

**Review Article**DOI: <https://doi.org/10.30750/ijpbr.6.4.8>**Pharmacological Review on Uricosuric activity**

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The naturally available uricosuric agents are *Tinospora cardifolia*, *Allium sepa*, *Cajanus Cajan*, *Piper nigrum* etc., Natural medicinal plants having no side effects are more preferred when compared to synthetic medications. Uricosuric agents increase the urinary excretion of uric acid hence the natural uricosuric agent is preferred to prevent many diseases like gout, arthritis, kidney stones etc., without side effect. Uricosuric medications are the substances that increase the excretion of uric acid in urine, thus reducing the concentration of uric acid in blood plasma. Prolonged and untreated hyperuricemia results into gout, a severe inflammatory condition. Sustain hyperuricemia leads to impaired blood pressure control, renal impairment and nephropathy. The common factors for deposition of uric acid in blood are drinking alcohol and taking high purine diet. The various screening methods for the uricosuric activity are uricosuric activity in mice, Potassium oxonate induced activity, and Phenol red excretion methods are explained in this review.

**Introduction**

Uricosuric medications are the substances that increase the excretion of uric acid in urine, thus they reduce the concentration of uric acid in blood plasma.

Prolonged and untreated hyperuricemia results into gout, a severe inflammatory condition. Sustain hyperuricemia leads to impaired blood pressure control, renal impairment and nephropathy<sup>1</sup>. The drugs used in treatment of hyperuricemia and for prophylaxis of gout include xanthine oxidase inhibitors like allopurinol and uricosuric agents like probenecid and benzbromarone<sup>2</sup>. Allopurinol is contraindicated in patients with compromised renal function<sup>3</sup> and frequently causes severe hypersensitivity reactions<sup>4</sup>. Febuxostat is contraindicated in liver failure<sup>5</sup>. Uricosuric agents furthermore can't be administered in patients with renal stones<sup>6</sup>. So, it is the need of the today to find out novel drug with minimal adverse effects.

**Uricosurics**

The Uricosuric medications are defined as the substances that increase the excretion of uric acid in urine. Thus they reduce the concentration of uric acid in the blood plasma. All drugs that reduce blood uric acid are not uricosurics there is another different mechanism to reduce blood uric acid concentration

by anti- gout medications. Uricosurics are often used in the treatment of gout.

Uricosuric drugs which increase the urinary excretion of uric acid, or XO inhibitors which block the terminal step in uric acid biosynthesis, can lower the plasma uric acid concentration, and are generally employed for the treatment of gout<sup>7</sup>. Allopurinol is a clinically used Xanthine oxidase inhibitor in the treatment of gout, but this drug suffers from many side effects such as hepatitis, nephropathy and allergic reactions<sup>8</sup>. Moreover allopurinol and its active metabolite oxypurinol is catalyzed by Xanthine oxidase itself, resulting in the generation of reactive oxygen species such as Superoxide anion (O<sub>2</sub><sup>-</sup>) is involved in various pathological states such as hepatitis, inflammation, ischemia, reperfusion, carcinogenesis and aging<sup>9-10</sup>.

**Etiology for deposition of Uric acid**

The common factors involved in deposition of uric acid in the blood plasma are

- Drinking alcohol
- High purine alcoholic beverages such as beer
- Taking sea food and meat in diet constantly
- Medical conditions like diabetes, obesity, high blood pressure

All these above factors are involved in the formation of uric acid in the blood plasma.

### Classification of Uricosuric Drugs <sup>11</sup>

The uricosuric drugs are classified into the following two types

1. Primary uricosurics
2. Secondary uricosurics
  1. Primary Uricosurics: The primary uricosuric drugs include
    - Probenecid
    - Benzbromarone
    - Sulfinpyrazone
  2. Secondary Uricosurics: Drugs with other primary uses and also having the properties of uricosuric drugs are known as secondary uricosurics.
    - Amlodipine
    - Atorvastatin
    - Fenofibrate
    - Losartan
    - Adrenocorticotrophic hormone
    - Cortisone

