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Nano-probiotics and nano-prebiotics potential applications

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ABSTRACT
Nanoparticles are everywhere, which makes them harmful. This calls for the development of nano-nutraceuticals from antioxidants, vitamins, fatty acids, fibers, probiotics, and prebiotics. In this mini-review, nanoparticles, nanolayers, nanobeads, nanoemulsions, and nanofibers are used with probiotics and prebiotics for numerous applications as found in cancer, microbial, antioxidant, and photo-reactive studies. Not so much could be discussed probably because of safety issues but a lot of practical potentials abounds.

KEYWORDS
nanoparticles; nutraceuticals; nanoprebiotics; nanoprobiotics; applications

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INTRODUCTION
Humans have always improved the means of solving life's challenges such as diseases. For example, chemically synthesized drugs are now replaced with less toxic ones, while the focus on potential applications of therapeutic or curative food-derived products is becoming more intense [1]. However, nutraceuticals or nutritional substances such as vitamins, polyunsaturated fatty acids, antioxidants, fibers, probiotics, and prebiotics, have not been fully explored for this purpose.

Probiotics and prebiotics have gained popularity among nutraceuticals. Microorganisms are integrated into life processes and the beneficial ones affect physiological homeostasis and host function; while prebiotics does not only support bifidobacterial and lactobacilli growth but are also now recognized for their metabolic readouts [2]. Many research show probiotics and prebiotics as nutritional substances that could complement pharmaceuticals and foods, as both often work synergistically to confer physiological and systemic benefits [3,4]. Considering potential enhancements of nanosized products in terms of properties and functions among others, and the curiosity on any potential safety risks, applying nanotechnology to probiotics and prebiotics presents an exciting area of research. This mini-review is straightly dealing with applications of nano-probiotics and prebiotics and some other noteworthy considerations.

APPLICATION OF NANO-PROBIOTICS AND PREBIOTICS
Some health benefits of probiotics include immunomodulatory [5], anti-inflammatory [6], anti-allergic [7], anticancer [8], antimicrobial [9], anti-diabetic [10], and anti-obesity [11] activities, while for prebiotics, anticancer [12], immunomodulatory [13], anti-cholesteremic [14], anti-obesity, constipation and anti-diabetic [15], and antioxidant [16] potentials have been reported. Prebiotics also support probiotic growth [17], reduce the risk of non-diabetic chronic disease [18] and enhance gut health via bacteriocins production [19].

Therefore, some recent studies have considered the emerging potentials of probiotics and prebiotics when some forms of nanotechnologies are applied to them. It is pertinent to know that probiotics and prebiotics could be regarded as microbial medicines, implying that other than being functional within the gut when ingested orally; they could deliver therapeutic effects also in drug-based formulations. For example, nano- probiotics have been used to prevent and treat neuroinflammation, and possess potential cancer immunotherapeutic functions [20]. In another study, a therapeutic strain of Salmonella typhimurium was engineered with nanoparticles for the detection, identification, and inhibition of prostate cancer cells at the targeted action sites [21].

Targeting the gastrointestinal tract, a study shows that probiotic spores may provide a good alternative delivery system for chemotherapeutic drugs [22]. Deoxycholic acid-modified spores were produced and loaded with doxorubicin and sorafenib to be orally administered chemotherapeutic nanoparticles with improved bioavailability in the gastrointestinal tract. The rate of release of broken hydrophilic deoxycholic acid and hydrophobic protein enhanced the stability of drugs in the gastrointestinal tract in order to overcome biological barriers of intestinal epithelium via the bile acid pathway, providing a promising strategy for oral drug and cancer therapy [22]. In another clime, MTT assay study of silver/Lactobacillus rhamnosus GG nanoparticles anticancer activity, demonstrated that viable HT-29 cell lines remarkably reduced after applying the highest nanoparticles concentration; which also resulted in apoptosis [23]. The study used an economically feasible technique, quite beneficial for biomedical applications of nanoprobiotics. Diarrhea among other gastrointestinal disorders could be treated with nanoprobiotics. For instance, the quantification of nanoparticles in commercial chocolates and subsequent evaluation of the particles' effect on a commercial probiotic formulation (B. coagulans, E. faecalis, and E. faecium) meant to treat infants diarrhea showed conventional probiotic activities such as biofilm formation, acid production, growth and antibiotic resistance, from isolated bacteria [24]. Moreover, isolated titanium dioxide nanoparticles from the chocolates reportedly inhibited the growth and activity of the probiotic formulation at 125–500 µg/mL concentration in vitro [24]. This particular study shows the potential of nanoprobiotics and their limitations in the presence of titanium dioxide once within the gastrointestinal tract, as against other studies.

