**Cephalosporin Production and Application**

Acremonium chrysogenum also known as Cephalosporium acremonium is the industrial producer of the antibiotic cephalosporin a beta-lactam antibiotic. cephalosporin and its derivatives are widely use in the treatment of number of infectious diseases caused by bacteria in the respiratory tract, infections of skin and infections of urinary tract. Different strains of Cephalosporium species such as Emericellopsis, Paecilomyces, chrysogenum , S. clavuligerus etc is used for the production of cephalosporin antibiotic. Acremonium chrysogenum is naturally found in soil, organic matter and plant debris and overgrows in humid environment forming grey and white colonies of loose interwoven hyphae.

**Generations of cephalosporins**

Cephalosporin is classified in to various generations on the basis of their antimicrobial potency against a number of Gram negative and Gram positive bacterial strains.

First generation cephalosporin (Narrow spectrum): This class of cephalosporins is known as narrow spectrum antibiotics with high beta lactamase sensitivity and activity against Gram positive bacteria e.g. Streptococcus, Staphylococcus etc.

Second generation cephalosporin (Intermediate spectrum): This class of cephalosporins is known as intermediate spectrum antibiotics because their activity lies between first and third generation cephalosporin with decreasing activity against Gram positive bacteria and increased potential against Gram negative bacteria e.g. E. coli, aemophilus influenzae etc.

Third generation cephalosporin (Broad spectrum): This class of cephalosporins is known as broad spectrum antibiotics with broad activity against Gram negative bacteria and beta lactamase resistance e.g. Pseudomonas, Staphylococcus aureus, Streptococcus pneumonia,

Enterobacteriaceae etc.

Fourth generation cephalosporin (Extended spectrum): This class of cephalosporins is an extended version of third generation antibiotics with increased activity against Gram positive & Gram-negative bacteria with high resistance to beta lactamas.



Figure: Activity spectrum of different cephalosporin generations

**Methods of production**

Cephalosporin production is an aerobic process, carried out either by conventional or non-conventional fermentation methods using free or immobilized fungi.

Conventional mode of production: Cephalosporin uses either surface liquid or solid-state fermentation in a batch bioreactor or continuous stirred tank reactor.

Limitation- oxygen limitation.

Non-conventional mode of production: Cephalosporin uses either packed bed or airlift bioreactor with an advantage of being operated in batch or continuous mode with proper oxygenation and agitation resulting in high yield of cephalosporin.

**Requirements of the fermentation process for cephalosporin production**

Carbon source i.e., glucose, sucrose, fructose, molasses, and lactose etc. It is required for morphological differentiation of the fungus. Organic and inorganic nitrogen sources i.e. peptone. urea, meat extract, yeast extract, casein, beef extract, ammonium sulphate,

ammonium chloride, ammonium nitrate, ammonium phosphate and potassium nitrate influence mycelium differentiation to swollen hyphae or metabolically inactive arthrospores. Thus, affecting biosynthesis of cephalosporin.

**Trace elements**

* Essential vitamins:

 • Aerobic conditions i.e., enough dissolved oxygen supply 40% or above.

* buffer for maintaining optimum pH.
* Silicone oil to control foaming
* Moisture.

Process: Cephalosporin is produced by Acremonium chrysogenum on the fermentation medium at 28°C for 144 hours. pH of the medium kept 7.2 and the temperature maintained at 28°C by passing water through the jacket. Dissolved oxygen maintained above 30% saturation by agitation and aeration. Most of the Cephalosporin produced in the idiophase.

Cephalosporin is separated from the liquid broth by the use of a number of separation and distillation techniques.

Downstream processing: Downstream processing of cephalosporin antibiotic involves a series of steps in a sequential manner to isolate and purify the produced antibiotic from the liquid broth by using a number of separation and distillation techniques depending on the physical and chemical nature of the product i.e., resin ion-exchange method or solvent extraction is used to separate the obtained antibiotic from the liquid broth. After that a purified form of the antibiotic is produced which is than ready for packaging and shipping.

Application

Cephalosporin is one of the mostly used antibiotic worldwide with broad activity spectrum making it suitable for used against numerous Gram negative and Gram positive bacterial strains for the treatment of various bacterial associated diseases.

Cephalosporins used to treat infections caused by susceptible bacteria, such as:

* Bone infections
* Ear infections (eg, **[otitis media](https://www.drugs.com/cg/ear-infection.html)**)
* Skin infections
* [**Upper respiratory tract infections**](https://www.drugs.com/cg/upper-respiratory-infection.html)
* [**Urinary tract infections**](https://www.drugs.com/mcd/urinary-tract-infection-uti).

Cephalosporins are not usually used as a first-choice antibiotic. They reserved for use when other antibiotics (often penicillins) cannot be used.