

Assessment of the Antibacterial Potential of Layered Double Hydroxides

Selina Ilunakan Omonmhenle^{1*}, Ikhazuagbe Hilary Ifijen²

¹Department of Chemistry,
Faculty of Physical Sciences,
University of Benin,
Benin City, Edo State,
Nigeria

² Department of Research Outreach,
Rubber Research Institute of Nigeria,
Benin-City, Edo State,
Nigeria

Email: selina.omonmhenle@uniben.edu

Abstract

Microbes play a crucial role in our lives, and certain pathogenic bacteria are responsible for a wide range of infectious illnesses, food safety, and environmental damage. Layered double hydroxide (LDH), a type of natural two-dimensional substance with a distinctive layered structure also known as anionic clays, has been established as a material that may be utilized to battle a variety of bacterial infections. The interesting properties of LDH include their ease of synthesis, unique structure, uniform distribution of different metal cations in the brucite layer, surface hydroxyl groups, flexible tunability, intercalated anions with interlayer spaces, swelling properties, oxo-bridged linkage, and high chemical and thermal stability, ability to intercalate different types of anions (inorganic, organic, biomolecules, and even genes), delivery of intercalated anions. In the field of biomaterials, LDH has gained prominence as a significant class of layered materials with promising applications. Here, emphasis has been placed on factors such as biocompatibility, anion exchange with the target ion, holding of guest species in the interlayer space, and controlled anion release in a given medium. By utilizing LDH's inherent biocompatibility, several studies have improved its antibacterial characteristics, enabling researchers to add active substances into its matrix for the treatment of bacterial-caused disease. Despite the fact that LDH's antibacterial capabilities have been the subject of several studies, there are currently very few reviews of such findings. Therefore, this study reviewed current developments in new LDH techniques to enhance their antimicrobial activity and provided background on their structures.

Keywords: Layered double hydroxides, antibacterial, biomaterial, biocompatibility

INTRODUCTION

Layered double hydroxides (LDH), often referred to as hydrotalcitelike anionic clay, are a subclass of ionic lamellar compounds made up of positively charged layers resembling brucite and charge-balancing anions and solvation molecules in the interlayer area (Zhang *et al.*, 2021). The general formula of LDH is $[M_1^{II}{}_x M_2^{III}(\text{OH})_2]^{x+} (\text{A}^n)_{x/n} \cdot m\text{H}_2\text{O}$ where M^{II} stands for divalent metal; M^{III} stands for trivalent metals and x is the mole ratio of $M^{III} / (M^{II} + M^{III})$, which is typically between 0.17 and 0.33,1 and subject to change for different applications

*Author for Correspondence

(Zhang *et al.*, 2021). In addition, LDH can contain M^+ and M^{4+} cations, such as Li^+ and Ti^{4+} , however these are only a few examples. Anions are balanced by an intercalated charge called an-. LDH have a wide range of applications, such as photochemistry, adsorption, CO_2 capture, drug delivery, and fire-retardant additives. However, the extent of their application as well as overall performance is severely constrained by the inevitable aggregation of the lamellar LDH flakes (Parida *et al.*, 2012; Pan *et al.*, 2016; Okolo *et al.*, 2015).

The synthesis of two-dimensional (2D) nanosheets of layered solids, such as metal chalcogenides, metal phosphates and phosphonates, layered metal oxides, as well as layered double hydroxides, has received a lot of attention in recent years (Wang *et al.*, 2017; Song and Hu, 2014; Yu *et al.*, 2017). The 2D nanosheet, with a thickness of about one nanometer and lateral sizes ranging from submicrometer to several tens of micrometers, has a higher specific surface area and more active sites, and it can be used for both fundamental research and as a building block to create a variety of functional materials (Ma and Sasaki, 2010).

Over the past ten years, significant advancements have been made in the synthesis of LDH, leading to new compositions and morphologies that enable improved applications in a variety of fields (Birgul *et al.*, 2012). Layered double hydroxides (LDH) have received a lot of attention in a number of technologically significant fields, including catalysis, separation, biomedicine drug storage-delivery agents, and environmental applications (Mohapatra and Parida, 2016; Omonmhenle and Shannon, 2016; Omonmhenle and Shannon, 2019a). This is because of their intriguing properties in anion exchangeability, compositional flexibility, and biocompatibility.

The recent interest in LDH is based on a number of characteristics: These materials exhibit a high degree of basicity, and the mixed oxides that result from thermal decomposition exhibit an even higher degree of basicity in relation to the oxide anions; intercalation of acidic anions results in systems with distinctive acid-base characteristics (Rives *et al.*, 2014). When mixed oxides (previously made by calcining some LDH at moderate temperatures) come into contact with solutions containing anions, they exhibit the so-called memory effect, or the capacity to regain their original layered structure (Mishraa *et al.*, 2018). Additionally, they have an anion exchange capacity (AEC) that is often greater than that of cationic clays. Contamination by microorganisms has emerged as one of the most important problems that needs academic or scientific attention.

Recent studies (Ifijen *et al.*, 2023a; Ifijen *et al.*, 2023b; Maliki *et al.*, 2022) have shown that infections caused by pathogenic microorganisms are a severe concern. This issue affects a wide range of businesses, including the textile and pharmaceutical industries, healthcare items, food packaging, and household goods (Busscher *et al.*, 2010; Ifijen *et al.*, 2022; Udokpoh *et al.*, 2023). It was suggested as a solution to this issue to intercalate the active antimicrobial molecule with an inorganic molecule that can hold it, enabling a very slow and controlled release under the right circumstances (Li *et al.*, 2020). LDH have a high potential as functional agent carriers due to their high biocompatibility, high chemical stability, and regulated release rate (Sokolova and Epple, 2008). However, there have only been a few studies on the use of LDH in active antimicrobial fields (Costantino *et al.*, 2008), therefore the rapid expansion of the use of antimicrobial LDH materials calls for a new analysis and more study. Regarding the structure and developments in their antibacterial uses, this review paper provides clear but in-depth information.

