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Diuretic Effects of Several Chemical and Herbal Compounds in Adult Laying Hens

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Abstract: Diuretic agents have been used in the treatment of several situations such as cardiopulmonary and urinary diseases in humans and animals, but they have not been extensively studied in poultry. Some Iranian poultry producers traditionally use urotropin (hexamine), alhagi (*Camelorum fisch*) and malt beverage to get therapeutic effect in broiler or laying hens. Diuretics may be used after drug therapy in order to get rid of tissue residues and in some toxicity conditions in birds. The purpose of this study was to evaluate the diuretic properties of several herbal and chemical agents in adult laying hens. Adult laying hens were randomly divided into 9 groups, each group consisting of 5 birds. Specific doses of diuretics were administrated to anesthetized hens (with xylazine and ketamine) following 24 h off-feed period. Urine samples were collected for 2 h after drug administration. Blood samples were also taken at 90 min. The concentrations of chloride, albumin, glucose, creatinine, uric acid and urea nitrogen were measured in serum and urine samples. Urine volume and specific gravity, sodium and potassium concentrations were also determined in urine. Statistical analysis of data showed that furosemide had a positive significant effect on urine volume compared to other agents. Urotropin also increased the urine volume but this effect was not significant. With respect to the effects on electrolytes (sodium, potassium and chloride), intramuscular furosemide, oral urotropin and hydrochlorothiazide exerted some changes, but no consistent pattern was observed with respect to the other factors measured in serum and/or in urine. Diuretic effect was more pronounced following intramuscular administration of furosemide.

Key words: Diuretic effect, herbal and chemical compounds, laying hens

INTRODUCTION

Unlike the classical bean-shaped kidneys in mammals, kidneys in birds are longitudinal in shape and are comprised of three lobes with no distinct cortex and medulla (Braun, 1982). The functioning units of each kidney are nephrons and these enable the birds to save their body water by concentrating the urine. The terminal collecting tubules empty into the ureters which directly open in the cloaca, a common vestibule into which the digestive and reproductive tracts end. Therefore, no renal pelvis and bladder is present in birds (Dicker and Haslam, 1966; Laverty and Dantzler, 1982). Birds make urine having a one fifth concentration compared to that in most mammals (Braun and Dantzler, 1972; Emery *et al*., 1972; Layton *et al*., 2000). Uric acid is the main nitrogenous waste product excreted largely by tubular secretion. Uric acid in the urine is present in a supersaturated colloid form suspension and does not contribute to the osmotic pressure (McNabb, 1974; McNabb and McNabb, 1975). Diuretics are substances that cause an increase in excretion of electrolytes and water so that body gets rid of any excess fluid. Their mechanisms of action vary and generally involve specific enzymes, transport proteins, hormone receptors and ion channels functioning directly or indirectly in renal tubular electrolyte reabsorption (Brater, 1998; Puschett, 1981). Osmotic diuretics, however, exert their effects by establishing an osmotic pressure gradient between plasma and tissue water compartments (Kang and Kim, 2005). Diuretics are used in several cardiovascular disorders such as congestive heart failure, hypertension, hyperkalemia, ascites, certain kinds of tissue edema and high intracranial pressure (Czaja *et al*., 1983; Dormans *et al*., 1998; Rodés, 1996; Roudebush *et al*., 1994; Vestweber *et al*., 1989; Wideman *et al*., 1995). These agents may also be used in certain types of toxicosis conditions in animals and human (Berg, 1977; Roscelli and Yu, 1970; Selye, 1969; Selye *et al*., 2006). Diuretic compounds have not been extensively studied in poultry. Traditionally, some Iranian poultry producers use urotropin, alhagi and malt beverage during heat stress periods and after vaccination of birds, or after an outbreak of infectious diseases and they claim to get positive therapeutic effects mainly due to their diuretic action. So, the aim of this study was to examine the diuretic effect of those agents and several other chemical and herbal products in laying hens.

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MATERIALS AND METHODS

Animals: Fourty five 60 week-old Bovans laying hens weighing 1.7-1.9 kg were purchased from Veterinary School Educational Farm of Shiraz University and were subjected to nine groups and were treated according to the followings. Hens were kept in 15 cages with similar conditions of environmental temperature, humidity, lightening and nutrition. Birds fed *ad lib* and had free access to drinking water. The feed was deprived to the hens 24 h before the experiment in order to reduce the amount of intestinal contents, but they had access to water during this period.

