Cardiovascular: Clinical Evidence and Mechanisms of Action of Far Infrared Therapy

1. **Far infrared therapy inhibits vascular endothelial inflammation via the induction of heme oxygenase-1** (Lin, Liu et al 2008)
   "The induction of HO-1 contributes to the ability of FIR therapy to inhibit the expression of EC adhesion molecules and the adhesion of monocytes to vascular endothelium."

2. **Heme oxygenase and the cardiovascular-renal system** (Abraham and Kappas 2005)
   "…the differential role of HO-1 could be a key factor in vascular wall remodeling in different clinical situations, such as occurs in hypertension or VSMC hyperplasia, or in the recovery of the vascular wall after mechanical injury, such as restenosis."

3. **Heme oxygenase and carbon monoxide in the physiology and pathology of the cardiovascular system** (Bełtowski, Jamroz et al, 2004)
   "…induction of HO-1 attenuates atherosclerosis and myocardial ischemia-reperfusion injury…."

4. **Role of Heme Oxygenase-1 in Vascular Disease** (Chung, Pae et al, 2008)
   Based on review of literature, HO-1 and its by-products, especially CO, has shown to exert protective actions in the vascular endothelium such as reduction of "oxidative stress, vascular inflammation, vasomotor tone, platelet aggregation, VSMC overgrowth, and EC apoptosis." So "the induction of this enzyme or its catalytic activity may represent an effective strategy to intervene in vascular diseases."

5. **Heme Oxygenase-1 against Vascular Insufficiency: Roles of Atherosclerotic Disorders** (Ishikawa 2003)
   Based on review of the literature, there is sufficient data suggesting "the possibility that up-regulation of HO-1 may be an important protective factor after balloon angioplasty inhibiting vascular smooth muscle cell proliferation."

6. **Conversion of biliverdin to bilirubin by biliverdin reductase contributes to endothelial cell protection by heme oxygenase-1—evidence for direct and indirect antioxidant actions of bilirubin** (Jansen, Hortmann et al 2010)
   HO-1 byproducts, bilirubin and carbon monoxide, are effective in reducing oxidative stress and chronic inflammation that may prevent cardiovascular diseases related to endothelial dysfunction.

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7. **Role of heme oxygenase in preserving vascular bioactive NO** (Pae, Son et al, 2010)
   Accumulating evidence in the literature suggest that HO-1 and its by-products offer vascular protection against injuries. Although the mechanisms have not yet been fully identified, their ability to improve vascular function may be from the enhancement of NO bioavailability
   through 3 pathways: "(1) modulate eNOS expression and activity, (2) prevent inactivation of vascular NO, and (3) compensate for the loss of vascular NO." Therefore, "HO-1 may offer a promising therapeutic strategy for vascular diseases associated with a reduced bioavailability of vascular NO."

8. **Targeting heme oxygenase: therapeutic implications for diseases of the cardiovascular system** (Peterson, Frishman et al 2009)
   "…HO-1 responses seem to have a protective role in the vascular wall against atherogenesis through multiple pathways. Interventions aimed at modulating the levels of HO in the vascular wall, therefore, might be a novel target to treat or prevent atherosclerotic diseases."

9. **Repeated sauna therapy increases arterial endothelial nitric oxide synthase expression and nitric oxide production in cardiomyopathic hamsters** (Ikeda, Biro et al 2005)
   Far Infrared Therapy has been found effective in improving endothelial dysfunction related to chronic heart failure (CHF) through induction of the eNOS/NO pathway.

10. **Repeated thermal therapy improves impaired vascular endothelial function in patients with coronary risk factors** (Imamura, Biro et al 2001)
    Far Infrared Therapy was shown to improve impaired vascular endothelial function in patients with risk factors for atherosclerosis.

11. **The effect of leg hyperthermia using far infrared rays in bedridden subjects with type 2 diabetes mellitus** (Kawaura, Tanida et al 2010)
    "In this study, repeated leg hyperthermia decreased plasma total 8-epi-PGF2α levels as a marker of oxidative stress", suggesting that Far Infrared Therapy may protect against oxidative stress, which may in turn mitigate skeletal muscle insulin resistance in diabetic patients.

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12. **Waon therapy improves the prognosis of patients with chronic heart failure.** (Kihara, Miyata et al 2009)
    A type of Far Infrared sauna therapy, Waon Therapy, was found to "decrease cardiac death and re-hospitalization in patients with CHF over a 60-month follow-up period," possibly due to its benefits in improving cardiac and vascular function and reducing ventricular arrhythmias in these patients.

13. **Repeated sauna therapy reduces urinary 8-epi-prostaglandin F(2alpha). (Masuda, Miyata et al, 2004)**
    Far Infrared Therapy was found to lower systolic blood pressure and urinary 8-epi-PGF2α levels (a marker for oxidative stress) in the treated group compared to the control group; suggesting that the therapy may protect patients against oxidative stress, and leading to the prevention of atherosclerosis.

14. **Beneficial effects of Waon therapy on patients with chronic heart failure: Results of a prospective multicenter study** (Miyata, Kihara et al 2008)
    This mutli-center study showed improvements in CHF patients' clinical symptoms and cardiac function, as well as decreased cardiac size.

15. **Waon therapy mobilizes CD34+ cells and improves peripheral arterial disease** (Shinsato, Miyata et al 2010)
    Far Infrared Therapy was found to improve symptoms of limb ischemia in patients with peripheral arterial disease by increasing circulating endothelial progenitor cells.

16. **Repeated sauna therapy improves myocardial perfusion in patients with chronically occluded coronary artery-related ischemia**. (Sobajima M et al 2013).
    Waon therapy extended treadmill exercise time (430 ± 185 to 511 ± 192 s, $p < 0.01$) and improved flow-mediated dilation of the brachial artery (4.1 ± 1.3 to 5.9 ± 1.8%, $p < 0.05$), but tended to decrease the number of circulating CD34-positive bone marrow-derived cells. Waon therapy improves CTO-related myocardial ischemia in association with improvement of vascular endothelial function. This therapy could be a complementary and alternative tool in patients with severe coronary lesions not suitable for coronary intervention.

17. **Far-infrared radiation acutely increases nitric oxide production by increasing Ca2+ mobilization and Ca2+/calmodulin-dependent protein kinase II-mediated phosphorylation of endothelial nitric oxide synthase at serine 1179**. (Park J-H et al 2013)
    "This study suggests that FIR radiation increases NO production via increasing CaMKII-mediated eNOS-Ser(1179) phosphorylation but TRPV channels may not be involved in this pathway. Our results may provide the molecular mechanism by which FIR radiation improves endothelial function"

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18. **Far-Infrared Therapy Induces the Nuclear Translocation of PLZF Which Inhibits VEGF-Induced Proliferation in Human Umbilical Vein Endothelial Cells. (Hsu YH et al, 2012)**
Hsu et al studied the molecular mechanisms by which FIR can stimulate the eNOS/NO pathway, to reduce graft stenosis and improve endothelial functioning. They found that "a non-thermal effect of FIR inhibited VEGF- induced proliferation in HUVEC's via the phosphoinositide 3-kinase/Akt signaling pathway"

19. **Far-infrared therapy for cardiovascular, autoimmune, and other chronic health problems: A systematic review**. (Shui S et al 2015)
"FIR therapy may be closely related to the increased expression of endothelial nitric oxide synthase as well as nitric oxide production and may modulate the profiles of some circulating miRNAs; thus, it may be a beneficial complement to treatments for some chronic diseases that yields no adverse effects."