Structural description of layered double hydroxide

In order to balance out the net positive charge, layered double hydroxides contain exchangeable intercalated anions between the layers of positively charged brucite-type divalent and trivalent metals (Wijitwongwan *et al.*, 2021). According to Paredes *et al.* (2011), layered double hydroxide has a structure that is comparable to that of brucite, or $Mg(OH)_2$, in which each Mg^{2+} ion is octahedrally surrounded by six hydroxide ions. The link between O and H is perpendicular to the octahedral layer and is formed when each octahedral unit shares its edges to generate infinite layers.

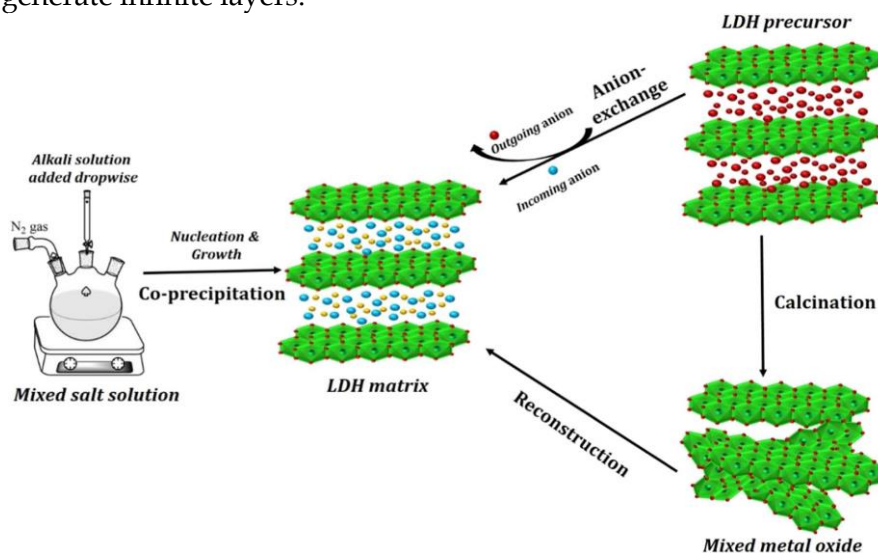


Fig. 1. Schematic representation of three methods of development and modification of LDH (Mishraa *et al.*, 2018)

Structure of layers

When double hydroxide is present in layers, the composition of the brucite structure can be changed by isomorphously substituting bivalent cations (M^{2+}) with trivalent cations (M^{3+}). This causes an excess of positive charge in the layer, which is counteracted by charge-balancing anions found in the interlayer galleries (Tang *et al.*, 2022). According to Tonelli *et al.* (2002), LDH has the generic formula $[M_{2+1-x}M_{3+x}(OH)_2]_x(Am^-)_x/m \cdot nH_2O$, where M^{3+} is trivalent cation, i.e., Al^{3+} , Fe^{3+} , and Cr^{3+} , and A is a counter anion with negative charge (m) and M^{2+} is bivalent cation, like Zn^{2+} , Mg^{2+} , Ca^{2+} , Ni^{2+} (Tonelli *et al.*, 2021). The centers of the edge-sharing octahedral structure are occupied by metal cations, according to Tang *et al.* (2002). Six OH^- ions make up each cation, and these ions point in all directions to produce infinite sheets. One of the primary structural characteristics of LDH materials is the uniform distribution of M^{2+} and M^{3+} cations in the hydroxide layers. Columbic attraction between positively charged layers and negatively charged interlayers exists in LDH composites. Additionally, hydrogen bonding occurs between the OH group of the metal hydroxides of the brucite type layers and the oxygen atom or any other electronegative atom of the intercalated anions.

With the notable exception of Al^{3+} (0.50 Å), which has an ionic radius of 0.50 Å, all divalent metal ions, from Mg^{2+} to Zn^{2+} , with an ionic radius in the range of 0.65-0.80 Å and all transition metal trivalent ions, with an ionic radius in the range of 0.62-0.69 Å, can enter the LDH hydroxide layers. The production of real brucite-like layers appears to be impossible at higher ionic radii (Ca, Cd, and Sc, La). The octahedral coordination will be lost by opening one side of the octahedron on the interlamellar domain, resulting to extra coordination with one interlamellar water molecule, if the radius of one of the metallic cations increases too much (Snyder *et al.*, 1990). These characteristics are shown in minerals from the hydrocalumite families, where the symmetry around the metal is reduced from $D3d$ to $C3v$.

Interlamellar anions

Anions and water molecules are present in the interlayer space of LDH. One of the key properties of LDH is that these interlamellar ions or molecules typically only form weak bonds with the host structure (Palinko *et al.*, 2022). Both during the creation of the lamellar structure and through subsequent anionic exchange, a wide range of anionic species may be found between the layers (Omonmhenle and Shannon, 2019b). The interlayer areas of LDH could be occupied by a huge number of anions, including organic and inorganic anions as well as the massive biomolecules (Palinko *et al.*, 2022). The interlayer arrangement depends on the interlayer packing related to the layer charge density as well as the anion size and the presence of water molecules; additional parameters such as the preparation method and the synthesis temperature may also have an impact (Wang *et al.*, 2022). The number of anions in the interlayer spacing is directly related to the charge density of the hydroxide layers, which can be controlled by the M_{2+}/M_{3+} ratio. These possible anions includes Biomolecules (DNA, amino acids, vitamins, peptides, nucleosides, etc.), Inorganic anions (F^- , Br^- , Cl^- , CO_3^{2-} , I^- , ClO_4^- , NO_3^- , $S_2O_3^{2-}$, SO_4^{2-} , $NiCl_4^{2-}$, CrO_4^{2-} , $Fe(CN)_6^{3-}$, $CoCl_4^{2-}$, and $Fe(CN)_6^{4-}$ etc.), anionic complexes (ferro and ferricyanide, $(PdCl_4)^{2-}$, etc.) and Organic anions (phosphonates, carboxylates, benzoates, alkyl sulfates, etc.).

