

**Medicinal plants Antimicrobial Activity against *Staphylococcus* spp. –
Literature Review****Atividade antimicrobiana de plantas medicinais contra *Staphylococcus*
spp. – Revisão de Literatura**

DOI:10.34117/bjdv5n10-111

Recebimento dos originais: 27/09/2019

Aceitação para publicação: 09/10/2019

Amandha Lara

Mestrado Profissional de Plantas Medicinais e Fitoterápicos na Atenção Básica,
Universidade Paranaense (UNIPAR)
Instituição: Universidade Paranaense - UNIPAR
Endereço: Praça Mascarenhas de Moraes n.4282. Bairro Zona III. CEP 87502-210,
Umuarama, Paraná, Brasil.
E-mail: lara_amandha@hotmail.com

Adriane Cordeiro Trevisani

Mestrado Profissional de Plantas Medicinais e Fitoterápicos na Atenção Básica,
Universidade Paranaense (UNIPAR)
Instituição: Universidade Paranaense - UNIPAR
Endereço: Praça Mascarenhas de Moraes n.4282. Bairro Zona III. CEP 87502-210,
Umuarama, Paraná, Brasil.
E-mail: adrianereunidos@hotmail.com

Isabela Carvalho dos Santos

Doutoranda em Ciência Animal com Ênfase em Produtos Bioativos na Universidade
Paranaense – UNIPAR. Bolsista CAPES
Instituição: Universidade Paranaense - UNIPAR
Endereço: Praça Mascarenhas de Moraes n.4282. Bairro Zona III. CEP 87502-210,
Umuarama, Paraná, Brasil.
E-mail: isabela_carvalhoxd@hotmail.com

Lidiane Nunes Barbosa

Docente no Programa de Pós-Graduação em Ciência Animal com Ênfase em Produtos
Bioativos, Universidade Paranaense (UNIPAR)
Instituição: Universidade Paranaense - UNIPAR
Endereço: Praça Mascarenhas de Moraes n.4282. Bairro Zona III. CEP 87502-210,
Umuarama, Paraná, Brasil.
E-mail: linuba2@gmail.com

Rosana da Matta

Mestrado Profissional de Plantas Medicinais e Fitoterápicos na Atenção Básica,
Universidade Paranaense (UNIPAR)
Instituição: Universidade Paranaense - UNIPAR
Endereço: Praça Mascarenhas de Moraes n.4282. Bairro Zona III. CEP 87502-210,
Umuarama, Paraná, Brasil.

E-mail: rosana.mtt@hotmail.com

Daniela Dib Gonçalves

Docente no Programa de Pós-Graduação em Ciência Animal com Ênfase em Produtos Bioativos e Docente no Mestrado Profissional de Plantas Medicinais e Fitoterápicos na Atenção Básica, Universidade Paranaense (UNIPAR)

Instituição: Universidade Paranaense – UNIPAR

Endereço: Praça Mascarenhas de Moraes n.4282. Bairro Zona III. CEP 87502-210, Umuarama, Paraná, Brasil.

E-mail: danieladib@prof.unipar.br

ABSTRACT

The *Staphylococcus aureus* is one of the most common bacteria in the clinical practice once it uses to colonize the human skin from up to 15% and is easily found in the nasal cavities. It can cause diseases that goes since a simple infection (pimples, boils and cellulitis) until serious infections such as pneumonia, meningitis, endocarditis, toxic shock syndrome, septicemia and others. The present study aimed to analyze the published literature regarding the medicinal plants Antimicrobial Activity against *Staphylococcus* spp., based on the main electronic libraries and database with the purpose of knowing the Antimicrobial Activity efficacy of some Medicinal plants. It is known that several bacteria are beneficial to their hosts, since they provide protection and nutrition against some pathogens and diseases, making difficult the harmful bacteria colonization; however, the bacteria that cause harm to the human health currently have high resistance to most antimicrobial and, based on this affirmative, several technological measures are suggested to solve the bacteria resistance problem, being one of them the look for new antimicrobial from vegetal species. Medicinal plants with therapeutic properties are of great relevance in all the world, especially in developing countries; and as much as the knowledge about medicinal plants is vast these days, it is necessary more and more researches, because for many times these plants are used in a wrong way, consequently, taking a great risk due to the active substances accumulation.

Keywords: *Staphylococcus aureus*, bacterial resistance, staphylococcal enterotoxin, hospital infection, phytotherapy.

RESUMO

O *Staphylococcus aureus* é uma das bactérias mais comuns na prática clínica, uma vez que costuma colonizar a pele de até 15% dos seres humanos e é facilmente encontrada nas fossas nasais. Pode provocar doenças, que vão desde uma simples infecção (espinhas, furúnculos e celulites) até infecções graves como pneumonia, meningite, endocardite, síndrome do choque tóxico, septicemia e outras. O presente estudo objetivou analisar a literatura publicada a respeito da Atividade Antimicrobiana de plantas medicinais frente a *Staphylococcus* spp., baseado nas principais bibliotecas eletrônicas e banco de dados com a finalidade de conhecer a eficácia da Atividade Antimicrobiana de algumas plantas Medicinais. Sabe-se que diversas bactérias são benéficas para o seu hospedeiro, pois realizam proteção e nutrição contra alguns patógenos e doenças, dificultando a colonização de bactérias nocivas; porém as bactérias que causam prejuízos à saúde humana possuem atualmente elevada resistência à maioria dos antimicrobianos, e baseado nessa afirmação; várias medidas tecnológicas são sugeridas para solucionar o problema da resistência das bactérias, sendo uma delas a procura

de novos antimicrobianos a partir de espécies vegetais. Plantas medicinais com propriedades terapêuticas são de grande relevância em todo o mundo, principalmente em países em desenvolvimento; e por mais que o conhecimento sobre plantas medicinais seja vasto nos dias de hoje, se faz necessário cada vez mais pesquisas, pois muitas vezes essas plantas são usadas de forma incorreta, conseqüentemente, correndo um grande risco devido ao acúmulo de substâncias ativas.

Palavras-chave: *Staphylococcus aureus*, resistência bacteriana, enterotoxina estafilocócica, infecção hospitalar, fitoterapia.

INTRODUCTION

The human beings, the animals and the plants are great bacteria reservoirs which can be easily found covering the skin, the mucosa and the gastrointestinal tract of humans and animals (Schaechter *et al.*, 2002).

The suspects that something could transmit diseases from one individual to other occurred at the Middle Ages where Dr. Francastorius, Italian doctor from Verona, in his book *De Contagione*, described the appearing of some diseases transmitted from one person to other, according to information collected from sailors who witnessed the diseases spread in expeditions, at the Colombian Era (Fernandes *et al.*, 2000; Rodrigues *et al.*, 1997; Pelczar Jr. *et al.*, 1996).

