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REVIEW

Microfluidization trends in the development of nanodelivery systems and applications in chronic disease treatments

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Abstract: Plant bioactive compounds are known for their extensive health benefits and therefore have been used for generations in traditional and modern medicine to improve the health of humans. Processing and storage instabilities of the plant bioactive compounds, however, limit their bioavailability and bioaccessibility and thus lead researchers in search of novel encapsulation systems with enhanced stability, bioavailability, and bioaccessibility of encapsulated plant bioactive compounds. Recently many varieties of encapsulation methods have been used; among them, microfluidization has emerged as a novel method used for the development of delivery systems including solid lipid nanocarriers, nanoemulsions, liposomes, and so on with enhanced stability and bioavailability of encapsulated plant bioactive compounds. Therefore, the nanodelivery systems developed using microfluidization techniques have received much attention from the medical industry for their ability to facilitate controlled delivery with enhanced health benefits in the treatment of various chronic diseases. Many researchers have focused on plant bioactive compound-based delivery systems using microfluidization to enhance the bioavailability and bioaccessibility of encapsulated bioactive compounds in the treatment of various chronic diseases. This review focuses on various nanodelivery systems developed using microfluidization techniques and applications in various chronic disease treatments.

Keywords: bioavailability, solid lipid nanoparticles, plant bioactive compounds, nanoemulsions

Introduction

Currently there is an increasing demand for natural plant bioactive compounds in the treatment of various chronic diseases like cancer and diabetes, and neurological and other age-related chronic diseases owing to lower side effects.[1–5] This demand has led to inter-collaboration across multiple research areas including medicinal, functional food, pharmaceuticals, and nutraceuticals. Owing to various process parameters during extraction, poor stability, oral environmental conditions, inaccessibility, and bioavailability, the application and development of various plant bioactive compound-based treatments for chronic diseases have been limited.[6–12] Therefore, an innovative approach that can protect bioactivity during oral treatments as well as provide enhanced bioavailability of those plant bioactive compounds for the successive treatment of chronic diseases is necessary.

Nanoencapsulation has been an efficient method of encapsulation of plant bioactive compounds to enhance the protection, stability, and bioavailability of plant bioactive compounds.[4,13,14] Various nanodelivery systems including solid lipid nanocarriers, nano-structured lipid carriers, nanoemulsions, and nanoliposomes have been efficiently used in the development of encapsulation of the plant bioactive compounds with

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their own merits and demerits for the treatment of chronic diseases.[2–5,13,15–17] Several techniques like emulsification, supercritical fluidization, high-pressure homogenization, and ultrasonication are most commonly used in the development of those nanodelivery systems.[18–21] However, the stability of these nanodelivery systems when loaded with plant bioactive compounds was not acceptable. This in turn affects the bioavailability and bioaccessibility of those plant bioactive compounds developed through nanodelivery systems using conventional techniques. Microfluidization techniques have been recently applied in the development of nanodelivery systems with enhanced stability and bioavailability of plant-based bioactive compounds.[22–24]

Novel stable nanodelivery systems have been developed with microfluidization techniques with enhanced stability of encapsulated compounds.[25] The major advantages of the techniques include higher stability with a smaller particle size, higher scale production of nanodelivery systems with higher reproducibility, no aggregation of developed nanodelivery systems along with lower fusibility, and higher encapsulation efficacy with lower usages of other solvents.[26–30] Further microfluidized nanodelivery systems with reduced particle size and higher bioaccessibility[31,32] can be effectively achieved using food grade biopolymer along with non-toxic and highly biodegradable carriers, which can broaden its application in nutraceutical and functional food development using plant-based bioactive compounds for chronic disease treatments. Recently, many different types of food grade polymer carriers including polysaccharides and proteins have been effectively used in the production of mini emulsion production for its uniformity in production and higher reproducibility using the microfluidization process. To the best of our knowledge, no review paper on the application of microfluidization in nanodelivery systems development for the effective delivery of plant bioactive compounds and its application in chronic disease treatment has been published.