The basal spacing of the layers is drastically altered depending on the size, charge, and layout of these interlamellar species (Wang *et al.*, 2022). However, it is more challenging to characterize the structure of interlamellar domains than it is the major layers. The anions position themselves to interact with the layers of positively charged hydroxide as much as possible. To ensure close connection between the oxygen atoms and the layer by generating hydrogen bonds, the CO_3^{2-} anions in pure LDH lie parallel to the hydroxide layers. When organic anions interact, their hydrophobic hydrocarbon chains are pushed far away from the surfaces of the hydrophilic layer and take on the lowest energy conformation (Feron *et al.*, 1994). This is because the anionic groups of organic anions are tightly hydrogen bound to the surface of hydroxyl groups. In order to improve the photoactivity with effective charge separation, the interlayer water and hydronium ions of the layered materials are crucial (Chen *et al.*, 2010). LDH's gallery height can hold a lot larger anion molecule. According to reports, the photocatalytic activity is increased when big anions are intercalated as opposed to the original layered oxides. This is caused by the interlayer gap, which promotes the reaction between the reactant molecules that prevent charge recombination and the photogenerated charge carriers (Zong and Wang, 2014). According to a report, LDH's OH groups may increase its antibacterial action. According to Moaty *et al.* (2016), the surface hydroxyl groups are changed into HO% radicals, the reactive oxygen species (ROS) that have the capacity to harm the DNA and cytoplasmic membrane of bacteria.

Advantages of LDH (Mishraa *et al.*, 2018)

- Although LDH are natural clays, a similar substance can be synthesized.
- Due to their great capacity for exchanging anions, various anions can be intercalated within the LDH interlamellar region.
- They have a wide range of uses, including in ceramics, fillers, diverse add-ons, fabric modifiers, etc.
- Under specific circumstances, they have the ability to sustain the discharge of the intercalated substance.
- they can be used to remove dangerous chemicals from water through adsorption and intercalation, which is known as environmental remediation.

Disadvantages of LDH (Mishraa *et al.*, 2018)

- The ratio of divalent to trivalent cations must be between 2:1 and 4:1 for appropriate LDH synthesis to occur. LDH fails to develop at levels below and above this percentage.
- If the precursor was calcined between 300 and 500 °C, reconstruction, or the so-called memory effect, will be possible. Beyond this point, LDH will establish a stable spinel structure and won't return to its initial configuration.
- The majority of LDH is not stable in neutral or alkaline pH, but is soluble in acidic pH, hence its composites are ineffective in this environment.

Layered double hydroxides (LDH) as antimicrobial biomaterials

Major societal and economic damages are caused by antimicrobial agent resistance. According to the World Health Organization, antibiotic resistance causes 700,000 deaths worldwide each year (Ifijen *et al.*, 2023c). Another difficult field of research is the creation of biomaterials with antibacterial characteristics, as many diseases in the modern world are brought on by germs (Maliki *et al.*, 2023). Numerous products, including medical implants, medical gadgets, food packaging, healthcare products, and household items, utilize biomaterials with antimicrobial capabilities (Costantino *et al.*, 2008; Saifullah and Hussein, 2015; Mokobia *et al.*, 2023). The LDH composite will act as expected depending on the type and function of the intercalated or included species, which is a well-known property of LDH. Therefore, the composite can act as an antibacterial material if some antimicrobial species are intercalated or incorporated into LDH. This idea was taken into account when nano silver was added to ZnAl LDH, and the composite's antibacterial activity was confirmed (Carja *et al.*, 2009). The substance was discovered to have effective antibacterial properties against both gram positive and gram-negative microorganisms.

Silver nanoparticles (NPs) have been shown to have potent antibacterial effects, but because of their high level of toxicity, they are used less frequently (Saifullah and Hussein, 2015). In order to make silver nanoparticles (NPs) more biocompatible, Marcato *et al.* (2013) created biogenic silver NPs (AgNPbio) with Mg/Al LDH. When they tested the biocompatibility of free AgNPbio, LDH, and AgNPbio LDH against the lung fibroblast cell line V79, they discovered that AgNPbio killed 50% of the cells at a concentration of 45 $\mu\text{mol/L}^{-1}$. LDH alone and AgNPbio LDH did not exhibit any toxicity, even at a concentration of 45 $\mu\text{mol/L}^{-1}$. This distinction can be linked to AgNPbio's immobilization on the surface of LDH, indicating that LDH may be employed as a means of bringing AgNPbio into compatibility with aesthetic and medicinal uses. The minimum inhibitory concentration (MIC) of AgNPbio is very low, measuring just 6.6 $\mu\text{g mL}^{-1}$ against Gram-positive (*S. aureus*) and 12 $\mu\text{g mL}^{-1}$ against Gram-negative (*E. coli*) bacteria (Marcato *et al.*, 2013). In addition, it was discovered that AgNPbio LDH hybrid material retained the antibacterial action. This appealing hybrid material is suitable for application in cosmetics, home goods, and biomedical technology. The manufacture of AgNPs on the surface of LDH (AgNP LDH) was a previous use of a technology comparable to this for the preparation of hybrid material (Carja *et al.*, 2009). AgNP LDH maintained the inhibitory zone against Gram-positive *S. aureus* and Gram-negative *E. coli*, according to their evaluation of the antimicrobial effects of AgNPs alone and hybrid AgNP LDH with regard to time.

