

Complementary and alternative remedies: an additional source of potential systemic nickel exposure

LUCIANA M. DE MEDEIROS¹, ANTHONY F. FRANSWAY², JAMES S. TAYLOR¹, MARCIA WYMAN³, JODITH JANES⁴,
JOSEPH F. FOWLER JR⁵ AND ROBERT L. RIETSCHEL⁶

¹Section of Industrial Dermatology, Department of Dermatology (A-61), Cleveland Clinic, Cleveland, OH 44195, ²Associates in Dermatology, Fort Meyers, FL 33919, ³Department of Pharmacy, Cleveland Clinic, Cleveland, OH 44195, ⁴Cleveland Clinic Alumni Library, Cleveland Clinic, Cleveland, OH 44195, ⁵Department of Dermatology, University of Louisville, Louisville, KY 40202, and ⁶Department of Dermatology, University of Arizona, Tuscon, AZ 85721, USA

Background: Systemic contact dermatitis from nickel has been reported from a number of sources including medical devices and following experimental oral exposure.

Objective: To identify other potential sources of systemic nickel exposure.

Methods: The internet and published medical literature were searched for complementary and alternative remedies which contain nickel.

Results: We identified and evaluated sources of nickel exposure in 4 homeopathic preparations, which are advertised to treat common skin diseases, as well as in a number of other homeopathic remedies, several herbal products and multivitamin mineral complexes.

Conclusion: Complementary and alternative remedies are an additional source of systemic nickel exposure and at highest doses the potential risk for systemic contact dermatitis in nickel allergic patients should be considered.

Key words: complementary and alternative remedies; herbal products; homeopathic preparations; internet; nickel; systemic contact dermatitis. © Blackwell Munksgaard, 2008.

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Systemic contact dermatitis (SCD) to nickel has been reported mainly following placement of dental braces (1), orthopedic prostheses (2), and venous catheters (3) as well as following oral exposure experimentally in nickel-sensitive individuals (4). We recently identified several potential new sources of nickel exposure in complementary and alternative remedies (CAR).

Methods

A published medical literature search was undertaken using PubMed/MEDLINE (from 1950) to find reports of SCD from metals in CAR. The Google internet search was also carried out to

identify CAR websites and products that contain nickel.

Results

The first and best-documented sources of nickel exposure found in CAR are preparations advertised to treat acne, eczema, seborrhea, and psoriasis (5). We identified 4 such products containing nickel in doses ranging from 0.5 to 1.5 mg per tablet (Table 1). Each is said to be available only by prescription and dosages are proportional to body weight. The company recommends caution in administration of these drugs to patients with nickel allergy, and confirmation by patch testing is

Table 1. Amount of nickel per tablet and dosage recommendation for 4 homeopathic remedies (Plymouth Pharmaceuticals) (5)

	Nickel (mg)	Starting dose (proportional to weight)	Max daily dose (proportional to weight)
Acunol [®]	0.5	0.25–1 mg/b.i.d	0.5–2 mg/b.i.d
Eczemol [®]	0.5	0.125–2 mg/day	0.25–4 mg/day
Psorizide Forte [®]	1.0	0.5–3 mg/day	1.5–9 mg/day
Psorizide Ultra [®]	1.5	0.75–4.5 mg/day	1.5–9 mg/day

mg, milligrams; tab, tablets; b.i.d, twice a day.

also suggested. In the presence of ‘nickel sensitivity or dyshidrotic eczema’ and in the absence of ‘extra-cutaneous hypersensitivity to nickel’ the company also recommends a nickel desensitization schedule beginning with gradually increasing doses taken at or before breakfast. These formulations also contain other chemicals such as potassium and sodium bromide, zinc sulfate, fumaric acid, and sulfur.

Other sources of nickel exposure (6–10) are non-prescription, oral alternative, homeopathic remedies, which may contain *Niccolum Metallicum* (Metallic Nickel) or *Niccolum Sulfuricum* (Nickel Sulfate) (Table 2). The amount of nickel present is not specified. A process of dilution as 3X through 30X is described, which indicates dilutions usually in distilled water from 1/10³ through 1/10³⁰, respectively, before addition to the remedy. This method is well known in homeopathy (11, 12).

