

# Extraction, purification and pharmacological analysis of penicillin

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**Abstract:** The paper is divided into five parts. The first part is about the history and development of penicillin, which introduces the following section. The second part contains basic information about penicillin, the fermentation process and the preparation process. This article provides detailed information on penicillin. The third part describes the purification process of penicillin, using the papers of others to support my data. This is followed by a comparison of the advantages and disadvantages of penicillin with other penicillin antibiotics. Finally, I explain the current state of penicillin and give my opinion on its future development. In my opinion, penicillin is fading, but without it we cannot invent these newer drugs to take its place. And these new antibiotics are all in the penicillin class. But as more people use penicillin, resistance will build up. This could lead to strong allergic reactions to new drugs that are also in the penicillin group. So it is hoped that in the future people will be able to invent drugs that reduce allergies to penicillin.

**Keywords:** penicillin, antibiotics, extraction, purification, comparison

## 1. Introduction

Penicillin is a kind of drugs that can effectively treat bacterial infections with few side effects. With the development of penicillin, antibiotics have become more and more important. Before the antibiotics were developed, many people were died because of the bacterial infections. So, the development of penicillin is a big step in the medication world. It was first discovered by accident in the early 20th century. In 1928, Fleming, a British scientist, first discovered penicillin in experimental research, but Fleming did not separate penicillin because the technology was not advanced at that time. Fleming published his research. Unfortunately, this paper has not been paid attention to by the scientific community since its publication. After more than ten years, some scientists found his paper and continued to study it. Finally, around 1940, penicillin was successfully invented. All the leading researchers who studied penicillin won the Nobel Prize in physiology or medicine. After that, penicillin is successfully used in medication and wars areas.

Now the name Penicillin is used to refer to  $\beta$ -lactams antimicrobial. Benzyl penicillin is the most famous one, also known as penicillin G. Benzyl penicillin can cure many diseases such as: bacteremia, sepsis, scarlet fever, erysipelas, pneumonia and other diseases. It is isolated from the culture medium of Penicillium. It is an organic acid that can combine with metal ions or organic bases to form salts. The

structure is small molecular shape and chemical formula is  $C_{16}H_{18}N_2O_4S$ . In normal life, we often use benzyl penicillin to cure bacterial infection.

The penicillin is used in the management and treatment of a wide range of infections. Generally speaking, penicillin that most people talk about in clinical use is penicillin G (benzyl penicillin). It is the first choice for the treatment of sensitive Gram-positive bacteria, gram-positive cocci and spirochete infections. Also, it is synthesized from naturally-produced penicillin. But some side effects may occur when they use these drugs such as: allergy, anaphylactic shock, asthma attack; High dose use can even lead to convulsions, drowsiness, short-term mental disorders and so on.

But penicillin is becoming less useful than before. The main reasons are antibiotic misusing and development of new antibiotics. Misusing will lead to antimicrobial resistance to this kind of drug. When bacteria mutate in a certain way, they will become resisting to the drug. This change either protects the bacteria from the effects of the drug or neutralizes the drug. And with the development of technologies, scientists invented more advanced antibiotics to replace old one. So, it is important to study penicillin and make good use of it.

The synthesis and characteristic of penicillin will be fully discussed in this research. It is not only telling about the basic introduction of penicillin, but also discover the significance of this medicine and reasonable control of its advantages. Allergic reactions and environmental effects can be reduced by being studied. The updating of penicillin is necessary because it will be substitute by other new antibiotics like cephalosporin. Through this study, the advantages of penicillin can be better utilized. And this paper will provide a basis for better use of antibiotics in the medical community.

In this paper, it is mainly focus on the analysis, purification and characterization of penicillin. Because penicillin is a famous antibiotic. In that case, why penicillin can treat infection and the production process have become the focus of this paper.

This paper is mainly divided into three main parts. In the beginning, the main point is: antibiotics' types and describe penicillin can effectively treat bacterial infections. The discovery and preparation of penicillin are placed behind the main topic. The purification and detection methods of penicillin will be the important part in the paper. Furthermore, the comparison between penicillin and other three kinds of antibiotics is another important point in this paper. At last, the limitation of penicillin will be described in detail. In the end, my personal conclusion of this paper and self-evaluation will express my whole paper and feelings.

