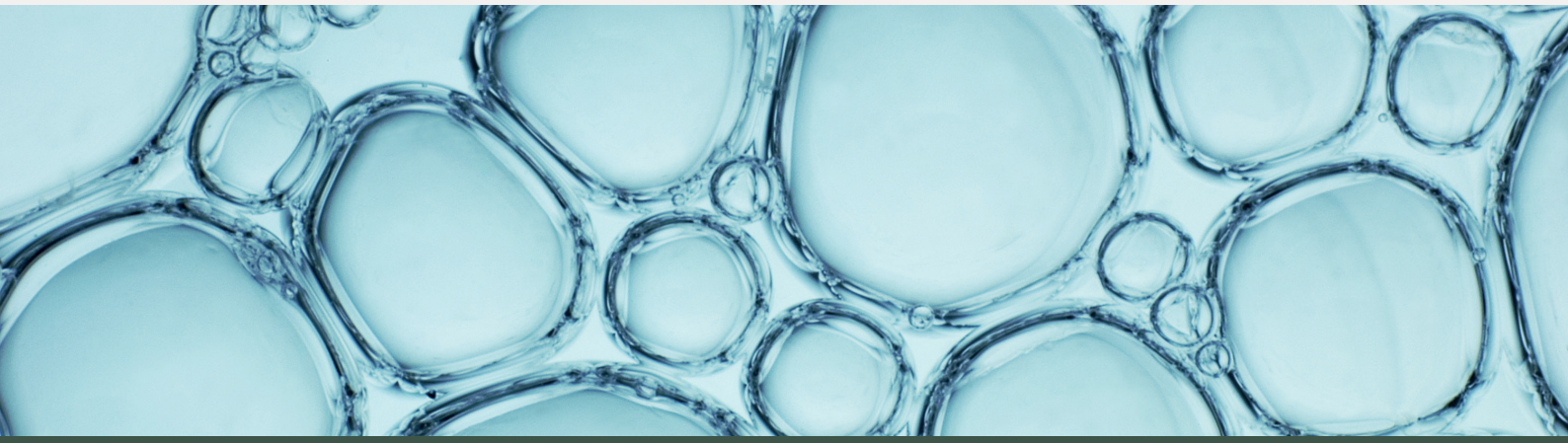
Fermentation of medicinal plants

UNLOCKING THE POTENCY OF NATURAL INGREDIENTS THROUGH TARGETED AND CONTROLLED TRADITIONAL FERMENTATION



Medicinal plants are rich sources of bioactive metabolites. However, many of these compounds have limited intrinsic bioavailability due to the plant matrix and their complex molecular structure. Many of these metabolites require enzymatic transformation by the gut microbiota before they can be efficiently absorbed and exert their biological effects.[1,2] As a result, the efficacy of medicinal plants can vary substantially between individuals due to differences in gut microbiome composition.[1]

Fermentation provides a biologically relevant strategy to address this limitation. By shifting these biotransformation processes from the variable gut environment to a controlled setting, fermentation enables a more consistent expression of plant bioactivity. Growing scientific evidence increasingly demonstrates that fermentation not only preserves medicinal plant functionality, but also adds functionality through the generation of fermentation-derived metabolites and postbiotic components. This emerging field is redefining how botanical ingredients are developed and applied.[1,3]

SCIENTIFIC REPORT

Fermedics
Fermented Ingredients

UNLOCKING NATURE'S POTENCY

ORIGINS OF FERMENTATION

Fermentation is one of humanity's oldest biotechnologies, with its origins dating back more than 14,000 years.[4] Long before its mechanisms were understood, early humans observed that food left to rest would undergo spontaneous fermentation. What began as chance observation gradually evolved into a deliberate and valued practice.

In Mesopotamia and Persia, fermented beverages and dairy products were already widely consumed. The Greeks and Romans embraced wine, fermented vegetables and fish sauces. At the same time, Asian cultures refined complex fermentation systems based on soy, rice and vegetables, while African societies applied fermentation to cereals and roots.[4,5,6]

FUNCTIONAL ROLE OF TRADITIONAL FERMENTATION

The widespread adoption of fermentation was driven by its important functional advantages in food systems. By inhibiting spoilage and pathogenic microorganisms through acidification and microbial competition, fermentation enabled perishable foods to be preserved for longer periods and transported over long distances. This was essential not only during migration and seasonal scarcity, but also for expanding trade routes and overseas trading activities.[2] Beyond preservation, fermentation also improved the sensory qualities of food, enhancing taste, aroma and texture. These changes increased palatability and contributed to the integration of fermented foods into traditional diets across cultures.[2]

EXAMPLES OF TRADITIONAL FERMENTED FOODS ACROSS CULTURES

Region	Food/Product	Raw Material	Key Microorganisms	Primary Function
Europe	Sauerkraut	Cabbage	Lactobacillus, Leuconostoc	Preservation, vitamin supply
Asia	Miso	Soybeans	Aspergillus oryzae, LAB, yeasts	Protein breakdown, flavor development
Asia	Kimchi	Vegetables	LAB	Preservation, digestive support
Caucasus	Kefir	Milk	LAB, yeasts	Improved digestibility, probiotic effects
Japan	Natto	Soybeans	Bacillus subtilis	Enzymatic activity, nutrient enhancement
Africa	Ogi	Cereals	LAB, yeasts	Nutrient availability, safety
South America	Chicha	Maize	Yeasts, LAB	Energy source, preservation

Table. Examples of traditional fermented foods.[5]

FERMENTATION: FROM TRADITION TO SCIENCE

For centuries, the benefits of fermentation were understood primarily through empirical observation and traditional practice. Fermented foods and botanicals were consistently associated with improved preservation, digestion, vitality and overall well-being long before the underlying biological mechanisms were known.

Advances in microbiology, biochemistry and microbiome science are now providing a scientific framework to explain these traditional observations. Modern research has revealed fermentation to be a highly dynamic biochemical process in which microorganisms transform complex food and plant matrices into a broad spectrum of metabolites. As a result, fermentation is increasingly being recognized not merely as a preservation technique, but as a biologically active process capable of fundamentally altering the functional properties of foods and medicinal plants.[1,3,7]

THE GUT HEALTH ADVANTAGES OF FERMENTATION

Fermentation has long been associated with digestive health and vitality across traditional food cultures worldwide. Fermented foods such as kefir, kimchi, sauerkraut, kombucha and fermented botanicals were historically valued for their beneficial effects on gut health and overall well-being.

Modern research is increasingly validating these traditional observations. A landmark 2021 study from the Stanford University School of Medicine showed that diets rich in fermented foods significantly increased microbiome diversity and reduced inflammatory markers, whereas high-fiber diets alone did not produce the same effects.[8] These findings suggest that the broad nutrient and metabolite diversity generated during fermentation play a more important role in microbiome modulation than fiber quantity alone.

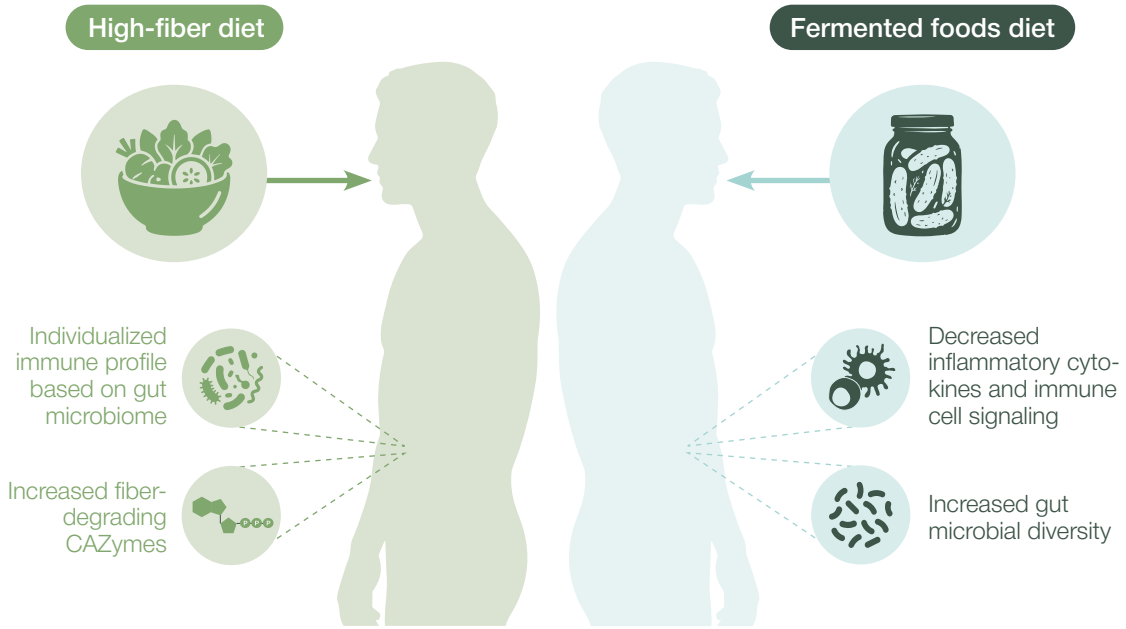


Fig. Gut-microbiota-targeted diets modulate human immune status. Cell. 2021[8]

MEDICINAL PLANT ACTIVITY IS MICROBIOME-DEPENDENT

A growing body of research highlights the central role of the gut microbiome not only in digestion, but also in the accessibility, transformation and efficacy of many dietary and botanical metabolites. Numerous polyphenols, glycosides, alkaloids and other plant metabolites depend on microbial enzymes to be converted into smaller, absorbable and biologically active forms.[1,9]

Modern lifestyle factors are placing increasing pressure on microbiome diversity and functionality. Diets low in plant diversity and rich in ultra-processed foods, frequent antibiotic exposure, chronic stress and other environmental influences have all been associated with a progressive loss of microbial diversity and metabolic capacity.[10,11] As microbiome functionality declines, so does the ability to efficiently convert many dietary and botanical compounds into their biologically active forms.

As a result, the efficacy of medicinal plants can vary considerably between individuals. Well-known examples include the deglycosylation of ginsenosides from Panax ginseng into more bioactive minor ginsenosides such as Compound K[12] and the conversion of ellagitannins and ellagic acid from pomegranate (Punica granatum) into urolithins. In the case of pomegranate, only around 40% of individuals appear capable of efficiently producing urolithin A[13], while substantial variability has also been reported for the microbial conversion of ginsenosides. These examples are not unique. A growing number of studies indicate that the metabolism of many plant-derived compounds is strongly influenced by gut microbial activity, resulting in significant interindividual differences in bioavailability and biological response.

