

ELECTROLYTES CHANGES INDUCED BY WEIGHT LOSS HERBAL DRUGS PHYTOLACCA AMERICANA AND PHYTOLACCA BERRY IN HYPERCHOLESTEROLEMIC RABBITS

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ABSTRACT

Present study deals to find out the effects of two herbal weight reducing drugs Phytolacca Americana (PA) and Phytolacca Berry (PB) on plasma electrolytes in common rabbits followed by the induction of hypercholesterolemia. In PA garlic, bladder wrack and grapefruit are the additional ingredients to poke weed while PB has poke weed only. Test animals of two groups were orally administrated PA and PB in doses of 33.3 mg/day and 1.15 mg/day respectively, for 37 days. Blood samples drawn on day 0, 3, 9, 14, 21, 27 and 37 were used to measure plasma Sodium (Na^+), Potassium (K^+) and Calcium (Ca^{++}). Both herbal drugs maintained plasma Na^+ to normal levels while plasma K^+ concentration that remained low returned to normal after four weeks of treatment, significantly ($p < 0.05$) depending on the duration of drug administrated. However, PA effectively returned the very high Ca^{++} concentration to normal level within one week of treatment whereas PB achieved the same normal level after three weeks of treatment. Thus it may be concluded that both weight reducing herbal drugs although maintained the plasma Na^+ , K^+ and Ca^{++} concentrations to normal levels when administrated for more than five weeks, showed pronounced alterations in plasma concentrations of K^+ and Ca^{++} during early period of treatment. This effect might be attributed to the interference of drugs with Na^+ - K^+ ATPase activity or blocking the Ca^{++} channels at the cellular level.

Keywords: Weight loss drugs, electrolytes, phytolacca americana, phytolacca berry, grapefruit.

INTRODUCTION

A large number of chronic and life-threatening diseases and conditions are associated with overweight and obesity (Shaw *et al.*, 2007; Logue *et al.*, 2011). High concentrations of cholesterol were significantly linked with overweight and obesity. (Mokdad *et al.*, 2003). Dashti *et al.* (2006) found an association between ketogenic diet, obesity and high cholesterol. Other studies proved that obesity and adiposity were significantly linked with high serum cholesterol and other lipids. (Neri *et al.*, 2007; Sertic *et al.*, 2009; Sacheck *et al.*, 2010).

Now a days herbal drugs and dietary supplements are available for the treatment of obesity and its related disorders (Shekelle *et al.*, 2003; Pittler and Ernst, 2004; Feng *et al.*, 2010; Bu *et al.*, 2011). Weight reduction has been found in people using herbal drugs (Boozer *et al.*, 2001, 2002; Feng *et al.*, 2010; Bu *et al.*, 2011). Poke weed is among the variety of herbs found efficacious in obesity (Willis *et al.*, 2008; Ravikiran *et al.*, 2011; Hasan *et al.*, 2012).

There is an interlink between intake of sodium with high caloric diet intake (Lin *et al.*, 1999) and various studies showed the involvement of sodium in obesity (Flodmark

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et al., 1992; Suzuki *et al.*, 1996; Riazi *et al.*, 2006). Mariosa *et al.* (2008) investigated the reduction of potassium in abdominal obesity. Also during the exercise testing in obese people the important role of potassium is explained by Salvadori *et al.* (2003). Although, experimentally calcium deficiency could not induce obesity (Paradis and Cabanac, 2005), however, clinical data showed the involvement of calcium in obesity. It has been found that calcium and parathormone are associated with obesity (Hultin *et al.*, 2010).

In the present investigation two herbal weight reducing drugs Phytolacca Americana (PA) with a combination of herbal ingredients including Poke weed, Bladder wrack, Garlic and Grape fruit and Phytolacca Berry (PB) with single ingredient of Poke weed are administered to hypercholesterolemic rabbits to evaluate the changes in plasma electrolytes concentrations, the underlying mechanism of action of ingredients as well as their side effects (Hasan *et al.*, 2011).

MATERIALS AND METHODS

Fifteen common rabbits (*Oryctolagus cuniculus*) 18 to 24 months old, ranging from 1,160 to 1,470g in weight were purchased from local market, and were kept in well ventilated barred cages (Lab standards). They were fed on normal diet including carrots, cabbage and alfalfa.

INDUCTION OF HYPERCHOLESTEROLEMIA

A modified diet containing 5g butter fat / 500g of diet was given daily for 15 days to induce hypercholesterolemia in all rabbits (Moghadasian *et al.*, 1999). Blood samples were drawn on day 0 and 15.

