الجمهورية الجزائرية الديموقراطية الشعبية

People's Democratic Republic of Algeria *N series ......*

وزارة التعليم العالي والبحث العلمي

Ministry of Higher Education and Scientific Research

جامعة الشهيد حمه لخضر الوادي

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Department of Cellular and Molecular Biology

END OF STUDY THESIS

In view of obtaining the degree of Academic Master in Biological Sciences

Speciality: Toxicology

THEME

Bibliographic summary of lactic acid bacteria and their relationship with human health

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Bb : *Bifidobacterium*

CAT :catalase

CLA: conjugated linoleic acid

E : *Enterococcus*

EPS: exopolysaccharides

GR: glutathione reductase

GPx : peroxidase enzymes

GSH : include glutathione

GTP : guanosine triphosphate

HFD: high-fat diet

IM: intestinal mucositis

LAB : Lactic acid bactria

LPS: lipopolysaccharide

Lb :*Lactobacillus*

Lc : *Lactococcus*

LPS : lipopolysaccharide

MALTs: membrane-associated lymphoid tissues

Strep: *Streptococcus*

SOD : superoxide dismutase

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Summary

Abstract

Lactic acid bacteria (LAB) are a heterogeneous group of bacteria that play an important role in a variety of fermentation processes. They ferment dietary carbohydrates and produce lactic acid as the main product of fermentation. In addition, the degradation of proteins and fats and the production of various alcohols, aldehydes, acids, esters and sulfur compounds contribute to the development of the specific flavor in various fermented food products. The main application of LAB is as starter farms, with a large variety of fermented dairy products (e.g. cheese, yoghurt, fermented milk), meat, fish, fruits, vegetables and grain products. Furthermore, they contribute to the flavour, texture and nutritional value of fermented foods and are therefore used as adjuvant cultures. Examples include accelerating cheese ripening, improving yoghurt texture through the production of exogenous sugars and controlling secondary fermentation in wine production. The production of bacteria and antifungal compounds has led to the application of bioprotective cultures in some foods. Furthermore, the well-documented health-promoting properties of some lactobacilli in association with bifidobacteria .

Keywords: Lactic acid bacteria; fermentation; fermented foods; meat; dairy products; health .

Résumé

Les bactéries lactiques (LAB) constituent un groupe hétérogène de bactéries qui jouent un rôle important dans divers processus de fermentation. Ils fermentent les glucides alimentaires et produisent de l'acide lactique comme principal produit de fermentation. De plus, la dégradation des protéines et des graisses et la production de divers alcools, aldéhydes, acides, esters et composés soufrés contribuent au développement de la saveur spécifique de divers produits alimentaires fermentés. La principale application de LAB concerne les fermes de démarrage, avec une grande variété de produits laitiers fermentés (par exemple fromage, yaourt, lait fermenté), de viande, de poisson, de fruits, de légumes et de produits céréaliers. De plus, ils contribuent à la saveur, à la texture et à la valeur nutritionnelle des aliments fermentés et sont donc utilisés comme cultures adjuvantes. Les exemples incluent l'accélération de l'affinage du fromage, l'amélioration de la texture du yaourt grâce à la production de sucres exogènes et le contrôle de la fermentation secondaire dans la production de vin. La production de bactéries et de composés antifongiques a conduit à l'application de cultures bioprotectrices dans certains aliments. En outre, les propriétés bénéfiques pour la santé bien documentées de certains lactobacilles en association avec les bifidobactéries .

Mots clés: bactéries lactiques; fermentation; aliments fermentés; viande ; les produits laitiers; santé .

ملخص

بكتيريا حمض اللاكتيك (LAB) هي مجموعة غير متجانسة من البكتيريا التي تلعب دورًا مهمًا في مجموعة متنوعة من عمليات التخمير. أنها تخمر الكربوهيدرات الغذائية وتنتج حمض اللبن باعتباره المنتج الرئيسي للتخمير. بالإضافة إلى ذلك، فإن تحلل البروتينات والدهون وإنتاج الكحوليات المختلفة والألدهيدات والأحماض والإسترات ومركبات الكبريت يساهم في تطوير النكهة المحددة في مختلف المنتجات الغذائية المتخمرة. التطبيق الرئيسي لـ LAB هو المزارع البادئة، مع مجموعة كبيرة ومتنوعة من منتجات الألبان المخمرة (مثل الجبن واللبن والحليب المخمر) واللحوم والأسماك والفواكه والخضروات ومنتجات الحبوب. علاوة على ذلك، فإنها تساهم في النكهة والملمس والقيمة الغذائية للأطعمة المخمرة، وبالتالي تستخدم كثقافات مساعدة. تشمل الأمثلة تسريع نضج الجبن، وتحسين قوام الزبادي من خلال إنتاج السكريات الخارجية والتحكم في التخمر الثانوي في إنتاج النبيذ. أدى إنتاج البكتيريا والمركبات المضادة للفطريات إلى تطبيق ثقافات الحماية الحيوية في بعض الأطعمة. علاوة على ذلك، فإن الخصائص المعززة للصحة الموثقة جيدًا لبعض العصيات اللبنية المرتبطة بالبكتيريا المشقوقة.

الكلمات المفتاحية: بكتيريا حمض اللاكتيك ؛ التخمير ؛ الأطعمة المخمرة ؛ لحمة ؛ منتجات الألبان ؛ صحة .

In recent years, more and more attention has been paid to the metabolism of lactic acid bacteria. Lactic acid bacteria (LAB) are a type of gram-positive bacteria that use carbohydrates as the only or main carbon source **(George *et al*., 2018).** Lactic acid bacteria are generally cocci or rods, and have strong tolerance to low pH. Although lactic acid bacteria include more than 60 genera, the frequently genera occur in food fermentation generally include *Lactobacillus*, *Lactococcus*, *Leuconostoc*, *Pediococcus*, *Streptococcus*, *Enterococcus*, *Weissella*, etc **(Mokoena, 2017)**. But it has recently been proposed to merge *Lactobacillaceae* and *Leuconostocaceae* in one family *Lactobacillaceae* . The genus *Lactobacillus* was also reclassified into 25 genera **(Zheng *et al*., 2020)** .

As a fermentation strain, lactic acid bacteria must possess several important metabolic properties. The metabolic properties of lactic acid bacteria and their applications in food industry from the aspects of degradation and biometabolism of lactic acid bacteria are reviewed. We hope to summarize the new development trends and promote the contribution of lactic acid bacteria related to metabolic engineering and food biotechnology in the food industry **(Yaqi Wang *et al*., 2021)** . The three main pathways involved in the synthesis and development of flavor in fermented food products are glycolysis, fermentation of sugars, lipolysis (decomposition of fats), and proteolysis (decomposition of proteins). Lactate is the main product resulting from carbohydrate metabolism and a portion of the intermediate pyruvate can alternatively be converted to diacetyl, acetoin, acetaldehyde or acetic acid (some of which can be important to typical yoghurt flavours). The contribution of LAB to lipolysis is relatively small, but proteolysis is the major biochemical pathway for flavor development in fermented foods. Lactic acid bacteria can be found in meat, vegetables, and dairy products **(Bintsis T, 2018)** .

LAB-driven fermentations often yield by-products with bioactivity and a diverse range of health-promoting effects, antioxidative, anti-inflammatory, anticancer, antimicrobial, immunomodulatory, and antihypertensive effects in the living body **(Ahmed *et al*., 2022)** .

to the international channel this theme the search for lactic bacteria is very important in the articlesfor example **Yalda *et al* en 2019** and working on the effects of EPS and the relationship of lactic acid bacteria with human health . **Dominika *et al* en 2022** The use of EPSs has been found to be a safer alternative in complex disorders such as cancer and immune-related diseases .**Heena *et al* en 2023** working on the compositional effects of LAB in fermented dairy products and the benefits and relationship for human health .

Other objective is better important of lactic acid bacteria and their consumption and their encorgenemt the different product ferments, The benefit of it is that I encourage the consumption of fermented products.

This memorandum is divided into three sections, which are as follows **Chapter I** General information on lactic acid bacteria, **Chapter II** Lactic acid bacteria in food products, **Chapter III** Therapeutic and prevention of LAB

I.1. History of lactic acid bacteria

Lactic acid bacteria are very old microorganisms whose ancestors may have emerged three billion years ago (before Cyanobacteria). They have been used for the fermentation of food for over 4000 years, without understanding the scientific basis of their use, but trying to produce food with better preservation and better quality **(Boudersa *et al*., 2017)**.

It will be necessary to wait for Pasteur and his work on fermentation in 1857 to establish a link between lactic fermentation and bacteria. The first pure bacterial culture will be a culture of *Lactococcus lactis* obtained and described by Joseph Lister in 1873 cited by **Penaud. (2006)**. In 1904, Metchnikoff isolated the "Bulgarian bacillus" (*Lactobacillus delbrueckii ssp. Bulgaricus*) present in yoghurt **(Mechai, 2009)**.

At the start of the 20th century, Elie Metchnikoff , noted that the longevity and good health of Bulgarian peasants was linked to their consumption of fermented milk products and suggested that certain microorganisms could exert beneficial effects on human health **(Daoudi, 2018)**.

I.2. Definition of lactic acid bacteria

Lactic acid bacteria are Gram-positive, non-spore-forming, non-respiring but aerotolerant, which produce lactic acid as one of the key fermentation products by utilizing carbohydrates during fermentation. These bacteria produce lactic acid as an end product of carbohydrate catabolism and also make organic substances that contribute to the flavor, texture, and aroma that result in unique organoleptic characteristics **Orla. (1919)** first published a monograph that laid the foundation for classifying lactic acid bacteria. This system of classification was linked to certain factors that entailed the following; glucose fermentation characteristics, cell morphology, capacity to utilize sugars, and optimum growth temperature range .This classification system thus recognized only four lactic acid bacteria genera: *Lactobacillus, Pediococcus, Leucononstoc, and Streptococcus* **(Quinto *et al*., 2014)**.

I.3. General characteristics of lactic acid bacteria

Lactic acid bacteria (LAB) are a group of microbes with increasing importance in biotechnology. They are widely used in milk processing. Traditionally, the use of LAB was mainly limited to the dairy, fermentation, fruit and vegetable, and animal feed industries. The importance of lactic acid bacteria is constantly growing because they are considered safe for humans and animals (Generally Recognized As Safe—GRAS) and show many beneficial effects on human health **(Chlebowska *et al*., 2019)**.

LAB are a large group of bacteria with the ability to ferment sugars into lactic acid. Lactic acid fermentation is an intracellular, anaerobic enzymatic process of converting sugars to lactic acid, which is one of the approaches to obtain the energy necessary for cell life processes in anaerobic conditions Morphologically **(Janiszewska-Turak *et al*., 2020)**, lactobacilli are not a homogeneous group. They include rods arranged in chains, such as the genus *Lacticaseibacillus, Carnobacterium, Weissella; cocci arranged in chains, such as species of Lactococcus, Enterococcus, Vagococcus; and Oenococcus (known as Leuconostoc oeni*), which was formerly referred to as *Leuconostoc*, and are arranged in the form of tetrads, such as the genus *Tetragenococcus*. These are relatively anaerobic, gram-positive, and nonspore-producing bacteria that usually do not have flagellas **(Othman *et al*., 2017; Zieli´ *et al*., 2018) .**

LAB can produce proteolytic enzymes inside the cell as well as in the external environment. The optimum pH for the development and growth of proteolytic bacteria in milk is 7–7.5. A low temperature inhibits the growth and development of these bacteria and decreases their enzymatic activity. Temperatures above that are optimal for bacterial growth rapidly inactivate proteolytic enzymes. In some cases, irreversible loss of proteolytic enzyme activity is observed after prolonged storage at low temperatures **(Worsztynowicz *et al*., 2020; Linares-Morales *et al*., 2020).** Many proteolytic bacteria have psychrotrophic properties. It should be noted that these bacteria can degrade milk proteins. This aspect has been observed in both bacilli and lactic streptococci, although to a lesser extent than that in typical proteolytic bacteria such as Proteus, Pseudomonas, Alcaligenes, Acinetobacter, Bacillus, Clostridium, and some strains of Micrococcus **(Cichosz *et al*., 2006) .**

LAB can degrade proteins, as exemplified by casein. The final products of this decomposition are most often the amino acids used by LAB as a source of nitrogen. Thermophilic lactobacilli species have stronger proteolytic abilities than rods or streptococci; however, each species has strains with highly varying activity in this respect. Depending on the species, subspecies, and even the strain, LAB show very diverse proteolytic activity. Among the cocci, the most active species are Lactococcus salivarius subsp. thermophilus (formerly named Streptococcus salivarius subsp. thermophilus) and Lc. lactis subsp. cremonis, while the least active is Lc. lactis subsp. lactis. Of the lactobacilli used in the dairy industry, the most proteolytically active species are *Lacticaseibacillus casei*, *Lactobacillus* delbrueckii subsp. bulgaricus, Lb. helveticus, and Lb. acidophilus, while the least active species is Lactiplantibacillus plantarum. In general, the activity of rods is greater than that of lactic streptococci **(Wa sko *et al*., 2012;Linares-Morales *et al*., 2020; Saidi *et al* ., 2020)** .

When discussing the proteolytic enzymes of LAB, it is worth mentioning lactococcal strains. Proteolysis of casein forms so-called bitter peptides, which are the cause of the bitter taste of dairy products **(Zhao *et al* ., 2016)** .

I.4. Classification of lactic acid bacteria

Lactic acid bacteria has also been classified into different genera/species (table 01) based on their acid production characteristics by fermenting sugars and its growth at specific temperatures **(Parvez *et al*., 2006)** . Additionally, the lactic acid bacteria can be classified as homofermentative or heterofermentative organisms based on their ability to ferment carbohydrates **(Mokoena, 2017)** .

Table 01 : Presentation of lactic acid bacteria species **(Bouguerra, 2021)**

Familles	Genres	Espèce type	Reference
Aerococcaceae	*Abiotrophia*	*Ignavigranum*	**(Bouguerra, 2021)**
	Aerococcus	*Ae. Viridans*	**(Belhamra, 2017)**
	Dolosicoccus	*Dc. Paucivorans*	**Bekhouche, 2006)**
	Eremococcus	*Ere. Coleocola*	**(Alard, 2017)**
	Facklamia	*F. hominis*	
	Globicatella	*Glo. Sanguinis*	
	Ignavigranum	*Ig. Ruoffiae*	

Carnobacteriaceae	*Alkalibacterium*	*Alk. Olivapovliticus*	**(Bouguerra, 2021)**
	Allofustis	*Af. Seminis*	**(Belkhir, 2017)**
	Alloiococcus	*Ai. Otitis*	**(Belyagoubi, 2014)**
	Atopobacter	*Ap. phocae*	
	Atopococcus	*Ac. Tabaci*	
	Atopostipes	*At. Suicloacalis*	
	Bavariicoccus	*B. seileri*	
	Carnobacterium	*C. divergens*	
	Desemzia	*D. incerta*	
	Dolosigranulum	*Dg. Pigrum*	
	Granulicatella	*Gra. Adiacens*	
	Isobaculum		
	Lacticigenium	*Is. Melis*	
	Marinilactibacillus	*Lg. Naphtae*	
	Trichococcus (incl.	*M. +psychrotolerans*	
	Lactosphaera(	*Tr.flocculiformis*	
	Catellicoccus	*Cat. Marimammalium*	
Enterococcaceae	*Enterococcus*	*E. faecalis*	**(Rakhis *et al*., 2016)**
	Melissococcus	*Me. plutonius*	
	Pilibacter	*Pi. Termitis*	
	Tetragenococcus	*Tet. Halophilus*	
	Vagococcus	*V. fluvialis*	
Lactobacillaceae	*Lactobacillus*	*Lb. Delbrueckii*	**(Bouguerra, 2021)**
	Paralactobacillus	*Pl. selangorensis*	
	Pediococcus+	*Ped. Damnosus*	
Leuconostocaceae	*Fructobacillus*	*Fru. fructosus*	**(Bouguerra, 2021)**

	Leuconostoc	*Ln. mesenteroides*	**(Alard , 2017)**
	Oenococcus	*O. oeni*	
	Weissella	*W. viridescens*	
Streptococcaceae	*Lactococcus*	*Lc. Lactis*	**(Belhamra, 2017)**
	Lactovum	*Lv. Miscens*	**(Bouguerra, 2021)**
	Streptococcus	*S. pyogenes*	
Other 'LAB'	*Bifidobacterium*	*Bif. Bifidum*	**(Negadi and Mekelleche, 2017)**

I.5. Biotechnology uses of lactic acid bacteria

The different biotechnological applications of lactic bacteria are now present in (figure 01)

I.5.1. Food products

The metabolic characteristics of lactic acid bacteria make them essential players during food fermentations. Lactic acid bacteria are classically involved in a large number of food fermentations, alone or with other microorganisms (transformation of milk, fermented drinks, salting, fermentation of plants) .