Over the years, several types of infections in hospitalized patients passed to be monitored, including patients with surgical incisions; because that time was frequent to found infected incisions (Al Temeier, 1979).

Joseph Lister at 1860 believed that the infection was caused by the harmful air penetration on wounds, saying that “the atmosphere septic properties” were due to the germs in suspension in the air and deposited in surfaces. Then, passed to use carbolic or phenoic acid, which were already widely used to disinfect latrines, stables and sewage, from observing the phenoic acid decreased the sewage odor and the cattle from such place were less sick. From there, they started to test in animals and humans and succeed after the application. Surgery rooms started to be sprayed with phenoic acid and, later, passed to use carbolic acid to instrumental disinfection. In 1883, Pasteur and Charles Chamberland, autoclave creators, showed that the sterilization by heating had superior efficacy (Pelczar Junior and Chan, 1996; Rodrigues, 1997).

Thus, followed up significant findings in the infectiology field, among which highlighted the gonococcus discovery, in 1879, by Albert Neisser. At the same period, Armauer Hansen discovered the leprosy bacillus and Pasteur discovered the streptococcus and staphylococcus.

Karl Joseph Eberth discovered the typhus bacillus and Kock discovered the tuberculosis microbe and the cholera bacillus. Albert Frankel discovered the tetanus bacillus, Theodor Escherich identified the coli bacillus and Anton Weichselbaum discovered the meningitis microbe. Richard Pfeiffer identified the flu bacillus or influenza. In 1892, William Welch discovered the gaseous gangrene bacillus, among other discoveries (Gordon, 1997).

Several bacteria are beneficial to their host, since they provide protection and nutrition against some pathogens and diseases, making the harmful bacteria colonization difficult (Santos, 2004). The *Staphylococcus aureus* known as an agent causative of several purulent diseases both in humans and in animals (Bean and Griffin, 1990), is also one of the most important causes of food poisoning (Penna *et al.*, 1998) due to the several enterotoxins production (Omoe, 2002); and it is present in the hospital infections where the concern is not limited only on the infection, but on the increasing of species diversity causing these infections and the changing of bacteria resistance pattern (Zecconi and Hahn, 2000).

The microbiota is an important part of our organism and although we don't see with naked eyes, it's estimate that 30-50% of healthy adults are colonized by *S. aureus*, representing an increased risk of subsequent infections (Klevens, 2007). Patients with diabetes type 1, drug users patients, patients on hemodialysis, surgical patients and patients with acquired immunodeficiency syndrome present a high staphylococcal colonizing rate. Patients with leukocyte function qualitative defects have also an increased staphylococcal disease risk (Lowy, 1998).

Staphylococcus aureus infection outbreaks, in the 50's and 60's, or by gram negative germs in the 70's, at some countries, increased the hospital costs, originating interest for hospital infection control measures, until nowadays. It is known that hospital infections are serious threats to the hospitalized patients' safety, constituting the most frequent and insidious complications; besides that, they contribute on increasing the morbidity and mortality rates, increasing the hospital costs, through prolonging the permanence and procedures spending, without considering the patient's time away from work (Pereira and Morya, 1995).

Currently, the main public health problem in the world is the antimicrobial resistance, independently if is a developed or underdeveloped country, and is caused by the antibiotic misuse; the wrong prescription from the health professional; uncomplying the stipulated therapeutic doses; the treatment dropout; among others... and it is known that staphylococcal infections are not only confined at intensive therapy units, acute care hospitals or any health institution (ANVISA, 2004).

There is a diversity of medicinal plants distributed across all the world aiming to treat diseases since medieval times, being many mechanisms unknown on these vegetal. It is known that the medicinal plants are being a rich source for obtaining molecules to be therapeutically explored; and can be classified according to their importance order: those directly used in therapies, followed from those constitute raw material for manipulation and, at last, those employed in the industry for obtaining active principles or as semi-synthesis precursors (Calixto, 2000; Carvalho, 2004).

With the objective of discovering compounds with antimicrobial activity compared to the traditional medicines, several studies have been developed with natural products and vegetal extracts; looking for a lower toxicity, efficient therapeutic action and lower environmental impact.

MATERIAL AND METHODS

A literature review was chosen, with the purpose of gathering and synthesizing the existent knowledge about Antimicrobial Activity against *Staphylococcus aureus*, using as temporal limitation the period between 1979 and 2018. The research was made based on online bibliographic data (Pub-Med, Medline and Scielo), in books and periodic. The used descriptors were: “Staphylococcus”, “aureus”, “infection”, “nosocomial”, “methicillinresistant”, “revisão”, “infecção”, “meticilina resistente” and “hospitales”.

RESULTS AND DISCUSSION

Etiologic agent

The *Staphylococcus* are Gram and catalase-positive coccus, with approximately 0.5 to 1.5 μm diameter, stationary, non-sporulated and generally non-encapsulated (Koneman *et al.*, 2001; Cassettari *et al.*, 2005; Trabulsi and Altherthum, 2005). The *Staphylococcus* was described for the first time in 1880, in surgical abscess pus, by the Scotland surgeon Alexandre Ogston and currently is one of the most common microorganisms in pyogenic infections all around the world (Santos, 2007).

The *Staphylococcus* gender pertains to the *Micrococcae* family, together with the *Planococcus*, *Micrococcus* and *Stomatococcus* genders. Currently, the *Staphylococcus* gender has 33 species, being that 17 of them can be isolated from human biological samples. The specie of greatest medical interest, especially in nosocomial environment, is the *S. aureus*, that

is frequently related with several infections in humans (Koneman, 2001; Cassettari *et al.*, 2005).

Staphylococcus aureus is one of the most common bacteria in the clinical practice once it usually colonizes the skin of up to 15% of humans and is easily found in the nasal cavities. It can cause diseases, ranging from a simple infection (pimples, boils and cellulites) until serious infections such as pneumonia, meningitis, endocarditis, toxic shock syndrome, septicemia and others (Koneman *et al.*, 2001; Cassettari *et al.*, 2005; Santos *et al.*, 2007).

A *Staphylococcus aureus* subtype called MRSA (*Methicillin-resistant Staphylococcus aureus*) is a *Staphylococcus* resistant to conventional penicillin treatment. Infections by MRSA have been increasingly frequent all around the world; and they are related to the increasingly widespread and most of time unnecessary antibiotic use; being this, the main microorganism responsible for infections in hospital environment and in health units (Alvarez, 2010).

It is estimated that around 30% of general population from the United States are infected with *Staphylococcus aureus* and 1.5% by *Methicillin-resistant Staphylococcus aureus* (Sigel *et al.*, 2007; Tenover, 2006; Elston and Barlow, 2009) and in Brazil, there is no systematized data that point the MRSA colonization rates in general population.

