Research Article

A Review on the Recent Advancements of Zinc Oxide Based Compounds in Different Applications

Ajay Jyothis R[1a)], Govind N Nampoothiri[1b)], Sasikanth SM[2*)]

[1]Department of Physics, Amrita School of Arts and Sciences, Amritapuri, Amrita Vishwa Vidyapeetham, India- 690525
[2]Department of Physics, Noorul Islam Centre For Higher Education, Kumaracoil, Thucklay, India- 629180
[a] Ajayjyothisr@gmail.com
[b] govindnn00@gmail.com
[*] vishnusasikanth@gmail.com

Article History: Received: 10 January 2021; Revised: 12 February 2021; Accepted: 27 March 2021; Published online: 28 April 2021

Abstract: Nanomaterials technology and development have successfully served progress various scientific areas. Because of its biocompatibility, special physicochemical characteristics and cost-effective mass production, zinc oxide (ZnO)-based nanocomposites has been the most viable techniques for biological applications. Latest developments in nano-engineering, moreover, technology enables the generation of specific three-dimensional structures and surface properties of ZnO nanocomposites which are efficiently developed on behalf of in vivo tests. Herein, our study showed current developments on the use of various ZnO NCs, by a specific emphasis of use. Production like immunotherapeutic vaccines adjuvants and tumor, and also their interfacial properties that interfere with both the immune system and the in vivo possible toxic impact. Eventually, as therapeutic and preventive vaccines towards pathogens, we summarise promising evidence-of-concept applications towards cancer. Moreover, the analysis of these composites is of highly significance due to their enhanced multifunctional properties, such as their mechanical, filter and antibacterial activities, the food processing materials sector. The knowledge of a nano-based biological frameworks among ZnO-based NCs and their immune-based response, along with the biologically effective strategy of nanomaterials by means of nano-architectural expertise, may open novel opportunities for the expansion of the therapeutic use of ZnO nanocomposites as an innovative platform for vaccines.

Keywords: ZnO nanocomposite, vaccine, cancer, packaging and barrier uses, mechanical properties.

Introduction

Among the most important accomplishments is the advancement of vaccines against different diseases on new research of medicine [1]. Over the last few years, immunotherapy vaccines have been established. Regulation of cancers and certain non-infectious disorders for decades [2-4]. Nevertheless, there have been plenty confronts and constraints that have prevented the production of powerful vaccinations against different vaccines evolving and re-emerging disorders, like the option of antigens, proper distribution of antigens, and adjunctive infections engineering [5]. To solve these problems, nanotechnology was already utilized, largely comes the vaccine development and production [6–10]. Various nanocomposites in optimized ingredients and proportions were revealed to enhance an elevation of antigenic distribution and immunogen through increasing the treating of antigen, improving the stability of antigen, and maintaining release. Nanocomposite (NC) compounds included in the production of various vaccines are those developed from natural substances such as poly(lactic-co-glycolic acid) (PLGA), polyethylene glycol (PEG), inulin and chitosan alongside synthetic nanoparticles (NPs) like silica-based particles [11].

Synthetic NCs dependent on metals, namely zinc oxide (ZnO), titanium dioxide (TiO_2), and iron owing to their complex processes, extended storage life, as well as the capacity to apply their inherent adjuvant-like characteristics and immune-stimulatory functions, oxides have lately been used as vaccine carriers [12]. Owing to the biocompatibility, durability, and lesser cost, ZnO, a good reported Food and Drug Administration (FDA) ratified material, was extensively utilized for many medicinal purposes [13]. In addition, elemental Zn influences many facets of an immune-based response and it could be competently expelled from that body via different channels, like sweat, urine and faeces, thus decreasing the body's effectiveness and possibility of aggregation [14-16] inside the body. Nonetheless an extent of in vivo toxicity and immune reactions have seemed to cause ZnO NCs. By generating pro-inflammation cytokines in the myeloid distinction main reaction protein-88 based way through Toll-like receptor (TLR) signal mechanisms when imparted through a pulmonary tract, ZnO NPs have become demonstrated to trigger lung infection [17]. ZnO when delivered subcutaneous injection or orally, it's also been

shown that NCs induce inflammation reactions [18-20] through the dissolution of Zn^{2+} and development of reactive oxygen species (ROS) [21].

It was also used as an adjuvant device because of the immunologic impact of ZnO, for different vaccines. Though perhaps not fully characterized, when coupled with vaccination antigens [22-26], some few studies have already shown the usage of ZnO NCs as a potential immune modulated signal. In addition, although employed as tumor antigen carriers, diverse categories of ZnO NCs has often reported to enhance anti-cancer tolerance [26].

Throughout the arena of food packaging, nanostructures make a sizeable impact by enhancing the various features of films for wrapping. Among many other things, ZnO NPs have acquired a critical function in enhancing packaging features, such as barriers, antibacterial and mechanical properties [27]. These ZnO NPs refer to different sizes of particles and forms are being synthesized via diverse paths. Their accessibility on a mass production has resulted in they are easily accessible and use explicitly in scientific studies. Packaging films comprising of NPs from ZnO various processing methods, like solvents, were developed alongside bio-polymers. Casting [28,29], exacerbating of melt [30], casting of solution [31-34], extrusion of twin-screws [35], extrusion blast molding [36], and volatilizing liquid [37]. This article discusses the usage of ZnO NPs in food packing substances to strengthen the gas protection and mechanical characteristics. Moreover, we also summarize the NC applications in the arena of as therapeutic vaccines towards pathogens, we summarise promising evidence-of-concept uses towards cancer.

Production of ZnO NCs

Numerous techniques was developed to synthesize ZnO based NCs whereas the shape and surface characteristics of the ZnO NCs could be nicely controlled as per in vitro circumstances, like chemical-based reactants, solvents, period and temperature [38]. Since ZnO NCs have been documented to respond differently to in vivo systems, it is necessary to respond differently based on the size, shape, and material property. To choose an effective approach of synthesis as per the important assignments. For ZnO Spherical primarily utilized are NPs, precipitation, micro-based emulsion, and sol-gel techniques [39]. Specifically, the methodology of sol-gel is the most common method since before Spanhel first recorded it [40,41]. Meulenkamp ZnO NP is generated in this process from zinc hydroxide, produced through reaction Zn dihydrate acetate in ethanol to hydroxyl anion. Usually, the hydrothermal approach has been utilized to ZnO nanowires (NWs) [38] are synthesized. ZnO NWs could be developed utilizing ZnO NPs on various receptors such as seeds. As contrasted with ZnO NP plants, solidification is thermodynamically favorable in a responding solution, to homogeneous nucleation. Although ZnO's surface area depends largely mostly on crystal plane, its feature proportion of ZnO could be regulated via facet measured NCs. Utilizing different surfactants to grow [42,43]. Furthermore, ZnO can be synthesized in different ways through PH, temperature and Zn precursor regulation [38]. Through using different natural and inorganic substances as templates, the geothermal approach could also be used for producing ZnO hybrid frameworks although ZnO NWs can be grown irrespective of the form of substrate [44]. To produce biocompatible ZnO nanostructures [45], green biosynthetic pathway utilizing non-toxic substances has developed in recent years. As it utilizes biological agents derived from plants, fungi, food, microalgae, it is a successful non-toxic and excellent biocompatibility process.

