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Research Article

Microbiota of the Vagina

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Abstract

The objective was to review and analyze the microbiota of the vagina. It was analyzed the composition, the different changes through the women's lives and, its defense mechanism. It was reviewed the websites of Pub Med, Google Scholar, Springer, Web of Knowledge, DOAJ, Hinari, Oxford Academic, JAMA Network, Embase, Research Life for English and Scielo, Lantidex, Imbiomed-L, Redalycy Google Scholar for Spanish. Publications from January 1970 to February 2021. Molecular biology technologies have allowed us to have a better vision of the bacterial diversity present in the vaginal microenvironment or microbiota, as well as have allowed us to discover or reveal the existence of bacterial categories until then unknown.

Keywords: Vagina; Microbiota; *Lactobacillus*

Introduction

It is well recognized that in the human body coexists with colonies or bacterials communities or conglomerates that are specific to specific sites of the body such as the testinal gastrointract, the oral cavity, the skin and the vagina, however, the scope of this relationship has recently been recognized with the use of high-performance sequencing techniques (siglas in English: HTS). It is now clear that microorganisms that are closely related to humans exceed the total number of human cells in a ratio of more than 10:1, in fact, the total number of genes in the human genome is surpassed by the number of genes that present the bacterial microbiome in a ratio greater than 1,000 to 1 [1,2].

A microbiome is the sum total of all cells or microorganisms that live in close relationship both inside and outside the human body and all their genes. The term microbiota refers to the bacterial community or colony at a specific site or organ of the human body and has been determined by studies of 16s RNA conducted with HTS techniques. Microorganisms and their communities or colonies or conglomerates have evolved with humans for more than thousands of years. It is now that we are beginning to understand the complex mechanisms that allow us to know the benefits of this mutual interaction but also the alterations of these microbiomes can cause diseases, which has improved our knowledge about this relationship and have a better knowledge and understanding of diseases and human health [2].

The human microbiome maintains a symbiotic relationship with the host that can behave as: 1. commensalism: does not affect the host; 2. mutualism: can positively affect the host and 3. pathogenic: negatively affects the functioning, immunity and supply of nutrients to the host. Thehumanma microbe that is acquired during childbirth changes during the course of the life of the host, especially that of the vagina [1,2].

Recent discoveries have demonstrated the potential of molecular microbiology that has allowed to reveal hitherto unknown characteristics of the human microbiome that are of great importance for human health. Molecular studies have shown the inadequacy of

some classical methods used in bacteriology and have shown that less than 10% of the microorganisms in the human microbiome are not cultivable by traditional techniques, depending on the anatomical location of the microbiome. The microbiome changes from birth through the years of human life for example in the vagina there is a close cooperation between microbes with the host permit ending a first line of defense against opportunistic microorganisms, this balance is called eubiosis, but when these opportunistic microorganisms exceed or alter this symbiotic balance occurs what is called dysbiosis, leading to an inflammatory process [1,3].

Materials and Methods

We searched the electronic pages of Pub Med, Google Scholar, Springer, Web of Knowledge, DOAJ, Hinari, Oxford Academic, JAMA Network, Embase, Research Life in the English-speaking literature and scielo, Lantidex, Imbiomed-L, Redalyc and Google Scholar in the Spanish-speaking literature, They were used and searched using the terms*:* microbiome, microbiota, vaginal microflora, vaginal microbiota, *Lactobacillus sp.* (a) articles of primary sources published in indexed journals, with a review nature, original research articles, comparative studies, evaluation studies, book chapter sand open access meta-analysis; b) articles in English and Spanish. Letters to the editor, case reports and uncontrolled studies were excluded from the review. Similarly, publications which did not have free access were excluded. We reviewed articles published from January 1970 to February 2021. The primary search yielded the meeting of more than 150,000 publications, after reviewing and analyzing them, they were used for 73articles.

Microbiota of the vagina

The female genital tract is formed by a succession of cavities: fallopian tubes, uterine cavity, endocervix and vagina, which communicate with the outside through the vulvar introito; these anatomical structures allow the exit or externalization of the menstrual flow and the passage of the fetus at the time of delivery, also allows the sexual act but also allow the entry of potentially pathogenic microorganisms that can produce infections in the female genital tract.

