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Chapter 11: Synergistic Nano-Targeted Therapeutics with Naturopathic Interventions

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Abstract

Cardiovascular diseases remain the leading causes of morbidity and mortality in all parts of the globe and novel approaches to treatment are sought after with respect to safety, innovation and integrations. The fast development of nanotechnology has also contributed to the revolution in the delivery of cardio-protective nutraceuticals that improve their solubility, stability, bioavailability, and functioning at the specific sites. Simultaneously, naturopathic methods, including herbal preparations, dietary optimization, and lifestyle measures, have full advantages as they reduce oxidative stress, suppress inflammation, enhance endothelial activity, and restore metabolic balance. This chapter focuses on the synergistic potential of nanotechnology-based delivery systems and naturopathic therapies in improving the outcomes of cardiovascular therapy. It mentions several types of nanocarriers such as liposomes, phytosomes, nanoemulsions and polymeric nanoparticles that have been used to enhance the delivery of plant-based antioxidants, flavonoids, polyphenols and other bioactive compounds traditionally used in natural medicine. Mechanistic viewpoints are given to describe the mechanisms by which these integrative mechanisms regulate molecular targets involved in atherosclerosis, hypertension, and myocardial damage. In addition, the chapter discusses preclinical results, translation opportunities, and safety profiles, and tackles major issues including the complexity of formulations, scalability of production, and regulatory standardization. Through the integration of modern nanoscience and evidence-based approaches to naturopathy, nano-integrative therapeutics is a prospective model of sustainable and personalized cardiovascular care.

Keywords: *Synergistic therapy, Nano-targeted delivery, Naturopathic interventions, Cardiovascular therapeutics, Bioactive compounds, Holistic medicine*

1. INTRODUCTION

The leading cause of mortality and morbidity in the world is cardiovascular diseases [1]. The Global Burden of Disease (GBD) Study 2019 shows that CVD deaths increased from 12.1 million to 18.6 million during the same period. In contrast, the incidence of CVD increased significantly from 271 million in 1990 to 523 million in 2019[2]. There are plenty of disorders listed within cardiovascular disease including heart disease, coronary artery disease, stroke, myocardial infarction, and congestive heart failure. Ageing and urbanization trends contributed to rapid changes in low- and middle-income nations, where over 80% of CVD incidents occur. In the majority of emerging nations worldwide, CVD is becoming a bigger issue. Therefore, effective interventions are required to manage the CVD crisis [3]. The persistent declines in CVD mortality in developed nations during the second half of the 20th century are largely attributable to improvements in secondary prevention and treatment, as well as decreases in the prevalence of major risk factors. These declines overlap with those observed for infectious diseases during the first half of the twentieth century [4]. Since 1990, age-standardized CVD mortality rates have reduced by around 30% worldwide, whereas crude (or "all ages") CVD mortality rates have only marginally declined. Furthermore, the number of deaths due to CVD has more than doubled throughout this time [2][3][4].

The complex disorder of myocardial infarction (MI) which includes both angina and stroke together with arrhythmias results from multiple physiological factors that operate over extended periods. The worldwide cardiovascular disease (CVD) epidemic results from four factors which include an aging population together with sedentary lifestyles and poor dietary practices and the increasing occurrence of metabolic disorders such as diabetes and obesity. Standard medical treatments show effectiveness for acute condition management yet produce only minor benefits in disease prevention while creating unwanted effects that decrease patient adherence to treatment. [7].

In addition to the limitations of existing therapies, there is an evident and urgent need for integrative, safer, and more sustainable therapeutic methods that target the underlying causes of cardiovascular disease (CVD) rather than only treating its symptoms[8]. Recent developments in nanotechnology have also transformed medication delivery, providing innovative answers to several bioavailability and targeting issues[9]. The purpose of nanocarriers, which include solid lipid nanoparticles, liposomes, phytosomes, nanoemulsions, and polymeric nanoparticles, is to encapsulate bioactive compounds and transport them to certain tissues or biological targets[10]. Pharmacokinetic and pharmacodynamic profiles are improved by these systems because they increase solubility, shield the therapeutic drug from early degradation, and permit regulated, site-specific release[11]. Nanotechnology is being investigated more and more in cardiovascular medicine to enhance the administration of cardio-protective medicines, such as natural substances and synthetic medications[12]. This chapter aims to explore the scientific foundation and possible therapeutic benefits of integrating naturopathic therapies with nano-targeted drug delivery technologies in relation to the implications of naturopathic treatments for cardiovascular disease.

2. CONCEPT OF SYNERGY IN CARDIOVASCULAR CARE

In cardiovascular care, synergy is bringing different therapeutic strategies together to ideally create a much better effect than what could have been generated by one method acting alone. Cases of cardiovascular disorders are hardly ever straightforward-they are an interplay of damaged vessels, inflammation at the site, oxidative stress, cholesterol imbalance, and hormonal alterations. Their complex nature makes it nearly imperative that treatment of these conditions be all-encompassing[13]. Neither a one-time intervention, nor even a combination of pharmacological therapy with lifestyle changes will be enough to manage the disease but a holistic and integrative approach, which facilitates a combination of two (or three) aspects, blending pharmacological therapy, lifestyle changes, and, in some cases, more advanced interventions, is necessary to govern the full range of the disease[14]. Elimination of dietary trigger substances is one of the most basic treatment options. As an example, baking soda and aspirin are some of the substances recommended to be avoided by some patients to avoid additional injury to kidneys. Overall, the treatment regimes involve the administration of statins, beta-blockers, ACE-inhibitors, and antiplatelet drugs, and they are supplemented with lifestyle changes, including a heart-friendly diet, regular physical activity, and non-smoking, which all positively influence cardiovascular and renal health outcomes[15]. Revascularisation, RA, and formal cardiac rehabilitation form the other points in advanced treatment. Research shows that pharmacological synergy exists when treatments given in conjunction, such as antiplatelet drugs and blood pressure drugs or dual antiplatelet therapy, significantly help reduce the incidence of heart attacks and related complications. But it's not just medicines. The care is team-based, involving cardiologists but also general practitioners and others, nurses, dietitians, physiotherapists ,all of whom help patients stick to their treatment plans so that risks can be caught early and the patient treated as a whole person. Combining lifestyle changes with proven medical therapy leads to further improvements in blood pressure control, cholesterol and overall cardiovascular health. The most effective care is delivered when the different interventions and professionals all work together consistently, reinforcing each other toward an overall comprehensive therapeutic effort[16].

2.1. Rationale for combining nanotechnology and naturopathy

Nanotechnology and naturopathy have a powerful therapeutic partnership potential because of the compounding effect of the natural bioactive compounds, which have low bioavailability, poor solubility, and rapid metabolic breakdown. Particularly effective in encapsulating phytoconstituents, to increase physicochemical stability, permit controlled release, and target tissue or cellular loci, are those nanocarrier systems that have been most selectively utilised, such as liposomes, polymeric nanoparticles, nanoemulsions, and metallic nanostructures, which optimise therapeutic efficacy and reduce off-target adverse effects and toxicity[17]. Naturopathic agents like polyphenols, flavonoids, alkaloids, and terpenoids are pharmacologically versatile and multi-monotherapeutic since they are antioxidants, anti-inflammatory agents and anticancer agents. However, there is still a lack of clinical translation due to the suboptimal pharmacokinetics and ecological instability of phytoconstituents in physiological conditions. Nanotechnological interventions can overcome these barriers by obtaining high therapeutic concentrations,

extending the duration of systemic circulation, and increasing permeability across biological barriers such as the blood-brain barrier and gastrointestinal epithelium to enhance more effective drug delivery[18]. Further advanced nanoformulations allow co-delivery of more than one phytochemical in a nanoformulation or co-delivery of phytochemicals and standard chemotherapeutics, and thus, synergistic interactions or overcoming multidrug resistance. This meeting is consistent with the growing paradigm of integrative and personalised medicine, which seeks the creation of safer, effective, and sustainable therapeutics that are based on natural sources.