Applications of ZnO NCs in therapeutic fields

In such a shaft furnace, ZnO was generated through warming zinc ore. As a vapor, metallic zinc is released for different applications, a flue ascends and condenses into an oxidized shape [46-48]. ZnO has for a long time been in our everyday lives, it is utilized as a component in medication, cosmetics and food coloring. ZnO piezoelectric has optoelectronics, sensors, transducers, and electricity generation have been commonly applied. Historical and current evidence indicates that ZnO is poor in toxins and biodegradability, with possible biomedicine applications [46,49]. The Charaka Samhita, an indigenous Medical textbook written about 500 B.C., discusses the possible usage of ZnO, referred to during the text as Pushpanjan, for diagnosis of eyes and open wounds [50]. During the first ZnO ointment, a Greek surgeon, Dioscorides, presents A.D. century [47]. ZnO was also addressed by Avicenna, a Persian philosopher and physician, in its book, as a favored treatment for various skin conditions, like skin cancer [51], Canon of Medicine.

Throughout the 20th century, material science flourished, and ZnO was among the initial metal oxide substances were studied in elaborative manner. ZnO was a semi-conductor device by a small energy gap straight and at ambient temperature, a larger excitation binding energy [52]. Its specific semiconductor characteristics make it suitable for different applications that are photo-induced, like photo-catalysts and photoemissions [53]. When ZnO absorbs the light smaller than 400 nm throughout the ultra-violet (UV) range, in the valence and conduction bands, electron–hole combinations can be formed. The conduction band was its band of atoms of electrons that leap through electrons stimulated from the band gap. The outer energy orbital of even an atom of a substance was its valence band. The bandgap was its difference in electricity between the Valence Band's extreme occupied level of

energy and the conduction band's lowest unoccupied level. Leaving holes (h+) throughout the valence band, excitons are transferred to a conduction band, and both ions and electrons may be included in cell physiological behavior. By reaction of oxygen or water, they may produce ROS like superoxide and hydroxyl radicals [39].

Interactions of ZnO NCs with that of immune-based cells

A number of phagocytic cells like monocytes easily absorb ZnO particles, macrophages and DCs, but instead impose immune-modulatory impact on these inherent immune properties [54-56] cells. Usually, these synergistic factors are influenced by the dissolution of intracellular Zn2+ the accumulation of inflammatory cells and cytokines throughout the lysosomes as well as the production of ROS in innate immune stimulation is cellular. These results throughout the immune response of antigen-specific as much as cell toxicity in vivo when co-administered to an antigen [55,57]. Additionally, ZnO NPs are influenced by non-immune-based cells, including as epithelial and neuron-based cells, mainly because they were prone to ZnO NP exposure compared to normal cell [58]. We mainly concentrate on a connection of ZnO NCs of phagocytosis innate and cancerous cells.

Uses of ZnO NCs for immune-based therapy and vaccines

A sequence of mechanisms are required to induce an appropriate immune statement in order to evoke an appropriate immune reaction. Appropriate adaptive immunity to particular antigens of the receptor. Next the antigen requires to be efficient, produced into APCs, like DCs, and extracted and addressed to T-cells efficiently. Diverse strategies antigen absorption and production by lysosomal or cytosol via major histocompatibility. It has been suggested that complex (MHC) I or MHC class II paths compensate for a DC's capacity to enhance the reactions of whichever helper-T (TH) cells or cytotoxic T lymphocyte (CTL). Secondly, manufacturing of controlling the differentiation, particular sub-types of T-cell rejoinders vs insult are strictly regulated via associations to APCs, naive T-cells into effector CD4 and 8 T-cells. DCs show a substantial part of translators among innate and adaptive immune system through the integration of tissue-derived signals infection or harm and the supply of many soluble and surface-bound indications to direct T-cells distinction of lymphoid secondary organs [59]. Then the complicated streams of antigen delivery to the APCs, efficient activating condition of DCs, and precise variation of T-cells throughout the preferred way need to be leveraged by a good vaccine method. A variety of vaccines dependent on nanotechnology are growing in structure, scale, shape, and surface characteristics which was accepted or are applicants for medical usage [60]. ZnO's immunomodulatory existence when incorporated into the composition of the vaccine [61], NCs impart great adjuvant ability. Nevertheless, leading to a shortage of basic knowledge of in vivo actions, problems remain. ZnO NPs that can act whether as a delivery plan to encourage the handling of antigens and/or as a delivery system. To trigger or boost immunity, an immune-stimulating adjuvant [62,63]. Furthermore, there has been the adjuvant ability of ZnO NCs in different systems has been investigated within just a few reports for vaccines or for use in immunotherapy [Table 1]. Herein, we recapitulate current developments in prophylactic/preventive use of ZnO NCs as adjuvant frameworks for vaccines.

Table 1. ZnO nanocomposites uses and its growth in the arena of vaccines and tumor immune-therapy *in vivo*.

S. No.	ZnO NCs	Disorder or antigen	Host mice	Vaccination path	Biology-based response	References
1	Mesophorous ZnO NP	Not associated (NA)	BALB/c	Sub-cutaneous	Improved CD4 and CD8 T cells, increased IgG2	[64]
2	ZnO NP	NA	(i) BALB/c	Intraperitoneal	Improved inflammation in intestine	[22]
			(ii) DBA/1J	Intraperitoneal	Enhanced in IL-4,5,17, IgG1 and IgE	[65]
3	ZnO NP	Scrub typhus	C57BL/6	Sub-cutaneous	Improved IFN-gamma^{+} CD4 and 8 T cells	[7]
4	ZnO tetrapod	HSV2/HSV2	BALB/c	Intravaginal	Stops viral-based shedding and decreased inflammation Improve T cell and Ab reactions; reduced death	[9]

