CHITOSAN, ZINC OXIDE AND PINK PEPPER ESSENTIAL OIL: POTENTIAL PROPERTIES AND APPLICATIONS

QUITOSANA, ÓXIDO DE ZINCO E ÓLEO ESSENCIAL DE PIMENTA ROSA: PROPRIEDADES E POTENCIALIDADES DE APLICAÇÕES

QUITOSANA, ÓXIDO DE ZINC Y ACEITE ESENCIAL DE PIMIENTA ROSA: PROPIEDADES Y POTENCIALIDADES DE APLICACIONES

Sonia Maria da Silva Garcia¹, Michelle Félix de Andrade², Ivo Diego de Lima Silva³, Iane Bezerra Vasconcelos Alves⁴, Severino Alves Júnior⁵, Ednaldo Cavalcante de Araújo⁶, Yêda Medeiros Bastos de Almeida⁷, Glória Maria Vinhas⁸

ABSTRACT

Objective: to describe properties and potential applications of chitosan, zinc oxide and pink pepper essential oil. **Method:** a descriptive study, of informative type, by surveying the universe of scientific production. **Results:** chitosan is a polymer that has characteristics such as biodegradability, biocompatibility, toxicity, low cost, natural product and exists in great quantity in nature. It is susceptible of being manipulated in the formats of slides, films, fibers and gels. It is an extremely functional molecule exerting mucoadhesive, anticoagulant, immunostimulating, healing, antitumor, hemostatic, hypolipemic, antimicrobial actions, among others. Zinc oxide is an antimicrobial with extraordinary bactericidal and fungicidal efficacy. Studies have investigated the pink pepper essential oil and identified that it possesses diuretic, astringent, antidiarrheal, anti-inflammatory, healing, bactericidal, antiviral, analgesic, sedative, expectorant, antipyretic, vermifuge and antiseptic activity. **Conclusion:** chitosan, zinc oxide and pink pepper essential oil have, individually or in combination, potential for applications in areas such as active packaging, water treatment, dressings and others, as a result of the competence to minimize or eradicate proliferation of pathogenic microorganisms. Anacardiaceae; Hydrogel; Zinc Oxid; Polymers; Biological Products; Chitosan.

RESUMO

Objetivo: descrever propriedades e aplicações potenciais da quitosana, óxido de zinco e óleo essencial de pimenta rosa. **Método:** estudo descritivo, tipo informativo, mediante o levantamento do universo da produção científica. **Resultados:** a quitosana é um polímero que possui características tais como biodegradabilidade, biocompatibilidade, atoxicidade, baixo custo, produto natural e existe em grande quantidade na natureza. É suscetível de ser manipulada nos formatos de lâminas, filmes, fibras e géis. É uma molécula extremamente funcional exercendo ação mucoadesiva, anticoagulante, imunoestimulante, cicatrizante, antitumoral, hemostática, hipolipêmica, antimicrobiana, dentre outras. O óxido de zinco é um antimicrobiano com extraordinária eficácia bactericida e fungicida. Estudos têm investigado o óleo essencial da pimenta rosa e identificado que ele possui atividade diurética, adstringente, antidiarreica, anti-inflamatória, cicatrizante, bactericida, antiviral, analgésica, sedativa, expectorante, antipirética, vermífuga e antisséptica. **Conclusão:** a quitosana, o óxido de zinco e o óleo essencial de pimenta rosa apresentam, individualmente ou em conjunto, potencialidades para aplicações em áreas tais como embalagens ativas, tratamento de água, curativos e outras, em consequência da competência para minimizar ou erradicar a proliferação de micro-organismos patógenos. **Descritores:** Anacardiaceae; Hidrogel; Óxido de Zinco; Polímeros; Produtos Biológicos; Quitosana.

RESUMEN

Objetivo: describir las propiedades y aplicaciones potenciales de la quitosana, óxido de zinc y aceite esencial de pimienta rosa. **Método:** estudio descriptivo, tipo informativo, mediante el levantamiento del universo de la producción científica. **Resultados:** la quitosana es un polímero que tiene características, tales como: biodegradabilidad, biocompatibilidad, atoxicidad, bajo costo, producto natural y existe en gran cantidad en la naturaleza. Es susceptible de ser manipulada en los formatos de láminas, películas, fibras y geles. Es una molécula extremadamente funcional, ejerciendo acción mucosidad, anticoagulante, inmuoestimulante, cicatrizante, antitumoral, hemostática, hipolipémica, antimicrobiana, entre otras. El óxido de zinc es un antimicrobiano con extraordinaria eficacia bactericida y fungicida. Los estudios han investigado el aceite esencial de la pimienta rosa e identificado que el posee actividad diurética, astringente, antidiarreica, cicatrizante, bactericida, antiviral, analgésica, sedante, expectorante, antipirética, vermífuga y antiséptica. **Conclusión:** la quitosana, el óxido de zinc y el aceite esencial de pimienta rosa presentan, individualmente o en conjunto, potencialidades para aplicaciones en áreas tales como envases activos, tratamiento de agua, curativos y otras, como consecuencia de la competencia para minimizar o erradicar la proliferación de micro-organismos patógenos. **Descriptores:** Anacardiaceae; Hidrogel; Óxido de Zinc; Polímeros; Productos Biológicos; Quitosano.

