

Review of the Effect of Imine, Azo, and Formazan Compounds on the Cell Membrane of Bacteria, Fungi, and Their Inhibition of Activity

Nagham Mahmood Aljamali^{1,*}, Atheraa Abdul Kadhim Wasaf², Mohammed Noaman Alanssari³

Abstract

The role of antibiotics is to reduce the resistance of bacterial and fungal cell membranes, thereby penetrating the cell membrane and causing bacterial death. Therefore, researchers have turned to preparing chemical compounds that mimic antibiotics in their ability to eliminate bacteria and microorganisms. Through ongoing research in the field of biological activity, recent decades have witnessed a significant increase in laboratory experiments involving imines, formazan, and other compounds in this area. Imines (Schiff bases), azo compounds, and formazan play a major role in inhibiting microbes. These compounds react with the negative charges of phospholipids and penetrate the cell membrane, increasing its permeability. This leads to leakage of vital cell contents, destruction of respiratory enzymes, and ultimately, death of the bacterial or fungal cell. Such chemical compounds contain hybrid atoms with electron pairs that play a crucial role in penetrating the cell wall membrane of microorganisms and interacting with it, indicating that these compounds are highly effective at killing microorganisms or at least inhibiting their activity and resistance. Bacteria are divided into two main groups: Gram-positive and Gram-negative. Both groups have a cell wall composed of peptidoglycan: in Gram-positive bacteria, the wall is thick, while in Gram-negative bacteria, it is thin. In Gram-negative bacteria, the cell wall is surrounded by an outer membrane. Chemical compounds, through electron pairs on hybrid atoms, such as oxygen and nitrogen, affect the cell membrane, thus penetrating it.

Keywords: Membrane cell, azo, imine, formazan, bacteria, fungi

INTRODUCTION

Azo Derivatives

Azo compounds: These compounds are well-known in all fields of pharmaceutical chemistry research due to their bridging group and electron pairs, which have a significant effect on the biological inhibition of most microbial cells and the penetration of the cell wall of bacteria and fungi. Some azo compounds or

derivatives are used in the preparation of drugs against intestinal worms. Researchers have studied numerous vital applications of Azo compounds in various fields of medicine, pharmaceuticals, and technology, yielding results of significant importance. Scientists have focused on preparing Azo compounds with biological activity, particularly antibacterial and antifungal properties. These compounds involve the association of Azo groups with heterocyclic compounds containing different atoms, such as oxygen, nitrogen, or sulfur, making them suitable antibiotics. Furthermore, these compounds exhibit a variety of antibacterial properties [1]. Such chemical compounds contain hybrid atoms with electron pairs that play a crucial role in penetrating the cell membrane of

*Author for Correspondence

Nagham Mahmood Aljamali

E-mail: dr.nagham_mj@yahoo.com

¹Professor, Department of Chemistry, College of Education, University of Kufa, Iraq

²Assistant Professor, Department of Chemistry, College of Education for Girls, University of Kufa, Kufa, Iraq

³Assistant Lecturer, Department of Chemistry, College of Education for Girls, University of Kufa, Kufa, Iraq

Received Date: June 01, 2026

Accepted Date: June 13, 2026

Published Date: July 20, 2026

Citation: Nagham Mahmood Aljamali, Atheraa Abdul Kadhim Wasaf, Mohammed Noaman Alanssari. Review of the Effect of Imine, Azo, and Formazan Compounds on the Cell Membrane of Bacteria, Fungi, and Their Inhibition of Activity. International Journal of Membranes. 2026; 3(2): 1–10p.

microorganisms and interacting with them. This indicates that these compounds are highly effective at killing microorganisms or at least inhibiting their activity and resistance (Figures 1 and 2).

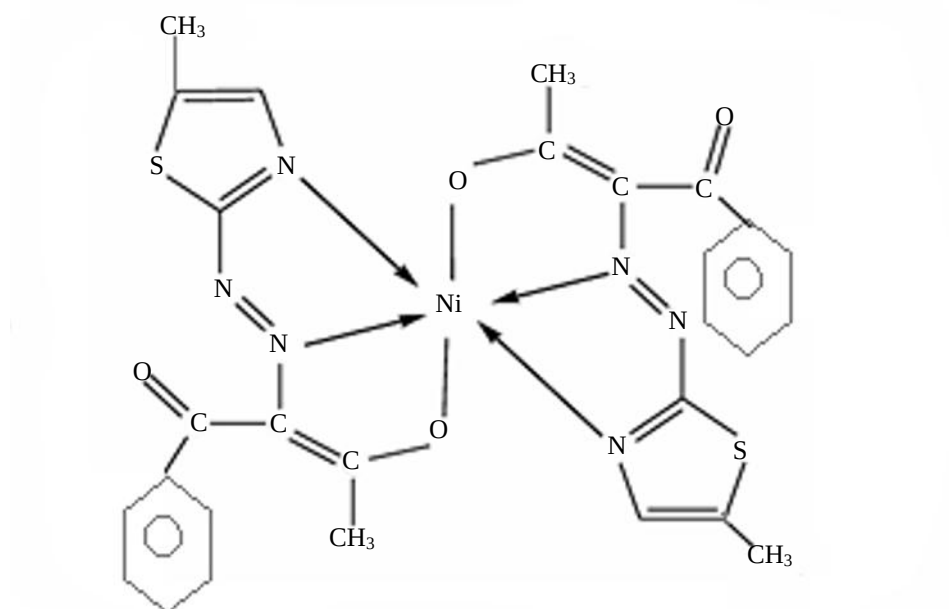


Figure 1. Azo derivative as antibacterial compound.

