

Rediscovering therapeutic virtues of herbal medicines for cardiovascular health

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Most of us would have come across individuals – be it family members, relatives, friends, or colleagues, who have been affected by heart attacks, high blood pressure, or stroke. The global burden of disease has witnessed a radical shift from communicable, maternal, neonatal, and nutritional causes to non-communicable diseases, such as cardiovascular diseases (CVDs) that remain the leading cause of death in both men and women all over the world (1). According to Centers for Disease Control and Prevention (CDC), 1 in every 4 deaths in the United States is caused by heart disease every year. Economic burden of heart disease costs the US about \$ 200 billion each year, which includes the cost of health care services, medications, and lost productivity (2). An estimate suggests that the number of deaths due to CVDs, mainly from heart disease and stroke, will increase to more than 24 million by 2030 (1).

Some of the risk factors responsible for CVDs include high levels of low-density lipoprotein (LDL) cholesterol, smoking, hypertension, diabetes, abdominal obesity, psychosocial factors, diet lacking fruits and vegetables, excess consumption of alcohol, and lack of regular physical activity. Although research has been able to link genetic factors, more complex lipid traits, and inflammatory markers as other risk factors involved in CVDs, INTERHEART study demonstrated that conventional risk factors account for more than 90% of the deaths (3).

HERBAL MEDICINES FOR HEART DISEASES

In the past couple of decades, a lot of efforts have been made to improve diagnostic and

therapeutic strategies for CVDs with the help of newer technologies and advancements in molecular medicine and biology and translational scientific efforts. However, higher potential for adverse effects related to pharmacotherapy is posing major challenges in treating various cardiovascular conditions. This has led to growing awareness among many individuals about the role of dietary factors and herbal medicines in the prevention of CVD and the possibility of their use in treatment (3).

Herbs have been the integral part of humans since the beginning of civilization, as they were well-appreciated not only for their culinary benefits but also for the inherent medicinal properties they possess. Resultantly, several herbal medicines and their derivatives have made a significant contribution in the progression of modern drug development process. Some of the botanicals like *Crataegus oxyacantha*, *Terminalia arjuna*, *Inula racemosa*, *Astragalus membranaceus*, *Digitalis purpurea*, *Rauwolfia serpentina*, and certain derivatives like aspirin, reserpine, digoxin have been found to have therapeutic benefit for the treatment of various cardiovascular disease conditions(4-6).

Increasing awareness of self-care and mounting concerns about inevitable adverse effects of conventional medicine has resulted in resurgence of the popularity of herbal medicines among patients in the West. Analysis of data from the 2015 National Consumer Survey on the Medication Experience and Pharmacist Role (NCSME-PR) revealed that more than one-third of respondents using herbal supplements with elderly people having higher education were associated with a higher use. Survey also revealed that compared to other population, people with chronic diseases were more

likely to use herbal medicines. Among these, patients with stroke were more likely to use herbal medicines than others (7). Furthermore, growing scientific evidence also suggest that several herbal medicines and their active ingredients contribute to the standard therapy for the management of CVDs (1).

CARDIOPROTECTIVE BENEFITS OF HERBAL INGREDIENTS: CLINICAL SUBSTANTIATION

Despite of a recent uptrend in the popularity of complementary and alternative medicine and natural products, not many herbal products have been clinically validated for their beneficial effects. This has resulted in enormous confusion and misunderstanding in the minds of both customers and researchers about their identification, efficacy, and safety. However, there are a few natural herbal ingredients that have undergone numerous clinical trials to prove their cardiovascular health support. For example, *Curcuma longa* (curcuminoids), *Commiphora mukul* (guggulsterones), *Saccharum officinarum* (policosanols, a mixture of higher aliphatic alcohols from the sugarcane wax), and *Terminalia arjuna* (arjunolic acid).

Curcuma longa

Curcuma longa (commonly referred as 'turmeric'), is one of the most revered herbs that has always been in the limelight and more so in recent times – owing to its plethora of therapeutic potential against scores of



health conditions, including cardiovascular benefits. Curcuminoids, a group of highly pleiotropic molecules, such as curcumin, demethoxycurcumin (DMC), and bisdemethoxycurcumin (BDMC), found in turmeric are known to be the main chemical constituents that possess myriad health benefits (8).

In a randomized, double-blind, placebo-controlled, parallel-group study, patients diagnosed with metabolic syndrome were supplemented with either curcuminoids – sample used was Sabinsa's patented Curcumin C3 Complex® (1000 mg/day; n=50) – in combination with a natural bioavailability enhancer piperine – BioPerine®, a standardized patented extract of black pepper from Sabinsa – or placebo (n=50) for 8 weeks. Results showed a greater reduction in serum triglycerides, total

cholesterol, serum LDL-C, non-HDL-C, lipoprotein (a), and increase in HDL-C concentrations in the curcuminoids group as compared to the placebo group. Overall, the combination was safe and effective adjuvant for controlling influence on lipid profile of patients with metabolic syndrome on standard treatment (9).

