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

Palanivel Ganesan1
Govindarajan Karthivashan2
Shin Young Park2
Joonsoo Kim2
Dong-Kug Choi1,2

1Department of Integrated Bio Science and Biotechnology, Konkuk University, College of Biomedical and Health Science, Nanotechnology Research Center, Konkuk University, Chungju 27478, Republic of Korea; 2Department of Applied Life Sciences, Graduate School of Konkuk University, Research Institute of Inflammatory Diseases, Chungu 27478, Republic of Korea

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 plant 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.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...
their own merits and demerits for the treatment of chronic diseases. Several techniques like emulsification, supercritical fluidization, high-pressure homogenization, and ultrasonication are most commonly used in the development of those nanodelivery systems. 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.

Novel stable nanodelivery systems have been developed with microfluidization techniques with enhanced stability of encapsulated compounds. 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. Further microfluidized nanodelivery systems with reduced particle size and higher bioaccessibility 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. 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. 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. 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 make the lipid carrier overcome its barrier. The pump driven by the compressed air mix the lipids and active compounds at very high velocities in the designed microchannels, thereby forming stable delivery systems of a nano size. 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. 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. 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, 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. 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. 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...
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. 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-inflammatory, 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. 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 prepa-
ration of those delivery systems using different equipment,
different characteristic effects were shown in the functional
properties of developed nanodelivery systems. 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 gener-
ated using microfluidizing techniques. 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. 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. SLNs showed higher
loading efficacy and bioavailability of various plant bioac-
tive 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. 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 includ-
ing high-speed homogenization, spray drying, cold homog-
enezation, hot homogenization, ultrasonication, double
emulsion, and supercritical technology. Usage of all those
techniques includes various advantages and disadvantages
in the development of SLNs. 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. 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 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. 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. 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. 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 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. Various methods are involved in the preparation and development of nanoliposomes for enhanced stability like ultrasonic injection, ethanol injection, and homogenizer methods. 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. 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. 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. 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. The particle size of the nanophytosomes developed by microfluidized method was about 92 nm, which was much lower than the traditional method. 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 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. 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. 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. 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. 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. 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 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. 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. 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. General medical practice includes radiation and chemotherapy, which lead to various other complications leading the patients in much stress. 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. 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. 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, 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. Treating obesity with plant-based bioactive compounds in the form of food, nutraceuticals, or drugs is practiced. 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. 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. Recently, oleoresin capsicum–loaded nanoemulsion was developed using microfluidization techniques with the particle size of about 50 nm showing enhanced anti-obesity 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. 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. 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. 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. Recently, Baicalein-loaded nanoemulsion was developed with a particle size of about 91 nm, showing excellent bioavailability of these compounds in rats and it could be possibly used in antcardiovascular 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. 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. 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. 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.

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.

Acknowledgments
This research was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Science and ICT (NRF-2017R1C1B2010276 and 2017R1A2A207001035).

Disclosure
The authors report no conflicts of interest in this work.

References
1. Dias MI, Ferreira IC, Barreiro MF. Microencapsulation of bioactives for food applications. Food Funct. 2015;6(4):1035–1052.
2. Jia Z, Dumont M-J, Orsat V. Encapsulation of phenolic compounds present in plants using protein matrices. *Food Biotech.* 2016;15:87–104.

3. Lacatusu I, Badea N, Niculae G, Bordei N, Stan R, Meghea A. Lipid nanocarriers based on natural compounds: An evolving role in plant extract delivery. *Eur J Lipid Sci Technol.* 2014;116(12):1708–1717.

4. Soukoulis C, Boht T. A comprehensive overview on the micro- and nano-technological encapsulation advances for enhancing the chemical stability and bioavailability of carotenoids. *Crit Rev Food Sci Nutr.* 2018;58(1):1–36.

5. Wang L, Guliati P, Santra D, Rose D, Zhang Y. Nanoparticles prepared by proso millet protein as novel curcumin delivery system. *Food Chem.* 2018;240:1039–1046.

