ARTÍCULO DE REVISIÓN

Review of *Lactobacillus* in the food industry and their culture media

Revisión de Lactobacilos en la industria alimentaria y sus medios de cultivo

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ABSTRACT

Lactic acid bacteria (LAB) are currently of great importance given their increasing use in the improvement of human and animal health and nutrition. They exhibit complex nutritional requirements, which is the reason why their production costs are high. Research efforts are being made aimed at evaluating different substrates for their production as well as the production of valuable metabolites from them. The purpose of this paper is to expose the main research and development trends for LAB production for industrial purposes with emphasis on the culture media required for their growth. The web of Science databases as well as the Google Patent Search tool were used in order to gather and analyze the scientific and technical information published in the last twelve years relating to LAB and their culture media. The use of milk, industrial cheese whey, cane molasses, hydrolyzed starches, lignocellulosic materials, organic food waste and bovine blood plasma, among others, have been proposed for *Lactobacillus* cultivation with the purpose of reducing costs and increasing performance in their production. Research groups and centers have the responsibility of intensifying their efforts to offer highly efficient technological alternatives to the industry that allow the production and application of LAB as a growth factor for the food sector. Also, research in prebiotic ingredients or additives derived from LAB that allow the enhancement of the benefits to the consumer must be continued. In this regard, it is necessary to increase the international visibility of Colombian scientific production in this area.

Key words: Lactobacillus, patent search, probiotics, starter culture, submerged fermentation.

RESUMEN

Las bacterias del ácido láctico (LAB) son actualmente de gran importancia dado su uso creciente en la mejora de la salud y nutrición humana y animal. Presentan requerimientos nutricionales complejos, por lo que sus costos de producción son altos. Se están realizando esfuerzos de investigación para evaluar diferentes sustratos para su producción, así como la producción de metabolitos valiosos a partir de ellos. El propósito de este documento es exponer las principales tendencias de investigación y desarrollo para la producción de LAB con fines industriales, con énfasis en los medios de cultivo necesarios para su crecimiento. Las bases de datos de Web of Science y la herramienta de búsqueda de patentes de Google se utilizaron para recopilar y analizar la información científica y técnica publicada en los últimos doce años relacionada con LAB y sus medios de cultivo. Se ha propuesto el uso de leche, suero de queso industrial, melaza de caña, almidones hidrolizados, materiales lignocelulósicos, desechos de alimentos orgánicos y plasma sanguíneo bovino, entre otros, para el cultivo de *Lactobacillus* con el fin de reducir costos y aumentar el rendimiento de su producción. Los grupos y centros de investigación tienen la responsabilidad de intensificar sus esfuerzos para ofrecer alternativas

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tecnológicas altamente eficientes a la industria que permitan la producción y aplicación de LAB como factor de crecimiento para el sector alimentario. Además, la investigación en ingredientes prebióticos o aditivos derivados de LAB que permite la mejora de los beneficios para el consumidor debe continuar. En este sentido, es necesario aumentar la visibilidad internacional de la producción científica colombiana en esta área.

Palabras clave: *Lactobacillus*, búsqueda de patentes, probióticos, cultivo iniciador, fermentación sumergida.

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INTRODUCTION

At the beginning of the 20th century the concept of lactic acid bacteria (LAB) emerged as an independent group. Today this group shows a huge biotechnological potential, and it is present in a large number of fermentative food processes destined for human consumption such as dairy, vegetables, meat and bakery products, as well as in silage for animal food (Lee *et al.*, 2013; J. C. Ramírez *et al.*, 2011). These bacteria not only contribute to the development of the organoleptic, rheological and nutritional characteristics of foods, but also generate unfavorable environments for the development of pathogenic microorganisms such as *Bacillus, Pseudomonas, Listeria and Escherichia* among others, given their bioconservative capacity to produce antimicrobial substances (Cizeikiene *et al.*, 2013; Topisirovic *et al.*, 2006). In addition to this important role in bio-conservation processes, some strains of lactic acid bacteria belonging to the genus *Lactobacillus* are beneficial to human and animal health, due to their potential in reducing enteric diseases in humans and farm animals, and the subsequent contamination of food products derived from them (Argyri *et al.*, 2013; Ávila *et al.*, 2010; L Axelsson, 1998). The purpose of this paper is to expose the main research and development trends in the production of lactic acid bacteria for industrial purposes with emphasis on the culture media required for their growth.

Search procedure

This review is, focused on presenting the alternatives of culture media for the production of *Lactobacillus* in the last 12 years, the study was divided into two parts: A synthetic literature review on the generalities of LAB, and a systematic review on specific media for cultivation of *Lactobacillus*. With this purpose, the Web of Science databases, consisting of KCL (Korean Journal Database), Russian Science Citation Index, SciElo Citation Index, Springer and ScienceDirect, was used. The following search terms were used: 1) for the Title field: *"Lactobacillus"* with connector "AND" and in Topic field: "culture media"; 2) published between 2005 and 2016; 3) type of document: articles; 4) language (English, Portuguese and Spanish). Once the records were obtained, filters were used to focus on the ten research areas in which this type of studies are done. In order to reduce the search size, the results were refined by using "Science and Technology" as research domain and even more specific research areas of this type of studies such as: "Food Science and Technology", "Applied Biotechnology and Microbiology", " Microbiology", "Applied Chemistry", and "Chemical Engineering".