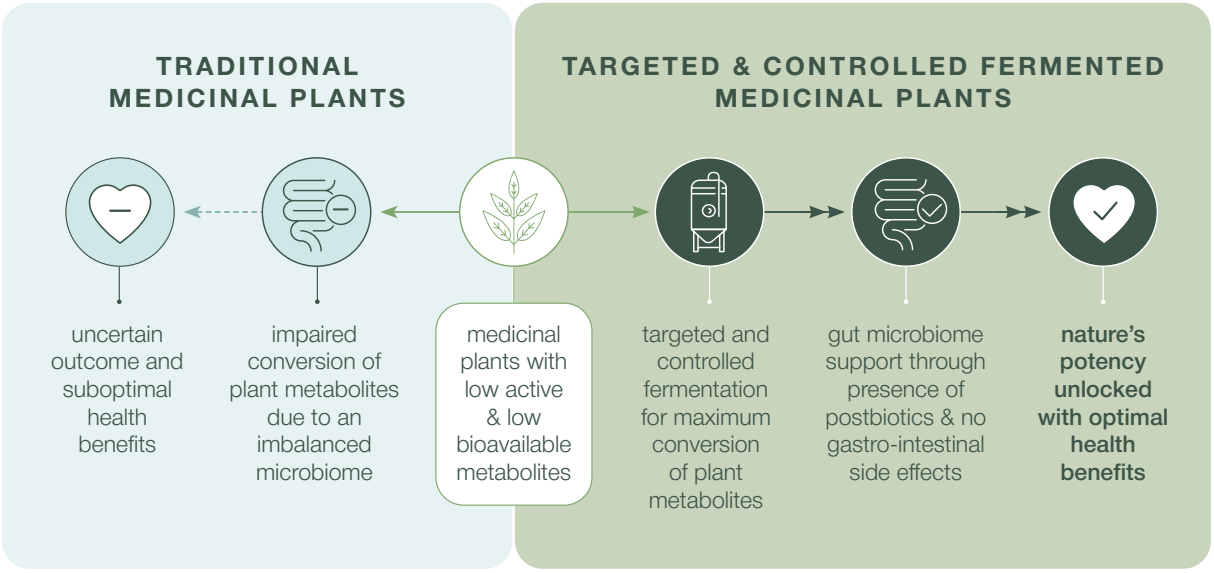


Fig. The benefits of fermented medicinal plants vs unfermented medicinal plants.

KEY ADVANTAGES OF FERMENTATION

By performing important microbial transformations before consumption, fermentation can reduce interindividual variability and lead to more consistent, reproducible and functionally active botanical ingredients.[1]

- ✓ Improved accessibility and absorption of plant compounds
- ✓ Conversion of precursor compounds into more bioactive metabolites
- ✓ Reduced dependence on individual microbiome variability
- ✓ Increased nutrient density and metabolite diversity
- ✓ Generation of beneficial postbiotic compounds and microbial metabolites
- ✓ Reduction of antinutritional compounds that impair absorption
- ✓ Enhanced consistency and reproducibility of botanical functionality
- ✓ Improved taste, aroma and sensory properties
- ✓ Preservation of the natural complexity and synergy of the whole plant matrix

QUALITY DIFFERENCES IN FERMENTATION TECHNOLOGIES

Not all fermentation processes produce the same outcomes. The biochemical transformations induced during fermentation depend strongly on the microbial strains used, substrate composition and process conditions such as pH, temperature, oxygen availability and fermentation time.[7]

As a result, fermentation generates a wide range of compositional profiles rather than a single uniform product. These differences can significantly influence the concentration, distribution and standardization of plant-derived metabolites, fermentation-derived compounds and microbial components.

TYPES OF FERMENTATION

Fermentation can broadly be divided into traditional and precision-based approaches.

Traditional fermentation, including spontaneous fermentation and starter culture fermentation, uses naturally occurring or selected microorganisms to transform whole plant or food materials through complex biological processes. These traditional systems are based on long-established practices and typically produce a broad range of compounds originating from the raw material itself.[7]

In contrast, precision fermentation is designed to produce specific target molecules using optimized or engineered microorganisms under highly controlled conditions. Rather than transforming the entire plant matrix, this approach focuses on generating defined and isolated compounds with high precision and consistency.

	TRADITIONAL FERMENTATION	PRECISION FERMENTATION
Substrate	**Whole foods** (fruit, vegetables, plants, spices)	**Defined substrates** (purified sugars, nutrients)
Microorganisms	**Spontaneous or selected microorganisms** (mixed or culture-defined)	**Engineered/ optimized microorganism** (single, well-characterized strain)
Process control	**Low control**	**High control**
Outcome	**Whole fermented matrix** Complex mixture of natural metabolites within native matrix	**Isolated compound** Single, specific molecule independent of plant matrix

Fig. The difference between traditional fermentation and precision fermentation.

FERMEDICS PHYTOFERM™ FERMENTATION TECHNOLOGY

Fermedics' PhytoFerm™ technology builds upon traditional fermentation by combining natural fermentation processes with advanced process control. Carefully selected botanical substrates are fermented using traditional food-grade (QPS-listed) microorganisms under tightly controlled conditions, including pH, temperature, oxygen availability and fermentation time.

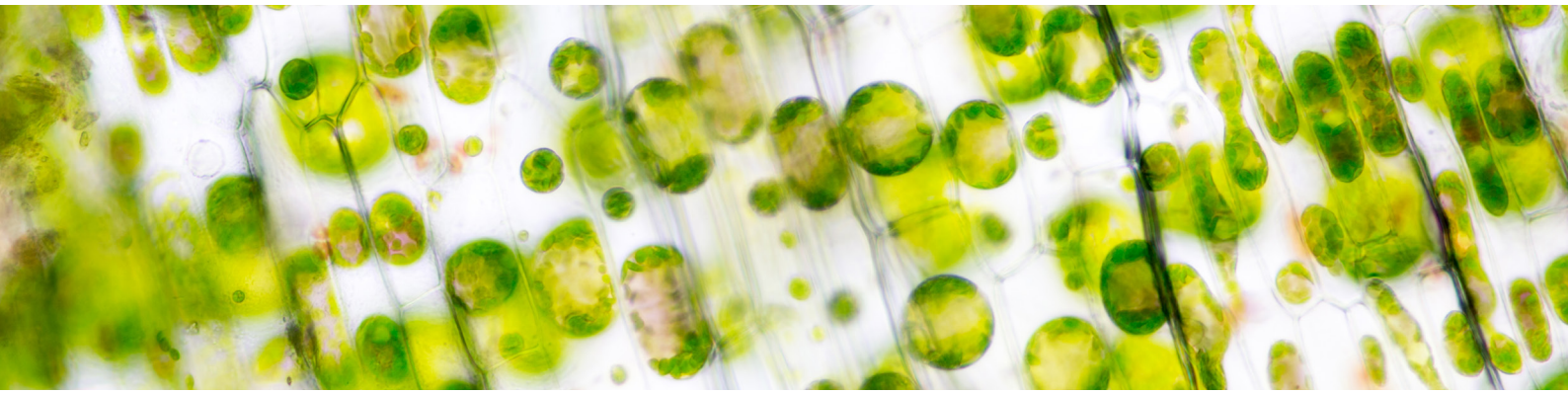
BENEFITS OF PHYTOFERM™ FERMENTATION

By combining the compositional complexity of traditional fermentation with advanced process control, Fermedics PhytoFerm™ technology delivers a highly reproducible and standardized fermentation strategy while preserving the natural integrity of botanical materials.

For each botanical, carefully selected food-grade microorganisms are chosen based on their natural ability to perform beneficial biotransformations within the plant matrix. This allows fermentation conditions to be tailored to the unique characteristics of each botanical while maintaining its full-spectrum complexity and naturally improving sensory characteristics through the modulation of taste- and aroma-active compounds.

This approach enables:

- ✓ Botanical-specific optimization of fermentation outcomes
- ✓ Targeted generation of bioactive metabolites through selected microbial strains
- ✓ More consistent and reproducible fermentation performance
- ✓ Reduced batch-to-batch variability
- ✓ Natural improvement of taste, aroma and overall sensory properties
- ✓ Preservation of the full-spectrum complexity and synergy of botanicals



KEY CHARACTERISTICS OF DIFFERENT TYPES OF FERMENTATION

TRADITIONAL SPONTANEOUS FERMENTATION	TRADITIONAL FERMENTATION WITH STARTER CULTURE	**FERMEDICS TRADITIONAL PHYTOFERM™ FERMENTATION**	PRECISION FERMENTATION
DEFINITION			
Natural fermentation driven by indigenous microorganisms	Natural fermentation using selected microbial strains	**Natural fermentation using selected microbial strains under controlled conditions**	Use of engineered or highly optimized microorganisms to produce specific target molecules
MICROBIAL SYSTEM			
Undefined, mixed microorganisms	Defined microbial strains	**Defined, QPS-listed microbial strains**	Optimized or engineered strains
SUBSTRATE			
Whole foods (fruit, vegetables, spices, plants, milk, cereals, ...)	Whole foods and specific food substrates	**Whole foods (fruits, vegetables, plants and spices)**	Defined substrates
LEVEL OF CONTROL & CONSISTENCY			
Low	Moderate	**High**	High
OUTPUT			
Broad, non-specific metabolite formation	Partial and predictable bioconversion of substrates	**Defined end-points of metabolites within their natural compositional range**	Production of isolated compounds independent of original plant matrix
SAFETY			
Risk of spoilage and formation of unwanted by-products	Reduced risk of spoilage and formation of unwanted by-products	**Consistent quality by robust process control and reliable end-product analysis**	Considerations related to the use of engineered microorganisms

FERMEDICS FULL MATRIX BENEFIT

Fermedics' fermented ingredients are developed as full-matrix botanical ingredients, preserving the natural complexity and compositional diversity of the original plant material rather than isolating single compounds. Fermentation enhances the functionality of this natural matrix while maintaining the broad spectrum of phytochemicals and fermentation-derived metabolites that contribute to biological activity.

This approach is gaining increasing scientific attention as researchers recognize that the health effects of botanicals often arise from the interaction of multiple constituents rather than a single isolated compound. Recent concerns regarding high-dose isolated phytochemicals have further renewed interest in full-matrix botanical ingredients that preserve a broader range of naturally occurring compounds in physiologically relevant proportions.[14]

A preserved full matrix supports complementary and synergistic biological interactions. For example, the activity of astragalus is influenced not only by its polysaccharides, but also by triterpenoid saponins and flavonoids.[15] Similarly, the benefits of turmeric extend beyond curcuminoids alone and include Ukonan-type polysaccharides, volatile oils and other bioactive constituents.[16,17,18,19] In fermented pomegranate, biological activity may arise from the combined action of native polyphenols, fermentation-derived metabolites and postbiotic components generated during fermentation.[20,21]

By preserving the full natural plant matrix while enhancing its functionality, fermentation supports a more holistic, balanced and physiologically relevant mode of action that better reflects the inherent complexity of botanical ingredients.

KEY CONVERSIONS DEFINING PHYTOFERM™ OUTCOMES

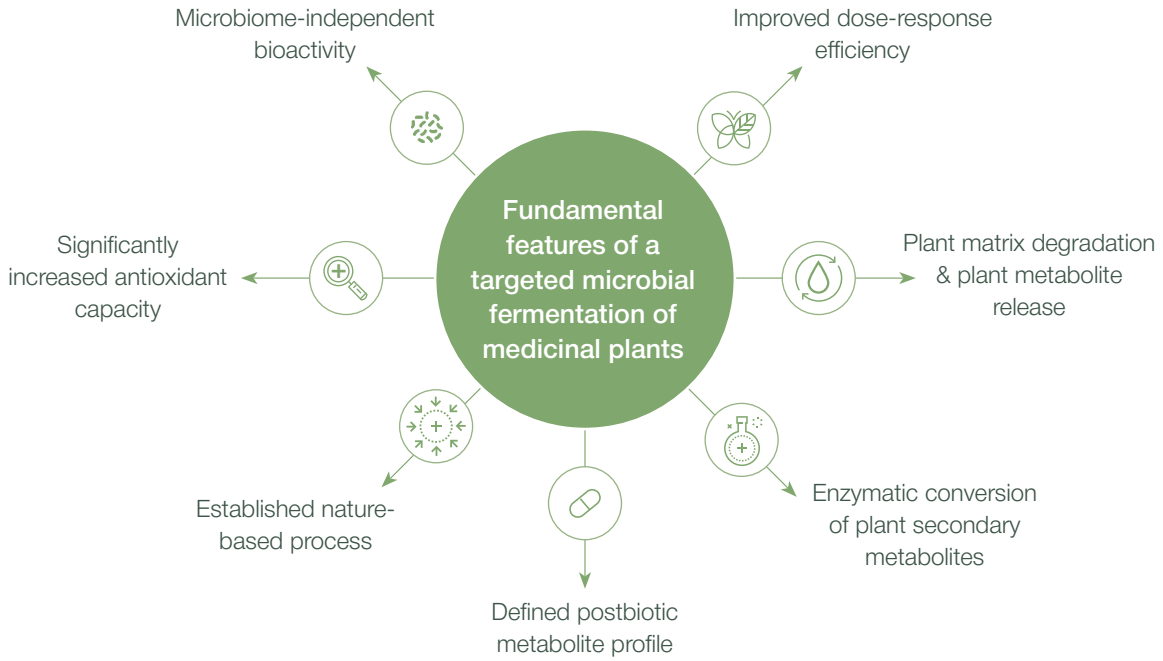
Through coordinated enzymatic biotransformations, PhytoFerm™ fermentation naturally modifies plant-derived metabolites through three interconnected mechanisms:

1 **Plant matrix breakdown**
Microbial enzymes partially degrade the complex plant matrix, releasing naturally occurring compounds from their structural surroundings and increasing their accessibility.

