Efficacy of Homoeopathic Medicine Urtica Urens Q In Controlling Uric Acid Levels in Wistar Rats

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Abstract

Hyperuricemia has increased in frequency among people all over the world over the last few decades.Although homoeopathic practitioners claim that the drug URTICA URENS is being effectively used with good results clinically in the treatment of hyperuricemia , gout no relevant researches have been done to establish this , no pre-clinical studies of this drug in this has been done to the best of our knowledge Therefore there is a sincere attempt to assess the effectiveness of URTICA URENS.Allopurinol is the standard treatment for hyperuricemia. Thegoal of the study was to determine whether *Urtica urens* Q had hypouricemic effects in a rat model of pyrazinamide induced hyperuricemia. Male and female Wistar rats, weighing 150-200 gm were used for acute model. The blood samples were collected through retro-orbital space, and send to the lab for determination of SUA. **RESULTS:** Rats initial serum uric acid levels were discovered to be between 3.5 and 4.5 mg/dl. After a week daily pyrazinamide administration at a higher dose (250 mg/kg) markedly raises the blood uric acid level upto 10 mg/dl. The homoeopathic medicine Urtica urens Q at dose of 40µL/100gmPO and 30C in distilled water have comparable hypourecemic activity with that of standard drug Allopurinol. **CONCLUSION**. As per the observation and the results analysed from the data, homoeopathic medicine Urtica Urens has highly significant effect in controlling serum uric acid levels. The current study pyrazinamide-induced that Urtica urens Q and 30C had antihyperuricemic potential in a rat model of hyperuricemia caused by pyrazinamide.

Keywords: Homoeopathy, Animal study, Hyperuricaemia, Allopurinol, Urtica urens

INTRODUCTION

In Hyperuricemia is a metabolic condition that affects millions of people worldwide and can increase blood urate/uric acid levels to as high as 6.8 mg/dL. Hyperuricemia is defined as plasma uric acid levels that are more than 6.8 mg/dL. Even though uric acid was just discovered a few years ago, there are still some unresolved pathophysiologic features of hyperuricemia. Currently, uric acid has been recognised as a marker for a number of metabolic and hemodynamic disorders. As opposed to allantoin, which is the more soluble end result of purine metabolism in lower animals, uric acid is the less soluble end product of purine metabolism in humans. [18,20,21]

Humans have greater uric acid levels than other animals due to a lack of the hepatic enzyme uricase and a reduced fractional excretion of uric acid. Two-thirds of the total amount of urate is produced by the body, and the other third is obtained from dietary purines. The intestines eliminate the remaining 30% of the body's daily urate production, leaving the kidneys to handle around 70% of it. With renal failure, the intestinal portion of urate excretion rises to make up for the kidneys' diminished capacity. The ratio of the rate of uric acid excretion to that of purine breakdown controls the amount of uric acid in the blood. [18,20,23]. In homoeopathy, as said by our master Dr. Hahnemann "the sole and raised mission of the doctor is to restablish the health to the sick which is called cure". Miasms are thought to be the root cause of every disease, including hyperuricemia which can be thought of under sycotic miasm . Miasms set the body up for a particular disease. Due to uric acid or lithic diathesis, the patient develops hyperuricemic symptoms and a tendency to build up uric acid crystals in his body, which is a constitutional dyscrasia.

Numerous medications used in modern medicine, such as febuxostat, allupurinol, NSAIDs, corticosteroids, anti-hyperuricemic drugs, and uricosuric agents, among others, have serious side effects like gastrointestinal distress, vomiting, hepatotoxicity, and hypersensitivity drug reaction blood loss, among others.[19]

In homoeopathic literature many medicines are given to treat hyperuricaemia like Ledum pal., Lycopodium, Colchicum, Benzoic acid, Lithium carb, Ocimum sanct. etc, Urtica urens is also used for the same. So, there is the dire need to find out an alternative medicine which can be used as the substitute for modern medicine so that there are merely no side- effects. [59,62] Chemicals like flavonoids, 13-hydroxy octa-decatrienoic acid, vitamin B, caffeic acid, terpenes, vitamin C, and vitamin k have all been mentioned in reports. To treat uric acid-related conditions like gout and uric acid diathesis, homoeopathyfrequently employs URTICA URENS. In its leaves anti-inflammatory, anti-arthritic, anti-bacterial, anti-oxidant, and anti-microbial properties have been demonstrated. Additionally, they have anxiolytic qualities (aerial part). [14,15,16]

The primary aim of the study was to examine the potential hypouricemic effects of Urtica urens Q on serum UA in Wistar rats with pyrazinamide-induced hyperuricemia.