Using the Web of Science search engine, the internal analysis of articles obtained in the last twelve years (a reduced sample greater than 500 articles) was performed using the following criteria: 1) The ten most important research areas; 2) the thirteen authors registered as the most important in these research areas; 3) the record of publications in the same period of time; and 4) the ten most important countries in this type of study. From this reduced sample, about 60 articles were selected using the following exclusion criteria: 1) Reports that do not contribute to the objective of this review by not making explicit the culture media for LAB; 2) papers that do not report the type of microorganism, substrate or supplement, type of fermentation, fermentation conditions, and biomass production. The extracted information was compiled in an MS Excel spreadsheet, designed with the search criteria used. In this format, some works published prior to the time period covered by this review were also included given their relevance and pertinence. Moreover, patents reported between 2000 and 2016 on *Lactobacilli* were consulted through the Google Patent Search using the same search criteria indicated above.

Search results on culture media for lactic acid bacteria

The initial search performed on *Lactobacillus* culture media, once the search criteria and the respective filters were applied, showed 594 records, which were analyzed for this review. From the records analyzed, 13.1% of the papers are authored by 13 researchers, who lead the studies on *Lactobacillus* in the last twelve years. These authors belong to research groups from Canada, Italy, South Africa, England, Poland, Japan, Argentina, Belgium, and the United States. Table 1 shows the 25 affiliation organizations of these authors. Taking into account the classification of research areas used by Web of Science, the articles found belong to the following

Table 1. Amount of publications of the 25 main organizations to which the research groups working on *Lactobacillus* belong between 2005-2016.

Organization (Country)	Records	Participation percentage
Institut National de Recherche Agronomique (INRA, France)	13	2.180
Consejo Nacional de Investigaciones Cientificas y Técnicas (CONICET, Argentina)	11	1.852
Consejo Superior de Investigaciones Cientificas (CSIC, Spain)	11	1.852
Universidade de São Paulo (Brazil)	11	1.852
Agriculture and Agri-Food Canada (Canada)	10	1.684
Istituto di Scienze di Alimentari (Italy)	9	1.515
Universidad Nacional de Tucumán (Argentina)	9	1.515
Universiti Putra Malaysia (Malaysia)	8	1.347
Islamid Azad University (Iran)	7	1.178
Jiangnan University (China)	7	1.178
Seoul National University (South Korea)	7	1.178
Technische Universitat München (Germany)	7	1.178
Centro de Referencia de Lactobacilos (CERELAC, Argentina)	6	1.010
Instituto de Investigación de la Leche (Uruguay)	6	1.010
Tohuko University (Japan)	6	1.010
University of Manchester (United Kingdom)	6	1.010
Universidad de Vigo (Spain)	6	1.010
Università della Basilicata (Italy)	5	0.842
Universiteit Gent (Belgium)	5	0.842
University of Helsinki (Finland)	5	0.842
Université Laval (Canada)	5	0.842
Universidad Nacional del Litoral (Argentina)	5	0.842
Stellenbosch University (South Africa)	5	0.842
University of Tehran (Iran)	5	0.842
Wageningen University (Netherlands)	5	0.842

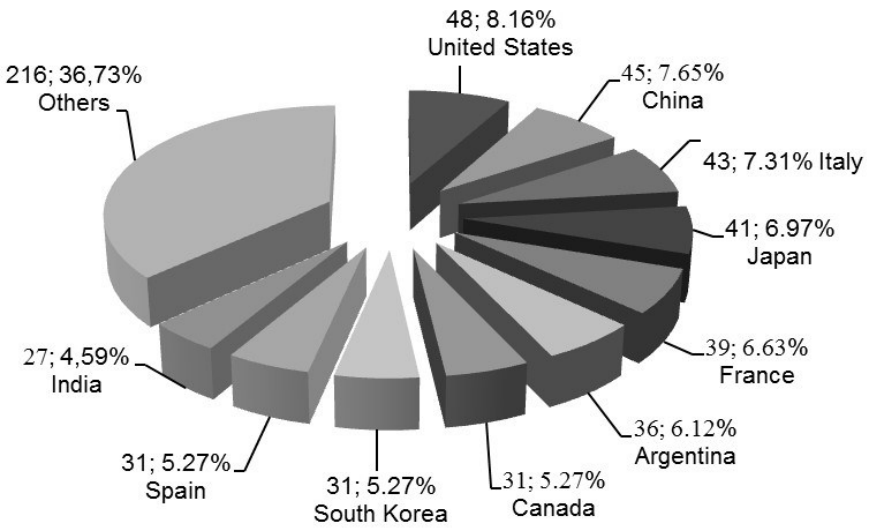

Figure 1. Distribution by country of the institutions to which the authors of articles on culture media for *Lactobacillus* belong in the period 2005-2016.

five research areas in descending order: Applied Microbiology and Biotechnology (196), Microbiology (176), Food Science and Technology (163), Molecular Biology and Biochemistry (31), Agriculture (28).

The ten countries with the highest participation in studies on culture media for *Lactobacillus* in the world in the last twelve years are shown in figure 1. It is noteworthy that only three records corresponding to Colombian researchers appear in Web of Science in the last twelve years, comprising a share of 0.5%. The amount of publications in the last twelve years was also consulted for this search in the selected databases and the results are illustrated in figure 2.

Patent search

The literature reports an important amount of patents on new *Lactobacillus* strains, as well as processes for differentiating and quantifying lactic bacteria in some natural products, the composition and enrichment of media for their cultivation, and processes for producing, characterizing and applying products with probiotic properties obtained from *Lactobacillus,* among others. Table 2 presents the list of patents found in the last decade (from 2005 to August 2016 as a reference period for the analysis) regarding *Lactobacillus*.

