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Effect of *Citrus aurantium Linn*., in paroxetine induced hyponatremia in albino mice

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ABSTRACT

The present study was undertaken to evaluate the effect of Citrus aurantium juice in paroxetine induced hyponatremia in albino mice. Paroxetine caused alterations in the levels of serum proteins, cholesterol, triglycerides, sodium, potassium and calcium, which were brought back to normal when treated with Citrus aurantium juice.

Key words: *Citrus aurantium*, paroxetine, htyponatremia.

INTRODUCTION

The study of sodium metabolism (Natrium in Latin) is fundamental to the understanding of electrolyte physiology and ECF, considerable amount is also present in bones, which act as a sodium reservoir. The daily intake of sodium varies considerably between 50 and 500meq/L. Normally about 13-20meq of sodium is filtered out every minute at the glomeruli [1]. The amount of sodium in our normal diet far exceeds the requirement of the body. Sodium excess due to increased intake is rare in the presence of normal kidney function [2].

Hyponatremia is the most common electrolyte disorder. It occurs in humans when the sodium concentration in the plasma falls below 135mmol/L. At lower levels, water intoxication may result which is an urgently dangerous condition. Severe hyponatremia may cause osmotic shift of water from the plasma into the brain cells. Typical symptoms include nausea, vomiting, headache and malaise. As the hyponatremia worsens, confusion, diminished reflexes, convulsions, stuper or coma may occur.

Hyponatremia can result from dysfunctions of the mineralocorticoid aldosterone (i.e. hypoaldosteronism) due to adrenal insufficiency, congenital adrenal hyperplasia, and some medications. Patients taking diuretic medications such as furosamide (Lasix), hydrochlorothiazide, chlorthalidone, etc., become volume depleted. Lack of adequate blood volume is a potent stimulus for vasopressin(ADH) secretion and hence for water retention.

Severe hyponatremia may result from few hours of heavy exercise in high temperature conditions, such as hiking in desert areas, or from endurance athletic events when electrolytes are not supplied. The runners in a Boston marathoa were at greatest risk of serious water intoxication with life threatening hyponatremia (serum sodium level < 120mmol/L**)** [3]. Paroxetine is a selective serotonin reuptake inhibitor (SSRI) used extensively in major depressive disorders, obsessive-compulsive disorder, panic disorder, and generalized anxiety disorder. In recent years, SSRIs have become the preferred agents in depression due to their relative safety and better tolerability. Gastro intestinal disturbances, central nervous system (CNS) side effects, and sexual dysfunction may be encountered as side effects during paroxetine therapy. Hyponatremia is an under-recognized and potentially serious complication of paroxetine therapy, especially in older patients.

Medicinal plants have been used in the treatment of various diseases from the time immemorial. The use of plants as a source of medicine lies deep in the root history of mankind [4].*Citrus aurantium* is one such plant belongs to the family Rutaceae. Fruits are orange to reddish in colour, up to 8.5cm in diameters. Fruits are loose skinned and the juice is sour in taste, with hollow core when ripe [5].The present study was designed to evaluate the effect of *Citrus aurantium* fruit juice against Paroxetine induced hyponatremia.

EXPERIMENTAL SECTION

Experimental animal
Male albino mice weighing about 50 – 60g were used as experimental animals. They were reared in ventilated poly propylene cages covered with stainless steel meshes. They were fed with normal rodent diet (pellet diet), and water *ad libitum.*

Experimental design
The animals were divided into 4 groups of 10 each.

Group I: Served as control.
Group II: Served as disease induced.
Group III: Animals fed with Citrus aurantium fruit juice alone.
Group IV:Animals fed with Citrus aurantium fruit juice(150ml/day) along with Paroxetine(0.5ml/kg of body weight).

Experimental hyponatremia is induced by the administration of Paroxetine (0.5 ml/kg of body weight). After stipulated period, animals were fasted overnight and sacrificed. Blood was collected and serum separated as used for further analysis.

Biochemical Analysis
The effect of *Citrus aurantium* juice in paroxetine induced hyponatremia was evaluated through various biochemical parameters such as Total serum protein, serum cholesterol, serum triglycerides, serum calcium, serum sodium, serum potassium using standard procedures.

RESULTS AND DISCUSSION

Hyponatremia is a clinical condition that may cause osmotic shift of water from the plasma in to the brain cells. Typical symptoms include nausea, vomiting, headache and malaise. As it worsens, confusion, diminished reflexes, convulsions, stupor or coma may occur. In the ancient days, several fruits and vegetables were used to overcome this problem. *Citrus aurantium* is one such important plant yielding fruits, used in making pickles and dishes and that is often advised by the practitioners of indigenous medicinal system to add in diet during excessive fluid loss to maintain electrolyte balance.

