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NATURAL ANTIMICROBIAL AGENTS: APPLICATION IN FOOD PRESERVATION AND FOOD BORN DISEASE CONTROL

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Abstract: Natural antimicrobial agents in food have gained much attention by the consumers and the food industry. The misuse of antibiotics has resulted in the dramatic rise of microorganisms that are antibiotic resistant and tolerant to several food processing and preservation methods. Additionally, increasing consumers' awareness of the negative impact of synthetic preservatives on health compared to the benefits of natural additives has caused interest among researchers in the development and usage of natural products in foods. This article reviews natural antimicrobial agents and their application in food preservation and food born disease control.

Keywords: natural antimicrobial agents, natural additives,food preservation, food born disease

Introduction

Food products are highly sensitive to microbial contamination that affect their quality characteristics and reduce their nutritional value. Moreover, the presence of microbial toxins or pathogenic microorganisms such as *Salmonella*spp., *Escherichia coli*, *Staphylococcus aureus*, *Bacillus cereus*, *Campylobacter*, *Clostridium perfringens*, and *Aspergillus niger* may endanger consumer safety and cause foodborn diseases - FBD (Nummer et al., 2012).Recent data indicate the existence of more than 1,340 registered plants from which more than 30,000 compounds exhibiting antimicrobial (AM) effects have been extracted (Hayek et al., 2013). The use of AM agents of natural origin is widely accepted by consumers, because it has GRAS status (GRAS - Generally Recognized As Safe). Today, isolates of *Listeria monocytogenes*, *Clostridium perfringens*, *Salmonella* spp. and *Escherichia coli* are considered the

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main causes of poisoning when consuming meat products (Ceruso et al., 2020; Cetin et al., 2020; Chang et al., 2020; Park et al., 2021).AM agents have various activities on different microorganisms due to their diverse physiologies, integrated either directly into food or to the packaging material where it is distributed over a period of time to maintain the safety and quality of the products, resulting in extended shelf life. The worldwide spread of pathogen-resistant bacteria threatens the public health of the population. Currently, infections caused by Gram-negative (Gr-) bacteria occur more often than Gram-positive (Gr+) bacteria in clinics. A report from the China Antimicrobial Resistance Surveillance System (CARSS) shows that Gr- bacteria account for 71.1% of 3.249.123 clinically isolated strains and the prevalence of Gr+ bacteria is 28.9% (Song et al., 2022).The increasing occurrence of dangerous infections caused by bacteria that are resistant to antibiotics of the latest generations (multidrug resistant - MDR) has made the research of new molecules in the field of medicine current on a global level.

Natural antimicrobial agents for food preservation

Compared to chemically synthesized substances, plants provide greater structural diversity and offer more opportunities for the identification of new AM compounds. Plants show excellent antibacterial effect due to their safety, efficacy, antimicrobial synergism and reduced drug resistance. The combination of herbs and chemical AM agents (of synthetic origin) for the treatment of infectious diseases is popular in clinical practice in China because of their synergistic or potentiating effects. Characterization of microorganisms can be very helpful for the selection of an AM agent such as cell wall composition – Gram-negative and Gram-positive, oxygen requirements- aerobes and anaerobes, growth stage - spores and vegetative cells, acid/osmosis resistance, optimal growth temperatures - mesophilic, thermophilic, psychotropic (Malhotra et al., 2015).

Alhough synthetic preservatives, nitrite and sulfites, proved to be highly effective against a broad range of pathogenic microorganisms in foods, their potential negative impact on human health has prompted the usage of naturally occurring antimicrobials to inhibit the growth of pathogens and prevent foodborn illness (Abdollahzadeh et al.,2014;Ahmedet al., 2014; de Oliveira et al.,2015). Natural AM agents can be obtained from various sources including plants, animals, bacteria, algae and fungi. Several studies related to plant antimicrobials have proved the efficacy of plant derivatives in food applications(Tajkarimi et al., 2010; Gyawali and Ibrahim, 2012). Natural plant

