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## RESEARCH ARTICLE

### TREATMENT OF GOUT FROM NUTRITIONAL VALUES & DIFFERENT PLANT EXTRACTED COMPOUNDS

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#### ABSTRACT

Gout was treated by bottle gourd and Ficus Palmata specie. 24 rats were divided into 4 groups: control, model, bottle gourd treated and Ficus Palmata treated. Gout is induced by direct oral dose of uric acid as 30mg/kg body weight. Bottle gourd and Ficus Palmata extracts were prepared in ethanol separately and given to rats as 80mg/kg body weight. After 6 weeks of treatment behavioral activities were monitored. After decapitation, biochemical tests were determined by calcium, magnesium, phosphorus and serum uric acid. Locomotor and stimulator activities significantly increases in bottle gourd and Ficus Palmata treated group, anxiety decreases while, recognition memory of both groups significantly increases as compare to model but decreases as compare to control. Bottle gourd and Ficus Palmata rats showed good effects to enhance magnesium level in blood, significantly reduces the serum uric acid level and maintained calcium phosphorus balance in blood. P-value <0.05 was statistically significant.

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## INTRODUCTION

Gout is a painful and common type of arthritis. (Kuo, 2017) The excess of uric acid in blood results in hyperuricemia which lead to develop gouty arthritis in most of the people. (Vargas-Santos and Neogi, 2017) Gout can be categorized as either primary or secondary. Primary gout is a result of increased production of purine and decreased renal clearance of uric acid. Secondary gout is an acquired disorder resulting from such causes as medication side effects such as diuretics (water pills), multiple myeloma, myeloproliferative disorders, renal disease, hypothyroidism, psoriasis, and lead poisoning, all of which can lead to a high uric acid level in the body. (Schirinzzi *et al.*, 2017) Gout can be cured by using different drugs like allopurinol, naproxen, corticosteroid etc. which also produces harmful effects on other organs in many cases. (Burns and Wortmann, 2011) Medicines for gout attacks are aimed at relieving pain and reducing inflammation. Other medicines are also the class of nonsteroidal anti-inflammatory drugs (NSAIDs), Colchicine and Corticosteroids. (Harris *et al.*, 1999) These medicines may be combined to treat a gout attack. Uric acid level is only mildly affected by diet. Therefore, dietary therapy does not play a large role in preventing gout. ([www.umm.edu/health/medical/reports/articles/gout](http://www.umm.edu/health/medical/reports/articles/gout)) Still, avoiding or reducing foods rich in purine can help. Bottle gourd or calabash is a delicately

flavored vegetable. It is considered as one of the chief culinary vegetables in many tropical and temperate regions around the world. (Tyagi *et al.*) Bottle gourd is one of the least calorie vegetable, providing just 14 calories per 100 g. It is also rich in Vit.C used in cancer therapy. The vegetables are a moderate source of thiamin, niacin (vitamin B-3), pantothenic acid (vitamin B-5), pyridoxine (vitamin B-6) and minerals such as calcium, iron, zinc, potassium, manganese and magnesium. (Lopes *et al.*, 2017) It is one of the vegetable also recommended by the dieticians in weight-control programs. Ficus palmata Forsk commonly known as 'Fegra Fig' belongs to the family of Moraceae or Urticaceae. (Christenhusz and Byng, 2016) Fegra plants are of common occurrence at places up to 1,000 meters above the sea-level, occasionally found in the forests, but grow well in villages, wastelands and fields, etc. The whole fruit, along with the seeds, is edible. The fruits are juicy, containing 45.2% extractable juice and 80.5% moisture. The total content of soluble solids of the juice is 12.1%, about 6% total sugars, the pectin content is 0.2%. It contains only 3.3 mg of vitamin C per 100 g of pulp and mineral elements like phosphorus, potassium, calcium, magnesium and iron were found to be 0.034, 0.296, 0.071, 0.076 and 0.004% respectively. (Yogesh Joshi *et al.*, 2014) They are principally used in diet for the treatment of constipation and diseases of the lungs and bladder. The sap is also used in the treatment of warts. Ficus palmata fruit is used in various disease e.g. gastrointestinal, hypoglycemic, antitumor, anti-ulcer, anti-diabetic, lipid lowering and antifungal activities ([www.pharmasm.com/pdf\\_files/Final%20Proceeding%20NPSS.pdf](http://www.pharmasm.com/pdf_files/Final%20Proceeding%20NPSS.pdf)). Therefore, the aim

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of the present study is the treatment of gout from nutritional values & different plant extracted compounds.

