Different NanoVehicles and Dietary Supplements

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Abstract

NanoVehicles are nanostructured delivery systems that transport natural health ingredients or active pharmaceutical ingredients in the bloodstream, ranging in diameter from 1 to 15,000 nanometers. These vehicles can be categorized into organic or inorganic types based on their composition. While fullerene, gold and silver NanoVehicles, and quantum dots have been extensively studied in medical research, they are not suitable for dietary supplements. Notably, the COVID-19 mRNA NanoVehicle vaccine and NanoVehicles with water-loving or oil-loving chemotherapeutics have shown promise in saving lives, particularly for cancer patients. However, these NanoVehicles require intravenous administration and high-energy processing, making them unsuitable for dietary supplements. Fortunately, there are other NanoVehicles that don't require high-energy processing, offering a highly impactful technology for dietary supplements. These NanoVehicles can enhance delivery into the bloodstream, and NanoPrime Labs has developed the technology to incorporate oil-loving natural health ingredients into egg- and dairy-free NanoVehicles, promoting consumer wellness and health.

1. Introduction

NanoVehicles are tiny, nanostructured vehicles that range in size from 1 nanometer to 15,000 nanometers. To put that into perspective, if a marble represented one nanometer, the Earth would be equivalent to one meter. Both eggs and milk contain NanoVehicles that carry essential nutrients, proteins, and lipids that are vital to our health.

Expanding our understanding of the various types of NanoVehicles can help us appreciate their diverse applications. These vehicles can be bioengineered to transport natural health ingredients (NHIs) or active pharmaceutical ingredients (APIs) in our bloodstream, with diameters typically falling within the nanometer range.

Previous white papers discussed milk fat globules, casein micelles, egg LDL micelles, egg granules, microemulsions, nanoemulsions, and micelles. These NanoVehicles have remarkably small diameters, ranging from 17 nanometers (egg LDL micelles) to 230 nanometers (casein micelles).

This white paper will explore additional types of NanoVehicles and their current uses, shedding light on the versatility and potential of these tiny vehicles.

2. Organic NanoVehicle 1: Fullerene

Figure 1(A) illustrates fullerenes, a type of organic NanoVehicle or nanoparticle. Organic NanoVehicles are defined as NanoVehicles containing carbon, nitrogen, sulfur, phosphorus, silicon, halogens, and oxygen.[1] Fullerenes are formed by 60 carbon atoms linked together in 5- or 6-membered rings, with diameters ranging from 25 to 500 nanometers.[2]

There are two main families of fullerenes: closed buckyballs and carbon nanotubes. The fullerene shown in **Figure 1(A)** belongs to the buckyball family. Despite being oil-loving NanoVehicles, fullerenes form stable NanoVehicles in water. They exhibit potent antibacterial activity and other attractive biological properties, including high-performance MRI and X-ray imaging contrast

agents, protein and therapeutic delivery, and photodynamic therapy for cancer treatment.[3]

While fullerenes have been extensively researched for their biological activities, they have not been approved by government regulations for ingestion as food or administration into the bloodstream. Therefore, they cannot be used in dietary supplements.

3. Inorganic NanoVehicle 1: Gold and Silver NanoVehicles

Figure 1(B) illustrates gold NanoVehicles, also known as gold nanoparticles, which fall under the category of inorganic NanoVehicles due to their composition of mostly gold atoms. Inorganic NanoVehicles are defined as those containing metals, minerals, and organometallic compounds.[4] Gold NanoVehicles have diameters ranging from 1 to 100 nanometers, and their solution changes color according to their diameter.[5]

As shown in **Figure 1(B)**, gold NanoVehicles consist of a golden core containing gold atoms, surrounded by a stabilizing layer (represented by the black outline) that can be modified to include targeting or imaging agents. Gold NanoVehicles have been extensively used in medical research for therapeutic delivery, tumor detection, gene therapy, radiotherapy dose enhancement, biosensors, and toxic gas detection.[5–7] Silver NanoVehicles, formed by substituting gold with silver, are primarily used for their antibacterial activity and have also been researched for chemotherapy and multi-drug resistance treatment.[8]

However, neither gold nor silver NanoVehicles have been approved for use in food or cancer therapy and are mainly used for medical and academic research purposes.[9] While they exhibit attractive biological activities, they cannot be used in dietary supplements, similar to fullerenes.