The microbiota or vaginal microflora (MBV), without a doubt, represents one of the most important defense mechanisms to maintain reproductive function in perfect conditions since it maintains a healthy environment and prevents the proliferation of potentially pathogenic microorganisms in the vagina [1,2,4].

History

Anton Van Leeuwenhoek, the father of the microbiol I heard and inventor of the microscope was the first to observe a colony or conglomerate or human bacterial community when used as a sample scraping of their teeth. At the beginning of the nineteenth century, the studios of numerous researchers of the time were added to través of techniques of culture aerobics and anaerobics that allowed to study the human microbiome, as well as, the increase in the knowledge of this area [4].

In 1892, Albert Döderlein was the first to describe the importance of bacteria in a woman's vagina, which produce lactic acid (AL), constituting the normal vaginal flora and being responsible for the inhibition of pathogenic ri anbacte such as facultative anaerobes. But it was Krönig in 1985, Döderlein's work company, who first differentiated lactobacilli cells from anaerobic bacteria. *Lactobacillus* is cultivated by Curtis in 1913 and was later named Mobiluncus curtisii by Spiegel and Roberts in 1984 but subsequently the name *Lactobacillus* acidophilus has been proposed for this bacterium [4].

At the beginning of the twentieth century, Manu in Fiji, studies and describes the vaginal flora in pregnant and non-pregnant women, as well as the vaginal flora from the birth of the girl to the senescence. Robert Schröder in 1921 describes 3 types of bacterial flora and vagina: 1. Normal aginal flora; 2. vaginosis bacteri ana (VB); 3.another bacterial flora. Then in 1930, Ludwig Nürnberger agrees with Döderlein's opinion that there are only 2 types of vaginal flora: normal and abnormal [4].

In recent years the emergence of new molecular and genetic technologies have allowed a more in-depth study of bacteria including *Lactobacillus,* as well as the interactions between them and with their biofilms, as well as determining the genetic differences of the different types of microorganisms of the vaginal flora. Before these techniques, it was known that there were microorganisms that could not be culture dados "ex vivo", so part of the human microbiome remained dark. With the advent of the teascnic as amplification, cloning and sequencing of bacterial genes using the technique of amplification of bacterial messenger RNA (if glas in English: rRNA 16S) in vaginal secretion samples has allowed a deeper and more adequate study of lactobaculation and all microbial species present in the sample. This has provided a better and more accurate description of the human ma microbe and of the MBV. Likewise, these techniques have made it possible to deter-

mine that *Lactobacillus sp*. (LB) is not always the dominant species in the MBV [5,6].

Molecular studies have shown the inadequacies of the methods of classical bacteriology and as mentioned above, these techniques have allowed to recognize, depending on the anatomical place studied, that less than 10% of the microorganisms that are part of the human microbiome are not cultivable. Similarly, these molecular microbiology techniques have proven to be potentially useful in revealing hidden or unknown characteristics of the human microbiome, and of course of the vaginal microbiota, as well as their impact on health [2].

One of the most important anatomical sites to study its microbiota is the vagina, in part because its bacterial microenvironment has been studied extensively using classical microbiology techniques and has allowed to establish or clarify the different colonies or conglomerates or communities of bacteria that colonize the vagina and their interactions that allows to maintain a vagina without pathology or infection.

There is a mutual relationship between the vaginal physiology of women and MBV, including with physiological or hormonal changes that occur during the menstrual cycle, from birth to postmenopausal, this means that the composition of the vaginal microflora is not constant and presents modifications or variations in response exogenous and endogenous factors [5,7-9]; these factors include the different stages of the menstrual cycle, menstruation, pregnancy, use of oral contraceptives, frequency of sexual relations, use of douches and vaginal deodorants, use or ingestion of antibiotics and drugs with immunosuppressive properties [1,3,5,9-11].

