Tattoo Pigments:

Regulation, Chemistry, Photostability, and Potential Complications in the Human Body

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Outline

- Regulatory status of tattoo inks and tattoo pigments
- Chemistry of tattoo pigments
- Potential impurities in tattoo pigments
- Photostability of tattoo pigments
- Tattoo marketplace
- Potential complications from tattooing and FDA responses

Regulatory status of tattoo inks in the U.S.

- Tattoo inks are mixtures of pigments and other components intended for introduction into the skin
  - Tattoo inks fall under the definition of a cosmetic
  - Pigments are regulated as color additives
  - Other components include water, isopropyl alcohol, glycerine, and witch hazel
- FDA traditionally has not exercised its regulatory authority over tattoo inks
  - Safety information is posted on FDA's website
- The practice of tattooing is regulated by state and local jurisdictions

Regulatory status of tattoo pigments in the U.S.

- Tattoo pigments impart color to tattoo inks and the human body
  - FDA defines *color additive* as any material that can impart color to a food, drug, cosmetic, or medical device, or to the human body
  - Therefore, tattoo pigments meet the definition of a color additive

- Color additives must be pre-approved by FDA for use in foods, drugs, cosmetics, and medical devices
  - Approved color additives are listed in the Code of Federal Regulations
  - 21 CFR Parts 73, 74, and 82

- No color additives have been approved for injected use
  - *See* 21 CFR 70.5(b)
  - Therefore, tattoo pigments are considered unapproved color additives

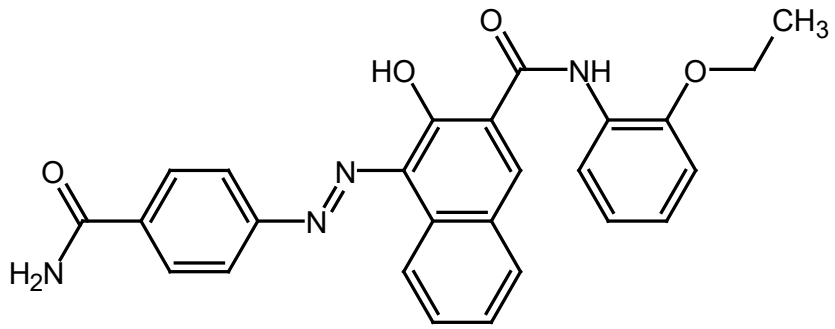
Types of tattoo pigments

- Inorganic pigments
  - Natural mineral or synthetic sources
  - E.g., metal oxides
- Organic pigments
  - Synthesized from carbon, hydrogen, nitrogen, sulfur, and oxygen

Classification of tattoo pigments

- Colour Index (C.I.) categories and numbers

- *Example:* C.I. Pigment Red 170



Inorganic tattoo pigments

- **Black**
  - Charcoal (C) . . . . . Pigment Black 7
  - Magnetite ($FeO \bullet Fe_2O_3$) . . . . . Pigment Black 11
- **Red**
  - Hematite (Fe_2O_3) . . . . . Pigment Red 102
- **Yellow**
  - Limonite ($FeO \bullet OH \bullet nH_2O$) . . . . . Pigment Yellow 43
- **White**
  - Anatase or rutile (TiO_2) . . . . . Pigment White 6
  - Barium sulfate ($BaSO_4$) . . . . . Pigment White 21
- **Blue**
  - [Phthalocyaninato (2-)] copper . . . . Pigment Blue 15

Limitations of inorganic tattoo pigments

- Iron oxides fade or change color
- Historically used mercury and cadmium salts are toxic

Potential impurities in inorganic tattoo pigments

- Elemental impurities
  - Lead (Pb)
  - Arsenic (As)
  - Mercury (Hg)
  - Cadmium (Cd)

- Can be determined by inductively coupled plasma (ICP) or atomic absorption (AA) techniques

