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Chapter 7: Liposomes, Phytosomes, and Niosomes for Nano-Targeted Cardio Nutraceuticals

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Abstract

Cardiovascular diseases (CVDs) ruling to be the world's leading cause of morbidity and mortality, new therapeutic approaches are required for both prevention, management and treatment. The technology's advances in the medicine industry which combines of nano-based delivery systems, specifically liposomes, niosomes, and nano-vesicles, with the other systems of medicine provide dual benefits. This enhances the solubility, stability, and targeted delivery of bioactive compounds has made them promising carriers for cardio-nutraceuticals. The design, development, and therapeutic potential of these novel drug delivery systems in cardiovascular care are examined and explained in this chapter. Various critical analysis are conducted of the ways in which liposomes and niosomes improves their bioavailability, shield nutraceuticals from deterioration, and enable site-specific drug delivery. Specifically phytoconstituents are focused in such a way that, when combined with nano-carriers, show cardio protective effects, such as polyphenols, flavonoids, omega-3 fatty acids, and plant sterols. To demonstrate their benefits over traditional formulations, comparative information about liposomal and niosomal systems, their surface modifications, and their stimuli-responsive characteristics is discussed. Clinical viewpoints, difficulties with large-scale production, safety, and regulatory issues for conversion into practical therapeutic use are also covered in this chapter. These cutting-edge delivery systems have the potential to completely transform naturopathic cardiovascular care by fusing nanotechnology and nutraceutical science.

Keywords*: Liposomes, Niosomes, Nano-vesicles, Cardio-nutraceuticals, Cardiovascular diseases, Targeted drug delivery, Naturopathy, Nutraceuticals.*

1. INTRODUCTION

As the technology progresses faster as the time progresses and the requirements in the improvement in the health sector are more demanding, treatment for the diseases has become the vital criteria for the growing population. Cardiovascular diseases has been one of the major concerns among the others so counteracting the worst effects and decreasing the mortality rate has also been on the other side of concern in order for the betterment of the healthcare of world population better methods of treatment. Nanotechnology which is recently on boom in the medical healthcare sector especially in the treatment of several diseases which was thought difficult to diagnose, treat and cure on(*Website*, n.d.-a). Nanoparticles which are used in formulation of targeted drug release which increases the effectiveness and thereby reducing the side effects . In this article we will discuss in brief about various nano-delivery systems used in cardiovascular care such as liposomes, Niosomes, Phytosomes also the cardio-protective phytoconstituents in nanoformulations and surface modifications and stimuli responsive characteristics, clinical applications, case studies, forthcoming challenges and its future perspectives(*Website*, n.d.-b).

2. NANO-DELIVERY SYSTEMS IN CARDIOVASCULAR CARE

The therapy of cardiovascular illnesses, especially atherosclerosis and myocardial infarction, has shown great promise in the realm of nanotechnology. A number of essential characteristics of nanosystems make them successful at treating various illnesses.These systems can target specifically on high risk atheromatous lesions, resulting in enhanced disease management,Nano systems exhibit stimuli response behaviour, enabling the controlled release of therapeutic agents in response to internal and external stimuli present in the atherosclerotic environment,Biomimetic particles such as macrophage membrane coated nanoparticles and platelet membrane cloaked nanoparticles mimics the properties of natural cells ,these biomimetic properties enhance targeted drug delivery models also had potential for promoting tissue regeneration and functional recovery in cardiovascular disorders ,including myocardial infarction.

Finding CADs early on gives patients a better chance of getting better and living longer. When the heart is damaged or stressed, biomarkers related to CAD, like cardiac troponins (cTns), myoglobin (Myo), creatinine kinase MB (CK-MB), C-reactive protein (CRP), and a number of miRNAs, are released into the blood. Consequently, a promising strategy for the early diagnosis of CADs is to create accurate, specific, straightforward, stable, and rapid blood analyses for these molecules. Mass spectrometry is commonly employed to identify potential biomarkers of CADs; however, its effectiveness is constrained by sensitivity and specificity owing to the low concentrations of biomarkers in human plasma.can provide high-affinity binding to targeted molecules and reduce nonspecific adsorption through surface modification or structure optimisation; the latter comprises two components: a biological sensing element for target recognition and a transducer for converting data into electrical signals. Nanosystems enhance the therapeutic potential of various agents such as nucleic acids, proteins, small molecule drugs, gas-signalling molecules and stem cells, for treatment of cardiovascular diseases, secondly they also improve drug delivery by providing sustained release and localized therapeutic effects,For example injectable hydrogels containing nano-complexes and therapeutic agents offer improved drug delivery to the targeted site(*Website*, n.d.-c). Nanoparticles can overcome biological barriers and enhance targeting to specific tissues or cells thereby increasing the efficacy of drug delivery while minimizing systemic side effects.Peptide modified nanoparticles for targeted delivery to the ischemic myocardium was still under research. Nanosystems have the efficacy to improve thrombus treatment by enhancing targeting, prolonging the halflife, and potentially reducing the side effects associated with current thrombolytic drugs. Combinatorial therapies using nanoparticles are investigated such as polymeric particles for reducing oxidative stress and muscle damage in cardiac myocytes. In addition nanosystems were developed to effectively cross the blood-brain barrier (BBB) for stroke treatment.The controlled release of drugs is facilitated by nanosystems such as liposomal amiodarone and platelet like fusogenic liposomes, these systems also promote angiogenesis, reduce infarction size, and improve cardiac healing. Advancements in cell-based drug vehicles offer promising prospects for targeted drug delivery and cell therapy in nanomedicine for cardiovascular applications.Delivery systems utilizing poly(DL-lactide-co-glycide) [PLGA] and porous silica nanoparticles (pSi) allow spatiotemporal release of growth factors. Sirolimus nanoparticles have been investigated for their potential in reducing inflammation and restenosis risk. Mesoporous silica nanoparticles [MSNPs] enhance the therapeutic effects of honokiol in inhibiting neointimal hyperplasia(*Website*, n.d.-d).