The development of effective natural product-based antimicrobial formulations is hampered by the thermal instability, photodegradation, and poor bioavailability of natural active components. By incorporating natural active substances into different nanostructures, these hereditary problems may be successfully reduced. Curcuminoids were added to Mg-Al layered double hydroxides using a unique green mechanochemical synthesis method

described by Madhusa *et al.* in 2021. Improved energy efficiency results from the one-pot, scalable synthetic technique that eliminates the need for time-consuming, harmful solvent-based processes. The surface and interlayer curcuminoids that make up the hydrotalcite-shaped nanohybrids exhibit weak interactions with layered double hydroxides, which is supported by X-ray diffractograms, X-ray photoelectron spectra, and Fourier transmission infrared spectra. The curcuminoids' structural and morphological characteristics contributed to their greater thermal stability. At pH 5.5, the release of the curcuminoids was slow and continuous for up to 7 hours (Fig. 2). The created nanohybrids showed zeroth-order dynamics, which encouraged transdermal application. In addition, the effectiveness of curcuminoid incorporated LDHs (CC-LDH) as an anticolonization agent was examined against four wound biofilm-forming pathogens, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, methicillin-resistant *Staphylococcus aureus*, and *Candida albicans*, using a broth dilution method and an *in vitro* biofilm model system. In produced nanohybrids compared to pure curcuminoids, microbiological investigations showed a 54–58% reduction in the ability of bacterial pathogens to build biofilms. In light of their enhanced dermatological/medical qualities, it is clear that these CC-LDH nanohybrids made by green chemistry are suitable for next-generation antimicrobial applications.

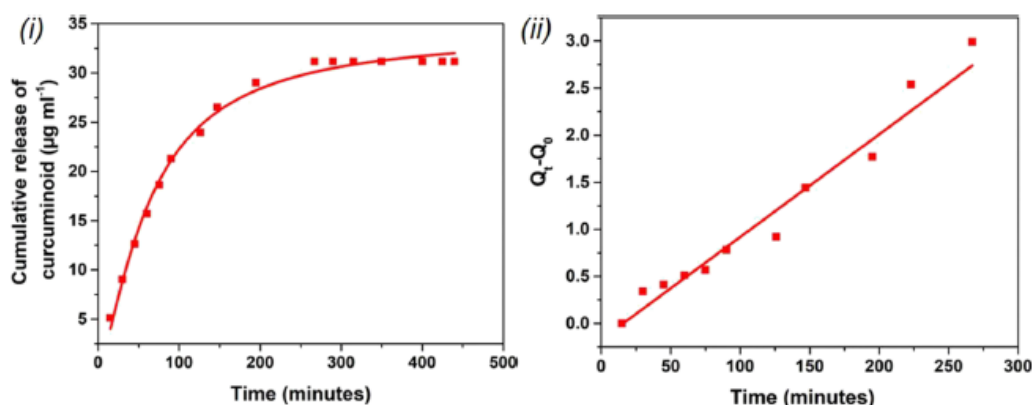


Fig. 2. (i) Release profiles of curcuminoids from CC-LDH at pH 5.5 under ambient conditions and (ii) best linear fit (zeroth-order model) of the release of curcuminoids (Madhusa *et al.*, 2021)

In order to make Mg²⁺ in MgAl-layered double hydroxides nanoparticles (MAI-LDHs, M: Mg²⁺, Cu²⁺, Ni²⁺, Co²⁺, and Mn²⁺) that might be employed as antibacterial agents, Li *et al.* (2020) used a straightforward strategy. XRD, FTIR spectroscopy, and TEM were used to examine the phase structural and morphological characterizations of MAI-LDHs. According to the findings, all MAI-LDHs showed normal layered structures with the exception of MnAl-LDH, which featured Mn₃O₄ phases. CuAl-LDH had a rod-like form, while MnAl-LDH had a specific morphology with ellipsoids, spherical, and rod-like structure. CuAl-LDH, NiAl-LDH, CoAl-LDH, and MnAl-LDH all had IC₅₀ values in the range of 800–1500 g/mL (the level exhibiting 50% antibacterial activity). In disk diffusion testing, the dosages of CuAl-LDH, CoAl-LDH, and MnAl-LDH with >10 mm inhibition zones were between 150 and 300 g/disk. The combined effects of the environment, surface contacts, particle shape, ROS, and metal ions may be responsible for the antibacterial properties of MAI-LDHs. The findings point to an easy way to create powerful antibacterial compounds based on LDHs, which may find use in antibacterial coating and water treatment.

By partially releasing metallic ions in an aqueous dispersion, the usage of layered double hydroxides (LDHs) as antibacterial materials may offer a strategy to lower the risk of bacterial infections and antibacterial resistance. The partial dissolution of various synthetic LDHs M^{II}-Al^{III} (M = Zn, Cu, Ni, Co, Mg) was investigated by Awassa *et al.* in Lysogeny Broth (LB) and

Tryptic Soy Broth (TSB), which are growth media for the bacterium *Escherichia coli* (*E. coli*) and *Staphylococcus aureus* (*S. aureus*), respectively. Crystallinity, the $M^{II}:Al^{III}$ ratio, the kind of intercalated anion (CO_3^{2-} , Cl^- , NO_3^- , ClO_4^-), as well as the makeup of the M^{II} cations, were all examined for their effects. Without any post-synthetic hydrothermal treatment, $Zn^{II}-Al^{III}$ LDH demonstrated a 6 times increased release of Zn^{II} ions. A similar result was seen when the $Zn^{II}-Al^{III}$ molar ratio was increased to 3:1 and carbonate anions were switched for cations with lower intercalating affinity. The dissolution characteristics of $M^{II}-Al^{III}$ LDHs were associated with the thermodynamic stability of their $M^{II}(OH)_2$ hydroxide counterparts, with the exception of Cu^{II} -based LDHs, which demonstrated an amplified release of Cu^{II} due to their irregular structure and flaws. Last but not least, Zn^{II} and Cu^{II} -based LDHs were the only ones with antibacterial activity reported. The kind of divalent metal itself and the quantity of released M^{II} ions into the culture media were both factors in the antibacterial impact of the LDHs under study. This impact was more clearly shown in $Zn^{II}-Al^{III}$ LDHs, where greater Zn^{II} ion release considerably reduced the minimum inhibitory concentration from 12 to 0.375 mg. mL⁻¹.