Results and Discussion

The composition and structure of the MBV has been studied and described very well since the use of the light microscope until today with the use of sequencing techniques. More than 250 species of bacteria have been described in mbv using HTS, these include (alphabetical order): *Actinomyces, Aerococcus, Allisonella, Alloscardovia, Anaerococcus, Arcanobacterium, Atopobium, Bacteroides, Balneimonas, Bifidobacterium, Blastococcus, Blautia, Bulleidia, Campylobacter, Citrobacter, Coriobacteriacea, Corynebacterium, Enterobacter, Escherichia, Facklamia, Faecalibacterium, Finegoldia,Gardnerella, Gemella, Haemophilus, Lachnospiracea, Massilia, Megasphera, Mobiluncus, Mollicutes, Moryella, Olsinella, Parvimonas, Peptinophilus, Peptostreptococcus, Prevotella, Porphyromonas, Proteobacteria, Providencia, Rhizobialis, Ruminococcaceae, Salmonella, Shigella, Shuttleworthia, Sneathia, Solobacterium, Staphylococcus, Streptococcus, Veillonella, Ureaplasma,* and *lactobacilli* sp. [4,12]. Table 1 shows the microorganisms most frequently found or isolated in the vagina and isolated by conventional procedures. Molecular sequencing techniques or HTS have allowed the detection of uncultivable bacteria that had not previously been recognized or isolated by conventional techniques, causing the establishment of types of colonies or unique microbial communities (acronyms in English: CSTs), based on the abundance and composition of the different bacterial species that colonize the vagina during the reproductive stage of the woman have been classified into 5 types: CSTI To CST-V [1,10,13]. CSTR-I, CST-II, CST-III and CST-V are characterized by the abundance of *L. crispatus, L. gassei, L. iners*, and *L. jensenii*, respectively [14]. However, CST-IV is characterized by being composed of a mixture of anaerobic facultative microorganisms with low levels of LB.sp. CST-IV has been divided into CST-IV-A and CST-IV-B. The CST-IV-A groups the species of the genera: *Anaerococus, Peptoniphilus, Corynebacterium, Provotella, Finegoldia and Sptreptococcus.* The CST-IV-B groups: *Atopobium, Gardnerella, Sneathia, Molbiluncus, Magsphera and Clostridiales* [1,10,13,14]. Kalia., *et al*. [1] mentions that it is debatable whether this CST-V represents a normal state or an asintomous state of abacterial vaginosis. However, some authors [1,10] consider that the composition of CSTs is not the only indicator of dysbiosis.

Coconuts and gram-positive bacilli aerotolerant anaerobes	*Lactobacillus* *Streptococcus*
Gram-positive coconuts and bacilli facultative anaerobes	*Corynebacterium* *Gardnerella* *Staphylococcus* (especially *S. epidermidis*)
Gram-negative bacilli facultative anaerobes	*Escherichia* *Klebsiella* *Proteus*
Mycoplasmas	*Mycoplasma* (especially *M. hominis*) *Ureaplasma*
Bacilli and gram-positive coconuts strict anaerobes	*Atopobium* *Peptococcus* *Peptostreptococcus* *Clostridium* *Bifidobacterium* *Propionibacterium* *Eubacterium*
Gram-negative bacilli strict anaerobes	*Bacteroides* *Prevotella*

Table 1: Common microorganisms in the vagina of healthy women.

Vaginal microbiota through the life of the woman

The vaginal mucosa acts as a protector of the lower genital tract against pathogens including the acquired non-deficiency in mu virus (HIV). The vagina produces a surfactant protein A (SP-A) that provides the natural defense to the vagina, producing opsonization of pathogenic microorganisms, alters the levels of pro-inflammatory cytokines, stimulates oxidative processes by causing cellular phagocytosis and stimulates the differentiation of antigens presented to cells; this adaptive immunity is linked to immunity innata [15]. Different studies have shown the composition of the MBV also, contribute to the defensive properties of the vaginal mucosa such as *L. crispatus* that increases or strengthens them and *L. iners* weakens them [16,17].