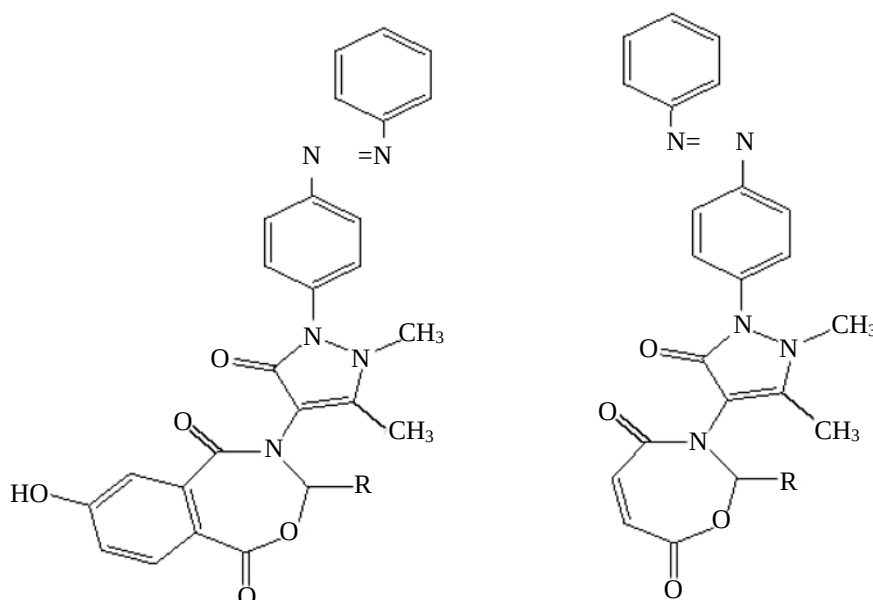


Figure 2. Azo derivative as antifungal compound.

Schiff Bases

These are primarily pharmaceutical organic compounds with biological applications and therapeutic behavior. After numerous studies, they have been used as antibacterial and antifungal agents, and as anti-inflammatories, antipyretics, and analgesics. Currently, they are being studied for their effectiveness against bacteria, fungi, and algae. They have also garnered significant attention for their ability to inhibit cancer cell division and act as antitumor agents. Their effectiveness against cancer is

attributed to the presence of a hybrid nitrogen atom in their structure, in addition to the presence of heterocyclic rings of hybrid atoms in some of their derivatives (Figure 3).

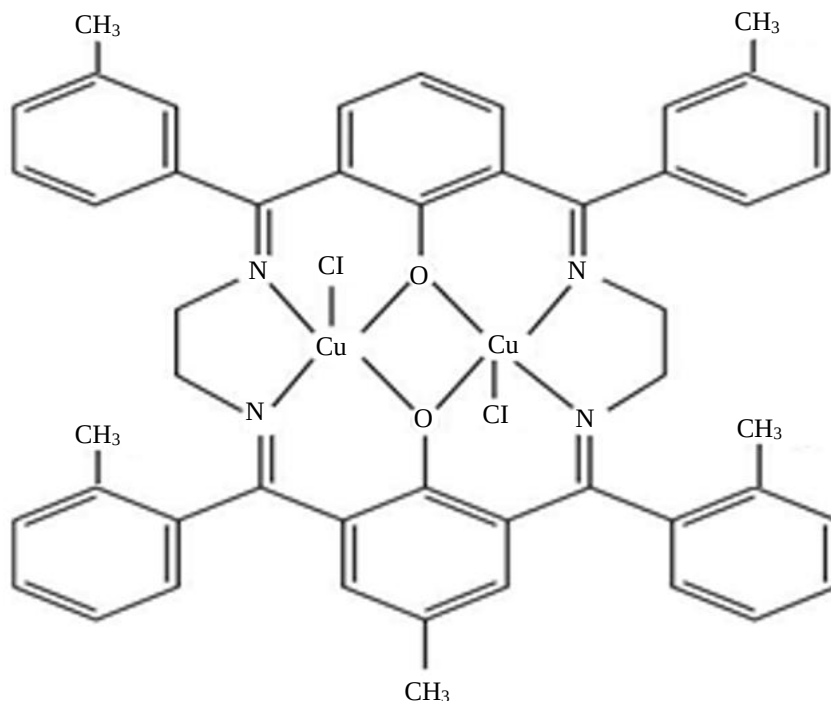


Figure 3. Imine derivative as antibacterial compound.

In the field of medicine, several imine derivatives have been prepared and used against types of bacteria known for their high resistance to antibiotics [2]. Some imine derivatives were prepared by linking them to heterocyclic rings of thiadiazole or oxazepine to increase their biological efficacy against *Staphylococcus aureus* bacteria, and these yielded good results during preliminary tests conducted by some researchers, also same derivatives tested against some types of fungi (Figure 4).

