Probabilistic modelling of prospective environmental concentrations of gold nanoparticles from medical applications

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Overall structure

- Motivations
- Objectives
- Methodological approach
- Limitations
- Results
- Conclusions
MOTIVATION
Motivation

- Increase in research with regard to gold nanoparticles (nano-Au) in the healthcare field due to
  - Unique properties at nanoscale
  - Ease of surface functionalisation
  - Easy synthesis
  - Relative biocompatibility


Motivation

- Some medical applications already in the market and some show high potential for translation for widespread diseases like cancer, diabetes
- No studies yet published to predict environmental concentrations of nano-Au from medical applications
- Increase in research with regard to nano-Au in other areas – catalysts for air and water purification, sensors for detecting harmful gases
- Nano-Au has been shown to be toxic to organisms in the environment
Objectives

- Estimate the yearly maximal possible consumption of nano-Au from current and prospective medical applications for the UK and US
- Model the concentrations in the transient compartments of Sewage Treatment Plants, Waste Incineration Plants and the environment compartments
- Perform environmental risk assessment
METHODOLOGICAL APPROACH
Methodological Approach

- **Model Type**: Probabilistic mass flow model developed by Gottschalk et al., 2009
- **Geographical regions**: UK and US
- **Consumption data**: 100% market penetration and all patients, irrespective of socio-economic status etc., have access
- **Risk assessment**: Probabilistic species sensitivity distribution (pSSDs) vs. Predicted environment concentration (PEC) method adopted from Gottschalk and Nowack, 2013
LIMITATIONS
Limitations: Model

- **Static**
  - Dynamic aspects not considered (time dependant particle release as well as kinetics)
  - Product use data of only one year

- **Size, shape and surface chemistry cannot be considered:** sphericity was assumed for all particles and the mass of nano-Au was calculated
Limitations: Data

- Many extrapolations to estimate nano-Au amount in *in vitro* diagnostic devices
- Due to time lag in reporting and updating disease incidence and prevalence data in disease registries, not all data are for the same year
- No ADME (absorption, distribution, metabolism, excretion) studies in humans
- Very few studies on fate and behaviour of nano-Au in the environment
- No studies on transformation and fate of nano-Au in waste incineration plants
- Less toxicity data available with respect to soil organisms
- Limited chronic toxicity data for aquatic organisms
RESULTS
ESTIMATION OF CONSUMED AMOUNTS OF NANO-Au
Applications selected

- Pregnancy and ovulation test kits
- Test kits to diagnose HIV/AIDS
  - Home based
  - Lab based
- Removal of SA from nasal carriages to prevent nosocomial infection prevention
- Treatment of gum diseases
- Diagnosing septicaemia and respiratory virus
- Genotyping diagnostic tests
- Diagnosis of different types of cancers and Chronic Kidney Disease via exhaled breath
- Treatment of cancers – thermal ablation
- Treatment of cancers – TNF delivery
- Diabetes management
Method to arrive at nano-Au consumption estimates

- Estimate the maximal possible nano-Au amount
  - mass of gold depending on particle size
  - amount required per test for *in vitro* diagnostic medical devices (IVD) or therapeutic dose

- Number of times a particular application likely to be used in a year or dose required for treatment

- Population estimate using disease incidence and prevalence data for the most recent year
## Consumption of nano-Au

<table>
<thead>
<tr>
<th>Application</th>
<th>UK</th>
<th>US</th>
<th>Unit</th>
<th>Waste compartment</th>
<th>Probability distribution function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin delivery for diabetes management</td>
<td>128</td>
<td>842</td>
<td>kg</td>
<td>Sewage</td>
<td>Uniform</td>
</tr>
<tr>
<td>Treatment of Periodontitis</td>
<td>0.28 -107</td>
<td>1 - 365</td>
<td>kg</td>
<td>Sewage</td>
<td>Uniform</td>
</tr>
<tr>
<td>Removal of <em>Staphylococcus aureus</em> from the nasal passage of patients</td>
<td>0.03- 53</td>
<td>0.11 -165</td>
<td>kg</td>
<td>Sewage</td>
<td>Uniform</td>
</tr>
<tr>
<td>Diagnostic test kits for infectious diseases</td>
<td>74</td>
<td>356</td>
<td>g</td>
<td>Hazardous waste</td>
<td>Uniform</td>
</tr>
<tr>
<td>Home based <em>in vitro</em> HIV test kits</td>
<td>18</td>
<td>87</td>
<td>g</td>
<td>Municipal waste</td>
<td>Uniform</td>
</tr>
<tr>
<td>Pregnancy and ovulation test kits</td>
<td>3 -100</td>
<td>15-463</td>
<td>g</td>
<td>Municipal waste</td>
<td>Uniform</td>
</tr>
</tbody>
</table>
## Consumption of nano-Au

