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Paper

Environmental assessment of a bottom-up hydrolytic synthesis of TiO_2 nanoparticles

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Green metrics evaluation of a bottom-up hydrolytic sol-gel synthesis of titanium dioxide (TiO_2) nanoparticles has been performed by following two different approaches, namely by using EATOS software and by LCA methodology. Indeed, it is well known the importance that engineered nanomaterials, are increasingly gaining worldwide in a plenty of high-technological applications. Due to the yet completely un-established environment and human health impact of nano-sized materials, the possibility to at least choose the greener synthetic strategy through accurate comparison of detailed environmental assessments, will soon become of absolute importance in both small as well as large scale production of these advanced inorganic materials. The present LCA study has been carried out following an ecodesign approach, in order to limit the environmental impacts and to protect the human health. The results of LCA analysis highlight that the highest environmental impact is mainly due to both energy and titanium isopropoxide precursor used in the synthesis process. Concurrently, the software EATOS has been employed to calculate the environmental parameters which account for the environmental and social costs related to all the chemicals involved in the analyzed synthesis. Being the EATOS approach purely based on synthetic chemical mechanism considerations, thus neglecting any energy contributions, its results cannot be directly compared to those arising from the LCA analysis. However, it will be shown that by simply neglecting energy contributions, similar and comparable outcomes are obtained, broadening the application fields of combined EATOS-LCA approach to the inorganic synthesis of engineered nanomaterials, highlighting the great potentialities of their synergy.

1 Introduction

Nowadays several evaluating parameters related to the environmental and human health impact of a particular chemical process are starting gaining increased interest and consideration side by side to the traditionally employed ones like yield, time and cost, as demanded by Green Chemistry, Green Engineering and Process Intensification developing philosophies.[1,5]

At this latter regard different metrics have been proposed during the last decades,[6,7] among which the E-factor[8] and the mass index (MI),[9,10] expressed respectively by equations 1 and 2, constituted the most studied and applied ones, leading also to the design and development of the software EATOS (Environmental Assessment Tool for Organic Syntheses) by Eissen and Metzger.[11]

$$E - factor = \frac{\sum waste(g)}{product(g)} \qquad (1)$$

$$MI = \frac{\sum substrate(g) + solvent(g) + auxiliary\_materials(g) + catalyst(g) + ...}{product(g)} \qquad (2)$$

Indeed, this free of charge software[12] allows utilization of easily available data for the calculation of the above mentioned mass metrics, and has been already applied to several studies, since it also permits to compare different synthetic strategies for the obtainment of a particular target compound.[11,13-17]

However, the most significant limitation of every mass metrics, thus including also the software EATOS, is the lack of any energy analysis together with its intrinsic character of being usually devoted to the gate-to-gate boundaries of a particular research laboratory or manufacturing plant. This means that several fundamental steps into the life cycle of employed chemicals like extraction of raw materials, production, transportation, sales, distribution, use and their final fate are not considered by such mass metrics.[7,18]

All of these latter shortcomings can be, on the other hand, overcome by applying Life Cycle Assessment (LCA) methodology, which is based on a cradle-to-grave approach.[19] However, mainly due to LCA intrinsic highly comprehensive nature as well as to the difficulty in finding several necessary inventory data, its use has been mainly limited to large scale production processes, rather than to the early stages of research for innovative and greener synthetic routes, having in this latter cases the software EATOS already demonstrated its applicability.[15] Nevertheless, numerous strategies have been

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proposed to simplify the LCA approach thus rendering it easily applicable also to a laboratory scale. Among these artifices for example it has been reported[20,21] the possibility to substitute chemicals which are absent into the LCA software database, with some analogues. Particularly, in those works different synthetic strategies have been evaluated and compared through both EATOS and LCA approaches. Noteworthy is the fact that similar assessments resulted although the two significantly different approaches on which they are based.

Although diffusion of the green chemistry developing philosophy usually involve the less environmentally-friendly considered organic reactions, it needs to be pointed out the impossibility to neglect the significant environmental impact that nanotechnology related research activities are increasingly engendering, particularly considering that the environmental as well as the human health effects of nano-sized materials are not yet fully established. In this last perspective, among the key issues related to minimisation of the impact of nanotechnology on the environmental and on the human health, which have been recently identified by Albrecht et al.[22], life cycle assessment and green chemistry metrics have been reported as mandatory.

Thus, the possibility to decide at least for the more green approach for the synthesis of target engineered nanomaterials (being understood the desired particles size and shape) should be highly recommended in order to pursue a more and more sustainable development.

LCA studies related to different nanomaterials have recently been reviewed[23] including also a few works necessarily related to titanium dioxide,[24-27] being the latter the most studied and applied semiconductor and photocatalyst, due to its unique physicochemical properties.[28,29] In general, the preparation routes for this material produce anatase, rutile, or an amorphous solid, depending on the experimental synthetic conditions employed. Nanosized anatase is the most attractive crystalline form of titanium dioxide for advanced and high-technological applications mainly because of its higher stability and photocatalytic activity with respect to rutile and brookite.

Consequently, the obtainment of anatase nanoparticles with high purity and precisely controlled structure and particle size is the main purpose of optimized synthetic methods, and many approaches have been proposed for that scope, such as inert gas condensation[30], sol-gel method[31,32] and hydrothermal synthesis[33]. Among these, the sol-gel technique is the most frequently applied for the synthesis of anatase nanoparticles with sizes ranging from 5 nm to several micrometers and a large variety of crystal shapes.

Aim of the present work is to apply two different green metrics evaluation tools, namely EATOS software and a detailed LCA study, to the hydrolytic sol-gel synthesis of TiO_2 nanoparticles, produced according to the method patented by one of the most important Italian company, supplier of chemicals for building and further industrial sectors,[34,37] and following an ecodesign approach. Then it has been compared the obtained results to evaluate for the first time the applicability of these combined approaches to the field of inorganic synthesis of engineered nanomaterials.

Indeed, similarly to what recently started being accepted by a part of the organic chemistry community, an environmental impact evaluation should always accompany any new synthetic strategy proposed for the synthesis of inorganic engineered nanomaterials, and of course the same should be valid also for already established and recognized preparation procedures, with the present manuscript representing a pioneering work in that precise direction. Being the most of the recently developed synthetic approaches for the obtainment of engineered nanomaterials, based on meticulous reaction mechanism premises (thus no longer based on prolonged solid state diffusion-controlled high temperature treatments) it should not be surprising that the environmental assessment of their chemical synthesis could be, as the case of the present work, evaluated with the aid of EATOS software, i.e. a tool originally developed for organic syntheses.

2 Experimental

The environmental performance of the hydrolytic synthesis of anatase TiO_2 nanoparticles has been evaluated by LCA methodology (according to the ISO 14040/44)[35,36] and by EATOS tool, according to the reaction mechanism considerations reported in the following paragraph.

