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Opinion Article

Deglycosylation of Ginsenosides by Human Intestinal Bacteria: A Key to Enhanced Bioactivity

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DESCRIPTION

Ginsenosides are bioactive compounds primarily found in *Panax ginseng*, a well-known medicinal herb in traditional Asian medicine. These compounds are considered the major pharmacologically active constituents of ginseng, associated with numerous health benefits, including anti-inflammatory, antioxidant, anti-cancer and neuroprotective effects. However, the bioavailability of ginsenosides, especially the primary or native forms (such as ginsenoside Rb1, Rc, Rd), is relatively low when consumed orally. This is because these primary ginsenosides are poorly absorbed in their native glycosylated form. Interestingly, human intestinal bacteria play an important role in converting these ginsenosides into more bioavailable forms through a process called deglycosylation. This article describes the deglycosylation process of ginsenosides by human intestinal bacteria and the significance of this transformation in enhancing their bioactivity.

Structure and classification of ginsenosides

Ginsenosides are triterpene saponins and their chemical structure comprises a dammarane path attached to various sugar moieties. Based on the sugar units and their attachment sites, ginsenosides are categorized into two main types: Protopanaxadiol (PPD) and Protopanaxatriol (PPT) ginsenosides. Protopanaxadiol ginsenosides like Rb1, Rc and Rd have sugar moieties attached to the C-3 and C-20 positions, whereas protopanaxatriol ginsenosides such as Re and Rg1 have sugars attached to the C-6 and C-20 positions.

The structural complexity and the attached sugar residues make native ginsenosides less bioavailable. These glycosylated ginsenosides are resistant to absorption in the upper gastrointestinal tract. However, they undergo transformation when they reach the large intestine, where the microbial community degrades the sugar moieties, thereby enhancing their absorption.

Role of human intestinal bacteria in ginsenoside deglycosylation

Human intestinal bacteria, particularly those residing in the colon, play a pivotal role in the deglycosylation of ginsenosides. This process involves the hydrolysis of sugar moieties attached to the ginsenosides, converting them into deglycosylated, aglycone forms that are more easily absorbed. The microbial enzymes, particularly glycosidases produced by various bacterial strains, are responsible for this transformation.

Several bacterial species have been identified for their deglycosylation activity, including *Bacteroides, Eubacterium, Clostridium* and *Lactobacillus*. For instance, *Bacteroides* species have been shown to efficiently convert ginsenoside Rb1 into compound K, which exhibits stronger biological effects. Similarly, *Lactobacillus* strains, commonly found in fermented foods, have been demonstrated to deglycosylate ginsenosides into bioactive metabolites.

The process of deglycosylation typically occurs in a stepwise manner. For example, the primary ginsenoside Rb1 is first converted into intermediate metabolites like ginsenoside Rd and F2, followed by the formation of the aglycone compound K. This deglycosylated form of ginsenoside Rb1 has significantly enhanced biological activities compared to its parent compound.

Metabolic pathway and key enzymes

The transformation of ginsenosides by gut bacteria involves a series of enzymatic reactions. The primary enzymes involved are β-glucosidases, α-rhamnosidases and arabinosidases, which cleave the sugar moieties attached to the ginsenoside method.

For example, β-glucosidase is an enzyme produced by certain bacterial strains that hydrolyzes the β-D-glucosidic bonds, removing the sugar molecules and leading to the formation of ginsenoside metabolites with fewer sugar units. In some cases, the intermediate metabolites themselves can be further

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hydrolyzed by different bacterial strains, leading to a complete deglycosylation of the ginsenoside.

The metabolic pathway of ginsenoside Rb1 to compound K is one of the most extensively studied transformations. It involves the following steps:

- Ginsenoside Rb1 → Ginsenoside Rd (removal of one sugar unit)
- Ginsenoside Rd → Ginsenoside F2 (further deglycosylation)
- Ginsenoside F2 → Compound K (complete removal of sugar residues)

Each step is mediated by specific bacterial enzymes that selectively hydrolyze the glycosidic linkages, highlighting the complex relationship between gut microbiota and ginsenoside metabolism.

Enhanced bioactivity of deglycosylated ginsenosides

The deglycosylation of ginsenosides leads to the formation of metabolites such as compound K, Rh1 and F2, which are known to have stronger pharmacological effects than their parent compounds. For example, compound K has demonstrated anti-cancer properties by inhibiting the growth of various cancer cells, including colon, liver and breast cancer cells. It also exhibits potent anti-inflammatory and neuroprotective effects, making it a potential candidate for therapeutic applications.

Moreover, the deglycosylated forms of ginsenosides have shown enhanced bioavailability. Compound K, for instance, is more readily absorbed by the intestinal cells, thereby increasing its concentration in the bloodstream and improving its therapeutic potential.

Implications for ginseng-based therapeutics

Understanding the role of intestinal bacteria in ginsenoside metabolism has important implications for the development of ginseng-based therapeutics. It highlights the importance of gut microbiota in modulating the bioavailability and efficacy of ginsenosides. Furthermore, this insight could lead to the development of probiotic supplements that enhance ginsenoside deglycosylation, thereby improving their therapeutic potential.

Additionally, personalized medicine approaches could consider an individual's gut microbiota composition to predict their response to ginseng supplementation. People with a gut microbiome rich in ginsenoside-degrading bacteria may experience more pronounced health benefits from ginseng consumption.

CONCLUSION

The deglycosylation of ginsenosides by human intestinal bacteria is a critical process that enhances the bioavailability and pharmacological effects of these compounds. By converting the native, poorly absorbable forms of ginsenosides into bioactive metabolites like compound K, gut bacteria play a major role in modulating the health benefits of ginseng. Future research on the interaction between gut microbiota and ginsenosides could prepare for more effective ginseng-based therapies customized to individual microbiome profiles.