Microfluidization

Plant bioactive compound-based nanodelivery systems development using microfluidization is an emerging technique to enhance the stability and bioavailability of the incorporated plant bioactive compounds.[26,33] Development of stable nanodelivery systems using plant bioactive compounds has been a research area of emerging delivery systems in the medical field, thereby facilitating oral delivery without much loss in activity.[33–35] Microfluidization mechanism is very essential to understand the development of stable nanodelivery systems, thereby enhancing the production of those systems with broader applications through the interdisciplinary approach of nutraceuticals and medicine.[36,37] The microfluidization process is a type of high energy process which works on the dynamics of the specially designed microchannels. The generated turbulence and momentum makes the lipid carrier overcome its barrier. The pump driven by the compressed air mixe the lipids and active compounds at very high velocities in the designed microchannels, thereby forming stable delivery systems of a nano size.[34,35] In the development of nanodelivery systems, two types of microfluidization are currently practiced. One is two-step, single-channel microfluidization and the other is single-step, dual-channel microfluidization, with their own advantages and disadvantages. In the case of the nanoemulsion-based delivery system, microfluidization-based nanoemulsion developed using a two-step single channel has many disadvantages like additional energy and more expensive wastage of lipid and oil for making coarse emulsion initially to be fed into the microfluidizer.[38] However, single-step dual-channel microfluidization overcomes the above disadvantages and thereby prepares the stable nanoemulsion with higher loading abilities, thereby having broader application in the medical, food, and nutraceutical sectors. Microfluidizing types are shown in Figure 1.

Microfluidization has several advantages over the development of nanodelivery systems. For example, microfluidization mechanism eases the development of the stable nanoemulsion with the particle size $<$160 nm.[39] The mechanism involves forcing the coarse emulsion through microchannels to the particular area by pneumatically powered pump by pressurizing compressed air up to about 150 MPa which results in nanoemulsion,[35,40] and the different passes lead to different sizes. It is also an easy-to-use and effective method for the development of other stable nanodelivery systems. Those developed nanodelivery systems show enhanced stability of the incorporated bioactive compounds, uniformity, and greater reproducibility, and food grade delivery systems can be effectively developed for greater application and development of functional food.[28,34,41–44] Recently, weighted orange oil terpenes used with different food grade polymers like modified gum arabic and modified starch to prepare nanoemulsion with the particle size of about 77 nm showed enhanced stability for the clear beverage development using microfluidization.[45] In addition, it has greater advantages in the medical field for its oral delivery with greater bioavailability and the sustained release of incorporated bioactive compounds. For example, orange oil nanoemulsion developed using ester gum incorporated in oil

