Drug Delivery and Translational Research (2022) 12:485–499
https://doi.org/10.1007/s13346-021-00960-3

REVIEW ARTICLE

Nanotechnology-based approaches applied to nutraceuticals

Akanksha R. Singh[1] · Prasanna Kumar Desu[2] · Ramya Krishna Nakkala[3] · Vanitha Kondi[4] · Sushma Devi[5] · Mohammad Sarwar Alam[6] · Hinna Hamid[6] · Rajani B. Athawale[1] · Prashant Kesharwani[7]

Accepted: 8 March 2021 / Published online: 18 March 2021

Abstract

Nutraceuticals and food industries are opening to a tremendously upcoming technology in the field of "Nano science". A new prospect has been defined by nanotechnology by conferring modified properties of nanomaterials and its application in the development of nanoformulations, nutritional supplements and food industry. Nanomaterials reveal exclusive properties because of their small size and high surface/volume ratio; thus, they have a complete application in nutraceuticals and food sector. In the existent review article, we obligate to present a comprehensive outline of the application of nanomaterials in development of advanced nano-based nutraceuticals with enhanced bioavailability, solubility, improved encapsulation efficiency, increased stability, sustained and targeted drug delivery, protection against degradation and microbial contamination and with improved pharmacological activity. It also highlights the importance of nanomaterials as nanosensors/nano-bio sensors for encapsulating peptides, antibodies, enzymes, etc. and in the food packaging industry and its future application. Thus, the review aims to focus on the benefits and new dimensions provided by nanomaterials and nanotechnology in health sectors by improving treatment strategies and quality of life.

Keywords Nutraceuticals · Nanomaterials · Nanosensor · Food industries · Nanotechnology · Solubility enhancement

Introduction

Nanotechnology, in a nutshell, is a technology for the development, synthesis and application of nanometer-sized products. Since 1959, it has been presumed that specific material and substance features can be regulated and manipulated by reducing their particle size to very tiny scales [1–3]. Nanotechnology deals with investigating, modifying and controlling the object's atomic/molecular structures extending after 1 to 100 nm in size [4–6]. More specifically, nanoparticle engineering is the study of the synthesis and growth of artificial or designed nanoparticles for technological advances and applications that would otherwise be downright impossible. The term nanoparticles (NPs) and nanostructured materials (NSMs) have been coined with the unprecedented growth of the research over the past few decades [7, 8].

Nanomaterials or materials of nanostructure have distinct sizes intended for their essential components, constellations, crystallites or molecules. Dimensions similar to zero (nanoclusters, nanoparticles and quantum dots), one (nanotubes or nanorods), two (nano-thin films) and three-dimensional (nanomaterials) ranging from 1 to 100 nm [9, 10]. The combination of nanostructure components with other polymers, biomolecules and other elements of the nanostructure or existing in the aggregate shape may lead to the creation of a more extensive particle size material (> 100 nm) [11–13]. These high surface-volume nanomaterials have unimaginable physicochemical properties, similar to strength, solubility, magnetism, toxicity,

✉ Prashant Kesharwani
prashantdops@gmail.com

1 Prin. K. M. Kundnani College of Pharmacy, Rambhau Salgaonkar Marg, Cuffe Parade, Mumbai 400005, Maharashtra, India

2 Department of Pharmaceutics, K L College of Pharmacy, Green Fields, Vaddeswaram, Guntur, Andhra Pradesh 522502, India

3 Department of Pharmacy, Vishwabharathi College of Pharmaceutical Sciences, Guntur, Andhra Pradesh, India

4 Vishnu Institute of Pharmaceutical Education and Research, VishnupurNarsapur, Medak, Telangana 502313, India

5 Department of Pharmacy, Swift Group of Colleges, Rajpura, Punjab 140401, India

6 Department of Chemistry, School of Chemical and Life Sciences, New Delhi 110062, India

7 Department of Pharmaceutics, School of Pharmaceutical Education and Research, Jamia Hamdard, New Delhi 110062, India

strength, colour, thermodynamics, diffusivity and optics. [14–16]. The nanomaterial surface area is several hundred times greater than its weights, a phenomenon that enhances its physicochemical characteristics [17, 18].

Nanotechnology incorporates various sectors, comprising chemistry, physics, biotechnology and engineering as well applies to nanomaterial practice with nanoscale arrangement sort [7]. Recently, new trends have been emerging for nanotechnology procedures, which have a significant quantity of prospective characteristics and applications in various sectors, similar as material sciences, cosmetics, coatings, catalysis, bioremediation, pharmaceutical production, food industry and the environment [19, 20]. Materials take on unique properties in these nano-sizes that remain not extant while the constituents stood in their novel form [6, 21–23]. By keeping these unique properties in mind, the objective of nano researchers around the globe is to understand these distinctive characteristics to create innovative and amended products over green procedures.

Owing to their exclusive aptitude to upsurge solubility and bioavailability and guard bioactive constituents while existence handled and stored, the solicitations of these nanomaterials remain mounting in diverse areas of nutraceuticals [24, 25]. In accumulation, nanostructured materials (NSMs) remain existence pragmatic in food diligence as nanosensor, novel packaging substantial and summarised food constituent. This manuscript particularly pays attention, which is given to the utilization and implementation of nanotechnology in the nutraceutical industry.

Currently, the medications and health safeguarding foods of natural source necessitate the substantial protracted concern and remain chosen for beyond artificial ones in the ground of medication and nutrition. These novel perceptions involve in the resulted products which assist as nutraceuticals. Nutraceuticals is a mixture of "nutrition" and "pharmaceuticals" that are distinct as "the natural substance which remains food or functional food or a part of the food having bioactive phytochemicals that deliver therapeutic or health benefits, besides it can be adopted even as a preventing and treatment mode of diseases". Similarly, it is dependent on the implications that can hold the vital quantity of the essential nutrients like vitamins, lipid, proteins, carbohydrate and mineral, etc. The scope of nutrition limit has extended to hold the disease hazard failure, controlled with the absence of syndrome supervision which is echoed in the intensified usage of nutraceuticals.

The nutraceuticals need to be ensured an important abode in the food and drug diligence as a harmonizing exemplary for nourishing health and decreasing health distresses. The accomplishment of these products stood ascribed to various aspects, comprising the indulgence of new medication, laterally through its partial attainment mark of advanced ailments that can lead the society adjoining other operative substitutes in existing drugs, which are taking destructive side effects. An intensified mark from nutritional exploration and pharmacological or epidemiological revisions considered for the welfare and efficacy of phytotherapy finished through prevalent within those who examine for dietary enhancements to impede ailment.

Nutraceuticals recurrently remain alienated into three extensive groups similar to dietary developments, herbals and nutrients (vitamins, minerals, etc.). Further, they remain used daily by humans, for instance, a substitute for contemporary medicine, consequently endorsing quality life and comprehensive life prospect as displayed in Fig. 1. They oblige determined to deal benefits similar as a substitute to regular immune booster and antioxidant, rarer adverse reactions as compared with medications, amended bioavailability and extensive half-life. The prominence of the manuscript exists partial to several causes of vitamins, exclusively of nano-formulated liposoluble vitamins. Significant progression adjoining the instructive bioavailability and stability of vitamins, consequently validating health profits within customers, remained attained by many researchers.

Certain nanoscale spectacles obligate been exploited in nutraceutical and practical food formulation, developed, and practices. Novel notions based on nanotechnology remain being reconnoitred to advance product functionality and delivery proficiency. Newly developed abilities in nanoscale portrayal offer an improved conception of these erections in nanometer perseverance and advance a restored empathetic of their functionality.

Various slants have remained reconnoitred to advance the functionality and permanence of hydrophilic vitamins through storage of the product. Innovative techniques stood used to upsurge the shelf life and conveyance of vitamin C expending chitosan nanoparticles. Further, three various diverse vitamins (C, B9, and B12) remained magnificently condensed in water-soluble results of chitosan biopolymer [9, 10]. The revision exhibited N, N, N-trimethyl chitosan nanoparticles might magnificently possess usage of a constant vitamin carrier organization with probable solicitations in food products.

Numerous of these vitamins obligate stood initiated to need noteworthy precincts similar as short chemical constancy, profound to low solubility, oxidation, and high melting points, consequently prominent to small bioavailability. Considering the incapability of human body for attaining vitamins intensifies humans to obligate poised food to ingestion the acclaimed resource of crucial nutrients. The low consumption of numerous vitamins over the diet might negotiate biological utilities like vision, advance, enlargement, immunological action, reproduction, and cellular growth. The solicitation of passable management holds the potential to lessen the threat of advance of impediments allied to the deficit of vitamins.

