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MINI REVIEW

Harnessing the dual nature of *W. coagulans* for sustainable production of biomaterials and development of functional food

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Abstract

Bacillus coagulans, recently renamed *Weizmannia coagulans*, is a spore-forming bacterium that has garnered significant interest across various research fields, ranging from health to industrial applications. The probiotic properties of *W. coagulans* enhance intestinal digestion, by releasing prebiotic molecules including enzymes that facilitate the breakdown of not-digestible carbohydrates. Notably, some enzymes from *W. coagulans* extend beyond digestive functions, serving as valuable biotechnological tools and contributing to more sustainable and efficient manufacturing processes. Furthermore, the homofermentative thermophilic nature of *W. coagulans* renders it an exceptional candidate for fermenting foods and lignocellulosic residues into L-(+)-lactic acid. In this review, we provide an overview of the dual nature of *W. coagulans*, in functional foods and for the development of bio-based materials.

INTRODUCTION

Bacillus coagulans was initially described in 1915 by Hammer, who isolated strain ATCC 7050 (also referred to as DSM1) from spoiled canned milk (Su et al., 2012). Recently, it has been phylogenetically reclassified as a distinct monophyletic clade called *Weizmannia* (Gupta et al., 2020). *W. coagulans* is a Gram-positive, lactic acid-producer, non-pathogenic and spore-forming bacterium (Konuray & Erginkaya, 2018) which is naturally distributed in a variety of niches as well as in food fermented from soybean, locust bean, maize, rice and others (Cho et al., 2023; Shudong et al., 2022). Since it has several health benefits, such as the production of prebiotic molecules, prevention of muscle damage during exercise, improvement of gastrointestinal disorders, ease of diarrhoea and prevention of bacterial vaginosis, it is widely used as a commercial probiotic, often in combination with other strains from *Bacillaceae* and *Lactobacillaceae* families (Bang et al., 2021; Kim et al., 2021).

Unlike other well-known probiotics, *W. coagulans* thrives optimally at temperatures between 35 and 50°C and a pH close to 6 (Rhee et al., 2011). It is regarded as "the king of probiotics" because of its ability to form spores, exhibiting strong resistance and survival rate under harsh conditions, i.e., low-oxygen environments of the gastrointestinal tract, stomach acids and bile salts as well as food processing (Zhou et al., 2020). For these reasons, *W. coagulans* is widely used in commercial foods such as dairy products, fermented meats and cereals (Konuray & Erginkaya, 2018). Worth-mentioning is the secretion of extracellular carbohydrate- and protein-degrading enzymes that enhance the quality and sensory properties of fermented foods (Konuray & Erginkaya, 2018; Olajuyigbe & Ehiosun, 2013). *W. coagulans* also produces compounds with antimicrobial activity against Gram-positive and Gram-negative food pathogens (Kim et al., 2021). The biotechnological potential of *W. coagulans* does not reside only in the food industry. Indeed, it is widely used also as a microbial cell factory for the eco-sustainable production of lactic acid (LA), providing an alternative to chemical synthesis (Huang, Tian, et al., 2023; Huang, Wang, et al., 2023; Pamueangmun et al., 2023). The moderately thermophilic nature of *W. coagulans* strains reduces the risk of microbial contamination, making them naturally suited for lactate production even in open fermentations (Aulitto et al., 2019). The ability to operate at high temperature also reduces the energy consumption needed for sterilization and cooling of the fermentation system (Su & Xu, 2014). To date, several *W. coagulans* strains have been utilised for LA production from lignocellulosic materials due to their temperature compatibility (50–55°C) with commercial enzymes currently used for the biomass saccharification (Li et al., 2021; Pol et al., 2016; Rhee et al., 2011; Walton et al., 2010).

Some molecular biology studies have been addressed to analyse the physiological response of *W. coagulans* during fermentation. For instance, the steam-explosion pre-treatment of lignocellulosic biomasses releases toxic compounds that hinder LA production as demonstrated for the MA-13 strain (Aulitto et al., 2017, 2019). Moreover, a comparative transcriptomic analysis revealed that sodium lactate induced downregulation and upregulation of glycolysis/gluconeogenesis and TCA cycle genes, respectively, thus affecting LA fermentation (Qin et al., 2015).

Moreover, a time-resolved transcriptomic and proteomic study shed light on the response mechanisms of *W. coagulans* during NaOH-buffered LA fermentation, highlighting the expression levels of the glycolytic and TCA cycle genes throughout the fermentation process (Huang, Tian, et al., 2023; Huang, Wang, et al., 2023).

Upon the identification of multiple strains of *W. coagulans* (65 strains reported on NCBI on 21 December 2023), comparative genomic studies have revealed that some strain-specific genetic traits can be exploited for diverse biotechnological fields. For instance, pangenomic scans offer insights into the comprehensive landscape of central carbon metabolism, as well as into the absence/presence of active virulence factor genes and/or prophage sequences highlighting that not all the available strains are suitable for targeted applications, especially in the field of the food industry (Aulitto et al., 2022; Su & Xu, 2014; Sun et al., 2023). Currently, only a limited number of reports are available on the potential role of *W. coagulans* as a whole-cell biofactory for the effective production of bioactive compounds (biomolecules and fermentation bioproducts). This mini-review aims to highlight the most recent advancements in *W. coagulans* as a probiotic as well as a producer of prebiotics and biotechnological relevant biomolecules in the food and feed sectors. Moreover, its emergence as a model system for the eco-sustainable synthesis of LA-based biomaterial is discussed with relevant examples from agri-food waste conversion.

FUNCTIONAL FOODS

Functional foods (often indicated also as 'natural health products' or 'healthy foods') exhibit beneficial effects on specific bodily functions beyond their nutritional value, such as improving general healthy conditions and/or decreasing the risk of chronic disease appearance (Henry, 2010; Kaur & Das, 2011). The global market for functional foods and beverages reached a value of $192 billion in 2020, driven by their increasing integration into consumers' daily diets worldwide (Konstantinidi & Koutelidakis, 2019). A well-known example of functional food is yogurt enriched with fruits, vegetables, cereals and other active compounds (such as honey, moringa, aloe vera extracts and essential oils etc) (Ahmad et al., 2022). Functional foods often contain bioactive compounds that support the activity of probiotics, by preventing the growth of pathogens and/or inhibiting the production of virulence factors (Damián et al., 2022). Overall, the combination of functional foods and probiotics promotes a synergistic effect on nutritional health (Ballini et al., 2023) and offers a reliable approach to enhance the ability of the probiotics to compete with harmful bacteria, supporting immune function and improving overall well-being (Silva et al., 2020).

Specifically, it is well known that *W. coagulans* contributes significantly to digestive health, nutrient absorption and human health through various mechanisms, including enzyme production, metabolite generation and modulation of the gut environment, as summarised in the Table 1 (Cao et al., 2020; Palomino et al., 2023).

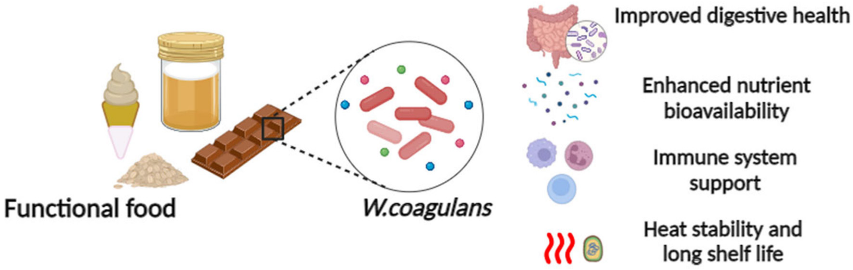
W. coagulans in food industries

Lactic acid bacteria (LAB), bifidobacteria and yeasts are well-researched and commonly used as probiotics in a wide range of food products (Palanivelu et al., 2022). However, the harsh environmental conditions encountered during food processing and storage often compromise the viability and activity of probiotics, thus affecting their effectiveness (Terpou et al., 2019). For instance, several *Lactobacillus* or *Bifidobacterium* spp. employed in functional foods formulations for the management of different intestinal disorders (Palanivelu et al., 2022), require freeze-drying processes or powdered formulations, which have a detrimental effect on their viability. It is worth noting that most of the *W. coagulans* strains isolated so far exhibit thermal resistance and high survival

TABLE 1 Beneficial health effects of *W. coagulans* consumption.

Beneficial effects on the health of the host		References
Interaction with gut microbiota	The consumption of *W. Coagulans* has been associated with an increase of lactobacillus and Bifidobacteria, while also competitively outcompeting opportunistic pathogens such as *Clostridium difficile* Reduction of toxic metabolites	Haldar and Gandhi (2016), Ianiro et al. (2016), Gibson et al. (2014), Kodali and Sen (2008)
Immunity response	• *W. coagulans* PTA-6086 enhances the activity of various human immune cells (increased phagocytic activity, maturation of mononuclear phagocytes). • *W. coagulans* reinforces the immune system and alleviates inflammation through cell-derived mediators, modifying the production of immune-activating, anti-inflammatory cytokines, chemokines and growth factors.	Benson et al. (2012), Jensen et al. (2010), Jensen et al. (2010), Sudha et al. (2015)
Amino acid absorption	• Absorption of specific amino acids, including those involved in blood flow regulation (citrulline) and recovery (glutamine).	Jäger et al. (2018)
Metabolite production	• *W. coagulans* produces metabolites like diacetyl, short-chain fatty acids (SCFAs) and vitamins. • Stimulates intestinal peristalsis, reducing harmful substances such as amines and promoting healthy bowel movements.	Nyangale et al. (2014)
Other health benefits associated with the intake of *W. coagulans*	• *Constipation Relief*: Studies show that *W. coagulans* administration effectively relieves constipation. • *Cholesterol Reduction*: Animal studies demonstrate that *W. coagulans* can reduce cholesterol levels by degrading cholesterol in blood serum. • *Bile Acid Metabolism Improvement*: Combination of soy pulp and *B. coagulans lilac-01* improves intestinal bile acid metabolism	Aminlari et al. (2019), Lee et al. (2016b), Minamida et al. (2015)

FIGURE 1 Benefits of incorporating *W. coagulans* in functional foods.



rates in gastrointestinal traits (Zhang et al., 2024), thus enhancing its potential as a probiotic.