6. Babhi S, Ben Ali R, Abidi A, Jameeddine S. The efficacy of plant extract and bioactive compounds approaches in the treatment of pulmonary fibrosis: A systematic review. *Biomed Pharmacother.* 2017;93:666–673.

7. Boniface PK, Baptista Ferreira S, Roland Kaiser C, Ferreira SB, Kaiser CR. Current state of knowledge on the traditional uses, phytochemistry, and pharmacology of the genus Hymenaea. *J Ethnopharmacol.* 2017;206:193–223.

8. Edwards CA, Havlik J, Cong W, et al. Polyphenols and health: Interactions between fibre, plant polyphenols and the gut microbiota. *Nutr Bull.* 2017;42(4):356–360.

9. Inada AC, Figueiredo PS, Santos-Eicher RAD, et al. Morinda citrifolia oil: oil–water nanoemulsions. *Process Eng.* 2016;56(13):2223–2230.

10. Raiola A, Errico A, Petruk G, Monti DM, Barone A, Rigano MM. Development and Evaluation of the Nanoemulsion Technique and investigation of their biological activities. *Nanoemulsions from Palm-Based Tocotrienol Rich Fraction by Microfluidization.* 2017;40(6):e12578.

11. Sharma A, Kasheyp D, Sak K, Tuli HS, Sharma AK. Therapeutic charm of quercetin and its derivatives: a review of research and patents. *Pharm Pat Anal.* 2017;7(1):15–32.

12. Torres-Contreras AM, Nair V, Cisneros-Zevallos L, Jacobo-Velazquez DA. Stability of Bioactive Compounds in Broccoli as Affected by Cutting Styles and Storage Time. *Molecules.* 2017;22(4):636.

13. Garcia-Moreno PJ, Özdemir N, Stephansen K, et al. Development of carbohydrate-based nano-structures loaded with fish oil by using electrohydrodynamic processing. *Food Hydrocoll.* 2017;69:273–285.

14. Yang R, Zhou Z, Sun G, Gao Y, Xu J, Ferritin XJJ. Ferritin, a novel beta-carotene containing high-energy emulsification–evaporation technique. *Microfluid. Molecules.* 2015;20(11):1993–19946.

15. Silvia HD, Cerqueira MA, Souza BWS, et al. Emulsões de betacaroteno preparadas por extracção assistida e bioatividades de Cyperus esculentus (C. esculentus L.) com lipídios hidrossolúveis. *J Food Process Pres.* 2018;42(7):e13668.

16. Jing S, Wang S, Li Q, et al. Dynamic high pressure microfluidization-assisted extraction and bioactivities of Cyperus esculentus (C. esculentus L.) leaves flavonoids. *Food Chem.* 2016;192:319–327.

17. Zeeb B, Saberi AH, Weiss J, McClements DJ. Formation and characterization of filled hydrogel beads based on calcium alginate: Factors influencing nanoemulsion retention and release. *Food Hydrocoll.* 2015;50:27–36.

18. You L, Zheng B, Zhang R, et al. Enhancing the bioaccessibility of hydrophobic bioactive agents using mixed colloidal dispersions: Curcumin-loaded zein nanoparticles plus digestible lipid nanoparticles. *Food Res Int.* 2016;81:74–82.

19. Malik P, Singh M. Study of curcumin antioxidant activities in robust microemulsion. *J Food Nutr Biotechnol.* 2017;58(1):1–36.

20. Zeng S, Wang S, Tian J, et al. Microfluidization isolated cross-linking of gliadin particles for structured algal oil emulsions. *Food Hydrocoll.* 2017;73:153–161.

21. Yan B, Park SH, Balasubramaniam VM. Influence of high pressure homogenization with and without lecithin on particle size and physico-chemical properties of whey protein-based emulsions. *J Food Process Eng.* 2017;40(6):e12578.

22. Cheng Z, Xiaoqian H, Wang MF, Tao NP. Fabrication of chia (Salvia hispanica L.) leaves flavonoids. *J Food Process Pres.* 2018;4(5):e13416.

