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Aspects of the therapeutic approach to vulvovaginal candidiasis

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ABSTRACT
Vulvovaginal candidiasis is an infection of the vulva and vagina caused by various types of Candida spp. This condition affects 75% of all women at least once in their lifetime, occurring more frequently during their childbearing years. The transmission of this fungal infection occurs through contact with mucous membranes and secretions on the skin of patients or patients, sexual contact, contaminated water and vertical transmission. Some other characteristic symptoms more seen in cases of VVC are white, creamy and flat lesions, being more intense in the premenstrual period, when the vaginal acidity increases. numerous antifungals are available on the market which are available for oral administration in tablet form or, for topical use, in the form of creams, lotions, vaginal tablets, suppositories and coated tampons. The general objective of the work was to analyze, through a literature review, conventional and alternative treatments for the therapeutic approach of Vulvovaginal Candidiasis in its context, using definitions, epidemiological data and its symptoms in society. The present work is an integrative review, which had data collection carried out from March 2021 to October 2021 in the Lilacs, Scielo, Google academic databases. The search resulted in 902 articles, of which 14 met the inclusion criteria. The search for treatments against vulvovaginal candidiasis has been shown to be wide according to the selected articles. We conclude that the vulvovaginal candidiasis pathology has been showing resistance in some therapeutic approaches, as well as some women do not adhere to any type of treatment, due to lack of knowledge about the pathology.

Keywords: Vulvovaginal Candidiasis, Therapeutic Approach, Treatment of Vulvovaginal Candidiasis.

1 INTRODUCTION

Vulvovaginal candidiasis is an infection of the vulva and vagina caused by several types of *Candida spp*, a genus of symbiotic fungi of the vagina and digestive mucosa. It can cause diseases in certain conditions that alter the vaginal environment (FIDEL, 2002).

The composition of the vaginal microbiota has as characteristic the presence of several microorganisms for environmental reasons of the vagina, when this vaginal environment undergoes certain changes can occur infections, among them the infection by fungi of the genus *Candida SP*, after this infection begins a pathological process named CVV vulvovaginal candidiasis (HICKEY et al., 2012; HOLLANDA AAR et al., 2007). To learn more about the pathology, we must know about the Gender *Candida ssp,* which consists of approximately 200 different species of yeasts, which

normally live in the most diverse body niches and, more, commonly in the vaginal region. Among the species that make up this genus, the species *Candida albicans* presents greater relevance due to its prevalence rate in normal conditions and disease (KURTZMAN et al., 1998; Odds et al., 1988; RIPPON, 1974). Being considered the most pathogenic species for humans, the *Candida albicans* presents virulence factors that include tissue adhesion, formation of hyphae and pseudohyphae, tissue invasion and formation of biofilms (CALDERONE & FONZI, 2001).

In the area of medicine, the word treatment has as its definition a set of means of any kind, whether hygienic, pharmacological, surgical or physical, whose purpose is the cure or relief of the disease or its symptoms, after the elaboration of a diagnosis, however, the availability of adequate antifungal drugs for the therapeutic approach to *Candida spp*. infections, is with deficit numbers (NAGLIK ET AL, 2003; BRAZIL, 2020).

Vulvovaginal candidiasis (CVV) affects 75% of all women at least once during life, occurring most often during childbearing age (ADESIJI et al., 2011, GANDHI et al., 2015). Going more into the prevalence, according to a study by Holanda et. al (2014) the incidence of vulvovaginal candidiasis is variable, ranging from approximately 25% in the general female population to 42% among adolescent women. This infection is also characterized by the second most common cause of vaginitis. It is estimated that between 70% and 75% of women of reproductive age will experience at least one episode of CVV throughout their lives and, of these, 50% will have a second episode of the infection (GONÇALVES et al., 2016).

The transmission of this fungal infection occurs through contact with mucous membranes and skin secretions of carriers or sick, sexual contact, contaminated water and vertical transmission during natural childbirth (BRAZIL, 2010). As previously stated, the yeasts of the genus *Candida* are part of the normal microbiota of the vagina of women, so sexual intercourse is not considered the main form of transmission of this microorganism (BRAZIL, 2006).