Lactic acid bacteria are essential, and their usefulness cannot be overemphasized in many food fermentation applications and preservation activities. Many traditional foods have been developed using lactic acid bacteria, which improve product characteristics and impart certain properties that enhance consumer acceptance and appeal. Most of the products that are developed by the use of lactic acid bacteria also provide superior health benefits to the consumer which is key to maintaining a healthy gastrointestinal system. Some of the fermented food products from lactic acid bacteria include kefir, cheese, butter, yogurt, sauerkraut, buttermilk, brined vegetables, sourdough, soya curd, koumiss, idly batter, uttapam, fermented meat, and beverages **(Gupta and Jeevaratnam, 2018)**.

Fermented milk products, alternatively referred to as cultured dairy products, include dairy foods that have been fermented by a consortium of lactic acid bacteria that are responsible for milk curdling or the souring of milk **(Wiley Press., 2003)** . Lactic acid bacteria are lactose fermenters that also preserve the taste and nutritional properties of milk. Bacterial members associated with fermented dairy products belong to the genera of

Lactobacillus, Lactococcus, Leuconostoc, Pediococcus, Bacillus, Propionibacterium, and Bifidobacterium. These bacteria live in the same ecological niches and act mutualistically. There are approximately 400 traditional and fermented milk products comprising a diverse group of microorganisms that give rise to different sensory properties **(Ghosh *et al*., 2019)** . **(table 02)** highlights several traditionally fermented milk products that use lactic acid bacteria along with the accompanying health derived benefits.

Table 02. Beneficial properties of ethnically fermented food products and associated microorganisms **(Raphael *el al*., 2020)**

Traditional Fermented Foods	**Microbiota**	**Associated Action**	**References**
Dahi	*Lactobacillus acidophilus*	Production of antibacterial substances	**(Balamurugan *et al*., 2014)**
Kefir	*Lactobacillus kefir, Lactobacillus kefiranofaciens,* and *Lactobacillus kefirgranum*	Production of bacteriocin enhances antibacterial activity Epithelial cells of the intestine have reduced inflammation Serum cholesterol level is reduced Produce an EPS known as kefiran.	**(Luo *et al*., 2011)** **(Seo *et al*.,2018)** **(Wang *et al*., 2008)** **(Bonczar *et al*., 2016)**
Tofu	*Lactobacillus plantarum*	Antioxidant activity	**(Li *et al*., 2012)**
Koumiss	*Lactobacillus sp.*	Excellent antimicrobial properties against pathogens	**(Guo *et al*., 2015)**
Swiss Cheese	*Lactobacillus helveticus R389*	Enhancement of the immune system by increasing IgA and CD4 positive cells.	**(Ghosh *et al*., 2019)**
Nunu	*Lactobacillus plantarum, Lactobacillus fermentum, and Saccharomyces cerevisiae*	Produces EPS, and β-galactosidase Produces bacteriocins known as plantaricins promoting antibacterial activity against pathogens	**(Akabanda *et al*., 2013)** **(Behera *et al*., 2018)**
Korean kimchi	*Lactobacillus plantarum*	Antimicrobial activity against pathogens	**(Kwak *et al*., 2017)**

I.5.2. Pharmaceutical products

Lactic acid is essential in pharmaceutical manufacturing as an electrolyte in parenteral/IV solutions and dialysis solutions for artificial kidney machines. It is preferred over sodium acetate for continuous ambulant peritoneal dialysis due to its lower side effects. Lactide-glycolide copolymers and polylactic acid (PLA) are preferred materials for controlled drug delivery systems. Ammonium lactate is used for treating dry skin disorders, preventing xerosis and callus formation, and in military lactate formulations for diseases like anemia, hypertension, and osteoporosis. Chiral chemistry is crucial in pharmaceutical processes, relying on natural chiral building blocks like lactic acid for desired stereochemistry **(Ramzi *et al*., 2015)**.

I.5.3. Cosmetic products

Lactic acid bacteria are beneficial to human health. Lactic acid bacteria have wide applications in food, cosmetic and medicine industries due to being Generally Recognized As Safe (GRAS) and a multitude of therapeutic and functional properties. Previous studies have reported the beneficial effects of lactic acid bacteria, their extracts or ferments on skin health, including improvements in skin conditions and the prevention of skin diseases. Lipoteichoic acid isolated from Lactobacillus plantarum was reported to inhibit melanogenesis in B16F10 melanoma cells. In particular, lipoteichoic acid also exerted anti-photoaging effects on human skin cells by regulating the expression of matrix metalloproteinase- 1. The oral administration of Lactobacillus delbrueckii and other lactic acid bacteria has been reported to inhibit the development of atopic diseases. Additionally, the clinical and histologic evidence indicates that the topical application of lactic acid is effective for depigmentation and improving the surface roughness and mild wrinkling of the skin caused by environmental photo-damage.

This review discusses recent findings on the effects of lactic acid bacteria on skin health and their specific applications in skin-whitening cosmetics **(Huey-Chun *et al*., 2020) .**

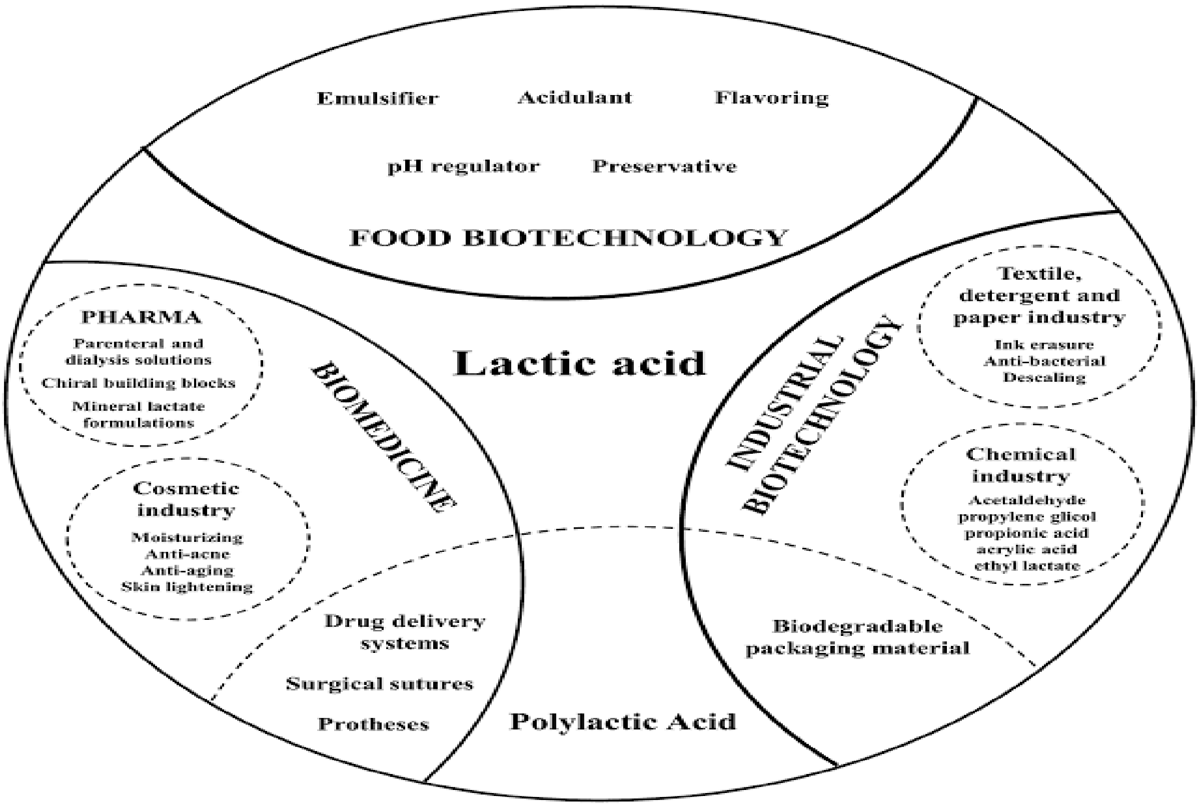

Figure 01: Biotechnological advances in lactic acid production by lactic acid bacteria

(Enrique *et al*., 2018)

Fermented foods are produced through fermentation of certain sugars by LAB and the origins of them are lost in antiquity. The most commonly LAB used as starter cultures in food fermentations are shown. It is well-known that the greatest proportion of them belong to the category of dairy products, namely cheese, yoghurt, fermented milks, while fermented meat products, fish products, pickled vegetables and olives and a great variety of cereal products are manufactured, nowadays, using starter cultures. These products, were produced in the past through back slopping and the resulting product characteristics depended on the best-adapted strains dominance, whereas, the earliest productions of them were based on the spontaneous fermentation, resulting from the development of the microflora naturally present in the raw material and its environment. Today, the majority of fermented foods are manufactured with the addition of selected, well defined, starter cultures with well characterized traits, specific for each individual product. For a detailed classification of starter cultures see **(Bintsis and Athanasoulas, 2015)**.

II.1. Functions of lactic acid bacteria in food

II.1.1. Metabolism of lactic acid bacteria

The use of sugars and the metabolism of nitrogen sources in food products by LAB are considered to be very important biochemical events in the development of the organoleptic and textural characteristics of a given food, hence their involvement in the food industry. . Furthermore, the production of organic acids in food thus lowers the pH and creates an unfavorable environment for the majority of pathogenic bacteria. The synthesis of volatile and aromatic compounds with the production of sugar polymers also determine a certain number of sensory and rheological characteristics desired in food products. Figure 02 shows the main metabolic pathways of LAB **(Saidi, 2020).**

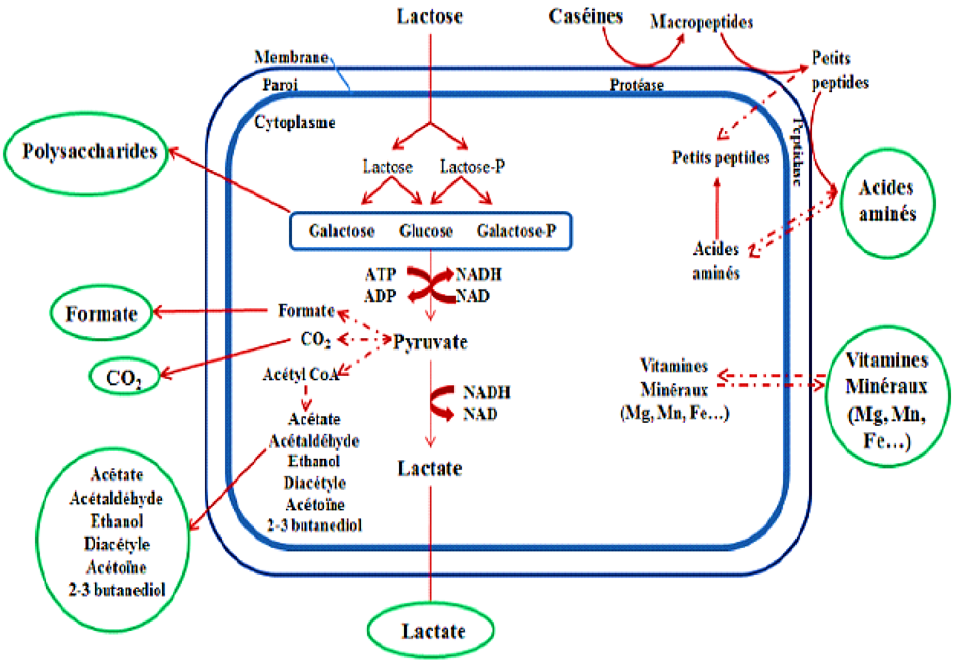

Figure 02: Main metabolic pathways of lactic acid bacteria **(Saidi, 2020).**

II .1.1.1. Sugar metabolism

Sugar catabolism provides the energy for anabolism in the form of ATP and generates reduced coenzymes in the form of NADH essentially. The major function of lactic acid production lies in the generation of these reduced coenzymes, however the amount of lactic acid produced is variable depending on the strains and the environment, and other metabolites such as formate, l acetate, ethanol and CO2 can also accumulate during fermentation (Novak and Loubière, 2000), the sugars are then catabolized according to one of three different pathways: the homofermentative pathway, the heterofermentative pathway and the bifid pathway **(Thompson and Gentry, 1994).**

Lactic acid fermentation is a metabolic process involving the conversion of sugars into lactic acid by lactic acid bacteria.. Several types exist, mainly related to the types of lactiques involved and the final products obtained. Lactic acid fermentation is an anaerobic process in some bacteria and animal cells, such as muscle cells. It occurs in the presence of oxygen or facultative anaerobic organisms. Lactate dehydrogenase catalyzes the interconversion of pyruvate and lactate, while homolactic fermentation converts glucose into two molecules of lactic acid, while heterolactic fermentation produces carbon dioxide and ethanol (figure 03) **(Battcock and Azam-Ali, 2019)** .

1. Homofermentative process

Homofermentative bacteria are a type of lactic acid bacteria that produce only lactic acid as a primary by-product in glucose fermentation. In biochemistry, homofermentative bacteria convert glucose molecules into two lactic acid molecules. They use this reaction to make two ATP molecules through substrate-level phosphorylation. Homofermentative bacteria include *Lactococcus* species, which is used in dairy starter cultures to rapidly-produce lactic acid in reduced pH conditions. In the dairy industry, *Lactococcus* species can be used in single-strain starter cultures or in mixed-strain cultures with other lactic acid bacteria such as *Lactobacillus* and *Streptococcus* **(Battcock and Azam-Ali, 2019*)*** .

$$\text{glucose} + 2\ \text{ADP} + 2\ \text{P}_i \rightarrow 2\ \text{lactate} + 2\ \text{ATP}$$

2. Heterofermentative process

The degradation of a molecule of glucose leads to the formation of a molecule of lactate, a molecule of ethanol (CH3CH2OH), a CO2 and an ATP. An enzyme specific for this pathway (D-xylulose-5-phosphate phosphoketolase) catalyzes the dissociation of xylulose-5-phosphate into acetyl-P and glyceraldehyde3-phosphate. The acetyl-P is then converted either into ethanol or into acetate according to the needs in ATP or NAD+. Glyceraldehyde-3-phosphate joins glycolysis to be converted into lactate. In general, sugars with 5 carbon atoms (or pentoses) can only be metabolized by this route. Some Leuconostoc and Lactobacillus bacteria use this heterofermentative pathway (Cherrad et al., 2020).

Heterofermentative bacteria produce less lactate and less ATP, but produce several other end products **(Battcock and Azam-Ali, 2019).**

$$\text{glucose} + \text{ADP} + \text{P}_i \rightarrow \text{lactate} + \text{ethanol} + CO_2 + \text{ATP}$$

Examples include *Leuconostoc mesenteroides*, *Lactobacillus bifermentous*, and *Leuconostoc lactis*.

3. Bifidum pathway

This route is taken by bacteria of the genus *Bifidobacterium*, it allows to have 1.5 molecules of acetate and 2.5 molecules of ATP from a molecule of hexose consumed (figure 03) ***(*Battcock and Azam-Ali, 2019*)***.

