

Cannabis Beverages contain NanoVehicles; NanoPrime Labs offers appropriate NanoVehicles

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Abstract

Cannabinoids, including THC and CBD, are oil-loving ingredients found in cannabis plants. To create cannabis NanoVehicles for beverages, specific ingredients are required. All cannabis beverages contain these NanoVehicles, which typically consist of six ingredients: lecithin, sucrose and sorbitan esters of fatty acids, polysaccharides, Quillaja extract, and poly(glycerol) esters of fatty acids. These ingredients, familiar in the food, cosmetic, and pharmaceutical industries, have been used for decades. While they help create shelf-stable cannabis beverages, they overlook the delivery and uptake pathway in our bodies. Moreover, these ingredients require high-energy processing, impossible to replicate in our stomachs, making them unsuitable for dietary supplements. Fortunately, NanoPrime Labs possesses the technology to produce suitable NanoVehicles powered by SMART IDS, designed to enhance the delivery of oil-loving natural health ingredients (NHIs). Without these appropriate NanoVehicles, an astonishing 99.99% of ingested oil-loving NHIs are lost in the digestive process. NanoPrime Labs is dedicated to improving the delivery of oil-loving NHIs with tailored NanoVehicles, powered by SMART IDS, to maximize their potential.

1. Introduction

NanoPrime Labs has established a solid educational foundation to understand the active ingredients in our food, identifying water-loving and oil-loving ingredients. The water-solubility challenges of oil-loving ingredients result in poor bioavailability, consistently observed in animal and human studies.¹⁻³ To address this, we broke down the uptake pathway into five steps, highlighting the second step - solubility in gastric fluid - as the bottleneck. Appropriate NanoVehicles are crucial to overcome this challenge. NanoVehicles, defined as nanostructured vehicles ranging from 1 nanometer to 15,000 nanometers, are familiar in milk and eggs, making them a natural solution. Fortunately, NanoPrime Labs possesses the technology to overcome this challenge, offering it in our softgels.

Cannabinoids, including THC and CBD, are oil-loving ingredients extracted and purified from cannabis plants. Initial legalized products in Canada

included cannabis oils, capsules, and vape cartridges, easily produced by diluting cannabis distillate into MCT oil. However, with the legalization of cannabis 2.0 in 2019, manufacturing stable and consistent cannabis beverages posed a challenge, given the water-loving nature of beverages and oil-loving cannabinoids.

2. Ingredient Structures

In the scientific and medical communities, it is widely acknowledged that cannabinoids are oil-loving ingredients. The two primary cannabinoids found in all cannabis plants are CBD and THC. CBD has been extensively studied for its beneficial effects on various conditions, including epilepsy, pain, arthritis, anxiety, depression, sleep disorders, acne, Parkinson's disease, nausea, and vomiting.⁴⁻⁶ THC, on the other hand, has been included in clinical trials for its potential to provide a recreational psychoactive experience and possibly work synergistically with CBD.⁷ It is important to



note that neither THC nor CBD can diagnose, cure, mitigate, or prevent any disease. While the benefits of cannabinoids have been demonstrated, incorporating them into cannabis beverages poses a challenge.

Nanoemulsions, previously discussed as NanoVehicles, have been extensively used in the pharmaceutical industry to enhance the delivery of oil-loving Active Pharmaceutical Ingredients (APIs). However, nanoemulsions require high-energy processing, such as ultrasonication or high-

pressure homogenization, which cannot be replicated in the stomach. The cannabis industry, dealing with oil-loving natural health ingredients (NHIs), has adopted nanoemulsions as a rapid manufacturing method for cannabis beverages. Analyzing currently marketed cannabis beverages in North America reveals the ingredients used, including lecithin, sucrose and sorbitan esters of fatty acids, polysaccharides, Quillaja extract, and poly(glycerol) esters of fatty acids (**Figure 1**). The following sections will explore how these ingredients are oriented in cannabis NanoVehicles and the limitations of these NanoVehicles.

