

University of Canterbury

End-of-year Examinations 2009

Prescription Number(s): CHEM 325

BCHM 302

Paper Title: Biological Chemistry

Time Allowed: Two hours

Number of pages: Eight

This paper is divided into TWO sections.

SECTION A: Answer **FOUR** questions out of FIVE.

SECTION B: Answer **FOUR** questions out of FIVE.

Both sections are worth equal marks.

TURN OVER

SECTION A

(Answer **FOUR** questions from this section.)

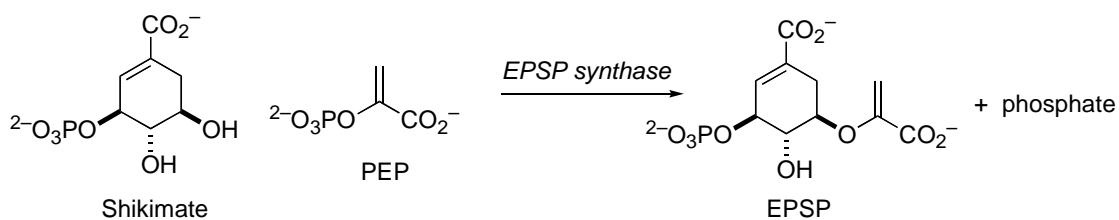
1. The Michaelis-Menten equation for the rate of an enzyme-catalysed reaction is:

$$v = \frac{k_{\text{cat}}[E]_0[S]}{K_M + [S]}$$

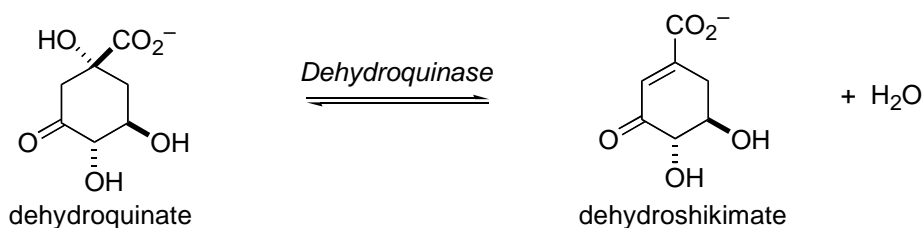
- (a) Define the five variables - v , k_{cat} , $[E]_0$, $[S]$ and K_M in this equation and define V_{max} in terms of these variables. Give units for each of these terms.
- (b) Qualitatively sketch the variation of v with $[S]$ that is predicted by this equation. On your sketch, indicate the values of V_{max} and K_M .
- (c) Explain the difference between the Michaelis-Menten and the Briggs-Haldane methods for deriving the Michaelis-Menten equation.
- (d) Explain why K_M is usually considered to be greater than K_S (where K_S is the dissociation constant for the enzyme-substrate complex).
2. Kinetic studies can play a useful role in learning about an enzyme-catalysed reaction, whether it is inhibited by an inhibitor or uninhibited.”

Discuss this statement.

3. EPSP synthase catalyses the formation of EPSP from shikimate and phosphoenol pyruvate (PEP).

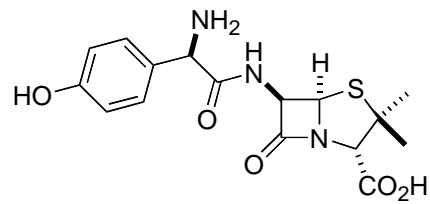


- (a) Describe the mechanism of this reaction.
- (b) The kinetic mechanism of the enzyme EPSP synthase is described as being ordered sequential. Explain what the terms ‘ordered sequential’ mean, and how this fits with the mechanism you have provided in part (a).
- (c) Describe what experiments would need to be carried out in order to demonstrate that the mechanism of this reaction is operating by a sequential kinetic mechanism.
4. Dehydroquinase catalyses the reversible dehydration of dehydroquininate to give dehydroshikimate. There are two distinct types of dehydroquinase, type I and type II.



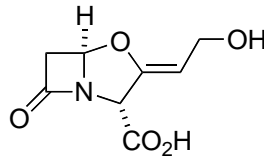
- (a) Describe labelling studies that can distinguish between type I and type II enzymes.
- (b) Describe the mechanisms of the two different types of dehydroquinase and explain how these mechanisms fit with the labeling studies described in part (a) above.

5. (a) Describe the molecular mechanism by which the antibiotic amoxicillin works.



amoxicillin

- (b) Explain, using mechanistic reasoning, why administration of amoxicillin with clavulanic acid can be far more effective than administration of amoxicillin alone.



