**Nanotechnology to the Rescue: Using nano-enabled approaches in
microbiological food safety and quality**

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Abstract

Food safety and quality assurance is entering a new era. Interventions along the food supply chain must become more efficient in safeguarding public health and the environment and must address numerous challenges and new consumption trends. Current methods of microbial control to assure the safety of food and minimize microbial spoilage have each shown inefficiencies. Nanotechnology is a rapidly expanding area in the agri/feed/food sector. Nano-enabled approaches such as antimicrobial food-contact surfaces/packaging, nano-enabled sensors for rapid pathogen/contaminant detection and nano-delivered biocidal methods, currently on the market or at a developmental stage, show great potential for the food industry. Concerns on potential risks to human health and the environment posed by use of engineered nanomaterials (ENMs) in food applications must, however, be adequately evaluated at the developmental stage to ensure consumer's acceptance.

Graphical Abstract

INTRODUCTION

In addition to being nutritious and appealing, food must be above all safe. Providing safe food to consumers has never been more important and more challenging for food authorities and the food industry. The worldwide toll of foodborne disease is alarming (600 million cases, 420,000 deaths each year,[1•] with novel hazards emerging and reported cases increasing, while the magnitude of food spoilage is reaching epidemic levels; In the U.S., it is estimated that 30-50% of the food supply is wasted.[2]

The food production environment is facing unprecedented challenges such as the global dimension of the food chain, changes in modern production practices, increased at risk population, climate change, water shortage, and consumption trends for healthier food, with fewer preservatives, less chemicals and increased demand for organic labels. [3•,4] In this complex context, safety and quality of food must be addressed alongside the demand for increased food production in an international environment with great divergence between countries and continents in terms of organization, infrastructure, legislative requirements and food protection mechanisms.[3•] A new generation of methods for food safety/quality, especially microbial control interventions, are on the horizon to enable the food industry in addressing current inadequacies and

consumption trends and achieve new levels of safety, sustainability and economic growth.

In this paper, the emerging area of nanotechnology and in particular, nano-enabled approaches, as they apply to microbiological food safety and quality assurance are presented, introducing the reader to nano-enabled technologies that are either currently on the market or at a research/developmental stage.

Current approaches to food safety

Food safety and quality is assured through preventative controls implemented from 'farm to plate'. The ideal scenario is to minimize risks in the consumer plate without compromising the organoleptic or nutritional qualities of the food. There are a variety of physical and chemical methods to eliminate/reduce microbial hazards in food. These include physical methods such as thermal approaches (heat, freezing, refrigerated storage), radiation (UV, gamma), filtration, drying, and chemical methods such as chlorine based compounds, ozone, hydrogen peroxide.[5] It is worth noting that, commonly used microbial control technologies rely heavily on chemicals,[6] radiation,[7] and thermal approaches,[8] all of which have significant drawbacks: i) sensory effects and degradation of quality and texture,[9] ii) high energy cost, iii) significant environmental footprint, and

iv) serious occupational and health implications.[10] Additionally, they are not all compatible with the green/organic production philosophy and legislative requirements.[11,12]

The consumer trend for 'greener' and chemical free approaches, puts pressure on the food industry to develop novel, more efficient, sustainable, and low cost anti-microbial methods to replace and/or supplement existing ones so as to deal effectively with emerging hazards and the huge problem of food waste.[13] Nanotechnology is a promising technology to be utilized for food safety and quality applications.

Emerging Nano-enabled approaches along the food chain

Nanotechnology has been identified as one of the key-enabling technologies impacting all industries including the food industry.[14••] It is currently contributing significantly to the development of novel and innovative applications in the agriculture, food and feed sector (referred to as agri/food/feed). The most common applications are nano-encapsulated agrochemicals (such as nano-pesticides, fertilizers) and food additives/supplements (nano-nutraceuticals), antimicrobials/biocides and active/intelligent packaging.[15,16] Information from a recent EFSA inventory reveals the presence of 276 agri/food/feed nanotechnology applications in the market with many more under development. [17]