Until de 80's, the MRSA strains were found only in health institutions and in people with some morbidity or other risk factors, *hospital-acquired* (HA-MRSA), however, infections in healthy people have been reported and related to a genetically and phenotypically modified MRSA strain compared to those commonly found in health institutions, *community-acquired* MRSA (CA-MRSA) (Simor *et al.*, 2007).

Transmission

Staphylococcus aureus are highly virulent and present high antimicrobial resistance; responsible for 12% of all hospital infections at the United States, being lungs, surgical wounds and bloodstream the most affected sites by these agent (Rodrigues and Richtmann, 2008).

The *S. aureus* nasal colonization is asymptomatic, which means, the individual doesn't develop infection, being with great clinical importance, once that, with the colonized nostrils, the individual contaminates its own hands and becomes a bacteria transfer vehicle on the infection mechanism by contact, which means, the individual acts like a microorganism carrier (Cavalcanti *et al.*, 2005; Reagan *et al.*, 1991).

Thus, especially in hospitals, the asymptomatic host may be a patient, a visitor or even a health professional, and the nasal carrying has also contributed for the bacteria transmission by air dissemination (Carvalho, 2005; Cavalcanti *et al.*, 2005; Reagan *et al.*, 1991).

The hospital control of endemic MRSA has been based on different complementary strategies: first of all, it is necessary to early identify and isolate the asymptomatic carriers to avoiding the dissemination. Washing the body with antiseptics; topical and/or systemic treatment; intense care about hands hygiene and other conventional precaution measures to reduce the carrier state are extremely important to help on minimizing the MRSA propagation. The antimicrobial control to reduce the antibiotic selective pressure, thereby reducing the MRSA infection carriers' rates in hospitals with endemic state (Alvarez *et al.*, 2010).

Staphylococcus can also be transmitted by ingesting a product or food containing the staphylococcal enterotoxin. Food companies must comply with the Good Practices for food services set out in the Resolution RDC-ANVISA n° 216/04; in order to ensure hygienic-sanitary quality and the food conformity with the sanitary legislation.

Food manipulated by people carrying the pathogen in nasopharyngeal secretions or with hands injuries, abscesses or acnes; products of animal origin and/or incorrectly manipulated, undercooked or improperly stored, kept at room temperature for a period that allows the organism multiplication... among other causes, are means for thermostable enterotoxin propagation and production. Furthermore, contaminated surfaces and equipment can also cause food poisoning (FDA/CFSAN, 2012).

Bacterial resistance aspects

The bacterial resistance emerges as a worldwide public health problem attracting the attention of national and international government bodies such as Sanitary Vigilance National Agency (ANVISA), World Health Organization (WHO), Centers for Disease Control and Prevention (CDC) and the hospital infections controllers associations, in addition the international pharmaceutical industry (Koneman *et al.*, 2001; Shale and Stirk, 1999; Helfand and Cowen, 1990). According to the Global Antimicrobial Surveillance System (GLASS), there is a generalized occurrence of antibiotic resistance among 500 thousand people suspect of bacterial infection in 22 countries. The resistant bacteria most commonly related were *Escherichia coli*, *Klebsiella pneumoniae*, *Staphylococcus aureus* and *Streptococcus pneumoniae*, followed by *Salmonella spp.* (WHO, 2018).

The antibiotic resistance is unavoidable and irreversible and is characterized by the microorganism capability, especially the bacteria, of resisting against the lethal action of one or more antimicrobial agents classes; and for the health professionals, it has become an increasing challenge, insofar as the therapeutic options for treating some infections caused by resistant microorganisms (MR) are increasingly more restrict and are evident in the worldwide scenario (Mota *et al.*, 2005).

The bacterial resistance is a natural consequence of the bacterial cell adaptation to antibiotic exposure and the antibiotics intense and inappropriate use most of times in medicine, food production for animals and agriculture have caused a bacterial resistance increasing in all the world (Santos, 2004).

The antimicrobial resistance in *S. aureus* can be chromosomally coded or mediated by plasmids. *Staphylococcus aureus* has three distinct mechanisms of methicillin-resistance: a) beta-lactamase hyperproduction; b) presence of a protein binding penicillin (PBP) changed named PBP 2a; c) modifications in the PBPs binding capability (Tomasz *et. al.*, 1989); which can still be present in a same sample, even interacting with each other (De Lancastre *et al.*, 1991).

Staphylococcus aureus has five PBPs. The PBPs are enzymes that catalyze the bacterial wall synthesis terminal phase and are in the bacterial cell membrane. The PBP 1, 2 and 3 are essential and have high affinity (site-target) with the beta-lactam antibiotics, uniting to them by covalent bond. The methicillin-resistance in staphylococcus is due to an additional PBP production, anomalous, named PBP 2a, that presents low affinity to the beta-lactam antibiotics. Such changed protein is coded by a chromosomic gene named as *mecA*, responsible for the staphylococcal methicillin intrinsic resistance to all the beta-lactam antibiotics (Chambers, 1988).

In the 70's, hospital infections had as main cause the Methicillin Resistant Staphylococcus and the Vancomycin was the only drug so far effective; however, after two decades using vancomycin, the resistance to this drug was attested, observing and following patients that didn't answer the adopted therapy, then emerging a new nomenclature: VISA (*Staphylococcus aureus* with intermediate resistance to vancomycin) and currently referred to simply as VRSA (vancomycin-resistant *Staphylococcus aureus*) (Rubin *et al.*, 1999).

Its resistance mechanism is associated to a cellular wall synthesis activation and due to a cellular wall components high production (mucopetide residues) that reduce the antibiotic amount that comes to its action site (cytoplasmic membrane) (Boyle-Vavra, 2001), occurs a

PBP2 and PBP2' protein binding penicillin hyperproduction, cell wall thickening and drugs entrapment.

Recently in Brazil, staphylococcus with glycopeptides resistance were found; however, an expansion is found in Japanese hospitals (Hiramatsu *et al.*, 1997).

The glycopeptide resistance was initially observed in staphylococcus that also presented methicillin and oxacillin resistance and in patients previously submitted to the vancomycin use, indicating the resistant mutants' selection pressure and not the enterococcus resistance genes transfer (Waldvogel, 1999).

Measures for reducing the risk of developing antibiotic and chemotherapeutic resistant bacteria strains is considerably hard, because it is necessary adopting criteria that reduce the risk of such strain development, combining a careful treatment guided as the patients comply with the drug posology and the established treatment time in its totality (Baddour *et al.*, 2006), since the multi-resistant microorganisms are reaffirming as a worldwide threat (Hayashi *et al.*; 2013).

What are medicinal plants?

The WHO defines medicinal plant as "all and any vegetal that possess, in one or more organs, substances that may be used with therapeutic purposes or that are semi-synthetic medicines precursors (Zhang, 1998). The medicinal plants have been being a rich source for molecules obtaining to be therapeutically explored; allowing humans to reconnect with the environment, accessing the nature power on helping the organism to normalize injured physiological functions, restore the weakened immunity, promote detoxification and rejuvenation (França *et al.*, 2008). Many species are used empirically, without scientific support regarding efficacy and safety, what shows that in a country such as Brazil, with a huge biodiversity, there is a huge gap between the plants supply and the lack of researches (Silva and Carvalho, 2004).