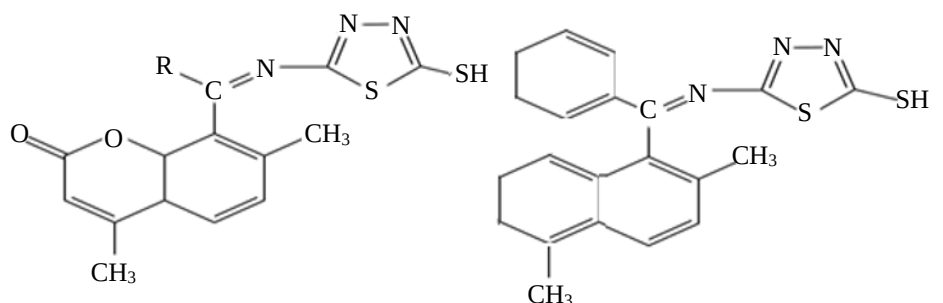


Figure 4. Imine derivative as antifungal compound.

Formazans are generally colored compounds resulting from the reduction reactions of tetrazolium salts. Their structures are characterized by multiple active groups ($-\text{NH}-\text{N}=\text{C}-\text{N}=\text{N}$) which automatically disrupt electron transport chains and impair the function of enzymes associated with the cell membrane, causing a breakdown in the membrane's electrical potential and the cessation of vital processes. They are often used to measure biological activity and kill cells (Figures 5–6).

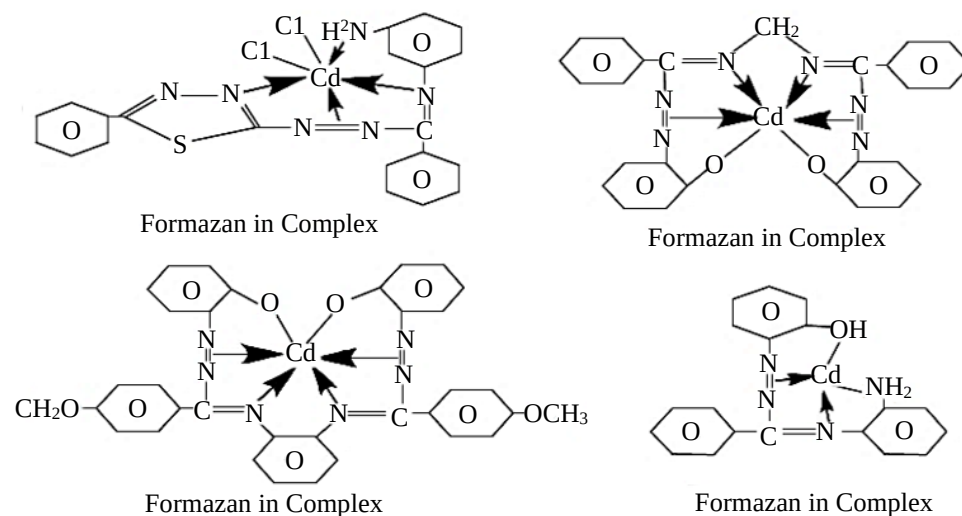


Figure 5. Formazan derivative as antimicrobial compound.

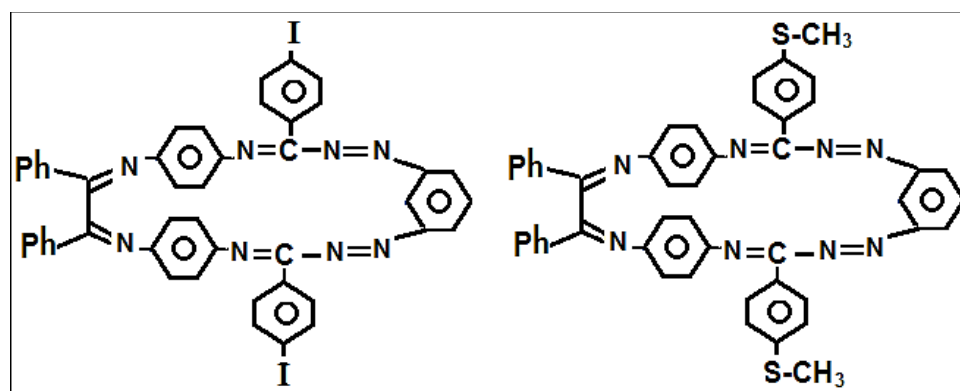


Figure 6. Formazan derivative as antifungal compound.

MECHANISM OF ACTION OF CHEMICAL COMPOUNDS ON THE CELL MEMBRANE

These chemically synthesized pharmaceutical compounds treat bacterial infections either by directly killing the disease-causing bacteria or by inhibiting their growth, reproduction, and activity, thus allowing the human body's immune system to eliminate them. These drugs are not used to treat viral infections because they are less effective against viruses than against bacteria and fungi [3].