Interestingly, after conducting in vivo and in vitro toxicity studies, a spore-forming strain of *W. coagulans* known as GBI-30, 6086 was recognised as Generally Regarded As Safe (GRAS) by the US Food and Drug Administration (FDA) and the European Union Food Safety Authority (EFSA) in 2013 (Konuray & Erginkaya, 2018). This relevant outcome has sparked increased interest in spore-forming probiotics because of their ability to withstand adverse environmental conditions (Ahmad et al., 2022). Moreover, reducing manufacturing costs and eliminating the need for freeze-drying processes are interesting features in food industries. Most importantly, the addition of *W. coagulans* spores did not compromise the sensory or nutritional characteristics of food. Over time, *W. coagulans* spores have been integrated into a wide range of functional foods, from pasta, chocolate and ice cream to heat-resistant cereal-based products, thanks to their ability to withstand high temperatures during food processing (Figure 1; Table 2) (Amini et al., 2022; Cao et al., 2020; Fares et al., 2015; Janipour et al., 2023; Kobus-Cisowska et al., 2019; Konuray & Erginkaya, 2018).

Furthermore, a recent study revealed the effectiveness of a novel organic functional beverage containing apple cider vinegar. This beverage with the supplementation of *W. coagulans* spores not only improved the serum lipid profile but also implemented the protection against HFD-induced hepatic steatosis in mice (Urtasun et al., 2020).

Interestingly, *W. coagulans* has been found to co-exist in complex hand-made ecological communities, such as Kombucha. Indeed, a study by Yang et al. (2022) analysed the microbial composition of nine different kombucha beverages that were prepared using various tea

TABLE 2 *W. coagulans* – based functional foods.

***W. Coagulans* strain**	**Functional foods**	**References**
GBI-30, 6086	Pasta	Fares et al. (2015)
GBI-30, 6086	Dark chocolate	Kobus-Cisowska et al. (2019)
n.r.	Ice cream	Janipour et al. (2023)
n.r.	Gluten-Free Cake Mix	Amini et al. (2022)
MTCC 5856	Fermented tea Kombucha	Yang et al. (2022)
GBI-30, 6086	Orange juice	Almada-Érix et al. (2021)
GBI-30, 6086	Yogurt	Almada-Érix et al. (2021)

varieties and different probiotic additions. The results of the study showed that *W. coagulans* was the most dominant strain under all the tested conditions (Yang et al., 2022). Furthermore, in 2021, a dynamic system designed to replicate the conditions of the gastrointestinal tract provided evidence that spore of *W. coagulans* GBI-30, 6086 strain exhibited remarkable survival when incorporated into orange juice and yogurt (Almada-Érix et al., 2021). Additionally, this commercially available strain has served as a reference control in studying the probiotic properties of newly isolated *W. coagulans* strains from corn, pickled cucumber, potato and tomato (Konuray Altun & Erginkaya, 2021).

Bioactive probiotic molecules

Multiple studies have provided evidence that *W. coagulans* possesses the capability to inhibit bacterial growth by balancing the microbiota through mechanisms including the production of bioactive effector molecules, such as LA and acetic acid, which serve the indirect role of antimicrobial agents by reducing the pH of the surrounding environment (Ibrahim et al., 2021). In this context, bacteriocins are small antimicrobial peptides or proteins that bacteria produce to inhibit the growth of closely related strains or other competing microorganisms. Bacteriocins are categorised into two main classes: (1) class I, undergoing post-translational modifications, and (2) class II, existing in a cyclic not modified form (Ríos Colombo et al., 2018). Moreover, several strains of *W. coagulans* (ATCC 7050, BDU3, MTCC 5856) produce lactosporins, a unique class of bacteriocins that does not belong to the conventional classification and exhibiting broad antimicrobial activity as well as shield ability on skin cells against UV-induced apoptosis (Abdhul et al., 2015; Riazi et al., 2009; Majeed et al., 2020).

Coagulins belong to class II of bacteriocins, and their mechanism of action involves the integrity disruption of the target bacterial cell membrane (Soltani et al., 2021). *W. coagulans* strain I4 and L1208 were found to produce a plasmid-linked antimicrobial peptide called coagulin active against foodborne bacteria (Cao et al., 2020; Contursi et al., 2014; Notomista et al., 2015; Zhang et al., 2024) (Figure 2).

A genetic arrangement that encodes for a non-lanthionine-antimicrobial peptide called circularin A was found in MA-13 and XZL9 strains by comparative genomic studies (Aulitto et al., 2019, 2022; Gabrielsen et al., 2014).

Some other strains may have lost certain genetic determinants during evolution, as observed in XZL4 where the *circC* gene involved in circularin A maturation was absent (Aulitto et al., 2022). Unlike circularin A and coagulin, which naturally occur as circular peptides, the presence of a gene encoding for a polypeptide antibiotic called bacitracin has been reported for MA-13 (Aulitto et al., 2022). Interestingly, among the nine strains examined, only MA-13 bears a complete pathway for bacitracin production including a signal transduction system (bceRS), along with adjacent efflux transporters (*bceA/B*) and an additional *bcrC* gene (Aulitto et al., 2022). Bacitracin acts by inhibiting bacterial cell wall synthesis and it is a widely used broad-spectrum veterinary antibiotic, commonly employed as a feed additive and as a preservative in meat, aquatic, vegetable and dairy industries (Cai et al., 2020; Choyam et al., 2021).

MICROBIAL CELL FACTORY FOR ENZYME PRODUCTION

Numerous studies have addressed the utilization of *W. coagulans* for the cost-effective production of valuable products suitable for diverse biotechnological applications such as hydrolytic enzymes that have been successfully applied in numerous food processing industries, including brewing, baking and dairy food (Aulitto et al., 2018; Konuray & Erginkaya, 2018; Pamueangmun et al., 2023).

Although many of the hydrolytic enzymes herein described are also produced by other microorganisms, the main advantage of exploiting those derived by a probiotic (such as *W. coagulans*), resides in their safe use in food manufacturing. Additionally, their potential extends to the pharmaceutical and biotechnological sectors, where they can be employed to enhance the production of desired compounds and facilitate biochemical transformations (Pamueangmun et al., 2023). A full description of *W. coagulans* enzymes is supplied to deepen its potential as a microbial cell factory for industrially relevant enzymes

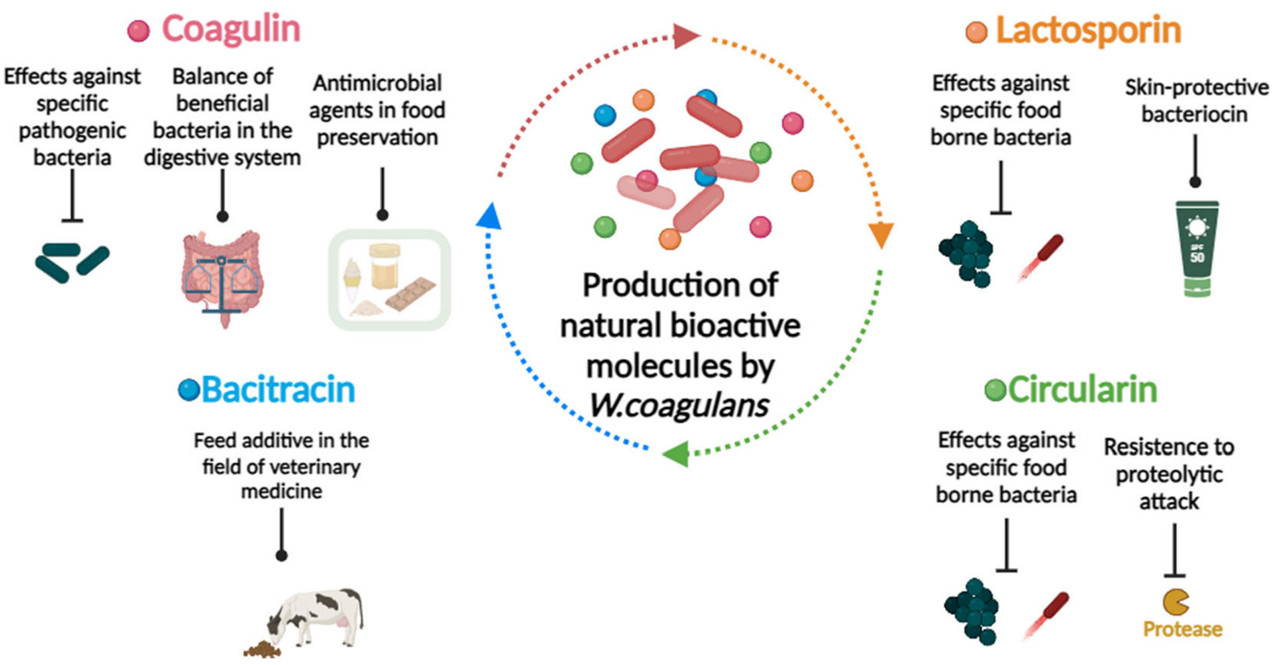


FIGURE 2 *W. coagulans* probiotic bioactive and effector molecules promoting human/animal health.

