



可降解骨植入镁合金表面抗菌涂层研究进展

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摘要:近年来,生物可降解植入材料的应用发展迅速,其中镁及合金因其具有良好的生物相容性与生物可降解性,成为新一代具有广阔发展前景的生物医用可降解金属材料,但存在镁合金本身由于快速腐蚀释放镁离子使周围环境碱化而具有的抗菌性和骨植入物需要长期保持力学性能之间的矛盾。本文总结了多种类型的金属及其氧化物、生物活性物质、天然抗菌物质、光热、光动力疗法在抗菌镁合金及表面抗菌涂层领域的研究进展,研究多种镁合金表面耐蚀抗菌涂层的制备方法,重点讨论了不同抗菌载体对镁合金耐蚀抗菌性的影响。结果表明:现阶段抗菌镁合金设计、镁合金抗菌耐蚀涂层制备的研究逐渐成熟,但也存在一些亟需解决的问题。同时,综合阐述了生物医用可降解镁合金表面抗菌涂层未来的发展方向。

关键词:镁合金;抗菌性;涂层;生物材料

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近年来,随着科技的发展,越来越多的新型医用金属材料层出不穷,由最初的不锈钢^[1-3]与钛合金^[4-7]双雄争霸,逐渐演化为镍钛合金(形状记忆金属)^[8-11]、贵金属^[12]、可降解金属(镁合金、锌合金)^[13-25]等遍地开花,特别是可降解镁基、锌基合金可有效避免二次手术,同时还表现出良好的促成骨功能,逐渐成为了现阶段研究的热点^[26]。

对于生物医用可降解镁合金,2006年,英国皇家科学院院士威廉姆斯(D. F. Williams)以“New Interesting Magnesium”为题撰写了可降解生物医用镁合金的评论,提出传统的金属植入材料在人体中的腐蚀产物对人体具有潜在的危害性。镁金属的腐蚀产物不仅没有害处,而且可能对人体有益^[27-28]。从此,揭开了21世纪镁合金医用研究的

序幕。随着研究的深入,镁合金良好的生物相容性、力学相容性、生物可降解性、密度和弹性模量与人体皮质骨相似、一定的抗菌性等优势逐渐被研究人员一一证实,其降解主产物镁离子也作为人体必需的微量元素,参加人体生命活动,并且多余的镁离子能通过人体自主的排泄过程排出体外,不会对人体产生额外的影响^[29]。

镁合金作为一种在生物医学领域具有广泛的应用前景的新型材料,可作为心血管支架^[30]、骨科内固定材料^[31]等。德国 Syntellix AG 公司的镁合金压缩螺钉(Compression Screw (CS), MAGNEZIX[®])是获得欧盟临床应用审批资质的可降解医用镁合金产品^[32]。2012年,苏州奥芮济医疗科技有限公司研发的胸部固定板获得了国内医用镁合金领域第

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一个医疗器械产品注册证。2014年11月3日,东莞宜安科技股份有限公司申请的“可降解镁骨内固定螺钉”产品通过国家食品药品监督管理总局创新医疗器械特别审批申请审查。2019年7月19日,该可降解镁骨内固定螺钉获批临床使用,标志着我国生物可降解金属植入物产业化步入了新阶段。2020年5月18日,该可降解镁骨内固定螺钉项目正式获欧盟CE认证,标志着我国镁金属材料医用产业化进程取得重大进展。我国镁资源丰富,镁合金种类繁多,Mg-Al合金、Mg-Ca合金^[33]、Mg-Li合金^[34]、Mg-Li-Ca合金^[35]、Mg-Zn合金^[36]、Mg-Zr合金^[37]、Mg-Sr合金^[38]、Mg-RE合金^[30]、Mg-Sc合金^[39]、Mg-Ge合金^[40]等都是比较典型的医用镁合金。

骨骼,作为人体中少数具有再生潜力的组织之一^[41],比较容易受到伤害后断裂。随着人口老龄化加剧,骨折将会成为我国医疗领域面临的巨大问题。据统计,2010年,我国的骨骼疾病患者多达百万例,由此导致的医疗费用大约为七百亿元。预计到21世纪中叶,每年在此方面所需的花费将会超过两千亿元^[42]。因此,新型骨植入材料的研发是医用生物材料领域的重点。镁合金作为骨固定材料的生物相容性已逐渐被证实^[43],特别是镁合金在人体中释放出的镁离子能促进成骨细胞的生长、增殖及分化,加速骨愈合^[44]。究其原因,是镁合金降解产生的镁离子可以刺激感觉神经末端释放出更多的神经递质降钙素基因相关肽(主要为CGRP),促进骨膜内干细胞的成骨分化直至形成新骨。研究表明,高于生理浓度的镁离子可显著提高脊髓背根神经元突触的可塑性,促进大鼠骨质疏松、骨折的愈合。因此,镁及合金可在骨折愈合初期为骨骼修复提供良好的骨细胞生长微环境和力学环境,降低应力遮挡效应、局部骨质疏松和再骨折的可能性。然而,骨折的愈合是一个复杂的过程。简单的骨折术后愈合需要分为四个周期^[45]: 1) 0~5 d,为骨折之后的血肿形成和炎症多发期; 2) 5~16 d,为软组织形成期; 3) 16~21 d,为硬组织形成期; 4) 21~63 d,为最终愈合阶段,硬骨重塑为成熟的层状骨。