As we mentioned previously, the composition of the MBV changes during the woman's life from birth; changes in the structure of the vaginal epithelium and hormonal changes have been suggested to play a fundamental role in this [1,3,10,11] (See figure 1).

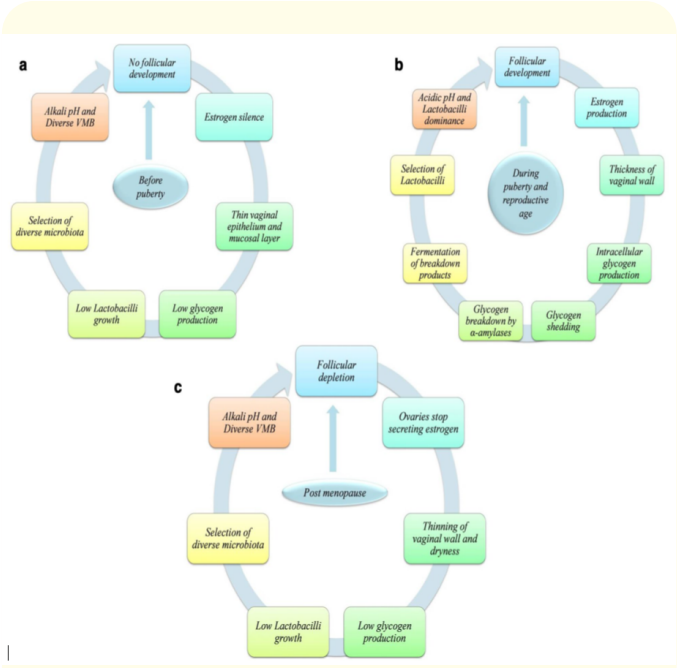

Figure 3: First post reduction splint.

At birth

The initial colonization of the vagina by microorganisms is carried out from the maternal vagina at the time of delivery or from the hands of the 1st person holding the girl during the cesárea [18]. Wylie col. [19] refer that the LB appears in the vagina of the newborn girl at 24-48 hrs. of birth. It is suggested that, within the first few weeks of birth, microorganisms are able to differentiate into different colones or communities in both vagina and intestines and skin [18]. During the first weeks of age, the girl possesses estrogens borrowed from the mother, which allows the proliferation and maturation of the vaginal epithelium plus the presence of the L *sp.*, favors the synthesis of AL [20]. At the time of its birth a full-term girl has the vagina impregnated with estrogens borrowed from the mother and you can find changes similar to those we will find when, the girl enters puberty, during adulthood and fertile stage, that is, with remarkable development of the vaginal epithelium. The 4 layers are distinguished and have a thickness of 500 to 1,000 µ, most of it is composed of the intermediate layer quite hyperplasia, composed up to 25 rows of intermediate cells. Of course, in the newborn girl, it is obtained in significant amounts of glycogen no by the action of the estrogens borrowed from the mother until the 3 to 4 weeks of birth when the estrogenic levels borrowed begin to fall or disappear [19]. These tantor anatomical, physiological and biochemical changes that can be observed in the newborn girl are transient and disappear when the estrogens borrowed from the mother are metabolized and eliminated. Then, towards the 2nd to the 4th day of birth, the cellular desquamation increases, likewise, as the borrowed estrogens are metabolized the epithelium is progressively reduced, and for the day to 14º, the epithelium only presents a few rows of basal cells.

Before puberty

Mbv during childhood presents a CST-IV, a neutral or elevated pH and a thin stratified flat mucosa with a thin epithelium with only 3 to 8 rows of cells with predominance of basal and parabasal cells. In the girl before the entry to puberty, the ovaries are at rest or do not produce estrogens, causing very thin mucosa and, the lack of glycogen production, by con following, a low growth of the L *sp*., which produces a neutral or alkaline pH in the vagina [21].

