

# Review on Antimicrobial Applications of Rare Earth-Doped Spinel Ferrites

Puja U. Tasalwar<sup>1</sup>, Aarti N. Wazalwar<sup>2</sup>

<sup>1,2</sup>Department of Physics, Dr. Ambedkar College, Deekshabhoomi, Nagpur-440010, India

## Abstract

Rare earth-doped spinel nano ferrites are gaining interest for their antimicrobial potential. This review examines their synthesis methods, structural properties and effectiveness against bacteria. Doping with rare earth ions influences factors like crystallite size and magnetic behaviour, which in turn enhances antimicrobial activity against both Gram-positive and Gram-negative bacteria. However, challenges such as cytotoxicity, environmental effects and complex synthesis needs to be addressed to maximize their use in biomedical applications.

**Keywords:** Spinel Ferrites, Rare Earth, Antimicrobial Activity

## 1. Introduction

The rise of antibiotic resistance is becoming a global public health crisis. While the misuse of antibiotics for treating human diseases is the primary cause of this issue, the overuse of antimicrobial agents in veterinary medicine, agriculture, and industry is also exacerbating the situation. In the poultry and livestock industries, the use of antibiotics to prevent potentially fatal infections in chickens, cattle, pigs, seafood, and farmed fish is a common practice worldwide [1]. This excessive use has led to mutations and the development of resistant bacterial strains. As this emerging health threat intensifies, there is an urgent need to develop innovative antimicrobial agents to control infections.

In this context, nanotechnology has rapidly evolved as a promising approach to tackling the complexity of antibiotic resistance. Nanotechnology-based materials, such as nanoparticles (NPs), have shown significant potential in combating microbial infections more effectively than conventional antibiotics. These NPs possess unique optical, electrical, and magnetic properties, and can be easily magnetized or demagnetized due to their soft and insulating nature [2].

Spinel ferrites (SF) are metal oxides that possess a spinel structure, represented by the general formula  $AB_2O_4$ , where A and B denote various metal cations located at the tetrahedral (A site) and octahedral (B site) positions in the crystal lattice, with at least one ferric ion present in the chemical formula. The properties of ferrites are highly dependent on the types, amounts, and positions of the metal cations within the crystallographic structure. These materials have wide-ranging applications from biomedical to industrial fields. The conjugation of ferrites with certain divalent metallic ions significantly enhances their properties. Spinel ferrites are ferromagnetic compounds typically composed of various transition metal oxides containing iron, such as  $ZnFe_2O_4$ ,  $NiFe_2O_4$ ,  $Zn/NiFe_2O_4$ ,  $CoFe_2O_4$ ,  $MnFe_2O_4$ , and  $MgFe_2O_4$ . SF nanoparticles are predominantly utilized as magnetic, refractory, and antimicrobial materials [3][4].

## 2. Health and disease

Health is a complex concept that can be measured through various parameters. It refers to an individual's overall well-being, including physical, mental, and social aspects, rather than just the absence of disease or infirmity[5]. In contrast, a disease is an abnormal condition that negatively impacts the structure or function of all or part of an organism, often identified by specific signs and symptoms. Moreover, microorganisms such as bacteria and viruses can cause diseases by entering the body through the air, water, food, or direct contact[6]. Antibiotic resistance is a critical concern in treating bacterial infections, as it renders standard antibiotics ineffective, leading to more severe illnesses and higher mortality rates[7].

The below table shows some diseases caused by microorganisms and their antibiotics:

S r. N o.	Disease	Causative Bacteria	Affected Body Part(s)	Common Antibiotic Treatment	Refere nces
1	Tubercul osis (TB)	<i>Mycobacte rium tuberculos is</i>	Lungs (primarily ) , can affect other organs	Combination therapy with isoniazid, ethambutol, and pyrazinamide	[8]
2	Strep Throat	<i>Streptococ cus pyogenes</i>	Throat tonsils	Penicillin or amoxicillin; alternatives include azithromycin or clarithromycin for penicillin- allergic patients	[9]
3	Scarlet Fever	<i>Streptococ cus pyogenes</i>	Skin (rash), throat	Penicillin or amoxicillin; early treatment is crucial to prevent complications.	[10]
4	Imbalanc e of vaginal bacteria	<i>Bacterial Vaginosis</i>	Vagina	Metronidazole or clindamycin to restore normal bacterial balance.	[11]
		<i>Streptococ cus</i>		Depends on the pathogen; options include macrolides (e.g., azithromycin), fluoroquinolones	

