Randomized open-label longitudinal cross-over study to assess the bioavailability of aluminium, formulated as aluminium chlorohydrate (ACH), after topical application of a representative antiperspirant formulation in healthy women using a [26Al] microtracer approach

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Primary ObjectiveTo assess the absolute bioavailability of aluminium in healthy female subjects after topical application.Secondary Objectives-To explore the impact of shaving of the axilla on the dermal bioavailability of aluminium;-To explore the...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON40938

Source
ToetsingOnline

Brief title
Bioavailability of aluminium after topical application

Condition

- Other condition

Synonym
general health

Health condition

general health

Research involving
Human

Sponsors and support

Primary sponsor: TNO
Source(s) of monetary or material Support: TNO

Intervention

Keyword: aluminium, antiperspirant, bioavailability, microtracer

Outcome measures

Primary outcome

Tolerability / safety endpoints

Assessment of adverse events and local tolerability.

Pharmacokinetic endpoints

Assessment of the pharmacokinetics (PK) after topical application of 26Al, as

[26Al]-ACH, and IV administration of 26Al, as [26Al]-AlCl3 in citrate-buffered

physiological NaCl solution.

Secondary outcome

Not applicable

Study description

Background summary

Antiperspirants are widely used in the western world and many products contain (water soluble) aluminium chlorohydrate (ACH). Currently, the databank on biokinetics of ACH in man is very limited and there are no solid data available on the dermal penetration of ACH. For assessment of the safety of aluminium (Al) as a cosmetic ingredient in e.g. antiperspirants, the dermal bioavailability is a crucial parameter. The dermal bioavailability is the fraction of the topically applied Al that passes the various layers of the skin to reach the systemic circulation. The fraction absorbed is determined by the absorption rate of Al in relation to the rate of removal of Al due for instance to loss of dead skin layers, perspiration, washing and shaving. Thus, personal care habits may influence the amount of Al absorbed.

Past estimates of the bioavailability of Al have been based on conservative default assumptions, animal studies, ex vivo human skin penetration studies. All of these have their specific limitations. Moreover, personal care products such as antiperspirants are typically used frequently, and not much is known about how repeated dosing influences bioavailability. Therefore, there is a growing need, also for regulatory authorities, for establishing a more reliable estimate of the dermal bioavailability of Al under realistic consumer conditions.

Study objective

Primary Objective
To assess the absolute bioavailability of aluminium in healthy female subjects after topical application.

Secondary Objectives
-To explore the impact of shaving of the axilla on the dermal bioavailability of aluminium;
-To explore the impact of regular product use on the dermal bioavailability of aluminium.

Study design

This will be a single centre, open-label, randomized, longitudinal cross-over study during which single doses of 26Al will be administered during each treatment period (4).

Intervention

Deodorant met gelabeled aluminum en intraveneuze toediening van gelabeled aluminum

Study burden and risks

In this study, 100 ng of [26Al]-AlCl3 in citrate buffered saline will be administered intravenously. Normal plasma aluminium concentration is believed to be 1 to 2 ug/L and, mostly within one week, greater than 95% of aluminium is eliminated by the kidney; ~2% in bile. To minimize the risk for hypersensitivity reactions, persons who have a history of an allergy for aluminium will be excluded from study participation as a precautionary measure.

Other risks to subjects mainly relate to the IV injection and venous blood sampling. Intravenous injection and the use of canulas (1 canula for IV injection and 1 canula for venous blood sampling) are known to carry a small risk of infection and hematoma.

All study product administrations will be performed in the clinic under medical supervision. The subjects receiving any study product will remain in the clinical unit for approximately 24 hours after each study product administration.

The Nuclear Research and Consultancy Group (NRG) has calculated the radiation burden of [26Al] as a result of participation in the study, 0.001 mSv, hereby declaring the safety of this low dose of radioactivity to volunteers

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Healthy female subjects, 18 to 45 years of age, inclusive. Healthy status is defined by absence of evidence of any active or chronic disease following a detailed medical and surgical history, a physical examination including vital signs, 12-lead ECG, haematology, blood chemistry, and urinalysis;
2. Body mass index (BMI) between 18 and 30 kg/m2, inclusive;
3. Able to communicate well with the investigator in the Dutch language;
4. Able to participate and willing to give written informed consent and to comply with the study restrictions;
5. Subjects should be used to frequent wet shaving with an appropriate female safety razor (electric shaving is not allowed, frequent defined as at least three times a week);
6. Sufficient venous access to allow blood sampling as per protocol.

Exclusion criteria

1. Any clinically significant abnormality as determined by medical history taking and physical examinations obtained during the screening visit that in the opinion of the investigator would interfere with the study objectives or compromise subject safety;
2. A positive pregnancy test and/or nursing at screening;
3. Use of aluminium-containing medications within 21 days prior to investigational product administrations, or less than 5 half-lives, whichever is longer, and during the course of the study;
4. Treatment for diabetes, hypertension, coronary heart disease, psychiatric conditions, inflammatory chronic disease - rheumatoid arthritis, Crohn*s disease, ulcerous colitis, chronic constipation, eating disorders, or any disease condition which interferes with ADME of the investigational product within 21 days prior to investigational product administrations, or less than 5 half-lives, whichever is longer, and during the course of the study;
5. Reported menopausal state at screening, or posthysterectomy;
6. Known allergy for aluminium;
7. Axillary hyperhydrosis;
8. Clinically relevant abnormal laboratory results, ECG, vital signs, or physical findings at screening that in the opinion of the investigator would interfere with the study objectives or compromise subject safety;
9. Participation in an investigational drug study within 3 months prior to screening or more than 4 times in the past year;
10. Any psychological conditions which, in the opinion of the investigator, might create undue

risk to the subject or interfere with the subject's ability to comply with the protocol;
11. History of alcohol or illicit drug abuse (alcohol abuse defined as alcohol consumption > 28 units/week);
12. Donation of blood within 3 months prior to screening or donation of plasma within 14 days prior to screening;
13. Not having a general practitioner;
14. Not willing to accept information transfer which concerns participation in the study, or information regarding health, like laboratory results, findings at anamnesis or physical examination and eventual adverse events to and from his general practitioner;
15. Not willing to give permission to have the general practitioner to be notified upon participation in this study;
16. Not willing to use effective (double barrier) contraception until at least 3 months after last investigational product administration;
17. Subjects who are part of the site staff of TNO or CHDR.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-08-2014
Enrollment:	12
Type:	Actual

Ethics review

Approved WMO

Date:	23-07-2014
Application type:	First submission

Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	27-08-2014
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	30-01-2015
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL49088.028.14