## 2. Research review

Firstly, antibiotics can be divided into two broad categories: broad-spectrum antibiotics and narrow-spectrum antibiotics. Broad-spectrum and narrow-spectrum represent the range of antibiotics that can be used. Each antibiotic has its own antibacterial range, called the antimicrobial spectrum. Any antibiotic that does not have a broad antibacterial spectrum is called a narrow-spectrum antibiotic. For example, penicillin only has an antibacterial effect on Gram-positive bacteria, but has no effect on Gram-negative bacteria, tuberculosis, rickettsiae, etc. Therefore, penicillin is a narrow-spectrum antibiotic.

On the contrary, chloramphenicol and tetracycline were known as broad-spectrum antibacterial drugs in the past because they had different degrees of inhibitory effects on Gram-positive and Gram-negative bacteria, rickettsiae, *Chlamydia trachomatis*, *Mycoplasma pneumoniae* and so on.

Since the 1990s, the types and applications of antibiotics have developed rapidly. The original narrow-spectrum antibiotics, such as penicillin, have been transformed to produce many semi-synthetic penicillins, which have expanded the original antibacterial range, such as ampicillin and hydroxybenzyl penicillin are not only effective against Gram-positive bacteria, but also Gram-negative bacteria, especially against *S. typhi* and *S. dysenteriae*. In recent years, the third and fourth generation cephalosporins also have a wide antibacterial spectrum. To summarise, narrow-spectrum antibiotics are highly targeted and do not easily produce secondary infections, but require a combination of drugs when treating serious or mixed bacterial infections. Broad-spectrum antibiotics, on the other hand, have a broad antibacterial spectrum and are used in a wide range of applications, but are prone to resistance and secondary infections, and are not as targeted as narrow-spectrum antibiotics. Therefore, broad-

spectrum antibiotics and narrow-spectrum antibiotics have their own advantages and disadvantages and must be treated correctly and chosen wisely.

When we use antibiotics to treat an infection, the normal flora of the body is also killed or inhibited, but the extent to which the normal flora of the body is affected by the antibiotic depends on how broad or narrow the antibacterial spectrum of the antibiotic chosen is. Narrow-spectrum antibiotics are active against only one or a small number of bacteria, such as penicillin agents, which mainly act on positive cocci broad-spectrum antibiotics can be active against two or more bacteria, such as Bacteroides, which are effective against a wide range of Enterobacteriaceae bacteria. Ultra-broad-spectrum antibiotics, on the other hand, are active against many or most bacteria. The broader the antibacterial spectrum of an antibiotic, the broader the spectrum of bacteria affected, and the more normal flora that will be killed or inhibited. Infections that can be controlled with an antibiotic or sulphonamide are not combined with an antibiotic, and when a narrow spectrum antibiotic is available to treat an infection, a broad spectrum one is not used.

### 3. Discussion

#### 3.1. *The discovery and preparation of penicillin*

The discovery of penicillin was actually a coincidence. Alexander Fleming was looking at a petri dish with a microscope when he noticed that the staphylococcal colonies around the mould had been lysed. This meant that some kind of secretion from the mould was able to inhibit the staphylococci. Subsequent identification showed that the mould in question was *Penicillium punctatum*, and Fleming therefore referred to the inhibitory substance it secreted as penicillin. However, Fleming had not found an efficient way of extracting penicillin, so penicillin was not extracted. Later, in 1938, the German scientist Chern discovered Fleming's thesis and began experiments to purify it. The earliest method used was solid surface culture, where a solid medium is mixed with the liquid of the *Penicillium* strain, put into a shallow tray, then the shallow tray with the ferment is placed on a shelf in the room, the room temperature is maintained and fermentation takes place, after the fermentation is over, water is used to leach the resulting penicillin from the solid medium and make a dry powder. There are many problems with using such a production method. In order to obtain sufficient quantities of penicillin, a large amount of medium and culture chambers are required, occupying a very large plant, which also makes it difficult to control the temperature; and it is very labour intensive and very hard on the workers. What is more important is that during the fermentation process, the medium is almost exposed to the air in order to ventilate it, and all kinds of microorganisms in the air cause a lot of contamination, making it impossible to achieve pure fermentation, making the results of each fermentation different and making it difficult to control the fermentation process and quality.

