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Hypocholesteremic and antioxidant effects of *Withania somnifera* (Dunal) in hypercholesteremic rats

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Abstract

Hypocholesteremic and antioxidant effects of *Withania somnifera* (WS) Dunal (Solanaceae) were investigated in hypercholesteremic male albino rats. When the root powder of WS was added to the diet at 0.75 and 1.5 gm/rat/day, hypercholesteremic animals registered significant decreases in total lipids (−40.54%; −50.69%), cholesterol (−41.58%; −53.01%) and triglycerides (−31.25%; − 44.85%) in plasma. On the other hand, significant increases in plasma HDL-cholesterol levels (+15.10%; +17.71%), HMG-CoA reductase activity (+19.51%; +26.02%) and bile acid content (+24.64%; +30.52%) of liver were noted in these animals. A similar trend was also noted in bile acid (+22.43%; +28.52%), cholesterol (+14.21%; +17.68%) and neutral sterol (+12.40%; +18.85%) excretion in the hypercholesteremic animals with WS administration. Further, a significant decrease in lipid-peroxidation (−35.29%; −36.52%) occurred in WS administered hypercholesteremic animals when compared to their normal counterparts. However, it appeared that WS root powder is also effective in normal subjects for decreasing lipid profiles.

Keywords: Anti-oxidant activity; Cholesterol metabolism; Coronary heart disease; Hypercholesteremia; Lipid profiles; *Withania somnifera*

Introduction

Elevated levels of plasma cholesterol and triglycerides have been implicated as causative factors in the development of atherosclerosis and coronary heart disease (Ross, 1999). Several modern drugs are being used as hypocholesteremic agents such as statins, fibrates, nicotinic acid and resins (Satoskar et al., 2003). Among the alternative therapies used to reduce blood cholesterol level are exercise, plant-based formulations and drugs. Various plant-based formulations are known till date, which in one way or the other are known to have an effect on cholesterol level. The plant-based formulations have been used since ancient times as remedial measures against various human and animal ailments. This has lead to the use of phytometabolites as cardio-protective agents, promoting a dramatic increase in their consumption as dietary supplements (Singh et al., 2003). *Withania somnifera* (WS) Dunal (Solanaceae) known as Ashwagandha is widely used in Ayurvedic system of medicine in India. Ashwagandha is the main component of a variety of formulations prescribed for common diseases of respiratory and reproductive tracts (Tripathi et al., 1996). Several studies on this plant indicated that it possesses anti-inflammatory, antitumor, antistress, antioxidant, immunomodulatory, hemopoetic and rejuvenating properties besides positively influencing the endocrine, cardiopulmonary and central nervous systems (Mishra et al., 2000). Despite the availability of literature on the medicinal properties of WS and its chemical constituents

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(Tripathi et al., 1996), no reports exist on its hypocholesteremic and antioxidant properties. We, therefore, have attempted to investigate the effect of WS on the lipid and antioxidant profiles of hypercholesteremic rats.

Materials and methods

Material preparation

Roots of WS were collected from university botanical garden, Sardar Patel University, Vallabh Vidyanagar. The roots were diced into small pieces, shade dried and powdered. The root powder was analyzed for it's crude fiber, phytosterols, polyphenols, flavonoids and ascorbic acid contents (Thimmaiah, 1999a,b; Goad and Akihisa, 1997; Yen and Hsieh, 1998; Schaffert and Kingsley, 1955) (Table 1).

Animals and experimental design

Three-month-old (inbred) Charles Foster male rats weighing 150–200 gm were selected and were used with the approval of Institutional Animal Ethics Committee (CPCSEA approved) for the present investigation. The animals were housed individually with free access to water with measured feed, in a well-ventilated animal unit (26±2 °C, humidity 62%, 12 h light/dark cycle). After a 10-day adaptation period, 48 animals were divided into six groups of eight animals each (NC, NWS-I, NWS-II, HC, HWS-I and HWS-II; Table 2) and the experiment was conducted for a 4-week duration. Hypercholesteremia was induced by addition of 0.5 gm% cholesterol and 1.0 gm% sodium taurocholate to the standard (basal) commercial diet and daily feed consumption was recorded. The standard diet was procured from Pranav Agro Industries, Vadodara, India and contained carbohydrates, proteins, fat, fiber and mineral mixture (Table 2).

Table 1. Phytoconstituents (values: mean±SD)

Phytoconstituents mg/gm dry tissue	*W. somnifera* (root)
Crude fiber	178.66±1.15 (17.866%)
Phytosterols	7.18±0.80 (0.718%)
Polyphenols	5.83±0.59 (0.583%)
Flavonoids	0.551±0.05 (0.0551%)
Total ascorbic acid	2.54±0.04 (0.254%)

Biochemical analysis

The plasma total lipids (TL), total cholesterol (TC) and triglycerides (TG) were estimated by spectrophotometric assays (Fringe et al., 1972; Wybenga et al., 1970; Mc Gown et al., 1983, respectively). The HDL-cholesterol (HDL-C) was separated (Burstein et al., 1970) and estimated (Wybenga et al., 1970). Plasma LDL-cholesterol (LDL-C), VLDL-cholesterol (VLDL-C) and atherogenic index (AI) were calculated (Friedewald et al., 1972). The liver TL was extracted in chloroform: methanol (2:1) (Folch et al., 1957) and estimated by gravimetric analysis. TC and TG were extracted (Folch et al., 1957) and estimated (Wybenga et al., 1970; Mc Gown et al., 1983, respectively). HMG-CoA reductase (EC 1.1.1.34) activity was determined as described by Rao and Ramakrishnan (1975). The hepatic bile acid was estimated by the method of Snell and Snell (1953). The fecal cholesterol, neutral sterol and bile acids were extracted (Kaiek et al., 1984) and estimated (Wybenga et al., 1970; Snell and Snell, 1954, 1953, respectively). The hepatic malondialdehyde (MDA) was estimated by the thiobarbituric acid method (Niehaus and Samuelsson, 1968). Activities of catalase (EC 1.11.1.6), superoxide dismutase (SOD; EC 1.15.1.1) and total ascorbic acid (TAA) content were determined by the methods of Cohen and Dembiec (1970), Aebi (1974), Kakkar et al. (1984) and, Schaffert and Kingsley (1955), respectively.

Table 2. Composition of diet (gm%)

Ingredient	NC	NWS-I	NWS-II	HC	HWS-I	HWS-II
Crude protein	22.12	22.12	22.12	22.12	22.12	22.12
Crude carbohydrates	55.67	55.67	55.67	55.67	55.67	55.67
Crude fat	4.06	4.06	4.06	4.06	4.06	4.06
Crude fiber	3.76	3.76	3.76	3.76	3.76	3.76
Mineral mixture	5.64	5.64	5.64	5.64	5.64	5.64
Cholesterol	—	—	—	0.5	0.5	0.5
Sodium taurocholate	—	—	—	1.0	1.0	1.0
WS root powder (gm/rat/day)	—	0.75	1.5	—	0.75	1.5

Abbreviations: NC – normal controls provided with basal diet; NWS-I – normal animals administered with 0.75 gm/rat/day *Withania somnifera* root powder; NWS-II – normal animals administered with 1.5 gm/rat/day *Withania somnifera* root powder; HC – hypercholesteremic animals administered with cholesterol and sodium taurocholate; HWS-I – hypercholesteremic animals administered with 0.75 gm/rat/day *Withania somnifera* root powder; HWS-II – hypercholesteremic animals administered with 1.5 gm/rat/day *Withania somnifera* root powder.