Understanding the role of homoeopathic preparation of *Berberis vulgaris* in mitigation of sodium oxalate-induced hyperoxaluria: An experimental approach

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Abstract

**Background:** Hyperoxaluria and calcium oxalate crystal deposition in the kidneys lead to overproduction of reactive oxygen species, resulting in the development of oxidative stress and renal injury. At the cellular levels, mitochondria and NADPH oxidase involved in reactive oxygen species production play a crucial role in the pathogenesis of hyperoxaluria-induced renal injury. **Objective:** The objective was to investigate the therapeutic effect of homoeopathic drug *Berberis vulgaris*, a potent antioxidant, upon regulation of NADPH oxidase against acute high-grade sodium oxalate-induced hyperoxaluria in rats. **Materials and Methods:** Hyperoxaluria was induced in male Wistar rats by administering a single dose of sodium oxalate (70 mg/kg body weight) intraperitoneally, and the treatment groups were pre-treated with homoeopathic drug *Berberis vulgaris* 6c (20 μl/100 g of body weight) ultra low dose for 7 days. **Results:** *Berberis vulgaris* significantly reduces hyperoxaluria-induced oxidative stress and restores antioxidant enzyme activities in kidney tissue. Histological analysis depicted that *Berberis vulgaris* treatment decreases renal epithelial damage and inflammation and restored normal glomerular morphology. Furthermore, immunoblotting analyses of NADPH oxidase revealed significant increased activity in the renal tissue of hyperoxaluric rats when compared to that of control rats. This has been brought back to normal by *Berberis vulgaris* treatment. **Conclusion:** Thus, our results emphasised that the Homoeopathy drug *Berberis vulgaris* has been effective in ameliorating sodium oxalate-induced acute hyperoxaluria in Wistar rats by modulating mitochondrial oxidative stress through the inhibition of NADPH oxidase.

**Keywords:** Acute hyperoxaluria, *Berberis vulgaris*, Homoeopathy, NADPH oxidase, Oxidative stress, Reactive oxygen species

**INTRODUCTION**

Hyperoxaluria is a major risk factor, and calcium oxalate (CaOx) is the chief constituent of most idiopathic urinary stones. Earlier studies reported that CaOx crystals and high oxalate (Ox) concentration are injurious to renal epithelial cells, which lead to the overproduction of reactive oxygen species (ROS) and the augmentation of oxidative stress in the kidneys.\[1\] In addition, Khan\[1\] and Thamilselvan et al.\[2\] elucidate that NADPH oxidase (NOX), involved in the production of ROS, is well known to play an imperative role in the pathogenesis of hyperoxaluria-induced nephrolithiasis on regulation of NADPH oxidase activation and its associated cell injury; it may be ameliorated by antioxidants and free radical scavengers. Based on the above deliberation, attention was currently focused on a novel approach of targeting the provocative sources of ROS (mitochondria and NADPH oxidase) to prevent accelerated oxidant production in hyperoxaluria, thereby eliminating pathological sources of ROS, further helping to comprehend the intricate procedure of stone formation.

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Since ancient times, herbal drugs which are the part of traditional medicine have been utilised as the major source for the treatment and prevention of diseases and health promotion, as well as for the enhancement of life span and quality of life. In the folklore of medicine, *Berberis vulgaris* holds a prominent place in treating urinary stone disease for more than 2500 years. *Berberis vulgaris* plant is extensively distributed in Europe and Asia; its root, bark, leaf and fruit exhibit medicinal properties such as antioxidant, anti-inflammatory, antimicrobial, antipyretic, anti-urolithic, anticonvulsant and antiarrhythmic activities. Our earlier study reported that Homoeopathy drug *Berberis vulgaris* proved to be a potent antioxidant and highlighted its effectiveness as a nephroprotective, in reducing oxalate deposition in tissues and protecting renal cell membrane integrity, thereby reducing the risk of stone formation.