3. Lecithin

Lecithin is a popular choice for cannabis beverage manufacturers, given its history in the pharmaceutical industry for producing nanoemulsions loaded with cancer chemotherapeutics and other Active Pharmaceutical Ingredients (APIs). Lecithin, a generic term for yellow-brownish fat substances found in animals and plants, has a distinct structure (**Figure 1(A)**) comprising two fatty acids, choline, and a phosphate group attached to one glycerol. It is a mixture of glycerophospholipids, including phosphatidylcholine and phosphatidylethanolamine, and can be sourced from egg yolk, soy, marine sources, and sunflower oil.^{8,9} When combined with MCT oils and cannabis distillate, lecithin forms NanoVehicles with a layer of lecithin (**Figure 2(A)**), exhibiting a zwitterionic charge. Lecithin's widespread use makes it an economical choice for cannabis beverages.

However, relying on lecithin in cannabis NanoVehicles comes with significant drawbacks, including poor uptake in the body and rapid clearance from the blood. While lecithin is suitable for storing cannabis beverages in aluminum cans or glass bottles, it neglects the five-step uptake pathway in the body. Although lecithin NanoVehicles dissolve in stomach acid, their

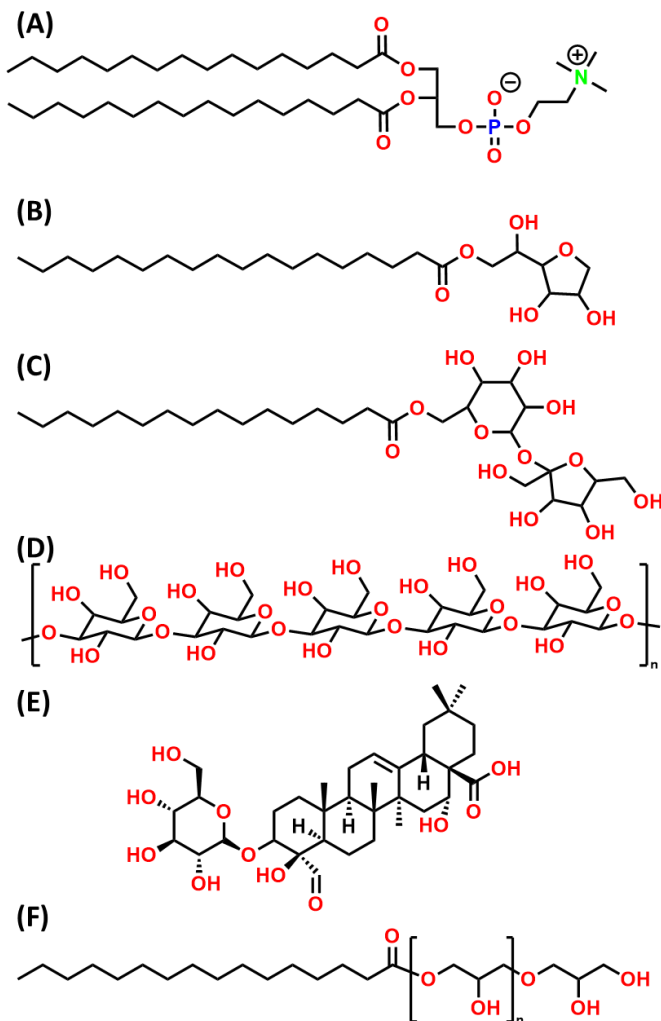


Figure 1. Chemical structures of the ingredients used to make the various NanoVehicles that include: A) lecithin, B) sucrose esters of fatty acids, C) sorbitan esters of fatty acids, D) polysaccharides, E) Quillaja extract, and F) poly(glycerol) esters of fatty acids.

intestinal uptake and microvilli transport are severely hindered, resulting in most of the NanoVehicle being excreted in the toilet. Lecithin may have worked well in the past, but it is not compatible with dietary supplements, requiring high-energy processing to manufacture stable NanoVehicles, which is impossible to replicate in the stomach. Therefore, lecithin cannot be used with

dietary supplements to create NanoVehicles powered by SMART IDS.