2.1 The hydrolytic sol-gel synthesis of TiO_2 nanoparticles

The hydrolytic sol-gel synthesis of anatase TiO_2 nanoparticles has been performed according to the procedure recently patented and actually employed by Colorobbia S.p.A., one of the most important Italian company supplier of chemicals for building and further industrial sectors for the preparation of aqueous TiO_2 suspensions.[34,37] It is well known[37,38] that in hydrolytic sol-gel syntheses of oxide nanomaterials, water acts both as a solvent and as a true reactant, with the reaction mechanism involving subsequent hydrolysis and condensation reactions. All of the possible hydrolytic reactions to which the organic metal precursors can undergo are reported in the following equations 3-6, in which titanium isopropoxide is considered as titanium precursor. Equation 7 can be alternatively used to summarise and group all the previous reactions.

$$\mathrm{Ti(OiPr)_4 + H_2O \rightarrow Ti(OiPr)_3OH + iPrOH} \quad (3)$$

$$\mathrm{Ti(OiPr)_3OH + H_2O \rightarrow Ti(OiPr)_2(OH)_2 + iPrOH} \quad (4)$$

$$\mathrm{Ti(OiPr)_2(OH)_2 + H_2O \rightarrow TiOiPr(OH)_3 + iPrOH} \quad (5)$$

$$\mathrm{TiOiPr(OH)_3 + H_2O \rightarrow Ti(OH)_4 + iPrOH} \quad (6)$$

$$\mathrm{Ti(OiPr)_4 + nH_2O \rightarrow Ti(OiPr)_{4-n}(OH)_n + niPrOH} \quad (7)$$

The next condensation reactions can obviously occur between both two hydroxylated metal species, leading to a Ti-O-Ti bond under the release of a water molecule (equation 8), and between a hydroxide and an alkoxide leading to the formation of a Ti-O-Ti bond under the release of an isopropyl alcohol molecule (equation 9).

$$\mathrm{\equiv Ti\text{-}OH + HO\text{-}Ti\equiv \rightarrow \equiv Ti\text{-}O\text{-}Ti\equiv + H_2O} \quad (8)$$

$$\mathrm{\equiv Ti\text{-}OiPr + HO\text{-}Ti\equiv \rightarrow \equiv Ti\text{-}O\text{-}Ti\equiv + iPrOH} \quad (9)$$

The chemical reactivity of the metal alkoxide towards hydrolysis and condensation mainly depends on the electrophilic nature of the metal atom, its ability to increase the coordination

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number, the steric hindrance of the alkoxy group, as well as the polarity, the dipole moment and the acidity of the solvent.[39] Therefore, the major problem of aqueous sol-gel methods based on the hydrolysis and condensation of molecular precursor is the control over the reactions rates. For most transition metal oxide precursors, these reactions are too fast, resulting in loss of morphological and structural control over the final oxide material. One of the possibilities to decrease and to adjust the reactivity of the precursor is the use of organic additives, which can act as chelating ligands thus modifying the reactivity of the precursors.

In the here reported specific case, for each Ti-O-Ti bridge formed a water or an alcohol molecule is generated and considering the product TiO_2 as the repetitive unit of the inorganic network and taking into account the octahedral coordination of Ti atoms and the trigonal-planar one of each oxygen atom, the stoichiometric reaction describing the overall hydrolytic sol-gel synthesis of TiO_2 nanoparticles can be considered the one reported in the following equation 10.

$$Ti(OiPr)_4 + 2H_2O \rightarrow TiO_2 + 4iPrOH \qquad (10)$$

The experimental synthetic procedure followed[37] exploited the use of concentrated nitric acid and Triton X-100 in order to control the alkoxide reactivity as well as the hydrolysis and condensation reactions rates, the latter acting also as dispersant agent for the as synthesised nanocrystals. The previous reaction (eq. 10), however, assumes that the complete hydrolysis of the metal precursor occurs first, leading to the formation of four molecules of isopropyl alcohol, with subsequent condensation reactions occurring only between tetra hydroxylated species, leading to the liberation of two water molecules for each TiO_2 repetitive unit formed.

In order to be more accurate as possible in pursuing an effective comparison between the two green metrics evaluation procedures (i.e. EATOS and LCA), reaction equation 11 has been considered. This is slightly different from equation 10, in fact equation 11 consider the water also into the reaction products.

$$Ti(OiPr)_4 + 4H_2O \rightarrow TiO_2 + 2H_2O + 4iPrOH \qquad (11)$$

2.2 Description of the life cycle of the bottom-up hydrolytic synthesis of TiO_2 nanoparticles

Fig. 1 shows the production process of the considered bottom-up hydrolytic synthesis of TiO_2 nanoparticles suspension. In particular the process consists of two main steps: the sol preparation and the addition of auxiliary materials used to prevent the flocculation of titanium dioxide. Since titanium isopropoxide, required for the sol preparation, has been not present in LCA databases, the representation of its synthesis route from titanium tetrachloride has been included in the present LCA study.[43] The same also applied to the synthesis of $TiCl_4$ precursor, thus a further step backward to its preparation from ilmenite has been necessarily accomplished.[43]

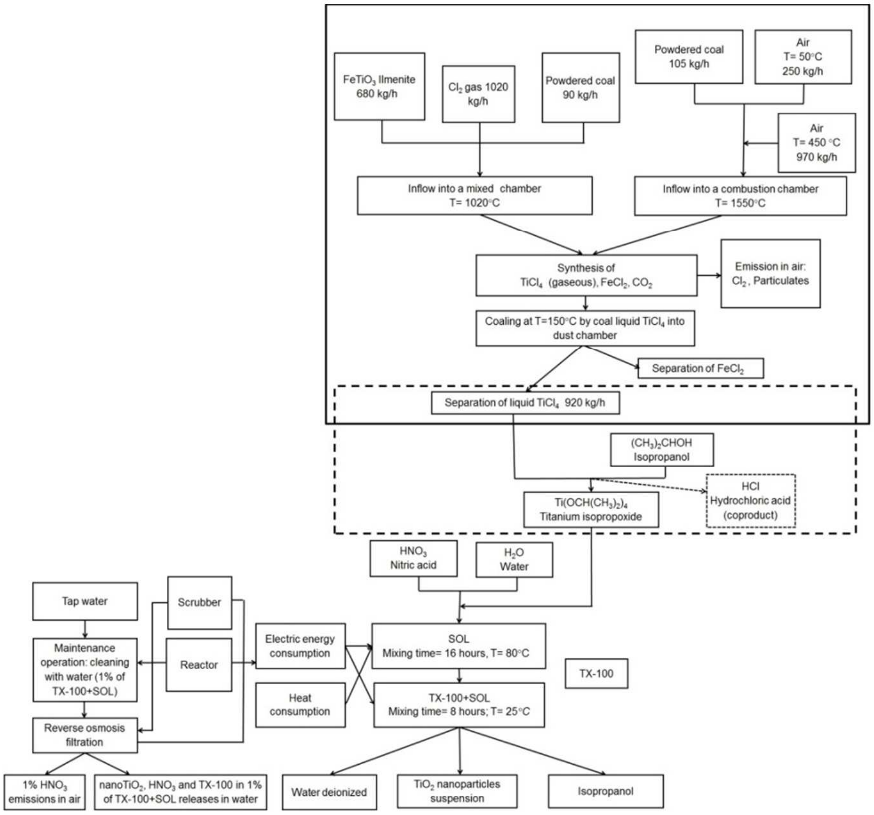

Fig. 1 Bottom-up hydrolytic synthesis of TiO_2 nanoparticles life cycle

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Table 1 Percent composition of chemicals used to produce nanoTiO_2 suspension (main product) and co-products

Chemicals	**wt%**
Titanium isopropoxide	23.22
Water	73.40
Nitric acid 63%	2.38
Triton X-100	1
Total	100
Recycled Isopropanol (*co-product*)	12
Remaining 88%	%
TiO_2 nanoparticles suspension (*main product*)	85.71
H_2O (*co-product*)	14.29
Total	100

2.2.1 Sol preparation

The chemicals used to produce anatase TiO_2 nanoparticles suspension are reported in Table 1. Titanium isopropoxide (TIP) and water are introduced in a closed 200 l volume glass reactor with nitric acid (HNO_3), as catalyst. This mixture is vigorously stirred for 16 hours at 80 °C, until it gradually transform into a translucent sol by peptization.