To increase the effectiveness of these antibiotic-free antibacterial agents, it is crucial to comprehend the mechanisms behind the interactions between layered double hydroxides (LDHs) and bacterial surfaces. Actually, the function of surface contacts in the antibacterial activity of zinc-based LDH nanoparticles is still poorly understood in comparison to that of dissolution and the production of reactive oxygen species (ROS). Awassa *et al.* (2022b) investigated the part surface interactions play in the antibacterial activity of $ZnAl$ LDH NPs. In contrast to $MgAl$ LDH, which is not bactericidal, $ZnAl$ LDH NPs demonstrated specific antibacterial action against *S. aureus* (Fig. 3). The enhanced antibacterial activity of nano-sized $ZnAl$ LDH NPs in comparison to micron-sized $ZnAl$ LDHs served as proof of the contribution of surface interactions to the antibacterial activity of LDHs. For comparable amounts, broth microdilution antibacterial experiments revealed that the MIC was 16 times lower for $ZnAl$ NPs, indicating an effect beyond the simple breakdown into Zn^{2+} antibacterial ions. Agar disk diffusion revealed an inhibition zone that was two times larger. The substantial morphological effects, such as membrane deformation, swelling, and dissociation into cell debris, that were seen on the surface of *S. aureus* cells after treatment with $ZnAl$ LDH NPs at MIC indicate that direct contact interactions must be taken into account. The surface adhesion interactions between the cell surface and LDHs were also investigated using LDH-functionalized AFM tips developed using AFM-based FS. High adhesion frequency *S. aureus* cell wall recognition was achieved by $ZnAl$ -functionalized AFM tips. Additionally, the comparison of the adhesion behavior of three different AFM tips, such as those coated with Al , those functionalized with $MgAl$, and those functionalized with $ZnAl$, showed the existence of particular surface contacts between $ZnAl$ LDHs and *S. aureus* cells. Such a discovery revealed the existence of a substantial association between the particular capacity of zinc-based LDHs to attach and destroy bacterial cell walls, confirming the hypothesis that pure LDHs have an antibacterial mechanism based on direct surface contacts.

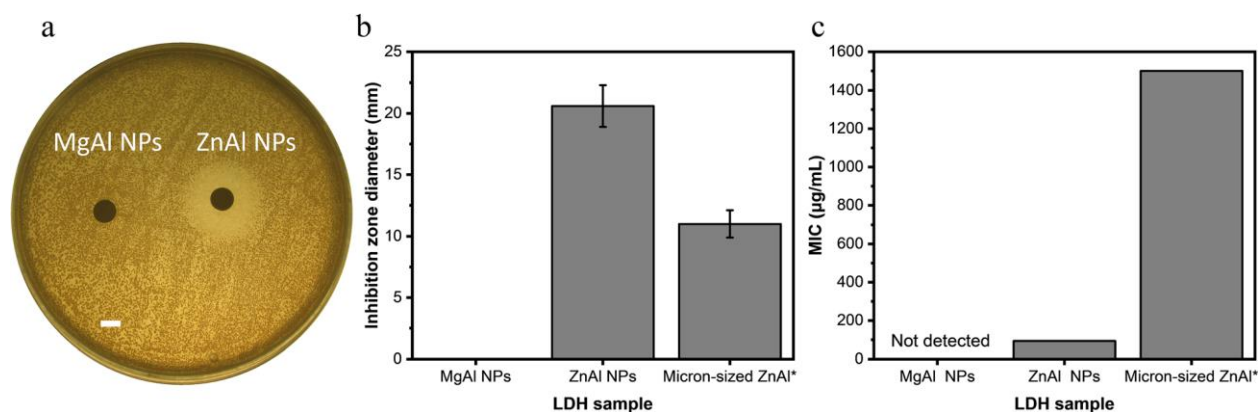


Fig. 3: ZnAl LDH nanoparticles antibacterial activity against *S. aureus*. (a) Agar disk diffusion test using 10 mg mL⁻¹ ZnAl and MgAl NPs suspensions (scale bar = 5 mm). (b) Mean zone of inhibition of MgAl, ZnAl NPs and micron-sized ZnAl LDH calculated as the average inhibition diameters of three repetitive trials. (c) MIC values for MgAl, ZnAl NPs and micron-sized ZnAl LDH calculated as the average MIC of three repetitive trials (Awassa *et al.*, 2022b).

A protein found in practically all living organisms is lysozyme. Animals generate the antibacterial enzyme lysozyme, which is a component of the innate immune system (Ferraboschi *et al.*, 2021). Tears, saliva, milk, and other fluids are all rich in lysozyme. In egg white, lysozyme can be detected in large quantities. The glycoside hydrolase lysozyme breaks down 1, 4-beta-linkages between N-acetylmuramic acid and N-acetyl-D-glucosamine residues in peptidoglycan, the main building block of the cell walls of gram-positive bacteria (Ferraboschi *et al.*, 2021). Lysozyme can be used to increase antibacterial activity against gram-positive bacteria rather than gram-negative ones, according to studies. In 2018, Wang *et al.* synthesized MgAl-LDH, ZnAl-LDH, and ZnMgAl-LDH covered with lysozyme, characterized the structure and morphology, tested the antibacterial capabilities in culture media, and assessed the biotoxicity in vitro and in vivo. The ZnMgAl-LDH flower-like structure has a rough surface, lysozyme covers it with a perfect ring, and exhibits good antibacterial properties that aid in mouse wound healing. Lyso@ZnMgAl-LDH has greater antibacterial activity than binary LDHs because the bloom floral structure of ZnMgAl-LDH may increase the loading rate of lysozyme while the rougher surface can adhere more bacteria.