2.2. Advantages over conventional therapies

The advanced or synergistic therapies work with CVDs to treat the multifactorial nature of cardiovascular pathologies with finer granularity, specificity, and swiftness. Generally, post-operative therapies of mono-therapy type are protocol-driven and may offer relief from symptoms or risk factor control. They hardly address complex comorbidities, stop disease progression, or assist long-term recovery. Conversely, the combination of drug therapy, biologics, and device-based therapies (drug-eluting stents, implantable cardioverter-defibrillators, etc.) appears to be more effective to employ in mortality reduction and enhanced recovery and patient discharge[19]. The digital health tools, remote patient monitoring, and AI-mediated diagnostics enable the use of the data in making decisions in real-time, which are not available in the traditional model. Individualised care plans informed by the genetic, phenotypic, and behavioural profiles also require such advanced options and can contribute to adherence and increased therapeutic response. Conversely, synergistic therapies have a tendency to promote multidisciplinary teamwork in order to provide care in a whole person approach through coordination of cardiology with pharmacology, rehabilitation and behavioural sciences. Such a paradigm shift reinforces clinical outcomes, as well as enhances cost-effectiveness by removing unnecessary interventions and enhancing the use of the available resources. As the art of cardiovascular treatment advances, the effectiveness of these new forms of treatment versus the traditional therapeutic methods is increasingly more evident in clinical and real-life studies[20].

3. NANOTECHNOLOGY IN CARDIO-NUTRACEUTICAL DELIVERY

Nanotechnology continues to demonstrate opportunities for improving therapeutics through its ability to enhance bioavailability and stability and targeted delivery of cardioprotective nutraceuticals which lead to improved therapeutic results in CVDs. Cardio-nutraceuticals such as omega-3 fatty acids, curcumin, resveratrol, quercetin, and coenzyme Q10 function as strong antioxidants with anti-inflammatory properties which decrease lipid levels, yet their clinical usefulness remains unachieved because of their low gastrointestinal tract bioavailability and poor water solubility and rapid metabolism [21]. The drug delivery systems which use nanotechnology include liposomes SLNs NLCs polymeric nanoparticles micelles and nanoemulsions because these systems focus on encapsulation to achieve controlled drug release with sustained therapeutic effects. For example, experimental models with polymeric nanoparticles containing resveratrol showed increased oral bioavailability and cardioprotection through enhancing endothelial dysfunction caused

by oxidative stress. All the above factors considered, the nanoemulsion formulations of omega-3 fatty acids have relative increments in absorption and serum triglyceride level and greater absorption and lower triglyceride level compared with conventional ointments of similar oils and fats[22]. Moreover, surface polymeric coating of nanoparticles with targeting peptides and antibodies enables focused delivery of the nanoparticles to atherosclerotic plaques, which minimises the off-target effects and improves the therapeutic accuracy. Other recent advances include nanocarriers that, in response to a change in pH, redox state, or enzyme concentration, release nutraceuticals encapsulated by the nanocarriers and that, during pathological conditions in cardiovascular tissues. Despite these developments, the lack of scalability of production, regulations, potential nanotoxicity, and the absence of long-term exposure studies are also significant and should still be considered. Nevertheless, nanotechnology in conjunction with cardio-nutraceuticals is an excellent and novel approach to the prevention and treatment of cardiovascular disease that paves the way to customised and precision therapies[23].

3.1. Liposomes, phytosomes and nanoemulsions

Nanocarrier systems such as liposomes, phytosomes, and nanoemulsions are the new systems promising to enhance bioavailability and therapeutic activity of nutraceuticals that have cardiovascular protective properties. Liposomes are systems described as spherical vesicles consisting of lipid bilayers and are able to entrap hydrophilic and lipophilic bioactives and enhance the solubility, stability and targeted delivery of cardio-protective lipid and workforce nutraceuticals, e.g. polyphenols, omega-3 fatty acids, and plant sterols[24]. Phytosomes, however, are a new complex of plant bioactives in association with lipids like flavonoids, saponins and terpenoids and phospholipids and enhance the absorption of membranes and systemic absorption compared with traditional herbal extracts. Oil-in-water or water-in-oil nanoemulsions with droplet diameters less than 200 nm, which boost the cardiovascular activity of lipophilic nutraceuticals like curcumin and resveratrol, and coenzyme Q10, through better dispersibility, increased encapsulation efficiency, and controlled release. Delivery systems based on such nanotechnology protect gastrointestinal degradation of fragile nutraceuticals, enhance time-delivery, and deliver to the cardiovascular system in a controlled way, significantly enhancing their therapeutic benefit to hyperlipidemia, oxidative stress and endothelial dysfunction.. The incorporation of liposomes, phytosomes, and nanoemulsions is a sophisticated innovation for overcoming bioavailability constriction and enhancing the clinical effectiveness of nutraceuticals for the heart, proposing a translation for functional foods and drugs[25].

3.2. Polymeric and lipid-based nanoparticles

The advances of delivery systems based on polymeric and lipid-nanoparticles have immensely contributed to the development of cardiac nutraceuticals delivery due to the properties that include bioavailability, improved stability, and controlled release of bioactive substances. These cardio-nutraceuticals that include such substances as polyphenols, flavonoids, omega-3 fatty acids and plant-derived antioxidants are low water soluble, have poor digestive stability and rapid metabolism, which altogether have rendered

their therapeutic prospects against CVDs to be very limited. The eco-friendly carrier system can be represented by various polymeric nanomaterials, e.g., based on biodegradable polymers (poly (lactic-co-glycolic acid) (PLGA), chitosan, and polyethylene glycol (PEG)) that are capable of not only encapsulating the hydrophilic and lipophilic nutraceuticals but also forming a protective layer around them against the enzymatic degradation and delivering the latter in a slow, stepwise, or on-demand manner[26]. Also, lipid-based nanocarriers, e.g. solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs) and liposomes have structural analogies to natural membranes and, therefore, have excellent biocompatibility, reduced side effects, and the fat-soluble cardio-protective agents resveratrol, curcumin, and coenzyme Q10 can be readily encapsulated. Such nanocarriers significantly improve not only the oral absorption and plasma half-life of nutraceuticals but also allow the delivery to cardiovascular tissues that are the target to thus facilitating the activity of antioxidants, anti-inflammatories, and lipid-lowering agents that are critical for atheroprotection and cardiac function[27]. New research, for example, points out that the coating of nanoparticles with ligands such as peptides, antibodies, or aptamers may lead to better endothelial targeting and fewer side effects, thus giving the possibility of using a precise approach in the treatment of CVDs. However, these benefits are accompanied by certain issues, such as mass production, regulatory approval, and long-term safety evaluation, which are still major obstacles that must be resolved before clinical translation can be reached. In general, polymeric and lipid-based nanocarriers are a state-of-the-art means to increase the therapeutic effect of cardioprotective and cardioprotective nutraceuticals, and they are a powerful resource for future interventions in cardiovascular health[28].

