Fungi in a One Health Perspective

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Fungi constitute a diverse group with highly positive and negative impacts in different environments, having several natural roles and beneficial applications in human life, but also causing several concerns. Fungi can affect human health directly, but also indirectly by being detrimental for animal and plant health, influencing food safety and security. Climate changes are also affecting fungal distribution, prevalence, and their impact on different settings. Searching for sustainable solutions to deal with these issues is challenging due to the complex interactions among fungi and agricultural and forestry plants, animal production, environment, and human and animal health. In this way, the "One Health" approach may be useful to obtain some answers since it recognizes that human health is closely connected to animal and plant health, as well as to the shared environment. This review aims to explore and correlate each of those factors influencing human health in this "One Health" perspective. Thus, the impact of fungi on plants, human, and animal health, and the role of the environment as an influencing factor on these elements are discussed.

Keywords: fungal infections ; plant health ; human health ; animal health ; mycotoxins ; antifungal resistance ; climate change

Kingdom Fungi is diverse and includes different types of organisms such as molds, yeasts, mushrooms, polypores, plant parasitic rusts, and smuts, totalizing more than 120,000 described species and between 2.2 and 5.1 million estimated species $^{[1][2]}$. This group includes saprotrophic, pathogenic, parasitic, commensal, and symbiotic organisms that can be found in the most variable ecosystems, from marine or freshwater to terrestrial environments $^{[1][3][4]}$. Their morphological traits aligned with exceptional metabolic diversity enable them to occupy numerous ecological niches and to create a panoply of interactions with other organisms $^{[1][4]}$.

Due to their unique but diverse characteristics, fungi are an essential component for the well-functioning of the ecosystems and have diversified roles in them. In terrestrial environments, fungi are crucial for soil fertility, decomposing organic matter and facilitating carbon and nitrogen flow, as well as for supporting plant species development ^[5]. Furthermore, microscopic fungi are an important food source for soil invertebrates and some of the macroscopic ones are eatable and valuable for humans' and animals' diets ^[4]. Furthermore, the observed diverse interaction skills and ability to produce different primary and secondary metabolites turn fungi into an interesting group for the pharmaceutical industry ^[6]. Most of the plant endophytic fungi produce compounds with both harmful and beneficial effects on plants, which, when extracted, may have agricultural or even medicinal value ^{[6][Z]}. For example, some secondary metabolites, such as alkaloids, may help a plant to resist to pests, to repel herbivores, and to adapt to changes in climatic conditions ^[6]. Others can be used as antibiotics (e.g., penicillin or cephalosporin), anticancer agents (e.g., illudin or paclitaxel), immunomodulatory substances (e.g., cyclosporine or mycophenolic acid), or antiviral agents (e.g., stachyflin), for example ^[2]. Therefore, fungal metabolites comprise a panoply of promising compounds and applications, but also potential harmful implications, in particular regarding mycotoxins in human and animal health ^{[6][Z][8]}, (**Figure 1**).



The most important mycotoxins are aflatoxins, fumonisins, ochratoxin A (OTA), deoxynivalenol (DON), zearalenone (ZEN), and ergot alkaloids which are mainly produced by *Aspergillus*, *Penicillium*, *Fusarium*, *Stachybotrys*, and *Claviceps* species ^{[9][10]}.

Mycotoxin contamination of food and feed may result in acute or chronic consequences such as carcinogenic, teratogenic, immunosuppressive, or estrogenic issues in humans and animals ^[9], which comprises a food safety concern. In this way, the European Commission set the maximum levels in raw materials, feed and processed food ^[11], which means that all the products containing mycotoxins above the thresholds are strongly devalued or even banned from being sold, which also affects the global economy. Furthermore, mycotoxins can also be inhaled, being other route to cause adverse human health effects. Exposure by means of inhalation of molds may happen in indoor residential, school, and office environments ^[12]. Additionally, in certain conditions, fungi can directly or indirectly cause allergies ^[13] and infections in humans ^[14], as well as in crops, compromising their yields ^[15]. Thus, the contamination of edible plants and of the surrounding environment is another possible route affecting human and animal health. In this way, this review will explore the negative impact of fungi on human health, under the "One Health" perspective. The "One Health" concept connects the health of plants, humans, animals, and the environment in a unifying approach, aiming to balance and optimize them as only one. Its points of action include food security and safety, the integrity of ecosystems, fungal infections including zoonosis and antimicrobial resistance control, and the promotion of health ^[12].

This review covers the most common mycological infestations of plants and animals with effects on human health either directly through dietary exposure or indirectly as environmental contaminants. Additionally, the subject of antifungal resistance induced by exposure to plant protection products will be explored and discussed, also under a "One Health" perspective.

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