

Mycotoxins: fungal toxins in our food
or
Fungi: friends or foes?

*Mummy: some of these walnuts are greenish/greyish inside:
I don't really fancy them!*



Alice Motola & Massimo Reverberi

Department of Environmental Biology, Sapienza University, Roma, Italy

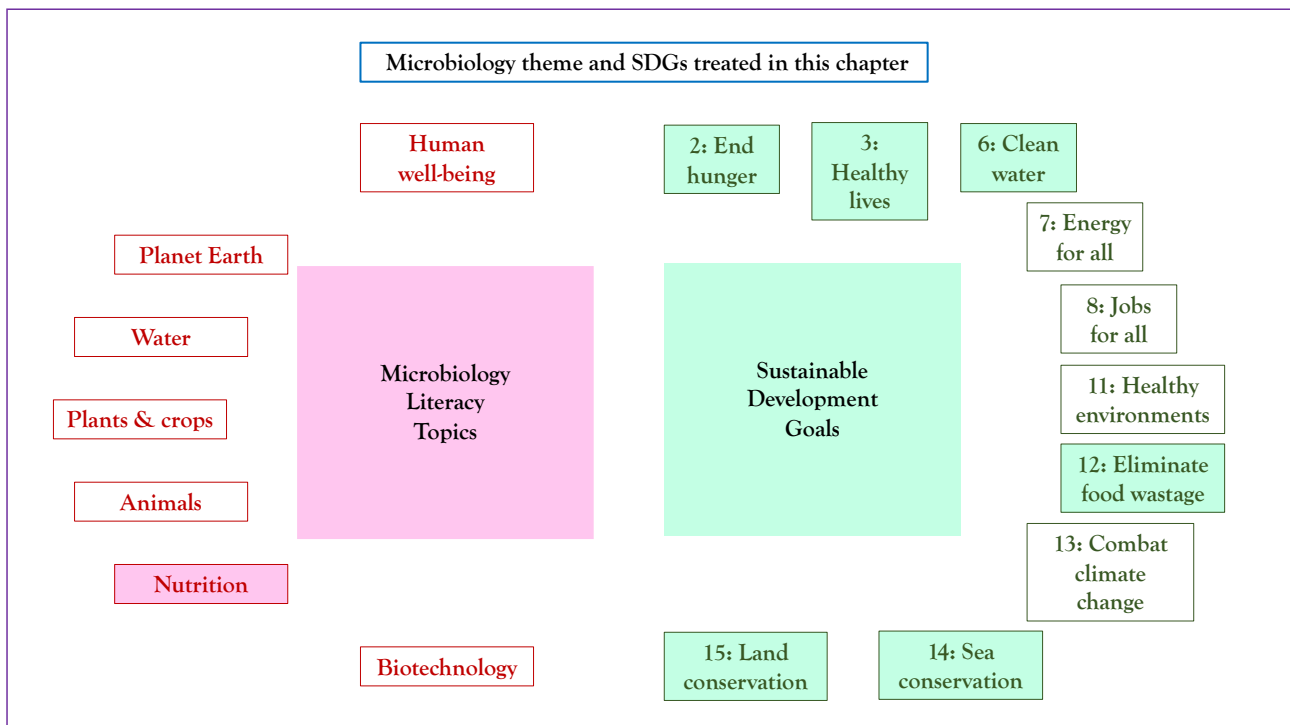
Mycotoxins

Storyline

Mycotoxins are low-molecular-weight compounds synthesised by filamentous fungi, which often occur in feed and foodstuffs and, due to their toxicity, are capable of causing disease and death in plants, animals and humans. The widespread and indiscriminate use of chemicals for the prevention of fungal colonization, and contamination with mycotoxins, has led to the development of strains resistant to anti-fungal chemicals, the presence of toxic residues in food, detrimental ecological effects, and environmental pollution. Additionally, it is predicted that climate change will exacerbate the environmental conditions conducive to mycotoxin production, and that the estimated rise of the global population to more than 9 billion people by 2050 will make it more difficult to guarantee food security, especially in developing countries. Thus, there is a need for the development of new alternative, safe and environmentally friendly strategies/agents which are both effective and economically feasible, in order to tackle the worldwide problem of mycotoxin contamination. The latter important topic thus has multiple consequences for Sustainable Development Goals.