(Aulitto et al., 2021). Moreover, the robustness of the enzymes deriving from the thermophilic nature of *W. coagulans* as well as their capability to work over wide temperature and pH ranges, represent an added value in several industrial applications (Ou et al., 2009).

Glycosyl hydrolases involved in food processing

The main enzymes involved in starch metabolism are amylases catalysing the hydrolysis of starch and related carbohydrates such as cyclodextrin glucanotransferase (CGTase) (Lim et al., 2021). These extracellular enzymes convert starch into cyclodextrins (CDs), i.e., 6–12 glucose units joined by α-1,4-glycosidic bonds, through a glycosyl transferase mechanism (Lim et al., 2021). The amylase capacity to break down starch into simpler sugars makes it valuable for processes like fermentation, dough rising, starch liquefaction and saccharification (Raveendran et al., 2018). The applications of *W. coagulans*-produced amylases span various industries, including food and beverage, starch processing, animal feed and more (Marzo-Gago et al., 2024). *W. coagulans* B49, releases a thermostable α-amylase when wheat bran is added to the culture medium, while *W. coagulans* CUMC 512, isolated from soil, produces an alkaline thermostable α-amylase and an extracellular CGTase, the latter one exhibiting a significant ability to convert about 60% of soluble starch into CDs in 20h at 50°C, widely utilised in food, pharmaceutical and chemical industries (Lim et al., 2021).

It is known that probiotic LAB and *Bifidobacteria*, typically present in the small intestine, could serve as natural suppliers of digestive enzymes, including α- and β-galactosidases, the former catalysing the hydrolysis of α-1,6-linked-galactose residues from galactose containing oligosaccharides, whilst the latter hydrolyzes the lactose into glucose and galactose (Kailasapathy & Chin, 2000). Several W. *coagulans* strains have been proven to encode for α-galactosidases and β-galactosidases and some of them have been biochemically characterised (Batra et al., 2002; Liu et al., 2019; Zhao et al., 2018). For instance, NRR1207 produces an α-galactosidase that enhances the nutritional value of soybean meal by breaking down α-galactoside linkages and making essential nutrients more accessible for absorption (Ra et al., 2018). Furthermore, among β-galactosidases, the *Bc*GalB enzyme from the MA-13 strain, besides lactose hydrolysis suitable for lactose-free dairy products, performs also a transglycosylation reaction, generating galactooligosaccharides (Aulitto et al., 2021). These latter can be incorporated into functional foods to promote gut health, allowing individuals with lactose intolerance to enjoy dairy-based functional foods without adverse effects (Park & Oh, 2010).

Industrial applications of *W. coagulans* enzymes

W. coagulans exhibits a multifaceted hydrolytic enzymatic repertoire, including phytases, lipases, xylanase and proteases. Phytases, such as those from *W. coagulans* IDCC 1201, enhance mineral bioavailability by breaking down phytic acid in plant-based feed ingredients (Lee et al., 2016a). Biofertiliser formulations combining *W. coagulans* and *Pseudomonas fluorescens* have been demonstrated to supply environmental benefits by reducing reliance on synthetic fertilisers and mobilizing native phosphorus for plant uptake (Yaashikaa et al., 2020).

Various *W. coagulans* strains produce lipases with alkaline properties, suitable for broad applicability in detergent and pharmaceutical industries. For instance, *W. coagulans* BTS-3 and ZJU318 produce lipases with optimal activity in a wide range of temperatures and pH values (Al-Ghanayem, 2021; Kumar et al., 2005). Interestingly, *W. coagulans* MTCC-6375 features a unique lipase with versatile activity, demonstrating changes in optimal pH under specific incubation conditions (Kanwar et al., 2006).

Furthermore, proteases derived from *W. coagulans* are utilized in various industries. For instance, an extracellular protease from a psychrotrophic strain is optimized to function at 37°C and a pH of 8 (Talebi et al., 2013). A thermostable protease from *W. coagulans* PSB-07 exhibits remarkable stability in organic solvents (Olajuyigbe & Ehiosun, 2013). Finally, xylanases from *W. coagulans* BL69 and B30 are efficient in xylan degradation, making them valuable in textile, pulp and paper industries (Heck et al., 2005; Sharma et al., 2013). A full list of the enzymes isolated and characterised is provided in Table 3 and Figure 3 and their working operational parameters are reported.

LA PRODUCTION FROM AGRI-FOODS

W. coagulans is recognised for its proficiency in LA production, a versatile compound with widespread applications in the food industry, pharmaceuticals, medical fields and personal care products (Abdel-Rahman et al., 2013; Huang, Tian, et al., 2023; Huang, Wang, et al., 2023). Moreover, LA serves as a building-block for the PLA (poly lactic acid), an eco-friendly alternative to traditional plastics made up of L-and D-isomers (de França et al., 2022). *W. coagulans* stands out for its robust metabolic pathways, ensuring efficient conversion of 5-or 6C sugars to L- and/or D-LA, and contributing to improved cost-effectiveness (Huang, Tian, et al., 2023; Huang, Wang, et al., 2023). Some studies have documented the effective utilization of *W. coagulans* for converting agri-food wastes into LA, exploring the potential of various agricultural residues, including wheat, rice and rye straw, along with sugar cane bagasse and corn stover (Hu et al., 2015; Jiang et al., 2016; Ouyang et al., 2020). Herein, we report the successful production of LA from food residues and/or leftovers by employing diverse strains of *W. coagulans* in different fermentation configuration (Figure 4, Table 4).

Coffee waste

Coffee residues, such as coffee pulp or spent coffee grounds, have high organic content, including carbohydrates that can serve as a substrate for LA production. Generally, during coffee production, a step of spontaneous fermentation is usually included by indigenous microbiota (e.g., yeasts and LA bacteria). For instance, Pereira et al. showed that *L. plantarum* LPBR01 was able to produce LA from the coffee pulp with a productivity of 1.33 g/L of LA after 24 h (Pereira et al., 2016). In this context, *W. coagulans* isolated from rape seed

TABLE 3 List of the biochemically characterised enzymes from *W. coagulans* strains, operating between 30° and 70°C and pH 4–9. Thermostability values are reported.

W. coagulans strains	Enzyme	T_{opt} (°C)	pH_{opt}	Thermostability (half-life)	References
ATCC 7050	α-Galactosidase	55	6	60°C for 30 min	Zhao et al. (2018)
T242	β-Galactosidase	50	6.8	n.r.	Xu et al. (2021)
RCS3	β-Galactosidase	65	6.8	65°C for 2 h	Batra et al. (2002)
NL01	β-Galactosidase	55–60	6	60°C for 3.5 h	Liu et al. (2019)
MA – 13	β-Galactosidase	60	5	60°C for 4 h	Aulitto et al. (2021)
IDCC 1201	Phytase	50	4	60°C for 3 h	Lee et al. (2016a)
n.r.	Cyclodextrinase	70°C	6	n.r.	Lim et al. (2021)
BTS – 3	Lipase	55°C	8.5	55°C for 2 h	Kumar et al. (2005)
n.r.	Lipase	30°C	8	n.r.	Al-Ghanayem (2021)
n.r.	Lipase	37°C	7	n.r.	Alkan et al. (2007)
MTCC-6375	Lipase	45°C	8.5	55°C for 20 min	Kanwar et al. (2006)
PSB – 07	Protease	60°C	8	50/60°C for 60 min	Olajuyigbe and Ehiosun (2013)
B30	Xylanase	50°C	9	n.r.	Sharma et al. (2013)
BL69	Xylanase	60°C	7	n.r.	Heck et al. (2005)

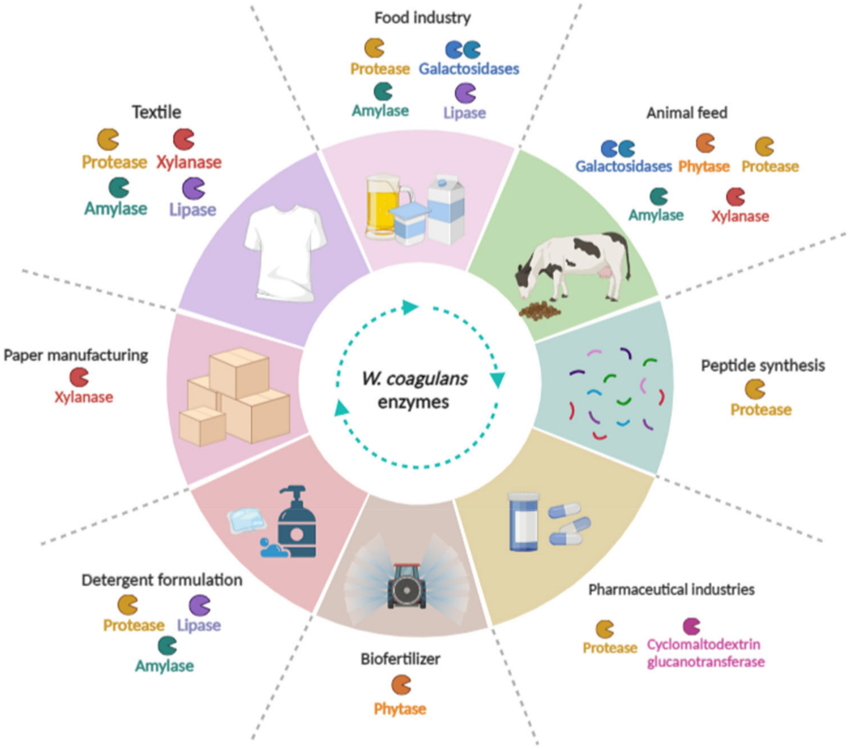


FIGURE 3 Production of enzymes from *W. coagulans* and their diverse applications in different fields.

