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Integrated Heart: Report for Clinicians

Use of Integrated Heart™ a Safe and Effective
Natural Treatment for Heart Disease

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EVIDENCE LEAD COMPLEMENTARY MEDICINE



李東垣

Li Dong Yuan

Integrated heart was first published in 1186 in a text written by Li Dong Yuan. It is important to note that while some Chinese Medicines are for an individual condition, this formula is listed as being beneficial for both the prevention and the treatment of a wide variety of illnesses. This formula was re-examined in every dynasty in China since its conception. Each time it was re-published new indications were added for its use. Traditionally this formula was used to treat chronic cough, increase heart function, regulate heart rate and protect against heat stroke. Integrated Heart remains one of the most elegant and powerful formulas ever devised in traditional Chinese medicine. Adding another dimension to this formula, we are bringing it to you.

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Active Constituents:

Examination of the active ingredients in Integrated Heart found that there are three main families of steroid-like compounds, glycosides and powerful anti-oxidants that work synergistically to increase mechanistic effects and boost efficiency in absorption. Their main actions include: vasodilatation, increasing myocardial contractility, anti-thrombosis actions, free radical scavenging, and anti-inflammatory effects. This information gives us a clear definition for the wide range of clinical activity available from Integrated Heart.

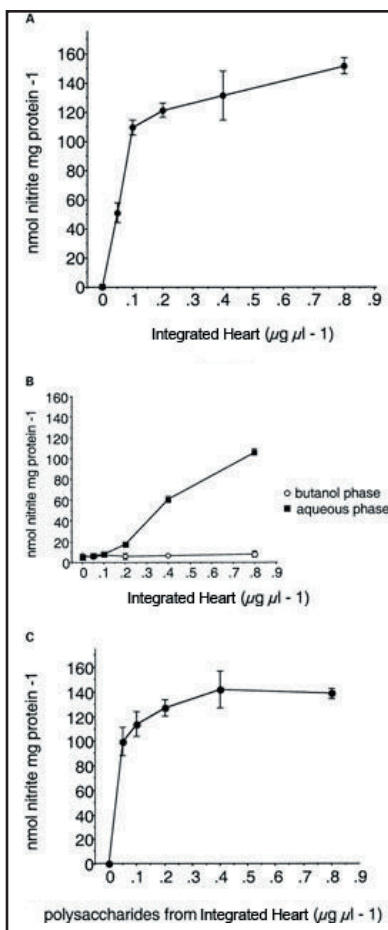
Pharmacodynamics:

The mechanisms of Integrated Heart can be separated into four main categories: vasodilatation, increased myocardial contractility, antioxidant activity and a reduction in platelet adhesions

Integrated Heart is an herbal formula composed of multiple ingredients. The chief herb enhances the release of Nitric Oxide (NO) from endothelial cells. NO is a powerful chemical compound within the body that stimulates blood vessels to dilate, among numerous other benefits. This herb has also been shown to decrease heart rate. It also has biphasic actions on blood pressure, which allows it to treat both high and low blood pressure. A further list of mechanism includes: inhibiting right ventricular hypertrophy, exhibiting anti fatigue actions on cardiac muscle cells and having an inhibitory effect on myocardial cell death. When both ischemia and reperfusion are present Integrated Heart can genetically signal heart tissue to begin killing itself. This is particularly problematic with heart transplants as well as in complications from heart attacks. Active components in this herb inhibit cardio-myocyte apoptosis by inhibiting expression of pro-apoptotic Bax gene and raising the ratio of Bcl-2/Bax.

Atherosclerosis is the build up of plaque within the walls of arteries. Atherosclerosis has been linked with various forms of heart disease, diabetes and cerebral-vascular diseases as atherosclerosis can build up and obstruct blood flow. This can increase blood pressure. Over time there is an increased likelihood of this plaque breaking free and causing heart a heart attack or stroke. Homocysteine (Hcy) is an independent risk factor in the development of atherosclerosis and other forms of vascular lesions. Compounds in Integrated Heart may have potential clinical applications in controlling Hcy-associated vascular diseases and other forms of vascular lesions.