Additional potential sources of nickel include contamination of various herbal remedies including Ginseng products (13), Indian herbal teas (14), Nigerian herbal remedies (15) (Table 3), and Chinese herbal plants (16) (Table 4). Some multivitamins as Centrum[®], One-a-day[®] and Century Advantage Complete Multivitamin[®] contain 5 µg of nickel per tablet. However, at the low

Table 2. Source of nickel in homeopathic remedies^a

Remedy	Nickel	Dilution
Bone Liqueescence [®] (6)	<i>Niccolum metallicum</i>	12X
Bone Stim Liqueescence [®] (7)	<i>Niccolum metallicum</i>	12X
Loma Lux [®] AcnePill (8)	<i>Niccolum sulfuricum</i>	6X
Loma Lux [®] Asthma (8)	<i>Niccolum sulfuricum</i>	6X
Loma Lux [®] Eczema (8)	<i>Niccolum sulfuricum</i>	6X
Loma Lux [®] Psoriasis (8)	<i>Niccolum sulfuricum</i>	3X
Loma Lux [®] Sinus and Allergy (8)	<i>Niccolum sulfuricum</i>	6X
Metex [®] (7)	<i>Niccolum sulfuricum</i>	30X
NatraBio Migraine Relief [®] (9)	<i>Niccolum metallicum</i>	6X
T5 Bone Liqueescence [®] (10)	<i>Niccolum metallicum</i>	12X

^aEach contains a number of ingredients in addition to nickel.

Table 3. Concentration of nickel contamination in Nigerian herbal remedies^a (15)

Nigerian herbal remedies	Nickel (mg) ^b
B-Success 28 Plant Operation Sweep	8.65
Aloe Vera Plus Bitter aloes	5
Zarausmacine	14.12
Virgy-Virgy Computer Worm-Expeller	6.32
Dorasine Powder	4.7
Sexual Energy	4.02
U&DEE Infection cleansing powder	5.97
U&DEE Sweet bitter	2.52
Natural Power Stone	12.27
Chama Black Stone	18
Portugal Antiseptic Soap	78
Edysol Antiseptic Soap	11.87
H-Nal	5.57
M-Reg	4.27
Veins Flocher	4.5
Diabor	3.32
C-Candi	6.6
C-Cysta	11.77
Firas	15.75
D-Diab	6.35
P-Pile	3.02
Infecta	13
Ribacin Forte	2.75
Aleo Vera Cure Formula	3.8
	3.07

mg, milligrams.

^aEach contains a number of ingredients in addition to nickel.

^bThe estimated dose was 1.0 g of total material per day.

levels of nickel present in some CAR, SCD seems unlikely to occur unless they are consumed in large quantities continuously.

Discussion

Almost all CAR can cause hypersensitivity reactions. These include contact dermatitis, the most common; various patterns of systemic drug eruptions and, less commonly, respiratory and anaphylactic reactions (17).

There are at least 2 reports of SCD from metals in homeopathic remedies. The first case was in a man who experienced a severe exacerbation of his eczema after oral intake of a chromium-containing homeopathic drug prescribed as a hyposensitizing therapy for treatment of his chromium hypersensitivity (18). Another report is an unusual case of baboon syndrome in a 5-year-old girl with prior positive patch test reactions to thimerosal and mercury who developed a maculopapular eruption that started 24 h after intake of a single tablet of a mercury-containing homeopathic cough remedy (19). We found no reports of SCD to CAR containing nickel.

Systemic reactions to metals, particularly to nickel, are regarded as controversial. Reactions to a ubiquitous hapten such as nickel are not easily identified with certainty because of the difficulty in

Table 4. Concentration of nickel contamination in Chinese herbal plants^a (16)