In another double-blind, placebo-controlled trial, 33 subjects were randomized to receive either curcuminoids (2 g/day) (Sabinsa's Curcumin C3 Complex®) or placebo for 8 weeks. Curcuminoids group significantly reduced LDL-C, VLDL-C, and serum triglyceride levels when compared to the placebo group. It was concluded that curcuminoids could be an effective supplement in the management of cardiovascular risk factors by possessing significant effect on cholesterol and triglyceride levels (10).

Commiphora mukul

Oleogum resin or guggul is a gum resin from the guggul tree, *Commiphora mukul*, which is native to India. Traditionally, guggul has been known for its cholesterol-lowering properties – to help support healthy levels of cholesterol and blood serum lipids (11). However, it was only in the 1960s that scientists were able to identify that guggulsterones like Guggulsterone-E and Guggulsterone-Z isolated from guggul are the bioactive constituents responsible for its cholesterol-lowering effects (12).

Short-term safety and efficacy of a guggul extract – Gugulipid®, a standardized extract from Sabinsa containing 2.5% guggulsterones – was evaluated in healthy adults with hyperlipidemia eating a typical Western diet. In this

double-blind, randomized, placebo-controlled trial, subjects received standard-dose guggul extract (SDG; 75 mg/day), high-dose guggul extract (HDG; 150 mg/day), or matching placebo for 8 weeks. Results showed that compared to placebo group, level of lipoprotein (a),



a known cardiovascular surrogate marker, was decreased by 7% and 5% in SDG and HDG groups, respectively (Figure 1) (13).

In a multi-center, 12-week, open-label trial, efficacy of guggul extract (Sabinsa's

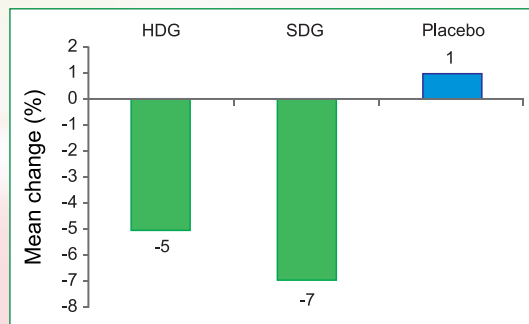


Figure 1 – Effect of guggul extract on Lp (a) levels.

Gugulipid®) was evaluated in 205 hyperlipidemic patients. All the patients completed 12-week open trial with guggul extract in a dose of 500 mg tds after 8-week diet and placebo therapy. A significant decrease in serum cholesterol (23.6%) and serum triglycerides (22.6%) levels was observed in 70-80% patients receiving guggul extract therapy. Similarly, in a double-blind, cross-over study, 125 patients were given guggul extract and 108 patients were provided clofibrate therapy. Decrease in serum cholesterol and triglycerides levels in guggul extract group was 11 and 16.8%, respectively, which was comparable with clofibrate – i.e. 10 and 21.6%, respectively. HDL-cholesterol was increased in 60% patients who responded to guggul extract, while clofibrate had no effect on HDL-cholesterol (14).

Saccharum officinarum

Policosanols is a natural mixture of higher aliphatic alcohols, found in plant waxes. Commercially, policosanols is isolated from sugarcane wax (*Saccharum officinarum*) that contains different components, such as 1-octacosanol, 1-dotriacontanol, 1-tetracosanol, 1-tetraatria-contanol, 1-hexacosanol, 1-heptacosanol, and 1-nonacosanol. Several clinical studies have demonstrated that these plant waxes may influence healthy cholesterol metabolism and thus help maintain normal cholesterol levels (15).

Influence of policosanols on lipid levels and inflammatory markers was evaluated in a randomized, double-blind study comprising of 40 patients (both men and women; aged: 18-65 years) with hypercholesterolemia (Type IIa), mixed dyslipidemia (Type IIb), and/or primary

hypertriglyceridemia for 24 weeks. These patients were randomized to receive oral medication of either policosanol (15 mg) or atorvastatin (10 mg) capsule daily before bed time.



levels in the policosanol group (18.38%) in comparison with the atorvastatin group (14.07%) was observed. Significant reduction in uric acid levels was also observed in policosanol and atorvastatin groups (14.09% and 20.10%, respectively) (15).

