

## **Hypouricemic Activity of *Pentopetia Androsaemifolia* Decne. (Apocynaceae) Hydro Alcoholic Extract in Mice**

***Randrianavony P., PhD***

***Reboza A. M., MSc***

Laboratoire de Pharmacologie Générale, de Pharmacocinétique et de Cosmétologie, Faculté des Sciences, Université d'Antananarivo, Madagascar

***Quansah N., PhD***

SIT Study Abroad Summer Program: Madagascar Traditional Medicine and Health Care Systems, Antananarivo, Madagascar

***Randimbivololona F., PhD***

Laboratoire de Pharmacologie Générale, de Pharmacocinétique et de Cosmétologie, Faculté des Sciences, Université d'Antananarivo, Madagascar

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### **Abstract**

The aim of this work was to investigate the uricemic and uricosuric activity of the hydro alcoholic extract of *Pentopetia androsaemifolia* in experimentally induced hyperuricemic mice. Hyperuricemia was induced in the mice by intraperitoneal injection of potassium oxonate. Oral administration of the extract at doses 50 to 200 mg/kg reduce hyperuricemia from  $218.78 \pm 7.50$  to  $72.29 \pm 16.88$  mg/l ( $P < 0.05$ ). The same doses of 50 to 200 mg/kg of the extract also reduce uricosuria from  $125.4 \pm 4.4$  to  $70 \pm 12.6$  mg/l ( $p < 0.05$ ). A direct correlation exists between plasma uric acid concentration and urine uric acid concentration ( $r = 0.99$ ). The hypouricemic activity of the extract could be due to xanthine oxidase inhibition by the flavonoids present in the extract.

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**Keywords:** *Pentopetia androsaemifolia*, hypouricemic, gout

### **Introduction**

Gout is a metabolic disease characterized by hyperuricemia, with a blood concentration superior to  $420 \mu\text{mol/L}$  ( $70 \text{ mg/L}$ ) (Bardin, 2007; Merriman T.R., and Dalbeth, 2011). Beyond this concentration, sodium urate precipitates in tissues, particularly in joints, provoking inflammatory reactions (Prigent & Berets, 1992). Acute gout can disappear on its own

within a short time without treatment. Whereas in the chronic state, it can lead to damages in joints and end up to be a permanent polyarthritis (Edwards *et al.*, 2011).

Treatment of gout can be symptomatic with nonsteroidal anti-inflammatory drugs, or in reducing uricemia by inhibiting xanthine oxidase (Choi *et al.*, 2005; Terkeltaub, 2003) or increasing uricosuria (Suresh & Das, 2012).

In the semi desert zone of the south of Madagascar, the local community is herdsman, and their main diet is beef. This population often suffers from joint problems, especially of the big toe. Drinking the beverage prepared with the leaves of *Pentopetia androsaemifolia* relieves the pain and reduces the edema. This field observation is the basis of our hypothesis, that this decoction may reduce uricemia or increase uricosuria.

### **Materials and methods**

The materials for this study were the leaves of *Pentopetia androsaemifolia* collected from the southern region of Madagascar in December 2015.

### **Preparation of the extract**

The leaves were dried in shade, aerated, at room temperature, and grounded. Five hundred grams of the powder were macerated 5 days in 5 liters of ethanol-water mixture (60:40), at room temperature. This macerate was filtered using Whatman paper n°3, and the filtrate was evaporated to dryness under vacuum with a rotative evaporator *Evapotec*® at the temperature of 80°C.

### **Animal used**

Albino mice, Swiss strain, of both sexes, aged 8 weeks, weighing 200 to 210 g were used during the experiments. The animals were bred in the animal house of the *Laboratoire de Pharmacologie Générale, de Pharmacocinétique et de Cosmétologie* (LPGPC) of the Science Faculty, University of Antananarivo, at a temperature of 22±2°C and kept under 12h/12h light/dark cycle. They were fed with LFL 1040® pelleted feed and had water *ad libitum*.

The mice were experimentally induced hyperuricemic by intraperitoneal injection of potassium oxonate aqueous solution at the dose of 200 mg/kg (Vogel *et al.*, 2002; Huang *et al.*, 2008).

BIOLAB® reagent made of 42µmol/l of potassium hexacyanoferrate, 450 UI of peroxidase, 0.150 mmol/l of amino-antipyrine and 120 UI of uricase, was used to dosage the uric acid concentration in the samples.

### **Study of the extract effect on uricemia**

The extract was dissolved in distilled water. The induced hyperuricemic animals were divided into 4 groups: one group served as control and 3 treated with the extract at 3 different doses. The control group received 10 ml/kg of distilled water, while the other groups were orally administered the extract at doses 50, 100, and 200 mg/kg respectively in 10 ml/kg of distilled water (Vogel *et al.*, 2002).