- *Destroying the Bacterial Cell Wall:* Some antibiotics (such as penicillin) work by attacking or preventing the formation of the bacterial cell wall, leading to leakage of cell contents and cell death.
- *Disrupting Protein Production:* Other antibiotics attack ribosomes (the protein factories) within the bacterial cell, hindering their ability to grow and survive.
- *Stopping DNA Replication:* Some types interfere with the process of DNA replication in bacteria, preventing them from multiplying and spreading [4].
- *Inhibiting Folic Acid Production:* Other drugs interfere with the vital processes bacteria need to produce folic acid to survive. To learn more about how to use these drugs safely and effectively,
- Trough killing bacteria by preventing them from building their cell wall or other cell components. Stopping bacterial reproduction by the mechanism in Figure 7.

The Effect of Chemical Compounds on the Cell Membrane of Bacteria and Fungi

The effect of prepared chemical compounds varies depending on the type of functional groups included in their structure, the active group, the number of these groups, the presence of hybrid atoms and electron pairs, the electronegativity of the hybrid atoms, and whether the substituent groups are electron-buffering or electron-withdrawing. All these factors differ depending on the type of cell membrane in bacteria compared to fungi, as follows:

- *Bacteria*: The degree of effect differs between Gram-positive and Gram-negative bacteria due to the difference in the thickness of the peptidoglycan cell wall. Some of these compounds (especially fluorine-substituted Schiff bases) penetrate easily into the cell membranes of Gram-negative bacteria.
- *Fungi*: Fungal cell walls are primarily composed of chitin. These compounds inhibit the enzymes responsible for building this wall, thus preventing fungal growth and damaging the primary plasma membrane surrounding the cytoplasm [5].

The cell wall is a rigid, semi-permeable outer structure that surrounds the plasma membrane in fungal, bacterial, and archaeal cells. This structure is one of the most significant differences between plant and animal cells, the latter of which completely lack it. The cell wall is not merely a passive covering, but a complex, dynamic organelle that performs a wide range of vital functions essential for cell survival, growth, and interaction with its environment [6, 7].

Schiff base compounds can split bacterial and fungal cells by penetrating the cell membrane, thus destroying the bacterial cell and killing the bacteria. This is found in the compounds shown in Figure 8.

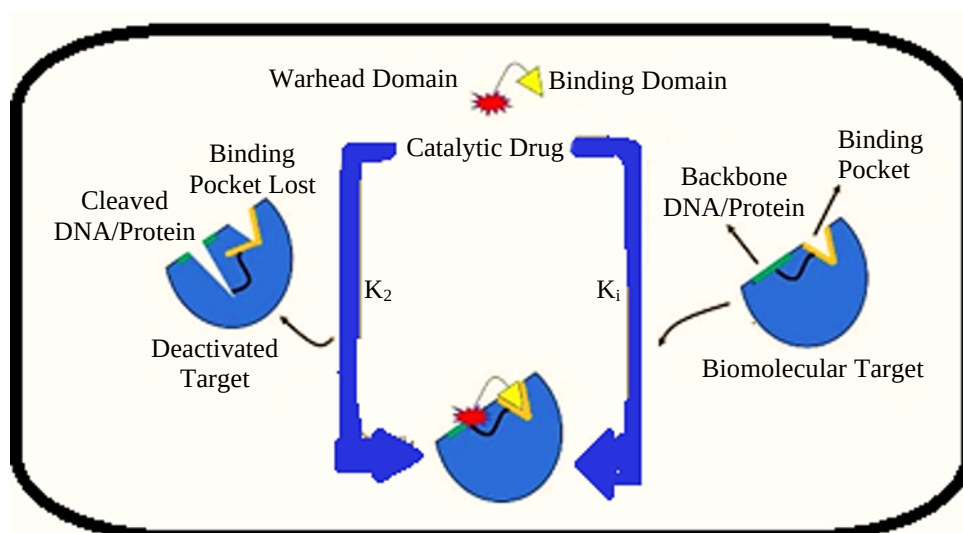


Figure 7. Effect of chemical compound on cell of bacteria.

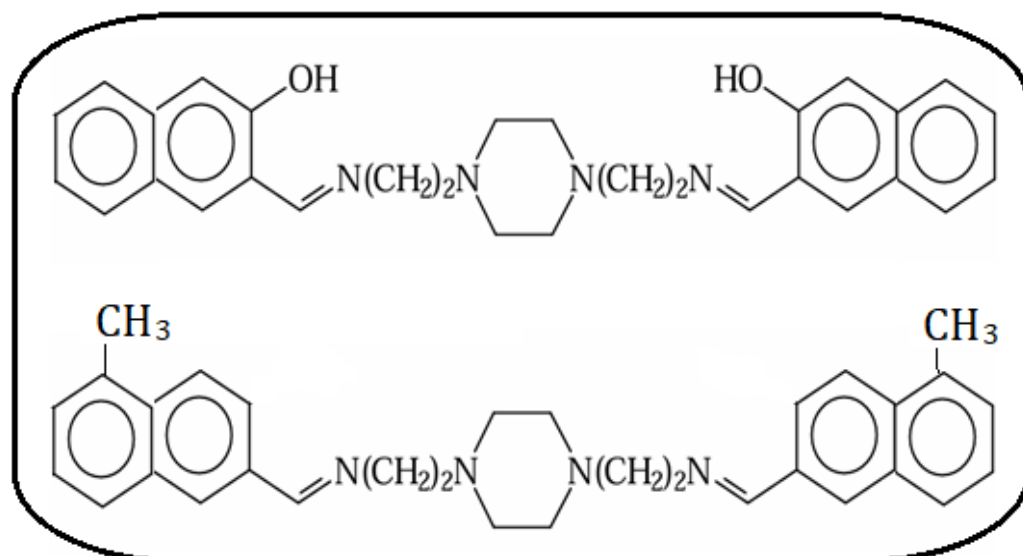


Figure 8. DNA-destroying base compounds of bacteria and fungi.