As crystallisation is an ongoing process associated with continued oxidative damage, its further consequence leads to renal epithelial injury, partially caused by ROS production, and the involvement of NOX might provide sites for crystal attachment and eventual retention within the kidney. At the cellular levels, NADPH oxidase and mitochondria are found to be the major sources of ROS present in the renal tissues as it has been found that these NADPH oxidase complexes play a crucial role in host defence and various signalling pathways leading to regulation of gene expression, and protein functions are disturbed under physiological conditions of oxidative balance. Hence, our main emphasis focused primarily on oxidative stress caused by ROS produced by NADPH oxidase and their effects on interactions to be targeted in order to reduce the function and downstream effects of NADPH oxidase.

Comprehensive studies recommend pre-treatment with antioxidants along with NADPH oxidase inhibitor, which significantly decreases renal CaOx crystal deposition, which is a surrogate marker of nephrolithiasis in animal models. Thus, the present findings were hypothesised to develop an inhibitor with increased efficiency and specificity with a combinatorial therapy based on the attenuation of oxidative stress with antioxidant, free radical scavenger and NADPH oxidase inhibition, which may completely ameliorate hyperoxaluric manifestations in acute sodium oxalate-induced rats.

### Materials and Methods

#### Drugs and chemicals

Homoeopathic preparation of *Berberis vulgaris* (6c, batch no: 2194) was procured from Hahnemann Publishing Co. Pvt. Ltd., Kolkata, West Bengal, India. The potentised homoeopathic drug, *Berberis vulgaris* 6c, used in the current study was suggested by the Central Council for Research in Homoeopathy (CCRH), which was used as the stock solution. All other chemicals and solvents used in the present study were procured from standard agencies and of analytical grade.

#### Animal model

Male Albino rats of Wistar strain weighing about 120 ± 150 g were obtained from the Central Animal House Facility, University of Madras, Taramani campus. The experimental protocol employed in this study received approval from the Institutional Animal Ethical Committee (IAEC no. 01 November 2015). The animals were acclimatised two per cage in large spacious cages under the conditions of controlled temperature (25°C ± 2°C) with 12/12 h light/dark cycle and were allowed food and water ad libitum. In addition, the animals were maintained on a commercial rat feed manufactured by Hindustan Lever Ltd., Mumbai, Maharashtra, India, under the trade name ‘Gold Mohur Rat Feed’. The feed constitutes 5% fat, 21% protein, 55% nitrogen free extract and 4% fibre (w/w) with adequate vitamins and minerals.

### Experimental protocol

In the present study, four groups, each comprising six rats (*n* = 6), were employed for the investigation. Potentials of a potentised homoeopathic drug, *Berberis vulgaris* 6c as an antioxidant and anti-urolithic, was used to treat acute high-grade hyperoxaluria in the current analysis.

- **Group I** (normal control) – Rats were maintained on standard food and water and no treatment was given.
- **Group II** (urolithic control) – Rats were administered a single injection of sodium oxalate (70 mg/kg/day intraperitoneal) in 0.89% normal physiological saline on the 8th day of the experiment, to induce rapid screening of calcium oxalate crystals.
- **Group III** (*Berberis vulgaris* 6c-treated group) – Rats were pre-administered with potentised homoeopathic drug, *Berberis vulgaris* 6c, (20 μl/day/100 g body weight, oral gavage) for 7 days with a single dose of sodium oxalate (70 mg/kg body weight) intraperitoneally on the 8th day as in Group II.
- **Group IV** (drug control) – Rats were pre-administered with potentised homoeopathic drug, *Berberis vulgaris* (20 μl/day/100 g body weight, oral gavage), alone for 7 days.

#### Sample collection

**Collection and analysis of urine**

The animals were housed in individual metabolic cages. Urine was collected in ice-jacketed flasks at 4°C for the assessment of renal function. The urine free from faecal contamination was collected for 24 h (at the end of the treatment, 8th day from the administration of sodium oxalate) with 0.2% sodium azide as a preservative. Cell debris and particulate matter were then removed from the urine samples by 1000 ×g centrifugation at 4°C for 15 min. The total urinary volume was measured by using a measuring cylinder and reported in millilitre. The pH of the freshly collected urine sample was measured using pH strips, and 24-h urine samples were analysed for its calcium, oxalate, phosphate, magnesium, uric acid and creatinine.