Puberty and reproductive age

With the arrival of puberty begins follicular development and therefore the production of estrogens (Es). Elevated levels of Es stimulate the proliferation and thickening of the vaginal epithelium with increased production of intracellular glycogen [3]. The desquamation and cytolysis of the cells of the vaginal epithelium promoted by hormonal changes, allows the availability of free gly-

cogen in the vagina, which is processed by the α-amylase present in the vagina [22]; glycogen and its products of metabolism such as maltose and maltotriosa are fermented by the *L. sp* producing AL, producing acidification of the vagina and bacterial domination of L. *sp.* in MBV (CST I, II, II and V) with the exception of CST-IV, which can be found in some women [3,23]. As mentioned above, during the phases of the menstrual cycle, the effect of hormones, estradiol (E2) and progesterone (P), produce changes in the vaginal epithelium that are manifested in the vaginal microenvironment such as the promotion of the growth of *Lactobacillus*. Estrogens stimulate the growth and maturation of the vaginal epithelium such as intermediate and superficial cells and stimulates the synthesis of intracellular glycogen in these cells. P promotes cytolysis of epithelial cells in the vagina. These glycogen-rich cells release glycogen that is metabolized by LB, as well as other bacteria that use glucose and maltosa, and produce AL that as we mentioned previously gives and maintains the acidic pH to the vagina. Different studies have shown that the MBV varies from one woman to another [24,25]. These studies have shown that in some women the MBV changes from one CST to another in a short period of time, while in others the MBV remains relatively constant, that is, without modifications or changes with dominance especially of *L. crispatus* [10,13]. These changes in TSA appear to be caused by menstruation [10,11]. In 81% of menstrual cycles, the levels of *Gardnetrella vaginalis* (Gv) together with *L. iners* increase significantly with the menstruación and decrease as the end of it approaches, while the levels of *L. crispatus and L. jensenii* behave in the opposite way [11]. This puede be attributed to the availability of iron during menstruation, favoring the growth of *Gv* and *L. iners.* Through the woman's years, while the ovaries are producing es, the levels of glycoor gene will remain high, which will remain stable until she reaches menopause [9,26].

Menopause and post-menopause

As the ovarian follicles are depleted, menopause manifests itself hormonally, biochemically, anatomically and histologically, the effects on the epithelium of the vaginal mucosa are observed. As a consequence of the depletion of the follicles, the synthesis of the Es begins to affect and lower their levels, which causes thinning of the thickness of the mucosa by the decrease of the num of rows of células of the different layers of the flat-stratified epithelium, also, it is accompanied by the decrease of the levels of glucógeno and with it of the levels of the LB that with leads to decrease of the levels of AL and elevation of the vaginal pH. In the post-menopause, the vaginal mucosa is observed with characteristics similar to the prepubertal stage; the MBV to predominance of lb changes to a microbial diversity that is to cst-IV with reduction of vaginal secretions, dryness, elevation or pH and therefore dyspareunia occurs when having sex. In other words, the MVB of the menopause land post-menopausal women resembles the MBV of the prepubertal stage, suggesting that reproductive physiology plays a fundamental role in the characteristics of the woman's MBV in her reproductive years [27].

Vaginal lactobacation

Since the first microbiological study of the human vagina, conducted by Döderlein, LB have been consistently described as the dominant microbes in it. Therefore, it is considered that they have a critical role in the maintenance of the vaginal ecosystem by preventing the excessive proliferation of undesirable microorganisms such as Gv, *also* prevents colonization by pathogenic microorganisms, generators of urogenital pathology [2]. It is also true that the vagina can be colonized by other alternative bacteria such as *Atopobium* so an MBV dominated by LB is not an absolute requirement [28,29], however, the presence of these microorganisms is sporadic so it is sique considering the presence of LB fundamental to maintain the homeostasis of the vagina or mbv [30].

Lactobacillus have various forms from very elongated to very short, from straight to curved and even spirited forms. They are usually included in the broad and heterogeneous group of lactic acid (LA) producing bacteria, characterized by being gram-positive, not sporulated and with a strictly fermentative catabolism of sugars, whose predominant final product is said organic acid. AL is produced in a sufficient amount to keep the pH of the vagina at an acidic level, between 3.5 to 4.5. In general, *Lactobacillus* are anaerobic bacteria tolerant of the aerobic medium and have a small genome so they are very demanding from the nutritional point of view.

