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Review

If exposure to aluminium in antiperspirants presents health risks, its content should be reduced

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ABSTRACT

Since aluminium (Al) pervades our environment, the scientific community has for many years raised concerns regarding its safety in humans. Al is present in numerous cosmetics such as antiperspirants, lipsticks and sunscreens. Al chlorohydrate is the active antiperspirant agent in underarm cosmetics and may constitute for Al a key exposure route to the human body and a potential source of damage. An in vitro study has demonstrated that Al from antiperspirant can be absorbed through viable human stripped skin. The potential toxicity of Al has been clearly shown and recent works convincingly argue that Al could be involved in cancerogenic processes. Nowadays, for example, Al is suspected of being involved in breast cancer. Recent work in cells in culture has lent credence to the hypothesis that this metal could accumulate in the mammary gland and selectively interfere with the biological properties of breast epithelial cells, thereby promoting a cascade of alterations reminiscent of the early phases of malignant transformation. In addition, several studies suggest that the presence of Al in human breast could influence metastatic process. As a consequence, given that the toxicity of Al has been widely recognized and that it is not a physiological component in human tissues, reducing the concentration of this metal in antiperspirants is a matter of urgency.

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Introduction

Up until now and even though US legislators recently proposed a crackdown on toxic cosmetics [1] the toxicity of ingredients in cosmetics such as heavy metals has been widely ignored. For example, notwithstanding consumer anxiety with regard to the lead contained in lipstick and its routine use for decades, it was only in December 2011 that the FDA addressed the subject, affirming that “the amount of lead found in lipstick is very low and does not pose safety concerns” [2]. While this statement is reassuring with regard to one heavy metal in a given formulation, it nonetheless appears necessary, rather than running the risk of a human health hazard, to envision toxicity testing before commercializing a cosmetic. In 2013, Liu et al. [3] studied the presence of other potentially harmful metals (aluminium, cadmium, chromium and manganese)

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in numerous cosmetics such as lip products. They concluded that cosmetics safety should be assessed not only by the presence of hazardous contents but also by comparing estimated exposures with health-based references. Moreover, aluminium (Al), a component of sunscreens/sunblocks, is a pro-oxidant and could significantly increase the potential for oxidative damage in the skin [4]. Several works have drawn attention to the toxicity of Al when used in antiperspirants [5,6].

Since Al pervades our environment, the scientific community has for many years raised concerns regarding its safety in humans [7]. Even though there exists no formal characterization of its health hazards, exposure to Al in industrial settings has led to the acceptance of an occupational exposure threshold, while for non-occupational exposure, limits have been set for food and water intake, though current regulations are primarily based more on practical than on health-related considerations [8]. The potential neurotoxicity of Al has been clearly shown. As observed as early as 1976 by Alfrey et al. [9], its accumulation and overload in the human can cause fatal encephalopathy in patients with reduced renal function, and the hypothesis that Al significantly contributes to Alzheimer's disease is built upon solid experimental evidence [10]. Whenever aluminium intake is limited, toxicity risk is correspondingly reduced.

Furthermore, aluminium salts, mainly aluminium chlorohydrate (ACH), are the active antiperspirant agents in underarm cosmetics blocking the sweat ducts by precipitating inside the eccrine sweat glands to produce insoluble aluminium hydroxide which then plugs the gland and blocks secretion of sweat onto the skin surface [11]. In humans, Minshall et al. [12] have shown that sweat is a major route for excretion of systemic Al; experimentally, on 20 healthy volunteers following mild exercise, the Al measured in sweat ranged from 234 to 7192 μg/day. This observation calls into question the practice of disrupting or blocking perspiration using Al-antiperspirants. At the very least, the latter may constitute a key exposure route to the human body of this metal [5] and a potential source of damage.

Wulf points out that in 1993, a petition was addressed to the US Food and Drug Administration concerning the safety of antiperspirants and, more particularly, the risk entailed by absorption of Al as ACH [5]. The possibly toxic role of this metal in antiperspirants, and more precisely the risk of adverse effects on human health was subsequently analyzed at length by Exley [13]. And in 2009, Darbre shed light on the question of antiperspirants/deodorants and breast cancer [14].

