

Black tattoo inks are a source of problematic substances such as dibutyl phthalate

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Summary

Background. Tattooing has recently become increasingly popular. Using tiny needles, tattooists place the tattoo ink in the dermis along with numerous unknown ingredients. Most tattoos consist of black inks, which are predominantly composed of soot products (carbon black with polycyclic aromatic hydrocarbons).

Objectives. Black tattoos cause skin problems, including allergic reactions, but the responsible substance frequently remains unknown.

Material/methods. We applied gas chromatograph–mass spectrometry analysis to search for hazardous compounds in 14 different commercially available black tattoo ink samples.

Results. The analysis revealed that all inks contained the softener substance dibutyl phthalate (0.12–691.2 µg/g). Some of the inks contained hexachloro-1,3-butadiene (0.08–4.52 µg/g), metheneamine (0.08–21.64 µg/g), dibenzofuran (0.02–1.62 µg/g), benzophenone (0.26–556.66 µg/g), and 9-fluorenone (0.04–3.04 µg/g).

Conclusion. The sensitizing agent dibutyl phthalate acts directly on keratinocytes and can drive Th2 responses following skin exposure via induction of thymic stromal lymphopoietin gene expression. Hexachloro-1,3-butadiene is genotoxic *in vitro* and 9-fluorenone is cytotoxic, generating reactive oxygen species under light exposure. The substances found in the inks might be partially responsible for adverse skin reactions to tattoos.

Key words: black inks; dibenzofuran; gas chromatography; health problems; phthalate; tattoo.

In recent years, tattoos have become very popular worldwide, and millions of people have mainly black-coloured tattoos. Despite the increasing number of tattooed individuals, there are currently few requirements, little legislation and few criteria for the safety of tattoos

and permanent make-up. The list of ingredients on black tattoo inks is usually missing or incomplete. Frequently, there is no information on packaging, such as expiration date, conditions of use, warnings, or the guarantee of sterility of the contents. Risk assessment should be an essential part of protecting human health, and this also applies to tattoos.

Tattooing is a practice whereby a pigment suspension is deposited in the dermis by intradermal injection of the inks with tiny solid needles. As black inks are produced by imperfect combustion, they consist mainly of carbon black. It is therefore unsurprising that such black inks contain high amounts of polycyclic aromatic hydrocarbons (PAHs) and phenol. As previously reported, we

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established an extraction procedure for the determination and quantification of 20 different PAHs in various commercially available black tattoo suspensions by using liquid chromatography detection (1).

Tattoo inks are not distributed by pharmaceutical companies, and in many countries regulation regarding such inks is still lacking. In Germany, the first tattoo regulation appeared in 2009; it prohibits the use of azo pigments that can be cleaved to hazardous aromatic amines. With black tattoo inks, PAHs and other substances can be introduced into the skin, and this might be responsible for the health problems associated with tattoos (2).

Therefore, we investigated black tattoo inks again by using gas chromatography (GC)–mass spectrometry (MS) analysis, and searched for other substances in 14 commercially available tattoo inks that might have the potential to be harmful for humans.

Materials and Methods

Materials

Fourteen commercially available black tattoo inks were purchased from different tattoo suppliers in Europe, the United States, and Asia: Tribal Black (Body Cult Tattoo Supply); Schwarz (Rotring); Black Magic (Faber); Liner-Black (Infernal Colour); Diabolo Genesis (Deep Colours!); Pitch Black (Scream Ink); Tattoo Outlining Ink (Kuro Sumi); True Black (Intenze Prod); National Pelikan (Pelikan); Sailor Jerry (Deep Colours!); Ink Black (Nova Ink); New Intense Black (Lynx); Black Liner Ink (Spaulding); and Calcutta Black (Spaulding).

Standard substances, including hexachloro-1,3-butadiene (HCBd), dibenzofuran (DBF), hexamethylene-tetramine (HET), 9-fluorenone (9F), benzophenone (BP) and dibutyl phthalate (DBP), were detected by MS (GC–MS) and obtained from Sigma Aldrich (Steinheim, Germany) as analytical pure standards. The references with a 1.0 mg/ml stock solution in acetonitrile were combined to obtain a 0.88 mg/ml calibration solution. The purity of each standard was approximately 98% as reported by the manufacturer.