Its importance lies in providing the mechanical support necessary to maintain cell shape, protecting it from osmotic stress that could lead to rupture, and serving as the first line of defense against pathogens and various environmental stressors. The chemical composition of the cell wall varies considerably among different biological kingdoms, reflecting the great diversity in its functions and the environments of the organisms that possess it. For example, the cell wall in plants is primarily composed of cellulose, while in fungi it is composed of chitin, and in bacteria it is composed of peptidoglycan [8]. This variation in chemical composition is what gives each cell wall its unique physical and biological properties, making it an ideal target for many applications, such as antibiotics, that target bacterial cell wall structure without affecting the host organism's cells. Understanding the structure and function of this complex structure is essential not only in basic biology but also extends to other vital fields such as agriculture, medicine, and biotechnology. Structure of cell wall is shown in Figure 9.

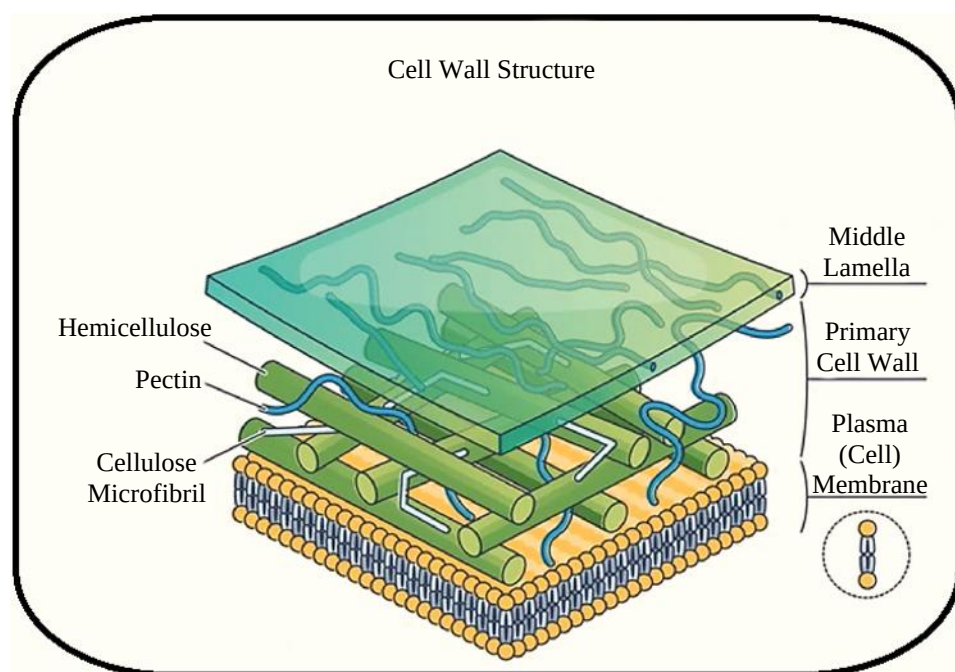


Figure 9. Structure of cell wall.

CELL WALL CHEMICAL COMPOSITION IN DIFFERENT KINGDOMS OF LIFE

The chemical composition of the cell wall exhibits remarkable diversity, reflecting the distinctive biochemical pathways of each kingdom of organisms [9]. This diversity is the basis for the varied properties we observe in these protective structures. The basic components of the cell wall can be summarized into the following main groups:

Cell Wall in Fungi

- **Chitin:** This is the primary structural component in most fungi. It is similar in structure to cellulose but consists of repeating N-acetylglucosamine units. Chitin provides structural support and strength to the fungal cell wall [10].
- **Glucans:** These are glucose polymers (such as beta-1,3-glucan and beta-1,6-glucan) that constitute the largest mass component of the fungal cell wall. They interact with chitin to form a strong network.
- **Glycoproteins:** These proteins, such as mannan, are attached to sugar chains on the outer surface of the cell wall and play an important role in interactions with the environment, cell adhesion, and cell recognition.
- **Bacterial Cell Wall: Peptidoglycan:** Also known as *murin*, this is the defining and essential component of the bacterial cell wall. It consists of long sugar chains of alternating N-

acetylglucosamine (NAG) and N-acetylmuramic acid (NAM) units. These chains are linked together by short peptide bridges, creating a strong, cohesive network structure that encloses the entire cell. This cell wall structure is a primary target for antibiotics such as penicillin [11–13].

