Heterocyclic Compounds as Commercial Antimicrobial Agents – *A Review*

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Abstract

Heterocyclic compounds are one of the fastest developing branches of synthetic chemistry, it grabs more attention because of their high existence in nature as well as their most important role in the creation of useful materials and drugs. Compounds such as carbon, hydrogen and methane does not show that much activity against microbes but heterocyclic compounds such as three-, four-, five-, six- and higher-membered rings containing drugs act as antimicrobial agents. There are different types of activities shown by the heterocyclic compounds. In this review paper some famous commercial drugs such as amphotericin B, amoxicillin, cephalexin, ceftriaxone, ciprofloxacin, fosfomycin, ketoconazole, miconazole, levofloxacin, penicillin, sulconazole, Voriconazole etc. along with their mode of action, dosage, and CAS ID will be discussed.

Keywords: Heterocyclic compounds, Commercial drugs, Antimicrobial agents.

Introduction

Heterocyclic compounds plays a major role naturally as well as synthetically and have broad spectrum of applications in our daily life, commercial life, agriculture life, in medicines, in our diets and it is present almost everywhere.[1] Scope of heterocyclic compound is very vast.[2] If we talk about petroleum, these are organic compounds and in that organic compounds there are mostly heterocyclic compounds.[3] In petroleum there is low concentration of nitrogen and sulphur containing heterocycles are present and next is coal which is a source of pyridine containing heterocycles by pyrolysis.[4] In our solar system many heterocycles are found in the chemistry of solar system such as meteorite, that meteorite which is a part of our solar system and that contain pyridine carboxylic acid.[5] Marine plants and animals, they are also has a big source of complex heterocycles for research purpose because they have wide range of compounds.[6] If we talk about heterocycles in our diet as such as carbohydrates chemistry and that contains disaccharides and polysaccharides such as furanose and pyranose that contain oxygen. So these are also important in monosaccharides such as D-glucose but these are actually the heterocycles or

derivatives of heterocycles.[7] Both plants and animals have a some sort of similar compounds such as plants have chlorophyll and animals have hemoglobin so these are both are the derivatives of heterocyclic compounds of porphyrin ring system, are the main components which necessary for the photosynthesis and for O2 transport in higher animals and plants.[8] On moon, molecules such as porphyrin are also found. There are thousands of nitrogen containing heterocyclic compounds such as alkaloids found in plant kingdom such as black pepper which is actually the alkaloid of nitrogen containing heterocycles such as piperine.[9]

In our essential diet ingredients are heterocyclic compounds. Pyridoxol (vitamin B6), riboflavin (vitamin B2), thiamine (vitamin B1) and the very famous (vitamin C) Ascorbic acid these all are the derivatives of heterocyclic compounds.[10] Among the twenty amino acids that are typically present in various proteins, basically proteins are made from amino acids, three, namely histamine, proline and tryptophan, are heterocyclic in nature.[11] In biological processes, carbohydrates, proteins and lipids, the nucleic acid bases, which are purine-derived compounds which is heterocyclic compounds.[8] Adenine, guanine and pyrimidine, namely thymine, cytosine these are actually involved in the replication of DNA and RNA. An example of one of these antibiotics is puromycin.[12] There are various purine alkaloids such as caffeine, theobromine and theophylline which are filled in the daily beverages that is tea, coffee as well as in the cocoa which is used as CNS stimulant and diuretic.[13]

As we all know that old antimicrobial agents are least effective to kill the microbes or slow down their growth so researchers have found new age antimicrobial agents.[14] New age antimicrobial drugs have potentially alleviated the present-day situation of drug resistance. They are the profitable source of recognition of therapeutic active agents. A new age antimicrobial can be produced economically with the next level of potency to improvise the pharmacokinetic characterization in pre drug clinical trial.

Beta-amino heterocyclic moieties manifest the probability of non-proteinogenic acid residues in peptide entreaty. They are used in the manufacturing of bioactive ligand composition due to their biological stability in proteolytic enzymes. It exhibits antimicrobial selective inhibitors of TNF (a converting enzyme). Additionally, they include metabolic resistance degradation and improve oral bioavailability.[15]

1. Motivation and purpose of study

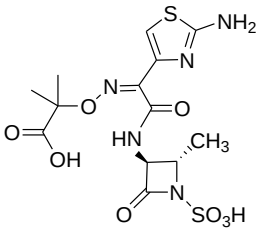
The study of Heterocyclic Compounds as Commercial Antimicrobial Agents is motivated by the critical need to address the growing global threat of antimicrobial resistance. As conventional antimicrobial treatments become increasingly ineffective, there is an urgent call for novel therapeutic strategies.[16] Heterocyclic compounds, with their inherent structural diversity and potential for unique biological activities, offer a promising avenue for combating infectious diseases. The motivation behind this study lies in harnessing the inherent properties of heterocyclic compounds to develop innovative antimicrobial agents that can overcome the challenges posed by resistant pathogens.[17] The purpose of this review is to comprehensively evaluate the potential of these compounds as commercial antimicrobial agents. By exploring their mechanisms of action, structure-activity relationships, and safety profiles, this study aims to contribute to the development of effective treatments that can mitigate the current antimicrobial crisis and safeguard public health.[18]

2. List of potent Antimicrobial Drugs and their mode of action

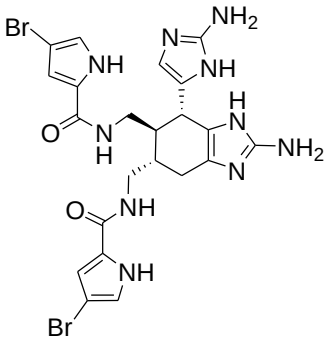
Several potent antimicrobial drugs have been developed to combat a wide range of infectious diseases, each employing distinct modes of action to effectively target and inhibit microbial growth.[19] For instance, antibiotics like penicillin and cephalosporins disrupt bacterial cell wall synthesis by inhibiting the enzymes responsible for cross-linking peptidoglycan strands, ultimately leading to cell lysis.[20] Macrolides, such as erythromycin, interfere with bacterial protein synthesis by binding to the 50S ribosomal subunit, preventing the elongation of peptide chains.[21] Fluoroquinolones, like ciprofloxacin[22], target bacterial DNA gyrase[23] and topoisomerase IV[24], disrupting DNA replication and transcription processes[25]. Antifungal drugs, like azoles[26], inhibit the synthesis of ergosterol, a vital component of fungal cell membranes, thereby compromising membrane integrity. Similarly, antiviral drugs, such as neuraminidase inhibitors[27] like oseltamivir[28], block the release of viral progeny from infected cells, while protease inhibitors like lopinavir[29] prevent the cleavage of viral precursor proteins, inhibiting viral maturation. These examples underscore the diversity of antimicrobial drug mechanisms, highlighting the importance of tailored approaches to effectively combat various types of pathogens and prevent the emergence of resistance.[30] Various potent antimicrobial drugs are discussed below with their mode of action. In the following, we present a comprehensive list of potent antimicrobial drugs, accompanied by a detailed overview of their respective modes of action.