The solvents used for extraction of PAHs, including benzene and acetone, were of reagent grade, and were obtained from Merck (Darmstadt, Germany). Acetonitrile as a solvent for GC analysis was of gradient-grade quality for liquid chromatography (LiChroSolv, Darmstadt, Germany). Millipore water as a solvent for HPLC analysis was freshly produced with a Milli-Q Advantage A10 system (TOC 5 ppb; Millipore, Molsheim, France). All substances were dissolved in 1 ml of acetonitrile and subjected to ultrasonic treatment (Bandelin Sonorex Super RK 103

H). As an internal standard (ISTD), hexamethylbenzene was obtained from Sigma Aldrich and prepared as a 0.2 mg/ml stock solution in acetonitrile.

Extraction procedure and sample preparation

As previously reported with PAH extraction, we used ultrasonic treatment of a defined amount of black ink suspension with benzene/acetone and centrifugation (1). The procedure was performed in triplicate. The residual compounds were resolved in 1 ml of acetonitrile, filtered with a polytetrafluoroethylene filter (CHROMAFIL®, O-20/15, organic, pore size 0.2 µm; Machery-Nagel, Düren, Germany), and analysed with the ISTD method, using GC–MS analysis. The selected compounds were previously detected in a qualitative GC–MS run of the ink extract samples.

Chromatography analysis

Analysis was performed with an Agilent Technologies GC/MS System, consisting of 7890 A GC and 5975C Inert XL EI/CI MSD with a CTC Pal Autosampler. Method settings: injection volume, 1.00 µl; He flow, 1 ml/min. Oven program: 40 °C for 3 min, then 15 °C/min to 280 °C for 5 min, then 25 °C/min to 300 °C for 5 min with splitless mode (1 min); injector temperature 250 °C. Transfeline temperature: 300 °C. The column used was an Agilent HP-5MS (30 m × 250 µm × 0.25 µm). Qualification and quantification were performed with an Agilent MSD ChemStation E.02.00.493 and NIST Mass Spectral Search Program for the NIST/EPA/NIH Mass Spectral Library Version 2.0f, 23 July 2008. For Matchfactor NIST > 900, a substance was regarded as clearly identified.

The concentrations of the investigated substances were quantified with the ISTD method. For each compound (i), the calibration factor (CF_i) was determined in a calibration run (single-level calibration). The respective concentration of the ISTD was chosen to be in the range of the concentration of the substances.

$$CF_i = \frac{f_{Tr}}{f_i} = \frac{m_i^K \cdot a_{Tr}^k}{m_{Tr}^K \cdot a_i^K} \quad (1)$$

Where f_{Tr} is the response factor of the ISTD, m_i^K is the mass of compound i in solution k, m_{Tr}^K and the mass of the ISTD in solution k. a_{Tr}^k is the area of ISTD in solution k, and a_i^K is the area of compound i in solution k.

Results

Quantitatively determined ingredients

Stock solutions (0.88 mg/ml) of each substance (HCBd, HET, DBF, DBP, 9F, and BP), which were qualitatively

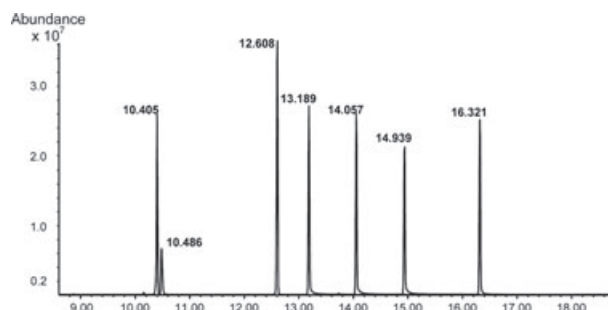


Fig. 1. Chromatography of the quantified substances. The retention times of the substances were 10.444 min (hexachloro-1,3-butadiene), 10.519 min (metheneamine), 13.229 min (dibenzofuran), 14.101 min (benzophenone), 14.982 min (9-fluorenone), and 16.349 min (dibutyl phthalate), and the retention time of the internal standard (hexamethylbenzene) was 12.642 min.

detected in a first GC run, were measured with the ISTD method to calibrate the system. Figure 1 shows clear separation of HCBd, BP, HET, 9F, DBF, and DBP. The corresponding retention times (RTs) of the substance peaks are listed in Table 1, with hexamethylbenzene (RT 12.608 min; 0.2 mg/ml) as ISTD. The chemical structures of these substances are shown in Table 2. The substances have some extended UV-active ring structures, a urotropine skeletal structure, or a six-fold chlorinated butadiene.

