darbre [3] advanced a hypothesis on a link between antiperspirants and breast cancer based on the high incidence of occurrence of the breast cancer in the upper outer quadrant, which is close to the site of general application of underarm antiperspirant application.

An epidemiological study of the number of antiperspirant launches and incidence of breast and prostate cancer was reported by McGrath [15]. In this study, obstruction of the Apocrine Sweat glands by antiperspirants was hypothesized to have a possible link with increasing number of breast and prostate cancer incidences. Although this report cautions reader on the need for further research between this correlation, it has been misconstrued and emphasized by some researchers as a confirmation of antiperspirants’ toxicity due to aluminum. It is unusual that this study’s sole focus was on a number of antiperspirant launches throughout the 20th century and it fails to account for numerous other factors such as changes in nutrition, diet, environment and lifestyle habits. One is bound to get a positive correlation if the same logic is applied to associations with any disorders like obesity, cardiovascular, cancer, etc., which have dramatically risen in the last few decades. Another epidemiological study from the same group [16] suggested a possible relationship between the use of aluminum based antiperspirants with an early detection of breast cancer in a cohort of breast cancer patients. The interpretations of this study should be approached with caution, as it did not have a control cohort of women, who did not have any incidence of breast cancer.

In an extensive epidemiological study with controls (813 women with breast cancer and 793 women with no history of breast cancer), Mirick et al. [17] did not find any support to the hypothesis that antiperspirant use increases the risks of developing breast cancer. In another, relatively smaller controlled epidemiological study (54 women with breast cancer and 50 women without breast cancer), Fakri et al. [18] did not find any association between the use of antiperspirants and breast cancer. Namer et al. along with a group of clinical experts in oncology performed a systemic review of available data and concluded that there is no conclusive evidence that antiperspirants are a factor of breast cancer [19].

**Is aluminum a pro-oxidant?**

In 2004, Exley [20] proposed a hypothesis mechanism to predict the pro-oxidant activity of Aluminum in the biological system. This hypothesis was later inconclusively extended to the potential pro-oxidant skin effects from aluminum present in sunscreens [21,22]. This is the only known hypothesis for the role of aluminum as a pro-oxidant in the skin and has not been followed-up by any other research group. There is no scientific data and evidence to support this theory to date.

**Do antiperspirants cause a buildup of toxins due to blockage of sweat glands?**

Although several researchers believe that the gut poorly absorbs aluminum and thus fecal route is the primary route of aluminum clearance [23,24], some consider transdermal perspiration plays a big role based on limited experimental datasets [25]. Minshall et al. [26] reported that Aluminum perspired in sweat was significantly higher in comparison to urinary excretion and thus, perspiration is a major route of excretion for aluminum. Also, the use of antiperspirants was called into question citing bioaccumulation concerns. In this study, the lack of inclusion of the comparison with fecal excretion of aluminum raises serious concerns. There are 1.6-5 million eccrine sweat glands which are distributed across the human skin with the highest densities on palms and soles, and the least on the back [27,28]. The number of the eccrine sweat glands under the armpits is a small fraction of the total number of the body. Antiperspirants are only intended for underarm sweat control and the notion that it would hinder the perspiration-dependent excretion of toxins (or even Aluminum), is a gross overestimation [29]. At the same time, one caveat for the use of antiperspirants issued by FDA [1] is for people with renal failure, due to the possible risk of increased exposure to aluminum contained in antiperspirant products. FDA recommends that people with renal failure conditions should consult their doctors before the use of antiperspirants. For people with normal renal function, the risk of Aluminum accumulation from unusual exposure to the underarm application of antiperspirant products (once or twice daily) is minimal [1].

**Does aluminum penetrate the skin?**

Anane et al. reported bioaccumulation of aluminum in the hippocampus of Swiss mouse when an aqueous solution of aluminum chloride (0.1 and 0.4 µg/day) was applied to the shaved mouse skin (4 cm2) for 130 consecutive days [30]. They reported a significant increase in the aluminum concentrations in serum and urinary excretion in comparison to control. In another study, they reported that dermal application of an aqueous solution of aluminum chloride (0.4 µg daily for 20 days) to pregnant mice resulted in a statistical increase of Al levels in serum, amniotic fluid, fetal brain, kidney and liver [31]. There are many concerns regarding the validity and interpretations of both these studies, especially when bioavailability of aluminum by dermal route is calculated to be greater than 100% [24].