3.3. Advantages in bioavailability and targeted delivery

One of the revolutionary changes that nanotechnology has brought about is its role in boosting the bioavailability and the target delivery of cardio-nutraceuticals by addressing many of the limitations associated with standard formulations. Cardiovascular diseases (CVDs) represent the leading causes of death throughout the entire world. The nutraceuticals polyphenols, omega-3 fatty acids, flavonoids and coenzyme Q10 together with other nutraceuticals show potential to provide deep heart support. Their therapeutic efficacy suffers from multiple issues which include their low solubility and low absorption as well as their fast metabolism and their unstable nature within the gastrointestinal system. Bioactive molecules can be loaded into nanocarrier-based systems like liposomes, solid lipid nanoparticles, polymeric nanoparticles, nanoemulsions, and dendrimers[29]. Hence, reactivity is increased and the protection of the molecules from enzymatic degradation is ensured, as well as prolonging systemic circulation. The small size of these masqueraders grants the ability of permeability through biological membranes to a great extent, thus, heightened gut absorption coupled with controlled release kinetics, which in turn allows higher bioavailability to be achieved than that of traditional dosage forms. Besides that, surface-altering procedures, including ligand conjugation or PEGylation, have the advantage of allowing targeted transport into the cardiovascular tissues. Hence, the nutraceuticals can be the ones to bring the most efficient use of the action site while at the same time avoiding the occurrence of off-target effects as well as systemic toxicity[30]. In addition,

nanotechnology platforms are optimal in terms of the co-delivery of various bioactive agents; when together, the agents can achieve a very impressive response when it comes to the activation of cardioprotective kinases by the agents, producing a synergistic anti-inflammatory, antioxidant and lipid-reducing response, which is truly remarkable. It has been found in many studies that nanoformulated resveratrol, quercetin, and curcumin have better pharmacokinetics and significant therapeutic effects in atherosclerotic, myocardial infarction, and hypertension animal models. To conclude, nanotechnology use in cardio-nutraceutical delivery holds an extremely bright prospect of overcoming the pharmacokinetic barriers, attaining the specific and regulated drug delivery, and eventually enhancing the clinical outcome of nutraceuticals in the prevention and treatment of cardiovascular diseases[31].

4. NATUROPATHIC INTERVENTIONS IN CARDIOVASCULAR HEALTH

4.1. Different Plant Extracts and Their Bioactive Compounds Used in the Prevention and Treatment of CVDs

The rising prevalence of cardiovascular diseases, safer and more effective treatments are essential. Plants provide multiple classes of bioactives—flavonoids, polyphenols, saponins, alkaloids and terpenoids. Following WHO pharmacovigilance guidelines is vital to ensure their safe use. Containing diverse bioactive compounds, these herbs exhibit antioxidant, anti-inflammatory, vasodilatory, and lipid-lowering effects, improving endothelial function and reducing oxidative stress and atherosclerosis. Their multi-target actions make herbal medicines valuable in preventing and managing various cardiovascular disorders.

Table 11.1: Mechanisms and Clinical Relevance of Cardioprotective Medicinal Plants and Bioactive Compounds

Plant / Compound	Active Constituents	Cardiovascular Actions	References
Digitalis purpurea (Foxglove)	Digoxin, Digitoxin (Cardiac glycosides)	Enhances cardiac contractility, regulates heart rate, alleviates heart failure and arrhythmia; narrow therapeutic index requiring toxicity monitoring	[32]
Allium sativum (Garlic)	Allicin, Sulfur compounds	Reduces LDL, BP, oxidative stress, platelet aggregation; prevents atherosclerosis, improves endothelial function	[33]
Crataegus spp. (Hawthorn)	Flavonoids, Proanthocyanidins	Enhances blood flow, lowers BP, prevents plaque formation, stabilizes heart rhythm	[34]
Crocus sativus (Saffron)	Crocin, Safranal	Reduces oxidative stress, inflammation, apoptosis; improves myocardial protection, lipid profile, cardiac function	[35] [36]
Centella asiatica	Asiatic acid, Asiaticoside, Madecassoside	Decreases hypertrophy, fibrosis, ischemic damage; improves microcirculation, nitric oxide availability	[37]
Panax ginseng	Ginsenosides	Promotes NO-mediated vasorelaxation, inhibits ACE, reduces inflammation, oxidative stress, thrombosis, cholesterol	[38]
Hibiscus sabdariffa (Roselle)	Polyphenols (Anthocyanins, Flavonoids)	Lowers BP, LDL, triglycerides; enhances antioxidant status and lipid metabolism	[39][40]
Ginkgo biloba	Ginkgolides, Bilobalide	Promotes vasodilation, inhibits ACE, reduces endothelial dysfunction, lipid accumulation, inflammation	[41][42]

Camellia sinensis (Green Tea)	Catechins (EGCG)	Decreases oxidative stress, BP, platelet aggregation, inflammation; improves endothelial function and lipid profile	[43]
Quercetin	Flavonoid (Antioxidant)	Prevents cardiac fibrosis, arrhythmia, hypertension, ischemia-reperfusion injury	[44]
Anchusa italica Flavonoids	Rutin, Quercetin, Kaempferol	Improves cardiac remodeling, reduces inflammation	[45]
Caffeic, Ferulic & Ellagic Acids	Phenolic acids	Antiplatelet, antioxidant, vasoprotective actions; reduces thrombus and platelet aggregation	[46][47]
Saponins (Various Plants)	Glycyrrhizic acid, Astragaloside IV, Tribulosin, Platycodin D	Exhibits antioxidant, anti-inflammatory, anti-ischemic, vasodilatory effects; enhances antioxidant enzymes, myocardial protection	[48]

4.2. Specific nutraceuticals with clinical evidence

Omega-3 polyunsaturated fatty acids (EPA/DHA, high-EPA formulations): According to several meta-analyses (2021–2024), taking omega-3 supplements can lower some cardiovascular outcomes, especially in high-risk or secondary prevention sub group. However, other analyses indicate that there may be a slight increase in the risk of atrial fibrillation in some populations, as well as little to no benefit. Benefit-harm balance is determined by dose, EPA vs. EPA+DHA mix, and baseline risk[49][50].

soluble fiber (such as psyllium) and plant sterols/stanols lower LDL cholesterol; these substances are still advised as lipid management adjuncts in guidelines and have consistent effects on LDL[51][52][53].The e ffects of nutraceutical supplements (phytosterols, red yeast rice, and L-tyrosol) in a group of individuals with polygenic hypercholesterolemia who were not responding to the M edDiet.The lipid profile, blood pressure, arterial stiffness, and endothelial function were theprimary charac teristics taken into account for the results[54].

4.3. Lifestyle-based naturopathic strategies

4.3.1. Physical activity, cardiac rehabilitation, and exercise:

Frequent resistance and aerobic exercise enhances secondary prevention results and lowers cardiovascular risk variables such as blood pressure, insulin resistance, and visceral obesity.

The biggest absolute risk reduction is achieved by lifestyle regimens that incorporate exercise, dietary changes , and behavioral adjustments. For post-MI and revascularization care, structured cardiac rehabilitation (CR) is still essential; however, more research is being done on modified naturopathic programs (such as adding yoga or mind-body techniques)[55].

4.3.2. Mind-body practices, stress management and sleep:

Stress, poor sleep, and autonomic instability are acknowledged contributors to cardiovascular risk. Mind-body therapies, including yoga, meditation, pranayama, and cognitive-behavioural therapy,

improve blood pressure, heart-rate variability, anxiety/depression, and some physiological biomarkers. Larger definitive outcome trials are being developed, however new randomized data indicates that yoga-based cardiac rehabilitation may provide benefits that are equal to or greater than those of traditional CR[56].

