# An assessment of exposure to benzophenones from cosmetics and potential health implications

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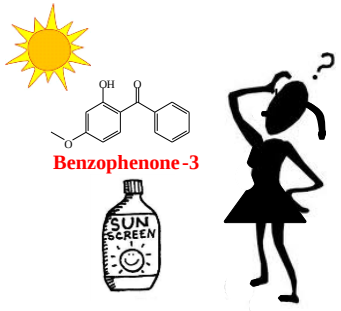
# What is in sunscreen products?

## Common UV filters in cosmetics

| | Generic name | Product name | Max concentration (%) | Spectrum of action | Approved |
|---|---|---|---|---|---|
| Chemical UV-filters | Benzophenone-3 | BP-3 | 6[b]–10[a,c] | UV-A, UV-B | EU, US, AU |
| | 2-Cyano-3,3-diphenyl acrylic acid | OCT | 10 | UV-B | EU, US, AU |
| | 3-Benzylidene camphor | 3-BC | 2 | UV-B | EU |
| | 3-(4-Methyl-benzylidene) camphor | 4-MBC | 4 | UV-B | EU, AU |
| | 2-Ethylhexyl 4-methoxy cinnamate | OMC | 7.5[b]–10[a,c] | UV-B | EU, US, AU |
| | Homosalate | HMS | 10[a]–15[b,c] | UV-B | EU, US, AU |
| | 2-Ethylhexyl 4-dimethylaminobenzoate | OD-PABA | 8 | UV-B | EU, US, AU |
| | 4-Aminobenzoic acid | PABA | 15[b,c] | UV-B | US, AU |
| Physical UV-filter | Titanium dioxide | | 25 | Physical | EU, US, AU |
| | Zinc oxide | | 25-no limit | Physical | US, AU |

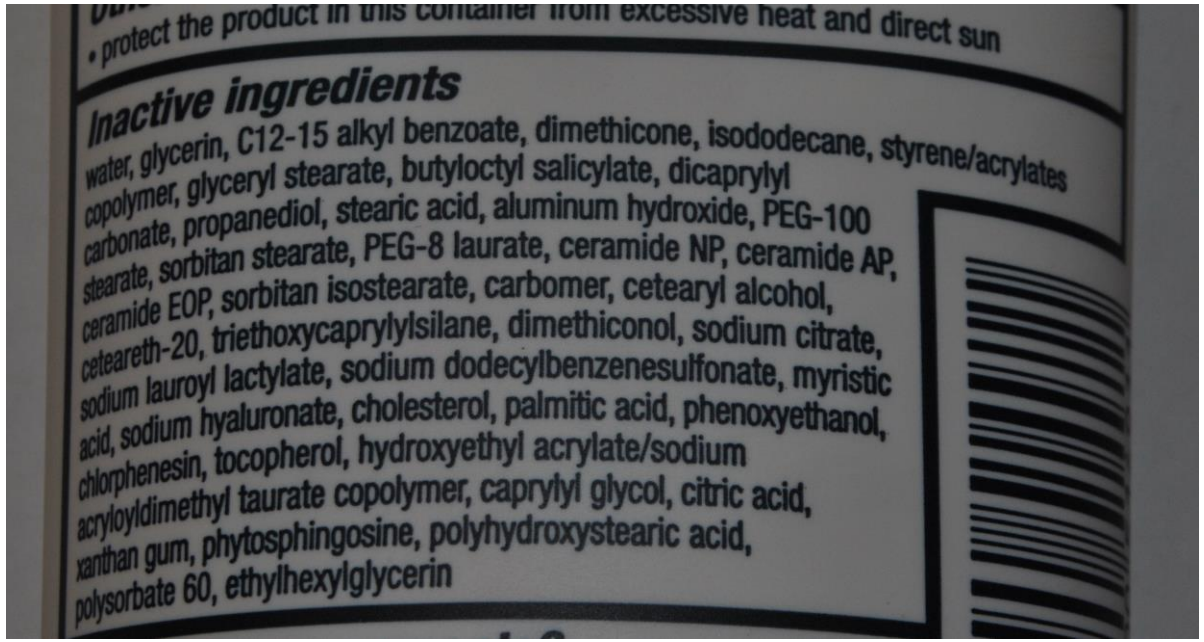
[a]List of permitted UV-filters in the Council Directive of the European Committee.
[b]List of permitted UV-filters in the US Food and Drug Administration monograph.
[c]List of permitted UV-filters in the Australian regulatory guidelines for over-the-counter medicines (ARGOM), by the therapeutic Goods Administration.

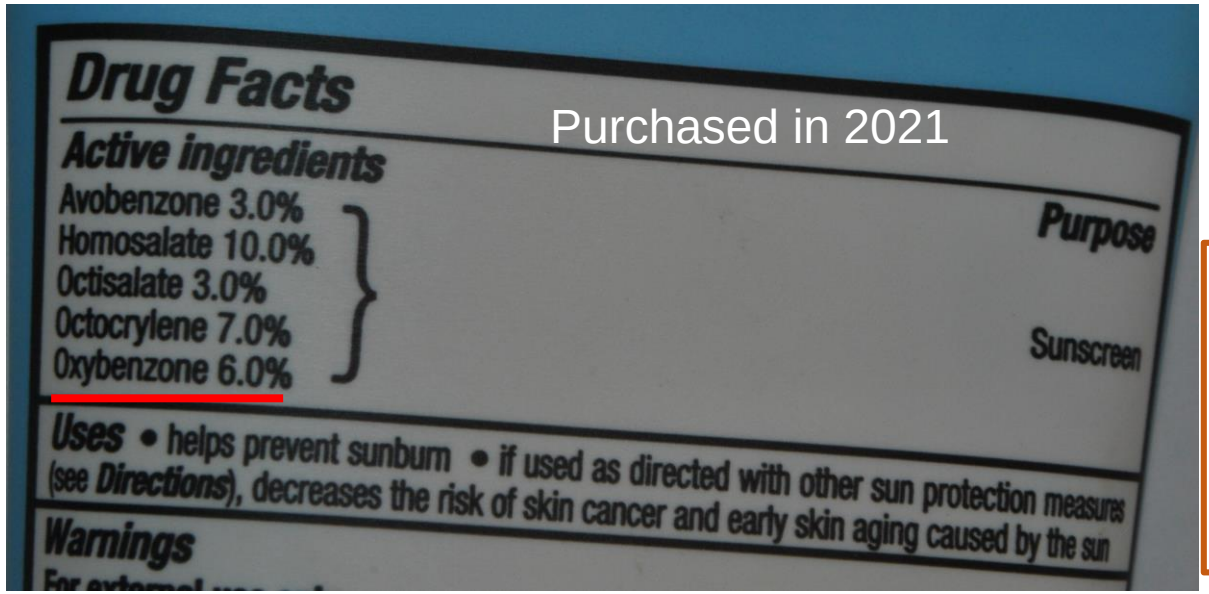
- **Organic (chemical) and inorganic (physical) UV filters**
- **FDA regulates them as OTC drugs; EU, AU as a cosmetic**




