Chapter 7

Essential Oils and Factors Related to Cardiovascular Diseases

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Additional information is available at the end of the chapter

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Abstract

Cardiovascular diseases (CVDs) are the leading cause of mortality and a major economic burden worldwide. Various drugs, including antihypertensive, antihyperlipidemic, and antiplatelet agents, are prescribed to treat CVDs, but these agents have side effects, including serious side effects such as bleeding. Therefore, efforts are being made to develop new drugs made of natural substances with relatively weak side effects. Essential oils are natural substances extracted from aromatic plants with biological effects, such as antioxidant and antiinflammatory activities. These oils have therefore long been used in traditional medicines. This chapter reviews the effects of essential oils on CVD-related factors. Essential oils have various effects, including improvements in lipid balance, liver function, and endothelial function; reductions in blood pressure, oxidative stress, thrombosis, and inflammation; promotion of vascular relaxation; and inhibition of diabetes development and angiogenesis. Therefore, essential oils and their active components may be promising therapeutic agents for CVDs. Further studies are needed to clarify their clinical effects and to elucidate their specific mechanisms of activity.

Keywords: essential oil, cardiovascular disease, dyslipidemia, hypertension, endothelial dysfunction

1. Introduction

Cardiovascular diseases (CVDs) are considered the leading cause of death worldwide. CVD-related deaths accounted for 31.5% of all global deaths in 2013 [1]. In 2010, the global economic burden of CVDs was 863 billion dollars, which was estimated to increase to 1044 billion dollars by 2030 [2]. Because the incidence of CVDs increases with age [3], the aging of society is expected to increase problems caused by CVDs. Traditional risk factors for CVDs, including

dyslipidemia, hypertension, and diabetes, cause oxidative stress. Fatty liver due to hyperlipidemia is also associated with increased lipid peroxidation [4]. Oxidative stress impairs vascular endothelial function, which is characterized by reduced nitric oxide (NO) bioavailability. Vascular dysfunction contributes to the impairment of vascular tone, characterized by a decrease in endothelium-dependent vasorelaxation [5]. Because endothelium-derived NO inhibits leukocyte adhesion, which causes inflammation [6] and inhibits platelet adhesion [7], endothelial dysfunction can lead to vascular inflammation and thrombosis. Activated platelets have been shown to increase inflammatory responses and the migration of vascular smooth muscle cells (SMCs) [8] (**Figure 1**).

Various drugs are prescribed to prevent and treat CVDs. For example, aspirin, clopidogrel, statins, beta-blockers and angiotensin converting enzyme (ACE) inhibitors are recommended for vascular protection in patients with stable angina [9]. Moreover, aspirin and statins have been reported to reduce the risks of atherosclerotic CVDs by 10 and 15%, respectively [10]. These drugs, however, have side effects [9]. For example, aspirin has been found to increase the risk of bleeding by 54% [10]. New drugs made of natural products with fewer side effects are therefore needed.

Essential oils are natural substances extracted from various organs of aromatic plants. Because these oils have pharmacological effects, they have been widely used in traditional medicines since the Middle Ages [11]. Studies have shown that essential oils and their main components have various biological properties in relation to CVDs. For example, neroli essential oil showed vasorelaxant activity, mediated by the NO-soluble guanylyl cyclase pathway and by ryanodine receptors, in mouse aortic rings [12]. Bergamot essential oil also induced