It should be noted that the patents on *Lactobacillus* granted in the period from 2000 to August 2016, show a great interest in the identification of new strains based on their natural substrates (mainly dairy and meat products), as well as their potential use as preventive or therapeutic agents against pathologies related to the human intestinal tract (Anonymous, 2005, 2016a; Bojrab, 2011; Connolly, 2008; Farmer, 2014). The companies filing patents on this topic aim their resources towards economic methods for production of *Lactobacilli* cultures at industrial level. Most patent documents refer to the use of whey (Yun *et al.*, 2015), corn starch (Li & Liu, 2014) and even whole milk (Anonymous, 2014a; Chen *et al.*, 2013). In other cases, the inventors resort to the design of synthetic media for the isolation of bioactive molecules, functional metabolites or production of LAB of interest (Elli *et al.*, 2002). For the enrichment of these media, the use of free bases, ribonucleosides, deoxyribonucleosides, casein hydrolysates, hydroxyproline, and glutamic acid was reported. Some patents introduced their inventions for preservatives, which enable the protection of the *Lactobacillus* culture, both in the subculture and during storage. It should be highlighted that, because of the recognized importance of probiotics, efforts are made to design growth media enriched with constituents such as sulfur amino acids, ovalbumin, bile powder, trehalose, and raffinose.

Features of lactic acid bacteria

Lactic bacteria are chemo-organotrophic microorganisms. Their morphology appears as cocci or bacilli, commonly associated in short chains, are Gram positive, non -sporulated, and aerotolerant. They are negative in the oxidase, catalase and benzidine tests. They lack cytochromes and generally do not reduce nitrate to nitrite. These bacteria synthesize lactic acid as the main product of carbohydrate fermentation (Lars Axelsson, 2004; Bovo *et al.*, 2014; Stieglmeier *et al.*, 2009;Vásquez *et al.*, 2009; Waldir *et al.*, 2007).

Table 2. Patents on *Lactobacillus* in the period registered 2000-2016.

Patent number	Country	Description	Reference
EP 2316278	South Korea	Method for producing fermented edible plants or animals and foods containing	Choi et al. (2013)
US 8613964	United States	Method for making shelf-stable poi food products from dryland and wetland taro	Day and Boiser (2013)
CA 2598539	Canada	Lactic acid and *Bacillaceae* fertilizer and method of producing it	Blais (2013)
CN 103857297	China	Probiotic fruit drinks	Anonymous (2016b)
EP 0698347	Sweden	Food composition containing reuterin	Dobrogosz and Lindgren (2006)
US 8697055	United States	Probiotic based on lactic acid-producing bacteria	Farmer (2014)
CN 103224895	China	A novel strain of *Lactobacillus reuteri* for use by improving autoimmune diseases	Anonymous (2014c)
US 8748124	United States	Biodegradation process and composition	López et al. (2014)
CN 101919879	China	Method for preparing probiotics preparation by taking attapulgite as carrier	Anonymous (2012)
US 8815539	United States	Methods for producing melanin and inorganic fertilizer from fermentation leachates	Popa and Nealson (2014)
CN 103154235	China	Improvement of *Lactobacillus* strains immunomodulatory properties	Anonymous (2016a)
CN 102994644	China	Quantitative detection method and kit for *Lactobacillus plantarum* and its application	Anonymous (2014b)
US 7888062	United States	Process and composition for the manufacture of a microbial-based product	Garner and Flint (2011)
CN 103550258	China	*Lactobacillus* strains for regulation of the immune response	Anonymous (2015a)
US7344867	United States	Selection and use of lactic acid bacteria for reducing inflammation in mammals	Connolly (2008)
US 7901925	United States	Strain of *Lactobacillus delbrueckii* ssp. *bulgaricus* and compositions	Bojrab (2011)
CN103275921	China	Method for improving cholate tolerance of *Lactobacillus*	Anonymous (2015b)
US 6340585	United States	Synthetic medium for cultivation of *Lactobacillus* and *Bifidobacteria*	Elli et al. (2002)
CA 2534013	Canada	*Lactobacillus* as a preventive or therapeutic agent against infections	Anonymous (2005)
US 7901925	United States	Strain of *L. delbrueckii* ssp. *bulgaricus* and its composition	Bojrab (2011)
CN 102952772	China	Enrichment of culture medium for *L. bulgaricus* and method of preparation	Chen et al. (2013)
CN 103305435	China	Method for preparation of *L. plantarum* culture	Anonymous (2014a)
CN 104212743	China	Culture medium and method for high density culture of *L. amylolyticus*	Li and Liu (2014)
CN 104531596	China	Improved culture medium with whey proteins and their applications	Yun et al. (2015)
CN 104560799	China	Method of active bacterial preparation of bacteriocins by *L. plantarum* ssp. *plantarum* Zhang-LL	Hongxing (2015)
US 9265270	United States	*Lactobacillus* culture and method for producing it	Hoshi et al. (2016)

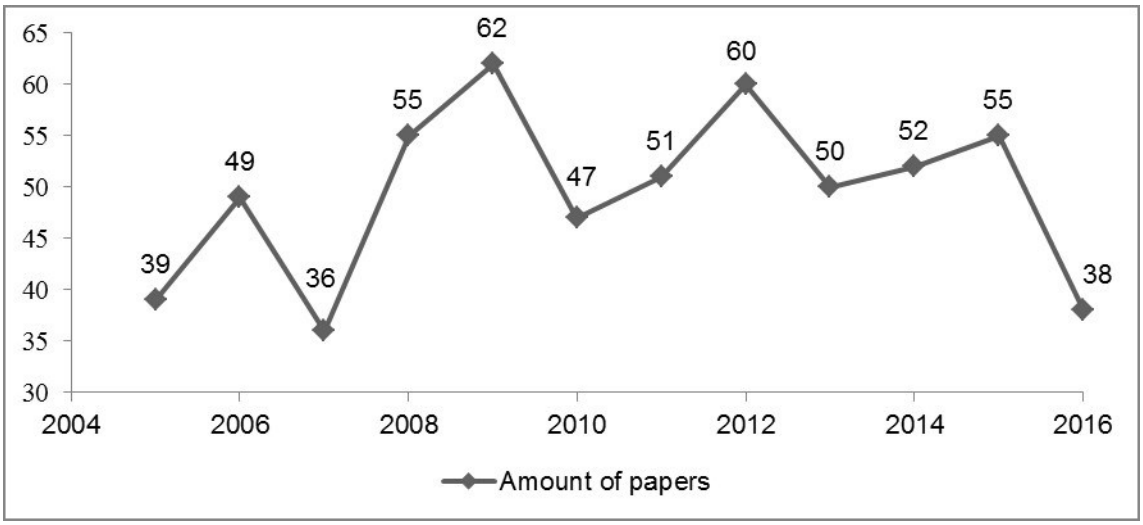

Figure 2. Amount of papers published on culture media for *Lactobacillus* in the period 2005-2016.

