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Urate as an endogenous antioxidant

by

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Abbreviations

UH_3 – Uric acid

AscH - Ascorbate

$ONOO^-$ - Peroxynitrite

$ROO^\bullet$ - Peroxyl radical

1. Contents

2. Abstract

Uric acid plays different roles in human body. This review focuses on function of uric acid as an endogenous antioxidant. Uric acid is able to react with different free radicals forming relatively stable urate radical and thus stopping radical reactions. Uric acid is thought to be involved in pathogenesis of different diseases. Main methods of detection of uric acid are also discussed.

3. Introduction

Uric acid is a naturally occurring product of purine metabolism, which plays different roles in human body.

Uric acid is present in plasma in relatively high concentrations: in men 302±60 uM; in women, 234±52 uM [1]. Humans have no enzyme to further oxidase uric acid, so an access of uric acid is excreted by kidney.

In normal condition the rate of synthesis of uric acid is equal the rate of its consumption and excretion (Fig. 1)

Increase of the concentration of uric acid could cause gout (Fig. 2). In this disease urates are deposited in joints (mainly in metacarpal) in needle-like form, causing terrible pain and changing shape of the joint.

However uric acid has a lot of beneficial functions in our body. It was shown to be a very important endogenous antioxidant. This paper will focus on antioxidative properties of uric acid

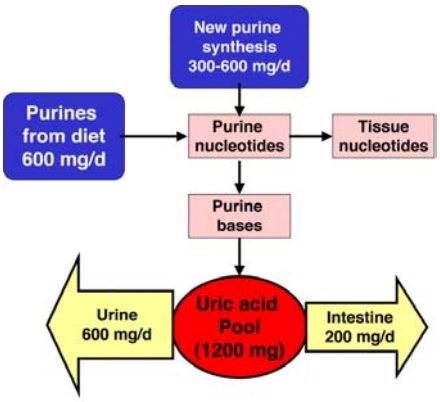
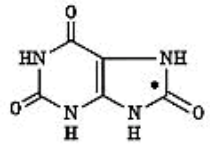


Fig 1. Synthesis of uric acid [from online sources]

Fig 2. Gout arthritis [from online sources]

4. Chemistry of uric acid

Uric acid, M_r 168.1, white odorless, tasteless crystals; one gram dissolves in about 15,000 parts of cold water [3].



(1)

Uric acid is an end product of purine catabolism (Fig. 3)

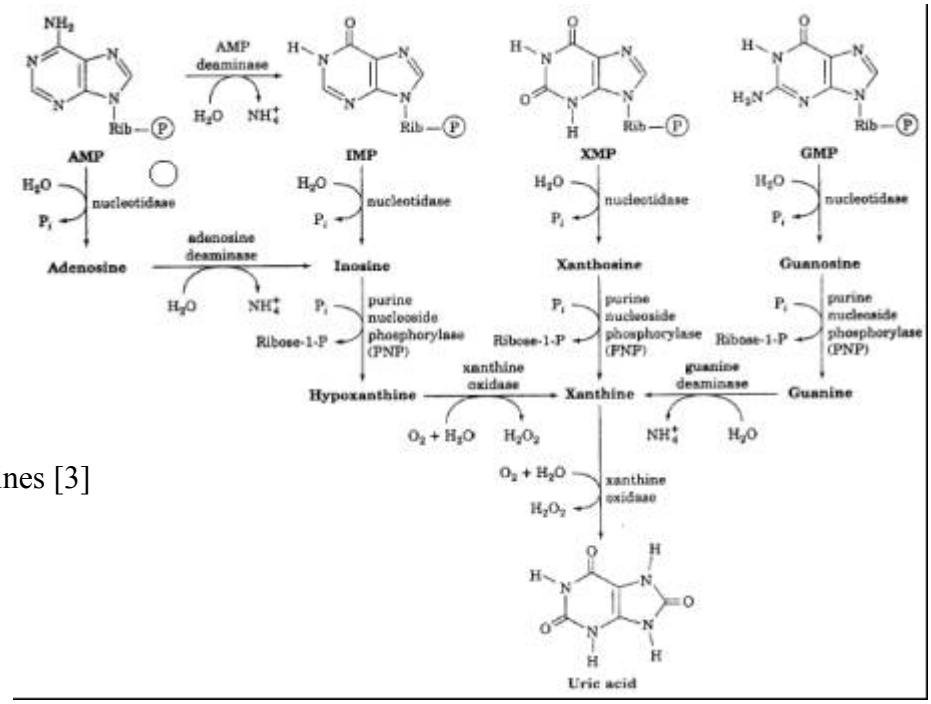
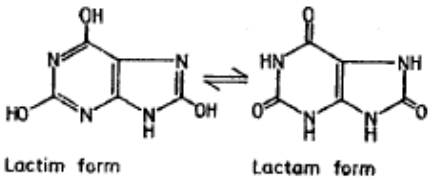