2.2.2 Addition of auxiliary material

After the sol production, TX-100 is added to the colloidal suspension in order to avoid the flocculation of the obtained nanoparticles. After 8 hours of stirring at 25 °C the anatase nanoparticles are generated, together with isopropyl alcohol and water as co-products (according also to equation 11).

2.2.3 Maintenance operations

The study evaluates the maintenance operations at the end of the process, particularly the cleaning of the reactor with water. It has been assumed that 1% of TiO_2 nanoparticles suspension remains on the reactor walls, so that the water used to clean the reactor results contaminated by nanoparticles. A reverse osmosis filtration process has been considered in order to purify the as-contaminated water.

2.2.4 Energy consumption

In the sol preparation step the heat consumptions to warm up the solution at 80°C and to keep the temperature constant for 16 hours have been evaluated. Similarly, the electric energy consumptions to mix the sol for 16 hours and to mix the TX-100 and the sol for 8 hours have been assessed. Moreover, the electricity used for the vacuum system and the reverse osmosis filtration has been considered. The electrical energy supply is assumed to be the Italian mix electrical energy generated by Ecoinvent database.[40]

2.2.5 Emissions and vacuum systems: assumptions and general considerations

The studied production system consists in a closed reactor, which allows avoiding nanoparticles air emissions, thus the only emissions to be assessed are those occurring in cleaning water (during maintenance operations).

The following assumptions have been considered:

- during the production and the purification steps a release into *air* of HNO_3 occurs and particularly the 1% of the total amount of material has been assumed to be emitted.
- during the maintenance operations, in particular in the purification process, the 1% of the TiO_2 nanoparticles suspension produced and composed of TiO_2, HNO_3, TX-100 and H_2O has been assumed to be released into the cleaning *water*.

Due to the above-mentioned emissions, a reverse osmosis filter equipped with a scrubber system, and a scrubber system solely, have been considered in the maintenance operations and production process respectively. The scope has been the reduction of the emissions to water and to air. In particular the scrubber system is able to capture the HNO_3 emissions while, the titanium dioxide nanoparticles, present in the obtained aqueous suspension, are entrapped by the reverse osmosis filter. The efficiency of the filter considered in the production process is 99.97%. The installation of reverse osmosis filter with high efficiency allows reducing the environmental impacts according to the ecodesign approach.

Regarding the end of life treatments, the part of filter that capture the emissions, together with the entrapped chemical substances, have been conferred recovered in a residual material landfill.

2.2.6 Mass balance

Table 1 shows the mass balance of the chemical synthesis; in particular 12% of the total is recovered as isopropanol (i.e. a reaction co-product) after the synthetic procedure. The remaining 88% is composed by 85.71% of TiO_2 nanoparticles suspension in water (main product) and a 14.29% of recoverable water considered as co-product.

The physical-chemical properties of the TiO_2 nanoparticles suspension are reported in Table 2. Particularly, the amount of TiO_2 nanoparticles in the aqueous suspension results of 6 wt%, and this value has been used to calculate a chemical reaction effective yield of 69.34%, which will be considered in the following EATOS calculations (see Section 4).

Table 2 Physical and Chemical properties of nanoTiO_2 suspension

Physical and Chemical properties	**Amount**
TiO_2 concentration (%w/w)	6
Density (g/ml)	1.15
Viscosity 20°C (mPa/s)	2
Nanoparticle size (nm)	30
Polydispersity index (pdI)	0.25
pH	5.5

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3 Life cycle assessment (LCA)

3.1 Aim definition

The aim of this LCA study is to assess the environmental impacts of a hydrolytic sol-gel synthesis of titanium dioxide nanoparticles suspension produced according to the procedure recently patented and actually employed by Colorobbia S.p.A. for the preparation of aqueous TiO_2 suspensions,[34,37] in order to identify its environmental loads.

3.2 System, functional unit and function of the system

The represented system is a multi-output process, which is based on the mass allocation criteria. The functional unit is represented both by the main product that is 0.75425 kg of the TiO_2 nanoparticles suspension and two co-products namely 0.12 kg of recovered isopropanol and 0.12575 kg of recovered water.

3.3 System boundaries

Fig. 1 highlights the system boundaries for the analysis, which include the upstream phases, from raw material extraction and chemicals production, till to the finished product packaging, thus obtaining “a cradle to the gate” overview. The production, maintenance and disposal of facilities, as well as the environmental burdens related to the production and disposal of packaging materials and other auxiliary materials have been also included in the present study. Emissions into the air and water, as well as the disposal of the part of filter that captures the nanoparticles or the volatile chemical compounds such as nitric acid have been taken into account. The transportation of chemical materials, facilities and packaging materials to the company that used them and the transportation of waste materials to a treatment facility have been also considered. In addition, energy consumptions required in all life cycle steps of TiO_2 nanoparticles suspension production have been evaluated as well.

3.4 Data quality and impact assessment methodology

The data for the study have been collected both directly from the authors of the patented procedure (primary data)[37] and from scientific literature (secondary data). In particular, primary data, referring to the optimized method for the preparation of aqueous dispersion of TiO_2 nanoparticles,[34,37] consist of the composition and the physical/chemical properties of TiO_2 nanoparticles suspension and energy consumptions. Where the data are somehow missing the study has been completed on the basis of secondary data obtained from the Ecoinvent database that exploited them to model the background processes (land use, materials production, fuel and electricity production and transports). The analysis is performed by using the SimaPro 7.3.3 software and IMPACT 2002+ evaluation method to assess the environmental impacts.

3.5 Life cycle inventory

In a LCA study, the quality and credibility of the results largely depend on the quality of the data included in the Life Cycle Inventory (LCI) stage. In accordance with ILCD Handbook[41] the inventory must state, in a specific and reliable way, all the inputs in the form of material and energy resources and all the outputs in the form of air emissions, emissions into water and soil, as well as the solid waste that is generated, for each of the stages of the life cycle of the system being studied (according to ISO/TS 14048)[42]. The inventory data has been modelled in SimaPro 7.3.3, taking the Ecoinvent database v2.2 as reference to configure the inventory of some chemicals (i.e. nitric acid and TX-100), natural gas, electricity, heat, transport, infrastructure, machinery and waste treatments. In those cases where the chemicals were missing, such as the case of titanium isopropoxide (reagent) and titanium tetrachloride (titanium isopropoxide precursor), they have been created using literature data.[43] The same approach has been followed for the vacuum system and the purification processes.

3.6 Impact assessment

Life cycle impact assessment (LCIA) results have been modeled by IMPACT 2002+ method using Simapro 7.3.3, to determine the environmental impacts related to the emissions released and resources consumed in the system under study.[44] This impact assessment method covers more impact categories than other methods and includes more substances, but the following additions and modifications have been implemented in order to describe the system considered in a more representative manner:

- Land use has been estimated by considering basic indicators of both land occupation and transformation. In the present study *Transformation, to forest intensive, normal, Transformation, to forest intensive and Transformation, to arable* have been introduced.
- Mineral extraction has been characterised in consideration of some additional resources such as *silver, gravel, sand, lithium, bromine and water in ground*, derived from the category Minerals of Eco-indicator 99 with the same characterisation factors.[45]
- Radioactive waste category has been added; particularly both this kind of waste and its occupied volume have been evaluated considering the same characterization and normalization factors of EPID 2003 method.[46] This category allows to take into account the possible damage of electric energy mix, which also includes the electricity generated by nuclear plants. This latter kind of energy produces radioactive waste, which have to be safely managed and disposed.

