AN EXPERIMENTAL STUDY ON ANTIHYPERURICEMIC ACTIVITY IN POTASSIUM OXONATE INDUCED RAT MODEL USING HOMOEOPATHIC MEDICINE LITHIUM CARBONICUM

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ABSTRACT

Hyperuricemia belongs to ICD-10 Code E79.0, is the most common disease which affects patients of all age groups and gender. Until their joints, kidneys, hearts, or other organs are impacted, the majority of people with elevated uric acid will not exhibit any symptoms. Gout-like symptoms are caused by a prolonged increase in blood uric acid. The course of disease pathology can be stopped if the elevated serum uric acid level is identified and prompt therapy is initiated. Long-term usage of the current standard treatment may have some negative effects on other important organs. For long-term care, homoeopathy will be an excellent choice because uric acid levels will fluctuate frequently. As a holistic approach, homoeopathy lowers uric acid levels and stops pathology from developing. In this study Homoeopathic medicine Lithium carbonicum 6C and 30C were used to show antihyperuricemic activity in hyperuricemia induced rat models. The rats were split up into five groups. Group 1 did not receive any medicine or induction. After an hour of fasting, other groups received an intraperitonial injection of potassium oxonate. After producing hyoeruricemia, the other three groups received an intervention, while Group 2 served as a negative control. Along with a histological study, the levels of creatinine and uric acid in the serum were measured. The result shows that when compared to allopurinol and lithium carbonicum 6C, the combined findings of the uric acid level and histopathological study demonstrated notable and consistent changes in lithium carbonicum 30C.

KEYWORDS: Antihyperuricemic activity, Invivo, Hyperuricemia, Homoeopathy, Lithium carbonicum.

INTRODUCTION

Hyperuricemia is the term used to describe elevated blood uric acid levels. More than 7 mg/dl is considered saturated and may result in symptoms. The usual upper limit of uric acid levels is 6.8 mg/dl. Reduced uric acid excretion, increased uric acid production, or both could be the cause of this elevated level.[1][2] Although gout and hyperuricemia seem to be closely linked conditions, 85–90% of hyperuricemia patients do not exhibit gout-like symptoms. Three phases—asymptomatic hyperuricemia, intermittent gout, and chronic gout—have been suggested as the temporal link between hyperuricemia and gout. Hyperuricemia without gout symptoms was referred to as asymptomatic hyperuricemia. It has been demonstrated that the level of hyperuricemia is a good predictor of flare-ups.[3] The threshold blood values for hyperuricemia were formerly set at 7.7 mg/dl for men and 6.6 mg/dl for women, or 7.0 mg/dl for men and 5.7 or 6 mg/dl for women.[3][4][5][6] Along with urate crystal formation in the joints, hyperuricemia has other pathophysiologic effects that lead to tissue inflammation, especially in the artery wall.[7] People with type 2 diabetes, hypertension, and related co-morbidities were found to have higher rates of hyperuricemia. The prevalence of hyperuricemia increased along with the duration of type 2 diabetes mellitus and hypertension.[8]

Establishing the worldwide adoption of safe, affordable, and efficient gout prevention and treatment methods will be crucial. Even if this is unlikely to be enough, it will be crucial to pay special attention to gout risk factors like a high purine diet, alcohol consumption, obesity, diabetes, and kidney disease in order to prevent and manage an epidemic of hyperuricemia and gout.[9] Lithium carbonicum is a homoeopathic medicine derived from lithium carbonate. Homoeopathic materia medica states that it specifically affects uric acid diathesis, which includes tophi and gout. In addition to being affordable, homoeopathic medicines don't have any known negative effects on important organs.[10] Lower serum uric acid levels were seen in one trial on the use of lithium carbonate to prevent hyperuricemia in pullets. Additionally, there was no proof that any lithium remained in the eggs or pullets' tissues.[11] Unfortunately, lithium carbonate's potential action on uric acid reduction was not investigated because there were no more trials to assess its efficacy. Therefore, the purpose of this study was to determine how well homoeopathic medicine Lithium carbonicum 6C and 30C reduced the uric acid level in rats that had been induced with hyperuricemia.

