**Microbial toxins Lec 3**

A **toxin** is a harmful substance produced within living cells or organisms; synthetic [toxicants](https://en.wikipedia.org/wiki/Biocide) created by artificial processes are thus excluded. The term was first used by organic chemist [Ludwig Brieger](https://en.wikipedia.org/w/index.php?title=Ludwig_Brieger&action=edit&redlink=1) (1849–1919) derived from the word [toxic](https://en.wikipedia.org/wiki/Toxic). **Microbial toxins** are [toxins](https://en.wikipedia.org/wiki/Toxin) produced by micro-organisms, including bacteria and fungi. Microbial toxins promote infection and disease by directly damaging host tissues and by disabling the immune system. Some bacterial toxins, such as *[Botulinum](https://en.wikipedia.org/wiki/Botulinum%22%20%5Co%20%22Botulinum)* neurotoxins, are the most potent natural toxins known. However, microbial toxins also have important uses in medical science and research.

Currently, new methods of detecting bacterial toxins are being developed to better isolate and understand these toxin. Potential applications of toxin research include combating microbial virulence, the development of novel anticancer drugs and other medicines, and the use of toxins as tools in [neurobiology](https://en.wikipedia.org/wiki/Neurobiology) and [cellular biology](https://en.wikipedia.org/wiki/Cellular_biology).

Bacterial production of secondary metabolites starts in the [stationary phase](https://en.wikipedia.org/wiki/Stationary_phase_%28biology%29) as a consequence of lack of nutrients or in response to environmental stress. Secondary metabolite synthesis in. bacteria is not essential for their growth, however, they allow them to better interact with their ecological niche.

 Many bacterial secondary metabolites are toxic to [mammals](https://en.wikipedia.org/wiki/Mammal). When secreted those poisonous compounds are known as [exotoxins](https://en.wikipedia.org/wiki/Exotoxin) whereas those found in the prokaryotic cell wall are [endotoxins](https://en.wikipedia.org/wiki/Endotoxins).

An example of a bacterial secondary metabolite with a positive and negative effect on humans is [botulinum toxin](https://en.wikipedia.org/wiki/Botulinum_toxin%22%20%5Co%20%22Botulinum%20toxin) synthesised by [*Clostridium botulinum*](https://en.wikipedia.org/wiki/Clostridium_botulinum). This [exotoxin](https://en.wikipedia.org/wiki/Exotoxin) often builds up in incorrectly canned foods and when ingested blocks cholinergic neurotransmission leading to muscle paralysis or death. However, botulinum toxin also has multiple medical uses such as treatment of muscle spasticity, migraine and cosmetics use.

Toxins vary greatly in their [toxicity](https://en.wikipedia.org/wiki/Toxicity), ranging from usually minor (such as a [bee](https://en.wikipedia.org/wiki/Bee) [sting](https://en.wikipedia.org/wiki/Stinger)) to almost immediately deadly (such as [botulinum toxin](https://en.wikipedia.org/wiki/Botulinum_toxin%22%20%5Co%20%22Botulinum%20toxin)). toxins may be classified as either

* [exotoxins](https://en.wikipedia.org/wiki/Exotoxin), being excreted by an organism,
* [endotoxins](https://en.wikipedia.org/wiki/Endotoxin), that are released mainly when bacteria are [lysed](https://en.wikipedia.org/wiki/Lysis)

 **Biotoxin**

The term "biotoxin" is sometimes used to clearly confirm the biological origin of toxin Biotoxins can be further classified, for example, as

* [fungal biotoxins](https://en.wikipedia.org/wiki/Mycotoxin),
* [microbial toxins](https://en.wikipedia.org/wiki/Microbial_toxin),
* [plant biotoxins](https://en.wikipedia.org/wiki/Phytotoxin), or animal biotoxins.

Toxins produced by [microorganisms](https://en.wikipedia.org/wiki/Microorganism) are important [virulence](https://en.wikipedia.org/wiki/Virulence) determinants responsible for microbial [pathogenicity](https://en.wikipedia.org/wiki/Pathogenicity) and/or evasion of the host [immune response](https://en.wikipedia.org/wiki/Immune_response).

Biotoxins vary greatly in purpose and mechanism, and can be highly complex (the [venom](https://en.wikipedia.org/wiki/Venom) of the [cone snail](https://en.wikipedia.org/wiki/Cone_snail) contains dozens of small [proteins](https://en.wikipedia.org/wiki/Protein), each targeting a specific nerve channel or receptor), or relatively small protein.

