

Research Article

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Evaluation of diuretic activity of gallic acid in normal rats

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Abstract

Objective: The present study was designed to evaluate the diuretic activity of Gallic acid in wistar albino rats. **Methods:** Animals were divided into 4 groups of 6 rat each. Group 1 and group 2 served as control and standard group respectively where as group 3 and 4 were test group which were treated with Gallic acid either at the dose of 25 mg/kg or 50 mg/kg orally. All the animals were fasted for 18hr before the experiment. All the animals were given with 2.5 ml/kg of normal saline to impose uniform salt load which was followed by drug treatment for each group. After that animals were kept individually in metabolic cages and observed for amount of urine collected. 24hr Urine samples were collected and analyzed for amount of sodium, potassium and chloride. **Results:** There was statistically significant increase in urine volume of standard and both the doses of Gallic acid ($p < 0.001$). Urinary excretion of sodium and chloride were increased when compared to control group ($p < 0.001$), Potassium excretion was also increased significantly in standard ($p < 0.001$) and Gallic acid treated group ($p < 0.05$). **Conclusion:** The result from present study shows that Gallic acid at the dose of 25 mg/kg and 50 mg/kg posses significant diuretic activity.

Keywords: Gallic acid, Diuretic, Furosemide, Urinary electrolytes.

Introduction

Gallic acid is a component of naturally occurring esters that belong to the larger group of plant polyphenols known as gallotannins. Gallotannins are polyphenolic compounds found in legumes, vegetables, fruits, and beverages. It is also chemically known as 3, 4, 5-Trihydroxybenzoic acid. Gallic acid exists in many plant materials in the form of free acids, esters, catechin derivatives and hydrolysable tannins. It is extensively used in tanning, ink dyes, as well as in the manufacturing of paper.¹ It is widely used as dietary herbal supplement; a recent study demonstrated that about thirty ayurvedic herbs and their formulation contained high percentage of Gallic acid, and these formulations are widely used for treatment of several diseases in India.^{2,3}

Gallic acid is reported to possess multiple biological activities which mainly consist of anticancer, antioxidant, antimicrobial and cardioprotective effects.⁴⁻⁷ Since gallic acid has shown antioxidant and cardioprotective activity it we decided to explore the nephroprotective effects of Gallic acid in a murine model of gentamicin induced renal damage. During the course of this study, it was noted that Gallic acid administered rats produced a high volume of urine formation. So this incidental finding prompted us to evaluate the diuretic potential of Gallic acid in normal rats.

Materials and Methods

Animals

Albino Wistar rats of either sex, inbred in the central animal house of A.J.Institute of Medical Science and Research center was used for the study. Rats were housed in clean polypropylene cages, three rats in each cage, in a controlled environment (24-26°C) with a 12 hour light and dark cycle with standard chow and water ad libitum. The rats were allowed to acclimatize to these conditions for one week. Experiments were performed during the light phase of the cycle (10:00-17:00hrs). The animals were maintained as per CPCSEA guidelines and regulations. The study was approved by institutional animal ethics committee.

Drugs and chemicals

Study drug

Gallic acid obtained from Hi-Media laboratory, given orally, dissolved in normal saline.

Standard drug

Furosemide (Sanofi Aventis Co.) at the dose of 10 mg/kg/day, orally dissolved in normal saline.

Study procedure

Rats were randomly assigned to 4 groups of 6 rats each as shown in table 1.

Table 1: Drug treatment schedule

| Group | Drug treatment | Dose |
|----------|----------------|---------------|
| Control | Normal saline | 10 ml/kg p.o |
| Standard | Furosemide | 10 mg/kg p.o |
| Test 1 | Gallic acid | 25 mg/kg p. o |
| Test 2 | Gallic acid | 50 mg/kg p.o |

All the drugs were dissolved in normal saline and administered to rats once daily.

Table 2: effect of Gallic acid on urine volume and diuretic action

| Group | Total urine volume (ml) | Diuretic action |
|------------------------|-------------------------|-----------------|
| Control | 6.80± 0.37 | - |
| Standard | 13.0 ±0.36** | 1.91 |
| Gallic acid (25 mg/kg) | 9.83 ±0.16** | 1.44 |
| Gallic acid 50 mg/kg) | 10.17 ±0.16** | 1.49 |

All the data are expresses as mean ± SE (standard error of mean). *p< 0.05, ** p<0.001 when compared to control.