Bifidobacterium bifidum utilizes a lactic acid fermentation pathway that produces more ATP than either homolactic fermentation or heterolactic fermentation ***(*Battcock and Azam-Ali, 2019*)* .**

glucose + 5 ADP + 5 Pi → 3 acetate + 2 lactate + 5 ATP 2

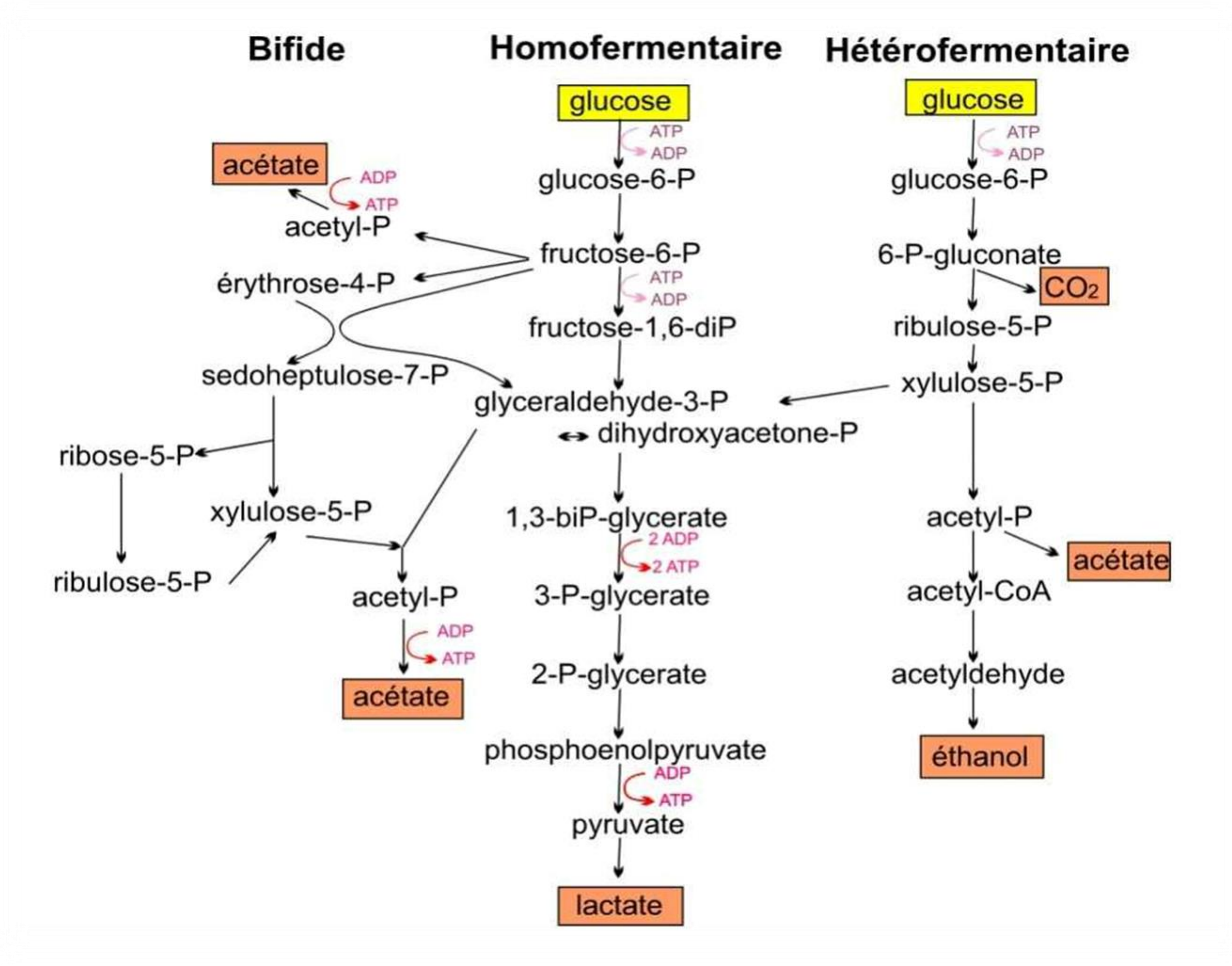

Figure 03: Diagram showing the different types of lactic acid bacteria fermentation **(Salminen and Von, 2004**).

II .1.1.2 Protein metabolism

LAB are fastidious microorganisms and are unable to synthesize many amino acids, vitamins and nucleic acid bases Depending on the species and the strain, LAB require from 6 to 14 different amino acids. Since free amino acids in milk are limited and amino acids are present as protein components, the growth of LAB requires the hydrolysis of milk proteins.

The hydrolysis of peptides to free amino acids and the subsequent utilization of these amino acids is a central metabolic activity in LAB, and proteolysis has been identified as the key process influencing the rate of flavour and texture development in most cheese varieties and has been reviewed and the catabolism of amino acids has been reviewed by Kunji et al.. The degradation of milk proteins to peptides is catalysed by proteolytic enzymes present in LAB, and peptides are then further hydrolysed by exopeptidases and endopeptidases to small peptides and amino acids **(AIMS Microbiol, 2018)**.

LAB have only weak proteolytic action on myofibrillar proteins in fermented meat products. However, some *Lb. casei*, *Lb. plantarum*, *Lb. curvatus* and *Lb. sakei* strains actively contribute to the hydrolysis of the sarcoplasmic proteins and to the subsequent decomposition of peptides into amino acids. Several peptidase activities have been reported in *Lb. sakei*, *Lb. curvatus* and *Lb. plantarum* isolated from sausages. Further, some *Lb. sakei*, *Lb. curvatus* and *Lb. plantarum* strains possess leucine and valine amino-peptidases, which contribute to the catabolism of proteins and peptides generating free amino acids, precursors of flavour compounds in the final product **(AIMS Microbiol, 2018)**.

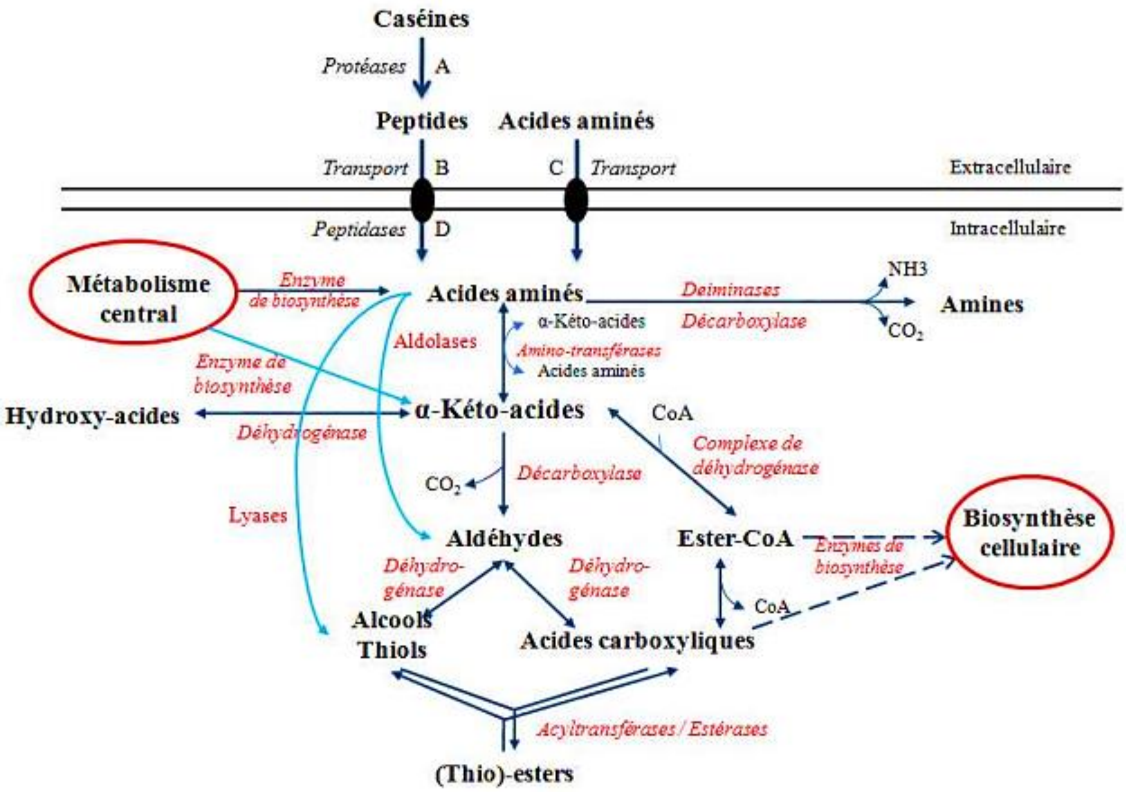

Figure 04: Overview of general protein conversion pathways relevant for flavor formation in dairy fermentations **(Smit *et al*., 2005)**.

II .1.3 Lipid metabolism

Bacterial lipases partly catalyze the production of long-chain fatty acids from mono and diglycerides (cut the ester bonds of triglycerides), while esterases allow the release of volatile fatty acids. They are also precursors for the formation of metylketones, alcohols, lactones and esters (figure06) illustrates the main pathways of lipolysis **(McSweeney and Sousa, 2000)** .

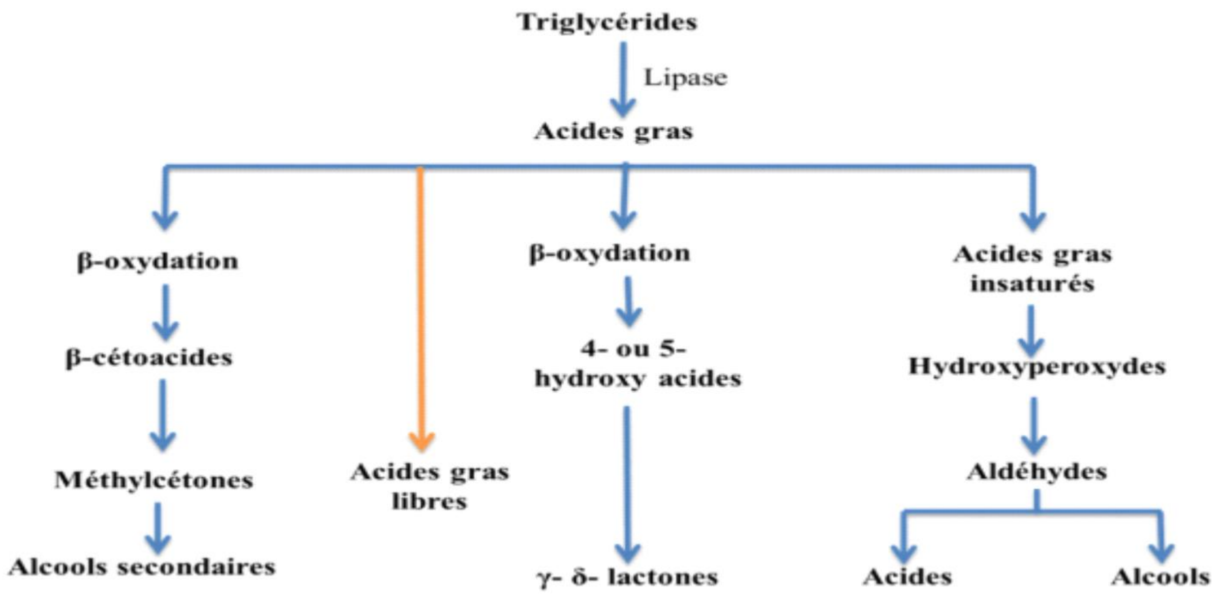

Figure 05: Main pathways of lipolysis **(Siegumfeldt *et al*., 2000).**

II .1.1.4 Metabolism of citrate and other carbonaceous substrates

Lactic acid bacteria are essential for their flavoring capabilities and are used in natural environments for food production. Citric acid is used by many species, including *Streptococcus*, *Lactococcus*, *Enterococcus*, *Pediococcus*, and *Leuconostacet Lactobacillus*. It is the main precursor of butter flavor and is involved in oenology. Pyruvate hydrolysis is also involved in citric acid metabolism. Some lactic acid bacteria ferment glycerol, producing trimethylene glycol and b-hydroxypropionic acid. This metabolic pattern can produce reuterin, an antimicrobial substance used in certain food products **(Nemkov *et al*., 2017)**.

II.2. Bacterinocins

Bacteriocins are heat-stable, ribosomally synthesized antimicrobial peptides. Both Gram-positive and Gram-negative bacteria, and archaea release antimicrobial peptides extracellularly in the late-exponential to the early-stationary growth phases **(Zheng *et al*., 2014)** . An essential attribute of bacteriocins is the antimicrobial activity against different bacteria, fungi, parasites, viruses, and even against natural resistant structures, such as bacterial biofilms **(Graham *et al*., 2017; Martín-Escolano *el al*., 2019)**.

II.2.1. Bacteriocin Overview

Bacteriocins are antimicrobial peptides with 20-60 amino acids, synthesized by ribosomal machinery, with genes involved in amino acid modification, export, regulation, and self-immunity proteins **(Ben Lagha *et al*., 2017; Noda *el al*., 2018)** .

Environmental factors influence bacteriocin secretion, with bacterial cell density, nutrient availability, acetic acid, and signaling peptides influencing their potency **(Bédard and Biron, 2018)**. Bacteria produce self-immunity proteins to protect against bacteriocins. **(Ben Lagha *et al*., 2017)** Bacteriocins effectively target pathogenic and opportunistic bacteria without discriminating between resistant and sensitive strains **(Cotter *et al*., 2013).** Bacteriocins synergize with antibiotics, reducing concentrations, side effects, and resistant strains **(Cavera *el al*., 2015) .**

II.2.2. Classification of Bacteriocins

umerous bacteriocins have been isolated from LAB and are described in several databases. They have different characteristics, structures, modes of action, biochemical properties, activity spectra, and target cell receptors **(Al Kassaa *et al*., 2019)**. Bacteriocins produced by Gram-positive bacteria have been classified into three groups according to their biochemical and genetic characteristics or the presence of disulfide or monosulfide bonds, molecular weight, thermal stability, proteolytic enzymatic stability, presence or absence of post-translational modification of amino acids, and antimicrobial action (table 03) **(Ahmad *et al*., 2017)** .

Table 03 Classification of bacteriocins **(Juan Carlos Hernández-González *et al*., 2021)**

Class of Bacteriocin	**Subclasses**	**Molecular Properties**	**Reference**
Class I Lantibiotic	Ia Lanthipeptides Ib Globular and inflexible bacteriocins Ic Sactipeptides	Small, heat-stable bacteriocins (<5 kDa), have a post-translational modification, resulting in the formation of atypical amino acids lanthionine and methyllanthionine	**(Ahmad *et al*., 2016) (Guder *et al*.,2000) (Bierbaum *et al*., 1996) (Alvarez-Sieiro *et al*., 2016) (Deegan *et al*., 2005)**
Class II Non-lantibiotic	IIa Pediocin-like IIb Two peptides IIc Leader less IId Non pediocin-like Single-peptide	Small and flexible bacteriocins (<10 kDa), with an amphiphilic helical structure. These peptides do not contain modified amino acid residues and are pH and heat-resistant.	**(Bédard and Biron, 2018) (Fimland *et al*., 2005) (Nissen-Meyer *et al*.,2009) (Oppegård *et al*., 2007) (Sawa *et al*., 2009) (Borrero *et al*., 2010) (Gabrielsen *et al*., 2014) (Iwatani *et al*., 2011)**
Class III	IIIa Bacteriolysins IIIb Nonlytic	High molecular weight bacteriocins (>30 kDa), thermolabile and unmodified peptides.	**(Nilsen *et al*., 2003) (Sun *et al*., 2018)**

Class I bacteriocins are small peptides with heat-stable structures and a modified amino acid sequence. They are divided into three subclasses: Class Ia, Class Ib, and Class Ic **(Alvarez-Sieiro *et al*., 2016)**. **Class II** bacteriocins are small and flexible, with an amphiphilic helical structure, and are pH and heat-resistant. They are divided into four subclasses based on structure and modifications: Class IIa bacteriocins, Class IIb, Class IIc, and Class IId. **Class**

III bacteriocins have high molecular weight and are thermolabile and unmodified peptides with a bacteriolytic or nonlytic mechanism of action. These bacteriocins have been poorly studied **(Sun *et al*., 2018)**.

