Chapter 6

Effect of tender coconut water on electrolytes, hormones and neurotransmitters in high fructose fed hypertensive rats

Previous studies demonstrate that chronic fructose feeding in rats altered the lipid and glucose metabolism associated with an elevation of blood pressure. TCW supplementation ameliorated the metabolic alterations and significantly decreased the fructose induced systolic and diastolic blood pressure. From these results it is evident that TCW contains a series of nutritional and therapeutic properties. The antihypertensive effects of TCW was discussed in chapter 3. TCW is a rich source of minerals reported to have blood pressure lowering effects.

Several studies have reported that electrolytes play a central role in blood pressure regulation. Renin–angiotensin system (RAS) (Rahn et al., 1999) and catecholaminergic system (Versterg et al., 1976) are also found to play an important role in hypertension.

The renin–angiotensin system plays a central role in the regulation of blood pressure, electrolyte and volume homeostasis. The metabolic changes associated with fructose induced hypertension are linked to increase in sympathetic activity (Hwang et al., 1987). Sympathetic activation stimulates renin secretion and the resulting Angiotensin II which further activates the sympathetic nervous system (Rahn et al., 1999). Angiotensin II increases the aldosterone secretion which causes sodium retention; it causes vasoconstriction...
through an increase in calcium influx (Holtback et al., 2000; Michael et al., 2007; Resnick, 1999b). It is reported that catecholamines like epinephrine and norepinephrine may participate in neurodegenerative disease process by causing oxidative stress and can form peroxide radical when metabolized (Siraki, 2002).

In the light of what is stated above we studied the effect of tender coconut water on electrolytes, hormones and neurotransmitters in high fructose fed hypertensive rats.

6.1 Materials and Methods

Experimental Groups

Male albino rats (Sprague Dawley strain) weighing 160-180 g, were used for the study. The rats were divided into 4 groups of six each and fed the following diet.

Group 1 Control rats

Group 2 Control rats + TCW

Group 3 High fructose fed (hypertensive) rats

Group 4 High fructose fed (hypertensive rats) + TCW

Rats were fed the respective diet and maintained for 5 weeks. All other experimental conditions were the same as described in chapter 3. At the end of experimental period they were sacrificed and blood and tissues (brain) were collected in ice cold containers.
6.2 Results

Following biochemical parameters were studied:

6.2.1 Concentration of electrolytes in serum

High fructose fed hypertensive rats showed decreased levels of calcium, magnesium and potassium and elevated sodium levels when compared to normal rats. Administration of tender coconut water in high fructose fed rats increased the levels of calcium, magnesium and potassium and decreased the sodium levels compared to high fructose fed rats (Table 19).

<table>
<thead>
<tr>
<th>Groups</th>
<th>Sodium (mMol/l)</th>
<th>Potassium (mMol/l)</th>
<th>Calcium (mg/dl)</th>
<th>Magnesium (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>123.21±4.35^b</td>
<td>5.3±0.3^b</td>
<td>12.48±0.4^b</td>
<td>3.46±0.3^b</td>
</tr>
<tr>
<td>2</td>
<td>122.21±4.6^b</td>
<td>5.6±0.17^b</td>
<td>12.9±0.3^b</td>
<td>3.78±0.27^b</td>
</tr>
<tr>
<td>3</td>
<td>135.71±3.1^a</td>
<td>3.05±0.4^a</td>
<td>9.5±0.5^a</td>
<td>1.7±0.2^a</td>
</tr>
<tr>
<td>4</td>
<td>129.4±1.4^b</td>
<td>4.96±0.3^b</td>
<td>11.8±0.4^b</td>
<td>3.3±0.2^b</td>
</tr>
<tr>
<td>F ratio</td>
<td>19.37</td>
<td>77.64</td>
<td>63.19</td>
<td>85.37</td>
</tr>
</tbody>
</table>

Values are mean ±SD for six rats. P<0.05, ^a indicates that the results are significantly different from group 1, ^b indicates that the results are significantly different from group 3.