5	Hollow ZnO NP	Cancer aTA	or	C57BL/6J	Subcutaneous	Improved CD4 and 8 T cells, slow cancer growth	[66] [67]

Use of ZnO NCs in Antigen distribution scheme

The crucial phase throughout the recruitment and activation of antigen via APCs to CD4 and 8 T -cells through the transmission path of an antigen was the MHC class I and II channels [68]. Along with different cellular mechanisms for the presentation of exogenous or endogenous antigen production, antigen production, the endo or phago-cytic monitoring systems normally connect to MHC-Class II-mediated networks. Processes to CD4 T-cells for presentation. Antigens throughout the cytosolic compartment, but at the other hand, they are produced in a proteasome-dependent way and introduced to CD88 through MHC class I molecules of T-cells [68,69]. The efficacy of the transmission of antigen to suitable cellular components is indeed essential to understanding the types and intensity of antigen-specific immune response. Formerly, our group has shown us that an antigen can be delivered into both containers by ZnO NCs. Inducing substantial and simultaneous enhancement of unique ZnO-associated CD4 and CD8 T cells antigenic agents [7,8,26]. Not only could antigens merged with ZBPs were affected by phagocytes, then APCs can also proficiently transmitted to the cytosol section, theoretically through specific cellular membrane insertion [7,8,70]. Efficient co-localization with lysosomal chambers of peptide antigens correlated with ZnO-based NPs was clearly found in DCs within several hours after incubation [8]. Hollow ZnO nanocrystals packed with ovalbumin (OVA) have been shown to significantly increase the intracellular uptake of a template antigen around in vitro APCs [24]. Through nurturing HEK293 of specific fan-sized ZnO NWs at the 4 °C, robust intra-cellular distribution of related peptides through straight membrane infiltration were verified. Because cellular activity, like endocytosis, was stopped at 4 °C, direct absorption of corresponding peptides via the cell membrane was indicated by the existence of peptides coating on ZnO NWs throughout HEK293 cells [70]. Furthermore the NC of 3D-structured ZnO the intracellular transmission of related DNAs could be mediated and the genetic variation may results in, clearly showing that ZnO NWs infiltrate membranes temporarily in order to keep peace intranuclear delivery DNA [70]. Intracellular distribution and cell proliferation of plasmid DNA through ZnO tetrapods other research [71] have also been published. Provided that ZnO NCs actively trigger cellular composite materials, ZnO nanocomposites may be autophagy [72], a major intracellular droplet impact that supplies lysosomes with cytoplasmic components for both MHC-class-I and II-limited antigen demonstration.

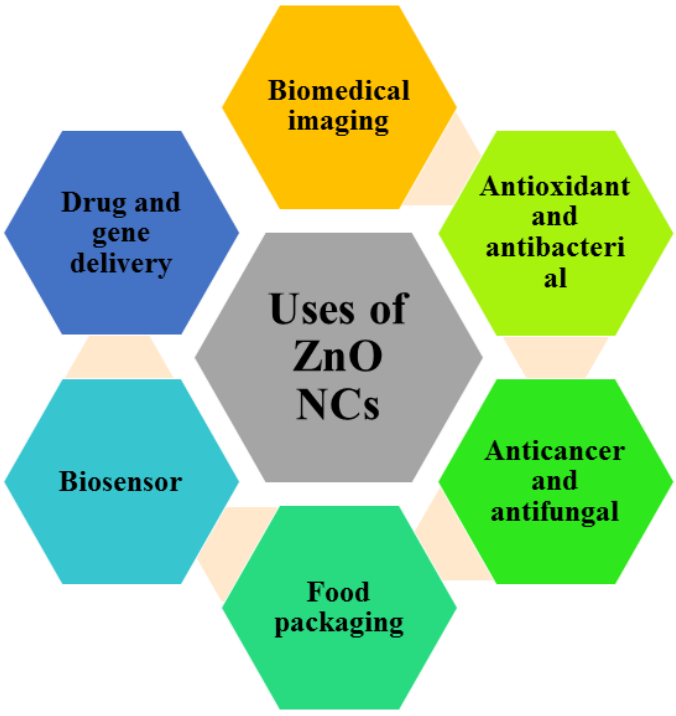

Figure 1. Various applications of ZnO NCs.

Inherently, thus, intra-cellular antigen treating has been further improved, since that requires to be checked in APCs. Collaboratively, nanocomposites based on ZnO possesses promising attributes in terms of the selection of antigen through both endocytic/phagocytic chambers and cytosols, therefore increasing the handling of antigen presentation through the pathways of MHC-class-I, II. Figure 1 depicts an applications of ZnO NCs in diverse fields.

Barrier features of (Bio)polymer or ZnO NCs

By offering multipurpose chemical functionality, NCs can strengthen barrier properties. Important increase in the barrier features of nanoparticles integrated into the NPs [73-76] polymers have been published. The transmission rate (OTR) of oxygen is refers to the quantity oxygen gas whereas under defined conditions of temperature, humidity and pressure, passes via a region until a certain time and its measurements are cm3/(m2.day). O_2 and CO_2 permeability coefficients were attained through multiply the OTR and CO_2-TR by a sample width respectively. While the primary mode of transmission of water vapor is the volume of water vapor transferred through it with a region until a certain time within defined humidity and temperature constraints and displayed in the following of g/(m2.day) [77]. The permeability of groundwater vapor is the result of specimen permeability and density (mm) [78]. Jasim et al. [36] stated that ZnO NPs mounting for both the OTR declined through 23.2 percent to 10 wt percent ZnO NPs-reinforced LLDPE materials. A homogeneous distribution in the matrix material of ZnO NPs this decline in OTR might lead to this. For a PLA/ZnO biological NC, a reduction in PO_2 and PCO_2 of 18 and 17% was shown, respectively owing to its uniformly distributed of ZnO nanoparticles in WVP was improved by 16 percent [35], the PLA matrices.

The PO_2 value was enhanced by the presence of 4 percent ZnO in PHBV for ZnO NPs dependent biological composites, owing to high interfacial adhesion to the polyester matrix, which has been shown to reduce by up to 35%, chain immobilization triggered [31]. ZnO/PHB biological NCs are 5 wt percent of ZnO throughout a case of ZnO/PHB, a loading value of NPs-PO2 was reduced by about 53% and a significant decrease also was identified for up to 38% WVP value for the similar ZnO loading NPs [32]. There had been a ZnO/PBAT composite for the significant decrease in OTR values increases the loading range of ZnO NPs from 0 to 10 % wt. The smallest one OTR value was reported for mounting of 10 wt % ZnO NPs [33].

In an analysis carried out on non-treated ZnO treated with 3-methacryloxypropyltrimethoxysilane by introducing 10 percent ZnO as well as ZnO (3-methacryloxypropyltrimethoxysilane preserved) NPs, NP reinforced-PLA NCs, PO2 plasticized PLA material quantities declined via 36.07 and 55.1 percent [36]. A strengthening of ZnO NPs of their large aspect proportion and its good circulation across the polymeric framework could be due to this tremendous decline in PO2 values [79]. PO2 was reduced within a research on Semolina reinforced to nano-based fillers by as much as 66 percent [21]. Wenhui Li et al. [37] published on NC PLA based on ZnO in their study OTR has been done by reducing the content of ZnO. The oxygen route is prolonged by the tortuous process and is the key explanation for the O_2 resistance development in nano-based blending films [80]. These were also a huge movement for WVP that may be attributed to nano-ZnO hydrophilicity, and the enhanced films' hydrophilic connection.