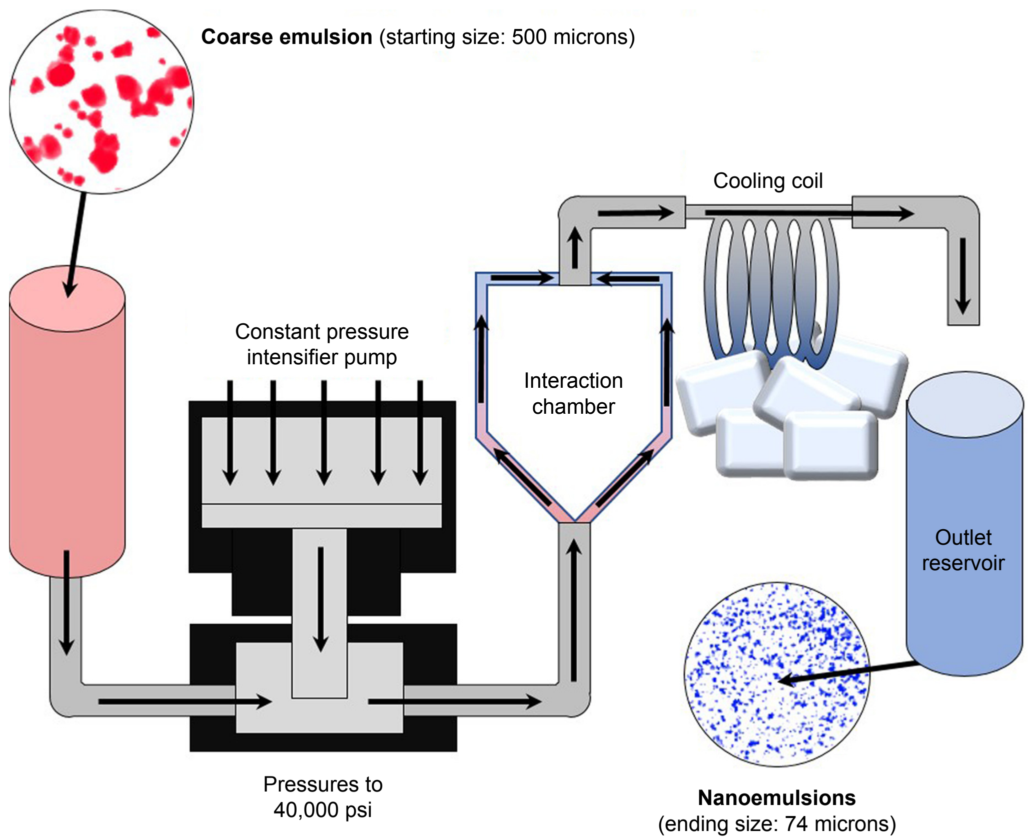

Figure 1 Microfluidization process for the preparation of nanodelivery systems.

phase and *Quillaja saponins* in continuous phase has higher stability of 2 weeks with the particle size of about 69 nm.[46]

Microfluidization-based nanoencapsulation of plant bioactive compounds

Plant bioactive compounds play a critical role in the prevention and treatment of various chronic diseases including cancers, type 2 diabetes, hypertension, obesity, and neurological diseases. Traditionally, food-based medicine or phytomedicine is followed generally throughout the world, and some bioactive compounds are documented in several countries.[6,10,11,47,48] In general practice, plant bioactive compounds are orally consumed in the form of either extracts or nutraceuticals, which benefit mankind by inhibiting or slowing down the occurrence of diseases by anticancer, anti-inflammation, antidiabetic, antiobesity, and antioxidation mechanisms. However, during oral consumption of plant bioactive compounds, their activity and mechanisms are fully achieved due to numerous factors in the gastrointestinal tracts. In order to overcome those factors, encapsulation of those bioactive compounds is a very efficient alternative, thereby enhancing activity and disease prevention. Several researchers have recently studied the development of various nanoencapsulation systems for higher encapsulation and greater efficacy in nanoencapsulated bioactive compounds using microfluidization. Nanoencapsulated plant bioactive compounds using microfluidization have greater stability of the developed systems and can also be repeatable in bulk production. In addition, a microfluidized delivery system can be produced in a uniform size, and there is less breakage and release of encapsulated bioactive compounds in comparison with other systems.[28,29,49–51] Furthermore, lower usage of the organic solvents is required, and a food grade carrier can be used to develop highly biodegradable, lower toxic delivery systems. Therefore, the current work focused on providing a detailed review of the developed nanodelivery systems for plant bioactive compounds using microfluidization and its application in various chronic disease treatments.

Development of microfluidization-based nanodelivery systems

Nanodelivery systems play a key role in the delivery of plant bioactive compounds in enhanced oral delivery mostly due to the smaller size and higher surface exposure of those bioactive compounds. However, based on the size and preparation of those delivery systems using different equipment, different characteristic effects were shown in the functional properties of developed nanodelivery systems.[6,10,11,47,48] In a recent study, solid lipid nanoparticles (SLNs) developed using microfluidization showed a smaller particle size of about 36–136 nm along with enhanced stability when generated using microfluidizing techniques.[52] Similarly, pickering nanoemulsions with very high stability were also developed using microfluidization by preventing droplet coalescence with surface coverage and achieving a higher bridging effect between the droplet. Based on the abovementioned few studies, the microfluidizing effect showed higher stability in the development of nanodelivery systems.[53] Therefore, it can enhance the bioavailability of those encapsulated compounds and can be helpful in the remedies for various chronic diseases. Microfluidized nanodelivery systems are shown in Figure 2. Briefly, some of the nanodelivery systems developed using microfluidization and their properties are discussed in this section.