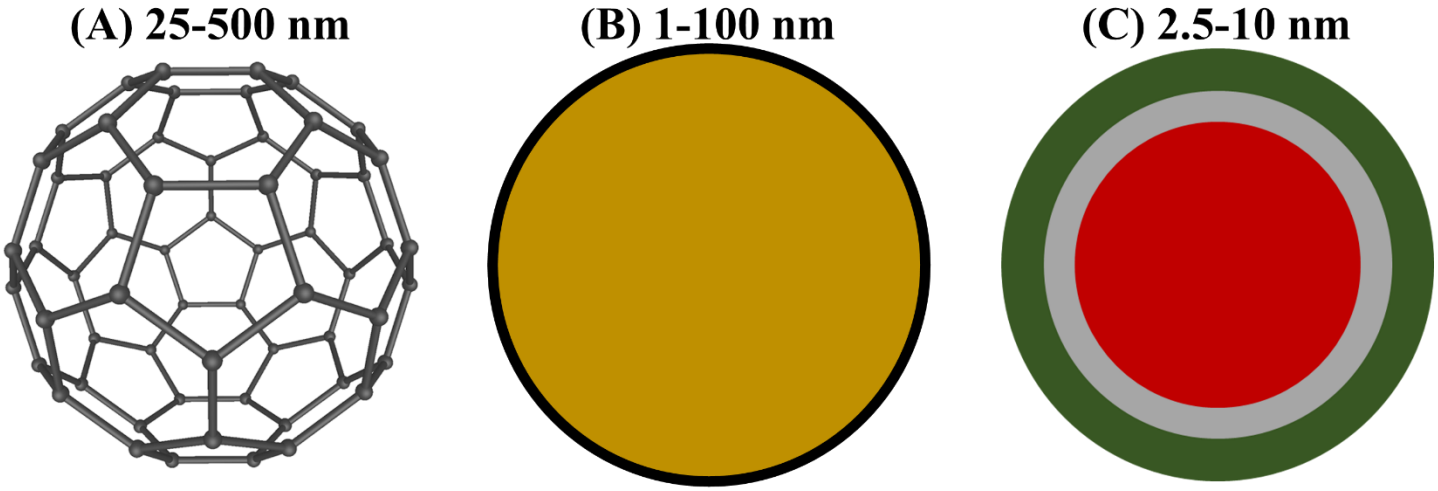

Figure 1. Schematic diagram showcasing the sizes and structures of different NanoVehicles including (A) fullerene, (B) gold NanoVehicles, and (C) quantum dots. The diameter of fullerene ranges from 25 to 500 nanometers and is shown with carbons as black dots, and the bonds between each carbon or black dot are represented as lines. The diameters of gold and silver NanoVehicles range from 1 to 100 nanometers and is shown with a golden core where the gold atoms are stored with a stabilizing layer represented by the black outlining. The diameter of quantum dots ranges from 2.5 to 10 nanometers and are shown with the core represented in red, the shell is represented in gray, and the stabilizer is represented in green. The fullerene was referenced from Rawn, J. D.; Ouellette, R. J. Organic Chemistry: Structure, Mechanism, Synthesis; Academic Press, 2018.

4. Inorganic NanoVehicle 2: Quantum Dots

Figure 1(C) illustrates quantum dots, another type of inorganic NanoVehicle. With diameters ranging from 2.5 to 10 nanometers, quantum dots consist of a core (red), shell (gray), and stabilizer (green). Their unique electronic and optical properties make them valuable for medical and academic research.

Quantum dots have shown promise in overcoming the blood-brain barrier, a significant hurdle in delivering therapeutics to the brain.[10] They have also been used for imaging purposes, outperforming traditional dyes.[11] Additionally, quantum dots have applications in photovoltaic cells, solar cells, and quantum dot displays, which surpass liquid crystal displays (LCDs) in performance.[12]

While quantum dots offer advantages due to their small diameters and electronic and optical properties, they are not approved for use in dietary supplements due to governmental regulations.

