

***Withania somnifera* Dunal (Ashwagandha): A Promising Remedy for Cardiovascular Diseases**

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Abstract: *Withania somnifera* Dunal (Ashwagandha), a popular medicinal herb of Ayurveda is used for health, vitality, longevity and rejuvenation properties. It is a common ingredient of polyherbal or herbomineral formulations and used for preventive or therapeutic polypharmaceutical use. Present article emphasized on the studies, which provides the pharmacological basis of its use in cardiovascular diseases. It has been demonstrated to possess adaptogenic, anti-inflammatory, antioxidant, anti-platelet, antihypertensive, hypoglycemic and hypolipidemic effects which may contribute to its cardioprotective properties.

Key words: Ashwagandha • Winter cherry • Myocardial infarction • Heart diseases

INTRODUCTION

Withania somnifera Dunal (family: Solanaceae), popularly known as Ashwagandha, Indian ginseng, or winter cherry has been used for millennia in Ayurveda, Indian system of traditional medicine. In Ayurveda, it is classified as a rasayana (rejuvenation) and acknowledged to increase longevity and vitality [1]. It is a reputed health food and herbal tonic and used for cardiovascular diseases in ethnomedicine. It is available for human use either as a single herb or an ingredient of polyherbal or herbomineral formulations. The human doses of ashwagandha are generally in the range of 4-6 g/day and expected to be safe and nontoxic. *Withania* contains active ingredients like steroidal alkaloids and lactones known as “withanolides”. Withaferin A and withanolide D are the two main withanolides contribute to the most of the biological actions of *withania* [2].

In the current decade, there has been a surge of research in its effect in animal models of atherosclerosis, hyperlipidemia, myocardial infarction, myocardial ischemia reperfusion injury, cerebral ischemia, cardiomyopathy, cardiac hypertrophy, cardiotoxicity and congestive heart failure. The hypolipidemic, hypoglycemic, diuretic, antioxidant, antiplatelet and antiobesity properties are ascribed to synergies the cardioprotective activity. Here, we have reviewed the work done so far on the role of *withania* in a variety of cardiovascular diseases.

Cardioprotective Effect: Myocardial infarction (AMI) and myocardial ischemia-reperfusion injury (M I-R), which occurs in a wide spectrum of patients, ranging from survivors of out-of-hospital cardiac arrest to AMI victims and patients undergoing cardiac surgery and represents a major public health burden, *withania* treatment found to increase the heart rate, contractility, relaxation and decrease preload along with improved antioxidant enzymes and inhibition of lipid-peroxidation comparable to vitamin E, a known cardioprotective antioxidant [3, 4]. In addition to antioxidant activity, the anti-apoptotic activity which contributes to cardioprotection was evidenced by up-regulated Bcl-2, an anti-apoptotic protein and decreased Bax, a pro-apoptotic protein as well as attenuation of terminal deoxynucleotidyl transferase biotin-dUTP nick end labeling (TUNEL) positivity; a hallmark of apoptosis [5]. Similarly, Thirunavukkarasu *et al.* 2006 found the energy boosting properties of a formulation comprising of *withania* in I-R compromised heart and recommended its use as a dietary supplement for cardioprotection. The formulation favorably altered the myocardial energy substrate, improved cardiac function and reduced infarct size [6]. In another study, Marutham, a polyherbal formulation containing *W. somnifera* has been found cardioprotective and antioxidant in isoproterenol-induced ischemic rats [7].

Anti-inflammatory Effect: Withania and withanolides being a potent inhibitor of pro-inflammatory transcription factors NF- κ B and AP-1 holds promise as a novel agent for the treatment of inflammatory cascade of cardiovascular diseases [8].

Cardiotonic Activity: The constituents of withania structurally being similar to digoxin are demonstrated to exhibit cardiotonic activity and provide a salutary effect in CHF [9].

Adaptogenic Activity: Stress, as a major cardiovascular risk factor leads activation of sympathoadrenal and hypothalamic pituitary adrenal (HPA) axis and causes oxidative stress. Withania possess a potent antistressor effect and reported to alleviate stress induced changes and provide cardioprotection in ischemic rats similar to the properties ascribed to adaptogens like *Panax ginseng*. It also increases heart weight and glycogen in myocardium and liver indicating intensification of the anabolic process and enhances the duration of contractility as well as coagulation time [10, 11].

Hypolipidemic and Anti-Atherogenic Activity: Withania has profound hypocholesteremic, hypolipidemic and antiatherogenic activity [12-15]. Mary *et al.* 2003 demonstrated the antiatherogenic activity of Caps HT2, a botanical medicine comprising of several plants including *W. somnifera* against vascular intimal damage and atherogenesis which leads to various types of cardiovascular diseases. The formulation scavenges free radicals, inhibited lipid peroxidation, delayed the plasma re-calcification time and enhanced the release of lipoprotein lipase enzyme. It also inhibited platelet aggregation comparable to heparin. The formulation altered atherogenic index and reduced the body weight with rise of high density lipoprotein cholesterol levels in hyperlipidemic rats. In a clinical study, an herbal cocktail containing withania used as an adjunct to conventional anti-ischemic drugs has been found to reduce total cholesterol, triglycerides and increase high density lipoprotein cholesterol in the post myocardial infarction patients [16]. The hypolipidemic and antiatherogenic potential is an additional benefit of its usefulness in cardiovascular diseases.

Positive Inotropic Activity: Withania has been reported to reduce blood pressure due to autonomic

ganglion blocking action and myocardial depressant effects as well as positive inotropic and chronotropic effects [17]. The alkaloids had a prolonged hypotensive, bradycardiac and respiratory-stimulant action [18].

Hypoglycemic Effect: Hyperglycemia is a major risk factor of cardiovascular diseases. Withania favorably alters blood and urine glucose levels, glycated hemoglobin and liver enzymes in diabetic rats [14, 19].

Chemotherapy Associated Cardiotoxicity: Dose-dependent and irreversible myocardial injury is a major side effect with doxorubicin, one of the effective antineoplastic agents for the treatment of solid and haemopoietic malignancies. Withania extract [20] as well as a polyherbal formulation containing CardiPro [21] has been shown to provide cardioprotection against doxorubicin associated cardiotoxicity as evidenced by reduced mortality, increased antioxidants and hypolipidemic action.

CONCLUSIONS

These studies on the cardioprotective effects of withania are fairly preliminary; however, the evidence for the beneficial effect of withania is encouraging. Till date, several activities such as antioxidant, anti-apoptotic, hypolipidemic, cardioprotective, anticoagulant, antiplatelet, adaptogenic, hypoglycemic and anti-inflammatory of *Withania somnifera* have been reported and these mechanisms were believed to contribute the cardioprotective effect. Considering its safety, efficacy and time tested utility in humans under different traditional systems of medicines, it is regarded as safe. Thus, *Withania somnifera* offer a natural alternative or as an adjunct with conventional agents with lesser side effects. However, for concrete evidence and its application as a drug in as per the stricter norms of drug development, more studies are warranted in clinical settings.

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