Krause et al. 2012 Int J Andrology, 35, 424-436

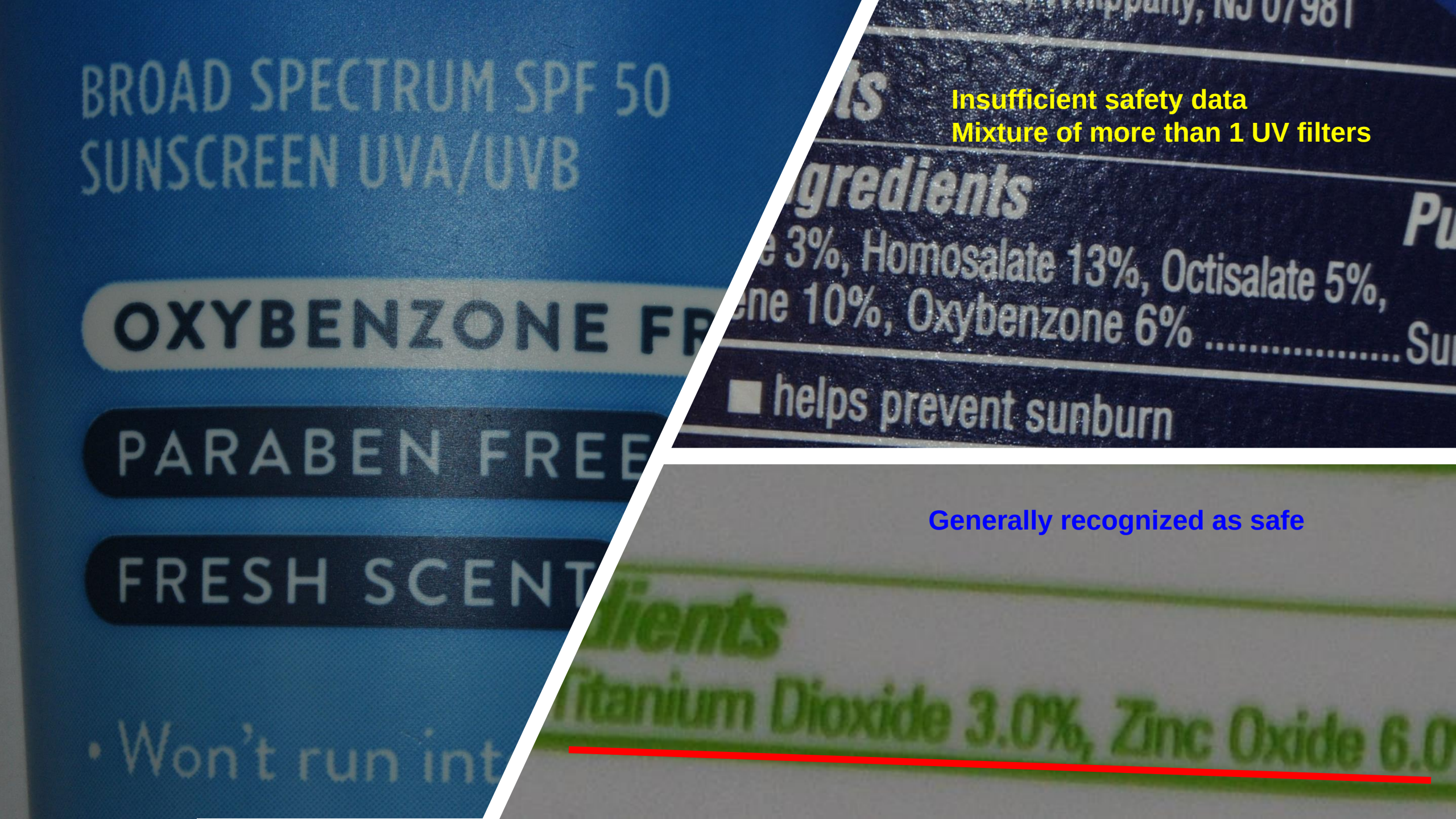
# Sunscreen products – active and inactive ingredients



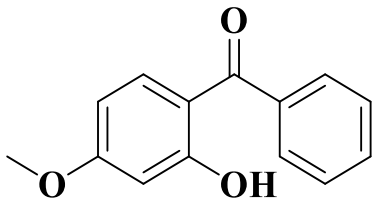


- **Active (20-30%) and inactive ingredients (50-60%; formulation stabilizers) and sensory enhancers (15-35%)**
- **16 active ingredients approved by the FDA; 8 commonly used – avobenzene, homosalate, octisalate, octinoxate, octocrylene, oxybenzone, TiO2 and ZnO**

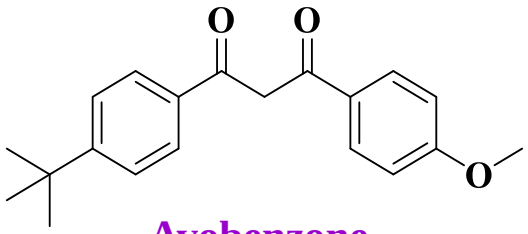

BROAD SPECTRUM SPF 50
SUNSCREEN UVA/UVB
OXYBENZONE FR
PARABEN FREE
FRESH SCENT
• Won't run int
Insufficient safety data
Mixture of more than 1 UV filters
gredients
3%, Homosalate 13%, Octisalate 5%,
ne 10%, Oxybenzone 6% .....
helps prevent sunburn
Generally recognized as safe
ients
Titanium Dioxide 3.0%, Zinc Oxide 6.0

# Benzophenone-3 (BP-3) or Oxybenzone or 2-Hydroxy-4-methoxy benzophenone

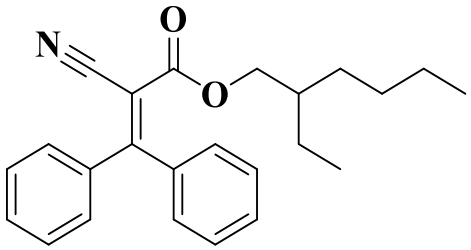
- UV radiation filter used in sunscreen, cosmetics, plastics and printing inks.
- Used in ¾ of the sunscreens marketed in the US in 2010s.
- 2016 - UV filters usage: 28,000 tons of each of 5 organic filters, octinoxate – 8600 tons; 5000 tons each of ZnO and $TiO_2$.
- Estrogenic and anti-androgenic – higher than BPA; 1000-100000 times lower than EE2