Antiperspirants with aluminium salts: the problem of percutaneous absorption

Studies on the subject have nonetheless been few and far between. Over the past 11 years, the only reported "in vivo" study in humans, with 2 healthy volunteers, was performed by Flarend et al. [15] through a single underarm application of ACH without occlusion bandage using radiolabeled aluminium (^{26}Al). Having shown that only 0.012% of applied aluminium was absorbed, the authors concluded that topical ACH does not significantly contribute to the body burden of Al.

But everything was turned topsy-turvy in 2004, when Guillard et al. [16] reported on the case of a woman with bone pain and fatigue symptoms. Since all the routine biological tests yielded normal results, the field of exploration was extended to minerals, and further examination revealed hyperaluminemia as high as 3.88 μmol/L (Al normal range: 0.1–0.3 μmol/L). Questioning showed that for 4 years, the woman had been making daily use of an antiperspirant applied on regularly shaved skin (corresponding all in all to a deposit of 157.3 g of this metal). While ours was a retrospective study limited to a single clinical case, interrogation on the possible sources of Al was thorough, and the answers given ruled out either consumption of medication containing sizable quantities of Al (antacids) or daily exposure (patient's profession: librarian) as a possible cause. Moreover, the measured concentration in this patient (3.88 μmol/L) is incompatible with fluid intake from either food or kitchen utensils. The only consequential source of Al absorption consisted in daily use of an antiperspirant on shaved skin. Cessation of antiperspirant application ensued without any concomitant modification of the patient's life style, and 8 months later, her plasma Al concentration and all clinical symptoms had returned to normal.

Given significant variations between individuals and the absence of specific clinical-biological signs as well as ethical and cost-based considerations, systematic measurement of plasma Al concentration in persons with non-medical exposure to non-prescription drugs such as users of Al-based antiperspirants is out of the question, and that is the main reason why no other biological data has been found in the literature.

The question to be put forward still revolves around the existence or non-existence of transdermal Al uptake in humans. Fairly recently, the French health product sanitary safety agency (ANSM) initiated an *in vitro* study of Al on the human skin as regards possible cutaneous penetration on healthy and stripped skin of the different commercial antiperspirant formulas. We conducted this study in accordance with the applicable Organization for Economic Cooperation and Development *in vitro* validated alternative test (OECD, 428 *in vitro* guideline 2004 revised 22 October 2010–Guidance Document for the Conduct of Skin Absorption Studies), using a Franz™ diffusion cell [17]. Results showed that subsequent to testing of the one-stick formulation, which is the most widely sold product on the market, transdermal Al uptake six times greater may be observed in stripped than in normal skin. In fact, the shaved or stripped skin with micro-cuts onto which antiperspirants are applied may constitute an important entranceway to the organism for Al. This work [17] lends additional credence to the hypothesis that application of Al-based antiperspirant may bring about the undesired presence or accumulation of Al in the tissues of the underarm and surrounding areas, including breast tissues [18]. Moreover, Exley et al. [19] have measured higher levels of Al from outer than from inner breast quadrants following use of an antiperspirant in breast tissue.

Antiperspirants with aluminium salts: their repercussions on breast cancer

In 2002, however, Mirick et al. [20] found no relationship between breast cancer and use of Al-based antiperspirants between a population of breast cancer patients ($n = 813$) and a group of non-affected controls ($n = 793$). In 2003, on the other hand, McGrath [21] reported with regard to a population of breast cancer patients that those who used more antiperspirant products on a shaved underarm tended to be diagnosed with breast cancer at an earlier age. Objectively speaking, the two studies [20,21] open the way to constructive questioning, which is sorely lacking in the hastily affirmative conclusions of Namer et al. [22] in 2008, who expressly refrain from suspecting any toxic effect emanating from the Al contained in antiperspirants and explicitly abstain from pursuing this line of inquiry.

And yet, clinical studies have shown a high incidence of breast cancer in the upper outer quadrant of the breast, thereby providing further evidence of the role of antiperspirants applied in the adjacent breast region in the development of breast cancer [18]. More precisely, the Al absorbed through application of antiperspirants may have consequences on human breast cancer cells by interfering with the functioning of oestrogen receptors. The studies published