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Thiol-Modification as Important Mode of Action for Allicin from Garlic (*Allium sativum*) †

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Abstract: Garlic is a common ingredient in food, normally used as spice but is also used since ancient times for its health beneficial activity. The thiosulfinate allicin is the first active compound in freshly damaged garlic tissue and reacts with thiol-groups. Hence, allicin is able to modify thiol groups, both of protein cysteine-residues and low-molecular weight thiols like glutathione. This thiol-modification is supposed to be an important mechanism for allicin's biological activity. Here, the mechanisms and possible targets for allicin in cells are discussed.

Keywords: garlic; *Allium sativum*; allicin; thiol; *S*-thioallylation

1. Introduction

Garlic (*Allium sativum* L.) is used as spice in food since ancient times and it is well known for its health-beneficial and even therapeutic properties. Its health properties have been documented in many scientific studies [1]. Therefore, garlic is potentially interesting for its nutriceutical use. However, the modes of action of garlic compounds are still not fully understood.

Allicin is the first compound that is produced in freshly damaged garlic tissue from the non-proteinogenic amino acid alliin. One clove of garlic produces about 50 mg allicin. However, allicin has a Janus-face. On the one hand, there are many different beneficial effects ascribed to allicin but, on the other hand, allicin is a broad-spectrum biocide, killing microbial and human cells [2]. Allicin is a very reactive thiosulfinate that is able to oxidize thiol groups in a reaction that is similar to the thiol-disulfide exchange reaction. Thus, the former thiol is oxidized to an *S*-thioallyl adduct, the process is called *S*-thioallylation [3]. In a second step it is possible that this adduct reacts with a second thiol within the protein to form a disulfide bridge; the *S*-thioallyl residue is reduced to allylmercaptane.

Both protein thiols and low-molecular weight thiols like glutathione are targets for *S*-thioallylation. The thioallylated glutathione (*S*-mercaptoglutathione) cannot be used as redox-buffer, although *S*-mercaptoglutathione is also a substrate for glutathione reductase, which recycles *S*-mercaptoglutathione to GSH and allylmercaptane using NADPH [4]. Consequently, the pentose-phosphate pathway (PPP), which is a primary source of NAPDH in the eukaryotic cell, is crucial to resist against allicin [5].

Furthermore, allicin reacts with protein thiol-groups. In a proteome-wide study of human cells, 232 proteins were found that are thioallylated upon exposure to sublethal concentration of allicin. Most of these proteins were related to the cytoskeleton. Also, enzymes involved in glycolysis were modified, which suggests that allicin impairs the primary metabolism of the cell directly. These are two examples how *S*-thioallylation might influence the cellular physiology and, thus, explain allicin's mode of action.

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