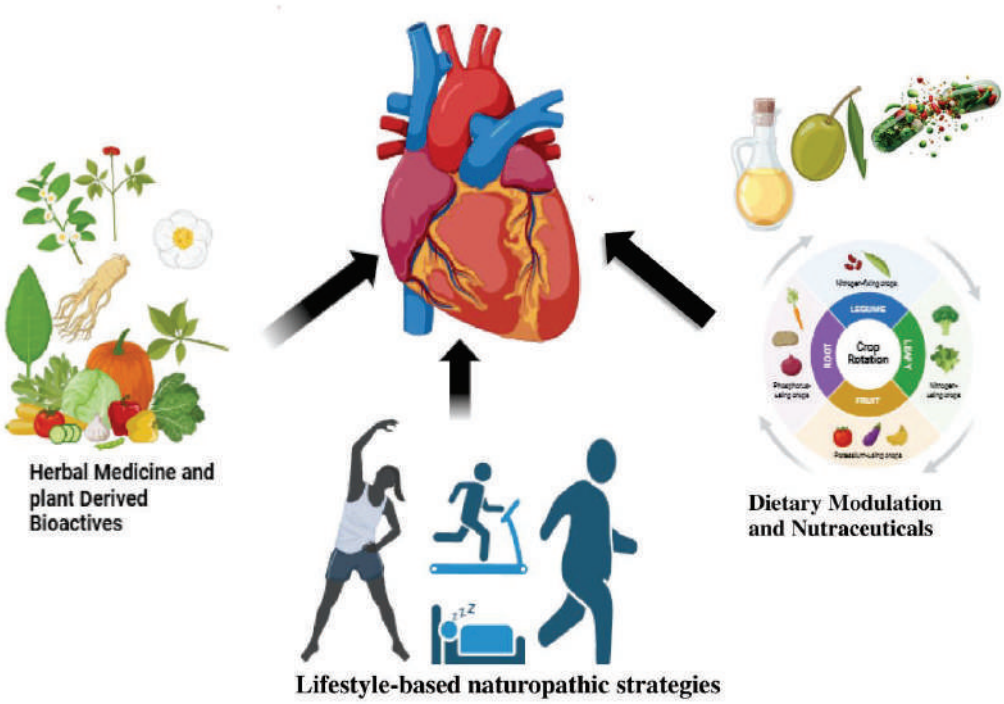

Figure 11.1: Natural and Lifestyle-Based Interventions in Cardiovascular Wellness

5. SYNERGISTIC MECHANISMS OF ACTION

5.1. Modulation of Oxidative Stress and Inflammation:

Every stage of cardiovascular diseases (CVDs), oxidative stress is a major factor that dynamically affects the course of the illness. When oxidized LDL, pro- inflammatory cytokines and advanced glycation and products cause early endothelial damage, NF- κB is activated endothelial dysfunction occurs, and inflammatory cells are drawn in, which starts the development of atheros clerotic plaque[57][58].

Plaque development and instability are further fueled by the production of foam cells, which are mediated by lipid uptake, macrophage polarization, and NLRP3 inflammasome activation.

Excess ROS produced by mitochondria, NADPH oxidase, and other sources worsen cardiac ischemia-reperfusion injury during acute ischemic episodes, encouraging inflammation, endothelial dysfunction, and c

ell death. Through the activation of MAPK, NF-κB, MMPs, and apoptotic pathways, chronic oxidative stress damages the integrity of cardiomyocytes and extracellular matrix, which leads to cardiac remodeling and heart failure[59].

Ironically, through signaling pathways such Nrf2, PI3K/Akt, and AMPK, moderate ROS levels can provide cardioprotection by improving redox homeostasis, antioxidant defenses, and mitochondrial function.

Overall, oxidative stress has effects that are very dose- and context-dependent, functioning as both a pathogenic driver and a possible protective mediator.

5.2 Effects on Lipid Metabolism and Endothelial Function

The endothelial dysfunction together with inflammatory responses and atherosclerosis development which poses a major threat to cardiovascular diseases results from metabolic disturbances in lipid and glycolipid pathways. The metabolic changes which occur in the body lead to disturbed fat and carbohydrate metabolism. This results in oxidative stress accumulation and vascular inflammation and plaque formation which are the main factors that cause cardiovascular and cerebrovascular diseases [60]. Metabolic by-products from lipid and carbohydrate breakdown lead to disease progression because they increase fat storage and insulin resistance and arterial calcification [61]. The main pathway through which metabolic disturbances lead to cardiovascular disease development operates through endothelial metabolic dysregulation which acts as the primary pathway that connects these two health conditions. Endothelial cells rely on glycolysis which produces a Warburg-like effect to generate energy needed for angiogenesis and barrier maintenance and nitric oxide (NO) production control [62]. The body achieves its metabolic balance through three main elements that include metabolic pathways and insulin and glucose levels. Pathological conditions which involve oxidative stress and hyperglycemia and dyslipidemia will disrupt this metabolic balance. This disruption results in two main effects which include and decrease mitochondrial function and NO production and reactive oxygen species (ROS) levels will rise [63].

5.3 Molecular pathways in CVD progression

The connection between vascular remodeling and inflammatory response together with metabolic changes and genetic factors leads to the development of CVD. The process of creating aneurysms occurs through three main factors which include extracellular matrix degradation and vascular smooth muscle cell loss and possible microbial involvement. The microbiota shows potential as a therapeutic agent because certain Acinetobacter Burkholderia and Escherichia bacteria species can damage vascular tissue. Genetic screening serves as an effective method to identify individuals who possess a higher risk of developing aneurysms because specific genetic mutations in FBN1 and COL3A1 and MYH11 genes lead to increased susceptibility. Inflammation creates vascular damage through activated macrophages who lose their ability to perform autophagy and through ATM-NF-kB signaling pathways. The dysregulated cytokines which include VEGF and TGF-β produce an additional weakening effect on arteries. Advanced ultrasonography enables the early detection of aneurysms through noninvasive methods. Allicin which comes from garlic shows potential

as a pulmonary hypertension treatment by its ability to decrease oxidative stress and improve nitric oxide signaling while preventing vascular remodeling. The combination of these discoveries enables the development of new CVD treatments and precise diagnostic methods.

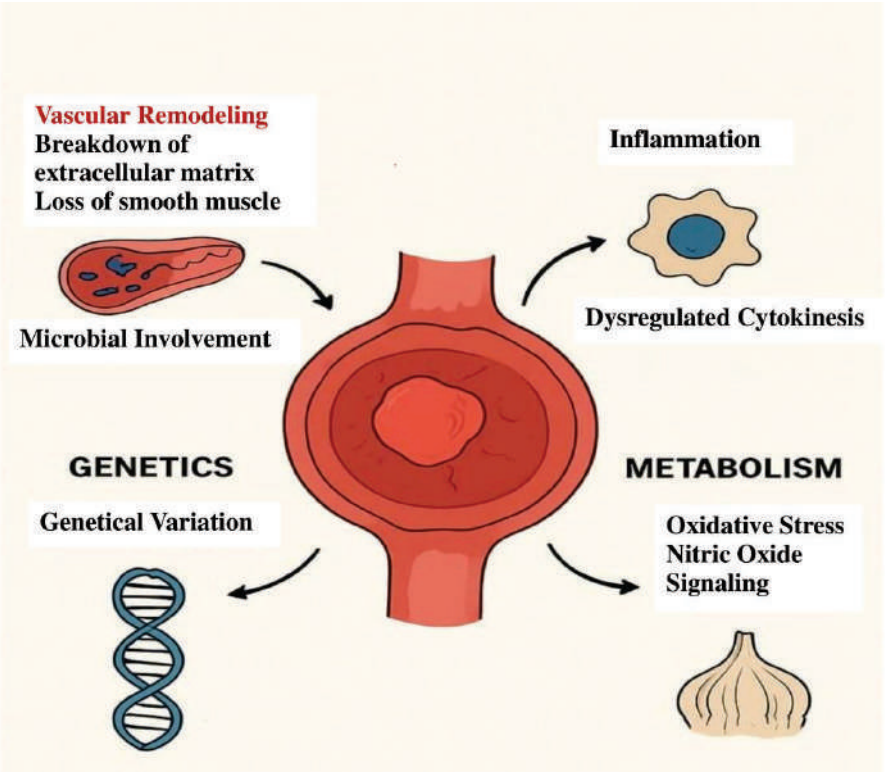

Figure 11.2: Interplay of Genetics, Metabolism, Inflammation, and Microbes in Vascular Pathology

6. ANIMAL STUDIES SUPPORTING NANO-NATUROPATHIC SYNERGY

The latest animal studies which have been conducted demonstrate that natural substances which have been nanoformulated deliver better results than their non-encapsulated counterparts. Dual-trigger systems for phytochemicals: Researchers created a system which used gelatin and perfluorohexane to construct core-shell nanodroplets that contained berberine chloride. The system used two activation mechanisms which allowed it to detect pH changes and ultrasound signals: The system released materials through a 89 percent cumulative release which occurred after ultrasound activation while only 15 percent of materials passed through the system at normal body temperature after 24 hours. The nanoparticles maintained their stability for approximately one month when stored at 4 °C[69]. Rodent studies about metabolic syndrome show that lipid nanoparticles which contain curcumin or quercetin (or both) produce better results in preventing inflammation through TNF-α and IL-6 reduction and increased insulin sensitivity and lower body fat levels than using the unbound substance[70].Antioxidant phytochemicals which include resveratrol and curcumin and plant flavonoids which were developed into nanoparticle drugs that targeted endothelial cells reduced tissue harm

and oxidative stress and plaque accumulation in mice and rat models of ischemia-reperfusion and atherosclerosis[71][72]. Polyphenol nanocarriers which contain resveratrol and epigallocatechin gallate have shown improved ability to cross the blood-brain barrier and decreased neuroinflammation and enhanced behavioral results in stroke and neurodegeneration research studies[73].

