Advances in Layered Double Hydroxides Coatings on Metallic Implants: A Mini Review

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Mini Review

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ABSTRACT

Surface modification strategies enable implants to exhibit bio functions, facilitating precise and localized treatments while minimizing systemic toxicity and ensuring prolonged therapeutic effects. Evaluated against criteria that include biodegradability, biocompatibility, corrosion control, and bio-functionality, Layered Double Hydroxide (LDHs) Nano sheets are considered exemplary coating materials, garnering considerable interest in the field of implant surface modifications. This mini-review concentrates on the considerable advancements in the development, synthesis, and clinical applications of LDH-based coatings for implants that have recently been accomplished.

Keywords: Layered double hydroxides; Metallic implants; Surfaces; Bio functions

INTRODUCTION

Layered Double Hydroxides (LDHs) are a class of inorganic two-dimensional nanomaterials. Their structure is commonly likened to a sandwich, with positively charged metal hydroxide layers analogous to the bread and intercalated anions representing the filling [1]. Notable features of LDHs include biodegradability, a tunable chemical composition (include metal element and interclated anions), anion exchange capacity, pH sensitivity, and "memory" effect [2]. Over the past decade, our group has conducted extensive work on modifying metal implants with LDHs nanosheets, endowing them with specific biological functions according to their particular medical application scenarios and limitations. The layered structure of LDHs can capture and block corrosive chloride ions, which prompted the initial development of their coating form for anti-corrosion on industrial metal substrates [3]. With the evolution of advanced biomaterials technology, provided the original author and source are credited.

investigative efforts on LDHs coatings have expanded to a range of metallic implants, Including Nickel-Titanium (NiTi) stents, Titanium (Ti)-based implants , and biodegradable Magnesium (Mg) based implants [4-11].

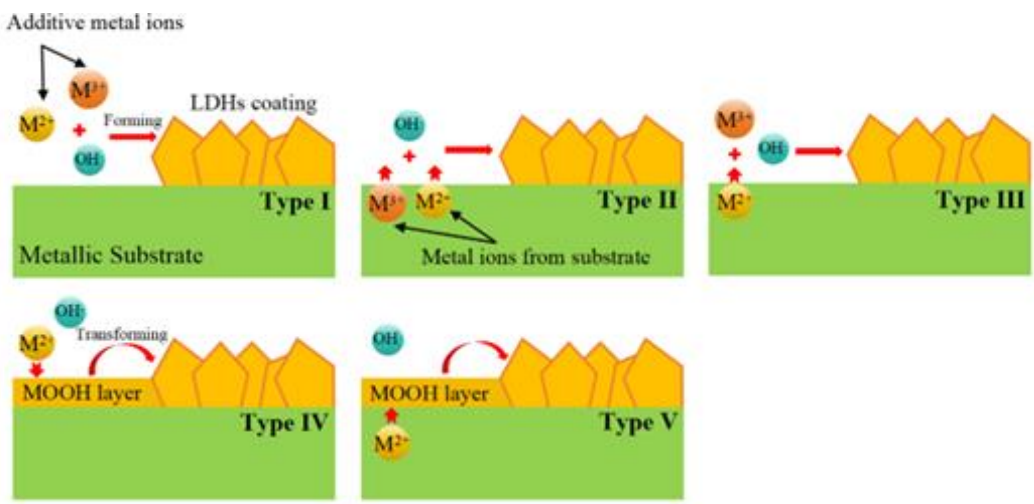
Substantial advances have been realized in the synthesis techniques for LDHs coatings, as well as in the study of their biological functions, investigation and comparison of properties, and the tailored design of various functional LDHs coatings [12].

Synthetic route and method

The synthesis of LDHs necessitates divalent (M^{2+}) and trivalent (M^{3+}) metal ions within an alkaline environment [13]. Initially, hydroxide ions precipitate with one type of metal ion. Subsequent substitution by another metal ion creates an excess charge, which is neutralized as anions intercalate into the interlayer space, culminating in the formation of LDHs Nano sheets with a characteristic layered structure [14]. Currently, classification of LDHs coating preparation route and method encompasses five methods as illustrated in the accompanying (Figure 1) (I) Co-precipitation of metal ions with different valences in an alkaline environment to form a coating on the substrate; (II) Corrosion-induced dissolution of two metal elements from the substrate in an alkaline medium, followed by simultaneous precipitation with OH-; (III) akin to the type II method, but, specifically involving substrate dissolution of divalent metal ions; (IV) To simulate the formation process of LDHs, initially, a layer of metal hydroxide is prepared on the surface of substrate to act as a precursor, and subsequent partial substitution of trivalent metal ions in the hydroxide with divalent metal ions transforms this precursor layer into an LDH coating; (V) Analogous to type IV method, involves additional divalent metal ions sourced from the substrate's dissolution.

Figure 1. Different routes and methods for fabricating LDHs coatings on metallic implants surface.