Composite film integrated with ZnO nanorods and cloves for bovine skin gelatin type-B by incorporating 2 percent of wt into matrix material, essential oil, PO_2 were reduced via 32.27 percent. A homogeneous spreading and higher aspect proportion of ZnO may be attributable to this decrease in PO_2 value nanorods into the framework of gelatin [34].

From penetrability study of ZnO NPs dependent (bio)polymer composite materials, it could be hypothesized it for semolina strengthened by nano-fillers [29], ZnO particles would be utilized in the form of nano-rods, an extreme reduction in PO2 value via approximately 66 percent is perceived. In reality, a 17 percent decreased in PCO_2 after an inclusion of 1 wt percent ZnO in ZnO/PLA biological composites [35] and 38 % decline in WVP value in ZnO/PHB nano-based biological composites [32] is recorded at 5 wt percent ZnO NPs packing. In short, a higher aspect ratio, uniform dispersion and lower absorption of NPs within a polymeric matrix will increase the barrier function of the NCs. The barrier characteristics are shown in Table 2 with respect to different ZnO NPs dependent (bio)polymeric materials.

Table 2. Barrier characteristics of ZnO biological polymeric composites.

S. No.	ZnO NCs	O_2 transmission rate	Water vapor permeability (WVP)	CO_2 permeability	References
1	PLA-ZnO NC films	NA	WVP declined on enhancing ZnO NP quantity from 1 to 3 wt. %	NA	[30]
2	ZnO/PHB biological NCs	PO2 declined by 53% at 5 wt. % ZnO NPs	WVP declined nearly 38% at 5 wt. % ZnO NPs	NA	[32]
3	ZnO/PBAT NCs	Small value of OTR identified for 10 wt. % ZnO NPs	NA	NA	[33]
4	An olive flounder jaw Gelatin-based ZnO NC	NA	WVP declined	NA	[81]
5	ZnO-based LDPE NCs	OTR declined through 17% on introducing Wt. % ZnO NPs	WVTR declined through 22% on introducing 5 wt percent of ZnO NPs	NA	[82]
6	ZnO PP NCs	OTR declined through 22 % on introducing 5 Wt. % ZnO NPs	WVTR declined through 12% on introducing 5 wt. % ZnO NPs	NA	[83]
7	ZnO-based PLA NC	Declined	Enhanced	NA	[37]
8	ZnO-reinforced PHBV Biological NCs	PO2 declined up to 35 % by 4 wt % ZnO	NA	NA	[31]
9	LLDPE films reinforced by ZnO NPs	OTR declined through 23.2% for 10 wt % ZnO addition	NA	NA	[36]
10	Semolina reinforced by Nano-based fillers	PO2 declined through 66%	NA	NA	[29]

Mechanical Characteristics of (Bio)Polymer or ZnO NCs

The introduction of ZnO NPs onto a matrices material have demonstrated the substantial impact on its mechanical features of a composite materials, including tensile strength, fracture toughness, youth modulus, yield tension, break pressure, elastic resilience and break deformation. Roberto Pantani et al. [30] stated that in tensile studies, PLA-ZnO NC films would have shown an improvement in Young's modulus and lower break elongation. The integration of a plasticizer into another process for the enhancement of these criteria, PLA-ZnO NC films could be mentioned. Tensile strengths on nano-based biological composites of ZnO/PHBV revealed that the Young module on 4 wt percent improved by 57 percent ZnO loading of NPs. The probability of a substantial increase in Young's module may be an improvement in a crystalline of PHBV, homo-geneous arrangement of NPs and good interfacial bond among the stages. With growing ZnO NPs material, although the strain at breaking was reduced by 30 %. The ductile stream of the polymer matrix was reduced due to filler strengthening that was also shown by lower straining at breakage values [31].

This situation of nano-based biocomposites of ZnO or PHB, a tensile power, the flexural asset of young people, and the effect of heavy interfacial adhesion, strength grew to 32 percent, 43 percent and 26 percent respectively. Through hydrogen binding connections among the matrix and the nano-based filler [32]. Tensile mobility and compressive strength in the situation of ZnO/PBAT nanoparticles, deformation at break values has

been increased. This should have been fine propagation in the polymer network of ZnO NPs [33]. Stated by Songee Beak et al. [81] assessment of impact strength mostly on bone gelatin-ZnO NC olive flounder. They were watching the compressive properties of the NC films was improved during break elongation. Decreased by 37 % ZnO NPs intermolecular forces with gelatin molecules have been accounted for enhancing the rigidity of a films with gelatin.

The qualities of split deformation and tensile strength in such a report on LDPE/ZnO NCs Agglomeration and low interfacial adhesion in polymer NCs have reduced [82]. For ZnO dependent PPP, a similar pattern of reducing flexural strength and tensile resistance was determined as [83] NCs. The above observations on the structural properties of ZnO could be interpreted from (bio)polymer fiber nanostructures with a maximum improvement in compressive properties of up to 32 % ZnO/PHB biological NCs [32] have been reported, although a 57 percent rise in young modulus has also been observed. ZnO loading in ZnO/PHBV biological NCs are recorded at 4 % wt [31].

ZnO NC as coating material for food

Packaged foods is a critical part of the manufacture of food. The extent of movement of packaging materials is a critical point in industrial packaged foods response to the growth awareness of consumers in accessing health care services. Consumers may refuse to eat stuff that is handled with ZnO NPs and worry about everything. Although there is, no reports conducted nearby the movement on ZnO NPs through polysaccharide. ZnO NP relocation from lower-density polyethylene (LDPE)-ZnO NC material as stated under diverse circumstances by Bumbudsanpharoke et al. [84]. Conditions shown are sterile water for aqueous-based food simulation, acetic acid 4 percent for acidic-based food simulation, C_2H_5OH 50 percent v/v for alcohol food simulation, and n-heptane for fatty acid food simulation. An outcome indicates the largest performance by ZnO NPs was 4 percent acetic acid movement w/v. A higher motion rate of ZnO NPs could be due to the acetic acid bioavailability that would have been the greatest in relation of another simulation methods utilized. But at an another hand, the n-heptane simulation solution did not detect zinc.

