Deliverable 2.1

Report of the selection of CNMs

Deliverable report for

Implementing Innovative Methods for Safety and Sustainability Assessments of Chemicals and Materials Particularly at Nano Level in The European Union

(CheMatSustain)

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Abstract

Deliverable 2.1 is the report that presents the considerations summarizing the methodology of selection process of chemicals, nanomaterials and materials (CNMs) investigated in the CheMatSustain project. The report includes: i) the list of pre-selected CNMs ii) the definition of the most crucial parameters that determine the selection process, iii) the identification of the most relevant groups of CNMs, iv) the discussion concerning the factors affecting the selection process (with particular emphasis on physicochemical, socio-economic aspects, environmental and application aspects of selected CNMs), and v) the conclusions and the final list of selected CNMs.

Keywords

Materials, nanomaterials, chemicals, selection process.

Disclaimer

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List of Abbreviations and Acronyms

Acronym	Description
AgNPs	Silver Nanoparticles
AuNPs	Gold Nanoparticles
AuNRs	Gold Nanorods
BNC	Bacterial Nanocellulose
CMS	CheMatSustain
CNCs	Cellulose Nanocrystals
CNF-s	Cellulose Nanofibrils
CNMs	Chemicals and (nano)materials
DSSCs	Dye-Sensitized Solar Cells
JRC	The European Commission's Joint Research Centre
MCC	Microcrystalline Cellulose
mNPs	Metallic Nanoparticles
NPs	Nanoparticles
PAMAM	Poly(amidoamine) dendrimers
PEG-SH	Poly(ethylene glycol) Methyl Ether Thiol
PS-NPs	Polystyrene Nanoparticles
PVP	Polyvinylpirrolidone
RS	Red Sentinel
RTMs	Representative Test Materials
SC	Sodium Citrate
TA	Tannic Acid
TOR	Tormentic Acid
TER	Triterpenic acids obtained from RS (Red Sentinel) callus extract

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Introduction

On the contents and scope of deliverable 2.1. Selection of CNMs

The specific objective of task WP2 is to identify select and supply four sets of chemicals, (CNMs – chemicals and (nano)materials) that will be tested in respect of chemical and physical attributes which will ultimately improve their safety and sustainability. Thus, in a first stage the pre-selection of CNMs included in the proposal is being confirmed and validated in Task 2.1 when the final selection of the CNMs will be based on an in-depth analysis. Next, selected CNMs will be synthesized or purchased (Task 2.2) and characterised in primary phase (Task 2.3). However, such progress requires a multi-faceted approach to the selection of materials as well as the knowledge about the application of individual materials and a preliminary assessment of its possible impact on the environment. Hence, the first stage of WP2 consists in selection and identification of materials for the project implementation that meet specific criteria resulting from the project assumptions. This report presents a summary of selection process along with a discussion of the detailed selection criteria.

List of pre-selected CNMs

To comply with the project implementation requirements, and to achieve its objectives, the CheMatSustain consortium has pre-selected a specific group of chemicals/(nano)materials (CNMs) that will be the basis on which the project will be implemented. This group of pre-selected CNMs samples respond to a threefold criterion, they are: 1) CNMs applicable to demonstrate the innovative concept of the project, 2) CNMs widely/commonly used in the health care/medical industry, and 3) CNMs acknowledged for their potential risks to humans and ecosystems.

A total pre-selected set of 31 CNMs, consists of: i) metallic nanomaterials (16) (spherical silver (6), rod-shaped silver (4), spherical gold (6)); ii) polymeric nanomaterials (PAMAM dendrimers (6) in full and half-generations); iii) micro/nano-materials (4) as a pair of the same materials in micro and nanoscale range size; iv) chemical substances often used for nanomaterials synthesis/stabilisation (5). The CheMatSustain diagram illustrating the project's pre-selected samples of CNMs is presented in Figure 1.

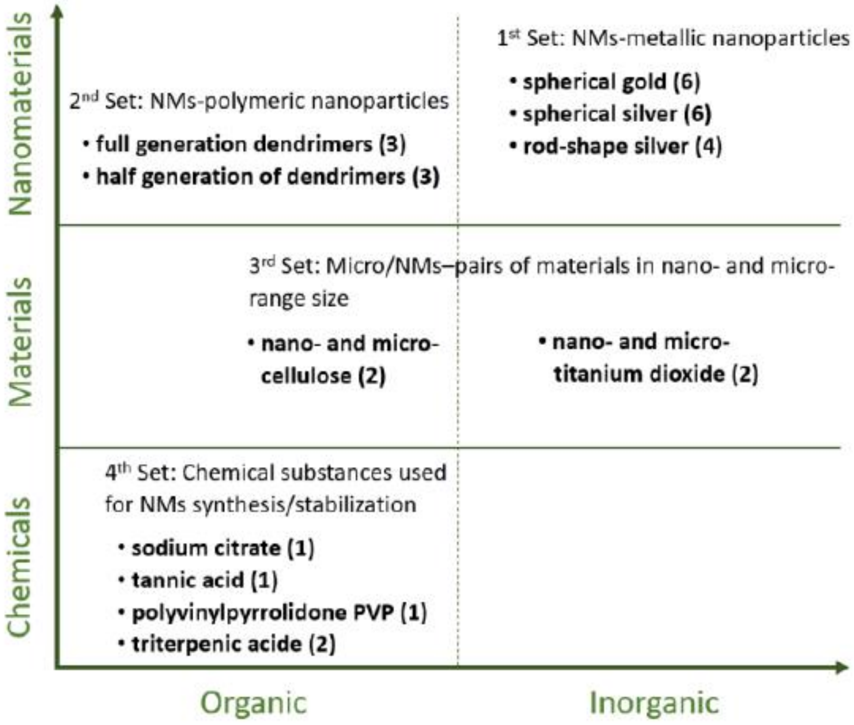

FIGURE 1. CheMatSustain diagram illustrating the project's pre-selected samples of CNMs.

The pre-selected samples of CNMs that are planned to be tested in the project consist of 31 different samples, that can be assembled into four groups:

1) Metallic nanomaterials (16 samples in total):
   - Spherical silver nanoparticles: in sizes 5, 10 and 50 nm, plus two out of five types of surfactants, giving a total of six (6) different samples.
   - Rod-shaped silver nanoparticles: with two lengths (diameters and lengths to be fixed), plus two out of five types of surfactants, giving a total of four (4) different samples.
   - Spherical gold nanoparticles: in sizes 5, 10 and 50 nm, plus two out of five types of surfactants, giving a total of six (6) different samples.

2) Polymeric nanomaterials (6 samples in total)
   - PAMAM dendrimers: in three generations (for example G2, G4 and G7). Thus, giving three (3) different samples.
   - PAMAM dendrimers: in three half-generations (for example G1,5, G3,5 and G6,5). Thus, giving three (3) different samples.

3) Micro/nanomaterials (4 samples in total) – pairs of the same materials in macro and nanoscale range size
   - Micro and nano titanium dioxide – one pair (2) of different samples.
   - Micro and nano cellulose – one pair (2) of different samples.

4) Chemical substances used for nanomaterials synthesis/stabilisation (5 samples in total)

- Sodium citrate – one sample (1).
- Tannic acid - one sample (1).
- Polyvinylpyrrolidone PVP – one sample (1)
- Triterpenic acids (2)

Pre-selection of CMNs

Definition of crucial parameters for CMNs selection

Nano-based technology has made enormous progress over the last decades. Nowadays, there is numbers of products that either contain or require nanomaterials for their production. This development is likely facilitated by their unique general properties that are the consequences of particle size, surface area, surface reactivity, charge, and shape. This enables a broad range of existing and possible applications, including cosmetical, pharmaceutical, medical, kitchenware, electronics, renewable energy, or even aerospace utilization. It has been anticipated that the increasing application of nanomaterials both quantitatively but also in terms of product diversity will lead to a diversification in emission sources into the environment. The objective of CheMatSustain is to assess consistently chemicals and materials, including nanomaterials. Because nanomaterials have different properties compared to their macro-counterparts, particle size has a key role in CheMatSustain. Therefore, for the proper implementation of the project, it was necessary to select micrometer-sized materials to fully identify, determine and understand the results obtained for nanomaterials. The selection of CNMs was performed within organic and inorganic substances and within those two main groups we identified the most important representatives of: chemicals, nanomaterials and materials. The selection process included CNMs necessary from the different point of views: i) CNMs important from the scientific point of view enabling the identification of relationships between materials (those are so-called “model materials” with precisely defined and repeatable physicochemical parameters); ii) CNMs widely used in industry; iii) CNMs with potential applications. This approach to the selection of materials will enable the development of methods for nanomaterials identification using model materials, then monitoring of the developed methods effectiveness by investigation of materials present in the industry and environment, and the assessment of possible threats, in the case of the investigation of materials with possible applications, before introducing them on the market.

Identification of the most important/relevant CNMs

The next step in the selection of materials was to indicate the representatives of individual groups: chemicals, nanomaterials and materials. Based on the threefold criterion mentioned (i) innovative concept of the project; ii) materials widely used in health care/medical industry and iii) materials acknowledged for their potential risks to humans and ecosystems, the following representatives were selected:

— Metallic nanoparticles

The main selection criterion for metallic nanoparticles (mNPs) was to test the scientific postulates of the CheMatSustain connected with the recognition of the nanomaterials by biological response. NPs have distinct physical and chemical proportions and cause distinct biological effects compared to their macro-counterparts. NPs differ from one another in material composition, size, shape, and dimension, the material core type and surface modifier present on the surface. NPs size plays a key role in their long circulation, biodistribution, and clearance [Pan, 2007] The nanoparticles' properties (material composition, size, shape, surface charge, and porosity) are intimately connected with their functionality and their effects on health and the environment [Yamini, 2023]. The size of individual particles can impact the properties and performance of a material or product. By understanding particle size and its effects, researchers and manufacturers can optimize their products and improve their efficiency. NPs made of the same material can show different biological effects [Orlowski, 2018] and the other way around, identical, or similar effects, may result from the use of nanoparticles made of different substances and of other sizes and shapes. Hence, in the CheMatSustain project we selected two types of metallic nanoparticles: gold and silver to investigate the impact of material composition (gold and silver) on the biological and quantum response. For each material we selected three equal sizes of nanoparticles (5, 10 and 50 nm) in order to find the relationship between the investigated parameters. Within one of the materials groups (silver) we selected nanomaterials with two different shapes (spherical and rod shape with two different aspect ratios) to investigate the impact of shape and aspect ratio of those nanomaterials on the biological response. It is known that the surface chemistry of nanoparticles also affects the biological response [Tomaszewska, 2022], hence, for spherical metallic nanoparticles two types of surface modifiers are planned to be investigated: sodium citrate and tannic acid. The variability of parameters within the mNPs group is relatively large (material core size, particle size, shape, surface chemistry) as those nanomaterials are kind of a "model materials" with precisely defined, repeatable morphology that allows the implementation of the scientific postulates of the CheMatSustain project.

