Evidence on the Developmental and Reproductive Toxicity of Bisphenol A

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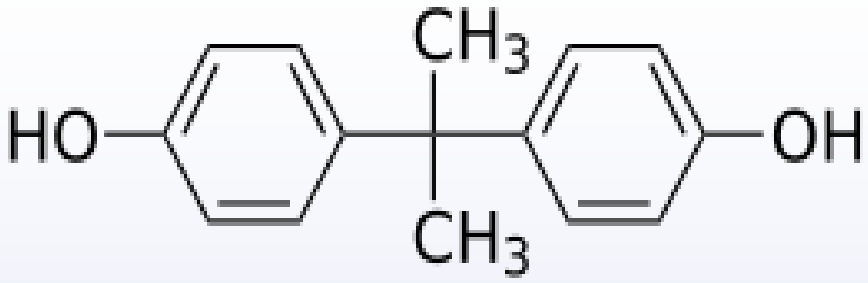
Chemical and physical characteristics of BPA



4,4'-dihydroxy-2,2-diphenyl propane

($C_{15}H_{16}O_2$)

Uses of BPA

- Produced in large quantities (2.3 billion pounds in 2004)
- Used primarily in the production of polycarbonate plastics and epoxy resins
  - Polycarbonate plastics used in:
    - food and drink packaging
      - water and infant bottles
    - compact discs
    - impact-resistant safety equipment
    - medical devices
  - Epoxy resins used as:
    - lacquers to coat metal products
      - food cans, bottle tops, and water supply pipes
    - dental sealants

Exposure to BPA

- The most common route of human BPA exposure is oral
  - BPA known to leach from:
    - dental composites
    - food containers (cans and polycarbonate plastic water bottles)
- Detectable levels of BPA in 92.6% of general population ≥ 6 years of age (0.4 µg/L to 149 µg/L, mean 2.6µg/L)
    - Child mean 4.5 µg/L
    - Adolescent mean 3.0 µg/L
    - Adult mean 2.6 µg/L
  - Neonates in intensive care 28.6 µg/L

General Toxicity of BPA

- Oral LD_{50}
  - >2,000 mg/kg in rat and mouse
- Dermal LD_{50}
  - >2,000 mg/kg in rabbit
- Acute inhalation
  - 6-hour exposure to 170 mg/m^3 produced slight and transient slight nasal tract epithelial damage in rats

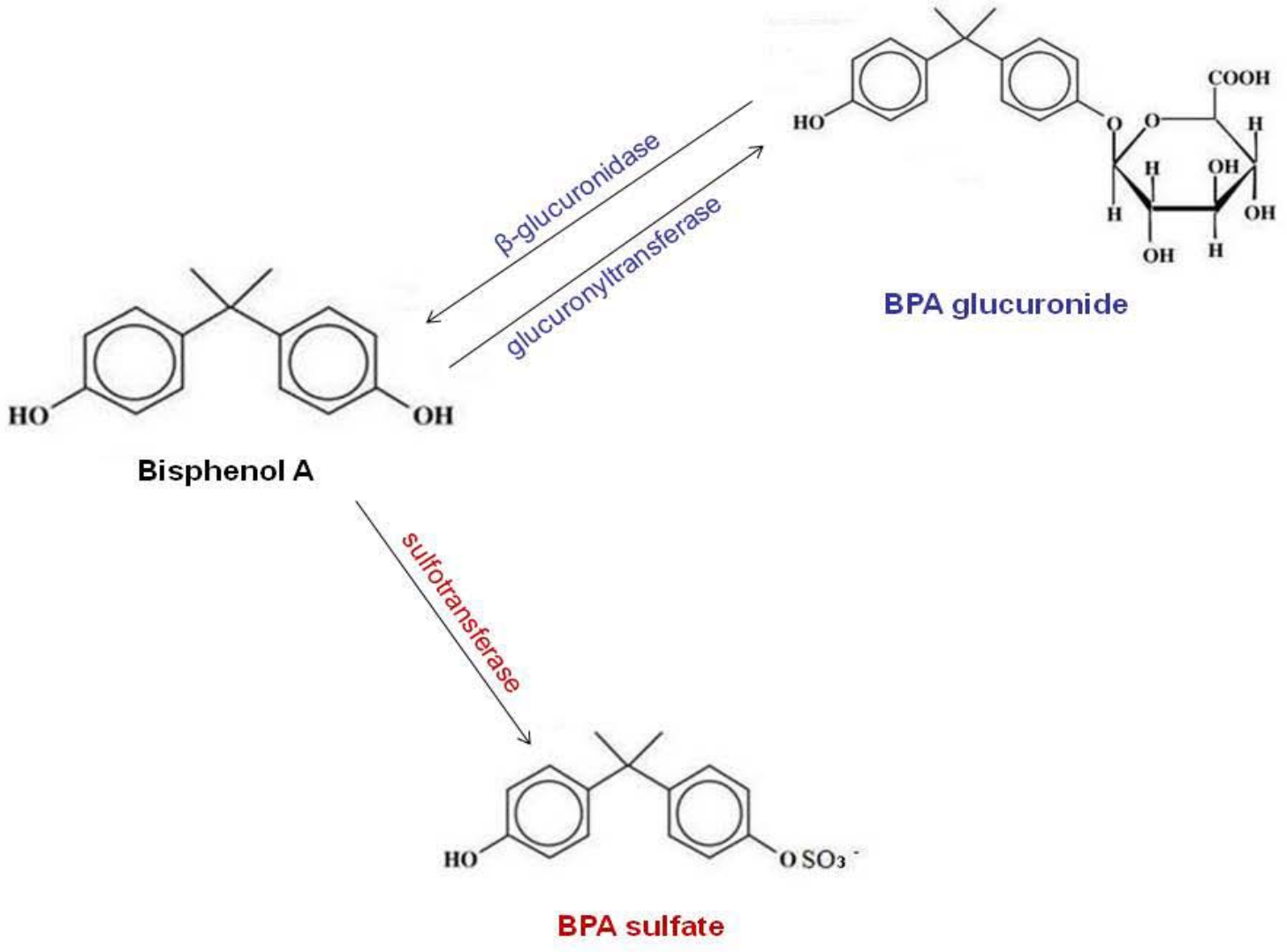
BPA Pharmacokinetics (PK)

- Absorption
- Metabolism
- Distribution
- Excretion
- Considerations for DART endpoints:
  - Routes of exposure
  - Age at exposure

BPA Pharmacokinetics (PK)

- Absorption
  - well absorbed by oral, i.p. or s.c. routes
  - less bioavailable from oral exposure than s.c. injection in rats and primates
  - similar bioavailability by oral and s.c. injection in neonatal mice at lower exposures

BPA Metabolism



BPA Pharmacokinetics (PK)

- Distribution
  - Widely distributed
  - Crosses placenta
  - Present in breast milk

BPA Pharmacokinetics (PK)

- Excretion
  - Rapidly excreted in urine
  - Undergoes enterohepatic recirculation in rodents
  - Higher levels of unconjugated BPA in rodents than humans

BPA Pharmacokinetics (PK)

- Considerations for DART endpoints:
  - Routes of exposure
  - Age at exposure
    - Maturation of glucuronidation and sulfation