

Review Article

Applications of Nanomaterials in Agrifood and Pharmaceutical Industry

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Nanotechnology recently emerged among the most exciting science-related innovations. Nanotechnology-produced metal nanoparticles got a lot of attention. This is emerging as a rapidly developing field due to its effective applications that targeted the manufacturing of new materials at the nanoscale level. There is considerable interest in the application of nanomaterials in many areas of industry including agrifood and biomedical products. In the agrifood area, nanomaterials have benefits in diverse areas which include fertilizers, herbicides, pesticides, sensors, and quality stimulants, among other food processing, food packaging, and nutraceuticals to improve nutritional value. These applications in agriculture result in enhanced quality and crop yield, reduction in pollution caused by various chemicals, etc. In the pharmaceutical area, nanomaterials are claimed to ameliorate drug safety and efficacy, as well as bioavailability. They are utilized for targeting various drugs to a specific location in the body. However, there are also concerns that some nanoparticles may have adverse effects on human health. These include titanium dioxide, copper oxides, and other nanomaterials which lead to liver damage, skin damage, lung damage, and various other human health-related problems. This review is aimed at presenting a briefing on the state of the art in the application of nanotechnology in food and human nutrition and drug administration, consumer attitudes, and their challenges and opportunities with future perspectives.

1. Introduction

In today's society, consumer demand for higher quality, safer, and healthier food and natural products is increasing [1–3]. Nanotechnology may play a significant role to protect and conveyance active compounds (hydrophobic and

hydrophilic) through incorporation into food products, to enhance nutraceuticals, functional foods [4, 5]. Nanotechnology typically refers to the use of nanomaterials between 1 and 100 nm in size [6–9]. The fundamentals of nanotechnology consist of materials adopting alternative and often more beneficial properties at their nanosize when

TABLE 1: Types of nanoparticles and their applications in biomedicine and food industry [25–29].

Type of nanoparticle	Structure	Properties	Functions	Application
Liposome	Phospholipid bilayer in an aqueous environment	(i) Biocompatibility (ii) Biodegradability	(i) Drug and gene delivery (ii) Texture in cosmetic products (iii) Application in dairy products	(i) Medicine (ii) Cosmetic industry (iii) Food industry
Polymer	Can be either polymer-protein conjugates or polymer-drug conjugates	(i) Polymer protein enhances protein stability (ii) Polymer drug promotes tumour targeting	(i) Drug delivery systems (ii) Functional foods	(i) Medicine (ii) Food industry
Carbon (i) Fullerenes (ii) Nanotubes	Many points of attachment for binding	(i) High symmetry (i) Electrical conductivity and strength (ii) Can be single or multiwalled	(i) Cleave DNA (ii) Drug delivery (i) Delivery of therapeutic molecules (ii) Uses in milk and other proteins	(i) Medicine (i) Medicine (ii) Food industry
Quantum dots	Coated in other materials to prevent leakage of toxic materials	(i) Semiconductors (ii) Fluorescent	(i) Cell tracking	(i) Medicine
Metal nanoparticles	Can be spherical, triangular, hexagonal, rod-shaped, polyhedral, cubic, etc.	(i) Biocompatibility (ii) Biodegradability	—	(i) Application in food industry (ii) Medicine
Metal oxide nanoparticles	Can be spherical, hexagonal, triangular, rod-shaped, polyhedral, cubic, etc.	(i) Biocompatibility (ii) Biodegradability	—	(i) Application in environmental remediation (ii) Pharmaceutical

N.B. Applications in medicine may also include nutritional supplements.