镁及合金应用于骨植入材料领域主要面临两个大问题: 过快的腐蚀速度和炎症。镁的标准电极电位为 -2.372 V ^[46],属于化学活性比较高的金属,在人体复杂环境中容易发生降解而失去力学性能。

过快的降解速度将直接导致材料的性能不能满足服役期的要求,在创伤未愈合时发生危险。炎症反应分为两种: 免疫调节反应和细菌感染^[47]。免疫调节反应多发生在植入材料生物相容性较低时,而细菌感染则是镁及合金临床应用面临的一个重大问题。因此,开发可控降解-抗菌一体化的功能镁合金表面十分必要。

1 常用的抗菌物质

具有抗菌性能的镁及合金骨植入材料,不仅能够抑制微生物的繁殖,同时可以避免因微生物繁殖而产生的酸性化境,减弱微生物腐蚀。现阶段,赋予镁及合金抗菌性能的方式主要分为两大类。一是通过在合金中添加具有抗菌性能的金属元素,例如: Cu、Zn、Ag等,在降解过程中释放离子起到杀菌效果。二是通过在镁及合金表面制备抗菌涂层或复合涂层。当然,表面涂层除了可以发挥抗菌作用,还可赋予镁合金表面其他的功能性^[48]。图1所示为常用的抗菌物质、特征及抗菌机制。本文中主要总结了金属及其氧化物、多肽与酶、天然抗菌剂、药物、光动力与光热疗法在镁合金表面耐蚀抗菌涂层制备领域的研究现状,所涉及到的抗菌机理包括: 抑制合金表面细菌黏附、破坏细胞膜结构导致细胞死亡、抑制DNA复制过程阻止细菌繁殖、抑制RNA转录导致细胞生物活动进程不能正常进行、热杀菌和活性氧杀菌等。下文我们将分类进行详细讨论。

1.1 金属及其氧化物

金属元素在抗菌领域的应用不仅体现在镁及合金(Mg-Ag, Mg-Cu, Mg-Cu)的合金化,同时也可以用于镁及合金的表面改性。研究发现,一些具有抑菌作用的Ag、Cu、Zn及其氧化物可以通过制备涂层的方式负载在镁合金表面,而后通过特殊的方式或者机制释放出来,起到杀菌效果。以下将对这些常用的具有抑菌作用的金属及其氧化物在镁合金抗菌领域的应用进行讨论。