5. Organic NanoVehicle 2: COVID-19 mRNA NanoVehicle Vaccine

COVID-19, caused by SARS-CoV-2, is a contagious disease that has had a significant global impact, resulting in a death toll of 3,078,473.[13] SARS-CoV-2 is the seventh member of the coronavirus family to infect humans.[14] The publication of its genetic sequence on January 11, 2020, has driven intense research and development efforts to create a vaccine.[15]

Moderna developed one of the first distributed vaccines, which utilizes NanoVehicles (lipid nanoparticles or liposomes) to store and deliver

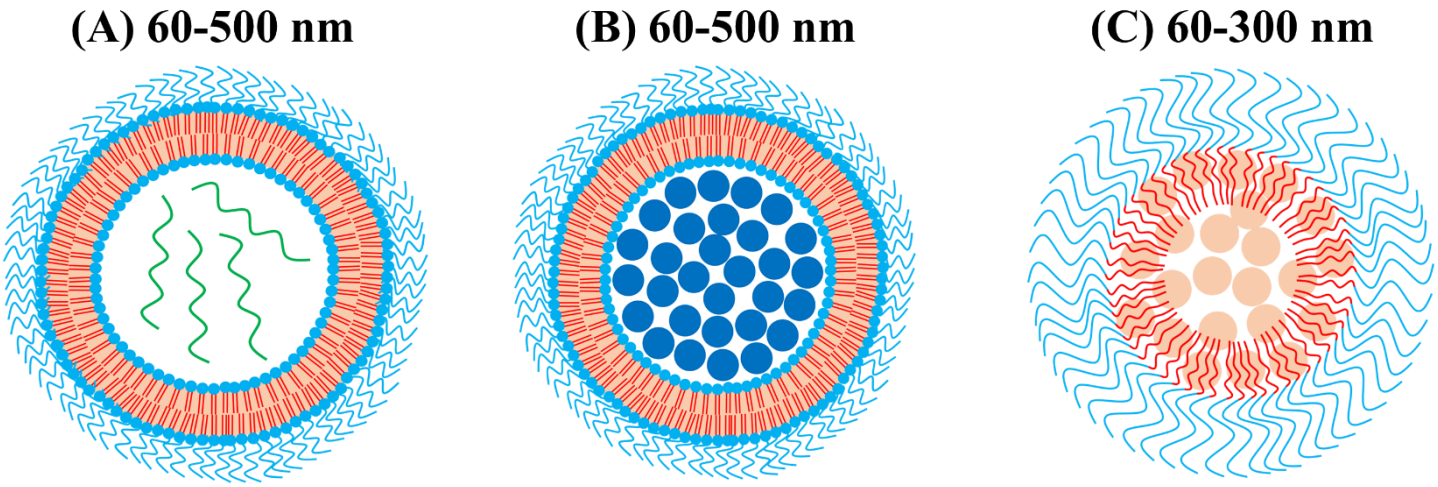

Figure 2. Schematic diagram showcasing the sizes and structures of different NanoVehicles including (A) COVID-19 mRNA NanoVehicles (B) NanoVechiles loaded with water-loving chemotherapeutics and (C) NanoVehicles loaded with oil-loving chemotherapeutics. The diameters of the COVID-19 mRNA NanoVehicle ranges from 60 to 500 nanometers (nm) and is composed of lipids that are represented in blue circles and red lines, an oil-loving layer represented in light red, with the water-loving core represented in white with the COVID-19 mRNA represented in green. The diameters of the NanoVehicles loaded with water-loving chemotherapeutics ranges from 60 to 500 nm and is shown similar to the COVID-19 mRNA NanoVehicle. The water-loving chemotherapeutics are represented by the dark blue circles. The diameters of the NanoVehicles loaded with oil-loving chemotherapeutics ranges from 60 to 300 nm and is composed of amphiphilic emulsifiers or polymers that include an oil-loving component represented by red lines and water-loving components represented by blue lines. These NanoVehicles are then loaded with oil-loving cancer therapeutics represented as light red circles.

mRNA-1273.[16] These NanoVehicles are essential for delivering mRNA, as it is rapidly degraded in the blood and has difficulty penetrating cells. The Moderna vaccine consists of mRNA-1273 and four lipids, with the NanoVehicle comprising the lipids surrounding the mRNA-1273 (**Figure 2(A)**).[17] This NanoVehicle is classified as an organic NanoVehicle and includes a lipid with a water-loving component, extending blood circulation and avoiding rapid clearance.[18]

Similar NanoVehicle technology is used in the Pfizer-BioNTech vaccine.[19] Both vaccines are globally distributed and have the potential to save millions of lives. However, these NanoVehicles are not suitable for use in dietary supplements due to their formulation, which requires intravenous injection for direct administration into the bloodstream.