2 **Bioconversion of plant metabolites**
Microbial enzymes naturally convert plant metabolites through fermentation, altering their physicochemical characteristics within the botanical matrix and resulting in improved bioavailability and biological activity.

3 **Generation of postbiotics and fermentation-derived metabolites**
Microbial metabolism generates a broad spectrum of bioactive metabolites, including organic acids, short-chain fatty acids and signaling molecules. Following Fermedics' PhytoFerm™ fermentation process, the microorganisms are inactivated, while their cellular structures and fermentation-derived metabolites remain present in the final ingredient as postbiotic components.

Together, these conversions improve solubility, accessibility and physicochemical properties of plant-derived metabolites.



PLANT MATRIX BREAKDOWN

Plant-derived ingredients consist of a complex structural matrix composed of cell wall components such as cellulose, hemicellulose, pectin and lignin, as well as proteins and lipids. This matrix can limit the accessibility of naturally occurring compounds by physically entrapping or binding them within the plant structure. For example, polyphenols are often associated with cell wall components, while curcuminoids in turmeric are embedded within a lipid-rich matrix.[22,23]

During fermentation, microbial enzymes such as cellulases, pectinases and proteases partially degrade these structural components. This controlled breakdown facilitates the release of embedded compounds and increases their accessibility within the fermented material.[1]

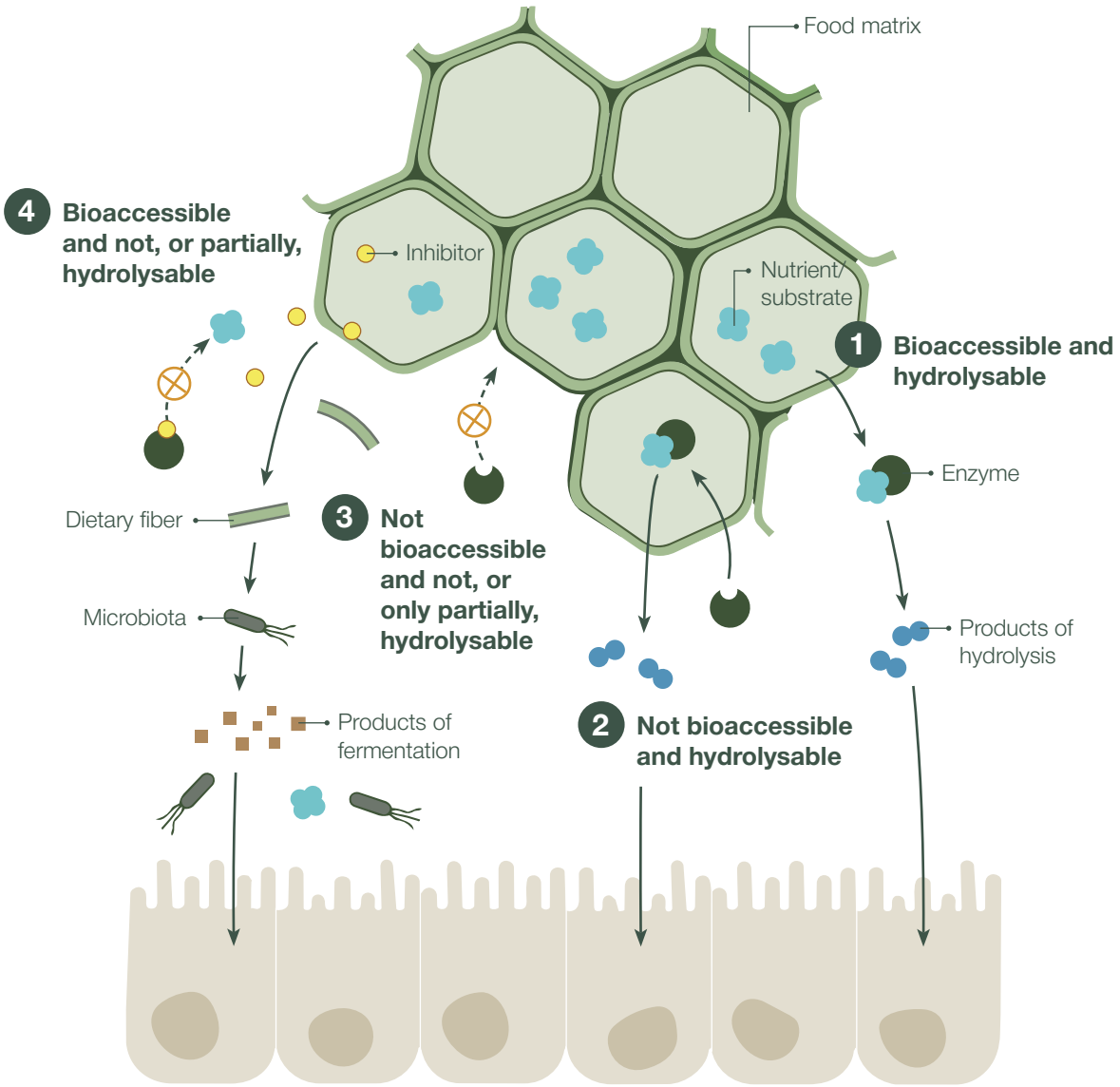
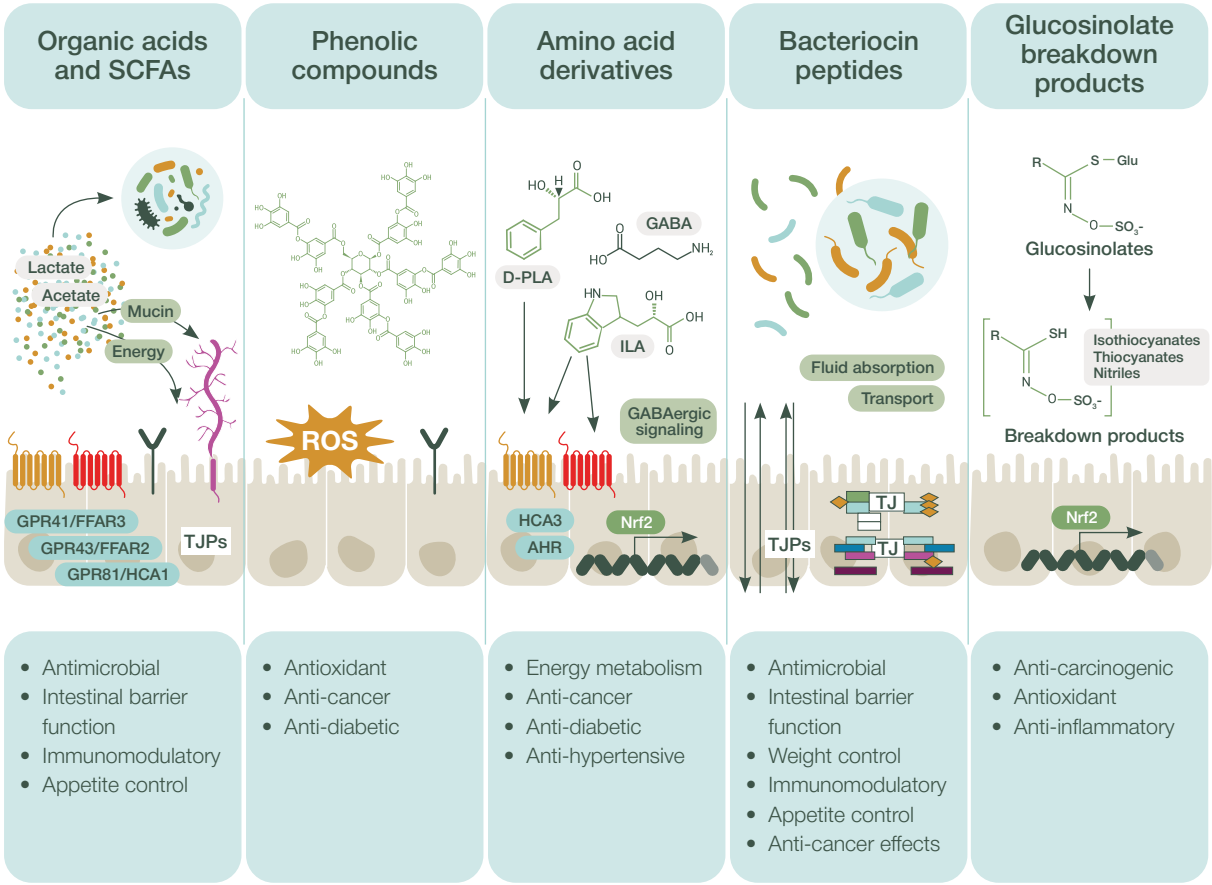


Fig. Bioaccessibility and associated concepts. Trends in food science & technology (2024).[24]

ENZYMATIC CONVERSIONS OF PLANT-DERIVED METABOLITES

In addition to matrix breakdown, fermentation involves the enzymatic conversion of plant-derived metabolites into different molecular forms. Many phytochemicals occur in bound or glycosylated forms, which can influence their solubility and interaction within the matrix.