## MATERIALS AND METHODS

Locally bred male Albino Wistar rats weighing about 180 to 200gm on arrival purchased from animal house, research institute of Agha Khan University Karachi Pakistan were used throughout the experiments. The rats were housed individually in specially designed cages with saw dust cover floor in a quiet room, with free access to cubes of standard rats' food and water for at least 3 to 4 days before starting the experiment so that rats could adapt them to the new environment. In this study 24 rats were used, divided into 4 groups containing 6 rats: control, model, test 1 and test 2. Control was given as 0.9% saline solution. Except control all rats were given uric acid as 30mg/kg body weight for inducing arthritis (Gout) for 3 weeks. After 3 weeks model was not treated but test 1 was treated with Bottle Gourd extract and test 2 with Ficus Palmata fruit extract. Extract was given orally to both groups as 80mg/kg body weight.

### Preparation of saline

For the preparation of saline 0.9gm of NaCl was taken and make up the volume up to 100ml of water.

### Preparation of plant extracts

All the plant compounds prepared individually by kept in 100% absolute ethanol for one week, residues were settled down on the bottom of flask from which all the ethanol was removed and added this to 0.9% saline solution to further dissolve.

### Handling

The oral administration of drugs to experimental rats require extensive handling and it is recommended that prior to experimental manipulation, such animals should be handled on a regular basis in non-life threatening situations like weighing, petting, giving food treats. This makes the animals respond positively to handling and learn to recognize individuals. To remove the rat from cage, it is picked up by the tail close to the base and placed on the flat surface of a laboratory bench. While still holding to the tail with the right thumb and forefinger, the scruff of the animal is reached for with your thumb and forefinger, positioning them firmly on either side of the animal's head at the level of the mandible. Simultaneously, the rest finger and palm of the left hand are used to firmly press the thorax or trunk down against the flat surface of the bench. There after the scruff (the loose skin over the neck) is gathered between the thumb and the forefinger and used to lift up the animal by the scruff. The tail may be held either firmly against the trunk with the fifth finger of the left hand or left hanging free. When held firmly this way, the rat is restrained and the esophagus is as straight as possible.

### Behavioral techniques

After one week of plant extracted compounds administration behavioral activities were monitored. The open field apparatus for locomotor activity was used in this experiment consist of a square area (76\*76cm) with walls 42cm high and floor divided into 25 equal squares. The experiment was performed under

day light, in a very quiet room to avoid any noise effect. An animal taken out from the cage and placed in the center square of the apparatus, rats move from the center square, crossing with all four paws, corner sitting, grooming, gnawing, these all activities scored for 5 minutes. Home cage (26\*26\*26) with saw dust cover floor was used as the no of cage crossing and increasing intensities of grooming and gnawing were monitored. Anxiety of rats was monitored with the help of Light and Dark box which consisted of two compartments. Both the compartments were of same size (26\*26\*26 cm), with a door (12 cm× 12 cm) between the compartments. One compartment was made up of black plastic walls while other with transparent plastic. Time spent in the light box was monitored for 5 minutes. The activity in this box was determined in a lighted place (360lux) using a 60W white light bulb. Novel object recognition test was used to assess recognition ability of rats. The apparatus used was an open field box (40×40×40 cm) made of gray painted wood. The floor was covered with saw dust. The objects to be discriminated were two similar transparent glasses filled with white cement (A1 and A2) and a metallic container of same size filled with white cement (new object, B). The test comprised of three phases; 1) Habituation phase, 2) Training phase and 3) Test phase. On the 1st day each rat was habituated to the open field box without any object for 15min. On the 2nd day each rat was placed in the open field for 15 min and allowed to freely explore two identical objects (two glasses filled with cement). On the 3rd day, during the test phase, one old object used during the training session was replaced by novel object (B) and rat was left to explore the objects for 5min. Both objects presented during the test session were different in texture, color and size. Recognition index was calculated by the ratio  $TB/(TA+TB)$  [TA=Time spent exploring the familiar object A; TB=Time spent exploring the novel object B].