The Microbiology and Societal Context

The microbiology: micro fungi, plant pathogens, post-harvest pathogens, secondary metabolites, mycotoxins. *And, peripherally for completeness of the storyline:* agricultural resource attribution, food safety, hazardous to animal and human health. *Sustainability issues:* health; hunger-food; environmental pollution; global warming.



Mycotoxins: the Microbiology

1. *Fungi: friends or foes?* In terms of the number of species, fungi represent one of the major kingdoms of living organisms. We mostly know them because some species are edible (e.g. truffles). However, the most famous fungi are those aiding us recover from bacterial disease, namely species such as those belonging to the genus *Penicillium*, which produce antibiotics. In this sense, we can consider fungi to be our “friends”. The flip side though is represented by the fact that some fungi can produce toxic substances, or at least substances that are toxic for us and for the other animals: notably, the *mycotoxins*.

2. *Mycotoxins: what are they?* Mycotoxins are low-molecular-weight compounds synthesized by filamentous fungi, which often occur in feed and foodstuffs and, due to their toxicity, can cause disease and death in plants, animals, and humans. Mycotoxins are **secondary metabolites** produced by some saprophytic filamentous fungi, which can be toxic to microorganisms, plants, invertebrates, animals, and humans. Unlike primary metabolites, which are made in order to grow, reproduce and carry out other essential cellular activities, secondary metabolites have no essential role in fungal growth, development and survival. They are usually synthesized in order to optimize interactions between fungi and their environment and, in this regard, mycotoxins were defined as “luxury molecules”.

3. *Mycotoxins are a very diverse group of molecules.* At present, more than 400 chemically different mycotoxins have been identified, which have low molecular weights ranging from about 200 to 500 Da. The primary classes of mycotoxins are aflatoxins of which aflatoxin B1 (**AFB1**) is the most prevalent, zearalenone (ZEA), trichothecenes - primarily deoxynivalenol (DON) and T-2 toxin (T-2), fumonisins, ochratoxins (**OTA**) and the ergot alkaloids. Mycotoxins are rather difficult to define and classify, owing to their diverse chemical structures, biosynthetic origins, biological effects, and their production by a wide number of different fungal species.

4. *Mycotoxins poison different parts of the body.* In fact, clinicians often group them according to the organ they affect, such as hepatotoxins, nephrotoxins, neurotoxins, immunotoxins, and so forth. Moreover, mycotoxin effects on animals and humans may be **acute**, resulting from a high-level dosage, or **chronic**, resulting from long-term, low-level exposure. Unfortunately, to date, no specific antidotes for aflatoxins exist.

5. *Mycotoxins are ubiquitous.* Mycotoxins are unavoidable, naturally occurring compounds in nature, because the fungi that produce them are common components of the surface (epiphytic) and internal (endophytic) microflora of staple crops. They are a hidden aspect of mould contamination and can remain on or in products well beyond the life cycle of the fungi.

6. *Reducing our exposure to mycotoxins involves reducing fungal contamination.* One approach to reducing food contamination with mycotoxins has been to treat crops with fungicides, poisons that kill fungi. However, the widespread and indiscriminate use of chemicals for the prevention of fungal colonization has led to the development of resistant strains, to the presence of toxic residues in food, to detrimental ecological effects, and to environmental pollution.

Other approaches to reduce mycotoxin contamination/to detoxify products include food processing operations such as: sorting, trimming, cleaning, milling, brewing, cooking, baking, frying, roasting, canning, flaking, alkaline cooking, nixtamalization, and extrusion. All are energy consuming and expensive.

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7. *Mycotoxin awareness started in 1962.* The term mycotoxin was coined in 1962, after the outbreak of the so-called Turkey “X” disease on a farm near London, which caused the death of 100,000 turkey poults. These had been fed with a groundnut meal purchased from Brazil, which was subsequently discovered to be contaminated with aflatoxins produced by *Aspergillus flavus*. Following this unfortunate incident, the study of mycotoxins – *mycotoxicology* – officially began. This was followed by a period of research known as the so called “golden age” of mycotoxins, during which many new fungal toxins were discovered from species of *Aspergillus* and other common moulds.

8. *But mycotoxins have been around for a long, long time.* It is known that these mysterious molecules have played a relevant role in the past, way before the Turkey “X” event. For example, ergotism, whose symptoms only now can be associated to the ingestion of mould-contaminated cereals, created significant demographic changes in the human population after the spread of pandemics. In fact, human mycotoxicoses have probably existed ever since the development of settled agricultural communities reliant on grain stores. Moreover, mycotoxins have been linked to ancient rituals during which their hallucinogenic properties were exploited and, more controversially, to witchcraft trials. Overall, mycotoxins represent a continued enigma and the risks they cause are as old as ancient human civilizations.