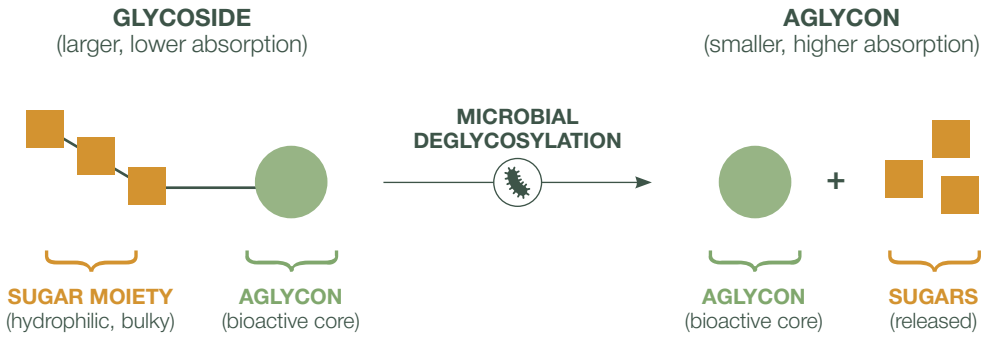
Microbial enzymes catalyze transformations such as deglycosylation, hydrolysis, depolymerization, oxidation–reduction reactions, decarboxylation and isomerization, converting the structure and physicochemical properties of these compounds.[1,9]



Overview of potential health-promoting properties exhibited by bioactive compounds from lacto-fermented fruits and vegetables. Wei et al. Lacto-Fermented Fruits and Vegetables: Bioactive Components and Effects on Human Health. Annu Rev Food Sci Technol. 2025[25]

DEGLYCOSYLATION OF PLANT-DERIVED METABOLITES

Many plant-derived metabolites such as phenolic compounds, terpenoids and saponins naturally occur in glycosylated forms, where sugar moieties are attached to the core molecule. These glycosylated structures are often highly polar, influencing their solubility and intestinal absorption. During fermentation, microbial enzymes such as glycosidases catalyze the removal of these sugar groups, a process known as deglycosylation. This conversion results in the formation of corresponding aglycone forms.[1,9]



These transformations are particularly relevant for adaptogenic botanicals, where key active constituents are often present in glycosylated forms. For example, in plants such as astragalus, ginseng, jiaogulan and ashwagandha, fermentation facilitates the enzymatic conversion of saponins and terpenoid glycosides into their corresponding aglycone forms.[1]

DEPOLYMERIZATION OF PLANT-DERIVED POLYSACCHARIDES

As for polyphenols, many botanicals also contain high-molecular-weight polysaccharides, such as those found in turmeric and astragalus. These complex structures again influence solubility, accessibility and interaction with immune-related pathways.

During fermentation, microbial enzymes partially depolymerize these polysaccharides into smaller and lower-molecular-weight fractions, altering their molecular size and physicochemical properties. Fermentation-induced depolymerization of turmeric and astragalus polysaccharides has been widely associated in the literature with enhanced solubility and increased measurable biological activity in vitro and preclinical models.[15,16,17,18,19]

DEPOLYMERIZATION OF PLANT-DERIVED POLYPHENOLS

Polyphenols and related compounds, including curcuminoids, are often present as complex or high-molecular-weight structures within raw plant materials, which can limit their dispersion, solubility and bioavailability.

During fermentation, enzymatic activity induces depolymerization, breaking down complex structures into smaller, lower-molecular-weight fractions. This transformation improves their solubility and is associated with increased antioxidant-related activity in all Fermedics fermented ingredients.[20]

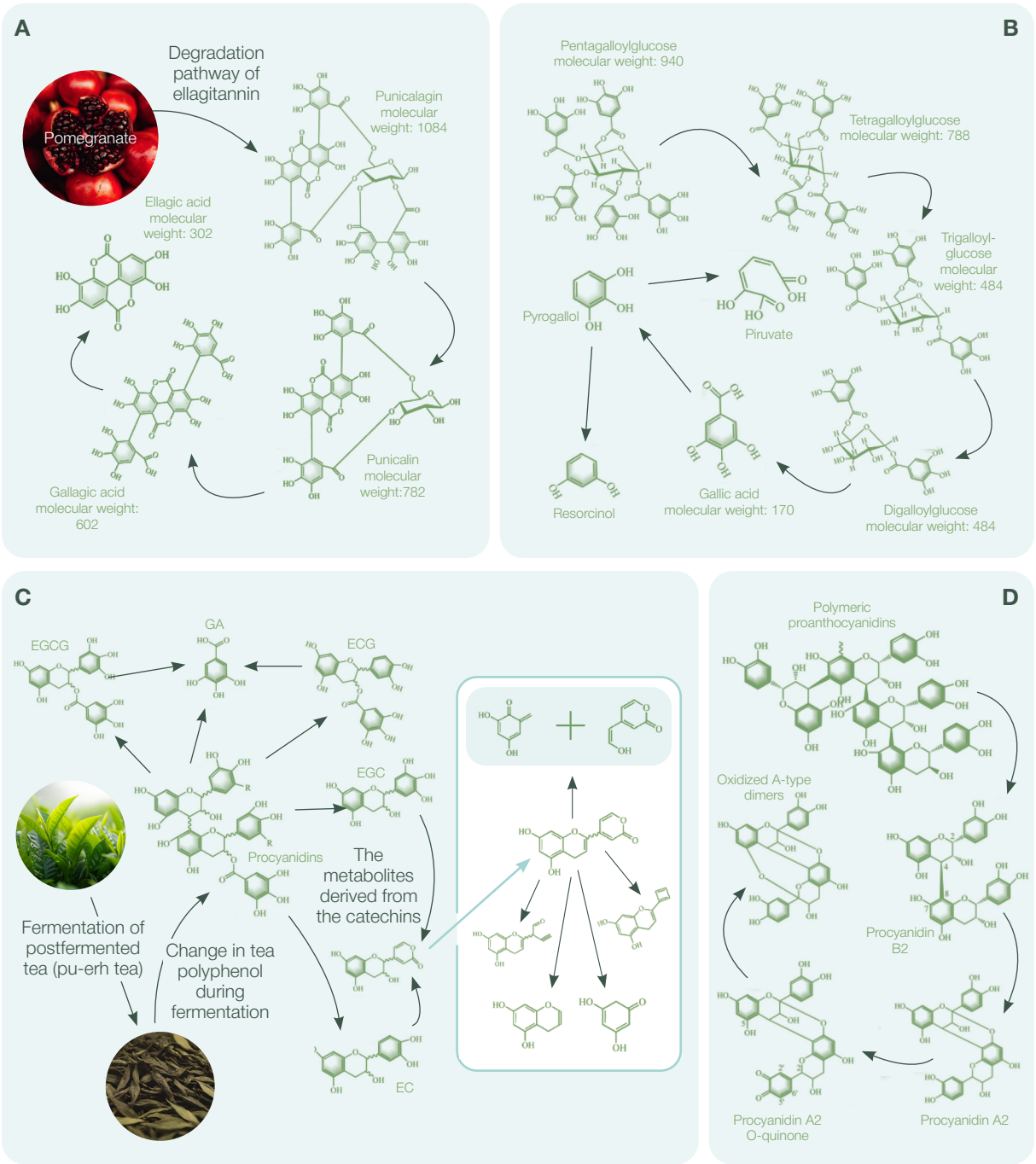


Fig. Effects of fermentation on bioactivity and the composition of polyphenols contained in polyphenol-rich foods. Foods (2023)[20]

FORMATION OF POSTBIOTICS AND POSTBIOTIC METABOLITES

In addition to transforming plant-derived compounds, fermentation also generates microbial-derived components and metabolites that contribute to the compositional complexity of fermented ingredients. These fermentation-derived compounds include both postbiotics and postbiotic metabolites.

POSTBIOTICS

During Fermedics' PhytoFerm™ fermentation process, microbial activity is carefully controlled and halted at the optimal stage through sterilization. Although the microorganisms become inactivated, important microbial structures remain preserved within the final ingredient.[27,28]

According to the International Scientific Association for Probiotics and Prebiotics (ISAPP), postbiotics are defined as "preparations of inanimate microorganisms and/or their components that confer a health benefit on the host."[29] These include non-viable microbial cells and structural components such as peptidoglycans, lipoteichoic acids and membrane-associated molecules.[27,28]

These microbial structures are known to interact with biological recognition systems, including pattern recognition receptors such as Toll-like receptors (TLRs), and have been associated with modulation of immune function, gut barrier integrity and inflammatory signaling pathways.[27,28,30]

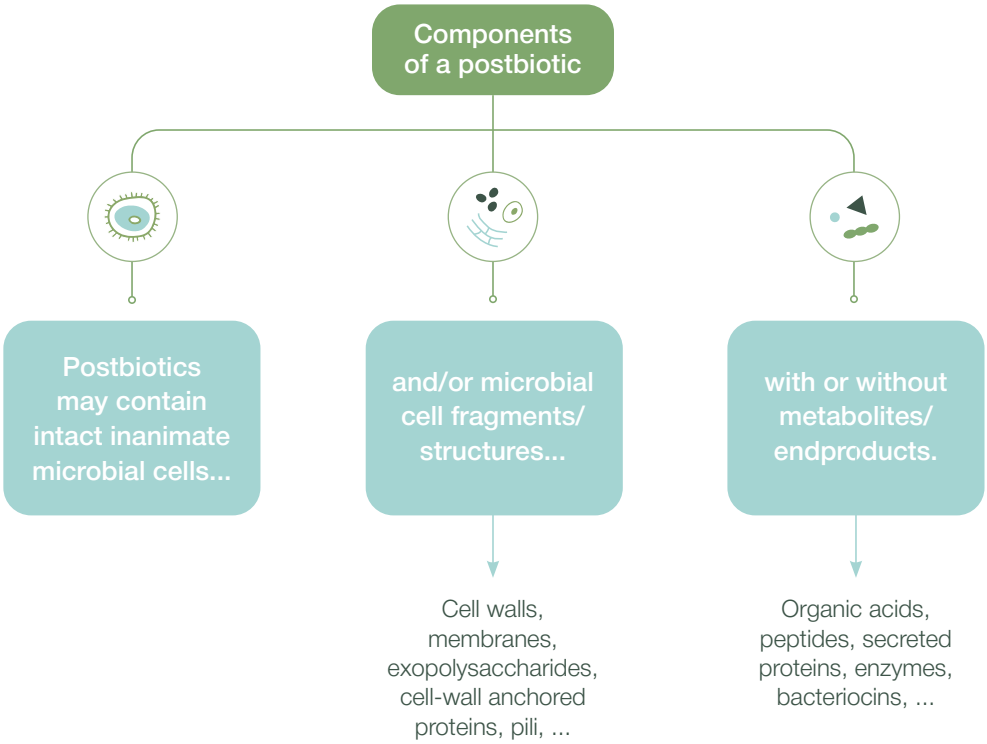


Figure. Schematic representation of the ISAPP definition and composition of postbiotics.
Adapted from the ISAPP postbiotics infographic.[33]

POSTBIOTIC METABOLITES

In addition to transforming plant-derived compounds, fermentation generates a broad spectrum of low-molecular-weight microbial metabolites through the metabolism of fermentable substrates. These include organic acids and short-chain fatty acids (SCFAs) such as acetate, propionate and butyrate, which are increasingly associated with gut barrier support, microbiome modulation and immune regulation.[30,31]

As a result, Fermedics PhytoFerm™ ingredients naturally contain a diverse range of fermentation-derived metabolites and postbiotic fractions, including microbial cell structures, organic acids and SCFAs. All PhytoFerm™ ingredients are standardized for specific postbiotic parameters, supporting greater compositional consistency, reproducibility and functional quality.

