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SHORT COMMUNICATION

Evaluation of a Method for Detecting Metal Release from Gold; Cysteine Enhances Release

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Gold has long been regarded as a controversial contact allergy (1). In order to induce or elicit contact allergy metals must be in an ionized state. For some metals spot analyses are available that can easily provide evidence of ionization (2–4), but for many metals, e.g. more precious ones, these do not exist.

There is a directive that regulates the use of nickel in items to be in contact with the skin, thus minimizing the risk of contact allergy. The release of nickel ions is based on findings when using artificial sweat (5, 6). For legislative purposes it would, of course, be very easy and logical if the analysis used for one metal could be used for all. For some metals, however, especially with regard to where/how they are used, this may not be possible. Artificial sweat has been tested for gold release, but has not yielded any positive results, i.e. no gold was detectable (7, 8).

The aim of the present study was to investigate gold release from various gold samples under different conditions.

MATERIALS AND METHODS

Artificial sweat, solutions of 0.1 M cysteine, 0.1 M glutathione, 0.1 M penicillamine, 0.5 M nitric acid, 0.1 mM sodium hydroxide, and 1% lactic acid were used. For details, see Appendix S1 (available from: http://www.medicaljournals.se/acta/content/?doi=10.2340/00015555-1541).

In the pilot study, extractions of gold-plated earrings in different solutions were performed. Extracts were analysed on days 4 and 5. For details, see Appendix S2 (available from: http://www.medicaljournals.se/acta/content/?doi=10.2340/00015555-1541).

Eleven metal discs (Allgemeine Gold- und Silberscheideanstalt AG, Pforzheim, Germany) with a thickness of 1 mm and diameter of 15 mm made of gold alloys frequently used for jewellery were used to study metal release in cysteine solution. In addition, pure gold foil was included. For details see Appendix S3 (available from: http://www.medicaljournals.se/acta/content/?doi=10.2340/00015555-1541).

The discs and the gold foil were pre-treated by cleansing in ethanol for 60 min. The metal discs were placed in polypropylene tubes, and 5 ml 0.1 M cysteine solution (pH 8) was added to each tube. The test tubes were placed on a rocker and shaken constantly and gently for 7 days at room temperature. After one week, a white precipitate was observed in the extraction solutions, believed to consist of cystine, a dimer of cysteine. The precipitate was dissolved before analysis by addition of 100 µl concentrated nitric acid.

The analysis was performed with an atomic spectrometer (AAS) with a detection limit of < 0.003 µg Au/ml. Each extraction solution was analysed 3 times. For details, see Appendix S4 (available from: http://www.medicaljournals.se/acta/content/?doi=10.2340/00015555-1541).

RESULTS

The pilot study showed no release of gold in artificial sweat, whereas release occurred when solutions containing serine, glycine, penicillamine and cysteine were used (Table I). In the actual extraction study the cysteine solution was chosen as extraction media. Gold release was enhanced when cysteine was used and as pH increased. Table II shows the extraction results, revealing no patterns regarding the amount of gold release for the different alloys and their gold content.

DISCUSSION

What are the reasons for questioning the conclusion drawn from the previous study (7), i.e. that there is no ion release from gold when in contact with the skin?

The method has been discussed previously (9, 10), and release of ions when gold is in contact with other solutions has been shown (11–13). The composition of artificial sweat can be discussed (10, 11). Cysteine is a

Table I. *Pilot study, gold release from gold-plated titanium earrings. Ear-rings (surface area 0.77 cm²) were extracted in 5 ml of each solution. The extraction solutions were analysed using atomic absorption spectrometry. Detection limit < 0.003 µg/ml*