6. Organic NanoVehicle 3: NanoVehicles loaded with Chemotherapeutics

Cancer treatment often involves chemotherapy, which utilizes chemotherapeutics (APIs) that are either water-loving or oil-loving. These chemotherapeutics target essential cell growth pathways, affecting non-cancer cells like cardiac and hair cells. However, NanoVehicles have improved the delivery of both types of chemotherapeutics.

Water-loving chemotherapeutics, like doxorubicin, benefit from NanoVehicles (lipid nanoparticles) that extend circulation time in the blood and eliminate rapid clearance (**Figure 2(B)**). These NanoVehicles provide a half-life of 35 hours compared to 9.6 minutes for doxorubicin alone.

Oil-loving chemotherapeutics face the challenge of dissolving in water and blood (90% water).[20] NanoVehicles ensure a substantial amount of the chemotherapeutic reaches cancer cells (**Figure 2(C)**). Researchers have investigated the pharmacokinetics of formulations containing oil-loving chemotherapeutics like docetaxel, showing extended half-lives (passed 6.9 hours) when loaded into NanoVehicles with water-loving components.[21]

Both types of NanoVehicles are administered directly into the bloodstream through IV administration, making them unsuitable for dietary supplements. However, these optimized formulations have the potential to save cancer patients' lives.

NanoVehicles have revolutionized cancer treatment by improving the delivery of chemotherapeutics. By encapsulating water-loving and oil-loving chemotherapeutics, NanoVehicles enhance circulation time, reduce clearance, and increase efficacy. While not suitable for dietary supplements due to IV administration, these optimized formulations offer hope for cancer patients.

7. Egg NanoVehicle 1: Egg Yolk Micelles

Different types of NanoVehicles were previously discussed, but is it possible to use egg NanoVehicle 1? As discussed in our previous white paper, the egg NanoVehicle 1, otherwise known as egg yolk micelle or low-density lipoprotein (LDL) micelle, is shown in **Figure 3(A).** Egg NanoVehicle 1 falls under the class of organic NanoVehicle and is found in all eggs that are part of a healthy diet. The egg NanoVehicle is overly complex to be used in a bioengineered process. The egg NanoVehicle 1 is composed of apolipoproteins of low-density lipoproteins (apoLDL), cholesterol, cholesterol esters, triglycerides, and phospholipids. These ingredients are not easy to incorporate oil-loving NHIs. Although egg yolks make a delicious breakfast with toasted bacon, the egg yolk micelles are not ideal to be used in dietary supplements. Instability and inappropriate ingredients are found in egg yolk micelles that cannot be used with dietary supplements. As eggs contain two types of NanoVehicles, the big question is if the egg NanoVehicle 2 can be incorporated with dietary supplements?