Chemical and herbal products: Drugs were purchased from local medical or veterinary drugstores. Herbal products were obtained from traditional producers in Shiraz. All solutions were freshly prepared from solid drug dosage forms.

Drug administration to various groups: Nine groups of hens were treated as the following:

- Control group for oral route (10 ml kg^{-1} distilled water administered directly into the crop by a plastic feeding tube).
- Control group for parenteral route (0.25 ml kg^{-1} distilled water injected intramuscularly into pectoral muscle).
- Malt beverage group (10 ml kg^{-1}; given orally).
- Alhagi group (10 ml kg^{-1}; given orally).
- Oral furosemide group (5 mg kg^{-1}; from a 0.05% drug solution after dissolving furosemide tablets in deionized water).
- Urotropin (methenamine; hexamine) group (50 mg kg^{-1}; from a 0.5% solution of the powder; given orally).
- Hydrochlorothiazide group (10 mg kg^{-1}; from a 0.1% drug solution after dissolving hydrochlothiazide tablets in deionized water; given orally).
- Spironolactone group (1 mg kg^{-1}; from a 0.01% drug solution after dissolving spironolactone tablets in deionized water; given orally).
- Parenteral furosemide group (2.5 mg kg^{-1}; from a 1% drug solution; given intramuscularly).

Anesthesia: Ketamine hydrochloride (12.5 mg kg^{-1}) and xylazine hydrochloride (5 mg kg^{-1}) were injected intramuscularly to induce general anesthesia. Small dose of ketamine hydrochloride (5 mg kg^{-1} at most) was re-administered to maintain anesthesia when required. Each anesthetized bird was placed by its back on a surgical board with the neck and wings extended. The legs were fixed to the board with masking tape.

Blood sampling: The site of bleeding was prepared by removing feathers and disinfected with 70% ethanol. Blood samples were taken from wing veins at 90 min after anesthesia. Samples were collected in tubes not containing any kind of anticoagulant agent and were left at room temperature for 2 h and sera were then separated by centrifugation at 1500g for 20 min. Glucose was measured right after blood centrifugation. The remaining sera were divided into several tubes and were kept at -20°C until analysis for albumin, creatinine, uric acid, blood urea nitrogen (BUN) and chloride.

Urine collection: Feathers were removed to expose the cloacal region and the area was disinfected. A small piece of gauze lubricated with mineral oil was inserted in the coprodeum of cloaca to prevent urine contamination with intestinal contents. Urine samples were intermittently collected, using a plastic syringe, from the fluid appearing in coprodeum. Each time the collected urine was emptied into a tube and was ultimately centrifuged at 2500 g for 10 min. After centrifugation, the volume of the supernatant was measured and aliquots were divided into plastic vials and kept at -20°C until analysis. Glucose was measured immediately after final urine collection. Other urinary biochemical parameters were measured at the end of *in vivo* experiments.

Analytical procedures: Glucose was measured with enzymatic-colorimetric (glucose oxidase) method (Barham and Trinder, 1972). Serum and urine albumin concentrations were determined using bromcresol green assay (Doumas *et al*., 1971; Tietz, 1976). BUN and UUN were measured by diacetyl monoxime technique (Evans, 1968). Uric acid was determined by phosphotungstate method in both urine and serum samples (Reece and Hobbie, 1972). Urinary and serum creatinine were estimated by the Jaffe reaction (Bartels *et al*., 1972; Fabiny and Ertingshausen, 1971). Colorimetric thiocyanate method was used to determine chloride concentrations in both serum and urine samples (Tietz, 1976). Flame photometry was employed to measure the concentrations of sodium and potassium in urine (Campbell and Coles, 1986; Dein, 1986). Specific gravity of urine was determined by refractometry (Campbell and Coles, 1986; Dein, 1986).

Statistical analysis: Results are expressed as Mean± SEM. unless otherwise stated. ANOVA test was used to analyze the data. The level of significance was considered to be $p \leq 0.05$.

RESULTS

(A) Urine physicochemical characteristics: The data with respect to the levels of various urinary parameters after administration of different compounds in hens are summarized in Table 1.