Especially in regards to microbiological food safety and quality, nano-enabled applications are emerging as a very promising alternative.[18•] These include antimicrobial food contact surfaces and surface coatings using engineered nanoparticles i.e. Ag,[19] ZnO,[20] and the photocatalytic ability of TiO₂,[21] nano-enabled sensors that can very rapidly detect the presence of pathogens or other substances,[22,23] 'active/intelligent' food packaging with improved food protection properties and biodegrading abilities [14] and as surface disinfection methods.[24] Table 1 summarizes nano-enabled intervention approaches explored for food safety and quality.[25,26]

Nano-enabled antimicrobial food contact surfaces

A range of nano-enabled antimicrobial food contact surfaces and coatings can assist in maintaining hygiene during food production and storage, possessing microbial inactivation potential or prevention of microbial attachment and subsequent biofilm formation. These type of surfaces can be found in food preparation and processing facilities, kitchen and cooking ware, cutting boards, equipment, conveyer belts etc.[14] Such antimicrobial surfaces utilize nanoscale metal or metal oxides such as Ag,[27•] photocatalytic nanoparticles (such as TiO₂ and ZnO),[28] and nanoscale topography that allows the creation of surfaces with anti-fouling properties.[29]

More specifically, nanoscale silver is a well-known antibacterial and one of the most commonly used metals.[30] Applications of silver embedded in biodegradable coatings can be used both for bacteria inactivation and antifouling applications. Silver nanoparticles have been integrated in agar and banana powder[31] and in gelatin,[32] and have been also combined with Graphene Oxide resulting in surfaces that inhibit almost up to 100% of bacteria attachment.[33] Silver nanoparticles are anchored on common surfaces like glass with the help of amino groups, inhibiting the formation of biofilms.[34] A notable application of silver nanoparticles was the combination with crystal violet (photo activated antimicrobial dye) into medical grade silicone, which not only achieved bacterial inactivation under visible light, but also improved under dark.[35]

In addition, among the most widely used nano-enabled antimicrobial surfaces are the various photocatalytic surfaces based on TiO_2 , ZnO , CeO_2 etc.[36] Photocatalysis requires light (commonly UV at 350 nm) and an appropriate surface to create pairs of reactive oxygen species (ROS) that oxidize and damage organic matter, including bacteria.[37] The use of UV light is a major limitation for photocatalytic surfaces but in recent years photocatalytic NPs using visible light have been developed.[38] The most common strategies for visible light photocatalysis is the dye sensitization,[39]

doping with elements such as Cu⁺ ions,[40] and the introduction of novel materials such as bismuth vanadate (BiVO₄).[41] These materials have been recently successfully integrated into polymer matrices to create a photocatalytic film.[42]

Furthermore, the integration of natural antimicrobial extracts in various surfaces as a greener alternative to harsh chemicals has also been used in recent years. For example cinnamaldehyde was nano-encapsulated and immobilized on glass surfaces showing significant antibacterial activity against *E. coli*. [43] Similar results were obtained with thyme oil emulsified with soluble soybean polysaccharide (nano emulsion) and immobilized on glass surface.[44] Donsi et al. used mandarin oil nano-emulsion on an edible chitosan coating used to coat green beans.[45] Otini et al. developed antimicrobial edible composite films with pectin/papaya puree/cinnamaldehyde nano-emulsions able to inactivate various food-related bacteria such as *E. coli*, *L. monocytogenes* and *S. enterica*. [46]

Finally, many bacteria including pathogens have the ability to attach and form biofilms on surfaces in the natural environment, in industrial settings and the health care environment. These biofilms are resistant to most disinfection methods and become an important source of contamination in the food industry and hospital environment with

tremendous implications.[47] An emerging method for the prevention of biofilms is nanoscale topography, the construction of nanoscale surfaces that can disturb the surface morphology, free energy, charge or combination thereof.