4. Lecithin and Sorbitan Esters of Fatty Acids

Lecithin NanoVehicles can be formulated with additional ingredients like sorbitan esters of fatty acids, such as sorbitan monopalmitate, to create a unique formulation. Sorbitan monopalmitate, used

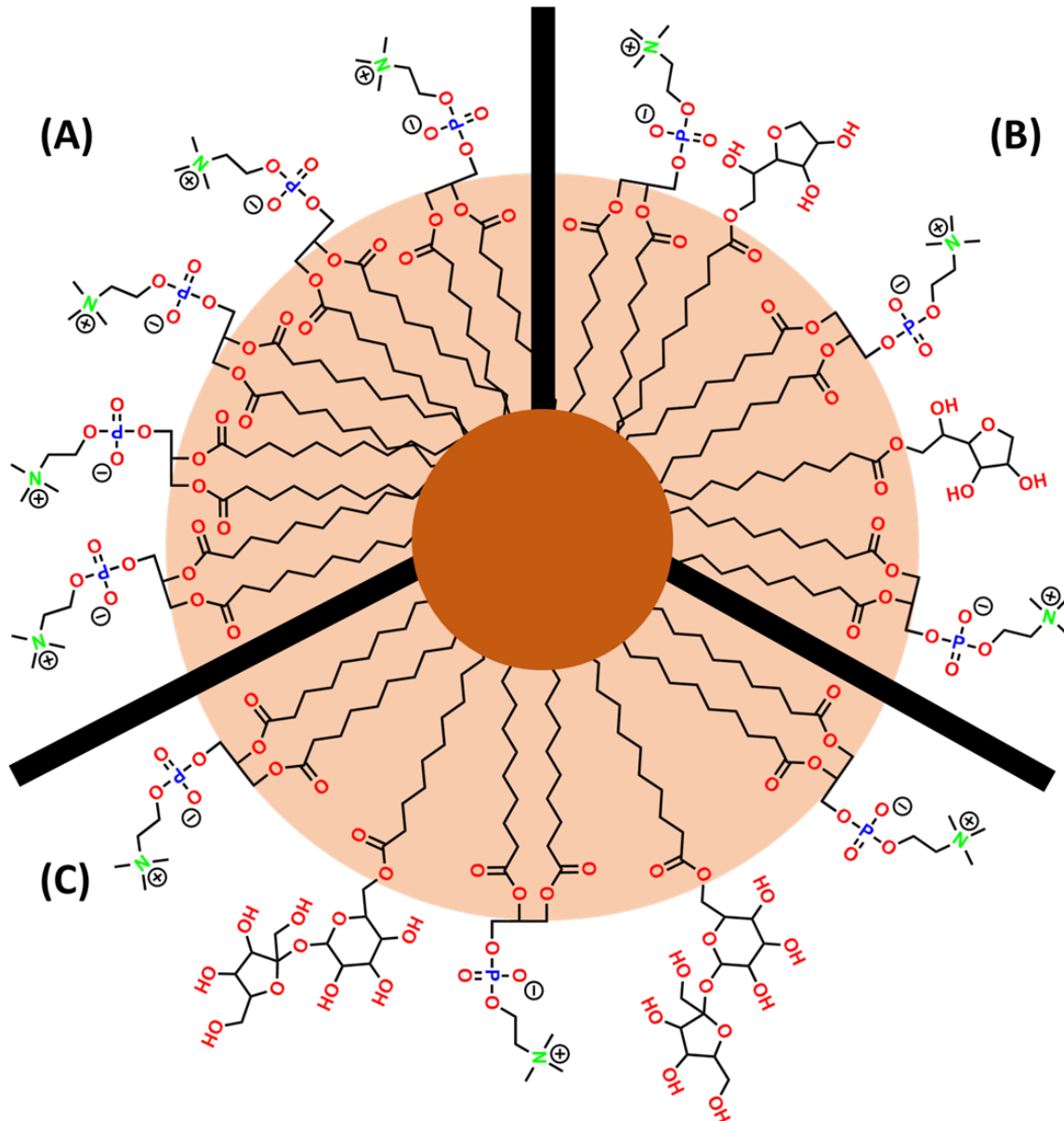


Figure 2. Schematic diagram of the various NanoVehicles present in cannabis beverages that include ingredients such as A) lecithin, B) lecithin and sorbitan esters of fatty acids, and C) lecithin and sucrose esters of fatty acids. The schematic diagram illustrates the oil-water interface of each NanoVehicle and represented the chemical structures that would exist in the interior and exterior of the NanoVehicle.