MATERIALS AND METHODS

Experimental animal

Fifteen Wistar albino rats weighing between 150 and 250 grams are used in this study, which was approved by the IAEC of The Dale View College of Pharmacy & Research Centre bearing approval No.1118/PO/Re/S/07/CPCSEA. A 12-hour light-dark cycle, 50–55% humidity, and a standard temperature of 25 degrees Celsius were maintained throughout the study.[12] Fifteen Wistar albino rats were split up into five groups of three. Potassium oxonate was used to create hyperuricemia in just four of these five groups.

Animal allotment:

GROUP 1: Normal control (no medicine)

GROUP 2: Hyperuricemic control

GROUP 3: Allopurinol (Standard control)

GROUP 4: Lithium carbonicum 6C

GROUP 5: Lithium carbonicum 30C

Hyperuricemia induction in rats

Urate is eliminated as uric acid, which is the final byproduct of purine degradative metabolism in humans. Rats had blood uric acid levels of about 20.93±6.98 µg/ml.[13] Allantoin, another oxidative metabolite of uric acid, is produced via purine metabolism in all mammals (with the exception of certain primates). The transfer of soluble allantoin from insoluble uric acid is controlled by the enzyme uricase. Because of an evolutionary mutation, humans no longer manufacture uricase, which is produced by the livers of most mammals.[14] By preventing hepatic uricase from working, potassium oxonate causes hyperuricemia in animals. An effective animal model for testing drugs to change blood uric acid levels and treatments for uric acid-related illnesses is the oxonate-treated rat.[12] In a 0.9% saline solution, 250 mg of potassium oxonate was dissolved.[15] Rats were given daily intraperitoneal injections of 250 mg/kg of potassium oxonate to produce hyperuricemia.[16]

METHODOLOGY

The study was carried out at the Dale View College of Pharmacy and Research Centre. Standard settings for the experiment were 25° Celsius, 50–55% humidity, and a 12-hour light/dark schedule. Before the trial began, the rats were kept in the lab for a week and given a standard diet and drink.[12] Before receiving a potassium oxonate injection for an hour each day, rats were deprived of food and given water instead. The rats in groups 2, 3, 4, and 5 received an injection of potassium oxonate (250 mg/kg in a 0.9% saline solution, not to exceed 1 ml)[15] for seven days after being denied food for an hour.[17] By inhibiting hepatic uricase, an enzyme mostly located in the liver and present in most mammals, potassium oxonate causes hyperuricemia in rats.

For seven days in a row, Allopurinol 5 mg/kg[15] (not more than 0.5 ml), Lithium carbonicum 6C (not more than 0.5 ml), and Lithium carbonicum 30C (not more than 0.5 ml) were administered orally once a day in distilled water, one hour after groups 3, 4, and 5 received an injection of potassium oxonate. On day 1, one hour after the potassium oxonate injection, one millilitre of blood was drawn from the rats retroorbital vein to confirm induction and on day 7, two hours after the drug treatment, the levels of creatinine and uric acid were measured. Animals were sacrificed on the seventh day, and their kidneys were removed and put in formalin buffer solution for histological analysis.

STASTICAL DATA

The study groups' mean uric acid levels varied statistically significantly ($F = 25.106$, $p < 0.001$) according to a one-way ANOVA. The hyperuricemic control group varied significantly from both the normal control group and the treatment groups that received Allopurinol, Lithium carbonicum 6C, and Lithium carbonicum 30C, according to a post hoc analysis using Tukey's HSD test. The remaining group comparisons showed no

statistically significant differences. These results imply that hyperuricemia significantly raises uric acid levels, although therapy with Allopurinol and Lithium carbonicum (6C and 30C) did not result in statistically significant changes in uric acid levels when compared to other treated groups.