23. Yi X, Liu Y-L, Guo J, Yin S-W, Yang Q. Microfluidization initiated cross-linking of gliadin particles for structured algal oil emulsions. *Microfluid.* 2017;3:1–36.

24. Guerra-Rosas MI, Morales-Castro J, Ochoa-Martinez LA, Salvia-Trujillo L, Martin-Belloso O. Long-term stability of food-grade nano-emulsions from high methoxyl pectin containing essential oils. *Food Hydrocoll.* 2016;52:438–446.

25. Ulusa S, Decker EA, McClements DJ. Optimization of Nanoemulsion Fabrication Using Microfluidization: Role of Surfactant Concentration on Formation and Stability. *Microfluidics.* 2017;40(11):52–59.

26. Bartheldyová E, Effenberg R, Mašek J, et al. Optimization of Nanoemulsion Composition and Characterization of filled hydrogel beads based on calcium alginate: Factors influencing nanoemulsion retention and release. *Food Hydrocoll.* 2015;50:27–36.
He Y, Yue Y, Zheng X, Zhang K, Chen S, Du, Z. Curcumin, Inflammation, and Chronic Diseases: How Are They Linked? *Molecules*. 2015; 20(5):9183–9213.

Singh N, Khullar N, Kakkar V, Kaur IP. Hepatoprotective effects of sesamol loaded solid lipid nanoparticles in carbon tetrachloride induced sub-chronic hepatotoxicity in rats. *Environ Toxicol*. 2016;31(5): 520–532.

Watkins R, Wu L, Zhang CM, Davis RM, Xu B. Natural product-based nanomedicine: recent advances and issues. *Int J Nanomed*. 2015;10:6555–6074.

Yadav VR, Suresh S, Devi K, Yadav S. Novel formulation of solid lipid microparticles of curcumin for anti-angiogenic and anti-inflammatory activity for optimization of therapy of inflammatory bowel disease. *J Pharm Pharmacol*. 2009;61(3):311–321.

Behbahani ES, Ghaedi M, Abbaspour M, Rostamizadeh K. Optimization and characterization of ultrasound assisted preparation of curcumin-loaded solid lipid nanoparticles: Application of central composite design, thermal analysis and X-ray diffraction techniques. *Ultrasomonochem*. 2017;38:271–280.

Cortés-Rojas DF, Souza CRF, Oliveira WP. Encapsulation of eugenol rich clove extract in solid lipid carriers. *J Food Eng*. 2014;127:34–42.

Kim JH, Baek JS, Park JK, et al. Development of Houttuynia cordata Extract-Loaded Solid Lipid Nanoparticles for Oral Delivery: High Drug Loading Efficiency and Controlled Release. *Molecules*. 2017; 22(12):2215.

Helgason T, Awad TS, Kristbergsson K, Mcclements DJ, Weiss J. Effect of surfactant surface coverage on formation of solid lipid nanoparticles (SLN). *J Colloidal Interface Sci*. 2009;334(1):75–81.

Kim JE, Park YJ. Paclitaxel-loaded hyaluronan solid nanoemulsions for enhanced treatment efficacy in ovarian cancer. *Int J Nanomedicine*. 2017;12:645–658.

Salminen H, Helgason T, Kristinsson B, Kristbergsson K, Weiss J. Formation of nanostructured colloidosomes using electrostatic deposition of solid lipid nanoparticles onto an oil droplet interface. *Food Res Int*. 2016;79:11–18.

Suter F, Schmid D, Wundrey F, Zülli F. Haptetptide-loaded solid lipid nanoparticles for cosmetic anti-aging applications. *Eur J Pharm Biopharm*. 2016;108:304–309.

Trujillo CC, Wright AJ. Properties and Stability of Solid Lipid Particle Dispersions Based on Canola Stearin and Poloxamer 188. *J Am Oil Chem Soc*. 2010;87(7):715–730.

