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EFFECTS OF CORNELIAN CHERRY (*CORNUS MAS L.*) FRUIT ON PLASMA LIPIDS, CORTISOL, T_3 AND T_4 LEVELS IN HAMSTERS

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ABSTRACT

The aim of present study was to investigate the effect of dietary cornelian cherry fruit (CCF) on plasma lipids, cortisol, T_3 and T_4 levels. Thirty six male hamsters were divided into four groups; Group1 (control) fed basal diet without CCF supplementation, group 2 which fed 5g CCF only at first daily meal, group3 which fed 10g CCF, at first and second daily meals and group 4 which fed 15g CCF, at first, second and third daily meals, for 20 continuous days. Dietary CCF caused significant changes in plasma total cholesterol (TC), triglyceride, high density lipoprotein-C (HDL-C) and low density lipoprotein-C (LDL-C) ($P<0.01$); TC and LDL-C are decreased in groups 2, 3 and 4, when compared with control (group 1), whereas triglyceride was increased in CCF supplemented groups (groups 2, 3, and 4). HDL-C was greater in groups 3 and 4, when it compared with control and group 2. The cortisol level was lower for groups 2, 3 and 4, when compared with control. But there were no any significant changes for thyroid hormones (T_3 and T_4) between experimental groups. It was concluded that dietary cornelian cherry fruit supplementation has hypolipidemic effect due to declining total cholesterol and LDL-C levels. Also, it can increase HDL-C (good cholesterol) and decrease cortisol level, without any considerable effect on thyroid hormones (T_3 and T_4) level. Dietary supplementation of cornelian cherry fruit for two meals daily is suggested to more efficient hypolipidemic effect.

Key words: Cornelian cherry fruit, glucose, insulin, Syrian hamster.

INTRODUCTION

The cornelian cherry (*Cornus mas L.*) is a medicinal plant with hypolipidemic and hypoglycemic effects (Seymour *et al*., 2009; Mirbadal and Shirdel, 2010; Shamsi *et al*., 2010). It has extensive grown in Eastern Europe and some Asian countries including Iran (Tetera, 2006). Iranian strain of cornelian cherry fruit (CCF) has greater concentrations of ascorbic acid (183.25 to 299.5 mg/100g), phenolic compounds (2695.75 mg gallic acid/ 100g fresh fruit) and antioxidant capacity upto 82.37% (Hassanpour *et al.*, 2011). The glucose and sucrose of CCF are in low concentration, and Fe, Ca, vitamins (α-tocopherol, biotin, riboflavin and ascorbic acid) are in high concentration in fresh CCF (Zargari, 1997). The nutrients contents of CCF are presented as table1.

Table1: Concentrations of some nutrients in fresh and dried cornelian cherry fruit (CCF), according to Craita-Maria *et al*., (2011) analysis.

Compound	Moisture (% DM)	Ascorbic acid (mg/100g DM)	Carotenes (mg/100g DM)	Total sugar (mg/100g DM)	Total protein (mg/100g DM)
Fresh fruit	327.53	419.08	6.58	48.41	0.5
Dried fruit	9.12	228.82	0.77	63.22	0.27

DM: dry matter.

About medicinal aspects of fruit and its application in ethno-pharmacology or novel medicine, the published reports have listed various and multifunctional characteristics for cornelian cherry. Results obtained from related studies shown antioxidative (Ersoy *et al*., 2011), antimicrobial (Dulger and Gonduz, 2004; Krisch *et al.*, 2008), hypo-lipidemic, hyper-insulinemic and weight losing effects (Jayaprakasam *et al*., 2006; Seymour *et al*., 2009; Shamsi *et al*., 2010; Mirbadal and Shirdel, 2010). In traditional medicine, CCF was used for treatment of diarrhea, fever, and kidney and urinary bladder dysfunctions (Zargari, 1997; Dulger and Gonduz, 2004).