METHODOLOGY

1. ETHICAL STATEMENT

The research proposal went through a process of ethical review by Institutional Animal Ethical Committee (IAEC), Bharati Vidyapeeth Medical College prior to the study commencement.

2. EXPERIMENTAL ANIMALS

Wistar albino rats (weighing between 150 and 250 g) were provided by the Bharati Vidyapeeth Medical College and Hospital's Department of Pharmacology's animal house. Rats were kept in polycarbonate cages of 47 x 34 x 18 inches square, with a maximum of four rats per cage. The study period was conducted under the same standard circumstances of humidity (50–55%), temperature (25–1 °C), and 12–12–hour light–dark cycle. Prior to the trial, rats were fed a regular meal and given access to unlimited amounts of water in a laboratory setting. The handling and usage of animals was limited to those with appropriate training and expertise.

3. DRUGS AND CHEMICALS

a. Pyrazinamide and allopurinol
b. Urtica urens Q and 30C of SBL brand

4. ESTIMATION OF INITIAL SERUM URIC ACID LEVELS

The blood samples were collected from each rat retro- orbital puncture and send for SUA estimation to a path lab.

5. EXPERIMENTAL SETUP

Each of the 5 groups, which each contained 8 animals, was made up of the animals. A lab assistant who was unaware of the purpose of the experiment divided the animals into the various groups at random. In order to check the baseline serum uric acid levels, blood samples from retro- orbital space were taken from each animal. Throughout the entire study, animals were also watched for negative outcomes like immobility, an inability to eat or drink, a change in body weight, or the death of any animal. During the administration of the medication, experimenters weren't blinded to the experimental groups.

6. HYPERURICAEMIA INDUCTION

As previously mentioned, rats were given pyrazinamide to cause hyperuricemia. In order to raise serum UA levels, pyrazinamide was given orally for 10 days at a rate of 250 mg/kg.

7. PREPARATION OF DIFFERENT DOSES OF DRUGS

Cold water can be used to dissolve pyrazinamide, which has a 15 mg/ml water solubility. Pyrazinamide dose titration was performed in this study at a rate of 250 mg/kg body weight. Pyrazinamide doses were estimated and made based on animal body weight and their solubility; for allopurinol, doses were 5 mg/kg body weight, and for Urtica urens, doses were 40 l/100 g body weight PO for Urtica urens Q, and 0.1 ml PO in distilled water for Urtica urens 30C.

8. EXPERIMENTAL DESIGN

S.NO	GROUP	TREATMENT SPECIFICATION	DOSE	ANIMALS PER GROUP
1.	CONTROL GROUP	-	-	8
2.	DISEASE CONTROL	NORMAL SALINE	-	8
3.	STANDARD DRUG	ALLOPURINOL	5mg/kg PO In distilled water	8
4.	TEST DRUG(Low Dose	URTICA URENS 30	0.1ml PO In distilled water	8
5.	TEST DRUG (High Dose)	URTICA URENS Q	40µL/100gmPO In distilled water	8

9. MEDICINEADMINISTRATION

Every medication, including the homoeopathic medicine and allopurinol, was administered orally once a day between 10 and 11 am. Allopurinol 5mg/kg, Urtica urensQ, and 30C were given orally to one of the five groups for eight days in each of the five groups. Two groups received distilled water: normal control and hyperuricemic control.

10.URIC ACID ASSAY

Initially on day 1 basal SUA was assessed, then on 10^{th} day for SUA levels were assessed after hyperuricaemia induction, then on 18^{th} day after administration of hypouricosuric agents. Blood samples were collected from rats retro- orbitally and given for SUA assessment in lab.