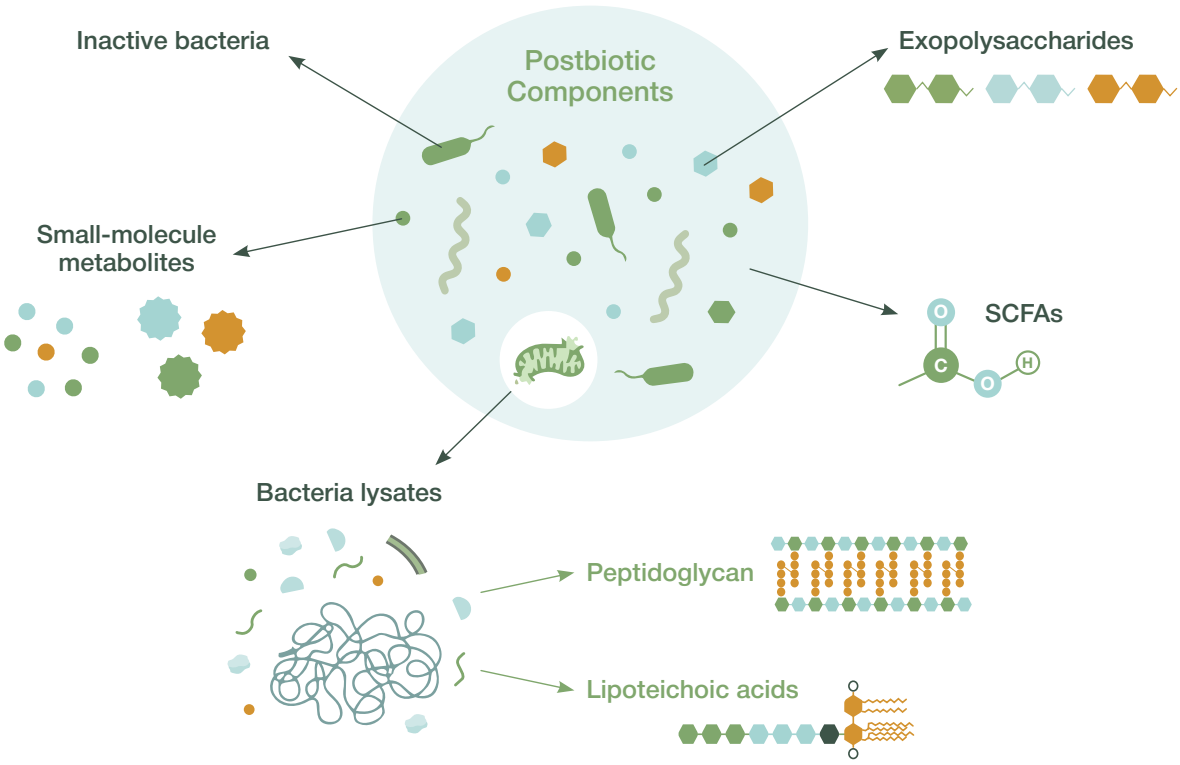
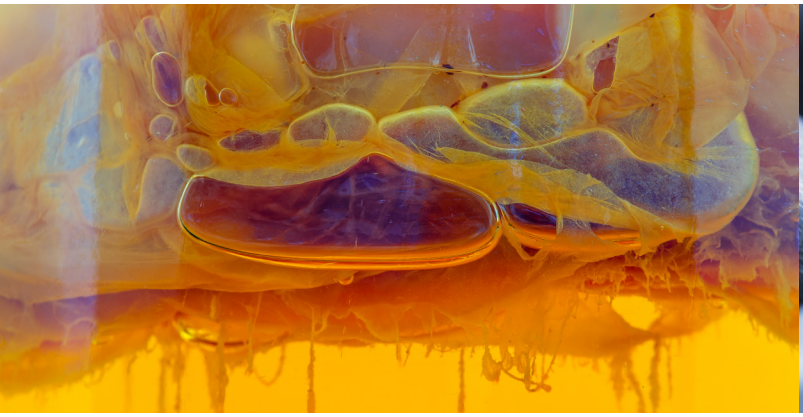


Fig. Postbiotics: Enhancing human health. eFood (2024)[32]



TRANSLATING MECHANISMS INTO FERMENTED INGREDIENTS

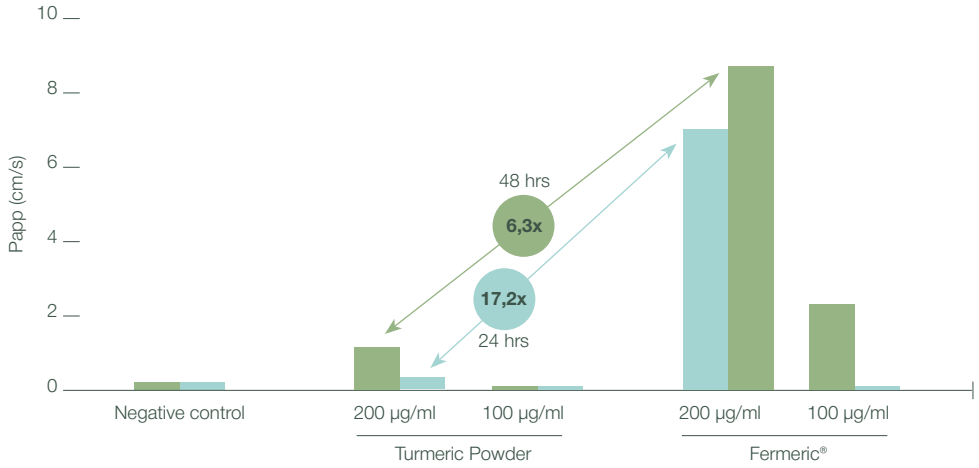
Fermedics has developed a portfolio of fermented botanical ingredients by applying the core biochemical mechanisms described above to a range of medicinal plants. These transformations are not merely theoretical concepts, but are directly reflected in the compositional and functional profiles of the resulting ingredients, where controlled PhytoFerm™ fermentation enables measurable shifts in metabolite distribution, bioactive accessibility and postbiotic composition within the natural plant matrix.

ENHANCED INTESTINAL ABSORPTION

Fermentation enhances the intestinal absorption of medicinal plant compounds by promoting the breakdown of the plant matrix and reducing molecular size. Microbial enzymatic activity facilitates the depolymerization of high-molecular-weight constituents and the conversion of complex glycosides into smaller, more permeable aglycones.[1,34,35,36] These transformations increase the accessibility of bioactive compounds and improve their ability to cross the intestinal barrier.

Test results for Fermeric®, fermented turmeric

This effect is well illustrated in fermented turmeric, where fermentation disrupts the plant matrix and converts curcuminoids into more bioavailable forms. As a result, significantly improved intestinal permeability and absorption have been observed compared to non-fermented turmeric preparations.[37]



Graphs. Apparent permeability coefficients (P app) – representing the appearance rate of curcumin in the receiver compartment of the test set-up, after transport across MDCK cells – after 24 and 48 hours. Transport across monolayers of MDCK cells (canine kidney epithelial cells) models the intestinal barrier for permeability assays. Source: TRI NEO BIOTECHNOLOGY

ENHANCED AGLYCONE PROFILE

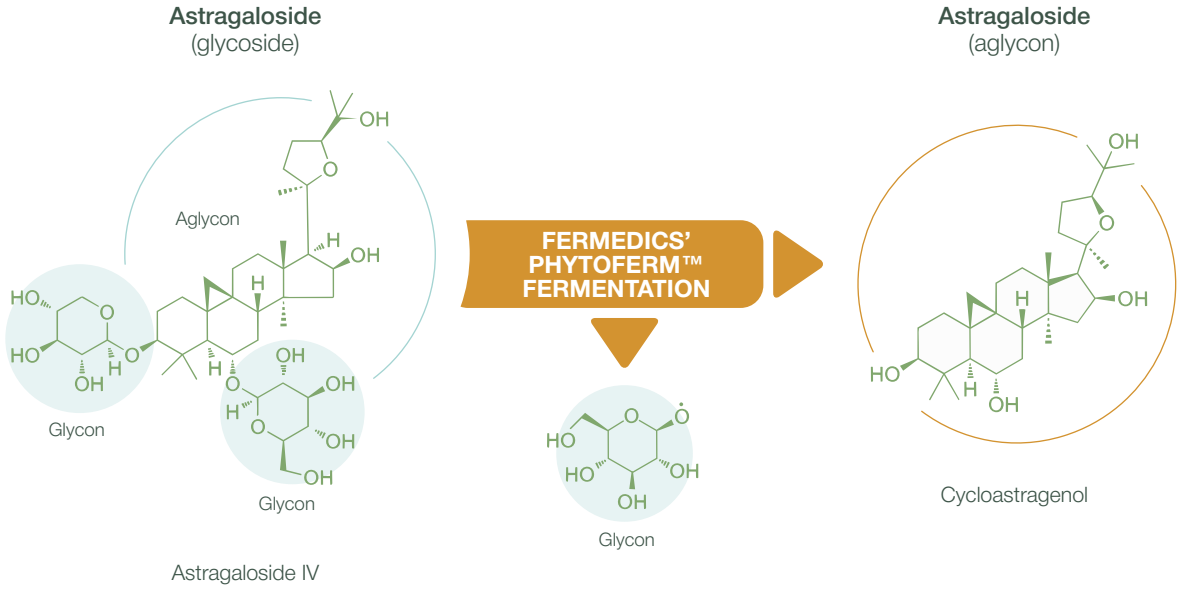
Fermedics' PhytoFerm™ fermentation supports the conversion of glycosylated plant compounds into their corresponding aglycone forms. As a result, Fermedics ingredients contain increased levels of fermentation-derived aglycone metabolites compared to their non-fermented botanical counterparts, while preserving the natural complexity of the plant matrix.

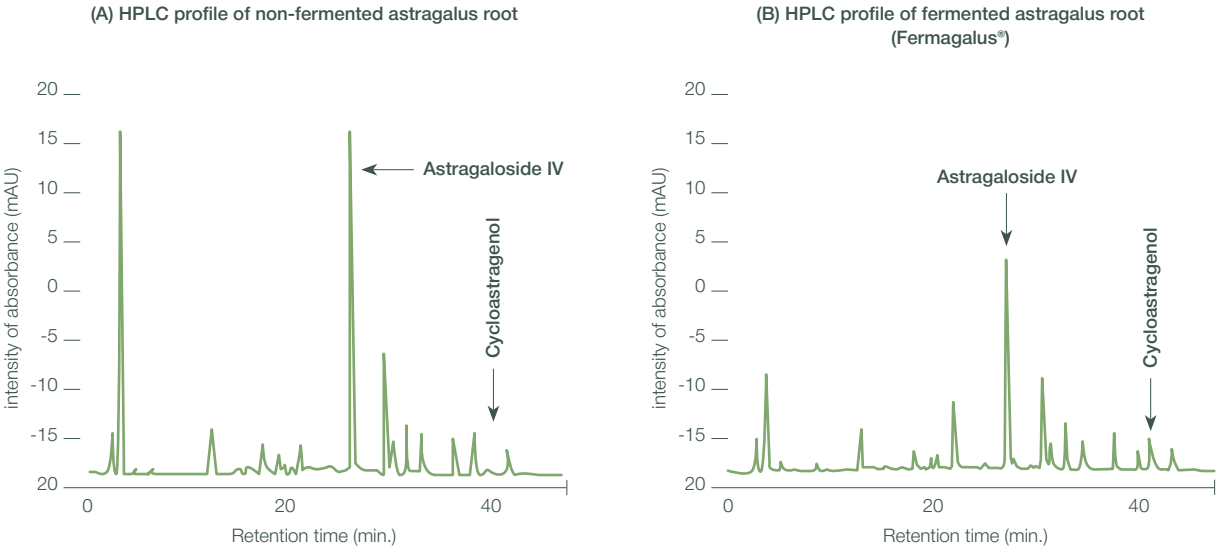
Fermented adaptogen	Enrichments* in bioactive aglycons or metabolites	Most prominent health effect
Fermagalus® Lactic acid fermented astragalus root	**33-fold more** cycloastragenol	Natural telomerase activator, slowing down the ageing process[38,39]
Fermanolide® Lactic acid fermented ashwagandha root	**70% more** withanolide A	Important candidate for tackling neurodegeneration[40,41]
Fermodiola® Saccharomyces cerevisiae fermented rhodiola root	**7.2-fold more** p-tyrosol	Protector against ischemic injury[42]
Fermogulan® Lactic acid fermented jiaogulan leaves	**13-fold more Compound K** **3-fold more ginsenoside Rg3** **2-fold more ginsenoside Rh2**	Rejuvenating power[12,43,44]