There are several historic registers about using plants for diseases treatment since 4,000 B.C. The first medical register deposited in the Pennsylvania Museum is dated of 2,100 B.C. and includes a formula collection of thirty different drugs derived from vegetal, animal or mineral (Helfand and Cowen, 1990; Toscano Rico, 2011) used for healing, preventing and treating diseases, serving as important source of biologically active compounds (Andrade, Cardoso and Bastos, 2007).

According to the WHO, the difference between medicinal plant and phytotherapeutical resides on the plant elaboration for a specific formulation, characterizing a phytotherapeutic. In the

past, the phytotherapy was more adopted by needy population due to the easy availability and lower costs, however, currently, using plants as a medicines source is predominant in developing countries as an alternative solution for health problems and is well established in some cultures and traditions, especially in Asia, Latin America and Africa (Shale and Stirk, 1999).

At beginnings of the 90's, the World Health Organization (WHO) published that 65-80% of developing countries population were dependent of medicinal plants as the only access to basic cares (Akerele, 1993), assisting in the health primary cares and an excellent therapeutic complement, compatible with the classical medicine.

A USA research made in 1997 showed that 42% of the population had already used medicinal plants, at least once in 1996, as alternative medical treatments. Such percentage is about 30% higher in relation to 1990, when the same research was made (Eisenberg, 1998).

The economic crisis that today affects Brazil, combined with the hard access to medical and pharmaceutical assistance by the population, such as the industrialized medicines cost, promote the medicinal plants use to consumers, as well as the ecological consciousness established in the last years (Simões, 1998).

In 2006 the National Policy of Medicinal Plants and Phytotherapeutic (PNPMF), the Decree n° 5,813 from June 22nd, 2006, the National Program of Medicinal Plants and Phytotherapeutic, the interministerial ordinance n° 2,960 from September 12th, 2008 and the National Policy of Integrative and Complementary Practices (PNPIC) were instituted in the SUS, the Decree n° 971 from May 03rd, 2006, with the purpose of ensure the legal frameworks for the phytotherapy implementing in the SUS. In 2008, the ANVISA put into effect the Normative Instruction-IN/05, with a list containing 36 plants with medicinal purposes.

In 2010, the ANVISA published the RDC n° 10 from March 10th, 2010, about selling the shaved vegetal drugs, and the RDC n° 14 from April 05th, 2010 about the phytotherapeutic registration. Still in 2010, the 5th Edition of the Brazilian Pharmacopoeia and the Public Consultation of the National Phytotherapeutic Form were published.

The RENISUS/2009 – National Relation of Plants interesting for the SUS was published by the MS Pharmaceutical Assistance Directorate, containing 71 vegetal species that may have their studies prioritized to ensure their use efficacy and safety. Recently, in April 20th, 2010 the Live Pharmacy was instituted within the Health Unique System through the Ordinance 886. The Live Pharmacies, within the National Policy of Pharmaceutical Assistance, should

proceed all steps, since cultivating, harvesting, processing and storing the medicinal plants and phytotherapeutic.

Medicinal plants already used against the *Staphylococcus aureus* species

Although many plants species have already been tested with therapeutic purposes, few studies with medicinal plants have been tested with antimicrobial purpose for determining the therapeutic safety and efficacy (Mahady *et al.*, 2008). Among the analyzed articles, different plants are reported such as those most sought and used by the population, as the Ginger (*Zingiber officinale* Roscoe), Baccharises (*Baccharis trimera*), Lemongrass (*Cymbopogon citratus*), Eucalyptus (*Eucalyptus globulus*), Rosemary (*Rosmarinus officinalis*), Pitanga (*Eugenia uniflora*), Tumeric (*Curcuma longa* L.) among others. Those plants have multiple uses such as in the medicine, flavoring, condiments and some of them present excellent repellent power, such as the Eucalyptus (*Eucalyptus globulus*) and the Lemongrass (*Cymbopogon citratus*) (Chagas *et al.*, 2002).

Regarding the extraction methods for obtaining the essential oils, they vary depending on plant's part where the odoriferous cells are found, which may be in the flowers, leaves, barks, stalks, roots and rhizomes, as well as the essential oils use purposes. The presented literature presents as the most common extraction methods: steam drag hydro-distilling, with Clevenger equipment, Soxhlet equipment, percolation, cold extraction (maceration) and enfleurage (Azmir *et al.*, 2013).

The extraction by percolation is the extraction process by preferably used solvents because it presents lower chemical reactions risk in the artifacts formation, derived of a combined action between solvents and high temperature (used by the Soxhlet system). In the acid-base extraction, partition processes between acid or basic aqueous solvents and organic solvents immiscible with water are used (ether, CHCl₃, AcOEt). For a single extraction (at cold or hot), generally a polar solvent is used (MeOH or EtOH); for more than one extraction, three types of solvents are used: nonpolar (hexane or petroleum ether), with moderate polarity (CHCl₃ or CH₂Cl₂) and polar (MeOH or EtOH). However, due to the international protocols that condemned the use of chlorinated solvents, prohibiting to be produced, these solvents should no longer be used for extracts preparation, being then, most indicated, a single extraction using MeOH or EtOH (Maciel *et al.*, 2002).

Institutions such as Embrapa, Universidade de São Paulo, Universidade Federal da Paraíba, Universidade Federal de Santa Catarina, UNESP have developed works that enable greater

clarity of traditional practices with medicinal species, collaborating for safely accessing the medicinal plants and phytotherapeutic (GONÇALVES, 2011). The table 1 shows some articles published in the 2007-2018 period, regarding the Antimicrobial Activity against *Staphylococcus aureus*, as well as the research result. And as much as knowledge about medicinal plants is vast nowadays, more and more researches are needed, because in many times these plants are incorrectly used, consequently, facing a great risk due to the active substance accumulation.

Table 1 – Medicinal Plants used against *Staphylococcus* spp. in the 2007-2018 period.