However, there are several risk factors for this transmission, the authors Rosa and Rumel, (2004) report that Antibiotics, oral contraceptives, diabetes, pregnancy, use of tight clothing, absorbents and specific immune deficiencies are part of these risk factors for CVV. It is believed that inadequate hygienic habits may also be possible predisposing factors of vaginal contamination by Candida, among them, the perineal hygiene performed in the direction of the anus to the vagina, and residues of feces present in the underwear (namely, panties), could be the origin of yeasts in the development of vulvovaginal candidiasis (ROSA E RUMEL, 2004). Another risk factor for the installation of this type of infection is changes in vaginal pH. With the change of pH in the vaginal region, caused most often by the variation of hormone levels and intimate hygiene habits (GUPTA S et, al., 2019). *Candida* sp is capable of causing infection in an acidic vaginal environment with a pH between 4.0 and 4.5, while vaginal infections caused by bacteria occur at an alkaline pH, greater than

4.5 (SOBEL, 2007; BRADFORD; RAVEL, 2017). It is also considered that hygiene practices, such as the use of vaginal douches, can cause local allergies and hypersensitivity reactions, facilitating the installation of *Candida* sp in the vaginal mucosa (PATEL et al., 2004).

Regarding the symptomatology of CVV, it is observed, in most cases, urinary and sexual complaints such as: dysuria and dyspareunia, as well as anxiety about the manifestations (RODRIGUES; SIMONS; DINIZ, 2009; MURDOCH et al., 2013). Some other characteristic symptoms most often seen in cases of CVV, are white, creamy and flat lesions, being more intense in the premenstrual period, when vaginal acidity increases (ALVARES et al., 2007; MORAES, 2008).

In addition, CVV may present a symptom considered typical of the disease: vaginal discharge, which is whitish with the appearance of cream, that is, semi-pasty, accompanied by an intense release of chemical substances in the region of the vaginal portion of the cervix, and may spread to the groin and anal region, causing irritation that causes intense itching on the skin (BENTO, 2004).

In the male case, as for the pathology, genital candidiasis turns into balanitis, in which accumulation of greater or lesser intensity of erythema, edema and white secretions is observed in the cleft of the foreskin of the glans (GUTEMBERG et al, 1990).

CVV is a frequent diagnosis in gynecology, being the most common type of vaginitis in tropical countries (HOLANDA et al., 2007). The diagnoses defined by culture are not common in field studies on CVV pathology, they are based on anamnesis and clinical diagnosis (ROSA, RUMEL; 2004). According to Almeida Filho (2001), to obtain the clinical diagnosis of CVV, the following aspects are evaluated: vulvovaginal itching and burning, excoriations, edema and vulvar erythema, dyspareunia, white vaginal secretion, flocculated, thick and odorless. The presence of one or more of these clinical signs allows the presumptive diagnosis of CVV. Patients who are immunosuppressed with severe diseases, by surgery or immunosuppressive therapy, may have more severe symptoms of CVV (ROSSI et al., 2011).

2 OBJECTIVES

2.1 GENERAL OBJECTIVE

To analyze, through a literature review, conventional and alternative treatments for the therapeutic approach of Vulvovaginal Candidiasis, contextuating it, using definitions, epidemiological data and its symptomatology in front of society.

2.2 SPECIFIC OBJECTIVE

Use the literature review to describe pertinent advances in the treatment of patients with vulvovaginal candidiasis.

3 JUSTIFICATION

Candida species are pathogenic, ubiquitous fungi and considered one of the most common causes of fungal mucosal infections in humans. *Candida albicans* is a polymorphic microorganism that reproduces by budding and that commonly lives commensal in the reproductive and gastrointestinal tract in approximately half of the population (FIDEL, 1998).

