Review Article

Thermal and Packaging-Related Nanoparticles in Food: Formation Pathways, Migration Mechanisms, and Toxicological Considerations

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The increasing prevalence of nanoparticles (NPs) in the food sector, either formed during thermal processing or released from packaging materials, raises critical questions regarding their potential health effects. This review explores the generation of food-derived nanoparticles (FDNPs), particularly fluorescent carbon nanoparticles (CNPs), during cooking and food processing, and the migration of engineered nanoparticles (ENPs), such as nanosilver, from food-contact materials. High-temperature cooking processes promote the formation of CNPs with diverse physicochemical properties, which can influence absorption, biodistribution, and potential toxicity. Migration studies reveal that ENPs can leach into food simulants. Migration rates generally increasing with temperature and storage duration, although usually remaining within current regulatory limits. Despite growing interest, significant gaps remain in the field of food nanotoxicology, particularly regarding long-term exposure risks and the relevance of current experimental models. This review emphasizes the urgent need for standardized analytical methodologies, mechanistic toxicological research, and comparative studies between industrial processing and domestic cooking scenarios to better assess the implications of nanoparticle exposure through the diet.

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Introduction

Food contamination is a global public health concern that significantly impacts human health and safety[1]. Contaminants enter the food chain through various means, including human activities like

industrial emissions and agricultural practices, as well as natural sources[2][3]. These contaminants pose a wide range of health risks, from acute toxicity to chronic diseases such as cancer, neurodevelopmental disorders, and endocrine disruption. Cooking plays a vital role in food safety by eliminating pathogens, improving palatability, and enhancing nutrient bioavailability[4]. However, it is important to recognize that cooking is not a chemically neutral process. Cooking can substantially alter the chemical composition of food, including the levels of existing contaminants and the formation of new, potentially toxic compounds[5][6][7]. The effects of cooking on contaminant concentrations can be both beneficial, by reducing levels, and detrimental, by increasing levels or generating new contaminants[8][9][10][11][12][13][14]. Accurate assessment of dietary exposure to food contaminants is crucial for effective risk management and public health protection. Relying solely on contaminant data from raw foods can lead to significant miscalculations, as cooking can dramatically alter these levels[5][15][7]. Therefore, understanding the impact of various cooking methods on contaminant concentrations is of paramount importance[16].

While there is existing literature on the influence of cooking processes on various organic pollutants and heavy metals in different food matrices[8][9][10][5][11][12][13], research on nanoparticles (NPs) and microplastics is much more limited. Regarding NPs specifically, key challenges include difficulties in accurately detecting and characterizing them in complex food matrices, the wide variety of engineered nanoparticles (ENPs), and the lack of standardized methods[17][18][19]. Additionally, NPs may interact with the food matrix, and those used in food packaging can migrate into food during cooking[20]. It is worth noting that limited data are available on specific cooking methods, as studies have generally focused on whether changes occur rather than comparing different methods.

Nanotechnology has rapidly emerged as a transformative field with diverse applications in the food industry, ranging from improved packaging to enhanced nutrient delivery[21][22][23][24]. However, alongside the intentional use of ENPs, there is growing awareness of the unintentional formation of NPs during food processing and preparation[25][26][27]. Specifically, thermal processing methods, such as roasting, frying, and baking, can generate food-derived nanoparticles (FDNPs), primarily fluorescent carbon nanoparticles (CNPs), with unique physicochemical properties and potential biological effects[28][29]. These FDNPs raise significant concerns due to their extremely small size, which allows them to penetrate biological barriers, and their potential for bioaccumulation in tissues and organs over time[30][31]. Understanding the formation, behavior, and potential health impacts of these FDNPs, as well as the

migration of ENPs from food packaging, is crucial for ensuring food safety and developing responsible nanotechnology applications[32].

When first mentioning "fluorescent carbon nanoparticles (CNPs)", their chemical structural features (e.g., presence of heteroatoms) should be provided to avoid confusion with carbon quantum dots (CQDs). CNPs are characterized by their graphitic carbon structure and the presence of surface functional groups such as hydroxyl and carbonyl groups, which facilitate their interaction with biological systems.

In 2022, the European Commission introduced a revised definition of nanomaterial, taking into account recent scientific advancements and insights from regulatory practice. The European Commission defines nanomaterials as “Natural, incidental or manufactured material consisting of solid particles present, either on their own or as identifiable constituent particles in aggregates or agglomerates, where 50% or more of these particles in the number-based size distribution fulfils at least one of three conditions related with dimensions”[33]. However, this size-based definition alone may not fully capture the unique properties of materials at the nanoscale, which can significantly influence their behavior in food systems and during biological interactions.

The use of nanoparticles as additives or ingredients in food products is becoming increasingly widespread, highlighting the importance of thoroughly assessing their potential toxicity when consumed[24]. Various studies have shown that ingesting NPs, especially those in solid form, can provoke toxicological responses in both animal models and cell cultures[34][35][36][37][38]. However, most toxicological investigations have focused solely on the effects of isolated NPs, often neglecting the potential interactions between NPs and food components in real-life scenarios. Research has highlighted the limitations of early analytical techniques in detecting particles in the nanorange and the potential toxic effects of plastic particles, adsorbed pollutants, and leached additives[39]. In turn, the potential interactions between NPs and food components has been emphasized[40], suggesting that NPs could affect nutrient absorption, and conversely, food components could modify NP absorption and toxicity[41]. These interactions highlight the importance of considering the food matrix when assessing the safety of NPs in food.