The total amounts of all clearly identified ingredients in selected black tattoo inks are shown in Table 3. After three repetitions of the extraction procedure, the values ranged from 0.18 to 716.94 µg/g. A detailed list of the quantified ink ingredients is given in Table 4. DBP was definitely quantified in all ink samples. The total amounts ranged from 0.12 to 691.2 µg/g. The six-fold chlorinated butadiene (HCBd) was found in six ink samples, with a total amount of 0.08–4.52 µg/g. High amounts of benzophenone (BP) were extracted, ranging from 0.26 µg/g for ink sample 14 up to 556.66 µg/g for ink sample 11. BP was detected in all ink extract samples

Table 1. Retention time of the substances

Retention time (min)	Reference substance
10.405	Hexachloro-1,3-butadiene
10.486	Hexamethylenetetramine
13.189	Dibenzofuran
14.075	Benzophenone
14.939	9-Fluorenone
16.321	Dibutyl phthalate
12.608	ISTD: hexamethylbenzene

ISTD, internal standard.

Table 2. Chemical structures of identified and quantified ingredients in black tattoo inks

Hexachlorobutadiene HCBd MW: 260.76 g/mol CAS: 87-68-3	Hexamethylenetetramine MW: 140.19 g/mol CAS: 100-97-0
Dibenzofuran MW: 168.19 g/mol CAS: 132-64-9	Benzophenone MW: 182.22 g/mol CAS: 119-61-9
9-Fluorenone MW: 180.19 g/mol CAS: 486-25-9	Dibutyl phthalate DBP MW: 278.34 g/mol CAS: 84-74-2

Table 3. The total amounts of quantified ingredients found in black tattoo inks

Ink*	Total amount* (µg/g)
1	96.08
2	42.38
3	21.28
4	25.76
5	0.48
6	13.04
7	0.24
8	164.88
9	14.86
10	0.18
11	556.78
12	14.92
13	716.94
14	6.12

*Names of traders and substances can be obtained from the authors.

except for samples 5, 7, and 10. Ink samples 2 and 13 contained all specified ingredients.

Qualitatively determined ingredients

Besides the six quantified ingredients, GC showed further peaks in several ink chromatograms. By use of the NIST database for MSD analysis, additional compounds could

Table 4. The amounts of the quantified ingredients found in black tattoo inks (µg/g)

Ink	HCBD	Methenamine	DBF	BP	9-F	DBP
1	—*	0.32	0.04	95.34	0.04	0.34
2	0.08	0.14	1.62	34.74	3.04	2.76
3	0.30	—	0.02	19.94	0.62	0.40
4	0.50	—	0.06	19.38	1.24	4.58
5	—	—	—	—	—	0.48
6	—	0.44	0.12	12.0	0.20	0.24
7	—	0.08	—	—	0.02	0.14
8	—	—	—	164.7	—	0.18
9	0.82	—	0.04	6.20	0.90	6.90
10	—	—	—	—	—	0.18
11	—	—	—	556.66	—	0.12
12	4.52	—	—	7.92	0.24	2.24
13	1.00	21.64	0.02	2.96	0.16	691.20
14	—	—	—	0.26	1.80	5.68

BP, benzophenone; DBF, dibenzofuran; DBP, dibutyl phthalate; HCBD, hexachloro-1,3-butadiene; 9F, 9-fluorenone.

*Value below detection limit.

Table 5. Qualitatively detected ingredients in black tattoo inks

Ink	Other ingredients
1	3,6-Dimethyl-1-heptyn-3-ol
2	1,6-Hexandiole
3	1,6-Hexandiole
4	Oleamide*; 7-hexyl-2-oxepanone
5	Propylene glycol; 7-hexyl-2-oxepanone
6	Propylene glycol
7	—†
8	1,1'-Oxybis-2-propanol; 2,2'-oxybis-1-propanol
9	7-Hexyl-2-oxepanone
10	Oleamide*; 7-hexyl-2-oxepanone
11	7-Hexyl-2-oxepanone
12	Oleamide*; 7-hexyl-2-oxepanone
13	Carbitol cellosolve‡ 1,2,3,4-tetrahydro-1-phenyl-naphthalene
14	7-Hexyl-2-oxepanone

*Oleamide: IUPAC name (Z)-9-octadecenamide.

†Value below detection limit.

