

University of Canterbury

End of Year Examinations 2007

Prescription Number(s):	BCHM 301 BIOL 331
Paper Title:	Biochemistry 3

Time Allowed: 2.5 HOURS

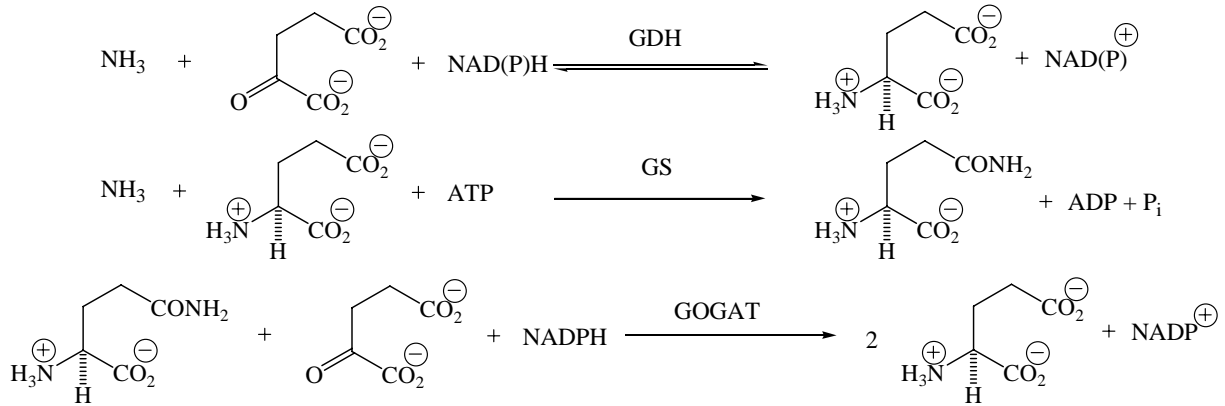
Number of pages: SIX

Answer **THREE** questions out of
FOUR.

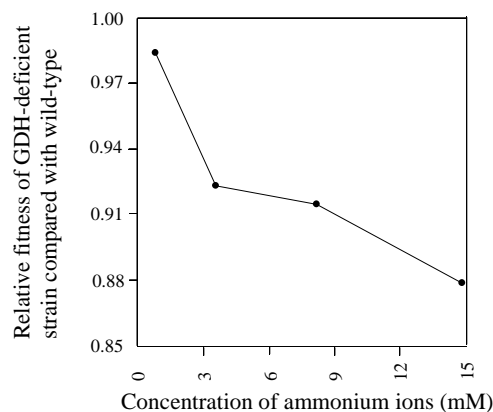
All questions are of equal value

TURN OVER

1. Give a critical account of the roles of the enzymes glutamate dehydrogenase (GDH), glutamine synthetase (GS) and glutamate synthase (GOGAT) in nitrogen metabolism. Your account you should include a discussion of the observations raised in (a) – (c).



- (a) The K_m for ammonia for GS from *E. coli* is approximately 0.1mM, whereas that for GDH is approximately 3mM.
- (b) Glutamate dehydrogenase from *E. coli* utilizes NADPH/ NADP⁺ as the redox co-factor, whereas the enzyme from animals utilises NADH/NAD⁺ for mediating this redox reaction. Furthermore GDH from animals is localised in mitochondria, and is allosterically regulated: ATP inhibits its activity and ADP stimulates it.
- (c) The role of GDH in *E. coli* has been addressed by comparing the growth of a wild-type *E. coli* strain with one in which the GDH has been mutated to a form that is inactive. It was found that when these two strains were grown competitively in glucose-rich media, the native strain and the strain deficient in GDH grew at exactly the same rate. However, when these organisms were grown in glucose-limited media it was found that the GDH-deficient strain was less fit than the native strain at higher concentrations of ammonium ions, as shown in the Figure.