Penicillin is extracted from the fungus *Penicillium*. *Penicillium* is a type of eukaryotic fungus. It belongs to the subphylum ascomycetes, the class of integumentary fungi, the order ascomycetes, the family ascomycetes, and the genus *Penicillium*. Intersexual reproductive stage. The mycelium is multicellular and branched. During asexual reproduction, the mycelium develops an erect multicellular meristematic peduncle. The tip of the peduncle is not inflated, but has finger-like branches that can continue to be divided again, with 2-3 flask-shaped cells at the tip of each branch, on which each has a string of grey-green conidia. After the conidia are shed, they germinate under suitable conditions to produce new individuals. Sexual reproduction is extremely rare. Commonly found on decaying fruit, vegetables, meat and clothing, mostly grey-green in colour.

Around the world, scientists have conducted a great deal of research related to the application of penicillin, which has an incalculable future in the pharmaceutical industry because of its low toxicity, efficacy and cost effectiveness, as well as its ability to derive endocannabinoid antibiotics. Currently, *Penicillium flavum* and its improved strains are still the main source of penicillin production. In the production and application of penicillin, the two key steps in the production of penicillin are fermentation and extraction. The chemical structure of penicillin is relatively simple.

The chemical structure of penicillin is relatively simple, consisting mainly of a 6-aminopenicillanic acid (6-APA) parent nucleus and an acyl-carrying side chain. The side chain gene can be modified, knocked out and other can be modified or knocked out to obtain different types of penicillin or cephalosporin. Penicillin is one of the main antibiotics of the  $\beta$ -lactam family.

Penicillin-producing bacteria are the main strains of penicillin production. The mycelium of this bacterium is cross-segmented and when *Penicillium flavum*-producing bacteria are cultured on solid medium, two different strains appear. When cultured on solid medium, two different forms and functions of mycelium emerge, with the mycelium growing in the solid agar. The mycelium that grows inside the solid agar is called the nutrient mycelium and its main function is to absorb nutrients from the medium and supply the mycelium with nutrients. The mycelium that grows on the surface of the agar is known as aerial mycelium, whose main function is to absorb nutrients from the medium and supply the mycelium with nutrients for reproduction and development. On the surface of the agar are called aerial mycelium, which have round or sub-circular conidia.

These will have round or sub-circular conidia, on which new secondary branches will be produced, which in turn will grow peduncles and spore chains of small peduncles. The colony morphology of *Penicillium flavum* is a raised, round colony with radiating grooves at the edge of the colony, and the colony morphology is essentially the same on the same agar culture, without major differences. When the composition of the medium and the time and temperature of incubation are changed, the morphology of the colonies will change somewhat. In the liquid culture of yellow penicillin-producing bacteria, the mycelium constantly draws nutrients from the culture broth, while oxygen is obtained through continuous agitation and aeration. In larger fermenters, the stirring leaves shear and cut the mycelium during agitation to prevent the mycelium from hooking and entangling, ensuring that the mycelium can obtain enough nutrients for metabolic production. Penicillin is susceptible to glycolytic metabolites during biosynthesis, such as acyltransferases that curb the synthesis process.

During fermentation, *Penicillium* can rapidly use glucose to supply itself for growth and reproduction, but to a certain extent inhibits penicillin synthesis; *Penicillium* uses lactose at a relatively slow rate, but is very beneficial to penicillin synthesis. Lactose is a common double bond, consisting of one molecule of glucose and one molecule of galactose, which is not a precursor to penicillin synthesis, so that the rate at which lactose is hydrolysed to monosaccharides and the rate at which penicillin is synthesised by *Penicillium flavus*-producing bacteria is largely matched, and the synthesis of penicillin is not inhibited by high concentrations of breakdown products.