components can be obtained from fruits and vegetables (onion, garlic, cabbage, pepper, xoconostle, and guava), seeds and leaves (olive leaves, parsley, caraway, nutmeg, fennel, and grape seeds), and herbs and spices (oregano, thyme, marjoram, basil, rosemary, sage, clove, and cardamom)(Tajkarimi et al., 2010). AM phytochemicals can be divided into several categories such as: phenolics and polyphenols; quinones; flavones, flavonoids, and flavonols; tannins; coumarins; terpenoids and essential oils; alkaloids; lectins and polypeptides (Cowan, 1999). Allyl-isothiocyanate is the mainAM component of mustard and horseradish oil which exhibitAM activity against Gram-negative bacteria with lesseffect on lactic acid bacteria (Delaquis and Mazza, 1995).

Accordingly, food business entities began to evaluate the use of environmentally friendly and consumer-friendly additives, of natural origin, instead of synthetic additives (Ryu and Lee, 2018; Câmara et al., 2020).

Lee et al. (2020) sublimated observations, suggestions and guidelines for researching the possibility of using antioxidants in the meat industry. The use of synthetic antioxidants is considered more cost-effective, safer and simpler, thus reducing the use of natural antioxidants (Pokorný, 2007; Mbah et al., 2019).

Essential oils(EOs)are considered as a natural AMremedyfor FBDinstead of using synthetic agents. The essential oils are well known for its AM and antioxidant (AOX) properties due to the presence of phenolic functional group (Vergis et al., 2013). Herbal extracts have already been used to control diseases that occur as a result of food poisoning and food preservation (Mostafa et al., 2018).Flavonoids are the most promising AM agents, showing favorable antibacterial activity. Most alkaloids exhibit a relatively weak antibacterial effect; however, berberine shows strong AM activity. Many terpenes and partial EOs show strong AM activity (Liang et al., 2022).Our experiences indicate that in the future it is necessary to improve the investigation of the use of plant EOs and extracts as AM agents, as well as the research of new approaches, such as the application of a small dose of a synergistic combination of plant extracts (Kurćubić et al., 2012a; 2012b; Kurćubić et al., 2014; Kurćubić et al., 2015).

By-products of different fruits and vegetables are potentially good sources of phenolics that have a broad range of AM properties (Chanda et al., 2010).

Natural agents of animal origin such as lactoferrin, chitosan, milk-derived peptides, lysozyme and many other present potential antimicrobials which could be used as food additives (Gyawali and Ibrahim, 2012).

Lactoferrin,iron-binding glycoproteinin milk, possess AM activity against a broad range of bacteria and viruses(Lönnerdal, 2011). The AM properties of Lactoferrin against FBD microorganisms including *Carnobacterium*, *L.*

monocytogenes, *E. coli*, and *Klebsiella* have beenreported (Al-Nabulsi and Holley, 2005; Murdock et al., 2007).

Chitosan, as a polycationic biopolymer naturally present in the exoskeletons of crustaceans and arthropods, has received considerable interest for commercial applications in food(Tikhonov et al., 2006).

Lysozyme, as an enzyme that is naturally present ineggs and mammalian milk, exerts antimicrobial activity against microorganisms, especially Gram-positive bacteria by hydrolyzing 1,4-β-bonds in the bacterial cell walls. Thus, this enzyme could be utilized in medical, pharmaceutical, and particularly in the food industry as a preservative in various products, such as fruits and vegetables, meat, milk, and dairy products (Khorshidian et al., 2022).

Milk-derived peptides such as casein and whey proteins have been reported to possesswide rangebioactivitiesincluding AM activity. These peptides exhibit activity against a broad range of pathogenic microorganisms such as *E. coli*, *Helicobacter*, *Salmonella, Listeria*,*Staphylococcus*, yeasts, and filamentous fungi (Fadaei, 2012).

Antimicrobials of bacterial origin such as bacteriocin (produced by *Lactococus lactis*) and reuterin (produced by *Lactobacillus reuteri*) present widely recognized natural preservatives (Arqués et al., 2011; Bian et al., 2011).