There is a remarkable link between anti-oxidants and heart disease reduction. Two of the herbs in Integrated Heart are powerful antioxidants and excellent sources of potassium which can up-regulate expression of



anti-oxidase. The effect of these herbs has been published as significantly stronger than Vitamin C on levels of superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px). These two markers are important factors involved in the pathogenesis and development of heart disease. A crude extract of another herb in this formula lead to marked changes in hemodynamics by adjusting left ventricular function in rats with heart failure following a heart attack. This same herb is also anti-inflammatory and anti-thrombotic and has been shown to regulate the expression of genes to protect vascular endothelial cells from programmed cell death.

Another component in Integrated Heart has been shown to protect the liver and heart from heat shock. In addition this component has been shown to reduce cardio-toxicity and also works as a powerful antioxidant. This same herb also has a cardio-protective function against ischemia reperfusion injuries. Reperfusion injury refers to damage to tissue caused by fresh blood supply when it returns to injured tissue after a period of ischemia.

Korean researchers studied a polysaccharide fraction extracted from Integrated Heart on radiation-induced alterations of specific antioxidant systems in the spleen of Balb/c mice. On the 5th day after sub-lethal whole-body irradiation, homogenized spleen tissues of the irradiated mice expressed increased mRNA levels of SOD (superoxide dimutase), catalase mRNA decreased to 50% of the amount in the control group.

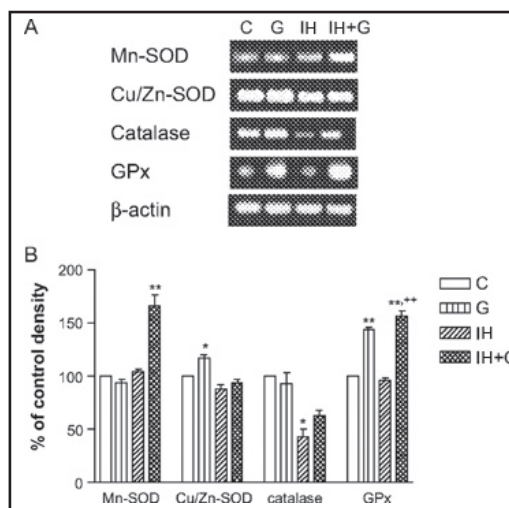
At the same time, in vivo treatment of non-irradiated mice with the same polysaccharide fraction extracted from Integrated Heart (100 mg kg⁻¹, intraperitoneal administration) had a significant effect on glutathione peroxidase (GPx) mRNA, increasing it 144% in comparison to the control.

It should be noted that the most biologically active species of each herb was selected, as tested by HPLC and have been verified to have the strongest cardiovascular efficacies.

When all of the herbs are prepared and used collectively, Integrated Heart has an anti-endotoxin shock effect. The combination of two of the raw herbs in this formula also appears to retain a powerful anti-oxidant compound from a third herb in the body and increase its bioavailability. This demonstrates that Integrated Heart is a synergistic formula for cardiovascular protection.

Human Trials:

In 1994 a comparative study between 98 cases of Coronary Heart Disease (CHD) and 110 healthy subjects determined that superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px) activity were significantly lower and malondialdehyde (MDA) level was significantly higher in the blood of CHD patients. The decrease in GSH-Px activity and increase in MDA level were considerably more apparent in patients with myocardial infarction (68 cases), when compared with those with angina pectoris (30 cases). This suggests that under conditions of myocardial infarction, the increased extent of myocardial ischemia could enhance free radical production and therefore lipid peroxidation reactions. Free radical mediated lipid peroxidation reaction is an important factor involved in the pathogenesis and development of CHD. In the same study patients with myocardial infarction were randomly divided into two groups. Integrated Heart was given via 3 granulated packets daily at total dose of 5.5 g, in addition to standard treatment. extracted herb daily for 28 days. After 2 weeks of treatment with



Integrated heart, patients had higher blood SOD and GSH-Px activities than those receiving standard treatment with a significant increase in enzyme activities being observed up to four weeks after the Integrated Heart treatment stopped.