These animal studies consistently show at least one or more of Increased bioavailability / plasma half-life, Targeted delivery to damaged/inflammatory tissues, Reduced required dose for effect (lower systemic toxicity) and Multi-pathway effects (antioxidant, anti-inflammatory, metabolic regulation). However, variations in species, route of administration, nanoparticle types (liposomes, polymeric, lipid, inorganic), dose regimens, and endpoints make cross-study comparison challenging[74].

Table 11.2. Representative animal studies supporting nano-naturopathic synergy

Natural compounds	Nano-carrier	Animal model	Route of administration	Key findings	References
Curcumin	Liposomal curcumin	Atherosclerosis (ApoE−/− mice)	IV / IP in some arms	Improved endothelial function, reduced plaque progression vs free curcumin; required lower effective dose.	[75]
Quercetin	Polymeric nanoparticles	Myocardial ischemia–reperfusion (rat)	IV	Reduced infarct size and oxidative stress; activation of Nrf2 pathway greater than free quercetin.	[76]
Resveratrol	Nanoemulsion	Diet-induced obesity (mouse)	Oral gavage	Improved lipid profile, reduced hepatic steatosis; higher plasma exposure than free resveratrol.	[77]
EGCG (green tea catechin)	BBB-penetrating lipid/polymeric carrier	Stroke / neurodegeneration (mouse)	IV	Enhanced brain uptake, reduced neuroinflammation, better behavioral recovery than free EGCG.	[78]
Berberine	Polymeric / lipid nanoparticles	Type 2 diabetes model (rat)	Oral	Greater glucose lowering and decreased inflammatory cytokines vs free berberine at equivalent/ lower dose.	[79]
Curcumin	Plant-derived lipid nanoparticles	Healthy volunteer PK (preclinical-to-human bridge; animal PK part reported)	Oral	Improved oral bioavailability in preclinical PK and supported translation to early human PK study.	[80]
Quercetin + Simvastatin	Nanoparticle co-delivery system	Atherosclerosis (ApoE−/− mice	IV	Additive plaque reduction and inflammation suppression vs separate dosing; improved plaque stability.	[81]
Plant polyphenols	Exosome-mimetic plant-derived nanoparticles	Myocardial infarction (rat)	IV	Reduced oxidative damage and infarct area; improved cardiac function vs free polyphenols.	[82]
Curcumin + Berberine	pH-responsive polymeric nanoparticles	Hypertension / endothelial dysfunction (rat)	Oral	Attenuated endothelial dysfunction and oxidative markers more effectively than single agents	[83]
Polyphenol	Polymeric	Myocardial ischemia–	IV	Combination nano-therapy	[84]

combinations	nanoparticles	reperfusion (rat)		reduced infarct size and inflammation more than free combination.	
Curcumin	Redox-sensitive micelles (macrophage-targeting)	Atherosclerosis (mouse)	IV	Preferential macrophage delivery in plaques, reduced macrophage inflammation and plaque progression.	[85]
Curcumin	Nanoencapsulated lipid nanoparticles	Hypertension model (rat)	Oral	Improved endothelial function, reduced blood pressure vs free curcumin; improved stability and bioavailability.	[86]

7. Challenges and Limitations

The medical system used natural compounds. The system checked the safety of nanocarriers because they could deliver natural compounds to patients. The system tested materials because certain polymers and cationic lipids and inorganic nanoparticles emit material-related dangers which cause oxidative stress and inflammation. The system used three properties which include size and surface charge and biodegradability to test their biocompatibility. Immunogenicity develops through repeated administration for chronic conditions which leads to complement activation and anti-carrier antibody formation against PEG. Non-biodegradable nanomaterials tend to build up in vital organs such as the liver and spleen and lungs. The long-term distribution and elimination of these nanomaterials must undergo complete examination to understand their behavior. The assessment process needs to track off-target connections because they have the potential to create disruptions in cellular signaling mechanisms and heighten oxidative stress levels. The interaction between nanomaterials and gut microbiota creates complex problems because it can either change metabolic processes or create new metabolic products. The optimization process of dose determination together with safety threshold establishment requires PK/PD modeling which includes the examination of genotoxicity and reproductive toxicity and immunotoxicity. The different ways that regulatory authorities classify nano-formulated botanicals as dietary supplements or pharmaceutical products create challenges for the industry. As such, compliance with regulatory practices like the FDA guidance on the characterization of nanomaterial, standardization of plant-derived extracts, and application of the Good Agricultural and Collection Practices (GACP) is mandatory. Scientifically, researchers and manufacturers should consider clear informed consent in terms of nanoparticle exposure, equitable allocation of benefits in terms of traditional knowledge, environmental protection with regards to nanomaterial wastes, and equitable access to novel therapies to avoid the expansion in disparities in healthcare access.

8. Future Perspectives

The current advancements in nano-naturopathic technologies resulted in the creation of smart and multifunctional delivery systems, which can provide fine-tuning therapy and adaptive reactions. Recent designs are the dual- or multi-stimuli-responsive nanoplatforms like pH- and ultrasound-responsive berberine nanodroplets, and redox-, enzyme-, and temperature-sensitive nanocarriers that are currently being preclinically evaluated. Theranostic nanostructures containing magnetic, fluorescent, or PET-based imaging

molecules enable the real-time detection of the biodistribution and pharmacodynamics of the agent which in turn enables adaptive dose changes. Immune evasion and tissue-specific targeting is also further improved by biomimetic vehicles of delivery, like exosome-mimicking particles or cell membrane-coated nanoparticles. Furthermore, spatiotemporal delivery of plant-derived bioactives can be achieved with modular nanocarrier platforms that can incorporate exchangeable ligands and therapeutic cargo, which can be conditional on the presence of reactive oxygen species (ROS), low acidic pH, light, or magnetic fields, and so on. At the same time, the emergence of personalized nutraceutical treatments applies biomarker-based stratification such as oxidative stress levels, inflammatory mediators, endothelial dysfunction, genomic and metabolomic signatures and microbiome composition to inform the choice and formulation of compounds. The addition of adaptive clinical trial models and digital health technologies, i.e. wearable sensors and mobile applications, enables continuous monitoring, dosage optimization, and personalized therapeutic modulation. Nanoengineered phytochemicals have potential related to adjuncts to current therapies in cardiovascular medicine by both targeting residual oxidative and inflammatory pathways to risk, and possessing preventive properties in patients at risk of metabolic or endothelial dysfunction. These nanotherapeutic procedures together with lifestyle-based interventions such as dietary optimization, exercise, and stress control offers a holistic and multifactorial model of cardiovascular treatment and care. However, their effective transfer into clinical practice will require strict clinical validation of their practical outcome benefits, and the setting up of supportive policy measures, standard regulatory rules, reimbursement policies, and fair access policies.