II.2.3. Mechanism of Action of Bacteriocins

The mechanism of action of bacteriocins depends on their primary structure. Some can exert their activity on the cytoplasmic membrane releasing compounds vital of susceptible bacterial (cell lysis); others can enter the cytoplasm and affect gene expression and protein synthesis (figure 06) **(Cotter *et al*., 2013).**

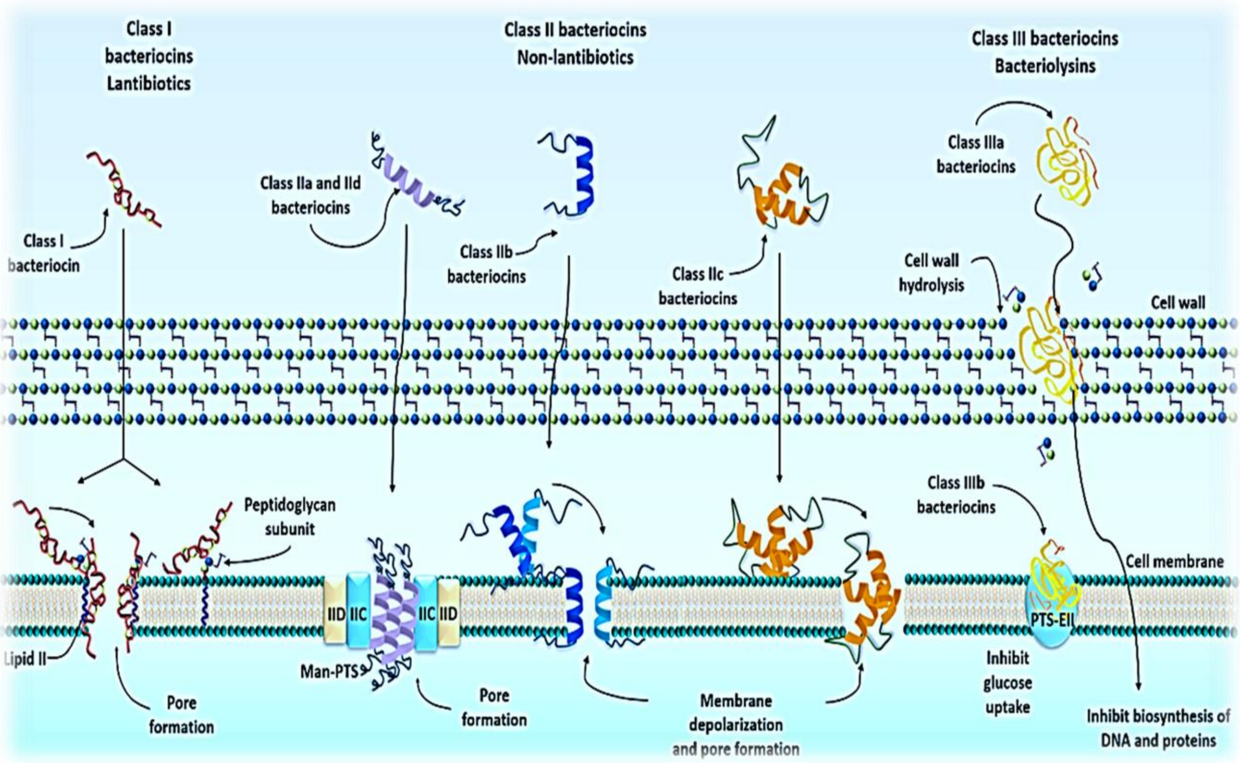

Figure 06: Mode Action of Bacteriocins **(Cotter *et al*., 2013).**

II.3. Lactic acid bacteria in food products

Lactic acid bacteria, also known as lactobacillary bacteria, are a group of bacteria that play an important role in the production of fermented foods such as yogurt, cheese, sauerkraut, kimchi and other similar products, are beneficial microorganisms used in the production of fermented foods. They contribute to the fermentation, preservation and improvement of the sensory and nutritional characteristics of food products.

As a fermentation strain, lactic acid bacteria should have several important metabolism characteristics, such as the ability to produce acid and aroma, the ability to hydrolyze protein, the ability to produce viscous exopolysaccharides and the ability to inhibit bacteria. In this review, the metabolic characteristics of lactic acid bacteria and its application in food industry were reviewed from the aspects of degradation and biosynthesis (table 04) metabolism of lactic acid bacteria. We hope to summarize the new development trends and promote the contribution of lactic acid bacteria related metabolic engineering and food biotechnology to the food industry (**Yaqi *et al*., 2021)**.

Table 04 Substances synthesized in food by lactic acid bacteria (**Yaqi *et al*., 2021)**.

Substance	**Metabolic Engineering works**	**Expanding applications in the food industry**	**Lactic acid bacteria strains (References)**
Lactic acid	Heterologous expression of gene encoding short-chain dehydrogenase for higher yield of D-lactic acid	Use dairy industry waste as a substrate to reduce costs	*Pediococcus acidilactici* **(Qiu *et al*., 2020),** *Lacticaseibacillus rhamnosus* B103 **(Bernardo *et al*., 2016)** *Lacticaseibacillus casei, Lactiplantibacillus pentosus* and *Lactobacillus sp.* **(Shirai *et al*., 2001)** *Enterococcus faecalis* **(Deibel and Niven, 1964)**
	Improve the yield of lactic acid by adding different nutrients such as the	Fermentation strategies and metabolic engineering are often	*Lacticaseibacillus* rhamnosus HN001 **(Wang**

	substrate glucose or vitamin B compounds or adopting pH control strategies	used to improve the yield and purity of lactic acid	***et al*., 2019),** *Pediococcus acidilactici* ZY271 **(Han *et al*., 2019)** *Lactiplantibacillus pentosus* CECT4023T **(Cubas-Cano *et al*., 2019)**
Other organic acids	The organic acid (formic acid, acetic acid, propionic acid, butyric acid, and succinic acid) production of lactic acid bacteria in fish infusion broth 3-Hydroxypropionic acid produced through glycerol metabolism The production of lactic acid, propionic acid was and succinic acid in	Detection of organic acids produced by lactic acid bacteria and improvement of food quality and safety 3-Hydroxypropionic acid is an important platform chemical The production of organic acids in fermented fish silages	*Lactobacillus lactis subsp. Lactis* **(Sezen *et al*., 2016)** *Limosilactobacillus reuteri* **(Kumar *et al*., 2013)** *Levilactobacillus brevis, Lactiplantibacillus plantarum, Pediococcus*
	fermented silages Heterologous expression of mvaES gene of *Enterococcus faecalis*	replaces the need of the addition of chemical additives for acidification Synthesize mevalonate	*acidilactici*, and *Streptococcus spp.* *Enterococcus faecalis* **(Wada *et al*., 2017)**
Bacteriocin	Gasserins has antibacterial activity against *Listeria monocytogenes* or *Bacillus cereus*	Inhibit the growth of *Listeria monocytogenes* in raw minced beef and	Lactiplantibacillus plantarum TN8 **(Trabelsi *et al*., 2019)**, Latilactobacillus sakei

		gilthead sea bream	CTC494 **(Costa *et al*., 2019)**
		Gassericin A can be an important tool for food preservation	*Lactobacillus gasseri* **(Pandey *et al*., 2013)**
	Sakacin P has antibacterial activity against Listeria monocytogenes or Bacillus cereus	Sakacin P exerts its antibacterial effect in fermented sausage	*Latilactobacillus* sakei **(Chen *et al*., 2012)**
Vitamins	Add passion fruit by-product and oligofructose to soy milk can produce folic acid	Synthesize folic acid in dairy products	Streptococcus,Lactobacillus and Lactococcus **(Khalili *et al*., 2020),** Lactococcus lactis NZ9000 **(Wegkamp *et al*., 2007),**
	Insert a 1059-bp DNA fragment into the upstream regulatory region of the rib operon of *Lactiplantibacillus plantarum*	Induce the overexpression of riboflavin biosynthesis	*Lactiplantibacillus plantarum* **(Ge *et al*., 2020)**
	Purine biosynthesis can trigger riboflavin secretion more effectively in Lactococcus lactis		*Lactococcus lactis* JC017 **(Chen *et al*., 2017**)
γ-aminobutyric acid	Mutations in the GadA or *gadR* gene facilitate the conversion of L-	Increase the GABA content in fermented	*Levilactobacillus brevis* **(Lyu *et al*., 2019)** *Levilactobacillus brevis*

	monosodium glutamate (MSG) to GABA	cereals	D17 **(Gong *et al*., 2019)**
	GadC transports L-glutamate into the cell		*Lactococcus lactis* **(Small and Waterman, 1998)**
	Glutamate decarboxylase and pyridoxal-5′-phosphate participate in the decarboxylation reaction of L-glutamate		*Lactococcus lactis* **(Cui *et al*., 2020)**
	The cell immobilization technology increase GABA production		*Levilactobacillus brevis* RK03 **(Hsueh *et al*., 2017)** *Levilactobacillus brevis* **(Shi *et al*., 2017)**
Flavor substances	SHMT gene encodes a serine hydroxymethyltransferase with threonine aldolase activity	Produce flavor substances (2,3-butanedione and 2,3-pentanedione, etc.) in wine, vinegar, bread, sourdough and cheese	*Streptococcus thermophilus* **(Chaves *et al*., 2002; Bancalari et al., 2017)**
	Heterologous expression of thl, hbd, and crt which encode thiolase, β-hydroxybutyryl-CoA dehydrogenase, and crotonase, and the Treponema denticola for higher yield of N-butanol		*Levilactobacillus brevis* **(Li *et al*.,2020)** ,*Lacticaseibacillus casei*, *Lacticaseibacillus rhamnosus* and *Streptococcus thermophilus* **(Bancalari *et al*.,2017)** ,*Streptococcus thermophilus* and *Lacticaseibacillus casei* **(Chammas *et al*., 2006)**
Antioxidant substances	*Lactiplantibacillus plantarum* fermentation	Produce antioxidant substances (active	*actiplantibacillus plantarum* **(Ge *et al*., 2019;**

	significantly enhanced the ability to scavenge free radical's DPPH when the fermenting conditions were optimized by the method of responsive surface design in fermenting sheep bone	phenol metabolites, chlorogenic acid glucoside, sulforaphane) have a variety of beneficial effects on the human body	**Mu *et al*., 2019; Ryu *et al*., 2019)**, *Lacticaseibacillus rhamnosus, Lactobacillus acidophilus* **(Kêska and Stadnik, 2018),** *Leuconostoc mesenteroides (***Nam *et al*., 2017)**
	Metabolize phenolic acid by decarboxylase and reductase	Reduce the damage of phenolic substances to the plasma membrane and cell wall of lactic acid bacteria	*Levilactobacillus brevis, Limosilactobacillus fermentum* and *Lactiplantibacillus plantarum* **(Filannino *et al*., 2018)**
	Hydroxycinnamic acid (*P*-coumaric, ferulic acid and caffeic acid) can be degraded. Hydroxybenzoic acid (gallic acid and protocatechuic acid) can be degraded.		*Lactiplantibacillus plantarum* NC8 **(Barthelmebs *et al*., 2000)**
		Promotion of glutathione synthesis in industry	*Lactiplantibacillus plantarum* CECT 748T **(Rodriguez *et al*., 2008)** *Lactiplantibacillus plantarum* **(Whiting and Coggins, 1971)**
	Convert oxidized glutathione taken from the environment into reduced glutathione	Increase dough rheology; promote the hydrolysis of egg white protein; improve the acid resistance of lactic acid bacteria	*Limosilactobacillus fermentum CECT* 5716 **(Surya *et al*., 2018)** *Streptococcus thermophilus* **(Qiao *et al*., 2018)**

	Mutant strain *Fructilactobacillus sanfranciscensis* DSM20451 *ΔgshR* lacking the glutathione reductase gene	Latilactobacillus sakei and Fructilactobacillus sanfranciscensis **(Loponenet *et al*., 2008)** Fructilactobacillus sanfranciscensis **(Xu *et al*., 2018)** Ligilactobacillus salivarius **(Lee *et al*., 2010)**

II.3.1. Lactic acid bacteria in dairy products

Mainly lactic acid bacteria are found naturally or added in fermented milk, yogurt and cheeses.

1. **Fermented milk**

Fermented milk is a type of dairy product that is produced by the action of lactic acid bacteria on milk. Lactic acid bacteria are a group of bacteria that convert lactose, the sugar present in milk, into lactic acid through the process of fermentation (table 05). This acidification gives fermented milk its characteristic tangy flavor and changes its texture.

Fermented milk products are popular worldwide due to their unique taste, extended shelf life, and potential health benefits. They are a source of beneficial bacteria known as probiotics, which can help maintain a healthy balance of gut microbiota and support digestion. Additionally, fermented milk products are often rich in nutrients like calcium, protein, and vitamins.

Table 05: The main Lactic Acid Bacteria associated with milk and milk product Fermentation **(Teshome Gemechu, 2015)** .

Species/ Subspecies	Their main uses in different milk product	References
Lactococcus ***Lc. Lactic subsp. Lactis***	Mesophilic starter used for many cheese types, butter and butter milk.	**(Broome *et al*., 2003)** **(Wouters *et al*., 2002)**
Lc. lactis subsp. actis biovar diacetylactis	Used in Gouda, Edam, Sour cream and lactic butter and butter milk.	**(Wood, 1997) (Leroy and De Vusyt, 2004)**
Lc. lactis subsp. Cremoris	Mesophilic starter used for many cheese types, butter and butter milk.	**(Weerkam *et al*., 1996)**
Streptococcus ***Sc. Thermophiles***	Thermophilic starter used for yogurt and many cheese types' particularly hard and semi hard high-cook cheeses.	**(Broome *et al*., 2003)** **(Beresford *et al*., 2001)**
Lactobacillus ***Lb. acidophilus***	Probiotic adjunct culture used in cheese and yogurt.	**(Briggiler-Marco *et al*., 2007)**

Lb. delbrueckii subsp. Bulgaricus	Thermophilic starter for yogurt and many cheese types, particularly hard and semi-hard high-cook cheeses.	**(Salaterry *et al*., 2010)**
Lb. delbrueckii subsp. Lactis	Used in fermented milks and high-cook cheese.	**(Broome *et al*., 2003) (Giraffa, 2010)**
Lb. helveticus		**(Broome *et al*., 2003) (Griffith and Tellez., 2013)**
Lb. casei	Thermophilic starter for fermented milks and many cheese types, particularly hard and semi hard high-cook.	**(Briggs, 2003)** **(Kongo, 2013)**
Lb. plantarum	Probiotic milk and cheese ripening adjunct culture. Cheese ripening adjunct culture.	**(Leroy and De Vuyst ., 2004)**
Lb. rhamnosus	Probiotic adjunct culture used in cheese.	**(Coppola *et al*., 2005)**
Leuconostoc		
Ln. mesenteroides subsp. Remoris	Mesophilic culture used for Edam, Gouda, fresh cheese, Lactic butter and sour cream.	**(Weerkam *et al*., 1996) (Slattery *et al*., 2010)**

2. Yogurt

Yogurt is a popular fermented dairy product in Western societies, particularly in the Netherlands and Scandinavian countries. It is a health-promoting, flavored, low-fat, drinkable, and probiotic-based product. The European Codex Alimentarius Commission defines yogurt as the product of milk fermentation by *Streptococcus* thermophilus and *L. bulgaricus*. However, different labeling laws allow for yogurt-like products, where *L. bulgaricus* can be substituted with other Lactobacillus species or yogurt containing probiotic bacteria (**Peláez and Martínez-Cuesta., 2019)** .

Yogurt is a rich source of macro- and micronutrients, including proteins, carbohydrates, minerals, and vitamins. It supports muscle growth and bone health due to calcium and phosphorus content. International agencies recommend incorporating fermented dairy products into daily diets, as they have additional health benefits. Studies show that regular consumption of fermented dairy products reduces bladder cancer and cardiovascular disease risk, and calcium intake positively impacts teeth health(**Peláez and Martínez-Cuesta., 2019)**.