OBSERVATIONS

GROUPS	**LABELLINGS**	**BASAL SUA**		**SUA AFTER 18 DAYS**
CONTROL GROUP	H1	3.2		3.2
	B1	3.4		3.4
	TI	3.6		3.6
	HB1	4.5		4.5
	RF1	1.5		1.5
	LF1	4.2		4.2
	RH1	3.8		3.8
	LH1	4.2		4.2
DISEASE CONTROL (NO TREATMENT)	**LABELLINGS OF RATS**	**BASAL SUA**	**SUA AFTER PYRAZINAMIDE (INDUCTION OF HYPERURICEMIA) AFTER 10 DAYS**	**SUA AFTER 18 DAYS**
	H2	3.2	7.7	10.4
	B2	1.8	7.3	11.4
	T2	3.2	8.1	15.0

	HB2	3.1	8.4	10.8
	RF2	3.7	9.0	12.7
	LF2	6.2	8.9	16.0
	RH2	5.2	7.4	12.6
	LH2	4.6	7.9	10.1
TREATED WITH ALLOPURINOL	**LABELLINGS OF THE RATS**	**BASAL SUA ON DAY 1**	**SUA AFTER PYRAZINAMIDE (INDUCTION OF HYPERURICEMIA) AFTER 10 DAYS**	**SUA AFTER TREATMENT BY ALLOPURINOL AFTER 18 DAYS**
	H3	1.2	7.9	1.8
	B3	2.2	7.7	2.4
	T3	2.5	7.2	3.5
	HB3	4.3	8.2	3.2
	RF3	1.7	7.3	4.5
	LF3	4.5	8.4	3.5
	RH3	4.6	8.1	4.3
	LH3	3.2	8.6	3.3
TREATED WITH URTICA URENS 30	**LABELLINGS OF THE RATS**	**BASAL SUA ON DAY 1**	**SUA AFTER PYRAZINAMIDE (INDUCTION OF HYPERURICEMIA) AFTER 10 DAYS**	**SUA AFTER TREATMENT BY URTICA URENS 30 AFTER 18 DAYS**
	H4	4.0	7.3	5.2
	B4	2.7	7.4	5.9
	T4	3.7	8.5	6.2
	HB4	3.5	8.0	HAEMOLYSED
	RF4	2.7	8.2	7.9
	LF4	2.5	7.9	7.8
	RH4	5.1	7.2	7.0
	LH4	3.4	8.4	8.0
TREATMENT WITH URTICA URENS Q	**LABELLINGS OF RATS**	**BASAL SUA ON DAY 1**	**SUA AFTER HYPERURICEMIA INDUCTION**	**SUA AFTER TREATM**