### Decapitation of rats

After 3 weeks of treatment rats were decapitated, by a specialized kit for dissection careful removal of fur under the neck, the jugular veins were exposed. The veins were then punctured with a clean and sharp syringe and the blood collected in the gel containing tube and then tube placed in an incubator for 30 minutes and the serum collected after centrifugation on a bench centrifuge at 300g for 15 min. Blood also collected in an anticoagulant containing tube to get plasma.

### Diagnostic analyzer

Roche Hitachi 902 analyzer and Sysmex XP-100 analyzer were used for biochemical and hematological tests.

### Statistical analysis

SPSS v.20 was used for statistical analysis. Results were represented as mean,  $\pm$  SD (n=6) significant difference by Tukey HSD and Duncan test \*  $P < 0.05$ , considered statistically significant level from C, M, T1 and T2 following one-way ANOVA.

## RESULTS

Fig 1(a) Effects of Bottle Gourd and Ficus Palmata treatment on open field behavior shows effects on control, model and test

groups of rats. Statically analyzed by one-way ANOVA (df4, 23) ( $F=8.73511$ ) ( $*p<0.002$ ) shows that after 6 weeks of treatment motor activity were markedly increased in test 1 group of rats as compare to control and model group of rats, but motor activity of test 2 group of rats was minor decreased as compare to control but markedly increase as compare to model group. (b) Home Cage activity statically analyzed by one-way ANOVA (df4,23) ( $F=17.4359$ ) ( $*p<0.01$ ) shows that after treatment stimulator activity were markedly increased in both the tests groups of rats as compare to control and model group. Fig 1 (c) Light and Dark activity statically analyzed by one-way ANOVA (df4,23) ( $F=3.99726$ ) ( $*p<0.04$ ) shows that anxiety significantly decrease as compare to model, but slightly decreases to control in both test groups. (d) Entries in light portion statically analyzed by one-way ANOVA (df4,11) ( $F=5.54517$ ) ( $*P<0.003$ ) shows that anxiety markedly decreases in tests groups as compare to control and model group of rats. Fig 1(e) Novel Object Activity statically analyzed by one-way ANOVA(df4,11) ( $F=7.88701$ ) ( $*p<0.04$ ) shows that

recognition memory of both test groups was decreased as compare to control but increases as compare to model. Fig 2 (a) Statically analyzed by one-way ANOVA (df4,23) ( $F=3.4372$ ) ( $p<0.05$ ) shows that magnesium level of both tests groups increases significantly as compare to model group, and slightly increases as compare to control group.(b) Statically analyzed by one-way ANOVA (df4,11) ( $F=4.44517$ ) ( $*P<0.001$ ) shows that Calcium level of both tests groups slightly increases as compare to control and model group, which are in normal range. Fig 2(c) Statically analyzed by one-way ANOVA(df4,11) ( $F=6.8510$ ) ( $*p<0.03$ ) shows that phosphorus level of both tests groups are slightly decreases as compare to control and model groups, but all groups were observed in normal ranges.(d) Statically analyzed by one-way ANOVA (df4,11) ( $F=5.3410$ ) ( $*p<0.04$ ) shows that Uric acid level of test groups specially Bottle Gourd treated group markedly decreases as compare to model group, and slightly decreases as compare to control group.

