

Comparison of the diuretic effects of frusemide and the *Karavi Panchaka* Ayurveda decoction

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Abstract

Objective To investigate the diuretic, natriuretic and kaliuretic effects of the antihypertensive Ayurveda drug *Karavi Panchaka* decoction and compare it with the diuretic frusemide.

Design An animal study using Sprague–Dawley rats. The volume of urine and the total sodium and potassium excreted in the urine by rats in response to orally fed *Karavi Panchaka* decoction were compared with rats fed with frusemide. Control experiments were done with rats receiving similar volumes of distilled water orally. The Ayurveda drug was prepared in accordance with the traditional method in the laboratory using medicinal plant specimens individually collected and identified.

Measurements The volume of urine excreted during a 24-hour period following administration of the Ayurveda drug, frusemide or water was measured. The total sodium and potassium ion concentrations in the urine samples were determined using flame photometry.

Results The *Karavi Panchaka* decoction clearly showed a statistically significant increase in urine excretion when compared with the control group that received only distilled water. The potassium ion excretion was significantly increased in the *Karavi Panchaka* decoction treated group when compared to the control group. This increase was statistically similar to that caused by frusemide. Neither drug had a significant effect on sodium ion excretion at the dosages used.

Conclusion Our results show that the *Karavi Panchaka* decoction significantly increases urine and potassium ion excretion in rats, but has no effect on sodium ion excretion at the dosage used. The effect of the Ayurveda drug on urine output as well as the sodium and potassium ion excretion is similar to that of frusemide administered at the dose used in our study.

Introduction

Hypertension is a major health problem because of the percentage of the population affected and the serious consequences of untreated hypertension. It is a major risk factor for stroke, congestive heart failure and coronary artery disease. In view of this the allopathic system of medicine has developed and established several lines of treatment for hypertension.

Over 3000 years ago, Susrutha described the existence of the circulatory system and its diseases as stated in

the ancient Ayurveda text "*Susrutha Samhitha*" [1]. He had even drawn a parallel between the shape of the heart with the aortic arch and a lotus bud attached to its petiole.

The practitioners of Ayurveda had a number of prescriptions to deal with diseases of the circulatory system. A few survive today in practice, and the prescription *Karavi Panchaka* decoction investigated in this study is one of them. *Karavi Panchaka* decoction is a simplified formulation of a bigger traditional prescription (*Karavyadi* decoction) used traditionally in Sri Lanka in the treatment of hypertension. The original prescription contained 22 ingredients. Of these 22 ingredients, five herbal ingredients have been selected by previous researchers for the preparation of the *Karavi Panchaka* decoction [2]. The decoction is an aqueous extract of fruit of *Carum carvi* Linn., roots of *Saussurea lappa* and *Ricinus communis*, leaves and stem of *Bacopa monniera* and roots of *Boerhavia diffusa* [2].

The efficacy of this decoction as an antihypertensive drug has been previously established [2]. Its effect as a cardiac depressant on the frog heart has been reported [3].

The control of hypertension in modern therapeutics is affected in many ways, and one approach is to reduce the body fluid volume [4]. This is achieved by stimulating diuresis. The objective of the present study was to investigate the presence of diuretic activity in the decoction and compare it with that of frusemide.

Methods

Preparation of the decoction (drug)

Fruit of *Carum carvi* Linn., roots of *Saussurea lappa* and *Boerhavia diffusa*, leaves and stem of *Bacopa monniera* were bought from a standard Ayurveda drug market from where patients make their purchases. Roots of *Ricinus communis* were collected fresh from its natural habitat as recommended in the prescription. The botanical identity of the samples were established by comparison with authentic samples.