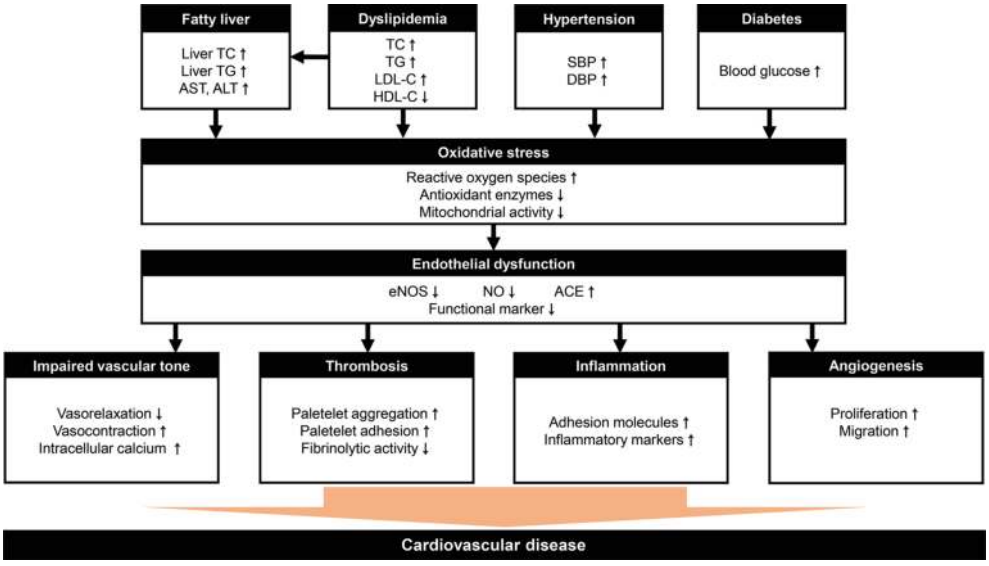

Figure 1. Flow chart showing the mechanisms of CVDs. Various risk factors increase levels of oxidative stress, thereby increasing endothelial dysfunction. Endothelial dysfunction, in turn, promotes abnormalities, such as impaired vascular tone, thrombosis, inflammation, and angiogenesis, which lead to CVDs.

vasorelaxation by inhibiting Ca^{2+} influx into mouse aortic rings [13]. The compound 1,8-cineole, a main component of eucalyptus essential oil, showed antioxidative and antihypertensive effects in chronic nicotine-induced hypertensive rats [14]. These findings have led to efforts to determine the efficacy and specific mechanisms of action of essential oils on CVDs. This review therefore describes the results of studies assessing the effects of essential oils on CVDs and provides new perspectives on future drug development using essential oils.

2. Effects of essential oils

The effects of essential oils on CVDs are summarized in **Table 1**.

2.1. Dyslipidemia

Dyslipidemia is a major risk factor for CVDs. Reductions in low density lipoprotein cholesterol (LDL-C) levels have been associated with decreased risks of major vascular events [53], whereas elevated triglyceride (TG) level and total cholesterol (TC)/high density lipoprotein cholesterol (HDL-C) ratios have been associated with increased risks of coronary heart disease, regardless of LDL-C levels [54]. Essential oils have been shown to improve blood lipid levels. For example, *Allium cepa* and *A. sativum* essential oils were found to reduce serum cholesterol and serum TG levels and β/α lipoprotein ratios in cholesterol-fed rabbits, suggesting that these oils have antiatherosclerotic properties [16]. *Dendropanax morbiferus* essential oil also showed antiatherogenic activity by reducing plasma TC, TG, and LDL-C levels and by increasing plasma HDL-C levels in high-cholesterol fed rats [26]. Similarly, *Syzygium aromaticum* essential oil significantly improved dyslipidemia by reducing plasma TC, TG, and LDL-C levels and by increasing plasma HDL-C levels in rats with metabolic syndrome induced by a high fructose diet [4]. Supplementation of a hyperlipemic diet with *Oenothera biennis* essential oil reduced plasma TG and TC levels and increased plasma HDL-C levels [43, 44], and intake of *Linum usitatissimum L.* essential oil reduced blood TC, TG, and LDL-C levels, in patients diagnosed with metabolic syndrome [34].

Efforts have been made to determine the specific mechanisms by which essential oils improve lipid metabolism. *Curcuma longa L.* essential oil improved dyslipidemia in hyperlipidemic rats by modulating the expression of peroxisome proliferator-activated receptor-α, liver X receptor-α, sterol regulatory element-binding protein (SREBP)-2, 3-hydroxy-3-methylglutaryl-CoA reductase (HMGCR) and genes involved in lipid regulation in the liver [24]. Oral administration of *Nigella sativa* essential oil to hyperlipidemic rats significantly reduced plasma TG levels and increased plasma HDL-C levels by reducing liver HMGCR activity [39]. Treatment of human hepatoma (HepG2) cells with *Pinus koraiensis* essential oil suppressed the expression of lipid-related genes, such as SREBP-1c, SREBP-2, HMGCR, fatty acid synthase, and glycerol-3-phosphate acyltransferase, increased the expression of low density lipoprotein receptors and inhibited the activation of human acyl-coenzyme A: cholesterol acyltransferases (hACAT) 1 and 2 [47]. Treatment of HepG2 cells with *Lippia alba* essential oil, especially the tagetenone chemotype, decreased lipid synthesis, lipid contents, and volume of lipid droplets via the mevalonate pathway [35]. Also, incubation of HepG2 cells with *Artemisia princeps* essential oil significantly increased LDL-R expression [21].

