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Review

Aspergillus oryzae: An opportunity for agriculture

Karen Berenice García-Conde, Ernesto Cerna-Chávez, Yisa María Ochoa-Fuentes*, Universidad Autónoma Agraria Antonio Narro. Calzada Antonio Narro Núm. 1923, Col. Buenavista, Saltillo, Coahuila, México. CP. 25315; **Jazmín Janet Velázquez-Guerrero,** Departamento de I+D, CULTA SA de CV. Boulevard Luis Echeverría Álvarez 1700, Col. Altavista, El Mante, Tamaulipas.

***Corresponding Author**:
Yisa María Ochoa-Fuentes
yisa8a@yahoo.com

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ABSTRACT

Aspergillus oryzae is a filamentous fungus capable of degrading various substances employing enzymes, which is why it is widely used in the biotechnological industry, pharmaceutical products, enzymes for industrial use, bleaching agents, anti-pollution textile treatments. However, few works focus on these microorganism's field applications. This manuscript reviews the potentially beneficial applications of *A. oryzae* and some by-products in agriculture as biological control, growth inducer, and bioremediation for soils contaminated with heavy metals.

Keywords: Bioremediation, nematicide, insecticide, microorganisms, metabolites, non-toxigenic.

INTRODUCTION

The fungi of the *Aspergillus* spp. genus are considered a complex group of ascomycetes that compose 350 accepted species (Kocsubé *et al.,* 2016). They are described as filamentous fungi, able to secrete a wide range of secondary metabolites and enzymes, whose function is to degrade and recycle biopolymers from plant tissues (El-Enshasy, 2007). The *Aspergillus* spp. genus is generally found in stored seeds, plants in decomposition and soil, where they develop as saprophytes (Mousavi *et al.,* 2016).

Although fungi from the *Aspergillus* spp. genus are not considered important sources of phytosanitary diseases, they are responsible for alterations in plants and stored products; since they are opportunist molds, they prosper under storage conditions (Awuchi *et al.*, 2021). This genus is also recognized for its production of mycotoxins, with around 300 and 400 identified, such as aflatoxins, secalonic acids, cyclopiazonic acid, aflatrem, citrinin, stregmatocystin, glycytoxin, ochratoxin A

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(OTA) and terrein (Navale *et al.,* 2021), with a potential health risk for humans and animals, as well as affecting the environment and having a negative effect on the world's economy (Bueno *et al.*, 2015). An important example of this type of toxic secondary metabolites are aflatoxins, which represent a hazard for farmers in postharvest and are considered indicators of biological soil degradation (Marshall *et al.,* 2020). They bring about qualitative nutritional and sensory changes in plant-based products, since the infection can produce unpleasant flavors or odors, rotting and discoloration (Kozakiewic, 1989).

Some fungi of the *Aspergillus* spp. genus, such as *A. flavus, A. nidulans, A. nomius* and *A. parasiticus,* are agronomically important, since they produce aflatoxins (AF) (Hesseltine *et al.,* 1970; Gomi, 2014). Mainly B1, B2, G1 and G2 have proven to be strong carcinogenic, cytotoxic and potentially mortal biotoxins for humans and cattle (Ráduly *et al.,* 2019). *A. flavus* has been reported as the cause of contamination with aflatoxins AFB1 in any stage of the peanut supply chain (imports, manufacturing and retail) in countries such as Malaysia, where the tropical climate conditions are favorable for the growth of this fungus (Norlia *et al.,* 2018, 2019). In Mexico, maize has been affected by contamination with aflatoxins, in the same way as grains such as rice, barley, bean, sorghum, wheat, some oleaginous plants and dried fruits are susceptible to these biotoxins, produced by *A. flavus* (AFB1 and AFB2), *A. parasiticus* and *A. nomius* (AFG1 and AFG2) (Anguiano-Ruvalcaba *et al*., 2005; Escobar *et al*., 2023).

It is worth highlighting the existence of non-toxicogenic strains within *Aspergillus* spp., which do not produce aflatoxins and which can be applied in the planting area, to then be installed, compete and displace the toxigenic strains, resulting in the reduction of aflatoxins (Marshall *et al.,* 2020; Senghor *et al.*, 2020). Non-toxicogenic *A. niger, A. sojae* and *A. oryzae* strains do not produce compounds that contain, essentially, a furan ring attached to the coumarin nucleus, important in the biosynthesis path of aflatoxins, and do not produce cyclopiazonic acid jointly with aflatoxins such as *A. flavus* (Dorner *et al.*, 2000; Padrón *et al.,* 2013).