6.2.2 Activity of plasma renin and aldosterone

High fructose fed hypertensive rats showed increased activity of plasma renin and aldosterone when compared to normal rats. Administration of tender coconut water in high fructose fed rats decreased the activity of plasma renin and aldosterone compared to high fructose fed control rats (Table 20).
Table 20  Activity of plasma renin and aldosterone

<table>
<thead>
<tr>
<th>Groups</th>
<th>Renin (ng/ml/hr)</th>
<th>Aldosterone (ng/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3.34±0.007&lt;sup&gt;b&lt;/sup&gt;</td>
<td>189.0±1.4&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>2</td>
<td>3.01±0.12&lt;sup&gt;b&lt;/sup&gt;</td>
<td>188.7±1.0&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>3</td>
<td>6.1±0.14&lt;sup&gt;a&lt;/sup&gt;</td>
<td>222.5±3.5&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>4</td>
<td>3.4±0.007&lt;sup&gt;b&lt;/sup&gt;</td>
<td>197±1.4&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>F ratio</td>
<td>104.76</td>
<td>115.13</td>
</tr>
</tbody>
</table>

Values are mean ±SD for six rats. P<0.05, <sup>a</sup> indicates that the results are significantly different from group 1, <sup>b</sup> indicates that the results are significantly different from group 3.

6.2.3  Concentration of epinephrine in serum

High fructose fed hypertensive rats showed increased concentration of serum epinephrine when compared to normal rats. Administration of tender coconut water in high fructose fed rats decreased the concentration of epinephrine when compared to high fructose fed rats (Fig. 19).

Fig. 19  Concentration of serum epinephrine

Values are mean ±SD for six rats. P<0.05, <sup>a</sup> indicates that the results are significantly different from group 1, <sup>b</sup> indicates that the results are significantly different from group 3.
6.2.4 Concentration of norepinephrine in serum

High fructose fed hypertensive rats showed increased concentration of serum norepinephrine when compared to normal rats. Administration of tender coconut water in high fructose fed rats decreased the norepinephrine concentration when compared to high fructose fed control rats (Fig. 20).

Fig. 20 Concentration of serum norepinephrine

Values are mean ±SD for six rats. 
P<0.05, a indicates that the results are significantly different from group 1, b indicates that the results are significantly different from group 3.

6.2.5 Activity of acetylcholine esterase in brain

High fructose fed hypertensive rats showed increased activity of acetylcholine esterase when compared to normal rats. Administration of tender coconut water in high fructose fed rats decreased the activity of acetylcholine esterase when compared to high fructose fed control rats (Fig. 21).
Fig. 21 Activity of acetylcholine esterase in brain

Values are mean ±SD for six rats. P<0.05, ^a^ indicates that the results are significantly different from group 1, ^b^ indicates that the results are significantly different from group 3.

6.2.6 Histopathological studies

High fructose diet caused congestion and hypercellularity of glomerular tuft of kidneys with infiltration of mononuclear cells. Tender coconut water supplementation reverted the congestion and hypercellularity of glomerular tuft (Plate 4).
Plate 4: Light microscopic appearance of the kidney sections stained with Hematoxylin-Eosin (x 400)

1. Control - Renal glomeruli shows normal structure. The renal tubules lined with low simple cubic epithelium. The tubules have a relatively regular distinct lumen.

2. Control + TCW- The kidney architecture same as that of control. No abnormal features.


4. Fructose fed hypertensive rats + TCW- Congestion and thickening of glomerular tuft is mildly reverted.
6.3 Discussion

In the study sodium levels increased in fructose fed hypertensive rats which was lowered by tender coconut water treatment. Cowley and Lohmeir (1979) reported that electrolytes play a central role in blood pressure regulation and thus sodium retention may be one of the causes for fructose-induced hypertension. Specifically, evidence has been presented that variation in NaCl intake will lead to changes in insulin sensitivity and plasma insulin concentration (Donovan et al., 1993). A moderate and transient sodium retention has been found in fructose-fed dogs (Sleder et al., 1988). Hyperinsulinemia in high fructose fed rats is shown to be associated with renal sodium retention (DeFronzo et al., 1976) which could contribute to the development of hypertension.

Serum potassium, calcium and magnesium levels lowered by high fructose diet was restored by TCW supplementation. TCW is a rich source of minerals viz potassium, calcium and magnesium. Potassium decreases urinary calcium excretion and increases body calcium balance, probably by increasing renal calcium resorption (Lawton et al., 1990). Potassium supplementation has been reported to lower systolic and diastolic blood pressure (Cappuccio et al., 1991; Syme et al., 1975).