The movement of ZnO NPs through commonly produced polypropylene (PP)-ZnO NC food containers (Nano Core, Ltd., Shanghai, China) was also the subject of some other analysis. Distilled water, 4% v/v acetic acid and n-heptane were the mimicking solution put on the vessel for the movement test. It was carried out at different temperatures. The outcome revealed that the sum of migrating ZnO NPs also improved as processing time improved [85]. Within higher-temperature circumstances, the migration rate was higher [85]. On acetic acid and n-heptane, the movement of ZnO NPs was observed to be higher [85]. The authors noticed that perhaps the organic food simulation solution would have a swollen effect on polypropylene, resulted as greater quantities of ZnO NPs migrating.

While ZnO is an authorized GRAS product through the FDA [86], ZnO's nano-size can produce toxic behavior. An evaluation of ZnO NPs, thus, in toxicity is necessary. The cyto-toxic impact of ZnO NPs was precisely tested by study by Barkhordari et al. against the cells of human spermatozoa [87]. The authors stated that NPs of ZnO in a dose- and time-dependent method, sperm cell death were induced. The results indicates the ZnO NPs the concentration of nearly 100 g per mL, nurtured with the spermatozoa for up to 90 min, resulting in much less cell death more than 10% . Somewhere else, ZnO NPs is added to cancerous cells by Wahab's research group and non-malignant cells [88]. These results indicates a ZnO NPs displayed the discouraging impact of a production of T98G cells, fairly efficient on KB cells and minimum harmful in the general HEK cells. The same impact of ZnO NPs on mouse cells were seen through Namvar et al. [89]. ZnO was tested by Namvar et al. against regular mouse fibroblast cells. ZnO NPs were also tested against different cancers for comparison. Cells and medications for tumor (paclitaxel or PTX) have been studied for cancer in the WEHI-3B cancer cell. The findings demonstrated that an existence of ZnO NPs reduced the expression of a different tumor cells. An involvement of PTX, meanwhile revealed the suppressing impact on cancer cells with WEHI-3B. ZnO NPs, but at the other hand showed no toxic effects of rodents to normal fibroblast tumor cells that use the MTT assay.

Conclusion

In this study, we summarized latest discoveries showing that ZnO NCs with both the correct composition, scale, and three - dimensional structure could've been applied as just an adaptive immunity adjuvant system. Owing to its special physicochemical characteristics, APCs are quickly absorbed by ZnO NCs, dissolve to intracellularly emit Zn ions, and consequently trigger intracellular Ros production. NCs are recognized by TLRs, thus effectively inducing innate immune cellular proliferation and encouraging pro-inflammatory reactions. Regulation of APCs, particularly DCs and the distribution of related antigen by ZnO NCs into intracellular compartments improve antigen-specific immune responses, like development of antibodies and T cell reactions. Although the forms of adaptive immunity stimulatory effects by ZnO NCs which differ depending on the distance of injection and the unique aspects of

antigen-complexed NCs, optimal forms of humoral and cellular immunity can be modified for particular target infectious agents via engineering the physico-chemical characteristics as well as 3D frameworks of ZnO NCs.
Latest in vivo experiments have accurate forecast evidence-of-concept proof for a production of prophylactic, vaccine production towards diseases and tumors utilizing ZnO NCs with special compositions and frameworks. Nonetheless, the use of ZnO NCs as in addition to immunotherapy agents, vaccine drug delivery are still at the initial phase of development. Several problems, including obstacles in the repeatable mass development of uniform properties and useful characteristics of ZnO NCs, a lack of basic interrelationship between nano-biological interfaces, and the possible toxic and biological distribution of NCs within a future research, it required to discussed during in vivo models. Besides that, it is possible to apply groundbreaking (bio)polymer/ZnO NC films As fabrics for packaged foods with enhanced properties. Centered on detailed investigations of A well-defined attribute of these NCs, ZnO NPs based (bio)polymer NCs, is then comparison to the normal size of NPs, this contributes to greater interfacial region.
With composites. An interfacial connection here among matrices material and ZnO NPs shows a key part of the end characteristics in enhancing them. A quality requirements of the system could be further enhanced after chemical modifications of these nanomaterials even at smaller wt percentages of NPs. Furthermore, there are some problems related to the manufacture of NCs, such as: (1) standardized NC development Displacement of NPs in the matrices and (2) the right choice of design strategies in the matrix. To control the degree of distribution of these NPs, which also has a major effect on these NPs. Along with end-product properties, stabilization. In addition, considerable research is necessary in enormous areas of research. To meet the requirements, the industrialization of ZnO/(bio)polymer nanocomposites is progressing towards a variety of technical areas. There is no dangerous chance of migrating ZnO NPs further into food, as numerous cytotoxicity studies have shown that ZnO NPs have limited effectiveness. Therefore, a tremendous possible for the use of ZnO NPs like a packaged food element, which shown the capacity to increase the shelf-life of food items and concerns with protection were limited. As also for their potential growth of polysaccharides, the movement of ZnO NPs through biopolymer to NC secure coating needs to be investigated. Rather than synthetic polymer dependent on petroleum to tackle the safety question of more the exact migration of ZnO NPs.

References

1. Pulendran, B., & Ahmed, R. (2011). Immunological mechanisms of vaccination. Nature immunology, 12(6), 509.
2. Zang, X., Zhao, X., Hu, H., Qiao, M., Deng, Y., & Chen, D. (2017). Nanoparticles for tumor immunotherapy. European Journal of Pharmaceutics and Biopharmaceutics, 115, 243-256.
3. Melief, C. J., van Hall, T., Arens, R., Ossendorp, F., & van der Burg, S. H. (2015). Therapeutic cancer vaccines. The Journal of clinical investigation, 125(9), 3401-3412.
4. Caspi, R. R. (2008). Immunotherapy of autoimmunity and cancer: the penalty for success. Nature reviews immunology, 8(12), 970-976.
5. Fauci, A. S., Touchette, N. A., & Folkers, G. K. (2005). Emerging infectious diseases: a 10-year perspective from the National Institute of Allergy and Infectious Diseases. International Journal of Risk & Safety in Medicine, 17(3, 4), 157-167.
6. Hu, X., Wu, T., Bao, Y., & Zhang, Z. (2017). Nanotechnology based therapeutic modality to boost anti-tumor immunity and collapse tumor defense. Journal of Controlled Release, 256, 26-45.
7. Ha, N. Y., Shin, H. M., Sharma, P., Cho, H. A., Min, C. K., Kim, H. I., ... & Kim, Y. K. (2016). Generation of protective immunity against Orientia tsutsugamushi infection by immunization with a zinc oxide nanoparticle combined with ScaA antigen. Journal of nanobiotechnology, 14(1), 1-12.
8. Cho, N. H., Cheong, T. C., Min, J. H., Wu, J. H., Lee, S. J., Kim, D., ... & Seong, S. Y. (2011). A multifunctional core–shell nanoparticle for dendritic cell-based cancer immunotherapy. Nature nanotechnology, 6(10), 675-682.
9. Agelidis, A., Koujah, L., Suryawanshi, R., Yadavalli, T., Mishra, Y. K., Adelung, R., & Shukla, D. (2019). An intra-vaginal zinc oxide tetrapod nanoparticles (zoten) and genital herpesvirus cocktail can provide a novel platform for live virus vaccine. Frontiers in immunology, 10, 500.
10. Zhao, L., Seth, A., Wibowo, N., Zhao, C. X., Mitter, N., Yu, C., & Middelberg, A. P. (2014). Nanoparticle vaccines. Vaccine, 32(3), 327-337.
11. Torres-Sangiao, E., Holban, A. M., & Gestal, M. C. (2016). Advanced nanobiomaterials: vaccines, diagnosis and treatment of infectious diseases. Molecules, 21(7), 867.
12. Marques Neto, L. M., Kipnis, A., & Junqueira-Kipnis, A. P. (2017). Role of metallic nanoparticles in vaccinology: implications for infectious disease vaccine development. Frontiers in immunology, 8, 239.