Organic tattoo pigments

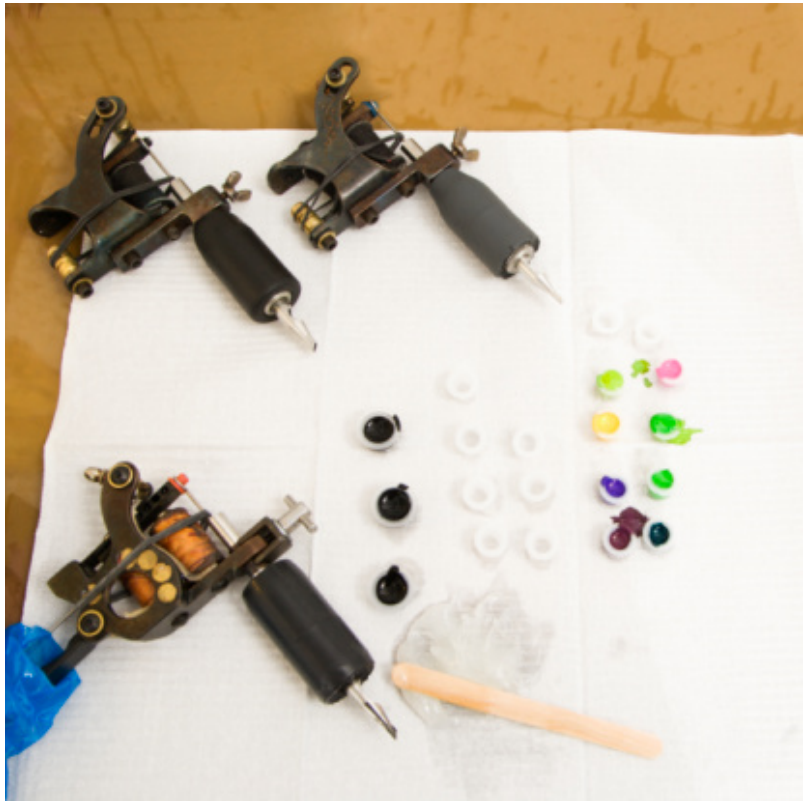
- Typically more intense colors than inorganic pigments
- Wider range of colors
- Some are removable by laser treatments

Potential impurities in organic tattoo pigments

- Polycyclic aromatic hydrocarbons (PAHs)
- Primary aromatic amines (PAAs)

- Many of these are known carcinogens
- PAHs can be determined by liquid chromatography or gas chromatography techniques

Marketplace – inks and implements



Tattoo inks

- Suspensions of non-soluble pigments with binders and solvents
  - Binders include polymers and shellac
  - Solvents include water, ethanol, isopropyl alcohol, and glycerine
- Finely dispersed pigment mixtures are stabilized
  - Stabilizers include surfactants and thickening agents
  - Otherwise the pigments will agglomerate
- Preservatives can be added to prevent microbiological spoilage

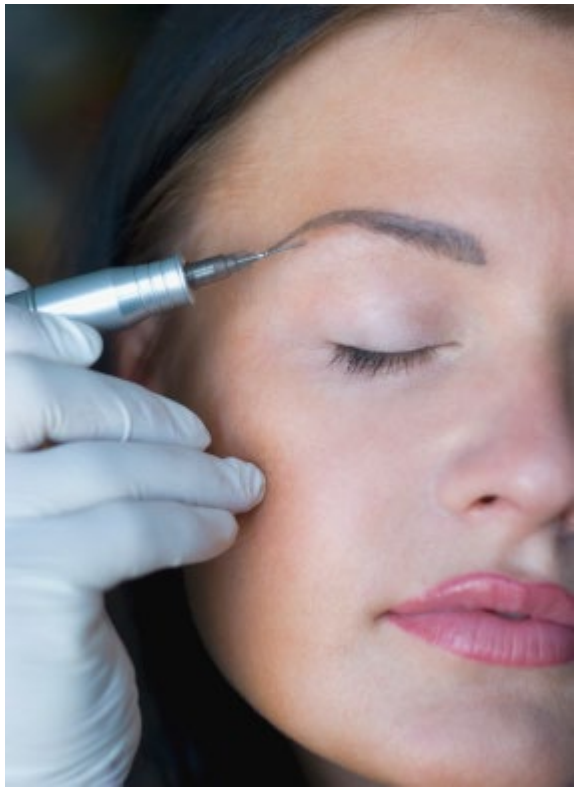
General body tattooing

Permanent makeup

- Until late 1970's, most tattoo artist avoided tattooing the face.
- Permanent makeup inks
  - Applied to face including eye area, lips
- Replaces traditional makeup
  - Eyeliner
  - Eyebrows
  - Lipliner
  - Full lips
  - Blusher
- Also called "micropigmentation"

Examples of permanent makeup

Eyebrows



Lips

Tattoo/permanent makeup industry

- Technicians diverse
  - Amateurs to RNs and MDs
- Salons/tattoo parlors regulated by state and local health departments
- Tattoos/permanent makeup in salon, home, workshop settings
  - No injected anesthesia
  - Varying sterile techniques
- Permanent makeup in medical setting
  - Injected anesthesia
  - Varying artistic ability

Complications from tattoos and permanent makeup

- Swelling, cracking, peeling, blistering, scarring
- Granulomas (small nodules of inflamed skin)
- Keloids (scars that grow beyond normal boundaries)
- Allergic reactions
- Photosensitivity
- Serious disfigurement
- MRI complications

Allergic reaction

Adverse reactions to permanent makeup

Adverse reactions to permanent makeup

- 1988 to 2003 – FDA received only five reports of adverse reactions
- 2003 to 2004 – FDA received more than 150 reports of adverse reactions
- FDA and CDC – identified 101 patients with adverse reactions
- Adverse reactions – tenderness, swelling, itching, and bumps
- Clinical diagnoses – allergic reactions or granulomas