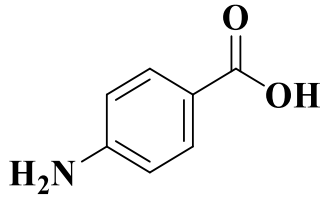
Benzophenone-3



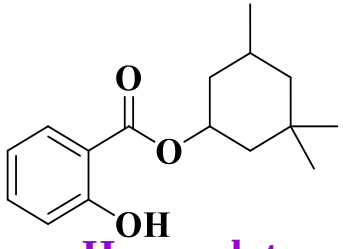
Avobenzone



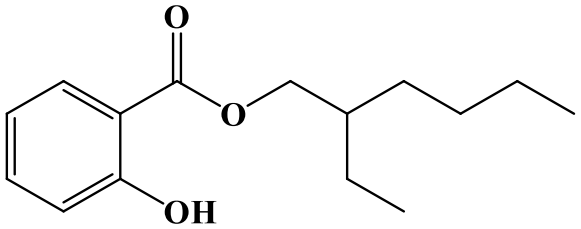
Octocrylene (cinnamate; can contain BP-3)



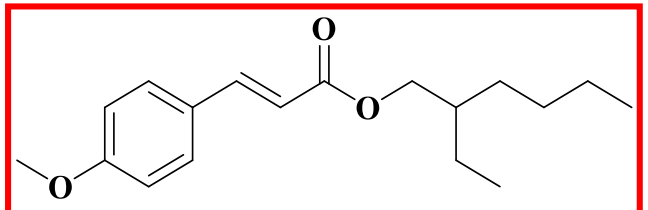
4-Aminobenzoic acid



Homosalate



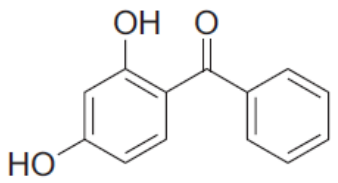
Octisalate



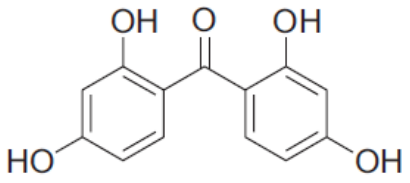
Octinoxate (cinnamate)

# Benzophenones

Parent chemicals

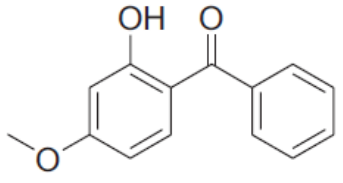



BP-1

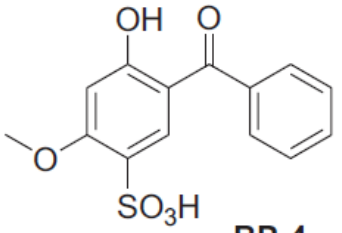



BP-2

herbicide

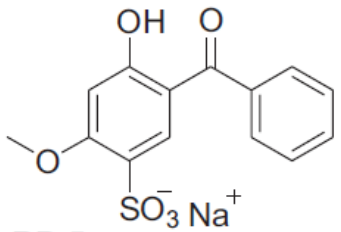



BP-3

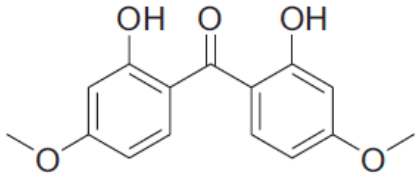



BP-4

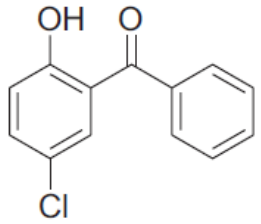
PCP and hair care




BP-5

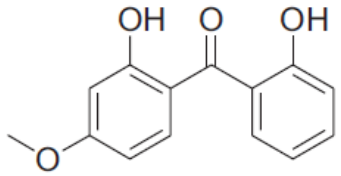



BP-6

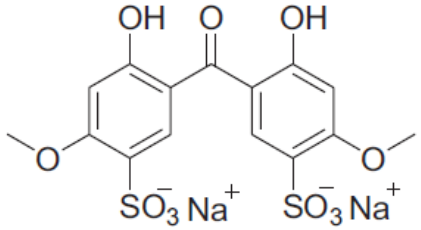



BP-7

fungicide




BP-8

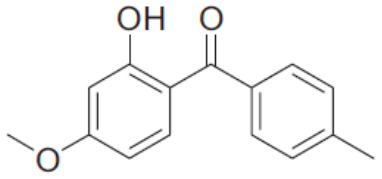



BP-9

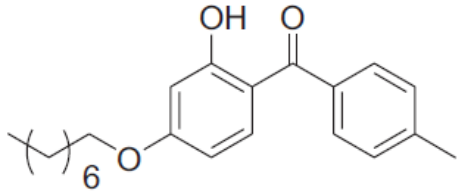
insecticide

BP-2 & BP-6

BP-11

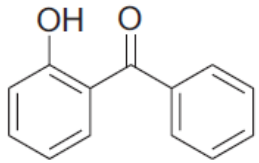



BP-10

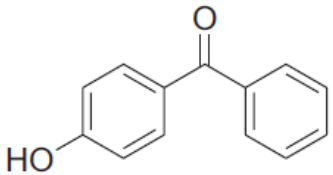



BP-12

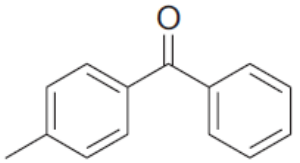
Metabolites




2-OH BP




4-OH BP




4-Me BP

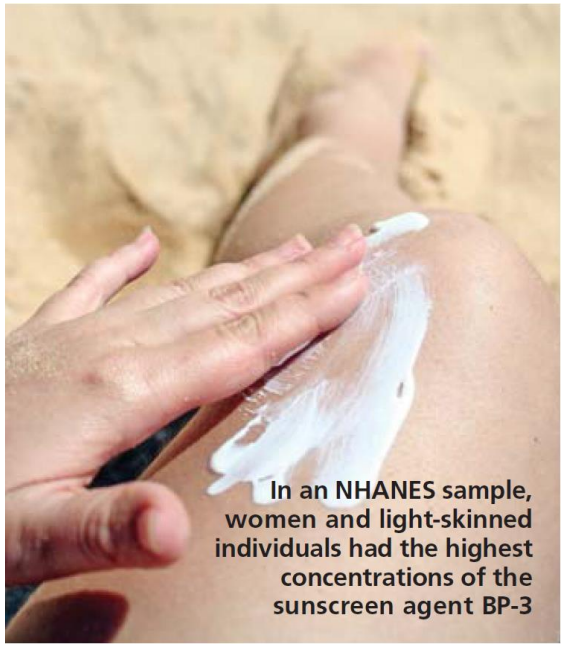
Environmental Health Perspectives • VOLUME 116 | NUMBER 7 | July 2008