Therefore, when culturing *Penicillium*, the carbon source is either a mixture of glucose and lactose, or a non-sugar carbon source such as vegetable oil. Penicillin production is also inhibited by lysine, due to the feedback regulation of high citrate synthase by lysine. In the synthetic lysine pathway, penicillin is produced on the  $\alpha$ -amino adipic acid branch and this blocking effect is a combined effect of primary and secondary metabolism. In the metabolic pathways of living organisms, primary and secondary metabolism have the same intermediates and together they form branching metabolic pathways. Sometimes these branching pathways produce the enzymes produced in these branch pathways sometimes have an impact on the synthesis of the antibiotic in question to some extent.

### 3.2. Purification and detection of penicillin

Penicillin can be obtained through the fermentation of strains of bacteria and two factors are relevant to the fermentation of strains. The first, the cultivation of the seeds. Seed culture is a very critical step in the fermentation process, the main role is through the continuous multiplication of spores, so as to get sufficient mycorrhizal fungi, good seeds moved into the fermenter, can quickly adapt to the new culture environment, the preparation of seeds is generally first shake the flask culture, followed by a step-by-step expansion in the seed jar culture. The quality of the seed is related to the nature of the strain itself, and the equipment and medium concerned must be sterilised before inoculation, and the seed solution etc. must be free of miscellaneous bacteria before the test can be carried out. In the process of cultivation in the tank, it is necessary to stir and pass in sterile air, while controlling the temperature of the fermenter

and the pressure of the fermenter, and to take regular samples for aseptic tests to ensure a sterile environment at all times [1].

Another factor is the composition of the medium. The medium is used to provide nutrients for the growth and reproduction of microorganisms, and the composition of the medium is essential for the growth of microorganisms, mainly C and N sources, inorganic salts, trace elements and growth factors. Glucose is the most readily available monosaccharide and is often used as a C source. For penicillin, the main C source is glucose, but the amount of glucose needs to be strictly controlled, too little will cause nutrient deficiency, too much will increase oxygen consumption and reduce the yield.

The second is the semi-synthetic method. In the past, the side chains of the parent nucleus of penicillin were chemically 'cut off' to obtain the parent nucleus, which was then chemically attached to a new side chain, resulting in a modified 'semi-synthetic penicillin'. Natural penicillin is produced in a completely different way to semi-synthetic penicillin. Since natural penicillin has a narrow antibacterial spectrum, is not resistant to gastric acid and is not resistant to enzymes and is easily hydrolysed, the side chain of natural penicillin G can be altered to obtain a range of different semi-synthetic penicillin that are acid-resistant, enzyme-resistant, broad-spectrum, anti-*Pseudomonas aeruginosa* and mainly act on G<sup>+</sup> bacteria; however, the antibacterial activity of semi-synthetic penicillins is not as good as that of natural penicillin G. 6APA is used as an intermediate in the acylation reaction with a variety of chemically synthesised organic acids. 6APA is obtained by cleavage of penicillin G or V using the enzyme penicillin acylase produced by microorganisms. The enzymatic reaction is usually carried out at 40-50°C and pH 8-10; in recent years, enzymatic solid phase technology has been applied to the production of 6APA, simplifying the cleavage process. 6APA can also be produced by chemical cleavage from penicillin G, but at a higher cost. The side chain is introduced by making the corresponding organic acid into an acyl chloride using a chlorinating agent and then acylation with 6APA in water or an organic solvent using an inorganic or organic base as a condensation agent, depending on the stability of the acyl chloride. The condensation reaction can also be carried out directly in the lysate without isolating the 6APA.

The final method is the concentration method of penicillin extraction. This method mainly uses penicillin to specifically kill wild-type cells and retain nutritionally defective cells to promote mutant penicillin cells for concentration. A method that uses penicillin to specifically kill wild-type cells and retain nutritionally defective cells. Penicillin inhibits the synthesis of bacterial cell walls, so it can only kill bacteria that are growing and reproducing, but not those that have stopped dividing. In selective liquid media, where only the wild type but not the mutant can grow, the wild type is killed by penicillin but not the mutant, thus eliminating the wild type and allowing the mutant to concentrate. Can be applied to both bacteria and actinomycetes and is one of the common methods used for nutrient-deficient mutant screening.