Based on the above, this review is aimed at examining current research on NPs in food, with a particular emphasis on: 1) the formation of FDNPs during cooking processes, focusing on the factors influencing their size, composition, and properties, 2) the analytical methods used to detect and characterize FDNPs, highlighting the challenges in distinguishing them from ENPs, 3) the biodistribution and potential

health impacts of FDNPs, including cellular uptake and toxicity studies, 4) the regulatory perspectives and knowledge gaps related to FDNPs in food. And 5) the migration of engineered nanoparticles (ENPs) from food packaging materials as a source of nanoparticles exposure.

Methods: Search Strategy

This review has examined the multifaceted presence of NPs in food, focusing on their sources, detection, properties, and potential impacts. Two primary pathways for nanoparticle occurrence in food have been identified: formation during cooking processes and migration from food packaging material. For it, a comprehensive and systematic literature search was performed using multiple scientific databases, including PubMed, Web of Science, Scopus, and Google Scholar. The search strategy combined keywords related to cooking processes ("cooking," "thermal processing," "food preparation," "boiling," "frying," "grilling," "baking," "microwaving," "steaming," "roasting"), and "nanoparticles," "engineered nanoparticles," "nanoplastics," "plastic additives," "phthalates", migration, and food. The search was limited to studies published in English from 2000 to early 2025. Additionally, relevant studies were identified through backward citation tracking (reviewing the reference lists of retrieved articles).

Studies were included if they quantitatively or qualitatively assessed the impact of one or more cooking methods on the levels of at least one of the target contaminants in a defined food matrix, provided sufficient methodological detail to allow for evaluation of the study's validity, and were original research articles, reviews, or meta-analyses. In contrast, studies were excluded if they focused solely on contaminant occurrence without assessing the effects of cooking, investigated the effects of food processing steps other than cooking (e.g., storage, packaging), were not available in full text, or were published in languages other than English.

Formation of Nanoparticles During Cooking Processes

While migration from packaging represents one pathway for nanoparticle exposure, cooking processes themselves can generate NPs. These food-derived nanoparticles (FDNPs), distinct from intentionally added nanostructured additives, form during thermal food processing and can have unique properties and biological effects. This section is primarily focused on fluorescent carbon nanoparticles (CNPs), the most commonly reported type of FDNP.

Mechanisms of CNP Formation

The formation of CNPs during cooking is a complex process, primarily driven by the Maillard reaction and caramelization, which occur at high temperatures (typically above 120°C)[42][43][44]. The Maillard reaction, a non-enzymatic browning reaction, occurs between reducing sugars (e.g., glucose, fructose) and amino acids (from proteins) at elevated temperatures. It leads to the formation of a wide range of complex molecules, including melanoidins, which are high-molecular-weight polymers with fluorescent properties. On the other hand, caramelization is a process that involves the thermal decomposition of sugars (primarily sucrose) in the absence of amino acids[42]. It also leads to the formation of complex, colored compounds, some of which may exist in nanoparticulate form.

The specific composition of the food being cooked (i.e., the relative amounts of proteins, carbohydrates, and lipids) significantly influences the type and amount of FDNPs formed, while higher temperatures and longer cooking times generally lead to increased CNP formation. The cooking method (roasting, frying, baking, grilling) also plays a role, as it affects the heat transfer and the presence of oxygen. Moreover, high-temperature cooking may generate Reactive Oxygen Species (ROS), which can further contribute to the oxidation and fragmentation of food components, potentially leading to CNP formation. Importantly, it must be noted that the exact mechanisms of CNP formation are still not fully understood and are an active area of research.

Meat-Derived Fluorescent Nanoparticles

Zhao et al.[45] reported the discovery of fluorescent NPs in roasted pork at different temperatures (180, 230, and 280°C). The size of these pork-derived NPs ranged from 5.93 to 7.49 nm, with no systematic variation observed across temperature conditions. Fourier-transform infrared spectroscopy (FTIR) and (X-ray photoelectron spectroscopy (XPS) analysis revealed that these NPs consisted primarily of graphitic carbon (sp^2) and carbon defects (sp^3), with abundant hydroxyl and carbonyl groups on their surface that facilitate interaction with biological systems. Using chamber tests, which serve as models for intestinal permeability, the authors demonstrated that these pork NPs could permeate through intestinal tissue in vitro. Mouse studies revealed notable accumulation of NPs in the liver, kidney, and testis, crossing the highly selective blood-brain barrier to enter the brain. While oral administration at a high dose (2 g/kg body weight) did not cause obvious acute toxicity in mice, significant effects on locomotion and lifespan were observed in Caenorhabditis elegans. In turn, Song et al.[46] investigated similar phenomena in roasted chicken breasts, reporting nearly spherical nanoparticles with an average size of 1.7 ± 0.4 nm,

significantly smaller than the pork-derived NPs. This size difference likely results from the different food matrix or specific roasting conditions. Biodistribution studies showed that these chicken-derived NPs distributed throughout the pharynx, intestine, liver, lung, and kidney, but unlike pork NPs, did not accumulate in the brain, highlighting potential food-specific differences in FDNP properties and biodistribution.

