

Dissolution and Reactive Oxygen Species Generation of Cobalt Compounds in Artificial Sweat

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Occupational and Environmental Exposures of the Skin to Chemicals

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Introduction

- Cemented tungsten carbides
 - Tungsten carbide bound in a cobalt (Co) matrix
- Applications
 - Cutting tools (metals) and drills (masonry, concrete)
- Skin exposure to Co
 - Sensitization and allergic contact dermatitis (ACD)
 - ACD prevalences: 7% (Europe) to 9% (USA)

Cobalt on Skin

- Soluble Co
 - Permeates (Linnainmaa & Kiilunen 1997)
- Metallic Co powder
 - Dissolves in simple artificial sweat
 - Permeates (Filon et al. 2004; Larese et al. 2007)
- Worker hands and necks
 - May be highly contaminated (Day et al. 2009)

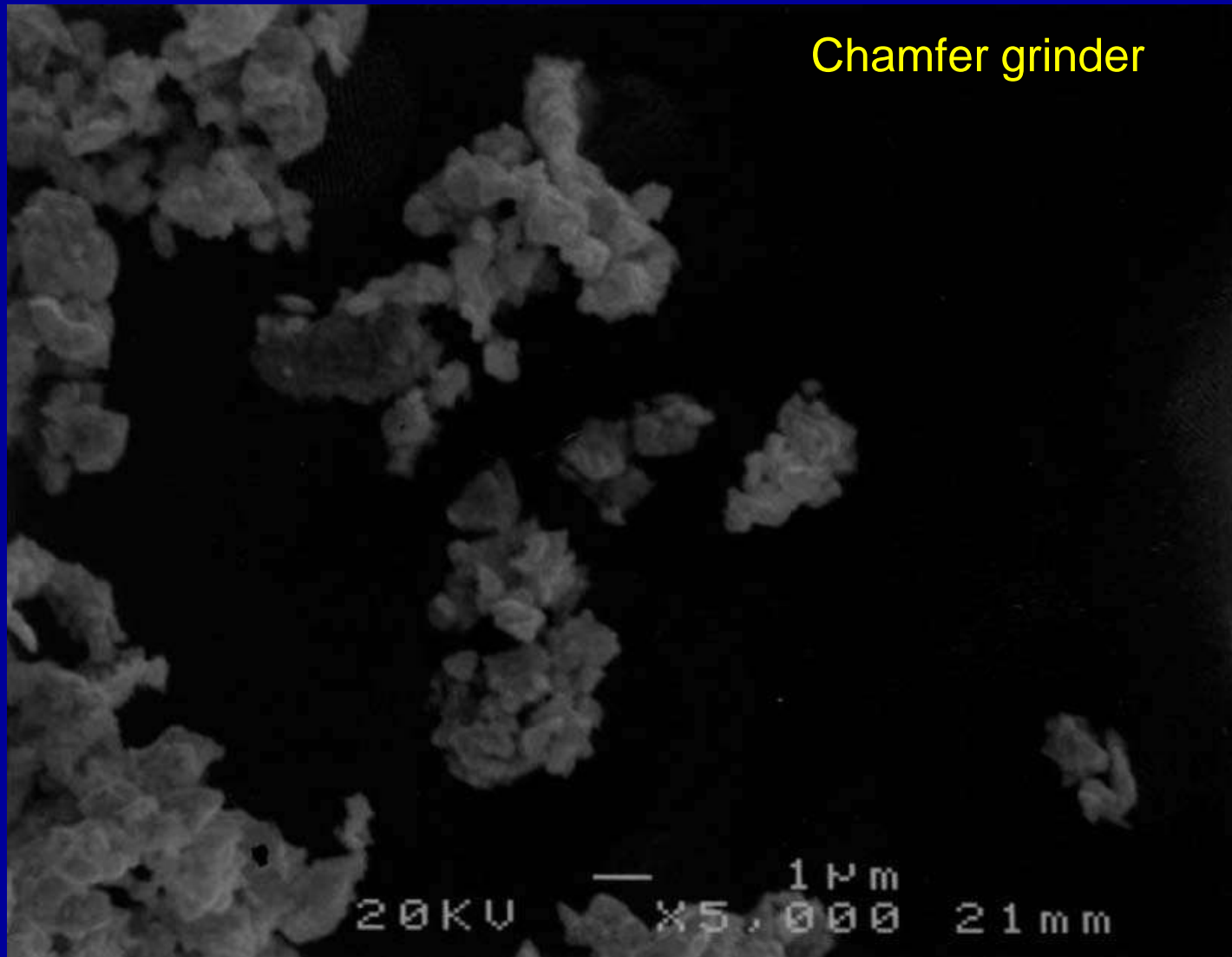
Co Sensitization and ACD

- Sensitization
 - Co^{2+} forms hapten complex in epidermis
 - Complex interacts with Langerhans cells (LCs)
 - LCs present complex to naïve T-lymphocytes
 - Formation of antigen-specific effector and memory T-cells
- ACD
 - Type IV (delayed hypersensitivity reaction)
 - Repeat contact
 - Memory T-cells recruited to the site of contact
 - Initiates inflammatory process