The cell wall is not merely a simple physical barrier; it performs a wide range of complex vital functions that ensure cell integrity and proper functioning. These functions are essential for organisms possessing this structure and highlight the pivotal role the cell wall plays in cell biology. Among these are:

THE BACTERIAL CELL WALL: A VITAL TARGET FOR ANTIBIOTICS AND CHEMICAL COMPOUNDS

The bacterial cell wall is a unique and vital structure, indispensable for bacterial cell survival in most environments. Its distinctive chemical composition, radically different from that of eukaryotic cells, has made it an ideal and effective target for antibiotic development. Targeting the cell wall structure allows for the selective elimination of bacteria without harming host cells (such as humans or animals) that lack this structure [14].

The essential and unique component of the bacterial cell wall is peptidoglycan. This giant network structure consists of long chains of polysaccharides linked together by short peptide chains. This intricate network gives the cell wall its immense mechanical strength, enabling it to withstand the extremely high internal filling pressure within the bacterial cell. Based on the thickness of the peptidoglycan layer and the presence of additional structures, bacteria can be classified into two main groups using Gram staining: Gram-positive and Gram-negative. Gram-positive bacteria possess a thick cell wall composed of multiple peptidoglycan layers, while Gram-negative bacteria have a very thin peptidoglycan layer sandwiched between an inner plasma membrane and a unique outer membrane. This difference in cell wall structure significantly impacts the effectiveness of various antibiotics [15, 16].

A large class of antibiotics, most notably the beta-lactam family (β -lactams), which includes penicillin and its derivatives, works by inhibiting bacterial cell wall synthesis. This process is achieved by targeting bacterial enzymes known as penicillin-binding proteins (PBTPs), which are responsible for forming the peptide crosslinks that hold peptidoglycan chains together. When these enzymes are inhibited, the bacterial cell loses its ability to synthesize a healthy cell wall or repair any damage to it. As the cell continues to grow and metabolize, the existing cell wall gradually weakens and fails to withstand the pressure of internal engorgement, ultimately leading to cell lysis and death [17–19]. The effectiveness of this method makes the bacterial cell wall one of the most important targets in chemotherapy against bacterial infections (Figure 10).

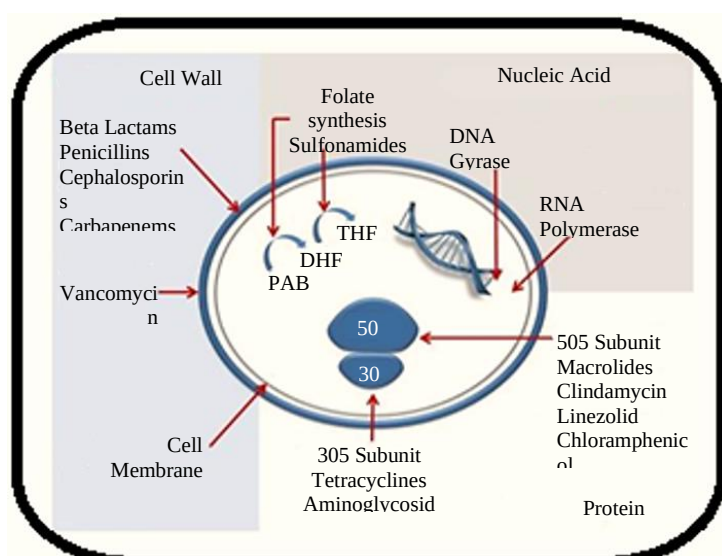


Figure 10. Effect of chemical drugs on cell wall.

THE FUNGAL CELL WALL: UNIQUE STRUCTURE AND SPECIALIZED FUNCTIONS

Although fungi share a cell wall with plants, the fungal cell wall has a unique chemical and functional structure that distinguishes it from its counterparts in other kingdoms. This wall is a fundamental biological structure for fungi, playing pivotal roles in maintaining cell shape, protecting it from osmotic stress, and mediating complex interactions with its environment, including interactions with host organisms in the case of pathogenic fungi. Understanding the structure of the fungal cell wall is crucial, especially since it contains components not found in human cells, making it an attractive target for antifungal drugs [20–22].

The fungal cell wall is primarily composed of a complex network of polysaccharides, most notably chitin and glucans. Chitin, a polymer of N-acetylglucosamine, is the main structural component that provides rigidity and strength to the wall, forming its inner layer. Glucans, polymers of glucose, make up most of the cell wall's mass and are found in multiple layers, contributing significantly to its strength and integrity [23–25]. In addition to these structural components, the outer surface of the fungal cell wall contains a layer of glycoproteins, such as mannoproteins, which play vital roles in surface adhesion, cell recognition, and colony formation. These surface proteins also act as receptors and antigens that can be recognized by the host organism's immune system. Although most bacteria possess a peptidoglycan-based cell wall, there are notable exceptions. The most prominent example is the genus *Mycoplasma*. These bacteria are microorganisms that naturally lack a cell wall. To overcome this structural limitation and cope with osmotic pressure, *Mycoplasma* incorporates sterol molecules, obtained from the host environment, into their plasma membranes. These sterols strengthen the membrane, making it more stable and resistant to osmotic degradation [26–29].

ARE CHEMICAL DRUGS THAT TARGET THE BACTERIAL CELL WALL RELATIVELY SAFE FOR HUMAN USE?