When the balance of normal flora is disrupted or immune defenses are compromised, Candida species can become pathogenic, causing recurrent diseases mainly in women, and in susceptible individuals. As a result, Candida infections are recognized as a serious public health challenge with high medical and socioeconomic importance.

Given the relatively limited number of adequate and effective antifungal drugs and the continuous increase in the incidence of *Candida infections*, there is still much to be studied regarding the identification of the fundamental pathogenic determinants for *C. albicans,* in addition to the reciprocal mechanisms of host protection against this fungus on mucosal surfaces and in invasive conditions (NAGLIK ET AL, 2003).

Another aspect that made us interested in the theme in question was to have participated, in an internship field, as students of the nursing course, in a research at the Clinical Research Unit of the Hospital das Clínicas, in the city of Ribeirão Preto - SP, in the development of an alternative therapeutic approach to vulvovaginal candidiasis (CVV), in which, women attended at the referred hospital and who presented CVV, were invited to test the alternative treatment under development based on propolis gel, made available in partnership with the private company: Apis Flora Industrial e Comercial Ltda.

In this sense, the present academic treatise aims to concern the analysis of data on treatments for vulvovaginal candidiasis infection, seeking to show the reader how much the disease is present in society, what types of treatments can be used, and in which cases they should be the method of choice.

4 METHODOLOGY

4.1 METHODS USED

4.1.1 The present work is an integrative review

The overall purpose of a research literature review is to gather knowledge on a topic, helping in the foundations of a meaningful study for nursing. Being a crucial task for reviewers/researchers (POLIT DF, BECK CT, HUNGLER BP, 2004). Taking this purpose into consideration, we elaborated, then, an integrative review with purpose directed to the definition of concepts and review of studies on the treatments used in fungal infection, vulvovaginal candidiasis (CVV).

According to Mendes et al. (2008) the integrative review is developed by six phases in which, in the initial stage, the guiding question is formed, constituting the most precious phase of the review; in the second stage, the inclusion and exclusion criteria of studies are analyzed; in the third stage, we

discuss data collection and literature collection; the fourth stage is limited to the categorization of the included studies; The fifth phase is restricted to the judgment of the data found in the selected works and, finally, the sixth and final stage addresses the presentation of the results, presentation of the review or composition of knowledge.

Once the data to be extracted from selected articles were defined, a detailed analysis of the selected literature was performed. The search strategy, objectives, and inclusion and exclusion criteria of the articles were defined throughout the research.

The guiding question defined for the development of this study was: *"What are the conventional and alternative treatments used in the therapeutic approach to vulvovaginal candidiasis?"*.

To survey the articles in the literature, a search was conducted in the following digital libraries: *Google Scholar* (Google scholar), *Medline* (Online System of Search and Analysis of Medical Literature), Scielo (Online Scientific Electronic Library), LILACS (Latin American and Caribbean Literature in Health Sciences).

The keywords used in the research with their respective combinations in Portuguese and English were "Vulvovaginal Candidiasis", "Therapeutic Approach", "Treatment of Vulvovaginal Candidiasis".

Next, the following inclusion and exclusion criteria were defined:

> Inclusion criteria: articles in Portuguese, Spanish and English; published in the last five years, which portrayed the theme related to the object of study of this integrative review, full texts freely available in the selected databases.

> Exclusion criteria: articles that were not presented in full in the databases used, that were not freely available, published more than five years ago and in languages other than Portuguese, English, Spanish. Some repeated articles were found in more than one database, which were selected in the first and excluded in the later.