^{1,2,3}Masters (PhD students), Postgraduate Program in Materials Science, Federal University of Pernambuco / UFPE. Recife (PE), Brazil. E-mail: sonia.garcia1@hotmail.com ORCID iD: <http://orcid.org/0000-0002-9340-7568>; E-mail: mifelixsilva@hotmail.com ORCID iD: <http://orcid.org/0000-0002-4798-1403>; E-mail: ivo.diego91@gmail.com ORCID iD: <http://orcid.org/0000-0001-7441-2305>; ⁴PhD (Postdoctor), Postgraduate Program in Materials Science, Federal University of Pernambuco / UFPE. Recife (PE), Brazil. E-mail: ianealvesji@gmail.com ORCID iD: <https://orcid.org/0000-0002-7662-1335>; ⁵PhD, Department of Fundamental Chemistry, Federal University of Pernambuco - Pernambuco / UFPE. Recife (PE), Brazil. E-mail: juniorbstr@gmail.com ORCID iD: <https://orcid.org/0000-0002-8092-4224>; ⁶PhD (Postdoctor), Postgraduate Program in Nursing - Master and Doctorate in Nursing, Federal University of Pernambuco / PPGENF / UFPE. Recife (PE), Brazil. E-mail: ednenjp@gmail.com ORCID iD: <http://orcid.org/0000-0002-1834-4544>; ⁷PhD, Department of Chemical Engineering, Federal University of Pernambuco - Pernambuco / UFPE. Recife (PE), Brazil. E-mail: yedamba@gmail.com ORCID iD: <http://orcid.org/0000-0003-1041-7144>; ⁸PhD, Department of Chemical Engineering, Federal University of Pernambuco - Pernambuco / UFPE. Recife (PE), Brazil. E-mail: gloria.vinhas@ufpe.br ORCID iD: <http://orcid.org/0000-0001-073-609X>

INTRODUCTION

Chitosan is a polymer that has applications in various areas, for example, food, waste treatment, pharmaceutical industry, process engineering and agronomy. However, the sector where chitosan proved extremely successful was in the biomedical field. The relevance of chitosan in this area correlates with its biological properties such as antimicrobial, biocompatibility, biodegradability, low toxicity and low immunogenicity.¹⁻²

The application of chitosan in the care of wounds is fundamentally due to the above mentioned biological peculiarities and also, to some degree, with the physical and mechanical characteristics. The use of chitosan in wounds anticipates tissue renewal as related to other established therapeutic procedures.³⁻⁴

Chitosan is referred to by scientists as a natural polysaccharide which has the function of enhancing neovascularization and the genesis of granulation tissue, two relevant steps in the wound healing process. This occurs by increasing the rate of infiltration of fibroblasts and inflammatory cells, the excitation of the generation of collagen by the fibroblasts and the activation of cytosine production by the cells, which makes chitosan effective as a dynamizer of tissue repair.⁴⁻⁶

Other properties of chitosan are acidic solubility and aggregation with polyanions that confer chitosan the characteristic of being an excellent gel former.

Hydrogels are three-dimensional polymer crosslinks that can inflate in an aqueous or biological liquid environment and preserve a large amount of water in your infrastructure without disintegrating. The hydrogels are based on hydrophilic polymers interlaced to prevent their dissolution in water and can therefore be employed to store cells, drugs or proteins. As a consequence of the existence of some functional groups in extending the polymer chains, hydrogels are often susceptible to environmental circumstances such as solvent constitution, pH and temperature.²

Chitosan hydrogels are used in the pharmaceutical, cosmetic, medical and especially for wound treatment, macromolecule aggregation and support for drug release. These uses are convenient for hydrogels because they exhibit peculiarities such as porosity of the solute, degree of tumescence, kinetics of absorbance of a liquid, ability to perceive and react to pH changes, non-existence of hydrophobic

influences and particular in vivo performance characteristics.²

The use of chitosan is possible in the condition of hydrogel mainly related to its biocompatibility.² Chitosan gel acts as an excellent dressing for lesions due to its healing specificities and, also, presents a predisposition of tissue adhesion leading to a significant contraction of the wound and anticipating its closure.³

With the current predisposition to use natural items, antimicrobial factors extracted from plants, such as essential oils, become increasingly evident with the use of these substances in treatments.⁷

The World Health Organization shows that 80% of the world's inhabitants use medicinal herbs in primary health care.⁸ Pink pepper, popularly known as aroeira, is used in the tenth position among 138 medicinal plants. This cited researcher reports that pink pepper is used in folk medicine for the treatment of most types of pain, venereal diseases, gingivitis, rheumatism, fever and diarrhea.⁹

There is a growing curiosity in discovering natural antimicrobial propellants for therapeutic application for the purpose of favoring synergistic activity or in exchange for chemical preservatives that have reduced use because of their imminent carcinogenic potential.¹⁰ In this way, better capital applications and research for the exchange of synthetic additives with natural preservatives in the plants and that carry out antimicrobial activity.

In addition to essential oils, as substances with bioactive principles, some metal oxides have also been investigated, such as zinc oxide (ZNO) with antimicrobial action.

OBJECTIVE

- Describe potential properties and applications of chitosan, zinc oxide and pink pepper essential oil.

RESULTS

♦ Chitosan

Chitosan is developed from chitin which is abundantly found in nature as a structural element of the exoskeleton of arthropods (including crustaceans, insects), algae and cell walls of some fungi. Structurally, chitin is a linear, water-insoluble mucopolysaccharide.¹¹ In figure 1, one can observe the chemical structure of cellulose, chitin and chitosan.

Figure 1. Chemical structure of cellulose, chitin and chitosan. Source:¹²

Chitosan (Figure 1) is a product of chitin deacetylation. It is a biodegradable, natural and renewable polymer of vast economic and environmental value. Chemically, it's a polyamine. This biopolymer has a molecular structure chemically identical to that of cellulose differing only in the functional groups -OH, -NHCOCH₃ e NH₂.¹³

The solubility of chitosan results from its biological origin, molecular weight and degree of acetylation.¹⁴ It is soluble in organic acid media (acetic, formic, citric) and inorganic (hydrochloric acid), constituting a cationic polymer with the protonation of the amino group resulting in the NH₃⁺ ion, which gives it peculiar characteristics: a viscous solution capable of developing coatings or coating films. The quality and characteristics of chitosan may change according to its manufacturing method that interferes with the characteristics of the final product. In the solid state, chitosan is a semicrystalline polymer.¹⁵

Chitosan is characterized by its molecular weight (MW) and degree of acetylation (DA). Chitosan, which is commercially available, has a degree of deacetylation > 85% (DA < 15%) and molecular weight contained between 100-1000 kDa. It is commonly recognized that low-weight chitosan has MW < 50 kDa; the medium, 50-150 kDa, and the high weight > 150 kDa.¹⁴

