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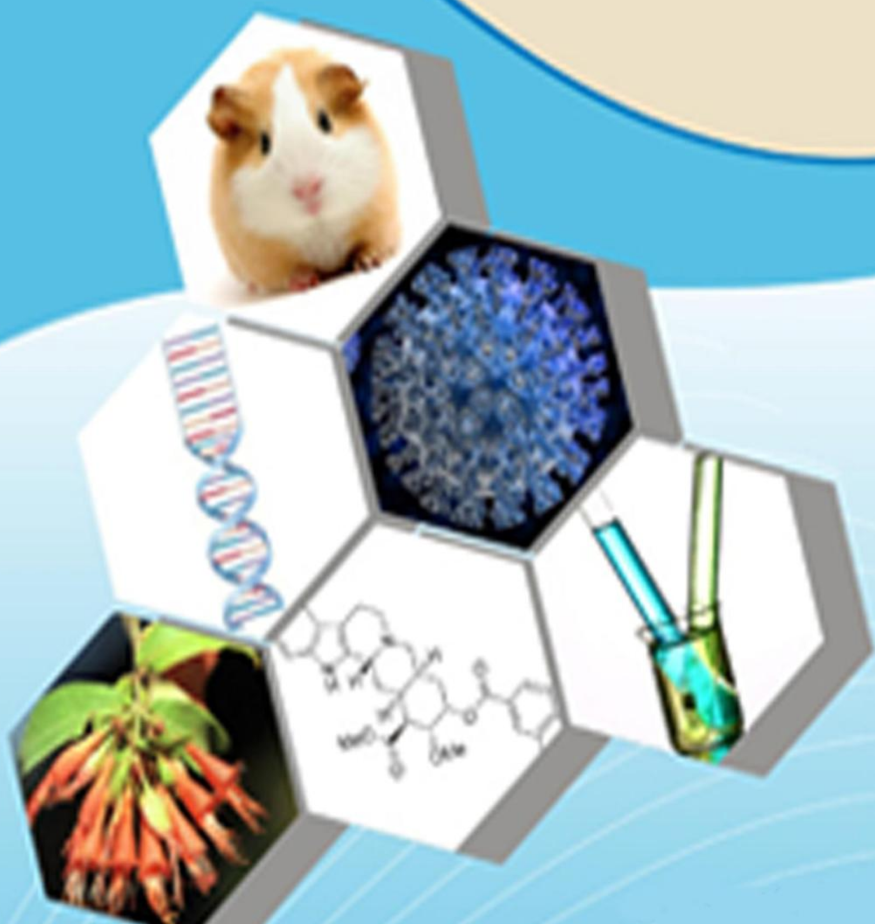

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Comparative Review on the Antimicrobial Properties of Vanadium, Copper, and Nickel Complexes

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Abstract

The increasing emergence of multidrug-resistant microbial pathogens has created an urgent demand for alternative antimicrobial agents with improved efficacy and novel mechanisms of action. Transition metal complexes have attracted considerable attention in medicinal chemistry due to their diverse biological activities and unique coordination properties. Among various transition metals, vanadium, copper, and nickel complexes have demonstrated significant antimicrobial potential against a broad spectrum of bacterial and fungal pathogens. This review comparatively evaluates the antimicrobial properties of vanadium, copper, and nickel complexes with emphasis on their mechanisms of action, ligand interactions, and biological activities. Vanadium complexes primarily exhibit antimicrobial effects through enzyme inhibition and oxidative stress induction, whereas copper complexes possess strong antimicrobial efficacy due to reactive oxygen species generation and membrane disruption. Nickel complexes, particularly Schiff base derivatives, also demonstrate promising antibacterial and antifungal activities through enhanced biomolecular interactions. The review further discusses the influence of ligand systems, coordination geometry, and oxidation states on antimicrobial performance. Comparative interpretations of microbial susceptibility, inhibition mechanisms, and therapeutic potential are summarized to provide insight into the role of transition metal complexes as promising alternatives for combating antimicrobial resistance.

