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Quantification of Sensitizing Metals in Tattooing Pigments by SF-ICP-MS Technique

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Abstract: Allergic reactions to metals and metal salts used in pigments for tattoos are surprisingly frequent. The objective of this study was to quantify the metal content of tattoo inks using the sector field inductively coupled plasma mass spectrometry analysis (SF-ICP-MS). The inks were subjected to a robust microwave digestion in a mixture of nitric and fluoridric acids, and hydrogen-peroxide. A total of 13 tattoo inks including various colors, as black, blue, brown, green, red, violet, white and yellow, were examined for the content of Cd, Co, Cr, Hg and Ni. The limits of detection and quantification were as follows (ng/ml): Cd, 0.02 and 0.07; Co, 0.06 and 0.20; Cr, 0.80 and 2.64; Hg, 0.50 and 1.65; and Ni, 0.40 and 1.32. The method was accurate reporting the following mean recoveries (%): Cd, 92; Co, 94; Cr, 96; Hg, 105; and Ni, 103. The precision of the method was calculated as intra-day (%) and inter-day repeatability (%) and results were: Cd, 2.09 and 5.20; Co, 1.58 and 2.67; Cr, 2.07 and 2.99; Hg, 3.88 and 4.55; and Ni, 4.05 and 5.11. All the tested metals were present in the tattoo pigments, but the relative contribution of elements to the tattoo ink compositions was highly variable between samples and even among like-colored pigments. The highest element was Cr in all the pigments (315-4720 ng/g) followed by Ni (37.5-2318 ng/g) and Cd (6.67-1150 ng/g); the lower elements were Co (2.78-125 ng/g) and Hg (<limit of quantification-179 ng/g). Since no rules regulate tattoo inks, this research can be a starting point for chemical safety assessment of commercial inks and for proposal of regulating legislation.

Keywords: Metals, tattoos, inks, SF-ICP-MS, allergic metals.

1. INTRODUCTION

Humans have always wanted to change and embellish their surroundings and their bodies. Body painting has always been an important part of the blemish ideals in all societies all over the world. Tattoos have a special place among body ornaments, because they cannot be washed or worn off like body paints. Tattoos pigments are entered under the top layer of skin by means of a needle, and this process ensures that the pigments cannot be removed and simultaneously the organism is exposed to the ingredients in the tattoo colors in a very direct way.

In a recent study at a small Midwest private college the 25% of 302 subjects had at least one tattoo [1] and among 491 university students in New York State the prevalence for tattooing was of 23% [2]. Gender distribution of the 105 adolescents with tattoos were 65% males and 35% females; in 1995 among 1762 students (nationwide) the proportion of adolescents with a tattoo was higher at 9% respect to 1993 and the average age of first tattoo dropped from 16 years in the 1993 study to 14.5 years [3].

An enormous "grey" area exists as regards to the colorants being applied. There are no uniform rules that describe the raw materials to be used for manufacture of pigments for tattooing, or that tell how the color itself should be tested. Only some of the ingredients used in tattoo inks are approved for use in cosmetics, foods, and medical devices (including iron oxides and titanium dioxide), although most are not. Moreover, only relatively few suppliers have documentation of the colorants, and it is difficult for tattooists assess the quality and significance of the documentation. In Italy, a specific legislation concerning tattoo practices is partially existing. In fact, the wide diffusion of tattoos has lead the National Ministry of Health to lay down in 1998 guidelines for practicing tattoos in safe conditions [4] with the purpose to implement good practices in order to prevent risks connected to tattoos. The main points are: hygienic requirements of the spaces, authorisation and license of the structure and the personnel, hygienic measures and provisions, information, training and control. As regards the requirements of the colorants used in pigments, the guidelines prescribed the need of "atoxicity" but no mention is made about chemical composition and chemical risk assessment.