9. *Mycotoxins constitute a significant problem for food security.* Globalization and the intensified trade of agricultural commodities, especially the food staples, represent today a significant potential vector for mycotoxin contamination worldwide. In a nutshell, mycotoxins, especially aflatoxins (AFs) and ochratoxin A (OTA), represent a serious global threat to food and feed production and safety, to plant, animal and human health and, last but definitely not least, indirectly to the environment, as great amounts of pesticides and fungicides are usually employed as the main strategy for mycotoxin control.

Additionally, it was predicted that climate change will exacerbate the environmental conditions conducive to mycotoxin production, such as: high temperatures, drought and insect attack, increasing the amounts of contaminated foods, especially in developing countries at lower latitudes close to the equator. Moreover, the estimated rise of the global population to more than 9 billion people by 2050 will make it more difficult to guarantee food security, especially in developing countries.

10. *Economic costs of mycotoxins:* The economic impact due to mycotoxins is mainly associated with reduction of quality foods for humans and animals, reduction in animal production due to feed refusal or diseases, increasing medical cost for toxicosis treatments, increased costs to find alternative foods, to design adequate management of contaminated supplies, to improve detection and quantification methods and to develop strategies that reduce toxin exposure.

Relevance for Sustainable Development Goals and Grand Challenges

The microbial dimension of mycotoxins relates to several SDGs (*microbial aspects in italics*), including

- **Goal 2. End hunger, achieve food security and improved nutrition and promote sustainable agriculture** (*end hunger and malnutrition, increase agricultural productivity*). The widespread occurrence of mycotoxins mainly in staple foods, such as cereals, nuts, milk, eggs and fruit, poses serious risks in terms of food security, especially in developing countries where diets are primarily based on these products and where they usually lack the knowledge, resources and legislation to address the mycotoxin contamination problem. More importantly, with the expected increase of the human world population, in the future more food will have to be produced and it will become more and more difficult to ensure that this food is safe and free from mycotoxins. More and more countries are introducing

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restrictions to limit the presence of toxic amounts of mycotoxins in feed and food. As a result, feed and food contaminated with mycotoxins above set limits are declared not fit for consumption and thus become waste. In some poorer regions, mycotoxin contamination is so high that the available options are either to consume toxic food or starve. Thus: finding and implementing new, non-polluting measures to reduce fungal growth and mycotoxin production on staple crops and foods is an integral component of strategies to end hunger.

- **Goal 3. Ensure healthy lives and promote well-being for all at all ages** (*improve health, reduce preventable disease and premature deaths*). Mycotoxins can cause chronic or acute intoxication, with damage especially of organs such as the gut, liver and kidneys. Animal and humans fed with high content of mycotoxins can die of hepatitis/cirrhosis (acute intoxication), whereas low, but regular, amounts of mycotoxins consumed with food can cause cancer, or at least depression of immune system function. Limiting mycotoxins in feed and food is thus a crucial step to ensure healthy lives and promote well being
- **Goal 12. Ensure sustainable consumption and production patterns** (*achieve sustainable production and use/consumption practices, reduce food waste, reduce production/pollutant release into the environment, reduce food losses along production and supply chains, including post-harvest losses*). Vegetables, grains, food and feed contaminated with high levels of mycotoxins are unfit for consumption and become food waste. For instance, maize grains contaminated with mycotoxins are used for ethanol or biofuel production, thereby converting food calory sources to energy sources. Limiting mycotoxins in food will reduce food wastage and lead to more sustainable use of food and feed.
- **Goals 6/14/15 Clean water/Conserve oceans/Protect terrestrial ecosystems** (*reduce pollution*). The indiscriminate and widespread use of fungicides and fungistatics as the main strategy in the fight against mycotoxins has caused a series of environmental problems, such as: fungal resistance, persistence of these chemicals in water and soil, alteration of the biogeochemical cycles of the elements, modification of the structure of the edaphic community of the soil, decrease of biodiversity, decrease in soil fertility, toxicity in organisms. Finding alternatives to fungicides to reduce fungal growth on crops and feeds will reduce pollution of surface and underground water bodies, including those that serve as sources of drinking water, and of land and soils.