Chitosan is susceptible of being manipulated in the formats of slides, films, fibers and gels. It is an extremely functional molecule exerting mucoadhesive, anticoagulant, immunostimulating, healing, antitumor, hemostatic, hypolipemic, antimicrobial, among others.¹³⁻⁹

Chitosan is biodegraded by the enzyme lysozyme generating non-toxic, non-immunogenic and non-carcinogenic amino compounds that are fully expelled by the body.¹⁵

This polysaccharide still has broad applications peculiar to the food industry. Among them are the development of biodegradable films and the preservation of food against microbial degradation. In the pharmaceutical and food industries, it is widely used in transportation for the release of bioactive drugs and compounds.¹¹⁻⁸ Among the numerous biological properties exposed for chitosan, anti-inflammatory, antimicrobial and healing competence is probably, the one of greater relevance for the health area.¹⁹

Chitosan has been investigated as an antimicrobial agent against a wide variety of microorganisms such as bacteria, yeasts, fungi and algae.¹³

This polymer generates inhibition of the growth or destruction of microorganisms such as *E. coli*, *S. epidermidis*, *S. aureus*, *S. faecalis*, *S. pyogenes*, *Vibrio*, *Shigella dysenteriae*, *Salmonella typhimurium*, *Bacillus cereus*, *P. aeruginosa*, *Candida*, *Xanthomonas campestris*, *Botrytis cinerea*, *Fusarium oxysporum*, among others.¹¹

Research shows that the form of antimicrobial action of chitosan is a consequence of the physicochemical properties of the polymer and the peculiarities of the microorganism's membrane. Three modes of antibacterial action were suggested.¹⁴⁻²²

1. Ionic interaction on cell surface resulting in cell wall opening: electrostatic forces between the positively charged

Garcia SMS, Andrade MF de, Lima ID de et al.

chitosan (NH + 3) molecule and negative residues on the cell surface possibly competing for Ca²⁺ by electronegative spots on the surface of the cell membrane. This fact generates disturbance in osmotic balance and / or hydrolyzes peptideoglycans in the membrane of the microorganism resulting in the detriment of potassium ions and low molecular weight protein constituents. This mechanism of action is the most accepted today.

2. Inhibition of mRNA and protein synthesis: the chitosan, after crossing the cellular membrane of the bacterium, enters the nucleus and joins the DNA avoiding the synthesis of mRNA and proteins.

3. Metal complexing: the chitosan develops an external hindrance by complexing metals and thereby eliminating essential nutrients for microbial growth.

Chitosan was evaluated as having bactericidal / bacteriostatic activity without differentiation between these activities.²³⁻⁴

Studies have shown that the antimicrobial activity of chitosan differs between Gram-positive and Gram-negative bacteria. In the case of Gram-positive, it is assumed that the chitosan fragments the membrane whereas, in the Gram-negative, the cytoplasm agglomerates and the intracellular space is expanded.²⁵

The antimicrobial property of chitosan has been proven by different researches emerging as a probable option against the antibacterials of synthetic origin usually employed.²⁵⁻⁶

There is no standardized method for presenting the results of antimicrobial testing of natural products. The plaque microdilution methodology is the most used and recommended to define the Minimal Inhibitory Concentration (MIC) or Minimum Bactericidal Concentration (MBC) of natural products, such as chitosan and essential oil, as a consequence of its sensitivity and minimal amount of reagents, which allows for a maximum number of replications, adding to the credibility of the results.¹³

As there is no standardization on the acceptable inhibition coefficient for natural products, when compared with standard antibiotics, the classification for plant derived materials based on MIC results was evaluated, such as: strong inhibition of MIC up to 500 µg / mL; moderate inhibition of MIC, from 600 to 1500 µg / mL, and as weak inhibition those exhibiting MICs above 1600 µg / mL.²⁷⁻⁸

♦ Chitosan Hydrogel

The hydrogels are conceptualized as systems, with two or more components,

Chitosan, zinc oxide and pink pepper essential...

constituted by the three-dimensional cross-linking of polymer chains and water that completes the environment between the macromolecules.²⁹⁻³⁰

Hydrogels are a relevant category of polymeric materials that can swell by retaining a significant amount of water within their structures without dissolving. Therefore, they can be referred to as a category of absorbent polymers.³¹ The existence of hydrophilic functional groups (-OH, -COOH, -CONH₂, -SO₃H) in the composition of hydrogels defines their ability to infiltrate and conserve large amounts of water. In turn, the presentation of crosslinking points produces their insolubility and stability.³²⁻⁴

Hydrogels can be categorized by various properties. According to crosslinking, hydrogels are categorized into physical or temporary hydrogels consisting of van der Waals forces, hydrogen bonds and their lattices can be broken by means of external stimuli such as: temperature, pH changes and saline solution. The second designation of the hydrogels, according to chemical or permanent crosslinks, is described as those connected fundamentally by covalent bonds. The development of crosslinks may be due to chemical reactions or to gamma ray, x-ray or ultraviolet radiation. The hydrogels achieved by chemical crosslinks, once the networks are synthesized, will no longer be able to undo.³⁴

As regards biodegradability, hydrogels are subdivided into biodegradable and non-biodegradable. Biodegradation can result from biological, physical and chemical actions. In vivo, biodegradable hydrogels undergo macromolecular decomposition by microorganisms such as bacteria, fungi, algae and enzymes, whereas non-biodegradable ones do not reach decomposition so as to be absorbed by nature.²³

According to the origin, the hydrogels can be natural, synthetic or hybrid. Natural hydrogels are developed by naturally occurring polymers, with or without chemical change, for example, hyaluronic acid, alginate, starch and chitosan. These hydrogels exhibit the benefit of being biocompatible and have biodegradability but, on the other hand, have low mechanical properties.³⁰