**Renal tissue analysis**

After blood collection, all animals, which were anaesthetised (with ketamine, 22 mg/kg body weight,
intramuscular), were sacrificed. The abdomen was cut open to remove both kidneys from each animal. The isolated kidneys were cleaned off extraneous tissue, rinsed in ice-cold physiological saline and used for tissue homogenate and histopathological analysis.

**Homogenate analysis**

The left kidney was finely minced and 10% homogenate was prepared in Tris-HCl buffer (0.01 mol/l, pH 7.4). The left kidney was finely minced and 10% homogenate was prepared in Tris-HCl buffer (0.01 mol/l, pH 7.4 and used for analysis of enzymatic and non-enzymatic antioxidants such as superoxide dismutase (SOD),[15] catalase (CAT)[15] and glutathione peroxidase (GPx);[17] glutathione-S-transferase activity (GST)[18] and the levels of Vitamin E[19] and Vitamin C (Omaye et al.[20]) as per standard protocols. Reduced glutathione was assayed by the method of Moron et al.[21]

**Histopathology**

The right kidney was fixed in 10% neutral buffered formalin, processed in a series of graded alcohol and xylene, embedded in paraffin wax, sectioned at 5 μm and stained with haematoxylin and eosin for examination under a light microscope.

**Western blot analysis**

Renal tissues were lysed with radiolmunooprecipitation assay (RIPA) buffer containing 1% protease inhibitor PMSF. The supernatant was gathered after centrifugation. All lysates were diluted with sodium dodecyl sulphate (SDS) loading buffer and boiled for 5 min. Equal amounts of protein (50 μg) were loaded into each lane of a 10% SDS-PAGE gel for electrophoresis. Proteins were then transferred onto a polyvinylidene fluoride (PVDF) membrane. Then, the membranes were blocked with 5% BSA for an hour and incubated with primary rabbit polyclonal antibodies against No×2 (1:1000) against β-actin (1:1000) or a mouse polyclonal antibody to urolithic group, and no remarkable changes were observed in drug alone-treated rats. Administration of sodium oxalate (7 mg/100 g, i.p.) statistically significantly (P < 0.05) attenuation of these parameters compared to urolithic vehicle control rats suggests its preventive effect on uroolithiasis. A single intraperitoneal injection of sodium oxalate (7 mg/100 g of body weight) administered caused statistically significant (P < 0.05) 7% reduction in body weight with increase in 45% relative body and 33% organ weight of rats in Group II compared to normal control rats.

Pre-treatment with the Homoeopathy drug *Berberis vulgaris* (6c) statistically significantly (P < 0.05) attenuated the gain in body (1.86%) and organ weight (16.78%) compared to urolithic group, and no remarkable changes were observed in drug alone-treated rats. Administration of sodium oxalate (7 mg/100 g, i.p.) statistically significantly (P < 0.05) decreased (18.42%) urine pH and (43.47%) volume as compared with that of Group I, and pre-administration of *Berberis vulgaris* caused a statistically significant increase (16.12%) in urinary pH and (61.53%) volume compared with that of Group II.

**Results**

**Effect of potentised homeopathic drug *Berberis vulgaris* on body weight, tissue weight, relative organ weight, urinary pH and volume of hyperoxaluria experimental rats**

Table 1 depicts the effect of *Berberis vulgaris* 6c for 7 days (20 μl/100 g of body weight) prevented (P < 0.05 vs. stone-forming group) the loss in body weight; significant attenuation of these parameters compared to urolithic vehicle control rats suggests its preventive effect on uroolithiasis. A single intraperitoneal injection of sodium oxalate (7 mg/100 g of body weight) administered caused statistically significant (P < 0.05) 7% reduction in body weight with increase in 45% relative body and 33% organ weight of rats in Group II compared to normal control rats.