1.1.1 Mg与MgO

镁及合金的降解产物 Mg^{2+} 本身具有较好的抗菌效果,对此,RODRÍGUEZ-SÁNCHEZ等^[29]对镁离子的抗菌机制进行了系统的研究,发现当体系

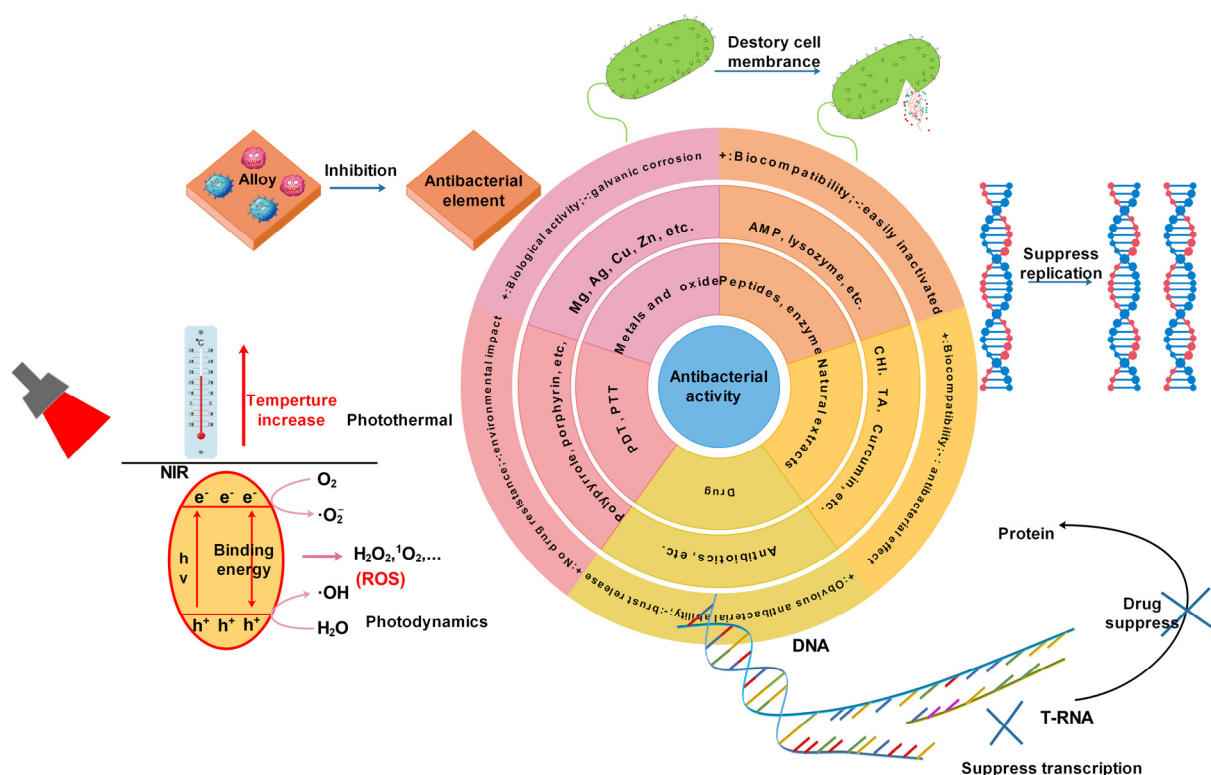


图 1 常用抗菌物质特征及机理

Fig. 1 Features and mechanisms of commonly used antimicrobial substances

pH 不变时, 更高的 Mg^{2+} 浓度会基于作用于细菌的更大的渗透压力, 导致细菌生理活动紊乱直至死亡, 从而表现出良好的抗菌性。687 mg/L 的 Mg^{2+} 可以杀死 50% 的革兰氏阳性、阴性菌, 因此, 口服或者静脉注射适量的 Mg^{2+} 有助于抑制术后炎症。另外, 镁及合金降解导致的碱性微环境也是其具有抗菌性的重要原因^[49]。当然尽管 MgO 在降解过程中由于 Mg^{2+} 的释放也表现出一定的抗菌性^[50-51], 但通过在镁合金表面制备 MgO 涂层实现抗菌功能的研究比较少。而且, 由于人体新陈代谢以及体液对 pH 值的缓冲作用, 镁合金本身因为 Mg^{2+} 和碱环境所产生的抗菌性能在体内并不适用^[52]。

1.1.2 Ag 与 Ag_2O

银由于可以和细菌酶蛋白形成结合键, 使得这些物质不能为微生物所利用, 从而破坏细菌细胞膜, 导致细菌死亡。研究表明, $Mg-Ag$ 合金表现出较低的细胞毒性和良好的细胞相容性, 对于金黄色葡萄球菌(*S. aureus*)和表皮葡萄球菌(*S. epidermidis*)两种常见致病菌的抑菌活性高于 90%^[53]。但铸态 $Mg-4\% Ag$ 合金的力学性能较差, 降解速度较快,

经过 T4 热处理后, 由于树枝状结构和部分析出物的溶解, 其降解速率与力学性能略有改善。侧向等径挤压处理也可以显著影响合金的微观组织和力学性能。总的来说, 降解速率加快是 Ag 用于合金化的最大弊端, 惰性的 Ag 会与活性的 Mg 形成原电池, 加快镁及合金的腐蚀速度^[54]。

因此, 研究者大多利用 Ag 构建涂层, 从而最大程度发挥 Ag 的抗菌作用^[55-56]。在镁合金表面, ZHAO 等^[57]采用层层组装(LbL)技术制备了纳米 Ag 多层膜, 而后通过聚硅烷包裹的方式, 使得纳米 Ag 可以实现缓慢持续释放, 在提高镁合金耐蚀性的基础上, 有效地实现了抗菌功能。LOPERENA 等^[58]在镁合金表面通过电沉积法制备了含 Ce 、 Mo 的复合涂层, 而后浸泡 $AgNO_3$ 溶液, 有效改善了 AZ91D 合金的耐蚀性, 同时赋予了其良好的抗菌性。ZHAO 等^[59]通过一步水热法在镁合金表面制备 Ag^+ 掺杂的水滑石涂层, 该涂层在提高合金的耐蚀能力的同时, 为涂层提供了抗菌功能。但对于载 Ag 涂层, 在 Ag^+ 的释放过程中, 一旦存在与镁基材接触的机会, 也不可避免的存在一定程度的电偶腐

蚀。

SONDI 等^[60]研究发现,除纳米 Ag 外,Ag₂O 由于可以破坏细菌 DNA 复制,也表现出良好的抗菌功能,是一种可以替代纳米 Ag 的抗菌材料,但其用于表面涂层的构建主要集中在钛合金上^[61-62],镁合金表面鲜有研究。