# Concentrations of the Sunscreen Agent Benzophenone-3 in Residents of the United States: National Health and Nutrition Examination Survey 2003–2004

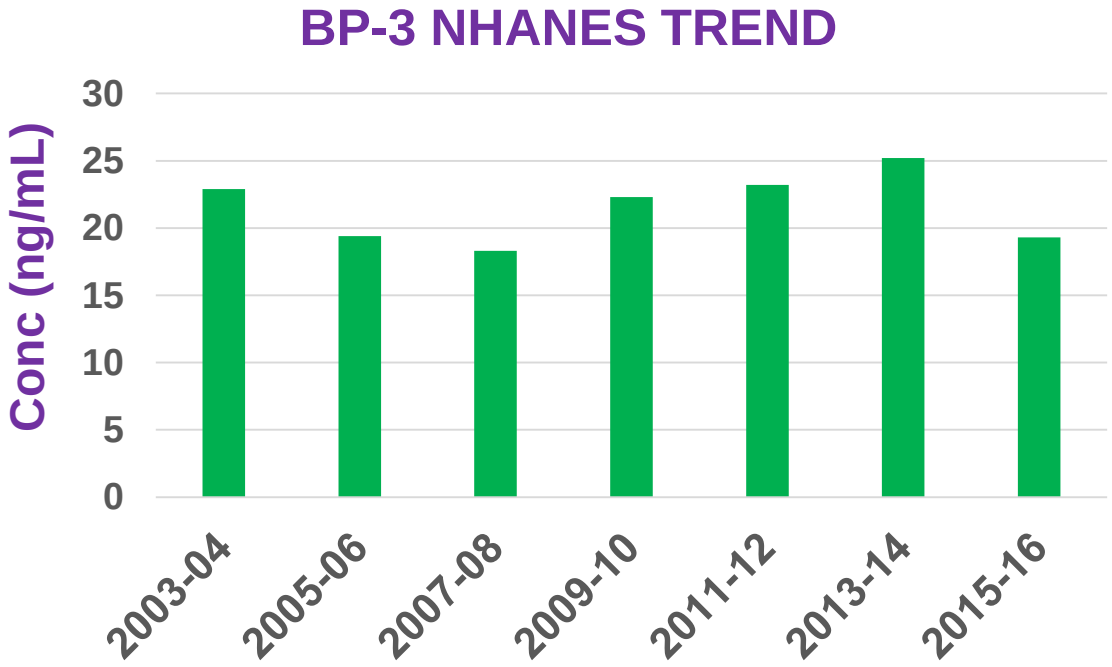
*Antonia M. Calafat, Lee-Yang Wong, Xiaoyun Ye, John A. Reidy, and Larry L. Needham*

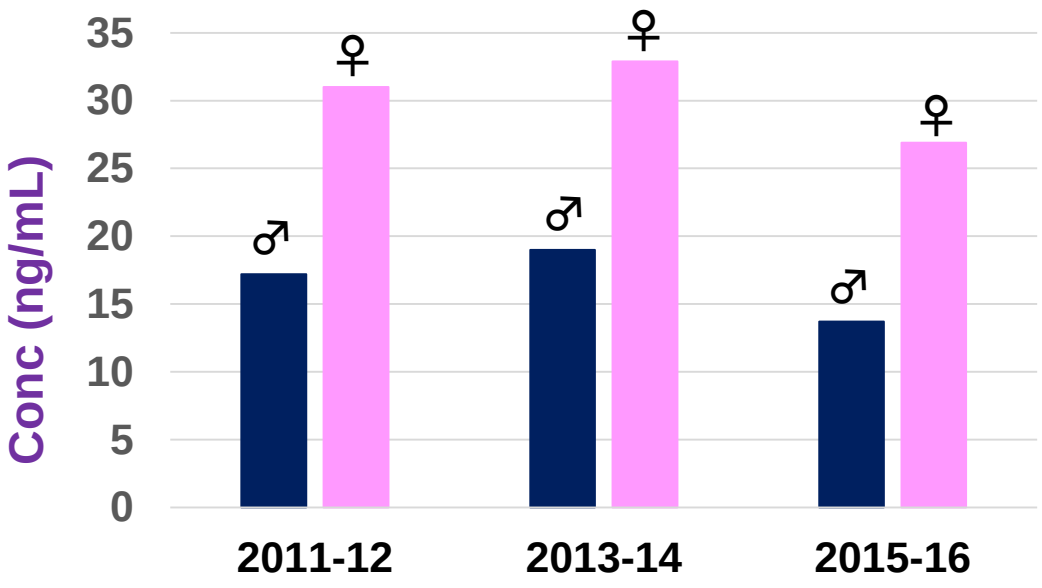
Division of Laboratory Sciences, National Center for Environmental Health, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

- **The National Health and Nutrition Examination Survey (NHANES) in 2015-16 urinary geomean concentration: 19.3 µg/L (or ng/mL)**
- **95th percentile 930 µg/L.**



In an NHANES sample, women and light-skinned individuals had the highest concentrations of the sunscreen agent BP-3




Data from CDC – NHAHES reports

Picture from EHP Vol 116, 2008, Page A306

PAPER 2010, 2, 707-713 www.rsc.org/methods | Analytical Methods

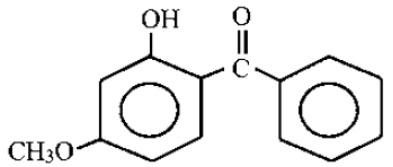
# Analysis of five benzophenone-type UV filters in human urine by liquid chromatography-tandem mass spectrometry

Tatsuya Kunisue,[a] Qian Wu,[a] Shinsuke Tanabe,[b] Kenneth M. Aldous[a] and Kurunthachalam Kannan*[ac]

*Received 23rd December 2009, Accepted 15th March 2010*

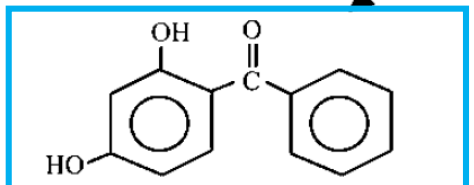
- **BP-3 metabolized to BP-1 and BP-8 and several other BPs; metabolites are more estrogenic**
- **Challenges in acquiring analytical standards, for metabolites**
- **Many other BPs remain not analyzed**
- **Studies reported skin penetration, as high as 20%; systemic absorption substantial. 1.2-8.7% excreted in urine**