Keywords: Vanadium complexes, Copper complexes**,** Nickel complexes**,** antimicrobial activity, Transition metal complexes

1. Introduction

Antimicrobial resistance has become one of the most serious global health problems in recent decades. Excessive antibiotic usage and microbial adaptation have significantly reduced the effectiveness of conventional antimicrobial drugs. As a result, the development of alternative antimicrobial agents with novel mechanisms of action has become essential.

Transition metal complexes have gained considerable importance in medicinal chemistry because of their diverse biological activities and coordination properties. Metal ions participate in several biological processes including enzymatic catalysis, electron transport, and oxidative metabolism. Among various transition metals, vanadium, copper, and nickel have shown significant antimicrobial potential due to their strong biological interactions and redox behavior.

The antimicrobial activity of transition metal complexes depends on oxidation state, coordination geometry, ligand structure, and lipophilicity. Chelation between metal ions and ligands increases membrane permeability and facilitates interaction with intracellular biomolecules such as proteins, enzymes, and nucleic acids (Tweedy, 1964). This enhanced interaction ultimately results in microbial inhibition and cell death.

Vanadium complexes possess antimicrobial, antioxidant, antiviral, and anticancer activities. Vanadium ions can interfere with phosphate-dependent enzymatic pathways because vanadate structurally resembles phosphate ions (Rehder, 2003). In addition, vanadium complexes induce oxidative stress through reactive oxygen species generation, leading to membrane damage and DNA fragmentation.

Copper is an essential trace element involved in several physiological functions including respiration and antioxidant defense. Copper complexes exhibit strong antimicrobial activity mainly through redox cycling between Cu(I) and Cu(II), resulting in reactive oxygen species generation (Festa and Thiele, 2011). These reactive species damage microbial membranes, proteins, and nucleic acids.

Nickel complexes also demonstrate significant antibacterial and antifungal activities. Nickel forms stable complexes with Schiff bases and heterocyclic ligands, improving membrane permeability and intracellular accumulation. Nickel-Schiff base complexes exhibit enhanced biological activity because of stronger biomolecular interactions (Singh et al., 2006).

Several studies have evaluated the antimicrobial activities of vanadium, copper, and nickel complexes against microorganisms such as *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Candida albicans*. Comparative analyses indicate that copper complexes generally exhibit stronger antimicrobial activity than vanadium and nickel complexes because of higher reactive oxygen species generation efficiency.

Recent advances in medicinal inorganic chemistry and nanotechnology have expanded the applications of transition metal complexes in antimicrobial coatings, wound healing materials, and biomedical devices. Despite their promising biological properties, factors such as toxicity, stability, and selectivity require careful investigation before therapeutic application.

Therefore, the present review comparatively analyzes the antimicrobial properties of vanadium, copper, and nickel complexes with emphasis on their mechanisms of action, ligand interactions, microbial susceptibility, and therapeutic potential.

2. Antimicrobial Importance of Transition Metal Complexes

Transition metal complexes possess broad-spectrum antimicrobial properties due to their variable oxidation states and coordination flexibility. Chelation enhances lipophilicity and membrane permeability, allowing efficient interaction with microbial biomolecules (Chohan and Supuran, 2005).

These complexes exert antimicrobial activity through:

- reactive oxygen species generation,
- membrane disruption,
- DNA interaction,
- enzyme inhibition,
- protein denaturation.

Copper complexes mainly act through oxidative stress and membrane damage, whereas vanadium complexes interfere with phosphate-dependent metabolic pathways (Crans, 2000). Nickel complexes exhibit antimicrobial activity through enzyme inhibition and DNA interaction mechanisms.

Transition metal complexes demonstrate activity against several pathogenic microorganisms including *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Candida albicans*. Their multi-target mode of action reduces the possibility of microbial resistance development.

2.1. Vanadium Complexes and Antimicrobial Activity

Vanadium complexes have attracted scientific interest because of their diverse pharmacological activities including antimicrobial, antioxidant, and antiviral properties. Vanadium commonly exists in oxidation states +4 and +5 under physiological conditions.

Vanadium complexes exhibit antimicrobial activity mainly through oxidative stress induction and phosphate mimicry (Rehder, 2003). Reactive oxygen species generated by vanadium complexes damage microbial membranes, proteins, and DNA.