Algae and mushrooms present natural sources of bioactive compounds that have a wide range of biological properties, such as AM, AOX, anti-inflammatory, cytotoxic, and other health promoting benefits.Algae and fungi can be consumed as dietary supplements in the form of capsules or tablets containing purified fungal or algae extracts and directlyused can be treated as a type of functional food(Ślusarczyk et al., 2021). The AM activity of different types of algae against pathogenic bacteria has been identified by several scientists as potential AM agents that may be useful in the food industry. AM activity of algae (*Himanthalia elongate*) and microalgae (*Synechocystis* spp.) against *E. coli* and *S. aureus* has been reported (Plaza et al., 2010).

The application of bioactive substances of plant origin is not always under the control of doctors, so the question of the safety of their use is open, because it can lead to the absence of biological or toxic effects (Rates, 2001; Kurćubić et al., 2022a, 2022b).In order to inhibit the growth of undesirable microorganisms and reduce lipid oxidation in meat products, bioactive compounds that exhibit strong AM and AOX power can be incorporated into the product formulation, coated on its surface or incorporated into the packaging material for packaging the product (Horita et al., 2018; Nikmaram et al., 2018).

Conclusion

The basis of progress lies in innovation and competitiveness, and the benefits of implementing the aforementioned "bioinitiatives" are, in addition to preserving the environment, improving the quality of existing foods, creating new, healthier or functional products with desirable techno-functional properties, enriched with the highest level of bioactive substances or reformulated, with positive repercussions on people's health.One of the unsolved challenges for many phytochemicals is tracing effective routes and forms of administration that can release the active antimicrobial compound at the target site during systemic infections. The selection of compounds responsible for antimicrobial activity in complex mixtures such as extracts and essential oils and their potential pharmacological interactions is also a puzzle. For this purpose, it is necessary to use modern technologies, antimicrobial tests with internationally recognized standardized protocols and the use of plant material with appropriate quality controls.

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References

Abdollahzadeh E., Rezaei M., Hosseini H. (2014). Antibacterial activity of plant essential oils and extracts: the role of thyme essential oil, nisin, and theircombination to control *Listeria monocytogenes* inoculated in minced fishmeat. Food Control 35,177-183.

Ahmed A.M., Rabii N.S., Garbaj A.M., Abolghait S.K. (2014). Antibacterial effect of olive (*Olea europaea* L.) leaves extract in raw peeled undeveined shrimp (*Penaeus semisulcatus*). International Journal of Veterinary Science and Medicine 2,53-56.

Al-Nabulsi A.A., Holley R.A. (2005). Effect of bovine lactoferrin against *Carnobacterium viridans*. Food Microbiology 22(2), 179-187.

Arqués J.L., Rodríguez E., Nuñez M., Medina M. (2011). Combined effect of reuterin and lactic acid bacteria bacteriocins on the inactivation of food- borne pathogens in milk. Food Control 22(3), 457-461.

Bian L., Molan A.-L., Maddox I., Shu Q. (2011). Antimicrobial activity of *Lactobacillus reuteri* DPC16 supernatants against selected food borne pathogens. World Journal of Microbiology and Biotechnology 27(4), 991-998.

Câmara A.K.F.I., Vidal V.A.S., Santos M., Bernardinelli O.D., Sabadini E., Pollonio M.A.R. (2020). Reducing phosphate in emulsified meat products by adding chia (*Salvia hispanica* L.) mucilage in powder or gel format: A clean label technological strategy. Meat Science 163,108085. https://doi.org/10.1016/j.meatsci.2020.108085

Ceruso, M., Clement, J.A., Todd, M.J., Zhang, F., Huang, Z., Anastasio, A., Pepe, T., Liu, Y. (2020): The Inhibitory Effect of Plant Extracts on Growth of the Foodborne Pathogen, *Listeria monocytogenes*. Antibiotics 9, 319. https://doi.org/10.3390/antibiotics9060319

Cetin E., Temelli S., Eyigor A. (2020). Nontyphoid *Salmonella* prevalence, serovar distribution and antimicrobial resistance in slaughter sheep. Food Science of Animal Resources 40, 21-33.https://doi.org/10.5851/kosfa.2019.e75