Five rabbits were kept as controls while remaining ten were equally divided into two groups as test 1 and test 2.

DRUGS

The two experimental weight reducing herbal drugs PA and PB available in tablet form were obtained from the local chemist shop. Drugs were administered with a daily oral dose of 33.3 mg and 1.15 mg of PA and PB to test 1 and test 2 animals respectively for 37 days.

BLOOD SAMPLING

Sampling was done on day 0, 3, 9, 14, 21, 27 and 37 by drawing the blood from the marginal vein of the ear with the help of 3cc disposable syringes (Moreland, 1965). Heparinized blood samples were centrifuged at 3500 rpm for 5 minutes and collected supernatants as plasma were stored at 4°C to be used for analysis.

BIOCHEMICAL AND STATISTICAL ANALYSIS

Commercial biochemical kits (QCA, Spain) were used to measure plasma electrolytes Na⁺, K⁺ and Ca⁺⁺. The absorbances of samples were read on Spectrophotometer (Model No. NV201, China). Statistical analyses of collecting data were performed by t-test and two - way ANOVA.

RESULTS

A consideration of table 1 indicates that, administration of modified diet to control and test rabbits for 15 days, significantly (p<0.05) increased the mean plasma concentrations of Na⁺ and Ca⁺⁺ and decreased the mean plasma K⁺ concentration.

CONTROL

After 15 days, in control rabbits the exclusion of butter fat from the diet resulted in a reduction of mean plasma concentrations of Na⁺ and Ca⁺⁺, while K⁺ increased to the normal concentration (Figs. 1,2,3).

Table 1. Effect of butter fat (5g/kg diet) on mean plasma electrolytes concentration (mmol/l) of rabbits *Oryctolagus cuniculus*.

Days	Sodium			Potassium			Calcium		
	C	T1	T2	C	T1	T2	C	T1	T2
0	169.44 ± 8.58	155.15 ± 10.355	163.41 ± 31.99	5.16 ± 0.56	5.65 ± 0.63	5.26 ± 0.20	0.85 ± 0.44	1.67 ± 0.71	1.38 ± 0.47
15	181.85 ± 8.10	190.05 ± 45.43	208.21 ± 33.46	4.13 ± 1.09	4.65 ± 0.63	4.26 ± 0.20	2.55 ± 0.68	3.07 ± 0.34	3.38 ± 0.43

Each figure is the Mean ± SD of five values. C = Control. T1 = PA (33.3 mg/day). T2 = PB (1.15 mg/day)

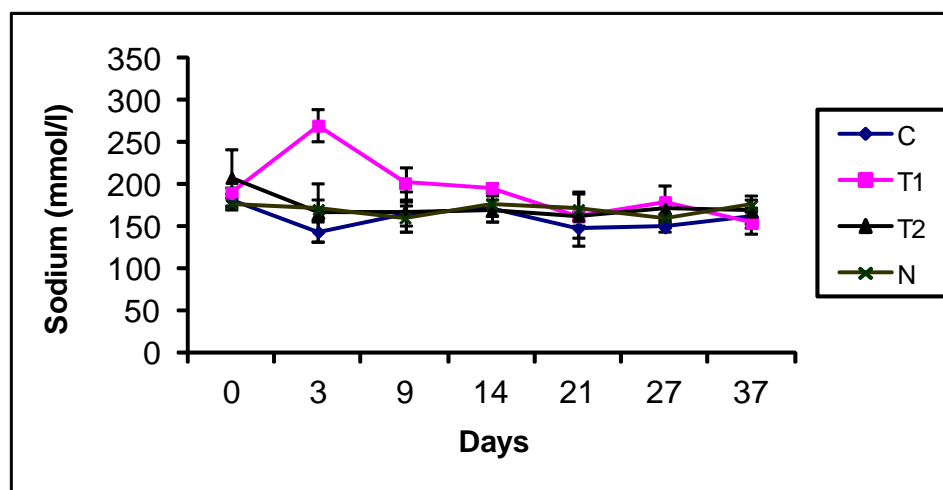


Fig. 1. Comparison of mean plasma sodium concentrations in control and test rabbits *Oryctolagus cuniculus* following the administration of weight reducing drugs.