Dietary intakes of Potassium, Calcium and Magnesium in combination also have been reported to lower blood pressure (Frank et al., 1995; Cutler and Brittain, 1990; Whelton and Klag, 1989; Witteman et al., 1989). Because these
cations exist together in commonly eaten foods such as fruits, nuts, vegetables, cereals and dairy products their intakes are highly correlated (Reed et al., 1985). Magnesium administration, concomitant with potassium, assist tissue replenishment of potassium (Shils, 1969). Magnesium administered parenterally has been used as a treatment for severe hypertension (Lee et al., 1984). Magnesium is a cardioprotective agent that plays a key role in neurochemical and muscular excitability (Naik et al., 1999). Magnesium is reported to decrease the peripheral vascular resistance and increase coronary vasodilation (Turplaty and Altura, 1980). Magnesium inhibits the contraction of vascular smooth muscles in pulmonary and coronary arteries (Naik et al., 1999). Proposed mechanisms involve stimulation of vascular prostacyclin release (Watson et al., 1986), renal vasodilation (Rude et al., 1989), vascular responsiveness (Lee et al., 1984), acceleration of cell membrane sodium pump (Saito et al., 1988). Low dietary Magnesium raises blood pressure levels in the rat (Berthelot and Esposito, 1983). Calcium supplementation is reported to lower systolic and diastolic blood pressure (Cutler and Brittain, 1990).

Mineralocorticoid aldosterone was found to be elevated in fructose fed rats which was restored to normal by TCW supplementation. Vascular RAS is upregulated in fructose fed rats which indicates that vascular RAS mediates vascular dysfunction and vascular oxidative stress in fructose fed hypertensives (Tobey et al., 1982). Aldosterone is reported to increase the blood pressure (Chen et al., 1989). In the study plasma renin activity was restored to normal.
levels by TCW treatment and it was raised by high fructose diet. Endothelium-derived relaxing factor is reported to inhibit renin release (Vidal et al., 1988). The presence of magnesium and antioxidant vitamin C may be an added advantage in reducing the elevated levels of catecholamines. Studies have shown that supplementation of vitamin C decreased circulating epinephrine levels (Peters et al., 2001). Magnesium reduces the incidence of epinephrine and norepinephrine induced arrhythmia and proved to be a potent cardioprotective agent (Zdanowicz, 1991).

Catecholamines namely epinephrine and norepinephrine levels raised in high fructose fed groups was restored to normal by TCW supplementation. Norepinephrine provides an indirect index of sympathetic neural activity. Elevated circulating catecholamines suggest a state of hyperactivity of the sympathetic system. Systolic blood pressure is increased by circulating catecholamines (Goldstein, 1982). It has been suggested that catecholamines may participate in neurodegenerative disease process by causing oxidative stress and can form peroxide radical. The presence of magnesium and antioxidant vitamin C in TCW may be an added advantage in reducing the elevated levels of catecholamines. Plasma norepinephrine elevated in fructose-fed rats accounts for hypertension because of its vasoconstrictor activity (Tobey et al., 1982). The elevated blood pressure in fructose-fed rats can also result from the development of skeletal muscle vascular resistance in these rats. This results in elevation of total peripheral resistance and an impaired blood
flow to skeletal muscle, which in turn favours the development of insulin resistance (Baron et al., 1993).

In the study TCW supplementation significantly decreased the activity of acetyl choline esterase (AChE) which increased in high fructose fed hypertensive rats. Acetyl choline esterase is the enzyme that catalyzes the catabolism of the neurotransmitter acetyl choline to acetate and choline. The inhibition of AChE lead to increased concentrations of acetylcholine and a prolonged action of the neurotransmitter (William et al., 2002). Vasodilator response to acetylcholine (which stimulates NO release from endothelial cells) is significantly reduced in humans with hypertension (Cardillo et al., 1998). Acetylcholine induces vasodilation by increasing NO synthesis (Collier et al., 1990). Inhibition of NO synthesis decreases renal blood flow and sodium excretion due to interaction between NO and renin-angiotensin system (Bachmann and Mundel, 1994).

The kidneys play a central role in the regulation of the balance of body salt and water, and disordered regulation of renal functions is responsible for the altered balance of salt and water in pathophysiological states including some experimental models of hypertension (Mohring et al., 1972). Histopathological studies of kidney revealed glomerular tuft congestion which was mildly reverted by TCW treatment. This suggests that renal dysfunction could be partly ameliorated by treatment with TCW which may be beneficial in the control of blood pressure.
The results indicate that the electrolytes, hormones and neurotransmitters play an important role in blood pressure regulation. Administration of tender coconut water maintained a homeostasis of electrolytes, hormones and neurotransmitters in high fructose fed hypertensive rats.