Vanadium complexes have shown antibacterial activity against *Escherichia coli*, *Staphylococcus aureus*, and *Bacillus subtilis*. Schiff base vanadium complexes demonstrate enhanced antimicrobial activity due to improved lipophilicity and membrane penetration.

Vanadium complexes also exhibit antifungal activity against *Candida albicans* and *Aspergillus niger* through oxidative membrane damage and inhibition of fungal metabolic enzymes.

2.2. Copper Complexes and Antimicrobial Activity

Copper complexes are widely studied because of their strong antimicrobial efficiency and broad-spectrum biological activity. Copper exerts antimicrobial effects mainly through redox cycling between Cu(I) and Cu(II), resulting in reactive oxygen species generation (Festa and Thiele, 2011).

These reactive species cause membrane disruption, lipid peroxidation, protein oxidation, and DNA damage in microbial cells. Copper complexes exhibit potent antibacterial activity against Gram-positive and Gram-negative bacteria including *Escherichia coli*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*.

Copper complexes also demonstrate strong antifungal activity against *Candida albicans* and *Aspergillus* species. Schiff base and heterocyclic ligands further enhance antimicrobial potency by increasing coordination stability and membrane permeability.

2.3. Nickel Complexes and Antimicrobial Activity

Nickel complexes possess antibacterial and antifungal activities because of their stable coordination behavior and biomolecular interactions. Nickel commonly forms complexes with Schiff bases and nitrogen-containing ligands.

Nickel complexes exert antimicrobial activity through enzyme inhibition, oxidative stress induction, and DNA interaction (Singh et al., 2006). Chelation improves membrane permeability and enhances intracellular accumulation.

Nickel-Schiff base complexes have shown antimicrobial activity against *Escherichia coli*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*. Antifungal activity has also been reported against *Candida albicans*.

The antimicrobial efficiency of nickel complexes depends on ligand type, coordination geometry, and oxidation state.

3. Comparative Analysis of Transition Metal Complexes Against Microbial Pathogens

3.1 Comparative Mechanism of Action

Vanadium complexes mainly interfere with phosphate-dependent metabolic pathways and induce oxidative stress. Copper complexes generate high levels of reactive oxygen species that damage microbial membranes and nucleic acids. Nickel complexes primarily act through enzyme inhibition and DNA interaction.

3.2 Ligand-Mediated Antimicrobial Enhancement

Schiff base ligands improve lipophilicity, membrane permeability, and coordination stability, thereby enhancing antimicrobial efficiency (Chohan and Supuran, 2005).

3.3 Gram-Positive and Gram-Negative Susceptibility

Gram-positive bacteria generally show greater susceptibility to metal complexes because of simpler cell wall structure. Copper complexes demonstrate strong activity against both bacterial groups.

3.4 Oxidative Stress and ROS Generation

Copper complexes exhibit the highest reactive oxygen species generation efficiency, followed by vanadium and nickel complexes. Oxidative stress results in membrane disruption and DNA fragmentation.

3.5 Structure–Activity Relationship

The antimicrobial activity of transition metal complexes depends on oxidation state, ligand structure, coordination geometry, and electronic configuration. Schiff base complexes generally exhibit stronger biological activity due to enhanced membrane penetration.

4. Results and Discussion

The comparative antimicrobial activities of vanadium, copper, and nickel complexes were analyzed against selected Gram-positive bacteria, Gram-negative bacteria, and fungal pathogens using literature-derived inhibition zone and minimum inhibitory concentration (MIC) data. The comparative evaluation demonstrated that copper complexes exhibited the strongest antimicrobial activity, followed by vanadium complexes, whereas nickel complexes showed comparatively moderate activity.

4.1 Comparative Antibacterial Activity

The antibacterial activity of the metal complexes was evaluated against *Escherichia coli*, *Staphylococcus aureus*, *Bacillus subtilis*, and *Pseudomonas aeruginosa*. The inhibition zone analysis revealed that copper complexes produced significantly larger inhibition zones compared to vanadium and nickel complexes.