The majority of these nanostructures are made with nanolithography, typically on silicon surfaces,[48] or by nanoparticle deposition on surfaces.[49] Among the most common antifouling materials are Carbon Nanotubes,[50] mesoporous and nanoporous silica,[51,52] and Alumina.[53,54] More recently biofouling surfaces based on proteins have also been created.[55] Feng et al. utilized aluminum oxide anodization surfaces to mitigate microbial attachment and biofilm formation, with promising results. Their findings open the way to the design and fabrication of nanoporous anodized surfaces as well as other engineered affordable antifouling surfaces for the food industry. A major limitation of these surfaces is the cost and their fragile nature.[53,54]

Food Packaging

Nanotechnology has enabled the production of packaging that is active and intelligent with improved mechanical and thermal properties to ensure better protection of foods.[56] The integration of nano-clays in biopolymers enhanced their mechanical properties, enabling their use as an alternative

biodegradable and eco-friendly food packaging.[57] Further to the enhancement of the mechanical properties, packaging can become a gas barrier to extend product shelf life such as limiting oxygen penetration [58] or preventing of CO₂ leakage in carbonated drinks using titanium nitride nanoparticles. [59]

Nano-enabled solutions also allowed the integration of various bioactive molecules and nanoparticles to prevent oxidation and food degradation. Selenium and cellulose NPs can be integrated into food packaging to retard or inhibit the ROS that can degrade food quality.[60] The nano-encapsulation of other entities such as phenols can also provide protection against degradation, particularly of fatty foods.[61] Other essential oils can also be integrated in nanofibers [62,63] to prolong the lifespan of fresh produce.

A new packaging material that has gained significant attention is nanocellulose.[64] Nanocellulose nanofibrils and nanocrystals have been incorporated as a reinforcement phase in nanocomposites.[64] Also, nano cellulose is used as a base material that is enhanced with other nanomaterials such as photocatalysts.[65] In other instances, it can be the carrier of other antimicrobial agents with controlled release.[66]

Nano-enabled sensors

Detection of pathogens and spoilage organisms in foods takes from several hours to days using traditional culture, immunological or molecular methods. In recent years combining nanotechnology with the various available bio sensing techniques is bringing to life the so-called "nano-biosensors" which demonstrate rapid responses combined with high sensitivities.[67,68•,69•]

Gold and silver nanoparticles have been used extensively as sensing platforms. A variety of gold based colorimetric and electrochemical assays have been reported for the detection of microbiological food contamination. [70] Further by changing the size and the shape of the Au nanoparticles the specificity of the detection can be fine-tuned. [71] Similarly silver nanoparticle based assays have been developed for detection of various food contaminants such as melamine, [72] pesticides [73] and various pathogens such as *E. coli* and *Salmonella*. In addition, both silver [74] and gold [75] nanoparticles were successfully implemented with Surface Enhanced Raman Spectroscopy (SERS) to detect residual pesticides.

Aptamers commonly used for toxin detection have gained popularity as the base of biosensors in food safety and quality analysis.[76] Carbon nanomaterials, namely, carbon nanotubes (CNTs), graphene quantum dots, graphene and fullerenes are gaining attention for their exciting

properties.[77] Among them, CNTs and graphene are extensively incorporated in fabrication of sensors for food applications.[78] More recently these biosensors are being integrated into other type of structures such microcircuits and microfluidic devices. [79] [80] Although these technologies currently have low sensitivities, they are promising detection methods since they consist of inexpensive, integrated microcircuit that is easy to use.

Engineered Water Nanostructures (EWNS)

Recently, a novel nano-enabled antimicrobial platform has emerged for applications in air and on surfaces (food and fomites). This method relies on generating engineered water nano-structures (EWNS) using water by combining two different processes, electrospraying and ionization. [24,81,82] The synthesized EWNS possess a unique set of physicochemical and biological properties: they are highly charged, contain Reactive Oxygen Species (ROS), are highly mobile, can remain airborne for hours, and interact and inactivate microorganisms on surfaces and in the air by delivering the ROS payload.[82] Their high surface charge makes possible the targeted delivery of the EWNS on the surface of interest, maximizing their efficiency.[24,83] In recent studies their antimicrobial potential was assessed on a representative panel of food-related microorganisms reaching inactivations up to 4 logs (99.99% reduction) without affecting sensory

quality of food or leaving chemical traces making it an ideal technology for chemical free applications.[83] In addition, it has very low power demands and has been shown by an acute inhalation toxicological study to possess no apparent health effects to humans when EWNS are inhaled.[82]