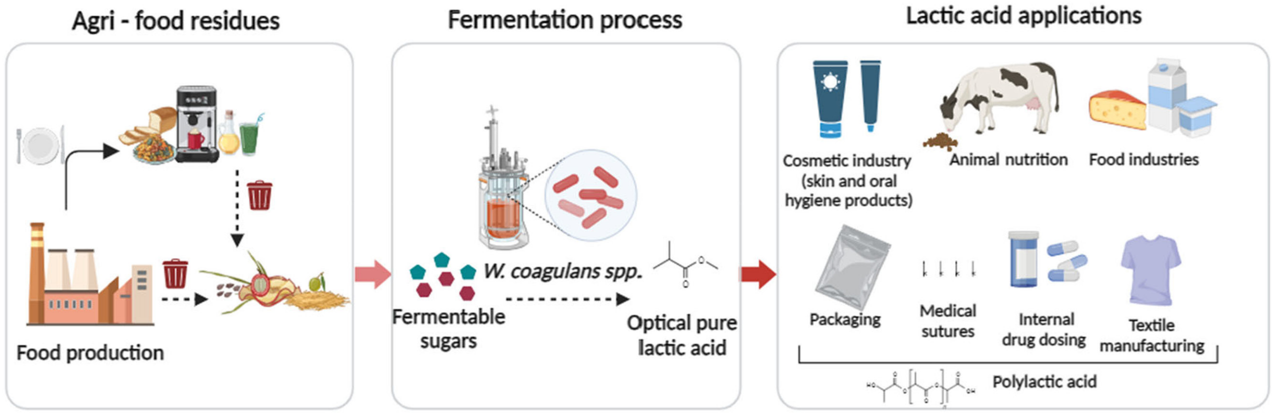


FIGURE 4 The process of LA production from agri-food residues through *W. coagulans* and its potential advantages.

meal was employed in fermentation experiments, using coffee mucilage as a renewable nitrogen source in LA fermentation (Neu et al., 2016). Interestingly, after a relatively short fermentation time (about 30 h), the resulting LA yield was 0.7 g/g of free sugars, using initial concentrations of 10.8 g/L sucrose, 21.5 g/L glucose and 27.8 g/L galactose/fructose/xylose, with LA production of 43.3 g/L (Table 2). When the fermentation was supplemented with 5 g/L of yeast extract, only the productivity was increased, but the LA yield was not affected (Neu et al., 2016). Considering that coffee waste amounts to 10 million tons per year, its valorization as a renewable alternative to commercial nitrogen sources, not only contributes to waste reduction but also enhances the economic feasibility and sustainability of the LA production process.

Pasta and bread waste

Pasta and bakery leftovers/by-products are significant contributors to food waste in many countries. Indeed, they typically contain 50%–70% starch, available for LA through fermentation processes. Several fermentation studies are reported and summarised in Table 4. López-gómez et al. (2022) have reported the ability of *W. coagulans* to produce LA starting from enzymatically treated pasta waste. Firstly, the enzymatic saccharification was successfully used to release 0.81 g sugars per gram of dry pasta waste. After preliminary comparative screenings of various *W. coagulans* strains, A559 was selected as the best performer in both laboratory and pilot scales. Indeed, during the lab-scale experiments, two fermentation modes were

TABLE 4 Valorization of diverse agri-food residues through *W.coagulans* fermentation.

W. coagulans strains	Agri-Food residues	Pre-treatment of raw materials	Process organization	Lactic acid (g/L)	Yield	Productivity (g/L·h)	References
n.r.	Coffee mucilage	–	Batch	43.3	0.7 g_{LA}/g_{sugars}	1.5	Neu et al. (2016)
A559	Pasta waste	Enzymatic hydrolysis	SSF	47.65	0.81 g_{LA}/g_{sugars}	n.r.	López-gómez et al. (2022)
A534	Sugar bread	Enzymatic hydrolysis	SHF	80	0.85 g/g	2.67	Olszewska-Widdrat et al. (2020)
n.r.	Crust bread waste	Enzymatic hydrolysis	SHF	62.2	0.57 $g_{LA}/g_{crust\ bread\ waste}$	2.59	Alexandri et al. (2020)
DSM1	Bread waste	Enzymatic hydrolysis	Fed-batch	155.4	0.85 $g_{LA}/g_{glucose}$	1.3	Cox et al. (2022)
JI12	Empty fruit bunch	Acid-catalysed and enzymatic hydrolysis	SSF	80.6	n.r	3.4	Ye et al. (2014)
LA1507	Sweet sorghum juice	Acid-catalysed hydrolysis	Batch	102	0.943 g_{LA}/g_{sugars}	2.9	Olszewska-Widdrat et al. (2019)
MA-13	Citrus waste	–	SSF Batch and Fed-batch	44.8	0.96 $g_{LA}/g_{glucose}$	1.9	Aulitto et al. (2024)

tested simultaneous saccharification and fermentation (SSF), and sequential hydrolysis and fermentation (SHF). This latter was proven to be more efficient compared to SSF, with a yield of 0.81 g of LA per gram of sugars (Table 2), highlighting the effectiveness of SHF for efficient LA production from pasta waste and demonstrating its potential as a sustainable and productive approach for valorizing this waste stream (López-gómez et al., 2022). Through batch experiments, it was observed that the strain *W. coagulans* A534 effectively metabolises different substrates, including acid whey, sugar beet molasses, sugar bread and tapioca starch (Olszewska-Widdrat et al., 2020). In continuous fermentations, the highest productivity was achieved using sugar beet molasses, with a remarkable value of 10.34 g/L·h. Moreover, the LA to sugar conversion yield reached 0.86 g/g demonstrating that LA can be efficiently produced in a continuous mode, regardless of the substrate employed (Olszewska-Widdrat et al., 2020; Table 2). Bread waste, which is rich in starch, has been employed for the production of LA through SSF using different strains of *Lactobacillus paracasei*. From this process, a very low yield (0.054 g/g) of LA from bread waste was achieved (Sadaf et al., 2021), compared to *W. coagulans*. Indeed, Alexandri et al. utilised crust bread waste, an alternative bakery residue, to produce LA using different strains of *W. coagulans* (Alexandri et al., 2020). Through enzymatic hydrolysis, they successfully achieved a production of 62.2 g/L of LA, with a conversion yield of 0.57 g/g of crust bread waste and a productivity rate of 2.59 g/L·h. Most recently, Cox et al. demonstrated an eco-friendly solution to valorise bread waste into LA through acidic and enzymatic hydrolysis using *W. coagulans* DSM1 under non-sterile conditions (Cox et al., 2022). The concentration of LA using waste bread and enzymatic hydrolysate reached remarkable levels (102.4 g/L and 129.4 g/L of LA), with yields of 0.75 and 0.83 g LA/g glucose (0.42 g/g feedstock), respectively. Employing enzymatic hydrolysate in a fed-batch process further enhanced the LA titre, reaching an impressive yield of 155.4 g/L, with a conversion yield of 0.85 g/g and a productivity rate of 1.30 g/L·h (Table 2). Additionally, the solid residues generated during the hydrolysis and fermentation stages were effectively utilised for the generation of biogas, with methane being the primary product. This integrated approach not only achieved an outstanding LA titre under non-sterile conditions but also represents a proof of concept of a waste bread-based integrated biorefinery, with the simultaneous production of valuable biogas from fermented residues.

Empty fruit bunch

Southeast Asia is a significant resource hub for palm oil production, accounting for over 80% of the global output. An interesting and valuable approach for the valorization of agricultural waste is the use of empty fruit bunch (EFB). Recently, Triwahyuni et al. focused on exploring LA production from EFB treated with alkali explosion and using cellulolytic enzymes and *Lactobacillus delbrueckii* through the SHF approach at 55° and 60°C. However, *W. coagulans* JI12 was previously demonstrated to have a remarkable ability to produce L-LA with exceptional optical purity of up to 99.5% due to a frameshift mutation observed in the D-LA dehydrogenase gene conferring regioselectivity (and enantiospecificify) to the encoded enzyme (Ye et al., 2014). By comparing the processes of simulated sugar mixtures and EFB hydrolysate with similar sugar compositions, it was found that the productivity of EFB hydrolysate (6.2 g/L·h) was lower than the simulated mixture (7.1 g/L·h) (Table 2). This slight decrease in productivity has to be traced back to the presence of inhibitors, such as furfural, hydroxymethylfurfural, acetic acid and other compounds that are generated during the pre-treatment process of the EFB (Ye et al., 2014). Therefore, the exploitation of *W. coagulans* strains able to withstand such toxic compounds represents a solution to exploit the full potential of EFB wastes. In this context, JI12 has shown remarkable capabilities in converting both glucose and xylose into LA because of its remarkable tolerance to high concentrations of acetate (20 g/L) and furfural (4 g/L). Notably, the strain can metabolise all furfural in acid-pre-treated EFB whole slurry, while simultaneously producing over 80 g/L of LA through detoxification, saccharification and fermentation.

