Assessment of airborne emissions during the use of a Cadmium Telluride Quantum Dots incorporating ink and a proposal to calculate their human health and freshwater effect factors

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Abstract. Quantum dots (QDs) confer a wide range of optical properties to pigments/inks. With new products and applications entering the market, the airborne emissions of QDs-incorporating inks during usage stage at consumer scale (e.g. household printing) and their corresponding impacts towards human health and the environment need to be investigated. In the present work Cadmium Telluride (CdTe) QDs have been selected as a case study. The targets of this study comprise: (i) the characterization under controlled conditions of the emissions during inkjet printing of a prototype of a CdTe QDs nanoadditivated ink and (ii) the assessment of the feasibility to derive human health and freshwater effect factors (EF) for potentially released CdTe QDs with the USEtox® consensus model. Mean particle size after 60 minutes inkjet printing corresponded to 59.52 nm. For human health EF calculation an extrapolation to the human EF of other nanomaterials has been proposed considering CdTe QDs' specific surface area whereas for the calculation of the freshwater EF, few of the data available have revealed suitable. A generic constraint to calculate both EFs for CdTe QDs released throughout the life cycle of a product incorporating them is related to the absence of information corresponding to their specific (eco)toxicological impacts.

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1 Introduction

The implementation of a life cycle perspective in the design phase of nanotechnology enabled products (NEPs) and applications (NEAs) needs to take into consideration releases of engineered nanomaterials (ENMs) taking place at multiple stages along their life cycle (e.g. during use). The chemical and physical forms of the emissions (releases) vary along these processes, as does the potential for human or ecological exposures and associated impacts. However, Salieri et al. [1] identified a total of 92 Life Cycle Assessment (LCA) studies of nanotechnologies out of which only 5 accounted for ENM releases [2-6].

The integration of the effects associated with pristine (or released) ENMs in LCA requires the calculation of characterization factors (CF). A CF is a substance-specific quantitative representation of the (relative) impact of a substance in the environment. CF calculation is based on models of cause-effect relationships for a specific impact category. The UNEP-SETAC toxicity model USEtox® is recommended for the calculation of CFs for human toxicity and freshwater ecotoxicity in Life Cycle Impact Assessment.

The USEtox® consensus model multiplies three aggregated parameters related to fate (fate factor, FF), exposure (exposure factor, XF), and toxicity (effect factor, EF) for the calculation of CFs, respectively, of a specific chemical [7, 8].

With the assumption of linear dose-response relationship, USEtox® calculates human health EF as

$$EF = 0.5/ED50 \quad (1)$$

where ED50 is the lifetime daily dose (ED corresponding to effective dose) resulting in 50% probability of effect.

USEtox® takes into consideration the inhalation and ingestion exposure routes and differentiates between the contributions of cancer and non-cancer toxicity impacts. Human EF is expressed by a loss of (healthy) life time expressed or disability adjusted life years (DALY) per kg intake. Examples of human EFs (HEFs) have been reported by Buist et al. [9] for ENMs including Ag, TiO_2, carbon black, high-aspect ratio, rigid and flexible multi-walled carbon nanotubes (MWCNT), all of them in their pristine form.

For ecotoxicological impacts, the freshwater ecotoxicity EF is determined using the linear slope of dose-response curves of the chemical up to the point where 50% of the species are affected. Therefore, the EF for ecotoxicity can be calculated as

$$EF = 0.5/HC50 \quad (2)$$

where HC50 is the hazardous concentration at which 50% of the species are affected above their EC50. Freshwater organisms include representatives of the trophic levels of algae, crustaceans and/or fish in order to reflect the variability of the physiology and to ensure a minimum diversity of biological responses. Freshwater EF is expressed as Potentially Affected Fraction (PAF) of freshwater species integrated over the exposed water volume per kg of bioavailable chemical in the aquatic environment (PAF m^3 kg^{-1}). According to Temizel-Sekeryan and Hicks [10], 29 freshwater CFs for different ENMs including carbon nanotubes (CNT), TiO_2; Ag or Au nanoparticles, amongst other, have been proposed to date.