Synthetic hydrogels are produced by polymerization of synthetic monomers having, for example, methacrylic acid, acrylamide, among others. Synthetic polymers commonly have a well-defined structure which can be altered in order to achieve the required degradability and functionality. Synthetic polymers correspond to a category of multifunctional materials because they offer

many applications, among which, are in the cosmetic and pharmaceutical fields.³⁰

Hybrid hydrogels are synthesized from the combination of natural and synthetic polymers, making it in many cases an excellent strategy to improve the properties of the material achieved.³⁰

The composition of the hydrogels network may be as macroporous, microporous or nonporous. Macroporous hydrogels exhibit pores with a diversified size of 0.1 to 1.0 µm. Microporous hydrogels have a pore with a tiny dimension between 100-1000 Å. Non-porous hydrogels have a pore with macromolecular size between 10-100 Å and have dense polymer chains, as well as providing completely restricted solubility conduction by diffusion through the free areas.³⁴

Swelling kinetics is one of the significant properties of the hydrogel. This is defined by the particularity of the porous structure, sample size, pore size, temperature and pH variation, among others. Stabilization in the swelling is produced by the equilibrium obtained by means of the osmotic force that benefits the solvent input and the counter elastic force that compensates the distension of the polymer network and avoids its deformation.³⁴

Several researches were found subsidizing the technological advance of hydrogels with emphasis in the biomedical area. Here some of them will be portrayed.

A chitosan hydrogel with nerolidol was synthesized and its antimicrobial and curative properties were investigated. The hydrogel was characterized by thermogravimetry, differential scanning calorimetry and infrared spectroscopy. The antimicrobial activity was tested against *Staphylococcus aureus* that showed bactericidal action. The chitosan hydrogel with 2% nerolidol exhibited extraordinary curative action because, on the 7th day of treatment, reepithelization and reorganization of the collagen occurred, demonstrating the cicatricial process. The authors concluded that the synthesized hydrogel was promising as a bactericidal and curative agent.³⁵

Chitosan was characterized and analyzed its implication in the cicatricial process in rats. The characterization was by means of elemental, thermogravimetric, spectroscopic analysis in the infrared region, in terms of viscosity, molar mass and degree of acetylation. The authors concluded that the chemical properties of chitosan (viscosity of 5 mPa s, low degree of acetylation (GA = 5.9%) and molar mass of 132.0 kDa) make it remarkable for use in different areas.

Regarding healing properties, chitosan generated a 81.4% decrease in lesion width, contributing to the treatment of cutaneous lesions, which confirms its potential for use in the medical area.⁴

Another study, also carried out with chitosan, was the development of a hybrid hydrogel consisting of chitosan and silver nanoparticles. The silver nanoparticles were synthesized and characterized by dynamic light scattering and transmission electron microscopy before being incorporated into the hydrogel. The silver nanoparticles presented a size of 7 nm and the spherical shape. The chitosan hydrogel was synthesized with silver nanoparticles and characterized by differential scanning calorimetry and scanning electron microscopy. The efficacy of silver ion release and the antimicrobial action were analyzed. In conclusion, it was identified that chitosan hydrogels, with or without silver nanoparticles, have sustained bactericidal activity against *S. mutans*.³⁶

A chitosan hydrogel with 1% silver sulfadiazine was studied and rheological, biological and therapeutic characterizations of this hydrogel were made. The authors identified that the chitosan hydrogel presented pseudoplasticity and bioadhesiveness that benefited the neovascularization and the inflammatory action in burns, as well, this gel showed adequate and coherent rheological properties for the mechanism of drug release.³⁷⁻⁸

The antimicrobial action of chitosan with chlorhexidine against *S. mutans* was analyzed. The antimicrobial action experiments were carried out using chitosan and chitosan / chlorhexidine solutions diluted in 1% acetic acid at various pH values (3.5 - 5.0) and concentration ranging from 0.1 to 1.5%. The author identified that the antimicrobial action increased with pH, chlorhexidine concentration, exposure time and with chitosan / chlorhexidine aggregation.³⁹

♦ Zinc oxide

Zinc oxide is an antimicrobial with extraordinary bactericidal and fungicidal efficacy. It offers reduced toxicity and is biocompatible. It acts by modifying the constituents of the cell membrane of the microorganism, altering and opening it, which induces the detriment of the intracellular elements and, as a consequence, the death of the microorganism. Currently, zinc oxide is used in the manufacture of ointments or antiseptic powders, deodorants, sunscreens and in active packagings. A new and prosperous sector for the use of zinc oxide is the sanitation of water for human

Garcia SMS, Andrade MF de, Lima ID de et al.

consumption.⁴⁰ Zinc oxide is used in the manufacture of cosmetics as a consequence of the particularities such as the wide spectrum of absorption and high photostability.⁴⁰

◆ Essencial oil

The use of medicinal plants for pharmacological purposes has increased significantly in recent decades, mainly as a consequence of World Health Organization (WHO) activities that have stimulated interest in private and governmental institutions.⁴¹

Essential Oils (EO) are oily-looking liquids formed by various volatile elements at room temperature and aromatic and produced by secretory cells in flowers, leaves, seeds, barks, fruits and roots of aromatic plants.⁴²

The International Standard Organization (ISO) distinguishes essential oils, also called volatile oils, such as: "products obtained from parts of plants by steam distillation, supercritical fluids, hydrodistillation, cold pressing, solvent extraction, turbodasting, enfleurage and microwave without solvent".⁴²⁻³

Essential oils consist of 20 to 60 components in various concentrations, but two or three are in concentrations significantly around 20 to 70%.⁴⁴⁻⁶

The essential constituents of an essential oil are part of the chemical classes of sesquiterpenes, oxygenated sesquiterpenes, oxygenated monoterpenes and monoterpenes.⁴¹ The difference in the biological performance of essential oils is conditioned by the constitution of their chemical components such as carvacrol, citral, limonene, pinene, furanodiene, cineole, caryophyllene, eucalyptol, elemene, eugenol and others.⁴³

These different mixtures of chemical constituents, presented by the essential oils, are in charge of the characteristics such as the antioxidant actions,⁴² antispasmodic, analgesic, anti-inflammatory, antiseptic,⁴⁴ antiviral, antibacterial, insecticidal and antifungal.⁴⁵⁻⁶ Still have repellent action against insects⁴⁵ and antitumor activity.⁴⁷

Chitosan, zinc oxide and pink pepper essential...