FDA and CDC actions

- July 2, 2004 – FDA alerted public to concerns with Premier Pigment brand of ink shades
  - "FDA Talk Paper" (press release) on FDA's website
- Sept. 27, 2004 – Product line recalled by manufacturer
- July 2005 – Case study in *Archives of Dermatology*
- June 28, 2007 – Publication in *New England Journal of Medicine*

Adverse reactions to tattoo inks without preservatives

- "Starbrite Colors" website bragged that no preservatives or other additives were used in their tattoo inks

- Claims included
  - *The inks are made with sterilized distilled water*
  - *The ink is not an alcohol-based tattoo ink*

Starbrite Ink microbial contamination

- 2004: Belgium withdrew “Starbrite Colors” tattoo ink from market because of microbial contamination
- FDA analyses found bacteria (*Pseudomonas aeruginosa)* and mold *(Acremonium)*
- Resulted in manufacturer recall of Starbrite ink
- Starbrite ink became contaminated because the manufacturer removed the alcohol preservative from their ink formula

More microbial contamination of tattoo inks

- In 2011 there were several outbreaks in the U.S. possibly linked to bottled tattoo ink
- Non-tubercular mycobacterium (NTM) was isolated from bottled ink
- Other pathogens have been isolated
- New England Journal of Medicine article
  - Kennedy, BS, Bedard B, Younge M, et al. Outbreak of Mycobacterium chelonae Infection Associated with Tattoo Ink. N ENGL J MED 2012; 367:1020-1024 September 13, 2012

Contamination sources

- NTM is commonly found in public water supplies
- Cannot be removed by filtration
- Spores can only be destroyed by sterilization
  - Problem: sterilization may affect pigments
- NTM and other pathogens may be introduced by the user
  - Diluting with water, pouring back unused ink, storing open containers

Recent example of microbial contamination

- FDA issued a Safety Advisory on May 15, 2019 warning consumers, tattoo artists, and retailers about using or selling certain tattoo inks contaminated with microorganisms
- Five tattoo ink products were voluntarily recalled
  - Four black inks and one red ink
- See https://www.fda.gov/cosmetics/cosmetics-recalls-alerts/fda-advises-consumers-tattoo-artists-and-retailers-avoid-using-or-selling-certain-tattoo-inks

Misleading websites

- Website claim by tattoo ink manufacturer:
  - FDA has approved polymethylmethacrylate (PMMA) for medical uses
  - Website claims FDA's approval of PMMA makes the ink safe for use in tattooing
- Problem: false claim!
  - FDA has NOT approved PMMA for use in tattooing
  - FDA has NOT approved any pigments for use in tattooing

Problems with tattoos and permanent makeup

- Tattoo pigments have not been approved by FDA for cosmetic purposes
  - Safety for skin injection has not been demonstrated
- No color additives have been listed for injected use
  - See 21 CFR 70.5(b)
- Adverse reactions have occurred
- Removal can be difficult

Tattoo removal

Laser treatments

- Painful
- Expensive
- Time consuming
- May result in discoloration of skin
- May not be complete
- Iron oxide and titanium dioxide pigments turn black

Surgery

- Painful
- Expensive
- Scarring

Current issues

- NTM contamination in sealed bottles of tattoo ink
- Alcohol preservation may not be bactericidal
- Sterilization methods are untested
- Industry has not demonstrated microbiological expertise
- FDA’s rapport with industry is limited

Questions for Industry Consideration

- Single vs. multiple use?
- Preservation requirements?
- Sterilization treatment options?
- Required labeling statements?

More information is needed

- Tattoo ink ingredients
  - FDA is in the process of sampling and testing tattoo inks to learn more about ingredients and contaminants
- Processing methods
  - FDA is planning to inspect more manufacturers to learn more about prevailing practices

FDA's future goals

- Better understanding of composition, methods of preservation and safe use
- Development of better tools to assess human health risks from tattoo inks and pigments
- Better understanding of the tattoo industry
- Continued outreach with all stakeholders
- Consideration of changing color additive enforcement policy

Summary of challenges

- Regulatory oversight
- Development of better tools to assess human health risks from tattoo inks and pigments risk
- Improvement in recognition of problems (both clinically and scientifically)
- Communication and outreach with stakeholders and constituents

Conclusions

- Marketplace – wide variety of pigments in tattoos and permanent makeup
- Adverse reactions – FDA has responded
- Misleading websites!!!
- Tattoos are difficult to remove!
- No pigments have been approved by FDA for tattooing for cosmetic purposes

Further information

- Current website “Tattoos and Permanent Makeup” https://www.fda.gov/cosmetics/cosmetic-products/tattoos-permanent-makeup-fact-sheet

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