13. Zhang, Y., R Nayak, T., Hong, H., & Cai, W. (2013). Biomedical applications of zinc oxide nanomaterials. Current molecular medicine, 13(10), 1633-1645.
14. Prasad, A. S. (2008). Zinc in human health: effect of zinc on immune cells. Molecular medicine, 14(5), 353-357.
15. Murakami, M., & Hirano, T. (2008). Intracellular zinc homeostasis and zinc signaling. Cancer science, 99(8), 1515-1522.
16. Mandal, G. P., Dass, R. S., Isore, D. P., Garg, A. K., & Ram, G. C. (2007). Effect of zinc supplementation from two sources on growth, nutrient utilization and immune response in male crossbred cattle (Bos indicus× Bos taurus) bulls. Animal Feed Science and Technology, 138(1), 1-12.
17. Chang, H., Ho, C. C., Yang, C. S., Chang, W. H., Tsai, M. H., Tsai, H. T., & Lin, P. (2013). Involvement of MyD88 in zinc oxide nanoparticle-induced lung inflammation. Experimental and Toxicologic Pathology, 65(6), 887-896.
18. Li, C. H., Shen, C. C., Cheng, Y. W., Huang, S. H., Wu, C. C., Kao, C. C., ... & Kang, J. J. (2012). Organ biodistribution, clearance, and genotoxicity of orally administered zinc oxide nanoparticles in mice. Nanotoxicology, 6(7), 746-756.
19. Yun, J. W., Yoon, J. H., Kang, B. C., Cho, N. H., Seok, S. H., Min, S. K., ... & Kim, Y. K. (2015). The toxicity and distribution of iron oxide–zinc oxide core-shell nanoparticles in C57BL/6 mice after repeated subcutaneous administration. Journal of Applied Toxicology, 35(6), 593-602.
20. Choi, J., Kim, H., Kim, P., Jo, E., Kim, H. M., Lee, M. Y., & Park, K. (2015). Toxicity of zinc oxide nanoparticles in rats treated by two different routes: single intravenous injection and single oral administration. Journal of Toxicology and Environmental Health, Part A, 78(4), 226-243.
21. James, S. A., Feltis, B. N., de Jonge, M. D., Sridhar, M., Kimpton, J. A., Altissimo, M., & Paterson, D. J. (2013). Quantification of ZnO nanoparticle uptake, distribution, and dissolution within individual human macrophages. ACS nano, 7(12), 10621-10635.
22. Roy, R., Kumar, D., Sharma, A., Gupta, P., Chaudhari, B. P., Tripathi, A., & Dwivedi, P. D. (2014). ZnO nanoparticles induced adjuvant effect via toll-like receptors and Src signaling in Balb/c mice. Toxicology letters, 230(3), 421-433.
23. Roy, R., Kumar, S., Verma, A. K., Sharma, A., Chaudhari, B. P., Tripathi, A., & Dwivedi, P. D. (2014). Zinc oxide nanoparticles provide an adjuvant effect to ovalbumin via a Th2 response in Balb/c mice. International immunology, 26(3), 159-172.
24. Wang, X., Li, X., Ito, A., Sogo, Y., Watanabe, Y., & Tsuji, N. M. (2017). Hollow ZnO nanospheres enhance anticancer immunity by promoting CD4+ and CD8+ T cell populations in vivo. Small, 13(38), 1701816.
25. Afroz, S., Medhi, H., Maity, S., Minhas, G., Battu, S., Giddaluru, J., & Khan, N. (2017). Mesoporous ZnO nanocapsules for the induction of enhanced antigen-specific immunological responses. Nanoscale, 9(38), 14641-14653.
26. Sharma, P., Shin, J. B., Park, B. C., Lee, J. W., Byun, S. W., Jang, N. Y., ... & Cho, N. H. (2019). Application of radially grown ZnO nanowires on poly-L-lactide microfibers complexed with a tumor antigen for cancer immunotherapy. Nanoscale, 11(10), 4591-4600.
27. Huang, Y., Mei, L., Chen, X., & Wang, Q. (2018). Recent developments in food packaging based on nanomaterials. Nanomaterials, 8(10), 830.
28. Arfat, Y. A., Ahmed, J., Al Hazza, A., Jacob, H., & Joseph, A. (2017). Comparative effects of untreated and 3-methacryloxypropyltrimethoxysilane treated ZnO nanoparticle reinforcement on properties of polylactide-based nanocomposite films. International journal of biological macromolecules, 101, 1041-1050.
29. Jafarzadeh, S., Ariffin, F., Mahmud, S., Hosseini, S. F., & Ahmad, M. (2017). Improving the physical and protective functions of semolina films by embedding a blend nanofillers (ZnO-nr and nano-kaolin). Food packaging and shelf life, 12, 66-75.
30. Pantani, R., Gorrasi, G., Vigliotta, G., Murariu, M., & Dubois, P. (2013). PLA-ZnO nanocomposite films: Water vapor barrier properties and specific end-use characteristics. European Polymer Journal, 49(11), 3471-3482.
31. Díez-Pascual, A. M., & Díez-Vicente, A. L. (2014). Poly (3-hydroxybutyrate)/ZnO bionanocomposites with improved mechanical, barrier and antibacterial properties. International journal of molecular sciences, 15(6), 10950-10973.