Chinese herbal plants	Nickel ($\mu\text{g/g}$)
<i>Acanthopanax</i> sp.	3.1
<i>Alisma Plantago-aquatica</i>	0.79
<i>Areca catechu</i>	<0.5
<i>Aristolochia debilis</i>	6.1
<i>Artemisia</i> sp.	2.3
<i>Astragalus membranaceus</i>	1.6
<i>Camellia japonica</i>	0.72
<i>Celosia argentea</i>	1.1
<i>Centella asiatica</i>	5.9
<i>Cinnamomum cassia</i>	<0.5
<i>Cydonia sinensis</i>	<0.05
<i>Desmodium styracifolium</i>	1.2
<i>Drynaria fortunei</i>	1.4
<i>Eriosema chinensis</i>	2.2
<i>Ilex rotunda</i>	3.3
<i>Imperata cylindrica</i>	1.9
<i>Leonurus artemisia</i>	2.0
<i>Magnolia officinalis</i>	0.66
<i>Michelia figo</i>	2.0
<i>Murraya paniculata</i>	<0.5
<i>Nelumbo nucifera</i>	<0.5
<i>Oryza sativa</i>	1.8
<i>Perilla frutescens</i> var. <i>crispa</i>	1.5
<i>Pinus</i> sp.	0.83
<i>Plantago major</i>	1.5
<i>Pogostemon cablin</i>	2.0
<i>Polygala sibirica</i>	2.0
<i>Pueraria</i> sp.	0.56
<i>Punica granatum</i>	0.86
<i>Rosa laevigata</i>	0.5
<i>Rubus parvifolius</i>	1.2
<i>Salix babylonica</i>	1.3
<i>Scrophularia buergeriana</i>	1.8
<i>Smilax glabra</i>	<0.5
<i>Sophora japonica</i> L.	7.2
<i>Syzygium aromaticum</i>	1.3
<i>Tamarix chinensis</i>	0.85
<i>Taraxacum officinale</i>	1.9
<i>Vitis thumbergii</i>	0.97
<i>Xanthoxylum avicennae</i>	0.75
<i>Zea mays</i>	<0.05
<i>Ziziphus jujuba</i>	0.74

$\mu\text{g/g}$: micrograms per gram.

^aEach contains a number of ingredients in addition to nickel.

measuring and controlling daily exposure through drinking water and diet.

The daily ingestion of nickel from food varies from 0.02 to 0.48 mg and depends both on the type of food and the production environment of the individual foodstuff. Foods with high nickel content include whole-grain flour, oats, soybeans, legumes, shellfish, nuts, licorice, and chocolate (20). The amount of nickel absorbed depends upon the simultaneous intake of other food products such as proteins and alcohol. Chelating medicaments can interfere with nickel absorption and metabolism and provoke systemic contact dermatitis. This has been well described for disulfiram (21).

The study of orally provoked flare-ups of nickel dermatitis was pioneered by Christensen and

Moller (22); who provoked 12 nickel-sensitive individuals with an oral dose of 5.6 mg nickel. Of the 12 patients, 9 reacted with SCD after an average of 8 h and the results have been repeated and confirmed by others (23, 24).

Recently, Jensen et al. (25) summarized the data from the oral exposure studies to determine an exposure threshold for elicitation of SCD following oral nickel ingestion. They estimated that intake of 0.55–1.33 mg and 1.27–3.06 mg of nickel would cause 10% and 50% of the sensitized patients, respectively, to react with signs of SCD.

In theory, these results indicate potential risk of SCD from nickel in those patients who take the recommended doses of homeopathic remedies (Table 1). In the case of homeopathic prescriptions of oral nickel available on the internet to treat common skin diseases, the amount of nickel intake may vary from 0.125 to 9 mg (Table 1). In a Nigerian report, herbal remedies were found to contain large, almost toxic amounts of nickel ranging from 2.525 to 78 mg/g (15) (Table 3). Based on the estimates of Jensen et al. (25), SCD would occur in more than 50% of sensitized patients at the highest doses of the Nigerian remedies and the homeopathic preparations. A recent study showed no toxic levels of nickel present in some Nigerian medicinal plants, however (26).

Complementary and alternative medicines are used for many ailments including asthma and atopic eczema. Recent surveys have shown an increasing use of unconventional treatments by as many as 42.1% of Americans (27, 28). Hypersensitivity reactions to complementary and alternative treatments are important concerns. Clinicians should be cognizant that these remedies can cause adverse reactions with patterns similar to those of conventional drugs. It is also important to ask patients about their use of CAR and to be aware of the potential for SCD in nickel allergy patients.

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Address:

James S. Taylor, MD
A-61, Department of Dermatology
Cleveland Clinic
9500 Euclid Avenue
Cleveland
OH 44195
USA
Tel: +1 216 444 5723
Fax: +1 216 636 0863
e-mail: taylorj@ccf.org