Other Food-Derived Nanoparticles

Cong et al.[47] extended the research to pizza, finding spherical fluorescent NPs with a diameter of approximately 3.33 nm, containing 68.21% carbon, 27.44% oxygen, 2.75% nitrogen, and 1.60% sulfur. The biodistribution pattern in mice was like that observed with chicken-derived NPs[46], with fluorescence detected in the stomach, intestine, liver, lung, and kidney, but not in the brain, heart, or spleen. Some FDNPs may have limited ability to cross the blood-brain barrier, in contrast to NPs derived from pork, which have demonstrated greater permeability.[45]. A recent study by Li et al.[48] investigated the oxidative modification of rabbit meat proteins and the associated changes in the physicochemical characteristics of the resulting CNPs across different roasting temperatures. The results demonstrated that roasting induces substantial alterations in protein structure, with the degree of oxidation rising in parallel with temperature. As roasting temperature increased from 180°C to 300°C, the relative elemental content in CNPs changed significantly: carbon increased by 12%, nitrogen decreased by 3%, while oxygen decreased by 9%. Correlation analysis revealed a positive relationship between protein oxidation degree and CNP fluorescence intensity, suggesting a mechanistic link between these processes. The results of that study provided valuable insights into the relationship between cooking conditions and CNP properties. Fu et al.[49] analyzed the colloidal properties and structural characteristics of CNPs during lamb soup stewing over periods ranging from 15 minutes to 5 hours. It was observed that with increasing stewing time, both particle size and colloidal stability increased. Protein secondary structure analysis showed that α-helix and β-turn content decreased, while β-sheet and random coil content increased during processing, resulting in more open CNP structures with a complex organization, in which proteins were encapsulated within lipids in the inner regions. It suggests that the cooking method and the interaction between different food components (proteins and lipids) can influence CNP structure. Recently, Nie et al.[50] conducted a study that expanded the range of cooking methods and food types investigated. These authors reported that high-pressure cooking significantly affected the properties of micro-nanoparticles in fish bone soup, decreasing particle size and enhancing the overall stability of the

colloidal system. The correlation network model revealed relationships between specific flavor compounds and the nanoparticle properties, highlighting the connection between processing conditions, nanoparticle formation, and sensory qualities.

Previously, Liu et al.[51] investigated the formation, physicochemical characteristics, elemental makeup, biodistribution, and interaction with human serum albumin (HSA) of fluorescent nanoparticles (FNPs) derived from roasted squid. They observed that increasing the roasting temperature from 190 to 250 °C reduced FNP size from 4.1 to 2.3 nm. Carbon, oxygen, and nitrogen were identified as the primary elements, with higher roasting temperatures leading to increased carbon and nitrogen content. After oral administration in mice, these FNPs accumulated in the stomach, intestine, and brain. Additionally, FNPs altered HSA structure by decreasing its α-helix content and increasing its morphological height, as shown by atomic force microscopy, which also revealed nanocorona formation between FNPs and HSA. In another study, Liu et al. (2020) assessed how fluorescent carbon dots (CDs) interact with human serum albumin (HSA) in roast beef, focusing on the development of protein coronas and their potential impact on toxicity. The CDs were found to be nearly spherical, measuring between 1 and 5 nanometers in diameter. Their composition was primarily carbon (68.68%), with notable amounts of nitrogen (10.6%) and oxygen (15.98%). Owing to their diminutive size and high solubility in water, these CDs were able to traverse the intestinal barrier with ease. The study also revealed a significant association between HSA and the CDs, indicating the likelihood of protein corona formation. The study found that HSA-CD complexes localized within cellular lysosomes, where they helped reduce the swelling typically induced by CDs and prevented the loss of mitochondrial membrane potential. Additionally, these protein coronas lowered the generation of reactive oxygen species (ROS) and minimized glutathione depletion caused by the CDs, thereby offering protection to the cells. These results highlight the beneficial role of protein coronas in mitigating cytotoxic effects.

Wang et al.[52] conducted a study aimed at examining how different baking temperatures could affect CDs derived from lamb meat. The research focused on characterizing the physicochemical properties of these CDs and evaluating their biological activities. The researchers employed various analytical techniques to investigate the temperature-dependent characteristics of the CDs. It was found that baking temperature significantly influenced the morphology, surface functional groups, fluorescent properties, and free radical scavenging abilities of the extracted CDs. To assess biocompatibility, Wang et al.[52] utilized flow cytometry, which revealed minimal toxicity of the CDs. Additionally, electron spin resonance methods were employed to measure the CDs′ capacity to neutralize free radicals. Using HepG2 cells as an

experimental model, the CDs′ protective effects against oxidative damage was shown, confirming their antioxidant capabilities. The results of that study established an important relationship between cooking conditions and the resulting properties of CDs. In turn, Song et al.[53] examined the formation, distribution, and cytotoxic effects of carbon quantum dots (CQDs) produced from roasted Atlantic salmon. X-ray photoelectron spectroscopy revealed that these CQDs primarily consisted of carbon, oxygen, and nitrogen. Their morphology, surface groups, and optical features varied significantly with roasting duration. In vivo studies in mice showed that CQDs accumulated in the digestive tract, kidneys, liver, and brain, suggesting their ability to cross the blood-brain barrier. Cell imaging demonstrated that CQDs could enter normal rat kidney cells, inducing autophagosome formation. At a concentration of 6 mg/mL, cell viability dropped to 34.62%, and cellular energy production shifted from aerobic to glycolytic pathways. On the other hand, Bi et al.[54] identified foodborne carbonaceous nanostructures (CNSs) in roasted pike eel. These CNSs exhibited strong photoluminescence under UV light and showed excitation-dependent emission behavior. Bi et al.[54] also investigated the effects of heating temperature on CNS properties and proposed a formation mechanism involving polymerization, pyrolysis, nucleation, growth, emergence, and blossom. The CNSs demonstrated excellent biocompatibility and were able to enter the cytoplasm of MC3T3-E1 cells without significant toxicity. The results highlighted the presence of tunable CNSs in roasted pike eel and their potential for cellular applications. Wang et al.[55] evaluated the toxicity of onion-like carbon nanoparticles (OCNPs) isolated from grilled turbot. Their findings showed that OCNPs could enter MC3T3-E1 cells without altering cell morphology, and no significant apoptosis or cellular damage was detected even at concentrations up to 20 mg/mL. Hemolysis assays indicated that OCNPs did not cause notable red blood cell lysis. Acute toxicity testing in zebrafish revealed a weak toxic effect, with an LC50 of 212.431 mg/L. However, in subacute exposure (30–40 mg/L for 10 days), zebrafish exhibited elevated reactive oxygen species (ROS) levels, which led to reduced activity of antioxidant enzymes and increased lipid and protein peroxidation, as evidenced by higher malondialdehyde and protein carbonyl levels. Assessing the chronic toxicity of onion-like OCNPs in zebrafish, it was found that oxidative stress occurred exclusively in groups exposed to high concentrations of OCNPs.