### Mechanism of action of Uricosuric drugs <sup>12</sup>

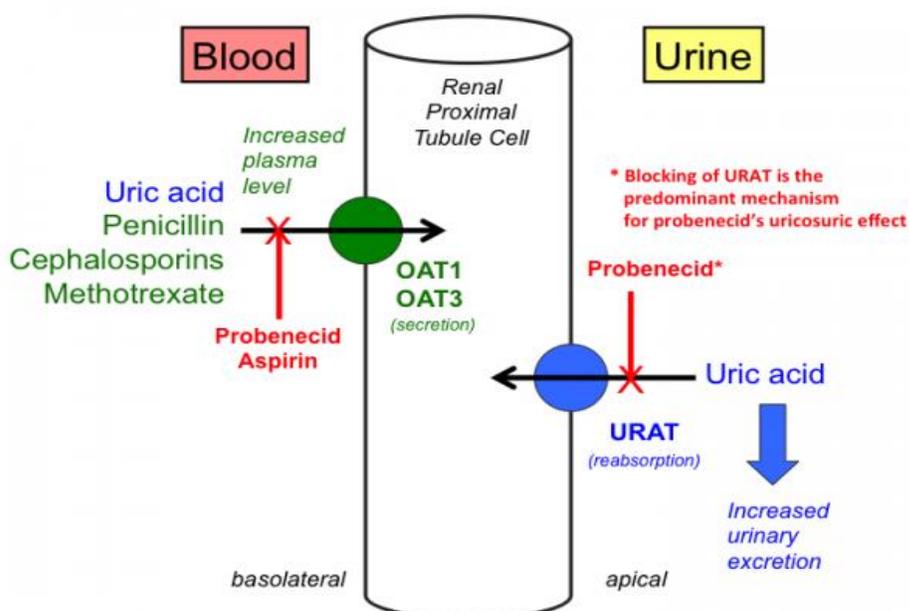


Figure 1: This figure describes the mechanism of action of uricosuric medications like probenecid

The general mechanism of action of uricosuric drugs is explained as follows

- Uricosuric drugs acts primarily on the proximal tubules in the kidney.
- They interfere with the absorption of uric acid from the kidney back into the blood
- Uricosurics act by blocking the function of a protein encoded by gene SLC22A12. It is also known as urate transporter 1 or URAT 1.
- URAT 1 acts as a central mediator in the transport of uric acid from kidneys into the blood.
- Thus the uricosuric drugs reduce the concentration of uric acid in the blood.

### Diagnosis Tests for Determination of Uric Acid <sup>13</sup>

The various diagnostic tests involved in the determination of uric acid in the blood and urine primarily depends on the chemical or enzymatic oxidation to allantoin. The various diagnostic tests are

- Manual colorimetric method
- Automated colorimetric method
- Manual enzymatic methods
- Automated enzymatic methods
- Chromatographic determination of uric acid and related purines
- Colorimetric titration.

## Uricosuric activity

Synthesis of uric acid primarily occurs in the liver, but the kidney has an important role in the patho-physiology of hyperuricemic syndromes. Because uric acid is poorly soluble, excessive amounts in the circulation may precipitate out into the tissues, particularly the joints, resulting in a painful arthropathy ("Gout"). In humans this condition is usually the result of faulty tubular transport of urate, resulting in increased net reabsorption.

Reduction of net uric acid synthesis by inhibition of xanthene oxidase is the preferred therapeutic approach. Xanthine oxidase catalyzes the oxidation of hypoxanthine and xanthenes to uric acid<sup>14</sup>.

### Methods for determining the uricosuric activity

The following methods were used to determine the uricosuric activity on animal models.

1. Uricosuric activity in mice.
2. Uricosuric activity after Potassium Oxonate treatment in rats.
3. Phenol red excretion in rats.

### Uricosuric activity in mice<sup>15</sup>

#### Procedure

1. Male NMRI mice weighing 25-30g are used.
2. On the evening prior to the experiment, food but not water is withheld.
3. In the morning, the mice are orally loaded with 50ml/kg 0.9% NaCl solution.
4. Together with the sodium load the test compound is applied by gavage in 2% starch suspension. Controls receive saline and starch suspension only.
5. Groups of 5 mice are placed into metabolic cages.
6. Urine is collected over 4h. In the urine sodium and potassium are determined by flame photometry, chloride by argentometrically with potentiometrical end point titration (Chloride titrator, Aminco). Uric acid is determined by the Uriquant-method.