2.1. Aztreonam

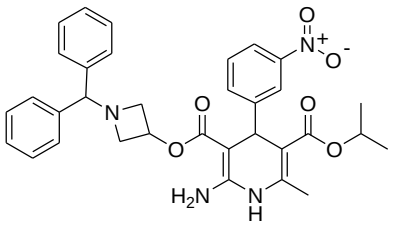
Aztreonam **1** also known as azthreonam; SQ 26,776 and it comes under the class of beta-lactam antibiotics which is the first member of monobactams. It is found to be more effective compared with cefamandole in urinary tract infections. Its mode of action is similar to penicillin; aztreonam prevents the crosslinking of peptidoglycans, which reduces the production of the bacterial cell wall. Its recommended dose is 2g in every 6 hours and in combination with avibactam 375-600mg every 6 hours for 10-14 days.[31]



Aztreonam
(78110-38-0)
1



Ageliferin
117417-64-8
2



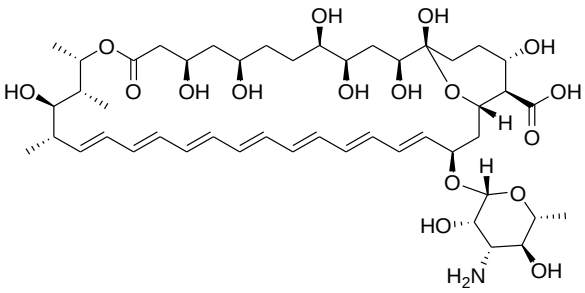
Azelnipidine
123524-52-7
3

2.2. Ageliferin

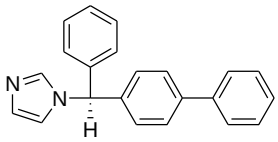
Ageliferin **2** is a rich marine substance synthesized via Acyl N-amidinyliminium Ion Rearrangement**.** Ageliferin is an alkaloid that belongs to the imidazole/pyrrole class of drugs. Ageliferin are capable of breaking the biofilm layer that bacteria formed to protect themselves from outside threats, such as antibiotics.[32]

2.3. Azelnipidine

Azelnipidine **3** comes under the class of Dihydropyridine a calcium channel blocker. It restricts trans- membrane influx of Ca^{2+} through smooth muscles in vascular walls.[33] Its recommended use is 4 mg oral dose in 14C-labeled Azelnidipine, 8-16 mg for an Adult.



Amphotericin B
1397-89-3
4



Bifonazole
60628-96-8
5

2.4. Amphotericin B

Amphotericin B **4**, polyene macrolide is a natural product antifungal agent derived from Streptomyces nodosus.[34] It creates membrane breakage in target cells, causing leakage of ions and tiny molecules leading to cell death. Amphotericin B is utilised to treat invasive fungal infections caused by Candida or Cryptococcus at doses of 3-6 mg/kg per day.[35]

2.5. Bifonazole

Bifonazole **5** works by inhibiting the production of ergosterol, ergosterol production is disrupted, resulting in holes appearing in the cell membrane and due to this essential constituent of the fungal cell can leak out and this kills the fungi.[36] Its recommended use is to apply the cream into the affected area for 2 weeks.

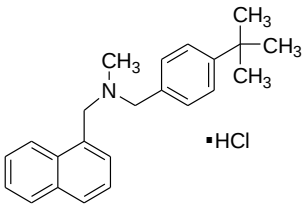
2.6. Butenafine

Butenafine **6** also known as (N-4-tert-butylbenzyl-N-methyl-1-naphthalenemethyl-amine hydrochloride) benzylamine antifungal agent were discovered to be more effective than clotrimazole.[37] The mode of action of butenafine is thought to be sterol synthesis inhibition. It inhibits the activity of the squalene epoxidase enzyme, which is required for producing sterols in the membranes of fungal cells. It is in the form of cream; recommended use is to apply on affected area and surrounding skin daily for 2-4 weeks.[38]

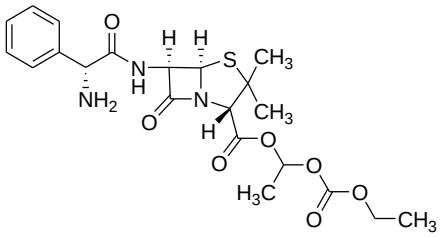
2.7. Becampicillin

A derivative of ampicillin called bacampicillin **7** is ethoxycarbonyloxyethyl ester that is quickly changed to active ampicillin, by unspecified esterases enzyme found in the serum and the intestine.[39] By esterases enzyme it is hydrolyzed in the intestinal lining during absorption from the gastrointestinal system. It has the same microbiologic activity as

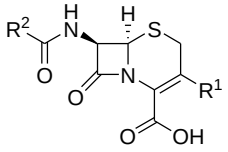
ampicillin and acts as a bactericide by inhibiting the formation of cell wall mucopeptides.[40] Its recommended use is to take 400-600 mg for every 8 hours for 6-12 days.[41]



Butenafine
101828-21-1
6



Becampicillin
50972-17-3
7



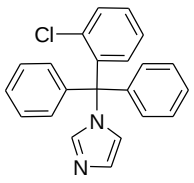
Cephalosporin
1820673-23-1
8

2.8. Cephalosporin

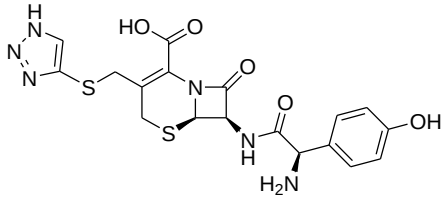
These are beta-lactam antibacterial drug **8** treat various kind of infections from gramme positive or negative bacteria.[42] Resistant bacteria, meningitis, and other infections, five generations of cephalosporin are useful to fight against these infections. The beta-lactam rings that bind to the penicillin-binding protein prevent it from doing its intended function. The bacteria perish as a result of their inability to produce a cell wall.[43] Its recommended use is 50-100 mg/kg/day for adults.

2.9. Clotrimazole

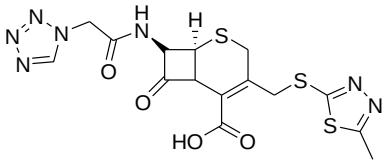
Clotrimazole **9** is imidazole containing drug, clinically used to treat vaginal infections and skin infections developed by yeasts and dermatophytes. Clotrimazale perform their work by suppression of modifying the permeability of the fungal cell wall in order to encourage the formation of distinct candidiasis or yeast cells.[44] Recommended use is 100 and 500mg vaginal tablets, applied once daily at bedtime for 6 days.



Clotrimazole
23593-75-1
9



Cefatrizine
51627-14-6
10



Cefazolin
25953-19-9
11

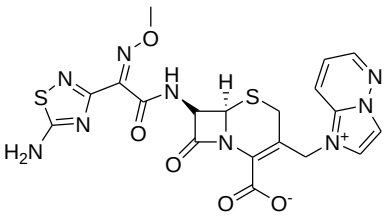
2.10. Cefatrizine

Cefatrizine **10** is also known as new oral cephalosporin compound having (1H-1,2,3-triazol-4-ylsulfanyl)methyl and [(2R)-2-amino-2-(4-hydroxyphenyl)]acetamido side-groups.[45] It

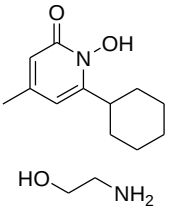
prevents the bacterial cell wall synthesis.[46] Its recommended use is 25-50 mg/kg for two to four equal doses per day.

2.11. Cefazolin

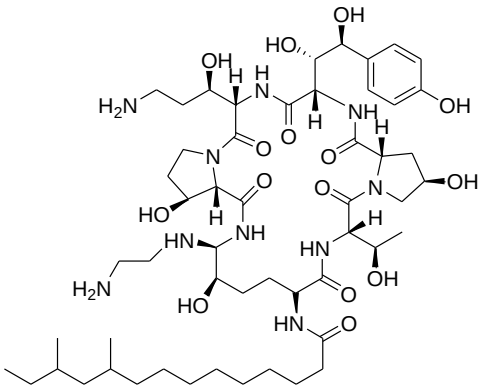
The antimicrobial activity of 1,3-*bis*-(2-benzimidazyl)-2-thiapropane ligand and its Pd (II) and Zn (II) halide complexes inhibits cell wall biosynthesis by the binding penicillin-proteins which stop peptidoglycan synthesis.[47] Its recommended use is to take 1-2 g for 4-7 days.