## Analysis of 5 BPs

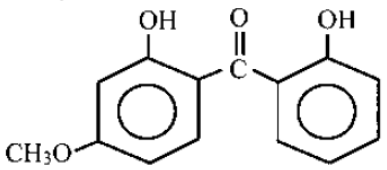



2-hydroxy-4-methoxybenzophenone
(2OH-4MeO-BP, BP-3)

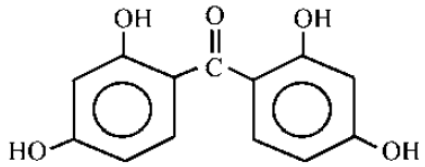
demethylation * * hydroxylation



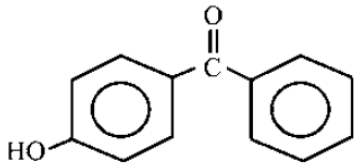

2,4-dihydroxybenzophenone
(2,4OH-BP, BP-1)



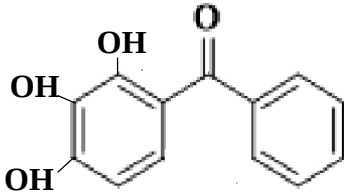

2,2'-dihydroxy-4-methoxybenzophenone
(2,2'OH-4MeO-BP, BP-8)




2,2',4,4'-tetrahydroxybenzophenone
(2,2',4,4'OH-BP, BP-2)




4-hydroxybenzophenone
(4OH-BP)



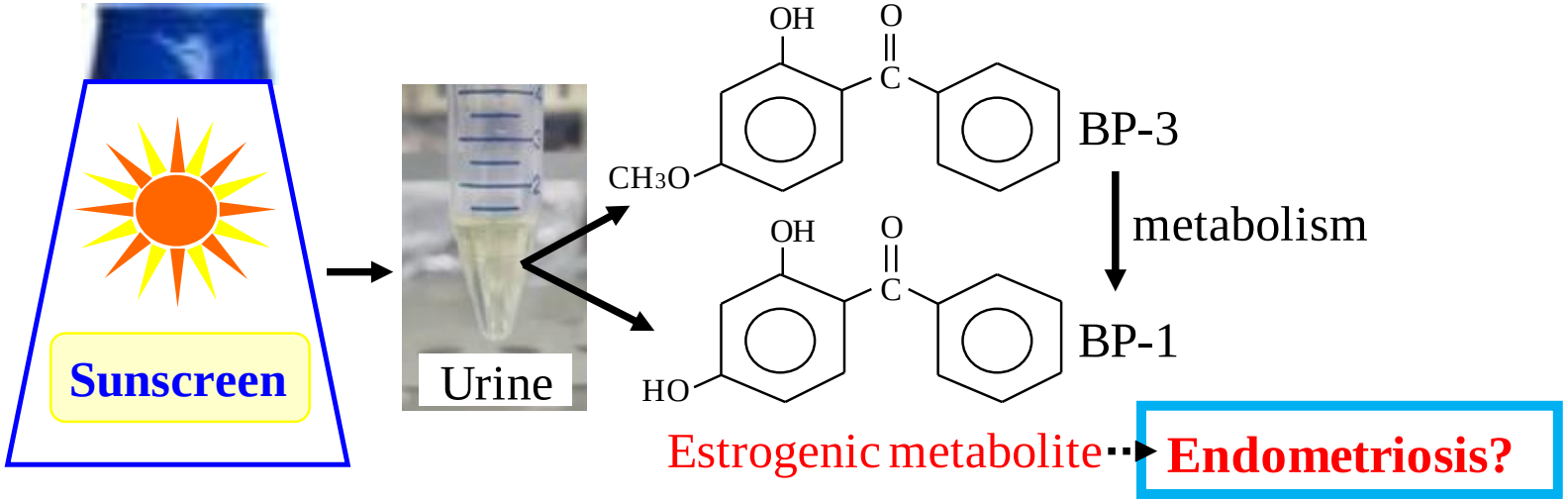

2,3,4-trihydroxybenzophenone
(THB)

Environmental Science & Technology
2012, 46, 4624-4632
Article
pubs.acs.org/est

## Urinary Concentrations of Benzophenone-type UV Filters in U.S. Women and Their Association with Endometriosis

Tatsuya Kunisue,[†] Zhen Chen,[‡] Germaine M. Buck Louis,[‡] Rajeshwari Sundaram,[‡] Mary L. Hediger,[‡] Liping Sun,[‡] and Kurunthachalam Kannan[†,§,*]

# Benzophenone Exposure and Endometriosis




**Showed the presence of benzophenones other than BP-3, in urine for the first time**

**BP-1 concentrations were similar to those of BP-3**

**BP-1 associated with endometriosis**

**Exposure to high levels of 2,4OH-BP (BP-1) was associated with endometriosis in women in an epidemiological study involving 600 women**

Environmental Science & Technology
2013, 47, 12532-12538
Article
pubs.acs.org/est

# Exposure in children

## Characteristic Profiles of Benzonphenone-3 and its Derivatives in Urine of Children and Adults from the United States and China

Lei Wang[†,‡] and Kurunthachalam Kannan[*,†]

| Conc (ng/mL) | BP-3 in total forms | BP-3 in free form | BP derivatives in total forms | | | |
|---|---|---|---|---|---|---|
| | | | 4-OH-BP | 2,4-diOH-BP (BP-1) | 2,2',4,4'-tetraOH-BP (BP-2) | 2,2'-diOH-4-MeO-BP (BP-8) |
| **Albany, NY, children (n=38)** | | | | | | |
| GM[a] | 9.97 | 0.290 | 0.913 | 4.21 | 0.238 | 0.258 |
| Median | 8.34 | 0.181 | 0.768 | 6.547 | 0.141 | 0.217 |
| DR %[b] | 97 | 76 | 100 | 87 | 29 | 68 |
| **Albany, NY, adults (n=30)** | | | | | | |
| GM | 15.7 | 1.04 | 0.330 | 4.37 | 0.289 | 0.161 |
| Median | 16.7 | 0.986 | 0.425 | 5.97 | 0.231 | 0.148 |
| DR % | 100 | 73 | 93 | 100 | 60 | 53 |

Children (3-10 years) and adults (15-66 years) from Albany, NY, 2011-2012.

BP-3 in conjugated form

BP-3 levels in Albany children were lower than those in adults, but BP-1 levels were similar.

Concentrations of BP-3 were significantly correlated with other BP derivatives.