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<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>Group IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight (kg)</td>
<td>147.56±11.42</td>
<td>137.33±13.78a*</td>
<td>139.89±13.93b*</td>
<td>145.74±12.91</td>
</tr>
<tr>
<td>Kidney weight (mg)</td>
<td>0.735±0.06</td>
<td>0.978±0.13a*</td>
<td>0.813±0.09b*</td>
<td>0.761±0.09</td>
</tr>
<tr>
<td>Relative organ weight (mg/g)%</td>
<td>0.49±0.04</td>
<td>0.69±0.05a*</td>
<td>0.55±0.06 b*</td>
<td>0.53±0.06</td>
</tr>
<tr>
<td>Urine pH</td>
<td>7.3±0.56</td>
<td>6.2±0.55 a*</td>
<td>7.0±0.87b*</td>
<td>7.1±0.05</td>
</tr>
<tr>
<td>Urine volume (ml)/24 h</td>
<td>4.6±0.33</td>
<td>2.6±0.24a*</td>
<td>4.2±0.41b*</td>
<td>4.3±0.18</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± SEM for six animals in each group. The letters ‘a’ and ‘b’ represent comparative study with Group I and Group II, respectively.

* Statistical significance at P<0.05, SEM: Standard error of mean.
Effect of potentised homoeopathic drug *Berberis vulgaris* on urinary stone-forming biochemical constituents in hyperoxaluric experimental rats

There was a significant increase in urinary oxalate excretion (43.87%) [Table 2] in hyperoxaluria-induced rats compared to the control group rats. Simultaneously, *Berberis vulgaris*-treated group showed a statistically significant ($P < 0.05$) decrease (15%) in urine calcium and (17.93%) oxalate content compared with that of Group II [Table 2]. Administration of sodium oxalate (Group II) caused a significant decrease in magnesium (24.91%) and (17.64%) phosphorus content in urine, whereas the uric acid (45.45%) and (16.66%) creatinine content increased compared with that of the untreated group (Group I). Significant increase in magnesium (24.87%) and (10.71%) phosphorus, whereas decrease in uric acid (90.68%) and (7.14%) creatinine were observed in *Berberis vulgaris*-treated group [Table 2], and no significant changes were observed in drug control group rats.

Effect of potentised homoeopathic drug *Berberis vulgaris* on enzymatic antioxidants in hyperoxaluric experimental rats

Figures 1 and 2 show the activities of antioxidant enzymes in the kidneys of normal and experimental rats. As a result of oxalate exposure, a statistically significant ($P < 0.05$) decline in the enzymic antioxidant activities (SOD, CAT, GPx, GR, GST and G6PD) was observed in Group II animals. These changes highlight the deteriorating antioxidant status in the hyperoxaluric group. Non-enzymic antioxidants showed a marked decline in the levels of non-enzymic antioxidants such as GSH and levels of Vitamins C and E in sodium oxalate-treated rats, whereas a statistically significant increase ($P < 0.05$) in the activity of non-enzymic antioxidant towards control range was obtained by pre-treatment with *Berberis vulgaris* (6c), indicating its protective effect against oxidative stress induced by hyperoxaluria. No significant changes were observed in drug control (Group IV) animals.

Effect of potentised homoeopathic drug *Berberis vulgaris* on renal tissue histology of hyperoxaluric experimental rats

The histopathological changes observed are highlighted in the photomicrographs in Figure 3. Group 1 (control) rats exhibited normal histoarchitecture of the kidney with normal glomeruli, tubules and interstitium. Sections from the kidney of rats with sodium oxalate (Group 2) administration showed glomerular shrinkage, tubular dilation and increased urinary space. An eosinophilic material was seen within the lumens of many of the tubules, and focal areas of interstitial inflammation were also observed. Group 3 rats (treated) showed amelioration of changes – glomeruli were normal and tubular dilatation was decreased. The renal tissue of Group 4 (drug control) rats showed normal histology, similar to that of control rats.