The basis for the beginning of this work was the existence of surveys which reported that there are many complications associated with the introduction of pigments into the skin. Local inflammation, infection, and allergic reactions are the most common adverse effects. In particular, allergic reactions to metals and metal salts used in pigments for tattooing are surprisingly frequent. Mercury together with Cr and Co have been reported as contact sensitizers with various type of skin reactions in tattooed areas. In particular, the red tattoo pigments (cinnabar and vermilion) was known to include Hg, and was able to produce a delayed hypersensitivity reaction [5]. A blue ink used for tattoo caused skin hypersensitivity for the presence of Co; in particular, the tattooed patient suffered of urticaria on the tattooed right deltoid [6]. Kang *et al.* found Co in 4 different henna dyes at a concen-

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tration of about 3 mg/kg and, in their opinion, this amount was able to provoke skin sensitization [7]. Other researchers have proposed that tattoo pigments containing Al and Ti can induce granulomatous reactions. A case study of a 21 year old man with delayed hypersensitivity granuloma formation in a tattoo has been reported. Four weeks after tattooing, three separate tumorous areas appeared in the violet areas of the tattoo and microscopic examination of the excised tumor indicated the presence of Al and Ti in the tissue [8]. A commercially available blue ink was revealed to contain a high concentration of Ti (36.82%) by quantitative EDX microanalysis [9], while in the 87% of 30 different tattoo inks studied, the most commonly identified element was Al [10]. A patient with a black and turquoise tattoo developed sarcoid granulomas on the areas of the black pigment; patch tests showed a positive reaction to Ni, Co and Cd and the spectrophotometric analysis of the black pigment revealed the presence of Ni and Co among other metals [11]. Biopsies from a red tattoos were examined histologically and the chemical composition of the red pigments revealed a variety of metallic elements including Al, Fe, Ca, Ti, Si, Hg and Cd [12].

Basing on this background, the metallic ingredients of pigments used for tattoos should be analysed and a systematic risk assessment with respect to potential health impacts should be performed. Contemporary, an appropriate methodology needs to be developed. To this end, in this investigation colors identified as some of the most used among professional tattooists were analyzed for their elemental composition and a method using the sector field inductively coupled plasma mass spectrometer (SF-ICP-MS) was developed. The results of this study would aim at ensure the safety of all the products in the trade and destined to the consumers and, in the meantime, the planning of a legislative activity at the national level.

2. MATERIALS AND METHODS

2.1. Sample Collection and Treatment

A total of 13 tattoo pigments were obtained from one tattoo ink supplier in Italy *via* a internet shopping mall. The kit comprised the following pigments: black ink, brite orange, canary yellow, country blue, deep blue, deep green, deep brown, deep turquoise, deep violet, golden yellow, lime green, red scarlet, white brite. All colors were liquids.

The samples were acid digested in a microwave (MW) oven (Milestone Ethos 900-Mega II, FKV Milestone, Milan, Italy), *ca.* 0.25 g of pigment being weighed in a Teflon vessel to which a mixture of 4 ml of ultrapur HNO_3 (Carlo Erba, Milan, Italy), 1 mL of supra-pure HF (Merck, Darmstadt, Germany) and 1 mL of supra-pure H_2O_2 (Merck) was added. Then, the vessel was closed and the mixture submitted to the following MW program: 5 min at 250 W; 5 min at 400 W; 10 min at 600 W. The attained solution was quantitatively transferred into polystyrene liners and the volume was completed to 15 mL by high purity deionised water (EASY-pure, PBI, Milan, Italy) and stored at +4°C until quantification. Samples were digested in duplicate and reagent blanks run together with matrices.

2.2. Sample Analysis

For the SF-ICP-MS analysis, the solutions were further diluted 1:4 v/v with high purity deionised water. An Element II SF-ICP-MS (Thermo Fischer, Bremen, Germany) equipped with Meinhard-type glass nebulizer, water-cooled Scott spray chamber, torch with guard electrode device and platinum interface cones, was used for metal quantification. Details on the radiofrequency power, gas flow rates, isotopes and mass resolution selected for the study are reported in Table **1**.

Table 1. SF-ICP-MS Operative Parameters

Instrument	ELEMENT II (Thermo Fischer, Bremen, Germany)
Geometry	Reverse Nier-Johnson, double focusing
Radiofrequency power (W)	1200
Nebulizer	Meinhard, glass type with water-cooled Scott-spray chamber
Interface	Pt cones
Gas flows (L/min)	Plasma, 14; auxiliary, 0.90; nebulizer, 0.90
Mass resolution (m/Δm)	Low (300) for Cd and Hg; Medium (3000) for Co, Cr and Ni
Analytical masses	^{114}Cd, ^{59}Co, ^{52}Cr, ^{202}Hg and ^{60}Ni
Internal standard	^{115}In

