EFFECT OF DIABETIC CONTROL ON SERUM URIC ACID LEVELS

THESIS

SUBMITTED IN PARTIAL FULFILMENT

FOR THE MASTER DEGREE IN

MEDICINE

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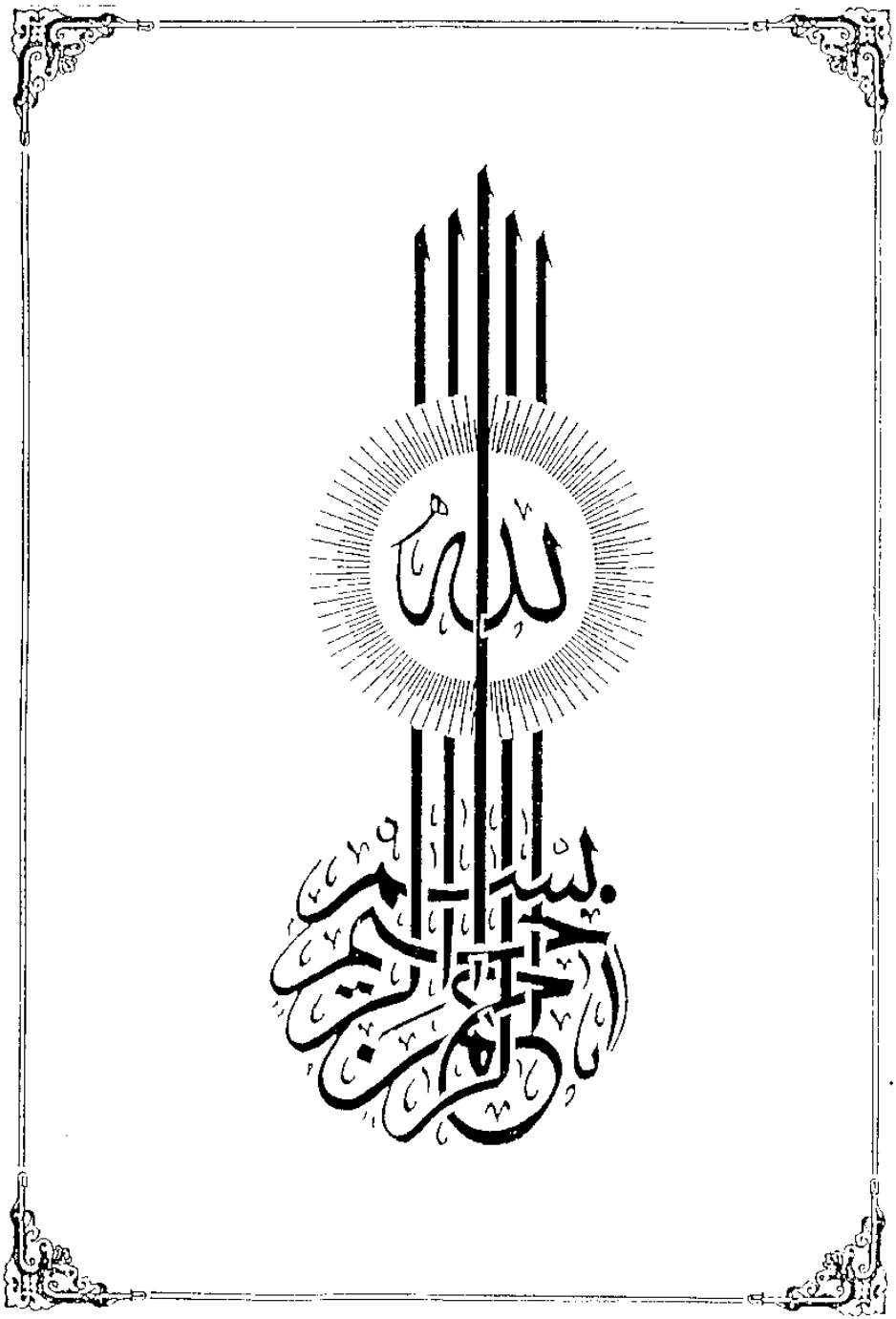

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INTRODUCTION AND THE AIM OF WORK