Wang R, Tian Z, Chen L. Nano-encapsulated liberated from barley protein microparticles for oral delivery of bioactive compounds. *Int J Pharm*. 2011;406(1–2):153–162.

Wang JL, Dong XY, Wei F, et al. Preparation and characterization of novel lipid carriers containing microalgae oil for food applications. *J Food Sci*. 2014;79(2):E169–E177.

Harwansh RK, Mukherjee PK, Bahadur S, Biswas R. Enhanced permeability of ferulic acid loaded nanoemulsion based gel through skin against UVA mediated oxidative stress. *Life Sci*. 2015;141:202–211.

Harwansh RK, Mukherjee PK, Biswas S. Nanoemulsion as a novel carrier system for improvement of betulinic acid oral bioavailability and hepatoprotective activity. *J Mol Liq*. 2017;237:361–371.

Karthik P, Ezhilrasari PN, Anandhamarakrishnan C. Challenges associated in stability of food grade nanoemulsions. *Crit Rev Food Sci Nutr*. 2017;57(7):1435–1450.

Lolah Kumar DH, Sarkar P. Encapsulation of bioactive compounds using nanoemulsions. *Environ Chem Lett*. 2018;16(1):59–70.

Li Y, Zheng J, Xiao H, Mcclements DJ. Nanoemulsion-based delivery systems for poorly water-soluble bioactive compounds: Influence of formulation parameters on Polymethoxylfaylene crystalization. *Food Hydrocoll*. 2012;27(2):517–528.

Ochoa AA, Hernandez-Beccera JA, Cavazos-Garduño A, Vernon-Carter EJ, Garcia HS. Preparation and Characterization of Curcumin Nanoemulsions Obtained by Thin-Film Hydration Emulsification and Ultrasonication Methods. *Rev Mex Ing Quim*. 2016;15(1):79–90.

Oliveira AEMFM, Duarte JL, Cruz RAS, Conceição ECDA, Carvalho JCT, Fernandes CP. Utilization of dynamic light scattering to evaluate Pterodon emarginatus oleoresin-based nanoemulsion formation by non-heating and solvent-free method. *Revista Brasileira de Farmacognosia*. 2017;27(3):401–406.
84. Yi J, Zhang Y, Liang R, Zhong F, Ma J, Jg M. Beta-carotene chemical stability in Nanoemulsions was improved by stabilized with beta-lactoglobulin-catechin conjugates through free radical method. J Agric Food Chem. 2015;63(1):297–303.

85. Zhong J, Liu X, Wang Y, Qin X, Li Z. γ-Oryzanol nanomulsions produced by low-energy emulsification method: an evaluation of process parameters and physicochemical stability. Food Funct. 2017;8(6):2202–2211.

86. Kotta S, Khan AW, Ansari SH, Sharma RK. Ali J. Formulation of nanoemulsion: a comparison between phase inversion emulsion method and high-pressure homogenization method. Drug Deliv. 2015;22(4):455–466.

87. Qian C, Mcbleems DJ. Formation of nanoemulsions stabilized by model food-grade emulsifiers using high-pressure homogenization: Factors affecting particle size. Food Hydrol. 2011;25(5):1000–1008.

88. Salvia-Trujillo L, Rojas-Graú MA, Soliva-Fortuny R, Martin-Bellos O. Effect of processing parameters on physicochemical characteristics of microfluidized lemongrass essential oil-alginate nanoemulsions. Food Hydrocoll. 2013;30(1):401–407.

89. Walker RM, Decker EA, Mcleems DJ. Physical and oxidative stability of fish oil nanoemulsions produced by spontaneous emulsification: Effect of surfactant concentration and particle size. J Food Eng. 2015;164:10–20.

90. Raviadaran R, Chandran D, Shin LH, Manickam S. Optimization of Silymarin Nanoliposomes against Isolated Methicillin-resistant Staphylococcus aureus. Food Res Int. 2014;64:492–499.