1.1.3 Cu 与 CuO

铜是人体不可缺少的微量金属元素,主要被胃和小肠吸收,经由胆汁排出体外。铜是体内多种酶和蛋白质的重要成分和催化剂,可以通过多种机制影响人体健康。基于铜的生物功能和益处,越来越多的生物材料研究者开始关注新型含铜生物材料的开发,这些材料在保护心血管系统、促进骨折愈合、发挥抗菌作用等方面具有独特的性能^[63]。关于铜的抗菌机制,主要是由于 Cu²⁺破坏细菌的细胞壁和细胞膜,吸附细菌电子产生活性氧(ROS),从而导致细菌和真菌的损伤和死亡^[64-65]。具有抗菌效果的 Mg-Cu 合金能够延长镁合金的抗菌时间,同时不影响合金的可降解性质。但需要注意的是,Cu 元素一般作为合金中的杂质元素,其掺杂量上限为 1×10^{-3} ,过多的 Cu 掺杂会加速镁及合金的腐蚀速度^[66-67]。关晓楠等^[68]研究发现,将镁铜合金的表面纳米化到 400 nm 时,伴随着位错胞及孪晶的形成,镁铜合金在氢氧化钠溶液中会出现明显的活化-钝化-过钝化现象,对腐蚀行为有所改善。

YAN 等^[69]在铸态及固溶处理的 Mg-0.6Cu 合金表面构建微弧氧化(MAO)涂层,研究发现,由于 Mg₂Cu 第二相的存在,Mg-0.6Cu 合金表现出明显的电偶腐蚀行为,但经固溶处理的 Mg-0.6Cu 合金表面 MAO 涂层耐蚀性与抗菌性明显优于铸态合金 MAO 涂层,其原因在于 Mg-0.6Cu 合金表面 MAO 涂层制备过程使得 MAO 结构外层具有一定量的 Cu,其多孔形貌又可以使得细菌与涂层直接接触,继而可以不经溶液体系的扩散过程,直接起到较好的接触性杀菌的作用。由此可见,载 Cu 的 MAO 涂层,可以兼顾较好的耐蚀性与抗菌性。于是,CHEN 等^[70]在 Mg-2Zn-1Gd-0.5Zr 合金表面构建了含 Cu 的 MAO 涂层,该涂层获得了较 MAO 涂层更好的耐蚀性,同时基于 Cu²⁺的释放,涂层抑菌率可达 96%以上。耐蚀性提高的主因可以归结于涂层中形成的 Cu₃(PO₄)₂产物可以稳定涂层结构不被破坏。

与 Cu 元素相似的,CuO 也作为抗菌的掺杂粒子。XU 等^[71]通过溶胶-凝胶法在镁合金 AZ60 的羟基磷灰石涂层中掺杂了 CuO 纳米颗粒,改善了羟基磷灰石涂层多孔的形貌,有效地提高了镁合金的耐蚀能力且使其具有抗菌性能。YANG 等^[72]将含 Cu 的生物活性玻璃纳米颗粒(Cu-BGN)载入聚己内酯涂层中,均匀分布的 Cu-BGN 释放的 Cu²⁺抑制了肉葡萄球菌(*S. carnosus*)和大肠杆菌(*E. coli*)的生长,提高了人骨肉瘤细胞(MG-63)的活力和增殖能力。

1.1.4 Zn 与 ZnO

锌抗菌的途径主要是通过参加细菌的 DNA 转录过程,进而通过影响有关蛋白质的合成来起到抗菌效果^[73],其在镁合金中的掺杂可有效改善镁合金的耐蚀和力学性能。QIN 等^[74]通过在镁基材中掺杂钕(Nd)、锌(Zn)、锆(Zr)三种金属元素,制备了一种新型的 Mg-Nd-Zn-Zr(简称 JDBM)合金,有效提高了镁基材的耐蚀抗菌性,不断扩散释放出来的 Zn²⁺也对 *E. coli*、*S. epidermidis*、*S. aureus* 起到了较好的抑制作用。

利用 Zn²⁺的抗菌性构建抗菌涂层,是实现其抗菌功能的一个重要应用^[75-76]。YANG 等^[77]通过一步水热法在镁合金表面制备了一种 Zn/Sr 掺杂的磷酸盐涂层,其中的 Zn 元素为涂层提供了优异的抗菌性能,所得涂层的耐蚀和促成骨功能也显著提高。ZOU 等^[78]则通过水热法在蒙脱石涂层层板间插入了 Zn²⁺离子,Zn²⁺作用于细菌的细胞膜,抑制了 *S. aureus* 和 *E. coli* 的生长并导致细胞质的泄漏和细菌的死亡。Zn²⁺的释放时间可达 144 h,可以应对医用植入物的早期感染。