Liposomes for Cardio-Nutraceuticals

Nutraceuticals come from foods that may be good for your health in some way. They are being made more and more with liposomal technology. Encapsulating liposomes makes these supplements easier to get and use, which is meant to make them work better.

Benefits of liposomal technology in Nutraceuticals:-

1. **Enhanced Bioavailability:**

   Liposomes have a bilayer of lipids that keeps hydrophobic nutraceuticals inside and an aqueous core that keeps hydrophilic ingredients inside. This makes it easier for the body to absorb them. Liposomes protect delicate nutrients from being broken down by stomach acid and digestive enzymes. It makes sure that the bloodstream gets more of the active ingredient(*Website*, n.d.-e)**.**

2. **Role in controlled release:**

   Liposomes can be sent exactly where they are needed. These are meant to keep nutraceuticals moving around the body in a precise and continuous way, either by slowly spreading their contents or by targeting certain areas(*Website*, n.d.-f).

3. **Reduced side effects:**

   The encapsulation of liposomes reduces Gastrointestinal irritation and also other negative effects which typically occurred with nutraceuticals(*Website*, n.d.-g)**.**

4. **Increased stability:**

   Liposomal encapsulation protects the nutraceuticals against degrading and oxidation thus prolonging their shelf-life(*Website*, n.d.-f))

Multilamellar vesicles (MLV) were several hundred nanometres (generally 100–400 nm) in diameter and made up of several concentric lipid bilayers with water-filled spaces in between. These were the first structures to form when phospholipids were spread out in water. Large unilamellar vesicles were single-layer vesicles that were bigger than 100 nm, while small unilamellar vesicles were single-layer vesicles that were 100 nm or smaller, with a theoretical minimum of about 20 nm.

Ingredients:

You can get phospholipids from lecithins made from different seed oils (soy, sunflower, and canola are all available for sale), egg yolks, and milk. The amount of phosphatidyl choline (PC) in lecithin and purified lecithin fractions is used to grade them. Raw lecithins have about 15% PC, while higher grades of lecithin fractions have 50% to 95% PC. PC has been used as a medicine for a long time and is thought to be the best phospholipid for making liposomes. Soy phospholipids have been used the longest, and soy lecithin is a great source of very high PC.nowadays soybean was not in use Sunflower PC has replaced soy in many commercial nutritional liposomes, but the global supply chain is currently unstable because large food companies are also trying to meet consumer demand. Phospholipids are good for your health on their own (not just as carriers), and PC is probably the most helpful of these. PC is the main structural support for cell membranes and a micellizing part of bile. It has been used in integrative and functional medicine for a long time.Unsaturated phospholipids from soy or sunflower produce a more flexible membrane that should function better for intraoral absorption, while stiffer phospholipids, such as hydrogenated phospholipids and saturated phospholipids, create stiffer membranes that may be better for GI absorption(Gunstone (Chemiker & Grossbritannien), 2008). 2,3 Other lipid molecules, both surfactant and nonsurfactant, as well as surface modifiers, have been employed to produce more stable, absorbable, or long-lasting structures, even though phospholipids are practically a defining feature of the liposome bilayer membrane. The most prevalent of these are membrane stiffeners like cholesterol, oils like medium-chain triglycerides (MCTs), and food-grade PEGs. Alginates, chitosan, and hyaluronic acid are examples of surface coatings for mucoadhesion. One useful and secure method for adding to liposome membranes is D-α-tocopheryl polyethylene glycol 1000 succinate (TPGS), a water-soluble vitamin E derivative of PEG. These micronized emulsions and coated liposomes have up to ten times longer circulation half-lives than liposomes without hydrophilic surface coatings and are more stable in biological settings but it has been proven ideal maintaining stability for longer

periods has been difficult since instability in surfactant system commonly seen as creaming of emulsions(Aoyagi, 2016; Wu, 2002).