Potential Implications for Decisions

1. *Individual*

- a. Avoid the frequent use of conserved products and try to substitute them with fresh foods. If obliged to follow a specific diet involving extensive of preserved, foods try to diversify the diet.
- b. Limit the use of foods potentially at high risk of mycotoxins contamination, such as dry nuts (e.g. pistachios), dry figs, salami, ham beer, coffee, cocoa
- c. If obliged to follow a specific diet, e.g. coeliac disease, limit the intake of foods derived from maize and favour those deriving from other cereals, such as rice.

2. *Community policies*

- a. Diffuse the knowledge of the risk of chronically ingesting mycotoxins and propose diets that limit their ingestion.
- b. Inform local medical and veterinary establishments of the mycotoxin problem and provide them with reports (also at scientific levels) on the associated risks.

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c. Become involved in the decision process of the daily diet at school and try to limit the mycotoxin ingestion. Mycotoxin intake limit thresholds are usually normed for adults with an average body weight of 65 kg. This is probably not safe for children with lower weights.

3. *National policies relating to mycotoxins*

- a. Food safety (e.g., national and supranational agencies)
- b. Public Health Institutions
- c. Private and public institutions controlling daily the quality of food and feed

Pupil Participation

1. *Class discussion of the issues associated with mycotoxins*

- a. Mycotoxins what are they? How dangerous are they?
- b. Are there environmentally friendly remediation processes to get rid of them?
- c. How can we modify a bit our diet to reduce their ingestion?

2. *Pupil stakeholder awareness*

- a. If you had to introduce this topic to a friend or a person who has never heard of mycotoxins before, what is, in your opinion, the best way to explain it?
- b. Can you think of anything that might be done to reduce the negative consequences of mycotoxin contamination, on a global level, especially in the food supply chain?
- c. What kind of advice would you give to your family and your friends to raise their awareness on the mycotoxin contamination risks?

3. *Exercises*

- a. Which small preventive actions could you take in your daily life in order to reduce the chances of ingesting mycotoxins and being exposed to their hazards?
- b. Which are the major problems stemming from the ubiquitous nature of mycotoxins? Name a few. Now reflect on how these problems could be connected to one another. If you believe they are, which could be the best approach to tackle all of them simultaneously?
- c. Chemicals such as fungicides are usually used in the fight against mycotoxins. What sustainable options and alternatives can you think of that could be more environmentally friendly? Which would be the direct benefits?

The Evidence Base, Further Reading and Teaching Aids

Bennett, J. W. (2010) 'An Overview of the Genus *Aspergillus*', *Aspergillus: Molecular Biology and Genomics*, (Caister Academic Press, U.K.). Available at: <https://www.caister.com/openaccess/pdf/aspergillus1.pdf>.

W. P. Blount, "Turkey 'X' Disease," (1961) *Turkeys*, 9: 52-61.

Khatoon, A. and Abidin, Z. ul (2018) 'Mycotoxicosis – diagnosis, prevention and control: past practices and future perspectives', *Toxin Reviews*. Taylor & Francis, 0(0), pp. 1–16. doi: 10.1080/15569543.2018.1485701.

Klingelhöfer, D. *et al.* (2018) 'Aflatoxin – Publication analysis of a global health threat', *Food Control*, 89, pp. 280–290. doi: 10.1016/j.foodcont.2018.02.017.

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- Medina, A. et al. (2017) 'Climate change, food security and mycotoxins: Do we know enough?', *Fungal Biology Reviews*. Elsevier Ltd, pp. 143–154. doi: 10.1016/j.fbr.2017.04.002.
- Ramos, A. J., Sanchis, V. and Marín, S. (2011) 'The prehistory of mycotoxins: Related cases from ancient times to the discovery of aflatoxins', *World Mycotoxin Journal*. Wageningen Academic Publishers, 4(2), pp. 101–112. doi: 10.3920/WMJ2010.1268.
- Reverberi, M. et al. (2010) 'Natural functions of mycotoxins and control of their biosynthesis in fungi', *Applied Microbiology and Biotechnology*, 87(3), pp. 899–911. doi: 10.1007/s00253-010-2657-5.
- Rodrigues, I. and Naehrer, K. (2012) 'A three-year survey on the worldwide occurrence of mycotoxins in feedstuffs and feed', *Toxins*, 4(9), pp. 663–675. doi: 10.3390/toxins4090663.
- Shephard, G. S. (2008) 'Impact of mycotoxins on human health in developing countries', *Food Additives and Contaminants - Part A Chemistry, Analysis, Control, Exposure and Risk Assessment*, 25(2), pp. 146–151. doi: 10.1080/02652030701567442.
- Thalita Calado, Armando Venancio, and L. A. (2014) 'Irradiation for Mold and Mycotoxin Control : A Review', 13, pp. 1049–1061. doi: 10.1111/1541-4337.12095.
- Whitlow, L. W. et al. (2002) 'Mycotoxins in feeds', pp. 74–78. Available at: http://fdsmagissues.feedstuffs.com/fds/Reference_issue_2010/13_Mycotoxins in Feeds.pdf.
- Zain, M. E. (2011) 'Impact of mycotoxins on humans and animals', *Journal of Saudi Chemical Society*. King Saud University, 15(2), pp. 129–144. doi: 10.1016/j.jscs.2010.06.006.