SLNs

SLNs are among the lipid nanocarriers developed for transporting the hydrophobic bioactive compounds with higher loading capacity along with the enhanced stability of the loaded bioactive compounds.[54–60] SLNs showed higher loading efficacy and bioavailability of various plant bioactive compounds like curcumin, resveratrol, quercetin, and catechin. These plant-derived bioactive compound–loaded SLNs showed higher potential in the prevention and cure of various chronic diseases.[61–66] Curcumin-loaded SLNs with some modification have been recently developed, showing a higher anticancer effect with enhanced loading efficacy. SLNs have been developed using different methods including high-speed homogenization, spray drying, cold homogenization, hot homogenization, ultrasonication, double emulsion, and supercritical technology. Usage of all those techniques includes various advantages and disadvantages in the development of SLNs.[67–69] The major disadvantages of the above systems in the development of SLNs include partitioning of the lipids, lower stability, and higher usage of the organic solvents, which limit its development in novel SLN development for chronic disease treatment. Recently, microfluidization was used for the development of SLNs with very high loading efficacy and higher bioavailability of those encapsulated compounds in the SLNs.[70–75] Microalgae oil contains a higher amount of docosahexaenoic acid (DHA; 22:6), which is among the essential fatty acids required in

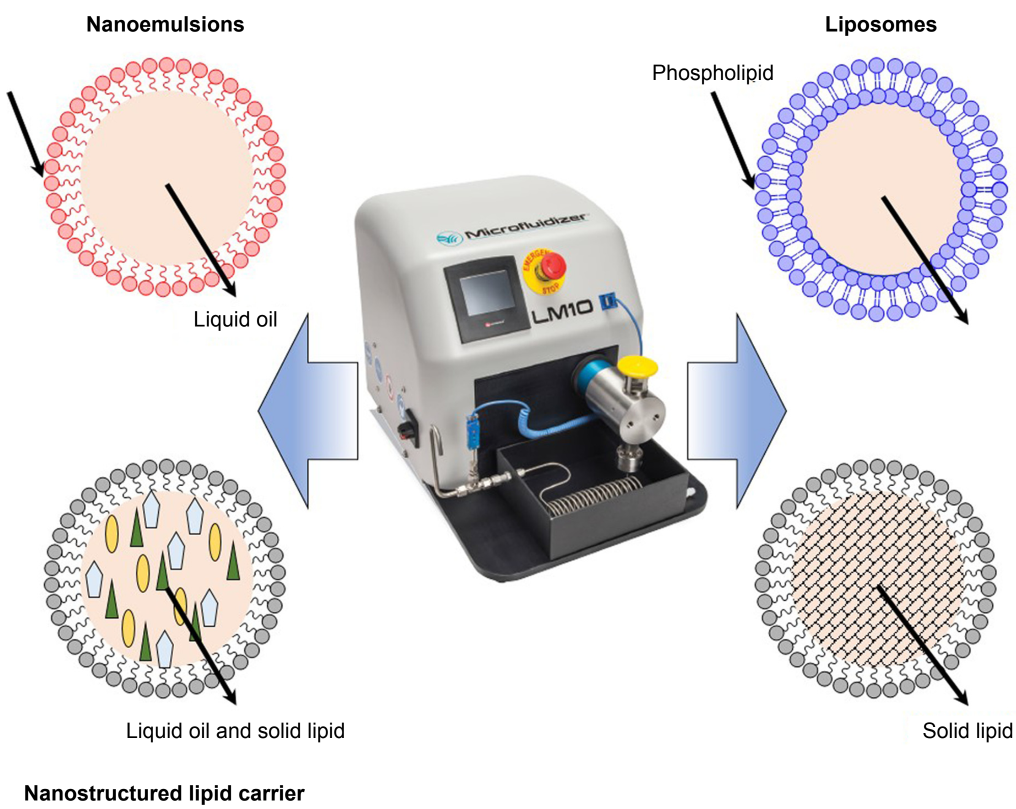

Figure 2 Applications of microfluidization process in the development of various nanodelivery systems.

healthy brain development and for various body functions. Consumption of the microalgae oil rich in DHA showed various beneficial activities in humans, including anticancer and antineurological properties and enhanced heart function. However, due to lesser stability and bioactivity loss during oral consumptions, alternatively SLNs were developed using microalgae oil. Higher encapsulation efficacy and lower particle size were highly achieved through the microfluidization techniques in the microalgae-loaded SLNs. Microalgae oil-rich DHA-loaded SLNs developed with the particle size of about 300–350 nm with uniform distribution of oil in the SLNs could be potentially applicable in functional food development[76] with prevention or treatment of chronic diseases. Similarly, transparent and stable SLNs can be developed using microfluidization techniques and could be highly applicable in the development of various plant bioactive compound–loaded SLNs.