The low resolution setting was used for Cd and Hg because not interfered by any relevant interference, while the medium resolution was necessary for Co, Cr and Ni quantification because these elements were heavily interfered by polyatomic species produced by a combination of isotopes coming from plasma, reagents and matrix. In particular, the major interferences coming from plasma were those of $^{36}Ar^{16}O$ on ^{52}Cr and $^{40}Ar^{18}OH$ on ^{59}Co. The use of HNO_3 and HF in the digestion mixture created interferences as $^{38}Ar^{14}N$ and $^{40}Ar^{19}F$ which overlapped the signals of ^{52}Cr and ^{59}Co, respectively. With the organic matrix containing high C concentration and other elements as Ca and Mg, the molecular ion $^{40}Ar^{12}C$ heavily influenced the ^{52}Cr signal while the species $^{44}Ca^{16}O$, and $^{24}Mg^{36}Ar$ hidden the ^{60}Ni signal. By using the medium resolution setting all these interferences were shifted away from the mass searching windows of the analytes, thus providing an high degree of selectivity.

The standard addition approach for calibration on 5 concentration levels was used in order to keep the matrix-induced variations under control. Additionally, in order to correct eventual instrumental drifts, In was added as internal standard to all samples and calibration standards.

3. RESULTS AND DISCUSSION

3.1. Method Validation

The method was validated for limits of detection and quantification (LoDs and LoQs), accuracy, intra-day and inter-day repeatability. The LoDs were calculated on 10 digested blanks and expressed as 3.3 times the standard deviation (SD) of the replicated measurements. The LoQs were calculated on 10 digested blanks and expressed as 10-fold the SD of the replicated measurements. Accuracy was evaluated by conducting a recovery study on 5 digested blanks at one spiked level containing all the elements under study. Intra-day repeatability was determined by the measurements of a digested pigment 10 times on the same day. Inter-day repeatability was determined by the analysis of a similar digested solution on 3 different days over a period of one week. Relative SD (RSD) was calculated for both series of analyses.

Table **2** summarizes the SF-ICP-MS validation data for the analysis of elements in tattoo pigments. The LoDs ranged from 0.02 ng/mL (Cd) to 0.8 ng/mL (Cr), while the LoQs varied from 0.07 ng/mL (Cd) to 2.64 ng/mL (Cr). The method was accurate reporting the following mean recoveries (%): Cd, 92; Co, 94; Cr, 96; Hg, 105; and Ni, 103. The inter-day RSD (%) were the following: 5.20 for Cd, 2.67 for Co, 2.99 for Cr, 4.55 for Hg, and 5.11 for Ni. These small values indicated the method was precise over a one weak period.

Table 2. SF-ICP-MS Method Performances

Parameter		Cd	Co	Cr	Hg	Ni
LoD (ng/ml)		0.02	0.06	0.80	0.50	0.40
LoQ (ng/ml)		0.07	0.20	2.64	1.65	1.32
Recovery (ng/ml)	Added	0.25	0.50	5.00	5.00	5.00
	Found	0.23	0.47	4.80	5.23	5.16
Intra-day repeatability (%)		2.09	1.58	2.07	3.88	4.05
Inter-day repeatability (%)		5.20	2.67	2.99	4.55	5.11

3.2. Metal Composition of Tattoo Pigments

The results of the analysis of pigments are given in Table **3** in ng/g. All the measured metals were present in the 13 colors, except for Hg which was absent in three colors (black ink, white brite and country blue). The overall ink composition varied widely between different inks, even in inks with the same gross color. Although the individual tattoo inks were a complex mixture with variable metallic composition, as a general behaviour, the highest concentration was observed for Cr, followed by Ni and Cd and, to finish, by Co and Hg. The following minimum and maximum concentrations were observed: Cr, 315-4720 ng/g; Ni, 37.5-2318 ng/g; Cd, 6.67-1150 ng/g; Co, 2.78-125 ng/g; and Hg, < LoQ-179 ng/g. Moreover, the presence of the five elements analyzed in like-coloured inks is shown in the Fig. **1a**, black; **1b**, blue (n = 3 inks); **1c**, brown, **1d**, green (n = 2 inks); **1e**, red (n = 2 inks); **1f**, violet; **1g**, white; **1h**, yellow (n = 2 inks).