compared to their normal size, due to an increase in surface area [10–13]. Nanomaterials can be created in one (nanoscale), two (nanowires and nanotubes), or three dimensions (nanoparticles) [14–16]. There are several techniques used to form nanomaterials; these include bottom-up and top-down approaches [17]. Bottom-up approaches involve the self-assembly of individual atoms using scanning tunnel microscopy; this process is time-consuming due to the vast number of atoms to be assembled. Top-down approaches are also used to create nanomaterials; large materials are transformed into smaller ones via atomic force microscopy. Current funding is supplied on a yearly basis; apart from a few expensive pieces of equipment, nanotechnology is relatively inexpensive [18]. Nanomaterials include nanofilms, nanotubes, and nanoparticles among others [17, 18]. Nanoparticles are a particular type of nanomaterial that can occur naturally, be created unintentionally, or indeed be engineered on purpose. Although benefits of these engineered nanoparticles (ENPs) are well recognised in many industries, more attention is needed on potential toxicity and its adverse effects [19]. Nanotechnology can be applied in a number of fields including medicine, agriculture, food science, food technology, recreation, and civil engineering [20–22]. There is exciting potential of nanotechnology in these areas, and some applications are already of great benefit to industries and consumers. Engineers have used nanotechnology to create substances for products, which are stronger, lighter, rustproof, and stain/fire resistant [23]. Advances in nanotechnology have been made in a number of areas; however,

development and acceptance of the technology are slow in the food industry [23]. This is mainly due to a mixed consensus from the public; many are unaware and do not understand nanotechnology as a science [24]. Nevertheless, consumers need to recognise that both natural and processed foods already contain nanoparticles. Milk is characterised as a nanofood, and meat is composed of nanosized protein fibres. Meat processing procedures practiced for many years alter the nanostructure of muscle [23]. In addition to that, we are exposed to naturally occurring and engineered nanoparticles every day (Table 1). This study will provide an overview of the current state of the art in the use of nanotechnology in food and human nutrition, medication administration, consumer attitudes, difficulties, and possibilities, as well as future prospects.

2. Applications of Nanomaterials in Agrifood Industry

Nowadays, with growing population, food demand is on the rise and food safety is a matter of concern. Nanoscience has emerged as one of the most innovative technologies in the field of agriculture and food industry chain. Nanomaterials can be utilized in the agrifood industries as nanoformulations for crop improvement, in crop protection for the identification of diseases, nanodevices for the genetic manipulation of plants, plant disease diagnostics, etc. [30]. A number of nanoparticles (mostly metal-based and carbon-based nanomaterials) have been exploited to improve the growth

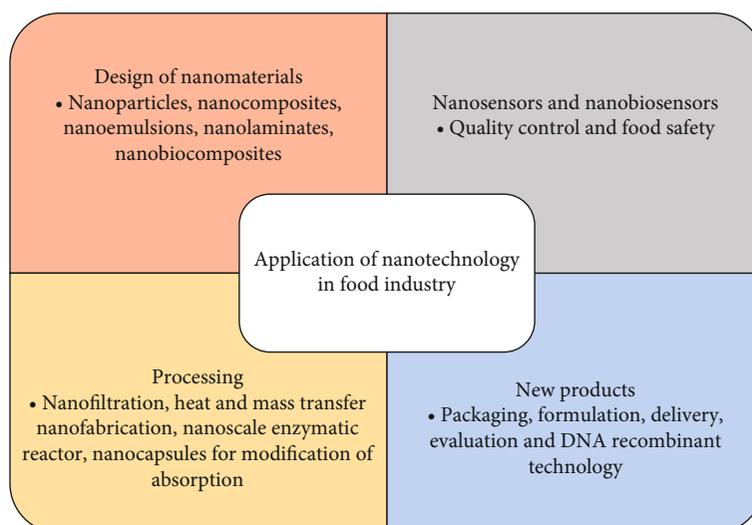


FIGURE 1: Application matrix of nanotechnology in the food industry.

and development of crop food plants [31]. This positive impact has led to enhanced germination percentage, biomass production along with enhancement of physiological parameters such as photosynthesis and nitrogen metabolism in many food crops including alfalfa, cucumber, corn, lettuce, onion, pumpkin, ryegrass, rape, radish, spinach, soybean, tomato, and wheat [32]. Nanomaterial has given a promise in plant protection, via genetically modified crops to produce a plant disease resistance to pathogen infections and is crucial to ensure sustainable food and agriculture [33]. Nanoencapsulation displays the advantage of more efficient use and safer handling of pesticides, fertilizers, and vaccines with less exposure to the environment that guarantees eco-protection [34]. Nanofertilizers have unique features like ultrahigh absorption which is a route to enrich the soil with adequate essential nutrients gradually, thus preventing pollution of water resources and it is well known to improve the quantity of fruit and biological production [35].