— Polymeric nanoparticles

Dendrimers were selected for the CheMatSustain project as the representatives of organic nanomaterials. Dendrimers are nano-sized, radially symmetric molecules with well-defined, homogeneous, and monodisperse structure that has a typically symmetric core, an inner shell, and an outer shell [Tomalia, 2005]. Dendrimers are constituted by repetitive units (so-called "generations") that are chemically bound to each other by an arborescent process around a multifunctional central core. Generally, dendrimers can be categorized by generation (layers between each cascade) and are associated with the branching cycles carried during synthesis and linked to molecular size [Abbasi, 2014]. The diameter of dendrimers increases linearly and surface groups increase exponentially with the increase in dendrimer generation [Tomalia, 2005]. There are several types of dendrimers depending on the central core type, e.g.: polyester, PAMAM, PPI, phosphorus based, PEG-polyester based, carbosilane, etc. However, the most widely used are the PAMAM dendrimers. The dendrimers cytotoxicity depended on the generation, the number of surface groups, and the nature of terminal moieties (anionic neutral, or cationic). Higher cytotoxicity occurred for higher-generation dendrimers and for dendrimers with positive charges on the surface [Zeng, 2016; Orlowski, 2028]. Therefore, three different generations of PAMAM dendrimers were selected for the project and research will be carried out on the possibility of recognizing both cationic and anionic types of dendrimers. Although the literature [Madaan, 2014] reports indicate the potentially high toxicity of all dendrimers, those nanostructures are recognized as potential pharmaceutical nanocarriers. Hence, for the CheMatSustain project dendrimers are selected as nanomaterials with acknowledged for their potential risks to humans and ecosystems.

— Micro/nanomaterials – pairs of materials in micro- and nanoscale range size

Within this subgroup, two pairs of materials were pre-selected: i) titanium dioxide and ii) cellulose, with the particle size in macro- and nanoscale range.

Titanium dioxide

Titanium dioxide was selected for the project due to its wide range of applications [Xiaobo, 2006] and presence in the environment. Titanium dioxide has an extremely high melting point of 1 843ºC and boiling point of 2 972ºC, so occurs naturally as a solid, and, even in its particle form, it is insoluble in water. TiO_2 is an insulator and absorbs UV light. This property makes it appear bright white under light, unlike other white materials that can look slightly yellow. Importantly, TiO_2 also has a very high refractive index (its ability to scatter light). This makes it an incredibly bright substance and an ideal material for paintings. Another crucial property of TiO_2 is that it can show photocatalytic activity under UV light. This makes it effective for environmental purification, for different kinds of protective coatings, sterilization and anti-fogging surfaces. Titanium dioxide is commercially used in both nano- and micro-forms. Nano-sized TiO_2 with the size about 5-50 nm is used in sunscreens due to its ability to block ultraviolet radiation while remaining transparent on the skin. Moreover, nano-TiO_2 is used in housing and construction as an additive to paints, plastics, cements, windows, tiles, and other products for its ultraviolet absorption and photocatalytic sterilizing properties. Nano-sized TiO_2 was pre-selected for the CNMs due to its wide range of commercial applications. The micro-sized counterpart of TiO_2 was also selected for the project in order to determine whether it is possible to distinguish the materials with the same chemical composition but originating from the nano- and micro-scale.

Cellulose

Cellulose is Earth's most abundant natural polymer, primarily found in plant cell walls and certain bacteria. It is a linear polysaccharide with β-(1→4) linked D-glucose units. The intrinsic properties of cellulose—such as biodegradability, renewability, and robust mechanical strength make it an ideal candidate for extensive research for both scientific and application purposes. Cellulose is sustainably sourced from wood, agricultural residues and other plant materials. Unlike petroleum-based polymers, cellulose does not contribute to net carbon emissions when degraded, making it an environmentally friendly alternative. Cellulose fibres naturally break down in the environment without leaving harmful residues, which is crucial for maintaining ecological balance. The degradation products of cellulose do not accumulate in the biosphere, thereby supporting life cycle assessments that favor materials with minimal environmental impact.

Cellulose's versatility allows for its use across various sectors, including construction, textiles, pharmaceuticals, cosmetics and even electronics. Nanoforms of cellulose are the perfect example of advanced functional materials [Kargarzadeh, 2018] innovations in nanotechnology have led to the development of cellulose nanocrystals and nanofibers, which exhibit remarkable strength and lightweight properties comparable to those of synthetic nanomaterials. Cellulose-based nanomaterials can be integrated into high-performance composites, flexible electronics, and barrier films, providing sustainable alternatives to conventional materials. The scientific and industrial community continues to explore cellulose due to its sustainable attributes, functional versatility, and innovation potential. The ongoing research argues that cellulose is not only a vital natural resource but also a cornerstone for future material science advancements. Encouraging further investigation into cellulose aligns with global sustainability goals and promotes the development of green technologies.

— Chemicals used for the synthesis and stabilization of nanomaterials and bioactive compounds

Within this subgroup, chemicals used for the preparation and functionalization of CNMs will be investigated. Those chemicals include the following compounds: i) sodium citrate (SC, the compound used for the synthesis of metallic nanoparticles with controllable size and shape using chemical reduction method in water); ii) tannic acid (TA, the natural origin compound used in the synthesis process of metallic nanoparticles using chemical reduction method); iii) polyvinylpirrolidone (PVP, an inert substance used as a stabilizer for dispersing titanium dioxide nanoparticles). Plant origin bioactive compounds will also be considered in this project such as : tormentic and triterpenic acids.

Selection of CNMs

Factors determining the selection of materials

The factors determining the final selection of materials includes physicochemical aspects of pre-selected CNMs based on the scientific postulates of the CheMatSustain project as well as the economic, sociological, environmental aspects and applications of the selected materials. This part of the report presents the discussion of individual factors and their impact on the final selection of CNMs.

1) Physicochemical aspects of selected CNMs

The physicochemical properties of the CNMs are the crucial parameters from the scientific point of view of the CheMatSustain project. Appropriate selection of materials is crucial for observation of the appropriate phenomena and to find the relationships constituting the scientific and cognitive basis of the project. In this part the most important physicochemical parameters of pre-selected CNMs will be discussed for each subgroup.

— Metallic nanoparticles

The nanoparticles pre-selected for the project include the two most used types of metallic nanoparticle: i) gold (AuNPs), and), and ii) silver nanoparticles (AgNPs). AuNPs are biocompatible with low cytotoxicity rendering them one of the safest candidates for biomedical applications like imaging (sensory probes), therapeutic drug delivery, and catalysis. AuNPs are postulated to exhibit minimal to no immuno-toxic, cytotoxic, or genotoxic effects in human cells. Hence, AuNPs are recognized as generally biologically inert [Salesa, 2023] which results in very high biocompatibility. Silver nanoparticles are used for a wide range of applications from disinfecting medical devices and home appliances to water treatment mainly as antibacterial agents [Palani, 2023]. Moreover, AgNPs are used in healthcare products, food storage, and textiles. Silver nanoparticles are reported as toxic to human cell lines and pose potential risks to human health [Ferdous, 2020; Xuan, 2023; Kumah, 2023]. Due to documented differences in biological activity and the influence on the human health and environment of gold and silver resulting from the material composition [Tomaszewska, 2022; Pudlarz, 2019; Orlowski and Tomaszewska, 2018], these metallic nanoparticles were selected for the project.

The size of a nanoparticle is a key physical property that directly influences the nanomaterial properties such as chemical, quantum or biological activity [Tomaszewska, 2022]. Smaller nanoparticles have a better chance of penetrate the cell membrane compared to larger sizes, which should be considered when predicting which nanoparticles may be hazardous. Hence, for the CheMatSustain project the nanoparticles with three different sizes were primary selected: 5, 10 and 50 nm. However, the deep analysis of the synthesis procedures of nanoparticles revealed that the preparation of gold and silver nanoparticles with proposed sizes using the same chemicals and synthesis protocols will not allow to obtain monodisperse materials. Especially, the process of preparation of nanoparticles with the size equal 50 nm leads to non-homogeneous nanoparticles both in terms of shape and size. Hence, such a polydisperse nanomaterial cannot be used as a “model” material. As the monodispersity of metallic nanoparticles is the most crucial parameter in the selection process of this subgroup, it was decided that the pre-selected nanoparticles with a size of 50 nm will be replaced with nanoparticles with a size of 30 nm. Such a change will not affect the scientific aspects of the project and will enable the use of material with a high degree of monodispersity. This ensures the use of the same preparation procedure for all selected colloids with the particle sizes equal: 5, 10 and 30 nm, respectively. This is extremely important from the scientific point of view for the examination of the influence of several nanoparticles’ physicochemical parameters, such as: metal core material, size, shape, and surface chemistry.