Cefozopran
113359-04-9
12



Ciclopirox olamine
41621-49-2
13



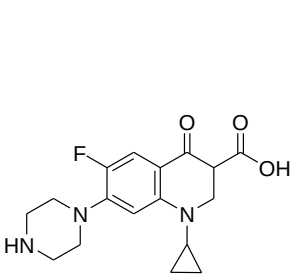
Caspofungin
179463-17-3
14

2.12. Cefozopran

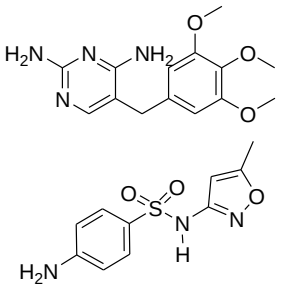
Cefozopran **12** is a fourth-generation cephalosporin developed to treat serious infections caused by staphylococci and enterococci in immunocompromised patients. It has a broad antibacterial scope which comprises both gramme-negative and positive microorganisms. It decreases the excretion rate of abacavir.[48] Its recommended use is to take 4mg/kg per day.

2.13. Ciclopirox olamine

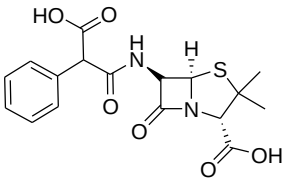
Ciclopirox olamine **13** is a hydropyridone antifungal agent which is a derivative of imidazole. Sterol biosynthesis is not affect by ciclopirox olamine. Both alteration of cell permeability and cell leakage observed only at high concentrations.[49] It is assumed that its principal mechanism of action is due to its high selectivity for trivalent cations, which prevents key enzyme cofactors from working. It comes in the form of ointment called ciclopirox olamine 1%, recommended use is to apply twice a day for 4 weeks around the affected area of skin.[50]



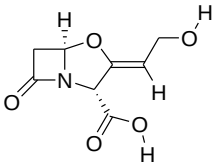
Ciprofloxacin
85721-33-1
15



Cotrimoxazole
8064-90-2
16



Carbenicillin
4697-36-3
17



Clavulanic acid
58001-44-8
18

2.14. Caspofungin

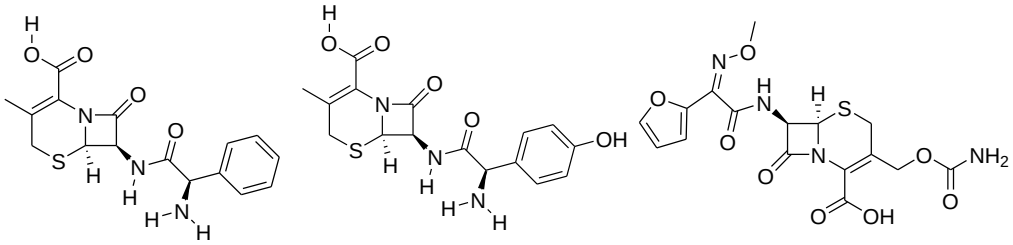
Caspofungin **14** belongs to the class of drugs called echinocandis. Caspofungin blocks the formation of beta-(1,3)-D-glucan, an important component of Aspergillus and Candida species cell walls.[51] Mammalian cells do not contain beta-(1, 3)-D-glucan. Beta-(1, 3)-glucan synthase is the main target. Caspofungin kills fungi by preventing them from forming a protective layer.[52] It is directly injected into the vein, recommended use is to inject once a day around 50-70mg infused over 1 hour.

2.15. Ciprofloxacin

Ciprofloxacin **15** is structurally linked to nalidixic acid and corresponds to the latest age of fluorinated quinolones. It has a wide range antibacterial agent that's extremely susceptible in vitro to most Gram-negative bacteria and moderately susceptible to various Gram-positive bacteria. Ciprofloxacin works by inhibiting bacterial DNA gyrase as its main mode of action.[53] Recommended use is 500 mg orally every 12 hour for 3-6 weeks.

2.16. Cotrimoxazole

Cotrimoxazole **16** drug was launched as combination of both trimethoprim and sulfamethoxazole as Cotrimoxazole.[54] It operates by inhibiting two sequential processes in the creation of nucleic acids and proteins, both of which are required for many bacteria to survive. Recommended dose for adults is 160mg trimethoprim and 800mg sulphamethoxazole twice daily, whereas for children 4mg/kg trimethoprim and 20mg/kg.[55]



Cephalexin
15686-71-2
19

Cefadroxil
66592-87-8
20

Cefuroxime
55268-75-2
21

2.17. Carbenicillin

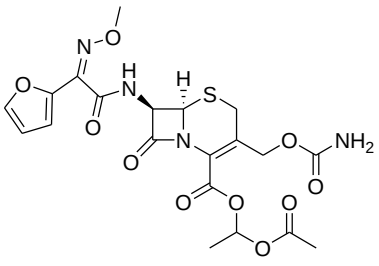
Carbenicillin **17** is bactericidal penicillin that belongs to the carboxypenicillin class.[56] Carbenicillin acts as a disinfectant by disrupting with resistant microbes terminal cell wall construction, and penicillins acylate the penicillin-sensitive transpeptidase C-terminal area by breaking the lactamase loop.[57] Its recommended use is to take 382-764mg 4 times a day for 3-7 days.

2.18. Clavulanic acid

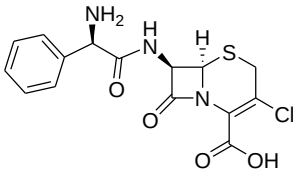
Clavulanic acid **18** is a naturally occurring potent inhibitor of bacterial -lactamases, is a significant -lactam antibiotic generated by the bacterium Streptomyces calvuligerus that is active against both Gramme-positive and negative bacteria. [58] Clavulanic acid, commonly known as clavulanate potassium salt, is FDA-approved for treating certain bacterial infections when combined with amoxicillin.[59] It belongs to a class of drugs known as beta-lactamase inhibitors by preventing bacteria from breaking down the amoxicillin antibiotic. Recommended dose for adults is to take 500mg every 8-12 hours, where as for children 20-45 mg/kg every 8-12 hours.

2.19. Cephalexin

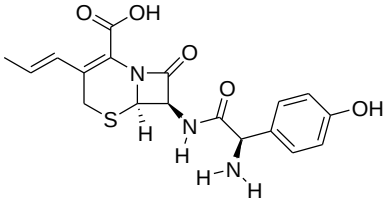
Cephalexin (desacetoxycephaloglycin) **19** comes under the class of first generation cephalosporins beta-lactam antibiotic.[60]It works by inhibiting the bacterial cell-wall synthesis. Recommended dose is to take 250-450mg every 4-8 hours for 6-12 days. A higher dose, up to 4 g daily in two to four evenly divided doses, may be required for more severe infections.[61]



Cefuroxime axetil
64544-07-6
22



Cefaclor
53994-73-3
23



Cefprozil
92665-29-7
24

2.20. Cefadroxil

Cefadroxil **20** comes under the class of medications called cephalosporin antibiotics.[62] It operates by attaching to one or more penicillin-binding proteins and suppressing bacterial wall production in actively dividing cells. As a result of the formation of an osmotically unstable defective cell wall and bacterial cell lysis.[63] Its recommended dose for adult's skin infection is 1 gram per day or in divided doses given 2 times a day.