It is quite well documented that colored inks used for tattooing practices contained a great variety of metal salts, which makes them a potential source for developing skin reactions, including allergic reactions, pseudolymphomas, systemic sarcoidosis and granulomatous or lichenoid reactions [13].

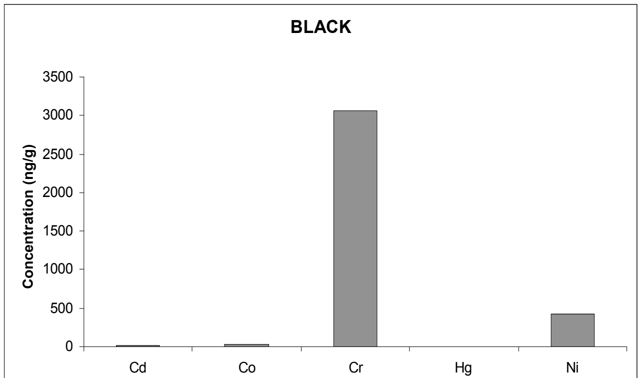
Black inks can be produced with India ink (containing carbon particles), logwood (containing Cr), or iron oxide. Sensitivity to black pigment is quite rare, but a case of sarcoid granulomas has been reported on the areas of a black pigment. The flame atomic absorption spectrophotometry analysis of the black pigment revealed Co (14,000 ng/g) and Ni (12,000 ng/g) at very high concentration among other metals [11]. Another case of intense pruritric erythematous papules scattered within and around the black tattoo area has been reported, and the inorganic components revealed multielemental peaks but no Ni was detected [14]. In this study, the composition of the black ink (Fig **1a**) was dominated by Cr (3064 ng/g) and Ni (424 ng/g), while traces of Cd and Co have been observed. Mercury was absent in the black ink.

Blue dyes are derived from a variety of cobalt salts and are notorious for deep granulomas as well as for urticarial symptoms [6, 15]. Light-blue colors are also derived from Co and may again cause granulomas [16]. Also Tazelaar *et al.* observed hypersensitivity to a light-blue tattoo, but, in this case, Cr was believed to be the responsible for the skin

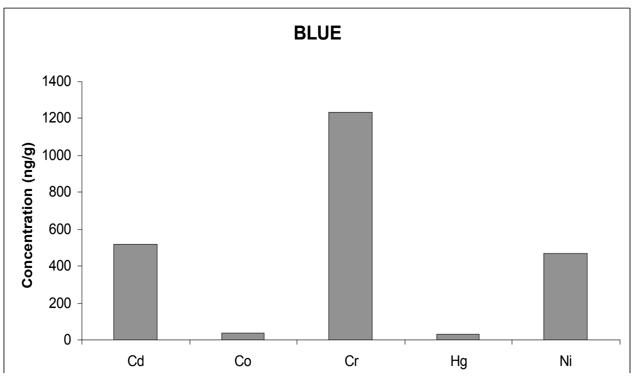
Table 3. Element Content in Tattoo Inks. Concentration in ng/g

Samples	Cd	Co	Cr	Hg	Ni
Black Ink	17.9 ± 1.5	24.7 ± 1.9	3064 ± 164	< LoQ	424 ± 16
Deep Blue	124 ± 8	65.0 ± 3.3	1368 ± 44	55.4 ± 6.0	348 ± 40
Country Blue	1150 ± 94	11.1 ± 0.7	521 ± 20	< LoQ	771 ± 28
Deep Turquoise	285 ± 14	34.5 ± 3.0	1809 ± 210	9.70 ± 1.1	283 ± 12
Deep Brown	7.65 ± 0.81	2.78 ± 0.31	451 ±89	43.5 ± 1.9	66.7 ± 7.2
Deep Green	361 ± 11	95.5 ± 8.3	4108 ± 133	179 ± 19	2318 ± 154
Lime Green	47.0 ± 2.2	43.0 ± 2.7	1791 ± 131	164 ± 10	564 ± 37
Red Scarlet	6.67 ± 0.59	16.6 ± 1.3	1073 ± 69	107 ± 5	179 ± 18
Brite Orange	13.7 ± 1.2	125 ± 10	4720 ± 350	66.1 ± 7.4	811 ± 61
Deep Violet	369 ± 19	32.3 ± 2.8	4046 ± 124	54.0 ± 5.7	1107 ± 94
White Brite	497 ± 33	11.0 ± 0.8	315 ± 38	< LoQ	602 ± 55
Canary Yellow	45.4 ± 2.0	24.5 ± 1.1	1900 ±129	128 ± 6	429 ± 34
Golden Yellow	48.9 ± 1.4	2.88 ± 0.35	357 ± 15	11.5 ± 1.3	37.5 ± 4.0

