Available online at www.sciencedirect.com

SCIENCE DIRECT®

Bioorganic Chemistry 33 (2005) 159–170

BIOORGANIC
CHEMISTRY

www.elsevier.com/locate/bioorg

Minireview

Structure and mechanism of tryptophylquinone enzymes

Victor L. Davidson*

Department of Biochemistry, The University of Mississippi Medical Center,
2500 N. State St., Jackson, MS 39216-4505, USA

Received 8 September 2004
Available online 11 November 2004

Abstract

Tryptophylquinone cofactors are formed by posttranslational modifications that result in the incorporation of two oxygens into a tryptophan side chain, and the covalent cross-linking of that side chain to another amino acid residue. Tryptophylquinone enzymes catalyze the oxidative deamination of primary amines, and utilize other redox proteins as electron acceptors. Mechanistic and structural studies of these enzymes are providing insight into how these enzymes utilize these highly reactive protein-derived quinones in a controlled manner to facilitate biologically important catalytic and electron transfer reactions.

Keywords: Amine dehydrogenase; Quinoprotein; Posttranslational modification; Protein-derived cofactor; Redox protein; Hydrogen tunneling

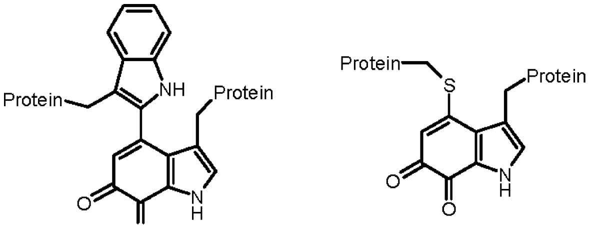
1. Introduction

Recent advances in enzymology have extended the scope of the field of cofactor-dependent enzyme catalysis. It has been documented that catalytic and redox-active prosthetic groups may be derived from posttranslational modification of peptide

---

* Fax: +1 601 984 1501.
E-mail address: vdavidson@biochem.umsmed.edu.

0045-2068/$ - see front matter © 2004 Elsevier Inc. All rights reserved.
doi:10.1016/j.bioorg.2004.10.001



Tryptophan tryptophylquinone
TTQ

Cysteine tryptophylquinone
CTQ

Fig. 1. Structures of tryptophylquinone cofactors of quinoprotein dehydrogenases. Tryptophan tryptophylquinone (TTQ) and cysteine tryptophylquinone (CTQ) are derived from amino acid residues of the polypeptide chain.

amino acid residues [1–3]. Such "new" prosthetic groups include covalently cross-linked amino acid residues, stable amino acid-based free radicals, and quinones derived from tyrosine and tryptophan residues. This review focuses on tryptophylquinone enzymes. Tryptophan tryptophylquinone (TTQ)[1] is the prosthetic group of methylamine dehydrogenase (MADH). This enzyme was first characterized in 1968 by Eady and Large [4], but the exact nature of its prosthetic group remained unknown for several years. The structure of the prosthetic group of MADH was determined in 1991 by McIntire et al. [5] using chemical and NMR spectroscopic methods, to be 2′,4-bitryptophan-6,7-dione. It was given the common name of TTQ. The structure was subsequently confirmed by X-ray crystallographic analyses of MADH [6]. In addition to MADH, TTQ has also been identified as the prosthetic group of aromatic amine dehydrogenase (AADH) [7]. Recently, the enzyme quinohemoprotein amine dehydrogenase (QHNDH) was shown to possess not TTQ, but cysteine tryptophylquinone (CTQ) as a cofactor [8,9]. In each of these enzymes two oxygens have been incorporated into a tryptophan side chain to generate a quinone, and the side chain has also become covalently cross-linked to another amino acid residue (either another tryptophan or a cysteine) to form the protein-derived cofactor (Fig. 1).

2. Physiological roles of tryptophylquinone enzymes

The TTQ and CTQ-dependent enzymes that have been characterized thus far are soluble enzymes localized in the periplasmic space of gram negative bacteria. Each is an inducible enzyme that allows the host bacterium to utilize particular primary amines as a sole source of carbon and energy. Each enzyme catalyzes the oxidative deamination of the primary amine. These dehydrogenases do not utilize NAD^+ or $NADP^+$ as electron acceptors. Instead, during the reductive half-reaction the

---

[1] *Abbreviations used:* CTQ, cysteine tryptophylquinone; TTQ, tryptophan tryptophylquinone; MADH, methylamine dehydrogenase; AADH, aromatic amine dehydrogenase; QHNDH, quinohemoprotein amine dehydrogenase.