Essential oil	Subject/route	Effects	Disease /model	Main component	Reference
Aframomum melegueta, Aframomum danielli	Pancreas and heart of rat	• Anti-diabetes • Anti-oxidation • ACE inhibition	—	*A. melegueta*: eugenol (82.2%) *A. danielli*: eugenol (51.1%)	[15]
Allium cepa, Allium sativum	Indian albino rabbit /PO	• Fibrinolysis • Lipid improvement	Athero sclerosis	*Allium cepa:* dimethyl-trisulfide (16.6%) *Allium ativum:* diallyl-trisulfide (33.6%)	[16]
Allium sativum	Human/PO	• Fibrinolysis	Myocardial infarction	Diallyl-trisulfide (33.6%)	[17]
Alpinia zerumbet	Wistar rat/IV	• Blood pressure reduction	Hyper tension	Terpinen-4-ol (28.1%)	[18]
Alpinia zerumbet	Wistar rat/PO, thoracic aorta of Wistar rat	• Blood pressure reduction • Vasorelaxation	Hyper tension	Terpinen-4-ol (57.4%)	[19]
Aniba rosaeodora	Wistar rat/IV, thoracic aorta of Wistar rat	• Blood pressure reduction • Vasorelaxation	—	Linalool (87.7%)	[20]
Artemisia princeps	HepG2 cells, isolated human LDL	• Anti-oxidation • Lipid improvement	—	1,8-cineole (20.1%)	[21]
Citrus bergamia Risso	MOVAS cells, EA.hy926 cells	• Intracellular calcium influx inhibition	—	ᴅ-Limonene (43.5%)	[22]
Citrus bergamia Risso	Wistar rat/IP	• Anti-oxidation • Angiogenesis inhibition	Vascular injury	ᴅ-Limonene (43.5%)	[23]
Curcuma longa L.	Golden Syrian hamster/PO	• eNOS expression • Anti-platelet • Lipid improvement • Liver function improvement • Vasorelaxation	Hyper lipidemia	Ar-turmerone (20.5%)	[24]
Curcuma longa L.	Wistar rat/PO, EA.hy926 cells	• Anti-inflammation	Myocardial ischemia/ reperfusion injury	Ar-turmerone (20.5%)	[25]
Dendropanax morbiferus	Wistar rat/PO	• Lipid improvement	Hyper lipidemia	γ-Elemene (18.6%)	[26]
Euphorbiaceae	Wistar rat/IV, thoracic aorta of Wistar rat	• Blood pressure reduction • Vasorelaxation	Hyper tension	Hexadecanoic acid, ethyl ester (46.1%)	[27]
Foeniculum vulgare	Swiss mouse/SC, thoracic aorta of Wistar rat, Guinea pig plasma	• Anti-platelet • Anti-thrombosis • Vasorelaxation	Pulmonary thrombo embolism	Anethole (75.8%)	[28]