Nanoemulsions

Nanoemulsions are one among the nanodelivery systems that play a key role in the delivery of plant bioactive compounds like curcumin, resveratrol, and quercetin for its enhanced application in the prevention and treatment of chronic diseases.[77–80] The advantages of incorporating bioactive compounds in nanoemulsion are smaller particle size, higher stability, and transparent emulsion, where the scattering effect of the light is very low compared with that of normal emulsions. The coalescence and flocculation effect of the plant bioactive compound–loaded nanoemulsion was much lower due to the small particle size, and thus the attractive forces between the droplets will be greatly reduced. Nanoemulsion can be effectively prepared using various methods like low energy methods including spontaneous formation by mixing or phase inversion and a high energy method including high-pressure homogenizer or sonication. Every method has its own advantages and disadvantages in the preparation of the nanoemulsion-loaded plant bioactive compounds.[81–85] The most common disadvantages of these methods are usage of synthetic solvents, emulsifiers or oils, bioavailability and potential toxicity of the solvents, and stability during oral delivery. To overcome the above disadvantages, a microfluidizer has recently been used in the development of the nanoemulsion with a smaller particle size, higher stability, and higher encapsulation efficacy of incorporated bioactive compounds.[35,38,45,86–89] The application of microfluidized nanoemulsions is shown in Figure 3. Curcumin is among the top bioactive compounds extensively used in traditional medicine for generations owing to its greater potential effects including anticancer, antihypertension, antidiabetic, and antineuroinflammatory effects. Owing to the lower solubility and lesser bioavailability of those compounds, many studies on the development of curcumin-loaded nanoemulsion

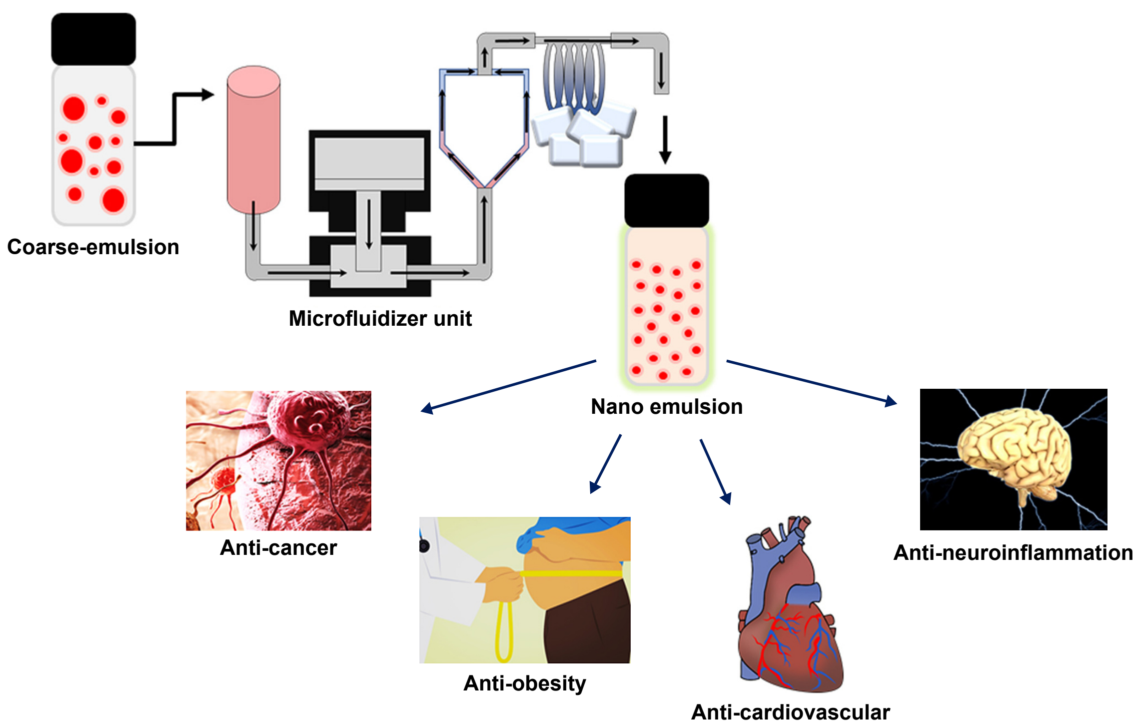

Figure 3 Microfluidized nanoemulsion applications in the treatment of various chronic diseases.

development have found higher beneficial effects in the treatment of various chronic diseases. In order to enhance its efficacy, various approaches have used curcumin-loaded nanoemulsion for the enhanced bioavailability of the curcumin. Microfluidized nanoemulsion can be obtained with a particle size of about 275 nm[90] with higher stability, which can scatter light weakly, and it could be highly applicable in food grade bioactive compounds or nutraceutical development.