The LAB exhibit two metabolic pathways for fermentation of monosaccharides: Homolactic fermentation or glycolysis (pathway Embden-Meyerhof-Parnas) and hetereolactic fermentation of the 6-phosphoglucanate (6FG) or pentoses pathway. Consequently, LAB have been classified as obligatory homofermentative, facultative heterofermentative, and obligatory hetereofermentative microorganisms (Lars Axelsson, 2004; Gänzle, 2015), The acidolactic bacteria shows slight proteolytic activity due to the proteases and peptidases attached to the cell wall or released by them, as well as weak lipolytic activity due to the action of intracellular lipases.

The culture media and main fermentation conditions for production of the main *Lactobacillus* species used for production of probiotics, starter cultures, and bacteriocins, are shown in table 3 (organized alphabetically by species name followed by the year of publication). Among the most individually studied *Lactobacillus* or a mixture of them, isolated from natural substrates, the following species should be highlighted for their probiotic and bio-preservation activities: *L. acidophilus, L. casei*, *L. delbruecki, L. plantarum, L. helveticus, L. rhamnosus,* and *Bifidobacterium bifidum*.

Culture media for lactic acid bacteria

A culture medium must contain the nutrients and growth factors required by the microorganism and be free of contaminating microorganisms (Garcia *et al.,* 2010). These requirements are characteristic of each species. LAB show complex nutritional requirements such as amino acids, peptides, derivatives of nucleic acids, vitamins, salts, fatty acids or esters of fatty acids, and fermentable carbohydrates (Parra, 2010). These requirements are usually met when the culture medium contains fermentable carbohydrates, peptone meat, and yeast extract. In general, for *Lactobacillus* it is desirable for the nitrogen to be organic in the form of amino acids or peptides. In this sense, glutamic acid, isoleucine and valine are considered as growth factors and must be present in the culture medium (González *et al.*, 2008). Many species require the presence of manganese, acetate and esters of oleic acid, especially Tween 80 (Berbegal *et al.*, 2015).

According to table 3 and figure 4, it can be observed that most studies on the production of *Lactobacillus* biomass still make use of whey and sugar cane molasses as source of carbon and energy. In recent years, the use of fruit juices, as well as of by-products and agro-industrial waste has gained importance for media formulation. The above corroborates the research trend in the search for feedstocks of high availability and lower cost with the purpose of reducing the sale price of the final products derived from the *Lactobacilli* biomass.

In Latin America, different research efforts have been reported aimed at the use of native products for LAB growth given the great availability of biological resources and economies with a high weight of the agriculture and agro-industry in these countries. For example, the growth kinetics of *Lactobacilli* with probiotic potential in the intestinal tract are being studied in Mexico using the agro-industrial residue derived from the fermentation of agave honey, a pre-Hispanic drink called *pulque* in that country (Yépez *et al.*, 2013).

In Colombia, the use of wastewater sludge from sugar cane processing as well as the sugar cane molasses has been proposed as feedstocks given the importance of the sugar industries including the industry for production

Table 3. Culture media and fermentation conditions for *Lactobacillus* production.
μ_{max}: maximum specific speed of growth; OD: optical density; X: concentration of cellular biomass; $Y_{P/S}$: product yield from substrate; $Y_{X/S}$: biomass yield from substrate; YE: yeast extract; WP: whey permeate.