91. Akhavan S, Assadpour E, Katouzian I, Jafari SM. Lipid nano scale Complex Liposomes as carriers of rainbow trout skin-derived antioxidant peptides. J Agric Food Chem. 2016;64(1):100–107.

92. Fung HW, Mikasa TJ, Vergara J, et al. Optimizing manufacturing and composition of a TLR4 nanosuspension: physicochemical stability and vaccine adjuvant activity. J Nanobiotechnology. 2013;11:43.

93. Hsu C, Zou LQ, Niu J, Liu W, Peng SF, Liu CM. The Stability, Sustained Release and Cellular Antioxidant Activity of Curcumin Nanoliposomes. Molecules. 2015;20(8):14293–14311.

94. Ren F, Fu J, Xiong H, et al. Complexes of Felodipine Nanoparticles by microfluidization using polymeric stabilizers: I. A Design of Experiment approach. Eur J Pharm Sci. 2015;69:111–121.

95. Rafiee Z, Barzegar M, Sahari MA, Maherni B. Nanoliposomal carriers for improvement the bioavailability of – valued phenolic compounds of pistachio green hull extract. Food Chem. 2017;220:115–122.

96. Yuan H, Li X, Zhang C, et al. Nanosuspensions as delivery system of (-)-epigallocatechin gallate through nanoliposome encapsulation. Int J Biol Macromol. 2017;103:100–107.

97. Chay SY, Tan WK, Saari N. Preparation and characterisation of lipid nano scale Complex Liposomes Containing Medium-Chain Fatty Acids and Vitamin C. Food Res Int. 2011;59(24):13004–13011.

98. Chen X, Zou LQ, Niu J, Liu W, Peng SF, Liu CM. The Stability, Sustained Release and Cellular Antioxidant Activity of Curcumin Nanoliposomes. Molecules. 2015;20(8):14293–14311.

99. Gong KJ, Shi AM, Liu HZ, et al. Preparation of nanoliposome loaded with IgG1 in rat serum and biological activities. J Nanobiotechnology. 2013;11:43.

100. Guldiken B, Gibis M, Boyacioglu D, Capanoglu E, Weiss J. Physical and chemical stability of anthocyanin-rich black carrot extract-loaded liposomes during storage. Food Res Int. 2018;108:491–497.

101. Lu T, Yang S, Liu W, et al. Preparation and Characterization of Nano-scale Complex Liposomes Containing Medium-Chain Fatty Acids and Vitamin C. Int J Food Prop. 2015;18(1):113–124.

102. Belloso O. Effect of processing parameters on physicochemical characteristics of microfluidized lemongrass essential oil-alginate nanoemulsions. Food Hydrocoll. 2013;30(1):401–407.

103. Peng S, Zou L, Liu W, et al. Storage stability and antibacterial activity of eugenol nanoliposomes prepared by an ethanol injection-dynamic high-pressure microemulsion method. J Food Prot. 2015;78(1):22–30.
124. Siddiqui IA, Sanna V. Impact of nanotechnology on the delivery of natural products for cancer prevention and therapy. *Mol Nutr Food Res*. 2016;60(6):1330–1341.

125. Abd-Rabou AA, Ahmed HH. CS-PEG decorated PLGA nano-prototype for delivery of bioactive compounds: A novel approach for induction of apoptosis in HepG2 cell line. *Adv Med Sci*. 2017;62(2):357–367.

126. Andrade KS, Ponceter D, Ferreira SRS. Sustainable extraction and encapsulation of pink pepper oil. *J Food Eng*. 2017;204:38–45.

127. Oliveira DA, Angonese M, Ferreira SRS, Gomes CL. Nanoencapsulation of passion fruit by-products for enhanced antimicrobial activity. *Food Bioprod Process*. 2017;104:137–146.

128. Lamprecht A, Ubrich N, Hombreiro Pérez M, Lehr C, Hoffman M, Maincent P. Biodegradable monodispersed nanoparticles prepared by pressure homogenization-emulsification. *Int J Pharm*. 1999;184(1):97–105.