Aspergillus spp. strains that do not produce aflatoxins can be used as fungal biocontrol agents in the prevention of contamination with biotoxins (Barberis *et al.,* 2019). Strains *A. westerdijkiae* 107*, A. fumigatos* C143*, A. tamarii* C122 and *A. niger* C187 have proven, in terms of inhibition and production of OTA, to have favorable results, with the strain *A. niger* C187 displaying an inhibition of 100% in the production of OTA and in the growth of *A. ochraceus, A. westerdijkiae, A. carbonarius* and *A. niger* in coffee grains (de Almeida *et al.,* 2019). Likewise, they are used in the pharmaceutical industry and in industrial processes such as the fermentation of foods, since they are abundant sources of enzymes such as proteases, amylases and amylglucosidases, and others (Schuster *et al*., 2002; Olempska-Beer *et al*., 2006; Samson *et al*., 2014; Gómez *et al*., 2016). The production of polygalacturonase (Exo-PGs), a consortium of enzymes required for the hydrolysis of pectin, is one of the applications of the strain *A. sojae* ATCC 20235, useful in the depectinization and clarification of fruit juices, the extraction of oils from the skins of vegetables and citrus fruits, and treating wastewater (Tari *et al.,* 2008).

Therefore, because *A. oryzae* has non-toxigenic strains, it figures as one of the most important species, due to its potential use as a biotechnological tool in degrading metabolic processes of diverse starches and proteins; in the metabolism of amino acids and amino acid and sugar absorption transporters (Machida *et al.,* 2005, 2008; Watarai *et al.,* 2019; Daba *et al.,* 2021). *A. oryzae* is considered by the FDA as "generally recognized as safe" (GRAS), which refers to any substance intentionally added to foods, which must be subjected to revision and approval before its commercialization, unless the substance is generally recognized among qualified experts (Gad, 2005; FDA, 2019). Therefore, the WHO endorses the security in the use of *A. oryzae* (He *et al.,* 2019), considering this microorganism adequate for its application in the food industry, such as the fermentation of foods, the production of alcohol and vinegar, in the pharmaceutical and cosmetics industries via the formulation of drugs and depigmenting agents. These applications are due to the production of enzymes and secondary metabolites such as lipases, cellulases, pectinases, β-galactosidase, amylases, kojic acid, malic acid, fumaric acid, pheluric acid and others (Daba *et al.*, 2021).

Therefore, this study focuses on reviewing investigation and literature studies on the diverse products derived from *A. oryzae,* their contributions and applications in the agricultural areas, such as bioremediators, growth enhancers and biological control agents. It is worth highlighting that, although the study of *A. oryzae* has focused mostly in the industrial area, this study only considered those studies and investigations in which their application is directed to the agronomic part. It focuses primarily on kojic acid and *A. oryzae* strains involved in its production, since the fermentation process presents sustainable characteristics, and its applications are novel for the agricultural area.

The main objective of this revision is to publish the potential of *A. oryzae* in scarcely studied areas of agricultural importance. Although *A. oryzae* has been studied on a large scale in industrial, food and medical areas, studies on its agronomic potential are few, and in Mexico its study is practically inexistent, hence part of this revision seeks the development in the future of scientific studies on *A. oryzae* aimed at the agricultural sector, contributing to the development and care of the Mexican countryside.

Morphology and description of *Aspergillus oryzae;* origin, isolation and development

Aspergillus spp. presents hyaline septate hyphae, with a 45° dichotomic ramification (Cuervo-Maldonado *et al.,* 2010). Growth forms extended mycelia that cover the entire surface of the culture media (Gomi, 2014) (Figure 1). The balloon-shaped vesicle has a diameter between 100 and 200 µm with a structure formed by oval-shaped conidia, 5 to 8 µm in length that contains four soft and slightly coarse nuclei. The phialides are found in the vesicle and may be uniseriate or biseriate sterigmata. The shoots are colorless and 1 to 5 mm in length, with a rugged texture (Moubasher, 1993; Powell *et al.*, 1994).

Ahlburg (1876) first isolated *A. oryzae* from köji, the material fermented by the mold of *A. oryzae* planted in a steamed rice solid medium (Machida *et al.,*