In the present work we have selected Cadmium Telluride Quantum Dots (CdTe QDs) as case study. CdTe QDs are characterized by their ease of tunability, high photoluminescence, quantum efficiency and stability in water [11] and their use as additive in inkjet printing inks has been reported [12]. Our objectives have included: the simulation of the printing at consumer scale of a prototype of a water based CdTe QD additivated inkjet printing ink, the characterization of corresponding airborne emissions in terms of mean particle size and the compilation of information of CdTe QDs for human toxicity via inhalation route and freshwater ecotoxicity for corresponding EF calculation using USEtox®. To the best of our

knowledge, no human health or freshwater ecotoxicity EFs have been proposed in the literature so far for CdTe QDs neither in their pristine nor in their released forms.

2 Materials and Methods

2.1. Experimental assessment of particle size of the emissions during the use of inkjet printing ink incorporating CdTe QDs

The average particle size of the airborne particles emitted during inkjet printing of a prototype of polyethylene glycol (PEG) CdTe QDs additivated water based ink provided by PLASMACHEM GmbH (Germany) was characterized under controlled conditions. The composition of the ink cannot be detailed due to confidentiality issues.

The protocol for the printing process was detailed by Blázquez et al [13]. Briefly, CdTe QDs containing ink was loaded into refillable ink cartridges which were subsequently inserted in a household inkjet printer (Pixma P7250, Canon). A pattern representing 65.71% coverage of a A4 paper was printed on recycled paper. The printer was enclosed in an aerosol exposure chamber with approximate dimensions of 0.74 x 0.55 x 0.59 m (0.24 m^3), to which clean air entered through a HEPA 14 capsule filter. The chamber was equipped with a scanning mobility particle sizer (SMPS Model 3936L25, TSI Inc.) measuring in a size range from 15 to 661 nm, a scan time of 100 s, a retrace time of 15 s, a 2 min recurrence interval and the sample flow rate was adjusted to 0.3 L/min. A 60 min printing cycle was performed followed by uninterrupted air monitoring during 60 min, to observe the evolution of particle sizes.

2.2. Compilation of (eco)toxicological information for Human Health and Freshwater Effect calculation and calculation of specific surface area

Different academic websites including Web of Knowledge, PubMed, Scopus or ScienceDirect were selected as a source for (eco)toxicological information. Several terms were displayed in combination to perform this search: “CdTe”, “Cadmium Telluride”, “Quantum Dots”, “EC50”, “ED50”, “carcinogenic”, “chronic inhalation toxicity”, “freshwater toxicity” … Data corresponding to QD formulations other than CdTe (e.g., CdS, CdSe) were disregarded. CdTe QD manufacturing processes that have moved beyond academic laboratory scale i.e. those with a technology readiness level (TRL) of 9, which is proven at commercial scale were prioritized to the possible extent since residual or solvent impurities resulting from not-optimized processes can affect the results of the (eco)toxicological tests. Despite that the coating is a particularly critical variable, as it affects solubility and therefore also (eco)toxicity, we have not taken into consideration surface functionalization due to limitations associated with USEtox®. Particle’s specific surface area (SSA) was calculated using the Sauter formula [14]:

$$SSA = 6/\rho L \quad (3)$$

where ρ and L correspond to particle’s density and diameter, respectively.

3 Results and discussion

For comparison purposes, the size corresponding to the pristine CdTe QDs reported by Blázquez et al. [13] has been taken as a reference. These authors detailed the use of CdTe QDs capped with PEG (750)-O-C(=O)CH2CH2-SH of 3 -5 nm size as nano additive in water-based inkjet printing ink. In the present work, a spherical diameter of 3.6 nm has been

assumed for CdTe QDs. Considering density of CdTe QDs (5.83 E+ 06 g/m^3) [15] and a spherical particle diameter of 3.6 nm, the SSA for pristine CdTe QDs corresponds to 286 m^2/g.

3.1. Characterization of emissions associated with inkjet printing

Particle sizes of the emissions measured in three different moments of the CdTe QDs inkjet printing under controlled conditions (times 0, 60 and 120 min, respectively) have been represented in Figure 1.