129. Lamprecht A, Ubrich N, Hombreiro Pérez M, Lehr C, Hoffman M, Maincent P. Influences of process parameters on nanoparticle preparation performed by a double emulsion pressure homogenization technique. *Int J Pharm*. 2000;196(2):177–182.

130. Sani SN, das NG, das SK. Effect of microfluidization parameters on the physical properties of PEG-PLGA nanoparticles prepared using high pressure microfluidization. *J Microencapsul*. 2009;26(6):556–561.

131. Martins C, Araújo F, Gomes MJ, et al. Using microfluidic platforms to develop CNS-targeted polymeric nanoparticles for HIV therapy. *Eur J Pharm Biopharm*. 2018 Jan 31.

132. Bai L, Mcclements DJ. Development of microfluidization methods for efficient production of concentrated nanoemulsions: Comparison of single- and dual-channel microfluidizers. *J Colloid Interface Sci*. 2016;466:206–212.

133. Chung C, Sher A, Roussett P, Mcclements DJ. Influence of homogenization on physical properties of model coffee creamers stabilized by quillaja saponin. *Food Res Int*. 2017;99(Pt 1):770–777.

134. Liu F, Zhu Z, Ma C, et al. Fabrication of Concentrated Fish Oil Emulsions Using Dual-Channel Microfluidization: Impact of Droplet Concentration on Physical Properties and Lipid Oxidation. *J Agric Food Chem*. 2016;64(50):9532–9541.

135. Qiu D, Yang L, Shi YC. Formation of vitamin E emulsion stabilized by octenylsuccinic starch: factors affecting particle size and oil load. *J Food Sci*. 2015;80(4):C680–C686.

136. Santos J, Calero N, Muñoz J, Cidade MT. Development of food emulsions containing an advanced performance xanthan gum by microfluidization. *Food Bioprod Process*. 2017;99(Pt 1):777–782.

137. Martinis C, Araújo F, Gomes MJ, et al. Using microfluidic platforms to develop CNS-targeted polymeric nanoparticles for HIV therapy. *Eur J Pharm Biopharm*. 2018 Jan 31.

138. Santos J, Calero N, Muñoz J, Cidade MT. Development of food emulsions containing an advanced performance xanthan gum by microfluidization technique. *Food Sci Technol Int*. 2018;24(5):373–381.

139. Stupak R, Makauskas N, Radzvevičius K, Valančius Z. Optimization of intracellular product release from Neisseria denitrificans using microfluidizer. *Prep Biochem Biotechnol*. 2015;45(7):667–683.

140. Wang FC, Acevedo N, Marangoni AG. Encapsulation of phytosterols and phytosterol esters in liposomes made with soy phospholipids by high pressure homogenization. *Food Funct*. 2017;8(11):3964–3969.

141. Zhang Y, Zhang J. Preparation of buccal and subcutaneous nanosuspensions for pulmonary delivery: Characterization, in vitro release and in vivo lung distribution studies. *Artif Cells Nanomed Biotechnol*. 2016;44(1):285–289.

142. Chen MJ, Wu IC, Chen YJ, et al. Nutritition therapy in esophageal cancer-Congress statement of the gastroenterological Society of Taiwan. *Dis Esophagus*. 2018;31(8).doi:1016.

143. Sani SN, das NG, das SK. Effect of microfluidization parameters on the physical properties of PEG-PLGA nanoparticles prepared using high pressure microfluidization. *J Microencapsul*. 2009;26(6):556–561.

144. Jafari E, Alavi M, Zal F. The evaluation of protective and mitigating effects of vitamin C against side effects induced by radiotherapy. *Radiat Environ Biophys*. 2018;57(3):233–240.

145. Zhao HD, Xie HJ, Li J, Ren CP, Chen YX. Research Progress on Reversing Multidrug Resistance in Tumors by Using Chinese Medicine. *Clin J Integr Med*. 2018;24(6):474–480.

