Human health characterization factors of TiO$_2$ nanoparticles in indoor and outdoor environments

Martina Pini
Nano-TiO₂ properties

Self-cleaning coatings

Photo-induced hydrophylic TiO₂ surface

Air depollution

Pollution removal mechanism of TiO₂ photocatalysis
Nanotoxicity assessment

• Uncertainties and knowledge gaps on behavior and toxicity of nanoparticles.

*We cannot remain silent!!*

• The LCA methodology can help to determine the potential impacts of nanoproducts and nanomaterials on human health and environment.


Aim of the project

• Determination of human characterization factors of TiO$_2$ nanoparticles.
• Focus on Indoor and Outdoor environments.
• USEtox™ model.

Collaboration

EMPA - Swiss Federal Laboratories for Materials Science and Technology, Technology and Society Laboratory, ERAM Group St. Gallen, Switzerland

Conference


Publication

USEtox™ model (1)

CF is a quantitative representation of the hazardousness or impact potential related to the emission of pollutant.

CF can be estimated through three steps: exposure, fate and effect.

• $\text{CF} = \text{XF} \times \text{FF} \times \text{EF} \ [\text{cases/kg}_{\text{emitted}}]$

  ▶ **XF (Exposure Factor)** is the fraction of mass taken in by the population every day $[\text{Kg}_{\text{intake}} \times \text{day}^{-1} \times \text{Kg}_{\text{in compartment}}^{-1}]$

  ▶ **FF (Fate Factor)** links the pollutant mass in a given compartment to the quantity released into any considered compartment. It accounts the multimedia transport between the environmental media (air, soil, water, run-off system, etc.) $[\text{Kg}_{\text{in compartment}} \times \text{kg}_{\text{emitted}}^{-1} \times \text{day}]$

  ▶ **EF (Effect Factor)** relates the quantity taken in by the population (via inhalation) to the probability of adverse effects of the pollutant in human $[\text{cases/kg}_{\text{intake}}]$
CF is a quantitative representation of the hazardousness or impact potential related to the emission of pollutant. CF can be estimated through three steps: exposure, fate and effect.

- \( \text{CF} = \text{XF} \times \text{FF} \times \text{EF} \) [cases/kg\text{emitted}]

- \( \text{iF} = \text{XF} \times \text{FF} \) [kg\text{intake}/kg\text{emitted}]

The fraction of an emission emitted into a compartment that is taken in by the exposed population through a given intake pathway.
Assumptions

• One-box model
• Steady state conditions
• Direct human exposure (e.g. inhalation of air, ingestion of water)
• Compartment: air
Indoor intake Fraction

\[ iF = \frac{\text{INH} \times \text{POP}}{V \times m \times k_{ex}} \]

- **\( \text{INH} \)** is the average human inhalation rate = \(13 \text{ m}^3\text{day}^{-1} \) USEtox™
- **\( \text{POP} \)** is the indoor exposed population (occupational exposure)
- **\( V \)** is the indoor volume
- **\( m \)** is the mixing factor (unitless) = 1 Humbert et al., 2011
- **\( k_{ex} \)** is the air exchange rate (h\(^{-1}\)) = 3 h\(^{-1}\) Humbert et al., 2011

**Independent of the studied substance**
Outdoor intake Fraction

\[ iF = \frac{INH \times POP \times FF}{V} \]

- \( INH \) is the average human inhalation rate = 13 m\(^3\)day\(^{-1}\)
- \( POP \) is the exposed population → Switzerland: 8112200 inhabitants
- \( V \) is the outdoor volume:
  - area of Switzerland: 41285 km\(^2\).
- \( FF = -\bar{K}^{-1} \), where \( \bar{K} \) is the rate coefficient matrix, which accounts transport and removal processes between the environmental media.
SimpleBoxModel4Nano (SB4N) assesses the ENPs transport and removal rates in and across air, rain, surface waters, soil, and sediment compartments.

Outdoor FF

One box model and Steady state conditions
Rate constant values for nano-TiO$_2$ calculated by SB4N

Meesters and co-author estimated the transport and removal processes for nano-TiO$_2$ considering the input parameters and systemic dimensions of Mueller and Nowack, 2008 study.