CONCLUSIONS

Nanotechnology and naturopathic medicine have met a critical turning point in integrative healthcare, and this merger of scientific accuracy and holistic methods in therapy is one of the most important developments. Nanotechnology is useful in drug delivery by increasing solubility, stability, bioavailability, and reducing degradation and off-target effects that reduce the conventional and natural therapy. Nano-formulations are effective when used together with phytochemicals, herbal extracts, and nutraceuticals to enhance therapeutic efficacy and minimize toxicity to facilitate personalized and patient-centered care. This integrative approach has demonstrated promise in the treatment of chronic, metabolic, inflammatory and neoplastic diseases in the combination of molecular precision with biological equilibrium. Controlled, site-specific release can be demonstrated with stimuli-responsive nanocarriers (e.g. pH-, enzyme-, redox-sensitive) that align with naturopathic principles of safety and minimal harm. However, the barrier to translating these innovations into clinical practice is associated with regulatory approval, scalability of manufacturing, durability with biocompatibility, and botanical component standardization. The future relies on interdisciplinary team work, strict clinical validation, and internationally standardized guidelines to guarantee safety, efficacy and accessibility. Finally, the combination of nano-targeted therapy and naturopathic modalities provides a prospective framework of precision and preventive medicine integrating technological advances and the restorative effects of nature to form a whole of sustainable health.

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Authors' Contributions

All authors contributed equally to the conception, design, writing, and finalization of this work. Each author was actively involved in literature review, data interpretation, manuscript preparation, and critical revision. All authors have read and approved the final version of the manuscript and agree to be accountable for all aspects of the work.

REFERENCES

1. Di Cesare M, Perel P, Taylor S, et al (2024) The Heart of the World. Glob Heart 19:11
2. Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, Barengo NC, Beaton AZ, Benjamin EJ, Benziger CP BA (2020) Global burden of cardiovascular diseases and risk factors, 1990–2019: update from the GBD 2019 study. J Am Coll Cardiol 76:2982–3021
3. Li Y, Cao G, Jing W, Liu J, Liu M (2023) Global trends and regional differences in incidence and mortality of cardiovascular disease, 1990−2019: findings from 2019 global burden of disease study. Eur J Prev Cardiol 30:276–286
4. Nedkoff L, Briffa T, Zemedikun D, Herrington S, Wright FL (2023) Global Trends in Atherosclerotic Cardiovascular Disease. Clin Ther 45:1087–1091
5. Xu S, Liu Y, Zhu M, Chen K, Xu F, Liu Y (2025) Global burden of atherosclerotic cardiovascular disease attributed to lifestyle and metabolic risks. Sci China Life Sci 68:2739–2754
6. Chong B, Jayabaskaran J, Jauhari SM, et al (2025) Global burden of cardiovascular diseases: projections from 2025 to 2050. Eur J Prev Cardiol 32:1001–1015
7. Malachias MVB, Kaiser SE, Albuquerque DC de, et al (2024) Risk of Adverse Health Outcomes in Patients with Poor Adherence to Cardiovascular Medication Treatment: A Systematic Review. Arq Bras Cardiol 121:e20240469
8. Smith SC, Benjamin EJ, Bonow RO, Braun LT, Creager MA, Franklin BA, Gibbons RJ, Grundy SM, Hiratzka LF, Jones DW L-JD (2011) AHA/ACCF secondary prevention and risk reduction therapy for patients with coronary and other atherosclerotic vascular disease: 2011 update: a guideline from the American Heart Association and American College of Cardiology Foundation endorsed by the Worl. J Am Coll Cardiol 58:2432–46
9. Patra JK, Das G, Fraceto LF, et al (2018) Nano based drug delivery systems: recent developments and future prospects. J Nanobiotechnology 16:71
10. Bakoyiannis I, Daskalopoulou A, Pergialiotis V, Perrea D (2019) Phytochemicals and cognitive health: Are flavonoids doing the trick? Biomed Pharmacother 109:1488–1497
11. Pattni BS, Chupin V V., Torchilin VP (2015) New Developments in Liposomal Drug Delivery. Chem Rev 115:10938–10966
12. Parikh KS, Omiadze R, Josyula A, Shi R, Anders NM, He P, Yazdi Y, McDonnell PJ, Ensign LM, Hanes J (2021) Ultra-thin, high strength, antibiotic-eluting sutures for prevention of ophthalmic infection. Bioeng Transl Med 6:e10204
13. Jaffe AS (2008) Key Issues in the Developing Synergism between Cardiovascular Imaging and Biomarkers. Clin Chem 54:1432–1442
14. Alter DA (2007) Therapeutic lifestyle and disease-management interventions: pushing the scientific envelope. Can Med Assoc J 177:887–889
15. Cardozo LFMF, Borges NA, Ribeiro M, Yee-Moon Wang A, Mafra D (2023) Protect the Kidneys and Save the Heart Using the Concept of Food as Medicine. J Ren Nutr 33:S110–S117
16. Buckley BJR, Lip GYH (2022) Current Concepts: Comprehensive "Cardiovascular Health" Rehabilitation—An Integrated Approach to Improve Secondary Prevention and Rehabilitation of Cardiovascular Diseases. Thromb Haemost 122:1966–1968
17. Ng PQ, Ling LSC, Chellian J, et al (2020) Applications of Nanocarriers as Drug Delivery Vehicles for Active Phytoconstituents. Curr Pharm Des 26:4580–4590
18. Teli D, Satasia R, Patel V, et al (2024) Nature meets technology: Harnessing nanotechnology to unleash the power of phytochemicals. Clin Tradit Med Pharmacol 5:200139
19. Singh H, Agrawal DK (2022) Recent advances in the development of active hybrid molecules in the treatment of cardiovascular diseases. Bioorg Med Chem 62:116706
20. Visco V, Ferruzzi GJ, Nicastro F, Virtuoso N, Carrizzo A, Galasso G, Vecchione C, Ciccarelli M (2021) Artificial