Microorganism	Substrate	Supplements	Fermentation conditions	Biomass production	Type of fermentation	References
Bifidobacterium bifidum	Medium 1: Sugar cane molasses 32 g/L	YE: 5.0 g/L	Anaerobic conditions	4.5 g/L-2.8 g/L	Discontinuous	*Vargas et al. (2004)*
	Medium 2: UHT			3.8 g/L-3.4 g/L		
	wastewater 45 g/L					
L. acidophilus	Medium 3: Sugar cane molasses 32 g/L	YE:5.0 g/L	37°C, 48 h, 100 rpm, 5-10% oxygen	5.5 g/L	Discontinuous	*Vargas et al. (2004)*
		Casein peptone: 10 g/L				
L. acidophilus ACC	Milk	YE: 0.3, 0.5 and 1%	37 °C, 100 rpm, controlled pH 6.5	CFU/ mL: 7.94×10^{7}-6.30×10^{9}	Discontinuous	*Avonts et al. (2004)*
				X_{max}: 1.2-3.5 g/L		
				μ_{max}: 0.36-0.92 h^{-1}		
L. acidophilus IBB 01	Milk	YE: 0.3, 0.5 and 1%	37 °C, 100 rpm, controlled pH 6.5	CFU/ mL: 7.94×10^{7}-6.30×10^{9}	Discontinuous	*Avonts et al. (2004)*
				X_{max}: 1.2-3.5 g/L		
				μ_{max}: 0.36-0.92 h^{-1}		
Lactobacillus bulgaricus RR	Medium: glucose (20g/L), Tween 80 (1.0 g/L), ammonium citrate (2 g/L), sodium acetate (5 g/L), $MgSO_4$ $7H_2O$ (0.1 g/L), $MnSO_4$ (0.05 g/L), K_2HPO_4 (2 g/L)	Yeast nitrogenous base (5 g/L) and Bacto casitone (10 g/L)	42°C, 12 h, pH 6.56	1.28×10^{8} CFU/mL	Discontinuous	*Kimmel and Roberts (1998)*
L. casei Imunitas	Milk	YE: 0.3, 0.5 and 1%	37 °C, 100 rpm, controlled pH 6.5	CFU/ mL: 7.94×10^{7}-6.30×10^{9}	Discontinuous	*Avonts et al. (2004)*
				X_{max}: 1.2-3.5 g/L		
				μ_{max}: 0.36-0.92 h^{-1}		
L. casei YIT 9029	Milk	YE: 0.3, 0.5 and 1%	37 °C, 100 rpm, controlled pH 6.5	CFU/ mL: 7.94×10^{7}-6.30×10^{9}	Discontinuous	*Avonts et al. (2004)*
				X_{max}: 1.2-3.5 g/L		
				μ_{max}: 0.36-0.92 h^{-1}		
L. casei	Sugar cane molasses 32 g/L	YE: 5.0 g/L	37°C, 48 h, 100 rpm, 5-10% oxygen	5.5 g/L	Discontinuous	*Vargas et al. (2004)*
L. casei NRRL 1445	Juice of Aloe vera variety barbariensis: 25, 50, 75 and 100%		30 °C,150 rpm, initial pH of medium: 6,5	*L. casei*: 1×10^{11} CFU/mL	Discontinuous	*González et al. (2008)*
L. casei Shirota	Sugar cane juice		37°C, 24 h	3.98×10^{7} CFU/mL	Discontinuous	*Magaña et al. (2008)*
	Coconut milk			1.58×10^{8} CFU/mL		
	Orange juice			1.58×10^{8} CFU/mL		
	Whey			3.16×10^{9} CFU/mL		
L. casei	WP from goat milk		Batch regime: 37 ºC, pH 5.5, effective volume 2 L, 300 rpm, inoculum concn. 0.5-1.0 g/L, concn., initial substrate concn. 33-50 g/L, 20 h	Productivity: 0.067 0.46 g biomass/(L×h)	Discontinuous	*Aguirre et al. (2009)*
			Fed-batch regime: 1 L supernatant replaced by 1 L fresh culture medium at 14 h	X: 2.5-3.5 g/L		
				$Y_{X/C}$: 0.0990-0.16 g biomass/g substrate)		
				5.17×10^{9} CFU/mL		
				Fed-batch: 2.43×10^{10} CFU/mL	Fed batch	
L. casei	WP from goat milk		Batch regime: 37 ºC, pH 5.5, effective volume 2 L, 300 rpm, inoculum concn. 0.5-1.0 g/L, concn., initial substrate concn. 33-50 g/L, 20 h	Productivity: 0.067 0.46 g biomass/(L×h)	Discontinuous	*Aguirre et al. (2009)*
			Fed-batch regime: 1 L supernatant replaced by 1 L fresh culture medium at 14 h	X: 2.5-3.5 g/L		
				$Y_{X/C}$: 0.0990-0.16 g biomass/g substrate)		
				5.17×10^{9} CFU/mL		
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μ_{max}: maximum specific speed of growth; OD: optical density; X: concentration of cellular biomass; $Y_{P/S}$: product yield from substrate; $Y_{X/S}$: biomass yield from substrate; YE: yeast extract; WP: whey permeate.