3. Kefir

Kefir is a traditional fermented dairy beverage produced by a complex natural microbiota from kefir grains. These grains are traditionally obtained from periodic coagulation of cow´s milk with calf or sheep abomasum (forth stomach) in goatskin bags. Kefir originated in the Caucasus but gained popularity in Eastern and Central European countries starting in the second half of the 19th century. Kefir can also be made with milk from other sources including as goat, sheep and buffalo milk (Bourrie, Willing et al. 2016). Distinctive microorganisms in kefir are homofermentative lactobacilli (*Lactobacillus kefiranofaciens*), which produces a kefiran complex that surrounds yeasts (*Saccharomyces cerevisiae*), and other bacteria (*Lactococcus*, *Leuconostoc*, thermophilic and mesophilic *lactobacilli* and acetic acid bacteria). Microbiological, technological, as well as nutritional, and health benefits of kefir have been recently summarized **(Kesenkas *et al*., 2017)** .

4. Cheese

Modern cheeses are made from pasteurized milk coagulated by recombinant enzymes or proteases, with *Lactococcus*, Lactobacillus, and *Leuconostoc* as starters. Traditional raw milk cheeses fermented by the microbiota are still produced in some Mediterranean countries. Raw milk contains over 400 bacterial species, with a decrease in core but persistence on surface. Cheese flavor develops through microbial metabolism during clotting and ripening (**Peláez and Martínez-Cuesta., 2019)**.

5. Traditional Algerian dairy products

Traditionally, cow's milk was considered as a staple in many diets. It is a healthy drink since consumption is associated with quality of food. It provides a matrix easily accessible and rich in a variety of essential nutrients: minerals, vitamins and easy to digest proteins. Therefore, it is essential for all functions of the body. Traditional Algerian dairy products, which have the commercial significance, include *Lben, Klila, Jben, Rayeb, Dhan, Zebda, Bouhezza*, *Takammarit*, etc. Figure 07 represents the main traditional Algerian preparations of these products **(Guetouache *et al*., 2020)** .

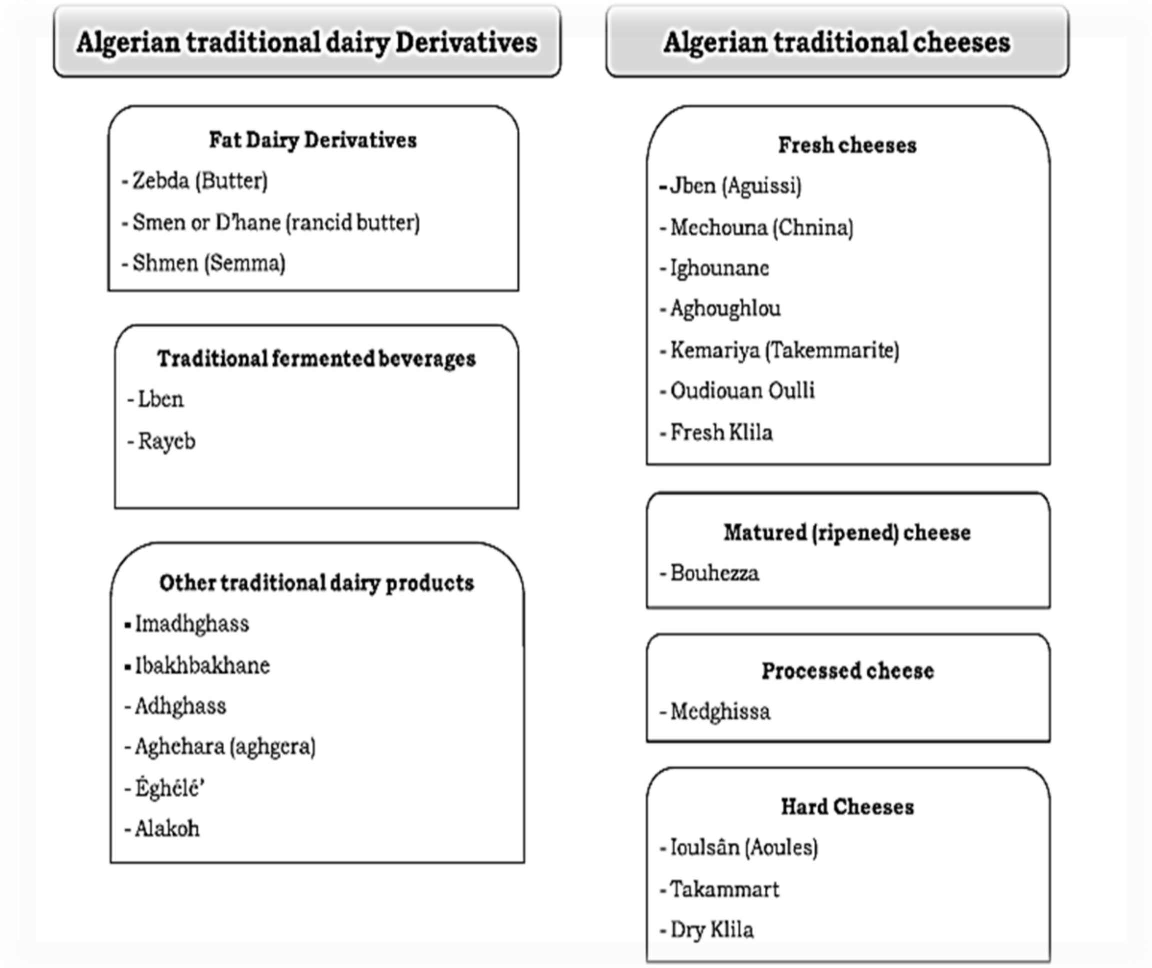

Figure 07: Algerian traditional dairy products **(Choubaila *et al*., 2019)**

In recent years, traditionally fermented dairy products have been considerably developed thanks to the consumers' interest in organoleptic, nutritional, therapeutic, and even hygienic qualities.

These fermented products result from fermentation by the dominant lactic acid bacteria *(Lactobacillus, Lactococcus,Leuconostoc*), accompanied by a slight fermentation in the presence of yeast (*Saccharomyces*), thanks to its rich and diverse composition .

Algeria produces traditional cheese, primarily Jben and Klila, using a family-scale manufacturing method. These cheeses have gained popularity in steppe areas due to their pleasant organoleptic and nutritional properties. The microflora plays a crucial role in sensory characteristics, and removal can reduce taste and aromas. Some cheeses also have inhibitory effects against pathogenic microorganisms **(Guetouache *et al*., 2020)** .

II.3.2. Lactic acid bacteria in meats

In fermented and cured meats, lactic acid bacteria are intentionally introduced during the processing. These bacteria contribute to the development of the characteristic flavors and textures of the final product. They lower the pH of the meat, creating an acidic environment that inhibits the growth of spoilage and pathogenic bacteria. The lactic acid produced by LAB also helps enhance the preservation of the meat by reducing its water activity **.**

Meat products harbor a diverse LAB microbiota, in which lactobacilli (*Latilactobacillus sakei*, *L. curvatus*, and *L. plantarum*) usually predominate **(Pisacane *et al*., 2015)** and play an important role in maturation. In certain cases, considerable populations of leuconostocs (*Ln. mesenteroides*, *Leuconostoc carnosum*) and enterococci (*E. casseliflavus*) are also present **(Maksimovic *et al*., 2018)** .Meat fermentation is a complex process, from the point of view of its microbial ecology, in which both LAB and coagulase negative staphylococci intervene, participating in the development of the typical sensorial properties of the product and in its biopreservation **(Carla *et al*., 2021) .**

LAB can either be used as meat starter cultures and/or as probiotics, interacting with native microorganisms in the product, or they can be part of the non-starter microbiota in fermented products. In both cases, their presence can have potential advantages for the end-products **(Todorov *et al*., 2017)**. The metabolic pathways of LAB on proteins in fermented meat products and the flavor substances produced are depicted in (figure 08). Fermentation allows to preserve meat products and to create a variety of fermented meats with different organoleptic characteristics, as a result of the microbial and endogenous enzymatic reactions taking place within their primary component – the animal muscle. The use of starter cultures, including probiotic microorganisms with health-promoting potential, such as the ability to reduce cholesterol content, contributes to promote product stability and safety, as well as consumer acceptance (**Carla *et al*., 2021)** .

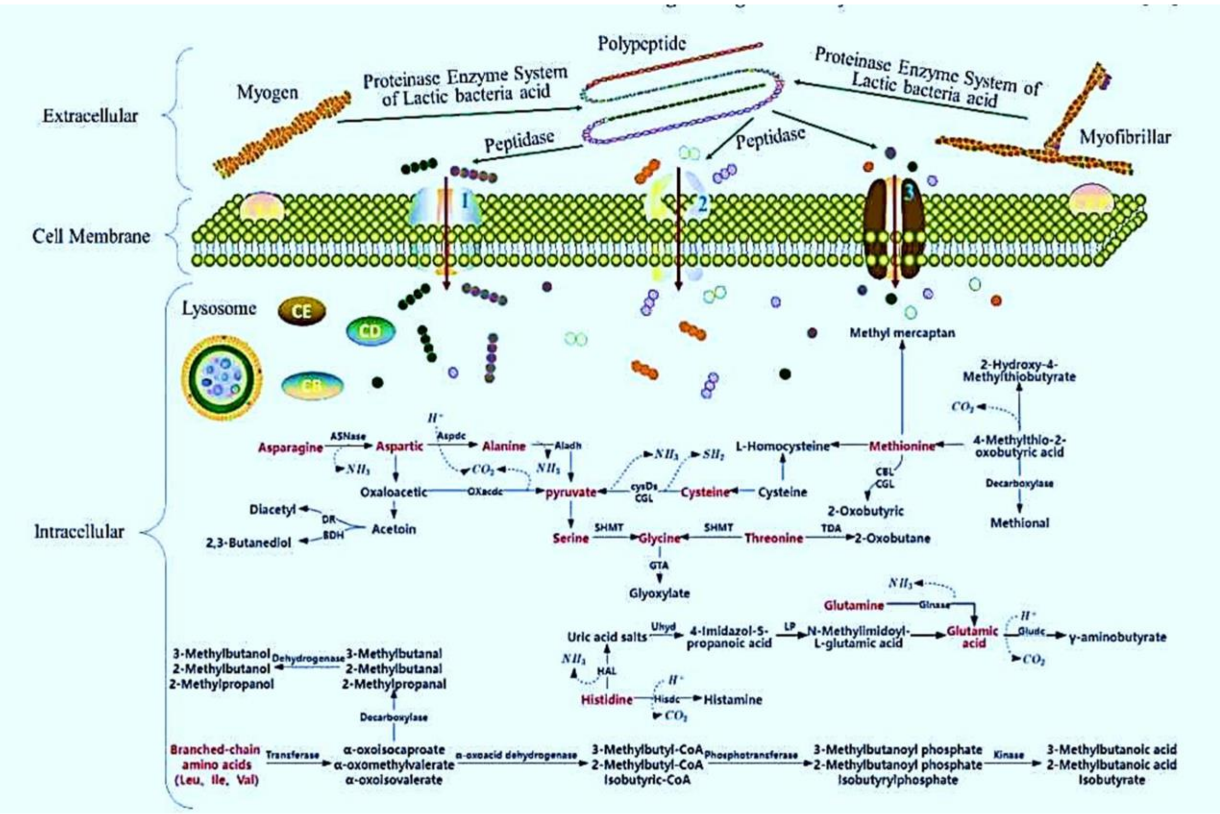

Figure 08: Metabolism of fermented meat products through lactic acid bacteria and the flavor of the substances produced**(Savijoki et al., 2006) .**

Several criteria should be considered to select LAB for the production of fermented meats. The ability to acidify and grow at low pH values are desirable factors for potential starter cultures for the meat industry and for spoilage-prevention, because they lead to increased safety and prolonged shelf life of the final products by inhibiting the growth of pathogenic and deterioration microorganisms, facilitating maturation, ensuring microbial stability during storage, stabilizing the product color, and improving its texture. Another desirable trait is proteolytic activity, which plays an important role in flavor developmentnduring the fermentation process, as is the case in raw sausage fermentation. During meat fermentation, LAB can positively influence protein degradation. The resulting peptides can be further converted into volatile compounds **(Carla *et al*., 2021).**

Proteolytic activity, acidification, and the ability to produce low final pH values were observed in LAB (figure 09) **(Todorov *et al*., 2017).**

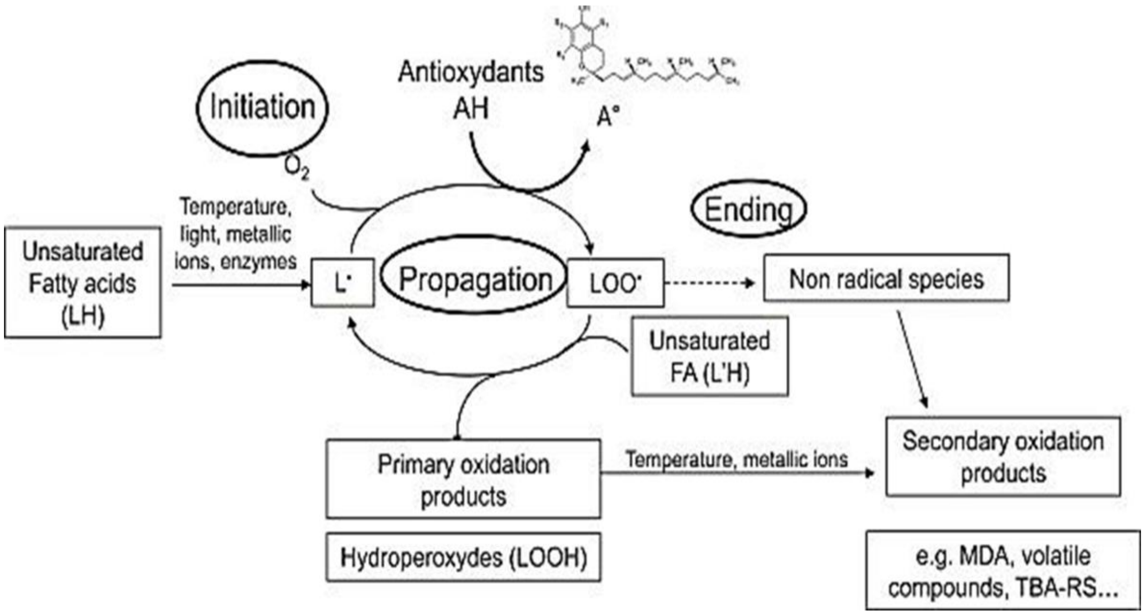

Figure 09: Mechanism of Proteinand lipid Oxidation in Fermented Meats **(Claire *et al*., 2016) .**

II.3.3. Lactic acid bacteria in vegetables

The diversity of LAB species present in the different fermented vegetables that can be found on the market is wide, and responds to the different compositions presented by raw material, the environment and the physicochemical conditions prevailing during the fermentation process **(Bautista-Gallegoa *et al* ., 2020)** .

In the specific case of table olives, the most representative genus, as mentioned above, is *Lactobacillus,* with *L. pentosus* and *L. plantarum* as the predominant species **(Benítez-Cabello *et al*., 2019; Botta and Cocolin, 2012)**, which show a great intra-specific diversity with the presence of different biotypes, depending on variety, type of processing, and geographical area. Other microorganisms identified during the fermentation process belong to the genera *Enterococcus, Pediococcus, Leuconostoc,* and *Lactococcus,* but always in a smaller proportion. Kimchi is also a fermented vegetable made with cabbages, radish, and various vegetables, and has great production and tradition in South Korea. As in the case of olives, there is also a great diversity of lactic bacteria, especially the genera *Weissella*, *Leuconostoc,* and *Pediococcus*. Furthermore, several species of *Lactobacillus* and

Leuconostoc have been identified in the fermentation of sauerkraut (cabbage). Finally, *P. ethanolidurans, E. thailandicus*, and different species of the genus *Lactobacillus* and *Leuconostoc* have been described as the most abundant species during the production of pickled cucumbers. **(Bautista-Gallegoa *et al*., 2020)** .