Bacteria are divided into two main groups: Gram-positive and Gram-negative. Both groups have a cell wall composed of peptidoglycan: in Gram-positive bacteria, the wall is thick, while in Gram-negative bacteria, it is thin. In Gram-negative bacteria, the cell wall is surrounded by an outer membrane. Chemical compounds, through electron pairs on hybrid atoms, such as oxygen and nitrogen, affect the cell membrane, thus penetrating it [30–34].

The key to safety lies in the principle of “selective toxicity.” Antibiotics, such as penicillin and cephalosporins, work by inhibiting the enzymes responsible for building and forming cross-links in the peptidoglycan network, the essential and unique component of the bacterial cell wall. When the formation of this wall is impaired, the bacterial cell becomes fragile and unable to withstand its own internal osmotic pressure, leading to cell death. Human cells, and generally eukaryotic cells, completely lack a cell wall and, therefore, lack the peptidoglycan and enzymes necessary to synthesize it. Because this molecular target is absent in our cells, these antibiotics have nothing to bind to or affect in the human body, enabling them to target bacterial cells specifically without causing significant harm to host cells., Structure of Membrane cell of Negative and Positive Bacteria in Figure 11.

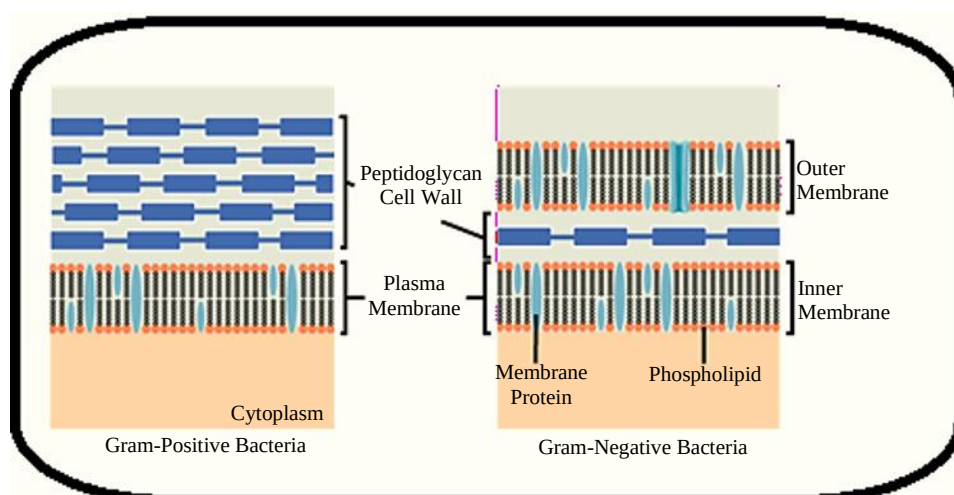


Figure 11. Structure of membrane for positive and negative bacteria.

CONCLUSIONS

The functions of the fungal cell wall extend beyond mere support and protection. It actively participates in growth and morphogenesis processes such as budding in yeasts or filamentous growth in molds. These processes are controlled by precise localized modifications of the cell wall, where it softens in specific areas to allow growth while hardening in others. In pathogenic fungi, the cell wall plays a dual role: it protects the fungus from host defenses while simultaneously displaying molecules on its surface that mediate adhesion to host tissues and the initiation of infection. This complexity in the structure and function of the fungal cell wall makes it an active area of research, aiming to develop novel therapies that target this unique and fundamental structure for fungal survival.