Table 1: Levels (Mean± SEM; n = 5) of urinary excretion of various parameters during 2 h after administration of different agents in laying hens

	Groups				
Factors (units)	DW (PO) (10 ml/kg)	DW (IM) (0.25 ml/kg)	F (IM) (2.5 mg/kg)	F (PO) (5 mg/kg)	HCT (PO) (10 mg/kg)
Volume (ml)	4.5±0.6^{ab}	3.4±0.8^{b}	6.5±0.9^{a}	4.2±0.8^{ab}	3.2±0.3^{b}
Glucose (mg/dl)	2.9±2.9^{a}	13.9±5.4^{b}	13.2±6.4^{b}	0±0^{a}	0±0^{a}
Chloride (mEq/l)	7.0±0.6^{a}	20.6±4.3^{c}	70.3±9.2^{b}	49.9±9.4^{b}	10.3±1.2^{a}
Albumin (g/dl)	0±0	0±0	0±0	0±0	0.04±0.03
Creatinine (mg/dl)	29.8±0.6^{a}	24.6±1.7^{a}	28.8±1.5^{a}	32.8±0.7^{a}	31.4±1.6^{a}
Uric acid (mg/dl)	23.5±2.5^{b}	7.9±1.9^{a}	27.3±3.5^{b}	10.3±1.1^{a}	25.6±2.4^{b}
Urea nitrogen (mg/dl)	6.3±2.1^{a}	13.6±3.9^{a}	4.3±1.0^{a}	13.5±1.9^{a}	9.6±2.1^{a}
Sodium (mEq/l)	365±32^{a}	447±69^{a}	2143±202^{b}	1175±228^{a}	424±37^{a}
Potassium (mEq/l)	386±61^{a}	309±40^{a}	608±86^{b}	657±98^{b}	457±51^{a}
Specific gravity (mg/ml)	1000.6±0.1	NM**	1001.1±0.1	1001.3±0.2	1001.0±0.2

	Groups			
Factors (units)	SPL (PO) (1 mg/kg)	UT (PO) (50 mg/kg)	AL (PO) (10 ml/kg)	MB (PO) (10 ml/kg)
Volume (ml)	2.3±0.4^{b}	4.1±0.7^{Ab}	2.2±0.5^{b}	2.0±0.5^{b}
Glucose (mg/dl)	5.6±3.8^{b}	12.5±6.2^{B}	20.6±8.6^{b}	0±0^{a}
Chloride (mEq/l)	4.2±1.2^{a}	3.6±1.1^{a}	2.3±1.0^{a}	6.4±2.0^{a}
Albumin (g/dl)	0±0	0±0	0±0	0±0
Creatinine (mg/dl)	26.3±1.7^{a}	28.6±0.6^{A}	35.9±1.1^{b}	38.2±2.3^{b}
Uric acid (mg/dl)	18.8±1.7^{b}	29.6±5.0^{b}	9.7±1.3^{a}	10.7±2.2^{a}
Urea nitrogen (mg/dl)	17.0±2.3^{a}	9.5±1.5^{A}	26.4±3.5^{b}	31.5±4.3^{b}
Sodium (mEq/l)	361±61^{a}	433±75^{A}	1103±280^{a}	2060±701^{c}
Potassium (mEq/l)	406±56^{a}	553±86^{A}	716±197^{b}	1520±393^{c}
Specific gravity (mg/ml)	1001.4±0.3	1001.2±0.2	1002.3±0.2	1002.3±0.4

*Alphabetical dissimilarities indicate significant difference ($p \leq 0.05$), **NM = Not measured

Key: DW: distilled water F: furosemide HCT: hydrochlorothiazide SPL: spironolactone
UT: urotropin AL: alhagi MB: malt beverage IM: intramuscular; PO: oral

Volume: Data showed that the highest amount of urine volume was produced after intramuscular administration of furosemide (Table 1). The difference between groups receiving alhagi, malt beverage, hydrochlorothiazide, spironolactone and injected control groups with the group received parenteral furosemide was significant ($p \leq 0.05$) with respect to the urine volume.

Glucose: The biggest amount of glucose in urine was achieved in group receiving urotropin, parenteral furosemide and distilled water. There was a significant difference ($p \leq 0.05$) among oral control with other groups (Table 1). In addition, no glucose was found in the urine samples of oral furosemide, hydrochlorothiazide and malt beverage groups.

Chloride: The highest levels of chloride ion were excreted in the groups receiving furosemide (im and oral). The difference among these two groups and other groups was significant ($p \leq 0.05$).