Another factor determining the biological response of nanomaterials is its shape. To investigate the influence of shape we pre-selected silver nanostructures with two different shapes: spherical and rod-shape nanoparticles with two different aspect ratios. However, the structural instability of silver nanorods and the challenges with obtaining homogeneous and uniform in shape nanomaterials prompted us to change this material to gold nanorods. Gold nanorods are much more stable and the precise control of morphology is possible. Moreover, the material is commercially available.

For the project we pre-selected the investigation of two types of chemicals used as a stabilizer of metallic nanoparticles. The pre-selection of such stabilizers contains: sodium citrate and tannic acid. It is well-known that the stabilizers should ensure the colloidal stability of nanoparticles. At the same time, the compound used as a nanoparticle stabilizer must also be stable over time (it cannot undergo chemical changes). Sodium citrate is an example of a stable chemical compound that provides electrostatic stabilization to nanoparticles. However, research carried out by our team revealed that tannic acid is unstable in metallic nanoparticle colloids and undergoes chemical transformations. Therefore, it cannot be used as a nanoparticle stabilizer in the CheMatSustain project due to its chemical instability. Tannic acid was replaced by other chemical compound poly(ethylene glycol) methyl ether thiol (PEG-SH) that is stable in metallic nanoparticle colloids and has been assumed to provide the NPs stability in salt water (ecotoxicological tests). Moreover, PEG-SH ensures surface binding to metallic nanoparticles. It will therefore constitute an example of a functional compound that chemically bound to the surface of nanoparticles and provides steric stabilization of NPs.

— Polymeric nanoparticles

Two types of nanoobjects were selected as representatives of nanostructures made of organic compounds. The first material, polymer nanoparticles, are composed of linear polystyrene molecules and the second material is branched dendrimer structures which are composed of PAMAM molecules. The main criterion for the selection of both nanomaterials was scientific goals, which allow to investigate the correlations between the structure of the tested nanostructures and their physicochemical properties and biological activity.

Dendrimers

The analysis of the literature [Madaan, 2014] revealed that dendrimers indicate high toxicity. Moreover, in the literature there is a lack of reliable physicochemical characteristics of dendrimers. This indicates the possible difficulties in characterizing dendrimers and the possible challenges to obtain the appropriate physicochemical data to create models. What is more, there is a small number of its commercial applications. These factors were the reason for the reduction of the number of dendrimers in the project from 6 to 3. Therefore, the half-generation dendrimers were abandoned, and three full generation dendrimers were selected in the project (generation 4, 5 and 6). Cationic dendrimers are recognized to be more toxic than anionic ones [Janaszewska, 2019], therefore it was proposed to replace them with other materials - polystyrene spheres, which also belong to the group of polymeric nanoparticles.

Polystyrene spheres

Polystyrene spheres are a material with a homogeneous shape and mono-modal size used in industry and present in the environment. *In vivo* and *in vitro* studies suggest that polystyrene nanoparticles (PS-NPs) may penetrate organisms through several routes i.e. skin, respiratory and digestive tracts. They can be deposited in living organisms and accumulate further along the food chain [Costa, 2016]. Polystyrene nanoparticles have been found to have numerous applications in scientific research, diagnostics, electronics, pharmaceuticals, and nanotechnology, such as purification and separation, and lateral flow detection. Two nano-sized polystyrene nanoparticles were selected with the size around 40 nm and 80 nm.

— Micro/nanomaterials – pairs of materials in micro- and nanoscale range size

Cellulose

Cellulose, a versatile and abundant natural polymer, is primarily found in various forms that differ in their physical and chemical properties. These forms cater to a range of applications from simple paper products to complex nanotechnology. To meet the basic requirement of the project, namely the ability to test materials in a variety of biological tests, the material must be in a form that allows its suspension in cellular culture media. Therefore, microcrystalline cellulose and nanocellulose were selected. Both forms of cellulose are available as chemically pure celluloses without other components originating from the biological material from which they were obtained. These impurities cannot influence the responses of the biological systems in which they will be tested.

Microcrystalline cellulose (MCC) is a refined form of cellulose that is widely used across various industries due to its properties and functionalities [Trache, 2016]. This biodegradable, non-toxic, and robust material is derived from cellulose, the most abundant polymer in nature. MCC is characterized by its small particle size and crystalline nature, which result from the controlled partial hydrolysis of cellulose. This process removes the amorphous regions of cellulose, enhancing its stability and making it less reactive. MCC is chemically inert, making it ideal for applications where non-reactivity is required. It does not undergo significant chemical changes when exposed to mild acids, bases, or organic solvents at room temperature. MCC is highly compressible, which makes it important in the pharmaceutical industry for tablet formulation. Its excellent binding properties facilitate the production of tablets by direct compression, thereby simplifying the manufacturing process. As a cellulose derivative, MCC is biodegradable under natural conditions, contributing to environmental sustainability.

Microcrystalline cellulose plays a pivotal role in various industries due to its desirable physical and chemical properties. Its functionality as a binder, stabilizer, and additive enhances the quality and efficiency of products ranging from pharmaceuticals to food items. The sustainability aspect of MCC also contributes to its growing popularity as industries seek greener alternatives in product formulations. The described features and important areas of practical applications of MCC, combined with a form that allows carrying out all planned toxicological and ecotoxicological tests, allow this material to be selected for research within the CheMatSustain project.

Nanocellulose refers to microcrystalline cellulose that has been engineered into nanostructures, exhibiting unique properties due to its high surface area-to-volume ratio and nanoscale dimensions. This advanced material is derived from the most abundant natural polymer on Earth—cellulose—and is gaining significant attention for its potential applications in various fields including the packing industry, medicine, electronics, and environmental technology [Brinchi, 2013]. Nanocellulose can be classified into three primary forms: cellulose nanocrystals (CNCs), cellulose nanofibrils (CNFs), and bacterial nanocellulose (BNC). Similar to MCC nanocellulose is biodegradable under natural conditions.

Of the three forms of nanocellulose mentioned above, cellulose nanocrystals (CNCs) were selected for research conducted as part of the CheMatSustain project based on the following criteria.

From a scientific point of view, it is crucial to limit the number of parameters changed within one group of tested materials. To be able to capture the relationship between the physicochemical features, quantum and biological effects of the tested material, we focused on changing the particle size of the tested celluloses while leaving other features as similar as possible. Microcrystalline and nanocrystalline cellulose are of plant origin and have a high degree of crystallinity. Another important criterion for selecting the CNMs was the possibility of achieving the best possible physicochemical characteristics. Cellulose in the form of nanocrystals has a much narrower distribution of geometric dimensions of particles compared to CNFs. Crystalline nanocellulose particles can also be characterized using the same methods as other tested CNMs, thus meeting the basic assumptions of the project.

The described features and important areas of practical applications of CNCs, combined with the fact that this form allows detailed physicochemical characterization and carrying out all planned toxicological and ecotoxicological tests, make this material valuable for research within the CheMatSustain project.

Titanium dioxide

Titanium dioxide exists in three common crystalline phases: brookite, anatase and rutile. However, in industry, the anatase and rutile are the mainly used crystalline phases of TiO_2, hence for this subgroup of the CNMs we selected anatase-TiO_2 and rutile-TiO_2 in the nano- and micro-forms. Titanium dioxide is the only material in the project that can have two nano- and macro- sizes for two different crystal forms: anatase and rutile. It was decided to introduce these two pairs of i) nano-TiO_2 (anatase and rutile) and ii) micro-TiO_2 (anatase and rutile) to the list of selected CNMs in order to check whether it is possible to distinguish two chemically identical materials with comparable particle size but with different crystal structures.

The list of CNMs in this subgroup has been increased by an additional nanomaterial – the titanium dioxide nanomaterial available in repository for Representative Test Materials (RTMs) in The European Commission's Joint Research Centre (JRC) [Rasmussen, 2014]. From the materials available in the repository the titanium dioxide NM-102 (nano-TiO_2 anatase) was selected as the well-defined, characterized and meeting the physicochemical requirements of the CheMatSustain project.

— Chemical substances (stabilizers and bioactive compounds)

The changes in the chemical compound subgroup initially selected for the CheMatSustain project include the removal of tannic acid from the list of chemicals as an unstable compound that undergoes chemical changes over time and is therefore very difficult/impossible to

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characterize. Poly(ethylene glycol) methyl ether thiol was included on the chemicals list, which is stable, ensures covalent attachment to metallic nanoparticles, stabilize nanoparticles sterically (unlike citrate which stabilizes nanoparticles electrostatically), and a potentially can ensure/increase nanoparticles stability in salt water in ecotoxicological tests. Bioactive compounds (tormentic and triterpenic acids) have been considered since they have health beneficial effects (for example they exhibit anticancer, antioxidant, anti-inflammatory, anti-atherogenic properties and hypoglycemic effects). Triterpenic acids are produced from Red Sentinel calluses to offer an independent supply of uniform biomass with enhanced production of active constituents. Furthermore, tormentic acid can be supplied by different companies that can consider using Red Sentinel calluses to produce high quantities of this compound.

2) Socio-economic, environmental and human health considerations of selected CNMs

The use of chemicals and materials with nanostructures is predicted to increase and can be a game changer for the technological development of, e.g., applications in medicinal products, construction materials and materials for energy distribution and storage. Nanomaterials also have a large potential use in more consumer-oriented applications such as packaging, sports equipment, and cosmetics. Whether the nanoform of a chemical or a material is technologically necessary or not is rarely made clear. There is always a risk that materials in nanoform are used in products simply because it is possible or to make a selling point. In research areas such as nanotoxicology and human exposure to chemicals, the potential additional risk due to the nanoscale has been studied and evaluated in several contexts. When it comes to engineered nanomaterials, the nanoform is generally considered to pose an increased risk for uptake and distribution, because particles are small enough to be inhaled and reach the smallest alveoli in the lung. There are also studies that show that particles can be absorbed via the skin and preferably via the so-called shunt routes. In the occupational setting, the use of e.g., nanoparticles in a process is considered to constitute a high risk environment with safety requirements and demands to use personal protective equipment. Occupational exposure tends to occur at higher concentration than consumer exposure or diffuse exposure from the abundant environment. This implies that the production and use of CNMs constitute a potential source for high occupational exposure as well as diffuse dispersion to the environment posing a risk of effects in wildlife and the general population. The societal implications of such a risk needs to be further assessed and evaluated. The selection of CNMs for the present project will therefore be examined and evaluated in other WPs using already established as well as state-of-the-art methods, i.e., material evaluation using Risk Assessment and Life Cycle Assessment approach will be used. Additionally, a methodology for the complementary use of Risk Assessment (RA) and Life Cycle Assessment will be developed in the project (WP6, T6.1)

3) *Application of selected materials*

Another criterion for selection of CNMs is their application. The pre-selected CNMs represent various groups of materials – the materials that are already commonly used in the industry and hence are present in the environment (e.g. titanium dioxide and cellulose), and materials with potentially wide applications in the future due to their unique properties (e.g. dendrimers). This approach to the selection of materials will allow not only the examination of materials that have a real impact on the environment but also the assessment of the suitability of the developed methods for materials testing that may become present in the environment in the near future.