Plant Popular Name	Plant Part	Research Target	Extract Compound	Biological Material Used	Research Result	Location	References
<i>Bactris gasipaes</i> <i>Kunth</i>	Bark	Evaluating the Peach-pal oil antimicrobial activity against the <i>Staphylococcus aureus</i> growing.	Essential oil from bark, pulp and seed.	<i>Staphylococcus aureus</i>	The bark oil from both Peach-palm species presents antimicrobial potential against <i>Staphylococcus aureus</i> strains. The pulp and seed oils don't present antimicrobial activity against <i>Staphylococcus aureus</i> development.	Acre, Brazil.	(Araújo <i>et al.</i> , 2012)
<i>Bactris dahlgreniana</i> (Peach-palm)	Pulp						
	Seed						
<i>Schinus terebinthifolius raddi</i> (Aroeira, Brazilian Peppertree)	Leaf	Evaluating the methicillin resistant <i>Staphylococcus aureus</i> positive presence in dogs, milk samples from cows with mastitis, animal health workers, graduation students from the Veterinary Medicine Faculty – UFPel; RS and control alternatives using medicinal plants.	Hydro-alcoholic extract	Methicillin resistant <i>Staphylococcus</i>	All the species present an efficient therapeutic alternative for infections caused by methicillin <i>Staphylococcus</i> .	Pelotas, RS Brazil	(Chaffe, 2014)
<i>Baccharis trimera</i> (Baccharises)							
<i>Syzygium cumini</i> (Jambolan)							

Tagetes minuta
(Chinchilla)

<i>Lippia origanoides</i> (Pepper Rosemary)	Leaf	Evaluating the <i>Lippia origanoides</i> essential oil antibacterial action against <i>Staphylococcus</i> sp. of animal origin.	Essential oil	<i>Staphylococcus</i> sp. isolated from food	The pepper rosemary essential oil (<i>Lippia origanoides</i>) presents antimicrobial activity against <i>Staphylococcus</i> sp. isolated from food.	Montes Claros, MG Brazil	(Queiroz <i>et al.</i> , 2014)
<i>Curcuma longa L.</i> (Turmeric)	Rhizome	Identifying, quantifying the constituents and evaluating the antibacterial activity of essential oils extracted from turmeric (<i>Curcuma longa L.</i>) and ginger (<i>Zingiber officinale Roscoe</i>) cultivated in the Manaus/AM conditions against 14 enteric salmonellas isolated from cooled chicken.	Essential oil	14 <i>Salmonella enterica</i> strains isolated from cooled chicken and 4 unidentified isolated, only confirming the <i>enterica</i> subspecies.	The research results allowed to evidence the ginger essential oil activity superiority compared to the turmeric against enteric salmonellas isolated from chicken, as well as the susceptibility variation of the confronted different strains.	Campinas, SP Brazil	(Majolo <i>et al.</i> , 2014)
<i>Zingiber officinale Roscoe</i> (Ginger)							
<i>Libidibia ferrea</i> (Brazilian Ironwood)	Bark	Testing the hydro-alcoholic extract antimicrobial activity from the Brazilian Ironwood bark (<i>Libidibia ferrea</i> (Mart. ExTul.) L. P. Queiroz), in different concentrations against microorganisms causing mastitis in goats.	Hydro-alcoholic extract	<i>Staphylococcus aureus</i>	There was a good inhibition of goat's milk contaminating microorganisms by using the extract, conferring a natural antimicrobial potential.	Mossoró, RN Brazil	(Paiva <i>et al.</i> , 2015)
<i>Eucalyptus globulus</i> (Common Eucalyptus)	Leaf	Proceeding tests to verifying antimicrobial effect with <i>Eucalyptus globulus</i> , <i>Justicia pectoralis</i> and <i>Cymbopogon citratus</i> aqueous extract against gram-positive and gram-negative bacteria strains.	Aqueous extract	<i>Staphylococcus aureus</i> ATCC 25923	Only <i>Eucalyptus globulus</i> has capability to inhibit the pathogenic <i>S. aureus</i> (ATCC 25923), proving that it has antimicrobial activity.	Sobral, CE Brazil	(Furtado <i>et al.</i> , 2015)
<i>Justicia pectoralis</i> (Freshcut - Chambá)							
<i>Cymbopogon citratus</i> (Lemongrass)							

<i>Spondias purpurea</i> L. (Jocote)	Leaf	Analyzing the medicinal plants extract modulatory activity of the <i>Spondias</i> genus against erythromycin resistant <i>Staphylococcus aureus</i> .	Ethanollic extracts by percolation	Erythromycin resistant <i>Staphylococcus</i> and not resistant strain (ATCC 25923)	Results indicate that <i>S. mombine</i> , <i>S. purpurea</i> may be a natural products source with potential to modify the antibiotics activity, may act as adjuvants in antimicrobial therapy.	Paraiba, Brazil	(Alencar <i>et al.</i> , 2015)
<i>Alpinia zerumbet</i> (Shell Ginger)	Leaf	Evaluating the <i>Alpinia zerumbet</i> essential oil and ethanolic extract efficacy against <i>Staphylococcus aureus</i> .	Ethanollic Extract (EE) and Essential Oil (OE)	<i>Staphylococcus aureus</i> isolated from cows with subclinical mastitis and standard strains ATCC 29213 and ATCC 25923	The <i>A. zerumbet</i> leaves OE and EE have significative action against <i>Staphylococcus aureus</i> .	Parnaiba, PI Brazil	(Castro <i>et al.</i> , 2016)
<i>Senna spectabilis</i> (Cassias)	Leaf	Determining the compared antibacterial activity among the <i>Senna spectabilis</i> , <i>Rosmarinus officinalis</i> and <i>Eugenia uniflora</i> extracts against a <i>Pseudomonas aeruginosa</i> ATCC 27853, <i>Staphylococcus aureus</i> ATCC 6538 and <i>Streptococcus pyogenes</i> ATCC 19615 standard strains.	Ethanollic extract: ethylic alcohol 70%; hexane (PA) and ethyl acetate (PA).	<i>Pseudomonas aeruginosa</i> ATCC 27853, <i>Staphylococcus aureus</i> ATCC 6538 and <i>Streptococcus pyogenes</i> ATCC 19615	The <i>R. officinalise</i> and <i>E. uniflora</i> hexane and ethyl acetate extracts were active for <i>S. aureus</i> . The <i>E. uniflora</i> ethyl acetate extract was active against the microorganism <i>S. pyogenes</i> . None of the extracts was effective against the gram-negative <i>P. aeruginosa</i> .	Umuarama, PR Brazil	(Arantes <i>et al.</i> , 2016)
<i>Rosmarinus officinalis</i> (Rosemary)							
<i>Eugenia uniflora</i> (Brazilian cherry)							
<i>Abarema cochliacarpus</i>	Bark	Evaluating the cyclohexanic, acetic and ethanolic extracts <i>in vitro</i> antibacterial activity of <i>Abarema cochliacarpus</i> bark (Gomes) Barneby & J.W. Grimes against bacteria isolated from dogs' skin wounds.	Cyclohexanic, acetic and ethanolic extracts	<i>Staphylococcus intermedius</i> , <i>Bacillus sp.</i> , <i>Pasteurella sp.</i> and <i>Escherichia coli</i>	All the three <i>Abarema cochliacarpus</i> bark extracts showed antibacterial activity against <i>Staphylococcus intermedius</i> and <i>Bacillus sp.</i> gram-positive strains isolated from dogs' wounds.	Pernambuco, Brazil	(Tenório <i>et al.</i> , 2016)