(**a**)



(**b**)



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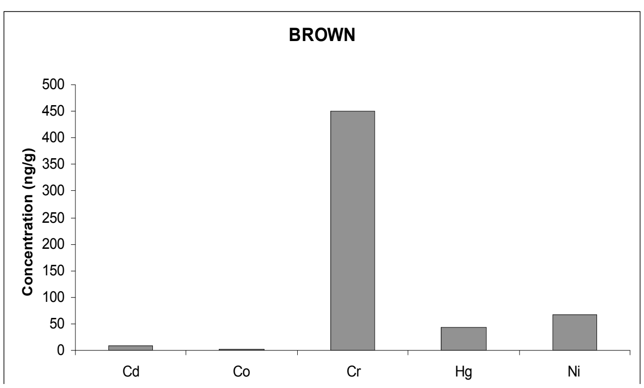


(**d**)

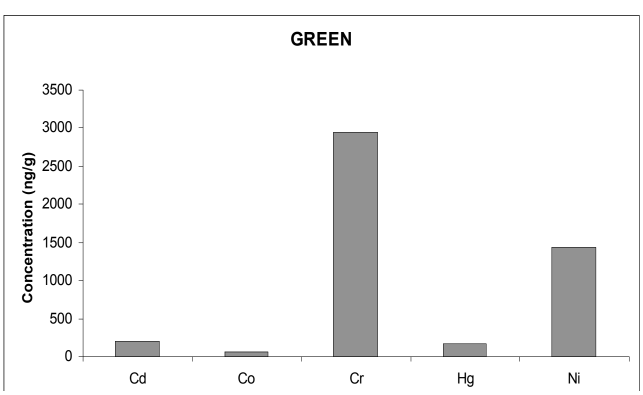
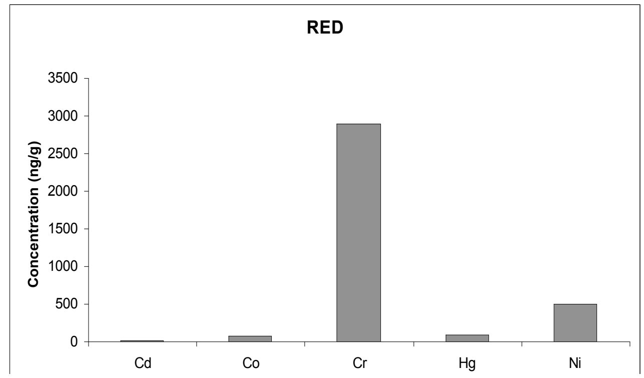


Fig. (1) contd…..

(**e**)



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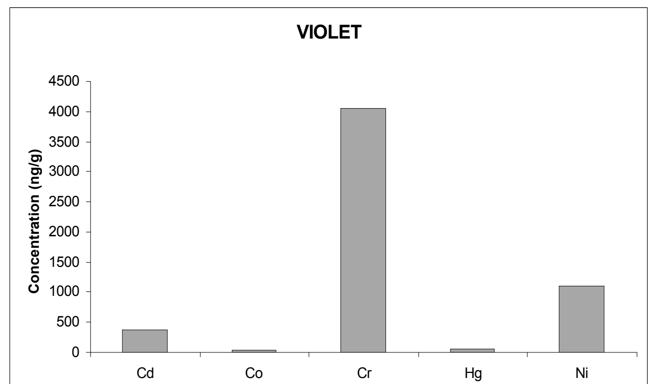
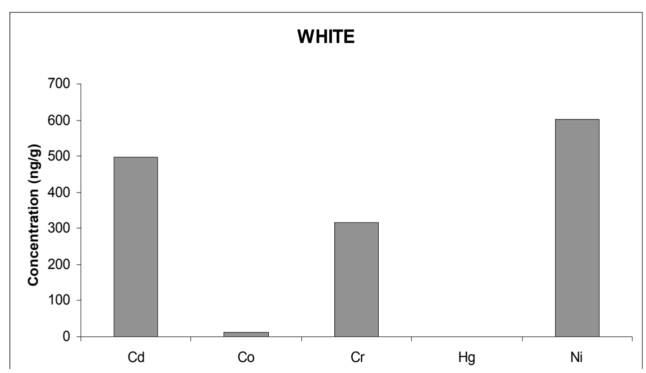