3. Applications of Nanomaterials in Food Industry

Nanotechnology has much potential to improve and produce new food concepts beyond capabilities in the current domain. It can be applied to all aspects of the food sector including agriculture, food processing, food packaging, and supplements. Food packaging may be developed in order to prevent the invasion of microorganisms or alert consumers if food is no longer edible via nanosensors. Through nanotechnology, food can also be made healthier for consumers [6]. However, such scientific breakthroughs may not be utilized if the public is uncertain about the technology. Applications in packaging are currently more accepted than uses in food itself; trust issues occur concerning naturalness. Nonetheless, it is predicted that nanotechnology will become increasingly important in the future [6]. Much research into nanotechnology is still warranted, especially in relation to food applications. Nanomaterials in food can

be described as both “soft” and “hard.” Soft nanomaterials are formed from natural ingredients or components of food during processing; examples include homogenised milk, ricotta cheese, and coenzyme Q10 (use in supplements). Hard nanomaterials however are more of a concern to the Food Standards Agency (FSA). Such materials are insoluble, and little is known regarding the properties in which they possess. Metals, among others, are characterised as hard nanomaterials [36]. As outlined by the FSA, current approval of nanotechnology foods and processes would be required in line with the “Novel Foods Regulation” (Regulation (EC) No. 258/97) [37].

Existing hazards associated with nanotechnology in the food industry are somewhat unknown. The EFSA expressed concern over the lack of methods in which to detect and measure engineered nanomaterials and the effect they may have on both consumers and livestock. Toxicity levels must be defined along with ways to identify engineered nanomaterial concentrations in food, feed, and biological tissues [38]. There is a need for greater awareness and understanding of nanotechnology; this will result in more productive and informed decisions. Following this, consumers may also perceive nanotechnology in a more positive light. Nanotechnology has wide range of applications within the food industry (Figure 1). However, some applications could fall into the arbitrary grey regions where overlapping of these categories occurs.

Table 2 shows specific examples of their potential usage into the four main categories related to agriculture, food processing, food packaging, nutraceuticals, and biomedicine [34, 36, 39]. Despite most of these applications being in the research and development (R&D) stages, food industries have been very careful in making decisions on whether or not to adopt these technologies due to concerns on consumer perceptions, which will be discussed in the later sections [39]. Advancing knowledge within this field in order to set the appropriate regulatory measures appears to be even more complex as it involves confidentiality, openness,

TABLE 2: Examples of current and potential nanotechnology application in the agrifood and biomedicine industry [49–53].

	Food processing	Food packaging	Nutraceuticals	Biomedicine
Agriculture				
Nanocapsules for the delivery of pesticides, fertilizers, vaccines, and other agrichemicals	Fumed silica (E551) as anticaking agent and carriers	Nanoclay embedded between PET layers for enhanced mechanical strength, heat resistance, gas permeability, and transparency	Nanosized powders for increased absorption of nutrients	Liposomes exploited in drug and gene delivery
Nanocapsules in the delivery of growth hormones in a controlled fashion	Nanosprayed dried salt with increased perception of saltiness as means to reduce salt levels in food	Nanosilver coated in reusable containers to inhibit microorganism growth	Cellulose nanocrystal composites as drug carriers	Dendrimers for targeted drug delivery
Nanosensors to detect animal and plant pathogens	Nanoparticles with selective binding properties to remove chemicals or pathogens in food	Titanium nitride in food packaging improving rigidity and strength	Nanodroplets with better vitamin absorption	Nanoshells for targeted cancer cells
Nanosensors to identify and preservation	Nanocapsule infusions of plant steroids as replacement of cholesterol	Nanoparticles with fluorescent properties with attached antibodies for detecting chemicals or foodborne pathogens	Nanocochleates for drug and nutrient delivery into the body	Quantum dots, gold nanoparticles, nanowires, and fullerenes as targeting and imaging agents
Nanosensors for soil condition monitoring and plant growth	Nanocapsule for flavour enhancers	Electrochemical nanosensors for detecting ethylene		Carbon nanotube for gene and drug delivery towards tumour cell
Nanotechnology for DNA molecular detection	Nanocapsules improving bioavailability of nutraceuticals			Nanobiosensors for diagnosis and detection of cancer agents
Nanochips for identity preservation and tracking	Nanotubes as gelation and viscosifying agents			

and transparency issues relating to commercial interests as addressed by [40]. Nowadays, consumers are increasingly demanding high-quality, safe, and healthy food products. Nanofood has the potential to change the whole food industry chain and is often associated with colour and flavour improvement, storage, preservation, pathogen detection, antimicrobial properties, and intelligent packaging [41].