### Plants with uricosuric activity<sup>18</sup>

**Table 1: Shows plants having Uricosuric activity**

S.No	Medicinal Plant Name	Part Used	Other Uses
1.	<i>Tinospora cardifolia</i>	Leaf	Diabetes, Hepatitis
2.	<i>Allium sepa</i>	Bulb	Hay fever, cold and cough
3.	<i>Barleria prionitis</i>	Root	Respiratory diseases, joint pains
4.	<i>Bauhinia variegata</i>	Flower	Astringent, dysentery
5.	<i>Brassica nigra</i>	Seed oil	Condiment, lubricant
6.	<i>Cajanus cajan</i>	Seed	Diabetes, food poisoning, constipation
7.	<i>Calamus rotang</i>	Stem bark	Chronic fever, antidote to snake venom
8.	<i>Cassia senna</i>	Leaf, fruit	Laxative, constipation

7. Creatinine is determined by the jaffe-reaction.

### Uricosuric activity after potassium oxonate treatment in Rats<sup>16</sup>

#### Procedure

1. Male Wistar rats weighing 250g are placed individually in metabolic cages.
2. They are offered a special diet containing 5% fructose, 3% Uric acid, 2% potassium oxonate (2,4-dihydroxy-1,3-triazine-6-carbonic acid) and 0.001% artificial sweetener.
3. Drinking water consists of a 0.5% solution of potassium oxonate solution.
4. The treatment is repeated on the second day.
5. On the third day 24 h urine is collected and the animals are sacrificed by exsanguinations.
6. Concentrations of uric acid and electrolytes (Na<sup>+</sup>, K<sup>+</sup>, and Cl<sup>-</sup>) are determined in blood and urine.

### Phenol red excretion in Rats<sup>17</sup>

#### Procedure

1. Phenol red (phenolsulfonphthalein) excretion is an indirect test for uricosuric activity.
2. Male Wistar rats weighing 120-150g are treated orally with the test compound or the standard compound.
3. 30min prior to intravenous injection via the tail vein with 2.5ml/kg of a 3% aqueous solution of phenolsulfonphthalein for intravenous application, 5.0 ml/kg of the test drug solution are injected immediately after the phenolsulfonphthalein injection followed by flushing with 2.5ml/kg saline.
4. By retro-orbital puncture blood samples are withdrawn after 30, 60 and 180 min.
5. Blood (0.2ml) is diluted with 2ml 0.9% NaCl- solution and centrifuged.
6. To 1ml of the supernatant 1 ml of 1% sodium carbonate solution and 8 ml of saline are added.
7. Using spectrophotometer extinction at 546 nm is determined.

9.	<i>Cissus quadrangularis</i>	Stem	Obesity, diabetes
10.	<i>Crataeva magna</i>	Root bark	Urinary problems
11.	<i>Crinum latifolium</i>	Leaf	Treatment of Prostatitis and adenoma
12.	<i>Crinum asiaticum</i>	Leaf	Anti- bacterial and anti- tumor
13.	<i>Cryptolepis buchananii</i>	Root	Fracture, Arthritis
14.	<i>Decalepis hamiltonii</i>	Root	Bactericidal
15.	<i>Enicostema axillare</i>	Whole plant	Rheumatism, abdominal ulcers
16.	<i>Gloriosa superba</i>	Tuber	Snake bites, parasitic skin diseases
17.	<i>Hemidesmus Indicus var.Indicus</i>	Root	Antinociceptive activity
18.	<i>Hemidesmus Indicus var.Pubescens</i>	Root	Used to make bevarages
19.	<i>Hygrophila auriculata</i>	Whole plant	Induce menstruation, diuretic
20.	<i>Piper nigrum</i>	Fruit	Condiment
21.	<i>Rauwolfia serpentine</i>	Root	Anti- hypertensive
22.	<i>Rubia cardifolia</i>	Root	Dysentery, chronic fever
23.	<i>Tinospora cordifolia</i>	Leaf	Rheumatoid arthritis, cancers
24.	<i>Trewia nudiflora</i>	Root	Healing wounds and injuries
25.	<i>Triticum aestivum</i>	Fruit	Anti- pyretic, sedative
26.	<i>Tribulus terrestris</i>	Whole plant	Reduce swelling
27.	<i>Aerva lanata</i>	Whole plant	Jaundice
28.	<i>Boerhavia erecta</i>	Whole plant	Jaundice, diarrhoea
29.	<i>Mimosa pudica</i>	Whole plant	Antivenom, anti- fertility
30.	<i>Phyllanthus nodiflora</i>	Leaf	Liver disorders, indigestion

The above table 1 describes about the medicinal plants with uricosuric activity and the other uses of the medicinal plants. These table can be taken as reference for further research on uricosuric activity.

## Conclusion

I would likely to take this time to summarize everything i have said in this blog regarding uricosuric activity. Uricosuric agents increase the excretion of uric acid thus reducing the concentration of uric acid in the body and increasing its rate of elimination. The medicinal plants having uricosuric activity and the screening models for uricosuric activity are explained in this activity. Therefore natural medicinal plants having no side effects are more preferred when compared to synthetic medications.

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