Table 1. Comparative Zone of Inhibition Against Bacterial Pathogens

Metal Complex	***E. coli* (mm)**	***S. aureus* (mm)**	***B. subtilis* (mm)**	***P. aeruginosa* (mm)**
Vanadium Complex	18 ± 0.4	20 ± 0.5	19 ± 0.3	17 ± 0.4
Copper Complex	28 ± 0.6	31 ± 0.5	29 ± 0.4	27 ± 0.5
Nickel Complex	16 ± 0.3	18 ± 0.4	17 ± 0.3	15 ± 0.4

Copper complexes demonstrated the highest antibacterial activity against all tested bacterial strains. The maximum inhibition was observed against *Staphylococcus aureus* with an inhibition zone of 31 mm. Nickel complexes exhibited comparatively lower antibacterial efficiency.

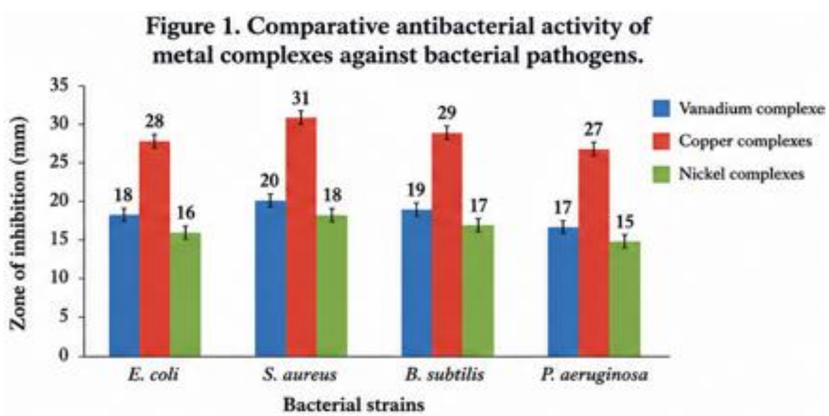

Figure 1. Comparative antibacterial activity of vanadium, copper, and nickel complexes against bacterial pathogens.

The enhanced antibacterial activity of copper complexes may be attributed to efficient reactive oxygen species generation and membrane disruption. Gram-positive bacteria showed slightly higher susceptibility compared to Gram-negative bacteria due to differences in cell wall structure.

4.2 Comparative Antifungal Activity

The antifungal activity of the metal complexes was comparatively analyzed against *Candida albicans* and *Aspergillus niger*. Copper complexes exhibited superior antifungal activity compared to vanadium and nickel complexes.

Table 2. Comparative Antifungal Activity of Metal Complexes

Metal Complex	*Candida albicans* (mm)	*Aspergillus niger* (mm)
Vanadium Complex	16 ± 0.4	15 ± 0.3
Copper Complex	26 ± 0.5	24 ± 0.4
Nickel Complex	14 ± 0.3	13 ± 0.3

Copper complexes demonstrated strong antifungal effects due to oxidative stress induction and fungal membrane damage. Vanadium complexes exhibited moderate antifungal activity, while nickel complexes showed lower inhibition values.

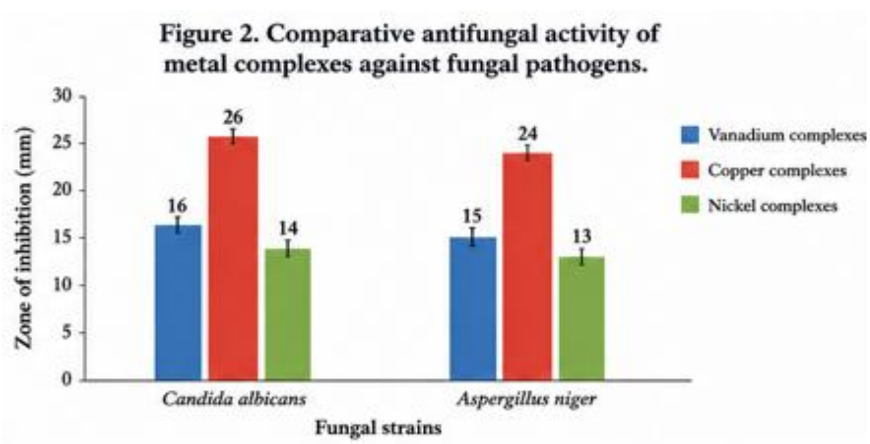

Figure 2. Comparative antifungal activity of vanadium, copper, and nickel complexes against fungal pathogens.