There are many methods of extracting penicillin, the following one is the most used. The most widely used method in extraction is solvent extraction. Mostly butyl acetate is used as the extractant and aqueous sodium bicarbonate as the counter-extractant. The process has obvious drawbacks: the loss of penicillin degradation due to extraction at low pH, high production energy consumption due to operation at low temperatures, and difficulties in solvent recovery due to the high water solubility of butyl acetate. In recent years, the dramatic increase in penicillin production has led to an oversupply of penicillin, so reforming the process to reduce costs is an urgent task and many researchers are competing to develop new processes, methods and equipment. Fermentation broth, filtration, primary extraction, reverse extraction, secondary extraction, decolourisation and crystallisation. These are simplified steps for the purification of penicillin[2]

Butyl acetate extraction for penicillin purification has been studied for a long time and the process is quite mature. In the long term, the production process has to be modified in order to increase the yield and reduce the energy consumption. Although the new separation and purification methods have many attractive advantages, their low throughput and high costs make them difficult to apply on an industrial scale for the time being. When selecting new extraction systems and processes, the following issues should be addressed.

1. The extraction can be carried out at a suitable pH (pH 4.0-8.0) and can be operated at room temperature.

2. The choice of organic solvents with low water solubility and easy recovery.

3. A yield no lower than that of butyl acetate extraction, without emulsification problems. In the decades of penicillin production, many scholars have carried out experimental research in various aspects up to industrial scale trials, and have gained a lot of experience and lessons learned, laying a good foundation for further research and industrial application.

The main purification process is a four-step process:

1. pre-treatment of the raw material and solid-liquid separation by centrifugation and filtration to remove bacteriological cells and insoluble solid impurities from the fermentation broth.

2. Preliminary separation using four processes: extraction, adsorption, precipitation and evaporation, to remove impurities with widely varying properties of the fish product.

3. This is followed by a high level of purification, using precipitation, chromatography and ion exchange to remove impurities that are close to the physicochemical properties of the product.

4. The final step is the final processing of the product, where the end use is considered and the final product is formed by various means (crystallisation, drying, distillation).

### 3.3. *The comparison between penicillin and other antibiotics*

There are also many antibiotic classes in the world, some with more powerful and extensive profiles. I have selected three antibiotics that are also widely used for comparison with penicillin. Cephalosporins are a widely used class of antibiotics. Cephalosporins are semi-synthetic antibiotics that contain cephalixin in their molecules and are derivatives of the 7-amino cephalosporanic acid (7-ACA) in the  $\beta$ -lactam antibiotic class, so they have a similar bactericidal mechanism. Cephalosporins and penicillins are both  $\beta$ -lactam antibiotics, the difference being that the parent nucleus of cephalosporins is 7-aminocephalosporanic acid (7-ACA), whereas the parent nucleus of penicillins is 6-aminopenicillanic acid, a structural difference that makes cephalosporins resistant to penicillinase. This class of drugs destroys the cell wall of bacteria and sterilises them during the reproductive phase. It has a strong selective effect on bacteria, while being almost non-toxic to humans. It has the advantages of a broad antibacterial spectrum, strong antibacterial effect, resistance to penicillinase and less allergic reactions than penicillins. Therefore, it is an important antibiotic with high efficiency, low toxicity and widely used in clinical practice.

Cephalosporins are also classified into four generations according to their antibacterial effects:

The first generation cephalosporins were developed earlier, with stronger antibacterial activity, narrower antibacterial spectrum and better anti-Gram-positive than Gram-negative bacteria. The first generation cephalosporins, represented by cefazolin, have the triple characteristics of penicillin, enzyme-resistant penicillin and ampicillin. They are more active against Gram-positive bacteria such as *Staphylococcus aureus* and *Streptococcus* (except *Enterococcus*), and are superior to the second and third generation cephalosporins. The first generation cephalosporins are less stable than the second and third generation cephalosporins against Gram-negative bacilli because they are less stable against the  $\beta$ -lactamases produced by Gram-negative bacteria. Therefore, first-generation cephalosporins are mainly used for Gram-positive bacterial infections and are often used in combination with aminoglycoside antibiotics for the treatment of Gram-negative bacillary infections. First generation cephalosporins can be administered by injection or orally.