since 1959, has been a common ingredient in various food products, including icings, marmalades, sorbets, food supplements, emulsified sauces, and chewing gum.¹⁰ Its structure (**Figure 1(B)**) features a palmitic fatty acid tail modified with a sorbitan sugar head group. Lecithin and sorbitan monopalmitate NanoVehicles (**Figure 2(B)**) appear similar, with the addition of sorbitan

sugar on the NanoVehicle surface. Both NanoVehicles have an oil-loving core for storing cannabinoids, stabilized by either lecithin or lecithin and sorbitan sugar. While lecithin NanoVehicles and those containing sorbitan monopalmitate share similarities, the focus lies in the distinct benefits offered by sorbitan monopalmitate.

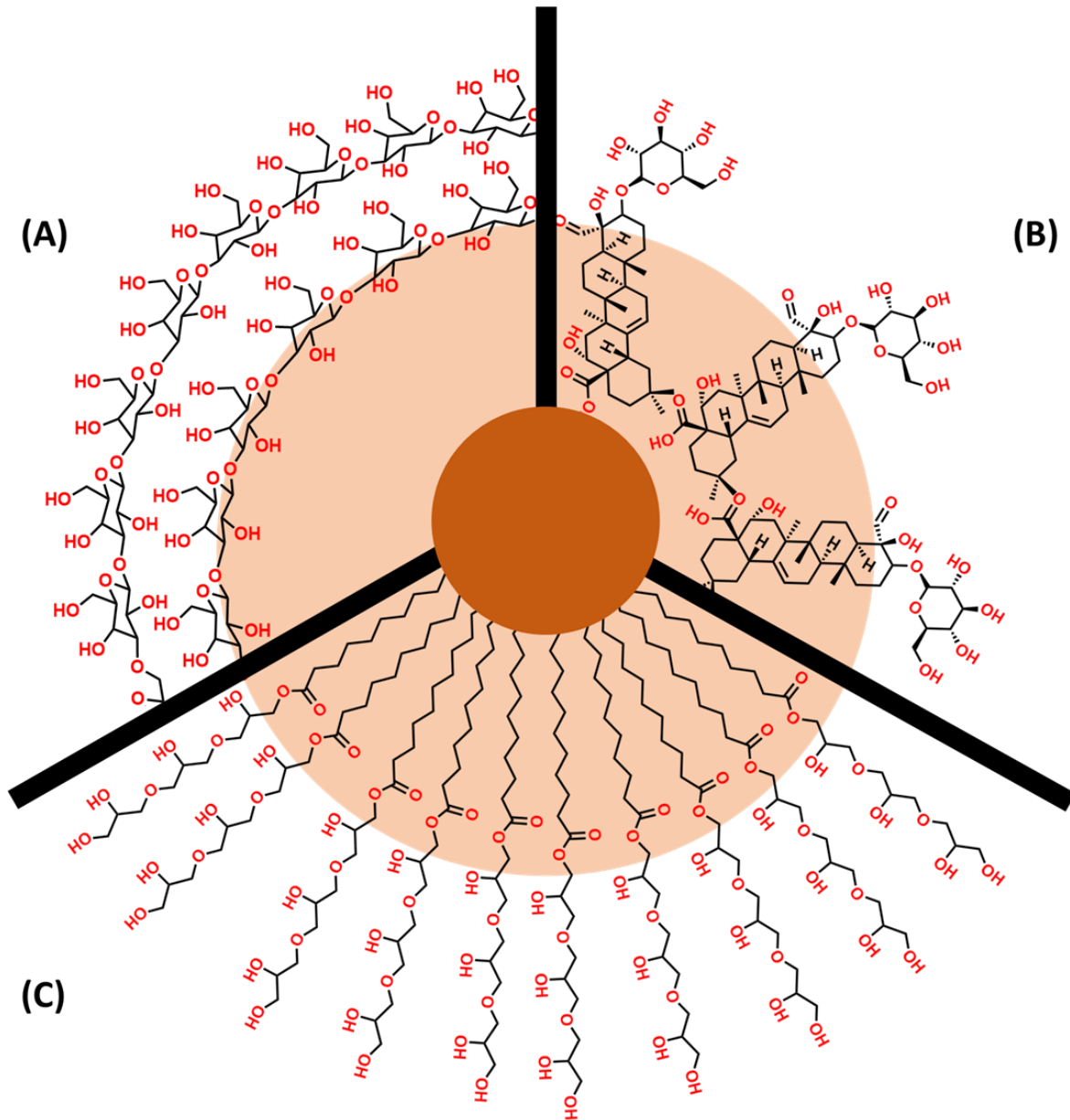


Figure 3. Schematic diagram of the various NanoVehicles present in cannabis beverages that include ingredients such as A) polysaccharides, B) quilaja saponin extract, and C) poly(glycerol) esters of fatty acids. The schematic diagram illustrates the oil-water interface of each NanoVehicle and represented the chemical structures that would exist in the interior and exterior of the NanoVehicle.

The incorporation of sorbitan monopalmitate may enhance the shelf-life stability of cannabis beverages, depending on the manufacturing process and ingredients used. However, this addition does not address the bioavailability challenges in the body. Similar to lecithin NanoVehicles, those containing sorbitan monopalmitate face difficulties in transporting through microvilli and entering the bloodstream. Additionally, these NanoVehicles require high-energy processing, impossible to replicate in the stomach. Therefore, sorbitan monopalmitate and lecithin are unsuitable for use with dietary supplements containing NanoVehicles powered by SMART IDS.

5. Lecithin and Sucrose Esters of Fatty Acids