Nanoliposomes

Nanoliposomes are yet another delivery vehicle made up of phospholipid bilayers, which contain aqueous compartments that can encapsulate various plant bioactive compounds for the controlled and sustained delivery of the encapsulated active compounds. Owing to the lower particle size and controlled delivery, it has a wide range of applications in medicine, pharmaceuticals, nutraceuticals, and functional foods.[91–95] Various methods are involved in the preparation and development of nanoliposomes for enhanced stability like ultrasonic injection, ethanol injection, and homogenizer methods.[96–102] The above methods are able to produce plant bioactive compound–loaded nanoliposomes, but the encapsulation efficacy and bioavailability of those encapsulated bioactive compounds vary with the methods.[103–108] Recently, the microfluidization method has been very effectively used for plant bioactive compound–loaded nanoliposome development, overcoming the above disadvantages in the preparation method and enhancing the sustained release of those bioactive compounds. Tea polyphenol–loaded nanoliposome was effectively prepared using the microfluidization method with a particle size of about 66 nm along with enhanced stability of those developed nanoliposomes.[107] The same research group also developed nanoliposome with different production technologies including a high-pressure homogenizer and ultrasonication methods with a particle size $>$100 nm. Higher stability and sustained release of the tea polyphenol–loaded nanoliposomes were observed in the microfluidized nanoliposomes, and it could be applicable in the development of food grade nutraceuticals and medicine. In a recent study, black carrot extract rich in anthocyanin-loaded nanoliposome was also developed with a particle size of $<$50 nm, and it could be helpful in the development of nutraceuticals.[109] Similarly, vitamin C–loaded nanophytosomes were also developed with a lower particle size and higher stability, and sustained release of vitamin C was achieved through the microfluidization method.[109] The particle size of the nanophytosomes developed by microfluidized method was about 92 nm, which was much lower than the traditional method.[110] The skin permeation study of vitamin C–loaded nanoliposomes developed using the microfluidization method was very high in comparison with liposomes and vitamin C during 24 hours. Similarly, curcumin-loaded nanoliposomes were also developed using microfluidization techniques with a lower particle size of about 68 nm and higher stability than the liposomes. The stability of the curcumin-loaded nanoliposomes was also enhanced against alkaline pH and metal ions. Refrigerated storage temperature also enhances the stability of microfluidized nanoliposomes along with the sustained release of the encapsulated curcumin.[111] Overall, the microfluidization method could be effectively used in the preparation of nanoliposome loaded with plant bioactive compounds for its enhanced application in the nutraceutical, functional food, pharmaceutical, and medicine industries.

Nanosuspensions

Microfluidized nanosuspensions are among the emerging techniques in the development of low soluble bioactive compound-based nanosuspension. Microfluidization helps to increase the bioavailability of those compounds by reducing the particle size and thereby increasing the surface area. Microfluidization-based nanosuspensions have several advantages over the traditional suspensions including lower particle size, higher stability, a simple process, and higher dissolution rate.[112–118] Several drug-based nanosuspensions were developed with higher efficiency in the bioavailability of those drugs in various chronic disease treatments. Recently, budesonide nanosuspension was developed using the microfluidization method with a smaller particle size of about 122 nm. The pulmonary delivery and distribution of the drug in the lung were higher than that of the normal-sized particles.[119] Similarly, another drug named ritonavir suspension was developed using the microfluidization process with a uniform lower particle size and higher efficacy of about 3.5-fold. In another study, the plant bioactive compound gambogenic acid nanosuspensions were developed using the solvent precipitation method with the particle size of about 183 nm with higher anticancer efficacy than gambogenic acid.[120] However, microfluidization-based nanosuspension will be an alternative approach in the delivery of many plant bioactive compound-based nanosuspensions with higher efficacy in the bioavailability of those compounds against various chronic diseases.

