8. Pharmacology and Biochemistry

1. MeSH Pharmacological Classification

**Dermatologic Agents**

Drugs used to treat or prevent skin disorders or for the routine care of skin. See a list of PubChem compounds matching this category.

2. Absorption, Distribution and Excretion

Allantoin administered to dogs orally as solid or solution was excreted in the urine to an extent of between 35 and 92 per cent within 24 hours. No allantoin was recovered either in urine or feces when given to rabbits orally. In man the recovery was 19 and 34 per cent in two individuals after massive doses. After intravenous administration recovery in the urine was practically quantitative with doses of 75 to 600 mgm. in the dog and in man. After 240 mgm. in man excretion continued for 72 hours. The results were similar after subcutaneous injection. Uric acid injected intravenously into a dog was converted into allantoin within two hours.

Young EG et al; J Pharmacol Exptl Ther 81 (1): 1-9 (1944)

3. Metabolism/Metabolites

In humans, uric acid is the final breakdown product of unwanted purine nucleotides. Uric acid is the last stage in purine degradation, because humans lack the enzyme uricase which converts uric acid into allantoin.

Abstract: PubMed

Hediger MA; Ther Umsch 61 (9): 541-5 (2004)

Allantoin in the presence of calcium ions has been implicated as a potential toxic agent in Reye’s syndrome. An investigation of possible alternative sources of allantoin in humans, which lack the enzyme uricase, has been initiated. Urate is a strong reducing agent which can reduce cytochrome c nonenzymatically, with the concomitant production of CO2 and H+. The stoichiometries measured for the various reactants and products were 1 urate:2 cytochrome c:1 H+:1 CO2. The initial reaction rate depended on the concentrations of both urate and cytochrome c, with reaction kinetics that were first order with respect to urate and second order with respect to cytochrome c. The participation of molecular oxygen in this reaction could not be detected. The pH and ionic strength optima for this reaction were determined to be 9.5-10.5 and 10(-5) M, respectively. Based on the results reported here, the following
balanced equation can be written: \text{urate}^{-2} + 2 \text{cytochrome c+3} + 2 \text{H}_2\text{O} \rightarrow \text{allantoin} + 2 \text{cytochrome c+2} + \text{H}^+ + \text{HCO}_3^- . /The authors/ propose that allantoin can be generated from the oxidation of \text{urate} by cytochrome c+3, and that this is a potential source of allantoin in human tissues.

**Abstract:** [PubMed](https://pubmed.ncbi.nlm.nih.gov)

Martens ME et al; Arch Biochem Biophys 252 (1):91-6 (1987) from HSDB

\text{Uric acid} is the main nitrogenous waste product in birds but it is also known to be a potent antioxidant. Hominoid primates and birds lack the enzyme \text{urate} oxidase, which oxidizes \text{uric acid} to allantoin. Consequently, the presence of allantoin in their plasma results from non-enzymatic oxidation.

**Abstract:** [PubMed](https://pubmed.ncbi.nlm.nih.gov)

Tsahar E et al; J Comp Physiol (B) 176 (7): 653-61 (2006) from HSDB

In most mammals \text{purine} degradation ultimately leads to the formation of allantoin. Humans lack the enzyme \text{uricase}, which catalyzes the conversion of \text{uric acid} to allantoin.

**Abstract:** [PubMed](https://pubmed.ncbi.nlm.nih.gov)


\text{Uric acid} ... acts as an antioxidant and /can/ react with biologically relevant oxidants to form allantoin. Therefore, measurement of allantoin in humans was proposed as a marker of oxidative stress. /The authors/ estimated allantoin in human plasma obtained from the patients with chronic renal failure before hemodialysis (n=30), patients with non-insulin dependent diabetes mellitus (n=30) and blood donors (n=30) ... . The preliminary reference range of allantoin in a group of blood donors is 4.76+/-2.99 umol/L. In the patients with chronic renal failure and the patients with non-insulin dependent diabetes mellitus ... allantoin levels in plasma of (27.1+/-13.8) umol/L and (11.08+/-5.90) umol/L, respectively/ were found/. It seems that allantoin is a possible indicator of free radical damage in vivo.

**Abstract:** [PubMed](https://pubmed.ncbi.nlm.nih.gov)


The concentrations of the major metabolites for \text{nitrogen} excretion and/or transport in maternal and fetal /rat/ blood and amniotic fluid during the last 2 days of gestation were investigated. \text{Alanine}, \text{glutamine}, \text{ammonia} and allantoin accumulated in amniotic fluid during late gestation. \text{Urea} concentrations increased in amniotic fluid though only during the last day of gestation, suggesting that \text{urea} is taken up by the mother through the amniotic membranes. \text{Glutamate} did not accumulate in amniotic fluid during late gestation although high concentrations of it were found in fetal blood in the same circumstances, suggesting the occurrence of a mechanism for preventing fetal \text{glutamate} disposal.