OBSERVATION AND RESULTS

In this study antihyperuricemic activity of Homoeopathic medicine Lithium carbonicum 6C and 30C was assessed. Hyperuricemia was induced in the rat groups and treated for 7 days. The results at the end of day 7 was given below.

Table 1: Comparison of Uric acid level in all groups

No. of rats	Normal control (NC) (mg/dl)	Hyperuricemic control (HC) (mg/dl)	Allopurinol (Al) (mg/dl)	Lithium carbonicum (LC) 6C (mg/dl)	Lithium carbonicum (LC) 30C (mg/dl)
Rat 1	1.78	4.6	2.3	1.8	1.71
Rat 2	1.6	5.3	1.8	1.7	1.82
Rat 3	1.89	4.2	2.97	2.6	1.75

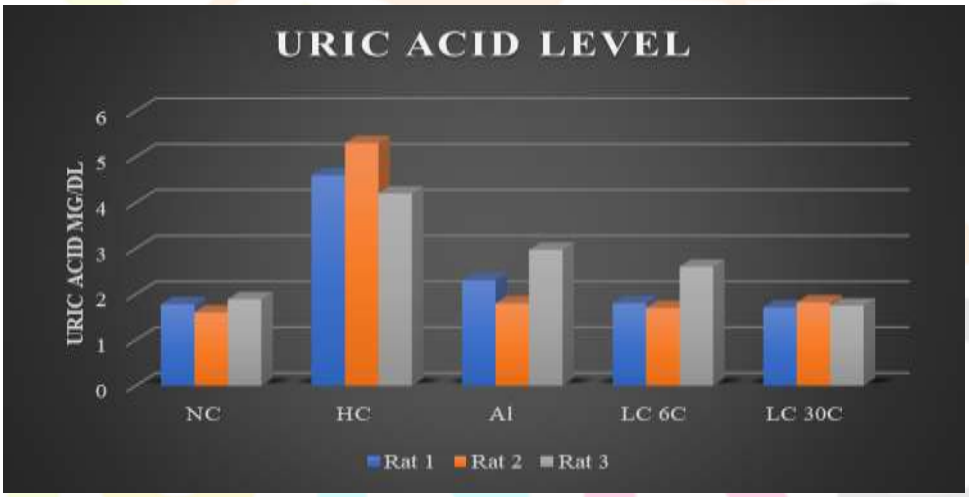

Figure 1: Uric acid level comparison between groups

Table 2: Comparison of Creatinine level in all groups

No. of rats	Normal control (NC) (mg/dl)	Hyperuricemic control (HC) (mg/dl)	Allopurinol (Al) (mg/dl)	Lithium carbonicum (LC) 6C (mg/dl)	Lithium carbonicum (LC) 30C (mg/dl)
Rat 1	0.40	0.48	0.45	0.40	0.40
Rat 2	0.35	0.42	0.42	0.43	0.44
Rat 3	0.44	0.45	0.48	0.47	0.37