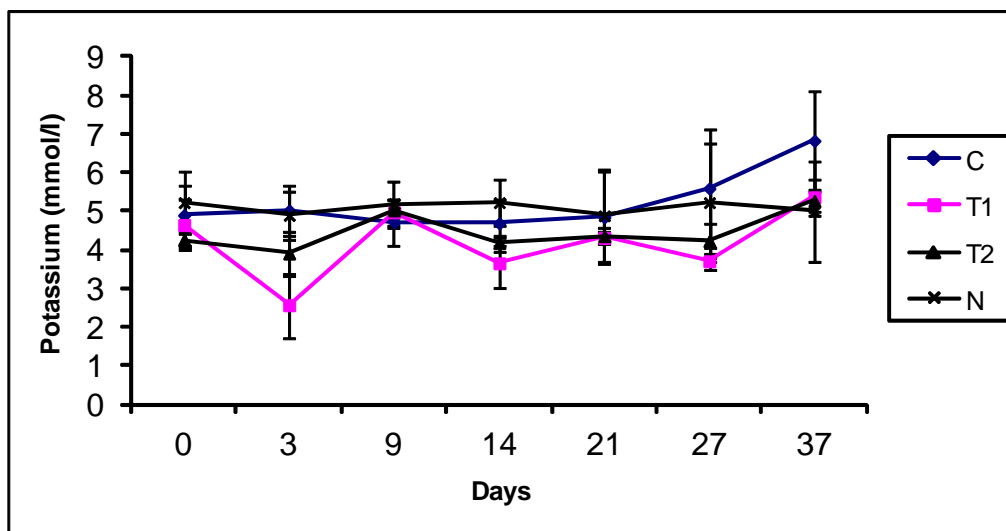


Fig. 2. Comparison of mean plasma potassium concentrations in control and test rabbits *Oryctolagus cuniculus* following the administration of weight reducing drugs.

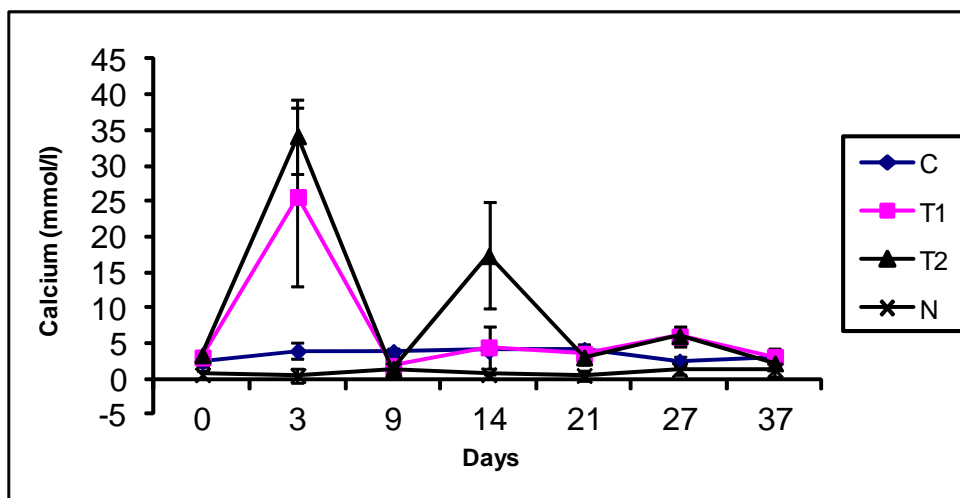


Fig. 3. Comparison of mean plasma calcium concentrations in control and test rabbits *Oryctolagus cuniculus* following the administration of weight reducing drugs.

Na⁺

On day 0, test 1 rabbits with high mean plasma Na⁺ concentration of 190.05 ± 6.14 mmol/l, when administered with a dose of 33.3 mg/day of PA for 37 days showed a further rise in Na⁺ concentration on day 3, followed by a significant ($P < 0.05$) reduction up to the end of treatment. On day 37, the Na⁺ concentration reached to 154.54 ± 13.34 mmol/l i.e. almost normal level (Fig. 1).

Test 2 rabbits with initial mean plasma Na⁺ concentration of 208.21 ± 33.45 mmol/l, when administered with a dose of 1.15 mg/day of PB for 37 days showed a reduction in Na⁺ concentration on day 3, followed by a constant, non-significant reduction till the end of the experiment (Fig. 1).