‡Carbitol cellosolve: IUPAC name 2-(2-ethoxyethoxy) ethanol.

be identified, for example alcohol-containing substances such as 3,6-dimethyl-1-heptyn-3-ol, 1,6-hexandiole, propylene glycol, and carbitol cellosolve, as well as substances such as oleamide, 7-hexyl-2-oxepanone, and urea (Table 5). Figure 2 shows a GC chromatogram of ink sample 13 as an example. Among quantitatively and qualitatively detected ingredients, the chromatogram still shows peaks that could not clearly be identified with the NIST database.

Discussion

Recently, we investigated commercially available black inks regarding PAHs by using high-performance liquid

chromatography technology (1). Using the established extraction procedure (3), we found total concentrations of PAHs in the different inks ranging from 0.14 to 201 µg/g. Even benz(a)pyrene, a known carcinogen, was found in four ink samples at a mean concentration of 0.3 ± 0.2 µg/g.

At the same time, we performed a nationwide survey in German-speaking countries to determine the incidence of health problems associated with tattooed skin (2). First, the survey showed that tattooed people have many (28%; ≥ 4) and large (36%; ≥ 900 cm²) tattoos requiring the injection of several grams of tattoo inks into skin, which partly spread in the human body and probably stay lifelong in human tissue (2). However, it is possible that people who like tattoos might have been more willing to participate in such a survey.

The participants described skin problems (67.5%) or systemic reactions (6.6%) directly after tattooing and related to the tattooing process. Six per cent of participants complained of persisting skin problems at the site of the tattoo, such as itching, burning, skin papules, small nodules, eczema, and redness of skin (erythema). In addition, 1.3% reported burning and itching of tattooed skin when it was exposed to solar radiation ('light sensitivity').

In light of these skin reactions, we analysed the extracts of such black tattoo inks in more detail by using GC–MS analysis to identify potential irritants or allergens. We found HCBD, HET, DBF, DBP, 9F, and BP, which were definitely quantified (Table 4). GC analysis and the NIST database revealed the presence of other substances in the black inks that could be not clearly identified and quantified (Table 5).

Below, we describe the usual sources of particular substances, and their effects *in vitro* and in the body, where known, with special regard to the skin. Any other health concerns regarding the substances are listed in Table 6.

Table 6. Assessment of other health risks

Dibutyl phthalate	Genotoxic (4), teratogenic (5, 6)
Hexachloro-1,3-butadiene	Genotoxic (7), carcinogenic (8), classified by the US EPA as a possible human carcinogen (Group C) (9)
Dibenzofuran	Not classifiable as to human carcinogenicity (Group D) (10)
Hexamethylenetetramine	Possibly genotoxic (11)
Benzophenone	Some evidence of carcinogenic activity (12)
9-Fluorenone	None