Another ingredient that can be added to lecithin NanoVehicles is sucrose esters of fatty acids, such as sucrose monostearate (**Figure 1(C)**). Sucrose monostearate consists of a sucrose molecule attached to the head group of stearic acid, an 18-carbon chain. The sugar and fatty acid components can be exchanged for other suitable options, depending on the desired properties of the end product. Sucrose esters are commonly used in food additives, fruit preservatives, cosmetics, and pharmaceutical NanoVehicles. For this white paper, we will focus on sucrose monostearate. The surface of a NanoVehicle containing both lecithin and sucrose monostearate is shown in **Figure 2(C)**, resembling the lecithin NanoVehicles with sorbitan monopalmitate. The question is, what benefits does sucrose monostearate bring to cannabis NanoVehicles?

The incorporation of sucrose monostearate into lecithin NanoVehicles may enhance shelf-life stability, a benefit for manufacturers, but offers little value in terms of cannabinoid absorption in the blood. The addition of sucrose monostearate has minimal effects on interacting with microvilli in the small intestines, and these NanoVehicles face the same delivery challenges as lecithin NanoVehicles.

Moreover, the processing of sucrose monostearate requires a high-energy step, identical to lecithin NanoVehicles, which is impossible to replicate in the stomach. Therefore, sucrose monostearate and other sucrose esters of fatty acids are unsuitable for NanoVehicles powered by SMART IDS.

6. Polysaccharides

Cannabis beverages without lecithin often contain polysaccharides, a type of carbohydrate consisting of long polymers or chains of sugar molecules (**Figure 1(D)**). Polysaccharides, abundant in food, include starch, dextrin, and gum arabic.^{11,12} When used in cannabis NanoVehicles, polysaccharides are found only on the exterior (**Figure 4(A)**), as they lack oil-loving components to incorporate into the oil cores. While starch can be processed into modified starch with potential benefits, polysaccharides' instability issues hinder efficient delivery.