Essential oil	Subject/route	Effects	Disease /model	Main component	Reference
Fructus Alpiniae zerumbet	HUVECs	• Anti-inflammation	High glucose induced injury	β-Phellandrene (16.4%)	[29]
Fructus Alpiniae zerumbet	HUVECs	• Anti-oxidation	oxLDL induced injury	β-Phellandrene (16.4%)	[30]
Hyptis fruticosa Salzm	Wistar rat/ IV, superior mesenteric artery of Wistar rat	• Blood pressure reduction • Vasorelaxation	—	1,8-Cineole (16.9%)	[31]
Lavandula hybrida	Human/Inhalation	• Endothelial function improvement	—	Linalyl acetate (36.2%)	[32]
Lavandula hybrida	Swiss mouse/PO, Guinea pig plasma	• Anti-platelet • Anti-thrombosis	Pulmonary thrombo embolism	Linalyl acetate (36.2%)	[33]
Linum usitatissimum L.	Human/PO	• Blood pressure reduction • Lipid improvement	Metabolic syndrome	α-Linolenic acid (41.0% of total fatty acid)	[34]
Lippia alba	HepG2 cells	• Lipid improvement	—	*L. alba* tagetenone: myrcenone (30.4%)	[35]
Mentha x villosa	Wistar rat/IV	• Blood pressure reduction	Hyper tension	Piperitenone oxide (95.9%)	[36]
Mentha x villosa	Wistar rat/IV, thoracic aorta of Wistar rat	• Blood pressure reduction • Vasorelaxation	—	Piperitenone oxide (95.9%)	[37]
Nardostachys jatamasi	Thoracic aorta of Sprague-Dawley rat, HUVECs	• Vasorelaxation • NO production increase	—	Calarene (38%)	[38]
Nigella sativa	Wistar albino rat/ PO	• Lipid improvement • Anti-oxidation	Hyper lipidemia	Thymol (32.0%)	[39]
Ocimum gratissimum	Wistar rat/IV, thoracic aorta of Wistar rat	• Blood pressure reduction • Vasorelaxation	Hyper tension	Eugenol (43.7%)	[40]
Ocimum gratissimum	Wistar rat/IV	• Blood pressure reduction	Hyper tension	Eugenol (43.7%)	[41]
Ocotea quixos	Swiss mouse/ SC, thoracic aorta of Wistar rat, Guinea pig plasma	• Anti-platelet • Anti-thrombosis • Vasorelaxation	Pulmonary thrombo embolism	Trans-cinnamaldehyde (27.8%)	[42]
Oenothera biennis	Rabbit/PO	• Anti-platelet • Angiogenesis inhibition • Lipid improvement	Hyper lipidemia	Linoleic acid (71% of total fatty acid)	[43]

Essential oil	Subject/route	Effects	Disease /model	Main component	Reference
Oenothera biennis	New Zealand rabbit/PO	• Anti-oxidation • Anti-platelet • Anti-thrombosis • Lipid improvement	Athero sclerosis	Linoleic acid (71% of total fatty acid)	[44]
Oenothera biennis, *Ribes nigrum*, *Borago officinalis*	Spontaneously hyper tensive rat/PO	• Blood pressure reduction	Hyper tension	*Oenothera biennis*: linoleic acid (71.0% of total fatty acid) *Ribes nigrum*: linoleic acid (45.0% of total fatty acid) *Borago officinalis:* linoleic acid (36.0% of total fatty acid)	[45]
Olea	Human/PO	• Blood pressure reduction • Anti-oxidation • Endothelial function improvement	High-normal BP, stage 1 essential HTN	oleic acid (55–83% of total fatty acid)*	[46]
Pinus koraiensis	HepG2 cells	• Anti-oxidation • Lipid improvement	—	Camphene (21.1%)	[47]
Radix Angelica sinensis	HUVECs	• Angiogenesis inhibition	—	3-Carene (32.1%)	[48]
Rosa indica L.	Thoracic aorta of rabbit	• Vasorelaxation	—	Acetic acid (percentage was not available)	[49]
Schisandra chinensis	HASMCs	• Anti-oxidation • Anti-inflammation • Angiogenesis inhibition	TNF-α induced injury	Borneol (43.6%)	[50]
Syringa pinnatifolia Hems1. var. alashanesis	Wistar rat/IG Kun ming mouse/IP Primary cultured rat myocyte	• Anti-oxidation • Anti-platelet	Myocardial infarction, hypoxia damage	α-Cadinol (19.9%)	[51]
Syzygium aromaticum	Sprague-Dawley rat/PO	• Anti-oxidation • Anti-inflammation • Lipid improvement • Liver function improvement	Metabolic syndrome	Eugenol (75.2%)	[4]
Trachyspermum ammi	Thoracic aorta of Wistar albino rat	• Vasorelaxation	—	Thymol (38.1%)	[52]

*Polyphenol-rich olive oil was used in this study.

Table 1. Effects of essential oils in CVDs.