The main application of selected subgroups of the CNMs:

- Metallic nanoparticles

Due to the unique physical, chemical, biological and optical properties of metallic nanoparticles, which differ significantly from their bulk counterparts, these nanoparticles have found extensive applications across various scientific and industrial fields. The increased surface area to volume ratio of metallic nanoparticles contributes to their exceptional reactivity and functionality, making them invaluable in catalysis, medicine, electronics, and environmental applications. In scientific literature [Mahendra, 2009], we can find information about the synthesis and testing of many metals in the form of nanoparticles. However, due to the requirement for the stability of metallic nanostructures that are to be used in practical applications, the most frequently used are gold and silver nanoparticles, which were selected for research as part of the CheMatSustain project.

One of the most significant properties of AgNPs is their broad-spectrum of antimicrobial activity, which inhibits the growth of bacteria and deactivate viruses [Orlowski, 2014]. This makes them invaluable in healthcare and consumer products. AgNPs are incorporated into catheters, wound dressings, and other medical implants to prevent infections. Silver-infused fabrics are used in medical textiles and active wear for their ability to kill bacteria and reduce odors. Antimicrobial coatings containing AgNPs are applied in hospital settings, on public transport, and in air filtration systems to mitigate the spread of pathogens. AgNPs are extensively used in electronics due to their high electrical conductivity. Silver nanoparticles are key components in conductive inks used for printing electronic circuits on flexible substrates, which are crucial for wearable electronics. The catalytic properties of AgNPs facilitate various chemical reactions. The unique optical properties of AgNPs, particularly their surface plasmon resonance, make them ideal for biosensing applications. AgNPs are used in biosensors to quickly detect pathogens and biomarkers quickly and other hazardous substances in the environment. Due to their antibacterial properties and aesthetic appeal, AgNPs are found in various consumer products. Silver nanoparticles are added to creams and lotions to enhance their antimicrobial effect and preserve the products. AgNPs are integrated into the surfaces of refrigerators, washing machines, and other appliances to inhibit microbial growth and prolong product life. Depending on their size, shape and surface modification, silver nanoparticles can be given various physicochemical properties and biological activities [x]. For each specific application, the appropriate structure of silver nanoparticles is selected to maximize their properties to the expected results.

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The biocompatibility and easy surface modification of AuNPs make them highly valuable in medical applications, especially in targeted drug delivery. AuNPs can be functionalized with various ligands, for example antibodies or drugs, enabling targeted delivery to specific disease sites, thereby reducing side effects and improving therapeutic efficacy. Combining therapeutic and diagnostic functions in a single platform, AuNPs are used in theranostic applications to diagnose, deliver targeted therapy, and monitor the response to treatment, particularly in cancer management. Due to their strong optical absorbance and scattering properties, AuNPs enhance the contrast in imaging techniques such as optical microscopy and photoacoustic imaging, improving the detection and diagnosis of diseases. AuNPs serve as effective catalysts due to their high specific surface area and active facets, which can be exploited in various chemical reactions. Gold nanoparticles catalyze a range of reactions including the oxidation of carbon monoxide and organic synthesis, offering pathways for more efficient and environmentally friendly chemistry. The conductive and plasmonic properties of AuNPs are advantageous in electronics and sensing applications. Gold nanoparticles are integral in developing biosensors and chemical sensors due to their quick and accurate detection of various biological and chemical species. Utilizing their plasmonic properties, AuNPs are used to fabricate devices that manipulate light at the nanoscale, such as in plasmonic photovoltaic cells, which enhance light absorption and increase solar cell efficiency. AuNPs are also incorporated into a variety of consumer products, leveraging their aesthetic and functional qualities. In the cosmetic industry, AuNPs are added to skin care products for their anti-aging properties and the perceived luxury they confer. Gold nanoparticles represent the pinnacle of nanotechnology's promise in revolutionizing industrial and scientific domains. As with silver nanoparticles, the sizes and shapes of AuNPs are tuned for specific applications. By modifying the surface of AuNPs, we can significantly influence their properties, which are particularly intensively used in the biomedical area of their applications.

Gold nanorods (AuNRs) are a type of gold nanoparticle characterized by their elongated, rod-like shape, which imparts unique optical and physical properties not found in AuNPs [Pérez-Juste, 2005]. The aspect ratio (length to diameter) of AuNRs can be finely tuned during synthesis, which allows precise control over their plasmonic resonance properties. This tunability makes AuNRs particularly useful in applications where enhanced light absorption or scattering at specific wavelengths is required. AuNRs are prominently used in photothermal therapy for cancer treatment. Their ability to absorb near-infrared light and convert it into heat can be utilized to selectively destroy cancer cells with minimal damage to surrounding healthy tissue. The longitudinal plasmon resonance of AuNRs, which can be tuned to the NIR window, is key to their effectiveness in this application, distinguishing them from spherical AuNPs which typically do not absorb NIR as effectively. AuNRs enhance contrast in optical coherence tomography, a non-invasive imaging technique used primarily in ophthalmology and tissue imaging. The strong scattering properties of AuNRs, particularly in the NIR region, improve the depth and resolution of optical coherence tomography images compared to spherical nanoparticles, which are less efficient scatterers at these wavelengths. Due to their sensitive optical properties, AuNRs are used in the detection of biomolecules. Changes in the local refractive index near the surface of AuNRs (caused by biomolecule binding) result in measurable shifts in their plasmonic resonance, enabling the sensitive detection of a variety of biological targets. This capability is enhanced in AuNRs over spherical AuNPs due to the larger surface area and aspect ratio-dependent plasmonic properties.

AuNRs are effective substrates for SERS applications, where their rod-shaped geometry facilitates the generation of "hot spots" at the tips of the rods. These hot spots significantly amplify the Raman signals of molecules adsorbed on the surface, providing greater sensitivity in chemical and biological sensing compared to spherical nanoparticles. The non-linear optical properties of AuNRs, such as second harmonic generation and two-photon luminescence, are more pronounced than in spherical AuNPs. These properties are exploited in the development of advanced optical devices and materials, including those used for optical switching and computing. Gold nanorods offer a range of applications that are distinct from those of spherical gold nanoparticles, primarily due to their shape-dependent plasmonic and optical properties. One of the most important limitation in practical implementation of AuNRs is extremely high price of this materials.

— Polymeric nanoparticles

Dendrimers are highly branched, monodisperse macromolecules characterized by a tree-like structure, which includes a central core, an interior dendritic structure (the branches), and an exterior surface with functional surface groups. This unique architecture endows dendrimers with a host of remarkable properties, such as a high degree of structural control, multifunctionality, and many reactive end-groups. These features make dendrimers a valuable tool in various industries, ranging from medicine and biotechnology to materials science and nanotechnology. Most of the uses described below are potential. Real applications still require a lot of basic and implementation research, including better knowledge of the toxicology and ecotoxicology of these materials.

Dendrimers have shown great potential in the field of biomedicine [Boas, 2004], where their precise molecular architecture allows for applications in drug delivery, imaging, and diagnostics. Dendrimers provide a versatile platform for drug delivery systems [Chauhan, 2018] due to their ability to encapsulate therapeutic agents within their interior voids or attach them to surface functional groups. This facilitates targeted delivery, which can significantly enhance drug efficacy and reduce toxicity. The cationic nature of certain dendrimers makes them suitable for gene delivery applications. Their ability to form complexes with DNA or RNA (through electrostatic interactions) enables the efficient transfer of genetic material into cells. Dendrimers are used as contrast agents in medical imaging due to their ability to be functionalized with imaging moieties and target specific tissues, enhancing the contrast in MRI, CT, and other imaging modalities. In catalysis, dendrimers are employed as both catalysts and catalyst supports. The ability to precisely place catalytic sites at specific locations within the dendrimer structure allows for selective catalysis. Enhanced selectivity and efficiency in chemical reactions, including organic synthesis and polymerization. Dendrimers contribute to the advancement of materials science, particularly in the development of advanced composite materials. Dendrimers are used to modify the properties of nanocomposites, enhancing their mechanical, thermal, and barrier properties. Functionalized dendrimers are incorporated into sensor technologies, where they can enhance sensitivity and selectivity for detecting gases, ions, and organic molecules. The functionality and structural precision of dendrimers extend to environmental applications, where they are used in water treatment. Dendrimers can remove toxic heavy metals and organic pollutants from wastewater through complexation and adsorption processes.

Dendrimers with amine groups have been explored for capturing carbon dioxide from industrial emissions, contributing to efforts to reduce greenhouse gas emissions. In the consumer products sector, dendrimers find applications in personal care products. Dendrimers are added to cosmetics and personal care products to improve delivery of active ingredients and enhance product stability. A factor that strongly limits the practical applications of dendrimers is their high price and known toxicity, especially ecotoxicity.