Effect of potentised homoeopathic drug *Berberis vulgaris* on the expression of NADPH oxidase of hyperoxaluria experimental rats

The expression of NADPH oxidase by Western blot analysis was markedly elevated in the sodium oxalate-induced acute hyperoxaluric rats when compared with normal control rats [Figure 4]. A marginal yet statistically significant ($P < 0.05$) decrease in No×2 expression was observed in the control group, and similar results were exhibited in *Berberis vulgaris*-treated and drug control groups when compared to the pathology group (Group II), indicating attenuation in renal oxidative stress.

Discussion

The results of the current study show that exposure to Ox and CaOx crystals is associated with elevated levels of oxalate and calcium in urine of hyperoxaluria-induced rats as this may cause precipitation of oxalate in urine due to the poor solubility of calcium oxalate. Further, it leads to heterogeneous nucleation followed by aggregation of calcium oxalate crystals in the renal tubules, thereby inducing functional damage too.$^{[22,23]}$ An earlier study conducted in our laboratory by Jyothilakshmi *et al.*, in 2013 strengthened that increased urinary excretion of oxalate might be a consequence of increased activity of oxalate-synthesising enzymes on ingestion of ethylene glycol that attributes to cause oxidative damage in the tubules of hyperoxaluria-treated rats.

Hyperoxaluria and hypercalciuria are often encountered in calcium oxalate stone formers, signifying hypercalciuria to be one of the secondary causative factors for stone formation.

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Table 2: Effect of potentised homoeopathic drug *Berberis vulgaris* on urinary stone-forming biochemical constituents in acute hyperoxaluria experimental rats

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>Group IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxalate</td>
<td>1.55±0.10</td>
<td>2.23±0.14*</td>
<td>1.83±0.12*</td>
<td>1.65±0.11</td>
</tr>
<tr>
<td>Calcium</td>
<td>0.16±0.01</td>
<td>0.20±0.01*</td>
<td>0.17±0.01*</td>
<td>0.167±0.01</td>
</tr>
<tr>
<td>Magnesium</td>
<td>2.57±0.20</td>
<td>1.93±0.13*</td>
<td>2.41±0.17*</td>
<td>2.54±0.18</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>0.34±0.03</td>
<td>0.28±0.02*</td>
<td>0.31±0.03*</td>
<td>0.33±0.03</td>
</tr>
<tr>
<td>Uric acid</td>
<td>0.11±0.01</td>
<td>0.16±0.02*</td>
<td>0.15±0.17*</td>
<td>0.14±0.02</td>
</tr>
<tr>
<td>Creatinine</td>
<td>1.24±0.14</td>
<td>1.4±0.15*</td>
<td>1.31±0.09*</td>
<td>1.26±0.13</td>
</tr>
</tbody>
</table>

Values are expressed as mean±SEM for six animals in each group. The letters ‘a’ and ‘b’ represent comparative study with Group I and Group II, respectively. *Statistical significance at $P<0.05$. SEM: Standard error of mean.
Figure 1: Effect of potentised homoeopathic drug of *Berberis vulgaris* on enzymatic antioxidants in acute hyperoxaluria experimental rats. (a) Superoxide dismutase. (b) Catalase. (c) Glutathione peroxidase. (d) Glutathione-S-transferase. Values are expressed as mean ± standard error of the mean for six animals in each group. The letters ‘a’ and ‘b’ represent comparative study with Group I and Group II, respectively. The symbol * represents statistical significance at $P < 0.05$.

Figure 2: Effect of homoeopathic drug *Berberis vulgaris* on non-enzymatic antioxidants in acute hyperoxaluria experimental rats. (a) Vitamin C. (b) Vitamin E. (c) Reduced glutathione. Values are expressed as mean ± standard error of the mean for six animals in each group. The letters ‘a’ and ‘b’ represent comparative study with Group I and Group II, respectively. The symbol * represents statistical significance at $P < 0.05$. 
Hypercalciuria could occur in both healthy and individuals with stone formation, wherein stone formers tend to excrete larger and aggregated particles than healthy individuals. Increased urinary calcium excretion in oxalate-induced rats favours the nucleation and precipitation of calcium oxalate from urine and subsequently crystal growth. Nevertheless, the present study corroborates an increased excretion of calcium in the urine of hyperoxaluric rats.