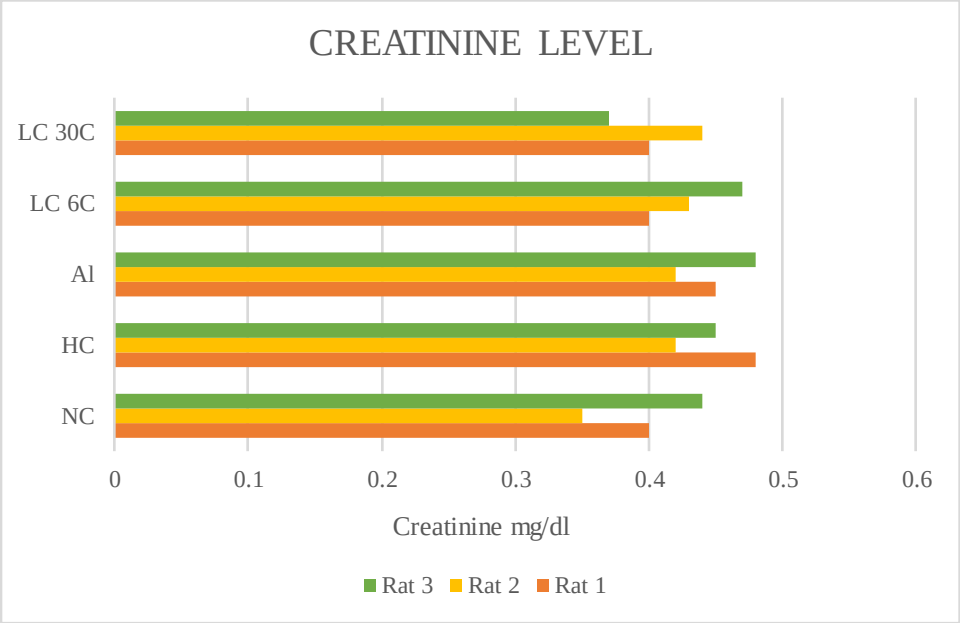

Figure 2: Creatinine level comparison between groups

The result shows that Lithium carbonicum 6C and 30C has antihyperuricemic activity by lowering the uric acid levels. But consistency of value was found better for Lithium carbonicum 30C than 6C. There was no elevation in creatine level for all the 5 groups so it was not significant.

Histopathological findings

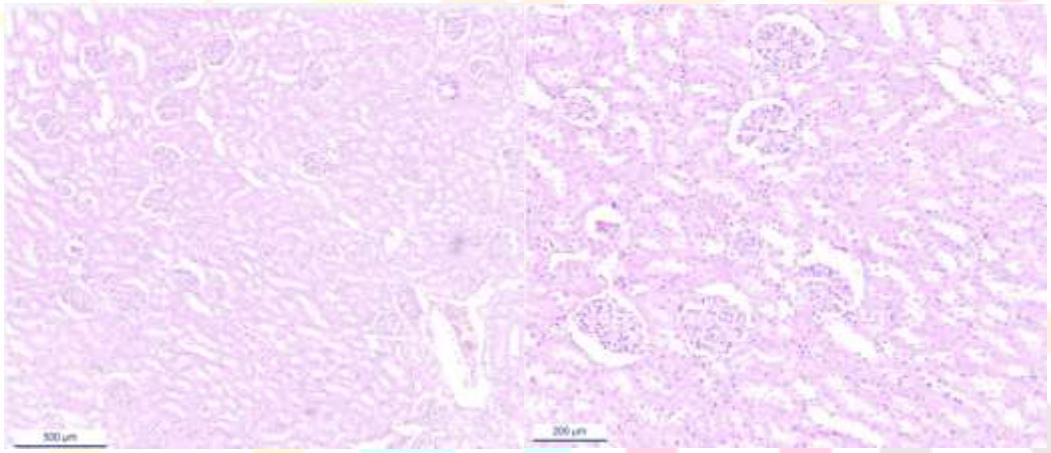

Figure 3: Hyperuricemic control group showing marked degree (+++) of tubular degeneration and moderate degree (++) of tubular dilatation