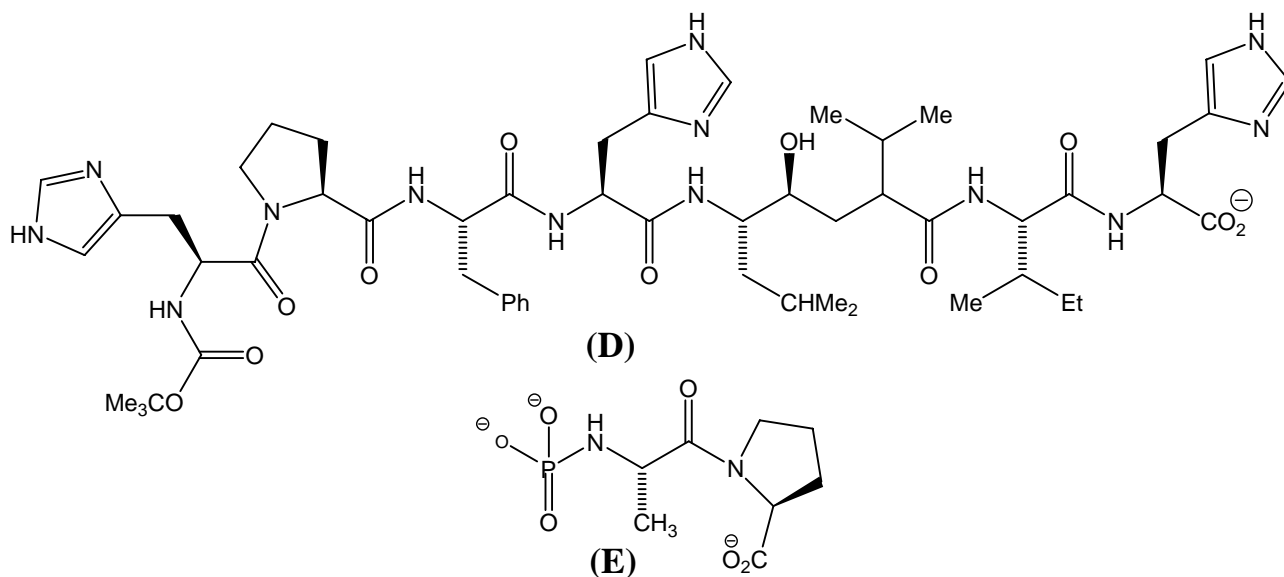
clavulanic acid

SECTION B

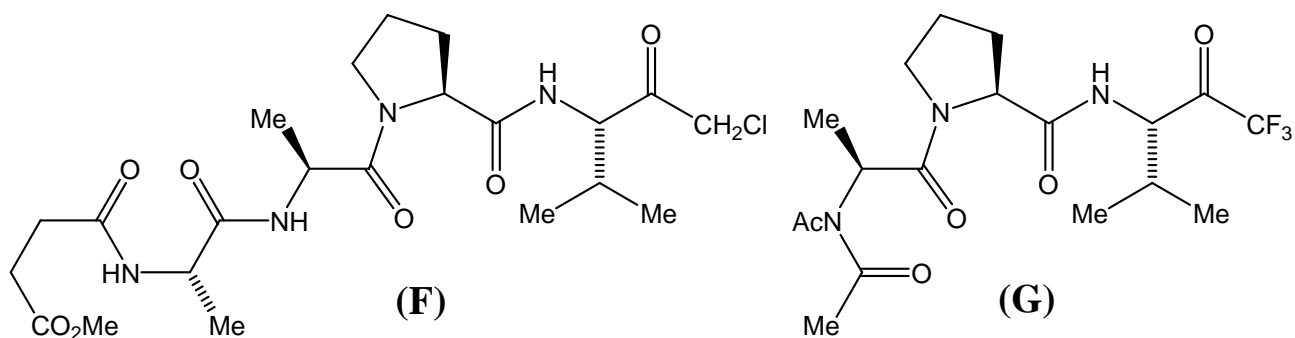
(Answer **FOUR** questions from this section.)

6. Angiotensin is a key hormone for the regulation of blood pressure. The final two steps of its biosynthesis are the renin-catalysed hydrolysis of angiotensinogen (**A**) to proangiotensin (**B**), and the further hydrolysis of (**B**) to angiotensin (**C**) by angiotensin converting enzyme (ACE).