Chanda S., Baravalia Y., Kaneria M., Rakholiya K. (2010). Fruit and vegetable peelsdstrong natural source of antimicrobics. Current Research, Technology and Education Topics in Applied Microbiology and Microbial Biotechnology 2, 444-450. Available: https://www.semanticscholar.org/paper/Fruit-and-vegetable-peels-strong-natural-source-of-Chanda/04f8e51d6b5d185e604319b0c109d58b31055f28

Chang S.H., Chen C.H., Tsai G.J. (2020): Effects of chitosan on *Clostridium perfringens* and application in the preservation of pork sausage. Marine drugs 18, 70. https://doi.org/10.3390/md18020070

Delaquis P.J., Mazza G. (1995). Antimicrobial properties of isothiocyanates and their role in food preservation. Food Technology 49, 73-84.

de Oliveira J.A.A., de Araujo G.H.G., Barbosa A.A., Carnelossi M.A., de Moura T.R. (2015). Stability, antimicrobial activity, and effect of nisin on the physico-chemical properties of fruit juices. International Journal of Food Microbiology 211,38-43.

Fadaei V. (2012). Milk proteins-derived antibacterial peptides as novel functional food ingredients. Annals of Biological Research 3(5), 2520-2526.

Gyawali R., Adkins A., Minor, R.C., Ibrahim S.A. (2014). Behavior and changes in cell morphology of Escherichia coli O157:H7 in liquid medium and skim milk in the presence of caffeine. CyTA -Journal of Food 12(3), 235-241.

Horita C.N., Baptista R.C., Caturla M.Y.R., Lorenzo J.M., Barba F.J., Sant'Ana A.S. (2018). Combining reformulation, active packaging and non-thermal post-packaging decontamination technologies to increase the microbiological quality and safety of cooked ready-to-eat meat products. Trends in Food Science & Technology 72, 45-61.https://doi.org/10.1016/j.tifs.2017.12.003

Khorshidian N., Khanniri E., Koushki M.R., Sohrabvandi S., Yousefi M. (2022). An Overview of Antimicrobial Activity of Lysozyme and Its Functionality in Cheese. Frontiers in Nutrition 9, 833618.

Kurćubić V.S., Mašković P.Z., Vujić J.M., Vranić D.V., Vesković-Moračanin S.M. Okanović Đ.G., Lilić S.V. (2014). Antioxidant and antimicrobial activity of *Kitaibelia vitifolia* extract as alternative to the added nitrite in fermented dry sausage. Meat Science97(4), 459-467. https://doi.org/10.1016/j.meatsci.2014.03.012

Kurćubić V.S., Stajić S.B., Dmitrić M.P., Miletić N.M. (2022a). Food safety assessment of burger patties with added herbal plant material. Fleischwirtschaft 11, 73-78.

Kurćubić V., Stajić S., Miletić N., Stanišić N. (2022b). Healthier food is fashionable - consumers love fashion. Applied Sciences 12(19), 10129. https://doi.org/10.3390/app121910129

Kurćubić V.S., Vujić J.M., Iličić M.D., Vranić D., Vesković-Moračanin S.M., Mašković P.Z. (2015). Effect of plant extracts of *Kitaibelia vitifolia* on antioxidant activity, chemical characteristics, microbiological status and sensory properties of Pirotski Kachkaval cheese. Hemijska Industrija 69(1), 85-93. https://doi.org/10.2298/HEMIND140129025K

Lee S.Y., Lee D.Y., Kim O.Y., Kang H.J., Kim H.S. Hur SJ. (2020). Overview of studies on the use of natural antioxidative materials in meat products. Food Science of Animal Resources 40, 863-880.https://doi.org/10.5851/kosfa.2020.e84

Liang J., Huang X., Ma G. (2022): Antimicrobial activities and mechanisms of extract and components of herbs in East Asia. Royal Society of Chemistry Advances 12, 29197. https://doi.org/10.1039/d2ra02389j

Lönnerdal B. (2011). Biological effects of novel bovine milk fractions. Nestle Nutrition Workshop Series Paediatric Programme 67, 41-54.