Taken together, the results of the above studies suggest that FDNP size and biodistribution vary by food type and cooking conditions, with implications for toxicity that remain unresolved. Simplified pathways of nanoparticle exposure in food are depicted in Figure 1.

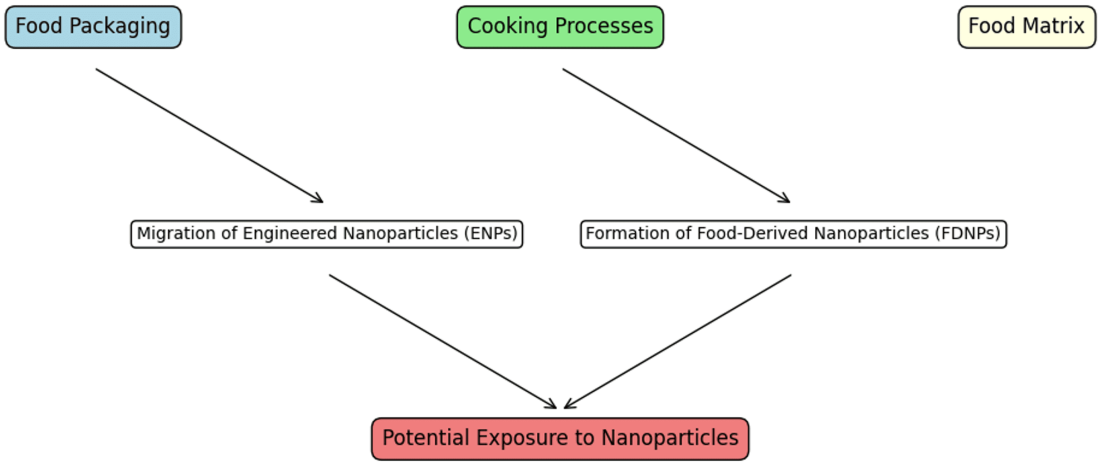

Figure 1. Simplified pathways of nanoparticle exposure in food.

Nanoplastics Release During Food Preparation

Beyond the formation of carbon-based NPs during cooking, recent studies have identified another source of food-related NPs: the release of nanoplastics from food containers during heating and cooking processes. This section discusses the differences between industrial processing and home cooking in terms of nanoplastics exposure. Son et al.[56] investigated the relationship between nanoplastics (NPs) release and the Maximum Service Temperature (MST) of five different plastic types, confirming a clear correlation under real-world conditions. NP release tended to reach its maximum at the material's MST, increasing with higher container content temperatures and longer cooking durations. Physical impacts were identified as the most significant contributors to NP release. Increasing the microwave power resulted in a higher amount of NPs being released, and this effect was more pronounced in polar substances than in non-polar ones. Based on these findings, Son et al.[56] recommended using containers made from non-polar materials with high MST to minimize nanoplastic ingestion during food preparation Previously, Hernandez et al.[57] investigated the release of microplastics and nanoplastics from plastic teabags during standard brewing. They found that steeping a single plastic teabag at 95 °C released about 11.6 billion microplastics and 3.1 billion nanoplastics per cup. Analysis by FTIR and XPS confirmed that these particles were composed of nylon and polyethylene terephthalate, matching the materials of the original teabags. The quantity of plastic particles released was several orders of magnitude greater than previously reported in other foods. Acute toxicity tests in invertebrates revealed

that exposure to these particles alone led to dose-dependent behavioral and developmental effects. Cella et al.[58] investigated the degradation of plastics into primary microplastics (pMP) and nanoplastics (pNP) during typical use of polyethylene rice cooking bags, ice-cube bags, and nylon teabags. Using a combination of Raman microscopy, XPS, and SEM, along with careful sample preparation, they characterized the chemical composition and morphology of the released particles. They also introduced a straightforward FTIR-based method to quantify pNP mass, finding that each nylon teabag released approximately 1.13 ± 0.07 mg of nylon 6. The research also demonstrated that temperature played a key role in altering the shape and clustering behavior of the materials that were released.

Industrial processing, such as ultra-high temperature sterilization, may result in higher nanoplastics release compared to home cooking due to the more extreme conditions and longer durations. However, both pathways contribute to overall nanoplastics exposure and warrant further investigation.

In conclusion, cooking, particularly at high temperatures, leads to the formation of FDNPs, primarily CNPs, through processes like the Maillard reaction and caramelization. The size, composition, and properties of these CNPs vary depending on the food matrix, cooking method, temperature, and time. Studies in model organisms have shown that these FDNPs can be absorbed and distributed to various organs, with some having the ability to cross the blood-brain barrier. The potential for nanoplastics release during food preparation adds another layer of complexity to nanoparticle exposure from food.

Migration of Nanoparticles from Food Packaging

The migration of NPs from food packaging materials represents a significant pathway for nanoparticle entry into food products. This section reviews studies focused on the migration of ENPs, primarily nanosilver and titanium dioxide, from various food contact materials.