As a summary, (table 06) shows the main LAB species identified in diverse types of fermented vegetables.

Table 06: Summary of LAB species identified in the main types of fermented vegetables **(Bautista-Gallegoa *et al*., 2020)** .

Vegetable Matrix	Specie	Reference
Table olives	*L. pentosus, L. plantarum, L. paraplantarum, L. parafarraginis, L. sanfranciscensis, Pediococcus sp., Lc. Mesenteroides*	**(Abriouel *et al*., 2012) (Hurtado *et al*., 2012) (Bautista-Gallego *et al*., 2013) (Benítez-Cabello *et al*., 2016, 2019)**
Kimchi	*L. curvatus, L. sakei, Lc. mesenteroides, Lc. gelidum, Lc. carnosum, Lc. gasicomitatum, P. pentosaceus, W. soli, W. cibaria, W. koreensis, W. cibaria*	**(Jung *et al*., 2013) (Jang *et al*., 2014) (Hong *et al*., 2015) (Ji, Jang and Kim, 2015) (Kyung *et al*., 2015) (Kim *et al*., 2017)**
Sauerkraut	*L. plantarum, L. pentosus, Lc. mesenteroides, L. brevis, L.sakei, L. curvatus, L. paraplantarum, L. coryniformis, P. pentosaceus, Lc. citreum, Lc. argentinum, Weissella sp.*	**(Johanningsmeier *et al*., 2007) (Plengvidhya *et al*., 2007) (Yan *et al*., 2015)**
Cucumbers	*L. pentosus, L. plantarum, L. brevis, L. paracasei; Weissella spp., P. ethanolidurans, Leuconostoc spp., Lactococcus spp*	**(Breidt *et al*., 2013) (Medina *et al*., 2016) (Pérez-Díaz *et al*., 2016)**
Other fermented Vegetables	*Enterococcus thailandicus E. casseliflavus, Lc. lactis, Lc. mesenteroides, W. hellenica. L. pentosus, L. plantarum, L. paraplantarum, L. brevis, L. citrtreum, L. alimentarius, L. paracasei, L. buchneri, P. ethanolidurans*	**(Breidt *et al*., 2013) (Tamminen *et al*., 2004)**

Lactic acid bacteria are known for their therapeutic properties for a variety of diseases, and this is due to their unique ability to ferment foods that are beneficial to human health and use them to apply treatments that have been discovered for several years. We will also see their terrible effectiveness in preventing diseases by these bacteria through the foods they contain. Hence, we will learn more about the benefits of these beneficial bacteria in treatment and prevention in this chapter.

III.1. Therapeutic application of probiotic lactic acid bacteria

In this part, we will explain the advantages of probiotics, including the antimicrobial role .

III.1.1. Antimicrobial activity

It has been well documented that probiotic LAB shows very good anti-bacterial, anti-fungal, and anti-viral properties by producing numerous anti-microbial compounds which include lactic acid, acetic acid, propionic acid, alcohol, and diacetyl (table 07) .These antimicrobial compounds produced by the LAB, interacts with the cell membranes of the harmful pathogens and inhibits their growth by intracellular acidification (lowering the pH) and denaturing the proteins of the membrane which leads to the dysfunction of the membrane permeability. In addition to these antimicrobial compounds, LAB also produces “Bacteriocins” which are ribosomally synthesized proteinaceous toxins which inhibit the growth of similar or closely related bacteria by making pores in the membrane of the pathogenic bacteria (table 07) and thus, disrupting the permeability of the membrane **(Rahul *et al*., 2018)** .

Table 07: Antimicrobial Substances produced by Lactic Acid Bacteria

(Rahul *et al.*, 2018) .

Antimicrobial compounds/metabolites	**Mechanism and target microorganisms**
Lactic acid, Acetic acid, Propionic acid, Reuterin, Diacetyl, Fatty acid	It inhibits a wide range of both gram-positive and gram-negative bacteria, clostridia, molds, some fungi as well as yeast by interacting with the membrane, denaturing membrane protein, causing intracellular acidification, and disrupting membrane integrity.
Hydrogen peroxide	It inhibits Pathogens and spoilage organism especially in protein-rich food by peroxidation of membrane lipid and thus causes membrane dysfunction
Antimicrobial Enzymes	**Mechanism and Target Microorganisms**
Lactoperoxidase system	It is a peroxidase enzyme which shows strong antimicrobial properties against pathogens and spoilage-causing bacteria (milk and dairy products) by the addition of hydrogen peroxide and thiocyanate.
Bacteriocins	**Mechanism and Target Microorganisms**
Class I bacteriocins (Lantibiotics)	Ribosomally synthesized bacteriocins that consist of one or two peptides which include nisin and other lantibiotics that go through
	post-translational modification to have lanthionine, β-methyllanthionine, dehydrated amino acid and some of them also have D-alanine. They are small peptides (<5kDa) which are further alienated into two subgroups: **Group Ia:** small cationic peptide which is flexible, amphipathic in nature, and having a screw-shaped structure that makes pores in the membrane by unspecific interaction and thus disrupting membrane permeability. **Group Ib:** globular shape peptides which are usually neutral or anionic in nature.
Class II bacteriocins (Non- lantibiotics)	Ribosomally synthesized low molecular weight peptide (<10kDa) which does not have any modified amino acid. They are heat stable and are generally produced as an inactive form. They become active when its N-terminal leader peptide is post-translationally cleaved. They are further sub-classified into different sub-groups: **Group IIa**: It consists of single peptide with strong anti-listerial activity and have consensus sequence YGNGGVXC near N-termini. It shows a broad range of anti-bacterial activity. **Group IIb**: This class of bacteriocins is called two-peptide bacteriocin because it requires two different peptides for anti-bacterial activity.

	Group IIc: These are circular bacteriocins that have a broad range of effects on target bacterial cells such as disruption of membrane permeability and cell wall formation.
Class III bacteriocins (Non-lantibiotics)	This class of bacteriocins are large, heat labile, antibiotic in nature-proteins and are least characterized with a molecular mass greater than 30kDa.
Class IV bacteriocins	This class of bacteriocins is complexed with lipids or carbohydrates moieties which is essential for their antimicrobial activity and are comparatively hydrophobic in nature and heat stable.

- These bacteria can produce antimicrobial metabolites such as bacteriocins, reutericyclin, reuterin, hydrogen peroxide, carbon dioxide, acetoin, diacetyl, ethanol, acetaldehyde, and organic acids : acetic and lactic acid (figure 10).

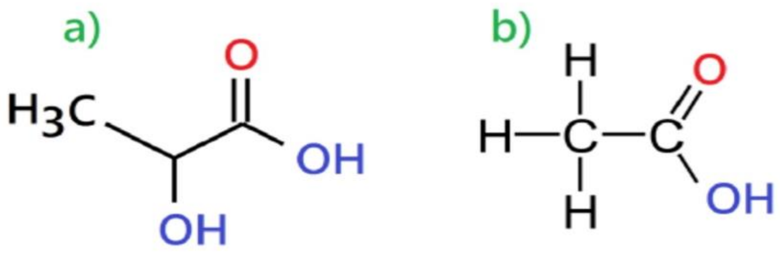

Figure 10 : Lactic acid (a) and acetic acid (b) as the main antimicrobial organic acids produced by LAB **(Mehran *et al*., 2022)** .

1. Lactic Acid Bacteria as Mucosal Immunity Enhancers and Antivirals through Oral Delivery

The mechanism of DC activation and the following immunological responses are strongly influenced by LAB strains. DCs, macrophages, and CD4+FoxP3+ cells' development and functionality are affected by lactobacillus. Tregs as well as CD4+CD8+ and CD4+FoxP3+ T cell differentiation in Peyer's patches (PPs). Specialized DCs from the mucosa of mesenteric lymph nodes, also known as membrane-associated lymphoid tissues (MALTs), carry out the counterattack of pathogens. The intestine's mucous epithelium is covered by this lymphoid tissue. MALTs resemble peripheral lymph nodes and are loaded with M and B cells that can engulf encroaching infections. Additionally, LAB can trigger a biological response by causing DCs to differentiate, which results in the production of cytokines that can encourage the differentiation of naive T cells into Tregs, a specialized T subset with particular regulatory mechanisms that (figure 11) **(Assad *et al.*, 2022) .**

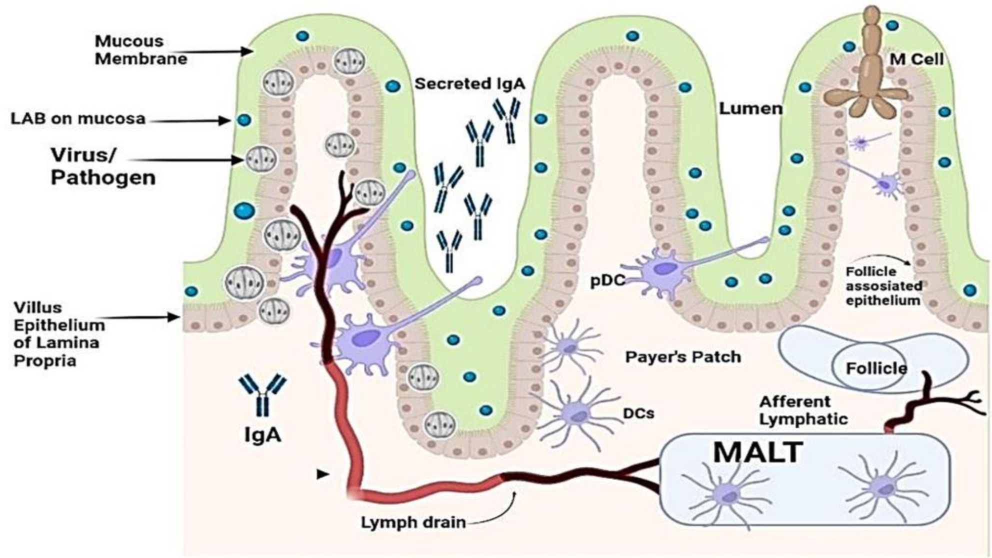

Figure 11 : Effect of orally administered LAB on activation of gut-induced mucosal immunityEffect of orally administered LAB on activation of gut-induced mucosal immunity **(Assad *et al.*, 2022)** .

2. LAB as Antivirals

The four primary processes that follow the mode of action of the antiviral properties of LAB are internal viral particle uptake into lymphoid tissue, production of an antiviral substance, suppression of viral absorption, and immunomodulation in the mucosa . The process by which LAB fights viruses is complex and irreversible . LAB may initially link to the viruses and conceal the binding sites of the virus surface and fusion proteins in order to prevent viruses from infecting the host cells . Second, LAB can lyse the virions and harm the viral envelope. L. crispatus not only affects the human immunodeficiency virus (HIV) but also HSV in a remarkable inhibitory manner. When L. delbrueckii subsp. bulgaricus OLL1073R-1 is found in fermented yogurt (figure 12) **(Assad *et al.*, 2022)** .

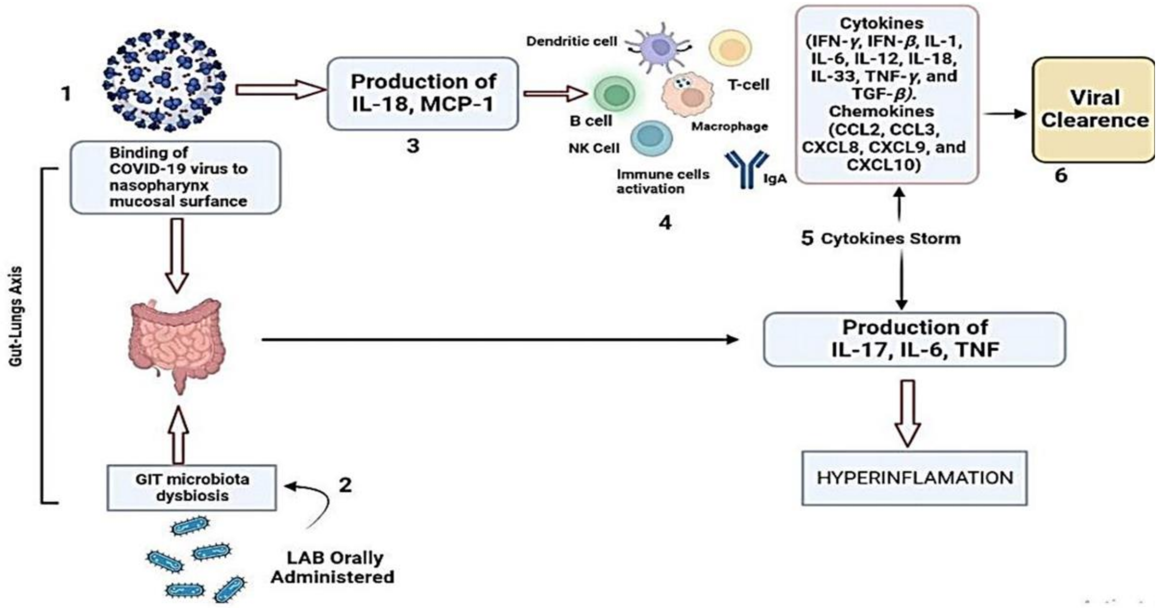

Figure 12 : Antiviral effects of LAB against SARS-CoV-2 **(Assad *et al.*, 2022)** .

3. Bacterioncin-Producing LAB and their role in diseases

Alteration in the normal microbiota of gut causes several chronic diseases, like joint pain, immune-related diseases, metabolic disorders, liver diseases, and various GI diseases . Bacteriocins may play a role in shaping the host microbiota and indirectly play an important role in correcting dysbiosis and the improvement of host health. Here, we have discussed a few important diseases that occur during the dysbiosis of the gut and their possible cure using bacteriocinproducing probiotic lactic acid bacteria. For clarity, a diagrammatic presentation of the same is depicted in (figure 13) **(Anjana and Santosh., 2022)** .

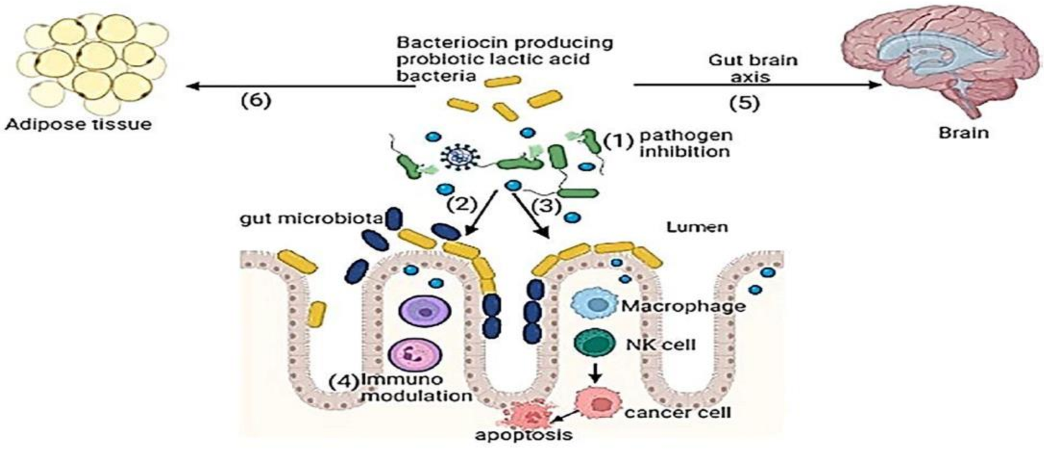

Figure 13 : Bacteriocin-producing probiotic lactic acid bacteria showing several potential functions: (1) inhibition of pathogens, (2) colonization of probiotic bacteria by competitive exclusion, (3) activation of macrophages, natural killer (NK) cells further interact with cancer cells causing apoptosis, (4) immunomodulation, (5) gut–brain axis balancing the gut microbiota, (6) antiobesity activity by reducing the adipose tissue **(Anjana and Santosh., 2022)**

III.2. treatment of intestinal inflammation

This review shows the potential uses of riboflavin and folates producing LAB for the biofortification of food, as therapeutics against intestinal pathologies and to complement antiinflammatory/anti-neoplastic treatments and will discuss the use of LAB as a natural alternative to increase riboflavin and folate concentrations in foods and provide an overview of the recent applications of LAB as a source of vitamins with anti-inflammatory/antioxidant activities against gastrointestinal tract inflammation.