# Excerpts from Human Biomonitoring Studies

- **Urinary concentrations of BPs were approximately an order of magnitude higher than those in serum (Zhang/Kannan et al. 2013).**
- **BPs can cross placental barrier; cord serum levels were similar to maternal serum levels; found in amniotic fluid (Song/Kannan et al. 2020).**
- **BP-1 and BP-3 were found in seminal plasma (median: 0.35 and 1.42 ng/mL, respectively) (Buck Louis et al. 2018).**
- **BP-3 was found in human adipose tissue at conc as high as 4940 ng/g wet wt (dermal application) (Wang/Kannan 2015).**
- **BP-3 was measured in breast tissue at concentrations as high as 26 ng/g (Barr et al. 2018).**
- **BP was found in U.S. breast milk at median concentrations of 9 ng/mL (Liu and Mabury 2019) and BP-3 at <LOD-10 ng/mL (Hines et al. 2015). Infant exposure = 9 ng/mL X 750 mL/d = 6750 ng/d or 1125 ng/kg bw/d (for a bw of 6 kg)**

Environmental Science & Technology
2014, 48, 4103-4109
Article
pubs.acs.org/est

# BP-3 in personal care products

## Widespread Occurrence of Benzophenone-Type UV Light Filters in Personal Care Products from China and the United States: An Assessment of Human Exposure

Chunyang Liao[†] and Kurunthachalam Kannan*[,†,‡]

| PCP category (ng/g) | n | GM | median | Range |
|---|---|---|---|---|
| Toothpaste | 5 | 71 | 140 | <1-785 |
| Hair care (shampoo/conditioner) | 15 | 115 | 73 | 2.4-6800 |
| Body wash (shower and facial cleanser) | 16 | 286 | 439 | 5.2-8200 |
| Sanitary products (odor eliminator) | 2 | 25500 | 33800 | 11600-56000 |
| Skin lotions (body/skin lotion, deodorant, sunscreen, eye cream and face cream) | 64 | 3000 | 1100 | 11-1285000 |
| Makeup products (liquid foundation, nail polish, lip cream, fragrance) | 12 | 2300 | 4600 | 34-815000 |

114 products, Albany, NY; purchased in 2012-2013; MTBE extraction, LC-MS/MS analysis

Sunscreens 100000 to 1280000 ng/g

Highest levels (ng/g)
Makeup cream: 800000
Deodorant: 37000
Lipstick: 180
Eye cream: 7000
Shampoo: 6800
Toothpaste: 700

# Dermal exposure dose (ng/d) to BP-3 from PCPs (adult females)

**Median exposure dose: 24.4 µg/d**

**For a person weighing 70 kg= 349 ng/kg bw/d**

**Skin lotions and face creams accounted for >80% of total exposures**

**Uncertainties exist (likely an underestimate)**

| Category | Daily usage (g/day) | Retention factor | GM (ng/d) | 95th percentile |
|---|---|---|---|---|
| Shampoo | 12.8 | 0.01 | 25.6 | 586 |
| Hair conditioners | 13.8 | 0.01 | 6.96 | 36.9 |
| Body shower | 14.5 | 0.001 | 1.30 | 9.55 |
| Facial cleanser | 4.06 | 0.001 | 1.97 | 30.4 |
| Toilet soaps (China) | 4.80 | 0.01 | 6.32 | 37.8 |
| Body lotions | 8.69 | 1.00 | 18100 | 4400000 |
| Face creams | 2.05 | 1.00 | 2200 | 54700 |
| Liquid foundations | 0.67 | 1.00 | 4060 | 705000 |
| Total dose | | | 24400 | 5160000 |

Liao and Kannan, 2014

# Relative Contribution of PCPs to BP-3 Exposure

**Total Daily Exposure Dose (extrapolated from urinary concentrations) =**

**Median concentration in urine (µg/L) x daily urine excretion rate (L/d)**

**30.7 (µg/L) X 1.5 (L/d) = 46.1 µg/d (70 kg: 659 ng/kg bw/d)**

Median exposure dose to BP-3 from PCPs = 24.4 **µg/d (for adult females)**

**Contribution of PCP to exposure = 24.4/46.1 X 100 = 53%**

Urine conc from Calafat et al. 2008

# BP-3 exposure from sunscreen usage – A day at the beach

- Median concentration of BP-3 found in 15 sunscreen products = 893000 ng/g or 893 µg/g or 0.893 mg/g (Liao and Kannan, 2014)

- 1 full day at beach, 3 oz (85 g) used (3 applications in 6 h at 1 oz every 2 h) = 76 mg BP-3 exposure

- For a person weighing 75 kg = 1.0 mg/kg bw/d at beach

- At 10% absorption = 0.1 mg/kg bw/d or 100 µg/kg bw/d (for BP-3).
- EFSA TDI for BP is 30 µg/kg bw/d.

Science of the Total Environment 537 (2015) 304–308

Contents lists available at ScienceDirect

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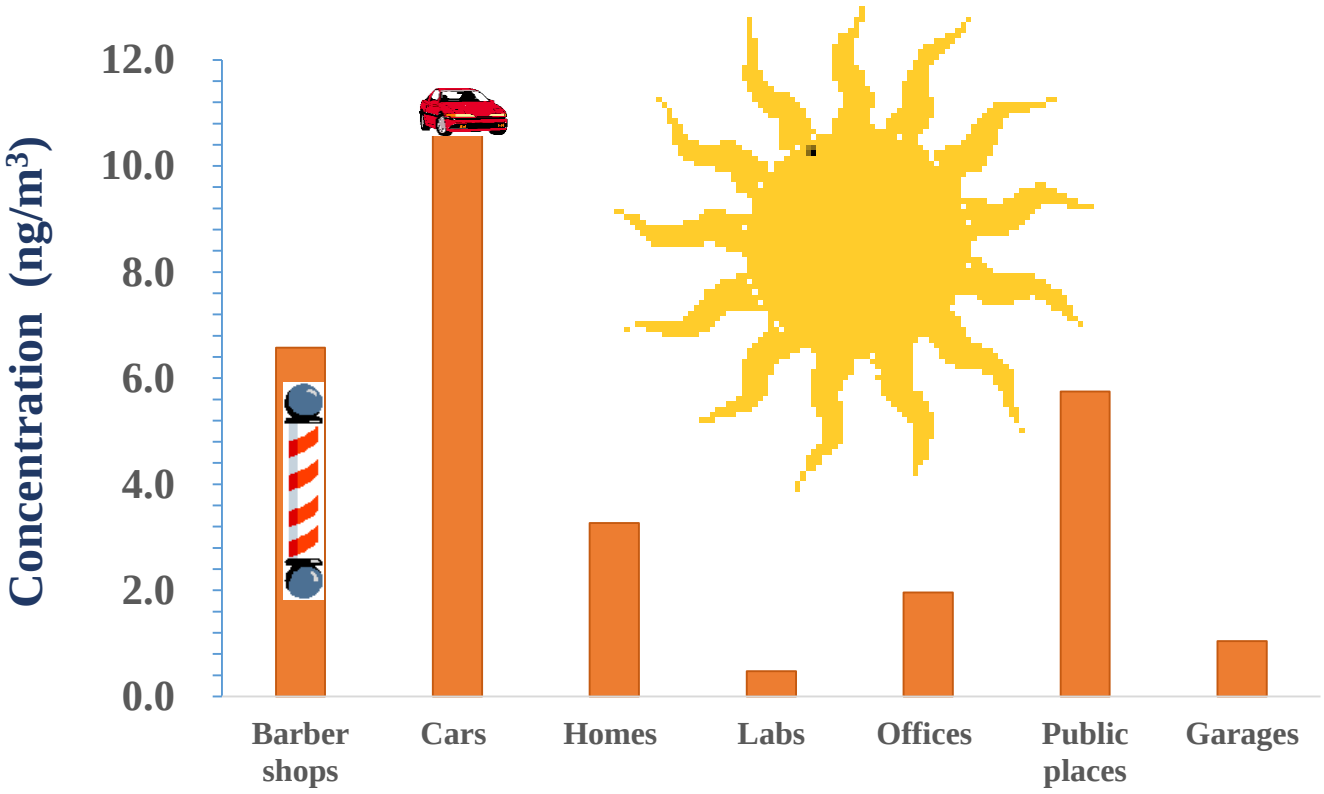
# Occurrence of benzophenone-3 in indoor air from Albany, New York, USA, and its implications for inhalation exposure