与 Ag、Cu 元素不同,ZnO 纳米颗粒是一种在镁合金表面应用更为普遍的抗菌氧化物。ZHOU 等^[79]通过一步法在 Mg₆₈Zn₂₈Ca₄合金表面制备了纳米羟基磷灰石(HA)/ZnO 涂层,该复合涂层内部致密的 ZnO 对镁合金起到了良好的保护作用,同时对 *S. aureus* 和 *E. coli* 起到了良好的体外抑菌作用。SUN 等^[80]利用微波水合成结合热处理制备了单层 ZnO 涂层,经紫外光辐照,抗菌性能明显提升。在 SBF 溶液中浸泡 14 d 后,ZnO 涂层表面有含碳酸盐的羟基磷灰石析出,且随着紫外光照射时间的增加,磷灰石的诱导能力显著提高,即生物活性、成骨活性显著提高。这主要是由于紫外光辐照,ZnO

涂层表面产生了 Zn-OH 官能团和羟基自由基。当然, 直接将 ZnO 纳米颗粒掺杂或负载于镁合金表面也是一种不错的方法^[81-82]。

综上所述, 抗菌金属及其氧化物可以通过合金化或涂层设计提高镁合金的抗菌性, 但普遍存在抗菌金属与镁合金之间的电偶腐蚀问题。金属及其氧化物对镁合金抗菌与耐蚀性能的影响如表 1 所示, 抗菌金属元素含量及合金化处理过程对抗菌镁合金性能具有直接的影响, 平衡抗菌镁合金的耐蚀性、力学性能与抗菌性之间的关系至关重要。从涂层设计的角度看, 如何在镁合金与抗菌涂层之间设置隔离带, 并且实现金属离子向外单向扩散十分关键。尽管人们认为银离子的抗菌性优于铜离子和锌离子, 且纳米银在抗菌领域更为常用, 但表 1 所述数据中, 铜离子和锌离子抑菌率更优于银离子。由此可见, 抑菌性能的优劣不仅与金属抗菌离子的种类有关, 更与金属离子在涂层中的存在形式、释放浓度等有关。Cu、Zn 氧化物的抑菌性明显优于其离子态, 但直接以金属氧化物纳米颗粒作为负载单元, 则将进一步衍生出涂层与镁合金表面的结合力问题。聚硅烷等聚合物相较于 MAO、HA 等无机涂层具有更好的物理阻隔作用, 因而所得涂层的耐蚀性优化效果更好。

1.2 多肽与酶

具有抗菌效果的多肽类物质是人类和其他生

物体产生免疫反应时的主要参与者。大多数的抗菌多肽是小于 50 个氨基酸的带电两亲性物质, 这类物质的常见抗菌机制在于能够破坏细菌的生物膜^[83]。迄今为止, 已经有超过 5000 种抗菌多肽可以通过人工合成, 抗菌多肽(AMP)的应用也得到了越来越多的关注。在镁合金表面利用抗菌多肽构建抗菌涂层时, 往往将多肽进行氨基化修饰, 使其更容易与镁基体或者内部涂层结合。TIAN 等^[84]将抗菌多肽 PSI 10(RRWPWWPWRR-NH₂)通过浸泡的方式直接吸附在镁合金 AZ91 表面的微孔板状 HA 涂层上, 随着降解过程中 PSI 10 的缓慢释放, 复合涂层浸泡 4 d 后依然保持超过 50%的抑菌率。近期, WANG 等^[85]对比了 caerin 抗菌肽 1.9(GLFGVLG-SIAKHVLPVVPVIAEKL-NH₂)和修改后的抗菌肽序列 1.1(GLLSVLGSAKHVLPVLPVLPVIAEHL-NH₂)在镁合金聚氨酯涂层表面的抑菌活性, 研究发现两种抗菌肽均能提高镁合金的耐蚀、抗菌性, 特别是可以有效抑制 MRSA 细菌, 且修改后的抗菌肽 1.1 比广泛使用的临床抗生素塔佐辛表现出更持久和更显著的抑菌性, 这可能与多肽、聚氨酯和金属基体形成的微观结构有关。ZHOU 等^[83]则通过旋涂法在氧化镁无机涂层表面利用丝纤蛋白负载了 CB((NH₂)-NGIVKAGPAIAVLGEAALCONH₂)抗菌肽, Mg²⁺与抗菌肽的协同作用抑制了细菌的黏附生长, 同时促进了可降解镁合金的成骨分化。抗菌肽在镁合金表面的应用取得了显著成效, 且比表

表 1 金属及其氧化物对镁合金抗菌与耐蚀性能的影响

Table 1 Effect of metal and its oxide on antibacterial and corrosion resistance of magnesium alloy