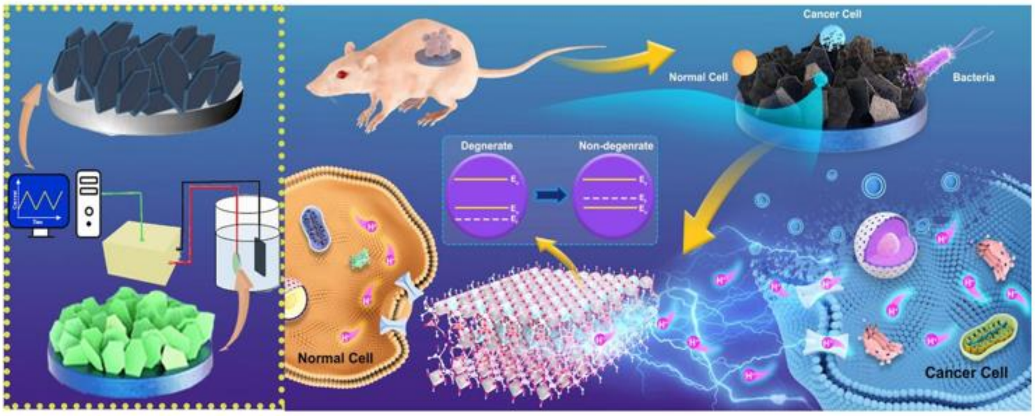
Note: Non *In-situ* grow method: Type I and type IV, *In-situ* grow method: Type II, III and V.



Biomedical applications involving various types of implants

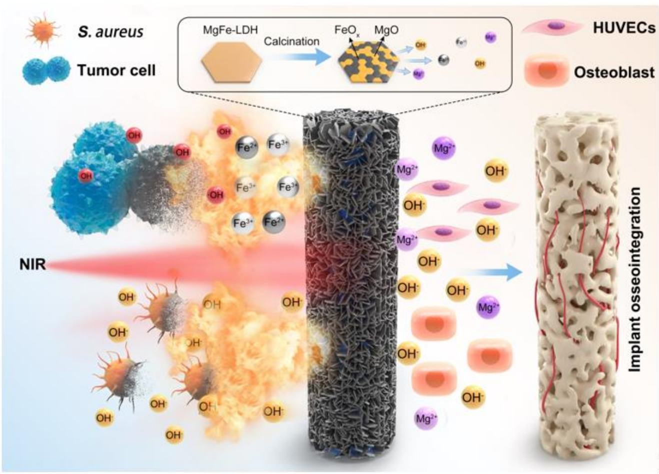
NiTi stent: The two high content metallic elements inherent in NiTi alloys are undoubtedly the best choice for preparing NiTi LDHs using type II method. Our group has successfully fabricated Ni-Ti LDH coatings, varying both in morphology and Ni/Ti ratios, on NiTi alloy substrates [15]. Building upon this foundation, our team engineered a suite of drug-loaded Layered Double Hydroxide (LDH) coatings capable of controlled drug release, using the micro environmental responsiveness of LDHs to acidity and hydrogen peroxide (H_2O_2). These drugs include doxorubicin, butyrate, and arsenic to achieve selective anti-tumor/bacteria effect according different needs [4, 6, 16]. Recently, Wang et al. reported a compelling study in which they developed a designed a degenerate Ni-Ti LDHs coating through electrochemical charging [17]. This innovative coating enables microenvironment-responsive electrotherapy, as depicted in (Figure 2), and possesses the capacity for timely and intelligent detection of physiological requirements. Upon contact with tumor cells, the coating transitions from a degenerate state, releasing holes that effectively target and neutralize the tumor cells. Conversely, when interacting with normal tissue, the rate of hole release is considerably slower, thereby inflicting minimal harm.

Figure 2. Schematic illustration of H^+-induced discharging of degenerate LDH films and their selective antitumor and antibacterial effects.



Ti-based implants: In contrast to NiTi alloys, the chemically stable surface of Ti impedes the dissolution of Ti ions and their involvement in the formation of LDHs coatings. Consequently, type I and IV method predominate in the preparation route. Tan et al. pioneered research in this domain by fabricating Mg-Al LDH coatings on pure Ti surfaces, followed by calcination at varying temperatures to produce surfaces conducive to distinct alkaline microenvironments [7]. They systematically investigated the influence of these alkaline microenvironments on bacterial and osteogenic responses, achieving equilibrium in their effects. In their subsequent studies, they employed the Type IV method to produce a Mg-Fe LDH coating, which, following thermal reduction in a hydrogen atmosphere, yielded a MgO/FeOx Nano sheet coating on a Ti substrate (Figure 3) [9]. This coating exhibited notable per oxidative and photo thermal activities, culminating in a combined chemo dynamic and photo thermal antitumor effect. Furthermore, the coating generated an alkaline microenvironment that suppresses bacterial energy metabolism, thus potentiating the photo thermal antibacterial efficacy. Additionally, the Mg^{2+} enriched alkaline environment on the film facilitated osteogenesis.

