Carcinogenic Tattoos?

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Today up to 36% of people younger than 40 years have at least one tattoo [1]. The toxic effects of tattoos have not been investigated systematically [1]. The Council of Europe (CoE, www.coe.int) has established guidelines and negative lists for tattoo products in 2003 and 2008 (www.coe.int/t/e/social_cohesion/soc-sp/resap_2008_1%20e.pdf). Single European countries have national regulations based on the European guidelines [2]. Switzerland introduced a regulation for tattoo products in 2005 (www.admin.ch/opc/de/classified-compilation/20050181/index.html). However, a nationwide survey in 2014 showed that still 126 of 206 tattoo products did not comply with the regulation (www.gd.bs.ch/dms/kantonslabor/download/berichte/berichte-2014/tattoo_pmu_2014_en-uk-/tattoo_pmu_2014_en(uk).pdf).

The main tattoo colorants (TCs) are a) azo and polycyclic pigments [3], b) amorphous carbon particles (Carbon Black) [2] and c) mineral pigments (titanium dioxide and iron oxides) [3]. A positive list of TCs does not exist. The German Federal Institute of Risk Assessment published a list of tests, which would be required for a TC to be placed on a positive list (www.bfr.bund.de/cm/343/anforderungen-an-taetowiermittel.pdf). The US FDA does not regulate the TCs.

The CoE established a list of 27 aromatic amines (negative list), which should neither be present in tattoos products nor released from TCs [2]. However, neither standardised analytical methods nor limits were proposed [2]. A working group of the European Union compiled all the methods and procedures to test TCs [2]. The yields of these procedures are very low and not sufficient to enable a sound scientific judgment of the tattoo safety.

TCs are injected under the skin. This leads to 0.6-9.4 mg of TC per cm^2 of skin [3]. The mean value [4] was estimated to be 2.5 mg/cm^2.

An in vivo animal model showed that about 30% of intradermal injected pigment red 22 disappeared from skin within six weeks after tattooing [5]. Fading of tattoos can occur through loss of TCs [3], through metabolism [6], or photo degradation [5]. Although the TC particles are poorly soluble, the TCs can be transported with the blood and lymphatic system to other parts in the body. However, only the transport of TCs to the lymph nodes has been reported [3]. TCs can be metabolised to aromatic amines [7]. Metabolism of TCs is also performed by the human skin microbiota [6].

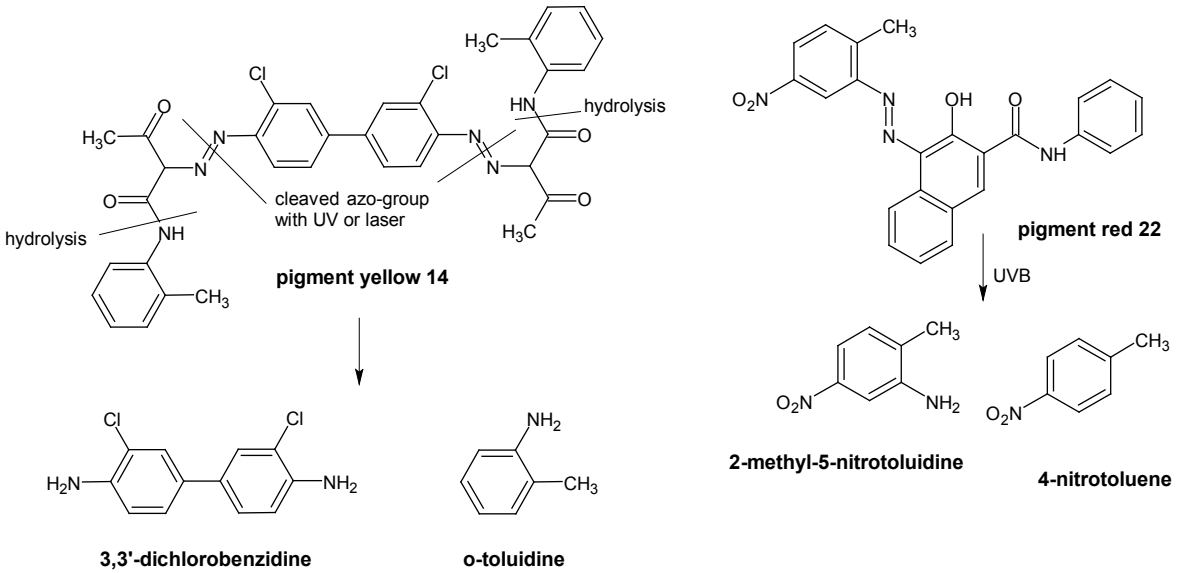
Light-induced decomposition of TCs has been tested recently [3, 5, 8]. Irradiation with simulated solar radiation for 32 days caused a TC reduction of about 60% in the skin [5]. In vitro studies showed the products resulting from photo degradation of TCs, for example pigment red 22. The found degradation products - 2-methyl-5-nitroaniline, and 4-nitrotoluene - indicate a reductive cleavage of the azo bridge (Figure 1) as well as cleavage at the site of the azo bond under loss of nitrogen. Other studies confirmed these results [8].