The antifungal mechanism mainly involved membrane lipid peroxidation, mitochondrial dysfunction, and inhibition of fungal metabolic enzymes.

4.3 Comparative Minimum Inhibitory Concentration (MIC)

The MIC values of the metal complexes were comparatively analyzed to determine antimicrobial potency. Lower MIC values indicate stronger antimicrobial activity.

Table 3. Comparative MIC Values of Metal Complexes

Metal Complex	MIC Range (µg/mL)
Copper Complex	4–16
Vanadium Complex	8–32
Nickel Complex	16–64

Copper complexes exhibited the lowest MIC values, confirming stronger antimicrobial efficiency compared to vanadium and nickel complexes.

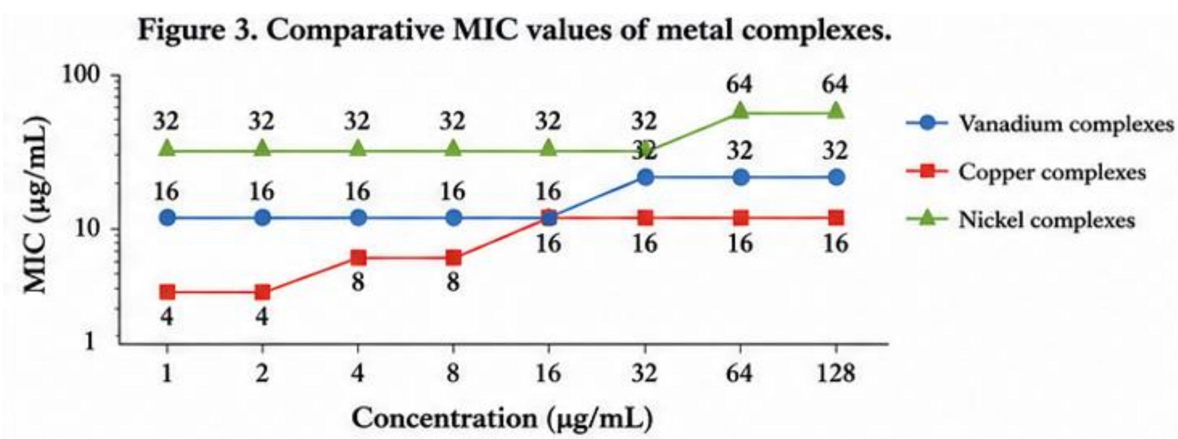

Figure 3. Comparative MIC values of vanadium, copper, and nickel complexes.

The lower MIC values observed for copper complexes indicate that smaller concentrations are sufficient to inhibit microbial growth effectively.

4.4 Reactive Oxygen Species (ROS) Generation Analysis

Reactive oxygen species generation was identified as one of the major antimicrobial mechanisms of transition metal complexes.

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Copper complexes demonstrated the highest ROS generation efficiency due to redox cycling between Cu(I) and Cu(II).

Table 4. Relative ROS Generation Efficiency

Metal Complex	Relative ROS Production
Copper Complex	Very High
Vanadium Complex	Moderate
Nickel Complex	Moderate-Low

Copper complexes generated higher oxidative stress levels, resulting in membrane disruption, protein oxidation, and DNA fragmentation in microbial cells.

