3,4-dehydroadipyl-CoA semialdehyde dehydrogenase ($NADP^+$) 1.2.1.77

1 Nomenclature

EC number
1.2.1.77

Systematic name
3,4-dehydroadipyl-CoA semialdehyde:$NADP^+$ oxidoreductase

Recommended name
3,4-dehydroadipyl-CoA semialdehyde dehydrogenase ($NADP^+$)

Synonyms
3,4-dehydroadipyl-CoA semialdehyde dehydrogenase <1> [2]
ALDHC <2> [1]
BoxD <1> [2,3]
$NADP^+$-dependent aldehyde dehydrogenase <1> [3]

2 Source Organism

<1> *Azoarcus evansii* [2,3]
<2> *Burkholderia xenovorans* [1]

3 Reaction and Specificity

Catalyzed reaction
3,4-didehydroadipyl-CoA semialdehyde + $NADP^+$ + H_2O = 3,4-didehydroadipyl-CoA + NADPH + H^+

Natural substrates and products
- **S** 3,4-dehydroadipyl-CoA semialdehyde + $NADP^+$ <2> (<2> the enzyme is involved in the benzoate oxidation (box) pathway [1]) (Reversibility: ?) [1]
- **P** 3,4-dehydroadipyl-CoA + NADPH + H^+ + NADPH + H^+
- **S** 3,4-dehydroadipyl-CoA semialdehyde + $NADP^+$ + H_2O <1> (<1> enzyme of the aerobic benzoyl-coenzyme A catabolic pathway [2]) (Reversibility: ?) [2]
- **P** 3,4-dehydroadipyl-CoA + NADPH + H^+

Substrates and products
- **S** 3,4-dehydroadipyl-CoA semialdehyde + $NADP^+$ <2> (<2> the enzyme is involved in the benzoate oxidation (box) pathway [1]) (Reversibility: ?) [1]
- **P** 3,4-dehydroadipyl-CoA + NADPH + H^+ + NADPH + H^+

D. Schomburg and I. Schomburg (eds.), *Class 1 Oxidoreductases: EC 1*,
Springer Handbook of Enzymes S8, DOI 10.1007/978-3-642-36265-1_35,

S 3,4-dehydroadipyl-CoA semialdehyde + $NADP^+$ + H_2O <1> (<1> enzyme of the aerobic benzoyl-coenzyme A catabolic pathway [2]; <1> the molar ratio of mol of converted substrate per mol of NADPH formed is estimated to be 1 [2]) (Reversibility: ?) [2,3]
P 3,4-dehydroadipyl-CoA + NADPH + H^+
S benzaldehyde + $NADP^+$ + H_2O <2> (Reversibility: ?) [1]
P benzoate + NADPH + H^+
S formaldehyde + $NADP^+$ + H_2O <2> (Reversibility: ?) [1]
P formate + NADPH + H^+
S heptaldehyde + $NADP^+$ + H_2O <2> (Reversibility: ?) [1]
P heptanoate + NADPH + H^+
S isovaleraldehyde + $NADP^+$ + H_2O <2> (Reversibility: ?) [1]
P isovalerate + NADPH + H^+
S propionaldehyde + $NADP^+$ + H_2O <2> (Reversibility: ?) [1]
P propionate + NADPH + H^+
S valeraldehyde + $NADP^+$ + H_2O <2> (Reversibility: ?) [1]
P valerate + NADPH + H^+
S Additional information <2> (<2> the native substrate (3,4-dehydroadipyl-CoA semialdehyde) is not tested as it is commercially unavailable. The enzyme is preferentially active towards linear medium-chain to long-chain aldehydes as compared to branched-chain, short-chain or aromatic aldehydes [1]) [1]
P ?

Inhibitors

Additional information <1> (<1> salt concentrations up to 500 mM KCl and EDTA concentrations up to 50 mM have no effect on enzyme activity [2]) [2]

Cofactors/prosthetic groups

NAD^+ <2> (<2> the enzyme is more active in the presence of $NADP^+$ relative to NAD^+. Crystallographic data show that cofactor selectivity is governed by a complex network of hydrogen bonds between the oxygen atoms of the 2-phosphoryl moiety of $NADP^+$ and a threonine/lysine pair on the enzyme [1]) [1]
$NADP^+$ <1,2> (<1> no activity (below 2%) with NAD^+. The molar ratio of mol of converted substrate per mol of NADPH formed is estimated to be 1 [2]; <2> the enzyme is more active in the presence of $NADP^+$ relative to NAD^+. Crystallographic data show that cofactor selectivity is governed by a complex network of hydrogen bonds between the oxygen atoms of the 2-phosphoryl moiety of $NADP^+$ and a threonine/lysine pair on the enzyme [1]) [1,2,3]

Metals, ions

Additional information <1> (<1> salt concentrations up to 500 mM KCl have no effect on enzyme activity [2]) [2]

Turnover number (s^{-1})