5 RESULTS

In the LILACS database, 119 (one hundred and nineteen) publications were found, of which 110 (one hundred and ten) were excluded due to age of publication, that is, they exceeded the stipulated time of 05 (five) years, other 03 (three) publications were excluded because they were repeated, 01 was also excluded, because it was not consistent with the theme presented in the present study. Therefore, from this database, 05 (five) publications were included which were in accordance with the inclusion and exclusion criteria already mentioned in the methodology. In the SciELO platform, 06 (six) publications were found, and only 01 (one) was in agreement with the theme of the present study. Thus, 05 (five) publications were excluded. Another database we used was Google Scholar, in which we found 777 (seven hundred and seventy-seven) publications, of which 343 (three hundred and forty-

three) were excluded, because they are unavailable for free consultation of the content, and 424 (four hundred and twenty-four) were excluded because they deviated from the theme proposed here. Thus, 08 (eight) publications met the criteria of this study and, therefore, were included. Therefore, for this bibliographic review, 14 publications were used, according to the distribution in table 1 below, and specified in table 2.

Table 1 – Distributions of selected publications in the databases.

DATABASE (SEARCH ENGINE)	**NUMBER OF ARTICLES - FOUND**	**SELECTION OF PUBLICATIONS**	
		N	(%)
LILACS	119	4	28,5%
SciELO	6	2	14%
Google Scholar	777	8	57,5%
Total	902	14	100%

Source: AUTHORS, 2021.

The 14 publications found for the research were described according to title, place of publication, year of publication, authors, method, and main points of conclusions of the research shown below in Chart 2.

Table 2: Summarization of the information related to the 14 selected articles.

Title	**Magazine/Year**	**Authors**	**Method**	**Key findings**
Susceptibility evaluation and resistance gene study of candida albicans isolates obtained from clinical specimens at the hospital de clínicas da unicamp	UNICAMP/2016	ISABELA HADDAD PERON	Field study	Clinical analysis of resistance of *candida albicans* to types of approach to vulvovaginal candidiasis, comparisons between drugs with low/high rate of resistance.
Prevalence of Candida spp. in cervicovaginal samples and in vitro susceptibility of isolates	Brazilian newspaper of Microbiology, 2017	Tchana Martinez Brandolt et al.	Cross-sectional study	Knowledge of the candida genus and their resistance in some types of treatments.
Risk factors associated with vaginal infection in pregnant women	Multimed. Medical Journal. Granma, 2019	FELIPE GONZALEZ, Nelvys et al.	Analytical Study	Analysis of factors and clinical manifestations in pregnant women, making it possible to

				identify the best type of treatment.
Brazilian Protocol for Sexually Transmitted Infections 2020: infections that cause vaginal discharge	Epidemiol. Serv. Health, Brasilia, 2020	Newton Sergio de Carvalho et al.	Analytical Study	Epidemiological aspects that guide the Brazilian system to deal with situations of sexually transmitted infections that cause vaginal discharge, prevention, symptomatology and treatment.
Garlic for the treatment of vaginal yeast infection Garlic for the treatment of vaginal candidiasis	Magazine chil obstet ginecol, 2020	Sandra Martínez Pizarro	Cross-sectional study	The vision of an alternative treatment, used in patients with vulvovaginal candidiasis.
Recurrent Vulvovaginal Candidiasis: The Role of the Nurse	Ibero-American Journal of Humanities, Sciences and Education – REASE/2021	Crislene da Silva Santos, Irailde Neves Bispo, Otaciana Almeida de Souza	Observational study	The nurse is fully imbued in this process of CVV treatment, being the main contributor to the insertion of new treatments for this infection, enabling the discovery of new clinical findings, to contribute to the therapeutic action.
Fluconazole and Propolis Co encapsulated in Mucoadhesive Nanoparticles for the Treatment of Vulvovaginal Candidiasis	Federal University of Goiás Graduate Program in Biology of the Parasite-Host Relationship/2020	Jacqueline Teixeira	Cross-sectional study	Application of an alternative treatment, used in patients with vulvovaginal candidiasis.
Liquid-crystalline systems as a potential strategy for vaginal administration of curcumin in the treatment of vulvovaginal candidiasis	Universidade Estadual Paulista Júlio de Mesquita Filho/2017	Camila Fernanda Rodero	Cross-sectional study	The antifungal potential of curcumin was potentiated through its incorporation into liquid-crystalline systems.
Treatment of Vulvovaginal Candidiasis and New Therapeutic Perspectives: A Narrative Review	Journal of Physical Therapy Research/2016	Mariana Robatto et al.	Observational study	Search for new means of treatment against vulvovaginal candidiasis.
Clinical characteristics, prevalence and diagnosis of vulvovaginitis in an outpatient clinic in the interior of Rio Grande do Sul	University of Santa Cruz do Sul (UNISC)/2016	Patricia Micheli Tabile, Hérika Lucena, Jessica Chaves, Juliana Fischborn, Renata Becker Juca.	Cross-sectional study	Vaginal discharge is a fairly common symptom in all vulvovaginitis including CVV, and is crucial for diagnosis and for choosing the type of approach to follow.