Microorganism	Substrate	Supplements	Fermentation conditions	Biomass production	Type of fermentation	References
L. casei ATCC 393	Uchuva pulp and glucose solution (14% p/p)		37 °C, 72 h, microaerophilic conditions	$5.40\pm2.36\times10^8$ to $7.34\pm7.88\times10^8$ CFU/mL	Discontinuous	*Cortés R (2009)*
L. casei	Deproteinized whey	Glucose (0 % and 5%)	Initial pH=6.05, 93 h	5.9×10^{10} CFU/mL	Discontinuous	*Escobar et al. (2010)*
L. casei var. *rhamnosus*	Whey	35-70 g/L lactose	37°C, pH 5.5, 300 rpm, volume 2 L, inoculum concn. 0.5-1.0 g/L	$Y_{X/S}$ = 1.5819 g/g $Y_{P/S}$ = 0.5684 g/g X: 5 g/L	Discontinuous	*Alvarez et al. (2010)*
L. casei IMAU60214 (isolated from commercial dairy products)	Wastewater from corn nixtamalization		37°C, 48 h	By absorbance (650 nm): 0.740	Discontinuous	*G. Ramírez et al. (2013)*
Lactobacillus delbrueckii ssp	MRS		42°C, 12 h, pH 6.56	1.62×10^8 CFU/mL	Discontinuous	*Kimmel and Roberts (1998)*
L. gasseri K7	Milk	YE: 0.3, 0.5 and 1%	37 °C, 100 rpm, controlled pH 6.5	CFU/ mL: 7.94×10^7-6.30×10^9 X_{max}: 1.2-3.5 g/L μ_{max}: 0.36-0.92 h^{-1}	Discontinuous	*Avonts et al. (2004)*
L. helveticus	Whey permeate (48g/mL of lactose)	YE: 20 g/mL, casein peptone: 5 g/mL	42 °C, controlled pH 5.9, 25 h	μ_{max} =0.477 h^{-1} X= 4.0 g/L	Discontinuous	*Amrane (2005)*
L. helveticus IMAU70129 (isolated from commercial dairy products)	Wastewater from corn nixtamalization		37°C, 48 h	By absorbance (650 nm): 0.735	Discontinuous	*G. Ramírez et al. (2013)*
L. johnsonii La1	Milk	YE: 0.3, 0.5 and 1%	37 °C, 100 rpm, controlled pH 6.5	CFU/ mL: 7.94×10^7-6.30×10^9 X_{max}: 1.2-3.5 g/L μ_{max}: 0.36-0.92 h^{-1}	Discontinuous	*Avonts et al. (2004)*
L. jonhsonii	Sugar cane juice		37°C, 24 h	3.98×10^7 CFU/mL	Discontinuous	*Magaña et al. (2008)*
	Coconut milk			1.58×10^8 CFU/mL		
	Orange juice			3.16×10^9 CFU/mL		
	Whey			1.58×10^8 CFU/mL		
L. paracasei HA9-2 (isolated from humans)	Media 1 and 4: Whey with 70 g/L carbohydrates	Medium 2: $MgSO_4.7H_2O$ (0.3 g/L), $MnSO_4.4H_2O$ (0,03 g/L)	Concn. inoculum: 1.0×10^8 CFU/mL, pH: 5.0, 5.5 and 6.0	1.5 to 3.53×10^9 CFU/mL	Discontinuous	*Vázquez et al. (2009)*
	Media 2 and 3: Whey	Medium 3: $MgSO_4.7H_2O$ (0.3 g/L), $MnSO_4.4H_2O$ (0.03 g/L) and YE (0.5%).				
		Medium 4: 0.5% and 1.0% acacia gum				
L. plantarum ATCC 8014	Media 1 and 2: Sugar cane molasses 3%	Medium 1: 0.5% YE, ammonium citrate and sodium acetate	35 °C, 24 h,	Productivity of medium 1: 0.0507 g/(L×h)	Discontinuous	*Villavicencio et al. (1999)*
		Medium 2: 0.5% YE, sodium acetate, ammonium phosphate and ammonium citrate, 0.1% Tween 80 and 0.005% MnSO4	150 rpm, 0.7 vvm	Productivity of medium 2: 0.0768 g/(L×h)		
L. plantarum	Medium 1: Sugar cane molasses 32 g/L	YE: 5.0 g/L	*Lactobacillus* spp.: 37°C, 48 h, 100 rpm, 5-10% oxygen	5.5 g/L	Discontinuous	*Vargas et al. (2004)*
	Medium 2: UHT wastewater 45 g/L					
	Medium 3: Sugar cane molasses 32 g/L	YE:5.0 g/L				
		YE:5.0 g/L				
		Casein peptone: 10 g/L				
L. plantarum (NCIMB 11718) and	Juice of *Aloe vera* variety *barbariensis*: 25, 50, 75 and 100%		30 °C,150 rpm, initial pH of medium: 6,5	1×10^9 CFU/mL	Discontinuous	*González et al. (2008)*

Table 3. Culture media and fermentation conditions for *Lactobacillus* production.
μ_{max}: maximum specific speed of growth; OD: optical density; *X*: concentration of cellular biomass; $Y_{P/S}$: product yield from substrate; $Y_{X/S}$: biomass yield from substrate; YE: yeast extract; WP: whey permeate.