Phytotherapeutics for thyroid dysfunction and optimization of releasing of T_3 and T_4 has an important role in helping to supports thyroid therapies (Dehghani *et* *al*., 2010; Shekar-Foroosh *et al*., 2012). In published studies, hypoglycemic and hypolypidemic effects of CCF are investigated in obesity and diabetic individuals, but the relation of this effect with endocrine hormones is somewhat unclear. The thyroid-cholesterol connection and its relation with possible hypothyroidism and hypercholesterolemia are stated by Feld and Dickey, (2001). Also, because of considerable role of cortisol and thyroid hormones in cholesterol metabolism (Fraser *et al*., 1999; Boone, 2009), it was suggested that the hypolipidemic effect of CCF is due to its effect on present endocrine hormones. In other hand, most of published studies in relation with CCFs hypo-lipidemic effect were investigated in diabetic or obesity conditions (Jayaprakasam *et al*., 2006; Mirbadal and Shirdel, 2010; Rafieian-Kopaei *et al*., 2011). The aim of present experiment was to investigate the possible effects of dietary supplemented CCF (one, two or three meals daily) on cortisol, thyroid hormones and plasma lipids of experimental model in healthy condition.

MATERIALS AND METHODS

Present study was conducted during Dec. 2011 to Apr. 2012 at animal rooms and laboratories of Islamic Azad University. Thirty six one-month-old male hamsters (*Mesocricetus auratus*) were divided into four experimental groups or treatments (9 animals in each treatment). All of experimental groups had one week pre-experiment adaptation period with same dietary regimen and environmental condition. Then, the dietary treatments were started by supplementation of dried CCF for one, two or three meals daily:

- Group1 (control): fed basal diets without CCF supplementation
- Group2: basal diets supplemented daily 5g CCF only for first daily meal.
- Group3: basal diets supplemented 10g CCF, for first and second daily meals.
- Group4: basal diets supplemented 15g CCF, for first, second and third daily meals.

The milled CCF was mixed with diets. At end of experiment (day- 20), three animals from each group were selected randomly and blood samples were taken via injection into heart, with regard to animal ethics recommendation of veterinary department-Islamic Azad University. The blood samples were centrifuged, and then separated serum was analyzed by Auto-analyzer (Alsyon 300, Abott-USA) and its commercial kits at Rastgoo bio-pathology laboratory (Tehran) for determining plasma lipids and hormonal parameters. Thyroid hormones were determined by Electrochemiluminescence immunoassay method.

Statistical analysis: The experiment was arranged in completely randomized design and the data obtained were subjected to analysis of variance technique through SAS software (Ver. 9.1) and Duncan multiple range test was applied for detection of possible significant difference between means. Results were recorded as significant, when the P-value was less than 0.05.

RESULTS AND DISCUSSION

The obtained results from laboratory analyze and statistical comparisons were presented in table1 and 2.

Plasma lipids: Supplementation of CCF caused significant changes in plasma total cholesterol (TC), triglyceride, HDL-C and LDL-C ($P<0.01$); TC and LDL-C were decreased in groups 2, 3 and 4, when compared with control (group1), whereas triglyceride was increased in CCF supplemented groups (groups 2, 3, and 4). HDL-C was greater in groups 3 and 4, when it compared with groups 1 or 2 ($P<0.01$; Table 2).

Table 2: Plasma lipid profile of animals fed cornelian cherry fruit, supplemented in daily meal.

Groups	Number of daily supplementation	Total cholesterol (mg/ml)	Triglyceride (mg/ml)	HDL-cholesterol (mg/ml)	LDL-cholesterol (mg/ml)
1 (control)	0	136.7^{a}	190.0	51.0^{b}	27.5^{a}
2	1	109.2^{b}	190.8	52.0^{b}	20.3^{b}
3	2	103.7^{c}	194.5	53.6^{a}	20.7^{b}
4	3	108.3^{b}	191.7	54.0^{a}	21.0^{b}
P value		<.0001	0.901	<.0001	<.0001
SEM*		1.070	1.800	0.707	0.276

Different letters (a,b or c) show significant differences between means of groups ($P<0.05$).
*The standard error of difference between the mean.

Hormonal measures: The supplementation of CCF caused significant effect on cortisol levels ($P<0.05$). Cortisol level was lower in groups 2, 3 and 4 in comparison with control. But there was no any significant difference for the thyroid hormones (T_3 and T_4) between experimental groups (table 3).

