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Potential uses of *Ustilago maydis*

Potenciales usos de *Ustilago maydis*

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Abstract:

Due to the high biodiversity of ecosystems in Mexico, there is a high variety of species, some of the most abundant are fungi, since there is an approximate record of 200 thousand endemic species of Mexico, traditionally the use given to these organisms is food and medicinal. One of the most characteristic species of our country is *Ustilago maydis* commonly known as *huitlacoche,* which has various properties in its high nutritional value. It is rich in amino acids, fats, antioxidants, proteins, and its ancestral use to treat different painful conditions. These applications have fostered the interest of different industries such as pharmaceuticals, since different studies show that *U. maydis* could have potential biotechnological uses. For this reason, this narrative review article aims to disseminate relevant biological aspects and the potential uses of huitlacoche.

Keywords:

Huitlacoche, medicinal mushrooms, antioxidant, edible mushrooms, nutrients

Resumen:

Debido a la alta biodiversidad de ecosistemas en México, existe una alta variedad de especies, unas de las más abundantes son hongos, ya que se tiene un registro aproximado de 200 mil especies endémicas en México, tradicionalmente el aprovechamiento que se le da a estos organismos es alimenticio y medicinal. Una de las especies más características de nuestro país es *Ustilago maydis* comúnmente conocido como huitlacoche, el cual presenta diversas propiedades en su alto valor nutrimental en aminoácidos, grasas, antioxidantes, proteínas y su uso ancestral para tratar diferentes padecimientos dolorosos. Estas aplicaciones han fomentado el interés de diferentes industrias como la farmacéutica, ya que diferentes estudios demuestran que *U. maydis* podría tener potenciales usos biotecnológicos. Por tal motivo, este artículo de revisión narrativa pretende difundir aspectos biológicos relevantes y los potenciales usos del huitlacoche.

***Palabras Clave**:*

Huitlacoche, hongos medicinales, antioxidants, hongos comestibles, nutrients

INTRODUCTION

Mexico is classified as a diverse country, occupying the fifth place in the world due to its wide number of species and endemisms, it is estimated that it represents 10% of the terrestrial diversity of the planet, due to its geographical location, topography, diversity of altitudes and climates, resulting in the diversification of habitats and different forms of life.[1-3] A clear example of this is fungi, which are considered to be the second most numerous organisms on Earth after insects[4], Mexico has temperate forests of gymnosperms and angiosperms, favoring the development of approximately 200,000 species of fungi of which only 3.5% to 5% have been reported including national and international research[4-6], among the uses and customs are gastronomic and medicinal. In pre-Hispanic times these were used to cure diseases of a spiritual nature such as the evil eye and witchcraft practices (*Dictyophora* and the lycoperdaceae)[7], currently, there has been an increased interest in modern pharmacology in the extraction and studies of chemical compounds from medicinal edible mushrooms.[8,9] Among the properties attributed to them are anti-inflammatory, antioxidant, and treating different types of pain such as headache, low back pain, among others.[10]

The endemic species of Mexico *Ustilago maydis*, is a basidiomycete parasitic fungus known in the world to cause the disease called common corn smut (*Zea mays*), this infection generates large tumors in the cob, culturally known as "huitlacoche" or "cuitlacoche" this fungus is used in the

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preparation of different dishes[11], however, the interest in this species also lies in the potential uses for its biochemical properties.

HOW IS HUITLACOCHE PRODUCED?

Fungi are eukaryotic organisms, heterotrophs, and chemoorganotrophs since they need organic compounds as the main source of energy, the vast majority of fungi take their nutrients by absorption since they release degrading exoenzymes of complex compounds, which allows them to use a great diversity of substrates as nutrients and energy sources. Filamentous fungi have a basic structure called hyphae, it is a tubular structure that branches as the fungus grows in an apical form, the set of hyphae that produces the fungus is called micelio.[12-14] *U. maydis* is a basidiomycete fungus, phytopathogenic, this species is dimorphic with a non-pathogenic yeast form and a pathogenic filamentous form which is responsible for the formation of tumors in corn, which makes it a non-obligated parasite, due to the above this species depends on living tissue for its proliferation and development[15,16], thus the symbiotic relationship between these two species (*U. maydis* and *Zea mays*) is merely parasitic since in this correlation only one species is benefited.[17] *U. maydis* requires one of its two hosts to complete its sexual cycle.[18-20] During its life cycle it can be divided into two phases, one of them saprophytic during which the fungus grows in the form of yeasts which, they reproduce by spores, the second phase is mycelial and pathogenic, where the fungus grows in the form of hyphae which only develop inside the host, most of the growth of the fungus occurs in meristematic tissues (embryonic tissue, poorly differentiated cells, responsible for growth and regeneration) of the plant[21], resulting in galls or tumors where the sporulation of the fungus subsequently occurs. The hyphae grow irregularly and fragment, covered with a thick, equinulate and pigmented wall. Symptoms in the plant can range from tumor formation, chlorosis, and distortions to plant dwarfism.[18,22] The production of huitlacoche can occur in two ways, natural and inoculated. The natural way is the “contamination of the cob” with the fungus strain without human intervention (Figure 1), the artificial way is the inoculation of each of the ears by means of an injection with the strain, carried out by farmers[11], it is required that the maize variety (host) be susceptible to the fungus, that the pathogen strain is virulent and the environment is favorable, with 80–85% relative humidity and a temperature of 16–32°C.[23]