- Area, Height, Volume of Atmosphere, Soil and Water
- TiO$_2$-NPs radius, TiO$_2$-NPs mass density, Aggregation and Attachment efficiency
# Outdoor intake Fraction

System Matrix of the rate constants *for each compartment and physical-chemical form* $\bar{K}$ [day$^{-1}$]

<table>
<thead>
<tr>
<th>$k$ [day$^{-1}$]</th>
<th>Free in atmosphere</th>
<th>Agg in atmosphere</th>
<th>Att in atmosphere</th>
<th>Free in rain</th>
<th>Agg in rain</th>
<th>Att in rain</th>
<th>Free in soil</th>
<th>Agg in soil</th>
<th>Att to soil</th>
<th>Free in water</th>
<th>Agg in water</th>
<th>Att in water</th>
<th>Free in sediment</th>
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<th>Att in sediment</th>
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<td>kdepRWfree</td>
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<td>kdepRWagg</td>
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</table>

Matrices: $\bar{FF} = - \bar{K}^{-1}$

$\bar{IF} = \bar{XF} \cdot \bar{FF}$
Effect Factor

1) The **human-toxicological** EF is calculated under the assumption of linearity in concentration–response up to the point in which the life time disease probability is 0.5.

2) \[ EF = \frac{0.5}{ED_{50h}^{lifetime}} \text{[cases/kg intake]} \]

3) \[ ED_{50h}^{lifetime} = \frac{ED_{50}^{a,t,j} \times BW \times LT \times N}{AF_a \times AF_t} \]

**Carcinogenic effects**

\( ED_{50}^{a,t,j} \) is the daily effect dose for animal \( a \), time duration \( t \) and exposure route \( j \) that causes a disease probability of 50% [mg*kg\(^{-1}\)*day\(^{-1}\)].

- \( AF_a \) = extrapolation factor for interspecies differences
- \( AF_t \) = extrapolation factor for differences in time of exposure
  (2 for subchronic to chronic exposure and 5 for subacute to chronic exposure)
- BW = body weight of humans
- LT = average lifetime of humans; N = number of days per year

**Non-carcinogenic effects**

\( ED_{50}^{a,t,j} \) can also be extrapolated from NOAEL (no-observed adverse effect level) and NOAEL from LOAEL (low-observed adverse effect level).

\[ ED_{50}^{a,t,j} = NOAEL^{a,t,j} \times AF_N \quad AF_N = 9 \text{ (Huijbregts et al., 2005)} \]

\[ NOAEL^{a,t,j} = LOAEL^{a,t,j} / AF_L \quad AF_L = 4 \text{ (Huijbregts et al., 2005)} \]
## Carcinogenic and Non-carcinogens effects (1)

<table>
<thead>
<tr>
<th>Human Effects</th>
<th>References</th>
<th>Type of study and toxicity indicator</th>
<th>Toxicity value</th>
</tr>
</thead>
</table>
| Carcinogens     | **NIOSH**
|                 | National Institute for Occupational Safety and Health, 2011               | • Sub-chronic oral study on rat.
|                 |                                                                           | • Benchmark dose associated with a 4% inflammatory response = 0.0144 m^2_{TiO_2}/g_{rat-lung}            | **ED_{4}^{rat,s-c,inh}** 0.3 mg/kg-bw/day |
| Non-carcinogens | **SCCS**
|                 | Scientific Committee on Consumer Safety, 2013                            | • Sub-chronic oral study on mice.
|                 |                                                                           | • NOAEL.                                                                                             | **ED_{50}^{mice,s-c,inh}** 62.5 mg/kg-bw/day |
Carcinogenic and Non-carcinogens effects (2)

**Indoor**
- N = number of working days per year = 240 days/year (*European labour law, 99/70/EC*)
- LT = 45-years working lifetime (*NIOSH, 2011*)