Microorganism	Substrate	Supplements	Fermentation conditions	Biomass production	Type of fermentation	References
L. plantarum LPBM10 (isolated from fermented cabbage)	Uchuva pulp and glucose solution (14% p/p)		37 °C, 72 h, microaerophilic conditions	1.64±1.57×10^9 to 3.23±3.35×10^9 CFU/mL	Discontinuous	*Cortés R (2009)*
L. plantarum WS417	Sterile molasses (5%, 10%, 20%, 25% and 30%)		25ºC, 30°C and 35ºC, 24 h, pH 5.2, 100 rpm	43×10^9 CFU/mL	Discontinuous	*Ossa et al. (2010)*
L. plantarum 1 H1 and *L.* plantarum 1 H2 (isolated from pig large intestine)	Medium 1: MRS	Medium 2: 14 g/L soy milk, 30 g/L wheat bran	32°C, 24 h, without pH control	MRS: 1.0×10^8 CFU/mL *L. plantarum* 1 H1 and 4.0×10^{12} CFU/mL *L. plantarum* 1 H2	Discontinuous	*Jurado et al. (2013)*
	Medium 2: 20 g/L sucrose, 130 g/L whey	Medium 3: 12 g/L soy milk, 10 g/L wheat bran		Medium 2: Not shown		
	Medium 3: 15 g/L sucrose, 120 g/L whey	Medium 4: 15 g/L soy milk, 15 g/L wheat bran		Medium 3: 1.0×10^{13} CFU/mL *L. plantarum* 1 H1		
	Medium 4: 10 g/L sucrose, 150 g/L whey			Medium 4: 4.0×10^{14} CFU/mL *L. plantarum* 1 H2		
L. plantarum CIDCA 83114 (isolated from Kefir grains)	Medium 1: WP with 80% lactose, 6% ash, 3% protein	Galacto-oligosaccharides	37°C,18 h	Medium 1: 4.75×10^8 ±7.07×10^7 CFU/mL, μ_{max} = 0.110 h^{-1}	Discontinuous	*Ayelén et al. (2016)*
	Medium 2: WP			Medium 2: 4.0×10^8 CFU/mL		
				μ_{max} = 0.160 h^{-1}		
L. reuteri	Medium 1: Sugar cane molasses 32 g/L	YE: 5.0 g/L	37°C, 48 h, 100 rpm, 5-10% oxygen	4.5-5.5 g/L	Discontinuous	*Vargas et al. (2004)*
	Medium 2: UHT wastewater 45 g/L					
	Medium 3: Sugar cane molasses 32 g/L	YE:5.0 g/L				
		YE:5.0 g/L				
		Casein peptone: 10 g/L				
L. reuteri DSPV002 of porcine origin (ileum)	Whey	<5% YE and 0.003% $MnSO_4$	37°C, 18 h		Discontinuous	*Fusari et al. (2014)*
		5% YE and 0.003 % $MnSO_4$				
		<5% YE and 0.003% $MnSO_4$				
	Whey	5% YE and 0.003 % $MnSO_4$				
	PSQ					
L. rhamnosus GG	Milk	YE: 0.3, 0.5 and 1%	37 °C, 100 rpm, controlled pH 6.5	CFU/ mL: 7.94×10^7-6.30×10^9	Discontinuous	*Avonts et al. (2004)*
				X_{max}: 1.2-3.5 g/L		
				μ_{max}: 0.36-0.92 h^{-1}		
L. rhamnosus ATCC 7469	Medium 1: Glucose 50 g/L and YE 60 g/L	KH_2PO_4 2.7 g/L; $MgSO_4.7H_2O$ 0.2 g/L; $MnSO_4.H_2O$ 0.05 g/L; Tween-80 1 ml/L; vitamins in solution (g/L): 12.8 pyridoxine HCl; pantothenic acid 1.0, niacin 1.0, riboflavin 1.0 and folic acid 1.0.	37 °C, constant pH 6.9, stirred-tank fermenter, N_2 injection, environment without O_2	Max cell viability.: 1.3×10^{10} CFU/mL (from 5.86 to 7.61 g/L)	Continuous	*Ling et al. (2006)*
	Medium 2: Glucose 40 g/L and YE 60 g/L.		Dilution rates: from 0.05 to 0.4 h^{-1}; constant volume 600 mL	$Y_{x/s}$ from 2.9 to 3.7×10^{11} CFU/g glucose (from 0.15 to 0.22 g/g glucose)		
L. rhamnosus	Apple juice concentrate	YE; tryptone; wheat; soy; YE and wheat; YE and soy	Initial pH 6.0, 2L fermenter, 500 rpm, 4.3 L/min air	Medium without supplements: OD_{max} =0.21, μ_{max}=0.27 h^{-1}	Discontinuous	*Champagne and Gardner (2008)*
				Max. biomass concn. for medium with YE and wheat: OD_{max} =0.51, μ_{max}=0.39 h^{-1}		
				Medium without supplements: OD_{max} =0.21, μ_{max}=0.13 h^{-1}		
				Max. biomass concn. for medium with YE and wheat: OD_{max}		
	Molasses	YE; tryptone; wheat; soy; YE and wheat; YE and soy molasses		=0.51, μ_{max}=0.47 h^{-1}		
L. rhamnosus GG	Wastewater from corn nixtamalization		37°C, 48 h	By absorbance (650 nm): 0.770	Discontinuous	*G. Ramírez et al. (2013)*
Lactobacillus sp. (isolated from *pulque*)	Medium1: Whole UHT milk with 7% lactose	Medium 2: 100% salts of MRS medium	23°C, 29°C and 37°C, pH 6.4, without agitation, with 2 and 5% inoculum, 34 h	35 to 42 g/L	Discontinuous	*Yépez et al. (2013)*
	Medium 2: Whole UHT milk with 7% lactose	Medium 4: 100% salts of MRS Medium 5: 100% salts of MRS medium and 0.25% YE				
	Media 3-6: whey with 7% lactose	Medium 6: 100% salts of MRS medium and 5 g/L YE				

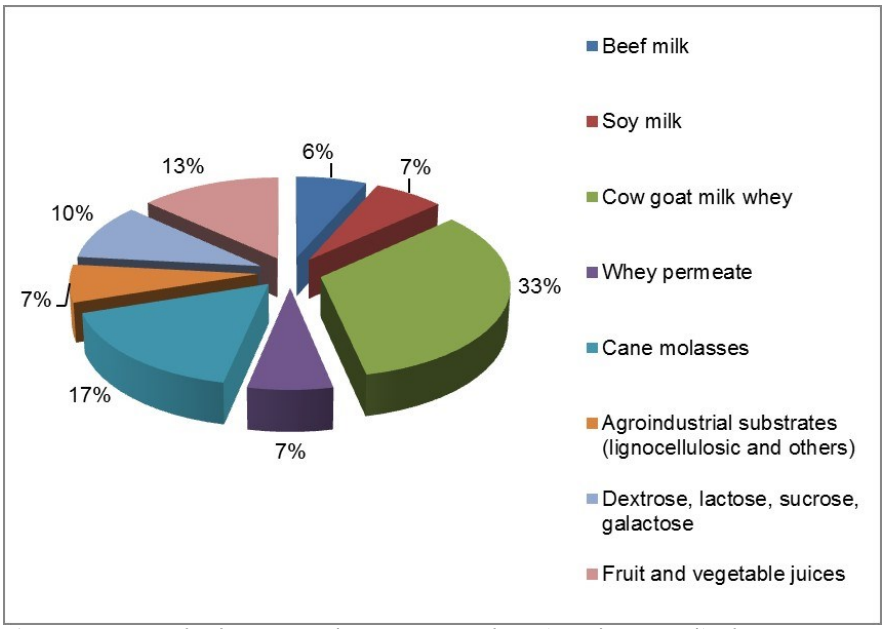

Figure 3. Type of substrate and percentage of use in culture media for *Lactobacillus* in the last fifteen years.