Vulvovaginal candidiasis in the gestational period: A theoretical approach	Catholic University Center of peccary/2015	Maria Jessica Fernandes, Victoria Pereira Pinho, Liene Ribeiro de Lima	Qualitative study	Cases of candidiasis in pregnancy, citing general aspects of the infection in this period, as well as its prevalence.
Vulvovaginal candidiasis: a literature review with approach to *Candida albicans*	Brazilian Journal of Surgery and Clinical Research – BJSCR/ 2019	Dagmar Mercado SOARES et al.	Observational study	Aspects emerged about the most predominant species in cases of CVV, data
Update on the management of vulvovaginal candidiasis (cvv) and recurrent vulvovaginal candidiasis (cvvr) aimed at improving care for women and pregnant women	Federal University of Minas Gerais/2015	Netya Aparecida Silva Areal	Observational study	Studies suggest that the essentially clinical diagnosis for vulvovaginitis, usual in clinical practice, is considered inadequate, considering the emerging antimicrobial resistance, given the known factors that contribute to trigger this resistance.
A review of the new therapeutic alternatives and main topical formulations used in the treatment of vaginal candidiasis.	Federal University of Santa Catarina Health Sciences Center/2021	Julia Conte	Cross-sectional study	Types of therapeutic approach to vulvovaginal candidiasis, its forms of application, mechanism of action, and its prevalence.

Source: AUTHORS (2021).

6 DISCUSSION

After reading the selected articles in full, the discussion followed in an attempt to answer some questions, among them the guiding question of this work: "What are the conventional and alternative treatments used in the therapeutic approach to vulvovaginal candidiasis?".

The search for treatments for vulvovaginal candidiasis has been broad according to the selected articles.

According to Johal et al (2014), the treatment against candida infection begins from the presentation of symptoms, with the aim of preventing the rampant growth of *Candida*, and in order to reduce the symptomatology. During the treatment for CVV, it is necessary to guide the success of the treatment, regarding the use of medications, being antifungals of topical and/or oral use, and regarding the rigid follow-up of the proposed regimens (AREAL, 2015). Currently, numerous antifungals are available in the market, which are found for oral administration in the form of tablets or, for topical use, in the form of creams, lotions, vaginal tablets, suppositories and coated tampons (SOBEL, 2007).

According to Brazil (2010) for the treatment of CVV, it is recommended Isoconazole nitrate, topical use, in the form of vaginal cream for seven days or eggs of this drug in a single dose. This azole antifungal is classified as imidazole, and its mechanism of action is intended to inhibit the biosynthesis

of ergosterol, which is important for the integrity and maintenance of the function of the cell membrane of fungi. (VON AHN A., 2011). As a second alternative, thioconazole is usually used, and some others such as; Miconazole, Terconazole, Clotrimazole, all of which act with a mechanism similar to Isoconazole. However, *Candida* resistance to antifungals remains a challenge, which may be due to the use of selective therapies with inadequate doses, or due to the increasing use of these drugs in the prophylaxis of fungal infections, which can lead to clinical resistance (GALLE; GIANINNI, 2004). However, according to Sanguinetti et al, (2015), some species of *Candida* may present resistance to treatment with the use of azoles for candidiasis, and this condition has emerged in individuals with opportunistic fungal infections such as candidiasis.