32. Díez-Pascual, A. M., & Diez-Vicente, A. L. (2014). ZnO-reinforced poly (3-hydroxybutyrate-co-3-hydroxyvalerate) bionanocomposites with antimicrobial function for food packaging. ACS applied materials & interfaces, 6(12), 9822-9834.
33. Venkatesan, R., & Rajeswari, N. (2017). ZnO/PBAT nanocomposite films: investigation on the mechanical and biological activity for food packaging. Polymers for Advanced Technologies, 28(1), 20-27.
34. Ejaz, M., Arfat, Y. A., Mulla, M., & Ahmed, J. (2018). Zinc oxide nanorods/clove essential oil incorporated Type B gelatin composite films and its applicability for shrimp packaging. Food Packaging and Shelf Life, 15, 113-121.
35. Marra, A., Silvestre, C., Duraccio, D., & Cimmino, S. (2016). Polylactic acid/zinc oxide biocomposite films for food packaging application. International journal of biological macromolecules, 88, 254-262.
36. Ahmed, J., Arfat, Y. A., Al-Attar, H., Auras, R., & Ejaz, M. (2017). Rheological, structural, ultraviolet protection and oxygen barrier properties of linear low-density polyethylene films reinforced with zinc oxide (ZnO) nanoparticles. Food Packaging and Shelf Life, 13, 20-26.
37. Li, W., Li, L., Cao, Y., Lan, T., Chen, H., & Qin, Y. (2017). Effects of PLA film incorporated with ZnO nanoparticle on the quality attributes of fresh-cut apple. Nanomaterials, 7(8), 207.
38. Baruah, S., & Dutta, J. (2009). Hydrothermal growth of ZnO nanostructures. Science and technology of advanced materials.
39. Mishra, P. K., Mishra, H., Ekielski, A., Talegaonkar, S., & Vaidya, B. (2017). Zinc oxide nanoparticles: a promising nanomaterial for biomedical applications. Drug discovery today, 22(12), 1825-1834.
40. Meulenkamp, E. A. (1998). Synthesis and growth of ZnO nanoparticles. The Journal of Physical Chemistry B, 102(29), 5566-5572.
41. Spanhel, L., & Anderson, M. A. (1991). Semiconductor clusters in the sol-gel process: quantized aggregation, gelation, and crystal growth in concentrated zinc oxide colloids. Journal of the American Chemical Society, 113(8), 2826-2833.
42. Joo, J., Chow, B. Y., Prakash, M., Boyden, E. S., & Jacobson, J. M. (2011). Face-selective electrostatic control of hydrothermal zinc oxide nanowire synthesis. Nature materials, 10(8), 596-601.
43. Zhang, T., Dong, W., Keeter-Brewer, M., Konar, S., Njabon, R. N., & Tian, Z. R. (2006). Site-specific nucleation and growth kinetics in hierarchical nanosyntheses of branched ZnO crystallites. Journal of the American Chemical Society, 128(33), 10960-10968.
44. Xie, X., & Melosh, N. A. (2015). Fabrication of sub-cell size "spiky" nanoparticles and their interfaces with biological cells. Journal of Materials Chemistry B, 3(26), 5155-5160.
45. Mirzaei, H., & Darroudi, M. (2017). Zinc oxide nanoparticles: Biological synthesis and biomedical applications. Ceramics International, 43(1), 907-914.
46. La Niece, S. C., Hook, D., Day, J., Almond, J., & Morgan, S. (1990). 2000 Years Of Zinc And Brass.
47. Rihll, T. E. The Oxford Handbook of Engineering and Technology in the Classical World edited by JP Oleson Oxford: Oxford University Press, 2008. Pp. xviii+ 870. ISBN 978--0--19--518731--1. Cloth $150.00.
48. Craddock, P. T. (2009). The origins and inspirations of zinc smelting. Journal of materials science, 44(9), 2181-2191.
49. Xiong, H. M. (2013). ZnO nanoparticles applied to bioimaging and drug delivery. Advanced Materials, 25(37), 5329-5335.
50. Sharma, P., Jang, N. Y., Lee, J. W., Park, B. C., Kim, Y. K., & Cho, N. H. (2019). Application of ZnO-based nanocomposites for vaccines and cancer immunotherapy. Pharmaceutics, 11(10), 493.
51. Kołodziejczak-Radzimska, A., & Jesionowski, T. (2014). Zinc oxide—from synthesis to application: a review. Materials, 7(4), 2833-2881.
52. Zhang, Y., Ram, M. K., Stefanakos, E. K., & Goswami, D. Y. (2012). Synthesis, characterization, and applications of ZnO nanowires. Journal of Nanomaterials, 2012.
53. Sruthi, S., Ashtami, J., & Mohanan, P. V. (2018). Biomedical application and hidden toxicity of Zinc oxide nanoparticles. Materials today chemistry, 10, 175-186.
54. Luo, Y. H., Chang, L. W., & Lin, P. (2015). Metal-based nanoparticles and the immune system: activation, inflammation, and potential applications. BioMed research international, 2015.
55. Roy, R., Parashar, V., Chauhan, L. K. S., Shanker, R., Das, M., Tripathi, A., & Dwivedi, P. D. (2014). Mechanism of uptake of ZnO nanoparticles and inflammatory responses in macrophages require PI3K mediated MAPKs signaling. Toxicology in Vitro, 28(3), 457-467.