Intelligence as a Business Partner in Cardiovascular Precision Medicine: An Emerging Approach for Disease Detection and Treatment Optimization. Curr Med Chem 28:6569–6590
21. Sindhu RK, Goyal A, Algın Yapar E, Cavalu S (2021) Bioactive Compounds and Nanodelivery Perspectives for Treatment of Cardiovascular Diseases. Appl Sci 11:11031
22. Patel P, Garala K, Singh S, Prajapati BG, Chittasupho C (2024) Lipid-Based Nanoparticles in Delivering Bioactive Compounds for Improving Therapeutic Efficacy. Pharmaceuticals 17:329
23. Liu H, Pietersz G, Peter K, Wang X (2022) Nanobiotechnology approaches for cardiovascular diseases: site-specific targeting of drugs and nanoparticles for atherothrombosis. J Nanobiotechnology 20:75
24. Atrooz O, Kerdari E, Mozafari MR, Reihani N, Asadi A, Torkaman S, Alavi M, Taghavi E (2024) A Comparative Review of Tocosomes, Liposomes, and Nanoliposomes as Potent and Novel Nanonutraceutical Delivery Systems for Health and Biomedical Applications. Biomedicines 12:2002
25. Choi SJ, McClements DJ (2020) Nanoemulsions as delivery systems for lipophilic nutraceuticals: strategies for improving their formulation, stability, functionality and bioavailability. Food Sci Biotechnol 29:149–168
26. Blanco-Llamero C, Fonseca J, Durazzo A, Lucarini M, Santini A, Señoráns FJ, Souto EB (2022) Nutraceuticals and Food-Grade Lipid Nanoparticles: From Natural Sources to a Circular Bioeconomy Approach. Foods 11:2318
27. Tang C-H, Chen H-L, Dong J-R (2023) Solid Lipid Nanoparticles (SLNs) and Nanostructured Lipid Carriers (NLCs) as Food-Grade Nanovehicles for Hydrophobic Nutraceuticals or Bioactives. Appl Sci 13:1726
28. Yang P, Ren J, Yang L (2023) Nanoparticles in the New Era of Cardiovascular Therapeutics: Challenges and Opportunities. Int J Mol Sci 24:5205
29. Manocha S, Dhiman S, Grewal AS, Guarve K (2022) Nanotechnology: An approach to overcome bioavailability challenges of nutraceuticals. J Drug Deliv Sci Technol 72:103418
30. Gul S, Miano TF, Mujeeb A, Chachar M, Majeedano MI, Murtaza G, Ahmed W, Khanzada YA, Ansari M (2024) Advancements in Nutraceutical Delivery: Integrating Nanotechnology and Microencapsulation for Enhanced Efficacy and Bioavailability. Matrix Sci Pharma 8:1–6
31. Sharma P, Sharma N (2022) Advances in Nanoformulated Polyphenols for Protection Against Cardiovascular Diseases. J Cardiovasc Pharmacol 80:648–660
32. Cuthbert JJ, Clark AL (2024) Diuretic Treatment in Patients with Heart Failure: Current Evidence and Future Directions – Part I: Loop Diuretics. Curr Heart Fail Rep 21:101–114
33. Zhao X, Cheng T, Xia H, Yang Y, Wang S (2024) Effects of Garlic on Glucose Parameters and Lipid Profile: A Systematic Review and Meta-Analysis on Randomized Controlled Trials. Nutrients 16:1692
34. Wu M, Liu L, Xing Y, Yang S, Li H, Cao Y (2020) Roles and Mechanisms of Hawthorn and Its Extracts on Atherosclerosis: A Review. Front Pharmacol. https://doi.org/10.3389/fphar.2020.00118
35. Zamani M, Zarei M, Nikbaf-Shandiz M, Gholami F, Hosseini AM, Nadery M, Shiraseb F, Asbaghi O (2022) The effects of saffron supplementation on cardiovascular risk factors in adults: A systematic review and dose-response meta-analysis. Front Nutr. https://doi.org/10.3389/fnut.2022.1055517
36. Hooshmand Moghadam B, Rashidlamir A, Attarzadeh Hosseini SR, Gaeini AA, Kaviani M (2022) The effects of saffron (Crocus sativus L .) in conjunction with concurrent training on body composition, glycaemic status, and inflammatory markers in obese men with type 2 diabetes mellitus: A randomized double-blind clinical trial. Br J Clin Pharmacol 88:3256–3271
37. Wang P, Yang J, Xu D, Zhang S, Lu S, Ji Y (2025) Madecassoside mitigates acute myocardial infarction injury by activating the PKCB/SPARC signaling pathway. Acta Pharmacol Sin 46:1624–1638
38. Hyun SH, Bhilare KD, In G, Park C-K, Kim J-H (2022) Effects of Panax ginseng and ginsenosides on oxidative stress and cardiovascular diseases: pharmacological and therapeutic roles. J Ginseng Res 46:33–38
39. Khongrum J, Yingthongchai P, Boonyapranai K, Wongtanasarasin W, Donrung N, Sukketsiri W, Prachansuwan A, Chonpathompikunlert P (2022) Antidyslipidemic, Antioxidant, and Anti-inflammatory Effects of Jelly Drink Containing Polyphenol-Rich Roselle Calyces Extract and Passion Fruit Juice with Pulp in Adults with Dyslipidemia: A Randomized, Double-Blind, Placebo-Controlled Trial. Oxid Med Cell Longev. https://doi.org/10.1155/2022/4631983
40. Elkafrawy N, Younes K, Naguib A, Badr H, Kamal Zewain S, Kamel M, Raoof GFA, M. El-Desoky A, Mohamed S (2020) Antihypertensive efficacy and safety of a standardized herbal medicinal product of <scp> *Hibiscus sabdariffa* </scp> and <scp> *Olea europaea* </scp> extracts (<scp>NW</scp> Roselle): A <scp>phase-II</scp> , randomized, double-blind, <scp>capt. Phyther Res 34:3379–3387
41. Kim H, Kang S, Go G (2024) Exploring the multifaceted role of ginkgolides and bilobalide from Ginkgo biloba in mitigating metabolic disorders. Food Sci Biotechnol 33:2903–2917
42. Yi Y, Zhang G, Lv S, Rong Y, Liu H, Teng J (2024) Comparative efficacy and safety of ginkgo-based Chinese patent medicines in patients with hypertension: A systematic review and network meta-analysis of randomized clinical trials. Medicine (Baltimore) 103:e37927
43. Kanu VR, Pulakuntla S, Kuruvalli G, Aramgam SL, Marthadu SB, Pannuru P, Hebbani AV, Desai PPD, Badri KR, Vaddi DR (2024) Anti-atherogenic role of green tea (Camellia sinensis) in South Indian smokers. J Ethnopharmacol 332:118298