Yanjian Wan [a,b], Jingchuan Xue [a], Kurunthachalam Kannan [a,c,*]




# BP-3 in indoor air and inhalation exposure

81 indoor air samples from Albany, NY, in 2014

BP-3 measured at 0.19-72 ng/m$^3$, highest in cars (GM: 2.67 ng/m$^3$)

Other BPs were not found.

Cars > saloons > malls > homes > offices > garages

Median Inh exposure: 36.5 ng/d (adults); minor pathway

# BP-3: Indoor dust exposure

ENVIRONMENTAL Science & Technology

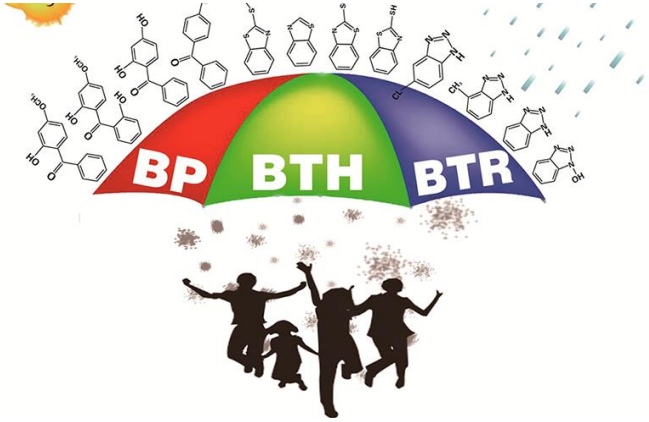
2013, 47, 4752-4759

Article

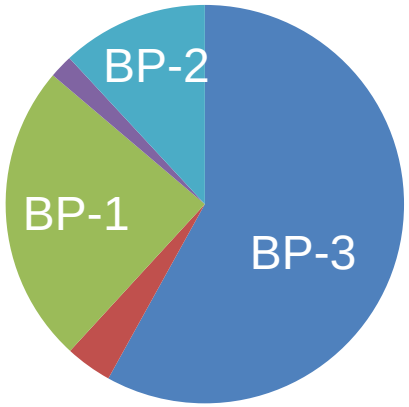
pubs.acs.org/est

## Benzotriazole, Benzothiazole, and Benzophenone Compounds in Indoor Dust from the United States and East Asian Countries

Lei Wang,[†,‡] Alexandros G. Asimakopoulos,[†] Hyo-Bang Moon,[§] Haruhiko Nakata,[∥] and Kurunthachalam Kannan[†,*]




| ng/g | BP-3 | 4OH-BP | BP-1 | BP-8 | BP-2 | ΣBPs |
|---|---|---|---|---|---|---|
| Median | 243 | 15.8 | 102 | 8.0 | 49.8 | 612 |
| Range | 65-1190 | 3.5-689 | 3.7-36400 | <1-56 | <1-1230 | 121-37400 |



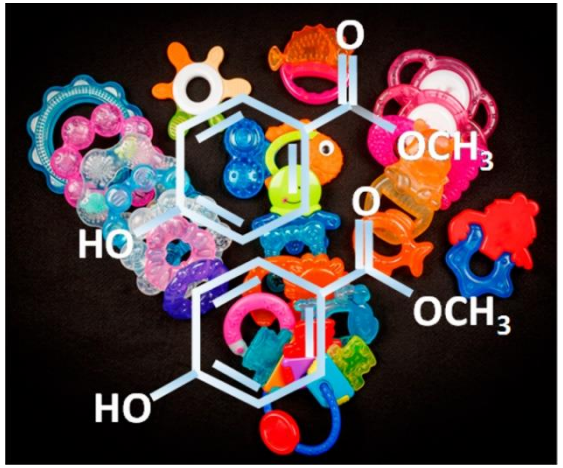

**40 house dust, Albany, NY, 2006-2010.**
**Median concentrations: 612 ng/g; BP-3 and BP-1 - 60% of the total.**
**Median dust ingestion exposure to BP-3: Adults 20 ng/d (MINOR)**

# BP-3: Other sources of exposure

**Clothing – reported in infant clothing (median conc: 5.9 ng/g [<2-157]), Minor contributor**

**Pantyhose – median: 205 ng/g [3.5-2410000]), Minor contributor**

**Infant teethers – median amount leached 5.4 ng [0.59-297 ng]), 2 h of extraction in water and meOH.**




**DIET, NOT KNOWN, BUT SEAFOOD HAS BEEN SHOWN TO CONTAIN BP-3 (oyster from Chesapeake Bay – 118 ng/g max)**

**Besides BP-3 other BPs were found in textiles, teether**

Xue/Kannan, 2017, EST 51, 5279; Li/Kannan, 2018, EST 52, 10812; Asimakopoulos/Kannan, 2016, EST 50, 13539