The identification of the species of *Lactobacillus* of the vagina will depend on the method used; a disparity in the findings can be observed when we use methods that identify the phenotypic characteristics of those methods that identify genotypic characteristics. The disparity between the methods of phenotypic (culture and isolation) and genotypic (HTS/16s RNA) identification appears to be due to the intraspecific biochemical diversity of vaginal *Lactobacillus* and the absence of some species in the database.

Taxonomy

The precise ascription of the *Lactobacillus* isolated from vagina to specific species will depend on the identification methods used, observing a disparity in the data obtained when using techniques that reveal phenotypic qualities and those that determine genotypic properties. In the dependent methods of cultivation are usually included within the genus *Lactobacillus* bacillary isolates, non-sporulated, gram-positive and catalase negative. Additionally, development in MRS medium can be used as a criterion, although this last requirement may leave out some species such as *L. iners.* In any case, in primary isolates lactobacilli behave like fastidious organisms, and incubation in media enriched with heme (hemin, hemoglobin or blood) and the atmosphere enriched in CO_2 or even anaerobic is advisable. Once purified, the isolated LB are usually subjected to identification tests that, traditionally, consist of determining the ability of the strain to ferment different sources of carbon and decrease in media with increasing concentrations of salt1 [2,18]. More recently miniaturized galleries have been used and both these tests and others indicate that the vagina is preferably colonized by *L. acidophilus* 4 [18,31,32] and/or *L. fermentum* [33]. However, when genotypic methods of identification are applied to the same germs, neither can be attached to either of these two species, and the predominant ones are *L. crispatus, L. gasseri* and *L. jensenii,* whether one analyzes the degree of homology of the chromosomal DNA [34,35] when determining the genetic fingerprinting [36] or the sequences of the 16S rRNA [28,37]. Through these methods are also detected in the vagina other species such as *L. iners* [27,38] and *L. vaginalis* [32]. This disparity between phenotypic and genotypic methods, as mentioned above, appears to be due to the intraspecific biochemical diversity of vaginal *Lactobacillus* cells and the absence of some species in the databases.

Larsen., *et al*. [38] reported that quantitative studies in vaginal washes have found ~107 *Lactobacillus* per gr of secretion. The most frequent LB are *L. acidophilus and L fermentum* and the least frequent or common are *L. plantarum, L. brevis, L. jensenii, L. casei, L. delbrueckii* and *L. salivarius.* Rogosa., *et al*. [31] mention that more than one species may be present in a woman.

Homeostasis vaginal

The properties of the MBV that allow it to colonize the mucosa and prevent the establishment or excessive proliferation of potentially pathogenic microorganisms are of two types: a) specific adhesion to epithelial cells and pathogenic microorganisms, and b) the production of antimicrobial compounds.

Specific adherence

The protection of the vaginal mucosa depends on the specific recognition between the superficial structures of the *Lactobacillus* (adhesins) and the epithelium (receptors).

Adhesins are part of the glycocaly of the cell wall and their composition seems to be varied, lipophilic acids [39], extracellular proteins [40], carbohydrates and glycoproteins [41,42] have been described. In relation to the receptors located on the surface of the epithelium does not knows much, however, it has been found that fibronectin, which is a glycoprotein that is part of the extracellular matrix, is recognized by the LB that have been isolated in the vagina whose union is favored by the acidic pH of the vagina, así, there are strains that do not bind at neutral pH as if they do at acidic pH of 4 [43]. Inaddition, the low binding capacity of anaerobic intestinal bacteria to fibronectin [44] favors the stability of MBV. Likewise, the union of the *Lactobacillus* could be directly to the glycolipids of the membrane of the cells of the vaginal epithelium in a process mediated by divalent cations [41]. The result of the association of lb and vaginal epithelium is the formation of a biofilm that protects it against colonization by unwanted and pathological microorganisms [41], to this fact is added the ability of vaginal LB toco-add with microorganisms potentially pathological. Most of the bacteria of the MBV have in the property of auto-add, this property that desaturase when adding the enzyme proteinase K, so this property depends on the production of an extracellular protein [41].