The antimicrobial action of essential oils has been conferred mainly on terpenes and derivatives. But the low-concentration components also support antimicrobial activity.⁴⁸⁻⁹

Several studies have analyzed the action against microorganisms of these compounds and have described different processes of action such as the blockade of nucleic acid synthesis, cytoplasmic membrane functions and energy metabolism.⁵⁰

The antimicrobial action of the essential oils can be due to three mechanisms: by the intervention in the double layer of phospholipid of the bacterial cell wall, by the increase of the permeability and deviation of the components of the cell and by modification of a diversity of enzymes as the participants in the production of cellular energy and synthesis of structural elements or elimination of genetic material.⁵¹

The antibacterial potential of the essential oils results from the hydrophobicity of these that allows the removal of the lipids of the cell membrane and mitochondria of the bacteria, causing the alteration of the cellular compositions and altering the permeability of the membrane, triggering the extravasation of fundamental molecules to their survival and inducing death of bacteria.⁴¹

◆ Pink pepper essencial oil

Schinus terebenthifolius Raddi (Figure 2) has different popular names such as: pink pepper, aroeira-pimenteira, aroeira-vermelho, aroeira-mansa, aroeira, beach aroeira, aroeira-do-brejo, aroeirado campo, aroeira-sabiá, aroeirinha, heart-of-bugre, sage-fruit, fox fruit, bunch-fruit, araguaraíba, corneiba, pepper tree, cabuí, cambuí and lentisco. It is a plant with abundant leaves, belonging to the family Anacardiaceae, native of South America, especially of Brazil, Paraguay and Argentina. The parts used that offer therapeutic properties are bark, leaves and fruits and these elements are widely used in folk medicine for the treatment of various diseases.⁵²⁻³

Figure 2. Pink pepper fruits. Source:⁵⁴

From 2009, through Administrative Order No. 2,982, of November 26, 2009, GM / MS of the Ministry of Health, the expansion of the supply and the availability of several phytotherapeutics in the Pharmaceutical Assistance of the UHS, as raw material, the pink pepper, among others.⁴¹

It is agreed among several researchers that pink pepper exerts diuretic, astringent, antidiarrheal, anti-inflammatory, cicatrizant, bactericidal, antiviral, analgesic, sedative, expectorant, antipyretic, vermifuge and antiseptic activity.⁵³⁻⁶

The chemical constitution of the fruits and leaves of the pink pepper was investigated and acids, terpene hydrocarbons and ketones were identified in its composition. The antimicrobial action of pink pepper against Gram-positive (*Staphylococcus aureus* and *Bacillus subtilis*) and Gram-negative bacteria (*Escherichia coli* and *Pseudomonas aeruginosa*), as well as against *Candida albicans*.⁹

The pink pepper essential oil has antioxidant and antimicrobial properties against Gram-positive and negative bacteria and food degenerating fungi.⁵⁶⁻⁷

The antimicrobial action of the essential oil of pink pepper, by the method of diffusion in agar in the presence of *Staphylococcus aureus* and *Escherichia coli*, was studied by Carvalho et al. For *S. aureus*, a discrete halo of inhibition (9.17 mm) conferred with the antibiotics ampicillin (35.00 mm) and tetracycline (29.17 mm) was investigated, while the *E. coli* bacterium showed no inhibition halo. Therefore, it did not exhibit antimicrobial action against this microorganism.⁵⁶

The pink pepper essential oils showed a promising antioxidant activity in vitro and exhibited cytotoxicity in the fight against breast cancer. The best biological action was localized in the essential oil which comprised

the higher sesquiterpene content. It was also verified the antimicrobial activity against microorganisms of food origin.⁵⁴⁻⁷

CONCLUSION

Chitosan and its structural alterations, such as acetylation degree and molar mass, have presented several biomedical applications, mainly as antimicrobial action, in drug release, tissue engineering and biosensors for clinical investigations.

Zinc oxide shows relevant performance for the body's immunity exerting influence on the proliferation and maturation of the defense cells.

The pink pepper essential oil has been shown as an alternative with antimicrobial potential.

These substances present, individually and / or together, potentialities for applications in areas such as active packaging, water treatment, curatives and others, as a consequence of the potential to minimize or eradicate the proliferation of pathogenic microorganisms.

REFERENCES

1. Rinaudo M. Chitin and chitosan: Properties and applications. Prog Polym Sci. 2006 July;31(7):603-32. Doi: <https://doi.org/10.1016/j.progpolymsci.2006.06.001>
2. Rafique A, Mahmood Zia K, Zuber M, Tabasum S, Rehman S. Chitosan functionalized poly(vinyl alcohol) for prospects biomedical and industrial applications: a review. Int J Biol Macromol. 2016 June; 87:141-54. Doi: [10.1016/j.ijbiomac.2016.02.035](https://doi.org/10.1016/j.ijbiomac.2016.02.035)
3. Alemdaroglu C, Degim Z, Celebi N, Zor F, Ozturk S, Erdogan D. An investigation on burn wound healing in rats with chitosan gel formulation containing epidermal growth factor. Burns. 2006 May; 32(3):319-27. Doi: [10.1016/j.burns.2005.10.015](https://doi.org/10.1016/j.burns.2005.10.015)

Garcia SMS, Andrade MF de, Lima ID de et al.

Chitosan, zinc oxide and pink pepper essential...