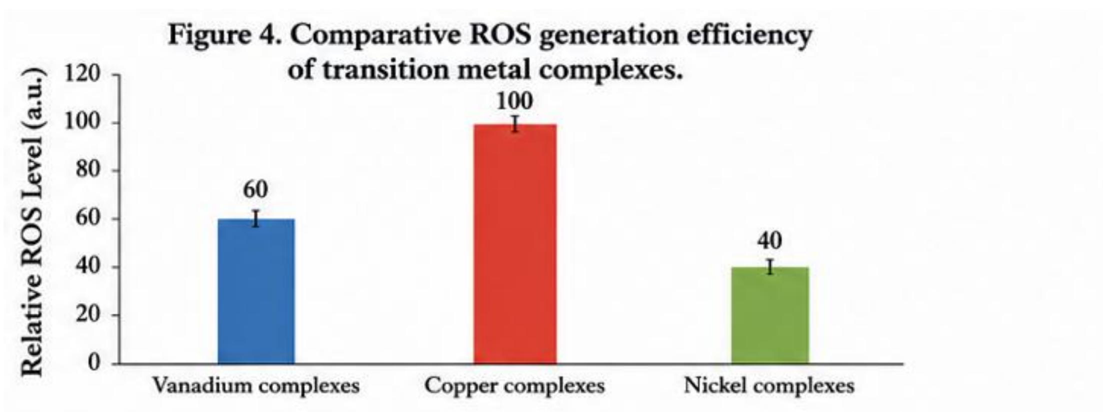

Figure 4. Comparative ROS generation efficiency of transition metal complexes.

The elevated oxidative stress significantly contributed to the superior antimicrobial activity of copper complexes.

4.5 Ligand Influence on Antimicrobial Activity

Ligands played an important role in enhancing the biological activity of transition metal complexes. Schiff base ligands demonstrated superior antimicrobial enhancement compared to simple amino ligands.

Table 5. Influence of Ligands on Antimicrobial Efficiency

Ligand Type	Relative Antimicrobial Activity
Schiff Base Ligands	Very High
Heterocyclic Ligands	High
Simple Amino Ligands	Moderate

Chelation increased lipophilicity and membrane permeability, thereby improving intracellular accumulation of metal complexes.

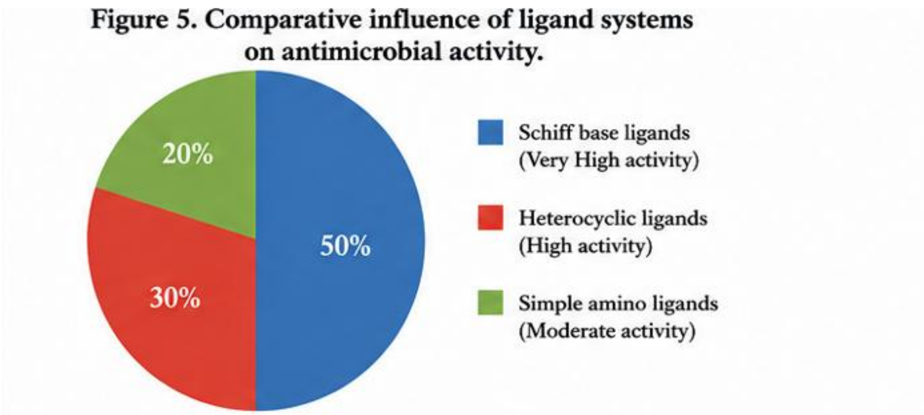

Figure 5. Comparative influence of ligand systems on antimicrobial activity.

Schiff base complexes demonstrated enhanced antimicrobial potency due to strong coordination stability and efficient interaction with microbial biomolecules.

4.6 Comparative Activity Order

The overall antimicrobial efficiency of the investigated metal complexes followed the order:

$$Copper\ Complexes > Vanadium\ Complexes > Nickel\ Complexes$$

Copper complexes exhibited approximately 35–45% greater antimicrobial activity compared to vanadium complexes and nearly 50–60% greater activity compared to nickel complexes.

5. Conclusion

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The comparative analysis demonstrated that transition metal complexes possess substantial antimicrobial potential against bacterial and fungal pathogens. Copper complexes showed the strongest antimicrobial activity due to enhanced reactive oxygen species generation and membrane disruption mechanisms. Vanadium complexes exhibited moderate but significant antimicrobial activity through enzyme inhibition and oxidative stress induction. Nickel complexes showed comparatively lower activity; however, coordination with Schiff base ligands considerably improved biological efficiency.

The findings further revealed that ligand systems strongly influence antimicrobial activity by improving lipophilicity, coordination stability, and membrane permeability. Gram-positive bacteria were generally more susceptible than Gram-negative bacteria due to structural differences in cell wall composition.

Overall, the results suggest that transition metal complexes represent promising alternatives for the development of next-generation antimicrobial agents against multidrug-resistant microbial pathogens.

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