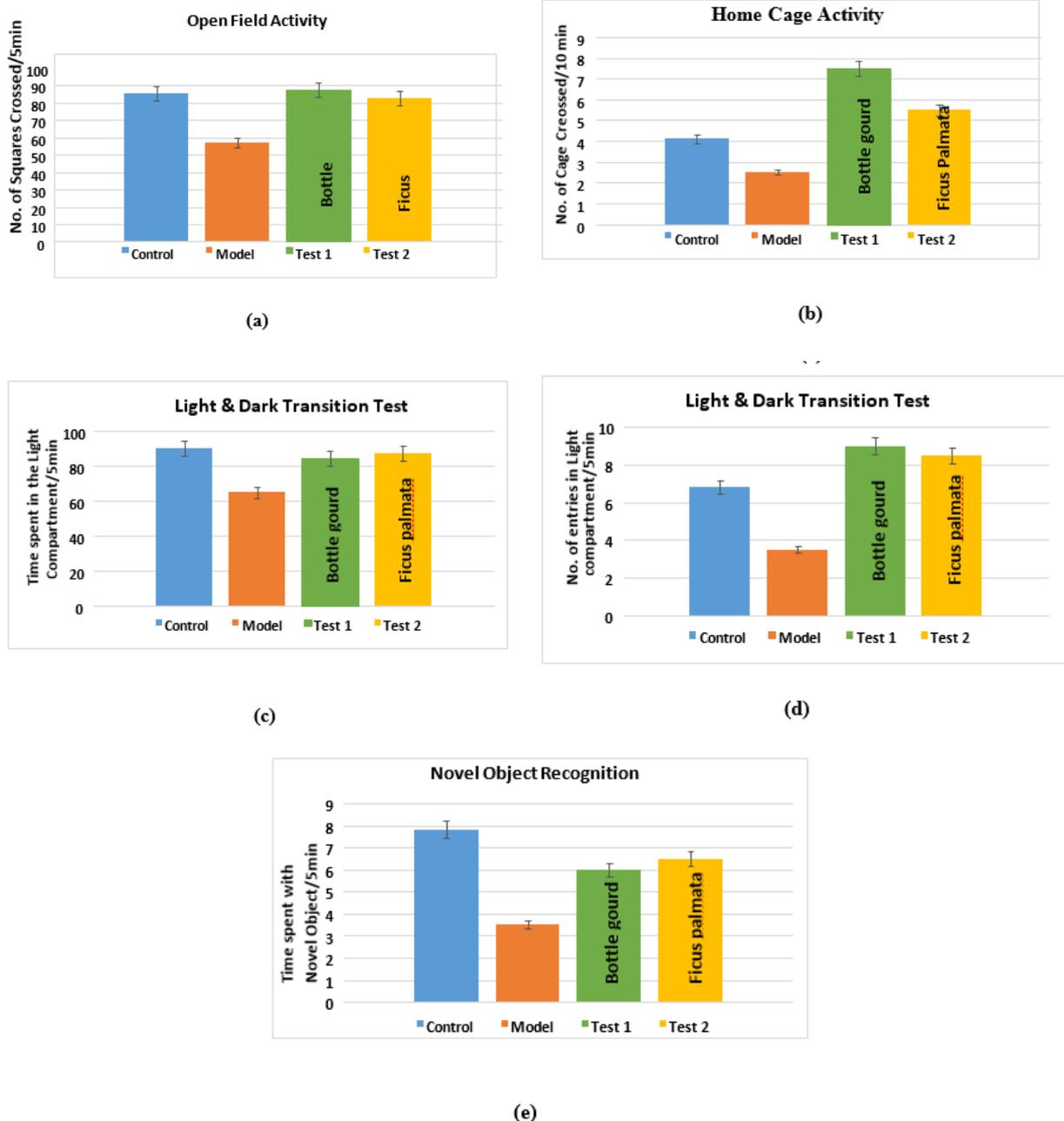


Fig. 1. Comparison of Behavioral Studies in Control, Model, Bottle Gourd and Ficus Palmata treated rats