Albumin: There was no detectable level of albumin in urine samples of most groups during the period of the experiment except for the group receiving hydrochlorothiazide.

Creatinine: The excretion of creatinine was relatively high after administration of malt beverage, alhagi, hydrochlorothiazide and oral furosemide (Table 1), but a significant difference ($p \leq 0.05$) was only noticed between the first two groups (alhagi and malt beverage) and other groups.

Uric acid: Birds receiving parenteral furosemide, oral urotropin, hydrochlrothiazide, spironolactone and distilled water excreted a significantly ($p \leq 0.05$) higher amount of uric acid in their urine compared to other groups (Table 1).

Urea nitrogen: Alhagi and malt beverage caused a significant ($p \leq 0.05$) increase in urinary urea nitrogen compared to other groups (Table 1).

Sodium and potassium: A significant ($p \leq 0.05$) and greater amount of urinary sodium concentration was noticed in groups receiving furosemide and malt beverage compared to other groups (Table 1). A similar, but lower level was obtained for potassium concentration in urine.

Specific gravity: Urine specific gravity was relatively unchanged (Table 1).

(B) Serum biochemical parameters: Values for various serum parameters after administration of different compounds in hens are summarized in Table 2.

Table 2: Serum levels (Mean ± SEM; n = 5) of various parameters 90 minutes after administration of different agents in laying hens

	Groups				
Factors (units)	DW (PO) (10 ml/kg)	DW (IM) (0.25 ml/kg)	F (IM) (2.5 mg/kg)	F (PO) (5 mg/kg)	HCT (PO) (10 mg/kg)
Glucose (mg/dl)	226±12[a]	224±8[a*]	212±11[a]	173±7[b]	212±8[a]
Chloride (mEq/l)	108±8	88±17	69±16	120±11	118±8
Albumin (g/dl)	2.1±0.2	2.9±0.2	3.1±0.2	NM**	2.1±0.1
Creatinine (mg/dl)	7.1±0.8[a]	4.0±0.8[a]	5.4±0.3[a]	6.9±0.3[a]	4.4±0.2[a]
Uric acid (mg/dl)	3.1±0.3	2.0±0.4	4.2± 0.6	3.2±0.2	2.6±0.2
Urea nitrogen (mg/dl)	0.6±0.4	2.6±0.5	4.1±1.2	3.1±0.7	2.5±0.9

	Groups			
Factors (units)	SPL (PO) (1 mg/kg)	UT (PO) (50 mg/kg)	AL (PO) (10 ml/kg)	MB (PO) (10 ml/kg)
Glucose (mg/dl)	204±15[a]	283±32[c]	215±6[A]	229±8[a]
Chloride (mEq/l)	116±4	82±15	129±16	113±6
Albumin (g/dl)	2.6±0.2	2.6±0.2	2.1±0.1	2.7±0.1
Creatinine (mg/dl)	13.0±3.1[b]	4.6±0.8[a]	3.3±0.3[a]	4.5±0.1[a]
Uric acid (mg/dl)	2.1±0.2	2.9±0.3	2.4±0.3	3.7±0.6
Urea nitrogen (mg/dl)	1.7±1.0	1.6±0.5	2.5±0.3	4.1±0.3

*Alphabetical dissimilarities indicate significant difference (p=0.05), **NM = Not measured

Key: DW; distilled water F: furosemide HCT: hydrochlorothiazide SPL: spironolactone
UT: urotropin AL: alhagi MB: malt beverage IM: intramuscular PO: oral

Glucose: Serum glucose levels were similar in all groups except for oral furosemide and urotropin. Maximum glucose concentration was found in urotropin group. In contrast, the minimum glucose level was obtained for oral furosemide trial (Table 2).

Chloride: The highest and the lowest chloride concentration in serum were found in alhagi and parenteral furosemide groups, respectively (Table 2). There was no significant ($p>0.05$) difference between all other groups.

Albumin: Maximum and minimum albumin levels were found in parenteral furosemide and oral control groups, respectively. No significant difference ($p>0.05$) was noticed among various groups (Table 2).

Creatinine: A significantly ($p\leq0.05$) greater amount of creatinine, was found in sera of birds in group receiving spironolactone. By contrast, other groups showed a non-significant ($p>0.05$) lower creatinine level. Maximum and minimum amounts of serum creatinine were respectively obtained for spironolactone and alhagi groups (Table 2).