Mechanistic Hypotheses of ACD

- Covalent binding (Goebeler et al. 1993, 1995)
 - Co^{2+} binds with nucleophilic proteins
- Radical generation (Van de Broeke et al. 1998)
 - Co^{2+} -mediated redox reactions
 - Radicals react with biological molecules
 - Form structural modifications

Materials and Methods



Solubility Studies

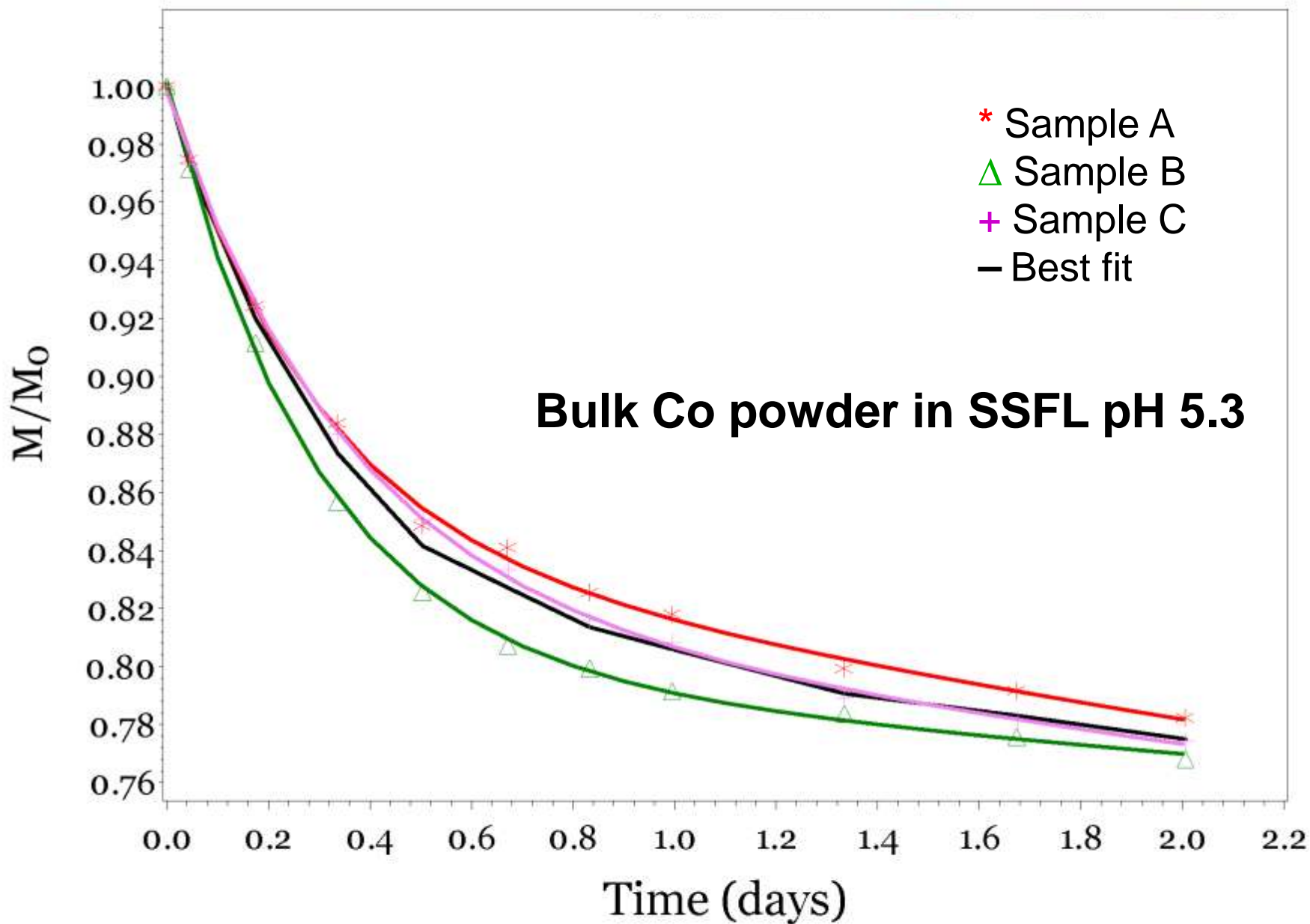
- Static dissolution
- Stefaniak & Harvey
 - Sebum lipids (10)
 - Sweat electrolytes and carbohydrate substances (5),
 - Buffered to pH 5
- Pedersen et al. (1998)
 - Sodium chloride
 - Buffered to pH 6