Glossary

Mycotoxins: Mycotoxins are low-molecular-weight natural compounds, produced as **secondary metabolites** by some saprophytic filamentous fungi, which can be toxic to microorganisms, plants, invertebrates, animals and humans.

Hallucinogenic effect: producing hallucinations, that is, a sensory perception (such as a visual image or a sound) that occurs in the absence of an actual external stimulus and usually arises from neurological disturbance.

Fluorescence: the emission of radiation, especially of visible light, by a substance during exposure to external radiation, as light or x-rays

Ultraviolet (UV) light: that portion of the electromagnetic spectrum extending from the violet, or short-wavelength, end of the visible light range to the X-ray region. Ultraviolet (UV) radiation is undetectable by the human eye, although, when it falls on certain materials, it may cause them to fluoresce—i.e., emit electromagnetic radiation of lower energy, such as visible light. Many insects, however, are able to see ultraviolet radiation.

Demography: is the statistical study of human populations. **Demography** examines the size, structure, and movements of populations over space and time. **Demography** is useful for governments and private businesses as a **means** of analyzing and predicting social, cultural, and economic trends related to population.

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Fungicides: Fungicides are pesticides, that is phytopharmaceuticals, chemical compounds used to kill fungi or prevent them from growing.

Variable: an element, feature, or factor that is liable to vary or change.

Biosynthesis: the production of complex molecules within living organisms or cells.

Metabolite: are the products and intermediates of cellular metabolism.

Global Warming: Global warming is the long-term heating of Earth's climate system observed since the pre-industrial period (between 1850 and 1900) due to human activities, primarily fossil fuel burning, which increases heat-trapping greenhouse gas levels in Earth's atmosphere.

Aflatoxin B1: (AFB1) is a secondary metabolite and a carcinogenic compound produced by the fungi species *Aspergillus flavus* and *Aspergillus parasiticus* when environmental factors are favourable in response to oxidative stress.

Ochratoxin A: is a mycotoxin and a carcinogenic compound produced by secondary metabolism of many filamentous fungi species belonging to the genera *Aspergillus* and *Penicillium*.

Pesticide: is any substance used to kill, repel, or control certain forms of plant or animal life that are considered to be pests.

Eco-friendly: not harmful to the environmental.

Evolution: descent with modification from pre-existing species; cumulative inherited change in a population of organisms through time leading to the appearance of new forms; the process by which new species or populations of living things develop from pre-existing forms through successive generations.

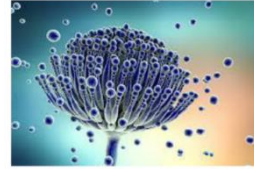
Holistic: characterized by the belief that the parts of something are intimately interconnected and explicable only by reference to the whole.

Multidisciplinary: combining or involving several academic disciplines or professional specializations in an approach to a topic or problem.

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Mycotoxins: A doggerel composed by Alice Motola & Massimo Reverberi

We introduce ourselves, we are the **Mycotoxins**,
whose presence in the world has no border and over time no end,
Beware of us, as we are not your friend!



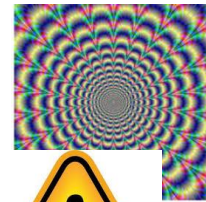
Caution not to ingest us you must have, indeed!
In fact, we contaminate many types of food and feed,



Because many of us are tasteless, odourless and invisible,
finding us is a tricky task,
So, yes, our presence is pretty much unavoidable, if you ask!