<i>Spondias mombin</i> L. (Yellow Mombin)	Leaf	Proceeding the <i>S. mombin</i> L. extract phytochemical screening and evaluating its <i>in vitro</i> antimicrobial action against <i>Staphylococcus aureus</i> , <i>Pseudomonas aeruginosa</i> and <i>Escherichia coli</i> .	Aqueous extract by maceration and decoction	<i>S. aureus</i> (ATCC 23235), <i>P. aeruginosa</i> (ATCC 25619) and <i>E. coli</i> (ATCC 29214)	The <i>Spondias mombin</i> L. extract showed bactericidal effect against the three bacteria types.	Natal, RN Brazil	(Alvez, 2017)
<i>Curcuma longa</i> L. (Turmeric)	Rhizome	Evaluating the <i>Curcuma longa</i> L. extract capability to control <i>S. aureus</i> , <i>P. aeruginosa</i> and <i>C. albicans</i> in vitro infection in murine macrophages (RAW 264.7), by analyzing the phagocytosis and immunoregulation processes.	Propylene glycol extract	<i>S. aureus</i> (ATCC 6538), <i>P. aeruginosa</i> (ATCC 15442) and <i>C. albicans</i> (ATCC 18804)	The <i>C. longa</i> L. extract effectively helped the murine macrophages (RAW 264.7) to control <i>in vitro</i> <i>S. aureus</i> , <i>P. aeruginosa</i> and <i>C. albicans</i> , infections as analyzed in the phagocytosis and immunoregulation processes.	São José dos Campos, SP Brazil	(Figueira, 2017)
<i>Zingiber officinale</i> Roscoe (Ginger)	Rhizome	Bibliographic review about the <i>Zingiber officinale</i> Roscoe and <i>Alpinia purpurata</i> (Vieill.) K. Schum. (Zingiberaceae) antimicrobial activity, commonly known as ginger and red-ginger, respectively, and their use in the Unique Health.			The results showed in this literature review about the <i>Z. officinale</i> and <i>A. purpurata</i> species provide a good vision about the medicinal potential of their bioactive compounds, especially as antimicrobial agents.	Umuarama, PR Brazil	(Soares et al., 2017)
<i>Alpinia purpurata</i> (Vieill.) K. Schum. (Red Ginger)							
<i>Jacaranda micranta</i> Cham. (Jacaranda)	Leaf	Proceeding a phytochemical screening and evaluating the gross aqueous extracts (EA) and hydro-alcoholic extracts (EH) biological activity of <i>Jacaranda micranta</i> Cham. (Jacaranda) against <i>Staphylococcus coagulase</i> positive and <i>Salmonella</i> spp. standard strains and isolated from products of animal origin.	Aqueous and hydro-alcoholic extract	<i>Staphylococcus aureus</i> ATCC 25923 and <i>Salmonella choleraesuis</i> ATCC 10708	Both <i>Jacaranda micranta</i> Cham. leaves extracts promote antibacterial activity.	Lajeado, RS Brazil	(Debres et al., 2018)
<i>Zingiber officinale</i> Roscoe (Ginger)	Rhizome	Extracting and isolating <i>Zingiber officinale</i> substances for antimicrobial evaluation and their virulence anti-factors effect of Methicillin Resistant <i>Staphylococcus aureus</i> .	N-hexane, ethyl acetate, ethanol and water extracts.	<i>Staphylococcus aureus</i>	Only the aqueous was not able on inhibiting the bacterial growth.	Lagarto, SE Brazil	(Santos, 2018)

Source: Author's elaboration

ACKNOWLEDGMENTS

The authors acknowledge the Universidade Paranaense (UNIPAR) for the provided financing to this research, the CNPq for conceding the productivity scholarship, the Fundação Araucária for the Basic and Applied Research Program scholarship and the CAPES for the PNPd scholarship.

REFERENCES

AKERELE, O. Summary of WHO guidelines for the assessment of herbal medicines. **Herbal Gram**, 1(28):13-19, 1993.

AL TEMEIER W. A.; BURKE, J. F.; PRUITT, B. A. Manual on the control of infection in surgical patients. **Philadelphia: Lippincott**; 202(2):29-30, 1976.

ALVAREZ, C.; LABARCA, J.; SALLES, M. Estratégias de prevenção de *Staphylococcus aureus* resistente à metilina (MRSA) na América Latina. **Brazilian Journal of Infectious Diseases**, 14(2):108-120, 2010.

ANDRADE, S. F.; CARDOSO, L. G.; BASTOS, J. K. Anti-inflammatory and antinociceptive activities of extract, fractions and populonic acid from bark wood of *Austroplenckia popunea*. **Journal of Ethnopharmacology**, 109(3):464-471, 2007. <https://www.sciencedirect.com/science/article/pii/S0378874106004211>

ANVISA, Agência Nacional de Vigilância Sanitária. **Universidade Federal do Estado de São Paulo**. Curso de Infecção Relacionada à Assistência à Saúde – IrAs. vs 1.0. 2004. 52p. <http://portal.anvisa.gov.br/documents/33852/3507912/Caderno+4+-+Medidas+de+Preven%3%A7%C3%A3o+de+Infec%3%A7%C3%A3o+Relacionada+%C3%A0+Assist%C3%Aancia+%C3%A0+Sa%C3%BAde/a3f23dfb-2c54-4e64-881c-fccf9220c373>

AZMIR, J. *et al.* Techniques for extraction of bioactive compounds from plant materials: A review. **Journal of Food Engineering**, 117(4), 426-436, 2013. <https://www.sciencedirect.com/science/article/pii/S0260877413000277>

BADDOUR, M. M.; ABUELKHEIR, M. M.; FATANI, A. J. Trends in antibiotic susceptibility patterns and epidemiology of MRSA isolates from several hospitals in Riyadh, Saudi Arabia. **Annals of Clinical Microbiology and Antimicrobials**, 5(30):1-11, 2006. <https://ann-clinmicrob.biomedcentral.com/articles/10.1186/1476-0711-5-30>

BEAN, N. H.; GRIFFIN, P. M. Foodborne disease outbreaks in the United States, 1973-1987: pathogens, vehicles, and trends. **Journal of Food Protection**, 53(9):804-817, 1990. <http://jfoodprotection.org/doi/abs/10.4315/0362-028X-53.9.804>

BOLETIM MENSAL DE COMÉRCIO AGRÍCOLA. Preços de cereais registram subida desde meados de 2003. **Boletim Mensal do Comércio Agrícola**, 1(67):4, 2004.

https://www.sei.ba.gov.br/index.php?option=com_content&view=article&id=48&Itemid=313