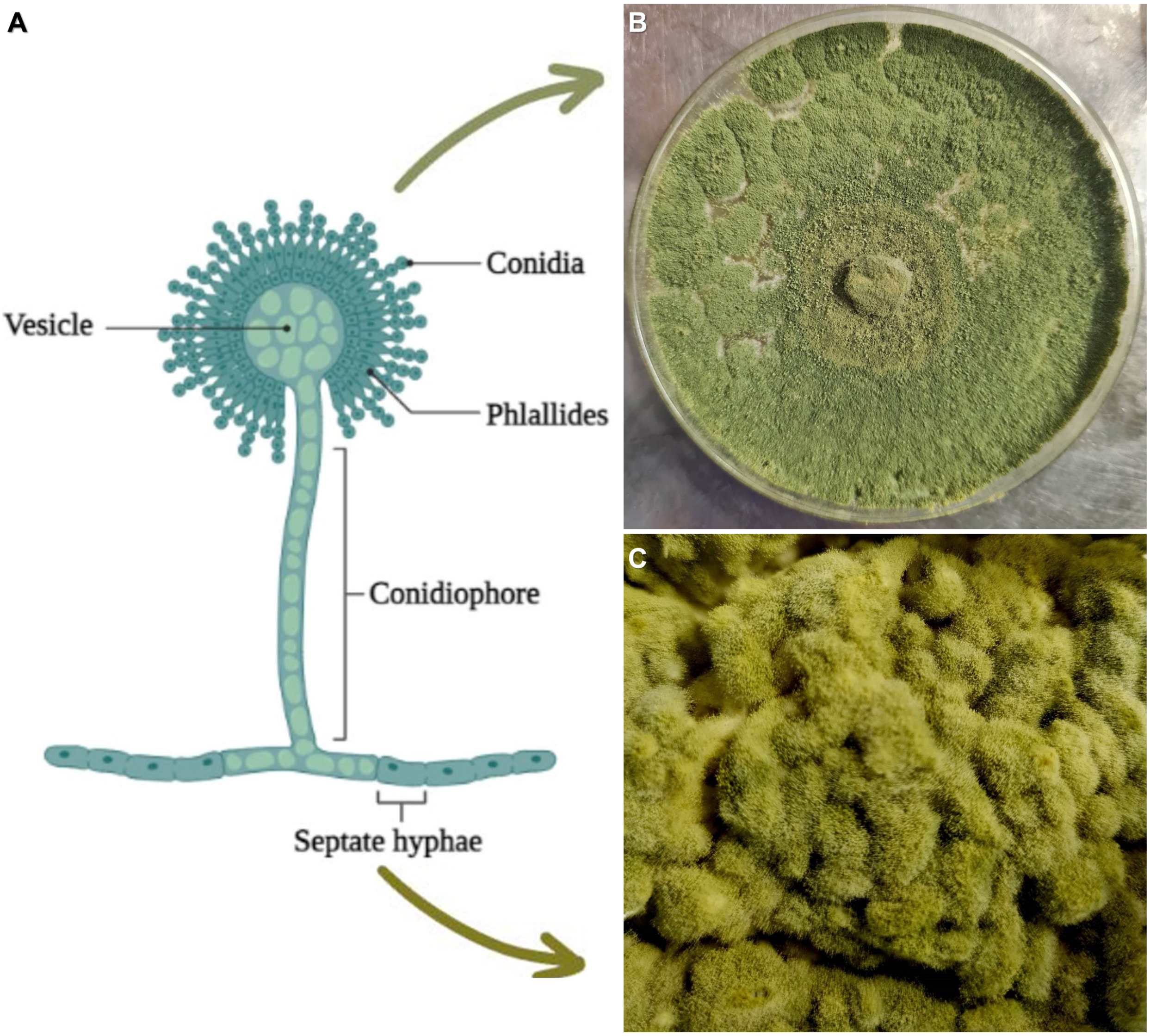


Figure 1. Morphology of *A. oryzae*; A) Parts and structures of the fungus (Adapted from "Structure of *Aspergillus* spp.", 2023), B) *A. oryzae* planted in a PDA medium and C) Growth of *A. oryzae* in steamed rice (köji).

2008). This fungus belongs to the Erotyomicetes class; Order: Eurotiales; Family: Trichocomaceae (Daba *et al.,* 2021). The use of *A. oryzae* in the production of sake (fermented rice alcoholic beverage), vinegar, miso (soybean paste) and soy sauce, has been reported for at least two millennia (Furukawa, 2012; Chang *et al.,* 2014). In general terms, it is considered safe and no strains that produce aflatoxins are known (Machida *et al.,* 2005).

The genes that codify the enzymatic pathway for the biosynthesis of aflatoxins are grouped in a 74 Kb region of the DNA in *A. flavus*. This group is found in *A. oryzae,* but it does not seem to be functional (Yu *et al.,* 2004). *A. oryzae* and *A. flavus* are morphologically similar. Several studies suggest they are ecotypes, which refers to a same species which have a different expression in different environments, due to the interaction of their genes with the environment in which they are found (Kurtzman *et al.,* 2018). This indicates that *A. oryzae* was the result of the domestication of *A. flavus* after centuries of planting it (Payne *et al.,* 2006).

