Biocatalysis and Agricultural Biotechnology 12 (2017) 104–115

Contents lists available at ScienceDirect

Biocatalysis and Agricultural Biotechnology

journal homepage: www.elsevier.com/locate/bab

An extensive review on L-methioninase and its potential applications

Kannan Suganya, Krishnamoorthy Govindan, Palanichamy Prabha, Marudhamuthu Murugan*

Department of Microbial Technology, School of Biological Sciences, Madurai Kamaraj University, Madurai 625021, Tamil Nadu, India

ARTICLE INFO

Keywords:
L-Methioninase
Optimal culture conditions
Mechanism of action
Biotechnological applications

ABSTRACT

L-methioninase (METs) catalyses the disintegration of methionine, an essential amino acid into ammonia, α-Keto glutarate and methanethiol. This enzyme has been extensively studied from a wide range of organisms, including plants, terrestrial and marine microbes. Clear and detailed information about the three dimensional structure and potential catalytic activity of L-methioninase from *Pseudomonas* and *Citrobacter* sp. have been well documented. This review catalogues the prominent sources of L-methioninase, methods of its production and purification, characterization and as well as its biological roles. In the same breath, this article reveals both the past and present applications of this important enzyme and discusses its upcoming scenarios.

1. Introduction

Enzymes are protein catalysts that have high specificity for the reaction catalyzed, the substrate acted on, and the products they produce. They are critically essential to cells, since most biological reactions are impossible without them. Indeed enzymes make life possible (Fogarty and Kelly, 1990). Thousands of enzymes have been identified, and many of them have been studied extensively. Quite a slight number of these enzymes have future of specific interest and drawn the attention of reliable bands of investigators. However, only a relatively rare has come up with special experimental advantages and becomes the objects of extensive studies (Wriston and Yellin, 1973). One of such enzymes is methionine- gamma-lyase is also known by extra names such as L-methionase, methioninase, methionine lyase,methionine demethylase, (MGL, EC 4.4.1.11) which has been the focus of several researches in the most recent years. From archea to plants excluding humans possess this idiosyncratic enzyme and it belongs to Aspartate Aminotransferase (AAT) family of fold 1 PLP dependent enzymes of which the internal aldimine was formed at lysine of N-terminus of the short helix at β-strand (Tanaka et al., 1977; Cooper, 1983). L-Methioninase depends on pyridoxal-5-phosphate (PLP) to transfigure sulfur containing amino acids such as methionine and cysteine to α- keto acids, ammonia, and volatile thiols by α, γ - elimination and γ replacement reactions (Salzmann et al., 2000; Percudani and Peracchi, 2003; Soda et al., 1983). Research on physiological competences of L-Methioninase was under study for more than half century, and a real bound forward was accomplished in 1953 when Wiesendanger and Nisman revealed the presence of L-methioninase in rumen bacteria (Wiesendanger and Nisman, 1953). In 1973, yet another breakthrough was achieved when Kreis and Hession demonstrated *C. sporogenes* methioninase against Walker carcinoma in rats (Kreis and Hession, 1973a, 1973b). Subsequently, numerous investigators focused on the purification, characterization, and therapeutic assessment of this enzyme as an anticancer agent against different types of human cancer cell lines (Kreis and Hession, 1973a, 1973b). Certain therapeutic approaches were developed to elicit the methionine dependency of tumor cells. Huiyan Guo through his investigations proved the tumor growing in nude mice can be induced by a methionine-free diet to have a methionine dependent cell cycle block (Guo et al., 1993). This methionine dependency of tumor cells lines artificially induced by using methioninase. Following this primary investigations, researchers have examined the activity of methioninase in combination with certain chemotherapeutic drugs such as cisplatin, 5-fluorouracil (5-FU), and 1,3-bis(2- chloroethyl)-1-nitrosourea (BCNU) have displayed a significant activity in mouse models of colon cancer, lung cancer, and brain cancer (Yoshioka et al., 1998; Hoshiya et al., 1997; Kokkinakis, 2006). Unfortunately, the *in vivo* therapeutic consequence of this enzyme constrained by various barricades such as *in vivo* proteolysis, hyperammoniemia, and antigenicity (Tan et al., 1998a, 1998b; Yang et al., 2004a, 2004b, 2004c). Further examinations done by El-Sayed explored the pharmacokinetic properties of PEGylated methioninase by lessening its antigenic properties, extending its half-life time and reducing the hyperammoniemia with maximum therapeutic efficacy (El-Sayed et al., 2012a, 2012b).