The huitlacoche in Mexico is not considered a pest, this species can naturally infect 1 to 5% of the crop, however, this percentage gives an economic gain to the farmer since the infected cob is marketable and many times its value is usually higher than that of the unparasitized cob.[22]

BIOACTIVE COMPOUNDS

Huitlacoche has been studied as a biofunctional food, which is composed of multiple vitamins (C and E), minerals that are biologically important for humans[24], phenolic compounds and flavonoids which exert antioxidant activity, as they protect from the action of cellular oxidizing species[25], the consumption of these compounds are associated with a lower incidence of chronic diseases such as diabetes mellitus and cardiovascular diseases.[26] The fatty acids (FAs) present in this species such as oleic and linoleic acids, are precursors of Omega 3 and Omega 6, which are essential for humans since their deficiency can produce serious metabolic and structural alterations at the cellular level.[27]

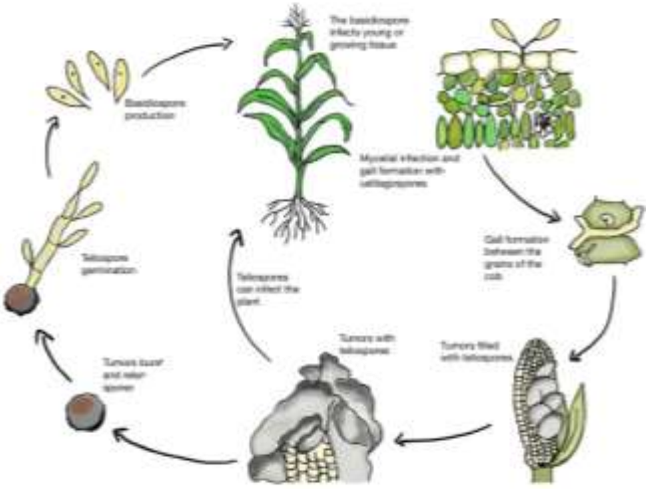

Figure 1. Life cycle without human intervention of *Ustilago maydis.*[18-20]

These FAs provide fluidity to cell membranes, which is essential for membrane proteins (ion channels, receptors, communicating junctions, catalytic receptors, enzymes, vesicle-forming structures, etc.) to have the mobility they require to perform their functions. It has been shown that in the formation of nervous tissue, particularly the brain, the fluidity of the membranes is especially important.[27] The high content of essential fatty acids suggests a high nutritional value of huitlacoche, which could be due to the fact that corn is one of the cereals with the highest content of fats and essential unsaturated fatty acids.[27,28]

The most commonly reported minerals are phosphorus, magnesium, zinc, iron, and sodium being metabolically indispensable for the body[25,28], it contains almost all the essential amino acids such as: lysine (most abundant amino acid), glycine, leucine, glutamic acid, aspartic acid, valine, isoleucine, phenylalanine, alanine, serine, tyrosine, proline, threonine, methionine, ornithine, tryptophan, γ-aminobutyric acid, ornithine and trichotomic acid.[25,29-31]

Regarding the protein value, it has been shown to have a considerable amount of protein in conjunction with other edible mushroom species (Table 1)[32-37], *Ustilago maydis* increases the percentage of protein in corn.[25,37] This mushroom provides advantages for the consumer over animal proteins by presenting antioxidant properties, antitumor, and antimicrobials. In the industry, protein concentrates, hydrolysates and fungal peptides are made to contribute to improving human health, in addition, edible mushrooms can be used to enrich traditional foods by increasing the protein value and functional qualities of the food, another important factor is the low-fat content, high fiber content[38], so it could be considered an alternative and complement in vegetarian diets.[28]