2.21. Cefuroxime

Cefuroxime **21** is a cephalosporin antibiotic (SEF a low spor in)51 that works by blocking the formation of bacterial cell walls. Cefuroxime has activity with both penicillinases and cephalosporinases in the presence of beta-lactamase of Gram-positive and Gram-negative bacteria. Recommended dose for adults and teenagers is 250-500mg two times a day 10 days.[64]

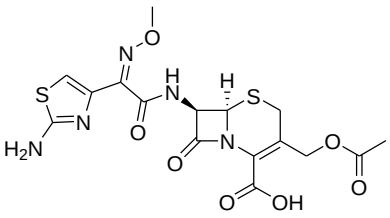
2.22. Cefuroxime axetil

Cefuroxime axetil **22** is a second-generation prodrug of the cephalosporin Cefuroxime, which has a beta-lactam ring structure like penicillin antibiotics. It has shown antibacterial action against gram-positive or negative bacteria organisms.[65] Several additional quinolones, cephalosporins, amoxicillin/clavulanic acid and macrolides were equally effective as the medication.[65] It works by binding to penicillin-binding proteins (PBPs). It hinders the last one stage of bacterium cell wall synthesis. Recommended dose for adults and teenagers is to take 250-500 mg twice a day for 10 days.[66]

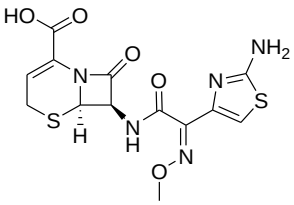
2.23. Cefaclor

Cefaclor **23** is a monohydrate of 3-chloro-7-d-(2-phenylglycinamido)-3-cephem-4-carboxylic acid.[67] It inhibited beta-lactamase-producing Haemophilus isolates and outperformed

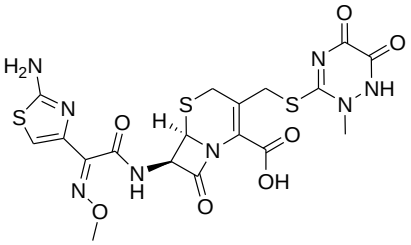
cephalexin against Haemophilus strains. Cefaclor is a semi-synthetic second-generation cephalosporin antibiotic that is used orally. Cephalosporins prevent the formation of cell walls.[68] Its Recommended dose for children is to take 20-40mg/kg/day and for adults 250-500mg/day for every 8 hours.[69]



Cefotaxime
63527-52-6
25



Ceftizoxime
68401-81-0
26



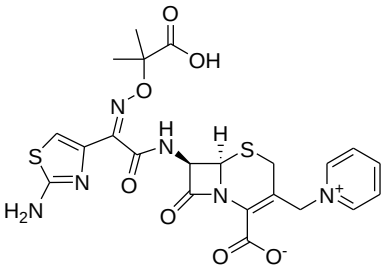
Ceftriaxone
104376-79-6
27

2.24. Cefprozil

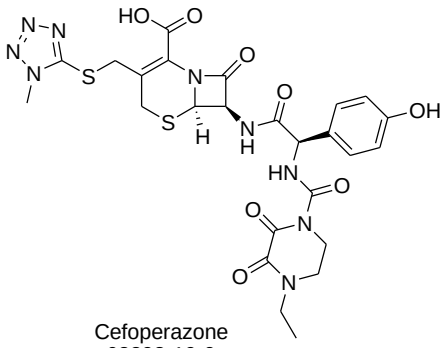
Cefprozil **24** is penicillin-like beta-lactam antibiotic. By adhering to certain penicillin-binding proteins (PBPs) present inside the bacterium cell wall, it suppresses the third one and final stage of bacterial cell wall formation. [70] For adults and teenagers, its recommended dose is 500 mg every 10 hours for ten days.[71]

2.25. Cefotaxime

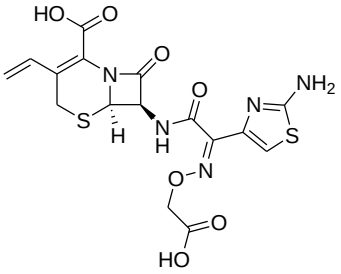
Cefataxime **25** is a cephalosporin antibiotic of the third generation that is effective against both Gramme positive and negative bacteria. Cefotaxime sodium and other brand names such as Claforan (Sanofi-Aventis) are available in market.[72] Cefotaxime sodium is an intravenous cephalosporin antibiotic that inhibits bacterial cell wall production. The structure of the molecule has been changed to make it immune to the Richmond I, III, IV, and V beta-lac enzymes.[73] Its recommended dose is to take 125-170mg/kg/day in 3-5 divided doses.[74]



Ceftazidime
72558-82-8
28



Cefoperazone
62893-19-0
29



Cefixime
79350-37-1
30

2.26. Ceftizoxime

Ceftizoxime **26** is a beta-lactam antibiotic of the third generation, related to penicillins.[75] It prevents the third one and final stage of bacterial cell wall formation by binding to certain penicillin-binding proteins (PBPs) located within the bacterial cell wall.[76] Its recommended dose is to take 100-200mg/kg/day every 6-8 hours.[77]

2.27. Ceftriaxone

Ceftriaxone **27** is a current third generation semisynthetic cephalosporin with a lengthy half-life, requiring a once-daily oral dose.[78] It can be given intravenously or intramuscularly and has vast antibacterial action against both gramme-negative and positive aerobic and oxygen deprived bacteria.[79] It works by preventing the bacterial cell wall from producing mucopeptides.[80] Its recommended dose is to take 3g in every 8 hours for 6-12 days.[81]

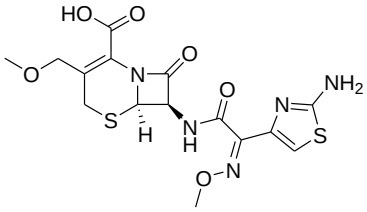
2.28. Ceftazidime

Ceftazidime **28** is a distinct type of cephalosporin that is given intravenously or intramuscularly. It exhibits a broad range of in vitro potency against both Gram-positive and Gramme negative aerobic microorganisms, is especially effective towards Enterobacteriaceae

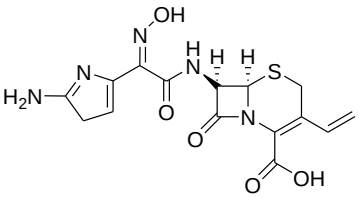
(including -lactamase-positive pathogens), and, like other subsequent-generation cephalosporins, is immune to disintegration by major -lactamases. [82] It inhibits the enzymes responsible for cell wall production as well as the penicillin binding protein.[83] Its recommended dose is to take 1-6g daily taken every 8-12 hours.

2.29. Cefoperazone

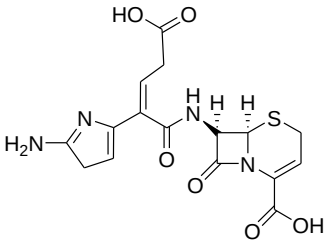
Cefoperazone **29** is third-generation cephalosporin, has wide anti-gram negative action.[84] Cefoperazone works as a bactericide by blocking bacterial cell wall formation, and sulbactam works as a beta-lactamase inhibitor to boost cefoperazone's antibacterial efficacy against beta-lactamase-producing bacteria. Its recommended dose is to take 2-4g/day for 10-14 days.[85]



Cefpodoxime
87239-81-4
31



Cefdinir
91832-40-5
32



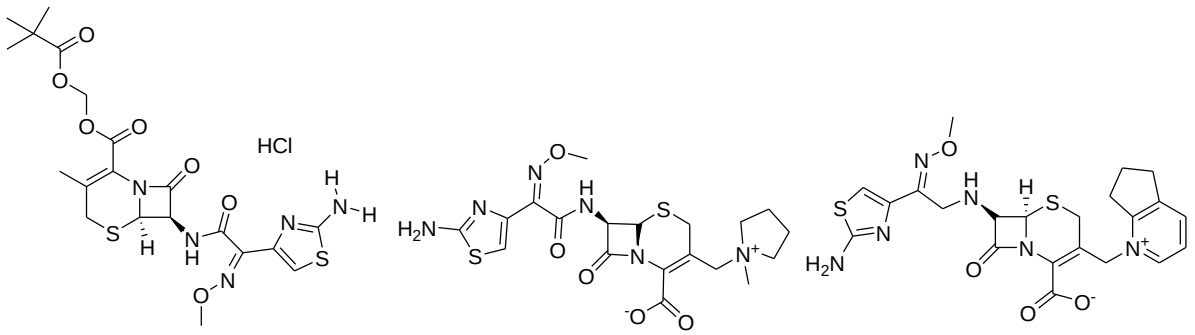
Ceftibuten
118081-34-8
33

2.30. Cefixime

Cefixime **30** is a semisynthetic, cephalosporin antibacterial.[86] It acts by inhibiting bacterial growth. This antibiotic is only used to treat bacterial infections.[87] Its recommended dose for adults is to take 200-400mg/day for every 12 hours and for children under the age of six months or 12 years is to take 8mg/kg.[88]