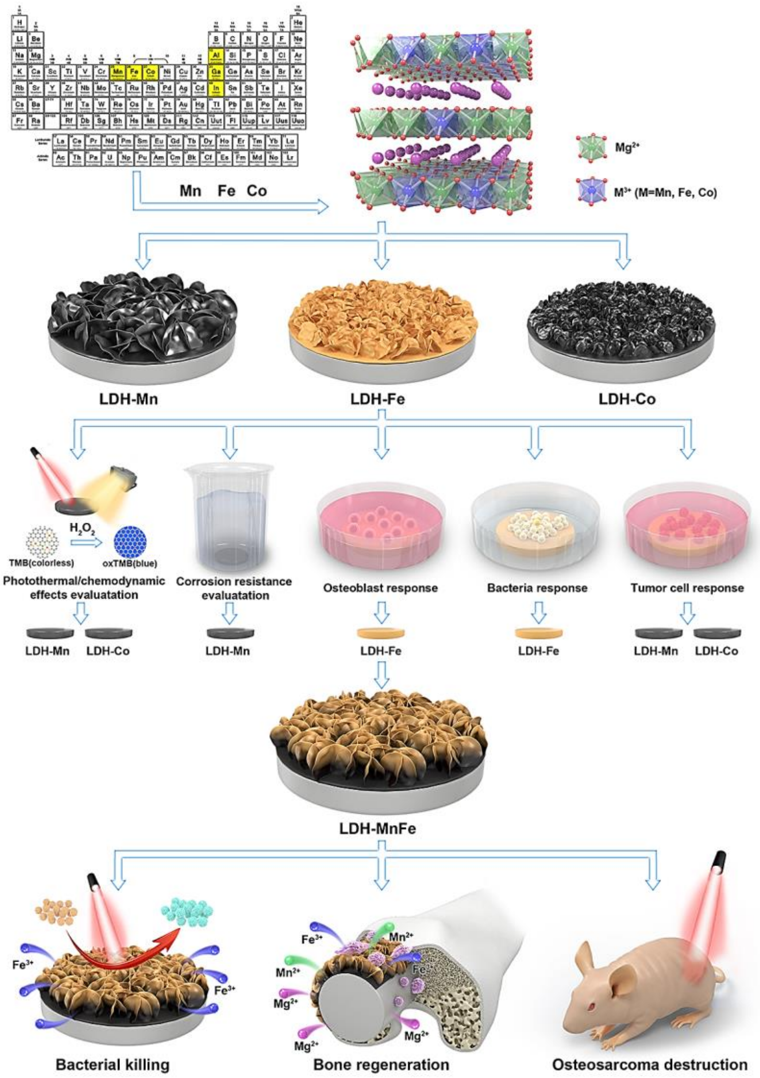
Figure 3. Mg-Fe LDH nanosheets mediated preparation of MgO/FeOx Coating and its synergistic antibacterial and osteogenic mechanism.



Biodegradable Mg-based implants: The high chemical reactivity of Mg surfaces has established the preparation of Mg-based LDHs coatings *via* type III and V method as the predominant approach. The advent of LDHs coatings on Mg alloys can be traced back to recent decades in industrial anticorrosion [18]. In this research domain, LDHs coatings have been serving as carriers for corrosion inhibitors. Our group was the first to extend the use of Mg-Al LDH coatings to the biomedical arena [19]. We have conducted systematic investigations into the properties of these coatings, thereby confirming their excellent anti-corrosion and biocompatibility. Furthermore, our research has incorporated functional agents into the Mg-Al LDH coatings, including 5-fluorouracil, zinc ions, and oleate, to engender coatings with targeted antitumor, antibacterial, and super hydrophobic properties, respectively [20-22].

However, the potential adverse effects associated with aluminum, such as neurotoxicity and dementia, must be carefully considered. Therefore, in our subsequent study (Figure 4), we synthesized three types of transition metal-containing LDHs (M=Mn, Fe, and Co), known as LDH-Mn, LDH-Fe, and LDH-Co, on Mg alloy using the type IV methodology [10,11,23]. The findings revealed that LDH-Mn offered superior corrosion resistance, while LDH-Fe demonstrated better enhanced cell compatibility and antibacterial qualities. LDH-Co was found to exhibit significant cytotoxicity, rendering it unsuitable for biomedical use. In light of these discoveries, a top Fe-riched and bottom Mn-riced layer double LDH coating was designed to achieve antibacterial, antitumor, and osteogenesis properties.

Figure 4. Schematic illustration of the comparison and experimental optimization design of transition metal-based LDHs coating on Mg alloys.



CONCLUSION

Over the past decade, significant advancements in this field have culminated in the establishment of a systematic approach to synthesizing LDHs coatings, along with a comprehensive elucidation of their physicochemical and biological characteristics. While there have been notable efforts to design tailored functionalized LDHs coatings, this area of research remains nascent. It requires additional studies focusing on the adhesion of coatings, fatigue resistance, and degradation patterns. Concurrently, as biomedical science progresses, there are ample opportunities to investigate and uncover the mechanisms underlying potential interactions between cells and bacteria in relation to these coatings.

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COMPETING INTERESTS

The authors declare no competing interests.

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