Polysaccharides' inability to incorporate into the NanoVehicle interior leads to stability and delivery problems. As shown in **Figure 4(A)**, polysaccharides on the exterior can interact with other NanoVehicles, causing coagulation and instability. Even if ingested, these NanoVehicles break apart quickly in stomach acid and the small intestines. If they reach systemic circulation, their circulation time is short. Moreover, polysaccharide-containing NanoVehicles require high-energy processing, impossible to replicate in the stomach, and cannot achieve diameters less than 200 nanometers, making them unsuitable for NanoVehicles powered by SMART IDS.

7. Quillaja Extract

The Soap bark tree, native to Chile, yields Quillaja extract, an intriguing ingredient used for decades as a foaming agent in beers and carbonated beverages. The cannabis industry adopted Quillaja extract for its foaming properties, but its base



chemical structure (**Figure 1(E)**) has multiple variations with different sugars and carbon chains. When used in cannabis NanoVehicles, Quillaja extract incorporates into the oil core with its oil-loving component (five 6-carbon rings) and water-loving component (sugar with multiple alcohol groups) on the exterior (**Figure 4(B)**). While Quillaja NanoVehicles resemble lecithin NanoVehicles (**Figure 3**), they share similar stability issues.^{13,14}

Despite its potential, Quillaja extract in cannabis NanoVehicles offers no observable benefits once ingested. Like polysaccharide-containing NanoVehicles, Quillaja NanoVehicles face coagulation and stability issues, breaking down in the acidic stomach and failing to deliver sufficient ingredients into the blood. Additionally, Quillaja-containing NanoVehicles require high-energy processing, impossible to replicate in the stomach. Therefore, Quillaja extract is unsuitable for NanoVehicles powered by SMART IDS.

8. Poly(glycerol) esters of fatty acids

Cannabis beverages can be prepared using a high-energy processing step to produce various NanoVehicles, including those incorporating poly(glycerol) esters of fatty acids (**Figure 1(F)**). These ingredients are prepared through polymerization, combining plant oils with glycerols. Poly(glycerol) esters of fatty acids are used to stabilize emulsions, foam, dispersions, and beverage clouding agents. Structurally similar to lecithin, sorbitan, and sucrose esters of fatty acids, they have a fatty acid ester (oil-loving component) and a poly(glycerol) component (water-loving component, represented by brackets). The poly(glycerol) component provides a superior water-loving component compared to lecithin. As shown in **Figure 4(C)**, poly(glycerol) esters of fatty acids are incorporated into NanoVehicles similarly to lecithin (**Figure 3**), with the fatty acid ester

embedding in the oil-loving core and the poly(glycerol) on the exterior.

Despite similarities with lecithin, poly(glycerol) esters of fatty acids have distinct chemical and structural differences when used in NanoVehicles. Like lecithin, they require a high-energy processing step to produce small-sized NanoVehicles, which poses the same problem as other ingredients in cannabis beverages. Moreover, poly(glycerol) esters of fatty acids have limited use in academic and pharmaceutical research, and their potential benefits or adverse effects are not well understood. Therefore, they are not suitable ingredients for NanoVehicles powered by SMART IDS.

9. Conclusion

Cannabis plants contain oil-loving ingredients like THC and CBD, which require suitable ingredients to create cannabis NanoVehicles. Six ingredients used in cannabis NanoVehicles were introduced: lecithin, sucrose and sorbitan esters of fatty acids, polysaccharides, Quillaja extract, and poly(glycerol) esters of fatty acids. Their chemical structures and orientations within cannabis NanoVehicles were discussed. These ingredients have been used in the food, cosmetic, and pharmaceutical industries for decades, which is why the cannabis industry adopted them. However, while they help create shelf-stable cannabis beverages, they neglect the delivery and uptake pathway in the body. Therefore, they are unsuitable for use with dietary supplements. Fortunately, NanoPrime Labs possesses the technology to produce NanoVehicles powered by SMART IDS, which enhance the delivery of oil-loving NHIs. Without these NanoVehicles, nearly 99.99% of ingested oil-loving NHIs are lost in the toilet. NanoPrime Labs strives to improve the delivery of oil-loving NHIs with SMART IDS-powered NanoVehicles, offering a superior solution for cannabis beverages.



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