According to Isabela Haddad (2016), antifungals are agents that prevent fungal infections, inhibit the proliferation of these in the body or cause their destruction, dividing into several classes according to their mechanism of action.

Another aspect exposed by Isabela Haddad (2016) concerns the resistance to antifungals, which intensified the search for new treatments, since several antifungals are used in the treatment of CVV, but 5% to 25% of patients have recurrences that may result in some cases in chronic CVV.

However, according to Freitas (2015), the effective therapeutic options currently known in the treatment of CVV are composed of four classes of antifungals, namely: polyenes, triazoles, echinocandins and fluocytosine (Chart 3).

Table 3- Groups of drugs used in the treatment.

Group	**Polyenes**	**Triazole**	**Echinocandins**
Examples	Nystatin	Fluconazole	Caspofugina
	Amphotericin B	Itraconazole	Micafungin
		Voriconazole	Anidulafungin
		Posaconazole	

Source: Adapted from Freitas, 2015.

6.1 POLYENICS

This class of antifungal represents the oldest ever developed, the beginning of its use occurred in the 1920s, and the two drugs belonging to this class most used are nystatin and amphotericin B. (SANTOS, 2018).

The two drugs belonging to the same class have basically the same mechanism of action, that is, they bind directly to ergosterol forming transmembrane channels, significantly increasing the permeability of the membrane and causing the release of monovalent ions K+, Na+, H+ and Cl−, and subsequent yeast cell death presenting fungicidal action, low antifungal resistance but, can interact with cholesterol, components of the human cell membrane and cause serious side effects such as nephrotoxicity (SANTOS, 2018).

Currently, there are few reports of resistance to antifungals of this class, the mechanisms used are not completely known, but there are limitations in use. An example of a consequence of the use of drugs of this group is in relation to amphotericin B, which is widely used in the treatment of invasive candidiasis intravenously and, depending on the case, can cause nephrotoxicity (CONTE, 2021).

6.2 AZOLE

The azoles or azoles, represent a group of antifungal agents, based on two imidazole and triazole nuclei, the main characteristic of this group is the inhibition action of the fungal enzyme lanosine-14a-demethylase, which is responsible for the conversion of lanosterol into ergosterol, directly affecting the fluidity of the membrane of the fungus and the enzymes attached to it. Some drugs known in the market of synthetic fungistatic agents, are derived from the class of azoles such as fluconazole, itraconazole, ketoconazole, voriconazole, feticonazole, isoconazole, posaconazole and ravuconazole, this group is considered quite effective for the treatment of candidiasis and are less toxic than amphotericin B (VIEIRA and SANTOS, 2016; SAINTS, 2018).

Soares et al., (2018) point out that drug therapy with oral azole agents has a slightly better cure rate than therapy with topical antifungals, and most women prefer oral therapy for the comfort of administration.

According to Julia Conte (2021), the presence of resistance to antifungals of the azole class is seen through attribution to prophylactic use, with prolonged exposures and low concentrations.

The use of drugs in the treatment of diseases of this type should be followed according to the etiological agent, identified by laboratory tests, taking into account the adequacy between the drug and the etiological agent (CONTE, 2021).

6.3 ECHINOCANDINS

Echinocandins are water-soluble lipopeptides that inhibit synthesis by non-competitive inhibition of the enzyme 1,3-β-glucan, fundamental for the osmotic balance of fungi, causing cell wall disruption and are available in a formulation. The mechanism of action of this class of drugs is unique within the class of antifungal drugs; Echinocandins have become attractive as they do not have cross-resistance with other drugs and their target is fungal and has no mammalian equivalent. Unlike amphotericin B and azoles (REVANKAR, 2019).

Caspofungin, micafungin, anidulafungin are also drugs belonging to this class, which represents an effective treatment against yeasts of the genus *Candida*, but its use in the treatment of CVV is not usual, because its form of administration is intravenous, which would not be possible, for example, for home treatment, where cases of CVV are actually treated (SANTOS, 2018).

