

# Tattoo Inks, Cancer and Other Chronic Diseases: Gaps in research and regulation

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<https://www.healthandenvironment.org/che-webinars/96733>

# Tattooing is an ancient custom, common to many societies

- Including “Ötzi the Iceman” preserved in a glacier above Bolzano, Italy for 5,300 years



<https://www.si.edu/stories/ancient-ink-iceman-otzi-has-worlds-oldest-tattoos>

(Photograph © South Tyrol Museum of Archaeology/EURAC/Samadelli/Staschitz)

# 32% of Americans have a tattoo

- AUGUST 2023 Pew Research Survey, Schaeffer K, Dinesh S.
  - <https://pewrsr.ch/3QFg5w1>

- Gender:
  - 38% of women
    - 56% of women 18 - 29
    - 53% of women 30 - 49
  - 27% of men

- Age:

• < 30:	41%
• 30 – 49:	46%
• 50 – 64:	25%
• >= 65:	13%

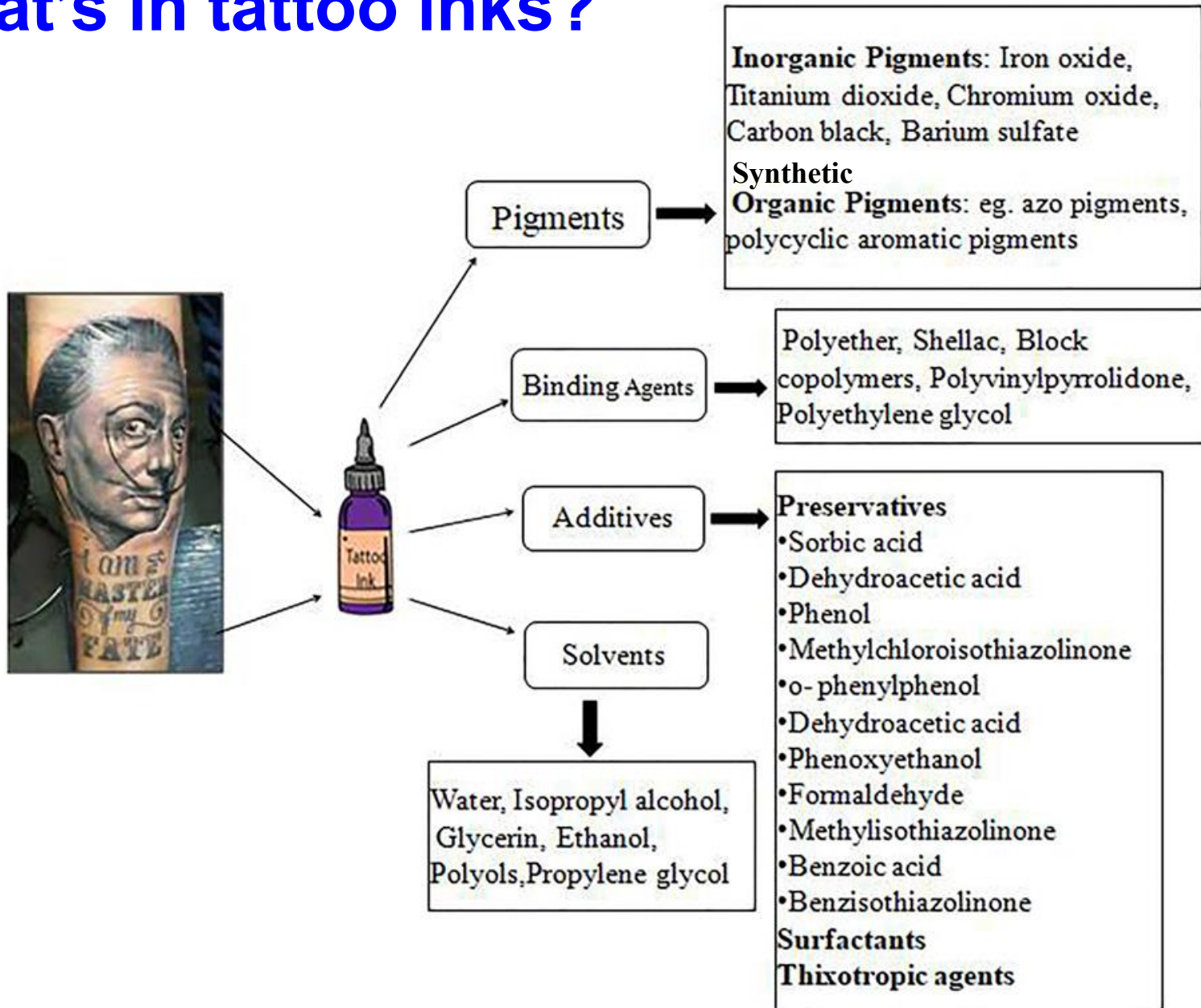


<http://www.besttats.com/colorful-unique-flower-sleeve-womans-tattoo/>

# The decision to get a tattoo often has deep personal significance

- AUGUST 2023 Pew Research Survey, Schaeffer K, Dinesh S.
  - <https://pewrsr.ch/3QFg5w1>
- Reasons for getting a tattoo:
  - 69% to honor or remember someone or something
  - 47% to make a statement about what they believe
  - 32% to improve their personal appearance.
- Regret: 24% say they regret getting one or more of their tattoos.

# What's in tattoo inks?



# Tattooing inks have become much more colorful (!), applied over wider areas, and with a wider array of ingredients

- Carbon black and other inorganics were typical in the past.