Malhotra B., Keshwani A., Kharkwal H. (2015). Antimicrobial food packaging: potential and pitfalls. Frontiers in Microbiology 6, 611.

Mbah C.J., Orabueze I., Okorie N.H. (2019). Antioxidants properties of natural and synthetic chemical compounds: Therapeutic effects on biological system. Acta scientific pharmaceutical sciences 3, 28-42.

Mostafa, A.A., Al-Askar, A.A., Almaary, K.S., Dawoud, T.M., Sholkamy, E.N., Bakri, M.M. (2018): Antimicrobial activity of some plant extracts against bacterial strains causing food poisoning diseases. Saudi Journal of Biological Sciences 25, 361-366. http://dx.doi.org/10.1016/j.sjbs.2017.02.004

Murdock C., Cleveland J., Matthews K., Chikindas M. (2007). The synergistic effect of nisin and lactoferrin on the inhibition of *Listeria monocytogenes* and *Escherichia coli* O157:H7. Letters in Applied Microbiology 44(3), 255-261.

Nikmaram N., Budaraju S., Barba F.J., Lorenzo J.M., Cox R.B., Mallikarjunan K., Roohinejad S. (2018). Application of plant extracts to improve the shelf-life, nutritional and health-related properties of ready-to-eat meat products. Meat Science 145, 245-255, https://doi.org/10.1016/j.meatsci.2018.06.031

Nummer B.A., Shrestha S., Smith J.V. (2012). Survival of *Salmonella* in a high sugar, low water-activity, peanut butter flavored candy fondant. Food Control 27, 184-7.

Park E., Ha J., Oh H., Kim S., Choi Y., Lee Y., Kim Y., Seo Y., Kang J., Yoon Y. (2021). High prevalence of *Listeria monocytogenes* in smoked duck: Antibiotic and heat resistance, virulence, and genetics of the isolates. Food Science of Animal Resources 41, 324-334.https://doi.org/10.5851/kosfa.2021.e2

Plaza M., Santoyo S., Jaime L., García-Blairsy Reina G., Herrero M., Señoráns F., et al. (2010). Screening for bioactive compounds from algae. Journal of Pharmaceutical and Biomedical Analysis 51(2), 450–455.

Pokorný J. (2007). Are natural antioxidants better and safer than synthetic antioxidants? European Journal of Lipid Science and Technology 109, 629-642. https://doi.org/10.1002/ejlt.200700064

Rates S.M.K. (2001). Plants as source of drugs. Toxicon 39(5), 603-613. https://doi.org/10.1016/S0041-0101(00)00154-9

Ryu Y.A., Lee J.S. (2018). Clean label guideline for entry into UK and EU agro-food markets. Food Ind Nutr, 23, 20-26.

Ślusarczyk S., Adamska E., Czerwik-Marcinkowska J. (2021). Fungi and Algae as Sources of Medicinal and Other Biologically Active Compounds: A Review. Nutrients 13, 3178.

Song L., Hu X., Ren X., Liu J., Liu X. (2022). Antibacterial Modes of Herbal Flavonoids Combat Resistant Bacteria. Frontiers in Pharmacology 13, 873374.https://doi.org/10.3389/fphar.2022.873374

Tajkarimi M., Ibrahim S., Cliver D. (2010). Antimicrobial herb and spice compounds in food. Food Control 21(9), 1199-1218.

Tikhonov V.E., Stepnova E.A., Babak V.G., Yamskov I.A., Palma-Guerrero J., Jansson H.-B., et al. (2006). Bactericidal and antifungal activities of a low molecular weight chitosan and its *N*-/2(3)-(dodec-2-enyl) succinoyl/-derivatives. Carbohydrate Polymers 64(1), 66-72.

Vergis J., Gokulakrishnan P., Agarwal R.K., Kumar A. (2013). Essential Oils as Natural Food Antimicrobial Agents: A Review. Critical Reviews in Food Science and Nutrition 55(10), 1320-1323.