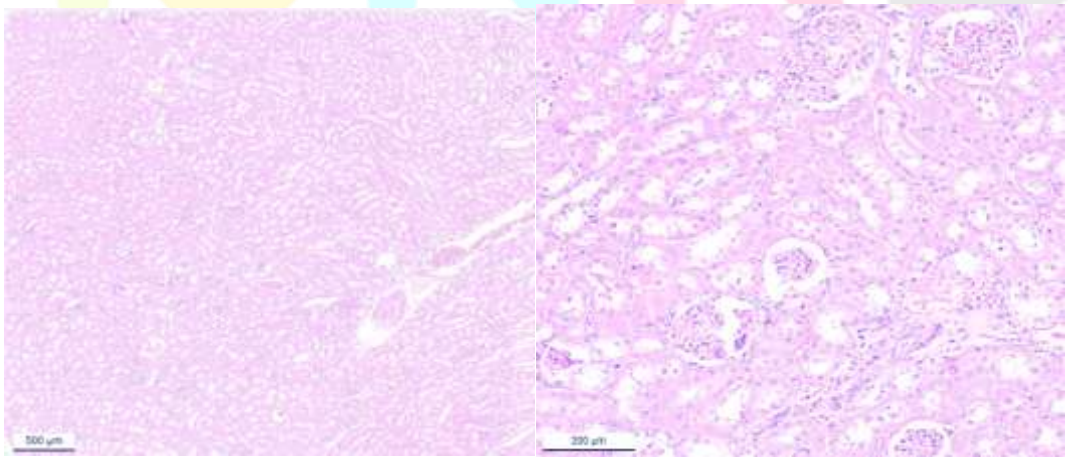

Figure 4: Allopurinol group showing mild degree (+) of tubular degeneration and mild degree (+) of tubular dilatation

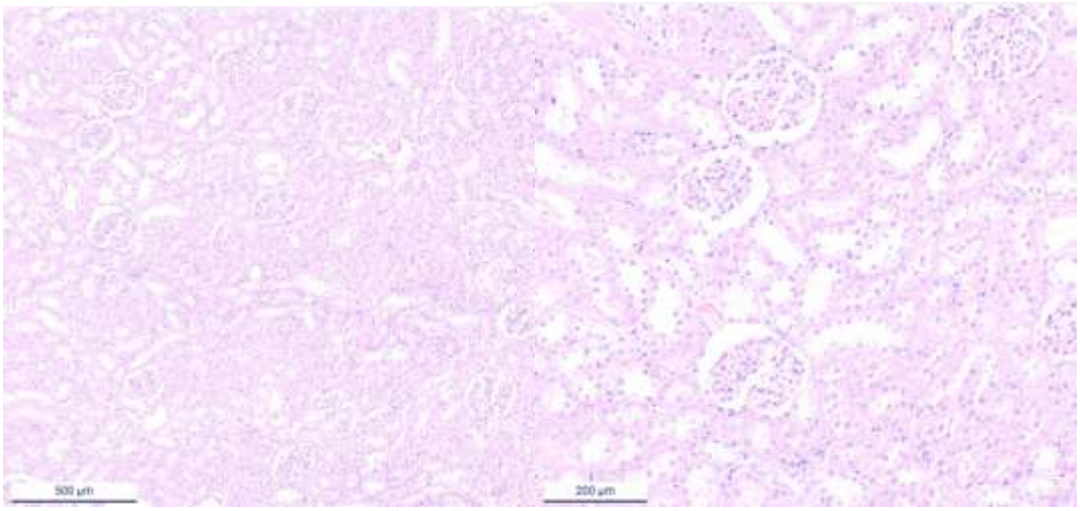

Figure 5: Lithium carbonicum 6C group showing moderate degree (++) of tubular degeneration and moderate (++) of tubular dilatation