2.2. Hypertension

Hypertension is also a major risk factor for CVDs. In the United States, the prevalence of hypertension in adults aged over 60 years was 67.2% from 2011 to 2014 and hypertension was the third leading cause of death from CVDs [55]. Thus, aggressive blood pressure control is needed and essential oils are thought to be helpful. Intragastric administration of *Alpinia zerumbet* essential oil to N-nitro-L-arginine methyl ester (L-NAME)-induced hypertensive rats for 30 days reduced systolic arterial pressure, diastolic arterial pressure, and mean arterial pressure in a time-dependent manner. These hypotensive effects of *A. zerumbet* essential oil were due to its vasorelaxing and Ca^{2+} antagonist effects [19]. In spontaneously hypertensive rats, *Ribes nigrum* essential oil reduced systolic blood pressure (SBP) significantly when compared with sesame oil [45]. Although *Oenothera biennis* and *Borago officinalis* essential oils also reduced SBP, these effects were not statistically significant. In addition, intravenous administration of *Ribes nigrum* essential oil reduced mean arterial pressure (MAP) in spontaneously hypertensive rats. Intravenous administration of *Alpinia zerumbet* [18], *Euphorbiaceae* [27], *Mentha x villosa* [36], and *Ocimum gratissimum* [40, 41] essential oils to deoxycorticosterone-acetate (DOCA)-salt induced hypertensive rats, reduced MAP. Moreover, *Aniba rosaeodora* [20], *Hyptis fruticosa Salzm* [31], and *Mentha x villosa* essential oils [37] reduced MAP in normotensive rats.

The antihypertensive effects of essential oils have also been demonstrated in human studies. In a randomized controlled trial, oral administration of *Linum usitatissimum* L. essential oil significantly reduced SBP and diastolic blood pressure (DBP) in patients with metabolic syndrome [34]. In addition, polyphenol-rich *Olea* essential oil reduced SBP and DBP in women diagnosed with stage 1 hypertension and those with high-normal blood pressure [46].

2.3. Fatty liver

Several essential oils effective in the treatment of dyslipidemia also improved liver fat contents and liver function. Oral administration of *Syzygium aromaticum* essential oil, the main component of which is eugenol, to rats fed a high fructose diet, was found to reduce total fat, TC, and TG levels in the liver. In addition, *S. aromaticum* essential oil reduced the plasma concentrations of alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin and direct bilirubin in these rats, thereby improving fatty liver and liver dysfunction [4]. Similarly, oral administration of *Curcuma longa* L. essential oil to hyperlipidemic hamsters not only reduced hepatic cholesterol levels but also decreased plasma ALT and AST concentrations [24].

2.4. Diabetes

Because chronic hyperglycemia associated with diabetes increases oxidative stress, a cause of vascular endothelial dysfunction, via several pathways such as polyol flux [56], the antidiabetic effect of essential oils is noteworthy. *In vitro* studies showed that the essential oils of *Aframomum melegueta* and *A. danielli*, the main component of which is eugenol, had antidiabetic properties. Although both essential oils inhibited α-glucosidase and α-amylase, *A. melegueta* essential oil had much higher inhibitory activities, indicating greater antidiabetic effects, than *A. danielli* oil [15].

2.5. Oxidative stress

Excessive production of reactive oxygen species (ROS) induces endothelial dysfunction, an early stage of atherosclerosis [57]. Patients with coronary artery disease (CAD) have higher lipid peroxidation activity but significantly lower antioxidant enzyme activities than individuals without CAD [58], indicating the importance of maintaining a balance between ROS production and antioxidant defense systems. Several essential oils have shown the ability to reduce oxidative stress. For example, pretreatment of human aortic SMCs with *Schisandra chinensis* essential oil blocked tumor necrosis factor (TNF)-α-induced ROS [50]. *Fructus Alpiniae zerumbet* oil attenuated oxidative stress in human umbilical vein endothelial cells (HUVECs) exposed to ox-low density lipoprotein (LDL), not only by reducing malondialdehyde (MDA) contents but also by increasing the activities of antioxidant enzymes such as superoxide dismutase (SOD), glutathione peroxidase, and catalase [30].

Essential oils have also been shown to be active in models of acute myocardial ischemia. For example, *Syringa pinnatifolia Hems1. var. alashanesis* essential oil inhibited the reduction of SOD activity and increased mitochondrial activity in cardiac myocytes [51]. *Aframomum melegueta* and *A. danielli* essential oils showed radical scavenging activity, as well as dose-dependently ameliorating lipid peroxidation in rat heart and pancreas [15]. Similarly, *Artemisia princeps* essential oil displayed radical scavenging activity and inhibited the production of thiobarbituric acid-reactive substances, a marker of LDL oxidation [21]. *Pinus koraiensis* [47] and *Olea* essential oils [46] also inhibited LDL oxidation.