2.31. Cefpodoxime

Cefpodoxime **31** is a third generation cephalosporin antibiotic that is used orally.[89] Cefpodoxime is a bactericidal agent that inhibits the formation of cell walls of bacteria. Cefpodoxime inhibits beta-lactamases in Gram-negative and Gram-positive bacteria, as well as cephalosporinases and penicillinases. Its recommended dose is to take 200mg/day for every 12 hours.[90]



Cefetamet Pivoxil
65243-33-6
34

Cefepime
88040-23-7
35

Cefpirome
84957-29-9
36

2.32. Cefdinir

Cefdinir **32** is an oral, third generation cephalosporin antibacterial drug with an enhanced spectrum. Cefdinir is a class IV medicine according to the Biopharmaceutics Classification Scheme (BCS).[91] Cefdinir is a bactericidal drug that works by interfering with cell wall construction to treat bacterial infections. Cefdinir is a wide-ranging antibacterial drug that's effective over both gram-positive and gram-negative bacteria. It is efficient against bacteria that produce beta-lactamase enzymes.[92] Its recommended dose is to take 300-600mg once a day for every 12 hours, taken for 5-10 days.[93]

2.33. Ceftibuten

Ceftibuten **33** acts as a bactericide by binding to critical proteins in the bacterial cell wall. This binding stops cell walls from forming.[94] Its recommended dose is to take 400mg two or three times weekly or a single dose of 9mg/kg.[95]

2.34. Cefetamet Pivoxil

Cefetamet pivoxil **34** is a prodrug ester of cefetamet, a microbiologically active cephalosporin. [96] Cefetamet Pivoxil Hydrochloride works as a bactericide by interacting with one or more penicillin-binding proteins found in the bacterial cell wall and inhibiting the final transpeptidation step of peptidoglycan production (PBPs).[96] Its recommended dose is to take 500 mg twice a day.[97]

2.35. Cefepime

Cefepime **35** inhibits bacterial cell wall production by covalently binding enzymes involved in the final phase of peptidoglycan wall synthesis, transpeptidation. This binding causes cell

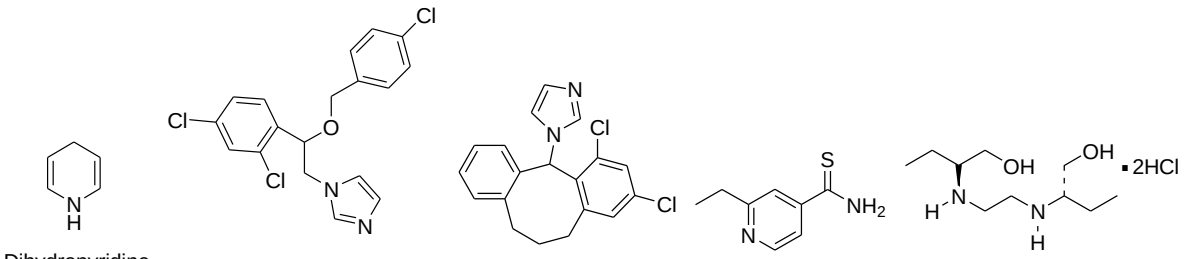
wall defects, this results in the process of autolysis and the living thing's mortality.[98] Its recommended dose is to take 50mg/kg for every 12 hours.[99]

2.36. Cefpirome

Cefpirome **36** (HR 810), a novel cephalosporin antibiotic featuring a 2,3-cyclopentenopyridine group in the 3-position side chain, was tested in vitro against 5 existing cephalosporins. [100] It works as a bactericide by inhibiting the activity of transpeptidase is an enzyme involved in the production of bacterial cell walls. The recommended dose is 1-2 g for every 12 hour.[101]

2.37. Dihydropyridine

Dihydropyridine **37** is a calcium channel blocker. It is accountable the blockage of voltage-gated L type muscle cells present in arterial blood vessels.[102] Its recommended use is 2.5-5 mg for 4 weeks, 10 mg/day for adults.



Dihydropyridine
3337-17-5
37

Econazole
27220-47-9
38

Eberconazole
130104-32-4
39

Ethionamide
536-33-4
40

Ethambutal hydrochloride
1070-11-7
41

2.38. Econazole

Econazole **38** is imidazole containing drug which is used for the treatment of infections of the cervix. Econazole nitrate is an effective antifungal drug. It inhibits ergosterol synthesis, which causes increased cellular permeability and leaking of cellular contents.[103]The recommended use is to apply on the affected area once or twice a day for at least 10 days.

2.39. Eberconazole

Eberconazole **39** inhibits ergosterol synthesis by suppressing the cell's lanosterol 14-demethylase enzyme fraction and has an effect on intracellular sterol synthesis and at high concentrations it gives rise to the flow out of small molecules from the fungal cells like

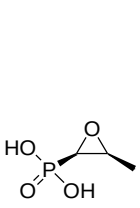
potassium ion, amino acids etc leading to cell death.[104] Its recommended use is by applying a thin layer into the affected parts for 4 weeks.

2.40. Ethionamide

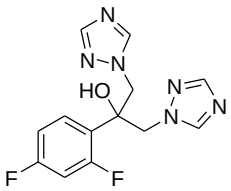
Ethionamide **40** is a prodrug that, like isoniazid, is activated by ethA, a monooxygenase presents in Mycobacterium tuberculosis, and subsequently binds NAD+ to form an adduct that inhibits InhA. The mode of action is thought to involve mycolic acid disruption.[105] Its recommended dose is to take 15-20mg/kg/day.[106]

2.41. Ethambutol hydrochloride

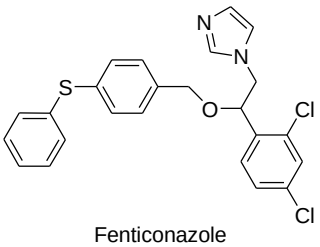
Ethambutol hydrochloride **41** is a bactericide antimicrobial drug used as a first-line treatment for tuberculosis (TB).[107] It blocks the transfer of mycolic acids into bacteria's cell walls, preventing bacterial cell development.[108] Its recommended dose is to take 25-30mg/kg.



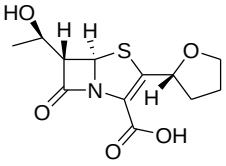
Fosfomycin
26016-99-9
42



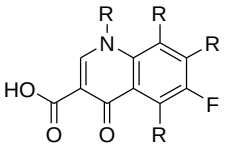
Fluconazole
86386-73-4
43



Fenticonazole
73151-29-8
44



Faropenem
106560-14-9
45



Fluoroquinolone
82419-36-1
46

2.42. Fosfomycin

Fosfomycin **42** was initially named phosphonomycin, derivative of phosphonic acid and used for the treatment of infections of the bladder.[109] It restricts the bacterial antibiotics interference in gram-positive and gram-negative.[110] Its recommended use is to dissolve the powder in 3-4 ounces of cold water for 3 days.[111]

2.43. Fluconazole

Fluconazole **43** is a Pyridoxine Bis-Triazolium Compounds shows their activity against pathogenic bacteria and fungi.[112] It interrupts the conversion of Lanosterol by binding with fungal cytochrome.[113] For adults- The first day, 400 mg, followed by 200 mg once a day for 10 to 12 weeks.