The common nutraceuticals formulated with liposomes:-

1. **Vitamins:**
   - **Vitamin C :** It enhanced the absorption compared to standard oral supplements(Purpura et al., 2024)
   - **Vitamin D:** It increases the bioavailability and efficiency especially in bone well-being.
2. **Minerals:**
   - **Magnesium :**

     Liposomal magnesium supplements are soluble and can be absorbed much more quickly and are less likely to trigger stomach discomfort
   - **Calcium:**

     Encapsulation increases the absorption of calcium and its utilization(Tinsley et al., 2022)
3. **Anti-oxidants:**
   - **Curcumin:**

     The active ingredient in turmeric,curcumin has low bioavailability, Liposomal formulations improves absorption as well as therapeutic effects(Bulboacă et al., 2019)
   - **Coenzyme Q10 (CoQ10) :**

     Liposomal CoQ10 boosts bioavailability and can aid in heart health and energy production

4. **Herbal extracts:**
   - **Resveratrol -**

     It is known for its anti-aging properties, where liposomal carrier is incorporated can improve the absorption
   - **Ginseng -**

     Extracts of Ginseng provide better absorption and effectiveness

5. **Omega 3 fatty acids:**
   - **EPA and DHA :-**

     Capsulating these essential fatty acids into liposomes improves the stability of their absorption and stability which benefiting cognitive and cardiovascular wellbeing(Tinsley et al., 2022)

Advantages:

- Higher Bioavailability and Absorption comparatively with other oral dosage forms
- Non-invasive avoids pain and discomfort
- Transmucosal (oral) uptake and absorption are enhanced by micronized encapsulation, which also shields against the harsh environment of the GI tract.
- More delivery within cells
- Capable of containing both hydrophilic and hydrophobic substances.
- Alternative for those who have trouble swallowing a tablet
- Can be given to adults and children as an option of incremental and adjustable dosage

- Economical, since a lower dosage can produce the desired results

Disadvantages concerning with it:

- Possibility of poor manufacturing
- Instability can occur
- Increased intracellular delivery

Niosomes for cardio-nutraceuticals:

Structure:

Niosomes are non-ionic surfactant based vesicle used for delivering nutraceuticals i.e bioactive compound of food that targets the cardiovascular system, thus promotes the enhancement in the cardiovascular therapy(Maisch & Oelze, 2006).Niosomes are structurally composed of vesicular structure consists of cholesterol and non-ionic surfactants (e.g., Span 60, Tween 60) which was commonly known as bilayer membrane(Baillie et al., 1985). Generally, niosomes are amphiphilic in nature that provides advantage of encapsulating both hydrophilic and lipophilic bioactive compounds.For instance, aqueous core encapsulates the hydrophilic compounds such as vitamins and peptides whereas lipophilic layers entraps the hydrophobic compounds such as curcumin, omega-3 fatty acids etc., this configuration of structure enhances the bioavailability, stability and controlled release of nutraceuticals(Moghassemi & Hadjizadeh, 2014).

Préparation:

There are a number of methods for preparation of niosomes by using non-ionic surfactants and cholesterol to form a bilayer membrane which enhances the capsulation of nutraceuticals.The most commonly employed method is thin-film hydration technique. In this method,a volatile organic solvent, such as methanol or chloroform, is used to dissolve a mixture of cholesterol and non-ionic surfactants, like Span or Tween series. A rotary evaporator is then used to evaporate the solvent under reduced pressure, forming a thin lipid layer on the inner wall of a round bottomed flask. Multilamellar vesicles are then formed spontaneously by hydrating this film with an aqueous solution containing the desired nutraceutical. In order to produce more consistent and stable niosomes, these vesicles can be further reduced in size using extrusion or sonication(Jana, 2025).

Other more advanced techniques are employed such as reverse phase evaporation method, where an aqueous solution contains the desired nutraceutical. In order to produce more consistent and stable niosomes, these vesicles can be further reduced in size using extrusion or sonication.the emulsion is prepared by mixing the hydrophobic phase (surfactant and cholesterol) and aqueous phase solvent containing nutraceuticals,followed by evaporation of solvent gives niosomes.The ether injection method involves slowly injecting a surfactant-lipid solution dissolved in ether into a heated aqueous phase, which causes the ether to evaporate and produce unilamellar vesicles.Microfluidization is a high-pressure technique that produces nanosized, homogenous niosomes by driving a cholesterol-surfactant combination through microchannels with high shear and turbulence(Winwar Study Expert, 2022).

All these methods has a unique advantages over one another in providing more stable and effective niosomes and also all these methods allow the efficient encapsulation of various cardioprotective nutraceuticals, including coenzyme Q10, omega-3 fatty acids, resveratrol, and curcumin(Anderson et al., 2013). The method of choice for preparation and formulation of niosomes has a direct influence on their release rate of active compound, stability and bioavailability of the final product(Miao et al., 2023).

Stability of niosomes:

Niosomes offer superior stability over liposomes by preventing oxidation, hydrolysis and temperature or environmental variations(Fadaei et al., 2024). Each ingredient in the formulation contributes to the stability of the product both physically and chemically, for example cholesterol in the bilayer prevents the leakage of drug by stabilizing the membrane and also contributes to prevent the hydrolysis as in other phospholipids. The non-ionic surfactant used in the formulation prevents the product from oxidation and also by choosing the appropriate surfactant and charge inducers (e.g., dicetyl phosphate) it

reduces the aggregation of vesicles(D. M. Brown, 2010). Most advantageous is that these preparations are stable at room temperature without using refrigeration. The stability can be enhanced by using cryoprotectants such as trehalose, sucrose, mannitol, glucose etc., (i.e. lyophilization). These stability properties make the niosomes in longer shelf life, simpler storage, lower production costs and also well-suited for nutraceutical delivery(Luo et al., 2023).