Table 3: Effect of Gallic acid on urinary electrolyte excretion

| Group | Urinary electrolytes excretion | | |
|------------------------|--------------------------------|------------------------|---------------|
| | Na ⁺ m.mol/L | K ⁺ m.mol/L | Cl m.mol/L |
| Control | 106.6±1.07 | 68.40±2.3 | 93.0±0.9 |
| Standard | 166.3±1.54** | 88.5±3.7** | 133.3±1.30** |
| Gallic acid (25 mg/kg) | 127.3±1.14** | 81.67±0.56* | 109.17±2.76** |
| Gallic acid (50 mg/kg) | 129.67±1.3** | 77.5±1.5* | 100.6±1.02* |

All the data are expresses as mean ± SE (standard error of mean). *p< 0.05, ** p<0.001 when compared to control

Evaluation of diuretic activity

The method of Lipschitz *et al.*^{8,9} was employed for the assessment of diuretic activity. According to this method,

the animals deprived of food and water for 18 hours prior to the experiment. All the drugs were freshly prepared and administered orally. Before treatment, all the animals were

administered with normal saline (0.9% NaCl) at a dose of 2.5 ml/kg orally to impose a uniform water and salt load. After administration of drug each animal was placed in a individual metabolic cage which is specially designed to separate faeces and urine at $20\pm 0.5^{\circ}\text{C}$ for 24hrs. During this period, no food and water was made available to the animals. 24 hr urine sample was analyzed for total urine volume, and concentration of Na^+ , K^+ and Cl^- in the urine.

The diuretic action of test drug was calculated by using the following formula:

$$\text{Diuretic action} = \frac{\text{Urinary excretion of test drug group}}{\text{Urinary excretion in control group}}$$

Statistical Analysis

The data was expressed as mean \pm SE. Results were analyzed using one-way anova followed by Dunnett's multiple comparison test. P value of < 0.05 was considered as statistically significant. Statistical analysis was carried out using the software package SPSS (Version 17.0).

Results

Effect on urine volume

There was no evidence of dehydration and animals were found normal at observed intervals of 5hr, 12hr and 24hr. As shown in table 2 the standard drug furosemide significantly increases the total urine volume (13.0 ± 0.36 ml) when compared to control group (6.80 ± 0.37 ml.) and diuretic action was 1.91. The test drug at the dose of 25 mg/kg and 50 mg/kg also showed a significant increase in urine volume (9.83 ± 0.16 ml and 10.17 ± 0.16 ml respectively) and a dose dependent increase in urine activity was also observed.

Effect on urinary electrolytes excretion

As shown in table 3 standard drug furosemide significantly increases urinary excretion of sodium, potassium and chloride ($p < 0.001$). whereas the Gallic acid at the dose of 25 mg/kg significantly decreases sodium, potassium and chloride excretion when compared to control ($p < 0.001$ when compared to control for sodium and chloride excretion) but significance level decreases for potassium excretion ($p < 0.05$ when compared to control for potassium excretion).

Gallic acid at the dose of 50 mg/kg also showed similar results like gallic acid 25 mg/kg and standard drug but significant level decreases for potassium and chloride excretion ($p < 0.05$ when compared to control).

Discussion

Diuretics are drugs that increase the rate of urine flow, sodium excretion and are used to adjust the volume and Composition of body fluids in a variety of clinical situations. Drug-induced

diuresis is beneficial in many life threatening disease conditions such as Congestive heart failure, nephritic Syndrome, cirrhosis, renal failure, Hypertension, and pregnancy toxemia .

Most diuretic drugs have the adverse Effect on quality of life including Impotence, fatigue, and weakness. High efficacy diuretics have the drawback of causing increased excretion of potassium in urine.^{10,11} Hence finding out newer drug with less adverse effect and potassium sparing activity is need of hour.

In the present study Gallic acid showed a significant increase in urinary excretion. There was also a significant increase in excretion of urinary electrolytes like sodium, potassium and chloride. The results of the study showed that Gallic acid posses significant diuretic activity but action was less than the standard drug. All the results were highly significant except the potassium excretion from Gallic acid treated group which had lower level of significance which may be attributed to little potassium sparing activity of drug.

Gallic acid is a naturally occurring polyhydroxy phenolic compound commonly found in gallnuts, grapes green tea, pineapple, bananas, strawberries etc. plants containing Gallic acid like *Alocasia macrorrhizos*,¹² *Camellia sinensis*,¹³ *Vitis vinifera* L¹⁴ has proven to have diuretic action. It may be because of presence of Gallic acid in these plants which has shown diuretic property. Gallic acid in its pure form caused diuresis more like a loop diuretic but multiple mechanisms seems to be appeared. In this study other electrolytes like bicarbonate, uric acid were not measured which may also have thrown some light on mechanism of action of drug.

Conclusion

To conclude Gallic acid at the dose of 25 mg/kg and 50 mg/kg showed a significant diuretic action. Further

detailed studies are required to explore the effect on different electrolytes and mechanism of action of the drug.

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