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The importance of ergothioneine synthesis in ancient time by organisms living in oxygen free atmosphere

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A B S T R A C T

The paper published by Ruczyszky and Liu (2017) reports on the biosynthesis of ergothioneine under both aerobic and anaerobic conditions. We would like to suggest a hypothesis as to what could be the reason that microorganisms on the Earth synthesized ergothioneine under anaerobic conditions.

Recently, Ruczyszky and Liu (2017) [1] published a paper reporting on the biosynthesis of ergothioneine under aerobic but even under anaerobic conditions. They cited the communication of Burns et al. (2017) [2] addressing the possibility that ergothioneine might play an important role in the survival of live protoorganisms under anoxic conditions. The authors hypothesized that the formation of ergothioneine preceded the appearance of atmospheric oxygen by 2.4 billion years. Khonde and Jardine (2015) [3] and Burns et al. (2017) [2] mentioned that the biosynthesis of ergothioneine from histidine, involving hercynine as an intermediate, was a phenomenon characteristic for bacteria, e.g. *Chlorobium limicola* (Fig. 1).

Moreover, Burns et al. (2017) [2] have demonstrated that *C. limicola* grows in illuminated anoxic water and conducts anaerobic photosynthesis using sulphides as electron donor for carbon dioxide fixation.

To comment on the above mentioned findings, we would like to propose a hypothesis as to what might be the reason that microorganisms on the Earth synthesized ergothioneine under anaerobic conditions: It is to be stated that in oxygen-free atmosphere there was no ozone protection from incidental radiation that degraded molecules of water in microorganisms resulting in the formation of free hydroxyl radicals (˙OH) – the most deleterious reactive oxygen species for any biostructure. To prevent damage of biostructures, ergothioneine donates hydrogen radical (˙H), thereby ˙OH radicals are scavenged.

Since a half-life of ˙OH radical is ca. 1 ns, it is comprehensible that ˙OH radical abstracts H˙ radical from any adjacent molecule. It means that if H˙ radical is abstracted from histidine or hercynine, the produced species of ˙C-, ˙N-, or ˙O-type can damage the biostructure due to their high reactivity. However, in case of the same mechanism of H˙ radical trapping from ergothioneine, one could state that while similar ˙C-, ˙N-, or ˙O-type radicals are generated, the formed ˙S-type radical should be classified as long-living, less reactive, which finally may recombine to form harmless disulfide type compounds (Fig. 2).

The energy necessary to abstract a hydrogen atom from its bond with biogenic atoms (C, N, O, S, P) predetermines the sulphur atom to act in its thiol – SH form as the most appropriate donor of hydrogen atom. It is just the thiol group in ergothioneine, which provides the necessary hydrogen atom to scavenge OH radicals. Since both hercynine and histidine are not thiols, they cannot act as donors of hydrogen atom from a thiol group but both molecules – hercynine and histidine – are donors of electrons.

Microorganisms synthesized ergothioneine under anaerobic conditions due to the ability of ergothioneine to scavenge ˙OH radicals forming by cosmic radiation, which was in oxygen free athmosphere enormously high.

At the same time, we point out that, interestingly, in further phylogenic development ergothioneine played a significant role as an antioxidant. In vertebrates it is not synthesized, but they possess a genetically coded transporter OCTN1 [3–5]. It indicates that in ancient times ergothioneine was synthesized and transported by organisms, which survived in anoxic environment. Besides ergothioneine, OCTN1 transports some further both endo- and exogenous agents including histidine and hercynine.

Ergothioneine is so far classified as an endogenous compound, which is ingested by individuals in a diet. However, since the synthesis of ergothioneine has been fully solved recently, up to date there are several commercial producers, who marketed this synthetic agent to be used as a nutritional supplement. So since currently ergothioneine is not classified as a medicament, its usage is just a nutritional supplement.

Conflict of interest

The authors declare no conflict of interest.

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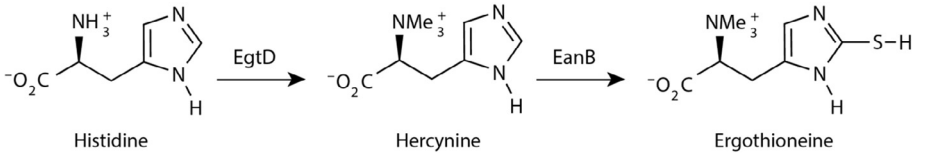

Fig. 1. Biosynthetic pathway of ergothioneine under anaerobic conditions adapted from Ruczyszky and Liu (2017) [1]: The enzyme EgtD converts the amino acid histidine into hercynine (Me, methyl group). The enzyme EanB catalyzes the synthesis of ergothioneine directly from hercynine in the presence of a sulphur donor under anaerobic conditions.

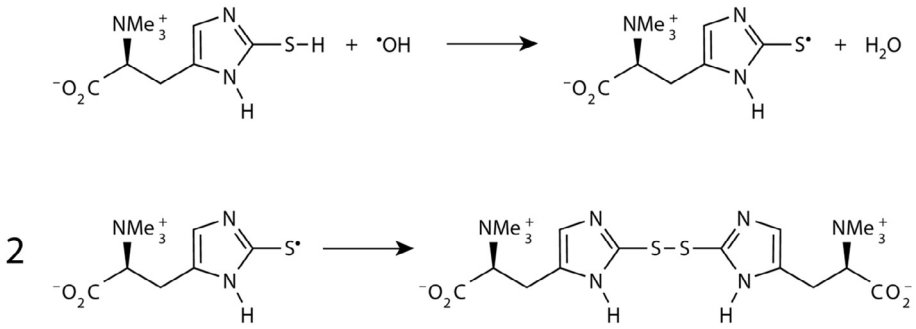

Fig. 2. Abstraction of the H˙ radical from ergothioneine resulting in the formation of ˙S-type radical, which undergoes recombination of two ˙S-type radicals to a disulfide type compounds.

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