Polystyrene nanoparticles, often referred to as PS nanolatex, are spherical particles of polystyrene that range in size from tens to hundreds of nanometers. Due to their uniform size, chemical stability, and ease of functionalization, these nanoparticles have found use across various fields including medicine [Loos, 2014], research, and industry. Most of the uses described below are highly specific or potential. Real applications still require a lot of basic and implementation research, including better knowledge of the toxicology and ecotoxicology of these materials. In the realm of biomedicine, PS-NPs are particularly valued for their applications in drug delivery and diagnostic assays. PS-NPs can be engineered to carry drugs, proteins, or genes, facilitating targeted delivery to specific cells or tissues. This targeted delivery system helps to maximize the therapeutic effect while minimizing side effects. Due to their uniformity and ability to be easily tagged with fluorescent markers, PS-NPs are commonly used in diagnostic applications, including as markers in flow cytometry and in various imaging techniques to track biological processes and cell interactions. PS nanoparticles are extensively used in scientific research, particularly in the study of particle behavior and dynamics in nanoscale environments [Kik, 2020]. Due to their well-defined size and stability, PS-NPs serve as model systems for studying colloidal science phenomena such as aggregation, adsorption, and interface behavior. In microscopy and flow cytometry, PS-NPs are used as size and fluorescence standards, helping researchers calibrate instruments with high precision. In materials science, PS-NPs contribute to the development of advanced materials and composites. By incorporating PS-NPs into polymer matrices, manufacturers can enhance the mechanical strength, thermal stability, and optical properties of the composite materials. Functionalized PS-NPs are added to coatings and adhesives to improve their properties such as scratch resistance, durability, and bonding strength. PS-NPs also find applications in various consumer products, enhancing performance and functionality. In the cosmetics industry, PS nanoparticles are used to improve the texture and application properties of products like creams and lotions. PS-NPs are incorporated into packaging materials to enhance barrier properties against moisture and gases, thereby improving the shelf life of packaged goods. While less common, PS-NPs have potential applications in environmental technology. Research is ongoing into the use of PS-NPs in water purification systems to adsorb and remove contaminants due to their large surface area and potential for surface modification. A factor that strongly limits the practical applications of PS nanolatex is their high price (especially for materials with highly narrow size distribution) and lack of knowledge about toxicity, especially ecotoxicity. A suspension of polystyrene nanoparticles can be treated as a model of micro and nanoplastics (depending on size).

— Micro/nanomaterials – pairs of materials in macro and nanoscale range size

Cellulose

Microcrystalline cellulose is extensively used as an excipient in the pharmaceutical industry. Its role as a binder, diluent, and disintegrant in tablet formulations is well-documented. Microcrystalline cellulose helps in improving the mechanical strength of tablets, controlling release profiles, and enhancing the bioavailability of drugs. In the food sector, microcrystalline cellulose serves as an anti-caking agent, fat substitute, emulsifier, and stabilizer. It is used in products like cheese, ice cream, and sauces to improve texture and stability without altering nutritional content. Microcrystalline cellulose is utilized in cosmetics for its thickening and texturizing properties. It is found in creams, lotions, and powders, enhancing their spread ability and consistency. In nutraceuticals, microcrystalline cellulose is employed as a fiber supplement and as a carrier for nutritional additives. Its inertness and fiber content make it suitable for dietary supplements that aid in digestive health.

The high strength and stiffness of cellulose nanocrystals, combined with their lightweight nature, make them ideal for reinforcement in nanocomposite materials. These composites are utilized in various sectors, including automotive, aerospace, and construction, where enhanced mechanical properties such as improved tensile strength and modulus are critical. Cellulose nanocrystals contribute to the development of materials that are not only stronger and lighter but also more sustainable compared to those reinforced with synthetic fibers. In the packaging industry, cellulose nanocrystals offer the potential for creating high-barrier films that are environmentally friendly. These films can provide excellent gas barrier properties, which are crucial for food packaging applications to enhance shelf life while reducing the use of traditional plastics. Cellulose nanocrystals can significantly alter the rheological properties of fluids, making them useful as rheology modifiers in industries such as cosmetics, pharmaceuticals, and food production. Their ability to increase viscosity and stabilize emulsions is valuable in formulations where precise control overflow properties is necessary. Cellulose nanocrystals play a role in environmental technology, particularly in water treatment and remediation. Their high surface area and modifiable surface chemistry enable them to act as effective adsorbents for removing pollutants and heavy metals from water, aiding in water purification efforts while being fully biodegradable.

Titanium dioxide

Titanium dioxide in its anatase form is one of the most widely used photocatalysts in various industrial applications [Dharma, 2022]. The anatase phase of TiO_2 , exhibits superior photocatalytic activity compared to its rutile counterpart. This high activity is attributed to the more effective charge carrier separation in anatase crystals. The industrial significance of anatase TiO_2 spans several sectors, highlighting its versatility and utility. The choice between rutile and anatase forms of TiO_2 largely depends on the specific requirements of the application. Rutile’s stability, high refractive index, and light scattering capabilities make it ideal for pigments, coatings, and optoelectronic devices, while anatase’s superior photocatalytic activity under UV light makes it the preferred choice for environmental and energy applications. Understanding these differences allows industries to tailor the use of TiO_2 to meet specific performance criteria, enhancing the functionality and efficiency of the end products.

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Anatase TiO_2 is renowned for its strong oxidizing power under UV light, making it a prominent choice for photocatalytic applications aimed at environmental cleanup. It is effectively used in the degradation of pollutants, both organic and inorganic, in water and air. This capability is pivotal in treating wastewater and breaking down airborne contaminants in industrial and residential settings, thereby contributing to pollution reduction and air quality improvement. The photocatalytic properties of anatase TiO_2 are exploited in the manufacturing of self-cleaning surfaces. When applied as a coating, TiO_2 can decompose organic compounds that settle on surfaces, such as buildings or vehicles, under sunlight exposure. Moreover, these coatings exhibit strong antimicrobial properties, killing bacteria and other microorganisms upon light activation, which is beneficial for medical equipment and public installations to maintain hygiene and reduce transmission of pathogens. Anatase TiO_2 is used as a key material in dye-sensitized solar cells (DSSCs), where it serves as a photoanode. Its ability to effectively generate electron-hole pairs upon light absorption leads to enhanced efficiency in solar energy conversion. This application is critical for the development of cost-effective and efficient renewable energy sources, aligning with global energy sustainability goals. In the paint industry, anatase TiO_2 is valued for its bright white pigment and UV protection properties. It is extensively used in paints and coatings to provide opacity and durability while protecting the substrate from UV degradation. This prolongs the life of the paint and preserves its aesthetic properties over time. Anatase TiO_2 is incorporated into various cosmetic products as a UV filter and whitening agent. Sunscreens provide effective protection against harmful UV rays, preventing skin damage and contributing to sunscreen's UV-blocking efficacy. Its non-toxic and inert nature makes it suitable for sensitive skin applications.

Titanium dioxide in its rutile form is the most stable and dense phase of this widely utilized oxide. TiO_2 is preferred in applications requiring a high refractive index and chemical inertness. The unique properties of rutile make it indispensable across various industrial sectors, from pigments to electronics. Rutile TiO_2 is the most commonly used white pigment in the world due to its excellent light-scattering properties. It is extensively used in paints, coatings, plastics, papers, inks, food, and cosmetics to provide whiteness and opacity.

These applications benefit from rutile's ability to impart superior coverage, brightness, and durability against UV degradation, which helps in extending the life of products exposed to sunlight and weather elements. In ceramics, rutile TiO_2 is used as an opacifier and to enhance mechanical properties such as fracture toughness and hardness. It is also employed in ceramic glazes for improving the appearance and durability of the final products. Rutile's high refractive index and optical properties are exploited in the manufacturing of optical components like lenses and dielectric mirrors. It is also used in the production of electronic components such as capacitors and resistors, where its stability and dielectric properties are crucial. In the field of photovoltaics, rutile TiO_2 is used in the manufacture of solar panels. Its high refractive index and dielectric constant make it an effective material for enhancing the efficiency of photovoltaic cells by minimizing electron-hole recombination and maximizing light absorption. This contributes significantly to the development of more efficient solar energy systems.

Depending on the particle size, TiO_2 can be categorized into micrometric (micron-sized) and nanometric (nano-sized) forms, each having distinct characteristics and applications. The study of titanium oxides with anatase and rutile crystal structure is extremely important both from the scientific point of view, allowing to indicate the differences in the biological activity of both forms depending on the size of the particles. Differences in the physicochemical properties and biological activity of both forms of TiO_2 mean that they are used in different application areas, although in some applications both forms or their mixtures may be used.

Nano-sized titanium dioxide is widely used across various industries due to its exceptional properties, such as high refractive index, chemical stability, and photocatalytic capabilities. Nano-sized TiO_2 excels in photocatalytic applications due to its increased surface area and enhanced photoactivity, which are not as pronounced in their micrometric counterpart. This makes nano-sized TiO_2 highly effective in environmental applications such as air and water purification, where it can degrade organic pollutants and disinfect them by breaking down bacteria and viruses under UV light. Due to its high surface area and the ability to exploit quantum effects, nano-sized TiO_2 is utilized in dye-sensitized solar cells (DSSCs) and other advanced solar energy systems. It serves as a photoanode where its properties significantly increase the efficiency of light absorption and energy conversion. The reactive surface of nano-sized TiO_2 has promising applications in medicine, particularly in drug delivery and antmicrobial treatments. The nanoparticles can be engineered to carry therapeutic agents or to produce reactive oxygen species that can kill microbes effectively, offering new solutions for treatment-resistant infections.

Micro-sized TiO_2 is predominantly used as a pigment due to its excellent opacity and ability to scatter visible light effectively. This makes it ideal for applications in paints, inks, coatings, and plastics where it enhances brightness, durability, and UV protection. Its larger particle size reduces the risk of photoactivity, which can cause degradation of the matrix material in some contexts. In sunscreens, micrometric TiO_2 is often preferred over nano-sized forms due to concerns about nanoparticle penetration through the skin. Micro-sized particles remain on the surface, providing effective UV protection without the potential risks associated with systemic absorption of nanoparticles.