Hence, in this review an effort has been made to illustrate the clear mechanism of action and structure of methioninase in an extensive way. This paper reviews the various sources of L-methioninase enzyme, methods that are being employed for its production, its assay methods, and its broad applications in the field of medicine and food.

* Corresponding author.
E-mail address: murubio2001@yahoo.com (M. Murugan).

http://dx.doi.org/10.1016/j.bcab.2017.09.009
Received 8 March 2017; Received in revised form 17 July 2017; Accepted 18 September 2017
Available online 21 September 2017
1878-8181/ © 2017 Elsevier Ltd. All rights reserved.

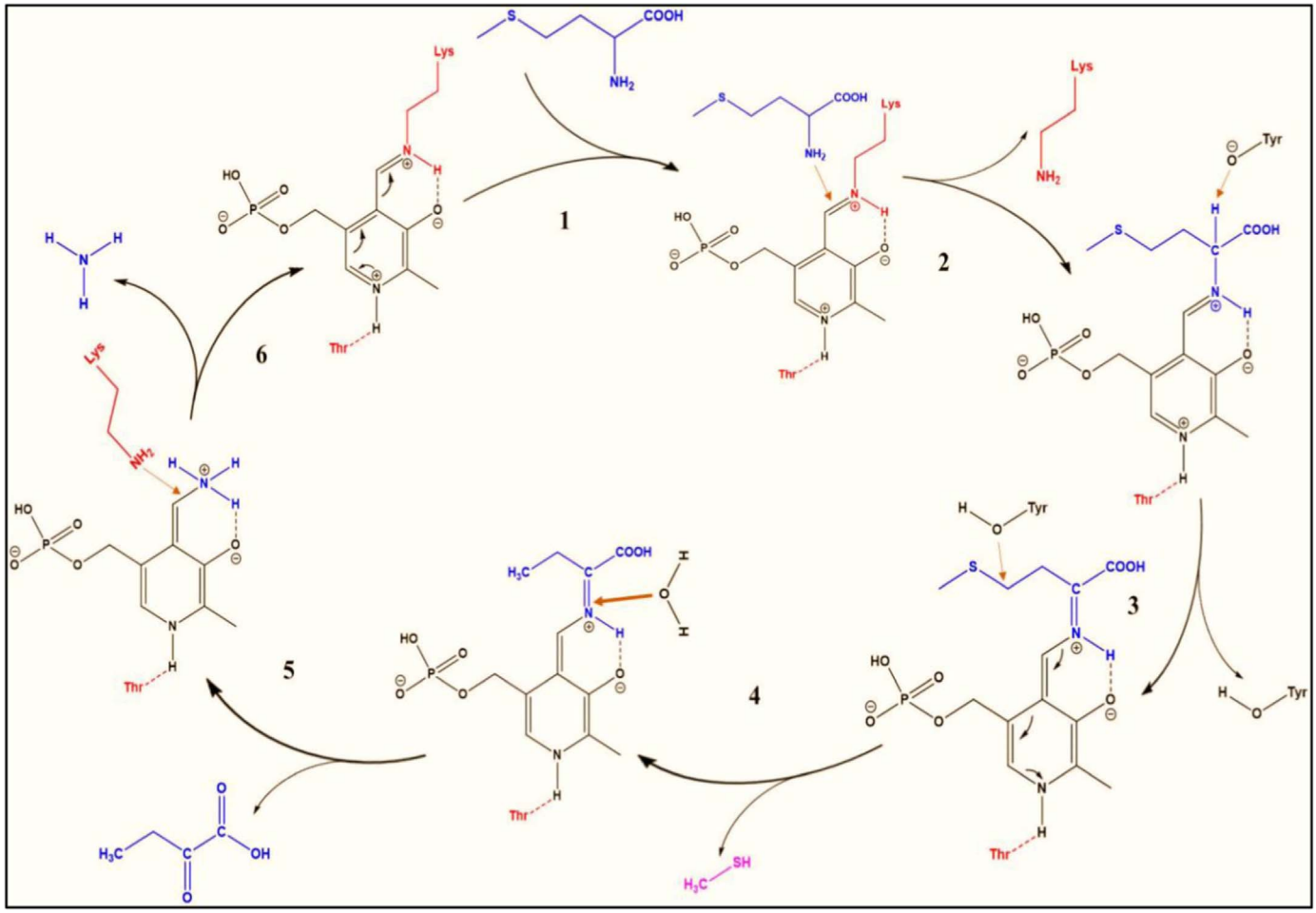

Fig. 1. Proposed reaction process of α, ϒ-elimination of methionine by methioninase [Substrates, intermediates, and products are shown in blue, while PLP is shown in black. Amino group reactions shown in red. Structures (1) to (6) correspond to the reaction intermediates explained in the text. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article)

1.1. L-methioninase mechanism of action

L -methioninase is a homotetrameric, multifunctional enzyme belongs to the $_{\gamma}$ family of PLP dependent enzymes and the active methioninase tetramer consists of two sets of strongly associated catalytic dimers (Motoshima et al., 2000; Nikulin et al., 2008a, 2008b). It catalyses α and $_{\gamma}$ removal with α $_{\gamma}$ replacement of L-methionine with the equimolar yield of α-keto acids (2-oxobutyrate and pyruvate), methanethiol, and ammonia (Inoue et al., 1995). Methionine is undergoing oxidative deamination with the presence of L-methioninase produces α-ketomethionine and further dethiomethylated with the production of methanethiol part of which oxidized to dimethyl disulfide and dimethyl trisulfide.α-ketobutyrate which is the key intermediate of methionine degradation can be converted to propionyl-CoA and subsequently methylmalonyl CoA, which can be converted to succinyl CoA, a citric acid cycle intermediate, and thus enter the citric acid cycle (Tokoro et al., 2003). The sulfur or oxygen atom at the β- or $_{\gamma}$-position of the substrate is substituted with the thiol during the β or $_{\gamma}$ replacement reactions. The comprehensive reaction mechanism catalyzed by L-methioninase comprise of 5 following steps (Fig. 1) (Tanaka et al., 1985; Chin and Lindsay, 1994; Faleev et al., 1996).