Calcium oxalate crystallisation of urolithiasis relies on various stone-promoting and -inhibiting factors. As far as the fact that calcium and phosphates are stone-promoting inorganic factors while magnesium is a stone-inhibiting factor is concerned, in the existing study, a diminished level of magnesium was observed in urolithic rats. In urolithiasis, glomerular filtration rate (GFR) decreases due to stones in the urinary system obstructing urine outflow, which leads to the accumulation of waste products in the blood, particularly nitrogenous substances such as urea, creatinine and uric acid. Sodium oxalate induced renal dysfunction as revealed by the renal profile is ameliorated on administration of Berberis vulgaris obviating its protective role.

Several studies have supported the involvement of oxidative stress in CaOx nephrolithiasis by treating hyperoxaluric rats with antioxidants. In our study, we found that Berberis vulgaris furnishes a strong defensive antioxidant activity against oxidative stress and thereby helps in the management of oxidative stress by protecting the renal tissue from oxidative stress. The antioxidant effect of Berberis vulgaris might be attributed to the predominant active compound berberine, an isoquinoline alkaloid, which has antioxidant property by nature.

Previously, Khan reported that calcium oxalate rat model nephrolithiasis is associated with the activation of NADPH oxidase, production of ROS, development of oxidative stress and renal injury. Among the NOX family members, NOX2 is expressed in macrophages and kidney cells that participate in excessive ROS generation. By inhibiting antioxidant defences, oxalate can induce oxidative damage in experimental rats and increase oxidative stress, which plays a crucial role in the
progression of renal disease. In our existing study, harmful cellular oxidative stress was suppressed on pre-treatment with Berberis vulgaris in treated group, thereby inhibiting oxalate-induced ROS production which may have prevented crystal adherence and the subsequent development of nephrolithiasis, suggesting that early activation of NADPH oxidase delayed the sequential events of urolithiasis.

This study has certain limitations. First, the mechanism by which NOX2 affects the kidney’s redox state, and inhibition of this enzyme to modulate oxidative stress and ROS production, remains to be delineated. Second, the extent oxidative stress-induced renal injury in renal tissue provoking the retention of calcium oxalate crystals, which forms the nidus and results to a cascade of events such as nephrolithiasis is not clear. Similarly, in-depth analysis of the genes that involve specific biological pathways triggered as renal tissue responses to hyperoxaluria, and ROS production remains to be further investigated.

**Conclusion**

Thus, these data suggest that a combination of antioxidants and NADPH oxidase inhibitor may synergistically inhibit nephrolithiasis progression and may be considered for the development of novel therapeutics. Potentised homeopathic drug Berberis vulgaris might ameliorate hyperoxaluria by eliminating oxidative stress of renal tissue, which plays a key role in the production of reactive oxygen species (ROS) with the involvement of NADPH oxidase as a potential target in the treatment and reoccurrence of renal stone disease. There is still a paucity of information on the exact physiologic and pathologic roles of NADPH oxidases in the kidney and hence further research should elucidate these effects.

**Financial support and sponsorship**

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**Conflicts of interest**

None declared.

**References**

La preparación homéopática de Berberis vulgaris inhibe la NADPH oxidasa y ameliora la hiperoxaluria aigue de haut grade induite par l’oxalate de sodium