In view of the incidence of hyperuricemia in diabetic patients (Aldsberg, 1949),and in the prediabetics (Herman,et al,1973; 1976; 1982)

Further evidence for interrelationship between, uric acid metabolism and/or gout, with diabetes mellitus; was sought in studying the effect of diabetic control on elevated serum uric acid in 20 diabetic patients, insulin dependent, and non insulin dependent variants.

review of literature

- CHEMISTRY OF URIC ACID :

. Structure and oxidation products:

The chemical structure of uric acid was shown to be 2,6,8 trioxypurine (Fig. 1). It is the most highly oxidized member of the purine class of compounds.

Further oxidation of uric acid in neutral or alkaline solution results in disruption of the purine ring , with removal of carbon-6 as carbon dioxide, and the formation of allantoin and other degradation products.

Alloxan is the product of uric acid oxidation in an acid solution. With the addition of ammonia it forms ammonium purpurate, the purplish red substance responsible for the well known, murexide test for uric acid . It is produced by heating uric acid, moistened with nitric acid, and adding few drops of ammonium hydroxide.

Other colorimetric procidures for quantitative determination of uric acid are based on the reducing properties of uric acid.

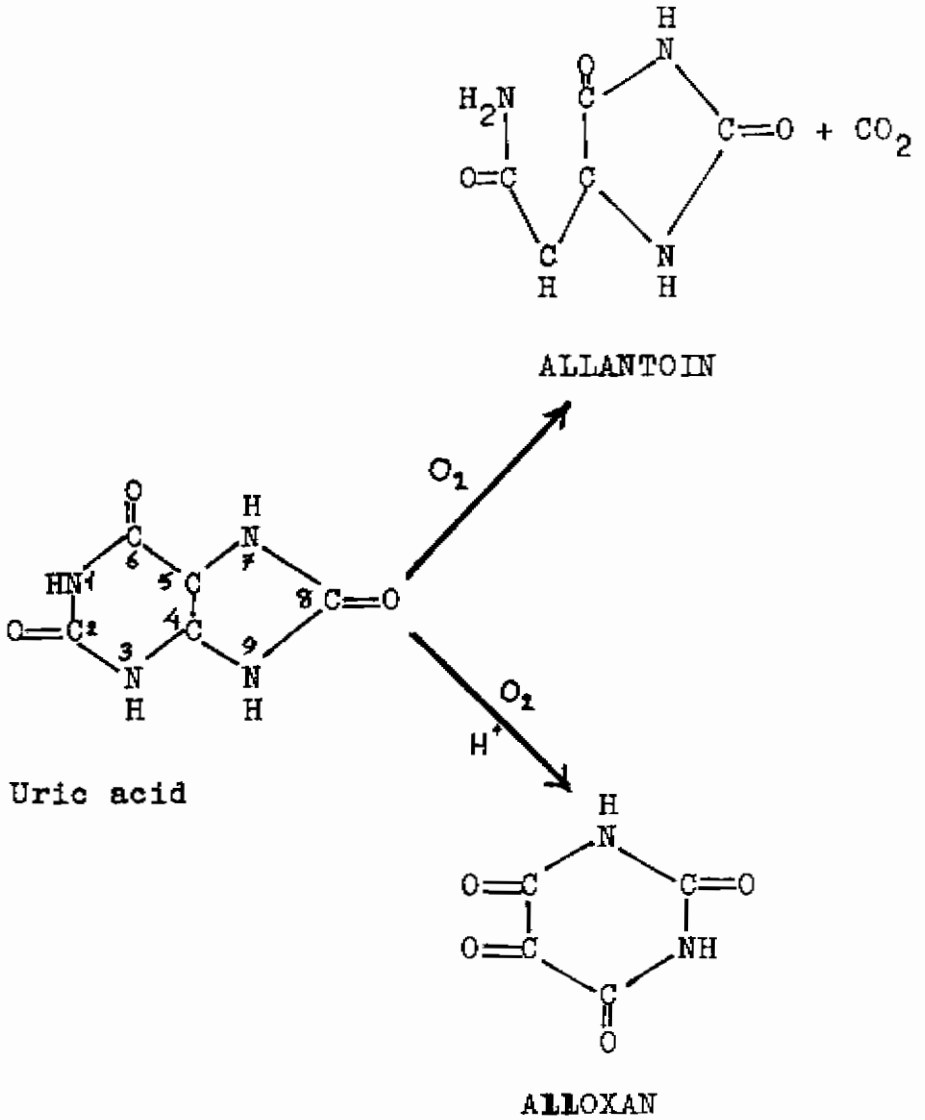


Figure (1) :