Citrus waste

Citrus waste, such as peels, pulp and other residues, offers significant potential as a renewable feedstock for LA production. Orange peel waste has been employed as a raw material for LA production utilizing *Lactobacilli* sp., resulting in conversion yields that ranged from 80% to 90% (Bustamante et al., 2020). Among the microbial strains, *W. coagulans* MA-13 is a resilient biocatalyst capable of efficiently fermenting lignocellulosic biomass into L-LA, even in the presence of inhibitory compounds derived from biomass. Recently, it was set up a one-step production of L-LA using *W. coagulans* MA-13 with untreated citrus waste as a sustainable feedstock (Aulitto et al., 2024). To enhance biomass degradation, a thermophilic enzymatic cocktail was employed in conjunction with the hydrolytic capabilities of MA-13, resulting in an impressive (up to 62%) increase in biomass degradation. Furthermore, batch and fed-batch fermentation experiments demonstrated the complete conversion of glucose into L-LA, achieving concentrations of up to 44.8 g/L, with a productivity of 1.9 g/L·h and yield of 0.96 g/g (Table 2).

Sorghum waste juice

Sweet sorghum juice (SSJ) is extracted by crushing the harvested stalks of *Sorghum bicolour*, a highly versatile grain with various culinary possibilities. Compared to cellulosic hydrolysates, the utilization of SSJ was proven to be more convenient and cost-effective for LA production, because of its high concentration of soluble sugars, including sucrose, glucose and fructose. In the study conducted by Wang et al., they investigated the use of acid hydrolysate from SSJ for fermentative production of L-LA (Wang et al., 2017) by employing strain LA1507. Results showed a maximum productivity of 2.90 g/L·h and an impressive yield of 0.943 g/g (Table 2) (Olszewska-Widdrat et al., 2019).

CONCLUSIONS AND PERSPECTIVES

Relevant features that make *W. coagulans* a valuable microorganism for a wide array of sustainable and eco-friendly technologies related to food manufacturing and biomaterial production are: (i) resilience towards diverse physiochemical conditions also due to the spore-forming capability, (ii) enzymatic versatility, (iii) thermotolerance, (iv) robustness towards inhibitory compounds, (v) probiotic/prebiotic properties and (vi) LA production. Indeed, thanks to its wide spectrum of enzymatic activities and production of prebiotics/antibacterials molecules, *W. coagulans* as a probiotic enhances the absorption of essential nutrients in the digestive tract and extends shelf life by inhibiting the growth of harmful bacteria. Interestingly, some studies and clinical trials have explored the use of *W. coagulans* as part of bacteriotherapy interventions for various gastrointestinal disorders, including irritable bowel syndrome.

Bacteriotherapy, utilizing *W. coagulans*, is a promising approach for preventing and treating dysbiosis in different body areas like the respiratory tract, skin and ears. Advances in additive manufacturing technologies enable the creation of bacterial cell-loaded devices for localised probiotic deployment. Techniques like electrospinning, electrospray and extrusion-based printing facilitate the production of structures that encapsulate diverse bacteria types, including *E. coli* and *Lactobacilli*. *W. coagulans* can be encapsulated within these structures and deployed using advanced manufacturing methods. Leveraging 4D bioprinting, researchers can optimise *W. coagulans* delivery, offering potential solutions for dysbiosis treatment in various body regions.

Furthermore, its metabolic versatility and excellent substrate utilization property during fermentation, enable the efficient conversion of diverse agri-food and lignocellulose residues into LA. New perspectives could be achieved by engineering *W. coagulans* to implement the production of LA and the expression of functional enzymes.

Overall, these features point to *W. coagulans* as an essential player in the usage of plant-based building materials towards the development of an eco-friendly, sustainable and greener future by reducing wastage, landfills and toxic emissions.

AUTHOR CONTRIBUTIONS

Emanuela Maresca: Conceptualization; writing – original draft; writing – review and editing. **Martina Aulitto:** Conceptualization; writing – original draft; writing – review and editing. **Patrizia Contursi:** Funding acquisition; supervision; writing – original draft; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

All the authors declare no competing interests.

ETHICAL APPROVAL

This article does not contain any studies with human participants or animals performed by any of the authors.

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REFERENCES

Abdel-Rahman, M.A., Tashiro, Y. & Sonomoto, K. (2013) Recent advances in lactic acid production by microbial fermentation processes. *Biotechnology Advances*, 31, 877–902. Available from: https://doi.org/10.1016/j.biotechadv.2013.04.002

Abdhul, K., Ganesh, M., Shanmughapriya, S., Vanithamani, S., Kanagavel, M., Anbarasu, K. et al. (2015) Bacteriocinogenic potential of a probiotic strain Bacillus coagulans [BDU3] from Ngari. *Int J Biol Macromol*, 79, 800–806. Available from: https://doi.org/10.1016/j.ijbiomac.2015.06.005

Ahmad, I., Hao, M., Li, Y., Zhang, J., Ding, Y. & Lyu, F. (2022) Fortification of yogurt with bioactive functional foods and ingredients and associated challenges – a review. *Trends in Food Science and Technology*, 129, 558–580 . Available from:https://doi.org/10.1016/j.tifs.2022.11.003.

Al-Ghanayem, A.A. (2021) Purification and characterization of thermo-alkaline stable lipase from *Bacillus coagulans* and its compatibility with commercially available detergents. *Romanian Biotechnology Letters*, 26, 2994–3001. Available from: https://doi.org/10.25083/rbl/26.5/2994.3001

Alexandri, M., Blanco-Catalá, J., Schneider, R., Turon, X. & Venus, J. (2020) High L(+)-lactic acid productivity in continuous fermentations using bakery waste and lucerne green juice as renewable substrates. *Bioresource Technology*, 316, 123949. Available from: https://doi.org/10.1016/j.biortech.2020.123949

Alkan, H., Baysal, Z., Uyar, F. & Doğru, M. (2007) Production of lipase by a newly isolated *Bacillus coagulans* under solid-state fermentation using melon wastes. *Applied Biochemistry and Biotechnology*, 136, 183–192. Available from: https://doi.org/10.1007/BF02686016

Almada-Érix, C.N., Almada, C.N., Cabral, L., Barros de Medeiros, V.P., Roquetto, A.R., Santos-Junior, V.A. et al. (2021) Orange juice and yogurt carrying probiotic *Bacillus coagulans* GBI-30 6086: impact of intake on Wistar male rats health parameters and gut bacterial diversity. *Frontiers in Microbiology*, 12, 623951. Available from: https://doi.org/10.3389/fmicb.2021.623951

Amini, K., Sharifan, A., Ghiassi Tarzi, B. & Azizinezhad, R. (2022) Preparation of a low-calorie, gluten-free all-in-one cake mix, containing *Bacillus Coagulans* using quinoa and inulin functionality. *Journal of Food Quality*, 2022, 1–12. Available from: https://doi.org/10.1155/2022/8550086

Aminlari, L., Shekarforoush, S.S., Hosseinzadeh, S., Nazifi, S., Sajedianfard, J. & Eskandari, M.H. (2019) Effect of probiotics *Bacillus coagulans* and lactobacillus plantarum on lipid profile and feces bacteria of rats fed a cholesterol-enriched diet. *Probiotics and Antimicrobial Proteins*, 11, 1163–1171. Available from: https://doi.org/10.1007/s12602-018-9480-1

Aulitto, M., Alfano, A., Maresca, E., Avolio, R., Errico, M.E., Gentile, G. et al. (2024) Thermophilic biocatalysts for one-step conversion of citrus waste into lactic acid. *Applied Microbiology and Biotechnology*, 108, 155. Available from: https://doi.org/10.1007/s00253-023-12904-7

Aulitto, M., Fusco, F.A., Fiorentino, G., Bartolucci, S., Contursi, P. & Limauro, D. (2018) A thermophilic enzymatic cocktail for galactomannans degradation. *Enzyme and Microbial Technology*, 111, 7–11. Available from: https://doi.org/10.1016/j.enzmictec.2017.12.008

Aulitto, M., Fusco, S., Bartolucci, S., Franzén, C.J. & Contursi, P. (2017) *Bacillus coagulans* MA-13: a promising thermophilic and cellulolytic strain for the production of lactic acid from the lignocellulosic hydrolysate. *Biotechnology for Biofuels*, 10, 210. Available from: https://doi.org/10.1186/s13068-017-0896-8

Aulitto, M., Fusco, S., Franzén, C.J., Strazzulli, A., Moracci, M., Bartolucci, S. et al. (2019) Draft genome sequence of *Bacillus coagulans* MA-13, a thermophilic lactic acid producer from lignocellulose. *Microbiology Resource Announcements*, 8, 13–15. Available from: https://doi.org/10.1128/mra.00341-19

Aulitto, M., Martinez-Alvarez, L., Fiorentino, G., Limauro, D., Peng, X. & Contursi, P. (2022) A comparative analysis of *Weizmannia coagulans* genomes unravels the genetic potential for biotechnological applications. *International Journal of Molecular Sciences*, 23, 3135. Available from: https://doi.org/10.3390/ijms23063135

Aulitto, M., Strazzulli, A., Sansone, F., Cozzolino, F., Monti, M., Moracci, M. et al. (2021) Prebiotic properties of *Bacillus coagulans* MA-13: production of galactoside hydrolyzing enzymes and characterization of the transglycosylation properties of a GH42 β-galactosidase. *Microbial Cell Factories*, 20, 1–17. Available from: https://doi.org/10.1186/s12934-021-01553-y

Ballini, A., Charitos, I.A., Cantore, S., Topi, S., Bottalico, L. & Santacroce, L. (2023) About functional foods: The probiotics and prebiotics state of art. *Antibiotics*, 12, 635. Available from: https://doi.org/10.3390/antibiotics12040635