Concerning the toxicity of nanoparticles, it is known that there are currently several major uncertainties and knowledge gaps with regard to the behavior, chemical and biological interactions and toxicological properties of engineered nanomaterials.[47] Despite this, a preliminary attempt to assess the toxicity of TiO_2 nanoparticles released in water on freshwater ecosystem and human health has been done. Particularly, the IMPACT 2002+ method has been furthermore exploited at this purpose as follow:

- *Particulates, <100 nm, in freshwater* (a representative substance of the damage on freshwater ecosystem) has been introduced in a new impact category named NanoTiO_2 Ecotoxicity in freshwater which refers to a new damage category with the same name and with a characterization factor calculated by Salieri et al..[48]
- *NanoTiO_2 Human toxicity, in freshwater* (a representative substance of a local damage on human health, considering the area of Emilia Romagna region in the north-east of Italy) has been introduced in a new impact category called *NanoTiO_2 carcinogens in freshwater* which refers to a

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new damage category with the same name and with a new calculated damage assessment factor.[49] This factor has been determined considering the Anandanl and Kumar study which evaluated the target organ toxicity dose (TTD) value for human liver cell toxicity in stream water of 8.33µg/L for the TiO_2 nanoparticles.[50] The new damage factor has been determined by Eco-indicator 99 calculation method for carcinogenic substances; in particular it consists of three main steps: fate analysis, effect analysis and damage analysis. It considers an emission released into freshwater during the purification of water contaminated by nanoparticles of 1kg/yr, a water body volume of Reggio Emilia province of $9E6m^3$ and a calculated nanoparticles concentration of $1.111E-7$ kg/m^3. The damage assessment factor obtained is of 7.14E-6 DALY/kg of TiO_2 nanoparticles released into water.

4 EATOS calculations

The list of the starting substances considered in the assessment made by means of the software EATOS and the categories to which they have been considered to belong are reported in Table 4. Table 4 summarizes the yield of the synthetic procedure as well as the useful amounts of obtained coupled products, the latter accounting for their possibility to be recovered and eventually recycled. All of the amounts reported in the two above-mentioned tables are in accordance with the functional unit considered into the LCA analysis (i.e. the amount of TiO_2 obtained from 1 kg of starting materials).

The amount of solvent has been considered completely recyclable (see Table 3), while the useful quantities of isopropyl alcohol and the remaining water (i.e. the second coupled product) have been settled in accordance to what indicated by the patented procedure[37] and off course to the amounts used into the LCA assessment, as reported in Table 1. In detail 120 g constituted the effectively recovered amount of isopropyl alcohol, while the maximum useful amount of the coupled product water has been established according to the yield of the reaction, assuming thus a maximum value of 69.34% of that theoretically obtainable. This yield value corresponds to a water amount which is significantly lower with respect to what indicated (Table 1) and considered in the LCA framework. The reason needs to be found in the fact that what considered by LCA as the water co-product, indeed refers to the amount of water effectively recovered after the synthetic procedure, the latter comprising both the effective water co-product and part of the water originally intended as the solvent.

Table 3 List of starting substances used for the EATOS environmental assessment of the hydrolytic sol-gel synthesis of TiO_2 nanoparticles, considering the stoichiometric reaction reported in equation 11

Substance	Category	Molecular weight (g/mol)	Quantity (g)
$Ti(OiPr)_4$	key substrate	284.2308	232.2
H_2O	substrate	18.0152	58.87
H_2O	solvent	18.0152	675.13 (recyclable quantity =100%)
HNO_3, 63%	catalyst	63.0128	23.8
Triton X-100	auxiliary material	646.8572	10

Table 4 List of product and coupled products considered in the EATOS environmental assessment of the hydrolytic sol-gel synthesis of TiO_2 nanoparticles, considering the stoichiometric reaction reported in equation 9

Substance	Category	Molecular weight (g/mol)	Useful quantity (% or g)	Yield (%), referred to the key substrate
TiO_2	product	79.8788	-	69.34
H_2O	coupled product	18.0152	69.34%	-
C_3H_8O	coupled product	60.0956	120 g	-

The software EATOS allows calculating four important environmental parameters: the mass index MI (eq. 2), the environmental factor E (eq. 1) together with EI_in and EI_out corresponding to the former ones in which each substance quantity is multiplied by its specific total weighting factor, Q_{tot}, which represents a mean value calculated among the different weighting factors Q*i* values. In detail the weighting factors allow evaluating and examining the specific chemical reaction with particular regard to the potential environmental and human health relevance of each substance employed.[51] The index *i* in the Q*i* notation, accounts for the *i*th weighting category among claiming of resources, risk, human toxicity, chronic toxicity, ecotoxicology, ozone creation, air pollution, accumulation, degradability, greenhouse effect, ozone depletion, nutrification and acidification. Each Q*i* can assume values ranging from 1 to 10 according to specific classifications internally made by the software algorithms. The software EATOS allows also selecting the opportune significance to associate to each weighting category.

The relevant information which determine the Qi value for that particular substance can be easily found into the Material Safety Data Sheet (MSDS) available from the supplier. Particularly in this work the MSDS considered have been those available on the Sigma Aldrich website,[52] and as concern the price, the biggest amount available has been selected.

5 Results and discussion

The Life Cycle Impact Assessment (LCIA) has been reported by both midpoint and endpoint assessment. Midpoint indicators are considered to be linked to the cause-effect chain (environmental mechanism) of an impact category. Common examples of midpoint characterization factors include ozone depletion potentials, global warming potentials, and photochemical ozone (smog) creation potentials. Endpoint indicators are instead considered to be linked to the cause-effect chain for all categories of impact (e.g., human health impacts, in terms of disability adjusted life years for carcinogenicity, climate change, ozone depletion, photochemical ozone creation, or impacts in terms of changes in biodiversity, etc.).[53]

5.1 LCA results

Single score damage is 988.87µPt for 1 kg of TiO_2 nanoparticles suspension produced. As Figure 2 shows, the electric energy consumption to mix the colloidal solution (sol) for 16 hours (indicated as E1) and the one necessary to mix the sol and TX-100 for 8 hours (indicated as E2) are the two contributions which are mainly responsible for the total damage (38.76% and 19.38% respectively), followed by the titanium isopropoxide (TIP) production (13.65%) and by the heat consumption (indicated as H2) to maintain the solution at 80°C (10.33%). A midpoint category interpretation is conducted, being the latter more appropriate to evaluate the environmental impacts of the various substances counted in the life cycle inventory. The impact categories considered are global warming, non-renewable energy, mineral extraction, carcinogens, non-carcinogens, respiratory inorganics, respiratory organics, aquatic ecotoxicity, terrestrial ecotoxicity, ionising radiation, ozone layer depletion, terrestrial acidification, aquatic acidification, aquatic eutrophication, radioactive waste, land occupation, nanoTiO_2 ecotoxicity in freshwater and nanoTiO_2 human toxicity.