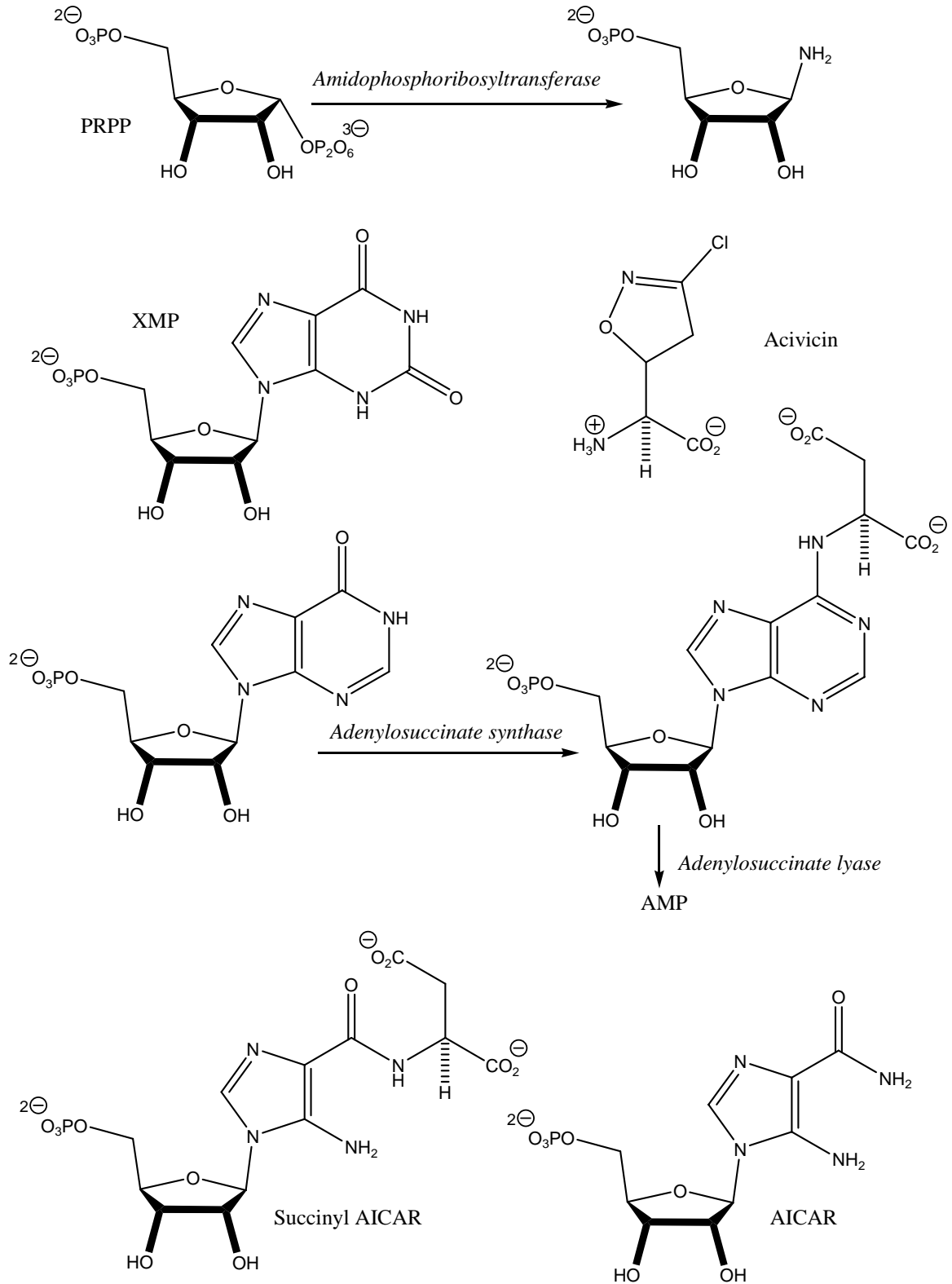
Figure

2. Structural information for this question is given in the **Scheme** on the following page.

Give a critical overview of the biological synthesis of purines. In your discussion you should give a critical discussion of some, or all, of the following issues: multifunctional enzymes; sequence homologies; regulation; nitrogen sources; *de novo* biosynthesis; and salvage. Your account should be illustrated with a wide range of specific examples and also discuss the observations in (a) and in **TWO** of (b) – (d).

- (a) Human GMP synthetase catalyses the synthesis of GMP from XMP and uses ATP as a co-factor. Either glutamine *or* ammonia can act as a nitrogen donor. Glutamine hydrolysis and ATP hydrolysis are coupled. The enzyme cannot use glutamine as nitrogen source if it has been treated with acivicin which forms an attachment to cysteine-104. Cysteine-104 lies within a predicted amidotransferase domain. The rate of inactivation by acivicin is accelerated by adding Mg^{2+} , ATP and XMP.
- (b) The enzyme adenylosuccinate synthetase from rabbit muscle uses GTP as a co-factor and is inhibited by AMP.
- (c) The active-site of adenylosuccinate lyase from *Neurospora crassa* also catalyses cleavage of succinyl-AICAR to give AICAR; this enzyme is homologous to a family of aspartase enzymes.
- (d) Genetic deficiency of Hypoxanthine Phosphoribosyl Transferase (HGPRT) gives rise to a crippling gouty arthritic disease known as Lesch-Nyhan syndrome.

Question 2 continued on following page

*Question 2 continued***Scheme****TURN OVER**

3. Discuss the childhood genetic disorders of glycosaminoglycan catabolism known as mucopolysaccharidoses (MPS) with reference to their genetic and biochemical basis, illustrating your answer with examples of the clinical phenotype of these diseases and methods for their diagnosis. Complete your answer by describing the therapies currently used for their treatment, including a discussion of how these therapies work.

4. Describe the roles of heparan sulfate proteoglycans in Alzheimer's disease. Illustrate your answer with 2 examples of the possible mechanisms involved, and discuss the development of new drugs which target each of these mechanisms.

END OF PAPER