i) Amine group of the methionine attacks the internal aldimine structure.
ii) Formation of external aldimine by the Schiff's base transformation and the lysine group of MGL released.
iii) Formation of ketimine, tyrosine moiety of MGL attacks and removes the hydrogen group from α- position of methionine.
iv) Formation of Quinonoid, the hydroxyl group of tyrosine moiety from MGL donates its hydrogen group to the β- position which leads to the release of thiol group.
v) Water moiety attacks the imine bond and releases the α-ketoacid.
vi) Formation of internal aldimine, amine group lysine moiety from MGL attacks the amine bond which forms aldimine structure and releases ammonia.

In the case of homoserines such as O-acetyl-L-serine, O-acetyl-L-homoserine, and O-succinyl-L -homoserine, the enzyme releases organic acids instead of thiols. L- Methioninase catalyses $_{\gamma}$-replacement reactions of the thiomethyl group of methionine with alkylthiols retain chain length below C_7 (Tanaka et al., 1977). In all living cells, the fate of methionine was implicated with various pathways in Fig. 4.

1.2. L –methioninase structure

Exploration has been carried out by several researchers to exemplify the clear configuration L-methioninase enzyme at the molecular level. Consistently the structure of L-Methioninase occurs as a tetramer and it is highly similar to the closely related cystathionine -β-lyase from *Escherichia coli* (Clausen et al., 1996; Johnston et al., 1979). Molecular structures of *Pseudomonas putida*, *Citrobacter freundii, Entamoeba histolytica, Micromonospora echinospora* and *Clostridium sporogenes* have been thoroughly investigated and their detailed structural data is accessible (Fig. 2) (Kudou et al., 2007; Nikulin et al., 2008a, 2008b; Kreis and

Download English Version:

https://daneshyari.com/en/article/5520420

Download Persian Version:

https://daneshyari.com/article/5520420

Daneshyari.com