The herbal ingredients of the prescription were washed and dried to a constant weight. The plant material so prepared was made into a coarse powder separately by using mortar and pestle. 50 g of each of the powdered ingredients were added to 5 litres of water and this volume was reduced to 1/8th the original volume by gentle boiling

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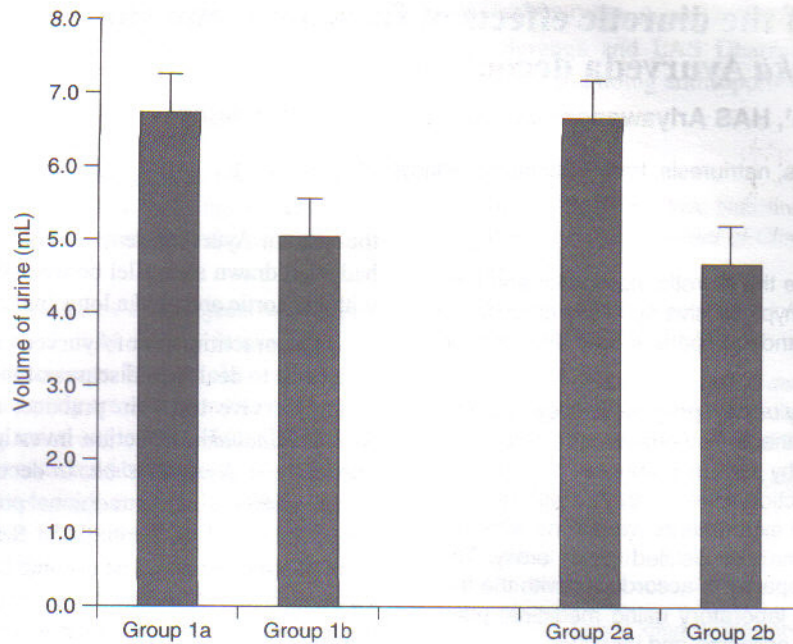


Figure 1. Effect of *Karavi Panchaka* decoction and frusemide on urine output. The vertical columns indicate the mean urine output with the standard errors of the means (SEM) given above the column. Group 1a and 1b represent the *Karavi Panchaka* decoction treated group and the corresponding control group that received water. Group 2a and 2b represent the frusemide treated group and the corresponding control group respectively.

using a controlled gas flame. The decoction so prepared according to tradition was filtered through a sieve and centrifuged at 1000 rpm. The resultant supernatant was lyophilised in aliquots and stored at -20°C for use.

Reconstitution of the drug for administration was done by dissolving the calculated weight of the lyophilised sample in an appropriate volume of distilled water to get the required concentration to suit the body weight of the test rat. The prepared drug was administered orally to partially anaesthetised animals.

Experimental

The experimental animals were healthy Sprague-Dawley albino rats weighing 140–240 g maintained on a standard diet of rat pellets with free access to water. The animals were divided into four groups 1a, 1b, 2a and 2b.

Group 1a: This group of rats ($n=22$) received 744 mg/kg body weight of lyophilised *Karavi Panchaka* decoction [2] dissolved in 1 ml/100g body weight of distilled water orally.

Group 1b: The rats of this group ($n=24$) constituted the control group for the above and received under identical conditions an equivalent volume of distilled water orally instead of the *Karavi Panchaka* decoction.

Group 2a: 18 rats were included in this group and each received the loop diuretic frusemide orally at a concentration of 40 mg/kg body weight.

Group 2b: The rats of this group ($n=17$) constituted the control group for the frusemide treated group, and

received an equivalent volume of distilled water orally instead of frusemide.

Administration of *Karavi Panchaka* decoction, frusemide or water to the rats was orally under light anesthesia. Following treatment the animals were placed separately in labelled metabolic cages and a 24-hour collection of urine was made. The urine output of each animal was measured and stored separately at -20°C . All the experimental animals were kept under observation for 48 hours to monitor the appearance of visible signs of alteration of behaviour indicating toxic effects of the decoction.

The sodium and potassium ion concentration of each urine sample as well as those of the *Karavi Panchaka* decoction were determined in duplicate by standard flame photometry.

All results were statistically analysed using the Student's t-test (SPSS 7.5 for Windows software) with $p < 0.05$ being considered significant.