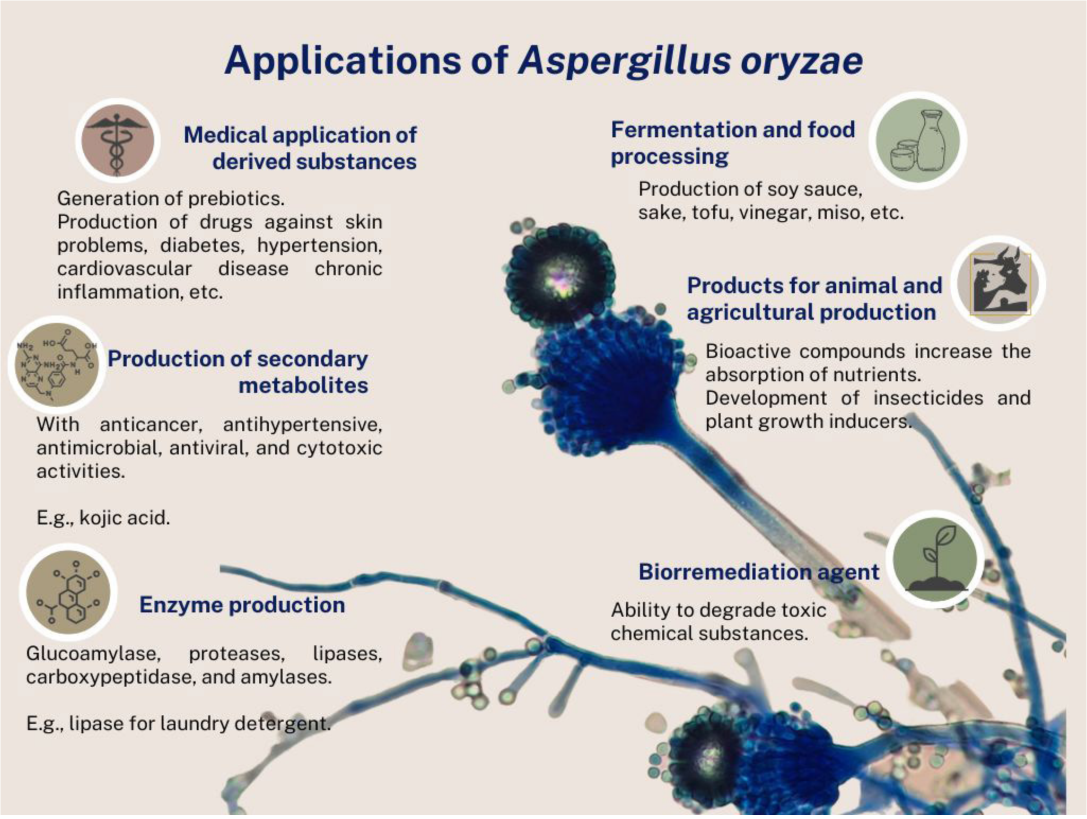
Because *Aspergillus oryzae* was reported as a domesticated microorganism, it cannot be found in nature. However, there are some reports that mention the isolation of *A. oryzae* from foods, plants and soils, appearing less frequently (Klich, 2002). A historical file described that *A. oryzae* should be isolated from a spike of rice, indicating that it could have existed in nature before its domestication (Murakami, 1980).

This fungus grows in several media, including potato dextrose agar, where it grows particularly fast in 7 days at 25 °C (Moubasher, 1993). Its stage of sporulation begins on day 7; when growth reaches 7 to 8 cm, yellow ring begins to form, and which will gradually turn green (Daba *et al.,* 2021). The ideal conditions for the development of *A. oryzae* include a slightly acidic pH between 5 and 6, its temperature must range between 32 and 36 °C (±1 °C), and variations in temperature above 44 °C inhibit its growth. These fungi show an efficient development in media with water activity above 0.8 and they rarely grow below this range (Gomi, 2014).

Applications of *Aspergillus oryzae* and its possible implementation in agriculture

The versatility of *A. oryzae* is reflected in the wide variety of areas in which it can be applied (Figure 2), since it is highly effective in the manufacturing of biotechnological products, due mainly to its metabolic and enzymatic diversity (El-Enshasy, 2007).

Lee and collaborators (2016) provided a metabolic profile obtained during the fermentation of köji with *A. oryzae,* which comprises the secondary metabolites secreted in the fermentation process, classifying them into; a) sugars (xylose, fructose and glucose); b) polyols (glycerol, erythritol, xylitol, sorbitol y myo-inositol); c) organic acids (succinic acid, glyceric acid, fumaric acid, malic acid,



Applications of *Aspergillus oryzae*

Medical application of derived substances

Generation of prebiotics.
Production of drugs against skin problems, diabetes, hypertension, cardiovascular disease chronic inflammation, etc.

Production of secondary metabolites

With anticancer, antihypertensive, antimicrobial, antiviral, and cytotoxic activities.

E.g., kojic acid.

Enzyme production

Glucoamylase, proteases, lipases, carboxypeptidase, and amylases.

E.g., lipase for laundry detergent.

Fermentation and food processing

Production of soy sauce, sake, tofu, vinegar, miso, etc.

Products for animal and agricultural production

Bioactive compounds increase the absorption of nutrients.
Development of insecticides and plant growth inducers.

Biorremediation agent

Ability to degrade toxic chemical substances.

Figure 2. Areas of application of *Aspergillus oryzae.*

kojic acid, citric acid and gluconic acid); d) phenolic acids (4-hydroxybenzoic acid and ferulic acid); e) amino acids (alanine, proline, glycine, serine, threonine, aspartate and GABA); f) fatty acids (palmitic acid, linoleic acid, oleic acid and pinellic acid); and g) vitamins (vitamin B3). Each one of these compounds has different antimicrobial, antioxidant, anticarcinogenic and antiviral properties, as well as hormonal compounds and metal chelators (Frisvad *et al*., 2018; Daba *et al*., 2021).

The application of *A. oryzae* in the production of malic acid and fumaric acid (Xu *et al.,* 2012; Brown *et al.,* 2013) proposes the possibility of the creation of a biorefining process for the production of organic acids and enzymes, replacing the currently used polymers derived from crude oil (Brink *et al.,* 2023). The biorefining process can be enhanced by incorporating agricultural by-products, inexpensive non-food substrates, reducing production costs and providing an option free of any chemical products (Jiménez-Quero *et al.,* 2020).

