BIOTRANS
LA ROCHELLE 2023

N°1277 / PC
TOPIC(s) : Biocatalytic cascade reactions

The Enzymatic Synthesis of S-Adenosyl-L-Homocysteine (SAH) and Its Derivatives for Enzyme-Catalyzed Methylation

AUTHORS

Xiaojin WEN / UNIVERSITY OF BASEL, MATTENSTRASSE 22, BASEL
Florian SEEBECK / UNIVERSITY OF BASEL, MATTENSTRASSE 22, BASEL

PURPOSE OF THE ABSTRACT

S-Adenosyl-L-homocysteine (SAH) and related nucleosides have been found as key regulator compounds in many biological transmethylation systems and their potential in the pharmaceutical and chemotherapeutic fields has been suggested.[1] So far, for enzymatic methylation, SAH has been used as the substrate for one-step regeneration of S-adenosylmethionine (SAM), the key co-substrate of most methyltransferases (MTs) in nature.[2-4] Due to their natural promiscuity, or as a result of introduced mutations, many MTs can also transfer larger alkyl chains or aromatic fragments to SAH to form plenty of SAM analogues.[5-7] Therefore, SAH and its derivatives have recently attracted great interest. However, SAH is so expensive that low-cost methods for SAH synthesis are in high command.[8,9] Herein, we developed a three enzyme-catalyzed cascade for in vitro SAH biosynthesis from two low-priced starting materials D/L-homocysteine thiolactone and adenosine. This enzyme cascade could also be used for production of SAH derivatives from their corresponding adenosine analogues.

FIGURES

FIGURE 1

FIGURE 2

KEYWORDS

S-Adenosyl-L-Homocysteine | Enzymatic Synthesis

BIBLIOGRAPHY

[1] P. M. Ueland, Pharmacol. Rev. 1982, 34, 223-253;

[2] C. Liao, F. P. Seebeck, Nat. Catal. 2019, 2, 696-701;

[3] X. Wen, F. Leisinger, V. Leopold, F. P. Seebeck, Angew. Chem. Int. Ed. 2022, 61, e202208746;

[4] F. Ospina, K. H. Schülke, J. Soler, A. Klein, B. Prosenc, M. Garcia-Borràs, S. C. Hammer, Angew. Chem. Int. Ed. 2022, 61, e202213056;

[5] Q. Tang, I. V. Pavlidis, C. P. S. Badenhorst, U. T. Bornscheuer, ChemBioChem 2021, 22, 2584-2590;

[6] Y. Motorin, J. Burhenne, R. Teimer, K. Koynov, S. Willnow, E. Weinhold, M. Helm, Nucleic Acids Res. 2011, 39, 1943-1952;

[7] C. Dalhoff, G. Lukinavicius, S. Klimasăuskas, E. Weinhold, Nat. Chem. Biol. 2006, 2, 31-32;

[8] G. de la Haba, G. L. Cantoni, J. Biol. Chem. 1959, 234, 603-608;

[9] S. Shimizu, T. Ohshiro, S. Shiozaki, H. Yamada, J. Biotechnol. 1986, 4, 91-100.