Antibacterial element	Antibacterial composition	Antibacterial ability	Corrosion resistance density, $J_{\text{corr}}/(\text{A} \cdot \text{cm}^{-2})$
Mg ^[49]	—	50%	—
Ag ^[53]	Mg-Ag alloy	90%	Decrease
Ag ^[57]	Ag nanoparticle	84.5%	Increase ($1.62 \times 10^{-5} \rightarrow 9.73 \times 10^{-8}$)
Ag ^[58]	AgNO ₃	Inhibition circle ($d=14 \text{ mm}$)	Increase ($1.05 \times 10^{-4} \rightarrow 3.00 \times 10^{-6}$)
Ag ^[59]	Ag-LDH	Weak ability	Increase ($2.56 \times 10^{-5} \rightarrow 2.09 \times 10^{-6}$)
Cu ^[69]	MAO (Mg-0.6Cu)	95% (3 h), 100% (6 h)	Increase ($4.5 \times 10^{-6} \rightarrow 5.0 \times 10^{-7}$)
Cu ^[70]	MAO-Cu (Mg-2Zn-1Gd-0.5Zr)	96%	Increase ($5.46 \times 10^{-6} \rightarrow 2.73 \times 10^{-7}$)
CuO ^[71]	HA@CuO (AZ60)	99.5%	Increase ($2.6 \times 10^{-5} \rightarrow 6.0 \times 10^{-7}$)
Zn ^[74]	Mg-Nd-Zn-Zr Alloy	94.8% (3 d)	Increase
Zn ^[77]	Zn/Sr	33.3%	Increase ($1.46 \times 10^{-4} \rightarrow 9.27 \times 10^{-6}$)
Zn ^[78]	Zn ²⁺	Inhibition circle ($d=32 \text{ mm}$)	Increase ($2.81 \times 10^{-5} \rightarrow 2.86 \times 10^{-7}$)
ZnO ^[79]	HA/ZnO (Mg ₆₈ Zn ₂₈ Ca ₄)	Close to 100%	Increase ($1.13 \times 10^{-4} \rightarrow 1.25 \times 10^{-5}$)

面积较大的无机涂层可以提高抗菌肽的负载量并实现缓释功能^[84]。

另外，酶也是一种具有潜在应用价值的镁合金表面抗菌物质，它可以通过改变生物外基质(ECM)、溶解细胞膜起到抗菌效果^[86]。例如：溶菌酶^[87]、内溶素^[88]等。蛋白酶和 DNA 解旋酶也具有一定的抗菌性能^[89]。研究表明，透明质酸交联溶菌酶对 *S. aureus* 具有很好的抑菌能力，同时有助于成骨细胞的增殖和分化^[90]。

多肽与酶在镁合金抗菌相关领域的应用仍然还是一个相对空白的领域，且大分子多肽的抗菌机制也不十分明确。如表 2 所示，所有抗菌多肽均需经过氨基化处理，使其在镁合金表面实现更好的结合，各抗菌多肽的抑菌效果也良莠不齐。另外，由于现有研究中的多肽涂层多为自组装分子膜，涂层厚度较薄，对镁合金耐蚀性的提升较为有限。如何保持抗菌肽、酶在制备、使用过程的生物活性问题是限制其应用的重要原因，通过多肽序列设计或复合涂层设计提高其耐蚀性与抗菌性是未来开展研究的重点。

1.3 天然抗菌剂

自古以来，人们就善于使用大自然中的天然物质来抵抗疾病。随着科学技术的发展，植物中的有效物质逐渐被分离、纯化，特别是一些多酚类提取液和类黄酮类有机物表现出较好的抗炎症、抗过

敏、抗血栓、抗癌和促进血脉舒张等作用，图 2 所示为常用天然活性物质分子式。

1.3.1 壳聚糖及其衍生物

壳聚糖(CHI)在镁及合金表面改性中的应用较为广泛，依靠接触型杀菌机制，CHI 及其衍生物的杀菌主要通过三种方式：1) 依靠自身的正电性与表面负电性的细菌结合，从而破坏细菌的细胞壁和细胞膜；2) 与金属离子结合，从而降低细菌生命活动必须的酶的活性；3) 穿透细菌的细胞膜，从而抑制 RNA 的转录。CUI 等^[91-92]利用 LbL 技术，分别在镁合金表面构建了 DNA/CHI、聚谷氨酸/CHI 多层，均表现出了较好的耐蚀、抗菌性。更多的研究则是将 CHI 与无机涂层结合，通过构建复合涂层达到研究目的。YU 等^[93]以 MAO 为内层构建了 MAO/CHI 复合涂层，研究表明，CHI 很好地封闭了 MAO 的多孔结构，降低了镁合金的降解速率，同时降解过程中表现出良好的 pH 缓冲与抗菌功能。GAO 等^[94]则利用 LbL 技术构建了 CHI/肝素化氧化石墨烯多层，涂层在提高基材耐蚀性的基础上，降低了溶血率和血小板黏附，同时促进内皮细胞的黏附和增殖。ALAEI 等^[95]和 BAHATIBIEKE 等^[96]则分别利用 CHI 与生物活性玻璃以及硅烷结合构建复合涂层，极大地提升了镁合金的耐蚀性和生物相容性。不难发现，研究者们后期更关注 CHI 对镁合金生物相容性的改善，而不仅仅局限于赋予镁合金抗菌性。另外，由于 CHI 的溶解性问题，单纯利用 CHI