56. Sahu, D., Kannan, G. M., & Vijayaraghavan, R. (2014). Size-dependent effect of zinc oxide on toxicity and inflammatory potential of human monocytes. Journal of Toxicology and Environmental Health, Part A, 77(4), 177-191.
57. Roy, R., Das, M., & Dwivedi, P. D. (2015). Toxicological mode of action of ZnO nanoparticles: Impact on immune cells. Molecular immunology, 63(2), 184-192.
58. Hanley, C., Layne, J., Punnoose, A., Reddy, K. Á., Coombs, I., Coombs, A., & Wingett, D. (2008). Preferential killing of cancer cells and activated human T cells using ZnO nanoparticles. Nanotechnology, 19(29), 295103.
59. Eisenbarth, S. C. (2019). Dendritic cell subsets in T cell programming: location dictates function. Nature Reviews Immunology, 19(2), 89-103.
60. Smith, J. D., Morton, L. D., & Ulery, B. D. (2015). Nanoparticles as synthetic vaccines. Current opinion in biotechnology, 34, 217-224.
61. Bisht, G., & Rayamajhi, S. (2016). ZnO nanoparticles: a promising anticancer agent. Nanobiomedicine, 3(Godište 2016), 3-9.
62. Ha, N. Y., Shin, H. M., Sharma, P., Cho, H. A., Min, C. K., Kim, H. I., ... & Kim, Y. K. (2016). Generation of protective immunity against Orientia tsutsugamushi infection by immunization with a zinc oxide nanoparticle combined with ScaA antigen. Journal of nanobiotechnology, 14(1), 1-12.
63. Zhao, L., Seth, A., Wibowo, N., Zhao, C. X., Mitter, N., Yu, C., & Middelberg, A. P. (2014). Nanoparticle vaccines. Vaccine, 32(3), 327-337.
64. Afroz, S., Medhi, H., Maity, S., Minhas, G., Battu, S., Giddaluru, J., & Khan, N. (2017). Mesoporous ZnO nanocapsules for the induction of enhanced antigen-specific immunological responses. Nanoscale, 9(38), 14641-14653.
65. Matsumura, M., Nagata, M., Nakamura, K., Kawai, M., Baba, T., Yamaki, K., & Yoshino, S. (2010). Adjuvant effect of zinc oxide on Th2 but not Th1 immune responses in mice. Immunopharmacology and immunotoxicology, 32(1), 56-62.
66. Antoine, T. E., Hadigal, S. R., Yakoub, A. M., Mishra, Y. K., Bhattacharya, P., Haddad, C., ... & Shukla, D. (2016). Intravaginal zinc oxide tetrapod nanoparticles as novel immunoprotective agents against genital herpes. The Journal of Immunology, 196(11), 4566-4575.
67. Wang, X., Li, X., Ito, A., Sogo, Y., Watanabe, Y., Tsuji, N. M., & Ohno, T. (2017). Biodegradable metal ion-doped mesoporous silica nanospheres stimulate anticancer Th1 immune response in vivo. ACS applied materials & interfaces, 9(50), 43538-43544.
68. Blum, J. S., Wearsch, P. A., & Cresswell, P. (2013). Pathways of antigen processing. Annual review of immunology, 31, 443-473.
69. Gerner, M. Y., Casey, K. A., Kastenmuller, W., & Germain, R. N. (2017). Dendritic cell and antigen dispersal landscapes regulate T cell immunity. Journal of Experimental Medicine, 214(10), 3105-3122.
70. Sharma, P., Cho, H. A., Lee, J. W., Ham, W. S., Park, B. C., Cho, N. H., & Kim, Y. K. (2017). Efficient intracellular delivery of biomacromolecules employing clusters of zinc oxide nanowires. Nanoscale, 9(40), 15371-15378.
71. Nie, L., Gao, L., Yan, X., & Wang, T. (2006). Functionalized tetrapod-like ZnO nanostructures for plasmid DNA purification, polymerase chain reaction and delivery. Nanotechnology, 18(1), 015101.
72. Yu, K. N., Yoon, T. J., Minai-Tehrani, A., Kim, J. E., Park, S. J., Jeong, M. S., ... & Cho, M. H. (2013). Zinc oxide nanoparticle induced autophagic cell death and mitochondrial damage via reactive oxygen species generation. Toxicology in Vitro, 27(4), 1187-1195.
73. Lange, J., & Wyser, Y. (2003). Recent innovations in barrier technologies for plastic packaging—a review. Packaging Technology and Science: An International Journal, 16(4), 149-158.
74. Duncan, T. V. (2011). Applications of nanotechnology in food packaging and food safety: barrier materials, antimicrobials and sensors. Journal of colloid and interface science, 363(1), 1-24.
75. Smolander, M., & Chaudhry, Q. (2010). Nanotechnologies in food packaging. Nanotechnologies in food, 14(2010), 86e-101e.
76. Avella, M., De Vlieger, J. J., Errico, M. E., Fischer, S., Vacca, P., & Volpe, M. G. (2005). Biodegradable starch/clay nanocomposite films for food packaging applications. Food chemistry, 93(3), 467-474.
77. Siracusa, V. (2012). Food packaging permeability behaviour: A report. International Journal of Polymer Science, 2012.
78. Patricia Miranda, S., Garnica, O., Lara-Sagahon, V., & Cárdenas, G. (2004). Water vapor permeability and mechanical properties of chitosan composite films. Journal of the Chilean Chemical Society, 49(2), 173-178.

79. Alebooyeh, R., MohammadiNafchi, A., & Jokar, M. (2012). The Effects of ZnOnanorodson the characteristics of sago starch biodegradable films.
80. Marra, A., Rollo, G., Cimmino, S., & Silvestre, C. (2017). Assessment on the effects of ZnO and Coated ZnO particles on iPP and PLA properties for application in food packaging. Coatings, 7(2), 29.
81. Beak, S., Kim, H., & Song, K. B. (2017). Characterization of an olive flounder bone gelatin-Zinc oxide nanocomposite film and evaluation of its potential application in spinach packaging. Journal of food science, 82(11), 2643-2649.
82. Polat, S., Fenercioğlu, H., & Güçlü, M. (2018). Effects of metal nanoparticles on the physical and migration properties of low density polyethylene films. Journal of Food Engineering, 229, 32-42.
83. Polat, S., Fenercioglu, H., Unal Turhan, E., & Guclu, M. (2018). Effects of nanoparticle ratio on structural, migration properties of polypropylene films and preservation quality of lemon juice. Journal of Food Processing and Preservation, 42(4), e13541.
84. Bumbudsanpharoke, N., Choi, J., Park, H. J., & Ko, S. (2019). Zinc migration and its effect on the functionality of a low density polyethylene-ZnO nanocomposite film. Food Packaging and Shelf Life, 20, 100301.
85. Liu, J., Hu, J., Liu, M., Cao, G., Gao, J., & Luo, Y. (2016). Migration and characterization of nano-zinc oxide from polypropylene food containers. Am. J. Food Technol, 11, 159-164.
86. Jin, T., Sun, D., Su, J. Y., Zhang, H., & Sue, H. J. (2009). Antimicrobial efficacy of zinc oxide quantum dots against Listeria monocytogenes, Salmonella enteritidis, and Escherichia coli O157: H7. Journal of food science, 74(1), M46-M52.
87. Barkhordari, A., Hekmatimoghaddam, S., Jebali, A., Khalili, M. A., Talebi, A., & Noorani, M. (2013). Effect of zinc oxide nanoparticles on viability of human spermatozoa. Iranian journal of reproductive medicine, 11(9), 767.
88. Wahab, R., Kaushik, N. K., Kaushik, N., Choi, E. H., Umar, A., Dwivedi, S., & Al-Khedhairy, A. A. (2013). ZnO nanoparticles induces cell death in malignant human T98G gliomas, KB and non-malignant HEK cells. Journal of biomedical nanotechnology, 9(7), 1181-1189.
89. Namvar, F., Rahman, H. S., Mohamad, R., Azizi, S., Tahir, P. M., Chartrand, M. S., & Yeap, S. K. (2015). Cytotoxic effects of biosynthesized zinc oxide nanoparticles on murine cell lines. Evidence-Based Complementary and Alternative Medicine, 2015.