Examples:

Curcumin:

Curcumin-loaded niosomes with Span 60 and cholesterol, optimised for nano-size and good entrapment efficiency. The niosomes exhibited a sustained release profile over 24 hours,which significantly increases curcumin's bioavailability. It also has the significant antioxidant capacity and also prevents the degradation in the gastrointestinal tract(Li Zhu Meijuan Sun et al., 2023).

Coenzyme Q10:

Coenzyme Q10 (CoQ10) is a lipophilic compound essential for mitochondrial energy production it reduces the oxidative damage to the tissues, which on encapsulation in niosomes increases its solubility and stability over degradation(Zhou et al., 2014).

Resveratrol:

Resveratrol niosomal preparation also has good encapsulation efficacy. It shows relatively increased stability and improved absorption. It has good antioxidant and vasorelaxation properties by modulating the NO metabolism thus reducing the oxidative stress(Singh et al., 2025).

Plant sterols:

Plant sterols such as β-sitosterol, stigmasterol etc., are encapsulated in niosomes and they showed good entrapment efficacy. They ensure improved cellular uptake and good therapeutic potential against cardiovascular diseases(Jaiswal et al., 2024).

3. PHYTOSOMES FOR CARDIO-NUTRACEUTICALS

Structure:

Phytosomes is a novel technology used as controlled and sustained release delivery. The term "phyto" means plant\herb and "some" means cell-like structure. This system consists of a phospholipid complex system of plant extract or phytochemicals in nano size range generally [<100nm] of particles(Shriram et al., 2022). Unlike other preparation, in phytosomes the active compounds is encapsulated within a lipid bilayer, phytosomes involve a direct interaction at the molecular level where the polar functional groups of the phytochemical such as hydroxyl or carboxyl groups form hydrogen bonds or electrostatic interactions with the polar head of the phospholipid. And results in an amphiphilic complex where it has both hydrophilic and lipophilic properties(Ruiz & Campos, 2016). This unique structure of phytosomes allows the poorly absorbed drugs such as curcumin, silybin, quercetin to deliver effectively into the body. It also shows better stability and great bioavailability(Kroon, 2025).

Preparation:

Phytosomes are produced by the reaction of a stoichiometric amount i.e. 1:1 or 1:3 of phospholipid (phosphatidylcholine) with the standardized plant extract or phytoconstituents in non-polar solvents(Aneja et al., 2025). The preparation of phytosomes begins by accurately weighing phosphatidylcholine and cholesterol, which are then dissolved in 10 ml of chloroform in a round-bottom flask. The mixture is sonicated for 10 minutes in a bath sonicator. Following this, the organic solvent is removed using a rotary evaporator maintained at 45–50°C. After complete removal of the solvent, a thin layer of the phospholipid mixture is obtained, which is subsequently hydrated with the methanolic extract of the plant in a rotary evaporator at 37–40°C for 1 hour. The hydrated mixture of lipid and plant extract is then sonicated for 20 minutes in an ice bath to allow heat dissipation. Finally, the obtained phytosomes are collected, transferred into amber-colored bottles, and stored in a freezer at 2–8°C for preservation(Patel et al., 2013);(Ruiz & Campos, 2016).

Stability of phytosomes:

Phytosomes show protection against degradation by protecting plants active from heat, light, oxidation, and enzymatic degradation(Kalita et al., 2017). It has better physical stability Compared to liposomes, phytosomes form more stable complexes due to stronger chemical bonding between phospholipids and phytoconstituents. Phytosomes prevent crystallization and improves compatibility with biological membranes(Bhumireddy et al., 2025). It is also resistant to gastric acid degradation thereby protecting sensitive phytochemicals from acidic environment. Hence easily formulated into stable solid dosage forms leading to improved shelf life and bioavailability(Ortega-Pérez et al., 2024).

Examples:

Polyphenols:

Polyphenols such as curcumin and resveratrol Complexation with phospholipids (e.g., *Curcumin Phytosome/Meriva*®) shows improved chemical stability, protects from oxidation, and enhances absorption up to 29-fold. Therapeutically used for Better antioxidant activity, improved endothelial function, reduced inflammation(M. Ahmed & Shafqat, 2025).

Flavanoids:

Flavonoids (e.g., Quercetin, Silybin) show Higher membrane permeability, stable in GI tract. It is used to enhance anti-inflammatory and anti-atherosclerotic effects(Toiu et al., 2025).

Omega 3-fatty acids:

Omega 3-fatty acids such as e.g., EPA, DHA when formulated as phytosomes shows better absorption and protects from oxidation. Used to lower the level of triglycerides and also has anti-inflammatory activity(L. Brown, 2018).

Plant sterols:

Sterols (e.g., Beta-sitosterol) shows Increased solubility and GI stability. Used to lower the LDL-cholesterol to a greater extent and also prevents plaque formation(*Website*, n.d.-h).