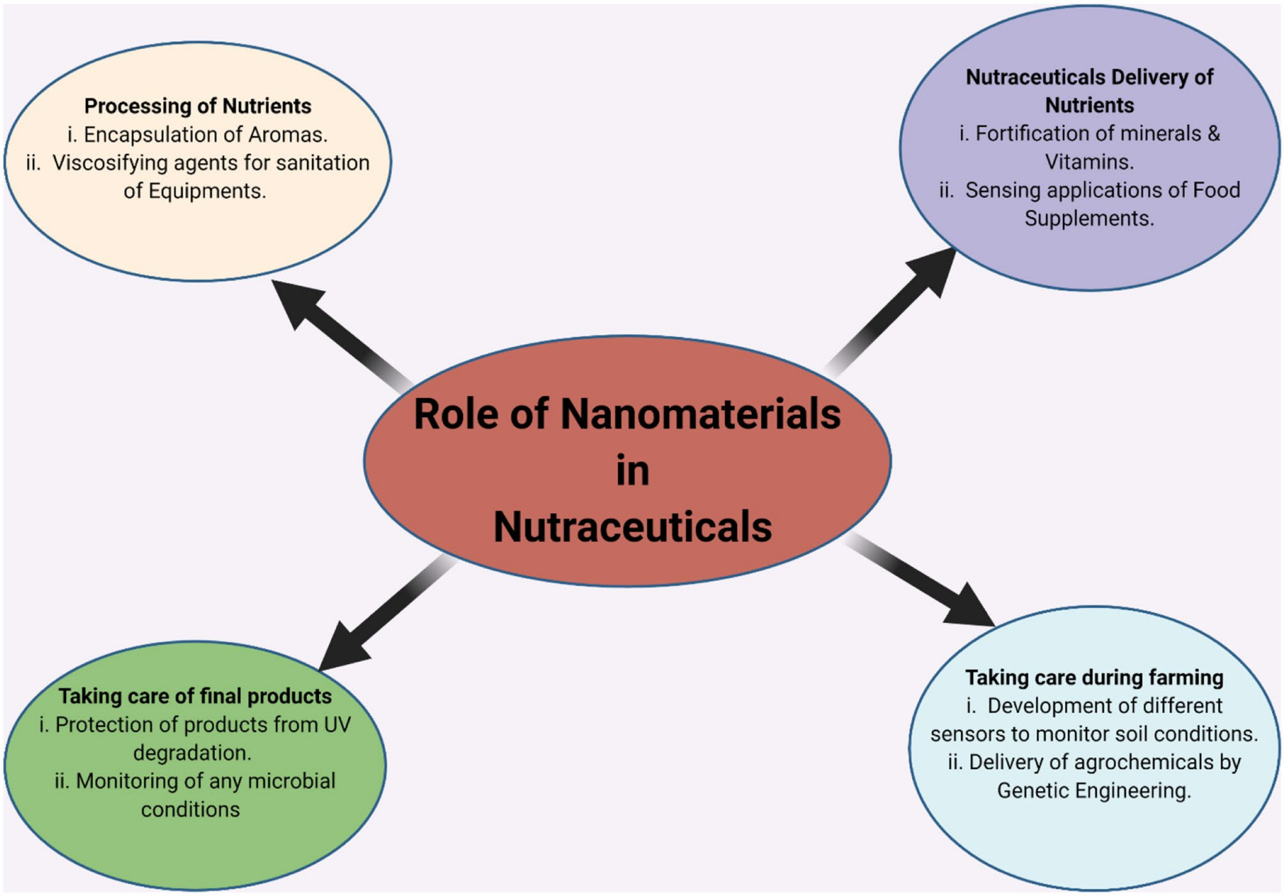

Fig. 1 Role of nanomaterials in nutraceuticals

Fortification of food and enhancements obligate strategies to thwart the absence of vitamins. Enhancement of nutritional premixes and exhilarated food to effort, the vitamins, and micronutrients confined in these produce requisites to endure active till depletion, which might not be frequent always and be the instance. Refreshed foods and premixes might lose a significant proportion of micronutrients and vitamin action formerly depletion through handling, packaging, storage, and transportation. Consequently, it calls for a need for vital prerequisite to progress, reconnoitre cost-effective, advanced methods which expands the permanence of nutraceuticals, exclusively liposoluble vitamins.

Possible nanomaterials in nutraceuticals

The provision of vitamins expending nanotechnology has fascinated attention freshly and remains anticipated as solitary of the probably advanced slants. Abundant methods suggested for the nanoformulations of liposoluble vitamins as described in Fig. 2**.**

Nanoemulsions

Dispersions of colloids entailing droplet of oil disseminated in aqueous medium of 5–200 nm sort recognised as nanoemulsion. They are isotropic schemes that remain constant on a kinetic basis paralleled to the predictable emulsions. Moreover, their tendency remains translucent or transparent to the naked eye. Also, they obligate similarly initiate and embrace distinct features similar to safeguard from oxidant and hydrolysis. There stand numerous sort of nanoemulsions, and the collective ones include oil in water, O/W type, water-in-oil (W/O) type, and the bi-continuous type, for instance, water-in-oil-in-water (W/O/W) type. Diverse provision practises for nanoemulsions stood probed diligently expending high and low energy. Several revisions on encapsulated O/W nanoemulsions of vitamins A, D, and E bioavailability improved and their aspects are distressing the stability. The emulsion schemes for vitamin E encapsulation exhibited the nanoemulsion preparation that amended the stability of emulsion through an average particle size of 277 nm as paralleled to the standard emulsion [26]. However, this seems that noteworthy exploration on nanoemulsions depicted upsurge

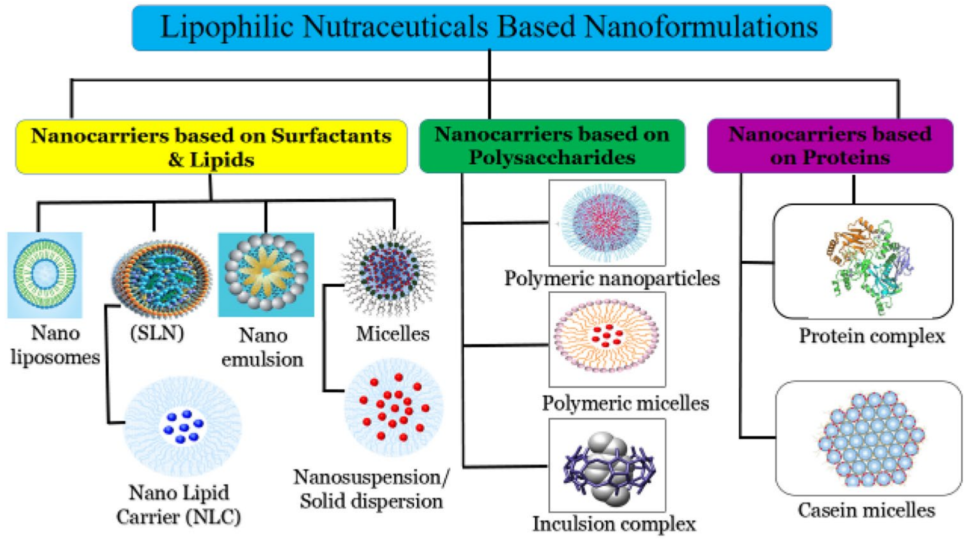

Fig. 2 Nanoformulations for lipophilic nutraceuticals

and emphasised requisite for further in vivo bioavailability revisions of foods exhilarated through lipophilic vitamins because their revisions are few owing to the high costs.

Polymeric nanoparticles

Polymeric nanoparticles (NPs) are the reliable carrier adept of adsorbing, dispersing, entrapping and attribute active constituents to medium size slighter than 1 µm. NPs remain fashioned after pre-formed polymer emulsion by the approaches like salting out, solvent evaporation, superficial fluid, dialysis and nanoprecipitation. Polymeric nanoparticles exhibited adequate stability, greater loading efficiency and controlled release of bioactive composites as paralleled to micelles, emulsion and liposomes [27]. Likewise, the obligate considered broadly in the field of nutraceutical because of appearances comprising amplified stability, ability to guard drugs etc.

Lipid nanoparticles

Lipid nanoparticles (LPs) stood advanced a substitute to traditional nanosystems similar to polymeric elements and liposomes. The lipid nanoparticles might be distinct as the colloidal particles poised of lipid stabilised by surfactants which remain solid at the ambient temperature through wavering sizes amid 40 and 1000 nm. The first nanoparticle (lipid) was solid lipid nanoparticles (SLN). The second-generation LPs remained a few years advanced entitled nanostructured lipid nanoparticles (NLC). NLC is finished after a composite of solid and liquid (oil) lipids [28]. Accumulation of oil in NLC preparation is intended to mislead the development of impeccably organised lipid crystals that initiate in SLN, consequently forming other room through interest ability intended for the summarised active.

Polymeric micelles

Polymeric micelles remain fashioned after block copolymers which obligate the amphiphilic character. It remains poised of water-liking and water-resisting parts. The concentration at which the micelles remain designed is known as the critical micelle concentration (CMC). In contrast, the temperature at which this micelle subsists is entitled as critical micellization temperature (CMT). They can remain exploited as medication transporters, by incorporation of the low soluble nonpolar constituents inside the micellar core and polar constituents on the micellar casing; consequences through intermediate polarity remain distributed amid the core and shell. The belongings permit the schemes for integrating inadequate aqueous soluble medications in the micellar core by chemical conjugation or physical interaction foremost to superior solubility ranges, for guarding the main drugs or the sensitive constituents from impulsive degradation and likewise decrease the drug toxicity [29]. While parallel to the conventional micelles, the polymeric micelles obligate minor CMC standards, which also remain stabilised even at concentrations beneath CMC.

Supercritical fluid technology

Approaches conferred in the preceding segments comprise the practice of the organic solvents that might divulge remaining moistness on nanoparticles thus fashioned. The supercritical fluid expertise, on the other hand, exploits the CO_2 that habitually augment the stability of these bioactive. They are significantly advocated meant for the conveyance of vitamins primarily owing to the physical forte, after that, owing to the capacity for safeguarding the actives from ecological aspects [30].

Nanomaterial technology used in nutraceuticals

In material classifications, the most existing NPs and NSM can be structured as follows:

Composite-based nanomaterials

Composite nanoparticles are sophisticated materials which, owing to their science and technological significance, have recently received increasing consideration [31]. Composite NMs are multi-phase NPs and NSMs with one nanoscale aspect phase that can mix NPs with other NPs or NPs coupled with larger or bulk components. The composites may be combined with any type of metals, ceramics, or bulk polymers of carbon-based, metal-based or organic-based NM [32].

Liu et al. introduced a new protein–lipid composite nanoparticle with a three-layered structure (a barley protein layer, α-tocopherol layer and phospholipid layer) and an inner aqueous compartment to load hydrophilic nutraceuticals. This delivery system showed efficient encapsulation of vitamin B12 (69%) and controlled release behaviour in simulated gastrointestinal media [33].

Carbon-based nanomaterials

Carbon NPs are made entirely of carbon. Carbon nanomaterials, due to their flexible structures, the dimension of which range from 0 to 3D and its tunable surface chemistry, have often been used as primary or as functional additives in various applications [34]. The functioning of carbon nanomaterials is possible using atoms such as nitrogen and fluorine, function groups like hydroxyl and carboxyl groups and polymers [35]. It can be divided into several subdivisions, including carbon nanotubes (CNTs), black carbon (activated carbon), carbon nanofibers, fullerenes and graphene [36].