Results

Effect on the urine output (Figure 1)

The results show a significant ($p=0.02$) increase in the average 24-hour urine output (6.7 ml) in the *Karavi Panchaka* decoction treated animals (group 1a) compared with the control animals (5.0 ml) of group 1b that received distilled water (Table 1). Administration of frusemide also resulted in a significant ($p=0.03$) increase of urine output (6.6 ml) when compared with the respective control group that received distilled water (4.6 ml). The urine output of the *Karavi Panchaka* decoction

Table 1. Effect of *Karavi Panchaka* decoction and frusemide on 24-hour urine output

	Group 1a (Test) n=22	Group 1b (Control) n=24	Group 2a (Test) n=18	Group 2b (Control) n=17	Group 1a (Test) n=22	Group 2a (Control) n=18
Mean (ml)	6.7	5.0	6.6	4.6	6.7	6.6
SEM	0.56	0.44	0.73	0.46	0.56	0.73
p value	0.02		0.03		0.96	

Group 1a and 1b represent the *Karavi Panchaka* decoction treated group and the corresponding control group that received water. Group 2a and 2b represent the frusemide treated group and the corresponding control group respectively.

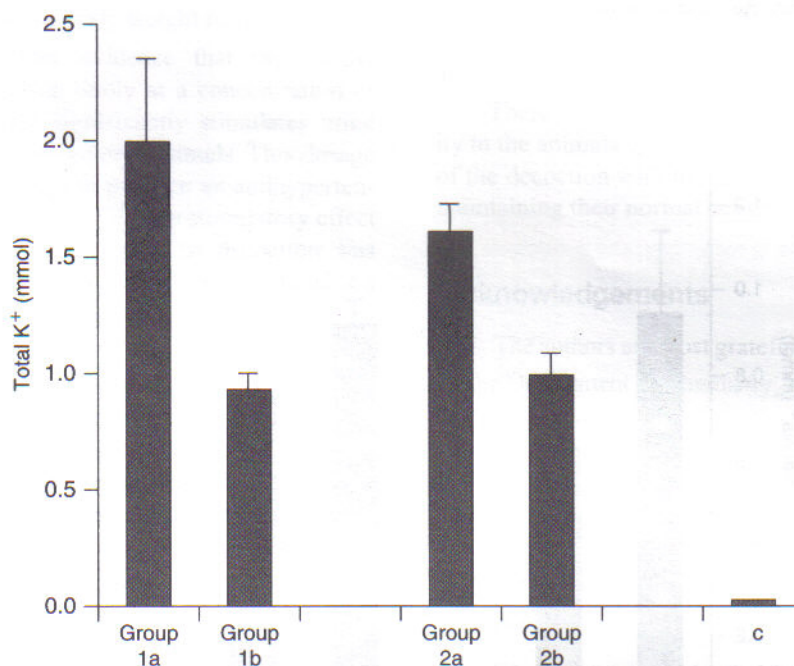


Figure 2. Effect of *Karavi Panchaka* decoction and frusemide on urinary K⁺ excretion. The vertical columns represent the mean total K⁺ excreted in 24 hours by the respective groups. The SEM values are given above each column. Groups 1a, 1b and 2a and 2b are the same as in Figure 1. The similar effect ($p=0.36$) of the *Karavi Panchaka* decoction and frusemide on the K⁺ excretion is illustrated by columns representing 1a and 2a. Column c illustrates the negligible amount of K⁺ in the *Karavi Panchaka* decoction.

treated group (group 1a) is statistically similar ($p=0.96$) to the group treated with frusemide (group 2a) at a concentration of 40 mg/kg body weight as shown in Table 1. The average urine output of the respective control groups (groups 1b and 2b) are also statistically similar ($p=0.6$).

Effect on K⁺ ion excretion (Figure 2)

The *Karavi Panchaka* decoction significantly increased ($p=0.01$) the urinary excretion of K⁺ (mean total = 1.99 mmol) compared to that of the control group (mean total = 0.92 mmol) as shown in Table 2 groups 1a and 1b. This is similar to the effect of frusemide administered at a concentration of 40 mg/kg body weight which stimulates a significant increase ($p<0.01$) in the excretion of K⁺ (mean total = 1.60 mmol) compared to that of the respective control group (mean total = 0.99 mmol) as shown in Table 2 groups 2a and 2b. There is no significant difference ($p=0.36$) between the total K⁺ excreted

in response to *Karavi Panchaka* decoction and frusemide, 1.99 mmol and 1.60 mmol respectively. The total amount of K⁺ in the *Karavi Panchaka* decoction is an insignificant 0.02 mmol (Table 2).