2.44. Fenticonazole

Fenticonazole **44** inhibits Candida albicans' release of protease acid, damages the cytoplasmic membrane, and inhibits cytochrome oxidases and peroxidases. Its recommended use is to use the cream twice a day for 3 days and use the applicator provided to insert 5 grams of cream high into your vagina.[114]

2.45. Faropenem

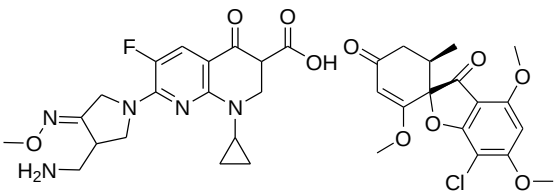
Faropenem [115] **45** the bacterial cell wall synthesis. It hinders cross-linking between the linear peptidoglycan polymer chains that make up a substantial portion of the cell wall of Gram-positive bacteria. Its recommended dose is to take 300mg/day for 7-10 days.[116]

2.46. Fluoroquinolone

Fluoroquinolone **46** operates functions by inhibiting two enzymes involved in bacterial DNA synthesis, the two of which resemble human DNA topography-modifying enzyme but are essential for bacterium reproduction of DNA, which renders it mutually specific and antimicrobial. Its recommended dose is to take 750 mg twice a day.[117]

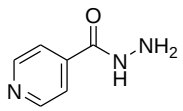
2.47. Gemifloxacin

Gemifloxacin **47** is an antibacterial agent that acts by binding to the enzyme DNA gyrase, which aids in the untwisting required to duplicate one DNA double helix into two.[118] Its recommended dose for adults is to take 320mg/day for 5-7 days.[119]

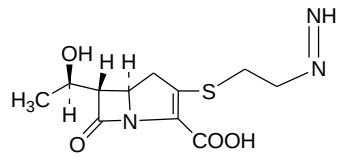


Gemifloxacin
175463-14-6
47

Griseofulvin
126-07-8
48



Isoniazid
54-85-3
49



Imipenem
74431-23-5
50

2.48. Griseofulvin

Mitosis and nuclear acid production are suppressed in fungal cells. Griseofulvin **48** also binds to alpha and beta tubulins, causing spindle and cytoplasmic dysfunction microtubule activity. Its recommended dose is to take 250 mg for every 12 hours or 500mg/day.[120]

2.49. Isoniazid

Isoniazid **49** inhibited the development of the mycobacterial cell wall. Isoniazid activation requires KatG, a bacterial catalase-peroxidase enzyme identified in Mycobacterium TB. Its

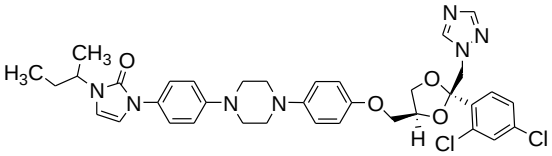
recommended dose for adults is to take 300mg/day and for children normal dose is 10mg/kg or 300mg/day.[121]

2.50. Imipenem

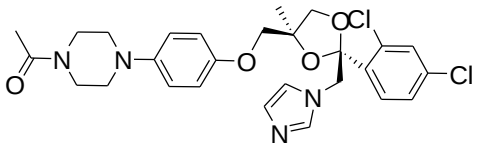
The mechanism of action of imipenem **50** is like that of other beta-lactam antibiotics, namely, inactivation of penicillin-binding proteins (PBP) and cell wall lysis or interference with cell wall synthesis. Its recommended dose is 250-500 mg (Powder for injection).[122]

2.51. Itraconazole

Itraconazole **51** inhibits the fungal cytochrome and blocks the conversion of lanosterol to ergosterol. Its recommended use is 100 mg/day for 2 weeks.[123]



Itraconazole
84625-61-6
51



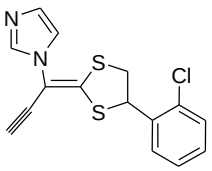
Ketoconazole
65277-42-1
52

2.52. Ketoconazole

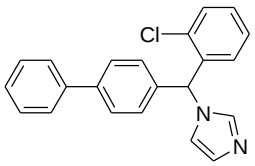
Ketoconazole **52** encounters 14 α-sterol demethylases, this inhibits ergosterol synthesis and increases fungal cellular permeability, resulting in lower levels of ergosterol in the fungal cell membrane. For adults 200-400mg/day, children under 2 years old and older 3.3-6.6mg/kg/day.[124]

2.53. Lanoconazole

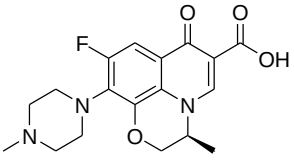
Lanoconazole **53** blockage of ergosterol biosynthesis by inhibiting 14-DM. Its recommended use is to apply once a day for 3 consecutive days.[125]



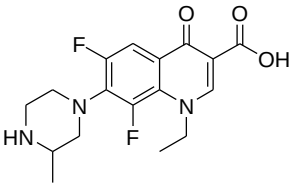
Lanoconazole
101530-10-3
53



Lombazole
60628-98-0
54



Levofloxacin
100986-85-4
55



Lomefloxacin
98079-51-7
56

2.54. Lombazole

Lombazole **54** is responsible for the inhibition of Sterol C_{14} demethylation in the ergosterol Biosynthesis. Its recommended use is to apply 2-6 weeks for proper treatment.[126]

2.55. Levofloxacin

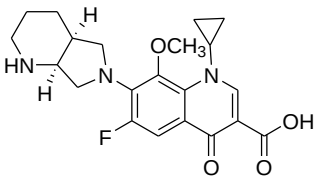
Levofloxacin **55** is a fluoroquinolone antibiotic that directly inhibits bacterial DNA synthesis. In vulnerable organisms, levofloxacin increases DNA strand breaking by blocking DNA-gyrase, which prevents supercoiled DNA from relaxing. Its recommended dose is 500 mg every 7-14 days or 750 mg every 5 days.[127]

2.56. Lomefloxacin

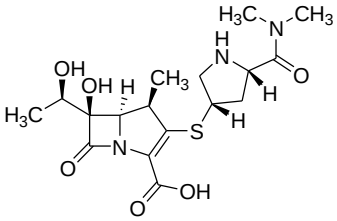
Lomefloxacin **56** bactericidal effect is due to interference with the bacterial enzymes DNA gyrase and topoisomerase IV, which are necessary for bacterial DNA transcription and replication. Gram-negative bacteria's principal quinolone target appears to be DNA gyrase. Recommended dose is 400mg/day orally for 10 days.[128]

2.57. Moxifloxacin

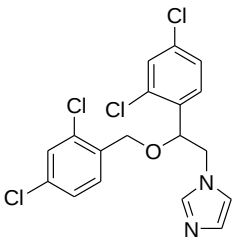
Moxifloxacin **57** is an antibiotic with a broad spectrum that kills both Gram-negative and Gram-positive bacteria. It operates by inhibiting bacterial DNA gyrase, topoisomerase IV, a type II topoisomerase, enzymes that break bacterial DNA. Recommended dose for adults is 400mg/day.[129]



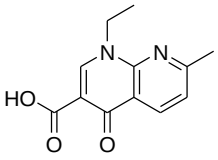
Moxifloxacin
354812-41-2
57



Meropenem
119478-56-7
58



Miconazole
22916-47-8
59



Nalidixic acid
389-08-2
60

2.58. Meropenem

Meropenem **58** is an antibiotic of some sort. The bactericidal effect of meropenem is due to its reduction of cell wall synthesis. Penicillin-binding protein (PBP) is bound by Meropenem targets within most gramme-positive and gramme-negative bacteria's cell walls. Its recommended dose is 2g every 8 hours.[130]

2.59. Miconazole

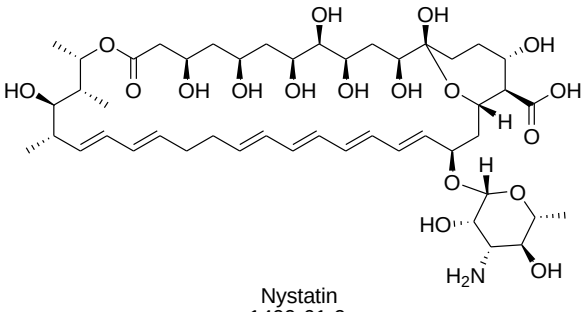
Miconazole **59** is imidazole containing drug and has shown to be equally efficient in the treatment of skin infections caused by Candida and dermatophyte. Miconazole is a cream used for the treat of vaginal infections. Miconazole stops the growth of Ergosterol which leads to death of organism.[131] For children under 2 years (20mg/g) (24mg/mL) gel: Apply 4 times daily, for adults 200-400mg for 4 days, and 1,200mg as a single dose.[132]