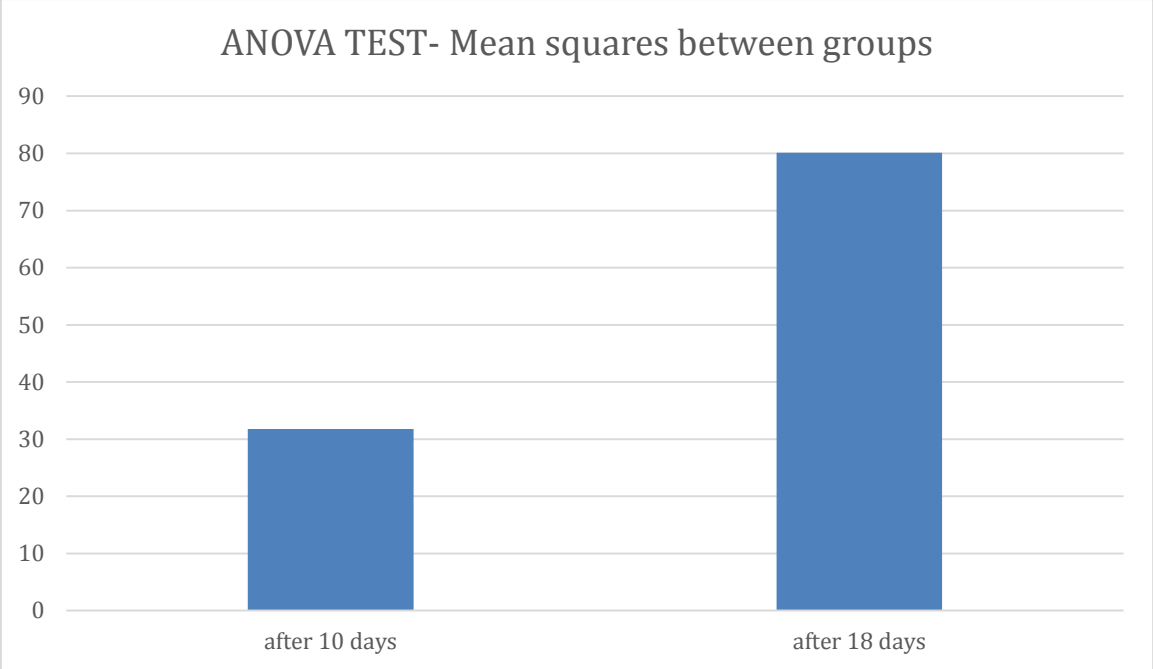
			ON DAY 10	**ENT BY URTICA URENS Q AFTER 18 DAYS**
	H5	3.4	8.6	7.8
	B5	3.5	8.5	7.3
	T5	3.3	7.7	7.1
	HB5	4.1	7.1	6.6
	RF5	2.9	7.8	7.0
	LF5	4.7	8.2	6.2
	RH5	4.9	7.7	6.2
	LH5	3.8	7.7	12.8

ANALYSIS- ANOVA test for readings between the groups

ANOVA						
		Sum of Squares	df	Mean Square	F	Sig.
After 10 days of induction	Between Groups	127.144	4	31.786	31.368	.000
	Within Groups	35.466	35	1.013		
	Total	162.610	39			
After 18 days	Between Groups	320.394	4	80.099	36.992	.000
	Within Groups	75.785	35	2.165		
	Total	396.179	39			

Table shows that after applying ANOVA test, there is significance difference after 10 days of induction of hyperuricemia and after 18 days of giving medicine between the groups with P value highly significant.

The result is represented in the graph shown below.



Tukey HSD test for Post Hoc analysis-

Multiple Comparisons						
Dependent Variable		(I) Group	(J) Group	Mean Difference (I-J)	Std. Error	Sig.
After 10 days of induction	Tukey HSD	Control Group	No treatment	-4.21250*	.50332	.000
			Allopurinol	-4.90000*	.50332	.000
			Urtica Urens 30	-4.41250*	.50332	.000
			Urtica Urens Q	-4.08750*	.50332	.000
		No treatment	Control Group	4.21250*	.50332	.000
			Allopurinol	-.68750	.50332	.653
			Urtica Urens 30	-.20000	.50332	.994
			Urtica Urens Q	.12500	.50332	.999
		Allopurinol	Control Group	4.90000*	.50332	.000
			No treatment	.68750	.50332	.653
			Urtica Urens 30	.48750	.50332	.867
			Urtica Urens Q	.81250	.50332	.499

		Urtica Urens 30	Control Group	4.41250*	.50332	.000
			No treatment	.20000	.50332	.994
			Allopurinol	-.48750	.50332	.867

			Urtica Urens Q	.32500	.50332	.966
		Urtica Urens Q	Control Group	4.08750*	.50332	.000
			No treatment	-.12500	.50332	.999
			Allopurinol	-.81250	.50332	.499
			Urtica Urens 30	-.32500	.50332	.966
	Dunnett t (2-sided)[b]	No treatment	Control Group	4.21250*	.50332	.000
		Allopurinol	Control Group	4.90000*	.50332	.000
		Urtica Urens 30	Control Group	4.41250*	.50332	.000
		Urtica Urens Q	Control Group	4.08750*	.50332	.000
After 18 days of treatment	Tukey HSD	Control Group	No treatment	-4.28750*	.73575	.000
			Allopurinol	4.61250*	.73575	.000
			Urtica Urens 30	.86250	.73575	.767
			Urtica Urens Q	.28750	.73575	.995
		No treatment	Control Group	4.28750*	.73575	.000
			Allopurinol	8.90000*	.73575	.000
			Urtica Urens 30	5.15000*	.73575	.000
			Urtica Urens Q	4.57500*	.73575	.000
		Allopurinol	Control Group	-4.61250*	.73575	.000
			No treatment	-8.90000*	.73575	.000
			Urtica Urens 30	-3.75000*	.73575	.000