**Biotoxins in nature have two primary functions:**

* [Predation](https://en.wikipedia.org/wiki/Predation), such as in the [spider](https://en.wikipedia.org/wiki/Spider), [snake](https://en.wikipedia.org/wiki/Snake), [scorpion](https://en.wikipedia.org/wiki/Scorpion), [jellyfish](https://en.wikipedia.org/wiki/Jellyfish), and [wasp](https://en.wikipedia.org/wiki/Wasp)
* Defense as in the [bee](https://en.wikipedia.org/wiki/Bee), [ant](https://en.wikipedia.org/wiki/Ant), [termite](https://en.wikipedia.org/wiki/Termite), [honey bee](https://en.wikipedia.org/wiki/Honey_bee), [wasp](https://en.wikipedia.org/wiki/Wasp), and [poison dart frog](https://en.wikipedia.org/wiki/Poison_dart_frog)

Some of the more well known types of biotoxins include:

* [Cyanotoxins](https://en.wikipedia.org/wiki/Cyanotoxin), produced by [cyanobacteria](https://en.wikipedia.org/wiki/Cyanobacteria)
* [Dinotoxins](https://en.wikipedia.org/wiki/Dinotoxin), produced by [dinoflagellates](https://en.wikipedia.org/wiki/Dinoflagellate%22%20%5Co%20%22Dinoflagellate)toxin in microor

 **Monitoring tools for toxin productions**

### Solid-phase adsorption toxin tracking (SPATT)

[SPATT](https://en.wikipedia.org/wiki/Solid_phase_extraction) is a useful tool in tracking algal blooms as it is reliable, sensitive, and inexpensive. One of the downsides is that it does not give very good results for water soluble toxins as compared to hydrophobic compounds. This tool is mainly used to determine intercellular concentrations of toxins but the cyanobacteria can also be lysed to determine the total toxin amount in a sample.

### Polymerase chain reaction (PCR)

[PCR](https://en.wikipedia.org/wiki/Polymerase_chain_reaction) is a molecular tool that allows for analysis of genetic information. PCR is used to amplify the amount of certain DNA within a sample which are usually specific genes within a sample.

### Immunochemical methods

This detection method uses mammalian antibodies to bind to microbial toxins which can then be processed in a variety of different ways. Of the commercial ways of using immunochemical detection would be [enzyme-linked immunosorbent assays](https://en.wikipedia.org/wiki/ELISA) (ELISA). This assay has the advantage of being able to screen for a broad range of toxins but could have issues with specificity depending on the antibody used

 **Well known toxins produce by microbial**

## Clostridial toxins

There are over 200 [Clostridium](https://en.wikipedia.org/wiki/Clostridium) species in the world that live in mundane places such as soil, water, dust, and even our digestive tracks. Some of these species produce harmful toxins such as botulinum toxin and tetanus toxin among others.

### *Botulinum* neurotoxin

[*Botulinum* neurotoxins](https://en.wikipedia.org/wiki/Botulinum_toxin) (BoNTs) are the causative agents of the deadly food poisoning disease botulism, and could pose a major biological warfare threat due to their extreme toxicity and ease of production.

### Tetanus toxin

[*Clostridium tetani*](https://en.wikipedia.org/wiki/Clostridium_tetani) produces tetanus toxin (TeNT protein), which leads to a fatal condition known as [tetanus](https://en.wikipedia.org/wiki/Tetanus) in many vertebrates (including humans) and invertebrates.

## Staphylococcal toxins

Immune evasion proteins from [*Staphylococcus aureus*](https://en.wikipedia.org/wiki/Staphylococcus_aureus) have a significant conservation of protein structures and a range of activities that are all directed at the two key elements of host immunity, complement and neutrophils. These secreted virulence factors assist the bacterium in surviving immune response mechanisms.

## Viral toxin

There is only one viral toxin that has been described so far: [NSP4](https://en.wikipedia.org/wiki/NSP4_%28rotavirus%29) from [rotavirus](https://en.wikipedia.org/wiki/Rotavirus). It inhibits the [microtubule](https://en.wikipedia.org/wiki/Microtubule)-mediated secretory pathway and alters [cytoskeleton](https://en.wikipedia.org/wiki/Cytoskeleton) organization in polarized [epithelial cells](https://en.wikipedia.org/wiki/Epithelial_cell). It has been identified as the viral [enterotoxin](https://en.wikipedia.org/wiki/Enterotoxin) based on the observation that the protein caused diarrhea when administered intraperitoneally or intra-ileally in infant mice in an age-dependent manner. NSP4 can induce aqueous secretion in the gastrointestinal tract of neonatal mice through activation of an age- and Ca2+-dependent plasma membrane anion permeability.

**Table   biological effects of some bacterial exotoxins with enzymatic activity**

|  |  |  |
| --- | --- | --- |
| **TOXIN** (subunit arr)\* | **ENZYMATIC ACTIVITY** | **BIOLOGICAL EFFECTS** |
| Choleratoxin (A-5B) | ADP ribosylates eucaryotic adenylate cyclase Gs regulatory protein |  Activates adenylate cyclase; increased level of intracellular cAMP promote secretion of fluid and electrolytes in intestinal epithelium leading to diarrhea |
| Diphtheritoxin (A/B) | ADP ribosylates elongation factor 2 | Inhibits protein synthesis in animal cells resulting in death of the cells |
| Pertussistoxin (A-5B) | ADP ribosylates adenylate cyclase Gi regulatory protein | Blocks inhibition of adenylate cyclase; increased levels of cAMP affect hormone activity and reduce phagocytic activity |