In addition to their intrinsic properties, certain strains of LAB have the capability of producing/releasing and/or increasing specific beneficial compounds in foods. While LAB are usually auxotrophic for several vitamins, it has been reported that certain strains have the ability to synthesize B group vitamins : riboflavin, folates, thiamine and cobalamin **(R Levit *et al.*, 2020)** .

III 2.1. Nutritional effect

1. **Riboflavin-producing LAB**

Riboflavin (vitamin B2) is the precursor of flavin mononucleotide and flavin adenine dinucleotide, two coenzymes that play a central role in metabolism by acting as hydrogen carriers in biological redox reactions . Riboflavin is a key nutrient for all aerobic forms of life, and is essential for normal cellular functions and growth. Although riboflavin is found in a variety of foods, suboptimal intakes can lead to ariboflavinosis. Riboflavin deficiency is associated with eye-related problems, cardiac risk, preeclampsia, anaemia, liver and skin damage and changes in cerebral glucose metabolism **(Levit *et al.*, 2018)** . a Some LAB strains are able to synthesize riboflavin and their use during fermentation improves the nutritional value of foods (table 08).

Furthermore, riboflavin concentrations can sometimes vary in certain products due to processing technologies and the action of the micro-organisms utilized during food processing. In this regard, it was shown that the addition of supplements, such as dietary fibres from fruit sources can increase riboflavin production **(Albuquerque *et al.*, 2020)** .

Riboflavin-producing LAB have been isolated from different ecological niches and showed the ability to increase the concentrations of this vitamin in food matrices such as milk, soymilk, whey and pseudocereals **(Rollan *et al.*, 2019)** .

Table 08 : Examples of LAB strains with ability of increasing the riboflavin concentration in different food matrices **(R. Levit1 *et al.*, 2020)** .

Strain	Matrice	Vitamine concentration
Lactobacillus acidophilus ATCC 314	Soymilk	657 036 mg l1
Lact. Acidophilus FTDC 8833	Soymilk	243 005 mg l1
Lact. Acidophilus FTDC 8633	Soymilk	113 002 mg l1
Lactobacillus plantarum CRL 725	Soymilk	70000 2000 ng ml1
Lact. Plantarum CRL 725 (G)	Soymilk	186000 2000 ng ml1
Lact. Fermentum KTLF1	Milk	150 mg l1
Lact. muocaseKTLF5	Whey	083 mg l1
Lact. Plantarum M5MA1-B2	Maize Kefir like	050 mg l1
Lact. Plantarum M5MA1-B2	Oat Kefir like	150 mg l1
Lact. plantarum UNIFGPL104 and UNIFGPL209	Bread	681 lgg1
Lact.Plantarum UNIFGPL104 and UNIFGPL209	Pasta	401 lgg1

- Riboflavin is synthesized in seven enzymatic stagesfrom guanosine triphosphate (GTP) and D-ribulose-5-phosphate precursors (figure 14) **,** andthe synthesis is strain dependent

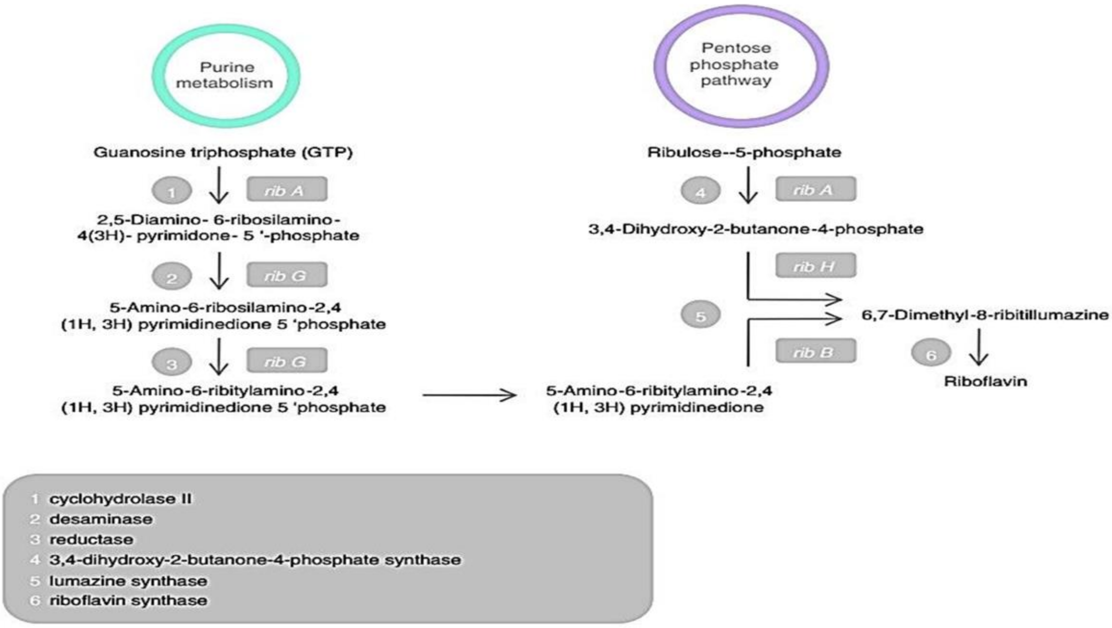

Figure 14. Riboflavin biosynthesis pathway in lactic acid bacteria **(R. Levit *et al.*, 2020)** .

2. Folate-producing LAB

The use of natural folic acid represents an alternative to synthetic folic acid to avoid adverse effects associated with its consumption and in this respect some LAB species are able to accumulate folate see biosynthetic pathway in (figure 15) in various substrates after the fermentation process (table 09) .

Table 09 : Examples of LAB strains with ability of increasing the folate concentration in different food matrices **(R. Levit *et al.*, 2020)** .

Strains	Matrices	Vitamin concentration
Streptococcus thermophilus CSCC2000	Skim milk	4000–5000 ng g1
Strep. thermophilus CRL 803Skim milk	Nonfat milk	6000–8000 µgl1
Strep. thermophilus 908	Nonfat milk	7661 329 ng ml1
Strep. thermophilus ABM5097	Oat flour	2000–2900 ng g1
Strep. gallolyticus subsp. macedonicus CRL 415	Nonfat milk	6000–8000 µgl1
Lact. delbrueckii subsp. bulgaricus CRL 863	Nonfat milk	6000–8000 µgl1
Strep. thermophilus CRL 803, Lact. delbrueckii subsp. bulgaricus CRL 871, and Strep. gallolyticus subsp. macedonicus CRL 415	Yogurt	18000 1000 µgl1
Strep. thermophilus CRL 803, Lact. delbrueckii subsp. bulgaricus CRL 871, Lact. amylovorus CRL 887, and Strep. gallolyticus subsp. macedonicus CRL 415	Yogurt	26300 240 µgl1
Strep. thermophilus TH-4 and Lact. rhamnosus LGG	Soy milk with passion fruit and fructooligosaccharides	192700 4900 ng ml1
Lact. plantarum P2R3FA	Wheat-based fermented Bread	4310 320 µgl1
Lact. plantarum CRL2106 and Lact. plantarum CRL 2107	Amaranth sourdough	13800 750 ng ml1
Lact. plantarum CRL 2107 and Lact. plantarum CRL 1964	Quinoa sourdough	160 020 µgg1
Lact. sakei CRL 2210	Tuber puree with amaranth and chia flour	190 µgg1
Lact. sakei CRL 2209 and Lact. sakei CRL 2210	Andean tuber purees	73000-148400 ng g1
L. lactis subsp. lactis FP368	Goat milk	31300 8100 µgl1

L. Lactis subsp. Cremoris	Cucumber juice	6000 190 ng ml1
L. lactis subsp. Cremoris	Watermelon juice	2600 160 ng ml1

However, the ability of microorganisms to produce folate is strain-specific and affected by growth conditions .The production of folate could also be affected by the coexistence of the starter cultures, the presence of prebiotics, and the external pH of R. Growth medium food , incubation temperature, and presence of chemical precursors GTP and 4-aminobenzoate, which is a product of the shikimate biosynthesis pathway : Savoy de Giori and LeBlanc 20. Use of folate for its growth. However, Lact. bulgaricus CRL 871 was able to synthesize intra- and extracellular folic acid. This strain inoculated with Strep. In vitamin content fermentation of oats and soybeans using LAB to improve folate content was also successful .

Lact. rhamnosus LGG and Strep. Thermophilus TH-4, used as a starter to produce fermented soy milk, was able to produce folate. Also, the addition of a passion fruit byproduct and oligosaccharides stimulated folate production by these strains during the fermentation process **(R. Levit1 *et al*.,2020).**

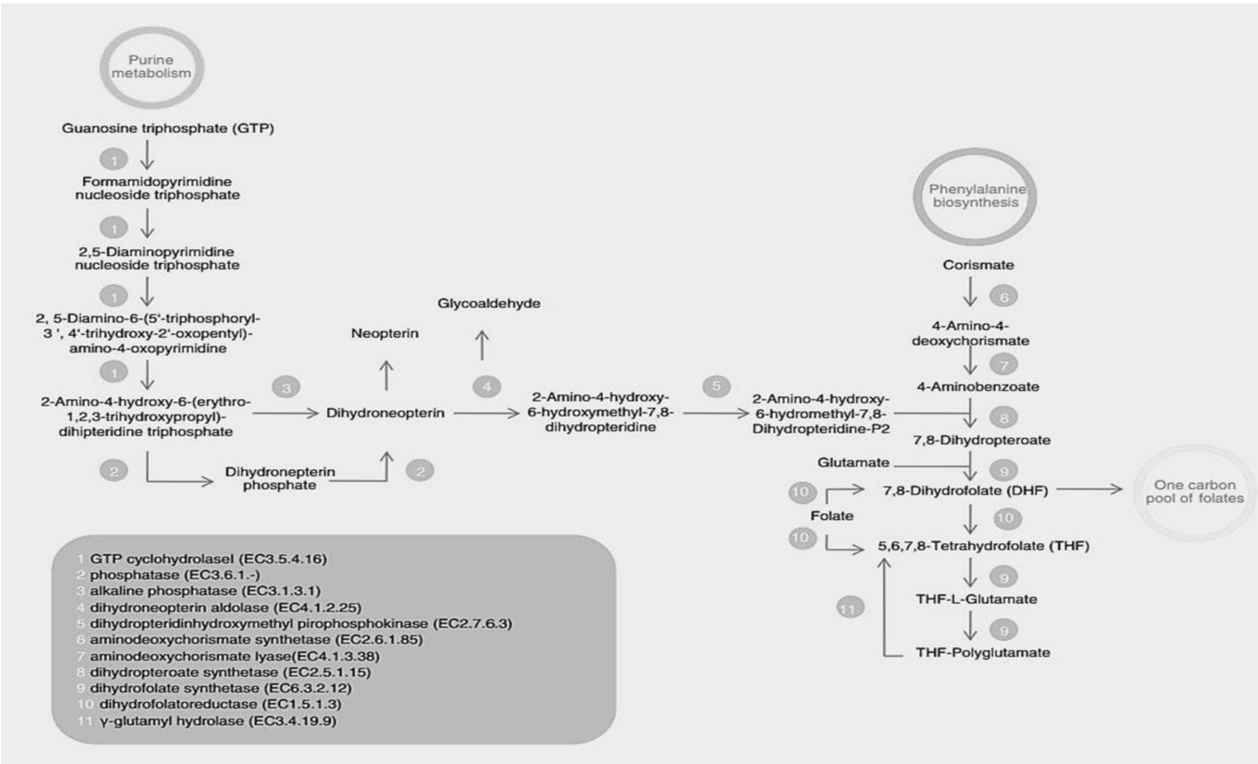

Figure 15 : Folate biosynthesis pathway in lactic acid bacteria **(R. Levit *et al*., 2020)** .

III.2.2. Preventive effect

All of these studies show that the use of vitamin-producing LAB could be a possible technique to reduce inflammation in patients with intestinal pathologies and to give patients vital nutrients that are typically depleted during intestinal pathologies. The utilization of LAB that produce riboflavin or folates for food biofortification was outlined in this review as a natural and more cost-effective alternative to fortification via chemical synthesis. The food business would benefit from this.

can develop meals that contain these bioactive chemicals in high amounts by choosing the right microorganisms and cultural factors. Considering the fact that people want food that provide certain health benefits in addition to providing nutrition advantages, this study gave a summary of recent studies that shown how vitamin-producing LAB can inhibit inflammatory processes in the GIT and supplements to anti-inflammatory ,These studies have shown that LABs that produce vitamins the ability to enhance the outcomes or lessen the traditional treatments' unfavorable side effects as well as provide as a source of vitamins **(R Levit *et al.*, 2020)** .

III.2.3.Therapeutic effect

1. **Vitamin production by LAB to counteract intestinal inflammation**

LAB have shown that can counteract inflammatory processes in the GIT through different mechanisms, this was demonstrated using animal models of IBD and intestinal mucositis (IM), and in clinical trials, being the intestinal microbiota and host's immune response modulation the most evaluated **(Yokota *et al.*, 2018; Choi *et al.*, 2019) .** LAB can also produce different vitamins, and some Vitamins' supplementation have proven to be effective against intestinal inflammation; so vitamin production has also been associated with the anti-inflammatory properties of certain LAB, in addition to the nutrition value of these strains, against intestinal pathologies (table 10) .

Table 10 : Examples of beneficial effects of folate and riboflavin-producing LAB strains **(R. Levit *et al*.,2020) .**

Strains/ product	Vitamin produced	Beneficial effect	Host/model
Lactobacillus plantarum CRL 2130	Riboflavin	Normalization of the intestinal morphology (villus size).	Riboflavin-depleted Mice
Lact. plantarum CRL 2130/fermented soy milk	Riboflavin	Reduction of IBD features (weight loss, intestinal inflammation, microbial translocation to liver and cytokines in intestinal fluids).	2,4,6-trinitrobenzene sulphonic acid (TNBS)- induced mice
Lact. plantarum CRL 2130, Lact.paracasei CRL 76, Lact. bulgaricus CRL 871 or Strep. thermophilus CRL 803	Riboflavin	Reduction of IBD features (intestinal inflammation, microbial translocation to liver, inducible nitric oxide synthase (iNOSs) enzyme producing cells, proinflammatory cytokines in intestinal fluids) .	TNBS-induced mice
Lact. plantarum CRL 2130	Riboflavin	Reduction of intestinal mucositis (IM) features (diarrhoea, alterations in the architecture of the small intestine, pro-inflammatory cytokines in serum and in intestinal fluids).	5-Fluorouracil (5-FU)induced mice
Lact. reuteri ATCC PTA 6475	Folates	Reduction of IBD features (macroscopic intestinal inflammation, weight loss, serum amyloid protein A) .	TNBS-induced mice
Strep. thermophilus CRL 808	Folates	Reduction of IM features (diarrhoea, alterations in the architecture of the small intestine, proinflammatory cytokines in serum) .	5-FU-induced mice
Strep. thermophilus 34v and Lact.plantarum16cv/fermented milk	Folates	Improvement of haematological parameters and villi height/crypt depth ratio in the small intestine .	Folate-depleted mice
Lact. plantarum CRL 2130, Strep. thermophilus CRL 808 and Strep. thermophilus CRL 807	Riboflavin –folates	Reduction of chronic IBD features (intestinal inflammation, and pro-inflammatory cytokines in intestinal fluids) and prevention of side effects of chronic anti-inflammatory therapy.	TNBS-induced mice
Lact. plantarum CRL 2107 and Lact. plantarum CRL 1964/fermented pasta	Riboflavin –folates	Normalization of the intestinal morphology (number and length of villi).	Folates and riboflavin-depleted mice

III.3. Role and mechanism of lactic acid bacteria in treating obesity

The composition, diversity, and functionality of the gut microbiota are substantially discordant between healthy and obese subjects in some studies. Indeed, obesity is a kind of low-degree inflammation reaction so it is associated with reduced intestinal barrier permeability . LABs are confirmed to regulate the composition abundance and structure of gut microbiota and improve inflammation and oxidation to achieve antiobesity effect. Substantial empirical evidence and published literature have shown that LAB supplements have had weight modifications effects both in animals and humans in the past 5 years **(Yi-Lin *et al.*, 2021)** .