Nanosilver Migration from Food Containers

Manufacturers of food storage containers often use nanosilver as an antimicrobial agent. However, the safety implications of nanosilver release remain incompletely understood. Huang et al.[59] conducted a study investigating the migration of nanosilver from commercial polyethylene plastic bags used for food storage. Bags were exposed to food-simulating solutions at temperatures ranging from room temperature to 50°C for periods of 3 to 15 days. Using Scanning Electron Microscopy with Energy-Dispersive X-ray (SEM/EDX), the presence of nanosilver particles in the packaging material was confirmed. Atomic absorption spectroscopy (AAS) analysis revealed a nanosilver concentration of

approximately 100 µg/g in the plastic. Both SEM/EDX and AAS demonstrated a time- and temperature-dependent migration of silver from the bags into the food simulants. Nevertheless, it is important to note that the study used food simulants, which might not perfectly replicate the complex interactions that occur with real food matrices. Moreover, the study focused on a limited range of temperatures and times. Despite these limitations, the results provided early, compelling evidence of nanosilver migration from food packaging, highlighting the potential for consumer exposure. Echegoyen and Nerín[60] conducted a study to assess the migration of nanosilver from three types of commercially available plastic food containers. Their investigation involved exposing these containers to various simulant solutions and subjecting them to different exposure durations. Inductively Coupled Plasma Mass Spectrometry (ICP-MS) and SEM-EDX were used to distinguish between dissolved silver ions and silver nanoparticles, a critical distinction for toxicity assessment. Silver migration was observed in all samples, with total values ranging from 1.66 to 31.46 ng/cm^2 (below permissible regulatory limits). Interestingly, the authors found that the size and morphology of the released silver nanoparticles varied considerably between different samples, ranging from 10 to 60 nm. In turn, Cushen ar al.[61] assessed the impact of both storage duration and temperature on the transfer of nanosilver and nanocopper from polyethylene nanocomposite packaging into boneless chicken breast. Their experiments measured silver migration at levels between 0.003 and 0.005 mg/dm^2, and copper migration between 0.024 and 0.049 mg/dm^2, under four storage scenarios that mimic typical conditions. However, the study found that variations in time and temperature did not produce significant differences in the extent of nanoparticle migration. The authors developed a migration and exposure model based on the Williams-Landel-Ferry equation. The exposure assessment estimated that the 95th percentile of human exposure to nanosilver ranged 5.89×10^{-5} to 8.9×10^{-5} mg kg(bw)$^{-1}$ day^{-1}. while for the measured migration of copper (under the same storage conditions), the exposure ranged from 2.26×10^{-5} to 1.17×10^{-4} mg kg(bw)$^{-1}$ day^{-1}. On the other hand, Addo Ntim et al. [62] examined the influence of aqueous food simulants (water, 10% ethanol, and 3% acetic acid) on the stability of silver nanoparticles (AgNPs). The authors used AF4, ultrafiltration, EM, and sp-ICP-MS. It was found that 3% acetic acid induced significant oxidative dissolution of AgNPs to silver ions, while water and 10% ethanol had minimal effects on the physicochemical properties of the AgNPs. This highlights the importance of the food simulant (and, by extension, the food matrix) in determining the fate and potential toxicity of migrated nanoparticles.

The studies above reviewed show that nanosilver can migrate from food packaging materials into food simulants, with migration rates generally increasing with temperature and storage time, although some

studies did not show significant effects. The type of food simulant significantly affects the stability and form of the released silver. While the reported migration levels are often below current regulatory limits, the use of food simulants, the limited range of packaging materials studied, and the analytical challenges in detecting very small nanoparticles suggest that actual exposure levels might be underestimated. Anyhow, migration represents one pathway for nanoparticle exposure.

Migration of Titanium Dioxide from Non-stick Coatings

Titanium dioxide (TiO2) is another significant nanoparticle found in food contact materials, often used in non-stick coatings[36]. Peters et al.[63] conducted a comprehensive investigation of TiO2 content and particle size distribution in 7 food-grade TiO2 materials, 24 food products, as well as 3 personal care products. Using electron microscopy, AF4-ICP-MS (asymmetric flow field- flow fractionation-ICP-MS), and sp-ICP-MS (Single-Particle ICP-MS), it was found that all E171 materials had primary particle sizes ranging from 60-300 nm, with approximately 10-15% of particles below 100 nm. The authors detected titanium in 24 of the 27 food and personal care products, ranging from 0.02 to 9.0 mg TiO2. Golja et al. [64] characterized commercially available non-stick coatings and investigated TiO2 nanoparticle migration. The coatings contained both micron- and nanosized rutile TiO2 particles and quartz SiO2 in a silicone polymer matrix. Migration tests into various simulants (deionized water, 3% acetic acid, and 5 g/l citric acid) at 100°C for 2 h showed Ti-containing particle migration at concentrations up to 861 µg/l (147 µg/dm^2). SEM-EDXS confirmed the presence of TiO2 nanoparticles in 3% acetic acid. Mechanical degradation studies suggested the release of microgram quantities of Ti-containing NPs. The results of that study highlighted the potential for both dissolution of the coating matrix and release of intact NPs. Thus, studies on TiO2 migration show that it can be released from non-stick coatings, with the amount and form (ionic vs. nanoparticulate) influenced by the food simulant. A critical limitation in assessing TiO2 exposure is the analytical challenge of detecting and quantifying nanoparticles below 20-50 nm.

In summary, migration from packaging represents one source of nanoparticle exposure to consumers. The amount and type of nanoparticle released depend on the packaging material, the food matrix (or simulant), temperature, and storage time. While studies suggest that migration levels are often below regulatory limits, analytical limitations and the use of simulants might be underestimating actual exposure.