Two hours after, the maxillary vein of the animal was pinpricked with a sterile pin. The blood was collected in non-heparinized glass tube, and centrifuged for 10 minutes at 3000 rpm with EBA 3S<sup>®</sup> centrifuge (Elin *et al.*, 1982).

After centrifugation, 25  $\mu$ l of supernatant were placed in glass tube containing 1 ml of BIOLAB<sup>®</sup> reagent. The mixture was left at room temperature for 5 minutes.

The concentration of uric acid in the samples was determined by colorimetric technic, using APUS<sup>®</sup> colorimeter, at the wavelength  $\lambda = 520$  nm, and a standard solution provided with the reagent (Wang *et al.*, 2010).

### **Study of the extract effect on uricosuria**

A raw beef juice was prepared by mixing 250 g of beef and 250 ml of 9‰ NaCl in a blender, used as source of purine. The extract was dissolved in this juice. All the animals were injected intra peritoneally with 200 mg/kg of potassium oxonate (Vogel, 2002; Huang *et al.*, 2008). One hour after, the animals were divided into 4 groups; one group serving as control, and 3 groups treated with the extract. The control group animals received 10 ml/kg of the beef juice while the 3 groups, were respectively administered by oral route the beef juice containing 50, 100, and 200 mg/kg of the extract in 10 ml/kg (Vogel *et al.*, 2002).

Afterwards, they were put individually in metabolism cages for 24 hours. Their urine were collected, and centrifuged for 10 minutes at 3000 rpm. The supernatant was recuperated, and 25  $\mu$ l of it was placed in glass tube containing 1 ml of BIOLAB<sup>®</sup> reagent. The mixture was left at room temperature for 5 minutes.

After this reaction, the uric acid concentration in the samples was determined. APUS<sup>®</sup> colorimeter was used at the wavelength of  $\lambda = 520$  nm, and a standard provided with the reagent was used to determine the concentration of uric acid in the samples.

### **Relation between uricemia and uricosuria**

Linear regression was established to evaluate the relation between uricosuria, uricemia and the dosage of the extract.

## Analysis and expression of results

Results were expressed as mean  $\pm$  s.e.m. They were compared using the Student 't' test. A value of  $P < 0.05$  was considered significant.

## Results

### Effect of the extract on uricemia and uricosuria

The uricemia and uricosuria of the induced hyperuricemic mice by intra peritoneal injection of potassium oxonate and treated with the alcoholic extract of *P. androsaemifolia* are inferior to those of the hyperuricemic control groups ( $P < 0.05$ ) (Table I).

**Table I.** Variation of uricemia and uricosuria of hyperuricemic mice, induced by potassium oxonate 200 mg/kg injected *i.p.* in the control group and treated with *P. androsaemifolia* alcoholic extract, administered by oral route, at the doses of 50, 100 and 200 mg/kg. ( $\bar{m} \pm$  e.s.m; n = 5; \* $P < .05$ ).

Animals	Control group	Treated with extract dissolved in beef juice		
Dosage (mg/kg)	Beef juice	50	100	200
Uricemia (mg/l)	227.89 $\pm$ 18.80	218.78 $\pm$ 7.50*	137.86 $\pm$ 30.42*	72.29 $\pm$ 16.88*
Uricosuria (mg/l)	148 $\pm$ 1.4	125.4 $\pm$ 4.4*	92.6 $\pm$ 10.1*	70 $\pm$ 12.6*

The correlation between the uricemia and uricosuria variation is very high ( $r=0.99$ ).

## Discussion

Mouse was used as experimental model in this experiment, because the urate elimination in mouse is similar to that of humans (Ding *et al.*, 2005). Injection of potassium oxonate by intra peritoneal route and the juice prepared with raw beef increase the uric acid concentration in the blood (Vogel *et al.*, 2002; Fukunari *et al.*, 2004; Wang *et al.*, 2010). Meanwhile, uricemia and uricosuria in animals treated with the alcoholic extract of *P. androsaemifolia* diminished, compared to the control group.

The main route of elimination of uric acid is the urinary tract. The diminution of uricemia could be explained by the increasing of uricosuria. Meanwhile, in this experiment, within the dosages used, the two parameters variate in the same way; both of them diminish in the treated animals.

This result means that the extract reduces the uricosuria and uricemia at the same time. Which let us deduce that the decrease in the concentration of uric acid in the urine is due to the reduction of the plasma uric acid concentration. From this observation, we advance a hypothesis that the alcoholic extract of *P. androsaemifolia* have diminished the plasma uric acid concentration by inhibiting its synthesis. The extract might inhibit the xanthine oxidase responsible for the synthesis of the uric acid (Zhifeng *et al.*, 2005; Huang *et al.*, 2008).

## Conclusion

Our results show that the alcoholic extract of *Pentopetia androsaemifolia* reduces both uricemia and uricosuria in hyperuricemic mice. This activity could be due to the inhibition of xanthine oxidase responsible for the synthesis of uric acid.

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