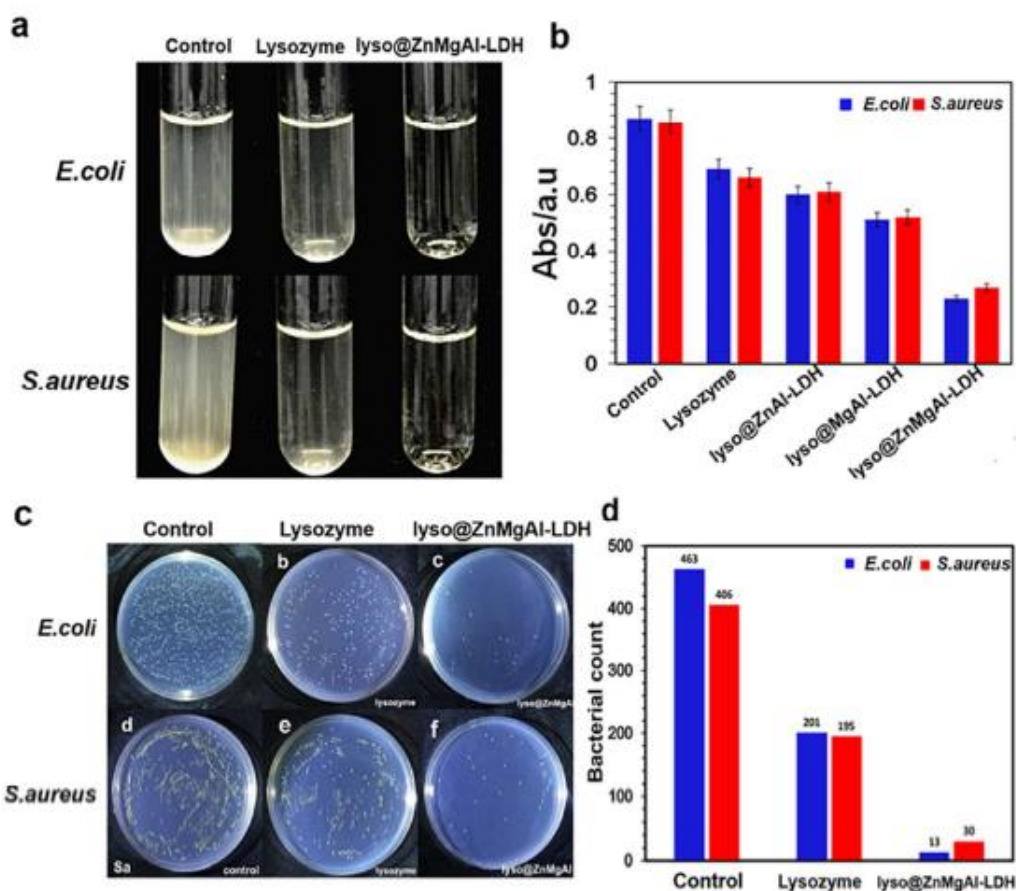


Fig. 4: Antibacterial activity comparison of lysozyme covered LDHs. Antibacterial activity of lyso@ZnMgAl-LDH in LB liquid medium with *E. coli* and *S. aureus* (a: the photo images of lyso@ZnMgAl-LDH with bacteria after culturing for 18 hours; b: the OD values of lyso@MgAl-LDH, lyso@ZnAl-LDH and lyso@ZnMgAl-LDH with bacteria samples; the agar plates pictures of control, lysozyme and lyso@ZnMgAl-LDH samples with *E. coli* and *S. aureus* (c), and the corresponding the number of bacterial colonies (d). (Control sample: only PBS was added into the media; the concentration of individual lysozyme group and lyso@ZnMgAl-LDH is 1.28 mg mL⁻¹, 1.28 mg lyso@ZnMgAl-LDH contains 0.41 mg lysozyme) (Wang *et al.*, 2018).

CONCLUSIONS

Superior host compounds that are capable of intercalating a variety of guest ions include layered double hydroxides (LDHs). The way the layers of the brucite-like structure are arranged gave rise to their distinctive structural properties. Its interlamellar gap, one of its unique properties, is what makes it most useful. By integrating active compounds with therapeutic qualities, several research have taken use of this characteristic to develop antibacterial therapeutics. They can also be formed with metallic materials either by intercalation or by surface contacts, resulting in remarkable material with enhanced antibacterial capability. They can intercalate a variety of anions, including medicinal drugs, biopolymers, and some biomolecules. This review effectively assessed LDH's potential for antibacterial research. LDH can be used to treat bacterial infections, according to the findings of their studies, but it can also be improved by intercalating with other substances.

Competing interests

On behalf of all authors, the corresponding author states that there is no conflict of interest.