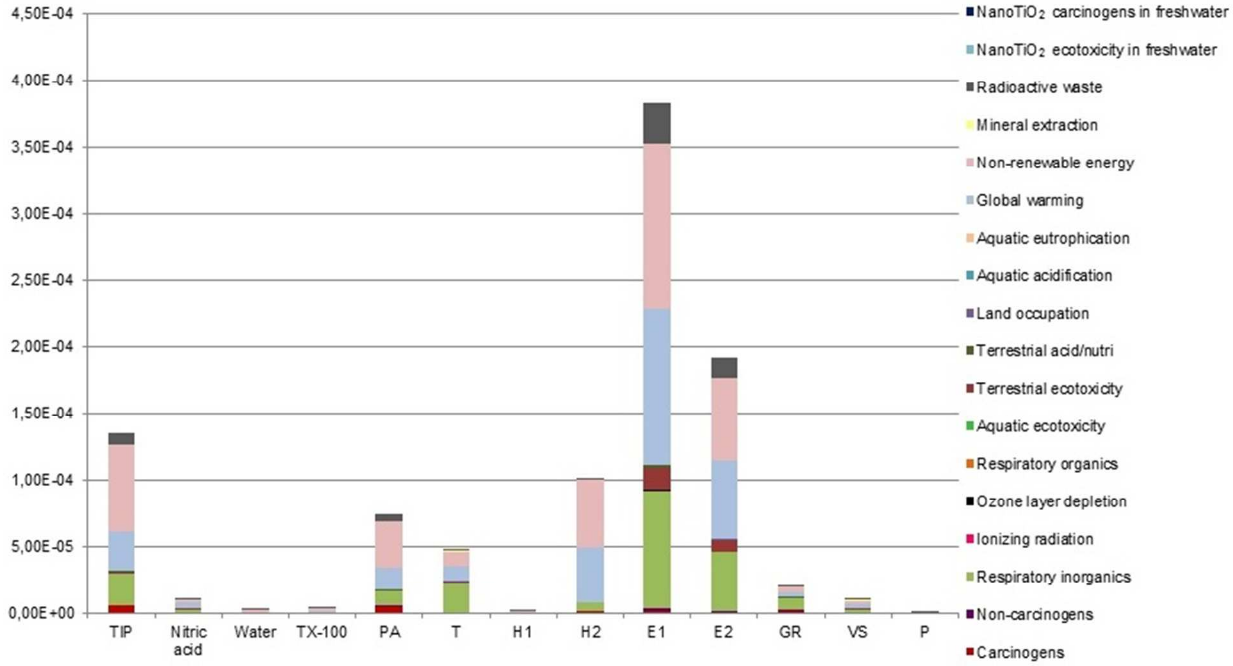

Fig. 2 Evaluation by single score of 1 kg of a bottom-up hydrolytic synthesis of TiO_2 nanoparticles, where TIP= Titanium isopropoxide; TX-100= Triton X-100; PA= Packaging of raw materials; T= Transport of raw materials; H1= Heat to warm up the solution at 80°C; H2= Heat to maintain the solution at 80°C; E1= Electric energy to mix the sol for 16 hours; E2= Electric energy to mix the sol and TX-100 for 8 hours; GR= Glass Reactor; VS= Vacuum system; WP= Water Purification.

Table 5 Characterised LCIA results

Midpoint results			Endpoint results		
Impact category	Unit	Total	**Damage category**	Unit	Total
Carcinogens	kg C_2H_3Cl eq	4,43E-2	Human Health	DALY	1,68E-06
Non-carcinogens	kg C_2H_3Cl eq	1,63E-2			
Respiratory inorganics	kg PM2.5 eq	2,13E-3			
Ionizing radiation	Bq C-14 eq	48			
Ozone layer depletion	kg CFC-11 eq	3,95E-7			
Respiratory organics	kg C_2H_4 eq	1,06E-3			
Aquatic ecotoxicity	kg TEG water	1,70E2	Ecosystem Quality	PDF*m^2*yr	0,503
Terrestrial ecotoxicity	kg TEG soil	52,8			
Terrestrial acid/nutri	kg SO_2 eq	4,39E-2			
Land occupation	m^2org.arable	2,91E-2			
Aquatic acidification	kg SO_2 eq	1,27E-2			
Aquatic eutrophication	kg PO4 P-lim	8,17E-4			
Global warming	kg CO_2 eq	2,86	Climate Change	kg CO_2	2,863
Non-renewable energy	MJ primary	55	Resources	MJ primary	55,15
Mineral extraction	MJ surplus	1,53E-1			
Radioactive waste	kg	6,37E-5	Radioactive waste	kg	6,37E-05
NanoTiO_2 ecotoxicity in freshwater	kg	6,63E-9	NanoTiO_2 ecotoxicity in freshwater	PAF*m^3*day	1,86E-09
NanoTiO_2 carcinogens in freshwater	kg	6,63E-9	NanoTiO_2 carcinogens in freshwater	DALY	4,73E-14

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Table 5 sums up the outcomes of the midpoint and endpoint analysis that are explained in detail hereafter. In particular, for the midpoint analysis the contributions of the main impact categories on the total damage are reported.