The microbial enzymes used in the industry have proven to be better in their application, as well as inexpensive and respectful to the environment in comparison with chemical products (Whiteley and Lee, 2006). They have technical-economic advantages, meaning shorter production times, better space per enzyme unit produced and unlimited potential in terms of availability of new enzymes (Scriban, 1985).

There are reports on the application of *A. oryzae* in the process of fermentation of grape pomace with the production of enzymes (cellulase, pectinase and tannase), which facilitate the aqueous extraction of polyphenols (gallic acid, sinapic acid and ferulic acid) with antioxidant and prebiotic properties, such as food additives, where *A. oryzae* has a greater production and selectivity of tannase under humid conditions, having a positive effect on the antioxidant activity, which can be influenced by the production of galic acid (Meini *et al.*, 2021). On the other hand, *A. oryzae* can stimulate ruminal fermentation by improving the consumption and digestion of the food and dry matter in cattle, by applying it as a microbial additive in the cattle feed (Sosa *et al.,* 2022). At the same time, the efficiency in the increase of volatile fatty acids has been proven, making *A. oryzae* an element of improvement to potentialize the diets of ruminants in a different way. It also exerts an influence on the supply of enzymes in maize, oat hay and alfalfa hay silage (Kong *et al.,* 2021).

Technological progress has taken advantage of the potential of *A. oryzae* (Matsunaga *et al.,* 2002) for industrial use in the development of detergents, pigments and antioxidants, (Christensen *et al.,* 1988; Machida *et al.,* 2008; Panchanawaporn *et al.,* 2022). Likewise, its application in the fermenting of foods (Machida *et al.*, 2008; Yasui *et al.,* 2020) and the implementation in the production of metabolites such as organic acids and plant growth regulators are important areas of study (El-Enshasy, 2007; Siddiqui, 2016). It can also be useful in biological activities such as in veterinary science as probiotics for poultry and livestock feed digestive (Lee *et al.*, 2006; Murphy, 2021; Podversich *et al.,* 2023).

A.oryzae as a soil bioremediator, growth enhancer and biological control

A. oryzae can be an alternative for the development of a sustainable and eco-friendly agriculture, specifically in Mexico, where their applications on the field are not a topic of study. The following information describes some areas of opportunity where this microorganism can be applied on the field, in order to pave the way for possible scientific studies aimed at the Mexican countryside.

Endophytic plant fungi are those which live on plant tissues and cause no visible harm. Due to this, a mutualistic relationship (endophyte-host) is occasionally identified, which unleashes the production of bioactive substances (secondary metabolites, enzymes etc.) which exert an influence on growth enhancement, the survival of the host under diverse environmental conditions, the reduction of susceptibility to diseases, and helping control pest insects and plant pathogen agents (El-hawary *et al*., 2020; Murali *et al*., 2012; Sharma and Singh, 2021).

Although *A. oryzae* is not commonly reported as a natural endophyte, information has been provided on its isolation in *Ginkgo biloba* roots in China (Machida *et al.,* 2005). Sun and collaborators (2018)*,* in the study of the inoculation of *Raphanus sativus* seeds with the strain *A. oryzae* BNCC341706, established it as a fungus with endophytic properties, since it did not affect the germination of the inoculated seed and instead promoted the growth of the *R. sativus* culture, which reached a height of 116 mm in comparison with the control, which had a height of 99.6 mm. Another effect of the use of *A. oryzae* was reflected on the health of its main pest insect *Plutella xylostella,* affecting its consumption parameters, weight of larvae and pupae, which opens the possibility of treating cruciferous seeds and the control of pest insects using *A. oryzae*.

Likewise, as bioremediating agents, endophytic fungi have proven to be efficient in the degradation of contaminants, leaving no traces of toxic by-products (Skinder *et al.,* 2022), which is advantageous, due to its biomass, long life cycle and network of hyphae (Sun *et al.,* 2012), along with its ability to degrade chemically toxic substances by modification or acting upon its chemical bioavailability (Bornyasz *et al.,* 2005). In the case of *A. oryzae* as a bioremediating agent, the *in vitro* study of the *A. oryzae* strains AM1 and AM2 displayed the ability to degrade atrazine (90%), endosulfan (56 and 76%) and chlorpyrifos (50 and 73%), while also obtaining an adequate development under high concentration of pesticides, which generates the possibility of degrading this type of chemical products (Barberis *et al.,* 2019).

The OTA is a microtoxin that affects human health and agricultural products, which has led to a search for control measures, therefore, biodegradation has been proposed as a promising method. The strain *A. oryzae* M30011 is able to degrade OTA by up to 94% in 72 h, at a pH of 8, a temperature of 30 °C and a concentration of the inoculant of 104 UFC mL^{-1}. On the other hand, a reduction in the levels of aflatoxins is an important matter, since they are a threat to worldwide food security (Xiong *et al.,* 2021). The strain *A. oryzae* M2040 has been proven capable of inhibiting the production of AFB1 by 87%, and the proliferation of *A. flavus*, under *in vitro* conditions, and in peanuts by successfully displacing the aflatoxin-producing fungus by secreting antimycotic compounds, which have not been reported (Alshannaq *et al.,* 2018). These studies back the potential of *A. oryzae* in the agricultural and food industry.