Several techniques of tuning probiotics into nanoprobiotics and their delivery thereof are continuously being explored. As examples, gold and selenium particles (10–1000 nm size), nanolayers (charged polyelectrolyte, a polymeric layer and a functionalized polysaccharide or polyether, among others), nanobeads (nanosized bacteria-enabled autonomous delivery system), nanoemulsions (liquid phase dispersion in another liquid phase with droplet size < 200 nm) and nanofibers are currently been explored as encapsulation nanoparticles of probiotics [1]. Encapsulation of probiotic cells aids their protection in a harsh environment like the gastrointestinal tract, and thus ensures their smooth release for more viability and activity in the host system. Important to note is that antibiotics create resistance and disrupt the microbial flora of the intestines. Therefore, well-encapsulated probiotics could serve as an alternative to the common antibiotics to curb the menace. For example, once P. acidilactidi was loaded into phthalyl dextran or phthalyl inulin nanoparticles, antimicrobial peptides production was more enhanced by probiotic cells in a self-defense mechanism, as compared to probiotics alone [25]. The antimicrobial effect recorded was against both Gram-positive and Gram-negative organisms and was an improved one. In the same manner, phthalyl pullulan nanoparticles loaded into L. plantarum via an energy-dependent and galactose transporter-dependent mechanism demonstrated antimicrobial effects against Escherichia coli K99 and Listeria monocytogenes [26]. It was reported that a higher amount of a natural antibacterial peptide (plantaricin) was secreted from the developed nanoprobiotics than from probiotics alone [26]. Figure 1 elaborates on nanoprobiotics and nanoprebiotics types, specific characteristics, and their potential applications.