According to Brasil (2020), the best form of treatment remains in the use of combined antifungals, even suggesting a schematized therapeutic approach for the treatment of CVV, as shown in chart 4.

Table 4. Therapeutic approach vulvovaginal candidiasis – drugs.

Clinical condition	Treatment	Observations
First option	Nystatin, an application, vaginally, at night when lying down for 14 days.	Sexual partnerships do not need to be treated, except symptomatic ones.
Second option	Fluconazole 150mg, orally, single dose or Itraconazole 100mg, 2 tablets, 2x/day, for 1 day.	It is common during pregnancy, and there may be relapses due to the favorable conditions of the vaginal pH that are established during this period.
Recurrent vulvovaginal candidiasis	Fluconazole 150mg, VO, 1x/day, on the 1st, 4th and 7th, or Itraconazole 100mg, 2 tablets, VO, 2x/day, for 1 day or Miconazole topical vaginal cream daily for 10-14 days.	Treatment in pregnant and lactating women: only vaginally. Oral treatment and the use of triazoles is contraindicated.
	Maintenance: fluconazole 150mg, VO, 1x/week, for 6 months or Miconazole topical vaginal cream, 2x/week or Miconazole vaginal egg, 1x/week, for 6 months.	

Source: Adapted from the Brazilian Protocol for Sexually Transmitted Infections 2020: infections that cause vaginal discharge.

The use of alternative treatments, that is, treatments without the use of controlled drugs, antifungals or drugs in general, has shown relevance in therapy, we describe some types below.

6.4 GARLIC (*ALLIUM SATIVUM*) FOR THE TREATMENT OF CVV

According to Pizarro (2020), some fungal strains are showing resistance to fluconazole belonging to the triazole group which has become a major concern, forcing a search for an alternative treatment.

In studies conducted in recent years, the use of garlic (Allium sativum) as a treatment of CVV, has been shown to be an alternative with antifungal relevance, being a natural product that inhibits the functions of *candida albicans* penetrating the cell membrane as well as the membranes of organelles, such as mitochondria, which causes the destruction of organelles and, ultimately, cell death (PIZARRO, 2020).

6.5 ESSENTIAL OILS

According to Julia Conte, (2021) herbal products have greater safety than synthetic products in general, noting that the search for natural products to treat infections is old and increasingly frequent, especially to replace conventional therapies in cases of drug resistance.

Essential oils can be synthesized in any organ of the plant, from the root to the seeds, these volatile and clear liquids, are produced by vegetables, having as main function the defense of the plant, in order to ensure its survival (PEREIRA, 2017).

In the human organism these substances produce several biological properties, being a mixture that can contain from 20 to 60 components, among these, the components of higher concentration are the majority in which they usually determine the biological properties of the essential oil (PEREIRA, 2017).

The mechanism of antimicrobial action of essential oils is multidirectional, causing everything from membrane disturbances to inhibition of protein synthesis or synthesis of genetic material. Lipophilic compounds access the cell wall more easily and cause damage to polysaccharides, fatty acids, and phospholipids, resulting in increased permeability of the microbial membrane. This mechanism causes an imbalance in the H+ and K+ cations, affecting the pH and subsequently the functioning of the organelles. (JULIA CONTE, 2021).

Still, according to Julia Conte (2021), oils can inhibit the synthesis of DNA, RNA, proteins and polysaccharides of fungi, as well as disintegrate the mitochondrial membrane.

6.6 HYDROGELS

In the search for another type of alternative therapeutic approach, Julia Andrigletto de Lima, (2015) reinforces that the use of gels as a semi-solid pharmaceutical form is indicated for the treatment of vaginal infections, as well as for topical release of contraceptives. Mainly because they present properties of consistency, adhesion on the surface for a reasonable period.

In general, hydrogels are materials obtained from the copolymerization of monomers or hydrophilic polymers, which when in contact with water, have the ability to retain it in its structure not dissolving (LIMA, 2015).