Table. Fermented botanicals have higher amounts of key bioactive components in comparison to non-fermented botanicals *identified by High Performance Liquid Chromatography (HPLC) analysis in fermented versus non-fermented plant material

Example 1: Fermagalus®, fermented astragalus root

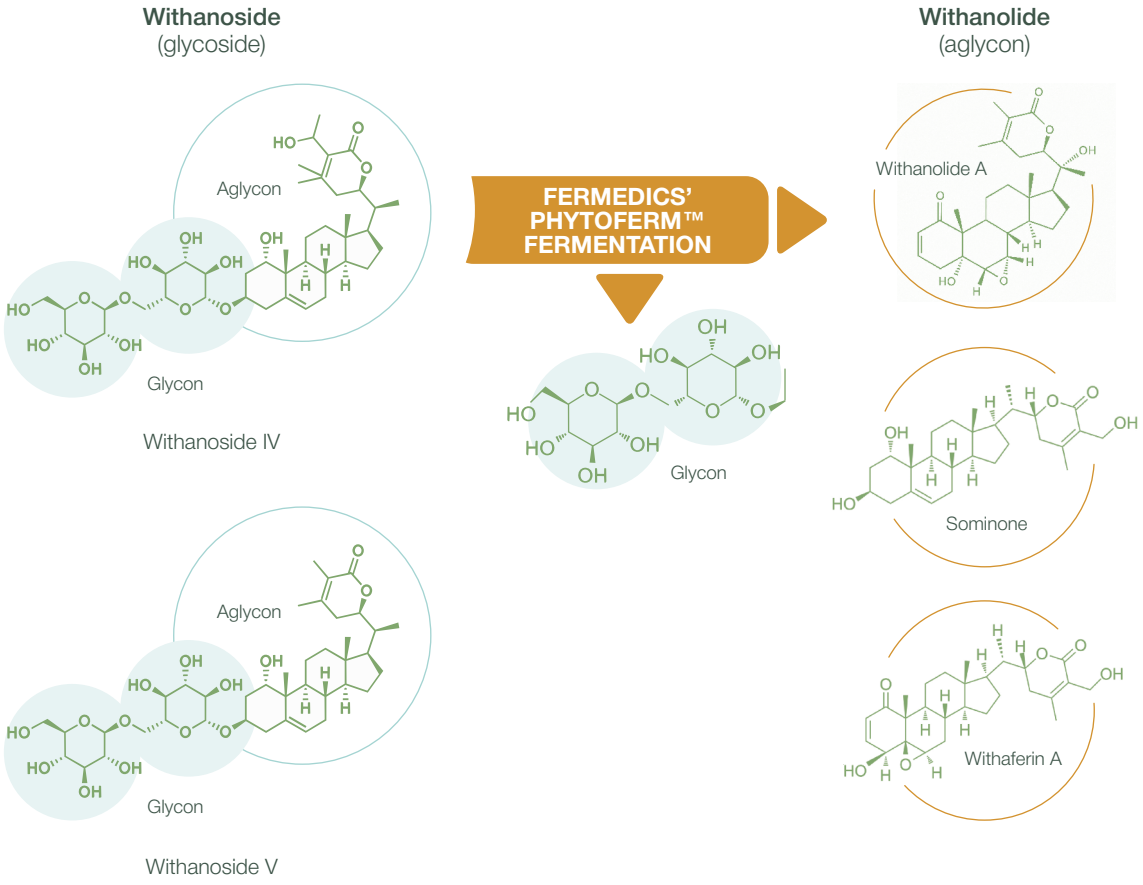
During fermentation astragaloside IV (a glycosylated triterpene) decreases in favour of cycloastragenol release (the corresponding 'bioactive' aglycon). Thanks to the targeted fermentation conditions, a standardization of 0.2% cycloastragenol is achieved and ensured.

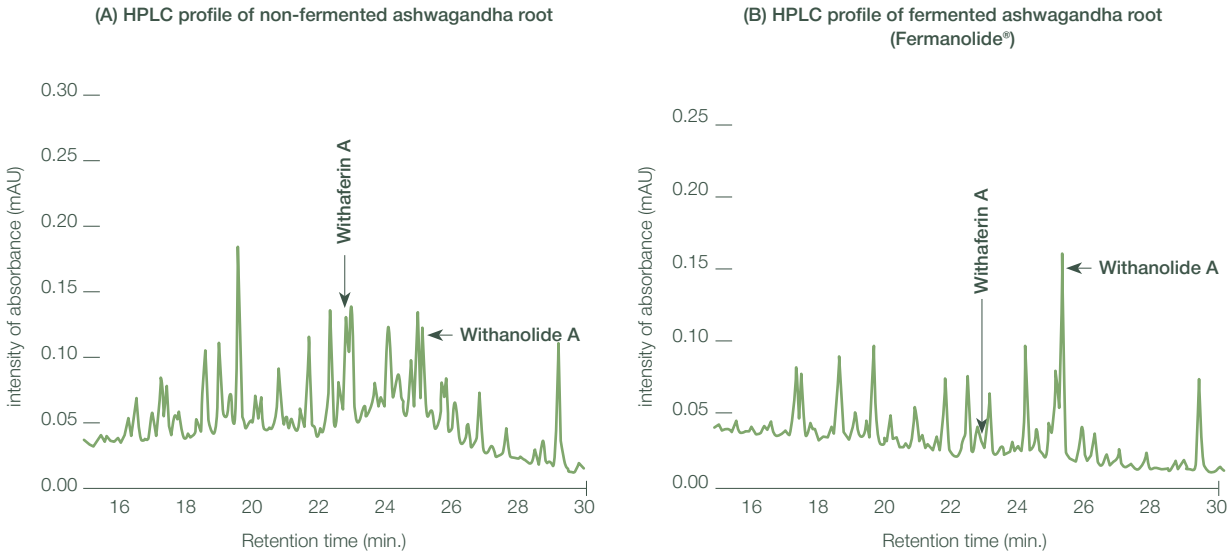




Example 2: Fermanolide®, fermented ashwagandha root

Under targeted fermentation conditions, glycosylated withanolide precursors are enzymatically converted, leading to an increased presence of withanolide A.[41] In parallel, further biotransformation results in the formation of sominone as a downstream metabolite.[49]

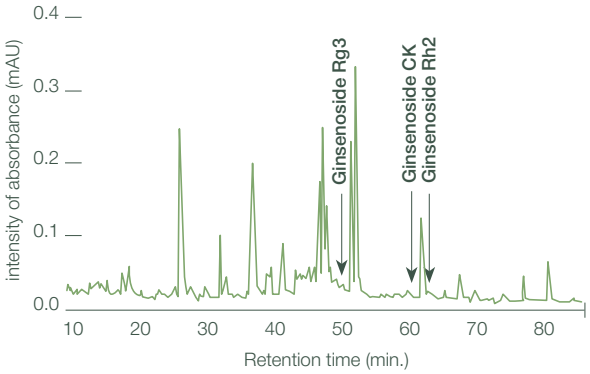




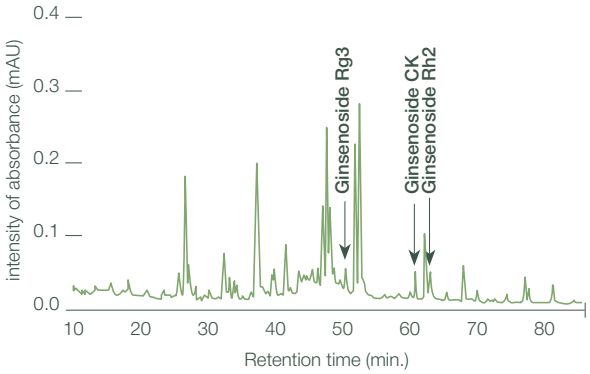
Example 3: Fermogulan®, fermented Jiaogulan leaves

During fermentation gypenosides (glycosylated saponins) are biotransformed into 'bioactive' aglycon metabolites (i.e. rare ginsenosides CK, Rg3 and Rh2) whose contents increased significantly. All 3 metabolites exhibit improved bioavailability following oral administration, as they are smaller and less polar in nature than their glycosylated precursors.[12,43,44]

(A) HPLC profile of native (unfermented) jiaogulan ginsenoside-type gypenosides



(B) HPLC profile of fermented jiaogulan ginsenoside-type gypenosides



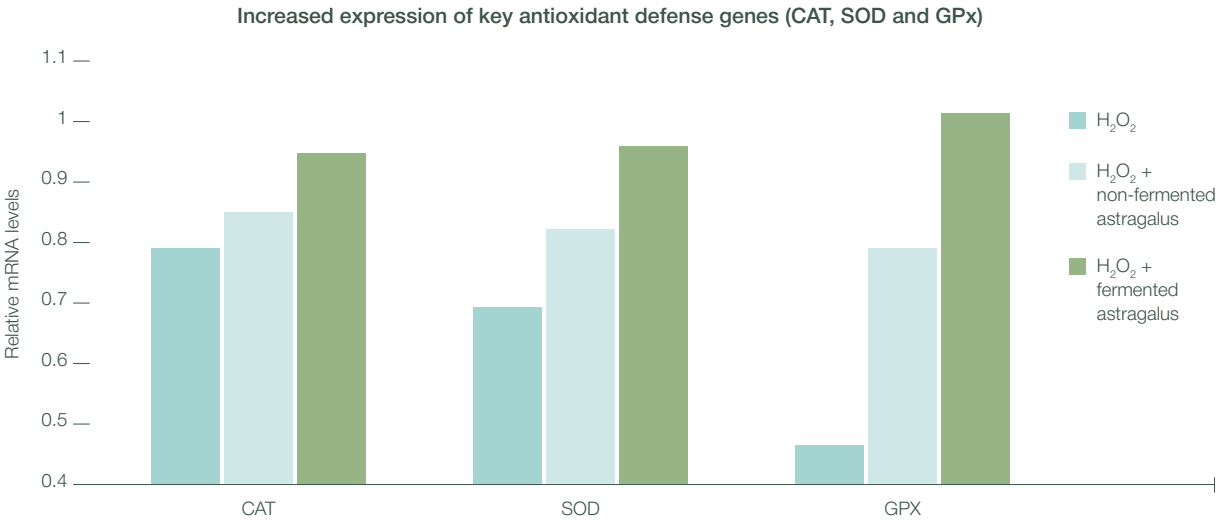
IMPROVED ANTIOXIDANT CAPACITY

Fermented medicinal plants are abundant in antioxidants. The observed antioxidant activity typically coincides an increase in total phenolic compounds. The fermentation process induces the structural breakdown of plant cell walls, leading to the liberation of various antioxidant compounds (e.g. flavonoids, simple phenolic compounds).[1]

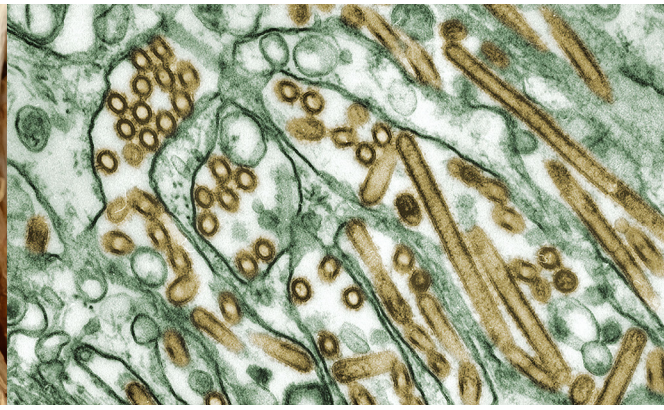
Flavonoids are broken down into smaller antioxidant molecules, often called SOD-like substances. These very stable molecules have an antioxidant property like that of superoxide dismutase (SOD). SOD forms the front line of defense against oxidative stress in the body.