Poly(lactic-co-glycolic acid) (PLGA)-based nanoparticles

PLGA-based nanoparticles are highly used in the delivery of various drugs and bioactive compounds as carriers for their sustained release and target-specific delivery. PLGA was widely accepted by the FDA owing to the lower toxicity; after hydrolysis, it can produce monomers without any harmful effects.[121–127] Various methods were used in the preparation of PLGA-based nanoparticles including emulsification, solvent precipitation, nanoprecipitation, and interfacial polymerization methods. Different methods have advantages and disadvantages in PLGA-based nanoparticle development and drug loading efficacy while the major limitations in most methods involve no uniformity and large-scale production limitations. This leads researchers to search for low energy, higher uniform bulk production, and microfluidization overcomes the limitation in the development of PLGA-based nanoparticles in the entrapment of various drugs[128–130] and plant bioactive compounds. Recently, efavirenz-loaded PLGA nanoparticles were also developed using the microfluidization method with a particle size of about 73 nm along with the higher permeability of about 1.3-fold higher than the normal drug, thus showing a higher anti-HIV effect. It makes the researchers in use of plant bioactive compound-based PLGA nanoparticles for the efficient delivery using microfluidization methods.[131] Recently, curcumin-loaded PLGA nanoparticles were developed using microfluidization methods with a particle size of about 30–70 nm, controlled delivery, and lower degradation of the curcumin. Higher anticancer efficacy of the developed nanoparticle was also observed against cancer cell lines.

Role of microfluidized nanodelivery systems loaded with plant bioactive compounds in chronic diseases

Microfluidization techniques help to produce various nanodelivery systems including SLNs, nanoemulsions, nanoliposomes, and PLGA nanoparticles loaded with drugs or plant bioactive compounds with enhanced stability and bioavailability of those loaded compounds.[132–139] Various in vitro or in vivo studies have confirmed that these microfluidized nanodelivery systems loaded with bioactive compounds showed enhanced protection in the treatment of chronic diseases including cancer, obesity, neurological diseases, and diabetes. A few of those studies are discussed in the following sections.

Anticancer effect

Cancer is among the major chronic diseases that cause major human death throughout the world, and scientists work diligently to produce various drugs for its treatment.[140–142] General medical practice includes radiation and chemotherapy, which lead to various other complications leading the patients in much stress.[143–145] Recently, nanomedicine has played a vital role in the treatment of cancer overcoming several side effects of traditional medicines, although nanodelivery systems loaded with drugs or plant-based bioactive compounds face critical challenges in the delivery of the bioactive compounds to the target sites and through the delivery systems.[146–149] Microfluidization techniques try to solve some disadvantages during the production of those nanodelivery systems developed using anticancer drugs or plant-based bioactive compounds. Curcumin, resveratrol, quercetin, and catechin are the most active compounds showing extensive benefits in anticancer activities. Recently curcumin-loaded palm oil–based nanoemulsion was developed with a smaller particle size, and it could be used in future food-based nanomedicine against various cancer treatments. Similarly, curcumin nanoliposome also produced using curcumin as an active compound by using microfluidization techniques with the particle size of about 68 nm showed sustained release of the curcumin, which could be useful for chronic diseases including cancer.[111] Recently, a plant-based bioactive compound known as camptothecin, a compound from Chinese tree bark, was used in the development of target-specific nanolipospheres owing to the potential toxicity of the active compound to the natural cells. Researchers developed target-specific nanolipospheres of $<$20 nm size by using those active compounds,[150] and further research is necessary in terms of their toxicity effects on normal cells during treatments.