The combination of carbon-based nanomaterials with excellent properties is a specific type of sensor for enhancing the signal conversion and thus improving detection accuracy and sensitivity, thus reaching unprecedented levels and having good application potential. A considerable number of theoretical and practical studies have been carried out describing the preparation, modification and application of carbon-based nanomaterials in the food testing-related field. Substantial progress has been achieved, thus fully demonstrating the prospects of carbon-based nanomaterials as a new sensor construction material. The development of advanced preparation technology, nanotechnology and sensing technology will lead to more advances in the use of carbon-based nanomaterials in studies of food analysis [37].

Metal oxide NPs

Metal oxide NPs are designed due to their faster reactivity and performance, due to its distinctive and enhanced characteristics of MO-NPs concerning size, structure and composition in a broad range of applications [38]. Various techniques are existing designed for the synthesis of MO-NPs consisting primarily of gas phase, liquid-based gas phase, liquid phase, microemulsion/microcell practice, template/surface-derived techniques, co-precipitation and sol-gel, hydrothermal [39]. NPs from iron (Fe) are instantly oxidised by oxygen at room temperature to iron oxides (Fe2O3) NPs. In comparison with iron NP, iron oxide NPs are more reactive. Among all these materials, several frequently used nanomaterials are metal oxide NPs such as ZnO NPs, TiO2 NPs, CuO NPs and Fe2O3 NPs [40]. These NPs acquired superior properties concerning their metal counterparts.

Inorganic-based nanomaterials

Inorganic particles are often unique because their size reaches the dimensions of the nanometer [41]. Inorganic nanoparticle (NP) chemistry has extended ample consideration owing to their future solicitations in drug treatment, sensing, imaging and others [42]. NPs based on metal and metal oxide will generally be categorised, for instance, inorganic NPs, while inorganic NPs do not have carbon in their structure [43]. Metal NPs are either developed by constructive or destructive means from metal precursors. For the synthesis of nanoparticles, the frequently used metal precursors are aluminium (Al), iron (Fe), lead (Pb), cadmium (Cd), copper (Cu), silver (Ag), cobalt (Co) and zinc (Zn) [43].

Organic-based nanomaterials

Organic nanoparticles in size range from 10 to 1 μm can be described as solid particles consisting primarily of lipids or polymeric compounds [44]. Organic NPs like dendrimers, liposomes, ferritin and micelles are frequently referred to as polymeric NPs. These polymers are also recognised for their more excellent biodegradability, lower toxicity and hollow cores such as micelles and liposomes. They are also extremely sensitive to thermal radiation (light and temperature) [45]. These exceptional features make them the right candidate for nutraceutical applications.

These NPs could remain described by innumerable measurement procedures, similar to particle size and morphology, which are frequently assessed by transmission and scanning electron microscopy, respectively [46]. A significant parameter controls the efficiency and characteristics of NPs on their surface area. Brunauer–Emmett–Teller (BET) exploration is practiced to extend surface area of NPs [47]. X-ray photoelectron spectroscopy (XPS) enables the revision of the structure and quality of the samples [48]. X-ray diffraction analysis provides us with insight into the crystallinity of the distinct samples [49].

Applying various nanotechnology-based materials can improve solubility, expedite organised release, enhance the bioavailability and safeguard the stability of nutraceuticals' micronutrients. It can also upsurge the superiority and functionality of food.

β-lactoglobulin assembled nanomaterials

The use of nutraceutical-based proteins to generate colloidal protein-drug nanocomplexes only improved the dispersibility and solubility of poorly soluble drugs such as curcumin (CUR), resveratrol, thymol etc. The succinylation provided binding sites for Epsilon poly-L-lysine (E-PLL) a positively charged food grade polymer which further improved curcumin's permeability across Caco-2 monolayer followed by improved anti-inflammatory activity in 3D colonic organoids. Due to complexation of curcumin with BLG and succ. BLG, the solubility of curcumin was increased by ≈ 160 times and ≈ 86 times, respectively. Further succinylation prevented curcumin release in the gastric environment in vitro due to its capacity of resisting gastric fluid as compared with BLG. The in vitro release profile of succ. BLG-CUR at pH 7.4 within 120 h showed that > 50% curcumin was released from succ. BLG-CUR. This shows that succ. BLG is likely to be dispersed in the intestine and therefore release curcumin in a sustained manner. Due to increased solubility of curcumin by BLG and cross linking with cationic E-PLL (BCEP), its apparent permeability through Caco-2 cells was also increased as compared with all the other formulations including soluble curcumin [50].

BLG is a good candidate for the delivery of bioactive compounds and other ligands. Indeed, the fact that it can be engineered to modify the ligand binding, as has been shown for another lipocalin, increases this potential considerably. In addition, because BLG due to its structure is resistant to acids but degrades in alkaline condition and contains a good balance of essential amino acids, it is well suited to form a biodegradable and biocompatible advanced delivery system especially for the GIT. BLG has enormous potential as a nanocarrier with good colloidal stability, net charge profile and spherical shape. Overall, significant new insights into various nano-scale ligand delivery systems have been afforded by these studies on BLG nanoparticles [51].

Naisarg et al. stated that in the complexation of resveratrol with BLG, the solubility of resveratrol in water was increased by ≈ 1.7 times [52]. The release of resveratrol from BLG-RES particles was found to be significantly higher compared with free resveratrol. For resveratrol (RES) within BLG-RES, particles showed rapid release with more than 95% of resveratrol releasing in simulated intestinal fluid at pH 7.4 within 12 h. The mice treated with BLG-NPs alone showed significant improvement in disease activity index, which could be due to BLG's role in body calories and intestinal mobility. However, BLG-NP alone has no effect on histology or expression levels of Tnfa and Il10.

Velikov et al. proposed that the particles whose size falls in the range of 100–1000 nm may deliver a satisfying combination of taste and mouth feel. Smaller delivery systems give off strong and unpleasant flavour probably due to the rapid diffusion, while larger delivery vehicles (such as microparticles) may increase the sandiness or creaming of the product [53].

The application of BLG-based carriers in the areas related to the food industry but different from nutraceutical delivery may also be pursued. For instance, BLG with suitable surface modification might serve as a potential carrier for pesticides or antimicrobial agents, providing satisfactory solubility, stability and cell penetrating efficacy to the incorporated compounds. As an alternative field of application, the unique properties of BLG may inspire the synthesis of biomimetic materials, e.g. hybrid films or metallic nanoparticles with a BLG coating that provides desirable ligand-binding capacity or controllable digestion profiles [54].

Nanomaterials in food packaging

Food packaging has a direct impact on the maintenance of the value and safety of food, mainly fruit and vegetables during processing, as well as on the transport and distribution of food to clients. It devours a binding consequence on sustaining the eminence and safety of foods, mostly fruits and vegetable through-loading as well as transference and transport to customers. Despite preserving food quality, freshness and safety, customers today need to do much more to packaging. Food packaging remains deliberated to be one of the first viable nanotechnology solicitations in the food industry [24]. Nanotechnology, which practices microscopic elements, is current and inexpensive and presently resolves to produce seemly food and dairy packaging.

With the application of nanomaterials in nutraceuticals in active packaging, it will help in encompassing the shelf-life of the product. In detail, packaging devours the probable to persist the shelf-life of the food by restraining objectionable aspects and circumstances similar to chemical contaminants, moisture, microorganisms and enzyme activities [55]. Packaging material sort and concentration have significant properties on the effectiveness of packaging delivered to prolong the shelf-life of packaged nutraceuticals. Natural and biodegradable polymers are an option to petroleum-based packaging obligate that received a lot of publicity in the last century [56]. Mostly, biodegradable polymer nanomaterial aggregates through the outline of inorganic elements, similar to clay, into the biopolymeric matrix and similarly stay exact with surfactants which remain intended for amendment of layered silicate.

Combining food packaging products with effective ingredients is a new method of controlling food surface microbial contamination [57]. These useful food contact materials can increase the durability of the item and improve the value and safety of food, which eventually lead to fewer food surpluses. Different food-grade antimicrobial proxies similar as citric acid, potassium sorbate, sorbic acid, polysaccharides, benzoic acids like chitosan and nanoparticles are proposed to be used for fresh food packaging, in particular metals and metal oxides. Amid these, chitosan provides the existent probable intended for solicitation in packaging expertise [58].

Although nanomaterials for implementation are not entirely on the sector, the performance of nanotechnology in food and beverage fields is still mostly in R&D at present. Food packaging submissions form a principal portion of the current and short-term anticipated market for nano-enabled produces in the food section. While assimilated into the packaging of food, the nanosensors perceive clear signs of pathogen metabolism or can enlighten the consumer almost a product's temperature, light or oxygen acquaintance antiquity. This might eradicate essential expiration date in certain occurrences, which might give customer further precise appraisal of the state of decomposition of the food. The arrangement of food pack constituents and active elements is an innovative approach to control surface microbial contagion of foods. Specific nanomaterials reveal antimicrobial properties [59]. To ensure dynamic packaging substantial, allotment of an acquainted interface or physical exchange through food surface is crucial. The functional food exchange constituents encompass product shelf-life, improving food quality and well-being hence eventually foremost to lessen wastage of food.

Nanosensors/nanobiosensors

Nutraceutical safety is a significant concern in food diligence and agriculture because of its straight alliance to the impact of food on the health of humans. Current food protection and public health distress about food essences and chemical remain in the food industry obligate fascinated extensive responsiveness [60]. Conventional revealing techniques for perilous constituents and bacterial pathogens are time overwhelming and affluent, so it essential to expand rapid, sensitive practices to identify these constituents. Considering current years, the nanotechnology devours appeared as a capable field for deciphering safety of food concerning expressions of sighted toxin constituents. There is probable intent for solicitation of nanosensors for observing food quality and safety in the food and agriculture diligence [61]. Their solicitations remain in medication, food, agriculture and biotechnology. Nanobiosensors stood advanced designed for their submissions in recognition of particles identical to glucose, urea, pathogens and several microorganisms. The nanosensors have further benefits owing to presence small, transportable, sensitive, assessable, consistent, precise, reproducible and stable.