The only *in vivo* study (to date) was performed by Flarend et al. [32]. They reported that only 0.012% of aluminum (0.25 µg/day) was absorbed through the skin surface (4 in. x 3 in.) after a single underarm application of antiperspirant in two subjects. This fraction represents about 2.5% of the aluminum, which would be typically absorbed by the gut in the same duration of time. As the experiments were performed in occluded conditions, it is expected that the absorption would be less under non-occluded conditions. Assuming that the human diet contains an average of 10mg/day of aluminum [23,33] and an intestinal uptake of 0.1% [32], the amount of aluminum absorbed through food is 10 µg/day. Thus, it was concluded that the body burden of aluminum from a one-time application of antiperspirants is not significant. The only *in vitro* Franz study (to date) was conducted by Pineau et al. [34], in which they reported less than 0.07% of transcutaneous penetration of aluminum in the receptor compartment. It approximately translates to 0.24 µg of aluminum absorbed across 1.76 cm2 diffusion area. In comparison with studies by Flarend et al., for a diffusion area of 75 cm2, this study deviates by a factor of 40 (10 µg/day). As the studies performed by Pineau et al. did not find any higher levels of aluminum than the blank samples in the receptor compartment, it is indicative of poor penetration of aluminum across the skin. Although *in vivo* transdermal experiments are considered as more accurate and reflective of body’s response, the lack of a number of subjects in the study by Flarend et al. [32] limits generalization of results. Although theoretically convincing, the hypothesis by Exley [35] that skin could act as a sink reservoir for aluminum does not have a substantive data to back up. It is imperative that more studies are needed to determine the effect of the damaged skin barrier and repeat applications of antiperspirants for a true reflection of the aluminum contribution to body’s bioburden in the long term.

There are a few more studies which indicate the safety of topical application of antiperspirants. Hostýnek et al. concluded that an insignificant amount of aluminum is believed to be absorbed by the sweat glands, which makes it very safe for topical antiperspirant applications [36]. Also, this study is supplemented by the finding by Quatrale et al. [8-10] which demonstrated that aluminum chlorohydrate and aluminum zirconium chlorohydrate glycine complex functioned at a superficial, stratum corneum level, whereas Aluminum chloride functioned at a level below the stratum corneum. No correlation was found between the efficacy of antiperspirants and the location of the plug within the eccrine sweat duct (whether at stratum corneum or deeper). This gives support to the notion that aluminum penetrates very poorly across the skin barrier and is relatively safe for topical application.

**What’s the link between antiperspirants, mammogram, and radiation therapy?**

Some of the speculations for the safety of antiperspirants stem from physician’s advice to discontinue use of aluminum-containing antiperspirants for women undergoing a mammogram screening and radiation therapy for breast cancer. For the first concern, the scientific rationale is to avoid the misinterpretation of the analysis from mammogram screening, since aluminum can appear as a shadow on the X-ray images and can be mistaken as an abnormality in the breast tissue. The latter concern is also more prevalent as 8 out of 10 physicians advice their patients to refrain from the use of antiperspirants during radiation therapy as there are concerns that aluminum might absorb more radiation dose on skin than intended, resulting in skin damage [37]. In a recent finding by a group at University of Pennsylvania [37,38], there was no change reported in the radiation dose absorbed by the skin in the control and treatment group of patients using antiperspirants. Thus, they concluded that the use of antiperspirants does not increase the amount of radiation dose received by the patients.

**Other Scientific Perspectives**

An extensive and critical review of the human health risk assessment for aluminum, aluminum oxide, and aluminum hydroxide was performed by Krewski et al. [24]. They provide an in-depth risk assessment analysis of aluminum from a holistic perspective. Willhite et al. [39] concluded that there is no clear scientific evidence to establish a cause and effect relationship between the use of Aluminum containing antiperspirants and risk of breast cancer. Leading scientific organizations like the American Cancer Society [20], Alzheimer’s Association [21], National Cancer Institute [40], World Health Organization [41] and German federal institute of risk assessment (BfR) [42] have indicated that there is lack of scientific evidence to establish a cause and effect relationship between the use of antiperspirants and adverse effects in humans. Similarly, for the use of parabens in underarm cosmetics, the Scientific Commission on consumer products (SCCP) reported to the European Commission that there is no evidence of risk for breast cancer [43]. In 2016, Allam [44] reported that a quantitative review of the association between breast cancer and aluminum is non-conclusive and further prospective studies are required.

In summary, the debate continues on the safety of the use of Aluminum containing antiperspirants, mainly because of conflicting results. Further research is needed to determine a true cause and effect relationship [45].

**Conclusion**

The scientific evidence on the topical toxicity of aluminum-based antiperspirants is scarce to-date. However, the consumer concerns with antiperspirants containing aluminum are on the rise. Thus, there is a need for further in-depth research on skin permeation kinetics, absorption routes and excretion mechanisms in the human body to conclusively establish the safety concerns associated with aluminum-based antiperspirants.

**Conflict of Interest**

The author declares no conflict of interest.

**Author Contribution**

All the authors, SMB, SPS and AM have contributed equally in writing this review article.

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