Bang, W.Y., Ban, O.H., Lee, B.S., Oh, S., Park, C., Park, M.K. et al. (2021) Genomic-, phenotypic-, and toxicity-based safety assessment and probiotic potency of Bacillus coagulans IDCC 1201 isolated from green malt. *J Ind Microbiol Biotechnol*, 48, 5–6. Available from: https://doi.org/10.1093/jimb/kuab026

Batra, N., Singh, J., Banerjee, U.C., Patnaik, P.R. & Sobti, R.C. (2002) Production and characterization of a thermostable β-galactosidase from *Bacillus coagulans* RCS3. *Biotechnology and Applied Biochemistry*, 36, 1–6. Available from: https://doi.org/10.1042/ba20010091

Benson, K.F., Redman, K.A., Carter, S.G., Keller, D., Farmer, S., Endres, J.R. et al. (2012) Probiotic metabolites from *Bacillus* *coagulans* GanedenBC30TM support maturation of antigen-presenting cells in vitro. *World Journal of Gastroenterology*, 18, 1875–1883. Available from: https://doi.org/10.3748/wjg.v18.i16.1875

Bustamante, D., Tortajada, M., Ramón, D. & Rojas, A. (2020) Production of D-lactic acid by the fermentation of orange peel waste hydrolysate by lactic acid bacteria. *Fermentation*, 6, 10–12. Available from: https://doi.org/10.3390/fermentation6010001

Cai, D., Zhang, B., Zhu, J., Xu, H., Liu, P., Wang, Z. et al. (2020) Enhanced bacitracin production by systematically engineering S-adenosylmethionine supply modules in *Bacillus licheniformis*. *Frontiers in Bioengineering and Biotechnology*, 8, 305. Available from: https://doi.org/10.3389/fbioe.2020.00305

Cao, J., Yu, Z., Liu, W., Zhao, J., Zhang, H., Zhai, Q. et al. (2020) Probiotic characteristics of *Bacillus coagulans* and associated implications for human health and diseases. *Journal of Functional Foods*, 64, 103643. Available from: https://doi.org/10.1016/j.jff.2019.103643

Cho, E., Kim, J.Y., Cho, B., Lee, J.S., Yoon, Y.C., Shin, Y.C. et al. (2023) Efficacy of fermented grain using *Bacillus coagulans* in reducing visceral fat among people with obesity: a randomised controlled trial. *Frontiers in Nutrition*, 10, 1148512. Available from: https://doi.org/10.3389/fnut.2023.1148512

Choyam, S., Jain, P.M. & Kammara, R. (2021) Characterization of a potent new-generation antimicrobial peptide of Bacillus. *Frontiers in Microbiology*, 12, 1–13. Available from: https://doi.org/10.3389/fmicb.2021.710741

Contursi, P., Farina, B., Pirone, L., Fusco, S., Russo, L., Bartolucci, S. et al. (2014) Structural and functional studies of Stf76 from the Sulfolobus islandicus plasmid-virus pSSVx: a novel peculiar member of the winged helix-turn-helix transcription factor family. *Nucleic Acids Research*, 42, 5993–6011. Available from: https://doi.org/10.1093/nar/gku215

Cox, R., Narisetty, V., Nagarajan, S., Agrawal, D., Ranade, V.V., Salonitis, K. et al. (2022) High-level fermentative production of lactic acid from bread waste under non-sterile conditions with a circular biorefining approach and zero waste discharge. *Fuel*, 313, 122976. Available from: https://doi.org/10.1016/j.fuel.2021.122976

Damián, M.R., Cortes-Perez, N.G., Quintana, E.T., Ortiz-Moreno, A., Noguez, C.G., Cruceño-Casarrubias, C.E. et al. (2022) Functional foods, nutraceuticals and probiotics: a focus on human health. *Microorganisms*, 10, 106. Available from: https://doi.org/10.3390/microorganisms10051065

Fares, C., Menga, V., Martina, A., Pellegrini, N., Scazzina, F. & Torriani, S. (2015) Nutritional profile and cooking quality of a new functional pasta naturally enriched in phenolic acids, added with β-glucan and *Bacillus coagulans* GBI-30, 6086. *Journal of Cereal Science*, 65, 260–266. Available from: https://doi.org/10.1016/j.jcs.2015.07.017

de França, J.O.C., da Silva Valadares, D., Paiva, M.F., Dias, S.C.L. & Dias, J.A. (2022) Polymers based on PLA from synthesis using D, L-Lactic Acid (or Racemic Lactide) and some biomedical applications: a short review. *Polymers (Basel)*, 14, 2317. Available from: https://doi.org/10.3390/polym14122317

Gabrielsen, C., Brede, D.A., Nes, I.F. & Diep, D.B. (2014) Circular bacteriocins: biosynthesis and mode of action. *Applied and Environmental Microbiology*, 80, 6854–6862. Available from: https://doi.org/10.1128/AEM.02284-14

Gibson, M.K., Pesesky, M.W. & Dantas, G. (2014) The Yin and Yang of bacterial resilience in the human gut microbiota. *Journal of Molecular Biology*, 426, 3866–3876. Available from:https://doi.org/10.1016/j.jmb.2014.05.029

Gupta, R.S., Patel, S., Saini, N. & Chen, S. (2020) Robust demarcation of 17 distinct bacillus species clades, proposed as novel bacillaceae genera, by phylogenomics and comparative genomic analyses: description of Robert Murray kyonggiensis sp. nov. and proposal for an emended genus bacillus limiting it only to the members of the Subtilis and Cereus clades of species. *International Journal of Systematic and Evolutionary Microbiology*, 70, 5753–5798. Available from: https://doi.org/10.1099/ijsem.0.004475

Haldar, L. & Gandhi, D.N. (2016) Effect of oral administration of *Bacillus coagulans* B37 and Bacillus pumilus B9 strains on fecal coliforms, Lactobacillus and Bacillus spp. in rat animal model. *Vet World*, 9, 766–772. Available from: https://doi.org/10.14202/vetworld.2016.766-772

Heck, J.X., Flôres, S.H., Hertz, P.F. & Ayub, M.A.Z. (2005) Optimization of cellulase-free xylanase activity produced by *Bacillus coagulans* BL69 in solid-state cultivation. *Process Biochemistry*, 40, 107–112. Available from: https://doi.org/10.1016/j.procbio.2003.11.044

Henry, C.J. (2010) Functional foods. *European Journal of Clinical Nutrition*, 64, 657–659. Available from: https://doi.org/10.1038/ejcn.2010.101

Hu, J., Zhang, Z., Lin, Y., Zhao, S., Mei, Y., Liang, Y. et al. (2015) High-titer lactic acid production from NaOH-pretreated corn stover by *Bacillus coagulans* LA204 using fed-batch simultaneous saccharification and fermentation under non-sterile condition. *Bioresource Technology*, 182, 251–257. Available from: https://doi.org/10.1016/j.biortech.2015.02.008

Huang, X., Tian, W., Wang, X. & Qin, J. (2023) Time-resolved transcriptomic and proteomic profiling of Heyndrickxia coagulans during NaOH-buffered L-lactic acid production. *Frontiers in Microbiology*, 14, 1296692. Available from: https://doi.org/10.3389/fmicb.2023.1296692

Huang, Y., Wang, Y., Shang, N. & Li, P. (2023) Microbial fermentation processes of lactic acid: challenges, solutions, and future prospects. *Food*, 12, 2311. Available from:https://doi.org/10.3390/foods12122311

Ianiro, G., Tilg, H. & Gasbarrini, A. (2016) Antibiotics as deep modulators of gut microbiota: between good and evil. *Gut*, 65, 1906–1915. Available from: https://doi.org/10.1136/gutjnl-2016-312297

Ibrahim, S.A., Ayivi, R.D., Zimmerman, T., Siddiqui, S.A., Altemimi, A.B., Fidan, H. et al. (2021) Lactic acid bacteria as antimicrobial agents: food safety and microbial food spoilage prevention. *Food*, 10, 1–13. Available from: https://doi.org/10.3390/foods10123131

Jäger, R., Purpura, M., Farmer, S., Cash, H.A. & Keller, D. (2018) Probiotic *Bacillus coagulans* GBI-30, 6086 improves protein absorption and utilization. *Probiotics and Antimicrobial Proteins*, 10, 611–615. Available from: https://doi.org/10.1007/s12602-017-9354-y

Janipour, R., Shekarforoush, S.S., Ghorbani, S. & Gheisari, H.R. (2023) Effects of partial replacement of sugar with fig syrup on the survival of *Bacillus coagulans* and the physicochemical properties of probiotic ice cream. *Food Technology and Biotechnology*, 61, 350–356. Available from: https://doi.org/10.17113/ftb.61.03.23.8152

Jensen, G.S., Benson, K.F., Carter, S.G. & Endres, J.R. (2010) GanedenBC 30TM cell wall and metabolites: anti-inflammatory and immune-modulating effects in vitro. *BMC Immunology*, 11, 15. Available from: https://doi.org/10.1186/1471-2172-11-15

Jiang, T., Qiao, H., Zheng, Z., Chu, Q., Li, X., Yong, Q. et al. (2016) Lactic acid production from pretreated hydrolysates of corn stover by a newly developed *Bacillus coagulans* strain. *PLoS One*, 11, 0149101. Available from: https://doi.org/10.1371/journal.pone.0149101

Kailasapathy, K. & Chin, J. (2000) Survival and therapeutic potential of probiotic organisms with reference to lactobacillus acidophilus and Bifidobacterium spp. *Immunology and Cell Biology*, 78, 80–88. Available from: https://doi.org/10.1046/j.1440-1711.2000.00886.x