146. Conte R, Luca ID, Luise AD, Pettillo O, Calcaro A, Peluso G. New Therapeutic Potentials of Nanosized Phytomedicine. *J Nanosci Nano- technol*. 2016;16(8):8176–8187.

147. Davatgaran-Taghipour Y, Masoomzadeh S, Farzaei MH, et al. Polypeh- nonanformulations for cancer therapy: experimental evidence and clinical perspective. *Int J Nanomedicine*. 2017;12:2689–2702.

148. Namdari M, Eatemadi A, Soleimaninejad M, Hammed AT. A brief review on the application of nanoparticle enclosed herbal medicine for the treatment of infective endocarditis. *Biomed Pharmacother*. 2017;87:321–331.

149. Wang Y, Zhang L, Wang Q, Zhang D. Recent advances in the nanotechnology-based drug delivery of Silybin. *J Biomed Nanotechnol*. 2014;10(4):543–558.

150. Loredo-Tovias M, Durañon-MEA, Villagran-Escareño MV, et al. Encapsulated ultrasmall nanoparticles as novel nanocarriers for highly hydrophobic anticancer drugs. *Nanoscale*. 2017;9(32):11625–11631.

151. Meng Y, Eirin A, Zhu XY, et al. Obesity-induced mitochondrial dysfunction in porcine adipose tissue-derived mesenchymal stem cells. *J Cell Physiol*. 2018;233(8):5926–5936.

152. Moharreri F, Asl SN, Behdani F, Ghaemi N. Evaluating of Psychiatric Activity. *Iran J Child Neurol*. 2012;1(1):26–36.

153. Donado-Pestana CM, Moura MHC, de Araujo RL, et al. Polypehnona from Brazilian native Myrtaceae fruits and their potential health benefits against obesity and its associated complications. *Curr Opin Food Sci*. 2018;19:42–49.

154. Hasan MM, Ahmed QU, Soad SZM, et al. Flavonoids from Tetracera indica Merr. induce adipogenesis and exert glucose uptake activities in 3T3-L1 adipocyte cells. *BMC Complement Altern Med*. 2017;17(1):431.

155. Mopuri R, Islam MS. Medicinal plants and phytochemicals with anti-obesogenic potentials: A review. *Biomed Pharmacother*. 2017;89:1442–1452.

156. Sido A, Radhakrishnan S, Kim SW, et al. A food-based approach that targets interleukin-6, a key regulator of chronic intestinal inflammation and colon carcinogenesis. *J Nutr Biochem*. 2017;43:11–17.

157. Somtimuang C, Olatunji OJ, Ovatlarnporn C. Evaluation of In Vitro α-Amylase and α-Glucosidase Inhibitory Potentials of 14 Medicinal Plants Constituted in Thai Folk Antidiabetic Formularies. *Chem Biodivers*. 2018;15(4):e1800025.

158. Udechuku MC, Abbey L, Nwodo U, Udenigwe CC. Potential of Moringa oleifera seeds and leaves as functional food ingredients for human health promotion. *J Food Nutr Res-Slov*. 2018;57(1):1–14.

159. Arent SM, Walker AJ, Pellegrino JK, et al. The Combined Effects of Exercise, Diet, and a Multi-Ingredient Dietary Supplement on Body Composition and Adipokine Changes in Overweight Adults. *J Am Coll Nutr*. 2017;36(2):111–120.

160. Hiroi K, Ushijima M, Uyeyama R, Uchihashi Y, Ikeda K. Effects of Capsaicin Coadministered with Eicosapentaenoic Acid on Obesity-Related Dysregulation in High-Fat-Fed Mice. *Biol Pharm Bull*. 2017;40(9):1581–1585.

161. Son HK, Shin HW, Jang ES, Moon BS, Lee CH, Lee JJ. Comparison of Antioxidity Effects Between Gochujangs Produced Using Different Koji Products and Tabasco Hot Sauce in Rats Fed a High-Fat Diet. *J Med Food*. 2018;21(3):233–243.