REFERENCES

1. Abd El-Rahim WM, Moawad H, Azeiz AZ, Sadowsky MJ. Optimization of conditions for decolorization of azo-based textile dyes by multiple fungal species. *J Biotechnol.* 2017;260:11–7.
2. Abe FR, Soares AM, de Oliveira DP, Gravato C. Toxicity of dyes to zebrafish at the biochemical level: Cellular energy allocation and neurotoxicity. *Environ Pollut.* 2018;235:255–62.
3. Abramian L, El-Rassy H. Adsorption kinetics and thermodynamics of azo-dye Orange II onto highly porous titania aerogel. *Chem Eng J.* 2009;150(2–3):403–10.
4. Wright S. Recombinant DNA technology and its social transformation, 1972–1982. *Osiris.* 1986;2:303–60.
5. Aljamali NM. Review in azo compounds and its biological activity. *Biochem Anal Biochem.* 2015;4(2):1–4.
6. Kaufmann SH. Concepts in vaccine development. *Biol Chem.* 1997;378(1):A2.
7. Aljamali NM, Farhan ZM. Anticancer study of innovative macrocyclic formazan compounds from trimethoprim drug. *Egypt J Chem.* 2023;66(1):217–30.
8. Knight HJ. Patent strategy: for researchers and research managers. 3rd ed. Chichester: John Wiley & Sons; 2012.
9. Strohl WR, Knight DM. Discovery and development of biopharmaceuticals: Current issues. *Curr Opin Biotechnol.* 2009;20(6):668–72.
10. Aljamali NM. Synthesis of antifungal chemical compounds from fluconazole with (pharmaceutical) studying. *Res J Pharm Biol Chem Sci.* 2017;8(3):564–73.
11. Abdullabass HK, Jawad AM, Aljamali NM. Synthesis of drug derivatives as inhibitors of cancerous cells. *Biochem Cell Arch.* 2020;20(2).
12. Jawad AM, Aljamali NM, Jwad SM, MJ A, MJ S. Development and preparation of ciprofloxacin drug derivatives for treatment of microbial contamination in hospitals and environment. *Indian J Forensic Med Toxicol.* 2020;14(2):1115–22.
13. Devi J, Yadav M, Jindal DK, Kumar D, Poornachandra Y. Synthesis, spectroscopic characterization, biological screening and in vitro cytotoxic studies of 4-methyl-3-thiosemicarbazone derived Schiff bases and their Co(II), Ni(II), Cu(II) and Zn(II) complexes. *Appl Organomet Chem.* 2019;33(10):e5154.
14. Aljamali NM. Synthesis and biological study of hetero (atoms and cycles) compounds. *Der Pharma Chem.* 2016;8(6):40–8.
15. Yu P, Deng J, Cai J, Zhang Z, Zhang J, Hamid Khan M, et al. Anticancer and biological properties of a Zn-2,6-diacetylpyridine bis(thiosemicarbazone) complex. *Metallomics.* 2019;11(8):1372–86.
16. Chohan ZH, Shad HA, Supuran CT. Synthesis, characterization and biological studies of sulfonamide Schiff's bases and some of their metal derivatives. *J Enzyme Inhib Med Chem.* 2012;27(1):58–68.
17. Abbas A, Irfan M, Khan S, Hassan A, Khan S, Javed R, et al. Microbes: Role in industries, medical field and impact on health. *Saudi J Med Pharm Sci.* 2021;7(6):278–82.
18. Lewis JW, Sandorfy C. Infrared absorption and resonance Raman scattering of photochromic triphenylformazans. *Can J Chem.* 1983;61(5):809–16.
19. Aljamali NM, Jawd SM, Hussein HA. Review on preventive instructions for controlling infectious diseases. *Int J Ind Biotechnol Biomater.* 2021;7(1):22–8.
20. Derakhshan S, Najar Peerayeh S, Bakhshi B. Association between presence of virulence genes and antibiotic resistance in clinical *Klebsiella pneumoniae* isolates. *Lab Med.* 2016;47(4):306–11.

21. Khan SA, Shahid S, Kanwal S, Hussain G. Synthesis characterization and antibacterial activity of Cr(III), Co(III), Fe(II), Cu(II), Ni(III) complexes of 4-(2-(((2-hydroxy-5-nitrophenyl) diazenyl)(phenyl)methylene)hydrazinyl)benzene sulfonic acid based formazan dyes and their applications on leather. *Dyes Pigments*. 2018;148:31–43.
22. Aljamali NM. Synthesis innovative cyclic formazan compounds for the first time and evaluation of their biological activity. *Int J Polym Sci Eng*. 2021;7(2):5–14.
23. Mubarak AK, Alkhefaji DQ, Radhi AW. In silico study, design, synthesis, and evaluation of anti-neoplastic activity of hybrid natural antioxidants as histone deacetylase inhibitors. *Wiad Lek*. 2025;2025(12):2685–97.
24. Jawad AM, Aljamali NM, Aseel MJ. Innovation, preparation of cephalixin drug derivatives and studying of (toxicity & resistance of infection). *Int J Psychosoc Rehabil*. 2020;24(4):3754–67.
25. Haseen M, Katiyar PK, Shukla B, Sharma A, Kumar P, Tyagi NT. Synthesis and characterization of sulfamethoxazole derivatives. *J Drug Deliv Ther*. 2025;15(8).
26. Aljamali NM, Jawad AM, Alfatlawi IO, Jawd SM. Review on hospital bacteria (causes, infections, prevention). *Infection*. 2020;11:16.
27. Jess T. Microbiota, antibiotics, and obesity. *N Engl J Med*. 2014;371(26):2526–8.
28. Steffen CA, Henaff L, Durupt A, El Omeiri N, Ndiaye S, Batmunkh N, et al. Evidence-informed vaccination decision-making in countries: Progress, challenges and opportunities. *Vaccine*. 2021;39(15):2146–52.
29. Alderete BL, da Silva J, Godoi R, da Silva FR, Taffarel SR, da Silva LP, et al. Evaluation of toxicity and mutagenicity of a synthetic effluent containing azo dye after advanced oxidation process treatment. *Chemosphere*. 2021;263:128291.
30. Zheng B, Wang X, Guo M, Tzeng CM. Therapeutic peptides: Recent advances in discovery, synthesis, and clinical translation. *Int J Mol Sci*. 2025;26(11):5131.
31. Narayana K. An aminoglycoside antibiotic gentamycin induces oxidative stress, reduces antioxidant reserve and impairs spermatogenesis in rats. *J Toxicol Sci*. 2008;33(1):85–96.
32. Ali N, Hameed A, Ahmed S. Role of brown-rot fungi in the bioremoval of azo dyes under different conditions. *Braz J Microbiol*. 2010;41:907–15.
33. Almeida EJ, Corso CR. Decolorization and removal of toxicity of textile azo dyes using fungal biomass pelletized. *Int J Environ Sci Technol*. 2019;16(3):1319–28.
34. Solís M, Solís A, Pérez HI, Manjarrez N, Flores M. Microbial decolouration of azo dyes: A review. *Process Biochem*. 2012;47(12):1723–48.