BOYLE-VAVRA, S.; LABISCHINSKI, H.; EBERT, C.C.; EHLERT, K.; DAUM, R.S. A Spectrum of Changes Occurs in Peptidoglycan Composition of Glycopeptide-Intermediate Clinical *Staphylococcus aureus* Isolates. **American Society For Microbiology**, 45(1):280-287, 2001. <https://aac.asm.org/content/45/1/280.short>

CALIXTO, J. B. Efficacy, safety, quality control, marketing and regulatory guidelines for herbal medicines (phytotherapeutic agents). **Brazilian Journal and Biological Research**, 33(2):179-189, 2000. http://www.scielo.br/scielo.php?pid=S0100-879X2000000200004&script=sci_arttext

CARVALHO, C.; BEREZIN, E. N.; PISTELLI, I. P.; MÍMICA, L.; CARDOSO, M. R. A. Monitoramento microbiológico sequencial da secreção traqueal em pacientes intubados internados em unidade de terapia intensiva pediátrica. **Jornal de Pediatria**, 81(1):29-33, 2005. <http://www.scielo.br/pdf/%0D/jped/v81n1/v81n1a07.pdf>

CARVALHO, J. C. T. **Fitoterápicos antiinflamatórios: aspectos químicos, farmacológicos e aplicações terapêuticas**. Ribeirão Preto, SP: Tecmedd, 2004. 480p.

CASSETTARI, V. C.; STRABELLI, T.; MEDEIROS, E. A. S. *Staphylococcus aureus* bacteremia: what is the impact of oxacillin resistance on mortality? **Brazilian Journal of Infectious Diseases**, 9(1):70-76, 2005. http://www.scielo.br/scielo.php?pid=S1413-86702005000100012&script=sci_arttext&tlng=es

CAVALCANTI, S. M. M.; FRANÇA, E. R.; CABRAL, C.; VILELA, M. A.; MONTENEGRO, F.; MENEZES, D.; MEDEIROS, A. C. R. Prevalence of *Staphylococcus aureus* introduced into intensive care units of a university hospital. **Brazilian Journal of Infectious Diseases**, 9(1):5663, 2005. http://www.scielo.br/scielo.php?pid=S1413-86702005000100010&script=sci_arttext

CHAGAS, A. C. S.; PASSOS, W. M.; PRATES, H. T.; LEITE, R. C.; FURLONG, J.; FORTES, I. C. P. Efeito acaricida de óleos essenciais e concentrados emulsionáveis de *Eucalyptus* spp em *Boophilus microplus*. **Brazilian Journal of Veterinary Research and Animal Science**, 39(5):247-253, 2002. <http://www.scielo.br/pdf/bjvras/v39n5/15836>

CHAMBERS, H. F. Methicillin-resistant staphylococci. **American Society For Microbiology**, 1(2):173-186, 1988. <https://cmr.asm.org/content/1/2/173.short>

DE LANCASTRE, H.; FIGUEIREDO, A. M. S.; URBAN, C.; TOMASZ, A.; RAHAL, J. Multiple mechanisms of methicillin-resistance and improved methods for detection in clinical isolates of *S. aureus*. **American Society For Microbiology**, 35(4):632-639, 1991. <https://aac.asm.org/content/35/4/632.short>

EISENBERG, D.; DAVIS, R. B.; ETTNER, S. L.; APPEL, S.; WILKEY, S.; ROMPAY, M. V.; KESSLER, R. C. Trends in alternative medicine use in the United States, 1990-1997. Results of a follow-up national survey. **Journal American Medical**, 280(18):1569-1575, 1998. <https://jamanetwork.com/journals/jamapsychiatry/fullarticle/188148>

ELSTON, J.W. T.; BARLOW, G. D. Community-associated MRSA in the United Kingdom. **Journal of Infection**, 59(3):149-155, 2009. <https://www.sciencedirect.com/science/article/pii/S016344530900187X>

FDA/CFSAN (2012). Bad Bug Book. *Staphylococcus aureus*. Atualizado em 20 de maio de 2013. Available in: <http://www.fda.gov/Food/FoodborneIllnessContaminants/CausesOfIllnessBadBugBook/default.htm>. Access in: August, 08, 2018.

FERNANDES, A. T., FERNANDES, M. O. V., RIBEIRO FILHO, N. A **Infecção Hospitalar e suas interfaces na área da saúde**. São Paulo (SP): Atheneu; 2000. 1812p.

FRANÇA, I.S. X.; SOUZA, J. A.; BAPTISTA, R. S.; BRITTO, V. R. S. Medicina popular: benefícios e malefícios das plantas medicinais. **Revista Brasileira de Enfermagem**, 61(2):201-208, 2008. <http://www.scielo.br/pdf/reben/v61n2/a09v61n2>

GORDON, R. **A assustadora história da Medicina**. Rio de Janeiro (RJ): Ediouro Publicações; 223p. 1997.

HAYASHI, M. A.; BIZERRA, F. C.; DA SILVA JÚNIOR, P. I. Antimicrobial compounds from natural sources. **Frontiers in Microbiology**, 4(1):195, 2013.

HELFAND, W. H.; COWEN, D. L. **Pharmacy: an Illustrated History**. New York, NY: Harry Abrams, Inc; 1990. 272p.

HIRAMATSU, K.; ARITAKA, N.; HANAKI, H.; KAWASAKI, S.; HOSODA, Y.; HORI, S. Dissemination in Japanese hospitals of strains of *Staphylococcus aureus* heterogeneously resistant to vancomycin. **The Lancet**, 350(9092):1670-1673, 1997. <https://www.sciencedirect.com/science/article/pii/S0140673697073248>

KLEVENS, R. M.; MORRISON, M. A.; NADLE, J.; PETIT, S.; GERSHMAN, K.; RAY, S.; HARRISON, L. H.; LYNFIELD, R.; DUMYATI, G.; TOWNES, J. M.; CRAIG, A. S.; ZELL, E. R.; FOSHEIM, G. E.; MCDUGAL, L. K.; CAREY, R. B.; FRIDKIN, S. K. Invasive Methicillin-Resistant *Staphylococcus aureus* Infections in the United States. **Journal American Medical Association**, 298(15):1763-1771, 2007. <https://jamanetwork.com/journals/jama/article-abstract/209197>

KONEMAN, E. W.; ALLEN, S. D.; JANDA, W. M. **Diagnóstico microbiológico**. 5 ed. Rio de Janeiro: Guanabara Koogan, cap.11, parte 1, 2001. 1760p.