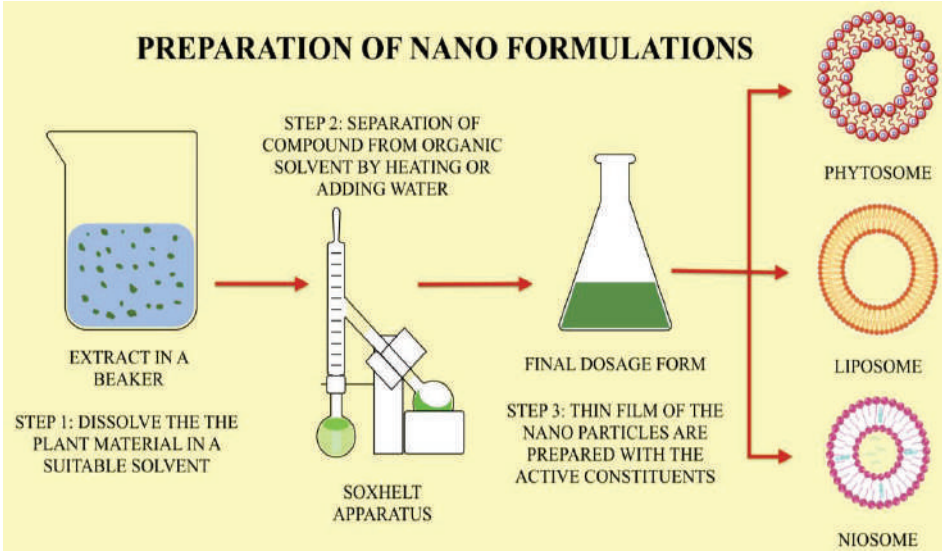

Figure 7. 1: Preparation of Nanoformulation

Table 7.1: Comparative Analysis of Different Nanoformulations

PARAMETERS	LIPOSOMES	NIOSOMES	PHYTOSOMES
Nature of core product	Aqueous core with lipid bilayer.	Aqueous core surrounded with non-ionic surfactant.	There is no typical core, phospholipid forms a molecular complex with phytoconstituents.
Encapsulation Efficacy	It can be moderate to high, depending upon the lipid composition and drug properties(Frontiers Editorial Office, 2023).	It is high, which is suitable for both hydrophilic and lipophilic drugs(Liga et al., 2024).	It is moderate i.e it is suitable only for certain specific phytoconstituents(Barani et al., 2021).
Stability	Low to moderate because it is prone to oxidative degradation and leakage without stabilizers(Barani et al., 2021; Frontiers Editorial Office, 2023).	Generally higher than liposomes; better physical and chemical stability(Liga et al., 2024).	High due to stable molecular complex, resistant to hydrolysis and oxidation(Barani et al., 2021).
Release Profile	May exhibit burst release which can be tailored with composition changes Followed by a sustained phase(Frontiers Editorial Office, 2023).	Sustained and controlled release profile(Liga et al., 2024).	Controlled release but the release depends on digestion and metabolism in the GI tract(Barani et al., 2021).
Specific site Targeting	High; easily modified for active targeting using ligands like PEG, antibodies, folate etc.,(Nakhaei et al., 2021)	Moderate to high; surface functionalization is possible(Liga et al., 2024).	Low; intended for systemic absorption via oral route rather than targeted delivery(Barani et al., 2021).
Toxicity	Generally low; but possible immune response or toxicity can occur if lipids are oxidized or not well-characterized(Nakhaei et al., 2021).	Low; non-ionic surfactants are generally safe, but some may cause irritation or allergy(Jana, 2025).	Very low; made from natural compounds and phospholipids, ideal for nutraceutical use(Barani et al., 2021).

Bioavailability	Improved for poorly soluble drugs and protects from degradation(Salla et al., 2024).	Enhanced bioavailability through improved permeation and sustained release(Baillie et al., 1985).	Significantly increased for plant-derived compounds due to better solubility and membrane permeability(Xu et al., 2024).
Limitations	-Increased production cost - Instability without cholesterol or stabilizers - Difficult to scale-up(Frontiers Editorial Office, 2023).	- Potential aggregation over time -Surfactant dependent toxicity - Batch reproducibility challenges(Liga et al., 2024).	- Only applicable to certain phytochemicals - Complex manufacturing process - Not suitable for synthetic drugs(Aneja et al., 2025).
Challenges	- Lipid oxidation - Short shelf life - Requires sterile and cold-chain storage conditions(Frontiers Editorial Office, 2023).	- Formulation optimization - Scale-up for commercial use - Long-term stability testing is required(Liga et al., 2024).	-Phospholipid and phytochemical ratio must be optimized - Limited data on long-term storage and clinical use(Barani et al., 2021).

4. CARDIO-PROTECTIVE PHYTOCONSTITUENTS IN NANOFORMULATIONS

Current research shows that plant-based natural phytoconstituents provide essential protection for cardiovascular health. Phytoconstituents which include polyphenols and flavonoids and omega-3 fatty acids and plant sterols and curcumin and ginsenosides and allicin and Lycopene and Coenzyme Q10 and other compounds serve as treatment options for cardiovascular diseases. The compounds show therapeutic effects because their bioavailability and solubility levels are extremely low and their metabolic processes occur at an accelerated rate. The researchers developed nanoformulations combined with targeted drug delivery systems as a solution to existing challenges.