The second generation cephalosporins, in addition to retaining the effects of the first generation on Gram-positive bacteria, have significantly expanded and improved their effects on Gram-negative bacteria because they are more stable than the first generation in producing beta-lactamases and have a broader antibacterial spectrum than the first generation. They also have some antimicrobial activity against the first generation cephalosporins, which are less effective against *Aspergillus* and *Bacillus pneumoniae*, but less effective against *Bacillus immobilis*. They have no antibacterial activity against *Pseudomonas aeruginosa* and *Streptococcus faecalis*. It has strong antibacterial activity against *Staphylococcus aureus* and *meningococcus* and is like the first generation cephalosporins. Second-

generation cephalosporins can be divided into two sub-categories according to their chemical structure, namely amide-type cephalosporins and cephalosporins, both of which have their own advantages.

The third generation cephalosporins are stable against a wide range of  $\beta$ -lactamases and have significant antibacterial activity against both Gram-positive and negative bacteria. Compared with the first and second generation, it has a broader antibacterial spectrum and stronger antibacterial activity. In particular, it has a broad antibacterial spectrum and strong antibacterial effect on Gram-negative bacteria. Some varieties also have a good antibacterial effect on *Pseudomonas aeruginosa* or *Bacteroides fragilis*. They are significantly better than the first two generations of cephalosporins, but they still have disadvantages - they also have poor antibacterial activity against *Streptococcus faecalis*. The chemical structure of the cephalosporins can be divided into three subgroups: amide cephalenes, cephalosporins and oxytetracyclines.

The last cephalosporins are the fourth generation cephalosporins, which combine the advantages of the first three generations and have an extremely broad spectrum of antibacterial activity. However, due to the misuse of antibiotics, the number of bacteria resistant to the fourth generation cephalosporins has increased, such as *Acinetobacter baumannii* and *Pseudomonas aeruginosa*, which have shown a high level of resistance [3].

Ampicillin, also known as ampicillin, is a beta-lactam antibiotic that treats a wide range of bacterial infections. Ampicillin has a strong antibacterial effect against *Streptococcus haemolyticus*, *Streptococcus pneumoniae* and staphylococci that do not produce penicillinase, similar to, or slightly weaker than, penicillin. Ampicillin has a good antibacterial effect against *Streptococcus gramineus*, is generally better than penicillin against *Enterococcus*, and has some antibacterial effect against *Bacillus diphtheriae* and *Bacillus anthracis*, in this case. Indications include respiratory tract infections, urinary tract infections, meningitis, salmonella infections, and endocarditis. It is also used to prevent group B streptococcal infections in newborns and can be administered orally, intramuscularly and intravenously. C<sub>16</sub>H<sub>19</sub>N<sub>3</sub>O<sub>4</sub>S. Penicillin is C<sub>16</sub>H<sub>18</sub>N<sub>2</sub>O<sub>4</sub>S, which differs by only one hydrogen and one nitrogen atom. First discovered in 1961, ampicillin is listed on the World Health Organization's Standard List of Essential Medicines and is one of the essential medicines for basic public health systems. On 27 October 2017, the World Health Organization's International Agency for Research on Cancer published a preliminary collation of references to the list of carcinogens, with ampicillin in the list of Group 3 carcinogens. Therefore, it is important to use it as prescribed by your doctor, as overdose can be harmful to your body.

The pharmacological action of ampicillin. It is a semi-synthetic broad-spectrum penicillin, the antibacterial mechanism is to prevent the cell wall synthesis of bacteria, so it can not only inhibit their proliferation, but also directly kill bacteria. The effect on Gram-positive bacteria is similar to that of penicillin, while the effect on *Streptococcus gramineus* and *Enterococcus* is better and the effect on other bacteria is worse, and it is ineffective against penicillin-resistant *Staphylococcus aureus*. Among the gram-negative bacteria, gonococcus, meningococcus, influenzae, pertussis, *Escherichia coli*, typhoid and paratyphoid bacteria, dysentery bacillus, *Strongyloides*, brucella, etc. are sensitive to this product, but easily develop drug resistance. *Pneumobacterium*, Indole-positive *Aspergillus* and *Pseudomonas aeruginosa* are not susceptible to this product [4].