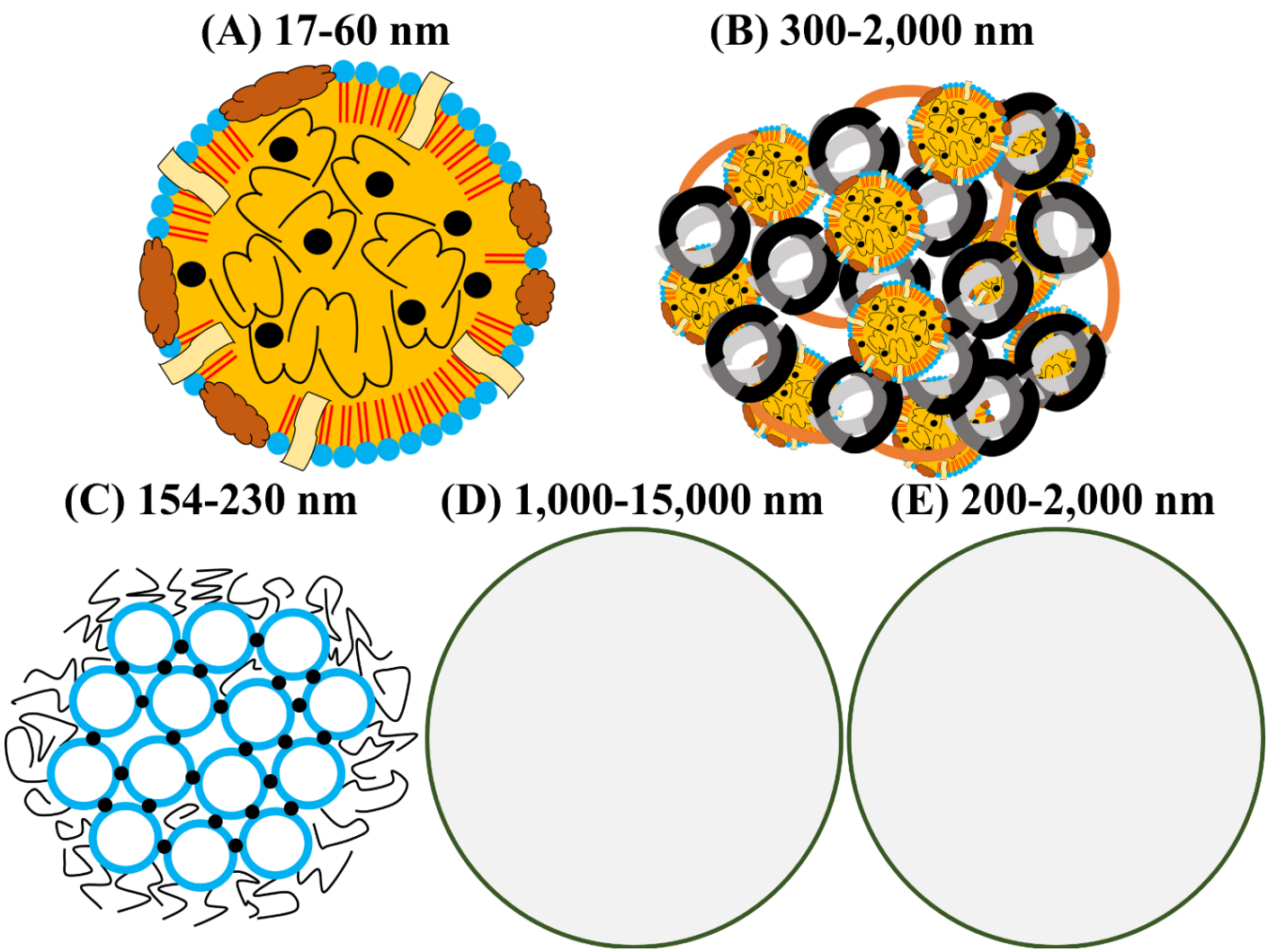

Figure 3. Schematic diagrams showcasing the sizes and structures of different NanoVehicles including (A) egg yolk micelle, (B) egg granules, (C) milk casein micelles, (D) raw milk fat globules, and (E) processed milk fat globules. (A) The egg NanoVehicle 1, otherwise known as low-density lipoprotein (LDL) micelles, are composed of apolipoproteins of low-density lipoproteins (apoLDL) represented as , cholesterol represented as , cholesterol esters represented as , triglycerides represented as , and phospholipids represented as . The diameters of egg NanoVehicle 1 ranges from 17 to 60 nanometers. (B) The egg NanoVehicle 2, otherwise known as egg granules, are a combination of LDL micelles represented as yellow circles, high-density lipoprotein (HDL) micelles represented as black and gray circles, and phosvitin integrating into the LDL and HDL micelles represented as a orange shape. The diameters of egg NanoVehicle 2 ranges from 300 to 2,000 nanometers. (C) The diameters of the milk NanoVehicle 1, otherwise known as milk casein micelles, ranges from 154 to 230 nanometers and is shown with calcium phosphate nanoclusters as back dots, and casein submicelles in light blue circles. (D) The milk NanoVehicle 2, otherwise known as raw milk fat globules, are composed of multi-layered liposomes with diameters ranging from 1,000 to 15,000 nanometers. (E) The milk NanoVehicle 2 can be homogenized to produce processed milk fat globules that comprise of the same multi-layered liposomes, but the processed milk fat globules have fine-tuned diameters ranging from 200 to 2,000 nanometers.