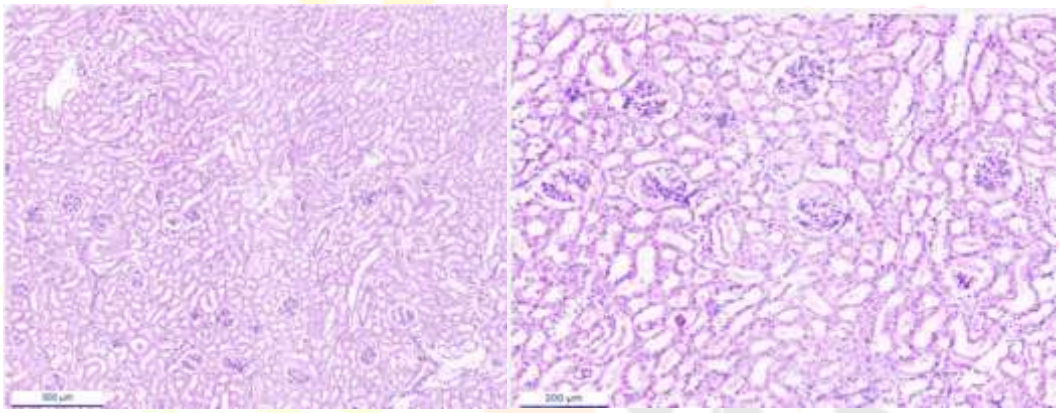

Figure 6: Lithium carbonicum 30C group showing no evidence of tubular degeneration and dilatation

DISCUSSION

The study uses potassium oxonate to induce hyperuricemia in a rat model in order to demonstrate the antihyperuricemic activity of lithium carbonicum in two potencies, 6C and 30C. An efficient uricase blocker that quickly causes hyperuricemia in rats is potassium oxonate. This model took less time and successfully show the hyperuricemic activity in rats. As a result, the effectiveness of medication will be precisely evaluated.

The study was carried out at The Dale View College of Pharmacy and Research Centre, Trivandrum. Five groups of three rats each were separated and kept in separate cages. Rats in each group had their retroorbital blood collected in order to measure uric acid and creatinine levels. After the rats were sacrificed, the kidneys were removed, sectioned, and viewed for histopathological analysis.

The uric acid level was significantly elevated in the hyperuricemic control group, with a mean value of 4.7 ± 0.56 mg/dl. It demonstrates the hyperuricemic model's efficacy. Serum uric acid levels in the usual treatment group, allopurinol, have significantly decreased to a mean of 2.36 ± 0.59 mg/dl. It exhibits its well-known conventional pharmacological effect. The average serumuric acid level in the lithium carbonicum 6C-treated group was 2.03 ± 0.49 mg/dl. In comparison to the hyperuricemic group, lithium carbonicum 6C demonstrated a moderate decrease in uric acid levels. Remarkably, the mean serum uric acid value for the

Lithium carbonicum 30C group was 1.76 ± 0.15 mg/dl. The serum uric acid level in the Lithium carbonicum 30C group has significantly decreased as compared to the Allopurinol and Lithium carbonicum 6C groups, demonstrating the animals' consistent response. However, all treatment groups' serum uric acid levels have recovered to normal following medication administration.

When taking into account the serum creatinine level, none of the five groups showed an increase. It indicates that increases in creatinine levels take time to manifest. Since the trial lasted for seven days, the creatinine level did not significantly alter. To see the variability in creatinine levels, more research with longer study durations is required.

Lithium carbonicum 30C has no anomalies in the renal structure, according to the histological analysis of the kidneys of the rats in each group. This indicates that this group has a notable effect by preserving kidney function. Tubular degenerative alterations and dilatation were seen in the hyperuricemic control group, indicating that hyperuricemia will impact renal structure even prior to an increase in blood creatinine levels. Lithium carbonicum 6C demonstrated moderate tubular degenerative change and dilatation, while the allopurinol group displayed minor tubular degenerative changes and dilatation. According to these histological results, the kidneys are affected by all treatment groups, with lithium carbonicum 30C showing the most significant effects.

CONCLUSION

By reducing the blood uric acid level back to normal, this study shows that the homoeopathic medication Lithium carbonicum 6C and 30C has antihyperuricemic activity. Lithium carbonicum 30C consistently lowers serum uric acid levels in all of the group's animals when compared to the usual medication Allopurinol. It is also clear from the histological analysis that lithium carbonicum 30C has a significant impact on the kidneys, sustaining uric acid excretion. According to the study's findings, lithium carbonicum 6C and 30C have a substantial therapeutic potential for treating hyperuricemia. When comparing the potencies, Lithium carbonicum's 30C potency offers greater anti-hyperuricemic capability.

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