(**g**)



(**h**)

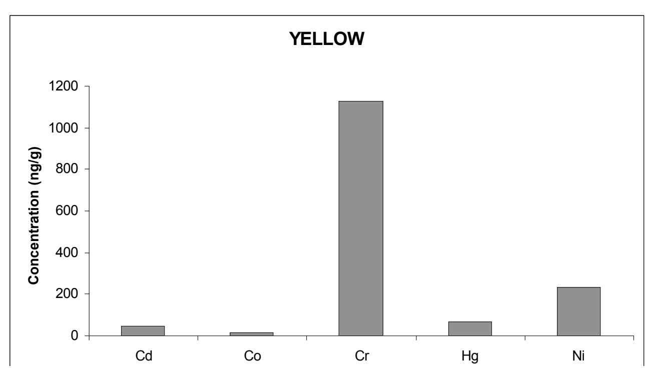


Fig. (1). Presence of metals in like-coloured inks: **1a**, black (n = 1); **1b**, blue (n = 3); **1c**, brown (n = 1); **1d**, green (n = 2); **1e**, red (n = 2); **1f**, violet (n = 1); **1g**, white (n = 1); **1h**, yellow (n = 2).

reactions [17]. In the blue dyes here examined (Fig. **1b**), Co was relatively low (i.e., 65.0 ng/g at maximum in the deep blue) and did not go above the Co concentration revealed in the other colored inks. Once more, the dominant metal in all the blue dyes was Cr ranging from 521 ng/g in the country blue to 1809 ng/g in the turquoise. Morales-Callaghan *et al.* found very high concentration of Cr (at 8%) in a turquoise pigment [11].

Brown dye may be formed *via* the use of either Venetian Red which is derived from ferric oxide or from cadmium salts. Reviewing the literature, allergies to a brown tattoo have never been observed. We found that the brown pigment (Fig. **1c**) showed a low content of Cr (451 ng/g), and Cd, Co, Hg and Ni were all at trace level. The unique literature data on the quantitative analysis of brown inks were those of Kim *et al.* [9], who showed a considerable amount of Fe, but unfortunately did not give indication about the metals we analyzed.

Green comes from Cr and can be a cause of allergic reactions both within the tattoo as well as generalized eczematous reactions on the body. Chromium oxide has a variety of names including Chrome green, Casalic green and Guignet's green. These variations while mixed in different suspensions may all cause significant and long term itching and other eczematous reactions that complete removal of the tattoo may be required [18, 19]. Other shades of green such as emerald green are formed from another type of chromium salt called chromium sesquioxide (aka veridan). In the emerald green, Cr was found at 72.66% [10]. The green pigments sampled in this study presented Cr equal to 4108 ng/g in deep green and 1791 ng/g in lime green. Surprisingly, both green showed Hg at the highest concentrations among all the tested colors (Fig. **1d**).

Red is the color most commonly associated with skin reactions at the red areas of the tattoo. Different allergic reactions have been observed, including granulomatous [12, 20], eczematous [21], pseudolymphomatous [22] and lichenoid reactions [23]. Mercury is the base metal in red tattoo dye, and may be known by the names mercury sulphide, cinnabar, vermillion and red cinnabar. In addition, cadmium sulphide and cadmium selenide might be the colouring agent in red and orange pigments. The skin reactions have usually been ascribed to Hg-hypersensitivity, though patch testing showed strong positivity also to Ni [23]. We found that (see Fig. **1e**), both in red and orange pigments, Hg was relatively low (107 ng/g) and Cd was at traces, while Cr still continued to be the predominant metal in the inks composition (4720 ng/g and 1073 ng/g in red and orange, respectively). Though previous experimental studies had never detected Ni in red pigments [10, 24], another study reported Ni at the concentration of 1900 ng/g which was proposed can be sufficient for dermal sensitization [23]. In this study, Ni concentration in red and orange pigments did not reach the μg/g level.