Extraction media	pH	Extraction time, days, *n*	Gold release µg/ml	Gold release µg/cm²
Artificial sweat	5	5	<0.003	<0.02
Artificial sweat	6.4	5	<0.003	<0.02
Artificial sweat	7.0	5	<0.003	<0.02
Artificial sweat	7.5	5	<0.003	<0.02
Nitric acid, 0.5 M	1.0	5	<0.003	<0.02
Lactic acid, 1%	1.0	5	<0.003	<0.02
Sodium hydroxide, 0.1 mM	10	5	<0.003	<0.02
Glutathione, 0.1 M	1.2	4	0.1	0.6
Glutathione, 0.1 M	7.2	4	0.3	1.9
Glutathione, 0.1 M	9.2	4	1.6	10.4
Penicillamine, 0.1 M	1.2	4	0.1	0.7
Penicillamine, 0.1 M	7.2	4	2.0	13.0
Penicillamine, 0.1 M	9.2	4	4.7	30.5
Cysteine, 0.1 M	7.0	5	2.7	17.5
Cysteine, 0.1 M	7.5	5	9.8	63.6
Cysteine, 0.1 M	8.0	5	29.5	192
Cysteine, 0.1 M	8.5	5	48.3	314
Cysteine, 0.1 M	9.0	5	70.5	458
Cysteine, 0.1 M	9.5	5	0.4	2.6

Table II. *Composition of gold alloys according to supplier and measured concentration of gold in extraction solutions using atomic absorption spectrometry. The different alloys were extracted in 5 ml 0.1 M cysteine, (pH 8) for 7 days. Area of gold discs (alloy 1–11) 4 cm², area of gold foil (12) 2 cm²*

Alloy	Gold type, (carat)	Other metals	Gold release µg/ml	Gold release µg/cm²	Relative SD (%)
1	Red gold (8)	Ag, Cu, Zn	1.2	1.5	3.6
2	Red gold (8)	Ag, Cu, Zn	8.3	10.4	6.5
3	Red gold (14)	Ag, Cu	5.0	6.3	2.8
4	White gold (14)	Ag, Cu	0.7	0.9	53.6
5	White gold (18)	Ag, Cu, Zn	3.1	3.9	2.0
6	Red gold (18)	Ag, Cu	7.1	8.9	2.0
7	Red gold (18)	Ag, Cu	6.2	7.7	22.9
8	Red gold (14)	Ag, Cu, Zn, Pd	1.4	1.8	14.3
9	Red gold (18)	Cu, Zn, Pd	5.1	6.4	1.9
10	Red gold (9)	Ag, Cu, Zn	1.1	1.3	5.0
11	Red gold (10)	Ag, Cu, Zn	0.6	0.8	10.3
12	Gold foil (24)	unknown	150	376	

SD: standard deviation.

sulphur-containing amino acid found in the skin (15), while artificial sweat does not contain any amino acids. The fact that contact allergy may be induced not only by skin contact makes the choice of extraction media used for scientific purposes extremely important, especially if conclusions are to be drawn with regard to possible legislative measures.

The use of medical implants in our bodies is increasing. There has been evidence that there may be a risk of reactions due to release of haptens from the implant surface (16–19). The crucial step for sensitization and elicitation is hapten formation (16). This formation will be influenced by several factors: the metals used, the alloy, and the structure and microstructure of the implant, but also the tissue where the implant is located. The best way to evaluate implant materials is through prospective studies in animals and humans. However, with regard to contact allergy there is a problem with animal studies (total exposure being different), and in humans these studies are often not feasible or ethical. In the present study with an *in vitro* method, we have shown that there is release of gold from both the pure metal and gold alloys, as previously shown by Brown et al. (13). Different solutions will determine how large the release will be. It also indicates that gold may react differently when found in different alloys (13). The study indicates that artificial sweat alone is not sufficient to cause ion release for all metals and is perhaps not the best solution to imitate the milieu on the skin surface, and especially not contact with other tissues.

The results of this study confirm that discussion of the surrounding tissue/body fluid where an implant is located is of the utmost importance, since the body fluids and tissue will make the implant react differently. The results emphasize the importance of taking corrosion and a possible contact allergy into consideration when choosing implant material.

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