Production of antimicrobial compounds

Organic acids (Acido láctico)

The physiological pH of the vagina is acidic with a range of 3.5 to 4.5,with an average value of 3.5 ± 0.2 and an average of 4; this acidic pH causes an acidic environment in the vagina, which is attributable to the accumulation of LA [2,22], partially or totally inhibits the development or growth of most of the bacteria from the digestive tract and those of environmental origin, this being a very effective natural protection mechanism of the vaginal mucosa [2]. As mentioned above, the origin of vaginal acidity is the LA that is generated as a final product of the fermentative metabolism of carbohydrates, specifically glycoallergen no, released by cytolysis of the desquamated superficial and intermediate cells of the vaginal epi-

thelium, by the *Lactobacillus*. This occurs from menarche to menopause so it is the glyc orgeno produced by the cells of the vaginal epithelium, considered the main source that allows to maintain the acidic pH of the vagina [1,2] because of this there is the widespread belief that the LB metabolize the glycogen to glucose and this in turn, to AL, however, different authors [18,30,44,45] have reported that the glycor geno produced by the céepithelial cells of the vagina is degraded or glucose by the cells of the vaginal epithelium themselves, so that the role of the LB would be only the degradation of glucose to LA responsible for maintaining the MBV and prevent the colonization of the vagina by unwanted microorganisms bless. The support for this assertion is based on finding the L (+) and D (-) isomers of LA in amounts similar to acid. The formation or generation of these isomers is characteristic of lb while epithelial cells generate the isomer L (+) [46,47]. However, Boskey., *et al*. [47] suggest that the vaginal protective level of LA depends primarily on the MBV, but the cells of the vagina contribute between 4 to 30% of the total LA produced in the vagina. As mentioned above 5 the LA present in the vagina comes in the form of two isomers: D(-) and L(+). Nasioudis., *et al*. [48] suggest that the amount of glycogen available in the vagina by exfoliation of surface and intermediate cells rich in glycogenois due to the action or activity of hyaluronidadse-1 and the matrix of metalloproteinase (acronym in Englishés: MMP), this allows the α-amylase to degrade the glyco geno available in the vagina, which, is converted into AL D(-) by the LB, however, no correlation was found between the isomer of AL L(+) with the α-amyltosa, suggesting the isomer D(-) is responsible for maintaining the vaginal pH ≤ 4.5 and prevent the growth of other bacteria. Hearps., *et al*. [49] suggest that these 2 isomers of AL induce an anti-inflammatory response in cervico-vaginal human cells against acquired immunodeficiency virus(HIV); likewise, Wagner., *et al*. [50] found that the D(-) and L(+) isomers of AL inhibit deacetylase, thus increasing dn are view, regulating the transcription or transcription of genes associated with them. Differences authors [23,51-53] has suggested that LA inhibits a wide variety of infectious agents including *Chlamydia trachomatis, Herpes Virus Simplex type 2 (HSV-2), HIV, HIV-1 and* a wide range against bacteria involved in the production of bacterial vaginitis tone. It has been shown that LA affects the immune response of the vagina through different mechanisms such as 1.- increased production of the anti-inflammatory mediator such as the interleuquine-1 antagonist receptor(IL-1RA) by vaginal epithelium cells, 2.- inhibition of the production of pro-inflammatory mediators such as Il-6, IL-8, tumor necrosis factor-alpha (acronym in English: TNF-α),the regulator of the activation of expressed and secreted T cells (Acronym in English; RANTES), and protein-3 alpha of the inflammatory macrophage(MIP3α) [48]; 3. the release of the growth-transforming factor-beta(TGF-β) to stimulate the antiviral response; 4. the stimulation of T Helper 17 (Th17) belonging to Tinfocytes, through the productionofIL-23 when exposed to bacterial polysaccharides; and 5. the increase of AL at the cytosolic level, which blocks the production of cyclic adenosine monophosphate (acronym in English: cAMP) which increases the autophagy capacity of the epithelial cells of the vagina to degrade microorganisms and maintain homeostasis. In general, these studies suggest different defensive properties of LA beyond the role or function of isomers. These separate properties or joints determine the susceptibility of the host and its relationship to the MBV [1].