2.60. Nalidixic acid

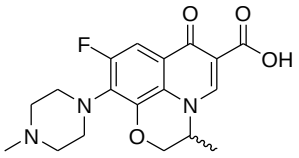
Nalidixic acids **60** block DNA gyrase function and cause the development of a relaxation band analogue. When sodium dodecyl sulphate is added to the complex, a double strand break in the DNA substrate occurs, this produces a linear molecule that appears to be covalently attached to protein. Adults should begin with 1 g taken four times per day for a period of one to two weeks.[133]

2.61. Nystatin

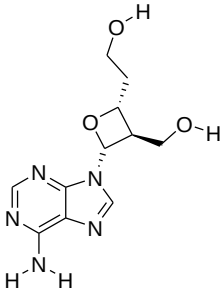
Nystatin **61** is a crucial element of the membranes of fungi, is where it binds. Adults and children aged 5 and older should take 4-6 mL (about 1 teaspoonful) four times each day. Four times a day, 1 mL, for infants who were premature or had low birth weight.[134]



Nystatin
1400-61-9
61



Ofloxacin
82419-36-1
62



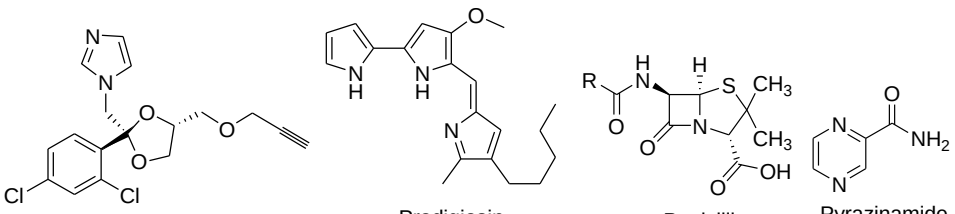
Oxetanocin A
6704-31-0
63

2.62. Ofloxacin

Inhibition of bacterial DNA gyrase is the mechanism of action of ofloxacin **62**. It has a wide range of action in vitro against aerobic Gram-negative and Gram-positive bacteria, but it is ineffective against anaerobes. The dosage range for adults is 200-800mg/day.[135]

2.63. Oxetanocin A

Oxetanocin A **63** is a novel nucleoside from bacteria. It prevents Viral replication by DNA polymerase inhibitor and also blocks the late stages of viral assembly. Its recommended use is 1-300mg/kg per day.[136]



Posaconazole
171228-49-2
64

Prodigiosin
82-89-3
65

Penicillin
1406-05-9
66

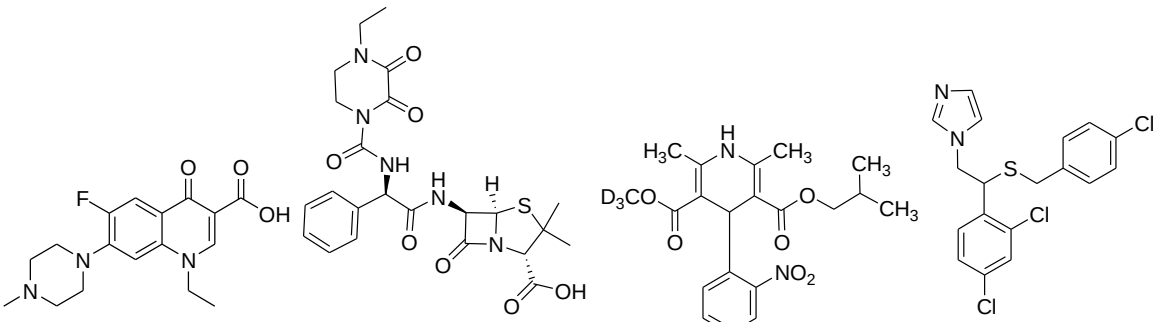
Pyrazinamide
98-96-4
67

2.64. Posaconazole

Posaconazole **64** inhibits the cytochrome P-450 dependent enzyme sterol 14 - demethylase in fungi by attaching to the enzyme's heme cofactor. This leads to impeding of fungal cell growth and eventually death. Its recommended use is 300 mg 2 times a day on the first day then 300mg/day.[137]

2.65. Prodigiosin

Prodigiosin **65** is a pyrrole containing proapoptic drug, belongs to highly red pigmented family prodiginnie.[138] Prodigiosin impede the cell growth by penetrating the cell membrane and slow down the targeted enzymes such as DNA gyrase. Its recommended dose is 10-470mg/m^2/day.[139]



Pefloxacin
70458-92-3
68

Piperacillin
66258-76-2
69

Qeiniodochlor
70

Sulconazole
61318-90-9
71

2.66. Penicillin

Penicillin Binding Proteins (PBPs) **66** are important participants in the bacterial cell cycle and antimicrobial resistance.[140] It inhibits the bacterial cell wall synthesis by induction of bacterial autolytic effect. Its recommended use is 100-150 mg for every 4-6 hours for 6 days.[141]

2.67. Pyrazinamide

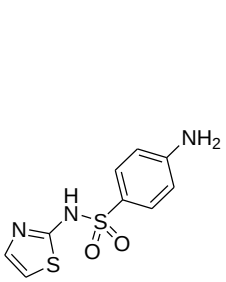
Pyrazinamidase enzyme (PZase) **67** in the cytoplasm converts the parent substance, which enters the bacteria passively, into pyrazinoic acid, the drug's active form. Its recommended dose is 15-30mg/kg/day orally.[142]

2.68. Pefloxacin

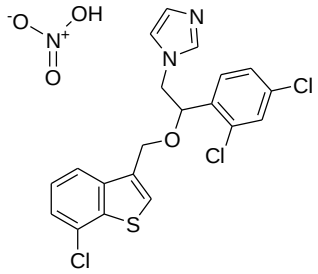
Pefloxacin **68** works by preventing cell division via inhibiting topoisomerase IV (an enzyme required to segregate replicated DNA) and DNA gyrase (a type II topoisomerase). Its recommended dose is 400mg bid 7-10 days taken along with food.[142]

2.69. Piperacillin

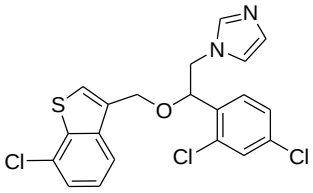
Piperacillin **69** binds to bacterial cell membranes and suppresses cell wall formation. Tazobactam prevents bacteria from producing beta-lactamase. Piperacillin has a bactericidal effect in susceptible organisms. Its recommended dose is 3-4 g taken every 4-6 hrs.[143]



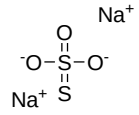
Sulfathiazole
72-14-0
72



Sertaconazole Nitrate
99592-39-9
73



Sertaconazole
99592-32-2
74



Sodium Thiosulphate
7772-98-7
75

2.70. Qeiniodochlor

Qeiniodochlor **70** works by killing the trophozoites (adult parasites) that are responsible for the development of cysts (infectious parasites). Its recommended dose is by applying a small layer to the afflicted region 3-4 times a day.[144]

2.71. Sulconazole

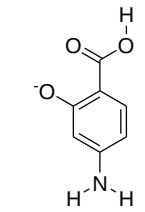
Sulconazole **71** inhibits the Cytochrome alpha demethylase by the binding of heme iron enzyme. Its recommended use is to apply once or twice a day for 2-3 weeks, whereas some requires up to 5 weeks of treatment.[145]

2.72. Sulfathiazole

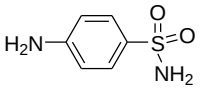
Sulfathiazole **72** blocks the conversion of p-amino benzoic acid to Coenzyme dihydrofolic acid. Its recommended use is 18 mg/kg/day for 13 weeks.[146]

2.73. Sertaconazole Nitrate

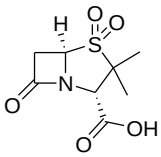
Sertaconazole nitrate **73** inhibits fungal cytochrome mediated 14 alpha- lanosterol demethylase enzyme. Its recommended use is 17 mg twice a day for four weeks.[147]