The key difference between micro-sized and nano-sized TiO_2 lies in their surface area-to-volume ratio. Nanoparticles, with their vastly greater surface area per unit mass, exhibit properties that are not observable in micrometric particles. This includes increased photocatalytic activity and quantum mechanical effects, which are capitalized on in advanced materials science and biomedical engineering. Conversely, the larger micrometric particles offer greater bulk properties like opacity and UV scattering, which are essential in coatings and pigments.

— Chemical substances (stabilizers and bioactive compounds) (5 samples in total)

Sodium citrate, the sodium salt of citric acid, is a versatile chemical compound with a wide range of applications in food, pharmaceuticals, and medical fields. Known chemically as trisodium citrate, it is recognized for its ability to act as a buffering agent, sequestrant, and anticoagulant. This compound’s unique properties make it valuable in various industrial and healthcare settings.

Sodium citrate is commonly used in the food industry as a flavor enhancer due to its mildly tart flavor. It is also employed as a preservative; its ability to control acidity levels helps preserve the stability and appearance of active ingredients in foods and beverages. In processed foods, particularly dairy products like cheese and ice cream, sodium citrate serves as an emulsifier. It helps in stabilizing fat emulsions, ensuring smooth textures and preventing separation in cheese sauces and dairy blends. Sodium citrate is included in electrolyte formulations of sports drinks. It helps replenish sodium lost through sweat and aids in the maintenance of osmoregulation and fluid balance, which is crucial during prolonged physical activity. In pharmaceuticals, sodium citrate is utilized as a buffering agent to maintain the pH of solutions. It is also used in effervescent tablets, where it helps control the reaction rate of the effervescent system, improving the dissolution and absorption of active ingredients. Sodium citrate is widely used as an anticoagulant in blood collection tubes. By chelating calcium ions in the blood, it prevents clotting, thereby preserving blood samples for various diagnostic procedures and tests. In the cosmetic industry, sodium citrate is added to products as a pH adjuster and preservative. It helps stabilize active ingredients and maintains the desired consistency and effectiveness of beauty and personal care products. The widespread use of sodium citrate is due to an extensive range of applications, The industrial production of sodium citrate is a well-established process characterized by its efficiency, friendliness for the environment, scalability and low price.

Poly(ethylene glycol) methyl ether thiol (PEG-SH) is a functional derivative of poly(ethylene glycol) (PEG) that is terminated with a thiol group (-SH) instead of the more typical hydroxyl groups. This modification imparts unique properties to the molecule, notably the ability to form disulfide bonds under oxidative conditions and to attach to gold and other metal surfaces via thiol groups. These characteristics enable its use in a variety of scientific and industrial applications. PEG-SH is extensively used in the formulation of drug delivery systems. Its ability to conjugate with other molecules and form stable, non-toxic, and water-soluble complexes makes it ideal for creating targeted drug delivery vehicles. PEG-SH can be used to modify the surface of nanoparticles, improving their circulation time in the bloodstream and reducing immunogenicity. PEG-SH is employed to modify proteins and peptides, enhancing their stability and solubility. This pegylation process helps to mask the therapeutic agents from the host's immune system, extending their half-life and increasing their efficacy in clinical applications. Due to its strong affinity for metal surfaces via the thiol group, PEG-SH is used to modify surfaces of materials like gold, silver, and platinum. These modifications can enhance the biocompatibility, lubricity, and anti-fouling properties of materials used in medical devices and implants. PEG-SH is used in the development of biosensors where it functions as a linker molecule to attach biomolecules to sensor surfaces. The thiol group ensures strong attachment to metal electrodes, which is crucial for the stability and sensitivity of the sensor. PEG-SH-modified surfaces can detect various biological targets, such as proteins, DNA, and small molecules, with high specificity and sensitivity. In nanotechnology, PEG-SH plays a crucial role in stabilizing metallic nanoparticles by preventing aggregation and providing a biocompatible interface. This stabilization is essential for the practical use of nanoparticles in medical imaging and therapeutic agents. PEG-SH serves as a versatile tool in numerous fields, largely due to its biocompatibility, functionalizability, and unique surface-attaching capabilities. One of the most important limitations in practical implementation of PEG-SH is the extremely high price of this class of compounds.

Polyvinylpyrrolidone (PVP), also known as povidone or polyvidone, is a synthetic polymer derived from the monomer N-vinylpyrrolidone. This water-soluble polymer is renowned for its excellent film-forming, adhesion, and non-ionic properties, making it extremely versatile in a range of industrial, pharmaceutical, and cosmetic applications. PVP is widely used as a binder in tablet formulations. Its ability to dissolve rapidly in water and other solvents makes it ideal for facilitating tablet disintegration, thereby enhancing the dissolution of the drug in the gastrointestinal tract. It acts as a dispersing agent to improve the solubility of drugs in liquid formulations. This property is particularly useful in the production of suspensions and solutions, where uniform dispersion of active ingredients is crucial. In transdermal drug delivery systems, PVP is used for its film-forming ability, which helps in forming a protective barrier over the drug, thus controlling the release rate of the medication. Due to its film-forming capability, PVP is a key ingredient in hair styling products such as gels and mousses, where it provides hold and texture without stickiness. In skincare, PVP functions as a stabilizer and binder in creams and lotions, enhancing texture and maintaining the stability of emulsions. In the industrial sector, PVP serves as an adhesive in applications requiring clear, strong bonds, such as in glass fiber or paper products. PVP stabilizes dyes in solutions, preventing them from settling out of suspension or adhering to unwanted surfaces. This is particularly useful in the textile and printing industries. PVP acts as a flocculant in water treatment processes. It helps in the aggregation of suspended particles to form larger flocs which are easier to remove during water purification. PVP enhances the binding of electrodes in battery manufacturing, particularly in lithium-ion batteries, contributing to improved battery performance and longevity. As research and development continues, the applications of PVP are expected to expand, further cementing its status as a crucial material in various industries. PVP is considered safe and non-toxic for humans and animals in controlled uses, its environmental friendliness is limited by its non-biodegradability and potential for persistence in natural ecosystems. Tormentic and Triterpenic acids bioactive compounds can be applied in the investigation of the production of the high-value secondary metabolites, which may be used as cosmeceuticals, nutraceuticals, and pharmaceuticals. These bioactive compounds continue to gain popularity for their several advantages: fewer side effects, better patient tolerance, and relatively less expensive and acceptable products due to a long history of use compared to synthetic ingredients.

The list of application of selected CNMs is presented in Table 1.

TABLE 1. The applications of selected CNMs.

Sample name	Sample characteristics	Applications
CMS_1a_AuNP	Gold nanoparticles, size 1, sodium citrate stabilized	Biomedical Applications: Drug Delivery, Diagnostic Imaging, Cancer Therapy (Photothermal Therapy, Radiotherapy Enhancement), Biosensing and Bioimaging Electronic and Optoelectronic Applications: Sensors and Actuators, Optical Devices Catalysis: Chemical Reactions, Fuel Cells, Photocatalysis Ingredients of cosmetics
CMS_2a_AuNP	Gold nanoparticles, size 2, sodium citrate stabilized	as above
CMS_3a_AuNP	Gold nanoparticles, size 3, sodium citrates stabilized	as above
CMS_4a_AuNP	Gold nanoparticles, size 1, PEG stabilized	similar to the above, but the use of a specific stabilizer narrows the fields of application
CMS_5a_AuNP	Gold nanoparticles, size 2, PEG stabilized	similar to the above, but the use of a specific stabilizer narrows the fields of application
CMS_6a_AuNP	Gold nanoparticles, size 3, PEG stabilized	similar to the above, but the use of a specific stabilizer narrows the fields of application
CMS_7a_AgNP	Silver nanoparticles, size 1, sodium citrate stabilized	Biomedical Applications: Antibacterial and Antimicrobial Agents, Wound Dressings, Medical Devices Environmental Applications: Water Treatment, Pollutant Detection Textile Industry: Antimicrobial Fabrics, Odor Control Consumer Products: Cosmetics and Personal Care, Household Products Electronic and Optoelectronic Applications: Conductive Inks, Thermal conductors, Sensors Food Industry: Food Packaging Energy Applications: Photocatalysis, Solar Cells Nanocomposites and Coatings
CMS_8a_AgNP	Silver nanoparticles, size 2, sodium citrate stabilized	as above
CMS_9a_AgNP	Silver nanoparticles, size 3, sodium citrate stabilized	as above
CMS_10a_AgNP	Silver nanoparticles, size 1, PEG stabilized	similar to the above, but the use of a specific stabilizer strongly narrows the fields of application but is important from the scientific point of view
CMS_11a_AgNP	Silver nanoparticles, size 2, PEG stabilized	similar to the above, but the use of a specific stabilizer strongly narrows the fields of application but is important from the scientific point of view
CMS_12a_AgNP	Silver nanoparticles, size 3, PEG stabilized	similar to the above, but the use of a specific stabilizer strongly narrows the fields of application but is important from the scientific point of view
CMS_13a_AuNR	Gold nanorods 1	AuNRs can potentially be used in areas similar to AuNPs, but elongated, rod-like shape, which imparts unique optical and physical properties open new set of applications: Photothermal Therapy, Optical Coherence Tomography (OCT), Sensing and Diagnostics, SERS-based Detection, Non-linear Optics. They are important from a scientific point of view for understanding the impact of a nanoobject's shape on its biological properties.
CMS_14a_AuNR	Gold nanorods 2	as above
CMS_15a_TNR	Nano TiO2, rutile	Photocatalysis, water and air purification Antibacterial coatings Photovoltaics Self-Cleaning Surfaces White pigments
CMS_16a_TMR	Micro TiO2, rutile	Matt architectural paints Field marking paints Synthetic resin plasters