Effect on Na⁺ excretion (Figure 3)

Neither the *Karavi Panchaka* decoction nor frusemide had a significant effect on Na⁺ excretion. The total Na⁺ excreted (0.94 mmol) by animals treated with *Karavi Panchaka* decoction was not significantly different ($p=0.19$) from the total Na⁺ excreted by the control animals (0.63 mmol) that received distilled water (Table 3, groups 1a and 1b). Table 3, group 2a and 2b illustrate this effect of frusemide. The frusemide treated animals of group 2a excreted a total of 0.92 mmol of Na⁺ whereas the respective control group excreted 0.75 mmol of Na⁺ which is not significantly different ($p=0.14$). The total Na⁺ excreted, 0.94 mmol and 0.92 mmol in response to *Karavi Panchaka* decoction and frusemide respectively

Table 2. Effect of *Karavi Panchaka* decoction and frusemide on 24-hour excretion of K⁺ in the urine

	Group 1a (Test) n=22	Group 1b (Control) n=24	Group 2a (Test) n=18	Group 2b (Control) n=17	Group 1a (Test) n=22	Group 2a (Control) n=18
Mean (mmol)	1.99	0.92	1.60	0.99	1.99	1.6
SEM	0.38	0.08	0.17	0.12	0.38	0.17
p value	0.01		0.01		0.36	

Total K⁺ in the dose administered = 0.02 mmol

Group 1a and 1b represent the *Karavi Panchaka* decoction treated group and the corresponding control group that received water. Group 2a and 2b represent the frusemide treated group and the corresponding control group respectively. The other abbreviations are the same as in Table 1.

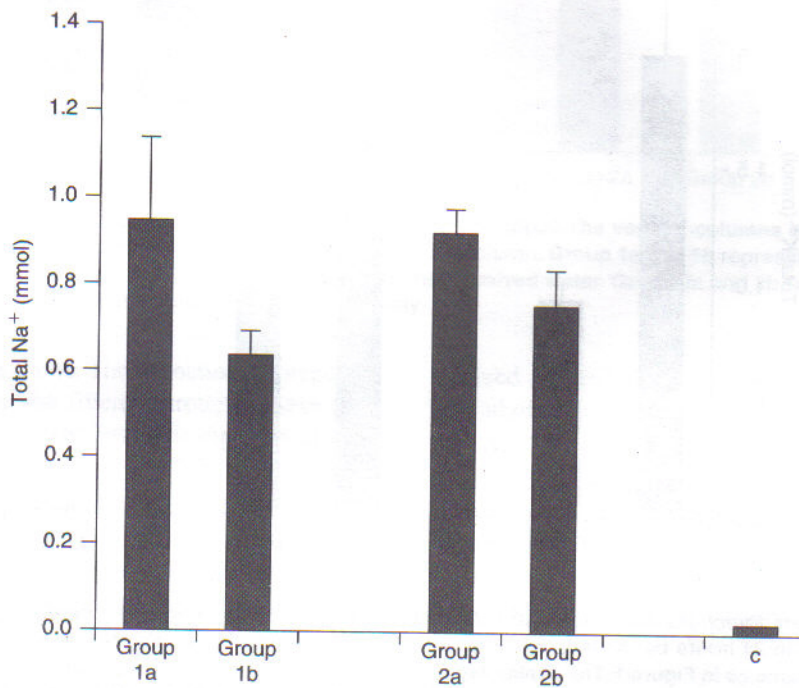


Figure 3. Effect of *Karavi Panchaka* decoction and frusemide on urinary Na⁺ excretion. The vertical columns represent the mean total Na⁺ excreted within 24 hours by the respective subgroups. The SEM values are given above each column. Groups 1a, 1b and 2a and 2b are the same as in Figure 1. The similar effect (p=0.91) of the *Karavi Panchaka* decoction and frusemide on the Na⁺ excretion is illustrated by columns representing 1a and 2a. Column c illustrates the insignificant amount of Na⁺ in the *Karavi Panchaka* decoction.