- Now thousands of compounds are used – many only recently invented.
  - Azo- pigments or polycyclic compounds are most common
  - Metals including arsenic, chromium, cadmium and nickel
  - Particles in the nano range are used to improve retention and color

# Tattoo inks contain carcinogens

- IARC Class 1 carcinogens found in inks\*:

Compound	Estimated concentration/300 cm <sup>2</sup> tattoo*
2-Naphthylamine	1950 ng
<i>o</i> -Toluidine	825 ng – 1648 µg
Arsenic	150 ng – 45 µg
Chromium	225 ng – 110 µg
Cadmium	7.5 ng – 5.9 µg
Nickel	23 ng – 7343 µg
Benzo[ <i>a</i> ]pyrene	5100 ng

*\* International Agency for Research on Cancer, Lyon France.  
Cited in: Foerster et al. Cancer Epidemiology 65 (2020) 101655*

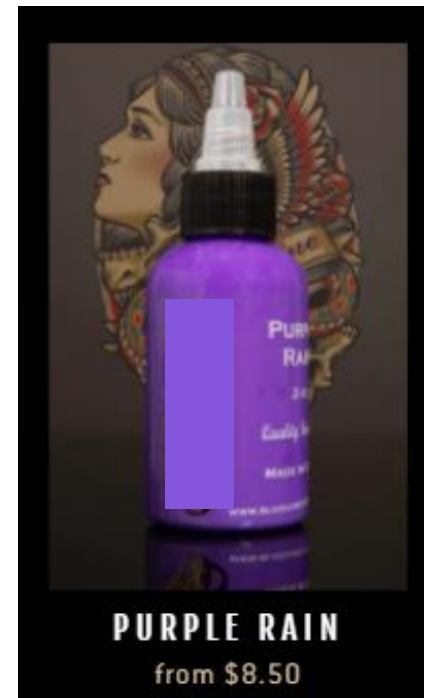
# **Tattoo inks also contain many chemicals whose toxicity is unknown**

- Tattoo ink formulators in the U.S. are under no obligation to evaluate the safety of chemicals before they use them
- There are many compounds in inks whose toxicity/safety is essentially unknown



# An example of a single tattoo ink pigment – picked almost at random for illustration

- From the website of a large tattoo ink supplier
  - *All our tattoo inks are processed with the utmost attention and care in the USA in our clean room. Everything from mixing, pouring, bottling, labeling, packing and shipping happens in our clean location. Our inks are cruelty-free, never tested on animals, vegan safe and Covid safe.*