Table 1 *Protein content of edible mushrooms*

Species	Protein amount*	References
Agaricus bisporus	19%	32,33
Boletus edulis	18.5	34
Pleurotus ostreatus	17.5%	35,37
Ustilgo maydis	13.46%	36
Amanita caesarea	13%	34

*Crude protein in dry matter

CONSUMPTION OF HUITLACOCHE FOR INFLAMMATION AND PAIN

The International Association for the Study of Pain (IASP) defines pain as an unpleasant sensory and/or emotional experience associated with actual or potential tissue damage[39,40], which can be classified depending on its duration, pathogenesis, location, course and intensity[41], as a result of cell damage, a process of inflammation is generated, which is a physiological response in order to repair damaged tissue; the inflammatory process begins when chemical compounds are released by the damaged tissue, in response, white blood cells produce substances that cause cells to divide and grow to rebuild tissue and thus repair the injury.

There are two types of inflammation, acute inflammation, which occurs in a short period of time and symptoms last for days, and chronic inflammation, which is described as slow and prolonged, which can last from months to years.[42] Inflammation can be due to different causes which can range from a blood clot inducing a stroke, immune system disorder, cancer, chemical exposure to polycyclic aromatic hydrocarbons, dioxins, smoking, physical injury including trauma, or a neurological condition.[43,44] Conditions of inflammation and pain can become disabling for those who suffer from it, impairing quality of life[45], however, it has been shown that prolonged use of Nonsteroidal anti-inflammatory drugs (NSAIDs) used to treat pain, fever and other inflammatory processes[46], such as naproxen, ibuprofen, ketorolac, can lead to adverse effects on the cardiovascular, gastrointestinal, hepatic and renal systems.[47]

Due to the above, there has been increased interest in offering alternatives or adjuvants to treat pain, demonstrating the efficacy and biosafety of the use of fungi and medicinal plants through research in biochemical and pharmacological analyses.[48] Generationally, *Ustilago maydis* has been used in painful and inflammatory situations such as intestinal pain, muscle inflammation and headaches[33,49,50], an ancestral use it is to make a poultice, which is placed on a cloth, and then applied directly to the area of inflammation[51], due to this, interest has been aroused in studying the compounds responsible for mitigating these discomforts; of the compounds recently evaluated for inflammatory and painful processes are ustilagols.[30] Ustilagols are compounds extracted from the mycelium of *U. maydis* that exhibit dopaminergic properties, offering pharmacological potential against some neuroleptic diseases[50], on the other hand, Ustilago C, E demonstrated anti-inflammatory properties, Ustilagol G showed that it can generate antiplatelet, similar to that observed with Aspirin®, Ustilagoles A – F demonstrated *in vitro* studies its potent anti-inflammatory and antithrombotic properties.[51] However, one cannot dismiss the ancestral knowledge in which it has been described that huitlacoche has been used to cure heart disease, colic, blisters, pimples, skin burns, athlete's foot, wounds, nosebleeds, rashes in babies, stop bleeding, heal animal bites, relieve dehydration and help with anxiety.[7,52-55] Nonetheless, there are still areas of opportunity to verify its multiple applications in pain and Inflammation and a possible future as an adjunct to a pharmacological treatment.

ANTIOXIDANT PROPERTIES

The antioxidant capacity of foods is derived from the cumulative synergistic action of a wide variety of antioxidants, such as polyphenols, flavonoids, vitamins C and E, carotenoids, terpenoids, Maillard compounds, and trace elements. These antioxidants play a role in the prevention of diseases related to oxidative[56-58], such as neurodegenerative diseases, in which progressive degeneration and neuronal death take place[59], due to an imbalance in the generation of oxidizing species of nucleic acids, proteins, and lipids resulting in mitochondrial dysfunction, glial cell activation, apoptosis, protein oligomerization, inflammatory response, alteration of the blood-brain barrier[60-62], however, phenolic compounds, flavonoids, and carotenoids have been shown to be antioxidant compounds that have potential health benefits, a potential industrial, pharmaceutical, and food application.[25]

According to National Institute of Statistics and Geography (INEGI) and National Population Council (CONAPO) the trend of the Mexican adult population is increasing[63], due to the increase in people's longevity, it is expected that there will be an increase in conical degenerative diseases[64], adding to this an unbalanced diet with an increase in the consumption of highly processed foods reducing traditional ethnic foods with high nutritional value.[65]

The consumption of antioxidants may be affected; therefore, it is opportune to encourage the Mexican population to consume foods with antioxidants. One of these foods is Huitlacoche (table 2)[66-70], this food when heat-treated (cooked as food) increases the concentration of phenolic compounds and flavonoids, benefiting its antioxidant capacity, therefore this food can contribute to an improvement in the state of human health, helping to reduce the damage generated during the oxidative stress of some metabolic processes.[24,55]