Terminalia arjuna

Terminalia arjuna, commonly termed as arjuna, is a well-known agent having cardioprotective potential. Its bark has been used as an ayurvedic remedy for anginal pain, hypertension, congestive heart failure, and dyslipidemia since vedic period. Several ancient Indian medicinal texts, such as Charaka Samhita, Sushruta Samhita, and Astang Hridayam have mentioned about its beneficial effects in promoting overall heart health (16).

In a double-blind, cross-over study, patients diagnosed with chronic congestive heart failure (CHF) were evaluated for the effect of *T. arjuna* (500 mg; every 8 h) post two weeks (phase-I) and 20-28 months (phase-II). The clinical, laboratory, and echocardiographic evaluation was carried out at baseline and at the end of therapy. Results demonstrated that group receiving *T. arjuna* showed improvement in signs and symptoms of heart failure, heart rate, and other parameters (Figure 4) compared to the placebo group (17).

In another double-blind, cross-over study, influence of *T. arjuna* on endothelial dysfunction, a hallmark of vascular diseases, e.g. atherosclerosis, in healthy male smokers (age: 28.16±9.45 years) was evaluated. For two weeks, smokers were given *T. arjuna* (500 mg; every 8 h), while age-matched, non-smokers were given matching placebo, followed by repetition of brachial artery reactivity studies to determine various parameters, including flow-mediated dilation after each period. Results showed a significant

improvement in endothelial functioning (as indicated by flow-mediated dilation) in the active group compared to the baseline values (9.31±3.74 v. 5.17±2.42%, p<0.005) (18).

CONCLUSION

Evidence clearly suggests that lifestyle changes along with nutritional transition are the major contributions that increase CVD risks. It is seen that the use of natural herbal ingredients and lifestyle modification with a healthy diet is what it takes to have a healthy heart.

Sabinsa has been a research-driven organisation, where the R&D constantly strives to revive the potential benefits of known age-old herbal medicines by applying newer technologies to standardize herbal extracts that are not just 'Ayurveda-inspired' but 'validated by science' as well.

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At the end of the study, policosanol compared favorably with atorvastatin in improving the serum lipid profile. Both the groups showed a significant decrease in the levels of total plasma cholesterol (policosanol=17.76%; atorvastatin=19.56%) (Figure 2), triglyceride (policosanol=33.87%; atorvastatin=35.53%) (Figure 3), LDL-C,

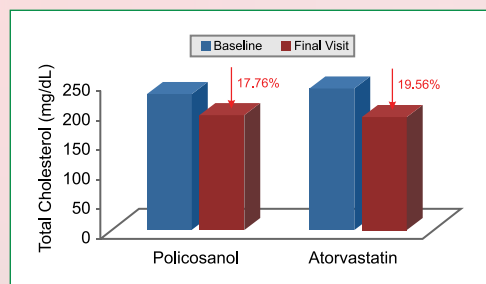


Figure 2 – Effect of policosanol on total cholesterol levels.

and VLDL-C compared to their respective baseline values. Both groups had increase in HDL-C. Additionally, policosanol group showed a significant reduction in the

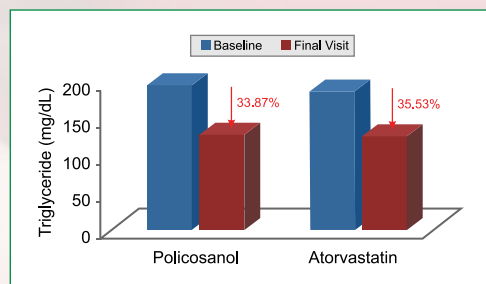


Figure 3 – Effect of policosanol on total triglyceride levels.

erythrocyte sedimentation rate (ESR), an early marker of inflammation (29.32%), while atorvastatin group showed non-significant ESR reduction (18.38%). Similarly, policosanol group showed better inhibition of high-sensitivity C-reactive protein (hs-CRP), a useful indicator of major tissue damage and CVDs, than atorvastatin group (36.33% vs. 22.95%).

An improvement in the liver function test, represented by a decrease in serum glutamic oxaloacetic transaminase (SGOT)

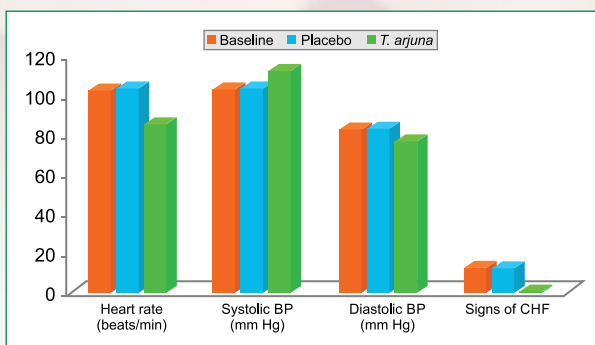


Figure 4 – Effect of T. arjuna on signs of CHF and related parameters.

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