The potential of the use of *A. oryzae* has been emphasized in the development of research work as a growth enhancer and a biological control agent, shown in Table 1.

The ability of *A. oryzae* to secrete enzymes is an alternative for the development of microbiological compounds, since biological activities are carried out which can be adapted in the area of agronomy. An example of this is the antifungal activity of xylanase produced by the strain *A. oryzae* MN894021, which displayed a reduction

Table 1. Use of *A. oryzae* as a growth enhancer, pest control agent and bioremediator od contaminated soils.

Application	Strain	Crop / Pest	Results	Reference
Arsenic biorremediator and growth enhancer	FNBR_L35	Oat (*Avena sativa*), Calendula (*Calendula officinalis*), Ashwagandha (*Withania somifera*)	Effects of bioaccumulation and biovolatilization of arsenic in concentrations of 100 to 10,000 ppm in a period of 21 days and enhancement of plant growth	Singh *et al.,* 2015
Entomopathogen	XJ-1	*Locusta migratoria*	Mortality in third instar of the insect	Zhang *et al.,* 2015
Growth enhancer and control agent	BNCC341706	Radish seeds (*Raphanus stativus*), *Puntella xylostella*	Greatest plant height. Inhibition of feeding and low weight of larvae and pupae	Sun *et al.*, 2018
Removal of glyphosate	AM1 and AM2	*In vitro*	Degradation of 50% in glyphosate concentrations, long periods of incubation and permanence of the fungus	Carranza *et al.,* 2019
Entomopathogen	USMN05 USMM03 NRRL2097	*Spodoptera litura*	Mortality of 20% and inability to produce aflatoxins	Fitriana *et al.,* 2021

of 75, 90 and 100% in the incidence of *Botrytis cinerea, Fusarium solani, F. chlamydosporum, F. incranatum, Macrophomina phaseolina, Rhizotocnia solani* and *Sclerotinia sclerotiorum* in broad bean seeds covered with xylanase, providing protection against the invasion of these phytopathogenic fungi (Atalla *et al.*, 2020). The results obtained from the xylanase produced by the strain *A. oryzae* MN894021 coincide with the activity of the xylanase from *Trichoderma harzianum* kj831197 against *Corynespora cassiicola, Alternaria* spp., *F. oxysporum* and *Botrytis fabae* (Ellatif *et al.,* 2022).

The control of phytopathogens is an important challenge for agriculture. The development of sustainable, environmental, easy and eco-friendly control processes is constant in current research; an option is the biogenic synthesis of bioparticles (Zhang *et al.,* 2020). The strain *A. oryzae* MTCC3107 has been implemented in the formulation of silver nanoparticles (AgNP), whose antimicrobial potential against *Sclerotinia sclerotium* reflected an inhibition of 100% at a concentration of 100 µL mL^{-1}. The role of *A. oryzae* in the formulation is due to the secretion of amylase, which catalyzed the AgNP production process, making it a green synthesis process (Gupta and Saxena, 2023).

The study and publication of information related to the potential of *A. oryzae* serve as a support for future investigations in the area of phytopathology, since it has been relatively scarcely studied. Despite *A. oryzae* having a wide margin of produced bioactive substances, those applied in this area are few. Some activities and metabolites are presented in Table 2.

Table 2. Activity of bioactive substances produced by *A. oryzae* against plant pathogens.

Bioactive substances	Strains	Application	Result	Reference
Kojic acid	NRRL 447, 552, 552, 1730 Y30038 (S-03)	Prevention of contamination by toxins in agricultural products	Reduction of aflatoxins in peanut	Dorner *et al.,* 1998
Kojic acid	*	Insecticide: *Glyphodes pyloalis*	Inhibition of phenyloxidase activity	Sharifi *et al.,* 2013
Oryzaeins A-D	KM999948	Antiviral: TMV	Rates of inhibition of 22.4 – 30.6%	Zhou *et al.,* 2016
Xylanase	MN894021	antifungal: *Alternaria alternata, Fusarium oxysporum, Phoma destructor, Rhizotocnia solani* and *Sclerotium rolfsii*	Reduction of the live growth Reduction in percentages of incidence of root rotting	Atalla *et al.,* 2020
Kojic acid	*	Antifungal activity: *Sclerotinia slerotiorum*	Inhibiyion of chitin and melanin synthesis Reduction of oxalic acid of the virulence factor	Zhu *et al.,* 2022