LOWY, F. D. *Staphylococcus aureus* infections. **The New England Journal of Medicine**, 339(8):520-32, 1998. <https://www.nejm.org/doi/full/10.1056/nejm199808203390806>

MACIEL, M. A. M.; PINTO, A. C.; VEIGA JÚNIOR, V. F. Plantas Medicinais: A necessidade de estudos multidisciplinares. **Química Nova**, 25(3):429-438, 2002. <http://www.scielo.br/pdf/qn/v25n3/9337.pdf>

MAHADY, G. B.; HUANG, Y.; DOYLE, B. J., LOCKLEAR, T. Natural products as antibacterial agents. **Studies in Natural Products Chemistry**, 35(1):423-444, 2008. <https://www.sciencedirect.com/science/article/pii/S1572599508800117>

MOTA, R. A.; DA SILVA, K. P. C.; FREITAS, M. F. L.; PORTO, W. J. N.; DA SILVA, L. B. G. Utilização indiscriminada de antimicrobianos e sua contribuição a multirresistência bacteriana. **Brazilian Journal of Veterinary Research and Animal Science**, 42(6):465-470, 2005. <http://www.periodicos.usp.br/bjvras/article/view/26406>

OMOE, K.; ISHIKAWA, M.; SHIMODA, Y.; HU, D.; UEDA, S.; SHINAGAWA, K. Detection of seg, seh, and sei genes in *Staphylococcus aureus* Isolates and Determination of the Enterotoxin Productivities of *S. aureus* Isolates Harborin seg, seh, or sei Genes. **Journal of Clinical Microbiology**, 40(3):857-862, 2002. <https://jcm.asm.org/content/40/3/857.short>

PELCZAR JR., M. J.; CHAN, E. C. S.; KRIEG, N. R. **Microbiologia: conceitos e aplicações**. São Paulo: Makron Books; 1996. 600p.

PEREIRA, M. S.; MORYA, T. M. **Infecção Hospitalar: estrutura básica de vigilância e controle**, 27(3):355-61, 1995.

REAGAN, D. R.; DOEBBELING, B. N.; PFALLER, M. A.; SHEETZ, C. T.; HOUSTON, A. K.; HOLLIS, R. J.; WENZEL, R. P. Elimination of coincident *S. aureus* nasal and hand carriage with intranasal application of mupirocin calcium ointment. **Annals of Internal Medicine**, 114(2):101-106, 1991. <http://annals.org/data/journals/aim/19720/aime199101150-00001.pdf>

RODRIGUES, E. A. C. **Infecções Hospitalares: prevenção e controle**. São Paulo (SP): Sarvier; 1997. 669p.

RODRIGUES, E. A. C.; RICHTMANN, R. IRAS - **Infecção Relacionada à Assistência à Saúde: orientações práticas**. São Paulo: Sarvier, 2008. 256p.

RUBIN, R. J.; HARRINGTON, C. A.; POON, A.; DIETRICH, K.; GREENE, J. A.; MOIDUDDIN, A. The Economic Impact of *Staphylococcus aureus* Infection in New York City Hospitals. **Emerging Infectious Diseases**, 5(1):9-17, 1999. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2627695/>

SANTOS, A. L.; SANTOS, D. O.; FREITAS, C. C.; FERREIRA, B. L. A.; AFONSO, I. F.; RODRIGUES, C. R.; CASTRO, H. C. *Staphylococcus aureus*: visitando uma cepa de importância hospitalar. **Jornal Brasileiro de Patologia e Medicina Laboratorial**, 43(6):413-423, 2007. <https://www.redalyc.org/pdf/3935/393541938005.pdf>

SANTOS, N. Q. La resistencia bacteriana en el contexto de la infección hospitalaria. **Red de Revistas Científicas de América Latina y El Caribe, España y Portugal**, 13(1):64-70, 2004.

SCHAECHTER, M.; ENGLEBERG, N. C.; EISENSTEIN, B. I.; MEDOFF, G. **Microbiologia: mecanismos das doenças infecciosas**. 3. ed. Rio de Janeiro: Guanabara Koogan, 2002. 664p.

SHALE, T.L.; STIRK, W.A.; VAN STADEN, J. Screening of medicinal plants used in Lesotho for anti-bacterial and anti-inflammatory activity. **Journal of Ethnopharmacology**, 67(3):347-354, 1999. <https://www.sciencedirect.com/science/article/pii/S0378874199000355>

SILVA, M. C.; CARVALHO, J. C. T. **Plantas Mediciniais: Aspectos químicos, farmacológicos e aplicações terapêuticas**. Ribeirão Preto: Tecmedd, 2004, 480p.

SIMÕES, C. M. O.; MENTZ, L. A.; SCHENKEL, E. P.; IRGANG, B. R.; STEHMANN, J. R. **Plantas da Medicina Popular do Rio Grande do Sul**. 5. ed. Porto Alegre: Ed. Universidade Federal do Rio Grande do Sul, 1998. 173p.

SIMOR, A. E.; STUART, T. L.; LOUIE, L.; WATT, C.; OFNER-AGOSTINI, M.; GRAVEL, D. Mupirocin-Resistant, Methicillin-Resistant *Staphylococcus aureus* Strains in Canadian Hospitals. **Antimicrobial Agents and Chemotherapy**, 51(11): 3880-3886, 2007. <https://aac.asm.org/content/51/11/3880.short>

TENOVER, F. C.; MCDUGAL, L. K.; GOERING, R. V.; KILLGORE, G.; PROJAN, S. J.; PATEL, J. B.; DUNMAN, P. M, Characterization of a Strain of Community-Associate Methicillin-Resistant *Staphylococcus aureus* Widely Disseminated in the United States. **Journal of Clinical Microbiology**, 44(1):108-118, 2006. <https://jcm.asm.org/content/44/1/108.short>

TOMASZ, A.; DRUGEON, H. B.; LENCASTRE, H. M.; JABES, D., MCDUGALL, L.; BILLE, J. New mechanism for methicillin-resistance in *S. aureus*: clinical isolates that lack the PBP 2a gene and contain normal penicilin-bindig proteins with modified penicilin-binding capacity. **American Society For Microbiology**, 33(11):1869-1874, 1989. <https://aac.asm.org/content/33/11/1869.short>

TOSCANO RICO, J. M. **Plantas Mediciniais**. Academia das Ciências de Lisboa, Instituto de Estudos Acadêmicos para Seniores, Lisboa, 2011. 244p.

TRABULSI, L. R.; ALTHERTHUM, F. **Microbiologia**. São Paulo: Atheneu, 2005. 718p.

WALDVOGEL, F.A. New resistance in *Staphylococcus aureus*. **The New England Journal of Medicine**, 340(7):556-557, 1999. <https://www.nejm.org/doi/pdf/10.1056/NEJM199902183400709>

ZECCONI, A.; HAHN, G. *Staphylococcus aureus* in raw Milk and human health risk. **Bulletin of IDF**, 345(1):15-18, 2000. <http://agris.fao.org/agris-search/search.do?recordID=BE2001000308>

ZHANG, X. Bulletin of the World Health Organization. **Regulatory situation of herbal medicines. A worldwide review**, Geneva, 1998. Available in: <https://apps.who.int/medicinedocs/pdf/whozip57e/whozip57e.pdf>. Access in: September, 13, 2018.