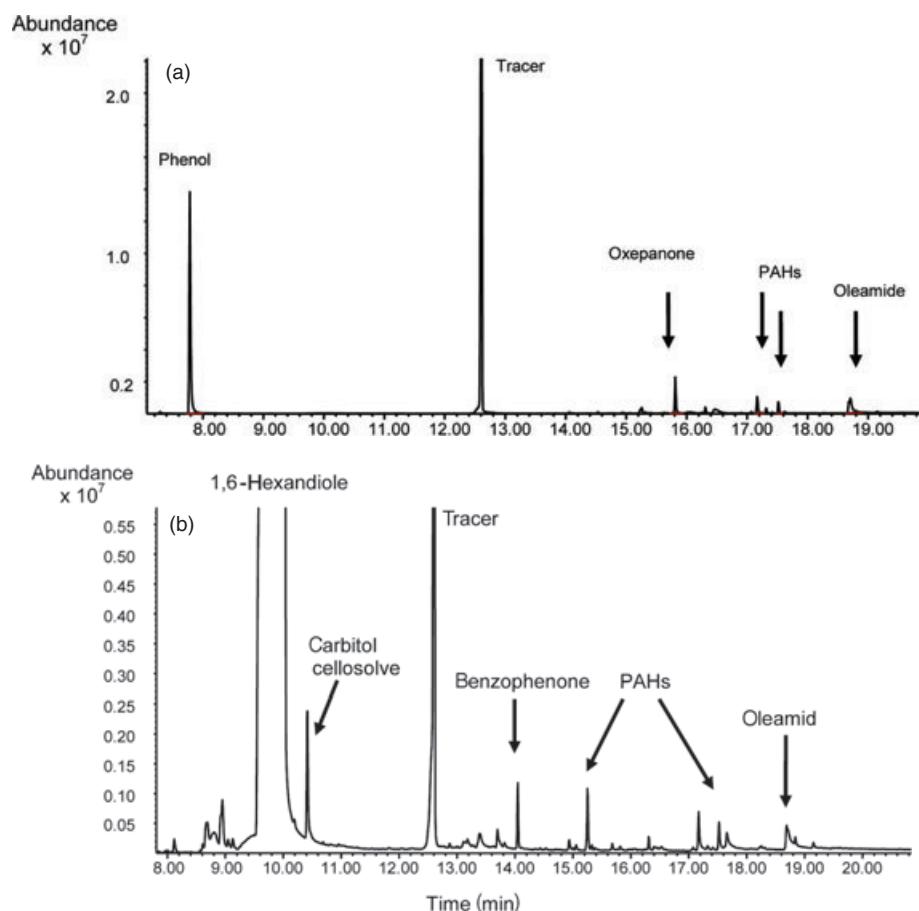


Fig. 2. Chromatograms of ink sample 13 (a) and ink sample 2 (b) showing additional substances that were either qualitatively determined or remained unknown. PAH, polycyclic aromatic hydrocarbon.

Dibutyl phthalate

In principle, synthetic materials, for example polyvinylchloride, contain several additives to provide special physicochemical handling properties, such as softness, elasticity, and plasticity (13). These synthetic materials are used in wallpapers, cloths, toys, plastic films, and artificial leather. Such phthalates are also present in dispersions and lacquers.

Thymic stromal lymphopoietin (TSLP) is an epithelial-derived cytokine expressed primarily in the lung, skin, and intestine, in response to inflammation, tissue damage, or Toll-like receptor ligation (14). In recent studies, it was shown that DBP is capable of inducing expression of TSLP in the skin (15, 16). Allergic contact dermatitis caused by DBP has been described (17).

In immunological experiments, DBP has been empirically included in the solvent system for fluorescein isothiocyanate (18). A study showed that stimulation of sensory neurons via TRPA1 and TRPV1 is involved

in the adjuvant effect during skin sensitization (18). This may reflect the connection between skin irritation and skin allergies. TRPA1 and TRPV1 may play a central role by transmitting noxious stimuli to the brain and immune cells, such as antigen-presenting cells, by sensing noxious compounds. Immunohistochemical analysis of skin after epicutaneous application of DBP showed a transient decrease in the number of C-type lectin-positive macrophages in the dermis (19).

Our results clearly show that DBP is present in all of the black inks under investigation, with concentrations up to 691 $\mu\text{g/g}$. When skin is tattooed, the black inks, together with DBP, enter the skin. In this way, DBP contacts nearly all skin cells that may trigger TSLP. An animal model showed, for coloured tattoo pigments, that such pigments can be partially transported to lymph nodes (20). Therefore, other ingredients of tattoo inks, such as DBP, might be transported away from the skin.

Hexachloro-1,3-butadiene

The chlorinated alkene HCBd is found predominantly as a byproduct from the manufacture of chlorinated solvents and related products. The substance was used as a fumigant for treating *Phylloxera* infection in the former Soviet Union, and to a lesser extent in southern Europe (21).

Rabbits have been epicutaneously exposed to pure HCBd (0.25–1.00 mg/kg) for 8 hr. HCBd has been found to be a skin penetrant and highly acutely toxic substance. HCBd led to epidermal and dermal necrosis, whereas the cutaneous changes increased with time for up to 5 weeks. The rabbits showed damage to the skin, liver, and kidneys (22). Out of the 14 black ink samples, we found HCBd in six samples, with concentrations up to 4.5 µg/g. So far, there are no case reports showing toxicity of HCBd in humans.

Dibenzofuran

DBF is the backbone of polychlorinated DBFs, which belong to the group of dioxin-like chemicals (23), and is listed in the US Environmental Protection Agency (US EPA) Toxic Substances Control Act (24). DBF is found as a combustion product in various percentages from the incomplete combustion of coal biomass, refuse, diesel fuel, and residual oil, as well as tobacco smoke (25). DBF is frequently used as wood preservative.