		Matt printing inks Coatings for paper and board Correction fluids Paper coatings Wallpaper coatings Lightweight coated paper (LWC paper) Matt emulsion paints Matt and lamination printing inks Synthetic resin plasters Conventional air-drying paints Silicate paints Silicone resin paints Flexographic inks Flexible PVC Plastisols, plasticiser pastes Impregnating baths for paper laminates Waterborne and solvent-based, high-gloss gravure and flexographic inks Packaging and can coatings Industrial coatings and wood finishes for interior use High-gloss gravure and flexographic inks UV-cured printing inks Reverse and lamination printing Packaging and can coatings Industrial coatings and wood finishes for interior use Thermoplastics concentrates Rigid PVC Rubber Linoleum PE melt extrusion coatings Polyolefin thin films White and colored automotive finishes Coil coatings Powder coatings High-quality industrial coatings PVC profiles and sidings Electroceramics Vitreous enamels Glazes Glass Ceramics Glass fibers Welding rods
CMS_17a_TNA	Nano TiO2, anatase	Photocatalysis, water and air purification Antibacterial coatings Photovoltaics Self-Cleaning Surfaces
CMS_18a_TNA	Micro TiO_2, anatase	White concrete Paper pulp Welding rods Electroceramics Glass enamels Rubber, Rubber threads Acrylic, rayon and acetate fibres UV-cured printing inks Leather finishes Masterbatches for polyester fibres Colouring pharmaceuticals Decorative cosmetics Sunscreens for cosmetics Personal care products Photocatalysis, water and air purification
CMS_19a_NC	Nanocellulose	Composite Materials: Reinforcement in Polymer, Aerospace and Automotive

		Paper and Packaging: Paper Strengthening, Biodegradable Packaging, High barrier coatings Biomedical Applications: Drug Delivery Systems, Wound Dressings and Tissue Engineering Electronics and Sensors: Flexible Electronics, Sensors Food Industry: Thickening and Stabilizing Agents, Edible Coatings Water Treatment: Water Purification Energy Storage: Batteries and Supercapacitors Environmental Remediation: Pollutant Adsorption Drilling Industry
CMS_20a_MC	Microcellulose	Pharmaceutical Industry: Tablet Binder and Filler, Disintegrant Food Industry: Fat Substitute and Calorie Reducer, Stabilizer and Thickener Cosmetic and Personal Care Products: Thickener and Stabilizer, Exfoliant Paper Products: Filler and Strengthening Agent Textile Industry: Textile Coating, Biocomposite Material Environmental Applications: Water Treatment Agricultural Applications: Carrier for Fertilizers and Pesticides
CMS_21a_DG4	PAMAM dendrimer, generation 4	Experimental and new biomedical applications: Drug Delivery, Gene Delivery, Diagnostics and Imaging, Antimicrobial Agents, Cancer Therapy
CMS_ 23a_DG5	PAMAM dendrimer, generation 5	as above
CMS_ 23a_DG6	PAMAM dendrimer, generation 6	as above
CMS_24a_PS1	Polystyrene spheres, size 1	Biomedical Applications: Diagnostic Assays, Flow Cytometry, Drug Delivery, Immunoassays, Cell Separation and Sorting Consumer Products: Cosmetics, Personal Care Products, latex dispersion for leather conservation Industrial Applications: Abrasives, Additives in Paints and Coatings Electronic and Optoelectronic Applications: Calibration Standards, Sensors
CMS_25a_PS2	Polystyrene spheres, size 2	as above
CMS_26a_CH_CIT	Sodium citrate	Food and Beverage Industry: Buffering Agent, Emulsifying Agent, Preservative, Stabilizing Agent Pharmaceutical Industry: Anticoagulant, Buffering Agent in Pharmaceuticals Cosmetics and Personal Care: pH Adjuster, Chelating Agent, Preservative, Cleaning and Detergent Industry, Water Softening Agent, Chelating, pH Buffer Chemical Industry: Chelating Agent in Electroplating, Buffer in Chemical, Sequestering Agent Textile Industry: Dyeing and Printing Water Treatment, Concrete Admixture, Antifreeze Agent
CMS_27a_CH_PEG	Poly(ethylene glycol) methyl ether thiol	Surface modifier of metals and metallic colloids, Biochemical reagent
CMS_28a_CH_PVP	Polyvinylpyrrolidone	Biomedical and Pharmaceutical Applications: Drug Delivery, Wound Dressings, Controlled Release Formulations Cosmetics and Personal Care: Hair Care Products, Skin Care Products, Oral Care Food Industry: Food Additive, Packaging Industrial Applications: Adhesives, Coatings and Films, Printing Inks Textile Industry: Dyeing and Finishing, Textile Coatings Nanotechnology: Stabilizer in Nanoparticle Synthesis Agriculture: Seed Coatings, Agricultural Formulations Electronics and Optoelectronics: Electrolytes, Electronic Components manufacturing Research and Development: Laboratory Reagent and colloid stabilizer
CMS_29a_CH_TOR	Tormentic acid	Biomedical Applications: Antioxidant and anti-inflammaging agents. Consumer Products: Anti-aging (prevention from age related diseases), cosmetics, nutraceuticals, antihypertensive, antihyperlipidemic and anti-diabetic
CMS_30a_CH_TER	Triterpenic acids obtained from RS (Red Sentinel) callus extract	Biomedical Applications: Antioxidant and anti-inflammaging agents. Consumer Products: Anti-aging (prevention from age related diseases), cosmetics, nutraceuticals, antihypertensive, antihyperlipidemic and anti-diabetic.

Conclusions and list of selected CNMs

The final selection of CNMs for the implementation of the CheMatSustain project was performed on the several criteria important from a scientific, socio-economic as well as application and environmental point of view. This allows to identify the specific representatives of chemicals, materials and nanomaterials that will be tested in respect of chemical, physical, quantum, toxicological and ecotoxicological attributes which will ultimately improve their safety and sustainability. The approach to the selection process of CNMs was multi-level. Consequently, the selected CNMs contains “model” materials, those widely used in industry and present in the environment as well as those with potential application. The selected CNMs allow the implementation of the CheMatSustain project's postulates.

The final list of CNMs selected for the CheMatSustain consist of 30 different samples:

1) Metallic nanomaterials (14 samples in total):
    - Spherical silver nanoparticles: in sizes 5, 10 and 30 nm, plus two types of surfactants, giving a total of six (6) different samples.
    - Rod-shaped gold nanoparticles: with two lengths (diameters and lengths to be fixed) (2) different samples.
    - Spherical gold nanoparticles: in sizes 5, 10 and 30 nm, plus two surfactants, giving a total of six (6) different samples.

2) Polymeric nanomaterials (5 samples in total)
    - PAMAM dendrimers: in three generations (G4, G5 and G6). Thus, giving three (3) different samples.
    - Polystyrene beads: with the size 20/40 nm and 80 nm. Thus, giving (2) different samples.

3) Micro/nanomaterials (6 samples in total) – pairs of materials in macro and nanoscale range size and different crystalline phases
    - Nano anatase (NM-102, JRC Repository)/rutile titanium dioxide – one pair (2) of different samples.
    - Micro anatase/rutile titanium dioxide – one pair (2) of different samples.
    - Micro and nano cellulose – one pair (2) of different samples.

4) Chemical substances (stabilizers and bioactive compounds) (5 samples in total)
    - Sodium citrate (SC) – one sample (1).
    - Poly(ethylene glycol) methyl ether thiol (PEG-SH) – one sample (1)
    - Polyvinylpyrrolidone (PVP) – one sample (1)
    - Tormentic acid (TOR) (1)
    - Triterpenic acids obtained from RS (Red Sentinel) callus extract (TER) (1)

The diagram illustrating the selected CNMs for the CheMatSustain is presented in Figure 2.

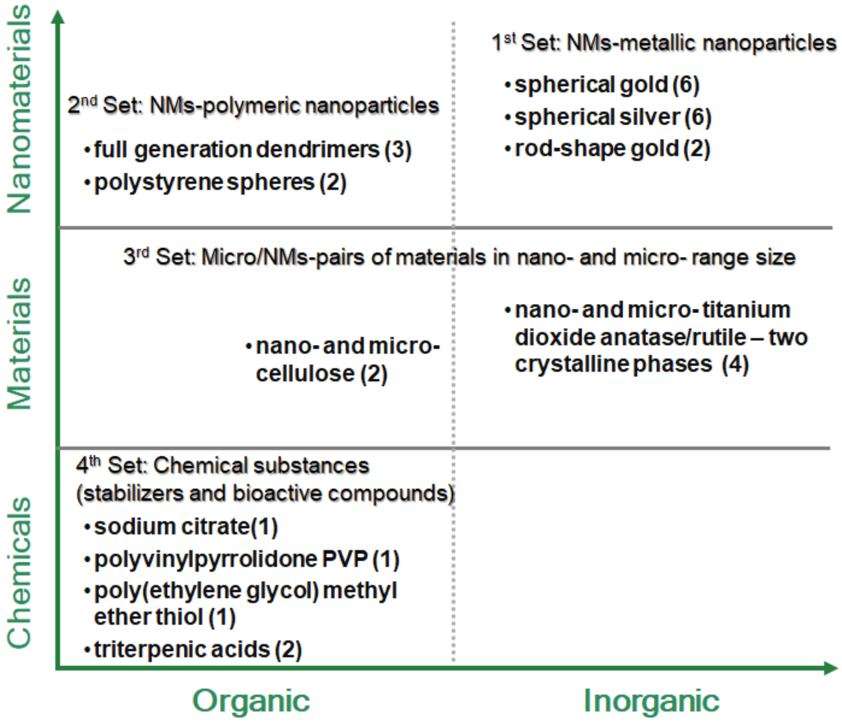

FIGURE 2. CheMatSustain diagram illustrating the selected CNMs.