5	Pneumonia	<i>pneumoniae</i> , <i>Haemophilus influenzae</i> , <i>Mycoplasma pneumoniae</i>	Lungs	(e.g., levofloxacin), or beta-lactams (e.g., amoxicillin-clavulanate).	[12]
6	Urinary Tract Infections (UTIs)	<i>Escherichia coli</i> , <i>Klebsiella pneumoniae</i> , <i>Proteus mirabilis</i>	Urinary tract (bladder, urethra, kidneys)	Trimethoprim-sulfamethoxazole, nitrofurantoin, or fosfomycin, depending on local resistance patterns.	[13]
7	Bacterial Meningitis	<i>Neisseria meningitidis</i> , <i>Streptococcus pneumoniae</i> , <i>Haemophilus influenzae</i>	Membranes covering the brain and spinal cord (meninges)	Empirical therapy often includes third-generation cephalosporins (e.g., ceftriaxone) and vancomycin, adjusted based on culture results.	[14]
8	Gastroenteritis (Food Poisoning)	<i>Salmonella spp.</i> , <i>Campylobacter jejuni</i> , <i>Escherichia coli</i>	Gastrointestinal tract	Many cases are self-limiting; severe cases may require antibiotics like ciprofloxacin or azithromycin, depending on the pathogen.	[15]
9	Skin Infections (e.g., Cellulitis)	<i>Staphylococcus aureus</i> (including MRSA), <i>Streptococcus</i>	Skin and underlying tissues	Non-MRSA: cephalexin or dicloxacillin; MRSA: clindamycin, trimethoprim-sulfamethoxazole, or doxycycline.	[16]

		<i>cus pyogenes</i>			
10	Gonorrhoea	<i>Neisseria gonorrhoeae</i>	Genital tract, rectum, throat	Due to rising resistance, dual therapy with ceftriaxone and azithromycin is recommended.	[17]
11	Cholera	<i>Vibrio cholerae</i>	Intestines	Rehydration is primary; antibiotics like doxycycline or azithromycin may reduce disease duration.	[18]
12	Diphtheria	<i>Corynebacterium diphtheriae</i>	Skin, joints, heart, nervous system	Antitoxin administration and antibiotics such as penicillin or erythromycin.	[19]
13	Whooping Cough (Pertussis)	<i>Bordetella pertussis</i>	Respiratory tract	Macrolide antibiotics like azithromycin or clarithromycin.	[20]
14	Tetanus	<i>Clostridium tetani</i>	Nervous system (muscle spasms)	Administration of tetanus immunoglobulin and metronidazole; supportive care.	[21]
15	Leprosy (Hansen's Disease)	<i>Mycobacterium leprae</i>	Skin, peripheral nerves, upper respiratory tract	Combination therapy with dapsone, rifampicin, and clofazimine over an extended period.	[22]
16	Syphilis	<i>Treponema pallidum</i>	Genital tract, skin, mucous membranes	Penicillin G is the treatment of choice; doxycycline for penicillin-allergic patients.	[23]

17	Plague	<i>Yersinia pestis</i>	Lymph nodes, lungs, bloodstream	Streptomycin or gentamicin; alternatives include doxycycline or ciprofloxacin	[24]
18	Anthrax	<i>Bacillus anthracis</i>	Skin, lungs, gastrointestinal tract	Cip	[25]
19	Legionnaires' Disease	<i>Legionella pneumophila</i>	Lungs	Levo	[26]

**Table 1: Diseases caused by microorganisms and their antibiotics.**

### 3. Factors Contributing to Antibiotic Treatment Failures:

The excessive use of antibiotics in human medicine, veterinary practices, and agriculture contributes significantly to antibiotic resistance. Not completing prescribed treatments allows partially resistant bacteria to thrive, complicating efforts to combat these strains, especially with few new antibiotics in development[27]. Resistant bacteria spread quickly, posing public health risks. To tackle this issue, a comprehensive strategy is needed, including responsible prescribing, increased funding for new antimicrobial research, and global public health initiatives to monitor and address antibiotic resistance. These measures are vital for protecting the effectiveness of antibiotics for future generations[28].

### 4. Antimicrobial Activity

Microbes, including bacteria, fungi, viruses, protozoa, and algae, are tiny life forms usually invisible to the naked eye. They exist in diverse environments, playing vital roles in ecology, human health, and industry. Bacteria are single-celled prokaryotes with various shapes (bacilli, cocci, spirilla). They thrive in many settings, often being beneficial by aiding digestion and nutrient cycling, though some can cause diseases[29]. Fungi are more complex eukaryotic organisms, encompassing unicellular yeasts and multicellular molds and mushrooms. They act as decomposers, recycle nutrients, and form beneficial relationships with plants. While many fungi are advantageous, some can lead to infections[30].

Antimicrobial activity involves substances called antimicrobials that inhibit the growth or destroy microorganisms, including bacteria, fungi, viruses, and parasites. They are crucial for treating infections, preventing disease spread, and maintaining hygiene [31].