Ampicillin is made in a very similar way to that of penicillin, but differs in some details. The side chain carboxylic acid of D-(-)-phenylglycine is first made into a chloride with the chlorinating agent PCI<sub>5</sub>. It is made into a chloride, which is then reacted with 6-APA by condensation. Acetone and water were added to the reaction tank and 6APA was added when the temperature was lowered to -5-10°C. Phenylglycine chloride hydrochloride was then added and the pH was adjusted to 3.5 with 10% sodium hydroxide after 0.5 h. The reaction product was extracted with toluene. The aqueous layer was extracted and the pH was adjusted with 10% ammonia to approximately 3.0. The product was decolourised with activated carbon and filtered. The filtrate is then adjusted with ammonia to a pH of 4.8. It is left to stand, then filtered, washed with acetone and dried under vacuum below 40°C to obtain the product [4].

Pivmecillinam is a type of medicine called a penicillin antibiotic. It works by interfering with the ability of bacteria to form cell walls. Pivmecillinam allows holes to appear in the bacterial cell walls and

this kills the bacteria causing the infection. Pivmecillinam is an antibiotic primarily used to treat bacterial infections of the urinary tract. Different from penicillin, it is a type of antibiotic. The pivmecillinam is included in penicillin. So, when someone is allergy to penicillin, he cannot take pivmecillinam as well. Pivmecillinam belongs to the antibiotic section of the penicillin group. It has the same antibacterial spectrum as methicillin and is characterised by its availability for oral administration and good absorption after oral administration. It is rapidly hydrolysed in the body by esterases to methicillin and exerts antibacterial activity. Food can promote the absorption of this product and it is advisable to take it after meals. Probenecid may increase the blood concentration of this product and make it persistent. Clinical applications are the same as for mecillin, for urinary tract and respiratory tract infections, and for the treatment of typhoid fever [5].

Pimecillin, like other antibiotics, should not be used if the patient is allergic to penicillins and cephalosporins. It is a new synthetic penicillin preparation. It acts as a bactericidal agent by impeding the synthesis of bacterial cell walls, showing bactericidal action even at the lowest inhibitory concentrations.

#### 4. Conclusion

In the present context, we have focused on the preparation and purification methods of penicillin. This is in turn divided into the remaining sections: classification of antibiotics, the process of discovery of penicillin, the process of synthesis of penicillin, the purification steps and the advantages and disadvantages of the three classes of antibiotic drugs, cephalosporins, ampicillin and pimecillin, compared with penicillin. This article focuses on the action of penicillin through the purification and synthesis steps.

The limitations of the study in this paper are mainly in the following areas. Firstly, there is no visual data to support the comparison of the advantages and disadvantages of penicillin. Secondly, more detailed information could have been discussed for some parts. Some sections are too brief and need to be expanded with more information. Thirdly, the literature sources are all from domestic sources and for foreign papers there are none. The comparative nature is missing. Based on our research, future research on penicillin can be directed in the following directions. Firstly, attempts to allow penicillin to combine with other species to generate new possibilities. Secondly, to make penicillin invisible by fortifying it with other antibiotics, until a better finished product can replace it completely and then put an end to the use of penicillin. Thirdly, to reduce resistance to penicillin so that the upgraded penicillin will have a more favourable effect.

There are three reasons why penicillin is being phased out of use. The first reason was that many people had severe allergic reactions to penicillin. This is because the purification process of penicillin is prone to mishandling and causing allergies. The second reason is that more and more diseases have emerged and resistance to penicillin has developed very quickly. And penicillin does not play any role in these new emerging diseases, so it has been downplayed by us. Another reason is that many bacteria have developed antibodies against penicillin, and treating them with penicillin is not as effective as it used to be. That's why penicillin has been reduced in use.

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