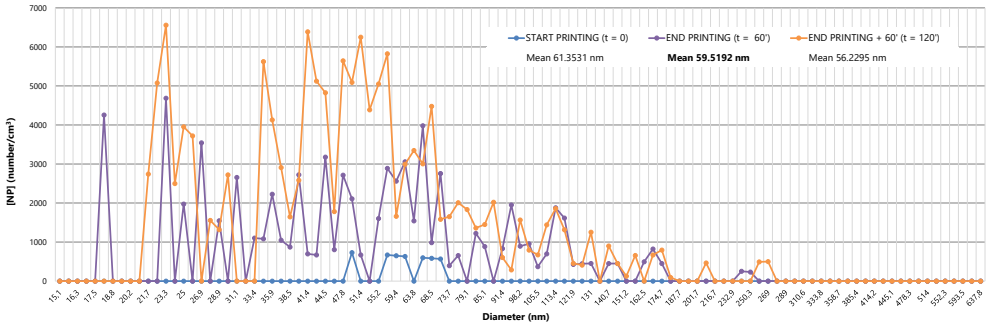

Figure 1: Particle size of emissions measured at the start of the printing process (t=0); at the end of the printing process (t=60'), and 60' starting from the end of the printing process (t=120'). Mean particle sizes and total particle concentration at t=0, t= 60 and t=120 corresponded to 61.35, 59.52 and 56.23 nm and to 69.25, 1167.97 and 2196.62 (#/cm^3), respectively. Whereas the mean particle size remained relatively constant, a time-dependent increase in the concentration of particles was observed. The mean particle size of 59.52 nm measured at the end of printing (t=60) has been selected as representative of the emissions associated with the usage stage of the CdTe QDs additivated inkjet printing ink.

3.2. (Eco)toxicological information and EF calculation

3.2.1. Human health toxicity data

The comparison of different studies executed with different CdTe containing QDs revealed challenging due to widely differing dose parameters used and insufficient data on Cd release by the QDs. As introduced earlier, another factor of importance is coating and/or functionalization of CdTe QDs. For instance, Bobine Serum Albumin (BSA) conjugated CdTe QDs are less cytotoxic than bare CdTe QDs [16]. Likewise, their conjugation with polyethylene glycol (or PEGylation) has a mitigating effect on QDs cytotoxicity [17]. In contrast, QDs with carboxylic surface groups are positive in the Comet assay, while QDs with other surface functionalizations are weakly positive or negative at the same dose [18]. No *in vivo* studies on CdTe genotoxicity performed in mammals have been encountered in public literature. An *in vitro* study by Wang et al. [19] using human umbilical vein endothelial cells (HUVECs), showed that a 12 h treatment with CdTe QDs, surface coupled with mercaptopropionic acid, induced DNA damage in a dose-dependent manner (ED50 approx. 50 µg/mL). Based on this limited evidence, no firm conclusion can be drawn with respect to CdTe QDs' genotoxicity.

As an alternative, the human health EFs (HEFs) derived by Buist et al. [9] have been taken as a reference to calculate a range of values providing an indication of the possible value of the CdTe QDs respiratory human health EF (Table 1). This range of values does not take into consideration the specific effects on human health of CdTe QDs, rather, an approximation to the HEF of other ENMs based on their SSA has been proposed.

Table 1: HEF for LCA, chronic inhalation exposure, for ENMs derived by Buist et al. [9] (Carbon black, Ag and TiO_2) and approximation to CdTe QDs based on calculated particle's SSA. Disability-adjusted life-years (DALYs) have been calculated based on a SSA of 286 m^2/g for pristine CdTe QDs. In the case of released forms of CdTe QDs (*in italics*), a SSA corresponding to 17.3 m^2/g has been calculated taking into consideration the selected average size of particles emitted during printing (59.52 nm) whereas the density has been assumed to remain equivalent to that of pristine CdTe QDs. Cases have been calculated based on 0.23 DALYs/case for chronic obstructive pulmonary disease (COPD).

ENM [Surface area (m^2/g)]	**Values (DALYs)** $(m^2/g)^{-1} \cdot kgintake^{-1}$	**Equivalent HEF for pristine CdTe QDs [SSA 286 m^2/g]**		***Equivalent HEF for released CdTe QDs [SSA 17.29 m^2/g]***	
		DALYs · kgintake^{-1}	**Cases · kgintake^{-1}**	***DALYs · kgintake^{-1}***	***Cases · kgintake^{-1}***
Carbon black [230]	0.0067	1.9	8.3	*0.12*	*0.50*
Ag [20]	0.15	42.9	186.5	*2.60*	*11.28*
TiO_2 [48]	0.013	3.7	16.2	*0.22*	*0.98*

Based on this comparison, the chronic HEF of pristine CdTe QDs could range between 1.9 and 42.9 DALYs kgintake^{-1} (8.3 and 186.5 cases kgintake^{-1}) representing low and high toxicity scenarios and corresponding to carbon black and Ag nanoparticles (NPs), respectively. HEF values adjusted to the SSA calculated for the average size of the particles emitted during the use of CdTe QDs-incorporating ink have also been presented. The present approach has not taken into consideration the composition of the released particles which will be integrated by CdTe QDs and the solvent ink. The proposed HEF for the usage stage should ideally be corrected by a quantified proportion of CdTe QDs contained in the total emitted particles. Furthermore, we have assumed that the CdTe QDs are closely aggregated and do not separate once lodged in the lungs. It is noteworthy that out of the four ENMs that have been selected as a reference, the closest scenario would be that of Ag NPs since both their mechanism of toxicity and that of CdTe QDs are based on the release of ions. The scope of the present work is limited to non-carcinogenic effects derived from the inhalation route.