Hydrogen peroxide

Hydrogen peroxide (H_2O_2) is another antimicrobial substance produced from the presence of O_2 and its production appears to be common among certain LB species such as *L. crispatus* and *L. jensenii,* while it is exceptional in others such as *L. fermentum* and in LB that preferably inhabit the intestine, such as *L. plantarum* and *L. casei,* even if they are isolated from the vagina [57,58]. O_2 levels in the vagina are low in order to maintain an atmosphere or anaerobic environment [1]. The strains producing H_2O_2 are more stable and sufficient in the vaginal environment [59] to protect the mucosa against alterations caused by unwanted microorganisms [1,2,60,61], including those producing sexually transmitted infections (STIss) such as *Neisseria gonorrhoeae* [62]. The antagonistic or bactericidal effect is greater when associated with LB species such as *L. crispatus* or *L. jensenii* [58]. Eschenbach., *et al*. [60] mentions that the H_2O_2 produced by LB in the vagina may be a non-specific antimicrobial mechanism to maintain the normal vaginal ecosystem or MBV. The bactericidal effect of H_2O_2 is determined by its oxidizing capacity and by the generation, from it, of metabolites such as the OH–radical, which damage the integrity of cellular DNA. This effect is enhanced by myeloperoxidase and halide radicals, such as Cl–, which are abundant in biological secretions and whose high concentration in the mucus of the cervix, especially during ovulation. Boris., *et al*. [41,42] showed that the H_2O_2 produced by the vaginal LB has a protective role against the Gv, suppress the overgrowth of *Candida* and the formation of hyphae. However, the protective role of H_2O_2 in MBV is debatable [1].

Bacteriocinas

They are polypeptides with antimicrobial activity that unlike peptide antibiotics, are synthesized in ribosomes. Lactic acid bacteria produce a multitude of bacteriocins, some of which, like nisin, are used as a food preservative. These molecules can produce the opening of pores in membranes and even cell lysis, since some bind to lipid II of the wall, this lipid is recognized by vancomycin [65,66]. Although multiple activities compatible with the production of bacteriocins by LB of vaginal origin have been described but there are only two in which there is evidence: one of them is a peptide of 3.8 kDa active on strains of Gv, while the other inhibits various strains of *Enterococcus*. Bacteriocins include bacteriocins IIa, IIc, and J46, acidic ACIDIC IF221A, gas sericin T and lanthbiotic type-A, which are protein substances with bactericidal activity and synthesized or produced by LB in particular by *L. crispatus* and *L. gasseri*. Bacteriocins permeate the cell membrane of pathogenic microorganisms such as *Staphylococcus aureus, Klebsiella spp., Escherichia faecalis and Escherichia coli,* playing a role in preventing their growth. However, the actual antagonistic role of bacteriocins is not well known, since their bactericidal effect has only been proven in *vitro* [2].

Surfactants

They are amphibyl compounds, called amphibophilic or unfriendly molecules, originate or produce a decrease in surface tension, favoring the solubilization of hydrophobic substances. Two surfactants have been described, one produced by the strain *L. acidophilus* and the other by *L. fermentum,* which inhibit the adhesion of *E. faecalis* and *E. coli,* but not that of *C. albicans,* to the silicone gum of urinary catheters). Unfortunately, it has not been proven whether they also inhibit the adhesion of unwanted bacteria to the cells of the vaginal epithelium. On the other hand, surfactants solubilize lipids, so that they could be lethal to enveloped viruses and mycoplasmas, which would be especially susceptible because they lack a cell wall.

Conclusion

In summary, for almost 2 decades with molecular microbiology techniques we have a better idea of the complexity of MBV that has allowed us to identify or know not known bacteria, which are important in MBV. Also, it has been learned that a single bacterium is not the only important component of MBV. HTS techniques have allowed us to have a better view of the bacterial diversity present in the vaginal microenvironment, as well as allowing us to discover or reveal the existence of bacteria categories hitherto unknown.

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