162. Sun L, Camps SG, Goh HJ, et al. Capsinoids activate brown adipose tissue (BAT) with increased energy expenditure associated with subthreshold 18-fluorine fluorodeoxyglucose uptake in BAT-positive humans confirmed by positron emission tomography scan. *Am J Clin Nutr*. 2018;107(1):62–70.

163. Surasmoo S, Min S-G, Bejrapha P, Choi M-J. Effects of surfactants on the physical properties of capsicum oleoresin-loaded nanocapsules formulated through the emulsion–diffusion method. *Food Res Int*. 2010;43(1):8–17.
164. Kim JY, Lee MS, Jung S, et al. Anti-obesity efficacy of nanoemulsion oleoresin capsicum in obese rats fed a high-fat diet. *Int J Nanomedicine* 2014; 9:301–310.

165. Scolaro B, Soo Jin Kim H, de Castro IA. Bioactive compounds as an alternative for drug co-therapy: Overcoming challenges in cardiovascular disease prevention. *Crit Rev Food Sci Nutr* 2018; 58(6):958–971.

166. Tam DNH, Truong DH, Nguyen TTH, et al. Ginsenoside Rh1: A Systematic Review of Its Pharmacological Properties. *Planta Med* 2018; 84(3):139–152.

167. Banjari I, Misir A, Šavikin K, et al. Antidiabetic Effects of *Aronia melanocarpa* and Its Other Therapeutic Properties. *Front Nutr* 2017; 4:53.

168. Braga ARC, Murador DC, de Souza Mesquita LM, de Rosso VV. Bioavailability of anthocyanins: Gaps in knowledge, challenges and future research. *J Food Compost Anal*. 2018:68:31–40.

169. Fang J, Little PJ, Xu S, Sw X. Atheroprotective Effects and Molecular Targets of Tanshinones Derived From Herbal Medicine Danshen. *Med Res Rev*. 2018;38(1):201–228.

170. Morais R, Morais A, Dammak I, et al. Functional Dehydrated Foods for Health Preservation. *J Food Quality*. 2018;1739636.

171. Olas B. The beneficial health aspects of sea buckthorn (*Elaeagnus rhamnoides*) oil. *J Ethnopharmacol*. 2018;213:183–190.

172. Huang ZF, Wang HS, Gao CS, Shen HY, Xe F. Drug Loaded Gold Nano-Particulates for Therapeutics of Myocardial Infarction in Rat Model. *J Biomater Tiss Eng*. 2018;8(2):197–205.

173. Jiange J, Ao J, He CY, et al. Preparation and characterisation of ginkgo volatile nanoparticles via the emulsion solvent evaporation method. *Micro Nano Lett*. 2018;13(5):636–640.

174. Katsuki S, Matoba T, Koga N, Nakano K, Egashira K. Anti-inflammatory Nanomedicine for Cardiovascular Disease. *Front Cardiovasc Med*. 2017;4:87.

175. Nakibanda A, Eskandani M, Omidi Y, et al. Combating atherosclerosis with targeted nanomedicines: recent advances and future prospective. *Biosensors*. 2018;8(1):59–75.

176. Yin J, Xiang C, Wang P, Yin Y, Hou Y. Biocompatible nanoemulsions based on hemp oil and less surfactants for oral delivery of baicalin with enhanced bioavailability. *Int J Nanomedicine*. 2017;12:2923–2931.

177. Businaro R, Corsi M, Asprino R, et al. Modulation of Inflammation as a Way of Delaying Alzheimer’s Disease Progression: The Diet’s Role. *Curr Alzheimer Res*. 2018;15(4):363–380.

178. Cho DY, Ko HM, Kim J, et al. Scoparone Inhibits LPS-Simulated Inflammatory Response by Suppressing IRF3 and ERK in BV-2 Microglial Cells. *Molecules*. 2016;21(12):E1718:1718.

179. Jo MJ, Kumar H, Joshi HP, et al. Oral Administration of α-Asarone Promotes Functional Recovery in Rats With Spinal Cord Injury. *Front Pharmacol*. 2018;9:445.