<table>
<thead>
<tr>
<th>Application</th>
<th>UK</th>
<th>US</th>
<th>Unit</th>
<th>Waste compartment</th>
<th>Probability distribution function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solid tumors (colorectal, pancreas, breast)</td>
<td>0.07-(0.42)-1</td>
<td>0.31-(2)-5</td>
<td>kg</td>
<td>Sewage</td>
<td>Triangular</td>
</tr>
<tr>
<td>Solid tumors (colorectal, pancreas, breast) – Compassionate use</td>
<td>0.42</td>
<td>2</td>
<td>kg</td>
<td>Sewage</td>
<td>Uniform</td>
</tr>
<tr>
<td>Head &amp; neck cancer and lung cancer</td>
<td>140 - 234</td>
<td>745 - 1241</td>
<td>kg</td>
<td>Sewage</td>
<td>Uniform</td>
</tr>
<tr>
<td>Head &amp; neck cancer and lung cancer – compassionate use</td>
<td>105 - 175</td>
<td>468 - 780</td>
<td>kg</td>
<td>Sewage</td>
<td>Uniform</td>
</tr>
<tr>
<td>Sensors for diagnosing cancer via breath</td>
<td>0.01 - 1589</td>
<td>0.03 - 4616</td>
<td>g</td>
<td>Hazardous waste</td>
<td>Uniform</td>
</tr>
</tbody>
</table>
CONCENTRATIONS IN ENVIRONMENT COMPARTMENTS AND RISK ASSESSMENT
Flows of nano-Au in the environment (UK)
Flows of nano-Au in the environment (US)
Concentration of nano-Au in the technosphere

<table>
<thead>
<tr>
<th></th>
<th>Hazardous waste</th>
<th>Landfill</th>
<th>Medical Waste</th>
<th>Municipal waste</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>μg kg⁻¹</td>
<td>μg kg⁻¹</td>
<td>Fly ash</td>
<td>Bottom ash</td>
<td>Fly ash</td>
<td>Bottom ash</td>
</tr>
<tr>
<td>Q15</td>
<td>23</td>
<td>3</td>
<td>36</td>
<td>27</td>
<td>39</td>
<td>28</td>
</tr>
<tr>
<td>UK Mode</td>
<td>34</td>
<td>4</td>
<td>28</td>
<td>23</td>
<td>51</td>
<td>28</td>
</tr>
<tr>
<td>Q85</td>
<td>130</td>
<td>5</td>
<td>518</td>
<td>393</td>
<td>67</td>
<td>52</td>
</tr>
<tr>
<td>Q15</td>
<td>20</td>
<td>3</td>
<td>30</td>
<td>23</td>
<td>31</td>
<td>30</td>
</tr>
<tr>
<td>US Mode</td>
<td>16</td>
<td>4</td>
<td>27</td>
<td>20</td>
<td>38</td>
<td>30</td>
</tr>
<tr>
<td>Q85</td>
<td>110</td>
<td>5</td>
<td>431</td>
<td>330</td>
<td>48</td>
<td>38</td>
</tr>
</tbody>
</table>

Concentration in non-hazardous waste is less than 0.1μg kg⁻¹
## Concentration of nano-Au in the ecosphere

<table>
<thead>
<tr>
<th></th>
<th>STP Effluent</th>
<th>Surface water</th>
<th>Sediment</th>
<th>STP sludge</th>
<th>Soil</th>
</tr>
</thead>
<tbody>
<tr>
<td>Units</td>
<td>pg L(^{-1})</td>
<td>pg L(^{-1})</td>
<td>ng kg(^{-1}) y(^{-1})</td>
<td>μg kg(^{-1})</td>
<td>ng kg(^{-1}) y(^{-1})</td>
</tr>
<tr>
<td><strong>UK</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q15</td>
<td>217</td>
<td>214</td>
<td>132</td>
<td>94</td>
<td>227</td>
</tr>
<tr>
<td>Mode</td>
<td>359</td>
<td>268</td>
<td>165</td>
<td>126</td>
<td>301</td>
</tr>
<tr>
<td>Q85</td>
<td>665</td>
<td>725</td>
<td>447</td>
<td>154</td>
<td>368</td>
</tr>
<tr>
<td><strong>US</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q15</td>
<td>95</td>
<td>3</td>
<td>3</td>
<td>119</td>
<td>121</td>
</tr>
<tr>
<td>Mode</td>
<td>168</td>
<td>4</td>
<td>5</td>
<td>145</td>
<td>147</td>
</tr>
<tr>
<td>Q85</td>
<td>271</td>
<td>7</td>
<td>8</td>
<td>171</td>
<td>174</td>
</tr>
</tbody>
</table>

Data rounded off to the nearest whole number.
Environmental Risk Assessment

Exposure
Measure concentrations in the environment: field sampling and chemical analysis
Predict environmental concentrations via modelling

Hazard
Bioassay toxicity tests
Acute and chronic toxicity tests

Risk
Probabilistic Mass Flow modelling (PEC)
Probabilistic Species Sensitivity Distribution
Details of data for creating the pSSD

- 12 relevant studies
- 26 values
- Endpoints selected: mortality and malformation, growth inhibition, reproductive impairment and acute immobilisation
- Relevant assessment factors used to account for chronic toxicity and to arrive at No Observed Effect Concentration
Probabilistic species sensitivity distribution (pSSD) for nano-Au in fresh water and soils
Probability distributions of the PECs and the pSSDs for nano-Au in surface water

UK

US

Concentrations log(ng/l)

Probability
Probability distributions of the PECs and the pSSDs for nano-Au in agricultural soils
CONCLUSIONS
Conclusions

- Total amount of nano-Au consumed in a year
  - UK: 540 kg
  - US: 2700 kg

- Significant release to the water compartment from therapeutics

- nano-Au concentration is surface water (0.0026 to 0.725 ng/L) is similar to background concentrations in freshwater (<1 ng/L to 50 ng/L)

- nano-Au concentration in sludge (126 & 145 µg/kg) is less than gold present in sludge (790 µg/kg - Sweden)

- No risk from nano-Au to aquatic and soil organisms, but more toxicity studies required
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