Hence it was hypothesized to determine the effect of *Citrus aurantium* fruit juice Paroxetine induced hyponatremia. Sodium plays a central role in the maintenance of normal distribution of water and osmotic pressure. In the present study, the serum protein level was increased in group II when compared to other groups (Table 1). This may be due to the stress proteins that are produced during electrolyte imbalance. In pseudohyponatremia the first symptom of the induction is the increase in the protein levels [6]**.** The animals belonging to group III showed mild increase in the protein levels but not significant when compared to the control group. Treatment with the juice of *Citrus aurantium* in the experimental group considerably reduced the protein level when compared to that of the animals of group II.

The serum cholesterol and triglyceride levels greatly fluctuate during experimentally induced hyponatremia (Table 1). The changes in the level of aldosterone, synthesized by the adrenal cortex, is regulated primarily by serum potassium but also is released in response to hypovolemia through the renin-angiotensin- aldosterone axis. Cholesterol is the precursor for aldosterone. Hypercholesterolemia in the group II is a clear indication of hyponatremic induction. Treatment with the *Citrus aurantium* juice brought back the altered levels to normal.

Serum sodium level was increased in group IV animals when compared to group II whereas potassium level was decreased in group IV when compared to group II (Table 2). These parameters were inversely proportional to each other. Normally, serum sodium concentration and serum osmolarity are maintained under precise control by homeostatic mechanisms involving stimulation of thirst, and renal handling of filtered sodium. Irreparable harm can befall the patient when abnormal serum levels are corrected too quickly or too slowly [7].Hyponatremia is physiologically significant when it indicates a state of extracellular hypoosmolarity and a tendency for free water to

shift from the vascular space to the intracellular space. Clinical manifestations of hyponatremia are related primarily to cellular edema that is evident by decreased calcium concentration [8].

The increase in the sodium, calcium and decrease in potassium levels in group IV clearly proved that there was a start for the reversal of normalcy after treatment (Table 2). Hence the extract from the *Citrus aurantium* fruit exhibited hypernatremic effect in case of paroxetine induced hyponatremia.

This is a tentative work and further experimentations should be carried out to determine the exact mechanism of the active principles of *Citrus aurantium* to cure hyponatremia.

Table 1: Estimation of serum Proteins, Cholesterol and Triglycerides in experimental and control groups

GROUP	SERUM PROTEINS (g/dL)	CHOLESTEROL (mg/dL)	TRIGLYCERIDES (mg/dL)
Group-I	4.02 ± 0.12	75.8 ± 0.4	5.25 ± 0.60
Group-II	4.53 ±1.01*	88.9 ±1.3*	8.15 ± 0.91*
Group-III	4.10 ± 0.81**	76.3 ±0.9**	5.73 ±0.83**
Group-IV	4.31 ± 1.06**	80.3 ± 0.74**	6.21 ±1.0**

**Statistically significant when compared with group I*
***Statistically significant when compared with group II*

Table 2: Levels of Calcium, Sodium and Potassium in control and experimental groups

GROUP	CALCIUM (mg/dL)	SODIUM (mequl/dL)	POTASSIUM (mequl/dL)
Group-I	80.3 ±0.04	123.0 ±0.16	93.2 ± 0.12
Group-II	68.01 ±0.02*	79.11 ± 0.39*	109.5 ± 0.67*
Group-III	83.09 ±0.07**	126.8 ± 0.23**	95.09 ± 0.10**
Group-IV	78.3 ±0.22**	96.0 ± 1.03**	101.3 ± 0.25**

**Statistically significant when compared with group I*
***Statistically significant when compared with group II*

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REFERENCES

[1] RS Satoskar; SD Bhandarkar. Pharmocology and pharmocotherapeutics,19th Edition, Popular Prakashan Publishers, **2005**.516-519.
[2] James Dooley. Disease of the liver and biliary system,10th edition,Wiley-Blackwell Publishers,**1997**.9-10.
[3] CS Almond; AY Shin; EB Fortescue; RC Mannix; D Wypiji; BA Binstadt; CN Duncan. *N Engl J Med*, **1990**,353 : 427-428.
[4] KR Kritikar; BD Basu. Indian medicinal plants,2nd edition, Bishen singh ,Mahendrapal singh Publishers,**1980**.
[5] SK Bhattacharjee. Handbook of aromatic plants, Pointer Publishers,**2000**,130-131.
[6] C Drummer; R Gerzer; M Heer. *Am J Physiol.*, **1992**; 262 (5) :744-754.
[7] HM Chung; R Kluge; RW Schrier; RJ Anderson. *Am J Med*., **1987**; 83: 905-908.
[8] PG Kennedy; DM Mitchell; BI Hoffbrand. *BMJ*. **1978**;2:1251-1253 .