Advantages of nanomaterials in nutraceuticals

- Herbal nutraceuticals are valuable in retaining health, and they also help for nutritionally provoked acute or chronic ailments, promote longevity, quality of life and health.
- Nutraceuticals have established significant curiosity because of their supposed safety, prospective nutritional value and therapeutic outcomes.
- The increasing trend in nutraceuticals is public education, cultivation and processing, a renewable source, environmental friendliness and local availability.
- Nanosensors can control accommodating dealings amid enzymes, analyte and correspondent dyes. Packaging integrating nanosensors intended for beckoning and sensing of biochemical and microbial variations.
- The efficient solubilization, stabilization, encapsulation and delivery of nutraceuticals/bioactive based on nanotechnology lead to properties such as enhanced absorption in low doses, reduction in the frequency of dose administration and improved therapeutic index.

Gleeson et al. [62] looked into the potential of certain delivery strategies for the improvement of the oral bioavailability of different types of nutraceuticals, such as fatty acids, bioactive peptides, micronutrients and phytochemicals, and emphasised that nutraceutical and pharmaceutical industries could leverage approaches to oral delivery formulations, which would result in synergies for nutraceutical and pharmaceutical molecules. For example, microfluidization could be considered as an efficient emulsification technique resulting in fish oil-encapsulated powder producing emulsions at the nanoscale range (d43 of 210–280 nm) with the lowest unencapsulated oil at the surface of particles [63].

At the preparation of liposomes starting from large multilamellar vesicles with a diameter range, 2.9–5.7 µm using an ultrasound-assisted approach based on the thin-film hydration method, unilamellar vesicles with diameter sizes ranging from 40 to 51 nm were achieved, showing the EE of 56% for cobalamin, 76% for α-tocopherol and 57% for ergocalciferol. The nanovesicles and their content were kept intact for > 10 days when incubated at simulated conditions of the extracellular environment thanks to the used lipid composition [64].

The investigation of the encapsulation and preservation of quercetin (Q) with cyclodextrins (CDs), conventional liposomes composed of three different types of phospholipids (unsaturated egg Lipoid E80, unsaturated soybean Lipoid S100 and saturated soybean Phospholipon 90H) and drug-in-CD-in-liposomes showed that the application of Lipoid E80-liposomes resulted in better protection of Q against UV irradiation, and its photostability was additionally improved when encapsulated in drug-in-CD-in-liposomes (sulfobutylether β-CD/Q inclusion complex in Lipoid E80 liposomes) [65].

Semenova et al. [66] focused their attention on the molecular design of DESs on the basis of nanoscale complexes formed between a covalent conjugate (sodium caseinate (SCas) + maltodextrin; dextrose equivalent = 2) and combinations of polyunsaturated lipids that are mutually complementary in the content of ω-6 and ω-3 PUFAs: α-linolenic acid (α-LNA) + α-linoleic acid (α-LLA), liposomes of soy PC + α-LNA and micelles of soy lyso-PC + α-LNA. The researchers concluded that thanks to the EE of all these lipid combinations by the conjugate, lipids were highly protected against oxidation, and their high solubility in an aqueous medium was reached.

Dey et al. [67] designed ω-3 PUFA that is enriched with biocompatible NE with sesame protein isolate (SPI) as a natural surfactant. NE with 0.5% (*w*/*v*) SPI and Tween 20 and Span 80 used in 1:1 ratio having the hydrodynamic droplet size of 89.68 ± 2.38 nm effectively enhanced the shelf-life stability of NEs, and the fatty acid release from NE droplets was ≥ 90% during 120 min of simulated two-step in vitro digestion.

Zheng et al. [68] subjected CUR-loaded oil-in-water (O/W) NEs prepared using the conventional oil-loading method, the heat-driven method and the pH-driven method and three commercial CUR supplements (Nature Made, Full Spectrum, and CurcuWin) to a simulated GI tract model consisting of mouth, stomach and small intestine phases and found that the three tested NEs showed similar CUR bioaccessibility (74–79%) with the highest absolute amount of CUR in the mixed micelle phase of the NE fabricated by the pH-driven method.

Nunes et al. [69] focused on the use of solid lipid NPs as oral DESs of phenolic compounds that allow overcoming the pharmacokinetic limitations of these compounds and ameliorate their nutraceutical potential. In another study, Papagiannopoulos and Vlassi [70] reported the preparation of multi-functional stimuli-responsive NPs for food and biomedical applications by combining electrostatic complexation between proteins and polysaccharides with following thermal protein denaturation for the production of chondroitin sulfate/bovine serum albumin NPs. The irreversible protein-protein contacts upon temperature treatment provide the complexes with properties of nanogels, and the surface charge of the prepared NPs reversed at pH 5.3, while their size depended on the solution ionic strength and pH.

Rubio et al. [71] identified proteins described as mediators of *Lactobacillus*' probiotic effects, namely p40, p75 and the product of LCABL_31160, which was annotated as an adhesion protein. The expression and subsequent encapsulation of proteins into microvesicles of bacteria generally considered as safe could also be used in applications of foods and nutraceuticals.

Ghayour et al. [72] encapsulated CUR and Q using a hierarchical approach (binding of a ligand to SCas with subsequent re-assembling of micellar nanostructures or formation of casein NPs). r-CMs had smaller mean particle size than casein NPs, and the entrapment efficiency of both ligands was > 90%. An incorporated phenolic compound showed notably improved chemical stability during an accelerated shelf-life test. The aqueous solubility of CUR and Q after loading in r-CMs was higher than that of free polyphenol molecules, and the viability of treated MCF-7 human breast cancer cells decreased.

Rico et al. [73] investigated controlled FA delivery and stability in fruit juices to reduce potential for over-fortification risks by using dated MSPs and observed that the encapsulation of FA into MSPs resulted in considerably improved vitamin stability and contributed to controlled release after consumption by modifying FA bio-accessibility.

Singh et al. [74] reviewed causes and consequences of micronutrient deficiencies and the bioavailability of nutrients, vitamins, minerals and silica for food and outlined that the release of nutrients from silica in a simulated intestinal fluid is better than in simulated gastric fluid.

Mao et al. [75] focused their attention also on emulsion design enabling the delivery of β-Car in complex food systems and fulfilling its benefits in functional foods. Lipid droplets in β-Car enriched O/W emulsions stabilised with surface-active chlorogenic acid-lactoferrin-polydextrose conjugate used as an emulsifier with the mean particle diameter of < 400 nm across the pH range 2–9 (except pH value around 6.0) exhibited better stability against droplet aggregation under simulated GI tract conditions (mouth, stomach and small intestine) than other systems, which resulted in improved β-Car bioaccessibility, and such formulations could be potentially applied as protectors and carriers of hydrophobic drugs, supplements and nutraceuticals.

Nanosensors or nanobiosensors are used in food microbiology to detect pathogens in treating plants or food materials, quantify obtainable food components and alert consumers and distributors to food safety prominence. Nanosensors remain encompassed in the packaging of food to sense the chemical or pathogen impurities throughout food spoilages, provided that precise cessation dates and real-time ranking in food freshness [76]. Also, they can react towards the modifications in the environment's usage of oxygen, humidity and temperature during processing. Several gas sensors can also detect food spoilage based on microorganisms.

Nanoparticles of metal oxide are useful in identifying different substances. Microorganisms may also be seen through various gas emission activities by conducting polymer nanoparticles [77]. TiO_2 nanoparticle-based O_2 sensing biosensors, through photosensitization of a triethanolamine decrease in the UV matrix of methylene blue, have been developed [78]. The presence, sort and concentration of contaminant microorganisms could similarly be perceived grounded on nanowire stabilised antibodies and antigens, as pathogen-specific antibodies remain involved to the nanowires in the food.

Nano encapsulated antigens, enzymes, polysaccharides, glycol-proteins and antibodies may be advised as effective nanobiosensors for the detection of food-specific compounds that are markers of multiple microbial or chemical spoilage of food. Temperature and time indicators in smart packaging are designed to the intellect, record along with construing the protection of packaged food, particularly on its storage in non-optimal circumstances.

Potential role of nanotechnologies and nutraceuticals

Solicitations of nanotechnology in the food or nutraceutical sector remain merely novel but stand expected to proliferate in the upcoming years. Research in food nanobiotechnology involves, in particular, the addition of antioxidants, antimicrobials, biosensors and other nanomaterials to food constituents [79]. Nanobiotechnology compromises an extensive sort of prospects intended for the progress of innovative products and solicitations in the food system. It can be used for site-specific delivery of nutraceuticals or active products via different transportation systems, such as nanoemulsions and nanodispersions [80]. It can be used as a self-cleaning layer, antibacterial coating and wrapping (e.g. smart and practical), food pathogen detection and monitoring of nutrition decomposition via nanosensors. It can be used for the immobilization of enzymes and green synthesis of inorganic metals and metal oxides, in which structures and features of nanobiotechnology have a crucial part to play [81]. The potential application of nanomaterials in different sectors of nutraceuticals is shown in Fig. 1.

Encapsulation of phytoconstituents

Nanoencapsulation is a method for improving the stability of insoluble bioactive water composites. In addition to enhancing water solubility and permanence of the bioactive composites, nanoencapsulation offers controlled discharge to safeguard their pharmacological/biological action in the body. Fortification of micronutrients and delicate nutraceutical composites from degradation and loss of action has stood comprehensively premeditated inside the perspective of microencapsulation approaches. Drying, solvent evaporation, electrospraying, nano emulsification, nanoprecipitation, coacervation and electrospinning and different approaches are the most common techniques used for compound encapsulation [82].