# PURPLE RAIN

## SDS | SAFETY DATA SHEET

ACCORDING TO FEDERAL REGISTER / VOL. 77, NO. 58 / MONDAY, MARCH 26, 2012 / RULES AND REGULATIONS  
DATE OF ISSUE: 01/30/2020  
VERSION: 1.0

TATTOO INKS

### COMPOSITION:

PIGMENT VIOLET 23 CI# 51319 PIGMENT WHITE 6 CI# 77891  
PROPYLENE GLYCOL CI# 57-55-6  
ETHYL ALCOHOL C.A.S #64-17-5  
AQUA C.A.S # 7789-20-0

**MATERIALS ARE CONSIDERED NON-HAZARDOUS BY OSHA UNDER 29 CFR 1910.1200(D).**

### ROUTE OF ENTRY: SKIN

SKIN CONTACT: CAN CAUSE MODERATE IRRITATION.

EYE CONTACT: CAN CAUSE MODERATE IRRITATION, TEARING AND REDDENING, BUT NOT LIKELY TO PERMANENTLY INJURE EYE TISSUE.

### OTHER HAZARDS

POTENTIAL HEALTH AFFECTS: EYES, SKIN, AND INGESTION SHOW NO KNOWN SIGNIFICANT EFFECTS OR CRITICAL HAZARDS.

POTENTIAL CHRONIC HEALTH AFFECTS:

CARCINOGENIC EFFECTS: NO KNOWN SIGNIFICANT EFFECTS OR CRITICAL HAZARDS.

MUTAGENIC EFFECTS: NO KNOWN SIGNIFICANT EFFECTS OR CRITICAL HAZARDS.

TERATOGENICITY/REPRODUCTIVE TOXICITY: NO KNOWN SIGNIFICANT EFFECTS OR CRITICAL HAZARDS.

OVER-EXPOSURE EFFECTS: NONE KNOWN.

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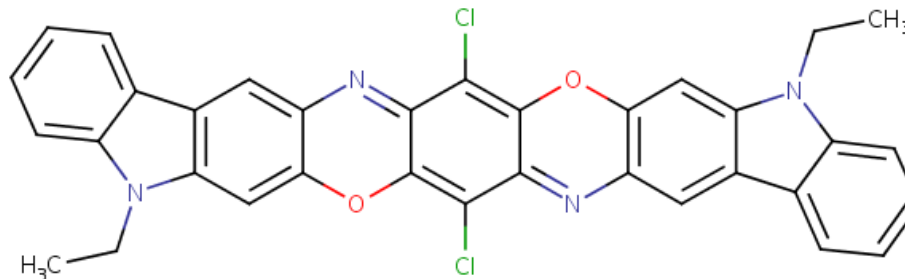
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# Violet 23 – CAS # 6358-30-1

8,18-Dichlor-5,15-diethyl-5,15-dihydrodiindolo[3,2-b:3',2'-m]triphenodioxazin



Synthetic organic dye, used in:

- Tattoo ink
- Cleaning products, air fresheners
- Construction and building materials
- Furniture and furnishings
- Caulk/sealant



## 8,18-Dichloro-5,15-diethyl-5,15-dihydrodiindolo[3,2-b:3',2'-m]triphenodio...

### Summary of Toxicology Information:

- **Cancer Information**

- ✘ No cancer slope factor
- ✘ No cancer unit risk values
- ✘ No cancer data
- ✘ No genotoxicity Data

- **Reproductive Toxicology**

- ✘ No reproductive toxicity data available

- **Chronic Toxicology**

- ✘ No chronic toxicity data available

- **Subchronic Toxicology**

- ✘ No subchronic toxicity data available

- **Developmental Toxicology**

- ✘ No developmental toxicity data available

- **Acute Toxicology**

- ✘ No acute toxicity data available

- **Subacute Toxicology**

- ✘ No subacute toxicity data available

- **Endocrine System**

- ✘ No endocrine disruption relevant data available

- **Skin / Eye**

- ✔ Skin / Eye Data: available: 1 [↗](#)