Laser treatment of 3,3'-dichlorobenzidine (DCBz)-based TCs such as pigment yellow 14, pigment yellow 83 and pigment orange 13 yielded DCBz (Figure 1) [3]. Therefore, laser removal [9] of tattoos will release substantial amounts of carcinogenic aromatic amines into the body.

TCs containing aromatic amines from the negative list established by the CoE are still used for tattoos.

The aromatic amines can be released metabolically or through photo and laser degradation. In humans, exposure to aromatic amines leads to bladder cancer. In the following, we estimate the cancer risk from such tattoos. In a 400 cm^2-tattoo

FIGURE 1. Photo degradation and hydrolysis of pigment yellow 14.



with pigment yellow 14 (Figure 1) 1000 mg TC are present. The photodecomposition of the TC can release maximally 385 mg of DCBz, which is a known carcinogen. Assuming a decomposition of the TC in 20 years, the daily dose of DCBz would be 0.053 mg/day. For a 70 kg-man, this corresponds to a dose of $7.5*10^{-4}$ (mg/kg/day). The US-EPA and the Californian Office of Environmental Health Hazard Assessment (OEHHA) use the cancer slope factor (CSF) to calculate the cancer risk for the lifetime time (70 years) exposure to environmental pollutants. The CSF has been established for many chemicals. The CSF of DCBz is 1.2 $(mg/kg/day)^{-1}$ (http://oehha.ca.gov/chemicals/33-dichlorobenzidine). Therefore, the Excess Lifetime Cancer Risk (ELCR) for an exposure period of 20-years to DCBz would be ELCR= CSF * dose * exposure period/lifetime=$3.87*10^{-4}$. Per molecule of pigment yellow 14 two molecules of o-toluidine can be released (Figure 1). The daily dose of o-toluidine would be $6.4*10^{-4}$ (mg/kg/day). The CSF of o-toluidine is 0.18 $(mg/kg/day)^{-1}$ (http://oehha.ca.gov/chemicals/o-toluidine). This yields an ELCR of $0.66*10^{-4}$. Therefore, for a 400 cm^2-tattoo with pigment yellow 14, additional 4.5 cancer cases per 10'000 people with tattoos are expected. The US-EPA tolerates a risk of one additional cancer case per 1 million people for lifetime time exposure to environmental chemicals. Therefore, the estimated cancer risk resulting from the exposure to pigment yellow 14 is too high. In comparison, 36'000 colon cancers per year are linked to meat consumption and 600'000 lung cancers per year are linked to tobacco consumption (www.iarc.fr). In the order to compare these values with the risk from tattoos the following assumption are made: The world population has $7*10^9$ people, $4*10^9$ eat meat and $1*10^9$ smoke. This yields roughly an additional lifetime cancer risk of 420 cancer cases per 10'000 (=(600'000cases/year)*70years/10^9) smokers and six cancer cases per 10'000 for meat-consumers.

This risk assessment is based on a single TC. Other TCs such as Carbon Black are used in tattoos. Carbon Black has been listed as possibly carcinogenic to humans (group 2B) by the International Agency of Research in Cancer (http://monographs.iarc.fr/ENG/Monographs/vol93/). Furthermore, high amounts of polycyclic aromatic hydrocarbons (up to 201 µg/g) were found in black TCs (10). Therefore, also other TCs add to the carcinogenic risk of tattoos.

In conclusion, millions of people worldwide have tattoos. The systemic effects of TCs have not been investigated. Toxicological and epidemiological studies are needed to clarify the impact of tattoos on human health. TCs with aromatic amines of the negative list should be forbidden for the use in tattoos since the released aromatic amines are a cancer risk.

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