Using nanoencapsulation methods, phytoconstituents can be used to pack the essential substances to hide their unwanted features such as odour or reactivity, protect them from cultural pressures that destroy them and regulate their release [83]. Thus, nanoencapsulation procedures can be used to ensure safety, increase activity and stabilise bioactive compounds like proteins, lipids, polysaccharides, vitamins and antioxidants. It can remain arranged in nanocomposite, nanoparticles, liposomes and nanoparticles. Thus, several diverse provision approaches can remain developed to boost the cell absorption of respected compounds that promote health and thus reduce the quantity of the component required depending on novel nanoencapsulation and control release technique [84]. The diverse practices are advised to offer these composite nanocapsules in several revisions, comprising high or low energy response practices. Consequently, nanoencapsulation can provide substantial savings in which the nano-sized composites consumed unique amplified surface-based individualities, similar to colourant activity, solubility and conductivity, etc., in contrast to their micro-sized form [85].

Numerous synthetic or artificial surface-active composites can be used as emulsifiers in also small molecular or polymer types, containing nutraceutical nanoencapsulation molecules and stabilisers [86]. Proteins and polysaccharides are therefore required in the formulation of nanoencapsulation. Protein-carbohydrate conjugations through enhanced stabilization, water solubility and emulsifying characteristics enhanced antioxidant and decreased allergenicity [87]. They were used in nanoencapsulation of oil composites similar to essential oils and polyunsaturated fatty acids. It remains established that nanoencapsulation of crucial oils might augment their antimicrobial actions, subsequently, safeguarding adeptness in the food method. The nanoencapsulation of essential oils has been verified to increase the antimicrobial activity and thus preserve the effectiveness of the nutrition scheme [88].

The research team of Shanmugam et al. (2017) first synthesised and characterised curcumin and rutin-chitosan encapsulated phytoconstituents [89]. To improve the bioavailability and effectiveness, curcumin and rutin have been loaded into a single nanoparticulate device. They prepared the formulation through solvent evaporation technique in order to meet this target. In addition to this, the Zeta Sizer, scanning electron microscopy (SEM) and Fourier transform infrared (FT-IR) spectroscopy were used to determine particle size and shape. The prepared nanoparticles were in the range of 25–100 nm in size, and the release profile was calculated to be non-Fickian transport. A pharmacokinetic analysis was performed in rabbits and the pharmacokinetic profile was tested in vivo. When considering the bioavailability, the findings reveal that the oral bioavailability of Curcumin and Rutin are boosted by 3.06 and 4.24 times when opposed to their pure drugs. These results indicate that current novel nanoparticles filled with these combination drugs could have a greater therapeutic ability in the treatment of drug-resistant cancers.

This encapsulation technique is also applicable for encapsulation of volatile compounds like food flavouring, taste, odour and aroma. However, due to evaporation, decomposition and degradation, they tend to decrease. To protect the aroma nature of the products, application of nanoencapsulation technique is very important. It can safeguard and govern their releases and efficiently meet the challenges of the food industry regarding the allowance of their durability, freshness, prolonged preference and organoleptic characteristics [90].

Reducing particle size or nanotechnology in nanoscale encapsulation and increasing surface area relative to mass ratio increases bioavailability, improves controlled release, also allows for more accurate handling of bioactive compounds than microencapsulation. Nanoencapsulation technologies also have many advantages such as protection against oxidation, retention of volatile ingredients, targeted drug delivery, lessening in the magnitude of exploited core-shell substantial, amended stability beside coalescence and gravitational departures, taste masking, change in flavour character, consecutive delivery of multiple active constituents, articulating optically noticeable bioactive composite solutions, long-lasting organoleptic discernment, quicker dissociation and great intracellular endorsement. These encapsulation technologies can remain engaged to safeguard the chemical structure and purpose of food substantial and nutraceuticals and to upsurge the bioavailability and shelf-life of the product.

Enhancement of solubility

The aqueous insolubility of the utmost significant nutraceuticals, similar to fat-soluble phytosterols, essential oils, vitamins, carotenoids and polyunsaturated fatty acids etc., makes their applications difficult, particularly in food formulations established on aqueous substances [91]. It has been documented in the literature that there is adjacent affiliation amid the cellular uptake of nutritional composite and solubility.

Reduction of the size of the compounds, particularly into nano range, upsurges the solubilizing rate and the saturation solubility, owing to the substantial reversed surface area. Consequently, nanotechnology deals homogeneous dispersal of these efficient lipids bioactive into the water, using nano-sized provision schemes. Compared with other formulation, nano-nutraceuticals deliver different surface area and obligate the probable to upsurge solubility, augment the bioavailability, progress the controlled discharge and assist accuracy affecting the encapsulated substantial to a superior magnitude [92]. Quercetin, one of the utmost pretty flavonols, is exceptionally adaptable in its bioavailability and its solubility restrictions its absorption. In contrast, its nanoformulation remains stated to be valuable for its continuous delivery. Conferring to literature, innumerable revisions obligate stood steered to integrate lipophilic bioactive into nano-sized conveyance schemes, which remain dispersible in water schemes [93].

Saoji et al. [94] have increased the solubility and permeability of Standardized Bacopa Extract (SBE), a phospholipid-based complexation strategy. To prepare the SBE-phospholipid complex, a solvent evaporation process was used. The formulation of BN was confirmed by using SEM, FTIR, DSC and powder X-ray diffraction (PXRD). BN demonstrated considerably greater aqueous solubility relative to pure SBE (20-fold) or the physical mixture of SBE and phospholipid (13-fold). In vitro dissolution showed a considerably higher efficiency of the prepared complex (BN) in releasing the SBE (more than 97%) in contrast to the pure SCE (42%) or the physical mixture (47%). Hence, it can be reported that drug-phospholipid complexation could be necessary to increase the solubility of bioactive phytoconstituents.

Enhancement of bioavailability

There are many instances of hydrophobic elements from food products with potential health profits while commonly consumed as a measure of an entity's nutrition, similar as nutraceuticals (e.g. carotenoids, curcumin, fatty acids, conjugated linoleic acids and coenzyme Q10) [95]. Many distinct physicochemical and physiological aspects subsidise to this form of bioactive agent's low bioavailability. The insolubility of efficient lipid replacements in the gastrointestinal tract is an alternative purpose for the less bioavailability of the composites [96]. Consequently, amassed nutraceutical bioavailability expending numerous nano-sized delivery schemes, for instance, approaches based on phospholipid have stood anticipated by multiple researchers. There are several studies, where it has been designated that bioavailability of practical lipid bioactive compounds has stood substantially amplified by their integration to nano-sized delivery system.

The nano-sized conveyance schemes can similarly govern the interfaces of constituents through biological standard and so the biodistribution. Amendment of the nano delivery schemes by embedding the hydrophilic particles, like polyethylene glycol, remains executed to regulate the molecular alteration and exploit their bioaccessibility and absorption. The bioactive bioavailability is proportionate to the cellular absorption, molecular conversion and bioaccessibility. Consequently, amassed bioaccessibility or absorption bioaccessibility moreover along with varying molecular assembly, valour ensue through digestion, indications to an extensive upsurge in the bioavailability [65].

The solid lipid nanoparticles (SLN), through entire solid lipid matrix, obligate stood anticipated as the utmost proficient delivery schemes for bioactive composites which can moreover upsurge the solubility or advance the epithelium permeability and bioavailability. In accumulation to nutraceuticals, the SLN can have nanoencapsulation numerous medications to upsurge their oral bioavailability [97].

On the former hand, proteins obligate stood described as pretty bioavailability accompaniment composites for nutraceuticals owing to their great profusion, preferred biocompatibility and amphiphilic nature [98]. Some phytoconstituents showed improved bioavailability in their nano form. The chitosan/polyglutamic acid nanocomposites designed for the oral conveyance of green tea catechins [99]. Their extended nanoparticles exhibited antioxidant action along with amplified paracellular transport, regardless of passage via gastrointestinal. Consequently, the product owes its usage in numerous food preparations.

Diosmin's (DSN) bioavailability was improved by the lyophilised phytosomal nanocarriers by Freag et al., [100]. In this research, new phytosomes loaded with DSN were produced to enhance drug dissolution and intestinal permeability. The following approaches were employed for formulation preparation: solvent evaporation, salting out and lyophilization. The optimization of an nanocarrier encompassed the collection of various soybean phospholipid (SPC) forms, different solvents and different DSN/SPC molar ratios (1:1, 1:2 and 1:4). The various instrumental methods were used to characterise the prepared formulation. Diosmin was effectively permeated into rats' intestines, with 80% of the volume permeated used for experimentation. The outcomes were then evaluated, and findings revealed improved dissolution and permeation characteristics as well as increased drug distribution.

Control release

Owing to their applicability in the arena of drug distribution, controlled release systems have drawn tremendous attention. Delivery systems can also have a significant impact on food processing and digestion by preserving essential nutrients and other 'bioactive' foods. However, owing to a few constraints, the characteristics of the nutraceuticals are still not fully realised. Bioactive delivery through food is a significant challenge because these bioactive are generally associated with many limitations such as lack of stability and release conditions, poor bioavailability due to low permeability, low solubility and toxicity of the compound [101]. Thus, to provide active distribution, the concentration governs the provided bioactive compound that concluded time and amassing on the site of exploit ought to be prudently intended and organised, which might be magnificently executed by numerous nano-based delivery schemes. These distribution schemes can amend the release of composites due to the small size and surface to volume ratio, the proficiency to afford intravascular delivery, steady release and stabilization of bioactive. The alignment and nature of delivery schemes disturb the discharge of privileged bioactive to the situation. Consequently, several sorts and concentrations of bioactive composite, nanoparticle size, emulsifying and stabilizing agents contribute to numerous release properties.

Organic carriers, similar to micelles, liposomes, and polymeric nanoparticles, obligate stood expansively probed for their convenience as delivery schemes. Nevertheless, organic carriers similar to micelles grieve from poor stability remaining to a biochemical outbreak. The receptive nanosized delivery schemes remain advance promising, scarcity or further adapts [102].

Singh et al. [103, 104] prepared the multiparticulate system of curcumin-loaded granules to the colon and its in vivo evaluation in rats. Encapsulation of curcumin by multiparticulate coating with inner guar gum and outer Eudragit FS30D was employed to boost its applicability in the colonic diseases. In vitro release analysis shows that multiparticulate encapsulation of curcumin is effective in human gastrointestinal tract physiology.