Fig. 3. Catabolism of purines [3]

Uric acid exists in two tautomeric forms [3]

(2)



Uric acid has the following acid-base equilibria [1]

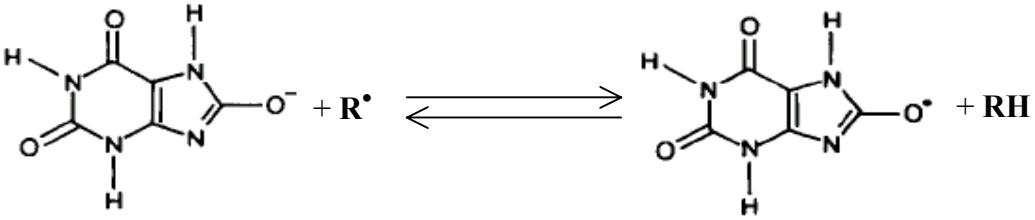
$$UH_3 \xrightleftharpoons{} UH_2^- \xrightleftharpoons{pK_{a2} = 9.8} UH^{2-}$$

(3)

5. Antioxidant properties of uric acid

Urate radical $^{\cdot}UH^{-}$ doesn't react with oxygen to give another peroxy radical, which makes urate a good oxidant.

A. Reaction of uric acid with radicals [1]



(4)

B. Uric acid reacts with peroxy radical [1]

$$ROO^{\bullet} + UH_2^{-} \longrightarrow ROO^{-} + UH^{\bullet -} + H^{+} \quad (5)$$

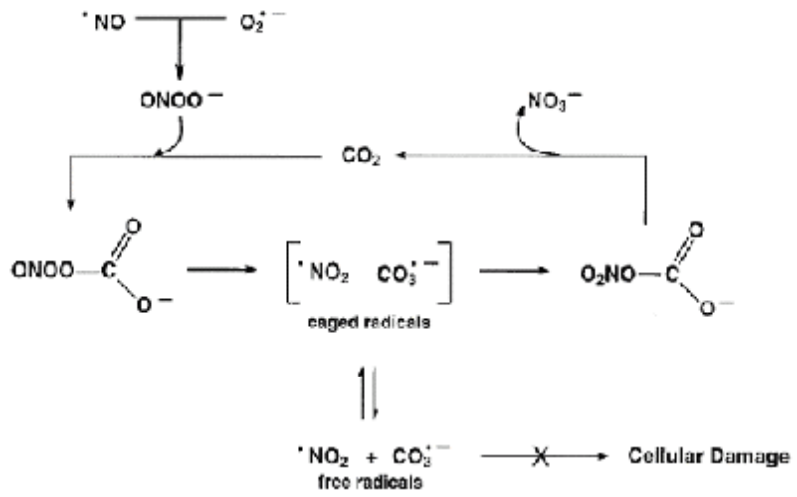
C. Reaction with ascorbate

The redox potential of uric acid at pH 7, $E_7 = 0.59$ V is considerably higher than the redox potential of ascorbate, E_7=0.28 V [1]. Ascorbate was shown to donate electron to ascorbate and thus prevent its deleterious effect on some enzymes [1].

$$UH^{\bullet -} + AscH^{-} \longrightarrow UH_2^{-} + AscH^{\bullet -} \quad (6)$$

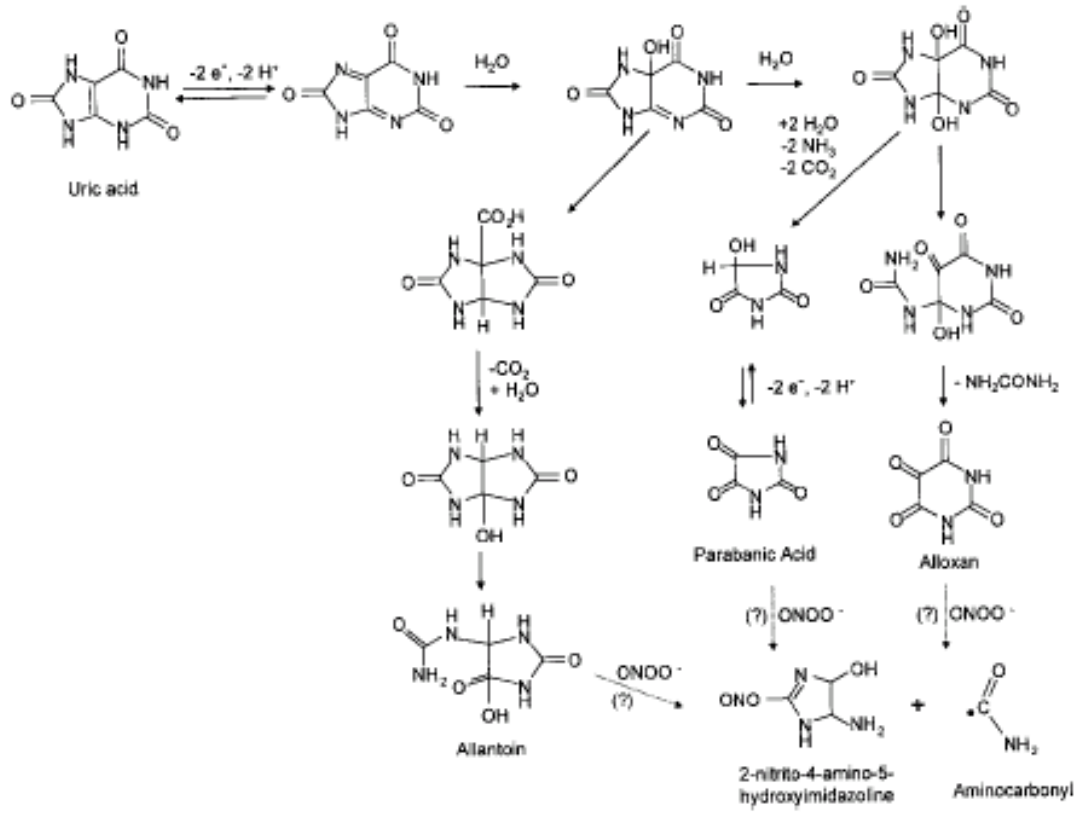
D. Reaction with peroxinitrite.