Kanwar, S.S., Ghazi, I.A., Chimni, S.S., Joshi, G.K., Rao, G.V., Kaushal, R.K. et al. (2006) Purification and properties of a novel extra-cellular thermotolerant metallolipase of *Bacillus coagulans* MTCC-6375 isolate. *Protein Expression and Purification*, 46, 421–428. Available from: https://doi.org/10.1016/j.pep.2005.10.007

Kaur, S. & Das, M. (2011) Functional foods: an overview. *Food Science and Biotechnology*, 20, 861–875. Available from: https://doi.org/10.1007/s10068-011-0121-7

Kim, Y.S., Lee, J., Heo, S., Lee, J.H. & Jeong, D.W. (2021) Technology and safety evaluation of *Bacillus coagulans* exhibiting antimicrobial activity for starter development. *LWT*, 137, 110464. Available from: https://doi.org/10.1016/j.lwt.2020.110464

Kobus-Cisowska, J., Szymanowska, D., Maciejewska, P., Szczepaniak, O., Kmiecik, D., Gramza-Michałowska, A. et al. (2019) Enriching novel dark chocolate with *Bacillus coagulans* as a way to provide beneficial nutrients. *Food & Function*, 10, 997–1006. Available from: https://doi.org/10.1039/c8fo02099j

Kodali, V.P. & Sen, R. (2008) Antioxidant and free radical scavenging activities of an exopolysaccharide from a probiotic bacterium. *Biotechnology Journal*, 3, 245–251. Available from: https://doi.org/10.1002/biot.200700208

Konstantinidi, M. & Koutelidakis, A.E. (2019) Functional foods and bioactive compounds: a review of its possible role on weight management and Obesity's metabolic consequences. *Medicine*, 6, 94. Available from: https://doi.org/10.3390/medicines6030094

Konuray, G. & Erginkaya, Z. (2018) Potential use of *Bacillus coagulans* in the food industry. *Food*, 7, 92. Available from: https://doi.org/10.3390/foods7060092

Konuray Altun, G. & Erginkaya, Z. (2021) Identification and characterization of *Bacillus coagulans* strains for probiotic activity and safety. *LWT*, 151, 112233. Available from: https://doi.org/10.1016/j.lwt.2021.112233

Kumar, S., Kikon, K., Upadhyay, A., Kanwar, S.S. & Gupta, R. (2005) Production, purification, and characterization of lipase from thermophilic and alkaliphilic *Bacillus coagulans* BTS-3. *Protein Expression and Purification*, 41, 38–44. Available from: https://doi.org/10.1016/j.pep.2004.12.010

López-gómez, J.P., Unger, P., Schneider, R., Pierrard, M. & Venus, J. (2022) Upgrading pasta wastes through lactic acid fermentations. *Food and Bioproducts Processing*, 135, 135–142. Available from: https://doi.org/10.1016/j.fbp.2022.07.010

Lee, S.H., Kwon, H.S., Koo, K.T., Kang, B.H. & Kim, T.Y. (2016a) Characterization of phytase from Bacillus coagulans IDCC 1201. *Korean J Microbiol Biotechnol*, 34, 28–34.

Lee, Y., Yoshitsugu, R., Kikuchi, K., Joe, G.H., Tsuji, M., Nose, T. et al. (2016b) Combination of soya pulp and *Bacillus coagulans* lilac-01 improves intestinal bile acid metabolism without impairing the effects of prebiotics in rats fed a cholic acid-supplemented diet. *British Journal of Nutrition*, 116, 603–610. Available from: https://doi.org/10.1017/S0007114516002270

Li, J., Shi, S., Wang, Y. & Jiang, Z. (2021) Integrated production of optically pure l-lactic acid from paper mill sludge by simultaneous saccharification and co-fermentation (SSCF). *Waste Management*, 129, 35–46. Available from: https://doi.org/10.1016/J.WASMAN.2021.05.008

Lim, C.H., Rasti, B., Sulistyo, J. & Hamid, M.A. (2021) Comprehensive study on transglycosylation of CGTase from various sources. *Heliyon*, 7, e06305.

Liu, P., Xie, J., Liu, J. & Ouyang, J. (2019) A novel thermostable β-galactosidase from *Bacillus coagulans* with excellent hydrolysis ability for lactose in whey. *Journal of Dairy Science*, 102, 9740–9748. Available from: https://doi.org/10.3168/jds.2019-16654

Majeed, M., Majeed, S., Nagabhushanam, K., Lawrence, L., Arumugam, S. & Mundkur, L. (2020) Skin protective activity of LactoSporin-the extracellular metabolite from Bacillus coagulans MTCC 5856. *Cosmetics*, 7, 76. Available from: https://doi.org/10.3390/cosmetics7040076

Marzo-Gago, C., Unger, P., Schneider, R., Venus, J. & López-Gómez, J.P. (2024) Valorising pasta industry wastes by the scale up and integration of solid-state and liquid-submerged fermentations. *Bioresource Technology*, 391, 129909. Available from: https://doi.org/10.1016/j.biortech.2023.129909

Minamida, K., Nishimura, M., Miwa, K. & Nishihira, J. (2015) Effects of dietary fiber with *Bacillus coagulans* lilac-01 on bowel movement and fecal properties of healthy volunteers with a tendency for constipation. *Bioscience, Biotechnology, and Biochemistry*, 79, 300–306. Available from: https://doi.org/10.1080/09168451.2014.972331

Neu, A.K., Pleissner, D., Mehlmann, K., Schneider, R., Puerta-Quintero, G.I. & Venus, J. (2016) Fermentative utilization of coffee mucilage using *Bacillus coagulans* and investigation of down-stream processing of fermentation broth for optically pure l(+)-lactic acid production. *Bioresource Technology*, 211, 398–405. Available from: https://doi.org/10.1016/j.biortech.2016.03.122

Notomista, E., Falanga, A., Fusco, S., Pirone, L., Zanfardino, A., Galdiero, S. et al. (2015) The identification of a novel Sulfolobus islandicus CAMP-like peptide points to archaeal microorganisms as cell factories for the production of antimicrobial molecules. *Microbial Cell Factories*, 14, 126. Available from: https://doi.org/10.1186/s12934-015-0302-9

Nyangale, E.P., Farmer, S., Keller, D., Chernoff, D. & Gibson, G.R. (2014) Effect of prebiotics on the fecal microbiota of elderly volunteers after dietary supplementation of *Bacillus coagulans* GBI-30, 6086. *Anaerobe*, 30, 75–81. Available from: https://doi.org/10.1016/j.anaerobe.2014.09.002

Olajuyigbe, F.M. & Ehiosun, K.I. (2013) Production of thermostable and organic solvent-tolerant alkaline protease from *Bacillus coagulans* PSB- 07 under different submerged fermentation conditions. *Current Biotechnology*, 12, 3341–3350. Available from: https://doi.org/10.5897/AJB2013.12219

Olszewska-Widdrat, A., Alexandri, M., López-Gómez, J.P., Schneider, R., Mandl, M. & Venus, J. (2019) Production and purification of L-lactic acid in lab and pilot scales using sweet sorghum juice. *Fermentation*, 5, 1–10. Available from: https://doi.org/10.3390/fermentation5020036

Olszewska-Widdrat, A., Alexandri, M., López-Gómez, J.P., Schneider, R. & Venus, J. (2020) Batch and continuous lactic acid fermentation based on a multi-substrate approach. *Microorganisms*, 8, 1–14. Available from: https://doi.org/10.3390/microorganisms8071084

Ou, M.S., Mohammed, N., Ingram, L.O. & Shanmugam, K.T. (2009) Thermophilic *Bacillus coagulans* requires less cellulases for simultaneous saccharification and fermentation of cellulose to products than mesophilic microbial biocatalysts. *Applied Biochemistry and Biotechnology*, 155, 76–82. Available from: http://doi.org/10.1007/s1201-008-8509-4

Ouyang, S., Zou, L., Qiao, H., Shi, J., Zheng, Z. & Ouyang, J. (2020) One-pot process for lactic acid production from wheat straw by an adapted *Bacillus coagulans* and identification of genes related to hydrolysate-tolerance. *Bioresource Technology*, 315, 123855. Available from: https://doi.org/10.1016/j.biortech.2020.123855

Palanivelu, J., Thanigaivel, S., Vickram, S., Dey, N., Mihaylova, D. & Desseva, I. (2022) Probiotics in functional foods: survival assessment and approaches for improved viability. *Applied Sciences (Switzerland)*, 12, 455. Available from: https://doi.org/10.3390/app12010455

Palomino, M.M., Allievi, M.C., Gordillo, T.B., Bockor, S.S., Fina Martin, J. & Ruzal, S.M. (2023) Surface layer proteins in species of the family Lactobacillaceae. *Microbial Biotechnology*, 16, 1232–1249. Available from:https://doi.org/10.1111/1751-7915.14230

Pamueangmun, P., Abdullahi, A.D., Kabir, M.H., Unban, K., Kanpiengjai, A., Venus, J. et al. (2023) Lignocellulose degrading Weizmannia coagulans capable of enantiomeric L-lactic acid production via consolidated bioprocessing. *Fermentation*, 9, 1689–1695. Available from: https://doi.org/10.3390/fermentation9080761

Park, A.R. & Oh, D.K. (2010) Galacto-oligosaccharide production using microbial β-galactosidase: current state and perspectives. *Applied Microbiology and Biotechnology*, 85, 1279–1286. Available from: https://doi.org/10.1007/s00253-009-2356-2