Out of the 14 black ink samples, we found DBF in seven samples, with concentrations up to 1.62 µg/g. We only detected the backbone of polychlorinated DBFs, and we cannot decide whether the chlorine atoms were present or cleaved prior to our investigations. The frequently described dermal, hepatic, and gastrointestinal health problems in humans are related to the brominated or chlorinated DBFs (26, 27).

In particular, little to no information is available on the effects of DBF exposure of skin. The information that does exist shows that short-term exposure to DBF can cause skin, eye, nose and throat irritation (28). Clear data in the medical literature about DBF are lacking, and the concentration in tattoo inks is low. Thus, it remains unclear whether this substance can cause health problems when tattooed into skin.

Hexamethylenetetramine

HET is used as a preservative in citrus washing solutions and in the manufacture of rubber, resins, and coatings, as well as in pharmaceuticals and cosmetics.

It is well known that preservatives used in cosmetics constitute an important source of allergic contact dermatitis (29). Some of the most problematic preservatives are

formaldehyde and formaldehyde-releasing agents (30). The formaldehyde-releaser HET, as a preservative in cosmetics, must not exceed a maximum authorized concentration of 0.15% (31). In addition, HET is known to cause respiratory allergies (30). In tattooing, HET is placed into the skin at concentrations up to 21.6 µg/g.

Benzophenone

BP, an aromatic ketone (diphenyl ketone), is an important compound in organic photochemistry and perfumery, as well as in organic synthesis. In the field of food packaging, BP is used as an initiator compound for hardening of printing inks by ultraviolet (UV) irradiation. Because of its volatile behaviour, BP is found in food.

According to the European Food Safety Authority (EFSA), BP is characterized as irritant but not genotoxic (32). A similar molecule is benzophenone-3 (2-hydroxy-4-methoxy-benzophenone), which is frequently used in sunscreens. It can cause photocontact allergy and other types of hypersensitivity reactions, such as contact allergy, photocontact urticaria, contact urticaria,



Fig. 3. Example of a simple flask containing black tattoo ink with no listing of ingredients.

and even cases of contact anaphylaxis (33). BP showed phototoxic reactions and caused photosensitization in the skin of guinea pigs under UV irradiation (34).

Previous studies in humans have indicated that the dermal absorption of organic UV filters during the application of sunscreens is very limited; in fact, only very low concentrations of these UV filters were detected in the blood after repeated, intensive application (35). However, dermal penetration is maximal for such substances during tattooing, and many of the black ink samples contained high concentrations of BP of up to 557 µg/g.

9-Fluorenone

9F is not commercially synthesized, but is obtained from the middle oil fraction of coal tar. It is used in the manufacture of antimalaria drugs and other pharmaceuticals. 9F may cause phototoxic reactions *in vitro* and *in vivo*, in particular in the oral mucosa (36, 37). Beyond that, little is known about adverse reactions to 9F, in particular regarding skin. 9F was found in 10 of the black ink samples at low concentrations (up to 3.04 µg/g), and it remains unclear to what extent 9F can harm the skin after tattooing.

Conclusion

The medical literature contains numerous case reports on dermatological diseases caused by tattoos, including pseudolymphoma, and allergic or granulomatous skin reactions (38–40). Considering the results of the survey in German-speaking countries, approximately 7.3% of tattooed people describe persistent skin reactions at the site of tattooing, including light sensitivity (2).

About 10% of the population are tattooed in Germany. If we extrapolate this percentage to all tattooed individuals, we tentatively assume that about 0.5 million people might have persistent skin problems with tattoos. The investigated black inks are from different countries, including the United States, where about 80 million people are tattooed (41). If the frequency of skin problems is the same in the United States, we tentatively calculate a number of about 5 million people with persistent skin problems at the tattooed site.

Carbon black in the inks is not suspected of causing allergic or irritant skin reactions. Thus, the described health problems are more likely to be caused by some of the ingredients listed in this investigation, although the listing might still be incomplete. Many of the 14 inks contain more than one ingredient that might lead to complex skin reactions. However, reports on adverse reactions in tattoos to the substances detected in this investigation are lacking so far. This first, but probably incomplete, list of tattoo ink ingredients may help physicians to search for the chemical trigger of adverse skin reactions.

In light of these results, we urgently recommend regulation of tattoo inks, so that only those inks without hazardous substances may be used. This could be started with a first step: substances that are not permitted to be used in cosmetics should be prohibited from being punctured into skin. Moreover, lack of knowledge (Fig. 3) should be remedied by requiring complete listing of the ingredients, as for cosmetics.

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