Peroxinitrite is on of the most important reactive species in human body [2].



(7)

Urate is able to protect from some of peroxinitrite-mediated cytotoxic effects [2]. Urate was shown to react with different reactive intermediates produced during peroxinitrite decomposition [2]. These intermediate are otherwise responsible for nitration of tyrosine residues [2].



(8)

E. Reaction with $NO_2^{\bullet}$

Uric acid reacts with •NO_2 and inactivates it [1]:

$$NO_2^{\bullet} + UH_2^- \longrightarrow NO_2^- + H^+ \quad (9)$$

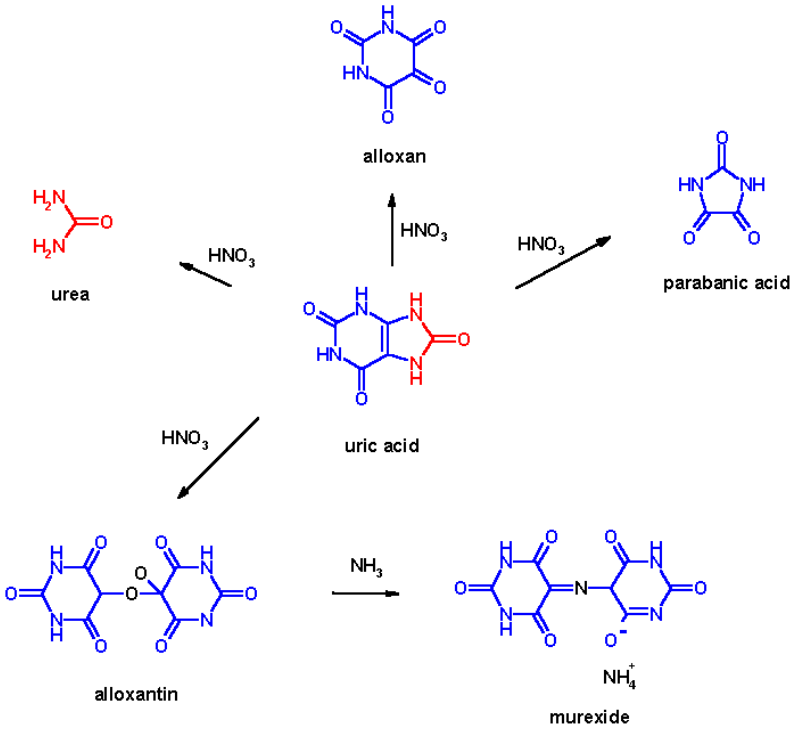
F. Repair of oxidative damage to DNA bases.

Uric acid was shown to reduce oxidative damage of DNA. One of the most important reaction of uric acid is reaction with guanyl radical

$$R\text{-}G^{\bullet}(\text{-}H) + UH_2^- \longrightarrow R\text{-}G + UH^{\bullet -} \quad (10)$$

6. Detection of uric acid

A common test for the presence of the acid in urine depends upon the formation of murexide (an ammonium salt), which is an intense reddish purple. Nitric acid is added to the urine, which is then evaporated. If uric acid is present, murexide is formed when ammonia is added to the residue.



(11)

7. Conclusions

Uric acid plays different roles in human body. Being an endogenous antioxidant its able to protect human body from different reactions involving free radicals. Protective role of uric acid was shown in

different diseases. These findings allow us to consider uric acid as a perspective diagnostic marker and therapeutical tool.

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