Answer both (a) and (b)

(a) Explain why (**D**) is a selective, tight-binding, inhibitor of renin.(b) Explain why (**E**) is a selective, tight-binding, inhibitor of ACE.Asp-Arg-Val-Tyr Ile-His-Pro-Phe-His-Leu-Val-Ile-His-protein (**A**)Asp-Arg-Val-Tyr Ile-His-Pro-Phe-His-Leu (**B**)Asp-Arg-Val-Tyr Ile-His-Pro-Phe (**C**)

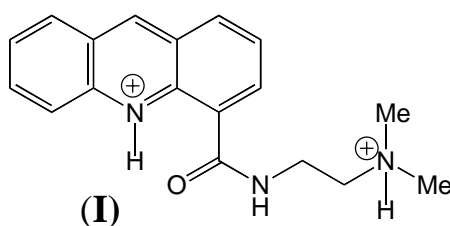
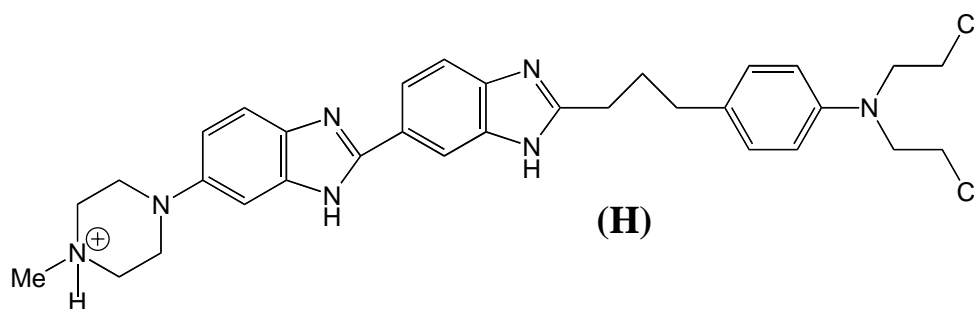
7. Elastase catalyses the hydrolysis of proteins in the lung and is a target for the treatment of emphysema. Explain the mechanisms by which compounds **(F)** and **(G)** act as selective inhibitors of human leukocyte elastase.



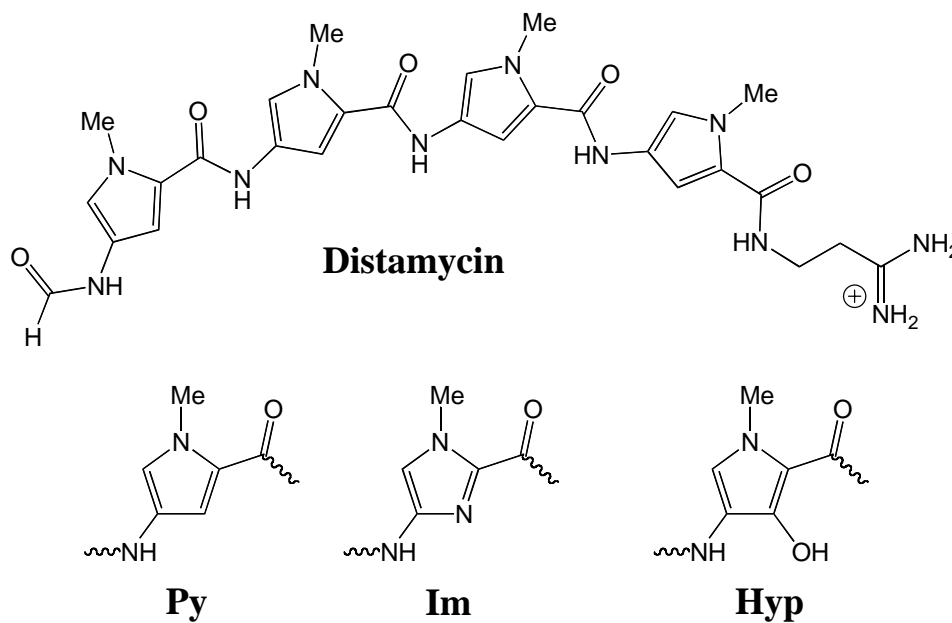
8. The two compounds **(H)** and **(I)** were both developed in New Zealand as potential anti-cancer drugs and have both been through clinical trials.

Answer both **(a)** and **(b)**

- (a) Explain why **(H)** binds selectively and irreversibly to AT-rich sequences of DNA.
- (b) Explain why **(I)** binds selectively, tightly and reversibly to GC-rich sequences of DNA



9. Peter Dervan's group discovered that Distamycin binds selectively to AT-rich DNA in a 2:1 ratio (Distamycin:DNA). Briefly explain this observation. Outline the way in which this observation has led to the creation of families of molecules related to Distamycin, incorporating **Py**, **Im** and **Hyp** building blocks, which recognise specific sequences of double-stranded DNA.



10. Combinatorial chemistry is an important area of research in chemical biology. Give a brief critical account of the way in which the systematic synthesis of combinations of building blocks is a powerful tool for the development of new therapeutic and diagnostic agents. Illustrate your account with specific examples.

END OF PAPER