**Outdoor**
- N = number of day per year = 365 days/year
- LT = average lifetime of humans = 70 years

<table>
<thead>
<tr>
<th>Human health effect</th>
<th>INDOOR $E_F_i$</th>
<th>OUTDOOR $E_F_o$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carcinogenic</td>
<td>1.45</td>
<td>6.11E-1</td>
</tr>
<tr>
<td>Non-carcinogenic</td>
<td>1.72E-2</td>
<td>7.26E-3</td>
</tr>
</tbody>
</table>
Characterization Factors nano-\(TiO_2\)

\[CF = iF \times EF \text{ [cases/kg}_{\text{emitted}}]\]

<table>
<thead>
<tr>
<th>Human Health effect</th>
<th>(iF_i)</th>
<th>(EF_i)</th>
<th>(CF_i) [cases/kg(_{\text{emitted}})]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carcinogenic (ED_4)</td>
<td>4.10E-04</td>
<td>1.45</td>
<td>5.93E-04</td>
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<tr>
<td>Non-carcinogenic NOAEL</td>
<td>4.10E-04</td>
<td>1.72E-2</td>
<td>7.04E-06</td>
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</table>

<table>
<thead>
<tr>
<th>Human Health effect</th>
<th>(iF_o)</th>
<th>(EF_o)</th>
<th>(CF_o) [cases/kg(_{\text{emitted}})]</th>
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<tbody>
<tr>
<td>Carcinogenic (ED_4)</td>
<td>2.53E-05</td>
<td>6.11E-1</td>
<td>1.55E-05</td>
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<tr>
<td>Non-carcinogenic NOAEL</td>
<td>2.53E-05</td>
<td>7.26E-3</td>
<td>1.84E-07</td>
</tr>
</tbody>
</table>

Humbert et al., 2009
**Particular Matter**
*North America scenario*
Indoor iF
Industry= 3.3E-5

Outdoor iF
Urban box= 6E-6

Humbert et al., 2011
**PM 2.5 \(\mu m\)**
*Generic continent*
Outdoor iF= 1.5E-5

*Europe*
Outdoor iF= 1E-5

<table>
<thead>
<tr>
<th>Benzene</th>
<th>USEtox - CF - Outdoor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancinogenic</td>
<td>1.47E-02</td>
</tr>
<tr>
<td>Non-carcinogenic</td>
<td>3.72E-03</td>
</tr>
</tbody>
</table>
Characterization Factors nano-TiO₂

CF = iF*EF [DALY/kg\textsubscript{emitted}]

**Severity assessment → Endpoint Characterization Factors**

Default damage severity factors of 11.5 DALY/cases(cancer) and of 2.7 DALY/cases(non-cancer) have been adopted (Huijbregts et al., 2005).

**DALY** = Disability-adjusted life year is a measure of overall disease burden, expressed as the number of years lost due to ill-health, disability or early death.

<table>
<thead>
<tr>
<th>Indoor</th>
<th>Human Health effect</th>
<th>CF\textsubscript{S,i} [DALY/kg\textsubscript{emitted}]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Carcinogenic ED\textsubscript{4}</td>
<td>6.82E-03</td>
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<tr>
<td></td>
<td>Non-carcinogenic NOAEL</td>
<td>1.90E-05</td>
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<tr>
<td></td>
<td>Non-carcinogenic LOAEL</td>
<td>9.51E-04</td>
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<table>
<thead>
<tr>
<th>Outdoor</th>
<th>Human Health effect</th>
<th>CF\textsubscript{S,o} [DALY/kg\textsubscript{emitted}]</th>
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<tr>
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<td>Non-carcinogenic NOAEL</td>
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<tr>
<td></td>
<td>Non-carcinogenic LOAEL</td>
<td>2.48E-05</td>
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</table>
Conclusions

- Human Health CFs of TiO$_2$ nanoparticles have been performed for both *indoor* and *outdoor* environments and *carcinogens* and *non-carcinogens* effects following USEtox$^\text{TM}$ model.

- Challenge: $\text{ED}_4 \rightarrow \text{ED}_{50}$ $\text{ED}_4 \leftrightarrow \text{ED}_{50}$

- Indoor $\text{iF}_i$ the $\text{FF}_i$ could be improved including aggregation, attachment rates in indoor environment.

- Outdoor $\text{FF}_o$ could be re-modeling for a wide geographic area using SB4N model.
Thank for your attention!

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