*(eye irritation)*

**Remember:**

**absence of evidence (of hazard)  
is not  
evidence of absence (of hazard)**

# Tattoo inks are poorly regulated

- In the U.S., the Food and Drug Administration (FDA) legally has responsibility for regulating tattoo inks, but has not done so.
  - “FDA has not approved any inks for injection into your skin.”
- In Europe, there is more control, under the EU comprehensive chemicals policy called REACH
  - Registration, Evaluation and Authorization of Chemicals, enacted in 2007
  - January 2022 - comprehensive European rules on tattoo ingredients



# The European Union has restricted more than 4,000 chemicals in tattoo inks

- Established maximum concentration limits for substances used in tattoo inks or permanent make-up.
- In the future automatically limits chemicals that are classified as:
  - carcinogen, mutagen or as toxic to reproduction
  - skin sensitizer
  - skin corrosive
  - skin irritant
  - eye irritant
  - eye damaging

# Notice: different approaches to regulation in the EU vs US

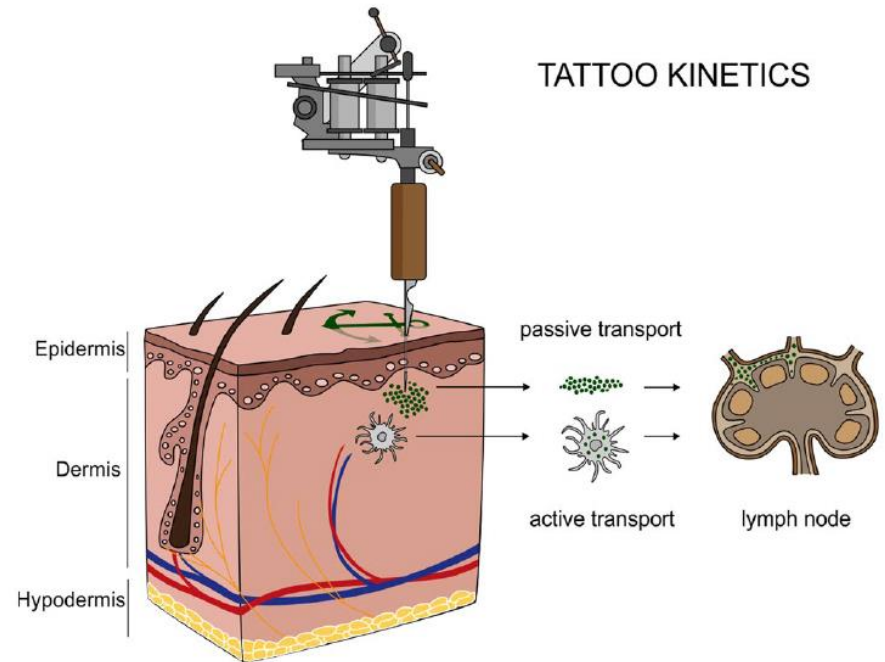
- The EU follows the precautionary principle:
  - *“when an activity raises threats of harm to human health or the environment, precautionary measures should be taken even if some cause and effect relationships are not fully established scientifically”*  
(1998 Wingspread consensus statement)
- The US follows the reactionary principle:
  - *“anyone is free to introduce a new hazard into the environment, and governments must wait until very strong evidence of risk is accumulated before intervening.”*

# What evidence is there that tattooing causes chronic disease?

- There is very little direct evidence
- A brief summary of what is known
  - Fate and transport of inks in the body
  - Immune responses to tattoos
  - Potential mechanisms for cancer and autoimmune diseases
  - Very limited human and animal evidence

# Tattoo ink fate and transport

- While the objective is permanent subcutaneous deposition, much of the ink ultimately is cleared.
  - There is a rapid clearance immediately after application, and then a slow phase lasting years.
- Clearance of insoluble particles via blood and lymph leads to accumulation in lymph nodes and other organs.
  - Adjacent lymphatic tissue is often found to contain large numbers of ink particles.