4. Nutritional Benefits of Using Nanoparticles

Foodborne microbial pathogens can potentially cause illness and fatality; this problem is hard to solve due to the increasing resistance of microbial strains [42, 43]. Nanotechnology can play a role in the detection of pathogens or pesticides in food. They can also monitor the temperature and pH of foods to prevent the presence of these unwanted organisms through the use of nanosensors [44]. Thin inorganic coatings act as protective layers on food products to enhance shelf life, by producing moisture- or oxygen-resistant materials. This knowledge led scientists and researchers to use similar methods to prevent spoilage by microbes and oxidation to prolong shelf life, using nanocomposite materials in food storage [42]. Nanocomposite materials favour conventional food packaging materials due to their superior polymeric properties reinforced by nanoparticles. This structure gives an advantage to food storage because it is less permeable to gases than other materials. Therefore, oxidation and consequently food spoilage are reduced. Nanocomposites with added nanoparticles can maintain resistance to these gases at half the thickness of others, meaning production costs are also reduced [42]. Macro- and micronutrients of low bioavailability have limited absorption in the body. However, by making these smaller with the use of nanotechnology, the particles can enhance bioavailability due to the increased surface area, improving absorption rates in the stomach and small intestine [42]. Therefore, nanotechnology has the potential to alter nutrient intakes through enriched and fortified food products [45]. Nanodrops have been used as an additive in canola oil which is designed to carry vitamins, minerals, and phytochemicals through the digestive system and urea [15].

Iron is the fourth most abundant mineral on earth, yet iron deficiency is the most common mineral deficiency in the world as over 2 billion people worldwide are anaemic [46]. It does not help that iron has an estimated lower bioavailability than other nutrients at 14–18% for mixed diets and 5–12% for vegetarian diets in subjects with no iron stores [47]. One solution to this could be to fortify foods with iron; however, this is often challenging because it can seriously affect the taste, smell, and appearance of foods [48]. Scientists in Switzerland addressed the problem of iron deficiencies and came up with a solution to enrich food with iron using nanotechnology. Iron was first dissolved in water then sprayed over a fire. The intense heat evaporated the water leaving minute iron crystals each about 10 nm in size. These nanoparticles can then be added to foods, and it was reported that they did not alter food in any way. However, this experiment was carried out in rats, so it is hard to determine if the taste of food was affected [48].

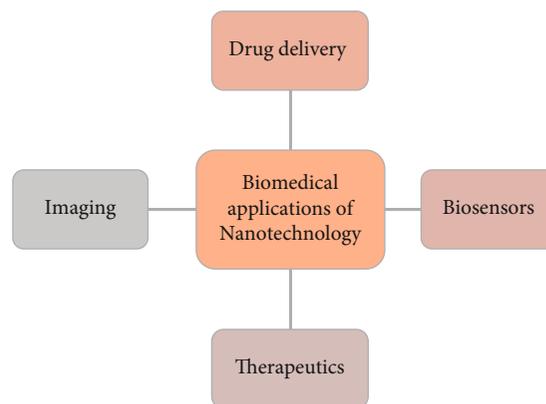


FIGURE 2: Application of nanotechnology in the biomedical sector.