Electron Spin Resonance Studies

- Primary focus on host defense
- “Fenton-like” reaction
 - Reaction of particles with macrophages
 - Subsequent interaction with H_2O_2
- Cell-free reaction system (H_2O_2 + Sweat)
 - DMPO spin trap
 - Production of $\bullet\text{OH}$ radicals by particles

Bulk Co powder in SSFL pH 5.3

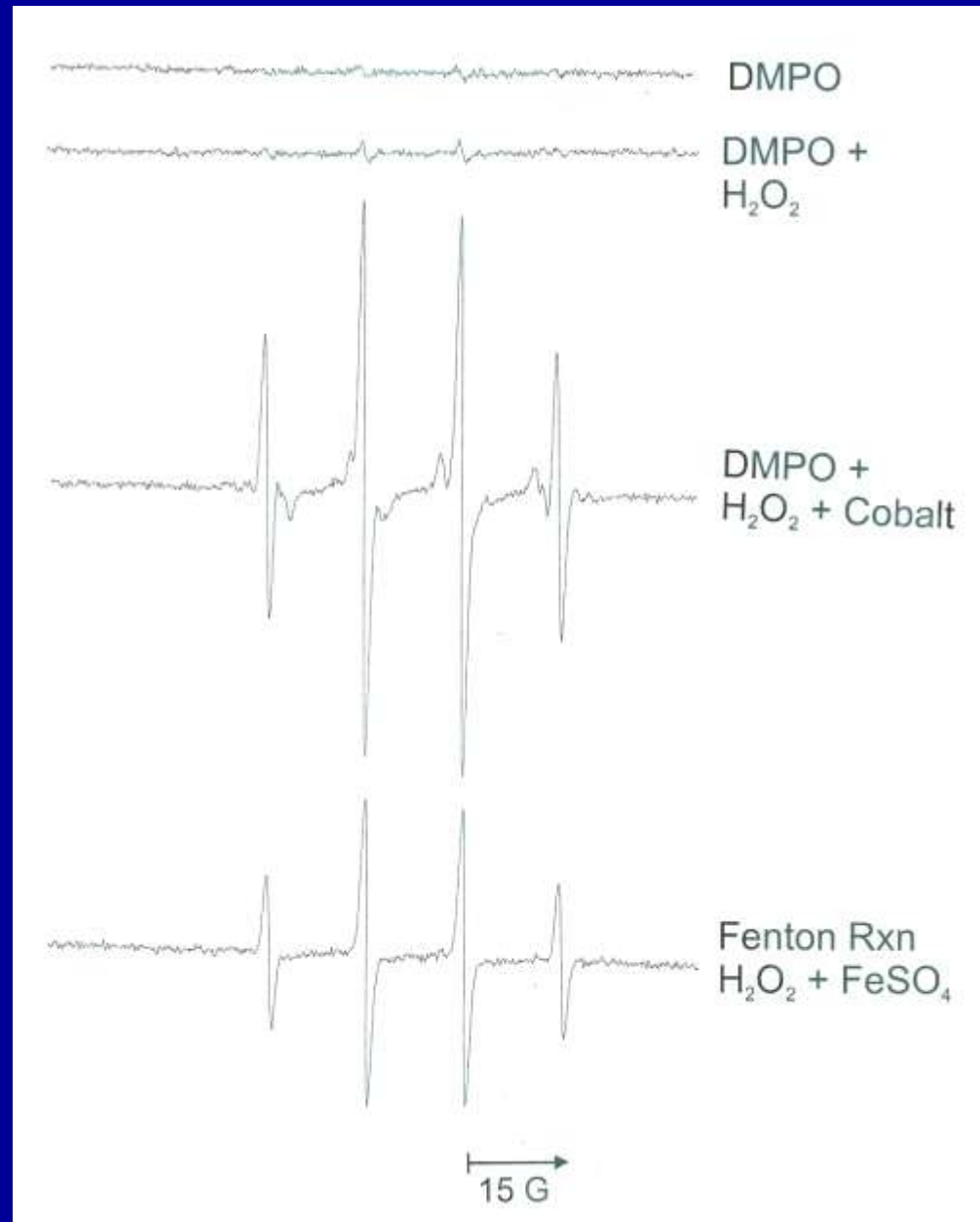


Size-Separated Powder Solubility

- SSFL (pH 5.3)
 - Co^{2+} released from all sizes of all compounds
 - Biphasic dissolution
- Parameters similar among sizes of compounds
 - Cobalt metal (3 sizes)
 - Admixture (3 sizes)
 - Spray dryer (2 sizes)
 - Chamfer grinder (1 size)