There are various types of antimicrobial agents, including antifungals, antivirals, and antiparasitic. Antimicrobial agents play a crucial role in protecting our health, and they come in several powerful forms: antifungals, antivirals, and antiparasitic. Each type is specifically designed to target and eliminate harmful pathogens, making them essential tools in the fight against infections and diseases. Embracing these agents is vital for maintaining our well-being and safeguarding public health [32].

### 5. Rare earth doped spinel nano ferrites

Rare earth-doped spinel nano ferrites are specialized magnetic nanomaterials that incorporate rare earth elements (such as  $\text{La}^{3+}$ ,  $\text{Ce}^{3+}$ ,  $\text{Pr}^{3+}$ ,  $\text{Y}^{3+}$ ,  $\text{Dy}^{3+}$ ,  $\text{Tb}^{3+}$ ) into their structure. This doping enhances their structural, electronic, magnetic, and antimicrobial properties, making them suitable for various applications[33][34].

Doping spinel nano ferrites with rare earth ions can significantly enhance their structural, electrical, magnetic, and dielectric properties. These modifications may influence the material's interaction with microbial cells, potentially contributing to antimicrobial activity. However, the direct relationship between rare earth doping and enhanced antimicrobial properties in spinel ferrites is not well established in the available literature. Further research is necessary to elucidate the mechanisms by which rare earth doping might impart or enhance antimicrobial activity in these materials[35][36].

The below table shows the antimicrobial activity of rare earth doped spinel nano ferrites:

Sr. No.	Ferrites	Dopant	Bacteria	Particle Size	Antimicrobial Activity	References
1	$\text{CuFe}_2\text{O}_4$	$\text{Ce}^{3+}$	<i>Klebsiellapneumoniae</i> , <i>Staphylococcus aureus</i>	16.53 nm to 25.36 nm	The antibacterial activity of $\text{Ce}^{3+}$ doped $\text{CoFe}_2\text{O}_4$ nanoparticles increases with higher $\text{Ce}^{3+}$ doping, linked to smaller grain size.	[37]
2	$\text{CoFe}_2\text{O}_4$	$\text{Ce}^{3+}$	<i>Klebsiellapneumoniae</i> , <i>Staphylococcus aureus</i>	18.53 nm to 25.36 nm	ZOI for <i>Klebsiellapneumoniae</i> is 17mm and <i>Staphylococcus aureus</i> is 19mm	[38]
3	$\text{CoFe}_2\text{O}_4$	$\text{Nd}^{3+}$	<i>S. aureus</i> , <i>E. coli</i> , and <i>C. albicans</i> .	15nm	The results showed improved bactericidal activity with Nd addition to cobalt ferrite.	[39]
4	Mn- $\text{ZnFe}_2\text{O}_4$	$\text{Dy}^{3+}$ = Y	<i>Escherichia Coli</i> , <i>S. aureus</i>	12.2 nm to 15.4 nm	The synthesis through ultrasonication demonstrated greater effectiveness against <i>Staphylococcus aureus</i> than against <i>Escherichia coli</i> .	[40]

5	Cd-substituted Ni-Co ferrite	Nd <sup>3+</sup>	<i>Escherichia Coli</i> , <i>S. aureus</i>	10.5 to 18.5 nm	Showed inhibitory action on the bacterial strains.	[41]
6	Mn-ZnFe <sub>2</sub> O <sub>4</sub>	Sm <sup>3+</sup> , Eu <sup>3+</sup>	<i>Escherichia Coli</i> , <i>S. aureus</i>	7-12 nm	A slight increase in activity was observed against <i>E. coli</i> .	[42]
7	Mn-ZnFe <sub>2</sub> O <sub>4</sub>	Ce <sup>3+</sup> / Dy <sup>3+</sup>	<i>E. coli and S. aureus</i>	8.6 to 18.5 nm	The antibacterial activity of gram-negative bacteria was slightly greater than that of gram-positive bacterial strains.	[43]
8	ZnFe <sub>2</sub> O <sub>4</sub>	Ce <sup>3+</sup>	<i>P. aeruginosa, S. aureus, Candida albicans</i>	7.75 to 11.63 nm	The ZOI for <i>P. aeruginosa</i> = 9.2 mm, <i>S. aureus</i> = 13.2mm, <i>Candida albicans</i> = 13.5mm	[44]
9	NiFe <sub>2</sub> O <sub>4</sub>	Gd <sup>3+</sup>	<i>E. coli and S. aureus</i>	13.31 and 15.23 nm	NPs actively killed the <i>E. coli</i> bacteria at all concentrations	[45]
			<i>B. subtilis and</i>			
10	MnFe <sub>2</sub> O <sub>4</sub>	Ce <sup>3+</sup>	<i>S. aureus, K. pneumonia and E. coli</i>	22 and 24 nm	Higher concentrations of Ce ions result in a larger zone of inhibition.	[46]
11	Ni-CoFe <sub>2</sub> O <sub>4</sub>	Pr <sup>3+</sup>	<i>Candida albicans</i>	10 to 17 nm	Increased dopant enhances the antifungal properties of the synthesized nanomaterial, suggesting that NSF's may be valuable in pharmaceuticals.	[47]