Antiobesity effects

Obesity is yet another major cause linked to various chronic diseases including hypertension, diabetes, and cardiovascular diseases. Consuming lipid-rich foods and sedentary lifestyle link to obesity, and it is a big burden to the well-being of mankind.[151,152] Treating obesity with plant-based bioactive compounds in the form of food, nutraceuticals, or drugs is practiced.[9,10,153–158] However, the bioavailability of those compounds through oral delivery faces many challenges. Recently, nanomedicine develops antiobesity bioactive compound–loaded nanodelivery systems, which has enhanced the delivery potential over traditional medicines. Recently, microfluidized nanomedicines developed using antiobesity bioactive compounds have enhanced the stability of nanodelivery systems. Capsaicin is among the major plant bioactive compounds extensively used in the treatment of obesity. Owing to higher pungency, odor, and low solubility, its usage and its bioavailability of the bioactive compounds in the treatment of obesity are limited.[159–162] Recently, microfluidization techniques have been extensively used in the development of food grade nanodelivery systems or nanomedicines for the enhanced bioavailability of the capsaicin and its related compounds.[163] Recently, oleoresin capsicum–loaded nanoemulsion was developed using microfluidization techniques with the particle size of about 50 nm showing enhanced antiobesity effects in a high-fat-induced rat. Similarly conjugated linoleic acid–loaded nanoemulsion was developed using microfluidizing techniques, which also showed an enhanced antiobesity effect.[164] Higher efficacy of the antiobesity plant-based bioactive compounds like zeaxanthin was also studied using microfluidization techniques by reducing its particle size. Further development of various nanodelivery systems using those antiobesity bioactive compounds is necessary to enhance its application.

Cardiovascular effect

Plant-derived bioactive compounds showed higher potential in the prevention of cardiovascular diseases.[10,165,166] Consumption of the plant bioactive compound–rich food showed higher prevention either by the prevention of the oxidation of lipoprotein or by the prevention of atherosclerotic lesion development. A diet rich in plant bioactive compounds showed an active preventive role in various mechanisms against the atherosclerotic effect.[167–171] However, the bioavailability of those bioactive compounds against atherosclerosis is very low and development of novel nanodelivery systems is currently playing a key role. Recently various nanodelivery systems were developed using plant bioactive compounds like nanoemulsion or nanoparticles for their effective preventive role against various chronic diseases including cardiovascular effects.[172–175] Recently, Baicalein-loaded nanoemulsion was developed with a particle size of about 91 nm, showing excellent bioavailability of these compounds in rats,[176] and it could be possibly used in anticardiovascular studies. Another potential anticardiovascular compound β-carotene was studied using the microfluidization technique, and are able to produce food grade nanoemulsion along with higher stability with a particle size of <200 nm.[176] However, the enhanced stability of those active compound loaded nanodelivery systems developed using microfluidization techniques are still limited in their protective role in the anticardiovascular effects.

Antineuroinflammation effect

Plant bioactive compounds like curcumin, resveratrol, and piperine play a significant role in antineuroinflammation and neuroprotection activity; they thereby can prevent various neuroinflammatory diseases including Parkinson's, Alzheimer's, and other brain diseases.[177–183] However, the delivery of those bioactive compounds is playing a key role in the prevention of the above neuroinflammatory diseases. Novel nanodelivery systems like SLNs, nanoemulsions, and nanoliposomes are successful in the delivery of various plant-based bioactive compounds in the treatment of neuroinflammatory diseases.[184–191] However, the stability and bioavailability of bioactive compound–loaded nanodelivery systems were greatly enhanced through microfluidization techniques. Curcumin, a potential antineuroinflammatory compound, was successfully loaded in zein nanoparticles using microfluidization techniques with a lower particle size and showed higher bioaccessibility.[192]

Conclusion

Microfluidization-based nanodelivery systems using plant bioactive compounds is a technology that is expected to make tremendous progress in producing various nanodelivery systems including SLNs, nanoemulsions, nanoliposomes, and PLGA nanoparticles. These techniques are able to produce stable and highly reproducible nanosystems of certain drugs with a lower particle size with the higher possibility of industrial scale production and application in the treatment of various chronic diseases. Stable nanodelivery systems developed using microfluidization techniques also showed higher bioavailability and bioaccessibility of those encapsulated plant-based bioactive compounds. Several microfluidized drugs are in the commercial market which are used in the treatment of various chronic diseases. Further research studies are also necessary in the design of microfluidization processing parameters for the development of particular nanodelivery systems using plant bioactive compounds in determining the stability and in the treatment of certain diseases. This will lead to the development of novel plant bioactive compound-based nanodelivery systems using microfluidization techniques with higher beneficial effects in the treatment of many chronic diseases.

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Disclosure

The authors report no conflicts of interest in this work.

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