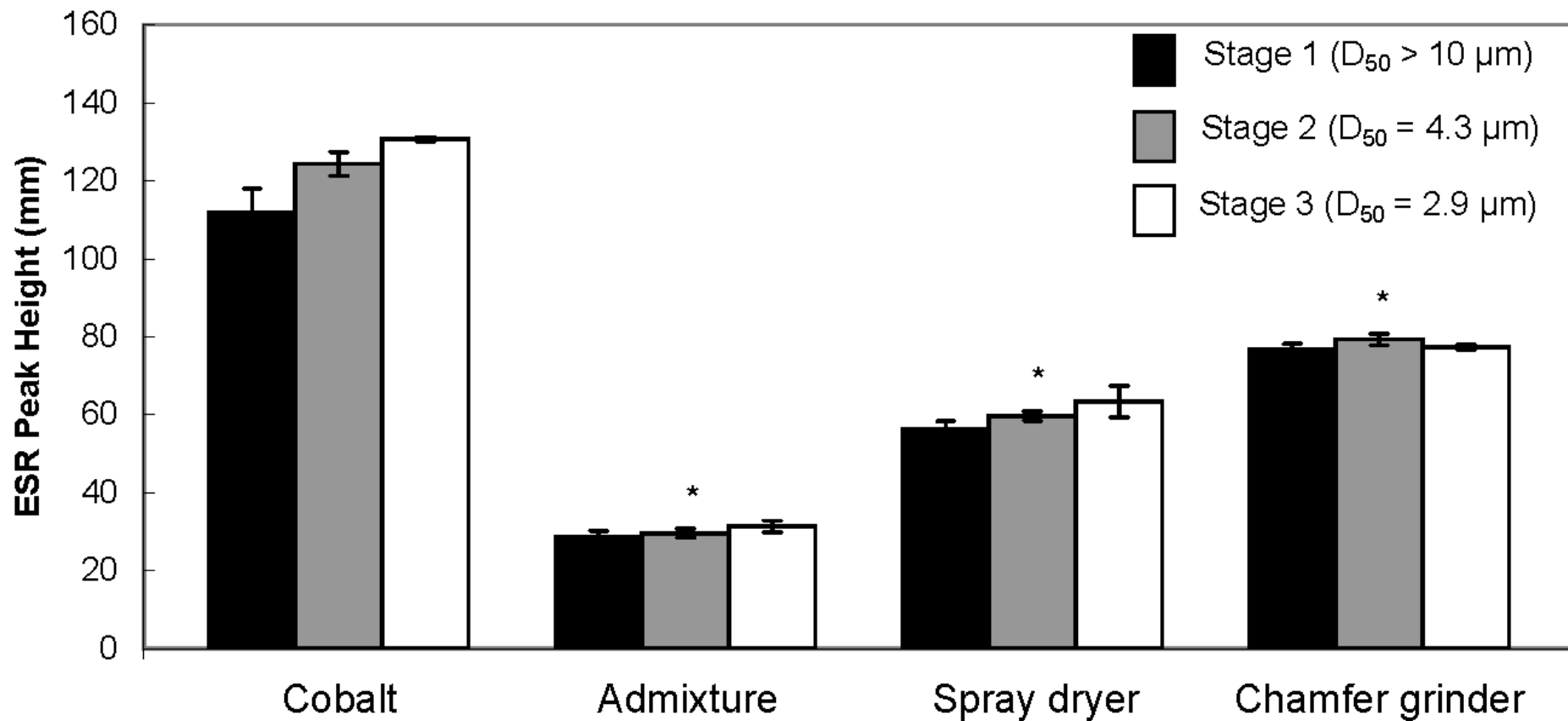
Cobalt-Free Radical Generation

- Artificial sweat
 - Generation of $\bullet\text{OH}$



Cobalt Free Radical Generation

- OH• radical levels
 - Co > chamfer grinder > spray dryer > admixture
 - Differed among all powders ($p < 0.05$)



Cobalt Solubility

- Bioaccessible in SSFL artificial sweat
 - Co^{2+} permeable form
- Bioavailability modeling
 - Amount on skin (Day et al. 2009)
 - Rate of dissolution (k)
 - Rate of permeation (Filon et al. 2004)
- Hapten binding with protein to form antigen

ROS Generation and ACD

- All cobalt powders generated $\bullet\text{OH}$ radicals
 - Pure cobalt highest
 - Supports plausibility of $\bullet\text{OH}$ generation on SC
- Radical generation and biomolecule alteration
 - Hapten induced-alternation in epidermis skin layer?

Summary

- Cemented carbide dusts in artificial sweat
 - Release Co^{2+}
 - Generate $\cdot\text{OH}$ radicals
- Potential for antigen formation and ACD
- Minimize skin exposure to Co in the workplace

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