5. Nanotechnology in Biomedical Application

Nanotechnology plays a significant role in biomedical and pharmaceutical products as it facilitates from syndrome diagnoses to drug delivery to human organs in order to target infectious diseases. Nanoparticles have unique biological properties which can be used for detection, prevention, and treatment of diseases, drug delivery, and gene therapy of cancer as well as pulmonary diseases [54, 55] (Figure 2), due to having capability to bind, absorb, and carry small-molecule drugs, DNA, RNA, and proteins with high efficiency [15]. Indeed, liposomal drug formulations (i.e., doxorubicin) are widely used for the treatment of breast and ovarian cancers and Kaposi's sarcoma successfully [56]. Incorporation of liposomal drug formulations to amphotericin and hamycin cancer drugs exhibited much better efficacy and safety as compared to conventional preparations [57]. Quantum dots are inorganic nanoparticles that consist of 10–50 atoms, and their diameter ranges from 2 to 10 nm [15]. Because of their high-sensitivity and multicontrast imaging properties, they have been used for the detection and diagnosis of cancer cells in *in vivo* conditions [58]. In addition to that, nanobiosensors can be employed for the early detection of leading causes of cancer such as environmental pollutants, pathogens, and carcinogenic gases [59, 60]. Nanomaterials have been incorporated into a drug formulation, such as active constituent (nanocrystals), excipients (drug-metal complexes), drug carriers (liposomes), or as complexes/conjugates (drug-protein) [54]. Nanotechnology may also have future nutritional health benefits. People with type one diabetes are expected to be able to consume a nanoengineered biodegradable material containing insulin, which can be released as a response to high blood glucose concentrations [61]. There is also interest in the application of nanotechnology-derived anti-inflammatory agents to the mucosal lining of patients with inflammatory bowel disease or Crohn's disease. It is also thought that the use of nanotechnology on some nutrients can enable individuals to expand their limited food tolerances or choices. There are various nanoparticle-based delivery systems that have been exploited for diagnostic and therapeutic applications as illustrated in Tables 1 and 2.

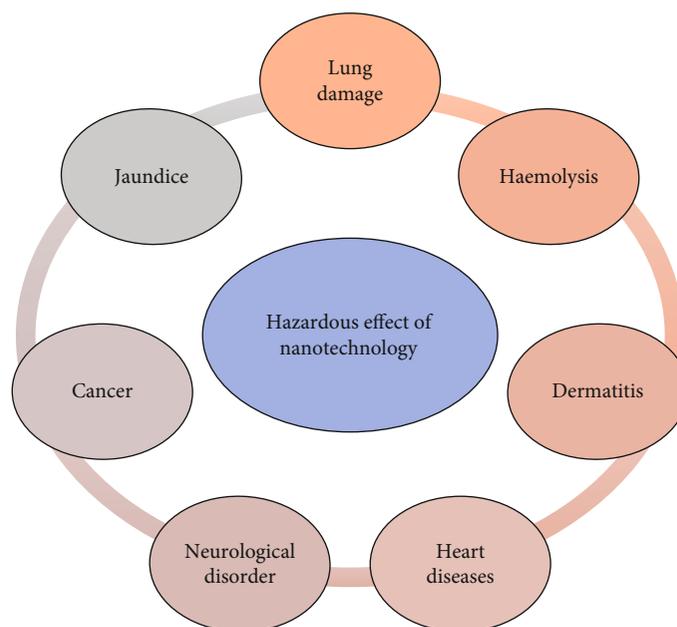


FIGURE 3: Hazardous effect of nanotechnology in human health.

6. Potential Hazards in the Use of Nanotechnology/Nanomaterials for Human Health

Although an increase in certain micronutrient intakes may be beneficial, it is also important to realise that the overconsumption of these nutrients can lead to toxicity, which may result in more severe problems (Figure 3). There are several potential challenges derived from the emergence of the use of nanotechnology. This includes toxicity and environment, health, social, ethical, legal, and cultural implications [62]. Nanoparticles are widely produced from nanotechnology and are presently utilized in a broad range of industrial sectors. These sectors include agriculture, healthcare, materials, and energy, therefore increasing the likelihood of exposure to consumers and workers [20]. Humans can be exposed to ENPs (engineered nanoparticles) from various pathways such as ingestion, inhalation, absorption through skin, and direct injection for medicinal purposes [63].