**Abstract:** [PubMed](https://pubmed.ncbi.nlm.nih.gov)


Fetal metabolic conversion and clearance of \text{hypoxanthine} was investigated in five pregnant rhesus monkeys. (14-C)\text{hypoxanthine} injected into the fetal
circulation disappeared rapidly and its metabolic break-down products uric acid and allantoin appeared in fetal plasma and erythrocytes. In amniotic fluid only hypoxanthine could be demonstrated. When (14-C)hypoxanthine was infused into the fetal circulation at a constant rate and metabolic conversion to uric acid and allantoin was inhibited with allopurinol, a constant level of hypoxanthine was obtained within 30 min. No uric acid or allantoin was demonstrated, but inosine monophosphate and adenine nucleotides appeared in the fetal erythrocytes...

Abstract: PubMed

... serum allantoin levels, oxidation products of uric acid, /were measured/ as a marker of free radical generation in rheumatoid arthritis. Fasting blood samples were obtained from 21 rheumatoid patients and 15 healthy controls. ... The mean allantoin and uric acid levels and ratios in the patient group were 22.1 +/- 11.3, 280.5 +/- 65.0 and 8.0 +/- 3.7 uM, while in the control group they were 13.6 +/- 6.3, 278.3 +/- 53.6 and 4.9 +/- 2.1 uM, respectively.

Abstract: PubMed

Urate oxidase (uricozyme) is an enzyme of non-human origin capable of oxidizing human uric acid to allantoin, a highly soluble product at renal tubule pH. /The authors/ report its efficacy in three patients with acute urate nephropathy due to tumor lysis in chronic lymphatic leukemia and high grade lymphoma. Two patients had an additional obstructive nephropathy due to ureretic urate crystals. An intravenous infusion (100 units/kg in 50 mL saline over 30 min) was given for between two and five consecutive days. All patients showed a rapid fall in serum urate levels with associated diuresis, correction of metabolic disturbance and full resolution of uremia within a week. The treatment was well tolerated and caused a rapid resolution of clinical symptoms in all cases.

Abstract: PubMed

The increased production of reactive oxygen species (ROS) from activated neutrophils in Behcet’s disease (BD) and recurrent aphthous stomatitis (RAS) may result in increased oxidative stress. Uric acid can react rapidly with neutrophil-derived ROS to form allantoin. The purpose of the study was to evaluate the serum levels of allantoin as a new marker of oxidative stress in BD compared with malondialdehyde (MDA) levels as a well-known marker. Blood samples were obtained from 23 BD patients, 22 RAS patients as positive controls, and 21 healthy controls. When compared to the healthy controls, /the authors/ found higher allantoin and MDA levels in the BD patients and higher MDA levels in the RAS patients. ... As allantoin is only a product of uric acid oxidation by reactive oxygen and nitrogen species, it may also be used as a marker of oxidative stress in BD.

Abstract: PubMed
Allantoin, the oxidation product of uric acid (UA), can be used as an in vivo marker of free radical generation. ...The study population was 20 infants of 24-30 weeks gestation, comprising 10 who subsequently developed chronic lung disease (CLD) and 10 without CLD. In the CLD infants, the plasma allantoin/UA ratio showed a significant increase after day 1 and continued to increase gradually to reach a peak on day 6 (6.5 +/- 4.1% for CLD and 2.1 +/- 0.9% for non-CLD infants). The allantoin/UA ratio in bronchoalveolar lavage fluid was also higher in CLD infants and the difference reached significance on days 4-6 (41.2 +/- 15.8% for CLD and 11.7 +/- 9.9% for non-CLD infants). ... 

Abstract: PubMed

4. Human Metabolite Information

Chemical metabolite information from the Human Metabolome Database (HMDB). Read more..

1. Metabolite Description

Allantoin is a diureide of glyoxylic acid with the chemical formula C4H6N4O3. It is also called 5-ureidohydantoin, glyoxyldiureide, and 5-ureidohydantoin. It is a product of oxidation of uric acid. It is a product of purine metabolism in most mammals except higher apes, and it is present in their urine. In humans, uric acid is excreted instead of allantoin. The presence of allantoin in the urine can be an indication of microbial overgrowth or it can be created via non-enzymatic means through high levels of reactive oxygen species. In this regard Allantoin is sometimes used as a marker of oxidative stress. Allantoin can be isolated from cow urine or as a botanical extract of the comfrey plant. It has long been used for its healing, soothing, and anti-irritating properties. Allantoin helps to heal wounds and skin irritations and stimulates the growth of healthy tissue. Allantoin can be found in anti-acne products, sun care products, and clarifying lotions because of its ability to help heal minor wounds and promote healthy skin. Allantoin is frequently present in toothpaste, mouthwash, and other oral hygiene products as well as shampoos, lipsticks, various cosmetic lotions and creams and other cosmetic and pharmaceutical products.