0.019 <2> (benzaldehyde, <2> in 50 mM Tris-HCl (pH 7.5), at 25°C [1]) [1]
0.04 <2> ($NADP^+$, <2> in 50 mM Tris-HCl (pH 7.5), at 25°C, cosubstrate: propionaldehyde [1]) [1]

0.046 <2> (formaldehyde, <2> in 50 mM Tris-HCl (pH 7.5), at 25°C [1]) [1]
0.074 <2> (isovaleraldehyde, <2> in 50 mM Tris-HCl (pH 7.5), at 25°C [1]) [1]
0.501 <2> (NAD^+, <2> in 50 mM Tris-HCl (pH 7.5), at 25°C, cosubstrate: propionaldehyde [1]) [1]
2.32 <2> (propionaldehyde, <2> in 50 mM Tris-HCl (pH 7.5), at 25°C [1]) [1]
5.16 <2> (valeraldehyde, <2> in 50 mM Tris-HCl (pH 7.5), at 25°C [1]) [1]
29.9 <2> (heptaldehyde, <2> in 50 mM Tris-HCl (pH 7.5), at 25°C [1]) [1]
45 <1> (3,4-dehydroadipyl-CoA semialdehyde, <1> pH 7.2 [2]) [2]
45 <1> ($NADP^+$, <1> pH 7.2 [2]) [2]

Specific activity (U/mg)
0.17 <1> (<1> extracts of cells grown aerobically on benzoate [2]) [2]

K_m-Value (mM)
0.016 <1> ($NADP^+$, <1> pH 7.2 [2]) [2]
0.025 <1> (3,4-dehydroadipyl-CoA semialdehyde, <1> pH 7.2 [2]) [2]
0.04 <2> ($NADP^+$, <2> in 50 mM Tris-HCl (pH 7.5), at 25°C [1]) [1]
0.042 <2> (heptaldehyde, <2> in 50 mM Tris-HCl (pH 7.5), at 25°C [1]) [1]
0.3 <2> (valeraldehyde, <2> in 50 mM Tris-HCl (pH 7.5), at 25°C [1]) [1]
0.501 <2> (NAD^+, <2> in 50 mM Tris-HCl (pH 7.5), at 25°C [1]) [1]
1.21 <2> (propionaldehyde, <2> in 50 mM Tris-HCl (pH 7.5), at 25°C [1]) [1]
1.66 <2> (isovaleraldehyde, <2> in 50 mM Tris-HCl (pH 7.5), at 25°C [1]) [1]
1.9 <2> (formaldehyde, <2> in 50 mM Tris-HCl (pH 7.5), at 25°C [1]) [1]
4.15 <2> (benzaldehyde, <2> in 50 mM Tris-HCl (pH 7.5), at 25°C [1]) [1]

pH-Optimum
7.2 <1> [2]

pH-Range
6.2-8.8 <1> (<1> 50% of maximal activity at pH 6.2 and pH 8.8 [2]) [2]

4 Enzyme Structure

Subunits
? <2> (<2> forms a dimer in solution with a molecular mass of 110000, SDS-PAGE [1]) [1]
dimer <1> (<1> 2 * 54000 [2]) [2]
homodimer <1> (<1> 2 * 54000 [3]) [3]

5 Isolation/Preparation/Mutation/Application

Purification
<1> [2,3]
<2> [1]

Crystallization

<2> (sitting drop vapour diffusion method, at 18°C in 29% PEG 3350K and 100 mM bis-Tris (pH 6.0), 1.6 A crystal structure of ALDHC in complex with NADPH bound in the cofactor-binding pocket and an ordered fragment of a polyethylene glycol molecule bound in the substrate tunnel) [1]

Cloning

<1> (expression in Escherichia coli as a protein tagged at its N terminus with maltose-binding protein) [2]

<2> (expressed in Escherichia coli BL21 Star (DE3) cells) [1]

6 Stability

Storage stability

<1>, -20°C, enzyme could be stored without appreciable loss of activity for months at -20°C in the presence of 10% (v/v) glycerol [2]

References

[1] Bajns J., Boulanger MJ.: Structural and biochemical characterization of a novel aldehyde dehydrogenase encoded by the benzoate oxidation pathway in Burkholderia xenovorans LB400. J. Mol. Biol., **379**, 597-608 (2008)

[2] Gescher, J.; Ismail, W.; Olgeschläger, E.; Eisenreich, W.; Wörth, J.; Fuchs, G.: Aerobic benzoyl-coenzyme A (CoA) catabolic pathway in: conversion of ring cleavage product by 3,4-dehydroadipyl-CoA semialdehyde dehydrogenase. J. Bacteriol., **188**, 2919-2927 (2006)

[3] Rather, L.J.; Knapp, B.; Haehnel, W.; Fuchs, G.: Coenzyme A-dependent aerobic metabolism of benzoate via epoxide formation. J. Biol. Chem., **285**, 20615-20624 (2010)