EP6.2

Succinate dehydrogenase (Optional extension)

In this activity you will use models to investigate the binding of a substrate to the active site of an enzyme. This will help you to understand why enzymes are so specific, and how some compounds can act as enzyme inhibitors.

Requirements

- molecular model kit

Introduction

Butanedioic acid (succinic acid) is oxidised to *trans*-butenedioic acid by removal of hydrogen. This reaction is catalysed by the enzyme *succinate dehydrogenase*.

$$\underset{\text{butanedioic acid}}{HOOC{-}CH_2{-}CH_2{-}COOH} \rightarrow \underset{\textit{trans}\text{-butenedioic acid}}{HOOC{-}CH{=}CH{-}COOH}$$

The enzyme is *inhibited* by propanedioic acid: $HOOC{-}CH_2{-}COOH$; in other words, its catalytic activity is less in the presence of propanedioic acid. This, together with other evidence, suggests that *two* –COOH groups are involved in binding the substrate to the active site.

The action of the enzyme is summarised in Figure 1.

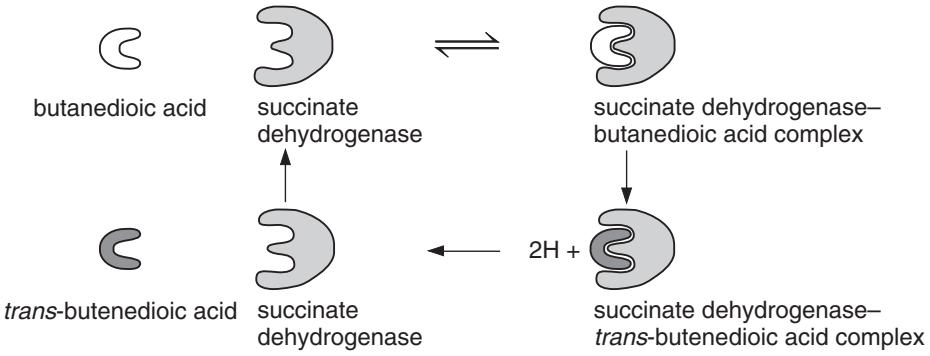

Figure 1 The action of succinate dehydrogenase

What you do

1 Make molecular models of the three acids (butanedioic acid, *trans*-butenedioic acid, and propanedioic acid).

2 Place the molecule of *trans*-butenedioic acid on a piece of paper so that all the atoms are touching the paper. Draw circles on the paper to mark the positions of the oxygen and hydrogen atoms of the –COOH groups. Note the position of the other hydrogen atoms. (Remember, this is the product of the oxidation reaction.)

3 Now manipulate your structure of butanedioic acid so that the hydrogens and oxygens of its –COOH groups can be placed on the same marks. One H atom of each $-CH_2-$ group should also be touching the paper. Note the positions of the other two H atoms – the ones which are removed by the enzyme.

4 Leave the model of butanedioic acid in place and superimpose your model of propanedioic acid on it so that the –COOH groups coincide. (You will need to 'close up' the butanedioic acid structure a little to achieve this.) Using a different colour, mark the new positions of the oxygen and hydrogen atoms of the –COOH groups.

This should show you that both butanedioic acid and propanedioic acid can be bound by their –COOH groups to the same site on the enzyme. The product of the oxidation reaction, *trans*-butenedioic acid, binds to this site less well and is released from the enzyme.

The oxidation (removal of hydrogen) occurs at another part of the active site. This must be where the C–C bond between the two central carbons of butanedioic acid naturally comes when it is placed as above.

Propanedioic acid is an inhibitor because it has no C–C bond to oxidise, but it can bind onto the site and block it.

5 Now consider pentanedioic acid: $HOOC{-}CH_2{-}CH_2{-}CH_2{-}COOH$.

Make a model of its structure. Try to fit it onto the marks you made in **4**. Decide whether you would expect it to:

- bind to the enzyme or not
- be oxidised by the enzyme to $HOOC{-}CH_2{-}CH{=}CH{-}COOH$
- be an inhibitor.