Uric acid: A lower serum uric acid level was observed in group receiving parenteral distilled water compared to the oral control group. The highest and the lowest amounts of serum uric acid were respectively found for groups receiving parenteral furosemide and distilled water. No significant difference ($p>0.05$) was noticed among groups.

Blood urea nitrogen (BUN): BUN level in urotropin group was close to the oral control group. Maximum and minimum BUN levels belonged respectively to the parenteral furosemide and oral control groups (Table 2). No significant difference ($p>0.05$) in the level of BUN was found among various groups.

DISCUSSION

Urine collection: Our attempt to collect urine from cannulated ureter (Okumura, 1976) was unsuccessful. Therefore, urine was obtained by inserting a parafinized piece of gauze into the cloaca allowing us to withdraw urine by suctioning it from coprodeum using a 5 ml plastic syringe. It is for the first time this method is reported. Employing the method in this experiment for 2 h caused no discomfort to the birds. It should be mentioned that the urine entering into the coprodeum should be collected soon, otherwise it will be partially reabsorbed that may affect the results.

Normal values of serum and urine biochemical parameters in laying hens: Urine and serum biochemical parameters were measured in birds anesthetized with ketamine and xylazine. So, it is possible that the data reported here be somehow different from the real normal values as anesthesia may affect the concentration of these parameters in serum and/or urine. Unfortunately, there is no considerable information in this respect and therefore, the impact of concurrent use of anesthetics on these values can not be elucidated or discussed. However, the range of biochemical parameters obtained in urine and serum are shown in Table 3. As the data indicates, serum glucose varies from 210-240 mg/dl which is similar to the previous reported values (Campbell and Coles, 1986; Dein, 1986). Serum albumin concentration was between 1.5 and 3 g/dl which is also in agreement with previous data reported (Campbell and Coles, 1986; Dein, 1986). Serum creatinine level is reported to be

Table 3: Normal levels (range) of various urine and serum biochemical parameters in anesthetized laying hens with ketamine and xylazine

Urinary factors (units)	Range	Serum parameters (units)	Range	Previous reported values*
Urine Volume (ml/h)	6-8	Glucose (mg/dl)	210-240	-
Glucose (mg/dl)	0-10	Albumin (g/dl)	1.5-3	200-450
Albumin (g/dl)	0-0.1	Creatinine (mg/dl)	2.5-10	1.2-3.6
Creatinine (mg/dl)	20-32	Uric acid (mg/dl)	1.5-3.5	0.74-1.83
Uric acid (mg/dl)	5-35	Blood urea nitrogen (mg/dl)	0.5-3.5	2-15
Urine urea nitrogen (mg/dl)	2.5-25	Chloride (mEq/l)	50-120	-
Chloride (mEq/l)	5-40	-	-	-
Sodium (mEq/l)	310-480	-	-	-
Potassium (mEq/l)	270-540	-	-	-
Specific gravity (g/ml)	1.001-1.004	-	-	1.002-1.330

from 0.74-1.83 mg/dl (Campbell and Coles, 1986; Dein, 1986) which is different from the data obtained in the present study (2.5-10 mg/dl; Table 3). Serum uric acid values obtained in this study (1.5-3.5 mg/dl) lie in the range of data reported elsewhere (2-15 mg/dl) (Campbell and Coles, 1986; Dein, 1986). Serum chloride levels were found to be from 50-120 mEq/l which is close to the previous reported figures (98-107 mEq/l) (Campbell and Coles, 1986; Dein, 1986).

No major reported data are available with respect to the biochemical parameters in urine. However, the urine specific gravity found in this experiment (1.001-1.004 g/ml) stays within the range of 1.002-1.330 g/ml reported by others (Campbell and Coles, 1986; Dein, 1986).

Diuretic effects of administered agents in hens: Diuretic agents may cause an increase in the volume of urine via various mechanisms such as: a) inhibition of chloride ion reabsorption followed by positive ions retention in urine (e.g., sodium, potassium and hydrogen ions) which consequently results in higher volume of urine; b) possessing hygroscopic or osmotic characteristics and c) inhibition of antidiuretic hormone. The ideal diuretic agent is the one that induces the most increase in urine excretion and exerts the least water and electrolyte imbalance (Brater, 1998).