The detriments caused by inhalation of nanoparticles, titanium dioxide (TiO_2) taken in food in rats and humans [64] and also in sunscreen and carbon nanoparticles in rodents [65, 66], were subject to investigation by researchers and found that inhaled particles into the lungs can lead to damage and scarring and this especially with long-term exposure could affect the lung wall, reduce absorbed oxygen, decrease carbon dioxide, and then trigger breathing difficulties [63]. Despite the lack of evidence for toxicity, results suggest that potential hazards of carbon nanotubes may cause inflammation in the lungs [65]. This is very similar to the process by which asbestos fibres cause asbestosis [63]. However, little research is known about toxicity of cerium oxide nanoparticles (CeO_2 NPs), which are used to increase fuel efficiency and reduce its emissions of car, but a recent study revealed it may cause lung cancer [67]. Studies

show that by reducing the surface area from large scale to nanoscale enables its toxicity to damage organs and the best example is nanocopper particles ingested by mice induce severely toxicological effects on the liver, kidney, and spleen [68]. Similarly, copper nanoparticles can enter the human body through food, water, drugs, cosmetics on the skin, nails, hair, [69], etc. If the intake of copper exceeds the capacity of the human body, it will result in toxic effects such as haemolysis, jaundice, and even death [68].

Furthermore, particles 7000 nm or smaller can penetrate the skin and have the ability to impair them [70]. Nanoparticles or nanoemulsions are used to manufacture sports equipment, biomedical applications, electronic components [71], clothing, cosmetics, shaving creams, sunscreens, shampoos, and toothpastes. Many of these are produced to deal with the skin and to treat damaged skin or hair and therefore can penetrate the skin. Such diseases such as dermatitis, acne, and psoriasis, as a result of simple actions, for instance, injuries (sunburns, cuts, or scrapes) or shaving, can lead to more cutaneous permeability [66]. Once particles are absorbed through the skin, they can be toxic to cellular and subcellular levels and damage the DNA [72].

However, the risks of toxicity of nanotechnology-derived food and food packaging for consumers are largely not very well understood [73], but recent studies demonstrate that silver nanoparticles (AgNPs) can be applied to food, food packaging, and other consumer products due to their antibacterial properties. These smaller AgNPs (AgNPs-5) can enter human cells much more easily than bigger ones (AgNPs-20 and AgNPs-50) which may lead to higher toxic effects than silver ions in cells [63, 74]. Research demonstrates that ENPs are able to cross the blood-brain barrier and induce direct damage to neuronal cells, neuroinflammation, and prooxidant changes because of their nanosizes [20]. It has been proposed that not all nanomaterials will

TABLE 3: Literature studies on potential nanotechnology-related health hazards.

Exposure via	Study outcomes	References
<i>Inhalation</i>	Inhaled titanium dioxide (TiO ₂) particles from food colouring into the lungs can lead to breathing difficulties.	[63, 79]
	Little known about toxicity of carbon nanotubes (CNTs) which may cause to inflammation in the lungs.	[65]
	Intake of TiO ₂ particles (150–500 nm) through food can translocate to the blood, liver, and spleen.	[64]
<i>Ingestion</i>	Copper nanoparticles enter the human body by ingestion from food and consumer product, leading to haemolysis, jaundice, and death.	[68]
	AgNPs-5 may lead to higher toxic effects than AgNPs-20 and AgNPs-50 in cells; ENPs cross the blood-brain barrier and cause damage to neuronal cells, neuroinflammation, and prooxidant changes.	[20]
<i>Skin penetration</i>	Particles size of 7000 nm or smaller can penetrate the skin and have ability to damage DNA.	[70]
	May be toxic to cellular and subcellular levels and damage to DNA; inconclusive data to show toxicity.	[66]

have adverse effects on human health due to differences in their surface, size, and formulation of the material in the products [75]. Although there are appropriate techniques available to assess many of the risks related to the consumer products and processes in which nanoparticles are involved, it seems to be not adequate to address all the hazards. Therefore, more studies should be done.

There are toxicity concerns with nanoparticles and ultra-fine particles in particular, due to their increased surface area and potential to bioaccumulate in cells [76]. The potential problems are unknown as they do not normally occur with bulk materials. However, most of this research is limited to animal models due to ethical reasons. Nanotechnology packaging also has its concerns due to the possibility of particle migration into foods [77]. Currently, safe limits are not defined by legislation due to limited knowledge in this area. Therefore, it is unknown if the levels used in food packaging or the food itself may be detrimental to health. Table 3 gives an overview of the potential hazards of exposure to nanomaterials via different routes. Assessment methods to detect the level of nanomaterials are limited; therefore, it is difficult to establish toxicity and exposure levels. For this reason, the development of technology is needed to establish a valid method of assessing nanomaterial exposure levels. Due to the novelty of this technology in food-related applications, long-term risks are not fully understood. Short-term studies must be considered carefully as their reliability is questionable [78].