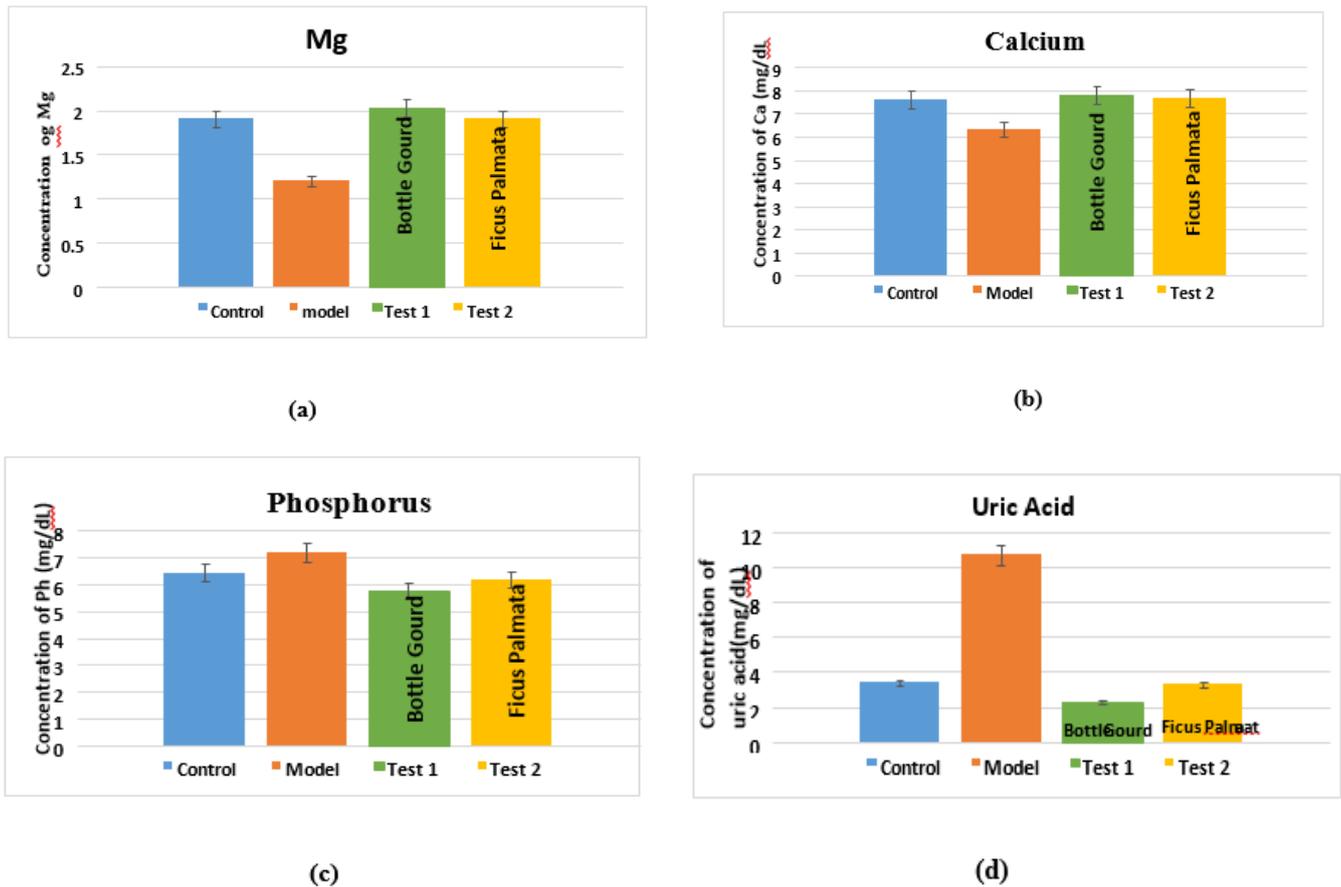


Fig. 2. Comparison of Biochemical Studies in Control, Model, Bottle Gourd and Ficus Palmata treated rats

Figure 1: Behavioral studies. Results were represented as mean,  $\pm$  SD (n=6) significant difference by student t-test  $p < 0.05$  level from C, M, T1 and T2 following one-way ANOVA. (a) open field activity (no. of square crossing) (b) Home cage activity (no. of cage crossed) (c) light and dark activity (time in second) (d) light and dark activity (entries in light portion) (e) Novel object recognition.

Figure 2: Biochemical Studies. Results were represented as mean  $\pm$  SD (n=6) significant difference by student t test  $p < 0.05$  level from C, M, T1 and T2 following one-way ANOVA. (a) Effect of Magnesium (b) Effect of Calcium (c) Effect of Phosphorus (d) Effect of uric acid.