Another team of Chinese researchers examined the effect of Integrated Heart on coronary heart dis

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ease (CHD) patients (30 angina pectoris and 68 acute myocardial infarction, AMI). In this study there was a focus on peroxidation related damage. The initial laboratory examinations showed that activities of superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px) levels were decreased and the content of malondialdehyde (MDA) in plasma were increased in CHD patients in comparison with healthy controls ($P < 0.001$). When Integrated Heart was administered orally to 38 of the AMI patients, both SOD and GSH-Px activities were increased and the level of MDA decreased ($P < 0.05$). These changes were even more significant when Integrated Heart was ingested for an additional two weeks ($P < 0.001$) after the trial period. At the same time, changes in SOD, GSH-Px and MDA levels in the control group (30 AMI patients not taking Integrated Heart) were not significantly different ($P > 0.05$) from their initial findings. Pathogenesis of CHD is associated with free radicals triggering a chain reaction of lipid peroxidation. Integrated Heart may act as an effective free radical scavenger, which can reduce and in some cases reverse lipid peroxidation related damage. Thus, Integrated Heart may be administered in the prevention and treatment of CHD.

Further clinical studies have shown that Integrated Heart can reduce the incidences of angina pectoris and the extent of myocardial damage caused by acute myocardial infarction, while also facilitating the repair of damaged myocardial tissue.

A study was published on the effect of Integrated Heart in the treatment of 100 patients with angina pectoris according to WHO standards. They were randomly divided into 2 groups. 50 cases in the trial group were treated with Integrated Heart and Nitroglycerine and 50 in the control group were treated with a combination of nitroglycerine, propranolol

hydrochloridum, nifedipine and isosorbide dinitrate. The treatment period consisted of 20 consecutive days.

Before the trial, routine physical and laboratory examinations including an ECG were taken for each patient. Long term ECG monitoring, ultrasound, chest x-ray, blood sugar, blood lipids and liver and kidney function test were also monitored when necessary. A graded treadmill exercise test was taken for patients with fatigue related angina pectoris. The dose of nitroglycerin was also recorded for each patient. Routine cardiograms were taken every 5 - 7 days to observe any change in the ST segment. Blood lipids, blood sugar and liver and kidney function are taken again after the 20-day treatment. Graded treadmill exercise test was taken again for patients with fatigue related angina pectoris and compared to their results before treatment.

Clinical effectiveness was determined as follows: **very effective** meant all the symptoms were gone and no more nitroglycerin was needed; **effective** meant chest pain was relieved and no more nitroglycerin needed. An improvement in ECG result meant their ST segment was rose more than 0.5mm. **No effect** was recorded if there was no change in those parameters.

Among the 24 **very effective** patients in the trial group, 8 of them had mild angina pectoris, 12 had medium angina, 4 had severe angina; among the 21 **effective** patients in the trial group, there were 3 with mild angina, 9 with medium angina and 9 with severe angina. Among the 23 **very effective** patients in the control group, 9 of them had mild angina, 12 had medium angina and 2 had severe angina. Among the 21 **effective** patients in the control group, 3 had mild angina, 8 had medium angina and 10 had severe angina. In the trial group 5 patients had **no effect**. In the control group 6 patients had **no effect**.

The total effective rate in the trial group was 90%, the improvement rate of their ECG results were 56% and all patients stopped taking nitroglycerin within 2 weeks of starting Integrated Heart. The total clinical effective rate in the control group was 88%, the improvement rate of their ECGs were 54%. Both

After one month of oral administration the total effective rate based on symptomatic improvement was 88.3% in the group treated with Integrated Heart. 61.7% of these patients also had improvements in their ECG results.

the effective rate and the improvement rate of their ECG results had no significant difference between the two groups.

Propranolol Hydrochloridum is a common drug choice in the treatment of myocardial ischemia. Nifedipine and Isosorbide Dinitrate are drugs of choice to enlarge the coronary blood vessels and reduce the cardiac pre and post-load. In the control group, different combinations of the three medicines in conjunction with low dose aspirin were given to patients according to their individual conditions. The trial group treated with Integrated Heart had no significant difference in effectiveness with that of the control group. This study indicates that Integrated Heart is an effective medicine in the treatment of angina pectoris.

After a 20-day observation period, Integrated Heart had no obvious effect on liver and kidney function, blood lipid and blood sugar and no side effects except for three cases of minor stomach discomfort.