The oxidation of uric acid. The oxidation to allantoin is catalysed by the enzyme uricase which is missing in the human species. Alloxan is a product of the chemical oxidation of uric acid at acid pH.

(Seegmiller, et al., : N.Engl.J.Med.,1963,268:712.

. Physical properties:

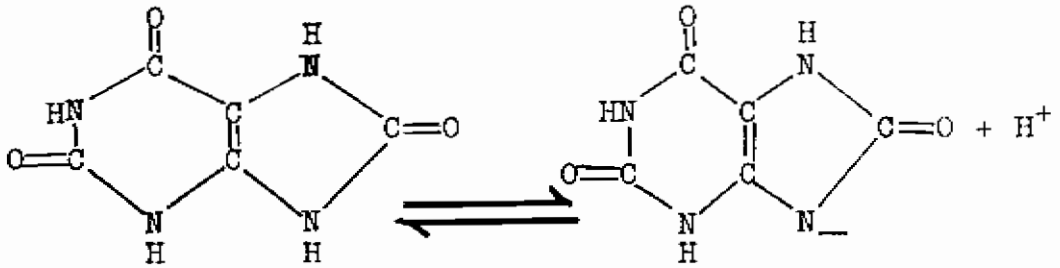
The property of the molecule responsible for the major clinical manifestations of gouty arthritis is the limited solubility of both the free uric acid and its monosodium salt (Fig. 2).

The weakly acidic nature of uric acid is due to the ionization of hydrogen atoms at position 9 and position 3 of the molecule.(Bergmann, et al., 1955).

The hydrogen atoms of position 1, and 7, do not ionize significantly. Cosequently, in body fluids at pH. 7.4, uric acid exists almost entirely as the monovalent urate ion.

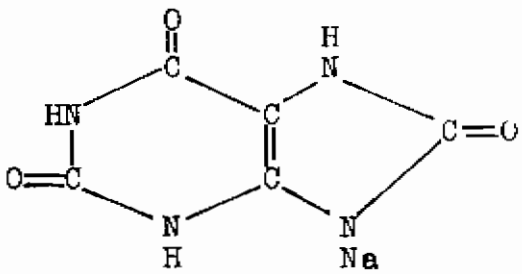
Solubility in water :-

Since the principal cation of extracellular fluids is sodium, the solubility properties of uric acid within the body fluids will be predominantly those of monosodium urate monohydrate, that accumulates in tophi of gouty patients.



Uric acid ⇌ Urate ion + H^+

Solubility 6.5mg/100ml H_2O — 120mg/100 ml H_2O



Monosodium urate
6.4 mg/100 ml /serum

Fig (2) :

Physical chemistry of uric acid. The limited solubility of uric acid and its salts is responsible for the major clinical manifestations of gout. (Bergmann, 1955)

The salt has a solubility in water of 120 mg./ 100 ml , which is substantially greater than the solubility in water of free uric acid (6.5 mg./ 100 ml).

Serum should be saturated with urate at a concentration of 6.4 mg./ 100 ml.(Peters, et al., 1946).

Crystalline forms :-

Monosodium urate occurs as a monohydrate, and in crystal forms that are characteristically needle or bar shaped. Very fine crystals that appear amorphous , are produced by rapid pricipitation.

Free uric acid, however, crystallizes in an orthorhombic crystal system, forming rhombic plates from pure solutions. It also crystallizes from urine with pigments in a variety of forms, most commonly as reddish brown or amber crystals.

Crystals of both monosodium urate and uric acid show special fringence when examined under polarised light. This property permits the ready detection of urate crystals in synovial fluid or tissue, and thus