4. Fráguas RM, Rocha DA, Queiroz ER, Abreu CMP, Sousa RV, Oliveira Júnior EN. Chemical characterization and healing effect of chitosan with low molar mass and acetylation degree in skin lesions. *Polímeros*. 2015 Mar/Apr; 25(2): 205-11. Doi: <http://dx.doi.org/10.1590/0104-1428.1778>
5. Howling GI, Dettmar PW, Goddard PA, Hampson FC, Dornish M, Wood EJ. The effect of chitin and chitosan on the proliferation of human skin fibroblasts and keratinocytes in vitro. *Biomaterials*. 2001 Nov; 22(22): 2959-66. Doi: [https://doi.org/10.1016/S0142-9612\(01\)00042-4](https://doi.org/10.1016/S0142-9612(01)00042-4)
6. Alsarra IA. Chitosan topical gel formulation in the management of burn wounds. *Int J Biol Macromol*. 2009 July; 45(1):16-21. Doi: <https://doi.org/10.1016/j.ijbiomac.2009.03.010>
7. Pereira MC, Vilela GR, Costa LMS, Silva RF, Fernandes AF, Fonseca EWN da, et al. Inhibition fungi growth through of utilization essential oils of spice. *Ciênc Agrotec*. 2006 July/Aug; 30(4):731-8. Doi: <http://dx.doi.org/10.1590/S1413-70542006000400020>
8. World Health Organization. Situação regulamentaria de los medicamentos herbários: uma resena mundial [Internet]. Geneva: WHO; 2000 [cited 2017 Oct 15]. Available from: www.apps.who.int/medicinedocs/es/d/Jwhozip58s
9. Dourado MT. Óleos essenciais e oleoresina da pimenta rosa (*Schinus terebinthifolius* Raddi): propriedades químicas e biológicas [thesis] [Internet]. Pelotas: Universidade Federal de Pelotas; 2012. Available from: [http://dctaufpel.com.br/ppgcta/manager/uploads/documentos/teses/tese_-_oleos_essenciais_e_oleoresina_da_pimenta_rosa_\(schinus_terebinthifolius_raddi\)_propriedades_quimicas_e_biologicas.pdf.pdf](http://dctaufpel.com.br/ppgcta/manager/uploads/documentos/teses/tese_-_oleos_essenciais_e_oleoresina_da_pimenta_rosa_(schinus_terebinthifolius_raddi)_propriedades_quimicas_e_biologicas.pdf.pdf)
10. Rauha P, Remes S, Heinonen M, Hopia A, Kähkönen M, Kujala T, et al. Antimicrobial effects of finnish plant extracts containing flavonoids and other phenolic compounds. *Int J Food Microbiol*. 2000 May; 56(1):3-12. Doi: [https://doi.org/10.1016/S0168-1605\(00\)00218-X](https://doi.org/10.1016/S0168-1605(00)00218-X)
11. Kumar MNVR. A review of chitin and chitosan applications. *React Funct Polym*. 2000 Nov; 46(1):1-27. Doi: [https://doi.org/10.1016/S1381-5148\(00\)00038-9](https://doi.org/10.1016/S1381-5148(00)00038-9)
12. Van Den Broek LA, Knoop RJ, Kappen FH, Boeriu CG. Chitosan films and blends for packaging material. *Carbohydr Polym*. 2015 Feb; 116:237-42. Doi:

- <https://doi.org/10.1016/j.carbpol.2014.07.039>
13. Mendes AA, Oliveira PC, Castro HF, Giordano RLC. Application of chitosan as support for immobilization of enzymes of industrial interest. *Quím Nova*. 2011;34(5):831-40. Doi: <https://dx.doi.org/10.1590/S0100-40422011000500019>
14. Goy RC, Britto D, Assis OBG. A review of the antimicrobial activity of chitosan. *Polímeros*. 2009; 19(3):241-7. Doi: <https://dx.doi.org/10.1590/S0104-14282009000300013>
15. Denkbaz EB, Kilicay E, Birlikseven C, Ozturk E. Magnetic chitosan microspheres: preparation and characterizations. *React Funct Polym*. 2002; 50(3):225-32. Doi: [https://doi.org/10.1016/S1381-5148\(01\)00115-8](https://doi.org/10.1016/S1381-5148(01)00115-8)
16. Kean T, Thanou M. Biodegradation, biodistribution and toxicity of chitosan. *Adv Drug Deliv Rev*. 2010 Jan; 62(1):3-11. Doi: <https://doi.org/10.1016/j.addr.2009.09.004>
17. Alexakis T, Boadi DK, Quong D, Groboillot A, O'Neill, Poncelet D, et al. Microencapsulation of DNA within alginate microspheres and crosslinked chitosan membranes for in vivo application. *Appl Biochem Biotechnol*. 1995 Jan; 50(1):93-106. Doi: <https://doi.org/10.1007/BF02788043>
18. Kanatt SR, Chander R, Sharma A. Chitosan glucose complex e a novel food preservative. *Food Chem*. 2008 Jan; 106(2):521-8. Doi: <https://doi.org/10.1016/j.foodchem.2007.06.036>
19. Singh HP, Mittal S, Kaur S, Batish DR, Kohli RK. Characterization and antioxidant activity of assential oils from fresh and decaying leaves of eucalyptus tereticornis. *J Agric Food Chem*. 2009 Aug; 57(15):6962-6. Doi: [10.1021/jf9012407](https://doi.org/10.1021/jf9012407)
20. Azevedo VVC, Chaves SA, Bezerra DC, Fook MVL, Costa ACFM. Quitina e Quitosana: aplicações como biomateriais. REMAP [Internet]. 2007 Jan [cited 2017 Aug 25];2(3):27-34. Doi: www2.ufcg.edu.br/revista-remap/index.php/REMAP/article/viewFile/46/81
21. Kulikov SN, Lisovskaya SA, Zelenikhin PV, Bezrodnykh EA, Shakirova DR, Blagodatskikh IV, et al. Antifungal activity of oligochitosans (short chain chitosans) against some *Candida* species and clinical isolates of *Candida albicans*: molecular weight-activity relationship. *Eur J Med Chem*. 2014 Mar; 74:169-78. Doi: <https://doi.org/10.1016/j.ejmech.2013.12.017>