Moreover, the microorganisms synthesize a range of antioxidants to protect themselves against oxidative damage (e.g. glutathione, exopolysaccharides) and add these to the final product.[2]

Example 1: fermented astragalus induced higher intracellular antioxidant enzyme levels than non-fermented astragalus (in vitro test[50])

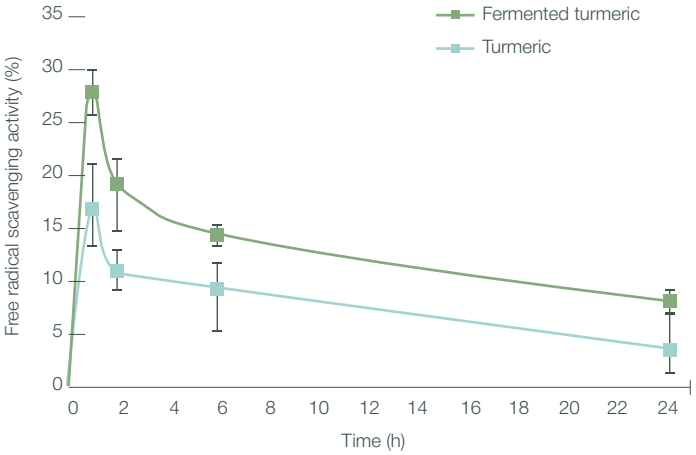


Graph. Antioxidant enzyme levels of CAT (catalase), SOD (superoxide dismutase) and GPx (glutathione peroxidase) in H2O2-induced HepG2 cells treated with non-fermented versus fermented astragalus. HepG2 is a cell line originating from a human hepatocellular carcinoma, and commonly used to study liver antioxidant defence mechanisms. Lactic acid fermented astragalus induced higher intracellular antioxidant enzyme levels than non-fermented astragalus ($p<0,05$). Source: Lee JY et al. Fermentation 2022; 8:34.[50]



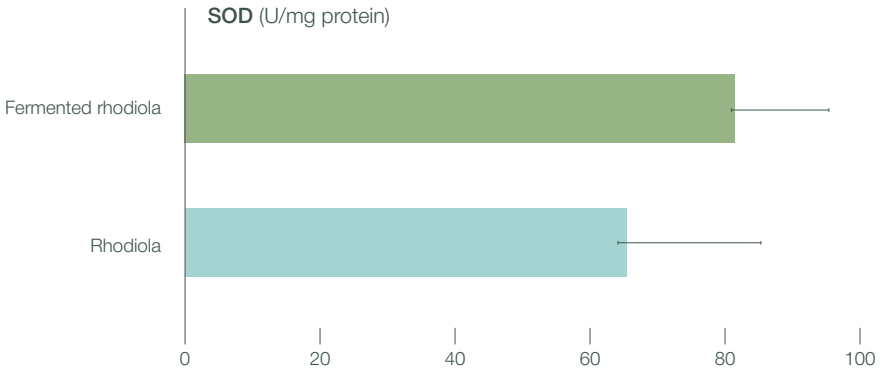
Example 2: fermented turmeric induced higher plasma antioxidant activity than non-fermented turmeric (rat experiment[37])

During Lactobacillus plantarum fermentation curcuminoids are biotransformed into the more powerful antioxidant metabolites.[9,26,37]



Graph. Plasma antioxidant activity after consuming turmeric versus fermented turmeric (rat experiment). Source: Pianpumepong P at al. Int J Food Sci Technol 2012; 47:2380-7.[37]

Example 3: fermented rhodiola induced higher liver antioxidant activity than non-fermented rhodiola (mice experiment[51])

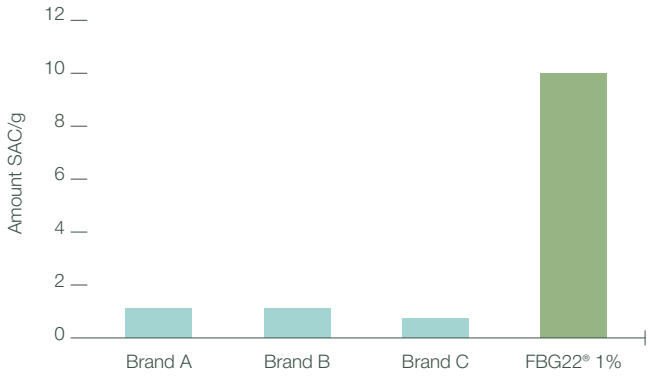


Graph. Hepatic SOD (superoxide dismutase) level in mice treated with Rhiodiola rosea extract (non-fermented) versus fermented Rhodiola rosea extract. Fermented rhodiola induced a higher SOD antioxidant level than non-fermented rhodiola ($p<0,05$). Source: Kang DZ et al. Prev Nutr Food Sci 2015; 20(1):38-42.[51]

Example 4: FBG22®, fermented black garlic

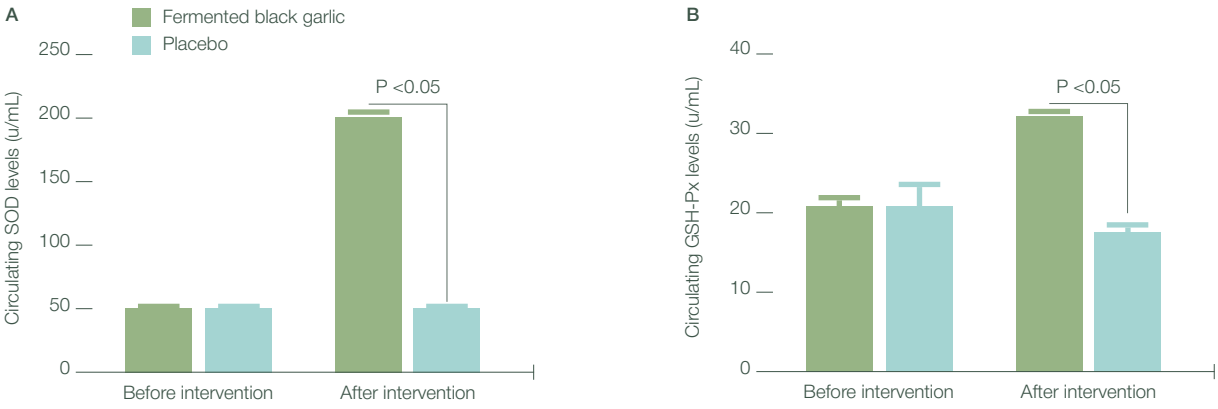
During fermentation of raw garlic, also referred to as ageing, the highly unstable compound allicin is progressively converted into more stable organosulfur compounds, among which S-allyl cysteine (SAC) becomes predominant. Thanks to targeted triple fermentation conditions, the formation of SAC is significantly enhanced, resulting in a more stable and bioactive antioxidant profile.

SAC has been extensively investigated in preclinical research and demonstrates a broad spectrum of biological activities, including antioxidant, anti-inflammatory, anti-apoptotic, anti-obesity, cardioprotective, neuroprotective and hepatoprotective effects.[52] These findings underline the importance of fermentation-driven biotransformation, making the optimization of SAC levels a key strategy in the development of value-added garlic-derived ingredients.



Graph. S-allyl-cysteine (SAC) content (mg/g) in fermented black garlic extracts. Based on internal analytical results using validated HPLC methodology.

Fermented black garlic induced an increase in plasma antioxidant activity in patients with coronary heart disease[53]



Graphs. Circulating antioxidant levels in blood plasma of CHF patients before and after intervention with fermented black garlic or placebo. A) SOD: superoxide dismutase; B) GSH-Px: glutathione peroxidase. Source: Liu J et al. Front Physiol 2018; 9:1435.

THE FUTURE OF FUNCTIONAL MEDICINAL PLANTS

Growing insights into microbiome science are reshaping how botanical functionality is understood. Many medicinal plant compounds depend on microbial conversion processes to become biologically accessible and functionally active.

At the same time, modern lifestyle factors are contributing to declining microbiome diversity and functionality, increasing interindividual variability in the response to medicinal plants.[1] This is driving growing interest in strategies that reduce dependence on variable gut microbial conversion while preserving the natural complexity of botanical ingredients.

In this context, controlled fermentation offers a biologically relevant solution. By performing key microbial biotransformations before consumption, PhytoFerm™ fermentation enables a more consistent and functionally active expression of plant-derived metabolites within the natural plant matrix.

Controlled fermentation is therefore emerging not merely as a traditional preservation process, but as a scientifically grounded platform for the development of next-generation medicinal plant ingredients.

CONCLUSIVE REMARK

Fermentation naturally optimizes the biochemical composition of plant-based materials through coordinated microbial and enzymatic biotransformations. By breaking down complex plant matrices, converting precursor compounds into bioactivated metabolites and generating fermentation-derived microbial components, fermentation enhances the accessibility, physicochemical properties and functional profile of botanical ingredients.[1,3]

These transformations are particularly relevant in the context of microbiome-dependent metabolism, where many phytochemicals require microbial conversion to become biologically accessible and functionally active. Interindividual differences in gut microbiome composition can therefore substantially influence metabolic conversion efficiency and biological response.

Controlled fermentation provides a biologically relevant strategy to reduce this variability by externalizing key microbial biotransformations prior to consumption. At the same time, fermentation preserves the compositional complexity and synergistic integrity of the natural plant matrix while increasing metabolite accessibility and postbiotic content.

Fermedics' PhytoFerm™ technology applies traditional food fermentation principles under controlled conditions using selected food-grade microorganisms and carefully standardized process parameters. This enables reproducible compositional outcomes and targeted modulation of plant-derived metabolites while maintaining the natural integrity and complexity of the original botanical material.

Taken together, controlled traditional fermentation represents a scientifically grounded approach for developing more consistent, microbiome-resilient and functionally active botanical ingredients.