			Urtica Urens Q	-4.32500*	.73575	.000
		Urtica Urens 30	Control Group	-.86250	.73575	.767
			No treatment	-5.15000*	.73575	.000
			Allopurinol	3.75000*	.73575	.000
			Urtica Urens Q	-.57500	.73575	.934
		Urtica Urens Q	Control Group	-.28750	.73575	.995
			No treatment	-4.57500*	.73575	.000
			Allopurinol	4.32500*	.73575	.000
			Urtica Urens 30	.57500	.73575	.934
	Dunnett t (2-sided)[b]	No treatment	Control Group	4.28750*	.73575	.000
		Allopurinol	Control Group	-4.61250*	.73575	.000
		Urtica Urens 30	Control Group	-.86250	.73575	.594
		Urtica Urens Q	Control Group	-.28750	.73575	.985

Table shows that after applying Tukey test, there is significance difference after 10 days of induction between the control group and all other groups. Dunnett test is applied because we have a control group.

After administration of drugs for 8 days i.e after total 18 days, Tukey test shows that

1. Statistical significance is observed between control group and allopurinol group as well as between control group and no treatment group.
2. Statistical difference is observed between no treatment and allopurinol group, Urtica Urens and no treatment group.
3. Statistical difference is observed between allopurinol and Urtica Urens group.
4. Dunnett test shows that no treatment group and allopurinol group against control group has statistical significant result.
5. As per the observation and the results analysed from the data, there is significant difference between the groups after 18 days of treatment.
6. When compared between each groups, Urtica urens 30 shows significant difference against no treatment and allopurional group. Also, Urtica Urens Q shows significant difference against no treatment and allopurional group.
7. If compared to allopurinol group, there is significant difference between allopurinol and each group i.e. control group, no treatment, Urtica Urens 30 and Urtica Urens Q group.

CONCLUSION

The present study evaluated the effects of *Urtica urens Q* and *30C* in pyrazinamide induced hyperuricemic rat model. The serum UA levels in all the groups significantly increased when compared to the normal control group, showing that the hyperuricemia rat model was successfully established. When the pathways that control uric acid are disturbed, hyperuricemia results. This study's experimental model for assessing antihyperuricemic action looked at pharmacological action on one symptom that is allopathically indicated (e.g. urate reduction). Allopurinol affects urate transporters and Cl/urate transporters, whereas homoeopathic medicines are thought to control pathological changes because the phenomenon is viewed as an expression of the dynamic vital force of the body.

After analyzing data with the help of ANOVA, Tukey's and Dunnetts test ,it was inferred that both Urtica Urens Q and 30C were potent in controlling SUA. Although in comparison to allopurinol the effect of homoeopathic medicine Urtica urens was less but it can be concluded that homeopathic medicines can also help in controlling serum uric acid levels.The goal of this study was to control serum uric acid levels, which was accomplished by using the homoeopathic drug Urtica urens.

AUTHOR CONTRIBUTIONS-

CONCEPTUALIZATION- Dr.Smriti Verma, Dr. Sameer S. Nadgauda
METHODOLOGY- Dr. Pallavi Khatavkar
DATA CURATION- Linpadmaja Thakur
WRITING: ORIGINAL DRAFT- Dr. Smriti Verma
WRITING: REVIEW AND EDITING- Dr. Sameer Nadgauda

CONFLICT OF INTEREST

The authors have no conflict of interest to disclose**.**

FUNDING-

The study was fully self- funded.

ETHICAL STATEMENT-

This study was carried out after the approval of IAEC(INSTITUTIONAL ANIMAL ETHICAL COMMITTEE) / CPCSEA approval with registration number BVDUMC/3056/2022/003/024.

DATA AVAILABILITY-

Datasets analysed during the study can be obtained from the institution.

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