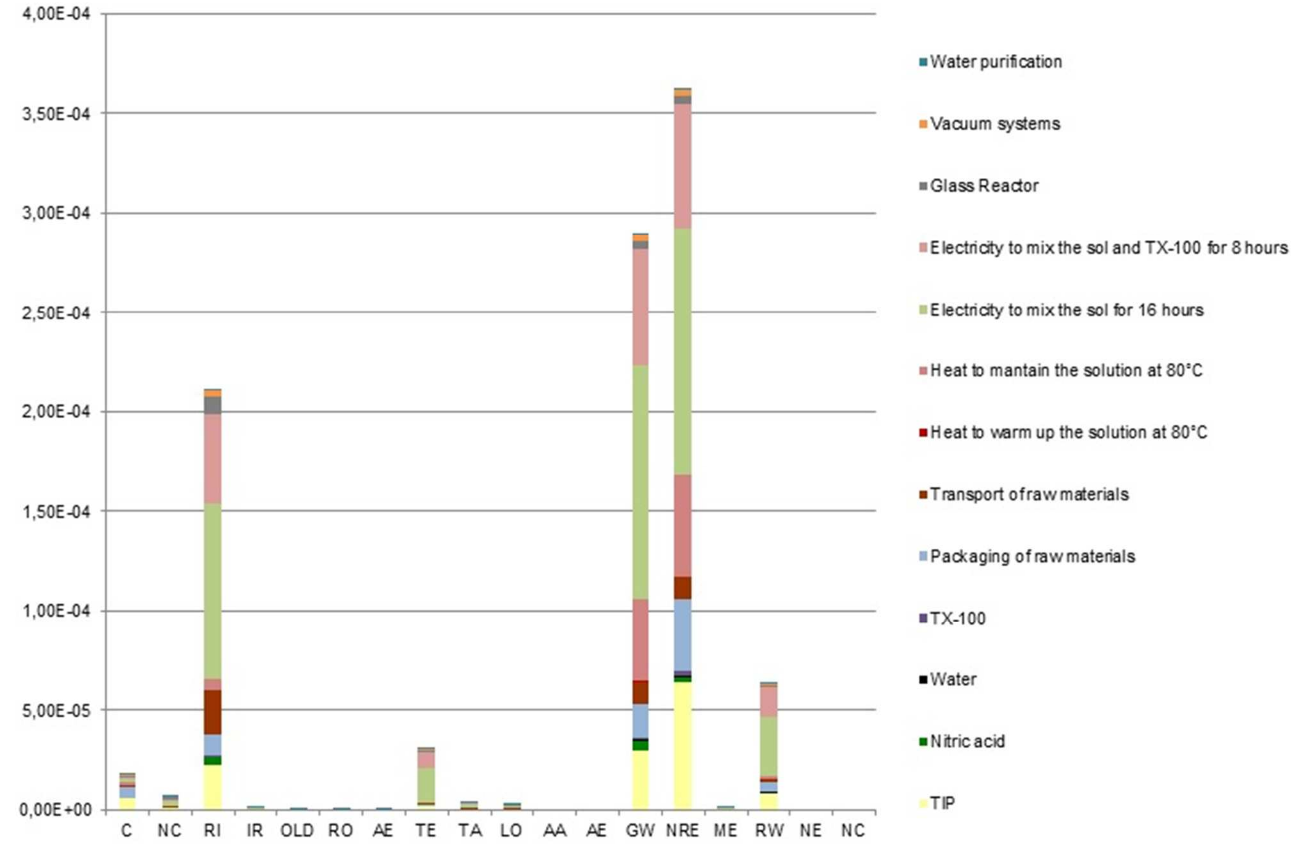

Fig. 3 Evaluation by impact categories of 1 kg of a bottom-up hydrolytic synthesis of TiO_2 nanoparticles, where C= Carcinogens; NC= Non-Carcinogens; RI= Respiratory Inorganics; IR= Ionizing Radiation; OLD= Ozone Layer Depletion; RO= Respiratory Organics; AE= Aquatic Ecotoxicity; TE= Terrestrial Ecotoxicity; TA= Terrestrial acid/nutri; LO= Land Occupation; AA= Aquatic Acidification; AE= Aquatic Eutrophication; GW= Global Warming; NRE= Non-renewable Energy; ME= Mineral Extraction; RW= Radioactive Waste; NE= NanoTiO_2 ecotoxicity in freshwater; NC= NanoTiO_2 carcinogens in freshwater

Figure 3 highlights that the most significant contribution to the total damage is due to Non-renewable Energy impact category which is primarily affected by natural gas (52.31%), crude oil (25.58%) and hard coal (11.23%) emissions. For all types of emissions the electric energy consumption to mix the sol for 16 hours is the process that produces the major environmental load (33.09%, 25.5% and 49.18% respectively). In particular in this process the emissions are mainly caused by the natural gas and crude oil production and the hard coal mining respectively.

Successively, the second major contribute to the total damage is generated by the Global warming impact category, mainly due to GHG (greenhouse gas) emissions (96.17%), which are for the 41.24% belonging to the electric energy consumption to mix the sol for 16 hours and in particular generated by the natural gas used to produce the electricity.

In Respiratory Inorganics the major contributions are due to the following emission to air: 37.3% of NO_x, 28.91% of SO_2 and 18.61% of particulates < 2.5 μm. All of these are mainly due to the electric energy consumption to mix the sol for 16 hours (38.77%, 49.65% and 45.54% respectively) and, in particular, generated for the first two (NOx and SO_2) during the heavy fuel oil combustion while for the latter one during the hard coal combustion.

In Radioactive Waste impact category, the volume occupied by low-active radioactive waste contributes for 65.31% on the total damage due to the electric energy production by nuclear power plants.

About the NanoTiO_2 ecotoxicity in freshwater and NanoTiO_2 carcinogens in freshwater impact categories the damage is totally due to the releases of 6,63 μg of *particulates, <100 nm* (anatase TiO_2 nanoparticles) and 6,63 μg *nanoTiO_2 human toxicity* in freshwater during the purification of contaminated water, which are obtained by the maintenance operation (reactor cleaning, see paragraph 2.2.3).

The endpoint analysis highlights (Fig. 4) that the total damage is affected for 23.9% the Human Health (2.36E-4 Pt), for 36.7% the Resources (3.63E-4 Pt), for 29.24% the Climate Change (2.89E-4 Pt), for 3.71% the Ecosystem Quality (3.67E-5 Pt), for 6.44% the Radioactive waste (6.37E-5 Pt), for 3.36E-6% the NanoTiO_2 ecotoxicity in freshwater (3.32E-11 Pt) and for 6.75E-7% the NanoTiO_2 carcinogens in freshwater (6.67E-12 Pt). In these latter two cases the damage is restrained since, as mentioned before, the LCA study has been set in an ecodesign approach, thus installing a specific filter for nanoparticles with a

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high efficiency (99.97%), in order to limit the nanoparticle releases.

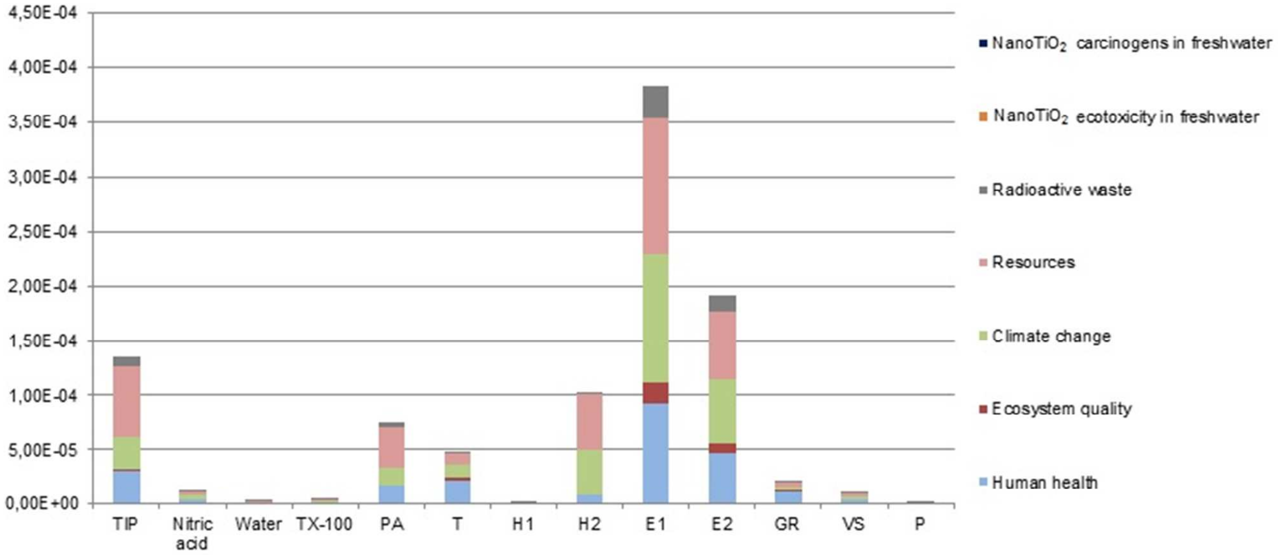

Fig. 4 Evaluation by damage categories of 1 kg of a bottom-up hydrolytic synthesis of TiO_2 nanoparticles, where TIP= Titanium isopropoxide; TX-100= Triton X-100; PA= Packaging of raw materials; T= Transport of raw materials; H1= Heat to warm up the solution at 80°C; H2= Heat to maintain the solution at 80°C; E1= Electric energy to mix the sol for 16 hours; E2= Electric energy to mix the sol and TX-100 for 8 hours; GR= Glass Reactor; VS= Vacuum system; WP= Water Purification