44. Zhang W, Zheng Y, Yan F, Dong M, Ren Y (2023) Research progress of quercetin in cardiovascular disease. Front Cardiovasc Med. https://doi.org/10.3389/fcvm.2023.1203713
45. Wang S, Zhao Y, Song J, Wang R, Gao L, Zhang L, Fang L, Lu Y, Du G (2020) Total flavonoids from Anchusa italica Retz. Improve cardiac function and attenuate cardiac remodeling post myocardial infarction in mice. J Ethnopharmacol 257:112887
46. Gualtero DF, Buitrago DM, Pinzón-García AD, Cely Veloza WF, Figueroa-Ariza LT, Torres-Morales S, Rodriguez-Navarrete JD, Jimenez VJ, Lafaurie GI (2025) Biopolymers of Polycaprolactone Loaded with Caffeic Acid and Trametes versicolor Extract Induced Proliferation in Human Coronary Artery Endothelial Cells and Inhibited Platelet Activity. Int J Mol Sci 26:4949
47. Anjali S, Padmakumari Soumya NP, Mondal S, Mini S (2022) Cardioprotective effects of Ferulic acid in Streptozotocin- induced diabetic rats. Bioact Compd Heal Dis 5:149
48. Lin Y-C, Lin Y-C, Kuo W-W, Shen C-Y, Cheng Y-C, Lin Y-M, Chang R-L, Padma V V., Huang C-Y, Huang C-Y (2018) Platycodin D Reverses Pathological Cardiac Hypertrophy and Fibrosis in Spontaneously Hypertensive Rats. Am J Chin Med 46:537–549
49. Qi X, Zhu H, Ya R, Huang H (2023) Omega-3 Polyunsaturated Fatty Acids Supplements and Cardiovascular Disease Outcome: A Systematic Review and Meta-Analysis on Randomized Controlled Trials. Rev Cardiovasc Med. https://doi.org/10.31083/j.rcm2401024
50. Khan SU, Lone AN, Khan MS, et al (2021) Effect of omega-3 fatty acids on cardiovascular outcomes: A systematic review and meta-analysis. eClinicalMedicine 38:100997
51. Geremew Kassa M, Alemu Teferi D, Asemu AM, Belachew MT, Satheesh N, Abera BD, Erku EG (2024) Review on psyllium husk: nutritional, functional, health benefits, food industry applications, waste treatment, and potential negative effects. CyTA - J Food. https://doi.org/10.1080/19476337.2024.2409174
52. Shah, Tapaskumar. (2020). Advancing Formulation Science in Diabetes and Migraine: From Conventional Therapies to Precision Drug Delivery. Journal of Cardiovascular Disease Research. 11. 358-372.
53. Madhusoodanan S, Shah P (2008) Management of psychosis in patients with Alzheimer's disease: focus on aripiprazole. Clin Interv Aging 3:491–501
54. Finicelli M, Di Salle A, Galderisi U, Peluso G (2022) The Mediterranean Diet: An Update of the Clinical Trials. Nutrients 14:2956
55. Kariuki JK, Imes CC, Engberg SJ, Scott PW, Klem ML, Cortes YI (2024) Impact of lifestyle-based interventions on absolute cardiovascular disease risk: a systematic review and meta-analysis. JBI Evid Synth 22:4–65
56. Sharma K, Basu-Ray I, Sayal N, et al (2022) Yoga as a Preventive Intervention for Cardiovascular Diseases and Associated Comorbidities: Open-Label Single Arm Study. Front Public Heal. https://doi.org/10.3389/fpubh.2022.843134
57. Dhalla NS, Elimban V, Bartekova M, Adameova A (2022) Involvement of Oxidative Stress in the Development of Subcellular Defects and Heart Disease. Biomedicines 10:393
58. Mishra R, Pal R, Khan Z, Sahoo S, Chawra HS, Kumar D. Solid lipid nanoparticles (SLNPs): a state-of-the-art formulation strategy and their applications against tuberculosis (TB) and analgesic effects. Nanoscience & Nanotechnology-Asia. 2025 Jun;15(3):E22106812379362.
59. Zhang Z, Guo J (2024) Deciphering Oxidative Stress in Cardiovascular Disease Progression: A Blueprint for Mechanistic Understanding and Therapeutic Innovation. Antioxidants 14:38
60. de Lima EP, Moretti RC, Torres Pomini K, et al (2024) Glycolipid Metabolic Disorders, Metainflammation, Oxidative Stress, and Cardiovascular Diseases: Unraveling Pathways. Biology (Basel) 13:519
61. Vasanth S, Mishra R, Sahoo S, Parveen S, Khan Z, Mumtaz, Ruqaiya, Pal R. Advancing Mitochondrial Health in Huntington Disease (HD): Small Molecule Therapies and Neurodegeneration. Current aging science. 2025.
62. Higashi Y (2023) Endothelial Function in Dyslipidemia: Roles of LDL-Cholesterol, HDL-Cholesterol and Triglycerides. Cells 12:1293
63. Carr SM, Scrivner O, Hekman KE (2025) Narrative review of endothelial cell metabolism and aberrations in atherosclerosis and peripheral artery disease. JVS-Vascular Sci 6:100285
64. Nemes-Nikodém É, Gyurok GP, Dunai ZA, et al (2024) Relationship between Gut, Blood, Aneurysm Wall and Thrombus Microbiome in Abdominal Aortic Aneurysm Patients. Int J Mol Sci 25:8844
65. Pachani, Raj & Shah, Tapaskumar & Soni, Dhruv. (2021). Advances In Peptide-And Antibody-Targeted Nanocarriers For Cancer Therapy And Imaging. 28. 392-419. 10.53555/3sadmc24.
66. Norgan Radler C, Ku K, Hodge A, Wang T, Moore P, Sathyamoorthy M (2025) The Novel Association of a Single Nucleotide Variant in the COL3A1 Gene with Diffuse Coronary Aneurysms. Curr Issues Mol Biol 47:82
67. Elbialy A, Kitauchi M, Yamanouchi D (2023) Antioxidants and azd0156 Rescue Inflammatory Response in Autophagy-Impaired Macrophages. Int J Mol Sci 25:169
68. Yamanouchi D (2025) Molecular Insights into Cardiovascular Disease: Unraveling Pathways for Diagnosis and Treatment. Int J Mol Sci 26:2067
69. Givarian M, Moztarzadeh F, Ghaffari M, Bahmanpour A, Mollazadeh-Bajestani M, Mokhtari-Dizaji M, Mehradnia F (2024) Dual-trigger release of berberine chloride from the gelatin/perfluorohexane core–shell structure. Bull Natl

Res Cent 48:65
70. Cao Y, Chen Y, Yu T, et al (2018) Drug Release from Phase-Changeable Nanodroplets Triggered by Low-Intensity Focused Ultrasound. Theranostics 8:1327–1339
71. Koli M, Shah TM, Dutta P, Patel N, Patel AK, Ghosh B, Singh A, Pal R. Non-Ionic Surfactants (NIOs) in Niosome Drug Delivery: In-Depth Review of Clinical Trials, Patents in Tuberculosis (TB) and Oncology. Current Nanomedicine. 2025. doi:10.2174/0124681873413153251014082026
72. Lv M, Sun Q, Yu Y, Bao J (2025) Nanocurcumin in myocardial infarction therapy: emerging trends and future directions. Front Bioeng Biotechnol. https://doi.org/10.3389/fbioe.2024.1511331
73. Ahmad MZ, Pathak K, Alam A, et al (2025) Improved antidiabetic potential of quercetin-loaded chitosan–lecithin nanoparticles for effective glycaemic control. J Drug Target 1–16
74. Shamsher E, Khan RS, Davis BM, Dine K, Luong V, Somavarapu S, Cordeiro MF, Shindler KS (2023) Nanoparticles Enhance Solubility and Neuroprotective Effects of Resveratrol in Demyelinating Disease. Neurotherapeutics 20:1138–1153
75. Teli S, Shah TM. Design solid lipid nanoparticle solid lipid nanoparticle (SLNs) of dapagliflozin for enhanced oral bioavailability and controlled release in type 2 diabetes. African Journal of Biological Sciences. 2022;4(1):287-306.
76. Hu S, Lv L, Hu W, Shen J (2025) Quercetin improves myocardial ischemia–reperfusion injury by regulating macrophage M2 polarization through Bcl-2/Beclin-1 complex. Eur J Med Res 30:780
77. Amar K, Sahoo S, Mishra R, Dutta P, Ghosh B, Pal R. Lipidic nanocarriers (liposomes): A potential targeting strategy for cosmeceutical and therapeutic applications—an in-depth review. Curr Nanomed. 2026;16:e24681873411316. doi:10.2174/0124681873411316251118051648.
78. Xia C, Gu C, Liu G, et al (2023) Preparation of a novel brain-targeted EGCG liposome and its antioxidative neuroprotection. J Funct Foods 111:105911
79. Wang Z, Wu J, Zhou Q, Wang Y, Chen T (2015) Berberine Nanosuspension Enhances Hypoglycemic Efficacy on Streptozotocin Induced Diabetic C57BL/6 Mice. Evidence-Based Complement Altern Med 2015:1–5
80. Pachani, Sachin & Shah, Tapaskumar. (2021). Formulation of Paclitaxel-Encapsulated Polymeric Micelles For Targeted Breast Cancer Therapy. Journal of Population Therapeutics and Clinical Pharmacology. 28. 936-951. 10.53555/m318xt37.
81. Tang J, Lobatto ME, Hassing L, et al (2015) Inhibiting macrophage proliferation suppresses atherosclerotic plaque inflammation. Sci Adv. https://doi.org/10.1126/sciadv.1400223
82. Kim J, Li S, Zhang S, Wang J (2022) Plant-derived exosome-like nanoparticles and their therapeutic activities. Asian J Pharm Sci 17:53–69
83. Boonla O, Kukongviriyapan U, Pakdeechote P, Kukongviriyapan V, Pannangpetch P, Prachaney P, Greenwald SE (2014) Curcumin improves endothelial dysfunction and vascular remodeling in 2K-1C hypertensive rats by raising nitric oxide availability and reducing oxidative stress. Nitric Oxide 42:44–53
84. Pal R, Pandey P, Chawra HS, Singh RP. Niosomal as potential vesicular drug nano-carriers for the treatment of tuberculosis (TB). Nanoscience & Nanotechnology-Asia. 2025 Feb;15(1):E22106812323829.
85. Momtazi-Borojeni AA, Abdollahi E, Nikfar B, Chaichian S, Ekhlasi-Hundrieser M (2019) Curcumin as a potential modulator of M1 and M2 macrophages: new insights in atherosclerosis therapy. Heart Fail Rev 24:399–409
86. du Preez R, Pahl J, Arora M, Ravi Kumar MN V., Brown L, Panchal SK (2019) Low-Dose Curcumin Nanoparticles Normalise Blood Pressure in Male Wistar Rats with Diet-Induced Metabolic Syndrome. Nutrients 11:1542