Table 1 summarizes the diverse sources, sizes, and biodistribution patterns of nanoparticles in food. Cooking-generated FDNPs (e.g., carbon NPs from meat) exhibit smaller sizes (1–8 nm) compared to ENPs

from packaging (10–300 nm), with distinct organ accumulation profiles.

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Nanoparticle Type	Source	Size Range (nm)	Detection Methods	Biodistribution	Potential Effects	References
Engineered NPs						
Silver (Ag)	Food packaging materials	10–60	SEM/EDX, AAS, ICP-MS, sp-ICP-MS	Temperature- and time-dependent migration	Antimicrobial properties; 95th percentile exposure: 5.89×10^{-5} to 8.9×10^{-5} mg kg(bw)$^{-1}$ day^{-1}	[59][60][61]
Titanium dioxide (TiO_2)	Food grade materials (E171), non-stick coatings	60–300 (10–15% <100 nm)	EM, AF4-ICP-MS, sp-ICP-MS	Present in both ionic form and as NPs	Migration up to 861 µg/l (147 µg/dm²) in acidic conditions	[63][64]
Cooking-Generated NPs						
Carbon fluorescent NPs (Pork)	Roasting (180–280°C)	5.93–7.49	TEM, FTIR, XPS	Liver, kidney, testis, brain	No obvious toxicity at 2 g/kg body weight in mice; effects on *C. elegans* locomotion	[45]
Carbon fluorescent NPs (Chicken)	Roasting	1.7 ± 0.4	TEM, XPS	Cytoplasm, digestive system, liver, lung, kidney (not brain/heart/spleen)	Cell cycle arrest and apoptosis at high concentrations	[46]
Carbon fluorescent NPs (Pizza)	Thermal processing	~3.33	TEM, XPS	Similar to chicken-derived NPs	Similar to chicken-derived NPs	[47]

Nanoparticle Type	Source	Size Range (nm)	Detection Methods	Biodistribution	Potential Effects	References
Carbon fluorescent NPs (Squid)	Roasting (190–250°C)	2.3–4.1	TEM, XPS	Stomach, intestine, brain	Interaction with HSA causing structural changes	[51]
Carbon fluorescent NPs (Beef)	Roasting	1–5	TEM, XPS	Can pass through intestine wall	Form protein coronas with HSA; coronas reduce cytotoxicity	Liu et al. (2020)
Carbon fluorescent NPs (Lamb)	Baking (200–350°C)	Variable	TEM, XPS	Cell membrane, cytoplasm	350°C baked CDs showed free radical scavenging capability	[52]
Carbon quantum dots (Salmon)	Roasting	Variable	XPS	Digestive tract, kidney, liver, brain	Reduced cell viability to 34.62% at 6 mg/mL; changed energy metabolism	[53]
Nanoplastics	Plastic food containers during heating	Variable	FTIR, XPS, SEM	Potentially absorbed through GI tract	Release correlates with Maximum Service Temperature; physical impacts are significant contributors	[56]
Nanoplastics	Plastic tea bags at brewing temperature (95°C)	<100	FTIR, XPS	Potentially absorbed through GI tract	~3.1 billion nanoplastics released per cup; dose-dependent behavioral and developmental	[57]

Nanoparticle Type	Source	Size Range (nm)	Detection Methods	Biodistribution	Potential Effects	References
					effects in invertebrates	

Table 1. Overview of Nanoparticle Types, Sources, and Characteristics in Food

Abbreviations: *SEM/EDX: Scanning Electron Microscopy with Energy-Dispersive X-ray; AAS: Atomic Absorption Spectroscopy; ICP-MS: Inductively Coupled Plasma Mass Spectrometry; sp-ICP-MS: Single-Particle ICP-MS; EM: Electron Microscopy; AF4: Asymmetric Flow Field-Flow Fractionation; TEM: Transmission Electron Microscopy; FTIR: Fourier-Transform Infrared Spectroscopy; XPS: X-ray Photoelectron Spectroscopy; HSA: Human Serum Albumin.*

Applications of Nanotechnology in Food Industry

The present review is essentially focused on the unintentional formation and potential risks of FDNPs. However, it is also important to remark that nanotechnology offers significant potential benefits for the food industry. Thus, nanomaterials can be used to improve food safety by inhibiting microbial growth, enhancing food preservation through nanoencapsulation of bioactive compounds, and developing sensitive nanosensors for detecting foodborne pathogens and contaminants[65][66][67]. In any case, a comprehensive assessment of these beneficial applications is beyond the scope of this review.

Detection and Characterization Methods for Nanoparticles in Food

The accurate detection and characterization of NPs in food, particularly FDNPs, presents significant analytical challenges. Researchers have employed a variety of complementary techniques to identify, quantify, and characterize NPs in food and food contact materials. Nevertheless, distinguishing FDNPs from ENPs and accounting for matrix effects remain major hurdles.

Imaging Techniques

Electron microscopy techniques, particularly scanning electron microscopy (SEM) and transmission electron microscopy (TEM), provide direct visualization of NPs, allowing determination of size, shape, and morphology. These techniques are often coupled with energy-dispersive X-ray spectroscopy (EDX or EDS) to provide elemental composition information. For example, Huang et al.[59] used SEM/EDX to confirm the presence and morphology of nanosilver in food packaging, while Song et al.[46] employed TEM to characterize the nearly spherical shape and size of NPs from roasted chicken. Electron microscopy can be limited by sample preparation artifacts and might not be suitable for quantifying NPs in complex food matrices.