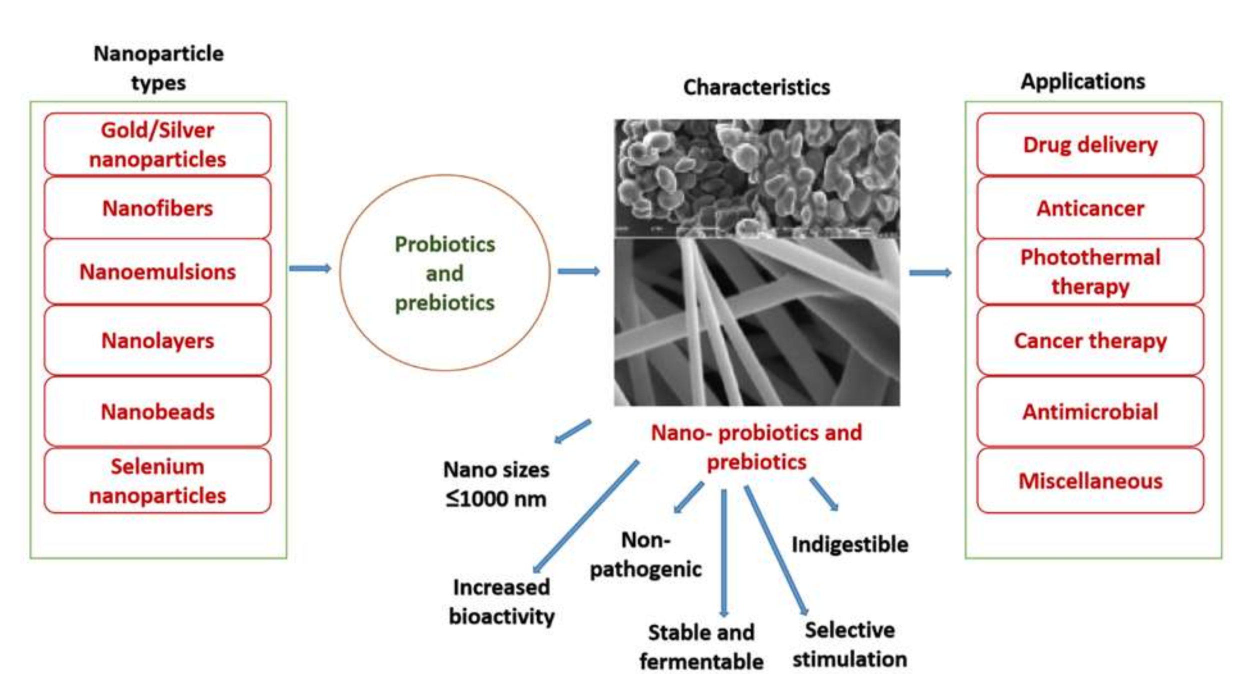

FIGURE 1: Nano-probiotics and nano-prebiotics types, specific characteristics and their potential applications.
Source: [4]

Nanosystems can also be created from the mechanism of using prebiotics to enhance probiotics' action and effect. For instance, the application of silver and titanium dioxide nanoparticles to L. casei ATCC 39392, L. plantarum ATCC 8014, and L. fermentum ATCC 9338 probiotic strains, with or without raffinose, lactulose, and inulin prebiotics, respectively, showed a decrease in the organisms' number by the nanoparticles in the presence of the prebiotics, which shows their antimicrobial potentials [27]. In another study, a prebiotic formulation comprising Pediococcus acidilactidi and phthalyl dextran nanoparticles with antimicrobial potentials was developed [28]. The researchers conjugated phthalic anhydride with dextran in the process and found that phthalyl dextran nanoparticles were internalized by probiotics based on time, temperature, and glucose transporters, enhancing antimicrobial peptides production and antimicrobial activity while increasing beneficial bacteria in mice through self-defense mechanism compared with probiotics themselves [28].

Nanofibers are also used as encapsulants of probiotics such as L. acidophilus and other lactic acid bacteria, to thermally protect probiotics in heat-processed foods and provide long-term stability for huge amounts of living bacteria if they are kept at ≤ 7 °C in vaginal drug delivery systems among others [29]. The studies mostly employed the electrospinning technique, due to its sterile nature, biocompatibility, adhesiveness, efficiency, and as a vehicle for controlled and sustained release in drug delivery, potentials highly sought after in the food and pharmaceutical industries [30]. Although the research carried out on nanoprebiotics is exhaustive, the ones that are known include the development of whey protein isolate/inulin nano complexes with prebiotic effects, and as a delivery system for various probiotics in food products, and the use of chitosan as a nanoencapsulant of L. acidophilus for enhanced viability and survival against gastrointestinal conditions [31].

FURTHER CONSIDERATIONS AND CONCLUSION

The potential applications of nano-probiotics and nano-prebiotics are huge be it in the pharmaceutical or food industries, and other sectors. Just as any engineered nanoparticles or materials attract some degree of attention due to limited comprehension of their mechanisms and health consequences, nano-probiotics and nano-prebiotics may need some degree of careful studies and detailed research. The safety of nanoparticles-based systems must be ascertained, along with their physicochemical characteristics for the sake of informed policies of regulatory bodies. In vivo and clinical research outcomes on nano-probiotics and nano-prebiotics are also few whereas they are essential and required to ascertain their effectiveness and safety. Conclusively, further investigations are required concerning the safety, bioavailability, and viability of these nanoproducts.

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