K⁺

Test 1 rabbits treated with PA have a low plasma K⁺ concentration with a mean value of 2.57 ± 0.83 mmol/l on day 3 which gradually raised and maintained up to the day 27, however a significant rise ($P < 0.05$) near to normal from day 9 was observed as administration of the drug continued till day 37 (Fig. 2).

The similar patterns of rise and fall in mean plasma K⁺ levels were obtained in test 2 animals on day 3 and day 9 respectively treated with PB. Afterwards further significant ($P < 0.05$) reduction in mean K⁺ concentration reaching to the normal values was observed (Fig. 2).

Ca⁺⁺

Fig. 3 shows the treatment of test 1 rabbits with PA resulted in a rapid rise of mean plasma Ca⁺⁺ level on day 3, i.e. 25.66 ± 12.48 mmol/l that immediately declined to low levels of 1.85 ± 0.76 mmol/l on day 9 followed by a gradual rise up to day 27. Further non-significant decrease in the mean Ca⁺⁺ level was evident on day 37.

Similar patterns of alterations in the mean plasma Ca⁺⁺ concentration were observed following the administration of PB to test 2 rabbits on day 3 and day 9. However, a rise and fall in the mean Ca⁺⁺ levels were observed on day 14 and day 21 respectively, maintained to normal levels onwards (Fig. 3).

DISCUSSION

Herbs and herbal preparations are effective in the treatment of diseases such as cancer, diabetes mellitus, obesity and cardiovascular diseases (York *et al.*, 2007). In the present study an attempt is made to find out the effects of two weight reducing herbal drugs PA and PB on mean plasma Na⁺, K⁺ and Ca⁺⁺ concentrations. Before the administration of drugs, hypernatremia, hypokalemia and hypercalcemia are induced in the experimental rabbits fed on a high butter fat diet. However, reversal to normal electrolyte concentrations is achieved when butter is excluded from the diet. PA, which is, a combination of different herbal constituents, administered to test 1 rabbits for five weeks returns the Na⁺ to normal concentration. In contrast, PB having only poke weed maintains the normal Na⁺ concentration within one week of treatment. Both the herbal drugs when administered for longer period significantly raise the mean plasma K⁺ to normal concentration. While the administration of these drugs for less than one week greatly elevate the mean plasma Ca⁺⁺ level, followed by a reduction in the later period of the experiment however, normal concentration is not achieved.

Above observations show that the herbal weight reducing drugs without having any effects on Na⁺ concentration, profoundly change the Ca⁺⁺ concentration and K⁺ concentration to a lesser extent. The laxative effect of bladder wrack and ultimate diarrhea is due to the presence of alginic acid in it which interferes with the absorption of Na⁺ and K⁺ (Newall *et al.*, 1996).

Several studies show that bladder wrack contains vitamins and minerals like Ca⁺⁺, Mg⁺⁺, K⁺, Na⁺, thus increasing their blood levels (Clark *et al.*, 2003). Normal mean Na⁺ concentration and a significant high K⁺ concentration may be attributed to the fact that herbal drugs interfere with enzyme ATPase, essential to transport these electrolytes across the membrane (Akpanabiatu *et al.*, 2005).

Two constituents of grapefruit i.e. flavonoid and naringenin have an inhibitory effect on ATPase activity (Middleton and Kandaswami, 1992; Conseil *et al.*, 1998) and voltage – operated Ca⁺⁺ channels (Summanen *et al.*, 2001). Further the concentration dependent vasorelaxant effect of naringenin (Saponara *et al.*, 2006), greatly reduced at high concentration of K⁺ (Ajay *et al.*, 2003) was in agreement with present results. However, grapefruit with low Na⁺ and Ca⁺⁺ concentrations is considered a good source of K⁺ (Ensminger, 1994). Another important component of PA is garlic which may be a good factor to maintain electrolyte balance by increasing serum Na⁺ and K⁺ levels (Oluwole, 2001). It has an inhibitory effect on Ca⁺⁺ channels, opens the K⁺-Ca⁺⁺ channels and close L - type Ca⁺⁺ channels promoting vasodilation (Siegel *et al.*, 1992; Eskardary *et al.*, 2001).

Finally it is concluded that experimental animals show a significant alteration in mean plasma K⁺ and Ca⁺⁺ concentrations in the initial period of treatment with PA and PB, that gradually return to near normal concentrations at the later part of the experiment. However, mean plasma Na⁺ is maintained to a normal concentration during the treatment. Thus the persons who are obese, especially with other obesity associated complications should use the herbal weight reducing drugs with caution as data on human studies are lacking.

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