III.3.1. Efects of LAB intervention gut microbiota resulta result in weight losson

As mentioned above, research has introduced the fact that LAB can alleviate obesity through effective approaches to improve gut microbial diversity, the F/ B abundance ratio, intestinal permeability, and barrier function as well as the anti-inflammatory and immune response. The effect of LAB on weight loss and lipid reduction may be mainly achieved by the following two mechanisms. One is that LAB can regulate the structure and diversity of intestinal microbiota, and the other is that various metabolites of LAB can participate in the host’s metabolic regulation and have apositiveinfluence. Firstly, phylum-level compositional patterns alteration is associated with obesity. What scientists found was an increased F/B ratio in obese versus lean samples . Also, LAB that can alleviate obesity generally reduces the F/B ratio and raise the diversity of gut microbiota **(kH Seo *et al.*, 2020)** . L. plantarum LC27 were reported to alleviate obesity in mice with the effect of reducing Firmicutes and Proteobacteria abundance in gut microbiota and lipopolysaccharide (LPS) production **(In Kim *et al.*, 2019)** . The diversity of gut microbiota was increased in the experimental group intervened by L. plantarum LMT1-48, which might help to ameliorate obesity in high-fat diet (HFD)-induced mice **(Yi-Lin *et al.*, 2021) .**

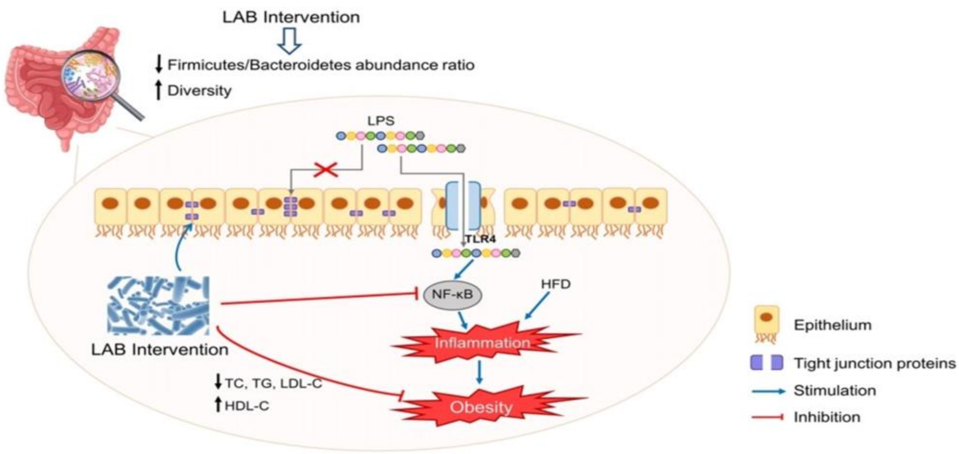

Figure 16: The possible mechanism of modulation in gut microbiota via LAB intervention to prevent obesity **(Yi-Lin *et al*., 2021)** .

We showed the pathogenic mechanism of HFD and LPS, as well as the effect of LAB to improve obesity through the intestinal tract in (figure 16). LPS is a component of the cytoblast of Gram-negative bacteria, which is composed of lipids and polysaccharides. The physiological effect of LPS is reflected by toll-like receptors on the cell membrane surface of host cells, particularly in immune cells and adipose tissue. HFD inhibits the expression of tight junction proteins zonulin and occludin so as to increase intestinal permeability of LPS, a pathogenic agent of endotoxin **(Sivamaruthi *et al.*, 2019)** . The anti-inflammatory LC27 can attenuate HFD-induced obesity, hepatic steatosis, and colitis by suppressing the gut microbiota of LPS-activated nuclear factor-κB (NF-κB) and inactivation that induce the expression of tight junction proteins in the colon **(In Kim *et al*., 2019)**.

III.3.2. Efects of metabolites of LAB on antiobesity

Studies that went deeper into the mechanism discovered that different metabolites of LAB can control the host's metabolism by blocking lipogenesis, speeding up lipolysis, and lowering appetite by way of the central nervous system. In addition, the production of organic acids like lactic acid can significantly lower the ecosystem's pH and REDOX potential Eh value, putting the intestine in an acidic state where it has a great inhibitory effect on pathogenic bacteria that can lead to disorders **(Sirichokchatchawan *et al.*, 2018)** . The impact and potential processes of the LAB's metabolites on obesity and various metabolic disorders will next be strongly addressed (figure 17) **(Yi-Lin *et al.*, 2021)** .

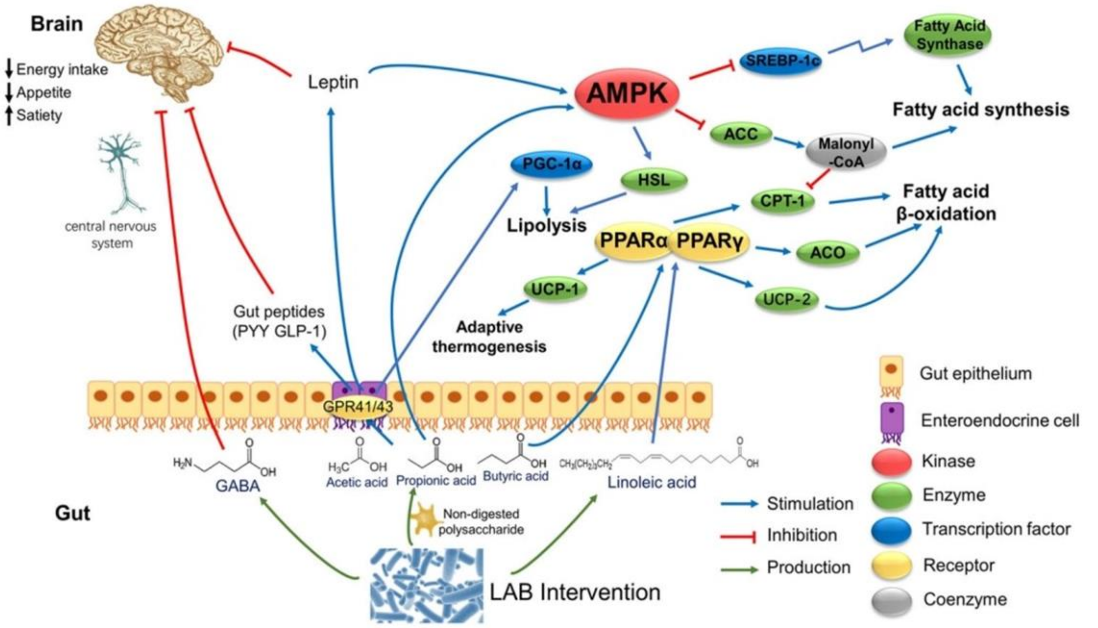

Figure 17 : The possible molecular mechanism of metabolites of LAB to prevent obesity **(Yi-Lin *et al.*, 2021)** .

III.4. Antioxidants and the human body

The human body has adapted defense mechanisms against oxidative stress; these involve a highly complex system of antioxidant comprised by enzymatic and nonenzymatic components. These components work synergistically to protect cells from oxidative stress.Under normal conditions, cells are capable of preventing ROS/RNS-induced oxidative damage, by generating endogenous antioxidants, which include glutathione (GSH), superoxide dismutase (SOD), catalase (CAT) and glutathione reductase (GR) and peroxidase (GPx) enzymes, and nonenzymatic antioxidants such as GSH, ubiquinol, and cysteine. However, endogenous antioxidants may not be sufficient to maintain their protective effect under promoted oxidative stress. In these cases, dietary antioxidants may be required for optimal cellular functions (figure 18) **(Aguilar-toala *et al.*, 2018)** .

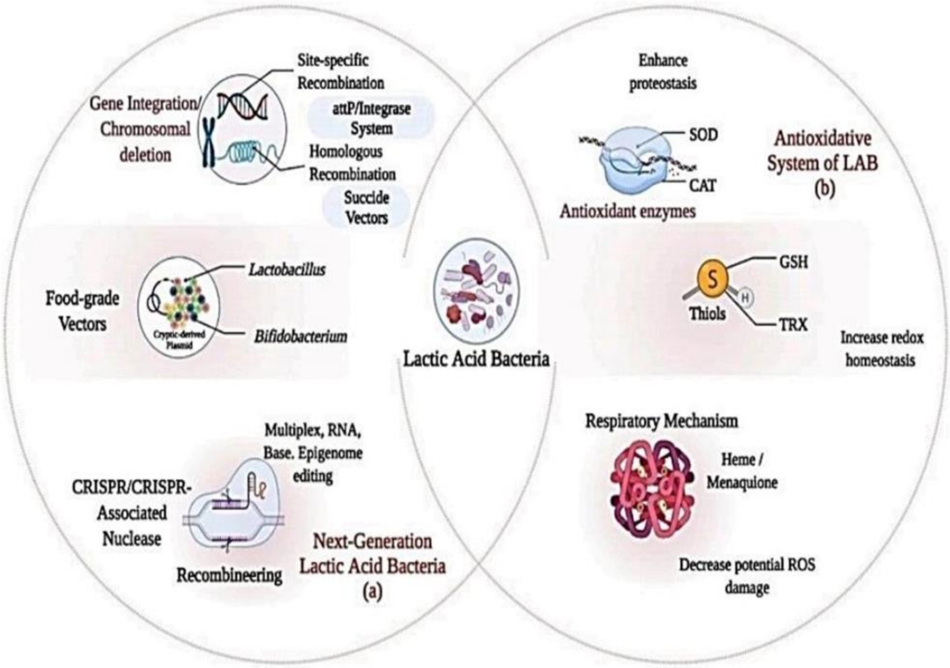

Figure 18 : Genomic Approaches and Antioxidative System of Lactic Acid Bacteria **(Sunday Bulus Peter *et al*., 2022)** .

III.4.1. Protective effect of some food-grade LAB against oxidative stress

Food-grade LAB are typically viewed as harmless microorganisms with a wide range of industrial applications. They make excellent microbial biopreservatives because their safety for humans has been established. They are also effective at low concentrations and active throughout refrigeration storage, and certain strains are thought to have benefits that are health-promoting. They also do not adversely change the nutritional characteristics of food. When consumed by people, certain food-grade LAB have been linked to a number of vital biological processes, such as altering the intestinal microbiota, eradicating pathogens, immunomodulation, promoting the proliferation of epithelial cells, strengthening the intestinal barrier, preventing diarrhea, and lowering lactose intolerance. Food-grade LAB are typically viewed as harmless microorganisms with a wide range of industrial applications **(Aguilar-toala *et al.*, 2018)** .

III.4.2. Production of antioxidant compounds by LAB

Antioxidant properties may be present in specific bioactive chemicals produced by LAB. Conjugated linoleic acid (CLA), exopolysaccharides (EPS), and bioactive peptides are some of these substances. reported that CLA is a powerful antioxidant, with a potency higher than -tocopherol and a level of effectiveness comparable to butylated hydroxytoluene. This fatty acid's primary mechanism is thought to involve its ability to scavenge free radicals by donating hydrogen atoms. The question of whether there are additional microorganisms able to produce CLA is raised by the fact that it is primarily produced by ruminal bacteria.Due to the possibility that LAB could create CLA in milk and growth media through linoleate isomerase activity, this hypothesis has led to substantial research in this area. These cultures may be added to milk to produce fermented milks with a 0.7–1.5-fold increase in CLA content **(Aguilar-toala *et al.*, 2018)**.

III.5. Improving gut and immune health in infants and young children

The colonization with microbes, which starts at birth, is essential for the infant gut's important developmental phases. The host's metabolic and immunological homoeostasis is significantly impacted by this colonization of the gut microbiota. Probiotic strains alter the gut microbiota and immunity to produce a wide range of health advantages. One of the most thoroughly researched probiotic strains is Lactobacillus reuteri. The synthesis of antimicrobial compounds (such reuterin and lactic acid) and the modulation of the acquired and innate immune systems all contribute to the promotion of gut health. A powerful anti-microbial substance called reuterin, which is generated by L. reuteri, can suppress a variety of pathogenic pathogens. L. reuteri produces antibiotic metabolites as well as biofilms that promote lipopolysaccharide-mediated synthesis of tumor necrosis factor **(Alam, 2022)** .

III.6. Suitability ofon the type of cancer cells involved. Some cells of the body have been subjected to autoph-LAB as Vectors

LAB haveagy as a result of treatments and some other tumorous cells may be treated with some become increasingly significant in therapeutic uses such as anti-viral, immunomodulatory,other different forms of cell death. It has been demonstrated that the LAB-produced EPSs anti-inflammatory, anti-oxidant, anti-tumor, anti-diabetic, enhanced colonization ofcan regulate the autophagy gene pathogens, anti-hypertensive, and Beclin-1cholesterol-lowering and also interrelate with apoptosis-related genes actions, as shown in (figure 19) **(OhS.H *et al*., 2021)** .

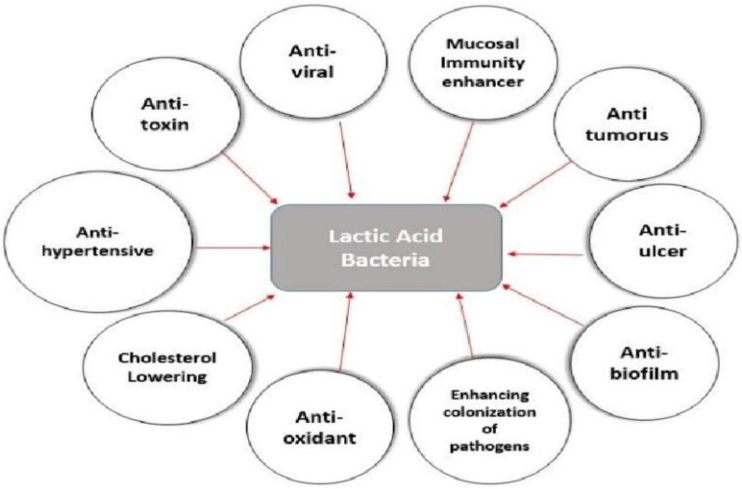

Figure 19 : Health and nutritional benefits of lactic acid bacteria in the schematic diagram **(OhS.H *et al.,* 2021)** .

Lactic acid bacteria (LAB) are microorganisms characterized by the production of organic acids, in particular lactic acid from the fermentation of sugars. They are used in industrial foods to improve these foods. Which consists of several germs including Lactobacillus, Streptococcus, Lactococcus, etc.

LAB are essential biotechnological agents used in milk processing, fermentation, and animal feed industries. They are considered safe for consumption and have beneficial effects on human health. LAB play a crucial role in proteolysis of casein, contributing to the sensory properties of dairy products. Some LAB strains, like Lactobacillus delbrueckii, have been found to inhibit atopic diseases and improve skin conditions when orally administered. Topical application of lactic acid has shown promising results in depigmentation and improving skin texture and appearance caused by environmental photo-damage. LAB are also used as starter cultures in food fermentations, particularly in dairy products like cheese, yogurt, and fermented milks. They play a central role in the degradation of milk proteins to peptides, influencing flavor and texture development in cheese. LAB also play a crucial role in the fermentation process of various foods, including fermented vegetables, meats, and milk products.

LAB have potential applications in food biofortification, intestinal pathologies treatment, and anti-inflammatory treatments. They can alleviate obesity by regulating gut microbial diversity, improving intestinal permeability, and modulating the immune response. LAB metabolites have antioxidant properties, contributing to the body's defense against oxidative stress. They also have antiviral properties, inhibiting viral absorption and modulating the mucosal immune response. The composition and functionality of the gut microbiota vary between healthy and obese individuals, thereby achieving an anti-obesity effect.

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