References

1. Hussain A, Bose S, Wang JH, Yadav MK, Mahajan GB, Kim H. Fermentation, a feasible strategy for enhancing bioactivity of herbal medicines. Food Res Int. 2016;81:1-16.
2. Hur SJ, Lee SY, Kim YC, Choi I, Kim GB. Effect of fermentation on the antioxidant activity in plant-based foods. Food Chem. 2014;160:346-356.
3. Sharma R, Diwan B, Singh BP, Kulshrestha S. Probiotic fermentation of polyphenols: potential sources of novel functional foods. Food Prod Process Nutr. 2022;4:21.
4. Arranz-Otaegui A, Gonzalez Carretero L, Ramsey MN, Fuller DQ, Richter T. Archaeobotanical evidence reveals the origins of bread 14,400 years ago in northeastern Jordan. Proc Natl Acad Sci U S A. 2018;115(31):7925-7930. doi:10.1073/pnas.1801071115
5. Cuamatzin-García L, Rodríguez-Rugarcía P, El-Kassis EG, et al. Traditional fermented foods and beverages from around the world and their health benefits. Microorganisms. 2022;10(5):1151.
6. Muhammed YMR, Minervini F, Cavoski I. From ancient fermentations to modern biotechnology: historical evolution, microbial mechanisms, and the role of natural and commercial starter cultures in shaping organic and sustainable food systems. Foods. 2025;14(24):4240. doi:10.3390/foods14244240
7. Gustaw K, Niedźwiedź I, Rachwał K, Polak-Berecka M. New insight into bacterial interaction with the matrix of plant-based fermented foods. Foods. 2021;10(7):1603.
8. Wastyk HC, Fragiadakis GK, Perelman D, et al. Gut-microbiota-targeted diets modulate human immune status. Cell. 2021;184(16):4137-4153.e14. doi:10.1016/j.cell.2021.06.019
9. Michlmayr H, Kneifel W. ß-Glucosidase activities of lactic acid bacteria: mechanisms, impact on fermented food and human health. FEMS Microbiol Lett. 2014;352(1):1-10.
10. Kang J, Choi Y, Keum GB, et al. Effect of diet and lifestyle changes on gut microbial diversity in healthy adolescents. J Microbiol Biotechnol. 2025;35:e2503018. doi:10.4014/jmb.2503.03018
11. Baldanzi G, Larsson A, Sayols-Baixeras S, et al. Antibiotic use and gut microbiome composition links from individual-level prescription data of 14,979 individuals. Nat Med. 2026;32:1351-1361. doi:10.1038/s41591-026-04284-y
12. Yang XD, Yang YY, Ouyang DS, Yang GP. A review of biotransformation and pharmacology of ginsenoside compound K. Fitoterapia. 2015;100:208-220.
13. García-Villalba R, Giménez-Bastida JA, Cortés-Martín A, et al. Urolithins: a comprehensive update on their metabolism, bioactivity, and associated gut microbiota. Mol Nutr Food Res. 2022;66(21):e2101019. doi:10.1002/mnfr.202101019
14. Lombardi N, Crescioli G, Maggini V, et al. Acute liver injury following turmeric use in Tuscany: an analysis of the Italian Phytovigilance database and systematic review of case reports. Br J Clin Pharmacol. 2020:1-13.
15. Chen Z, Liu L, Gao C, et al. Astragali Radix (Huangqi): a promising edible immunomodulatory herbal medicine. J Ethnopharmacol. 2020;258:112895.
16. Choi EH, Son SU, Shin KS. Structural characterization of rhamnogalacturonan-I purified from Curcuma longa and its anti-lung cancer efficacy via immunostimulation. Food Sci Biotechnol. 2024;33(15):3591-3606.
17. Qiu Y, Zhang A, Lian X, et al. Unraveling the link between structural properties of polysaccharides and anti-inflammatory activity: a review. Carbohydr Res. 2025;555:109583.
18. Chandrasekaran CV, Sundarajan K, Edwin JR, Gururaja GM, Mundkinajeddu D, Agarwal A. Immune-stimulatory and anti-inflammatory activities of Curcuma longa extract and its polysaccharide fraction. Pharmacognosy Res. 2013;5(2):71-79.
19. Son SU, Choi EH, Shin KS. Effects of rhamnogalacturonan-I type polysaccharide purified from Curcuma longa on immunostimulatory and intracellular signaling pathway mechanisms of macrophages. Food Biosci. 2023;53:102589.
20. Yang F, Chen C, Ni D, et al. Effects of fermentation on bioactivity and the composition of polyphenols contained in polyphenol-rich foods: a review. Foods. 2023;12(17):3315. doi:10.3390/foods12173315
21. Pontonio E, Montemurro M, Pinto D, et al. Lactic acid fermentation of pomegranate juice as a tool to improve antioxidant activity. Front Microbiol. 2019;10:1550. doi:10.3389/fmicb.2019.01550
22. Liu X, Le Bourvellec C, Renard CMGC. Interactions between cell wall polysaccharides and polyphenols: effect of molecular internal structure. Compr Rev Food Sci Food Saf. 2020;19(6):3574-3617. doi:10.1111/1541-4337.12632
23. Nasef NA, Loveday SM, Golding M, et al. Food matrix and co-presence of turmeric compounds influence bioavailability of curcumin in healthy humans. Food Funct. 2019;10(8):4584-4592. doi:10.1039/c9fo01063g
24. Grundy MML, Moughan PJ, Wilde PJ. Bioaccessibility and associated concepts: need for a consensus. Trends Food Sci Technol. 2024;145:104373. doi:10.1016/j.tifs.2024.104373
25. Wei L, Van Beeck W, Hanlon M, DiCaprio E, Marco ML. Lacto-fermented fruits and vegetables: bioactive components and effects on human health. Annu Rev Food Sci Technol. 2025;16(1):289-314. doi:10.1146/annurev-food-052924-070656
26. Aggarwal BB, Deb L, Prasad S. Curcumin differs from tetrahydrocurcumin for molecular targets, signaling pathways and cellular responses. Molecules. 2014;20(1):185-205.
27. Siciliano RA, Reale A, Mazzeo MF, Morandi S, Silvetti T, Brasca M. Paraprobiotics: a new perspective for functional foods and nutraceuticals. Nutrients. 2021;13:1225.
28. Piqué N, Berlanga M, Miñana-Galbis D. Health benefits of heat-killed (tyndallized) probiotics: an overview. Int J Mol Sci. 2019;20(10):2534.
29. Salminen S, Collado MC, Endo A, et al. The International Scientific Association of Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of postbiotics. Nat Rev Gastroenterol Hepatol. 2021;18(9):649-667. doi:10.1038/s41575-021-00440-6
30. Teame T, Wang A, Xie M, et al. Paraprobiotics and postbiotics of probiotic Lactobacilli, their positive effects on the host and action mechanisms: a review. Front Nutr. 2020;7:570344.
31. Cuevas-González PF, Liceaga AM, Aguilar-Toalá JE. Postbiotics and paraprobiotics: from concepts to applications. Food Res Int. 2020;136:109502.
32. Da M, Sun J, Ma C, et al. Postbiotics: enhancing human health with a novel concept. eFood. 2024;5(4):e180. doi:10.1002/efd2.180
33. International Scientific Association for Probiotics and Prebiotics (ISAPP). Postbiotics [infographic]. Accessed June 25, 2026. Available at: https://isappscience.org/resource/postbiotics/.
34. Gu Y, Wang G, Pan G, Fawcett JP, Jiye A, Sun J. Transport and bioavailability studies of astragaloside IV, an active ingredient in Radix Astragali. Basic Clin Pharmacol Toxicol. 2004;95(6):295-298.
35. Devkar ST, Kandhare AD, Sloley BD, et al. Evaluation of the bioavailability of major withanolides of Withania somnifera using an in vitro absorption model system. J Adv Pharm Technol Res. 2015;6(4):159-164.

36. Zhu J, Lee S, Ho MKC, et al. In vitro intestinal absorption and first-pass intestinal and hepatic metabolism of cycloastragenol, a potent small molecule telomerase activator. Drug Metab Pharmacokinet. 2010;25(5):477-486.
37. Pianpumepong P, Anal AK, Doungchawee G, Noomhorm A. Study on enhanced absorption of phenolic compounds of Lactobacillus-fermented turmeric (Curcuma longa Linn.) beverages in rats. Int J Food Sci Technol. 2012;47:2380-2387.
38. Yu Y, Zhou L, Yang Y, Liu Y. Cycloastragenol: an exciting novel candidate for age-associated diseases. Exp Ther Med. 2018;16(3):2175-2182.
39. Salvador L, Singaravelu G, Harley CB, Flom P, Suram A, Raffaele JM. A natural product telomerase activator lengthens telomeres in humans: a randomized, double blind, and placebo controlled study. Rejuvenation Res. 2016;19(6):478-484.
40. Patil D, Patwardhan B. Determination of withaferin A and withanolide A in mice plasma using high-performance liquid chromatography-tandem mass spectrometry: application to pharmacokinetics after oral administration of Withania somnifera aqueous extract. J Pharm Biomed Anal. 2013;80:203-212.
41. Baitharu I, Jain V, Deep SN, et al. Withanolide A prevents neurodegeneration by modulating hippocampal glutathione biosynthesis during hypoxia. PLoS One. 2014;9(10):e105311.
42. Sun L, Fan H, Yang L, Shi L, Liu Y. Tyrosol prevents ischemia/reperfusion-induced cardiac injury in H9c2 cells: involvement of ROS, Hsp70, JNK and ERK, and apoptosis. Molecules. 2015;20(3):3758-3775.
43. Kim EH, Kim W. An insight into ginsenoside metabolite compound K as a potential tool for skin disorder. Evid Based Complement Alternat Med. 2018;2018:8075870.
44. Song BK, Kim KM, Choi KD, Im WT. Production of the rare ginsenoside Rh2-MIX (20(S)-Rh2, 20(R)-Rh2, Rk2, and Rh3) by enzymatic conversion combined with acid treatment and evaluation of its anti-cancer activity. J Microbiol Biotechnol. 2017;27(7):1233-1241.
45. Li S, Liu C, Zhang Y, Tsao R. On-line coupling pressured liquid extraction with two-dimensional counter current chromatography for isolations of natural acetylcholinesterase inhibitors from Astragalus membraneceus. Phytochem Anal. 2021;32:640-653.
46. Pan L, Zhang XF, Wei WS, Zhang J, Li ZZ. The cardiovascular protective effect and mechanism of calycosin and its derivatives. Chin J Nat Med. 2020;18(12):907-915.
47. Deng M, Chen H, Long J, Song J, Xie L, Li X. Calycosin: a review of its pharmacological effects and applications prospects. Expert Rev Anti Infect Ther. 2021;19(7):911-925.
48. Gong G, Zheng Y, Yang Y, Sui Y, Wen Z. Pharmaceutical values of calycosin: one type of flavonoid isolated from Astragalus. Evid Based Complement Alternat Med. 2021;2021:9952578.
49. Kuboyama T, Tohda C, Komatsu K. Withanoside IV and its active metabolite, sominone, attenuate Abeta(25-35)-induced neurodegeneration. Eur J Neurosci. 2006;23(6):1417-1426. doi:10.1111/j.1460-9568.2006.04664.x
50. Lee JY, Park HM, Kang CH. Antioxidant effect via bioconversion of isoflavonoid in Astragalus membranaceus fermented by Lactiplantibacillus plantarum MG5276 in vitro and in vivo. Fermentation. 2022;8:34.
51. Kang DZ, Hong HD, Kim KI, Choi SY. Anti-fatigue effects of fermented Rhodiola rosea extract in mice. Prev Nutr Food Sci. 2015;20(1):38-42.
52. Yudhistira B, Punthi F, Lin JA, Sulaimana AS, Chang CK, Hsieh CW. S-Allyl cysteine in garlic (Allium sativum): formation, biofunction, and resistance to food processing for value-added product development. Compr Rev Food Sci Food Saf. 2022;21(3):2665-2687.
53. Liu J, Zhang G, Cong X, Wen C. Black garlic improves heart function in patients with coronary heart disease by improving circulating antioxidant levels. Front Physiol. 2018;9:1435.
54. Sultana T, Okla MK, Ahmed M, Akhtar N, Al-Hashimi A, Abdelgawad H, Haq IU. Withaferin A: from ancient remedy to potential drug candidate. Molecules. 2021;26:7996.
55. Ivanova Stojcheva E, Quintela JC. The effectiveness of Rhodiola rosea L. preparations in alleviating various aspects of life-stress symptoms and stress-induced conditions—encouraging clinical evidence. Molecules. 2022;27(12):3902.
56. Akter S, Park JH, Jung HK. Potential health-promoting benefits of paraprobiotics, inactivated probiotic cells. J Microbiol Biotechnol. 2020;30(4):477-481.
57. Anna BW, Pavol F, Paulina C, Dominika P, Alicja S, Katarzyna P, Monika J. Antimicrobial and prebiotic activity of mannoproteins isolated from conventional and nonconventional yeast species—the study on selected microorganisms. World J Microbiol Biotechnol. 2022;38(12):256.