Alterations in biochemical parameters, both in serum and urine, do not follow a regular pattern in most groups. The most profound changes are as the following:

Urotropin had a relatively high effect on serum glucose in a way that it caused an increase of about 30% compared to the control group. Elevation of glucose absorption from gastro-intestinal tract, inhibition of glucose metabolism and/or increase in the rate of glycogenolysis may be among possible mechanisms by which urotropin exerts its hyperglycemic action. The other possible mechanism of its action is the release of formaldehyde in the nephrons which may affect the normal structure of glomeruli and hence excretion of glucose into the urine may occur.

No considerable changes occurred in serum concentration of albumin, creatinine, uric acid and BUN. In comparison to the control groups, serum chloride decreased in parenteral furosemide, hydrochlorothiazide and urothropin groups, but increased in other groups. Based on the proposed mechanism of action of furosemide in mammals (Bosch *et al*., 1977; Hirai *et al*., 1992), it may increase chloride ion excretion in urine via inhibition of its reabsorption from thick ascending limb of Henle's loop and therefore, excretion of greater amounts of Cl^- may decrease its serum concentration.

According to the data obtained in this study (Table 1, 2 and 3), the group receiving parenteral furosemide produced the highest amount of urine which is in accordance with the effect in other species such as sheep and mare (Gronwell, 1985; Zimmerman *et al*., 1978). The urine formed in that group is around 2-4 times greater than the urine volume in other groups.

The presence of albumin in one urine sample (hydrochlorothiazide group; Table 1) may be due to the contamination of urine with diffused materials (feces or oviduct secretions).

The highest and the lowest amounts of excreted creatinine were observed in groups receiving parenteral furosemide and spironolactone, respectively. Parenteral furosemide and malt beverage were two groups respectively illustrating maximum and minimum quantities of urine urea nitrogen and uric acid. It was expected that hydrochlorothiazide, through competition with uric acid, causes a decline in urinary uric acid and an increase in serum uric acid, but the data did not support this phenomenon.

Birds in hydrochlorothiazide group excreted more chloride in urine possibly via inhibition of sodium reabsorption in proximal part of distal tubules. This is supported by a decrease in serum chloride (Puschett, 1981).

No study has so far shown the diuretic effect of urotropin. As serum chloride was moderately declined in the group receiving urotropin compared to the control groups, it may be deduced this agent can have a weak diuretic effect.

A dose-dependant increase in diuresis in cats along with parallel increase in the excretion of sodium and chloride ions was confirmed by Klatt *et al*. (1975). In 1976, Cohen and coworkers proved that IV administration of furosemide in the dog results in a significant increase in urine volume, sodium and potassium.

Bosch *et al.* (1977) suggested that chronic administration of furosemide in drinking water could enhance urinary sodium excretion in dogs, especially in the first day. Stephens and Robertson (1985) confirmed that addition of furosemide to the fresh water increases urine volume, sodium, potassium and chloride in turtles which lack Henle's loop. Vestweber *et al.* (1989) reported that IV administration of furosemide in clinically normal Holstein cows brought about a statistical mean increase in urine sodium, potassium and chloride besides serum sodium. There was also a significant decrease in the mean serum potassium. In 1992, Hirai and colleagues showed that IV administration of furosemide causes a diuretic effect accompanied with an extreme increase in the excretion rate of sodium and chloride in the anesthetized dog. Roudebusch *et al.* (1994) came to this conclusion that furosemide therapy with sodium restricted diet in normal dogs causes no clinically meaningful changes in the serum electrolytes, urea nitrogen or creatinine concentrations.

Spironolactone is believed to exert its diuretic effect through competition with aldosterone, so it was expected to increase sodium excretion, but such a pattern was not noticed in hens.

With respect to the hygrophobic nature of urothropin, small increase in urine volume plus a positive effect on the urinary excretion of sodium, potassium and chloride can be expected.

Conclusion: Administered drugs and herbal products have illustrated different effects on biochemical factors both in serum and urine. Parenteral furosemide was the most potent diuretic drug with respect to the volume of urine produced in laying hens. Furosemide also exerted the highest influence on the concentration of ions including sodium, potassium and chloride, particularly in urine. Similar results were not demonstrated with oral furosemide, even with greater dosage, which can probably be due to the delayed absorption of the drug from gastrointestinal tract in hens.

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