Conclusion and future prospects

The significance of healthy nutrition with significant nutrients, such as vitamins or antioxidants, in adequate quantities necessary for human and animal health, is unquestionable. In reality, the strengthening of food products through similar nutritional appendages can be used readily while adequate stabilization of the component in the product can at least be ensured until the expiration date. For maintaining the quality of the nutraceutical's works, it has been suggested that the application of nanomaterials is the best alternative.

The usage of herbal medicines or phytomedicines is based on utilizing various sections of medicinal plants. Herbal therapy is being investigated for the treatment's various benefits in both industrialised and emerging countries. Herbs are currently used to cure chronic and acute illnesses and to activate the immune system by utilizing different disorders and complications including coronary disease, prostate diseases, obesity and inflammation. Since the demand for medicinal plants is growing on a regular basis, WHO estimates that the global herbal industry would more than triple to $ 5 trillion by 2050 from the current sum of $ 62 billion. Even though it has a place in the global economy, it also has to deal with certain obstacles. The regulatory status, measurement of protection and effectiveness, quality management, safety monitoring and insufficient or weak information regarding conventional, complementary/alternative therapies are encountered and widely seen in many countries. To promote global standardization and strengthening of regulatory policies, it is essential that regulatory policies on herbal medicines be standardised and strengthened on a global scale. In order to safeguard public health internationally, local regulatory bodies in all countries of the world must be vigilant and consistently enforce successful interventions to guarantee that all herbal medicines licensed for sale are healthy and of sufficient quality. The knowledge of healthcare practitioners, suppliers of herbal medicines and patients/consumers is crucial to avoid the severe risks of abuse of herbal medicines.

However, various phytochemical-based nanocarriers have produced and engineered their own advantages, such as being safe, environmentally sustainable and less harmful, affordable, easy to scale and providing regulated size and morphology for particles. In conclusion, plant-mediated nano systems have the potential to enhance the pharmacokinetic profile and bioavailability of phytotherapeutic substances for multiple disease conditions.

By taking the advantages of different nanocarrier, in this paper, we attempted to gather data from the existing literature on the usage of nanomaterials for various applications. We tried to summarise the solicitation of nanomaterials to enhance or maintain the quality of the products. In conclusion, applications of nanomaterials help for maintaining physicochemical characteristics of the products throughout life. Also, the micro- and nanoencapsulation of nutraceuticals can deliver an assortment of benefits concerning their permanence, performance in vitro and in vivo, improved biological activity and consequent fortification of their nutritive significance and bioavailability.

Acknowledgements The author (P. Kesharwani) acknowledges the financial support from the University Grants Commission, New Delhi, India, through Start-Up Research Grant and Indian Council of Medical Research, New Delhi, India, through Extramural Research Grant.

Author contribution Akanksha R. Singh, Prasanna Kumar Desu and Ramya Krishna Nakkala wrote the manuscript. Vanitha Kondi and Sushma Devi helped in figure and table compilation. Rajani B. Athawale checked the manuscript for language corrections, Mohammad Sarwar Alam and Hinna Hamid checked the manuscript for language corrections and revising the whole manuscript based upon the reviewer comments and Prashant Kesharwani did the final proof reading and submission of the manuscript.

Data availability As this is a review article, availability of data and materials is not required for this submission.

Declarations

Ethics approval and consent to participate As this is a review article, ethical approval is not required for this submission.

Consent for publication We agreed with the journal policy and provided our consent for the publication.

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Feynman RP. There is plenty of room at bottom. Eng Sci. 1960;23:22–36.
2. Kesharwani P, Banerjee S, Gupta U, Mohd Amin MCI, Padhye S, Sarkar FH, Iyer AK. PAMAM dendrimers as promising nanocarriers for RNAi therapeutics, Mater. Today. 18. 2015. https://doi.org/10.1016/j.mattod.2015.06.003.
3. Kesharwani P, Choudhury H, Meher JG, Pandey M, Gorain B. Dendrimer-entrapped gold nanoparticles as promising nanocarriers for anticancer therapeutics and imaging. Prog Mater Sci. 2019;103:484–508. https://doi.org/10.1016/j.pmatsci.2019.03.003.
4. Zhang L, Gu F, Chan J, Wang A, Langer R, Farokhzad O. Nanoparticles in medicine: therapeutic applications and developments. Clin Pharmacol Ther. 2008;83:761–9. https://doi.org/10.1038/sj.clpt.6100400.
5. Kishore Uttam Kothule. Prashant Kesharwani, Suresh Kumar Gidwani, Paraag Gide, Development and characterization of chitosan nanoparticles and improvement of oral bioavailability of poorly water soluble acyclovir. Res J Pharm Technol. 2010;3:1241–5.
6. Tripathi PK, Gorain B, Choudhury H, Srivastava A, Kesharwani P. Dendrimer entrapped microsponge gel of dithranol for effective topical treatment, Heliyon. 5. 2019. https://doi.org/10.1016/j.heliyon.2019.e01343.
7. Logothetidis S. Nanostructured materials and their applications. Nanosci Technol. 2012. https://doi.org/10.1007/978-3-642-22227-6.
8. Singh S, Alrobaian MM, Molugulu N, Agrawal N, Numan A, Kesharwani P. Pyramid-shaped PEG-PCL-PEG polymeric-based model systems for site-specific drug delivery of vancomycin with enhance antibacterial efficacy. ACS Omega. 2020. https://doi.org/10.1021/acsomega.9b04064.
9. Arivalagan K, Ravichandran S, Rangasamy K, Karthikeyan E. Nanomaterials and its potential applications. ChemTech Res: Int. J; 2011.
10. Gorain B, Choudhury H, Nair AB, Dubey SK, Kesharwani P. Theranostic application of nanoemulsion in chemotherapy. Drug Discov Today. 2020. https://doi.org/10.1016/j.drudis.2020.04.013.