Polyphenols:

People recognize polyphenols as natural compounds which protect against oxidative damage and reduce inflammation through their resveratrol and quercetin content. The grape and red wine compound resveratrol protects the heart by enhancing endothelial function and minimizing oxidative damage and preventing platelet clumping. The flavonol quercetin, which occurs in onions and apples and berries, assists with blood pressure control and reduction of oxidative damage. Their medical applications remain restricted because of their low bioavailability and high metabolic rates. The development of nanoformulations, which include nanoemulsions and solid lipid nanoparticles and polymeric nanoparticles through PLGA-based systems, helps to improve the solubility of Reveratrol while providing protection against degradation and achieving controlled release. The use of Nanoencapsulation through lipid-based carriers and chitosan

nanoparticles and dendrimer systems enables quercetin to achieve higher absorption rates while extending its bioavailability duration.(Yang et al., 2020).

Flavonoids:

Flavonoids exist as a primary category which contains polyphenolic compounds that are found in all fruit and vegetable products as well as in all types of medicinal plants. The substances provide multiple heart health benefits because they protect against oxidative harm and prevent LDL cholesterol from oxidizing and they improve blood vessel function and their anti-inflammatory effects. The clinical use of flavonoids such as kaempferol and luteolin and hesperidin faces limitations because of their poor solubility and low oral bioavailability. The application of nanotechnology-based delivery systems which include nanomicelles and nanosuspensions and nanostructured lipid carriers (NLCs) results in improved compound dissolution and permeability rates. The formulations enable efficient delivery through biological membranes while they enhance stability and deliver continuous product release which optimizes their ability to protect heart health. (F. Ahmed et al., 2025).

Omega-3 fatty acids:

The omega-3 fatty acids eicosapentaenoic acid and docosahexaenoic acid work together to protect heart health through their ability to decrease triglyceride levels and stop abnormal heart rhythms while they also fight against inflammation in the body. However, the water-insoluble compounds become ineffective because they face two challenges which include their tendency to break down when exposed to light and oxygen. To solve this problem scientists developed nanoformulations which include nanoemulsions and liposomes and self-emulsifying drug delivery systems (SEDDS) to improve omega-3 fatty acids stability and bioavailability while protecting them from oxidation and enabling better gastrointestinal absorption which leads to improved cardiovascular risk reduction.(Arshad et al., 2025);(Ashfaq et al., 2023).

Plant Sterols:

Plant sterols are natural compounds that have a cholesterol-like chemical structure. The use of plant sterols leads to successful cholesterol reduction which helps to avoid atherosclerosis and heart disease medical conditions. The restricted usage of the product occurs because it has two main issues which prevent effective use. The delivery system of nutraceuticals needs enhancement through the application of nanoformulation techniques which include nanoparticle systems and nanoemulsions and nanoliposomes. The process of biopolymer and cyclodextrin encapsulation results in enhanced solubility and stability which creates an effective dietary solution for treating hypercholesterolemia and cardiovascular disease risk reduction.(Sharma et al., 2025).

Curcumin:

The potent antioxidant capacity and anti-inflammatory effects of curcumin establish its function as a protector against cardiovascular diseases. The treatment has demonstrated effectiveness in decreasing cardiac fibrosis and myocardial hypertrophy while enhancing endothelial function. The substance cannot be used in medical practice because it suffers from two major problems which make it difficult to use. Scientists have developed targeted delivery systems through the use of polymeric nanoparticles which include PLGA and chitosan, liposomes, and nanogels, to solve existing obstacles. The functionalized nanoparticles which carry targeting ligands enable curcumin to reach inflamed vascular tissues, which improves the treatment results for cardiovascular diseases.(Datz, 2017).

Ginsenosides:

Ginsenosides (Rg3 and Rb1) function as saponins which provide proven cardiovascular advantages. The compounds enhance endothelial function while decreasing oxidative stress and protecting against myocardial apoptosis. The drugs show pharmacokinetic limitations because they exhibit low solubility and undergo extensive first-pass metabolism. Researchers have utilized lipid-based nanoparticles and phytosomes and nanocrystals to develop methods which improve drug bioavailability and specifically deliver medicine to cardiovascular tissues. The new drug formulations demonstrate enhanced treatment effectiveness for ischemic heart disease. (Adnan et al., 2023).

Allicin:

The sulfur-containing molecule Allicin produces three medical benefits which include lipid reduction and blood pressure reduction and prevention of atherosclerosis. The unstable nature of Allicin causes it to break down rapidly which restricts its application. Scientists have developed three types of delivery systems which include nanoemulsions and liposomes and cyclodextrin complexes to protect allicin from degradation while enabling its scheduled delivery. The systems provide two functions which include transporting the substance to blood vessels and delivering its heart protection effect. (Devi, 2025).