7. Consumer Attitudes to Nanotechnology

Consumer perceptions of nanotechnology applications in the food industry are varied. This mixed consensus is thought to be largely accounted to limited awareness and understanding of the emerging nanotechnology science. Numerous studies have shown that consumer attitudes towards nanotechnology in the food industry differ according to the application [79]. Research carried out in France by [6] suggested that French citizens were sceptical about both nanotechnology food and packaging applications. However, research in Switzerland suggested consumers tended to accept the concept of nanotechnology packaging

but not the application of nanotechnology in food. These two pieces of research could suggest that the consumer's attitude towards nanotechnology has changed within the time period between the two studies. Conversely, it could be that different cultures have different perceptions of nanotechnology, creating a need for cultural perceptions to be addressed individually.

The consumers' opposition to nanotechnology applications in the food industry is thought to be multifactorial:

- (i) Poor knowledge of the concept of nanotechnology
- (ii) Lack of trust in governmental agencies
- (iii) Low perceived level of naturalness
- (iv) Limited knowledge of the benefits

It is advisable to acknowledge sceptical consumer outlooks in the early stage of developing nanotechnology products in order to gain consumer trust. To encourage public approval of nanotechnology, the government and NGOs will need to address the subject appropriately to ensure the public develops an informed view of the technology [6]. Consumer willingness to buy health beneficial foods, produced using nanotechnology, has recently been investigated [80]. The finding displayed evidence for naturalness has been a very important factor in deciding whether or not to purchase functional food. Hence, as consumers currently view nanotechnology as unnatural, they will need to be convinced that the concept is natural before they willingly purchase nanotechnology functional foods. Vandermoere et al. [24] completed a study using risk-benefit trade-offs to distinguish supporters (benefit > risk), doubters (risk = benefits), and opponents (risk > benefit) of nanotechnology food packaging and nanotechnology food.

When familiarity of nanotechnology was accounted for, there were no differences in opinion between gender and/or educational background. Prior to the survey, 57.6% of the participants were not aware of what nanotechnology was and only 5.1% reported having good knowledge of nanotechnology. This demonstrates the limited public knowledge of nanotechnology and provides evidence that there is a need to educate the public about nanotechnology. There

are fears that consumers may express negativity towards nanotechnology applications as it becomes commercialised; this concern stems from the adverse public reaction to GM (genetically modified) applications. Therefore, the learnings as to why consumers did not trust GM when the concept was released must be unraveled and where possible applied in the context of nanotechnology in order to reduce the potential negativity which is speculated [79]. Currently, there is no legislation regarding labelling of nanotechnology products, although it is often discussed. One study investigated how labelling nanotechnology products affected consumer perception. The findings suggested that labelling sunscreen as “nanotechnology sunscreen” was reason of a higher level of perceived risk and a lower level of perceived benefits. Although this is not a food product, consideration is needed as the consumer attitude would likely be similar for food [81].

8. Conclusion

Nanotechnology plays a significant role in biomedical and pharmaceutical products. Nanomaterials are an efficient tool for the improvement of agricultural and pharmaceutical industry. They are utilized for the protection of plants, crop improvement, drug delivery, biosensors, etc. Though it shows different activities, nanotoxicological effects need to be found out. Different factors may be responsible for the negative impact of nanomaterials. Therefore, research is needed to clarify a number of issues including knowledge and understanding from both industry and consumer perspectives, detection methods of nanomaterial exposure levels, and effects of long-term exposure to consumers. If these problems are addressed appropriately, the public may start to accept the use of nanomaterials for industrial purposes.

Data Availability

The data used to support the findings of this study are included within the article.

Conflicts of Interest

The authors declare no conflict of interest.

Authors' Contributions

Hiwa M. Ahmed wrote the first draft of the manuscript; Arpita Roy revised the manuscript and added; Muhammad Wahab, Mohammed Ahmed, Gashaw Othman-Qadir, Basem H. Elesawy, Mayeen Uddin Khandaker, Mohammad Nazmul Islam, and Talha Bin Emran have read and improved the whole manuscript and supported. All authors read and agreed to the final submitted version.

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