Julia Andrigleto de Lima, (2015) brings into focus how harmful is the use of antifungals, such as polyenes that have their use limited to skin and mucous membrane infections, caused by *candida*, and can trigger adverse effects such as vomiting and diarrhea.

6.7 GREEN PROPOLIS

According to Jacqueline Teixeira da Silva, (2020) propolis has been shown to be an efficient alternative in the therapy against CVV, it presents itself in varied forms when applied at different

temperatures, being sticky, soft and malleable at high temperatures, and can reach a liquid state when at 60 ºC, 70 ºC or 100 ºC, and solid, brittle when at low cooling temperatures.

Propolis is formed by a set of substances collected from plants, such as nectar and pollen, by bees, mainly of the species *Apis miellifera* (JACQUELINE TEIXEIRA DA SILVA, 2020).

The use of propolis by man is dated back to antiquity, being used from the maintenance of health to the preservation of food. It has been used in pharmaceuticals, food, cosmetics such as facial and body creams, and as oral hygiene formulations (JACQUELINE TEIXEIRA DA SILVA, 2020).

7 CONCLUSION

Each modality of therapeutic approach presents advantages and disadvantages, according to its applicability, its pharmacokinetic and pharmacodynamic process among other possible means that may suggest which would be the most appropriate means of treatment for each case of CVV, as shown below.

Polyenics have some advantages like; wide aspect of action, fungicide, low commercial cost, rare cases of resistance, but some disadvantages are present as; A higher degree of toxicity, use only topical and intravenous, side effects are; Nausea, vomiting, nephrotoxicity, hepatotoxicity, cardiotoxicity and hemolytic anemia.

The use of azoles in the approach has some advantages, because they are of the class of fungicides as well as the previous approach, the use can be topical (cream, lotion, shampoo) and also systemic (tablet), are specific to the cytochrome P450 enzyme, as well as the extended spectrum of action: dermatophytes, fungi, filaments, yeasts and dimorphic fungi. The disadvantages of its use are due to the adverse effect affecting hepatotoxicity and the presentation of cases of apparent resistance.

The Echinocandins are also used as a form of treatment, their advantages are for presenting rare cases of resistance, excellent activity against a variety of candida species, and their low toxicity rate. On the other hand, its adverse effects are; fever, chills, flushing (flushing), skin rash (skin irritation), vomiting and phlebitis.

The use of Garlic (*Allium sativam),* It is also indicated for this type of therapeutic approach, it has advantages for being of low commercial cost, presents rare cases of resistance in addition to being a natural treatment. Already the disadvantages of its use, can be related to low market acceptance and side effects such as; Digestive problems, cramps, gas, vomiting, diarrhea, headache, kidney pain and dizziness, in addition to its use being only topical.

Essential oils, in turn, have the advantages of being; natural, use an antimicrobial mechanism of action being multidirectional. About the side effects found after its use, it can occur; skin irritations, opening of cracks and wounds, its use is only topical.

The use of Hydrogels in the treatment may have advantages such as; be natural and biodegradable, it is presented in topical use and tablets. The disadvantages presented by hydrogels are their high price in trade and their adverse effects; intense burning, redness or irritation on the skin.

The use of green propolis in treatment is also validated by its advantages, being a natural product and of wide aspect, as well as its adverse effects as; allergic reaction in which it causes symptoms such as swelling, redness, itching or hives on the skin, in addition to having a low acceptance in the market.

After analysis, we highlight that currently the therapeutic approach to vulvovaginal candidiasis is comprehensive, but it is possible to identify some aspects to be improved in each type of approach, offering the carrier of the pathology the most effective treatment, taking into account that the choice for the therapeutic approach to be followed should follow a whole individual context of each clinical case presented.

As can be seen, vulvovaginal candidiasis is still a frequent disease among women. Although there are already treatments available, all have the disadvantage of generating some severe adverse effect. Therefore, it is clear the need for the search by the various research groups and pharmaceutical industries for new alternatives for the resolution of this disease in order to find an effective, low-cost drug that brings little or no side effects to patients.

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