8. Egg NanoVehicle 2: Egg Granules

Egg NanoVehicle 2, also known as egg granules, have diameters ranging from 300 to 2,000 nanometers and fall under the class of organic NanoVehicles (**Figure 3(B)**). While they are composed of various micelles (LDL, HDL, and phosvitin), they are not suitable for loading oil-loving natural health ingredients (NHIs) due to their variable diameters and composition. Therefore, egg NanoVehicle 2, like egg NanoVehicle 1, is not a suitable NanoVehicle for use with dietary supplements. Let's explore the milk NanoVehicles as a potential alternative.

9. Milk NanoVehicle 1: Casein micelles

Milk NanoVehicle 1, also known as casein micelles (**Figure 3(C)**), are organic NanoVehicles composed of casein submicelles and casein proteins. While they may be able to load oil-loving ingredients, their suitability for dietary supplements is limited. As seen in the example of THC BioMed's THC Kiss beverage, using milk ingredients, including casein micelles, as a delivery system for oil-loving cannabinoids is not optimized for absorption into the bloodstream.[22] Instead, the milk ingredients only helped dissolve the cannabinoids in water. Therefore, milk NanoVehicle 1 is not a suitable vehicle for dietary supplements. Let's explore milk NanoVehicle 2 as a potential alternative for efficiently delivering oil-loving natural health ingredients (NHIs).

10. Milk NanoVehicle 2: Raw Milk Fat Globules

Milk NanoVehicle 2, also known as raw milk fat globules (**Figure 3(D)**), are organic NanoVehicles with varying diameters (1,000 nm to 15,000 nm). While they resemble the COVID-19 NanoVehicle vaccine, they are not suitable for delivering oil-loving natural health ingredients (NHIs) due to difficulties in loading and uncontrollable parameters. As a result, raw milk NanoVehicle 2 is not a viable option for dietary supplements.

11. Milk NanoVehicle 2: Processed Milk Fat Globules

Processed milk NanoVehicle 2, also known as processed milk fat globules (**Figure 3(E)**), are organic NanoVehicles with diameters ranging from 200 to 2,000 nanometers, resulting from homogenization of raw milk.[23] While homogenization extends shelf life, inactivates bacteria, and enhances milk's appearance and texture, it's still not possible to load oil-loving ingredients into these processed milk fat globules. Similar to raw milk fat globules, there are many uncontrollable parameters, making them unsuitable for use in dietary supplements.

12. Egg- and Dairy-free NanoVehicle 1: Nanoemulsions

Nanoemulsions (**Figure 4(A)**) are organic NanoVehicles with diameters ranging from 5 to 100 nm, suitable for oil-loving ingredients. However, their high-energy manufacturing process, requiring large devices like ultrasonicators or high-pressure homogenizers, makes them impractical for dietary supplements. Additionally, nanoemulsions are typically administered through IV administration, which is not suitable for oral consumption. While they have applications in the cannabis industry, enhancing water solubility and shelf life of cannabis beverages, their limitations make them unsuitable for use in dietary supplements.

13. Egg- and Dairy-free NanoVehicle 2: Microemulsions

Microemulsions (**Figure 4(B)**) are organic NanoVehicles with diameters similar to nanoemulsions, containing an oil core, amphiphilic emulsifiers, and water-loving components. Unlike nanoemulsions, microemulsions don't require high-energy processing and can be easily packaged into dietary supplement soft gels. Once ingested and broken down in the stomach, microemulsions spontaneously form, allowing for the delivery of multiple oil-loving ingredients into the bloodstream. This makes microemulsions an ideal NanoVehicle

for dietary supplements, offering enhanced delivery and versatility. A deeper exploration of microemulsions will be discussed in an upcoming white paper.

14. Egg- and Dairy-free NanoVehicle 3: Micelles

Micelles (**Figure 4(C)**) are egg- and dairy-free NanoVehicles similar to microemulsions, but without an oil core. They simplify formulation and are commonly used to deliver cancer chemotherapeutics (APIs) to cancer cells.[24] Like microemulsions, micelles can be loaded with multiple oil-loving natural health ingredients (NHIs) and packaged into softgels. Upon breakdown in the stomach, these softgels form micelles that effectively solubilize oil-loving NHIs in stomach acid, enabling delivery for various therapies. While micelles are not as powerful as microemulsions, they offer a valuable delivery solution, and their differences will be explored in an upcoming white paper.

15. Conclusions

This text provides a comprehensive overview of NanoVehicles, their types, and applications. NanoVehicles are defined as nanostructured delivery systems that carry natural health ingredients (NHIs) or active pharmaceutical ingredients (APIs) in the blood, with diameters ranging from 1 to 15,000 nanometers.