REFERENCES

- Awassa, J., Cornu, D., Soule, S., Carteret, C., Ruby, C., and El-Kirat-Chatel, S. (2022b). Divalent metal release and antimicrobial effects of layered double hydroxides. *Applied Clay Sci.* 216: 106369.
- Awassa, J., Soulé, S., Cornu, D., Ruby, C., and El-Kirat-Chate, S. (2022a). Understanding the role of surface interactions in the antibacterial activity of layered double hydroxide nanoparticles by atomic force microscopy. *Nanoscale*.14: 10335.
- Birgul, Z.K., and Ahmet, A. (2012). Layered double hydroxides – multifunctional nanomaterials. *Chem. Pap.* 66: 1–10.
- Busscher, H.J., Rinastiti, M., Siswomihardjo, W., and Mei, V.D.H.C. (2010). Biofilm formation on dental restorative and implant materials. *J. Dent. Res.* 89: 657–665.
- Carja, G., Kameshima, Y., Nakajima, A., Dranca, C., and Okada, K. (2009). Nanosized silver anionic clay matrix as nanostructured ensembles with antimicrobial activity. *Int. J. Antimicrob. Agents* 34: 534–539.
- Carja, G., Kameshima, Y., Nakajima, A., Dranca, C., and Okada, K. (2009). Nanosized silveranionic clay matrix as nanostructured ensembles with antimicrobial activity. *Int. J. Antimicrob. Agents* 34: 534–539. *Chemical Lett.* 31(6): 1511-1515.
- Chen, X., Shen, S., Guo, L., and Mao, S.S. (2010). Semiconductor-based photocatalytic hydrogen generation. *Chem. Rev.* 110: 6503–6570.
- Costantino, U., Ambrogi, V., Nocchetti, M., and Perioli, L. (2008). Hydrotalcite-like compounds: versatile layered hosts of molecular anions with biological activity. *Microporous Mesoporous Mater.* 107: 149–160.
- Fernon, V., Vichot, A., Colombet, P., Damme, H., and Bégin, F. (1994). Synthesis and structure of calcium aluminate hydrates intercalated by aromatic sulfonates. *Mater. Sci. Forums* 152-153:335–338.
- Ferraboschi, P., Ciceri, S., and Grisenti, P. (2021). Applications of Lysozyme, an Innate Immune Defense Factor, as an Alternative Antibiotic. *Antibiotics* 10(12): 1534.
- hydroxide assembled with transition metals *via* a facile preparation method. *Chinese*
- Ifijen, I.H., Ikhuoria, E.U., and Omorogbe, S.O. *et al.* (2023a). Chemical, plant and microbial mediated synthesis of tin oxide nanoparticles: antimicrobial and anticancer potency. *Braz. J. Chem. Eng.* DOI: <https://doi.org/10.1007>.
- Ifijen, I.H., Maliki, M., and Anegebe, B. (2022). Synthesis, photocatalytic degradation and antibacterial properties of selenium or silver doped zinc oxide nanoparticles: A detailed review. *OpenNano.* 8: 100082.
- Ifijen, I.H., Maliki, M., Udokpoh, N.U., Odiachi, I.J., and Atoe, B. (2023b). A Concise review of the antibacterial action of gold nanoparticles against various bacteria. In: TMS 2023 152nd Annual Meeting & Exhibition Supplemental Proceedings. TMS 2023. *The Min. Met. Mater. Series. Springer, Cham.* https://doi.org/10.1007/978-3-031-22524-6_58.
- Ifijen, I.H., Udokpoh, N.U., Maliki, M., Ikhuoria, E.U., and Obazee, E.O. (2023c). A review of nanovanadium compounds for cancer cell therapy. In: TMS 2023 152nd Annual Meeting & Exhibition Supplemental Proceedings. TMS 2023. *The Min. Met. Mater. Ser. Springer, Cham.* DOI: https://doi.org/10.1007/978-3-031-22524-6_59.
- Li, M., Li, L., and Lin, S. (2020). Efficient antimicrobial properties of layered double hydroxide assembled with transition metals *via* a facile preparation method. *Chinese Chemical Lett.* 31(6): 1511-1515.
- Ma, R., and Sasaki T. (2010). Nanosheets of oxides and hydroxides: Ultimate 2D charge-bearing functional crystallites. *Adv. Mater.* 22(45): 5082-104.
- Madhusa, C., Rajapaksha, K., Munaweera, I., de Silva, M., Perera, C., Wijesinghe, G., Weerasekera, M., Attygalle, D., Sandaruwan, C., and Kottegoda, N. (2021). A novel green approach to synthesise curcuminoid-layered double hydroxide nanohybrids: adroit biomaterials for future antimicrobial applications. *ACS Omega.* 6: 9600–9608.