of non-centrifugal sugar or solid brown sugar (called *panela* in that country) (Ossa *et al.*, 2010). Likewise, the use of lignocellulosic materials for LAB production with probiotic functionality by submerged fermentation, such as wheat bran, has been reported (Jurado *et al.*, 2013). Obtained *Lactobacillus* may be used to produce probiotics, which can colonize the intestine when consumed orally. This would open new possibilities in the diversification of the feedstocks basis for industrial fermentation processes. Other researchers have proposed the use of cereals like barley and malt for the development of lactic acid bacteria with probiotic potential such as *L. plantarum* NCIMB 8826 and *L. acidophilus* NCIMB 8821 (Rathore *et al.*, 2012). Complex or enriched liquid media are currently being used supplemented with some components that increase the production costs of lactic cultures. Particularly, as can be seen in this review, the nitrogen sources used such as yeast extract, tryptic casein peptone, and meat extract have a high cost in industrial fermentations. Table 3 shows the most widely used substrates in the last twelve years, supplements added to the media, conditions of fermentation, type of fermentation, and data on production of biomass obtained. Table 3 does not report the average biomass yields since these data are scarcely published in the available literature, being risky to make any comparation about the performance of synthetic media related to those based on agro-industrial waste. Considering the final viable biomass concentration (in CFU/mL), the medium based on whey and sucrose as carbon sources, and soy milk and wheat bran as nitrogen sources employed by Jurado *et al.* (2013) allowed reaching the highest concentration of *L. plantarum*. In the case of *L. casei*, the best medium was almost exclusively based on a by-product (or waste) from the dairy industry (Escobar *et al.*, 2010): the cheese whey (see table 3). These outcomes suggest that the utilization of waste materials for media formulation is an attractive way to enhance the performance of LAB cultivation, enabling, at the same time, the decrease in the feedstock costs during production of probiotic microorganisms and starter cultures. In this sense, the evaluation of lignocellulosic hydrolyzates for LAB fermentation could be a promising research trend in the near future. In general, the range of cell concentrations (in CFU/mL) for main LAB presented in table 3 is as follows: *L. acidophilus* 7.94×10^{7} – 6.30×10^{9}, *L. casei* 7.94×10^{7} – 6.30×10^{9}, *L. plantarum* 4.0×10^{8} – 4.0×10^{14} and *L. rhamnosus* 7.94×10^{7} – 3.7×10^{11}. It should be noted that the papers reviewed for this work reported the data on biomass concentrations with different units (CFU/mL, g/L, Optical Density); this difficults the comparison among the different media used in those papers.

Culture conditions for *Lactobacillus*

The temperature for the cultivation of mesophilic and thermophilic LAB found in this study ranges from 23 to 37°C and 42°C, respectively, with incubation times from 18 to 93 hours and a pH from 5.2 to 6.9. The discontinuous cultivation was the type of fermentation used in almost all the studies reviewed (table 3), which does not allow a more precise evaluation of other alternative regimes that are more efficient like the continuous culture.

The highest production of viable cells (4.0×10^{14} CFU/mL) mentioned above, corresponded to a batch system for production of two *L. plantarum* strains. More research efforts are required at the bench and pilot levels in continuous and discontinuous fermentations in order to assess the efficiency of alternative cultivation regimes for *Lactobacillus* production.

Applications of LAB

Lactic acid bacteria are increasingly used in the improvement of human and animal health and nutrition (Senz *et al.*, 2015; Süle *et al.*, 2014). It has been known for several decades that LAB have an inhibitory potential in food against the development of altering microorganisms and pathogens, which is useful for prolonging shelf-life and increasing the hygienic quality of foods (Concha-Meyer *et al.*, 2011; Forney *et al.*, 2004; Siamansouri *et al.*, 2013). Therefore, LAB are widely investigated as natural biological agents because of their antimicrobial potential and as a response to the demand for safe, fresh or minimally processed foods, without preservatives and with a longer shelf-life (Serna & Enríquez, 2013). In general, from the industrial viewpoint, LAB are being applied in the production of antimicrobial substances, sugar polymers, sweeteners, aromatic compounds, vitamins, and are also used as probiotics (Aro & Rojas, 2013; Leroy & De Vuyst, 2004).

The term probiotic was redefined in 2002 by the United Nations Food and Agriculture Organization (FAO) and the World Health Organization (WHO) as a "living microorganism that ingested in the right amounts confers a healthy benefit to the host" (Colombo *et al.*, 2014; Miranda *et al.*, 2013). Fermented dairy products are the most used foods to carry probiotic bacteria. The probiotic strains predominating in these dairy derivatives are *L. acidophilus, L. casei,* and *B. lactis* (Geng & Boyer, 2014; Tabasco *et al.*, 2014). These bacteria have been used in recent decades as probiotic supplements in functional food and animal nutrition (Senz *et al.*, 2015). Also, a limited amount of LAB species are used as a starter culture in the meat industry; the main cultures are *L. sakei, L. curvatus, L. plantarum*, *Pediococcus pentosaceus*, and *P. acidilactic*.

CONCLUSIONS

Most papers on *Lactobacillus* production are focused on the production of lactic acid and, in some cases, on evaluating the growth of *Lactobacillus* of industrial importance, mainly for human and animal health, and food. Currently, the best production system for LAB corresponds to the submerged fermentation in a batch regime at mesophilic conditions using whole whey or whey permeate supplemented with nitrogenous materials like yeast extract, soy milk or wheat bran.

Research efforts are being made all over the world to improve the production systems, as well as cultivation methods and media for LAB production. In the case of Colombia, research groups and centers have the responsibility of intensifying their efforts to offer highly efficient technological alternatives to the national industry, that allow the production and application of LAB as a growth factor for the food sector. In this regard, among other aspects, it is necessary to increase the international visibility of Colombian scientific production in this area, as it is evident from the results of this review. Thus, national researchers will contribute to supply the demand for high quality scientific knowledge on starter microorganisms for fermented foods such as meat, dairy and vegetables, among others; as well as on the culture media in which they are grown (including the use of agro-industrial wastes as raw materials). Furthermore, research in prebiotic ingredients or additives derived from LAB allowing the increase of the benefits to the consumer must be continued.

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