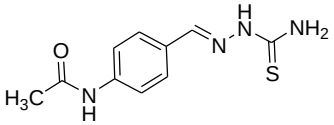
Sodium Amino salicylate
6018-19-5
76



Sulphonamide
63-74-1
77



Sulbactam
68373-14-8
78



Thiacetazone
104-06-3
79

2.74. Sertaconazole

Sertaconazole **74** works by slowing the growth of fungi and helps in relieving the symptoms of the fungal infection such as itching, redness, etc. Its recommended use is to apply twice a day for four weeks.[148]

2.75. Sodium Thiosulphate

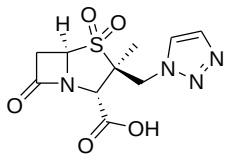
Sodium Thiosulphate **75** is a neutralizing agent that produces antidotal synergy. It penetrates the late test reactions and responsible for active sensitization. It is used for the treatment of cyanide poisoning. It acts as a Sulphur donor and causes antidotal effect. The dose prescribed is 12.5 g injected in the vein.[149]

2.76. Sodium Amino salicylate

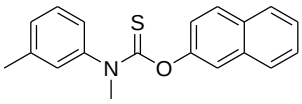
Sodium Amino salicylate **76** is an anti-tuberculous drug that is responsible for Bacterial multiplication. It restricts the folic acid synthesis and Cell wall component. It is recommended dose for adults and teenager 13 years of age and older 3.3-4g every eight hours or 4-5g for every 12 hours.[150]

2.77. Sulphonamide

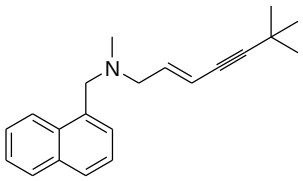
Sulphonamide **77** are synthetic antimicrobial agents that contain the sulfonamide group. It inhibits bacterial growth by acting as a competing inhibitor of the p-aminobenzoic acid implicated in the folic acid metabolism cycle. Its recommended dose for adults and teenager is to take 2-4 g for the 1st dose, then 750mg to 1.5 grams every 4 hrs; or 1-2 g every 6 hours.[151]



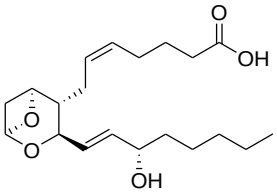
Tazobactam
89786-04-9
80



Tolnaftate
2398-96-1
81



Terbinafine
91161-71-6
82



Thromboxane A2

83

2.78. Sulbactam

A variety of susceptible bacterial infections are treated with the beta-lactamase inhibitor antibiotic sulbactam in combination with other antibiotics. Because sulbactam **78** binds to and inhibits the beta-lactamase produced by bacterial cells, it can stop the enzyme from decreasing the effectiveness of antibiotics. Sulbactam is an irreversible inhibitor of beta-lactamase. Its recommended dose is 80-100 mg/kg/day.[152]

2.79. Thiacetazone

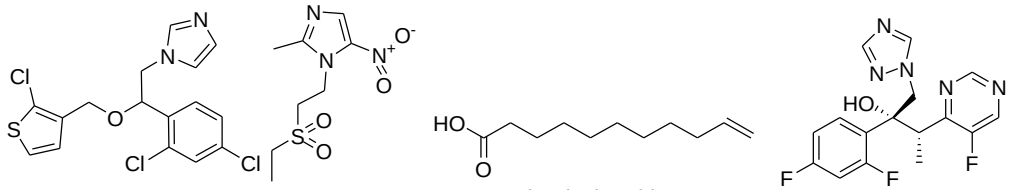
Amithiozone, also referred to as thioacetazone **79**, is an oral antibiotic used to treat tuberculosis. Due to toxicity and the emergence of more effective anti-tuberculosis medications like isoniazid, it has almost completely fallen out of use. It functions as a prodrug and a bacteriostatic agent by preventing the formation of mycolic acid cyclopropane. Children should take 15–125 mg per day, while adults should take 50–300 mg per day.[153]

2.80. Tazobactam

Tazobactam **80** prevents the restricts beta lactamase as well as destruction of piperacillin. The recommended use is 90 mg/kg for every 8 hours.[154]

2.81. Tolnaftate

In most areas, tolnaftate **81**, a synthetic thiocarbamate used as an anti-fungal agent, may be purchased over-the-counter. It is offered in the following forms: cream, powder, spray, liquid, and liquid aerosol. Jockey's itch, athlete's foot, and ringworm are all fungal disorders that are treated with tolnaftate. Stop the production of ergosterol by blocking squalene epoxidase. Additionally, it has been observed to alter hyphae and stifle mycelial development in vulnerable species. For 2-4 weeks, apply once or twice daily to the afflicted region.[155]



Tioconazole
65899-73-2
84

Tinidazole
19387-91-8
85

Undecylenic acid
112-38-9
86

Voriconazole
137234-62-9
87

2.82. Terbinafine

Terbinafine **82** is an antifungal drug that combats fungal infections. Scalp fungal infections are treated with terbinafine granules. Terbinafine particularly disrupts the early phases of fungal sterol synthesis. As a result, ergosterol levels drop and squalene accumulates inside cells, killing the fungus.[156] Terbinafine inhibits squalene epoxidase in the fungal cell membrane. The adult dosage is determined on body weight. The typical dosage is 250 mg administered once daily for six weeks. Children aged 4 and older typically receive a dose of 250 mg once daily for six weeks. The typical dosage for youngsters between the weights of 25 kg and 35 kg is 187.5 mg once daily for six weeks.[157]

2.83. Thromboxane A_2

Thromboxane A_2 **83** belongs to the eicosanoids class of lipids. It stimulates the activation of new platelets and increases platelet aggregation. Its recommended dose is 50 mg/day.[158]

2.84. Tioconazole

Tioconazole **84** is a derivative of imidazole used for the treatment of vaginal infections and do not taken as oral tablets, it is available in the form of creams.[159] It impedes ergosterol synthesis which results in increased cellular permeability, causing leakage of cellular contents and leading to cell death. Recommended as single dose vaginal applicator and each applicator full will deliver approximately 4.6 gms.[160]

2.85. Tinidazole

Tinidazole **85** is nitroimidazole antiprotozoal which is widely used antimicrobial drug against anaerobic bacteria. The toxic free radical of Tinidazole covalently bind to DNA, damage this DNA cause cell death. Its recommended use is usually taken with once a day as a single dose for 2-5 days.[161]

2.86. Undecylenic acid

By transporting protons across the plasma membrane, undecylenic acid **86** can also prevent the formation of germ tubes and inhibit an enzyme involved in lipid metabolism. By interacting with unspecific cell membrane components, undecylenic acid has antibacterial effects. Apply to the skin's afflicted region twice per day.[162]

2.87. Voriconazole

Voriconazole **87** is an antifungal triazole. inhibits the lanosterol-dependent demethylation caused by cytochrome P450 (CYP 450). Its recommended use is 200-400 mg orally twice a day.[163]

3. Conclusion

The main problem is that people facing so many fungal and bacterial infections, so heterocyclic compounds play major role naturally as well medicinally. This article provides an overview of certain well-known commercial drugs that prevent the growth of microorganisms inside of our bodies, like amoxicillin (AX), which contains CA-Mg Fe2O4 nanocomposites. Their antibacterial and anti-biofilm activities were also investigated in relation to certain harmful microorganisms.

4. Future prospective

As we all know that old antimicrobial agents are least effective to kill the microbes or slow down their growth so researchers have found new age antimicrobial agents. A new age antimicrobial can be produced economically with the next level of potency to improvise the pharmacokinetic characterization in pre drug clinical trial. But the problem is that there are very few antifungal drugs available on the market so clinically used drugs leads to complications and poor outcomes in patients. Researchers should focus on the production of antimicrobial agents which might be used as clinically effective drugs in future.

Acknowledgements

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