Table 3. Effect of *Karavi Panchaka* decoction and frusemide on 24-hour excretion of Na⁺ in the urine

	Group 1a (Test) n=22	Group 1b (Control) n=24	Group 2a (Test) n=18	Group 2b (Control) n=17	Group 1a (Test) n=22	Group 2a (Control) n=18
Mean (mmol)	1.94	0.63	0.92	0.75	0.94	0.92
SEM	0.22	0.07	0.06	0.09	0.22	0.06
p value	0.19		0.14		0.91	

Total Na⁺ in the dose administered = 0.02 mmol

Group 1a and 1b represent the *Karavi Panchaka* decoction treated group and the corresponding control group that received water. Group 2a and 2b represent the frusemide treated group and the corresponding control group respectively. The other abbreviations are the same as in Table 1.

at the given dosages do not show a statistically significant difference ($p=0.91$) as shown by Table 3. The total Na^+ in the *Karavi Panchaka* decoction was insignificant (0.02 mmol) as shown in Table 3.

Discussion

The results of our study show a remarkable similarity between the Ayurveda antihypertensive drug *Karavi Panchaka* decoction and the diuretic frusemide with respect to the diuretic, natriuretic and kaliuretic effects when administered orally at concentrations of 744 mg/kg body weight and 40 mg/kg body weight respectively.

This study provides evidence that the *Karavi Panchaka* decoction given orally at a concentration of 744 mg/kg body weight significantly stimulates urine output in rats compared to control animals. This dosage has been previously shown to produce an antihypertensive effect in a previous study [2]. The stimulatory effect on urine output by *Karavi Panchaka* decoction was statistically similar to that of frusemide administered at a dosage of 40 mg/kg body weight.

The results also show a remarkable similarity between the natriuretic and kaliuretic effects of *Karavi Panchaka* decoction and frusemide. The pattern of K^+ and Na^+ excretion in urine in response to *Karavi Panchaka* decoction and frusemide are similar with respect to effect as well as extent at the given concentrations.

Both *Karavi Panchaka* decoction and frusemide significantly increased K^+ excretion in the urine, and the increases are statistically similar. In contrast, neither drug had a significant effect on the Na^+ excretion at the dosages used. This is an unexpected observation, since frusemide is well known to cause natriuresis. Further, if *Karavi Panchaka* decoction, which is used in the treatment of hypertension, brings about the lowering of blood pressure by reducing the extracellular fluid volume, a natriuretic effect should be evident. The unexpected absence of natriuresis could be explained if *Karavi Panchaka* decoction is also a loop diuretic like frusemide and the Na^+ excretion at the given concentrations of the respective drugs is insufficient to overwhelm the reabsorption of Na^+ occurring in the distal renal tubule.

Loop diuretics inhibit $\text{Na}^+/\text{K}^+/\text{Cl}^-$ co-transport mechanism of the ascending limb of the loop of henle resulting in the accumulation of these ions in the tubular fluid. However, when the tubular contents with the resulting load of $\text{Na}^+/\text{K}^+/\text{Cl}^-$ pass through the distal convoluted tubule of the kidney, Na^+ and Cl^- ions are actively reabsorbed. In the terminal part of the distal convoluted tubule, where the Na^+-K^+ exchange site responsible for the fine tuning of K^+ is located, Na^+ are absorbed from the tubular fluid and K^+ secreted [5].

The absence of natriuresis and the presence of kaliuresis in this study could be accounted for if the Na^+ load presented to the distal convoluted tubule due to

Karavi Panchaka decoction and frusemide at the given dosages is more or less equal to the tubular absorption of Na^+ of the distal convoluted tubule.

Since the dosage of the *Karavi Panchaka* decoction used in this study is equivalent to the dosage used in a previous study to establish its antihypertensive property [2], the mode of action of this antihypertensive drug is unlikely to be due to its diuretic property, as the extracellular fluid volume cannot be significantly reduced without natriuresis. However with five different medicinal plants included in the preparation of the *Karavi Panchaka* decoction, the drug might possess other effects towards reducing blood pressure such as the blocking of β -adrenoreceptors and inhibition of angiotensin converting enzyme.

There were no manifestations of any signs of toxicity to the animals up to 48 hours after the administration of the decoction with the animals feeding normally and maintaining their normal activity.

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