22. Tayel AA, Ibrahima SI, Al-Saman MA, Moussa SH. Production of fungal chitosan from date wastes and its application as a biopreservative for minced meat. *Int J Biol Macromol.* 2014 Aug; 69:471-5. Doi: <https://doi.org/10.1016/j.ijbiomac.2014.05.072>
23. Costa RAS. Síntese e Teste de Hidrogéis Inteligentes para a Liberação Controlada de Fármacos [dissertation] [Internet]. Bragança: Instituto Politécnico de Bragança; 2013 [cited 2017 Aug 21]. Available from: <https://bibliotecadigital.ipb.pt/bitstream/10198/9231/1/Rita%20Costa.pdf>
24. Elsaka SE, Elnaghy AM. Antibacterial activity of calcium hydroxide combined with chitosan solutions and the outcomes on the bond strength of RealSealer sealer to radicular dentin. *J Biomed Res.* 2012 May; 26(3):193-9. Doi: [10.7555/JBR.26.20110136](https://doi.org/10.7555/JBR.26.20110136)
25. Batista ACL, Dantas GC, Santos J, Amorim RVS. Antimicrobial Effects of Native Chitosan against Opportunistic Gram-negative Bacteria. *Microbiol J.* 2011; 1(3):105-12. Doi: <https://scialert.net/abstract/?doi=mj.2011.105.112>
26. Kim KW, Min BJ, Kim YT, Kimmel RM, Cooksey K, Park SI. Antimicrobial activity against foodborne pathogens of chitosan biopolymer films of different molecular weights. *LWT Food Sci Technol.* 2011 Mar; 44(2):565-9. Doi: <https://doi.org/10.1016/j.lwt.2010.08.001>
27. Holappa J, Hjalmsdóttir M, Másson M, Rúnarsson Ö, Asplund T, Soininen P, et al. Antimicrobial activity of chitosan N-betainates. *Carbohydr Polym.* 2006 July; 65(1):114-8. Doi: <https://doi.org/10.1016/j.carbpol.2005.11.041>
28. Aligiannis N, Kalpoutzakis E, Mitaku S, Chinou IB. Composition and antimicrobial activity of the essential oils of two organum species. *J Agric Food Chem.* 2001 Sept; 4(9): 4168-70. Doi: [10.1021/jf001494m](https://doi.org/10.1021/jf001494m)
29. Ferreira EA, Silva VA, Silva EA, Silveira HRO. Hydrogel efficiency and physiological responses of seedless citrus cultivars seedlings under water deficit. *Pesqui Agropecu Trop.* 2014 Apr/June; 44(2):158-65. Doi: <https://dx.doi.org/10.1590/S1983-40632014000200009>
30. Hoffman AS. Hydrogels for biomedical applications. *Adv Drug Deliv Rev.* 2012 Dec; 54(1):3-12. Doi: <https://doi.org/10.1016/j.addr.2012.09.010>
31. Moghadam HRT. Super absorbent polymer mitigates deleterious effects of arsenic in wheat. *Rhizosphere.* 2017 June; 3(1):40-3.

Doi:

- <https://doi.org/10.1016/j.rhisph.2016.12.003>
32. Nascimento MHM, Lombello CB. Hyaluronic acid and chitosan based hydrogels for cartilage tissue engineering. *Polímeros.* 2016 Oct/Dec; 26(4):360-70. Doi: <https://dx.doi.org/10.1590/0104-1428.1987>
33. Patel A, Mequanint K. Hydrogel biomaterials. In: Fazel-Rezai R, editor. *Biomedical Engineering: frontiers and Challenges.* London: InTech, 2011.
34. Ganji SS, Ganji DD, Sfahani MG, Karimpour S. Application of AFF and HPM to the systems of Strongly Nonlinear Oscillation. *Curr Appl Phys.* 2010 Sept; 10(5): 1317-25. Doi: <https://doi.org/10.1016/j.cap.2010.03.015>
35. Schoen FJ, Hoffman AS, Ratner BD. *Biomaterials science: an introduction to materials in medicine.* Waltham: Elsevier; 2013.
36. Ferreira MOG, Leite LLR, Lima IS, Barreto HM, Nunes LCC, Ribeiro AB, et al. Chitosan Hydrogel in combination with Nerolidol for healing wounds. *Carbohydr Polym.* 2016 Nov; 152(5):409-18. Doi: <https://doi.org/10.1016/j.carbpol.2016.07.037>
37. Sámano-Valencia C, Martínez-Castañón GA, Martínez-Martínez RE, Loyola-Rodríguez JP, Reyes-Macías JF, Ortega-Zarzosa G, et al. Bactericide efficiency of a combination of chitosan gel with silver nanoparticles. *Mater Lett.* 2013 Sept; 106(1):413-6. Doi: <https://doi.org/10.1016/j.matlet.2013.05.075>
38. Nascimento EG, Sampaio TBM, Medeiros AC, Azevedo EP. Evaluation of chitosan gel with 1% silver sulfadiazine as an alternative for burn wound treatment in rats. *Acta Cir Bras.* 2009 Nov/Dec; 24(6): 460-5. Doi: [http://dx.doi.org/10.1590/S0102-86502009000600007](https://dx.doi.org/10.1590/S0102-86502009000600007)
39. Oliveira RA. Avaliação do efeito antimicrobiano in vitro de quitosana e da associação quitosana/clorexidina sobre saliva e *Streptococcus mutans* [dissertation] [Internet]. São Carlos: Escola de Engenharia de São Carlos; 2014 [cited 2017 Aug 28]. Available from: <http://www.teses.usp.br/teses/disponiveis/82/82131/tde-19012005-103055/pt-br.php>
40. Porto RCT, Uchôa PZ, Peschel LT, Justi B, Koslowski LAD, Nogueira AL. Zinc oxide nanoparticles synthesized by the polyol method: characterization and evaluation of the antibacterial activity. *Matéria.* 2017 Jan;22(Suppl 1):e11912. Doi: [http://dx.doi.org/10.1590/s1517-707620170005.0248](https://dx.doi.org/10.1590/s1517-707620170005.0248)

Garcia SMS, Andrade MF de, Lima ID de et al.

Chitosan, zinc oxide and pink pepper essential...