- Maliki, M., Ifijen, I.H., and Ikhuoria, E.U. *et al.* (2022). Copper nanoparticles and their oxides: optical, anticancer and antibacterial properties. *Int Nano Lett* **12**, 379–398.
- Maliki, M., Omorogbe, S.O., Ifijen, I.H., Aghedo, O.N., and Ighodaro, A. (2023). Incisive Review on Magnetic Iron Oxide Nanoparticles and Their Use in the Treatment of Bacterial Infections. In: TMS 2023 152nd Annual Meeting & Exhibition Supplemental Proceedings. TMS 2023. *The Min. Met. Mater. Series*. DOI: <https://doi.org/10.1007>.
- Mishraa, G., Dasha, B., and Pandeya, S. (2018). Layered double hydroxides: A brief review from fundamentals to application as evolving biomaterials. *Applied Clay Sci.* **153**: 172–186.
- Moaty, S.A.A., Farghali, A.A., and Khaled, R. (2016). Preparation, characterization and antimicrobial applications of Zn-Fe LDH against MRSA. *Mater. Sci. Eng. C* **68**: 184–193.
- Mohapatra, L., and Parida, K.M. (2016). A review on the recent progress, challenges and perspective of layered double hydroxides as promising photocatalysts. *J. Mater. Chem. A*. **4**: 10744–10766.
- Mokobia, K.E., Ifijen, I.H., and Ikhuoria, E.U. (2023). ZnO-NPs-coated implants with osteogenic properties for enhanced osseointegration. In: TMS 2023 152nd Annual Meeting & Exhibition Supplemental Proceedings. TMS 2023. *The Min. Met. Mater. Ser. Springer, Cham*. DOI: https://doi.org/10.1007/978-3-031-22524-6_27.
- Okolo, P.O, Omonmhenle, S.I., Abdulsalaam, A.O., and Ofunne, C.N. (2015). Novel applications of locally sourced montmorillonite (MMT) clay as a disintegrant in the formulation of pharmaceutical product. *Bayero J. Pure and Applied Sci.* **8**(1):153.
- Omonmhenle, S.I., and Shannon, I.J. (2016). Synthesis and characterization of surfactant enhanced Mg–Al hydrotalcite-like compounds as potential 2-chlorophenol scavengers. *Applied Clay Sci.* **127–128**: 88–94.
- Omonmhenle, S.I., and Shannon, I.J. (2019a). Influence of varying synthetic routes on the physicochemical properties of Mg–Al–CO₃ and Zn–Al–CO₃ hydrotalcite-like compounds: a comparative study. *European Scientific J*: **15**(12): 52–66.
- Omonmhenle, S.I., and Shannon, I.J. (2019b). Effect of Interlamellar Composition on ZnAlHydrotalcites: Synthesis and Characterization. *European Scientific Journal*. **15**(12): 317.
- Palinko, I., Sipos, P., Berkesi, O., and Varga, G. (2022). Distinguishing anionic species that are intercalated in layered double hydroxides from those bound to their surface: a comparative ir study. *J. Phys. Chem. C*. **126**(36): 15254–15262.
- Pan, H., Wang, W., Shen, Q., Pan, Y., Song, L., Hu, Y., and Lua, Y. (2016). Fabrication of flame-retardant coating on cotton fabric by alternate assembly of exfoliated layered double hydroxides and alginate. *RSC Adv.* **6**: 111950–111958.
- Paredes, S.P., Valenzuela, M.A., Fetter, G.S., and Flores, O. (2011). TiO₂/Mg–Al layered double hydroxides mechanical mixtures as efficient photocatalysts in phenol degradation. *J. Phys. Chem. Solids* **72**: 914–919.
- Parida, K., Satpathy, M., and Mohapatra, L. (2012). Incorporation of Fe³⁺ into Mg/Al layered double hydroxide framework: effects on textural properties and photocatalytic activity for H₂ generation. *J. Mater. Chem.* **22**: 7350.
- Rives, V., del Arco, M., and Martín, C. (2014). Intercalation of drugs in layered double hydroxides and their controlled release: a review. *Appl. Clay Sci.* **88–89**: 239–269.
- Saifullah, B., and Hussein, M.Z., 2015. Inorganic nanolayers: structure, preparation, and biomedical applications. *Int. J. Nanomed.* **10**: 5609–5633.
- Snyder, E.E., Buoscio, B.W., and Falke, J.J. (1990). Calcium (II) site specificity: effect of size and charge on metal ion binding to an EF-hand-like site. *Biochem.* **29**(16): 3937–43.

- Sokolova, V., and Epple, M. (2008). Inorganic nanoparticles as carriers of nucleic acids into cells. *Angew. Chem. Int. Ed.* 47: 1382–1395.
- Song, F., and Hu, X. (2014). Exfoliation of layered double hydroxides for enhanced oxygen evolution catalysis. *Nat. Commun.* 5: 4477.
- Tang, L., Xie, X., Li, C., Xu, Y., Zhu, W., and Wang, L. (2022). Regulation of structure and anion-exchange performance of layered double hydroxide: function of the metal cation composition of a brucite-like layer. *Mater* 15: 7983.
- Tonelli, D., Gualandi, I., Musella, E., and Scavetta, E. (2021). Synthesis and Characterization of Layered Double Hydroxides as Materials for Electrocatalytic Applications. *Nanomater.* 11(3):725.
- Udokpoh, N.U., Jacob, J.N., Archibong, U.D., Onaiwu, G.E., and Ifijen, I.H. (2023). Utilizations of graphene-based nanomaterials for the detection and treatment of *mycobacterium tuberculosis*. In: TMS 2023 152nd Annual Meeting & Exhibition Supplemental Proceedings. TMS 2023. *The Min. Met. Mater. Series.* Springer, Cham. DOI: <https://doi.org/10.1007>.
- Wang, X., Zhao, H., Chang, L., Yu, Z., Xiao, Z., Tang, S., Huang, C., Fan, J., and Yang, S. (2022). First-principles study on interlayer spacing and structure stability of nial-layered double hydroxides. *ACS Omega.* 7(43): 39169-39180.
- Wang, Z., Yu, H., Ma, K., Chen, Y., Zhang, X., Wang, T., Li, S., Zhu, X., and Wang, X. (2018). Flower-like surface of three-metal-component layered double hydroxide composites for improved antibacterial activity of lysozyme. *Bioconjugate Chem.* 29(6): 2090–2099.
- Wijitwongwan, R.P., Intasa-Ard, S.G., and Ogawa, M. (2021). Preparation of MgGa layered double hydroxides and possible compositional variation. *Nanomater.* 11(5): 1206.
- Yu, j., Wang, Q., O'Hare, D., and Sun, L. (2017). Preparation of two-dimensional layered double hydroxide nanosheets and their applications. *Chem. Soc. Rev.* 46: 5950-5974.
- Zhang, Y., Xu, H., and Lu, S. (2021). Preparation and application of layered double hydroxide nanosheets. *RSC Adv.* 11: 24254.
- Zong, X., and Wang, L. (2014). Ion-exchangeable semiconductor materials for visible light induced photocatalysis. *J. Photochem. Photobiol. C: Photochem. Rev.* 18: 32–49.