HUITLACOCHE AS FOOD

With the information that is available from prehistory to the present times, the huitlacoche is used as a food in Mexico, mainly in the center and southeast, because of this there is a great variety of ways of preparing this fungus, the National Autonomous University of Mexico published a book entitled 'Cujtlacochi el huitlacoche', an open-access version describes What is it?, How is it made?, trade, life cycle, traditions, history and phylogeny of this species; this book includes approximately 31 recipes ranging from Avocados stuffed with Cuitlacoche (Figure 2) to Salmon with sweet cuitlacoche sauce,[71] in this way, the versatility of this species as a food is shown. With all the scientific support that has been given to huitlacoche, it is considered an excellent food, the best way to take advantage of its properties is cooked[24,55], it is important to emphasize that the low use of oil is essential in any dish, in this way it is considered a complement in food plans and highly adaptable to different lifestyles, so promoting its consumption is important.

***Table 2** Antioxidant compounds recorded in huitlacoche.*

Group	Derived compound	Reference
Phenolics	ferulic	24,28,55,66,67
	Sinapic	
	Chlorogenic	
	p-coumaric	
	caffeic	
Flavonoids	Anthocyanins	25,28,55,67
	Quercetin	
	Naringenin	
	Catechin	
Carotenoids	β-carotene	67,68
	β-cryptoxanthin	
Phytosterols	campesterol-3-β-glucoside	28,69,70
	Δ7-stigmasterol	
	Δ7-avenasterol	
	Ergosterol	

FUTURE OF MUSHROOMS

As mentioned above, most mushrooms have a broad profile of essential amino acids, which can contribute to different dietary requirements, while fungi have economic advantages over plant and animal sources.[72] With the passage of time the food industry seeks to meet the demand for food. It is predicted that by 2050 the world's population will exceed 9 million people. The Agriculture Organization (FAO) says that agricultural production will have to increase food production by 70% to meet demand.[73] Due to the nature of fungi, they can be produced industrially in a high quantity and in a short period of time. Within the biotechnological field, multiple species of fungi have been used for processes such as bioconversion, biorefining, bioremediation, biodegradation, antimicrobial and antifungal agents, although *Ustilago maydis* is more studied to be a complementary and functional food for the population, its biotechnological potential cannot be discarded, since it was shown that it can be used as a complement in biological control for wine production at the beginning of fermentation since *U. maydis* produces an effective toxin against *Brettanomyces bruxellensis* yeast deteriorating.[74]

Figure 2. A, B: Raw Huitlacoche for sale at the Pachuca Hidalgo supply center, C: Avocados stuffed with huitlacoche and cheese (Recipe based on the book Cujtlacochi el huitlacoche).*[71]*

The antimicrobial and antifungal activity of this species is relevant since its extracts have shown to be effective against yeasts, bacteria and molds, its glycolipids showed efficacy against Staphylococcus aureus and *Salmonella enterica, Typhimurium, Aspergillus terreus and Candida albicans,* which shows that *U. maydis* has potential application in the food, pharmaceutical and industrial industries.[30,75-77] As has been shown in different molecular studies, fungi are strictly evolutionarily related to animal cells, consequently many of the cellular processes are conserved between these groups; cell model systems of fungi such as yeasts have contributed to the understanding of different cellular pathways, as they have a good genetic accessibility, a short generation time and simple culture form, the role that species like *U. maydis* is that they have an advantage as a yeast. *U. maydis* was shown to have an unexpected similarity in the engines of microtubule organization, long-distance transport and mitosis, with higher eukaryotic cells, this discovery demonstrates that *U. maydis* has a large number of genes closely related to human genes, this supports the use of this species as a model system for the study of cellular processes that may favor the genetic study of our species.[78]

CONCLUSION

As has been demonstrated through the generations, huitlacoche has a wide variety of uses, from gastronomic to medicinal. It is important to bear in mind that there are still areas of opportunity in which different investigations can be carried out to demonstrate and rectify such uses. The interest in this species in different industries such as pharmaceutical, food and biotechnology has shown that this species is being considered a good model to study different cellular metabolic processes and at the same time has compounds that could have pharmaceutical potential, although there is still much to be investigated, however, with the already existing evidence. The huitlacoche is undoubtedly a good complementary food for the Mexican diet, taking into account its multiple benefits due to antioxidants, fats and proteins that it contains, adding that the preparation of this is a representative dish in Mexican culture.

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