The usual metallic salt used for violet-colored tattoos contains manganese. An acute dermatitis overlaying an immunological granuloma has been reported at the site of violet tattoos; the skin reaction was observed 3 weeks after the injection and atomic absorption spectrometry revealed a large amount of Mn in the biopsy specimen [25]. Unfortunately we did not analyze Mn, but we found that the violet ink had high contents of Cr (4046 ng/g) and Ni (1107 ng/g) (Fig. **1f**).

The white tattoos are achieved usually from titanium or zinc oxide or from the use of lead carbonates. These may have the potential to contain metallic derivatives. No allergic reactions to white tattoo have been described. In this study, the white pigment (Fig. **1g**) showed Ni as the prevailing metal (602 ng/g) followed by Cd (497 ng/g). Traces of Cr and Co have been observed. The white ink was mercury-free.

Cadmium sulfide is the most common salt used in yellow tattoo ink and can be a cause of reactions within tattoos [26]. Not only may Cd produced local or generalized eczematous reactions; it has also been associated with phototoxic reactions when exposed to light [27]. We were unable to see a prevalence of Cd in the yellow pigments (Fig. **1h**) respect to the other colors analyzed. Chromium was present at 1900 ng/g in one yellow pigment (canary), but turned to be low in the golden yellow

Even if the concentrations of allergenic metals as Cd, Co, Cr, Hg and Ni we found in the tattoo inks were relatively low (i.e., less than 1.1 ppm for Cd, < 0.12 ppm for Co; < 4.7 ppm for Cr; < 0.18 ppm for Hg and < 2.3 ppm for Ni), it should be considered that the metals in tattoos remain on the skin for a prolonged period of time, and it is hard to completely rule out the possibility of allergenic metals playing a role in inducing contact dermatitis. Also, even if these metals are irrelevant to the development of contact dermatitis by tattoos, they can provoke sensitisation, contributing to the occurrence.

Moreover, our data on Cr and Ni can be compared with the published maximum levels defined as allergologically safe for consumers exposed to products containing metals; for example, Allenby *et al.* reported that patients with normal skin previously sensitised to Ni can develop contact dermatitis at 1 ppm-10 ppm and at 0.5 ppm if the skin has been irritated with sodium dodecyl sulphate [28]. Similarly, Basketter *et al.* indicated that on normal skin, the patch test threshold was 10 ppm for Cr, and, in the presence of an irritant, the threshold was closer to 1 ppm [29]. As a consequence of these studies, it was recommended that products in contact with the skin adhere to a standard of a maximum concentration of 1 ppm for Cr and Ni, with an ultimate target of 0.5 ppm of contamination. In this study, 9 colors out of 13 had Cr higher than 1 ppm, while Ni was higher in 2 colors out of 13. The contact with such quantities of Cr and Ni contained in inks might be responsible for cases of contact dermatitis or skin sensitization in tattooed patients.

CONCLUSIONS

Professional tattoos have different colors and consist of a variety of pigments and neither the tattoo artist nor the tattooed patient has any information about the compounds punctured on the skin. Because tattoo compounds in comparison with cosmetics are not officially controlled, the origin and the chemical structure of these colouring agents are hardly unknown. This study wanted to characterize the metallic composition of tattoo dyes sold in Italy, so that a formal risk assessment could be carried out. The data obtained showed, not unexpectedly, that individual tattoo inks were variable mixtures of metals and that also among like-colored pigments the variability was very high. We quantitatively analysed the existence of Cr at a median concentration of 1791 ng/g, of Ni at a median value of 429 ng/g in addition to traces of Cd, Co and Hg in tattoo inks. Being the quantity of Cr and Ni, in some cases, over the standard limit for skin reactions, the contact with pigments can be thought to be relevant to the development of contact dermatitis by tattoos, or to be sufficient to provoke skin sensitisation. Therefore, we believe that additional research in this field with clinical examinations should be done for further evaluation.

ABBREVIATIONS

EDX = X-ray energy-dispersion spectrometry

LoDs = Limits of detection

LoQs = Limits of quantifications

MW = Microwave

RSD = Relative standard deviations

SD = Standard deviations

SF-ICP-MS = Sector field inductively coupled plasma mass spectrometry analysis

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