In addition, essential oils have also been found to reduce MDA contents. For example, *Citrus bergamia Risso* essential oil reduced MDA production in carotid arteries injured by balloon angioplasty [23] and *Nigella sativa* essential oil reduced plasma MDA formation in hyperlipidemic rats [39]. In rabbits, an atherogenic diet supplemented with *Oenothera biennis* essential oil inhibited platelet MDA production [44]. Oral administration of *Syzygium aromaticum* essential oil to rats with metabolic syndrome reduced plasma MDA concentrations [4].

2.6. Endothelial dysfunction

NO is a typical vasodilatory substance produced from L-arginine by the enzyme endothelial NO synthase (eNOS) in vascular endothelial cells [59]. Thus, endothelial dysfunction is associated with decreased NO bioavailability [57]. In hyperlipidemic hamsters, *Curcuma longa* L. essential oil, at a concentration of 300 mg/kg body weight, increased the expression of aortic eNOS, suggesting that *C. longa* L. essential oil protects against endothelial dysfunction [24]. Treatment of HUVECs with *Nardostachys jatamansi* essential oil increased NO production by phosphorylating eNOS, a reaction mediated by the phosphatidylinositol 3-kinase/protein kinase B signaling pathway and changes in intracellular Ca^{2+} [38]. *Aframomum melegueta* and *A. danielli* essential oils were found to inhibit ACE activity *in vitro*, suggesting that these oils have antihypertensive activity, with *A. danielli* oil having greater activity than *A. melegueta* oil [15].

Flow mediated dilatation (FMD) is a widely used marker of vascular endothelial cell function. A study of night-shift medical workers found that FMD was significantly higher after a 30 min inhalation of *Lavandula hybrida* essential oil than before inhalation and than in a control group

[32]. A randomized crossover study in women with stage 1 hypertension or high-normal BP found that a diet containing polyphenol-rich *Olea* essential oil increased hyperemic areas after cuff-induced ischemia, another test of vascular endothelial function [46].

2.7. Impaired vascular tone

Many essential oils have been found to induce vascular relaxation *in vitro*. In a hyperlipidemic animal model, oral administration of *Curcuma longa* L. essential oil, at a dose of 300 mg/kg body weight for 28 days, restored acetylcholine-induced vasorelaxation, as well as increasing eNOS expression and decreasing cholesterol contents in the aorta [24]. *Ocimum gratissimum* essential oil showed partial endothelium-dependent vasorelaxing activity in aortic rings from DOCA-salt induced hypertensive rats. This vasorelaxant activity was mainly attributed to an inhibition of Ca^{2+} influx rather than Ca^{2+} release from the sarcoplasmic reticulum [40]. In addition, essential oils of *Aniba rosaeodora* [20], *Euphorbiaceae* [27], *Foeniculum vulgare* [28], *Mentha x villosa* [37], *Nardostachys jatamasi* [38], *Rosa indica L.* [49], and *Trachyspermum ammi* [52] were found to induce vasorelaxation in rat thoracic aorta pre-contracted with KCL or phenylephrine. In particular, the vasodilatory effects of *Nardostachys jatamasi* essential oil were mediated by increased NO production [38]. *Ocotea quixos* essential oil also relaxed aortic rings pre-contracted with U46619 [42]. *Alpinia zerumbet* essential oil was also shown to relax aortic rings pre-contracted with KCL or phenylephrine. *A. zerumbet* oil also inhibited $CaCl_2$-induced vascular contraction, an effect resulting from the inhibition of Ca^{2+} influx through voltage-operated and receptor-operated Ca^{2+} channels [19]. Similarly, the treatment of the rat superior mesenteric artery with *Hyptis fruticosa Salzm* essential oil resulted in vascular relaxation and inhibition of $CaCl_2$-induced vascular contraction in a concentration-dependent manner [31]. Adequate regulation of cytosolic Ca^{2+} is important in maintaining vascular tone. *Citrus bergamia Risso* essential oil inhibited Ca^{2+} influx into HUVECs [22].