# Summary

- **Cosmetics and personal care products are the major sources of daily exposure to BP-3 in the general population.**
- **Indoor air, dust ingestion and textiles are minor sources of exposure to BP-3 (<5% of the total dose).**
- **Studies describing occurrence of other BPs (BP-1, BP-2, BP-4 etc) in cosmetics are not available.**
- **Contribution of diet to total BP exposures is not known.**
- **Daily BP-3 exposure doses from cosmetics and PCPs are 10-100 times below the tentative reference value (TDI) suggested by the EFSA.**
- **BP exposure dose from sunscreen use on a beach day can exceed the EFSA reference value.**

# Thank you

# Sunscreen ingredients

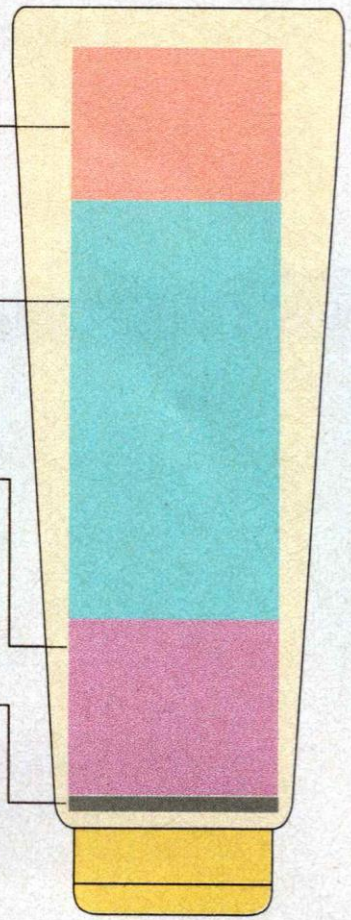
**These are the ingredients in most sunscreens.**

**Active ingredients, 20%**
Compounds that filter the sun, such as avobenzone and zinc oxide

**Formulation stabilizers, 55%**
Solvents, preservatives, thickening agents, and emulsifiers

**Sensory enhancers, 23%**
Compounds that improve the feel or scent of the formula, such as fragrances, moisturizers, and emollients

**Added extras, 2%**
Compounds that don't influence how the sunscreen works, such as aloe and blue-light protectors



**Sources:** Perry Romanowski, various sunscreen companies.
**Note:** Percentages are approximate.

CEN Jul 26, 2021 page 22-23

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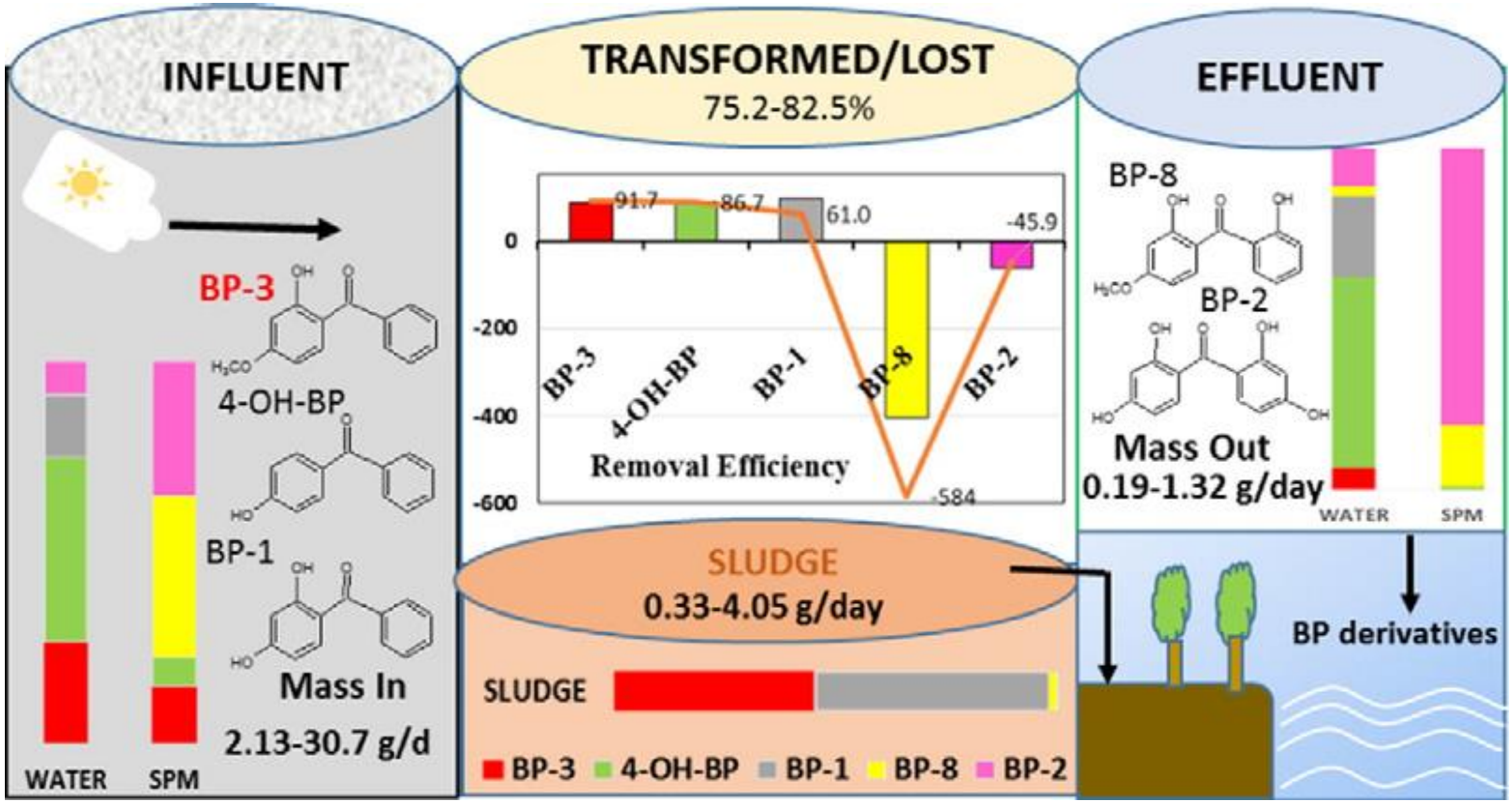
# Mass loading and emission of benzophenone-3 (BP-3) and its derivatives in wastewater treatment plants in New York State, USA

Wei Wang [a], Kurunthachalam Kannan [a,b,*]




- Mass loading and fate of benzophenone UV filters were studied in two WWTPs.
- Sorption to sludge accounted for 13.2–15.7% of ΣBPs' mass reduction
- A negative removal efficiency was found for BP-8 and BP-2
- The mass loading of ΣBPs in WWTPs was ~102–276 mg/d/1000 people
- ~55–94 mg/d/1000 people of ΣBPs was discharged into the environment from WWTPs.