12	CoFe <sub>2</sub> O <sub>4</sub>	Sm <sup>3+</sup>	E. coli, P. aeruginosa, S. typhimurium, S. aureus, B. cereus, and S. faecalis	29nm to 31.37nm	The sample exhibited antibacterial properties against both gram-positive and gram-negative bacteria, with inhibition zones measuring 12 to 14.5 mm in diameter.	[48]
13	Li-NiFe <sub>2</sub> O <sub>4</sub>	Dy <sup>3+</sup>	Staphylococcus Aureus, Bacillus Subtilis, Escherichia Coli and Proteus Mirabilis	32.79 – 11.13 nm	The antifungal potential was studied against <i>Candida albicans</i> and <i>Aspergillus Niger</i> .	[49]
14	ZnFe <sub>2</sub> O <sub>4</sub>	Ce <sup>3+</sup>	<i>S. aureus</i> , <i>P. vulgaris</i> , <i>P. mirabilis</i> , <i>p. aeruginosa</i> , <i>E. coli</i> , <i>K. pneumonia</i> , and <i>S. typhi</i> .	7.75 and 11.63 nm,	ZOI for <i>P. aeruginosa</i> is 9.5 mm, <i>S. aureus</i> is 13.2 mm, <i>Candida albicans</i> is 13.5 mm.	[50]
15	CoFe <sub>2</sub> O <sub>4</sub>	Gd <sup>3+</sup>	<i>C. albicans</i> , <i>Aspergillus Niger</i> , <i>S. aureus</i> , <i>E. coli</i>	54nm-47.2nm	The substitution of gadolinium (Gd) significantly enhances the antimicrobial activity of cobalt ferrite.	[51]
16	Ni- CoFe <sub>2</sub> O <sub>4</sub>	Ce <sup>3+</sup>	B. subtilis, S. aureus. coli and P. multicide	29.71 to 24.95 nm	The maximum inhibition zone (20 mm) was recorded for E. Coli	[52]
17	Mg-CdFe <sub>2</sub> O <sub>4</sub>	Gd <sup>3+</sup>	Staphylococcus aureus, salmonella typhi, Candida Albicans	46 to 35 nm	Gram-positive bacteria exhibited slightly higher activity compared to Gram-negative bacterial strains.	[53]

**Table 2: Antimicrobial activity of rare earth doped spinel nano ferrites**

## 6. Mechanisms of Antimicrobial Action

The antimicrobial activity of these doped ferrites is attributed to several mechanisms

6.1 Disruption of Microbial Membranes: The interaction of nanoparticles with microbial cell membranes can increase permeability, leading to cell lysis.

6.2 Generation of Reactive Oxygen Species (ROS): Doped ferrites can induce ROS production, causing oxidative stress and damage to essential cellular components in microbes.



6.3 Release of Metal Ions: The leaching of metal ions from the ferrite matrix can interfere with microbial enzymatic functions and metabolic pathway[54].

### 7. Limitations of rare earth doped spinel nano ferrites

Due to their unique properties, rare earth-doped spinel nano-ferrites show great potential for antimicrobial applications. However, several challenges must be addressed to maximize their effectiveness. Key concerns include cytotoxicity, which raises safety issues for human cells, and resource limitations that can affect production costs and scalability[55]. The complex synthesis processes required can complicate industrial applications, while the environmental impact of their creation and disposal needs careful consideration.

Furthermore, ensuring the long-term stability of these nano-ferrites under various conditions is essential for maintaining their antimicrobial properties. Overcoming these hurdles is crucial to fully exploit the benefits of rare earth-doped spinel nano-ferrites in antimicrobial uses[56][57].

### 8. Future scope

Rare earth-doped spinel nano ferrites exhibit promising antimicrobial properties, positioning them as potential candidates for future applications in healthcare and environmental sectors. Ongoing research focuses on optimizing rare earth ion doping to enhance antimicrobial efficacy, developing advanced synthesis methods for consistent nanoparticle production, and conducting comprehensive biocompatibility and environmental impact assessments to ensure safe and sustainable use. These efforts aim to harness these materials' unique structural and magnetic properties for innovative antimicrobial solutions.

### 9. Conclusion

Rare earth-doped spinel ferrite nanoparticles exhibit enhanced antimicrobial properties, making them potential candidates for addressing challenges posed by resistant microbial strains. The ability to tailor their structural and magnetic properties through controlled doping and synthesis methods enables the optimization of their antimicrobial efficacy. However, comprehensive studies on their biocompatibility, cytotoxicity, and environmental impact are essential to ensure safe and effective integration into biomedical and environmental applications.

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