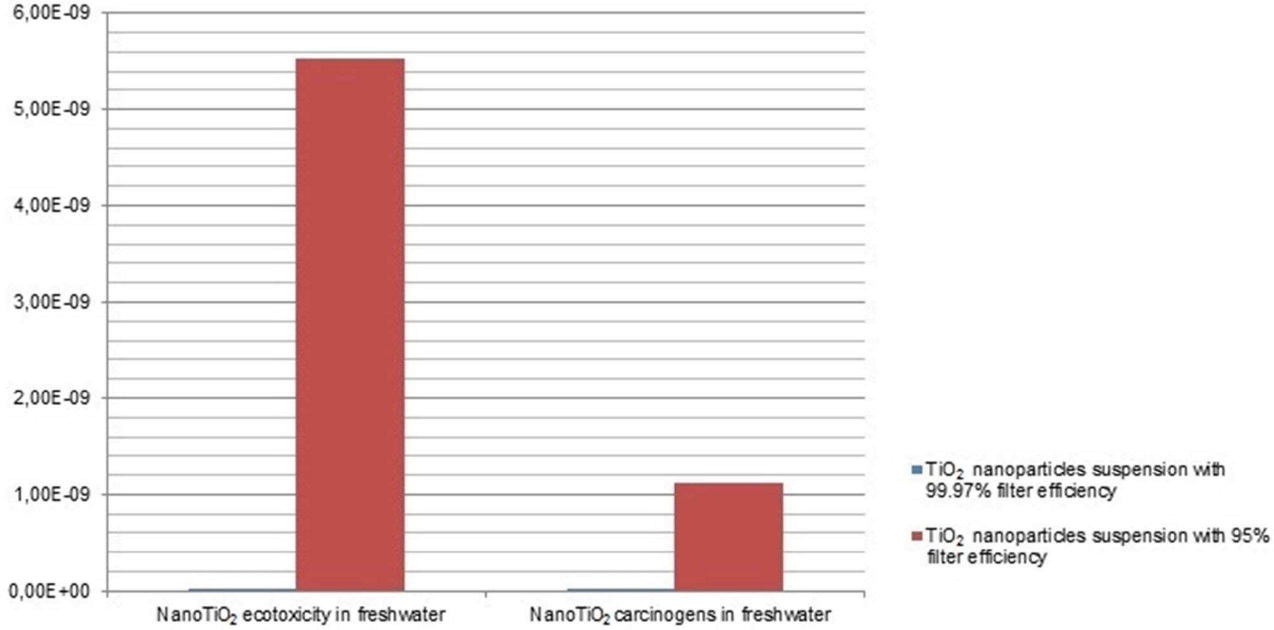

Fig. 5 Comparison of environmental impact values (Pt) for 99.97% and 95% filter efficiency

Indeed, Figure 5 shows that the variation of the sole filter efficiency from 99.97% to 95% leads to an increase of the damage in $NanoTiO_2$ ecotoxicity in freshwater and $NanoTiO_2$ carcinogens in freshwater impact categories equal to 165.67%.

Furthermore, a life cycle cost analysis has been carried out. Internal and external costs have been assessed. The first takes into account all input materials cost and the latter considers environmental costs caused by the hydrolytic synthesis of TiO_2 nanoparticles.

The results for 1 kg of TiO_2 nanoparticles suspension show that internal and environmental costs values are 29.125 euro and 1.289 euro respectively, being them mainly caused by electric energy consumptions.

5.2 EATOS results

Results returned by the software EATOS in terms of the evaluation of histograms for the metrics MI, E-factor, EI_in and EI_out are reported in Figure 6. The green metric EI_out parameter, expressed in Potential Environmental Impact (PEI; the bigger its value is, the worse the process will impact on the environment) per kg of product, accounts for the environmental damage potentially induced by the reaction waste. Particularly, as

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detailed in Table 6 its total value of 9.6195 is mainly attributed to coupled products, since only a limited amount of isopropyl alcohol is recovered. The category by-products accounts for the fact that being the yield of the synthetic process equal to 69.34 some unspecified by-products need to be considered.

More interestingly, in the particular framework of a direct comparison with the LCA results, the potential environmental and human health relevance of each substance employed in the total inward materials flux related to the hydrolytic synthesis of anatase TiO_2 nanoparticles suspension should be considered. At this latter regard, the green metrics parameter EI_in reaches a total value of 16.0896 PEI/kg, and it is for its 83.9% due to the titanium isopropoxide precursor, for its 8.5% to catalyst, for its 2.1% to auxiliary materials and for its 2.4% to the solvent (i.e. water). Noteworthy is that this latter finding is in perfect agreement with previously discussed LCA results. Indeed, by simply neglecting the energy contributions, the LCA outcomes show that the total damage is mainly caused by titanium isopropoxide for the 87.98% and by nitric acid for the 7.22%.

According to this latter approximation, Figure 7 reports the comparison between LCA and EATOS outcomes in terms of the main factors affecting the single score damage and EI_in respectively, revealing a tremendously similar trend.

It needs to be specified that for the present EATOS analysis the weighting categories considered have been those in which the corresponding values for at least one substance have been found and consequently inserted, i.e. human toxicity, chronic toxicity, ecotoxicology and accumulation (to which an influence of 25 % has been assigned). The possibility of Q=0 assignment has been considered as well.

A further possibility offered by the EATOS software, is to calculate and present the different entry items, such as substrates, solvents, and so on by the so-called economic index, i.e. COST INDEX (CI). The different contributions to the CI (expressed in eur/kg) deriving from the different input materials used for the synthesis under consideration are detailed in Table 7.