2.8. Thrombosis

Platelet aggregation and adhesion play important roles in thrombus formation. *Curcuma longa* L. essential oil has been shown to reduce hyperlipidemia-induced platelet activation by suppressing platelet aggregation and adhesion in hyperlipidemic hamsters [24]. Other essential oils were found to inhibit platelet aggregation or adhesion. For example, essential oils of *Foeniculum vulgare* [28], *Lavandula hybrida* [33], and *Ocotea quixos* [42] not only inhibited agonist-induced platelet aggregation *in vitro* but also inhibited thrombin-induced clot retraction in guinea pig plasma. In addition, these three essential oils prevented paralysis in an animal model of acute pulmonary thromboembolism, indicating that these oils had antithrombotic activity. *Syringa pinnatifolia Hems1. var. Alashanesis* essential oil was found to inhibit agonist-induced platelet aggregation in rat whole blood. This result, together with its antioxidant effects, suggests that *Syringa pinnatifolia Hems1. var. Alashanesis* oil has cardioprotective activity [51]. In addition, an atherogenic diet enriched with *Oenothera biennis* essential oil reduced agonist-induced platelet aggregation in whole blood and platelet thromboxane B2 production, thereby inhibiting platelet activation [44]. Both *Allium cepa* and *A. sativum* essential oils have been shown to increase the fibrinolytic activity of garlic and onions in atherosclerotic rabbits [16]. In addition, *A. sativum* essential oil was found to significantly increase the fibrinolytic activity in patients with chronic myocardial infarction and in patients after acute myocardial infarction [17].

2.9. Inflammation

The levels of expression of intercellular adhesion molecule (ICAM)-1 and vascular cell adhesion molecule (VCAM)-1 in endothelial cells increase during inflammation [60], with the expression of these adhesion molecules being regulated by inflammatory cytokines such as interleukin (IL)-1 and TNF-α [61]. Several essential oils have been shown effective in inhibiting this process. For example, the treatment of HUVECs exposed to high glucose with *Fructus Alpiniae zerumbet* essential oil was shown to reduce the secretion of IL-8, TNF-α, ICAM-1, and VCAM-1 by inhibiting nuclear factor kappa B (NF-κB) signaling, suggesting that this essential oil has endothelial protective effects [29]. Similarly, the treatment of human aortic SMCs with *Schisandra chinensis* essential oil decreased TNF-α-induced matrix metalloproteinase-9 (MMP-9) activation, inducible NO synthase and cyclooxygenase-2 (COX-2) expression by inhibiting NF-κB signaling [50]. In an animal study, oral administration of *Curcuma longa* L. essential oil to rats exposed to myocardial ischemia/reperfusion injury reduced endothelial cell-induced inflammation by decreasing the expression of E-selectin and ICAM-1 [25]. Similarly, *Syzygium aromaticum* essential oil reduced plasma TNF-α concentration in rats fed a high-fructose diet [4].

2.10. Angiogenesis

The proliferation and migration of vascular SMCs play essential roles in the pathophysiological changes of cardiovascular systems. *Radix angelica* essential oil was found to dose-dependently inhibit HUVEC proliferation and migration, and, at concentrations above 20 μg/ml, to reduce endothelial tube formation, indicating that *R. angelica* essential oil has antiangiogenic effects [48]. Similarly, *Schisandra chinensis* essential oil effectively decreased the TNF-α-induced migration of human aortic SMCs. These findings, together with the antiinflammatory and antioxidant effects of this oil, suggested that *Schisandra chinensis* oil has antiatherosclerotic activity [50].

Animal studies have also assessed the effects of essential oils on angiogenesis. For example, supplementation of a hyperlipidemic diet with *Oenothera biennis* essential oil for 6 weeks reduced endothelial lesions of the aorta and neointimal proliferation of the arterial wall in rabbits [43]. *Citrus bergamia Risso* essential oil reduced the neointima/media ratio and the cross-sectional area of the carotid artery in rats that underwent balloon-induced vascular injury, with these effects accompanied by decreased expression of lectin-like receptor for oxidized LDL [23].

3. Conclusions

Essential oils are natural substances extracted from aromatic plants with biological properties, including antioxidant and antiinflammatory activities. This chapter reviewed the effects of essential oils on CVD-related factors. Evidence has shown that essential oils have multiple effects, improving lipid balance, liver function, and endothelial function; reducing blood pressure, diabetes induction, and oxidative stress; enhancing vascular relaxation; and inhibiting thrombosis, inflammation, and angiogenesis. Essential oils and their active components may therefore be promising therapeutic agents for CVDs. Studies are needed to clarify the effects of these oils on patients and to elucidate their specific mechanisms of action.

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Conflict of interest

None.

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