The text discusses various types of NanoVehicles, including: fullerenes (organic, 60-300 nm). gold and silver NanoVehicles (inorganic, 1-100 nm), quantum dots (inorganic, imaging agents), COVID-19 mRNA NanoVehicle vaccine (organic), NanoVehicles with water-loving and oil-loving chemotherapeutics (organic), nanoemulsions (organic, require high-energy processing), Egg- and dairy-free NanoVehicles (organic, suitable for dietary supplements), NanoPrime Labs is highlighted as a company that holds the technology to incorporate oil-loving NHIs into egg- and dairy-

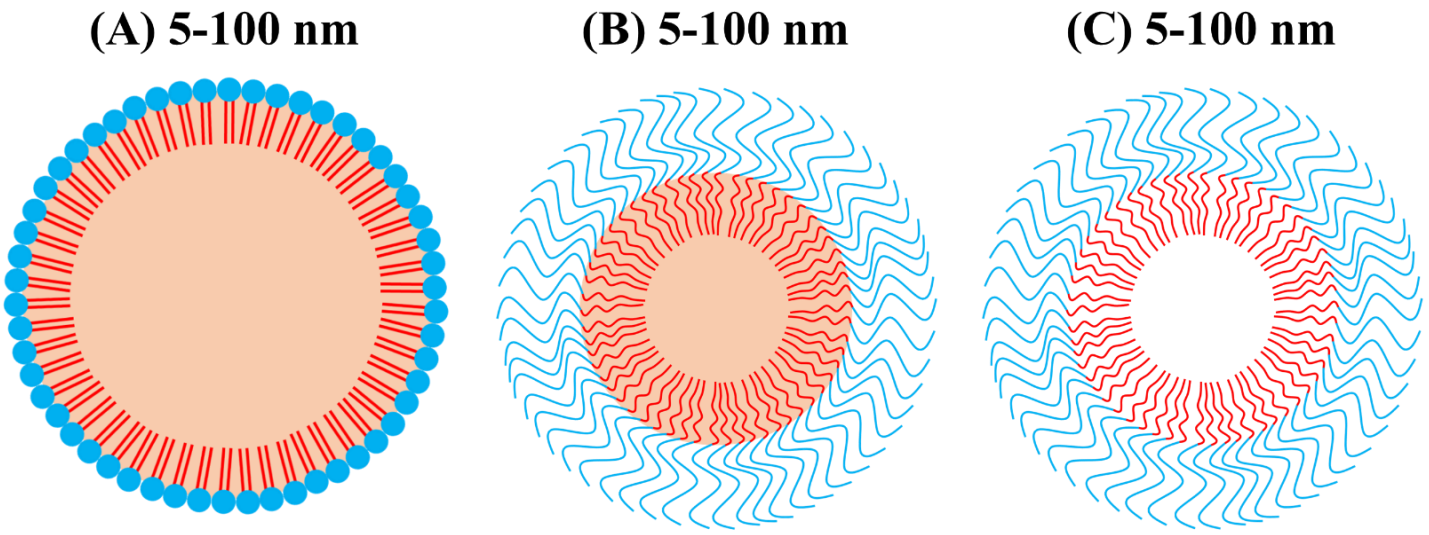

Figure 4. Schematic diagrams showcasing the different egg- and dairy-free NanoVechicles of (A) nanoemulsions, (B) microemulsons and (C) micelles. The diameters of nanoemulsions ranges from 5 to 100 nanometers, and is represented with an oil core in light red, amphiphilic emulsifiers with the oil-loving component represented in red lines, and the water-loving components represented in light blue circles. The diameters of microemulsions also ranges from 5-100 nanometers, and the oil core is represented with light red, amphiphilic emulsifiers with the oil-loving component represented with red lines, and the water-loving components represented with light blue lines. Micelles are similar to microemulsions in terms of structure and size, but micelles do not have an oil-containing core. However, the core of the micelles may be loaded with oil-loving Natural Health Ingredients (NHIs).

free NanoVehicles, enhancing consumer wellness and health.

Overall, the text provides a thorough exploration of NanoVehicles, their characteristics, and applications, emphasizing their potential impact on dietary supplements and consumer health.

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