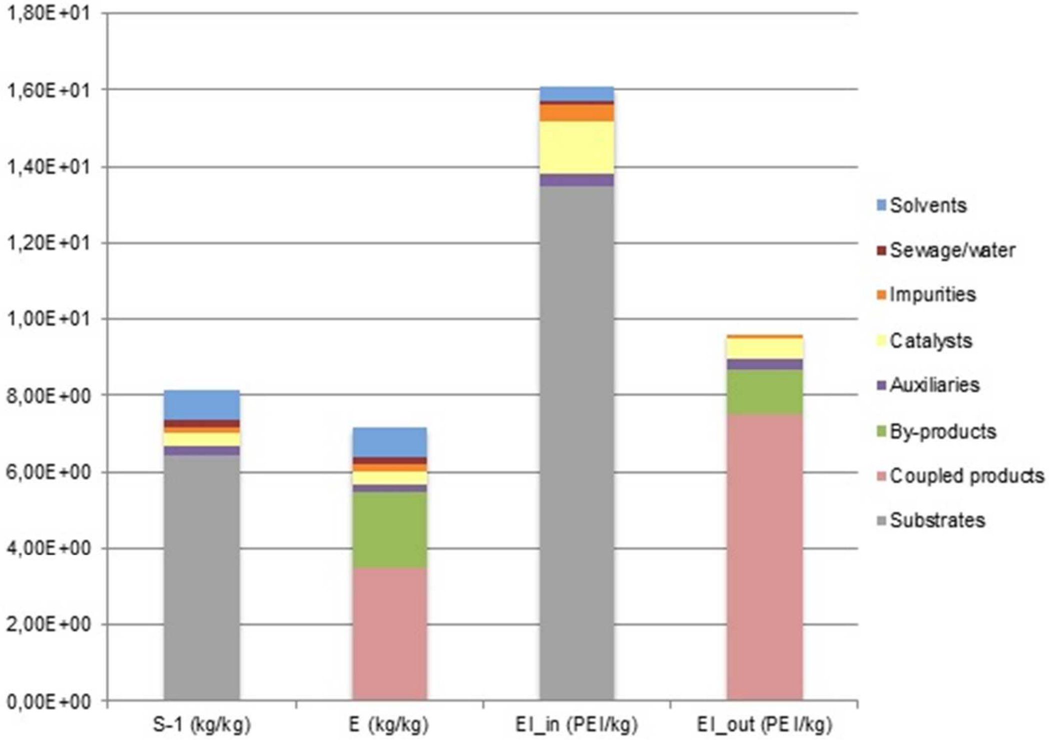

Fig. 6 EATOS results

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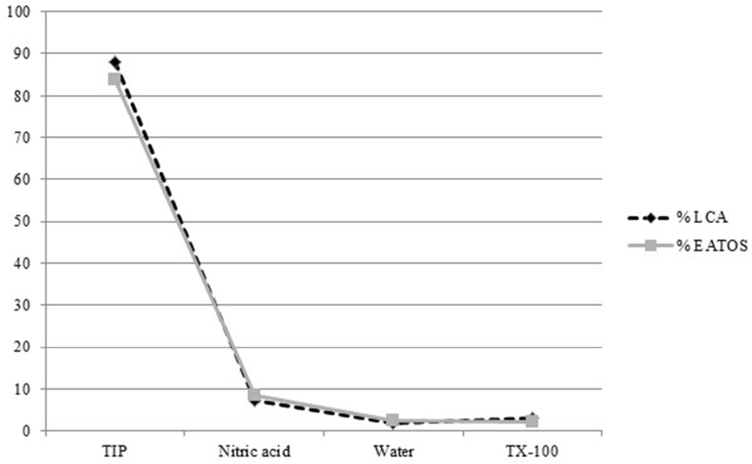

Fig. 7 EATOS and LCA (excluding energy consumptions) results comparison

Table 6 Contributions of all the substances to the metrics S-1, E, EI_in and EI_out

Category	Substance	S^{-1} (kg of starting material/kg of product)	E (kg of waste/kg of product)	EI_in (PEI/kg)	EI_out (PEI/kg)
Substrates	Titanium isopropoxide and water	6.4728	0.0402	13.4997	/
Coupled products	Isopropanol and water	/	3.4604	/	7.5233
By-products	Unspecified	/	1.9723	/	1.18
Auxiliaries	Triton X-100	0.2278	0.2278	0.3418	0.2848
Catalysts	Nitric acid	0.3416	0.3416	1.3665	0.5124
Impurities	Unspecified	0.1587	0.1587	0.3968	0.119
Sewage/water	Water+unspecified	0.2006	0.2006	0.1003	/
Solvents	Water	0.7691	0.7691	0.3845	/
Total		**8.1706**	**7.1707**	**16.0896**	**9.6195**

Table 7 Detailed quantification of the different contributions to the CI, for the hydrolytic sol-gel synthesis of anatase TiO_2 nanoparticles investigated with EATOS tool.

Substance category	CI (EUR/kg)
Substrates	454.948
Auxiliaries	8.9115
Catalysts	17.6381
Impurities	13.6392
Solvent	**7.9986**
Sewage/water	**2.0866**
Total	**505.222**

6 Conclusions

The environmental assessment of the bottom-up hydrolytic sol-gel synthesis of anatase TiO_2 nanoparticles has been concurrently performed by the software EATOS and by LCA methodology and, although the different philosophies on which they are based, similar conclusions can in some conditions be drawn.

EATOS software has been originally developed for organic chemists and mainly applies to fine chemical processes, relying on data which are easily available from the material safety data sheets. On the contrary, Life Cycle Assessment is a much more detailed and versatile method, suitable to assess industrial scale procedures, but it is hardly adaptable to small scale ones,[54] due to its intrinsic time-consuming nature and to the difficulty to source necessary inventory data. Particularly for chemical processes, the databases to which the LCA methodology refers to, are still significantly inadequate. Therefore, when the required chemical is not included in databases it is necessary either to consider chemicals with similar properties, among those comprised in the databases, or to recreate the synthesis of that particular substance *ex novo*.

Despite its immediacy, EATOS suffers from the major strong approximation of neglecting any energetic contribution. Precisely the typical limitations and drawbacks of both EATOS and LCA contributed to highlight their complementary character, which has been extensively exploited in the environmental and human health assessments of several organic reactions.

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The present work represents, to the best of authors' knowledge, the first example in which, the synergy between LCA methodology and EATOS software, has been applied to the green metrics evaluation of the inorganic synthesis of engineered nanomaterials.

In details the studied hydrolytic sol-gel synthesis route generates a suspension of TiO_2 nanoparticles, characterized by high purity and crystallinity, according to the patented procedure.[37] The evaluated ecodesign approach (based on the installation of 99.97% efficiency filter and the use of closed reactor) together with the employed aqueous solvent and the low processing temperature, contribute to well fit the here presented synthetic protocol into a green chemistry perspective.

The LCA results evidenced that the most environmental loads are generated by the electric energy consumption (58.14%), followed by titanium isopropoxide (13.65%) and heat consumption to maintain the solution at 80°C (10.33%). A better environmental performance can be achieved by:

- using renewable energy sources (e.g. solar power, geothermal, biomass, etc.), in order to reduce the non-renewable energy consumption.
- using microwave dielectric heating of reaction mixture, which has recently been significantly employed not only in organic chemistry but also in inorganic synthesis of a wide variety of engineered nanomaterials,[55] due to its intrinsic advantages over conventional heating techniques based on heat transfer mechanisms (rather than on energy transfer ones).
- substituting titanium tetraisopropoxide with a different metal oxide precursor, more environmentally friendly and less costly.

At this latter regard, the use of the software EATOS alone, can furnish a first reliable approximation for the environmental assessment of synthetic strategies employing different metal oxide precursors. Indeed, in the present study, neglecting any energy contributions, the comparison between the results obtained using LCA methodology and EATOS software, highlighted the reaching of similar conclusions from both approaches. Particularly, they returned very similar environmental impacts with the more affecting factor resulting in the titanium isopropoxide, followed nitric acid and with aqueous solvent and auxiliary triton X-100 showing pretty close contributions.

In conclusion EATOS provides fast and functional results, which are comparable to LCA results when energy consumptions are neglected. Furthermore, EATOS is a free of charge and user-friendly software, so it is particularly suitable when a choice among different synthetic strategies needs to be considered for the preparation of the desired engineered nanomaterial.

This work represents the first example of the application of EATOS software (originally developed for the synthesis of fine chemicals) to inorganic synthesis of transition metal oxide nanostructures, and the natural progression of the research activities in this direction, actually in progress, will involve the comparison among the most widely employed synthetic strategies for the obtainment of the desired inorganic nanocrystals. However, a later deeper investigation by a complete LCA study should be carried out since LCA methodology provides more detailed and accurate results. Indeed midpoint and endpoint analysis give a complete knowledge on: *i)* the impact and damage categories that mainly affect the total environmental and human health impacts of the studied process, *ii)* the substances that cause these impacts and *iii)* the compartments (air, soil, water, raw) that result more paining.

The main conclusion of the present work, which would like to be a recommendation to inorganic chemists and materials scientists worldwide, is to always combine an environmental assessment to any new proposed strategy for the synthesis of engineered nanomaterials, so that the strict requirement of using the most environmentally friendly procedure very soon could accompany traditional requests of a desired size and shape.

The assessment by means of easily available and accessible EATOS tool, although able to furnish trustworthy indications, should be later on integrated by a complete Life Cycle Assessment study, thus allowing considering also the impacts of the energy consumption, which usually represents the most impacting parameter of the whole process.

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