3.2.2. Freshwater toxicity data

Values accounted for the calculation of the Frshwater Ecotoxicity EF have been reported in Table 2.

Table 2: Values accounted for the calculation of the Freshwater Ecotoxicity EF. *In vivo*, acute exposure data have been retrieved only: chronic values are calculated by a factor of 0.5 in agreement with the general provisions of USEtox®. Subsequently, (i) log(10) is calculated for each chronic EC50 value [corresponding to EC50i], (ii) the average of EC50i values for the three trophic levels considered is calculated [corresponding to the aggregated EC50] and, finally, (iii) the aggregated HC50 value is calculated as the antilogarithm of EC50.

Organism	**Effect endpoint**	**Exposure duration (h)**	**EC50 (mg/L)**	**Chronic values**	**log(10) of chronic values [EC50i]**	**avlog (EC50i) [EC50]**	**10^EC50 [HC50]**
Algae *(Chlamydomonas reinhartii)* [20]	Growth	72	5.00	2.50	0.40	0.12	1.34

Organism	Effect endpoint	Exposure duration (h)	EC50 (mg/L)	Chronic values	log(10) of chronic values [EC50i]	avlog (EC50i) [EC50]	10^EC50 [HC50]
Crustacean *(Daphnia pulex)* [21]	Death	48	0.25	0.125	-0.90		
Fish *(Danio rerio)* [22]	Death	120	15.28	7.64	0.88		

A Freshwater Ecotoxicity EF for CdTe QDs calculated as $0.5/HC50.10^3$ and corresponding to 374.10 Potentially Affected Fraction (PAF) of freshwater species m^3/kg is proposed. Ecotoxicty data used for the calculation of the freshwater EF are limited to one value per trophic level which conveys a high uncertainty in the proposed value (interim). In addition to *in vivo* data reported in Table 2, the use of fish cell lines in *in vitro* toxicity studies for CdTe QDs has also been reported. For instance, Gagné et al. [23] performed an *in vitro* test with primary cultures of hepatocytes of rainbow trout *Oncorhynchus mykiss* (48 h exposure). Though the fish cell line RTgill-W1 has been recently accepted as an alternative to predict fish acute toxicity [24], the currently available version of USEtox® cannot take into consideration results from *in vitro* tests for the calculation of freshwater EF.

3.2.3. General remarks and limitations

Information of (eco)toxicological nature has been retrieved in the absence of clear standard operating protocols for ENMs' (eco)toxicity assessment. Moreover, tests were done with the same compound but different materials (size, shape, functionalization…). Concerning the HEF, an approximation based on SSA only has been considered for CdTe QDs whereas the ENMs taken as a reference have different compositions and, thus, associated toxic effects. An exception is represented by Ag nanoparticles with toxicity mechanisms associated with the release of ions, as in the case of CdTe QDs. The absence of dosimetry studies (nominal versus measured exposure levels) represents an additional limitation.

4 Conclusions

The toxicity of CdTe QDs is not fully understood. As an alternative, an extrapolation to the HEF of better known ENMs considering the SSA of both pristine and released forms of CdTe QDs has been proposed. Only one ecotoxicity value per trophic level representative of the freshwater compartment has been used for EF calculation, which increases its uncertainty. Future updates of USEtox® should integrate the results from *in vitro* tests for fish acute toxicity for RTgill-W1. The average particle size of the airborne emissions associated with 60 minutes inkjet printing of a CdTe QDs-additivated ink corresponded to 59.52 nm. A generic constraint to calculate both freshwater and human EF of the released forms is related to the absence of specific (eco)toxicological information of the CdTe QDs emitted throughout the life cycle of products incorporating them such as during printing (use stage). Hereby proposed EFs will need to be adjusted as new information corresponding to the impacts of the released forms of CdTe QDs becomes available.

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