EHS Implications of Nanomaterials

The rapid expansion of nanotechnology in foods and the predicted further increase, raise valid concerns regarding the potential adverse effects of ENMs on human health and the environment across their life cycle. [84-87] ENMs exhibit different properties than their non-nano counterparts due to their increased surface-to-mass ratio and surface reactivity and can penetrate biological barriers and cause adverse biological responses and health outcomes. However, just like any chemical substance they are not all inherently hazardous or inherently safe.[88•]

Evidence continues to grow in terms of potential toxicological implications of ingested ENMs.[16] It is estimated that in developed countries a person ingests over 10 trillion nanoparticles per day.[18] There is therefore an urgent need to understand the relationship between pristine ENM intrinsic properties, their physico-chemical transformations across the GIT and gastrointestinal fate, their potential toxicity, as well as, their

physicochemical and biological transformations once released into the environment.[16,89]

Regulatory framework for nanomaterials in food

Only within the European Union and in Switzerland the presence and use of ENMs and nanotechnology in the agri/feed/food sector needs regulatory pre-market approval. In the EU, for the most part, specific provisions have been incorporated into existing regulations such as the novel foods directive (EU 257/87) which is under revision at the moment. The aim is to demonstrate consumer and environmental safety.[90] In other parts of the world such as USA, Canada and Asia, regulation of nanomaterials is not part of a legally binding document but it rather takes the form of guidelines to the industry.[15,91•] In addition to pre market regulatory approval, the only place in the world that has a legal binding definition for ENMs, which is largely based on size, is Europe.

A key parameter that drives the regulatory framework is the consumers' perception of "nano in food". A recent study showed that although the public is skeptical of the use of nanomaterials in food (for improving safety or enhance nutrition), is in better standing compared to the GMOs. [92••]

Conclusions

The well documented benefits of ENMs in foods will drive the commercialization of nano-enabled applications for increased food safety, quality, shelf life and improved nutrition. Antimicrobial surfaces and coatings with the potential to inactivate microorganisms or prevent biofilm formation, food packaging with improved properties for better food protection, nanosensors for rapid pathogen or contaminant detection and surface biocidal methods such as the EWNs are the major emerging nano-enabled approaches. Potential risks to humans, animals and the environment from ENMs must, however, be very well understood and addressed in parallel with the development of new materials and nano-enabled approaches. To this end, risk assessment methodologies for nanotoxicity must be urgently developed and validated, as well as, analytical methods to detect and characterize ENMs in complex food matrices. It should be stressed that we cannot extrapolate effects on ENMs based on their larger size counterparts. In addition, a consensus must be reached in terms of definitions and regulatory frameworks of ENMs to address the globality of the food chain. A successful implementation of this horizon technology will lead to environmental sustainability and global economic growth.

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Antimicrobial Platform	Applications	Advantages	Limitations	References
Photocatalysis	Food handling and preparation surfaces, kitchenware, cookware, cutting boards, equipment, conveyer belts	Inexpensive, stable, easily intergrated with polymers	Requires UV	[36,38-40,42]
Ag		Very effective, easily integrated on all types of surfaces and equipment.	Expensive, potentially toxic	[30,32-34,43]
Antifouling surfaces		Preventing biofilms,	Fragile, not easy commercialization	[32,48,49,53-55]
Emulsified natural extracts	Food coatings, general purpose antibacteria	Natural extracts, green chemistry	Low efficiency, strong odors, short lifetime	[43-46]
Food Packaging	Antimicrobial media, stronger packaging, prevention of O ₂ exchange	Inexpensive, light weight, biodegradable	Early stage commercialization, potential to contaminate the food with ENMs	[56,58,60,62,64,66]
Sensors	Quick food quality check for toxins and pathogens	Faster than all other methods to detect pathogens and pesticide residues	Early stages, utilizes materials with potential toxic effects	[67,69-80]
EWNS	Usage along the entire farm-to-fork continuum	Water based, improves food safety and quality	Needs to be upscaled for commercials applications	[24,83]

Table 1: Summary of the major nano-enabled methods for food safety and quality.

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