Another study examined the effect of Integrated heart on 117 patients with stable angina pectoris between May 2004 to June 2006. The patients were randomly divided into two groups. There were 60 cases in the trial group (41 male and 19 female with an average age of roughly 62 and average course of disease of roughly 6 years). In the control group there were 57 cases (39 male and 18 female with average age of roughly 64 and average course of disease of roughly 6 years). The patients stopped all anti-myocardial-ischemia medicine for at least 5 half-life periods before the trial.

Blood and urine routine test, liver and kidney function, blood lipid, blood sugar and ECG were tested in all patients before and after the trial. Blood pressure, frequency, location, degree, duration, inducing factors, amount of consumed nitroglycerin, on-set time of nitroglycerin and its side effects of each attack of angina pectoris were also recorded daily.

Clinical effectiveness was determined as follows: **very effective** meant no attacks of angina pectoris or the frequency of attack decreased more than 90% & a decrease of nitroglycerin requirement by 90%; **effective** meant the amount of consumed nitroglycerin decreased 50%-90%; **no effect** meant that the patient did not meet the above standards; **aggravated** meant the frequency of angina attack and the amount of consumed nitroglycerin increased more than 50%. Clinical effectiveness of ECG results were determined as follows: very effective meant that their ECG went back into normal range; effective meant the ST seg-

ment in cardiogram rose but not enough to be to considered normal range normal, or T wave changes from upside-down to flat or from flat to erective; no effect meant the patient did not meet the above standards; aggravated meant that the ST segment declined 0.5mm below the level established before the trial, or the upside-down T wave declined below the level established before the trial, or changed from erective to flat or from flat to upside-down.

The frequency of angina pectoris attack and cardiogram had no significant difference between the two groups before treatment ($P>0.05$). After one month of treatment, the total effective rate of the trial group was 88.3% and 91.3% in the control group. There was no significant difference between two groups ($P>0.05$) according to the patients' symptoms. After treatment, the total effective rate in the trial group was 61.7% and 63.2% of the control group. There was no significant difference between two groups ($P>0.05$) according to their ECG results.

In the trial group, TC, TG and LDL all decreased distinctly after the treatment and the difference was significant before and after treatment ($P<0.05$). HDL increased slightly but had not a significant difference. The blood lipids in the control group did not change significantly after treatment ($P>0.05$). The blood pressure, blood and urine routine test, liver and kidney function and blood sugar also had no significant difference after treatment in both groups. Three cases in the trial group had stomach discomfort and gastric acid reflux. Those symptoms disappeared when the medicine was taken with meals. In the control group 14 cases had headache and head distention, 7 cases had burning and flushed face, 9 had dizziness.

Modern pharmacological research has proven that Integrated Heart can increase myocardial contraction, reduce peripheral vascular resistance and myocardial oxygen consumption, as well as scavenge free radicals and inhibit the lipid peroxidation, thus protecting the heart. This formula is also rich in potassium and its components are very similar with glucose, insulin and potassium (GIK). This brings actions as an anti-arrhythmic, improves myocardial ischemia, resistant myocardial apoptosis, enforces myocardial contractility and slows down the hear rate. Further this formula has actions as an anti-oxidant & free radical scavenger. This also protects heart tissue against the ischemia. Isosorbide Dinitrate is an allopathic medicine used for

angina pectoris but it has side effects including: headache, head distention and burning face, esp. when continuously taking nitric acid esters for long term 70%-80% of patients will develop a drug resistance to this medication and in some cases it may affect a patients' ability to keep taking the treatment and the effectiveness of it is reduced. Integrated Heart doesn't have the above side effects. The total effective rate based on symptoms was 88.3% in the trial group after treatment and 91.3% in the control group. The total effective rate based on ECG results was 61.7% in the trial group after treatment and 63.2% in the control group. No significant difference was found when comparing the two groups ($P>0.05$) based on symptoms or ECG. This shows us that Integrated Heart is equal to Isosorbide Dinitrate in the treatment of angina pectoris.

Please take your own clinical notes:

Conclusion

With Integrated Heart it is possible to present a highly evaluated adjunct natural therapy to help boost the quality of life in patients with heart disease. Given the scientific background of this treatment there is sound reason to include this therapy with your patients.