Lycopene:

Lycopene, a carotenoid found abundantly in tomatoes, has antioxidant properties and reduces LDL oxidation and improves vascular health. The substance becomes difficult to absorb because of its hydrophobic characteristics. Lycopene delivery to patients requires the development of three nanocarrier systems which include nanoliposomes and solid lipid nanoparticles and nanoemulsions. The nanoformulations provide two benefits because they protect the substance from degradation while increasing its bioavailability which makes lycopene an effective substance for cardiovascular health enhancement. (Kaczor & Baranska, 2016).

Coenzyme Q10:

Nutraceuticals which support cardiovascular health usually contain Coenzyme Q10. The compound functions as an essential component for mitochondrial ATP synthesis while providing strong antioxidant protection to heart muscle cells. The lipophilic properties of CoQ10 restrict its absorption through the gastrointestinal tract.(Sharma et al., 2025).

The use of Nano formulations like liposome, niosomes, etc will definitely have greater therapeutic effect when compared to the conventional drug delivery system since the Preparation of Nanoformulations doesn't require much ingredients when compared to conventional drug delivery systems. The nano formulations also have some disadvantages like sophisticated instruments, higher making cost. Etc. This Nono formulation is used for cardiovascular disease as a protective manner and immunobooster is still not proven. But it is proven that the NDDS will increase the therapeutic range and increase the shelf life and prolong drug release in the body. (Jha et al., 2024; Pires et al., 2023; Yao et al., 2025).

Surface modifications:

Surface Modification is a change in the surface of the Nono particle which makes the increase in the physiochemical property and enhances stability, targeting capability, biocompatibility, and functionality for drug delivery and other applications.

The surface modification in cardio vascular Nano formulation helps to increase the therapeutic effect & stability of the drug which can also overcome the disadvantages of the novel drug delivery systems.

Chemical Surface Modification

- Covalent Conjugation: Functional groups (e.g., carboxylic acids, amines, thiols) on the nanoparticle surface are chemically linked with polymers (like PEG), ligands, or targeting agents using coupling reagents such as EDC/NHS (carbodiimide chemistry) or maleimide-thiol chemistry. This enhances properties like circulation time (stealth coating), stability, and active targeting(*Website*, n.d.-i).
- Silanization: Common for nanoparticles with hydroxyl groups (e.g., silica, cellulose), organosilanes are attached to the surface, improving dispersibility in nonpolar solvents and increasing compatibility with other materials(Mahtabani, 2021).
- Plasma Treatment: Plasma creates reactive groups on a nanoparticle surface, which are then used for further functionalization(Kharkwal & Janaswamy, 2016).

Physical Surface Modification

- Surface Adsorption: Surfactants or polymers are adsorbed onto the nanoparticle surface to improve colloidal stability or impart specific functionalities. This is easily reversible and often used for initial property tuning(Alzobaidi, 2019).
- Laser and Ion Implantation: High-energy sources like lasers or ion beams modify the surface to alter microstructure and enhance properties such as hardness, wear resistance, and reactivity(Coffa et al., 1995).

- Physical Coating: Techniques such as layer-by-layer assembly deposit thin films or shells onto nanoparticles for added stability or functional responsiveness(Rawtani & Agrawal, 2014).

Biological Surface Modification

- Ligand Attachment: Nanoparticles are coated with biological ligands (antibodies, peptides, aptamers) to confer active targeting to specific cell types or tissues, enabling receptor-mediated uptake and enhanced therapeutic selectivity(Kesharwani, 2022).
- Biocompatible Coatings: Zwitterionic, synthetic, or protein coatings reduce immunogenicity and non-specific interactions. A prominent example is PEGylation (attachment of polyethylene glycol), which prolongs blood circulation and reduces immune clearance(Suk et al., 2016).

Clinical Applications and Case Studies:

1. Chronic heart failure and GISSI-HF: n-3 polyunsaturated fatty acids (PUFAs)

   Participants and design: double-blind, randomised, placebo-controlled study. In all, over 7046 chronic heart failure patients were registered in Italy.

   Dosage and intervention: n-3 PUFA (≈1 g/day) versus placebo.

   Hospitalisations for cardiovascular conditions and all-cause mortality are the main results(Aleksova et al., 2013).

2. Q-SYMBIO — Chronic heart failure and coenzyme Q10 (CoQ10)

   Participants and design: Multicenter, double-blind, randomised, placebo-controlled study of chronic heart failure patients.

   Intervention and dosage: oral administration of Coenzyme Q10 (ubiquinone) as an adjuvant treatment; the precise dosage schedule is described in the PubMed abstract.

   Hospitalisation, death, and major adverse cardiovascular events (MACE) are the main outcomes.

   Important conclusions: Patients who received treatment reported improvements in their symptoms as well as decreases in MACE, cardiovascular mortality, and all-cause mortality(Chopra et al., 2024).

3. Dietary inorganic nitrate and beetroot juice: HFpEF exercise and haemodynamics

   Participants and design: Randomised crossover/controlled studies in elderly individuals with preserved ejection fraction (HFpEF) and heart failure.

   Intervention and dosage: For brief periods of time (e.g., 1 week), daily beetroot juice (a source of inorganic nitrate) is administered.