Pereira, G.V.d.M., de Carvalho Neto, D.P., Medeiros, A.B.P., Soccol, V.T., Neto, E., Woiciechowski, A.L. et al. (2016) Potential of lactic acid bacteria to improve the fermentation and quality of coffee during on-farm processing. *International Journal of Food Science and Technology*, 51, 1689–1695. Available from: https://doi.org/10.1111/ijfs.13142

van der Pol, E.C., Eggink, G. & Weusthuis, R.A. (2016) Production of l (+)-lactic acid from acid pretreated sugarcane bagasse using Bacillus coagulans DSM2314 in a simultaneous saccharification and fermentation strategy. *Biotechnol Biofuels*, 9, 1–12. Available from: https://doi.org/10.1186/s13068-016-0646-3

Qin, J., Wang, X., Wang, L., Zhu, B., Zhang, X., Yao, Q. et al. (2015) Comparative transcriptome analysis reveals different molecular mechanisms of *Bacillus coagulans* 2-6 response to sodium lactate and calcium lactate during lactic acid production. *PLoS One*, 10, 0124316. Available from: https://doi.org/10.1371/journal.pone.0124316

Ríos Colombo, N.S., Chalón, M.C., Navarro, S.A. & Bellomio, A. (2018) Pediocin-like bacteriocins: new perspectives on the mechanism of action and immunity. *Current Genetics*, 64, 345–351. Available from:https://doi.org/10.1134/S000629791905002X

Ra, S.H., Renchinkhand, G., Park, M., Kim, W. & Paik, S. (2018) Hydrolysis of non-digestible components of soybean meal by α -Galactosidase from *Bacillus coagulans* NRR1207. *Journal of Agroalimentary Process and Technologies*. 28, 1347–1353.

Raveendran, S., Parameswaran, B., Ummalyma, S.B., Abraham, A., Mathew, A.K., Madhavan, A. et al. (2018) Applications of microbial enzymes in the food industry. *Food Technology and Biotechnology*, 56, 16–30. Available from: https://doi.org/10.17113/ftb.56.01.18.5491

Rhee, M.S., Moritz, B.E., Xie, G., Glavina del Rio, T., Dalin, E., Tice, H. et al. (2011) Complete genome sequence of a thermotolerant sporogenic lactic acid bacterium, *Bacillus coagulans* strain 36D1. *Standards in Genomic Sciences*, 5, 331–340. Available from: https://doi.org/10.4056/sigs.2365342

Riazi, S., Wirawan, R.E., Badmaev, V. & Chikindas, M.L. (2009) Characterization of lactosporin, a novel antimicrobial protein produced by Bacillus coagulans ATCC 7050. *J Appl Microbiol*, 106(4), 1370–1377. Available from: https://doi.org/10.1111/j.1365-2672.2008.0410

Sadaf, A., Kumar, S., Nain, L. & Khare, S.K. (2021) Bread waste to lactic acid: applicability of simultaneous saccharification and solid-state fermentation. *Biocatalysis and Agricultural Biotechnology*, 32, 101934. Available from: https://doi.org/10.1016/j.bcab.2021.101934

Sharma, N., Ranchan, S. & Pathania, S. (2013) Production, purification and characterization of cellulase free-xylanase by *Bacillus coagulan* s B30 using lignocellulosic forest wastes with different pretreatment methods. *Journal of Agroalimentary Process and Technologies*. 19, 28–36.

Shudong, P., Guo, C., Wu, S., Cui, H., Suo, H. & Duan, Z. (2022) Bioactivity and metabolomics changes of plant-based drink fermented by *Bacillus coagulans* VHProbi C08. *LWT*, 156, 113030. Available from: https://doi.org/10.1016/j.lwt.2021.113030

Silva, D.R., Sardi, J.d.C.O., Pitangui, N.d.S., Roque, S.M., Silva, A.C.B.d. & Rosalen, P.L. (2020) Probiotics as an alternative antimicrobial therapy: current reality and future directions. *Journal of Functional Foods*, 73, 104080. Available from: https://doi.org/10.1016/j.jff.2020.104080

Soltani, S., Hammami, R., Cotter, P.D., Rebuffat, S., Ben, S.L., Gaudreau, H. et al. (2021) Bacteriocins as a new generation of antimicrobials: toxicity aspects and regulations. *FEMS Microbiology Reviews*, 45, 1–24. Available from: https://doi.org/10.1093/femsre/fuaa039

Su, F., Tao, F., Tang, H. & Xu, P. (2012) Genome sequence of the thermophile *Bacillus coagulans* hammer, the type strain of the species. *Journal of Bacteriology*, 194, 6294–6295. Available from: https://doi.org/10.1128/JB.01380-12

Su, F. & Xu, P. (2014) Genomic analysis of thermophilic *Bacillus coagulans* strains: efficient producers for platform bio-chemicals. *Scientific Reports*, 4, 3926. Available from: https://doi.org/10.1038/srep03926

Sudha, M.R. & Arunasree, K.M. (2015) Anti-inflammatory and immunomodulatory effects of Bacillus coagulans Unique IS2. *Int J Probiotics Prebiotics*, 10, 1.

Sun, Q., Yin, S., He, Y., Cao, Y. & Jiang, C. (2023) Biomaterials and encapsulation techniques for probiotics: current status and future prospects in biomedical applications. *Nanomaterials*, 13, 2185. Available from: https://doi.org/10.3390/nano13152185

Talebi, M., Emtiazi, G., Akhavan Sepahy, A. & Zaghian, S. (2013) Zymogram analysis of alkaline keratinase produced by nitrogen-fixing *Bacillus pumilus* ZED17 exhibiting multiprotease enzyme activities. *Jundishapur Journal of Microbiology*, 6, 7974. Available from: https://doi.org/10.5812/jjm.7974

Terpou, A., Papadaki, A., Lappa, I.K., Kachrimanidou, V., Bosnea, L.A. & Kopsahelis, N. (2019) Probiotics in food systems: significance and emerging strategies towards improved viability and delivery of enhanced beneficial value. *Nutrients*, 11, 1591. Available from: https://doi.org/10.3390/nu11071591

Urtasun, R., Díaz-Gómez, J., Araña, M., Pajares, M.J., Oneca, M., Torre, P. et al. (2020) A combination of apple vinegar drink with *Bacillus coagulans* ameliorates high fat diet-induced body weight gain, insulin resistance and hepatic steatosis. *Nutrients*, 12, 1–19. Available from: https://doi.org/10.3390/nu12092504

Walton, S.L., Bischoff, K.M., Van Heiningen, A.R.P. & Van Walsum, G.P. (2010) Production of lactic acid from hemicellulose extracts by *Bacillus coagulans* MXL-9. *Journal of Industrial Microbiology & Biotechnology*, 37, 823–830. Available from: https://doi.org/10.1007/s10295-010-0727-4

Wang, Y., Chang, J., Cai, D., Wang, Z., Qin, P. & Tan, T. (2017) Repeated-batch fermentation of L-lactic acid from acid hydrolysate of sweet sorghum juice using mixed neutralizing agent under unsterilised conditions. *Journal of Chemical Technology and Biotechnology*, 92, 1848–1854. Available from: https://doi.org/10.1002/jctb.5195

Xu, Y., Wu, Q., Bai, L., Mu, G., Tuo, Y., Jiang, S. et al. (2021) Cloning, expression, and bioinformatics analysis and characterization of an α-galactosidase from *Bacillus coagulans* T242. *Journal of Dairy Science*, 104, 2735–2747. Available from: https://doi.org/10.3168/jds.2020-18942

Yaashikaa, P.R., Kumar, P.S., Varjani, S., Tamilselvi, S. & Saravanan, A. (2020) Formulation and combinatorial effect of Pseudomonas fluorescens and *Bacillus coagulans* as biocontrol agents. *Biocatalysis and Agricultural Biotechnology*, 30, 101868. Available from: https://doi.org/10.1016/j.bcab.2020.101868

Yang, J., Lagishetty, V., Kurnia, P., Henning, S.M., Ahdoot, A.I. & Jacobs, J.P. (2022) Microbial and chemical profiles of commercial kombucha products. *Nutrients*, 14, 670. Available from: https://doi.org/10.3390/nu14030670

Ye, L., Bin, H.M.S., Li, Z. & Wu, J.C. (2014) Simultaneous detoxification, saccharification and co-fermentation of oil palm empty fruit bunch hydrolysate for l-lactic acid production by *Bacillus coagulans* JI12. *Biochemical Engineering Journal*, 83, 16–21. Available from: https://doi.org/10.1016/j.bej.2013.12.005

Zhang, S., Li, P., Lee, S., Wang, Y., Tan, C. & Shang, N. (2024) *Weizmannia coagulans*: an ideal probiotic for gut health. *Food Science and Human Wellness*, 13, 16–26. Available from: https://doi.org/10.26599/FSHW.2022.9250002

Zhao, R., Zhao, R., Tu, Y., Zhang, X., Deng, L. & Chen, X. (2018) A novel α-galactosidase from the thermophilic probiotic *Bacillus coagulans* with remarkable protease-resistance and high hydrolytic activity. *PLoS One*, 13, 1–16. Available from: https://doi.org/10.1371/journal.pone.0197067

Zhou, Y., Zeng, Z., Xu, Y., Ying, J., Wang, B., Majeed, M. et al. (2020) Application of *Bacillus coagulans* in animal husbandry and its underlying mechanisms. *Animals*, 10, 454. Available from: https://doi.org/10.3390/ani10030454

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