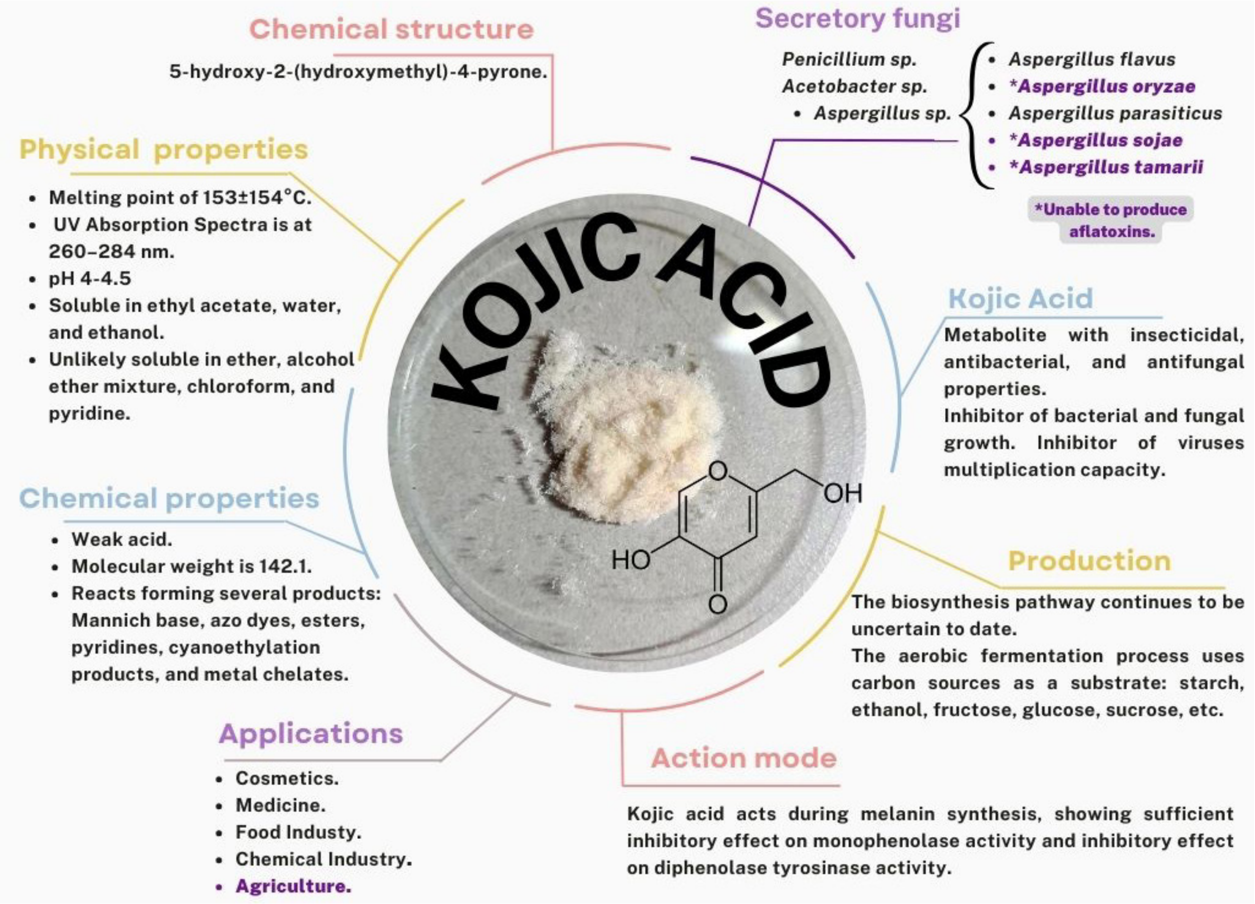
*Strain not provided by the author.

Kojic acid, secondary *A. oryzae* metabolite; alternative for the control of plant pathogens

Within the main secondary metabolites produced by *A. oryzae*, kojic acid is one of the most relevant (Figure 3) (Yamada *et al.,* 2014). Its application in the control of phytopathogenic agents and pest insects is a relatively new topic; however, the investigation reports show that this application may be a feasible alternative for the control of pests in crops.

A. oryzae has bactericidal, fungicidal and insecticidal effects (Mohamad *et al.,* 2010). It acts in relation with the inhibition of oxidative enzymes in both plants and arthropods. Studies have shown that kojic acid efficiently inhibits the rate of formation of pigmented products and absorption of oxygen when compounds such as catecholamines (DL-DOPA, dopamine and norepinephrine), are oxidized by the enzyme tyrosinase (Kahn, 1995; Kahn and Ben-Shalom, 1997).

Mahmoud and collaborators (2023) analyzed the insecticidal activity of kojic acid produced by the strain *A. oryzae* ASU44 (OL314732), against *Aphis*



Chemical structure

5-hydroxy-2-(hydroxymethyl)-4-pyrone.

Secretory fungi

Penicillium sp.
Acetobacter sp.
- *Aspergillus sp.*
  - *Aspergillus flavus*
  - ***Aspergillus oryzae**
  - *Aspergillus parasiticus*
  - ***Aspergillus sojae**
  - ***Aspergillus tamarii**

***Unable to produce aflatoxins.**

Physical properties

- Melting point of 153±154°C.
- UV Absorption Spectra is at 260–284 nm.
- pH 4-4.5
- Soluble in ethyl acetate, water, and ethanol.
- Unlikely soluble in ether, alcohol ether mixture, chloroform, and pyridine.