   Blood pressure, vascular function, and exercise tolerance (submaximal endurance, peak VO_2) are the main results(Tilly, 2013).

4. Red yeast rice extract, or xuezhikang, as a supplementary preventive measure after MI

   Participants and design: Chinese individuals with a history of myocardial infarction participated in a randomised experiment.

   Intervention and dosage: Xuezhikang, a red yeast rice extract that contains monacolins, which are naturally occurring substances that resemble statins.

   Cardiovascular death and recurrent coronary episodes are the main outcomes(Trogkanis et al., 2024).

5. A meta-analysis of hawthorn extract for chronic heart failure

   Participants and design: Meta-analysis of randomised studies investigating the effects of extracts from Crataegus (hawthorn) on chronic heart failure.

   Intervention and dosage: Different standardised hawthorn extracts were used in each study.

   Exercise tolerance, functional improvement, and symptoms (fatigue, dyspnoea) are the main results(Dunning, 2013).

6. Systematic review: Xuezhikang and red yeast rice in the prevention of cardiovascular disease

   Participants and Design: Systematic evaluation of randomised studies evaluating the safety and effectiveness of red yeast rice extracts for cardiovascular outcomes and cholesterol reduction(Wilkinson et al., 2021).

Challenges:

1. Formulation Heterogeneity

   Assessing effectiveness is made more difficult by variations in the concentration, purity, and bioavailability of active ingredients (such as polyphenols, CoQ10, and omega-3 PUFAs).

   Reproducibility is decreased when commercial items and clinical trial preparations are not standardised. For instance, the amount of monacolin K in various red yeast rice formulations varies, which influences the results of lipid-lowering(Keane, 1999).

2. Limited Evidence of High Quality

   Instead of using concrete outcomes like death or significant cardiovascular events, many studies are small, have a limited duration, or employ surrogate endpoints (blood pressure, cholesterol levels, exercise tolerance). While there is quite strong evidence for omega-3 and CoQ10, meta-analyses show that bigger, longer-term RCTs are needed for other nutraceuticals, such as hawthorn, beetroot, and polyphenols(Pittler et al., 2005).

3. Variability Among Individuals

   Response to nutraceutical therapies is influenced by comorbidities, baseline nutritional status, gut flora, and genetics. Clinical studies seldom examine personalised therapies(Murga-Garrido et al., 2021).

4. Safety and Regulatory Issues

   There are worries about contamination, adulteration, or incorrect labelling because dietary supplements are subject to less stringent regulations than medicines. There is a chance of drug-nutraceutical interactions, particularly when red yeast rice contains chemicals that resemble statins or when large dosages of omega-3 have anticoagulant effects(*Website*, n.d.-j).

5. FUTURE PERSPECTIVES

1. Personalised and Accurate Nutrition

   Optimising patient-specific nutraceutical regimens may be possible through the integration of genetic, metabolomics, and microbiome data. Potential to reduce side effects and increase effectiveness(Lagoumintzis & Patrinos, 2023).

2. Quality Control and Standardisation

   Creating pharmaceutically standardised nutraceutical formulations (nano-formulations, phytosomes) to increase repeatability, effectiveness, and bioavailability. Regulatory supervision might improve security and make clinical practice integration easier(Rath et al., 2024).

3. Combination Treatments

   Combining nutraceuticals (such as omega-3 + CoQ10 or polyphenols) with traditional medication may have synergistic effects that improve cardiovascular health. To create safe and efficient combinations, mechanistic research and RCTs will be essential(Rakel & Minichiello, 2022).

4. Large-Scale, Long-Term RCTs

   Hard outcomes (mortality, hospitalisation, serious adverse cardiovascular events) have to be established. The specific function of nutraceuticals in the prevention and treatment of cardiovascular disease may be determined via comparative efficacy studies with conventional medication(Risom et al., 2025).

5. New Technologies

Targeted delivery, absorption, and solubility can all be enhanced by liposomal, phytosomal, or nanotechnology formulations. Potential for creating "cardio-nutraceuticals" that target certain organs, such as the endothelium or myocardial(Cicero et al., 2020; Kar et al., 2024).

CONCLUSION

The development of cardio-nutraceuticals through advanced nano-delivery systems which use liposomes, niosomes, and phytosomes as delivery methods has created an effective supplementary method for treating cardiovascular diseases.Clinical research shows that their treatment results in better lipid profiles and improved endothelial function and enhanced exercise capacity and better heart failure results. Although precise nutrition methods and standardised nanoformulations and controlled clinical trials still need to overcome three main barriers which include product variation and insufficient long-term research and uncertain regulatory procedures. The combination of these nutraceuticals with standard medication practices which follow research-based guidelines shows potential to improve cardiovascular results and patient care for both primary and secondary prevention purposes.

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Authors' Contributions

Partha Sarathi Das contributed equally to the conception, design, drafting, and finalization of this work. All authors were actively involved in the literature review, data interpretation, manuscript preparation, and critical revision for intellectual content. Additionally, the manuscript was carefully edited for clarity, coherence, and grammatical accuracy. All authors have read and approved the final version of the manuscript and agree to be accountable for all aspects of the work.

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