We were used during ancient rites for our **hallucinogenic effect**,
And even after numerous historical and scientific studies, our mysteries
haven't been revealed all yet and
more information about us you humans must collect!



It is known though, that because of us in the past many women were
accused
of witchcraft, as their brains we brought to insanity,
So many of them were burned on the stake,
But only now we know that killing them was a terrible mistake
And that their lives were unfairly wasted, indeed, it's such a pity!



Also, we can be visually determined as we emit green or blue **fluorescence**
when we are put under **UV light**,
This of ours, is no doubt a fascinating and mind-blowing property, right?



Throughout history with epidemics we varied the **demography**
of human populations, whenever their food we would spoil,
And the recent indiscriminate use of **fungicides** to control us
has polluted the planet's water and soil.

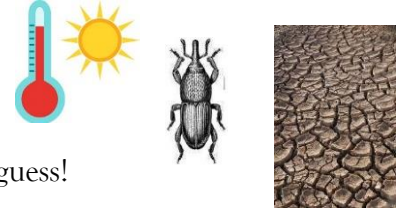


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However, the mycotoxin problem still persists today,
Because of our existence most of the world is completely oblivious!
And our concentrations in many food and feedstuffs remain conspicuous,
To the scientists' utmost dismay!



Us Moulds often produce mycotoxins because of high temperatures,
drought and insect attack, all of which cause us stress,
In fact, between these environmental **variables** and the **biosynthesis** of
our dangerous **metabolites** a link has been established, as you can also easily guess!



And alas, with the increase of the global population
and **global warming** at this rate,
If the only staples left will be contaminated,
you will not have enough food on your plate!



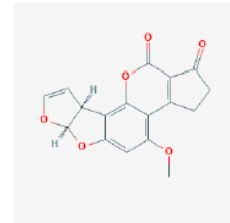
Here we are, **Aflatoxin B1** and **Ochratoxin A**,
guilty of harming many of Earth's inhabitants,
Such as humans, animals and plants,

By causing them death and disease,
As our toxicity their **immune systems** can weaken,
Which overall will make their natural defence mechanisms decrease.



Acute Toxic

Hi, I'm the aflatoxin, also known by the nickname **AFB1**,
Hopefully, in your kitchen of my **molecules** there are none!



I can give you some hints of where I might be,
As there is absolutely no chance that with your naked eye you could see me!

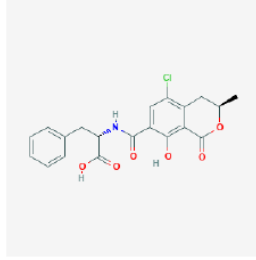


For example, I've been detected in many of the things you eat,
Such as cereals, peanuts, milk and meat,



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Instead, I am **OTA**, the ochratoxin,
And AFB1 and I are very much akin.



So, just like her I could be in different kinds of grains,
And if you swallow me in high doses, to your body I can inflict great
pains!



But, as long as I'm not in your pint of beer or glass of wine,
You can get drunk, have fun, and hopefully you'll be just
fine!



Several countries banned 50% of all their **pesticides**.
So safe and **eco-friendly** methods to control us must be discovered and
fast!
Only then the planet would be happier and healthier, at last!



Dear humans you are surrounded by the greatest and most obvious
source of ideas, that is, Nature, that's for sure!
Which no doubt more than you is shrewd and mature.



As indeed Life, during its approximately 3.8 billion years of **evolution**,
has had plenty of time to develop for any problem that exists, more than one solution!



As a matter of fact, many fungi, bacteria and plants can aid us by producing
magical molecules which cause no harm to you or your pet,
Yet, are strong in fighting against the “bad fungi”, on this you can bet!



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Therefore, a **holistic** and **multidisciplinary** approach is needed. Simultaneously of humans, animals and the environment as a whole we must care, So that the benefits we can then together all share!



Since, as the philosopher **Giordano Bruno** wisely affirmed in many years bygone:



<< In the universe separation does not exist! >>.

Indeed;

" ONE IS ALL AND ALL IS ONE!"



Giordano Bruno: was an Italian Dominican friar, philosopher, mathematician, poet, cosmological theorist, and Hermetic occultist. He is known for his cosmological theories, which conceptually extended the then-novel Copernican model. He proposed that the stars were distant suns surrounded by their own planets, and he raised the possibility that these planets might foster life of their own, a philosophical position known as cosmic pluralism. He also insisted that the universe is infinite and could have no "center".