表 2 多肽与酶对镁合金抗菌耐蚀性能的影响

Table 2 Effects of peptides and enzymes on antibacterial and corrosion resistance of magnesium alloys

Antibacterial molecule	Antibacterial composition	Antibacterial ability	Corrosion resistance
Antimicrobial peptide PS10 ^[84]	HA coating	50% (4 d)	Increase (Weightlessness rate 36.13±1.5%→7.62±0.74%)
1.9(GLFGVLGSIAKHVLPHVVPVIAEKL-NH ₂) ^[85]	PU coating	Effective antibacterial area about 245 mm ² (stretch), about 370 mm ² (toughness)	—
1.1(GLLSVLGSAKHVLPHVLPVVPVIAEHL-NH ₂) ^[85]	PU coating	Effective antibacterial area about 60 mm ² (stretch), about 110 mm ² (toughness)	—
CB((NH ₂)-NGIVKAGPAIAVLGEAALCONH ₂) ^[83]	MgO coating	95%	Slightly increase

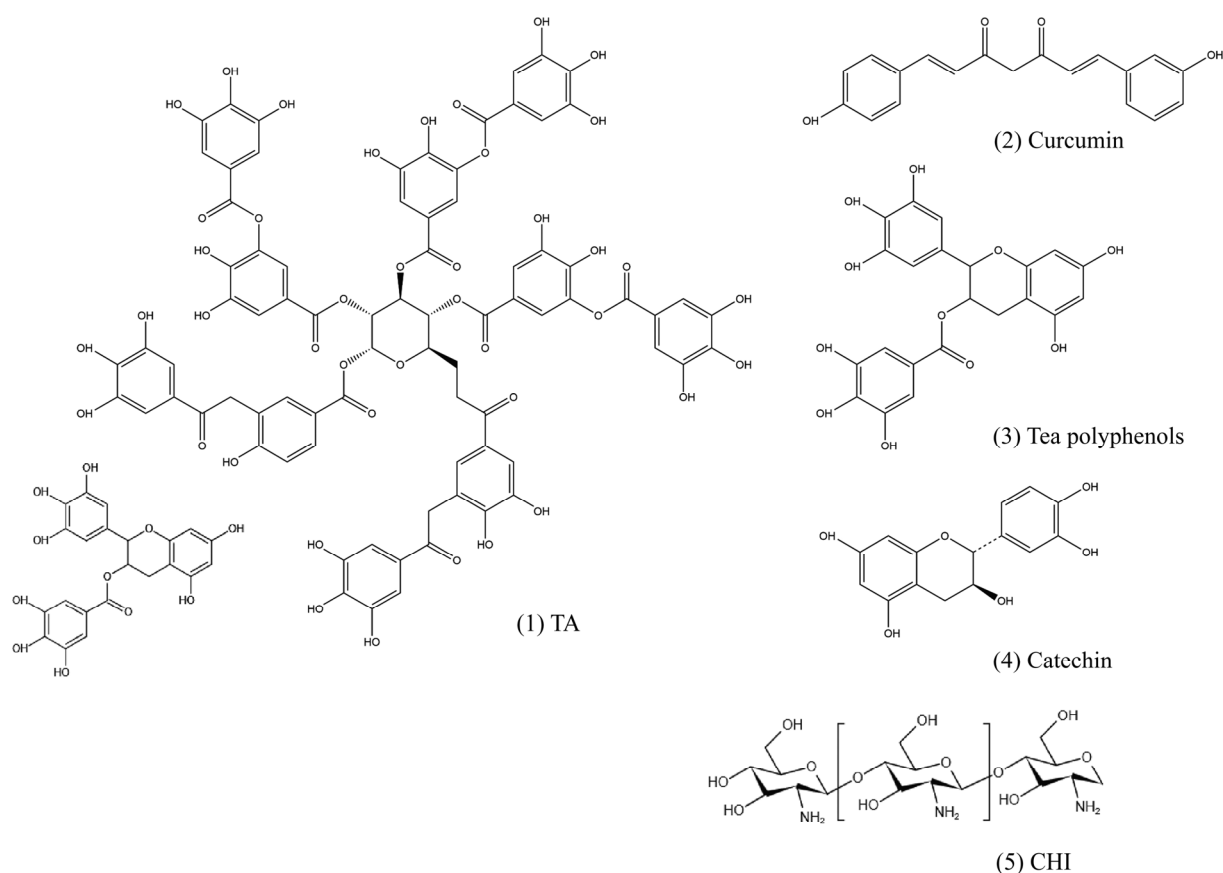


图 2 常用天然活性物质分子式

Fig. 2 Molecular formula of commonly used biologically active substances

改善镁合金的耐蚀性存在较大难度, 制备过程往往需要通过调节溶液 pH 尽可能减小酸性溶液对镁合金的腐蚀。

1.3.2 单宁酸

单宁酸(TA)也称鞣酸, 由五倍子中提取, 是一种典型的多元酚类有机分子。其抗菌机制主要是基于 TA 分子中的酚羟基破坏细菌的细胞壁和细胞膜^[97]。同时, TA 可以络合金属离子, 降低细菌中维持正常生命活动的金属酶的活性^[98-99]。FACCHI 等^[100]制备了一种聚阳离子缩合 TA/多糖基聚电解质多层膜来防止微生物在基材表面的黏附行为, 从而起到较好的抗菌效果。CUI 等^[101]将 TA 添加于微弧氧化电解液中制备抗菌 MAO 陶瓷涂层, 研究表明, TA 有效提高了植酸系 MAO 涂层的厚度, 降低了涂层的孔径和孔隙率, 赋予了涂层较好的抗菌性。WANG 等^[102]在 Mg-Zn-Y-Nd 合金表面制备了 TA 修饰的氟化镁复合涂层, 除了 TA 的酚羟基表现出良好的抗菌性外, TA 还表现出优异的自由基清除与血小板排斥能力, 并且能够有效促进内皮细胞的生