# Tattoos continuously attract immune cells, a normal defensive response

- Langerhans cells (LCs) are recruited to the site
  - Skin-resident macrophages involved in immune responses to foreign agents
- LCs continually surveil skin for antigens, bacteria, viruses
  - They phagocytize particles and present them to other immune cells for removal
- Precursor cells are recruited and differentiate to continually renew the local population of LCs
  - Karanth, Exp Dermatol 1996; 5:168-172

# Tattoos continuously attract immune cells, a normal defensive response

- In other words, the immune system is continuously stimulated by a tattoo
- Is this a problem?
  - We don't know
  - But it is possible that this could lead to immune dysregulation and errors in immune cell replication
  - The cell-mediated immune response is very complex, and there is still much we don't understand about normal and abnormal function

# Could tattoos be carcinogenic?

- Chronic inflammation?
- Immune dysregulation?
- Prolonged local exposure to specific carcinogens?
- Foerster et al. hypothesize that non-Hodgkin lymphomas (NHL) might be expected from chronic immune stimulation.
  - (Foerster M. Cancer Epidemiology 65 (2020) 101655)

# Could tattoos trigger autoimmune diseases?

- Could chronic immune stimulation lead to immune system dysfunction?
  - We don't know
- Causes of autoimmune diseases are poorly understood, but may arise from immune dysregulation
  - Rheumatoid arthritis?
  - Sarcoidosis?
  - Lupus erythematosus?



# Animal evidence

- Limited evidence, very few studies

# Human case reports

- There are many case reports of skin cancers in people with tattoos:
  - Melanomas
  - Basal cell carcinomas
  - Squamous carcinomas
  - (Kluger N., Lancet Oncol 2012; 13: e161–68)
- Also many case reports of pseudolymphoma, lymphoid hyperplasia, and other similar conditions
  - (Mitteldorf C, J Cutan Pathol. 2020 Jan;47(1):76-97.)
- But these could easily be the result of chance co-occurrence of tattoo and disease

# The only epidemiologic evidence – one case control study of 2 types of hematologic cancers

- Population based study in BC, Canada, of NHL (2000 - 2004) and multiple myeloma (2009 – 2013)
  - Self-reported tattoo prevalence was low ~ 6%
    - Not surprising given mean age ~60 years
  - Weak evidence of an association for 2 types of cancer
  - T cell lymphoma:
    - Odds ratio = 1.47 (95 % confidence interval = 0.49–3.66)
  - “other B cell” lymphoma:
    - Odds ratio = 1.27 (95% CI = 0.68–2.30)
- Warner FM, et al., Cancer Epidemiol Biomarkers Prev. 2020 Jul 22. doi: 10.1158/1055-9965.EPI-20-0515.

# Some common misperceptions

- “If a chemical is allowed on the market, it must have been tested for safety”
  - This is false
  - Tattoo artists are licensed, but this is to ensure sterile technique, and there are no U.S. laws about ink ingredients
- “Tattoos sit in the very top layer of skin, and they stay there forever, so they must be isolated from the rest of the body, out of reach of the blood stream.”
  - This is false

# Some common misperceptions

- “People have been getting tattoos forever. So, if they were dangerous, we would know it”
  - This is false
  - A major reason why epidemiology exists:
    - in order for a common exposure causing a common disease to be “noticeable” to the public (or physicians) the risk must be very large
- It’s hard to “see” that smoking causes lung cancer
  - Most life-long smokers don’t get lung cancer

# What is to be done?

- People should be able to tattoo safely, but we don't know enough to identify safe inks
- Research is urgently needed
  - epidemiology
  - clinical studies
  - toxicology
- In the U.S., we should demand that FDA regulate tattoo inks