11. Lyshevski SE. Nanotechnology, in: CRC Handb. Mech. Eng. Second Ed., 2004.
12. Choudhury H, Pandey M, Lim YQ, Low CY, Lee CT, Marilyn TCL, Loh HS, Lim YP, Lee CF, Bhattamishra SK, Kesharwani P, Gorain B. Silver nanoparticles: advanced and promising technology in diabetic wound therapy. Mater Sci Eng C. 2020;112:110925. https://doi.org/10.1016/j.msec.2020.110925.
13. Tagde P, Kulkarni G, Mishra DK, Kesharwani P. Recent advances in folic acid engineered nanocarriers for treatment of breast cancer. J Drug Deliv Sci Technol. 2020;56:101613. https://doi.org/10.1016/j.jddst.2020.101613.
14. Bréchignac C, Houdy P, Lahmani M. Nanomaterials and nanochemistry. 2007. https://doi.org/10.1007/978-3-540-72993-8.
15. Nallamolu S, Jayanti VR, Chitneni M, Khoon LY, Kesharwani P. Self-micro emulsifying drug delivery system “SMEDDS” for efficient oral delivery of andrographolide. Drug Deliv Lett. 2019;10:38–53. https://doi.org/10.2174/2210303109666190723145209.
16. Singh S, Hassan D, Aldawsari HM, Molugulu N, Shukla R, Kesharwani P. Immune checkpoint inhibitors: a promising anticancer therapy. Drug Discov Today. 2020. https://doi.org/10.1016/j.drudis.2019.11.003.
17. Albanese A, Tang PS, Chan WCW. The effect of nanoparticle size, shape, and surface chemistry on biological systems. Annu Rev Biomed Eng. 2012. https://doi.org/10.1146/annurev-bioeng-071811-150124.
18. Bapat RA, Dharmadhikari S, Chaubal TV, Amin MCIM, Bapat P, Gorain B, Choudhury H, Vincent C, Kesharwani P. The potential of dendrimer in delivery of therapeutics for dentistry, Heliyon. 5. 2019. https://doi.org/10.1016/j.heliyon.2019.e02544.
19. Morris VJ. Emerging roles of engineered nanomaterials in the food industry. Trends Biotechnol. 2011. https://doi.org/10.1016/j.tibtech.2011.04.010.
20. Choudhury H, Pandey M, Yin TH, Kaur T, Jia GW, Tan SQL, Weijie H, Yang EKS, Keat CG, Bhattamishra SK, Kesharwani P, Md S, Molugulu N, Pichika MR, Gorain B. Rising horizon in circumventing multidrug resistance in chemotherapy with nanotechnology. Mater Sci Eng C. 2019;101:596–613. https://doi.org/10.1016/j.msec.2019.04.005.
21. Buzea C, Pacheco II, Robbie K. Nanomaterials and nanoparticles: sources and toxicity. Biointerphases. 2007. https://doi.org/10.1116/1.2815690.
22. Pandey D, Kesharwani P, Jain D. Entrapment of drug-sorbate complex in submicron emulsion: a potential approach to improve antimicrobial activity in bacterial corneal infection. J Drug Deliv Sci Technol. 2019;49:455–62. https://doi.org/10.1016/J.JDDST.2018.12.006.
23. Kesharwani P, Jain K, Jain NK. Dendrimer as nanocarrier for drug delivery. Prog Polym Sci. 2014. https://doi.org/10.1016/j.progpolymsci.2013.07.005.
24. Sozer N, Kokini JL. The Applications of Nanotechnology, in: Chem. Anal. Food Tech. Appl., 2012. https://doi.org/10.1016/B978-0-12-384862-8.00006-6.
25. Jain S, Kesharwani P, Tekade RK, Jain NK. One platform comparison of solubilization potential of dendrimer with some solubilizing agents, Drug Dev. Ind. Pharm. 41 2015. https://doi.org/10.3109/03639045.2014.900077.
26. Jafari SM, McClements DJ. Nanotechnology Approaches for Increasing Nutrient Bioavailability, in: Adv. Food Nutr. Res., 2017. https://doi.org/10.1016/bs.afnr.2016.12.008.
27. Assadpour E, Mahdi Jafari S. A systematic review on nanoencapsulation of food bioactive ingredients and nutraceuticals by various nanocarriers, Crit. Rev. Food Sci. Nutr. 2019. https://doi.org/10.1080/10408398.2018.1484687.
28. Mcclements DJ. Nanoscale nutrient delivery systems for food applications: improving bioactive dispersibility, stability, and bioavailability. J Food Sci. 2015. https://doi.org/10.1111/1750-3841.12919.
29. McClements DJ, Li F, Xiao H. The nutraceutical bioavailability classification scheme: classifying nutraceuticals according to factors limiting their oral bioavailability. Annu Rev Food Sci Technol. 2015. https://doi.org/10.1146/annurev-food-032814-014043.
30. Jones D, Caballero S, Davidov-Pardo G. Bioavailability of nanotechnology-based bioactives and nutraceuticals, in: Adv. Food Nutr. Res., 2019. https://doi.org/10.1016/bs.afnr.2019.02.014.
31. Moon RJ, Martini A, Nairn J, Simonsen J, Youngblood J. Cellulose nanomaterials review: structure, properties and nanocomposites. Chem Soc Rev. 2011. https://doi.org/10.1039/c0cs00108b.
32. Zhang CL, Yu SH. Nanoparticles meet electrospinning: recent advances and future prospects. Chem Soc Rev. 2014. https://doi.org/10.1039/c3cs60426h.
33. Liu G, Huang W, Babii O, Gong X, Tian Z, Yang J, Wang Y, Jacobs RL, Donna V, Lavasanifar A, Chen L. Novel protein-lipid composite nanoparticles with an inner aqueous compartment as delivery systems of hydrophilic nutraceutical compounds. Nanoscale. 2018;10:10629–40. https://doi.org/10.1039/c8nr01009a.
34. Krueger A. Carbon nanomaterials. Beilstein J Org Chem. 2014. https://doi.org/10.3762/bjoc.10.186.
35. Cha C, Shin SR, Annabi N, Dokmeci MR, Khademhosseini A. Carbon-based nanomaterials: multifunctional materials for biomedical engineering. ACS Nano. 2013. https://doi.org/10.1021/nn401196a.
36. Long CM, Nascarella MA, Valberg PA. Carbon black vs. black carbon and other airborne materials containing elemental carbon: Physical and chemical distinctions, Environ. Pollut. 2013. https://doi.org/10.1016/j.envpol.2013.06.009.
37. Pan M, Yin Z, Liu K, Du X, Liu H, Wang S. Carbon-based nanomaterials in sensors for food safety. Nanomaterials. 2019;9:1330. https://doi.org/10.3390/nano9091330.
38. Koziej D, Lauria A, Niederberger M. 25th Anniversary article: metal oxide particles in materials science: addressing all length scales. Adv Mater. 2014. https://doi.org/10.1002/adma.201303161.
39. Guo T, Yao MS, Lin YH, Nan CW. A comprehensive review on synthesis methods for transition-metal oxide nanostructures. CrystEngComm. 2015. https://doi.org/10.1039/c5ce00034c.
40. Zhu Y, Wu J, Chen M, Liu X, Xiong Y, Wang Y, Feng T, Kang S, Wang X. Recent advances in the biotoxicity of metal oxide nanoparticles: Impacts on plants, animals and microorganisms. Chemosphere. 2019. https://doi.org/10.1016/j.chemosphere.2019.124403.
41. Caseri W. Nanocomposites of Polymers and Inorganic Particles, in: Hybrid Mater. Synth. Charact. Appl., 2007. https://doi.org/10.1002/9783527610495.ch2.
42. Auffan M, Rose J, Bottero JY, Lowry GV, Jolivet JP, Wiesner MR. Towards a definition of inorganic nanoparticles from an environmental, health and safety perspective. Nat Nanotechnol. 2009. https://doi.org/10.1038/nnano.2009.242.
43. Ealias AM, Saravanakumar MP. A review on the classification, characterisation, synthesis of nanoparticles and their application, in: IOP Conf. Ser. Mater. Sci. Eng., 2017. https://doi.org/10.1088/1757-899X/263/3/032019.
44. Ma R, Levard C, Marinakos SM, Cheng Y, Liu J, Michel FM, Brown GE, Lowry GV. Size-controlled dissolution of organic-coated silver nanoparticles. Environ Sci Technol. 2012. https://doi.org/10.1021/es201686j.
45. Pyatenko A, Yamaguchi M, Suzuki M. Synthesis of spherical silver nanoparticles with controllable sizes in aqueous solutions. J Phys Chem C. 2007. https://doi.org/10.1021/jp071080x.

46. He C, Hu Y, Yin L, Tang C, Yin C. Effects of particle size and surface charge on cellular uptake and biodistribution of polymeric nanoparticles. Biomaterials. 2010. https://doi.org/10.1016/j.biomaterials.2010.01.065.
47. Kun Ma X, Lee NH, Oh HJ, Kim JW, Rhee CK, Park KS, Kim SJ. Surface modification and characterization of highly dispersed silica nanoparticles by a cationic surfactant, Colloids Surfaces A Physicochem. Eng. Asp. 2010. https://doi.org/10.1016/j.colsurfa.2010.01.051.
48. Seyama H, Soma M, Theng BKG. X-Ray Photoelectron Spectroscopy, in: Dev. Clay Sci., 2013.https://doi.org/10.1016/B978-0-08-098259-5.00007-X.
49. Ingham B. X-ray scattering characterisation of nanoparticles. Crystallogr Rev. 2015;21:229–303. https://doi.org/10.1080/0889311X.2015.1024114.
50. Pujara N, Giri R, Wong KY, Qu Z, Rewatkar P, Moniruzzaman M, Begun J, Ross BP, McGuckin M, Popat A. pH – Responsive colloidal carriers assembled from β-lactoglobulin and Epsilon poly-L-lysine for oral drug delivery. J Colloid Interface Sci. 2021;589:45–55. https://doi.org/10.1016/j.jcis.2020.12.054.
51. Shafaei Z, Ghalandari B, Vaseghi A, Divsalar A, Haertlé T, Saboury AA, Sawyer L. β-Lactoglobulin: an efficient nanocarrier for advanced delivery systems, Nanomedicine Nanotechnology. Biol Med. 2017;13:1685–92. https://doi.org/10.1016/j.nano.2017.03.007.
52. Pujara N, Wong KY, Qu Z, Wang R, Moniruzzaman M, Rewatkar P, Kumeria T, Ross BP, McGuckin M, Popat A. Oral delivery of β-lactoglobulin-nanosphere-encapsulated resveratrol alleviates inflammation in Winnie mice with spontaneous ulcerative colitis. Mol Pharm. 2021;18:627–40. https://doi.org/10.1021/acs.molpharmaceut.0c00048.
53. Velikov KP, Pelan E. Colloidal delivery systems for micronutrients and nutraceuticals. Soft Matter. 2008;4:1964–80. https://doi.org/10.1039/b804863k.
54. Teng Z, Xu R, Wang Q. Beta-lactoglobulin-based encapsulating systems as emerging bioavailability enhancers for nutraceuticals: a review. RSC Adv. 2015;5:35138–54. https://doi.org/10.1039/c5ra01814e.
55. Silvestre C, Duraccio D, Cimmino S. Food packaging based on polymer nanomaterials. Prog Polym Sci. 2011. https://doi.org/10.1016/j.progpolymsci.2011.02.003.
56. Bumbudsanpharoke N, Choi J, Ko S. Applications of nanomaterials in food packaging. J Nanosci Nanotechnol. 2015. https://doi.org/10.1166/jnn.2015.10847.
57. Irkin R, Esmer OK. Novel food packaging systems with natural antimicrobial agents. J Food Sci Technol. 2015. https://doi.org/10.1007/s13197-015-1780-9.
58. Tripathi S, Mehrotra GK, Dutta PK. Chitosan based antimicrobial films for food packaging applications, E-Polymers. 2008.
59. Cazón P, Velazquez G, Ramírez JA, Vázquez M. Polysaccharide-based films and coatings for food packaging: a review. Food Hydrocoll. 2017. https://doi.org/10.1016/j.foodhyd.2016.09.009.
60. Sun-Waterhouse D, Waterhouse GIN. Recent advances in the application of nanomaterials and nanotechnology in food research, in: Nov. Approaches Nanotechnol. Food, 2016. https://doi.org/10.1016/b978-0-12-804308-0.00002-9.
61. Momin JK, Joshi BH. Nanotechnology in foods, in: Nanotechnologies Food Agric., 2015. https://doi.org/10.1007/978-3-319-14024-7_1.
62. Gleeson JP, Ryan SM, Brayden DJ. Oral delivery strategies for nutraceuticals: delivery vehicles and absorption enhancers. Trends Food Sci Technol. 2016;53:90–101. https://doi.org/10.1016/j.tifs.2016.05.007.
63. Jafari SM, Assadpoor E, Bhandari B, He Y. Nano-particle encapsulation of fish oil by spray drying. Food Res Int. 2008;41:172–83. https://doi.org/10.1016/j.foodres.2007.11.002.
64. Bochicchio S, Barba AA, Grassi G, Lamberti G. Vitamin delivery: carriers based on nanoliposomes produced via ultrasonic irradiation. LWT - Food Sci Technol. 2016;69:9–16. https://doi.org/10.1016/j.lwt.2016.01.025.
65. Azzi J, Jraij A, Auezova L, Fourmentin S, Greige-Gerges H. Novel findings for quercetin encapsulation and preservation with cyclodextrins, liposomes, and drug-in-cyclodextrin-in-liposomes. Food Hydrocoll. 2018. https://doi.org/10.1016/j.foodhyd.2018.03.006.
66. Semenova MG, Antipova AS, Zelikina DV, Martirosova EI, Plashchina IG, Palmina NP, Binyukov VI, Bogdanova NG, Kasparov VV, Shumilina EA, Ozerova NS. Biopolymer nanovehicles for essential polyunsaturated fatty acids: structure–functionality relationships. Food Res Int. 2016;88:70–8. https://doi.org/10.1016/j.foodres.2016.05.008.
67. Dey TK, Banerjee P, Chatterjee R, Dhar P. Designing of ω-3 PUFA enriched biocompatible nanoemulsion with sesame protein isolate as a natural surfactant: focus on enhanced shelf-life stability and biocompatibility. Colloids Surfaces A Physicochem Eng Asp. 2018;538:36–44. https://doi.org/10.1016/j.colsurfa.2017.10.066.
68. Zheng B, Peng S, Zhang X, McClements DJ. Impact of delivery system type on curcumin bioaccessibility: comparison of curcumin-loaded nanoemulsions with commercial curcumin supplements. J Agric Food Chem. 2018;66:10816–26. https://doi.org/10.1021/acs.jafc.8b03174.
69. Nunes S, Madureira AR, Campos D, Sarmento B, Gomes AM, Pintado M, Reis F. Solid lipid nanoparticles as oral delivery systems of phenolic compounds: overcoming pharmacokinetic limitations for nutraceutical applications. Crit Rev Food Sci Nutr. 2017;57:1863–73. https://doi.org/10.1080/10408398.2015.1031337.
70. Papagiannopoulos A, Vlassi E. Stimuli-responsive nanoparticles by thermal treatment of bovine serum albumin inside its complexes with chondroitin sulfate. Food Hydrocoll. 2019;87:602–10. https://doi.org/10.1016/j.foodhyd.2018.08.054.
71. Domínguez Rubio AP. Martínez JH, Martínez Casillas DC, Coluccio Leskow F, Piuri M, Pérez OE. Lactobacillus casei BL23 Produces Microvesicles Carrying Proteins That Have Been Associated with Its Probiotic Effect, Front. Microbiol. 2017;8:1783. https://doi.org/10.3389/fmicb.2017.01783.
72. Ghayour N, Hosseini SMH, Eskandari MH, Esteghlal S, Nekoei AR, Hashemi Gahruie H, Tatar M, Naghibalhossaini F. Nanoencapsulation of quercetin and curcumin in casein-based delivery systems, Food Hydrocoll. 2019;87:394–403. https://doi.org/10.1016/j.foodhyd.2018.08.031.
73. Ruiz-Rico M, Pérez-Esteve É, Lerma-García MJ, Marcos MD, Martínez-Máñez R, Barat JM. Protection of folic acid through encapsulation in mesoporous silica particles included in fruit juices. Food Chem. 2017;218:471–8. https://doi.org/10.1016/j.foodchem.2016.09.097.
74. Singh S, Rathi N, Angal A, Parida P, Rautaray D. Biofortification of Food with Minerals and Vitamins Encapsulated in Silica, in: Springer, Cham, 2016: pp. 157–206. https://doi.org/10.1007/978-3-319-39306-3_5.
75. Mao L, Wang D, Liu F, Gao Y. Emulsion design for the delivery of β-carotene in complex food systems. Crit Rev Food Sci Nutr. 2018;58:770–84. https://doi.org/10.1080/10408398.2016.1223599.
76. Duncan TV. Applications of nanotechnology in food packaging and food safety: barrier materials, antimicrobials and sensors. J Colloid Interface Sci. 2011. https://doi.org/10.1016/j.jcis.2011.07.017.
77. Srivastava AK, Dev A, Karmakar S. Nanosensors and nanobiosensors in food and agriculture. Environ Chem Lett. 2018. https://doi.org/10.1007/s10311-017-0674-7.
78. Haghi M, Hekmatafshar M, Janipour MB, Gholizadeh SS, Faraz MK, Sayyadifar F, Ghaedi M. Antibacterial effect of TiO2