41. Ministério da Agricultura, Pecuária e Abastecimento (BR), Secretaria de Desenvolvimento Agropecuário e Cooperativismo. Boas Práticas Agrícolas (BPA) de plantas medicinais, aromáticas e condimentares [Internet]. Brasília: MAPA; 2006 [cited 2017 Oct 21]. Available from: bvsms.saude.gov.br/bvs/publicacoes/cartilha_plantas_medicinais.pdf
42. Bakkali F, Averbeck S, Averbeck D, Idaomar M. Biological effects of essential oils: a review. Food Chem Toxicol. 2008 Feb; 46(2): 446-75. Doi: <https://doi.org/10.1016/j.fct.2007.09.106>
43. Busato NV, Silveira JC, Costa AOS, Costa Junior EF. Modeling strategies for essential oil extraction by hydrodistillation and steam distillation. Ciênc Rural. 2014 Sept; 44(9): 1574-82. Doi: <http://dx.doi.org/10.1590/0103-8478cr20121330>
44. Freire JCP, Nóbrega MTC, Oliveira-Júnior JK, Freire SCP, Dias-Ribeiro E, Lima EO. Atividade antifúngica de fitoterápicos sobre espécies de Candida: uma revisão de literatura. Arch Health Invest. 2016 Dec; 5(6):307-10. Doi: <http://dx.doi.org/10.21270/archi.v5i6.1790>
45. Mendes SS, Bomfim RR, Jesus HC, Alves PB, Blank AF, Estevam CS, et al. Evaluation of the analgesic and anti-inflammatory effects of the essential oil of Lippia gracilis leaves. J Ethnopharmacol. 2010 June; 129(3):391-7. Doi: <https://doi.org/10.1016/j.jp.2010.04.005>
46. Schuck VJA, Fratini M, Rauber CS, Henriques A, Schapoval EES. Evaluation of the antimicrobial activity of Cymbopogon citratus. Rev Bras de Ciênc Farm. 2001 Jan/Apr; 37(1):45-9.
47. Carmo ES, Lima EO, Souza EL. The potential of origanum vulgare L. (lamiaceae) essential oil in inhibiting the growth of some food-related aspergillus species. Braz J Microbiol. 2008 Apr/June; 39(2):362-7. Doi: <http://dx.doi.org/10.1590/S1517-83822008000200030>
48. Silva HSRC, Santos KSCR, Ferreira EI. Chitosan: hydrossoluble derivatives, pharmaceutical applications and recent advances. Quím Nova. 2006 July/Aug; 29(4):776-85. Doi: <http://dx.doi.org/10.1590/S0100-40422006000400026>
49. Gutierrez L, Escudero A, Batlle R, Nerín C. Effect of Mixed Antimicrobial Agents and Flavors in Active Packaging Films. J Agric Food Chem. 2009 Sept; 57(18): 8564-71. Doi: [10.1021/jf901459e](https://doi.org/10.1021/jf901459e)
50. Burt S. Essential oils: their antibacterial properties and potential applications in foods

- a review. Int J Food Microbiol. 2004 Aug; 94(3):223-53. Doi: <https://doi.org/10.1016/j.ijfoodmicro.2004.03.022>
51. Cushnie TPT, Lamb AJ. Antimicrobial activity of flavonoids. Int J Antimicrob Agents. 2005 Nov; 26(5):343-56. Doi: [10.1016/j.ijantimicag.2005.09.002](https://doi.org/10.1016/j.ijantimicag.2005.09.002)
52. Kalembe D, Kunicka A. Antibacterial and antifungal properties of essential oils. Curr Med Chem. 2003 May; 10(10):813-29. Doi: <https://dx.doi.org/10.2174/0929867033457719>
53. Clemente AD. Composição química e atividade biológica do óleo essencial da pimenta-rosa (Schinus terebinthifolius Raddi) [thesis] [Internet]. Viçosa: Universidade Federal de Viçosa; 2006. Available from: locus.ufv.br/bitstream/handle/123456789/2077/texto%20completo.pdf?sequence=1
54. Romani VP. Desenvolvimento de embalagem ativa utilizando matérias-primas renováveis [dissertation][Internet]. Rio Grande: Universidade Federal do Rio Grande; 2015. Available from: <https://www.ppgalimentos.furg.br/images/stories/dissertacoes/2015/viviane%20romani%20desenvolvimento%20de%20embalagem%20ativa%20utilizando%20matrias-primas%20renovveis.pdf>
55. Lins R, Vasconcelos FHP, Leite RB, Coelho-Soares RS, Barbosa DN. Clinical evaluation of mouthwash with extracts from aroeira (Schinus terebinthifolius) and chamomile (Matricaria recutita L.) on plaque and gingivitis. Rev bras plantas med. 2013; 15(1): 112-20. Doi: <http://dx.doi.org/10.1590/S1516-05722013000100016>
56. Bulla MK, Hernandez L, Baesso ML, Nogueira AC, Bento AC, Bortoluzz BB, et al. Evaluation of photoprotective potential and percutaneous penetration by photoacoustic spectroscopy of the Schinus terebinthifolius Raddi Extract. Photochem Photobiol. 2015 May/June; 91(3):558-66. Doi: [10.1111/php.12419](https://doi.org/10.1111/php.12419)
57. Matsuo AL, Figueiredo CR, Arruda DC, Pereira FV, Scutti JA, Massaoka MH, et al. α -Pinene isolated from Schinus Terebinthifolius Raddi (Anacardiaceae) induces apoptosis and confers antimetastatic protection in a melanoma model. Biochem Biophys Res Commun. 2011 July; 411(2):449-54. Doi: <https://doi.org/10.1016/j.bbrc.2011.06.176>

Garcia SMS, Andrade MF de, Lima ID de et al.

Chitosan, zinc oxide and pink pepper essential...

Submission: 2018/02/20
Accepted: 2018/03/08
Publishing: 2018/04/01

Corresponding Address

Sonia Maria da Silva Garcia
Universidade Federal de Pernambuco
Av. Professor Moraes Rego, 1253
Cidade Universitária
CEP: 50670-901 — Recife (PE), Brazil