Contexte: La hiperoxaluria y el depósito de cristales de oxalato de calcio en los riñones entrañan una supresión de especies reactivas del oxígeno, entrainant le développement d’un stress oxydatif y de lésions rénales. Au niveau celular, las mitocondrias y la NADPH oxidade impliqué en la producción de especies reactivas de l’oxygène jouent un rôle crucial dans la pathogénese des lésions rénales induites par la hiperoxaluria. Objectif: L’objectif était d’étudier l’effet thérapeutique du médicament homéopathique Berberis vulgaris, un antioxydant puissant, sur la régulation de la NADPH oxidase contre l’hiperoxalurie induite par l’oxalate de sodium chez le rat. Matériel et méthodes: Une hyperoxalurie a été induite chez des rats mâles Wistar en administrant une dose unique d’oxalate de sodium (70 mg / kg de poids corporel) par voie intrapéritonéale, et les groupes de traitement ont été prétraités avec le médicament homéopathique Berberis vulgaris 6C (20 µl / 100 g de corps) pendant 7 jours. Résultats: Berberis vulgaris a réduit de manière significative le stress oxydatif induit par la hyperoxalurie et restauré les activités enzymatiques antioxydantes dans les tissus rénaux. L’analyse histologique a montré que le traitement par Berberis vulgaris diminuait la concentration et l’inflammation et rétablait la morphologie glomérulaire. En outre, les analyses d’immunoempreinte de la NADPH oxidase ont révélé une activité accrue significative dans le tissu rénal des rats hyperoxaluriques par rapport à celle des rats témoins. Conclusion: Ainsi, nos résultats ont souligné que le médicament homéopathique Berberis vulgaris est efficace pour améliorer l’hiperoxalurie induite par l’oxalate de sodium chez les rats Wistar en modulant le stress oxydatif mitochondrial par l’inhibition de la NADPH oxidase.

La preparación homoeopática de Berberis vulgaris inhibe la NADPH oxidasa, y mejora la hiperxaluria aguda de alto grado inducida por oxalato sódico

Antecedentes: La hiperoxaluria y la deposición de cristal de oxalato de calcio en los riñones conducen a la sobreproducción de especies reactivas de oxígeno, lo que resulta en el desarrollo de estrés oxidativo y lesión renal. A nivel celular, las mitocondrias y la NADPH oxidasa que participan en la producción de especies reactivas de oxígeno desempeñan un papel crucial en la patogénesis de la hiperxaluria inducida por la lesión renal. Objetivo: El objetivo era investigar el efecto terapéutico del fármaco homoeopático Berberis vulgaris, un potente antioxidante, sobre la regulación de la NADPH oxidasa contra la hiperxaluria aguda inducida por oxalato de sodio de alto grado en ratas. Materiales y métodos: Se indujo hiperxaluria en ratas Wistar masculinas mediante la administración de una dosis única de oxalato sódico (70 mg/kg de peso corporal) intraperitoneal, y los grupos de tratamiento fueron pretratados con el medicamento homoeopático Berberis vulgaris 6C (20 µl/100 g de peso corporal) para la hiperxaluria y restauró las actividades enzimáticas antioxydantes en el tejido renal. El análisis histológico describió que el tratamiento con Berberis vulgaris disminuyó el daño epitelial renal y la inflamación y restauró la morfología glomérular normal. Además, los análisis de inmunotransferencia de NADPH oxidasa revelaron un aumento significativo de la actividad en el tejido renal de ratas hiperxalurícas cuando se comparan con las ratas control. Esto fue llevado de vuelta a la normalidad por el tratamiento de las ratas Wistar. Conclusion: Así, nuestros resultados enfatizaron que el fármaco de Homeopatía Berberis vulgaris es eficaz en la mejora de la hiperxaluria aguda inducida por oxalato sódico en ratas Wistar, modulando el estrés oxidativo mitochondrial a través de la inhibición de la NADPH oxidasa.
Tamilarasan, et al.: Plausible role of a potentised Homoeopathy drug, Berberis vulgaris, in ameliorating sodium oxalate-induced acute hyperoxaluria in Wistar rats

Berberis vulgaris is an effective antioxidant that inhibits NADPH oxidase, thereby reducing the oxidative stress and restoring antioxidant enzyme activities in the kidney tissue. The histological analysis showed that Berberis vulgaris treatment reduced renal epithelial damage and inflammation and restored normal glomerular morphology. Furthermore, immunoblotting analysis of the NADPH oxidase showed a significantly increased activity in the hyperoxaluric rats compared to the control rats. This was corrected to normal with Berberis vulgaris treatment.

**Conclusion:** Therefore, our results underscore that the homoeopathic medication Berberis vulgaris is effective in improving sodium oxalate-induced acute hyperoxaluria in Wistar rats through the modulation of mitochondrial oxidative stress by inhibiting NADPH oxidase.