Investigation on diabetic animal models shows hypolypidemic effects of CCF more efficient than similar effect of chemical drugs (Mirbadal and Shirdel, 2010). In the literatures, there is reported considerable hypolipidemic or anti-obesity effect for cherry family of fruits. In this regard, Seymour *et al*. (2009) reported that in obese laboratory rats fed a high-fat diet, physiologically relevant tart cherry consumption reduced various phenotypes of metabolic syndrome and reduced systemic and local inflammation, considerably. Also, in Ataie-Jafari *et al*., (2008) report, TC and LDL-C were decreased significantly following dietary supplementation of sour cherry juice in diabetic individuals.

Table 3: Plasma cortisol, T_3 and T_4 levels of animals fed cornelian cherry fruit supplemented in daily meal.

Groups	Number of daily supplementation	Cortisol (ng/ml)	T_3 (pg/ml)	T_4 (ng/ml)
1 (control)	0	45.8^a	0.70	6.8
2	1	30.3^b	0.72	6.8
3	2	34.0^b	0.71	6.9
4	3	28.8^b	0.70	6.8
P value		0.010	0.981	0.115
SEM*		2.821	0.030	0.129

Different letters (a,b or c) show significant differences between means of groups (P<0.05).
* The standard error of difference between the mean.

In present study, decreased TC and LDL-C, and also increased HDL-C following CCF supplementation may indicates inflammatory reactions and its effects on arachidonic acid and decline free radicals production and specially effect on oxidation of LDL-C (Thakur *et al*., 2001). Anthocyanin is a bioactive compound of CCF that can affect activity of hepatic enzymes in lipid metabolism (Lila, 2004). Flavonoids have significant hypolipidemic effect and they can decrease plasma TC (Borradaile *et al*., 2002). More total flavonoid (669 mg catechin equivalent per 100 g fresh weight basis) content in Iranian genotype of CCF (Hassanpour *et al*., 2011) may be able to declining TC and LDL-C in CCF fed animals. So, findings of present study (table 2) were in accordance with Seymour *et al*., (2009) and Mirbadal and Shirdel, (2010) findings in obese and diabetic animal models.

Relationship between cortisol and TC has been documented in an earlier study (Schwertner *et al*., 1984). But, between cortisol level and HDL-C was a significant negative or inverse correlation (Fraser *et al*., 1999). The cortisol affect cholesterol metabolism to HDL-C formation, and Long-term elevation in glucocorticoids releases explain in part the risk associated with hypercholesterolemia (Fraser *et al*., 1999). The lowest HDL-C levels are noted in subjects with the highest cortisol releasing rate (Fraser *et al.*, 1999). The findings of present study (tables 2 and 3), declined TC and cortisol level following CCF supplementation are in agreement with suggested relation by Schwertner *et al*., (1984). Since cholesterol is a precursor to cortisol, it is equally possible that declined TC can cause a subsequent decline in cortisol concentration. Also, greater HDL-C level in groups with lower cortisol level (tables 2 and 3) is in agreement with Fraser *et al*., (1999).

However the thyroid hormones have considerable role in cholesterol metabolism, there was no any changes in T_3 or T_4 in groups with different TC concentrations (Tables 2 and 3). So, differences in TC, HDL-C and LDL-C rates in experimental groups are not associated with thyroid hormones level.

In this regard, studies on different animal modes had indicated that there are no correlations between thyroid hormones and plasma lipids (Nazifi *et al*., 2002, 2007; Eshratkhah *et al*., 2012). It shows that the hyperlipidemia caused by CCF supplementation is not due to changes in thyroid hormone.

It was concluded that cornelian cherry fruit supplementation has hypolipidemic effect via declining total cholesterol and LDL-C levels. Also, it could increase HDL-C (good cholesterol) and decrease cortisol level, without any considerable effect on thyroid hormones (T_3 and T_4) level. The hypolipidemic effect of cornelian cherry fruit can be expressed following supplementation only for one meal daily. But supplementation for two meals daily is suggested to more efficient hypolipidemic effect.

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