Spectroscopic and Analytical Methods

Spectroscopic methods provide crucial information about nanoparticle composition and structure: X-ray photoelectron spectroscopy (XPS) for elemental composition determination and surface chemistry analysis; Fourier transform infrared spectroscopy (FTIR) for identification of functional groups on nanoparticle surfaces, atomic absorption spectroscopy (AAS) and inductively coupled plasma mass spectrometry (ICP-MS) for quantitative analysis of metal-containing NPs, and fluorescence spectroscopy for characterizing optical properties of carbon-based NPs formed during cooking. Although these techniques are useful, they often require extensive sample preparation, which can alter the properties of FDNPs.

Separation and Size Characterization Techniques

Advanced separation methods like asymmetric flow field-flow fractionation (AF4), frequently used in combination with ICP-MS, enable NPs to be separated and analyzed based on their size.S ingle-particle ICP-MS (sp-ICP-MS) represents another sophisticated approach for detecting and characterizing individual NPs in complex matrices, but may have limitations in detecting very small NPs.

Analytical Challenges Specific to FDNPs

Despite these advanced techniques, a major challenge remains in the detection and characterization of FDNPs: distinguishing them from ENPs. It is often difficult to determine whether a nanoparticle found in cooked food is naturally formed or originated from packaging or other sources. In addition, FDNPs may be present at very low concentrations in food, making detection and quantification difficult. On the other

hand, the complex composition of food (proteins, lipids, carbohydrates, etc.) can interfere with analytical measurements, leading to inaccurate results, while sample preparation methods (e.g., homogenization, extraction, digestion) can alter the size, shape, aggregation state, and surface properties of FDNPs, potentially leading to artifacts. As highlighted by Peters et al.[63], current methods often have practical size detection limits (e.g., 20-50 nm for TiO2 potentially leading to a significant underestimation of the number of smaller FDNPs. In any case, there is a critical need for standardized analytical methods to enable comparisons between studies and to support regulatory efforts.

Biodistribution and Potential Health Impacts

The studies reviewed provide important insights into the biodistribution and potential health impacts of food-related NPs, particularly FDNPs. Several studies have investigated how FDNPs interact with biological systems following ingestion.

Absorption and Tissue Distribution

Evidence from multiple studies indicates that FDNPs can be absorbed through the intestinal barrier and distribute to various organs. The extent of absorption and the specific organs affected appear to depend on the properties of the FDNPs (size, composition, surface functional groups) and potentially on the food matrix. In Ussing chamber experiments, Zhao et al.[45] demonstrated the ability of fluorescent NPs derived from roasted pork to permeate intestinal tissue in vitro. Their biodistribution studies in mice revealed accumulation in the liver, kidney, and testis, with particles even crossing the blood-brain barrier, which suggests that these specific pork-derived NPs have properties that allow them to overcome the restrictive blood-brain barrier. Song et al.[46] and Cong et al.[47] found similar biodistribution patterns for chicken- and pizza-derived NPs, with distribution to the stomach, intestine, liver, lung, and kidney in mice. However, unlike the pork-derived particles, these NPs did not accumulate in the brain, heart, or spleen. This difference highlights the potential for food-specific differences in FDNP properties and biodistribution.

Cellular and Molecular Interactions

At the cellular level, food-derived nanoparticles have been shown to localize within the cytoplasm of cells, often within lysosomes[68][69]. Cytotoxicity assessments by Song et al.[46] and Cong et al.[47] revealed that FDNPs can cause cell cycle arrest at the G0/G1 phase and induce apoptosis at high

concentrations, suggesting potential dose-dependent toxicity. Several mechanisms may contribute to the observed cellular effects: cellular uptake, oxidative stress, inflammation, mitochondrial dysfunction, autophagy and protein corona formation. For example, oxidative stress may arise from ROS generated by FDNPs, potentially damaging cellular components like lipids and DNA, as observed in Wang et al.[55].

It must be emphasized that the specific molecular targets and mechanisms of action of FDNPs are still largely unknown and require further investigations.

In Vitro vs. In Vivo Models

Current studies on NPs toxicity rely heavily on in vitro models (e.g., Caco-2 cells) and in vivo models (e.g., mice, zebrafish). While in vitro systems allow controlled mechanistic studies, they may oversimplify NPs interactions with the gut microbiome or immune system. In contrast, in vivo studies capture systemic effects but face challenges in extrapolating doses to human exposure. Future work should integrate organ-on-chip models or human biomonitoring to bridge this gap.

Risk Assessment Considerations

While acute toxicity appears limited in the studies conducted thus far, often requiring high concentrations of FDNPs, the observed cellular effects, biodistribution patterns, and behavioral impacts in model organisms suggest potential for biological activity that merits continued research attention. Key considerations for risk assessment include: dose-response relationships, chronic low-dose exposure, potential for interactions between different FDNPs and between FDNPs and other food components, considering that interactions can modify the bioavailability and toxicity of FDNPs. Age-Dependent Susceptibility needs also special attention because vulnerable populations such as children, the elderly, and individuals with pre-existing health conditions, may be more susceptible to the effects of FDNPs. A deeper understanding of the mechanisms by which FDNPs interact with biological systems at the cellular and molecular levels is another key issue for accurate risk assessment. This includes identifying the specific molecular targets of FDNPs and the pathways involved in their toxicity.

Epidemiological data on the health effects of FDNPs are currently limited. However, theoretical daily intake (TDI) calculations can provide valuable insights. For example, based on the migration levels of nanosilver from food packaging[59][60], the estimated TDI for an average adult would be significantly below the regulatory limits. Nevertheless, these calculations should be interpreted with caution due to

the uncertainties in exposure assessment and the potential for cumulative effects from multiple sources of nanoparticle exposure.