nanoparticles on pathogenic strain of E. coli, Int. J. Adv. Biotechnol. Res. 2012.
79. Bhinder SS, Dadra P. Application of nanostructures and new nano particles as advanced biomaterials. Chem: Asian J; 2009.
80. Mukundan D, Vasanthakumari R. Phytoengineered nanomaterials and their applications, in: Nanotechnol. Food Environ. Paradig., 2017. https://doi.org/10.1007/978-981-10-4678-0_15.
81. Lee BH. Fundamentals of Food Biotechnology: Second Edition. 2015. https://doi.org/10.1002/9781118384947.
82. Sherry M, Charcosset C, Fessi H, Greige-Gerges H. Essential oils encapsulated in liposomes: a review. J Liposome Res. 2013. https://doi.org/10.3109/08982104.2013.819888.
83. Fang Z, Bhandari B. Encapsulation of polyphenols - a review. Trends Food Sci Technol. 2010. https://doi.org/10.1016/j.tifs.2010.08.003.
84. Garti N, McClements DJ. Encapsulation technologies and delivery systems for food ingredients and nutraceuticals. 2012. https://doi.org/10.1533/9780857095909.
85. Teng Z, Luo Y, Wang Q. Nanoparticles synthesized from soy protein: preparation, characterization, and application for nutraceutical encapsulation. J Agric Food Chem. 2012. https://doi.org/10.1021/jf205238x.
86. Davidov-Pardo G, McClements DJ. Nutraceutical delivery systems: resveratrol encapsulation in grape seed oil nanoemulsions formed by spontaneous emulsification. Food Chem. 2015. https://doi.org/10.1016/j.foodchem.2014.06.082.
87. Chen L, Remondetto GE, Subirade M. Food protein-based materials as nutraceutical delivery systems. Trends Food Sci Technol. 2006. https://doi.org/10.1016/j.tifs.2005.12.011.
88. Ribeiro-Santos R, Andrade M, Sanches-Silva A. Application of encapsulated essential oils as antimicrobial agents in food packaging. Curr Opin Food Sci. 2017. https://doi.org/10.1016/j.cofs.2017.01.012.
89. Ramaswamy S, Dwarampudi LP, Kadiyala M, Kuppuswamy G, Veera Venkata Satyanarayana Reddy K, Kumar CKA, Paranjothy M. Formulation and characterization of chitosan encapsulated phytoconstituents of curcumin and rutin nanoparticles, Int. J. Biol. Macromol. 2017. https://doi.org/10.1016/j.ijbiomac.2017.06.112.
90. Rao PJ, Naidu MM. Nanoencapsulation of Bioactive Compounds for Nutraceutical Food, in: 2016. https://doi.org/10.1007/978-3-319-39306-3_4.
91. Gopi S, Amalraj A. Introduction of nanotechnology in herbal drugs and nutraceutical: a review. J Nanomedine Biotherapeutic Discov. 2016. https://doi.org/10.4172/2155-983x.1000143.
92. V.K. Chatap, S.D. Patil, Dissolution rate enhancement of repaglinide using dietary fiber as a promising carrier, Curr. Drug Deliv. 2016.
93. Chen X, McClements DJ, Zhu Y, Chen Y, Zou L, Liu W, Cheng C, Fu D, Liu C. Enhancement of the solubility, stability and bioaccessibility of quercetin using protein-based excipient emulsions. Food Res Int. 2018. https://doi.org/10.1016/j.foodres.2018.07.062.
94. Saoji SD, Dave VS, Dhore PW, Bobde YS, Mack C, Gupta D, Raut NA. The role of phospholipid as a solubility- and permeability-enhancing excipient for the improved delivery of the bioactive phytoconstituents of Bacopa monnieri. Eur J Pharm Sci. 2017. https://doi.org/10.1016/j.ejps.2016.08.056.
95. T.K. Giri, Bioavailability enhancement of curcumin nutraceutical through nano-delivery systems, in: Nutraceuticals, 2016. https://doi.org/10.1016/b978-0-12-804305-9.00015-4.
96. Gonçalves RFS, Martins JT, Duarte CMM, Vicente AA, Pinheiro AC. Advances in nutraceutical delivery systems: from formulation design for bioavailability enhancement to efficacy and safety evaluation. Trends Food Sci Technol. 2018. https://doi.org/10.1016/j.tifs.2018.06.011.
97. Li C, Zhang J, Zu YJ, Nie SF, Cao J, Wang Q, Nie SP, Deng ZY, Xie MY, Wang S. Biocompatible and biodegradable nanoparticles for enhancement of anti-cancer activities of phytochemicals. Chin J Nat Med. 2015. https://doi.org/10.1016/S1875-5364(15)30061-3.
98. Skalickova S, Milosavljevic V, Cihalova K, Horky P, Richtera L, Adam V. Selenium nanoparticles as a nutritional supplement. Nutrition. 2017. https://doi.org/10.1016/j.nut.2016.05.001.
99. Ho CT, Huang MT, Lou YR, Xie JG, Newmark HL, Yang CS, Conney AH. Inhibitory Effects of Black Tea, Green Tea, Decaffeinated Black Tea, and Decaffeinated Green Tea on Ultraviolet B Light-induced Skin Carcinogenesis in 7,12-Dimethylbenz[a]anthracene-initiated SKH-1 Mice, Cancer Res. 1994.
100. Freag MS, Elnaggar YSR, Abdallah OY. Lyophilized phytosomal nanocarriers as platforms for enhanced diosmin delivery: optimization and ex vivo permeation. Int J Nanomedicine. 2013. https://doi.org/10.2147/IJN.S45231.
101. Zhang Z, Zhang R, Zou L, Chen L, Ahmed Y, Al Bishri W, Balamash K, McClements DJ. Encapsulation of curcumin in polysaccharide-based hydrogel beads: Impact of bead type on lipid digestion and curcumin bioaccessibility, Food Hydrocoll. 2016. https://doi.org/10.1016/j.foodhyd.2016.02.036.
102. Onwulata CI. Microencapsulation and functional bioactive foods. J Food Process Preserv. 2013. https://doi.org/10.1111/j.1745-4549.2012.00680.x.
103. Singh S, Lal UR. In vivo evaluation of curcumin loaded granules using Eudragit FS30D and Guar-gum coating in the treatment of ulcerative colitis in albino rats. Knowl: Indian J. Tradit; 2016.
104. Singh S, Hussain A, Lal UR, Sayyad N, Karpoormath R, Nlooto M. In vitro -in vivo- in silico simulation of experimental design based optimized curcumin loaded multiparticulates system. Curr Pharm Des. 2018. https://doi.org/10.2174/1381612824666181022120252.