Kojic Acid

Metabolite with insecticidal, antibacterial, and antifungal properties.
Inhibitor of bacterial and fungal growth. Inhibitor of viruses multiplication capacity.

Chemical properties

- Weak acid.
- Molecular weight is 142.1.
- Reacts forming several products: Mannich base, azo dyes, esters, pyridines, cyanoethylation products, and metal chelates.

Production

The biosynthesis pathway continues to be uncertain to date.
The aerobic fermentation process uses carbon sources as a substrate: starch, ethanol, fructose, glucose, sucrose, etc.

Applications

- Cosmetics.
- Medicine.
- Food Industy.
- Chemical Industry.
- Agriculture.

Action mode

Kojic acid acts during melanin synthesis, showing sufficient inhibitory effect on monophenolase activity and inhibitory effect on diphenolase tyrosinase activity.

Figure 3. Characteristics and basics of kojic acid based on reports by Phasha *et al*. (2022) and Siddiquee (2018).

gossypii, vector of the Cotton leafroll dwarf virus (CLRDV) (Mahas *et al.,* 2022). They evaluated the difference between the kojic acid extracted from the strain *A. oryzae* ASU44 (OL314732) and synthetic kojic acid, and indicated that the kojic acid produced by *A. oryzae* ASU44 (OL314732) was more efficient against *Aphis gossypii,* with a medium lethal concentration (CL_{50}) of 11.2 ppm, a lethal concentration (CL_{90}) of 50.3 ppm, and a lethal time of (LT_{90}) of 7 days, since the results are lower than those for synthetic kojic acid, highlighting their application as an efficient and inexpensive *in vitro* evaluation model (Mahmoud *et al.,* 2023).

Likewise, the antifungal activity of kojic acid has been evaluated with *A. terrus, A. flavus, A. parasiticus, A. fumigatus, Penicilium* and *Sclerotinia sclerotiorum* (*Kim et al.,* 2012; Kim and Chan, 2014; Zhu *et al.*, 2022). In the case of *S. sclerotiorum,* kojic acid inhibits the biosynthesis of melanin, which affects the development of sclerotia and the biosynthesis of chitin and β-1,3-glucanos, which alters the cell walls and the growth of the mycelium, reducing in its entirety the symptoms of

S. sclerotiorum in soybean pods with 50 mM de ácido kójico. It has the ability to prevent and inhibit symptoms of *S. sclerotiorum*. In turn, it is more effective than commercial fungicides (carbendazim and prochloraz) (Zhu *et al.,* 2022).

More frequently, phytoparasitic nematodes have been pointed out as the cause of important economic losses in several crops, fluctuating around $77 billion dollars worldwide, which raises concerns in agriculture, horticulture and forestry (Yadav, 2017; Seo *et al*., 2019). For example, *Meloidogyne* spp., the gall-forming nematodes, is responsible for annual losses of up to $100 billion dollars. Kim and collaborators (2016) established a method to control these nematodes using kojic acid as the active ingredient, which was produced by the strain *A. oryzae* EML-DML3PNa1 obtained from white dogwood (*Cornus alba*). During their experiments, an inhibiting effect was displayed on the hatching of eggs and the development of larvae, and the use of kojic acid was suggested along with a dispersing, penetrating or surfactant agent, in order to improve absorption and the effect of the product on the crop (Kim *et al.,* 2016). The nematicidal action of the kojic acid reported a mortality of 87.6% in juvenile *Meloidogyne incognita* under conditions of 20% of a filtrate of a fermentation broth. It displayed inhibition in the incubation of the nematode and a mortality dependent on the dose, with mean effective concentration values (CE_{50}) of 195.2 µg mL^{-1} and 238.3 µg mL^{-1}, respectively, 72 h after exposure, which suggests that is has potential as a biological control agent (Kim *et al.,* 2016).

Interest in safe agricultural products for human health and free of contaminants is on the rise, due to awareness on residual toxicity caused by the use of pesticides. The implementation of microorganisms with nematocidal activity is recommended, since they are respectful with the environment because they are obtained from natural products, as in the case of kojic acid, therefore its implementation in agronomy opens a door for the development of sustainably inexpensive, environmentally friendly products that, above all, do not harm the health of people who apply them.

CONCLUSIONS

This study highlights the potential of the *A. oryzae* strains and its derivatives (enzymes and secondary metabolites), considering the ability to compete with commercial chemical products as pesticides, since it presents insecticidal, fungicidal and nematocidal characteristics, which represent an inexpensive and sustainable alternative, since the way in which it is produced excludes the use of costly products. Developing new investigation work and opting for the application of products based on *A. oryzae* at a greenhouse level is required to confirm its adaptability in conditions outside the laboratory and verify if the benefits of *A. oryzae* are maintained or reduced in such a way that they can be used in the field. Finally, the study of *A. oryzae* and its by-products is scarcely studied in Mexico, making it a debatable topic to be exploited for the benefit of the Mexican countryside, since it opens a new aspect of study for the development of products that benefit crops and for the control of phytopathogenic agents.

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