Regulatory Perspectives and Knowledge Gaps

Current Regulatory Frameworks

Regulatory approaches to NPs in food vary globally, with different definitions, testing requirements, and risk assessment methodologies. The European Food Safety Authority (EFSA) has issued dedicated guidelines for evaluating the safety and potential risks of nanomaterials used in food and animal feed[70]. The European Commission's recommendation defines nanomaterials based on size distribution (50% or more particles with at least one dimension between 1-100 nm). On the other hand, the US Food and Drug Administration (US FDA) has evaluated nanomaterials under existing regulatory frameworks on a case-by-case basis. The US FDA focuses on whether nanoscale materials exhibit different properties due to their small size. A key challenge for regulators is the evolving nature of nanomaterial definitions and the difficulty in distinguishing between naturally occurring FDNPs and engineered nanoparticles (ENPs). This distinction is crucial for developing appropriate regulatory approaches.

Research Needs and Future Directions

Several critical knowledge gaps remain in the understanding of NPs in food, particularly FDNPs. Thus, standardized detection methods are required. Development of validated, standardized analytical methods capable of reliably detecting, quantifying, and characterizing the full spectrum of FDNPs in complex food matrices is needed. It includes methods that can distinguish FDNPs from ENPs based on subtle differences in composition, structure, or surface properties. Research on the absorption, distribution, metabolism, and excretion (ADME) of different FDNPs, particularly under chronic low-dose exposure scenarios, is also essential. This should include studies in relevant animal models and, if possible, human biomonitoring studies. Moreover, deeper investigation into the mechanisms by which FDNPs interact with biological systems at the cellular and molecular levels is required. It means identifying the specific molecular targets of FDNPs and the pathways involved in their toxicity (e.g., oxidative stress, inflammation, mitochondrial dysfunction). Developing methods and criteria to clearly differentiate between naturally occurring FDNPs and ENPs is another crucial issue for informing appropriate regulatory approaches. This may involve analyzing isotopic signatures, trace element profiles, or other

unique characteristics. The influence of the food matrix on the formation, properties, bioavailability, and toxicity of FDNPs, are other important gaps that need to be systematically investigated. In addition, research on consumer awareness, understanding, and acceptance of nanotechnology applications in food and food packaging is important for informed public discourse and policy development. It is also important to thoroughly evaluate the environmental effects of nanomaterials, such as FDNPs, across all stages of the food system, from production through to disposal.

Consequently, future investigations should be aimed at developing more realistic in vitro and in vivo models that better mimic human exposure to FDNPs. It means using advanced analytical techniques (e.g., cryo-EM, single-particle ICP-MS, hyphenated techniques) to characterize FDNPs in complex food matrices, investigating the potential for synergistic or antagonistic effects between different FDNPs and other food components, conducting long-term, low-dose exposure studies in relevant animal models to assess the chronic health effects of FDNPs, and developing strategies to minimize the formation of potentially harmful FDNPs during food processing.

Conclusions

The present review has highlighted the diverse pathways through which NPs can enter and interact with food, including formation during cooking processes and migration from food packaging. Cooking processes generate FDNPs, particularly fluorescent CNPs, whose biological interactions and health implications require further investigation. The size, composition, and surface properties of FDNPs vary depending on the food matrix and cooking conditions. Engineered nanoparticles such as nanosilver and titanium dioxide can transfer from packaging materials into food, with their migration influenced by storage time, temperature, and food composition. While migration levels remain below current thresholds, the adequacy of these limits for long-term, low-dose exposure warrants scrutiny, especially given evidence of NP accumulation in organs remain uncertain. Protein corona formation and interactions with food components can modify nanoparticle bioavailability and toxicity, necessitating more comprehensive risk assessments that account for the complexity of the food matrix. Additionally, the emerging issue of nanoplastics release during food preparation introduces further concerns that must be addressed through regulatory oversight and improved consumer guidance.

Nanotechnology presents significant opportunities in food science, particularly in enhancing food safety, preservation, and bioavailability of nutrients. However, standardized detection methodologies, in-depth toxicological studies, and clear regulatory frameworks are essential to mitigate potential risks. Future

research should focus on long-term exposure studies, elucidating the mechanisms of NPs interaction with biological systems, distinguishing FDNPs from ENPs, and developing sustainable nanotechnology applications in food processing.

Overall, a balanced approach is required, one that leverages the benefits of nanotechnology while minimizing health risks through rigorous scientific evaluation and transparent regulatory policies. Ensuring food safety in the context of NPs, and particularly FDNPs, requires multidisciplinary collaboration between toxicologists, food scientists, analytical chemists, regulatory agencies, and industry stakeholders. A proactive and precautionary approach is warranted to address the potential risks associated with FDNPs and to ensure the safe and sustainable application of nanotechnology in the food industry. This includes developing strategies to minimize the formation of potentially harmful FDNPs during food processing and preparation.

In conclusion, while the potential risks of FDNPs and ENPs in food warrant further investigation, it is important to provide practical guidelines for consumers. Key practical recommendations include: (1) preferring gentler cooking methods (steaming, boiling) over high-temperature techniques (frying, grilling) to minimize CNP formation, (2) selecting food containers with high maximum service temperatures and non-polar compositions to reduce nanoplastic release, and (3) avoiding prolonged cooking times for protein-rich foods at temperatures above 180°C. Future research should prioritize the development of sensitive detection methods and investigation of long-term biological effects, while regulatory efforts are essential to fully understand and mitigate the health implications of NPs in food.

Statements and Declarations

Conflicts of interest

The author declares that he has no known competing financial interests or personal relationships that could appear to influence the work reported in this paper.

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Declarations

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