## DISCUSSION

The Open Field Activity was performed to determine locomotor activity in rats, the most direct evidence that activation of noradrenaline receptors can produce locomotor activity comes from intraventricular infusion experiments. (<https://books.google.com.pk/books?isbn=1468431803> Leslie Iversen) Present study shows that orally administration of Bottle Gourd and Ficus Palmata extracts gradually increases the locomotor activity in rats, by activation of noradrenaline receptors. Home cage activity specific for simulator activity living in their home freely. These activities were monitored as the number of cage crossing, increasing intensities of grooming and gnawing. The present study shows that after Bottle Gourd and Ficus Palmata treatment simulator activity of treated rats significantly increased as compare to control and model. Simulator activities are associated with dopamine levels in

brain. Dopamine is an important neurotransmitter in the brain with several potential functions. (Larson, Garret *et al.*, 2017) Increase dopamine levels in brain increase stimulation. Light and dark activity is specific for anxiety. By using light and dark box it can be determined that whether the drug or any plant compound is anxiolytic or anxiogenic. Anxiety associated with different types of neurotransmitters in brain such as GABA, serotonin, epinephrine, dopamine etc. (Ray *et al.*, 2017) Serotonin appears to be specifically important in feelings of well-being, and deficiencies are highly related to anxiety and depression. Present studies show that after treatment of Bottle Gourd and Ficus Palmata, anxiety of treated rats was decreased as compare to model but slightly increases as compare to control. Recognition memory is a subcategory of declarative memory. (Martin *et al.*, 2017) Essentially, recognition memory is the ability to recognize previously encountered events, objects, or people. When the previously experienced event is re-experienced, this environmental content is matched to stored memory representations, eliciting matching signals. Present study shows that after treatment of Bottle Gourd and Ficus Palmata treated groups the recognition memory decreases as compare to control because of induction of uric acid, but the recognition memory of tests groups increases as compare to model by enhancing the dopaminergic neuronal activity. Magnesium level of tests groups increases significantly as compare to model group, and slightly increases as compare to control group. Previously, it was known that magnesium is an alkaline mineral, it maintains the blood circulation smoothly which helps to prevent the crystallization of uric acid in joints, also helps to prevent other diseases like cardiovascular disorder, osteoporosis, prevents migraine headache and

regulates calcium potassium and sodium level in body. (Ismail) Calcium level of test groups slightly increases as compare to control and model group, which are in normal range. Calcium is important to maintain strong bones, calcium deficiency causes osteoporosis, osteopenia, but if, the level of calcium is high in blood can lead to form calcium pyrophosphate crystals (CPPC) in joints and causes pseudogout. (Huo *et al.*, 2016) Phosphorus level of test groups are slightly decreases as compare to control and model groups, but all groups are in normal ranges. Uric acid level of test groups specially Bottle Gourd treated group markedly decreases as compare to model group, and slightly decreases as compare to control group. This significant decrease in uric acid is due to vitamin Curicosuria effects, this effect reduces the reabsorption of uric acid at the proximal tubules of kidneys and enhance the excretion of uric acid through urine. Gout is an autoinflammatory disease associated with increased blood levels of urate due to deposition of monosodium urate crystals in and around joints. (Kou *et al.*, 2015) Over recent decades, the prevalence of hyperuricemia is steadily increasing and gout is becoming one of the most common causes of inflammatory arthritis. In the present study, gouty arthritis rats treated with Bottle Gourd and Ficus Palmata specie which shows positive results on behavioral and biochemical tests.

### Conclusion

In conclusion antigout effects of Bottle Gourd and Ficus Palmata species were observed in rats with uric acid induced gouty arthritis in which Bottle Gourd and Ficus Palmata species reduce the serum uric acid level by neutralizes the uric acid and uric acid crystals in and around the joints. In addition, it reduces serum uric acid through its uricosuria effect. In last, both bottle gourd and Ficus Palmata specie contain vitamins, minerals and dietary fibers that keep the body well nourished, and prevent to cause and cure hyperuricemia and gout.

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