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References

[Abbasi, 2014] Abbasi E, Aval SF, Akbarzadeh A, Milani M, Nasrabadi HT, Joo SW, Hanifehpour Y, Nejati-Koshki K, Pashaei-Asl R, Dendrimers: synthesis, applications, and properties, *Nanoscale Res Lett.* 9 (2014) 247, doi: 10.1186/1556-276X-9-247

[Boas, 2004], Boas U, Heegaard P (2004) Dendrimers in drug research. *Chem. Soc. Rev.* 33 (2004) 43-63, doi:10.1039/B309043B

[Brinchi, 2013] Brinchi L, Cotana F, Fortunati E, Kenny JM, Production of nanocrystalline cellulose from lignocellulosic biomass: Technology and applications, *Carbohydr. Polym.*, 94 (2013) 154-169, doi:10.1016/j.carbpol.2013.01.033

[Chauhan, 2018], Chauhan A, Dendrimers for Drug Delivery, *Molecules* 23 (2018) 938, doi:10.3390/molecules23040938.

[Costa, 2016] Costa J, Santos PSM, Duarte AC, Rocha-Santos T, (Nano)plastics in the environment – Sources, fates and effects, *Sci. Total. Environ.*, 566–567 (2016) 15-26, doi:10.1016/j.scitotenv.2016.05.041

[Dharma, 2022] Dharma HNC, Jaafar J, Widiastuti N, Matsuyama H, Rajabsadeh S, Othman MHD, Rahman MA, Jafri NNM, Suhaimin NS, Nasir AM, Alias NH. A Review of Titanium Dioxide (TiO_2)-Based Photocatalyst for Oilfield-Produced Water Treatment, *Membranes (Basel)* 12 (2022) 345, doi: 10.3390/membranes12030345

[Ferdous, 2020] Ferdous Z, Nemmar A. Health Impact of Silver Nanoparticles: A Review of the Biodistribution and Toxicity Following Various Routes of Exposure, *Int J Mol Sci.* 21 (2020) 2375 doi: 10.3390/ijms21072375

[Janaszewska, 2019] Janaszewska A, Lazniewska J, Trzepiński P, Marcinkowska M, Klajnert-Maculewicz B. Cytotoxicity of Dendrimers, *Biomolecules*, 9 (2019) 330, doi: 10.3390/biom9080330

[Kargarzadeh, 2018] Kargarzadeh H, Mariano M, Gopakumar D, Ahmad I, Thomas S, Dufresne A, Huang J, Lin N, Advances in cellulose nanomaterials, *Cellulose* 25 (2018) 2151–2189, doi:10.1007/s10570-018-1723-5

[Kik, 2020] Kik K, Bukowska B, Sicińska P. Polystyrene nanoparticles: Sources, occurrence in the environment, distribution in tissues, accumulation and toxicity to various organisms. *Environ Pollut.* 262 (2020) 114297, doi: 10.1016/j.envpol.2020.114297.

[Kumah, 2023] Kumah EA, Fopa RD, Harati S, Human and environmental impacts of nanoparticles: a scoping review of the current literature. *BMC Public Health*, 23 (2023) 1059, doi:10.1186/s12889-023-15958-

[Loos, 2014] Loos C, Syrovets T, Musyanovych A, Mailänder V, Landfester K, Nienhaus GU, Simmet T. Functionalized polystyrene nanoparticles as a platform for studying bio-nano interactions. *Beilstein J Nanotechnol*. 5 (2014) 2403-12. doi: 10.3762/bjnano.5.250.

The project CheMatSustain under No. 101137990 has received funding from the European Union under the Horizon Europe Programme.

[Madaan, 2014] Madaan K, Kumar S, Neelam P, Viney L, Pandita D, Dendrimers in drug delivery and targeting Drug-dendrimer interactions and toxicity issues, *J. Pharm. Bioallied. Sci*., 6 (2014) 139-150, doi:10.4103/0975-7406.130965

[Mahendra, 2009] Mahendra R, Alka Y, Aniket G, , Silver nanoparticles as a new generation of antimicrobials Author links open overlay panel, *Biotechnology Advances* 27 (2009) 76-83, doi:10.1016/j.biotechadv.2008.09.002

[Orlowski, 2014] Orlowski P, Tomaszewska E, Gniadek M, Baska P, Nowakowska J, Sokolowska J, Nowak Z, Donten M, Celichowski G, Grobelny J, Krzyzowska M. Tannic acid modified silver nanoparticles show antiviral activity in herpes simplex virus type 2 infection, *PLoS One*, 12 (2014) e104113. doi: 10.1371/journal.pone.0104113

[Orlowski, 2018] Orlowski P, Zmigrodzka M, Tomaszewska E, Ranoszek-Soliwoda K, Czupryn M, Antos-Bielska M, Szemraj J, Celichowski G, Grobelny J, Krzyzowska M, Tannic acid-modified silver nanoparticles for wound healing: The importance of size, *Int J Nanomedicine* 13 (2018) 991 – 100716, doi:10.2147/IJN.S154797

[Orlowski and Tomaszewska, 2018] Orlowski P, Tomaszewska E, Ranoszek-Soliwoda K, Gniadek M, Labedz O, Malewski T, Nowakowska J, Chodaczek G, Celichowski G, Grobelny J and Krzyzowska M (2018) Tannic Acid-Modified Silver and Gold Nanoparticles as Novel Stimulators of Dendritic Cells Activation. *Front. Immunol.* 9 (2018) 1115, doi: 10.3389/fimmu.2018.01115

[Palani, 2023] Palani G, Trilaksana H, Sujatha RM, Kannan K, Rajendran S, Korniejenko K, Nykiel M, Uthayakumar M. Silver Nanoparticles for Waste Water Management, *Molecules* 28 (2023) 3520, doi: 10.3390/molecules28083520

[Pan, 2007] Pan Y, Neuss S, Leifert A, Fischler M, Wen F, Simon U, Size-dependent cytotoxicity of gold nanoparticles, *Small* 11 (2007) 1941-1949, doi: 10.1002/smll.200700378.

[Pérez-Juste, 2005] Pérez-Juste J, Pastoriza-Santos I, Liz-Marzán L, & Mulvaney P, Gold nanorods: Synthesis, characterization and applications, *Coordination Chemistry Reviews*, 249 (2005) 1870-1901, doi:10.1016/J.CCR.2005.01.030.

[Pudlarz, 2019] Pudlarz AM, Ranoszek-Soliwoda K, Czechowska E, Tomaszewska E, Celichowski G, Grobelny J, Szemraj J. A Study of the Activity of Recombinant Mn-Superoxide Dismutase in the Presence of Gold and Silver Nanoparticles, *Appl. Biochem. Biotechnol*. 187(2019)1551-1568, doi: 10.1007/s12010-018-2896-y

[Rasmussen, 2014] Rasmussen K, Mast J, De Temmerman P, Verleysen E, Waegeneers N, Van Steen F, Pizzolon J, De Temmerman L, Van Doren E, Jensen K, Birkedal R, Levin M, Nielsen S, Koponen I, Clausen P, Kofoed-Sørensen V, Kembouche Y, Thieriet N, Spalla O, Giuot C, Rousset D, Witschger O, Bau S, Bianchi B, Motzkus C, Shivachev B, Dimowa L, Nikolova R, Nihtianova D, Tarassov M, Petrov O, Bakardjieva S, Gilliland D, Pianella F, Ceccone G, Spampinato V, Cotogno G, Gibson P, Gaillard C, Mech A.

Titanium Dioxide, NM-100, NM-101, NM-102, NM-103, NM-104, NM-105: Characterisation and Physico-Chemical Properties. EUR 26637. Luxembourg (Luxembourg): *Publications Office of the European Union*; 2014. JRC86291

[Salesa, 2023] Salesa B, Ferrús-Manzano P, Tuñón-Molina A, Cano-Vicent A, Assis M, Andrés J, Serrano-Aroca A, Study of biological properties of gold nanoparticles: Low toxicity, no proliferative activity, no ability to induce cell gene expression and no antiviral activity, *Chemico-Biological Interactions* 382 (2023) 110646, doi:10.1016/j.cbi.2023.110646

[Tomalia, 2005], Tomalia AD, The dendritic state, *Materials Today* 8 (2005) 34-46, doi:10.1016/S1369-7021(05)00746-7

[Tomaszewska, 2022] Tomaszewska E, Ranoszek-Soliwoda K, Bednarczyk K, Lech A, Janicka M, Chodkowski M, Psarski M, Celichowski G, Krzyżowska M, Anti-HSV Activity of Metallic Nanoparticles Functionalized with Sulfonates vs. Polyphenols. *Int. J. Mol. Sci.* 23 (2022) 13104, doi:10.3390/ijms232113104

[Trache, 2016], Trache D, Hussin M, Chuin C, Sabar S, Fazita M, Taiwo O, Hassan T, Haafiz M, (2016). Microcrystalline cellulose: Isolation, characterization and bio-composites application-A review, *Int. J. Biol. Macromol.* 93 Pt A (2016) 789-804, doi:10.1016/j.ijbiomac.2016.09.056

[Xiaobo, 2006], Xiaobo Ch, Samuel SM, Titanium Dioxide Nanomaterials: Synthesis, Properties, Modifications, and Applications, *Chem. Rev.* 107 (2007) 2891–2959, doi:10.1021/cr0500535

[Xuan, 2023] Xuan L, Ju Z, Skonieczna M, Zhou PK, Huang R. Nanoparticles-induced potential toxicity on human health: Applications, toxicity mechanisms, and evaluation models. *MedComm* 4 (2023) e327, doi: 10.1002/mco2.327

[Yamini, 2023] V. Yamini VS, \ Rameshpathy M, Venkatraman G, Ramanathan G, Garalleh ALH, Hashmi A, Brindhadevi K, Rajeswari VD, Environmental effects and interaction of nanoparticles on beneficial soil and aquatic microorganisms, *Environ. Res.* 236 (2023) 116776, doi:/10.1016/j.envres.2023.116776

[Zeng, 2016] Zeng Y, Kurokawa Y, Win-Shwe TT, Zeng Q, Hirano S, Zhang Z, Sone H. Effects of PAMAM dendrimers with various surface functional groups and multiple generations on cytotoxicity and neuronal differentiation using human neural progenitor cells. *J. Toxicol. Sci.* 41(2016) 351-70, doi: 10.2131/jts.41.351