长和分化。另外, TA 还可以用做 HA 等含金属离子无机涂层的诱导剂^[103]。

1.3.3 姜黄素

姜黄素是一种从生姜中提取的具有抗菌、消炎、抗癌、促成骨功能的二酮类有机物^[104-106], 具有优异的生物活性, 对于缓解艾兹海默证也有一定的效果^[107]。研究发现, 姜黄素作为抗菌剂的作用方式主要分为两大途径: 1) 参与细菌的调节过程(QS), 能够有效的抑制细菌的增殖; 2) 能够靶向识别细菌的细胞膜、细胞壁、蛋白质、DNA 等, 从而影响细菌的生命活动^[108]。

最初, 姜黄素主要被用于食品防腐领域。而近些年来, 姜黄素在抗菌材料领域的应用越来越多, 也逐渐延伸到了合金表面的功能化设计。HUANG 等^[109]设计了一种具有抗菌功能的姜黄素负载纳米 MOF 结构, 这种结构不仅能够有效的杀死细菌, 还能控制姜黄素的释放。LI 等^[110]在镁合金表面设计制备了一种含姜黄素的三层复合涂层, 该复合涂层表现出良好的自修复和促成骨分化功能, 姜黄素在

复合涂层中的缓慢释放主要起到调节免疫微环境的作用，从而促进骨髓干细胞的骨分化和细胞外基质矿化。也有研究发现，姜黄素具有一定的促进伤口愈合的功能^[111]。

1.3.4 其他

自古以来，就有用茶叶粉末涂抹伤口来防止伤口发炎的方法。研究者通过对茶叶中的有效成分进行分析提纯后发现，茶多酚和儿茶素等物质具有灭菌功能。例如，早期 TAKAHASHI 等^[112]发现儿茶素对耐甲氧西林金葡萄球菌具有抗菌功能。MARCHESE 等^[113]通过模仿胃部和肠道的生理活动过程与茶多酚进行比较，发现了茶多酚具有杀死金葡萄球菌的能力。但在镁及合金表面，仅 ZHANG 等^[114]利用绿茶多酚，通过 LbL 技术诱导富 Mg²⁺ 多层转化膜，用以增强 AZ31 镁合金的耐蚀性，促进表面的原位内皮化，但相关抗菌能力并未提及。另外，诸如没食子酸、鞣花酸、芦荟苷、丹参酮等均属于植物提取的天然抗菌剂，值得广大研究者予以关注。

天然抗菌剂因其良好的生物相容性逐渐在镁及合金表面涂层中获得关注，如表 3 所示，利用天然抗菌剂制备涂层时大多利用其分子结构特征，通过层层组装技术制备多层膜或通过无机涂层负载，其抑菌能力相较于传统抗生素、金属离子等弱，且抑菌范围较为有限，无法应对复杂的感染环境。当出现大量死细菌黏附或者形成细菌生物被膜时，接触型杀菌机制能够发挥的作用也被极大地降低。所得涂层对镁合金的保护能力，取决于其涂层制备方法，原则上结合无机涂层负载相较于层层组装多层的耐蚀性更优，这主要是由于层层组装多层往往较

薄，无法屏蔽腐蚀性离子的侵蚀。由此可见，结合一些其他聚合物分子制备涂层对耐蚀性的提高更有利。另外，如何在发挥天然抗菌剂的抗菌能力的同时，更好地利用其促进细胞分化、伤口愈合等其他功能值得广大研究者进一步关注。

1.4 药物

临床环境下的抗感染主要以抗生素等药物为主，即在涂层中负载药物仍是赋予镁及合金抗菌能力最有效的方式，常用的药物包括环丙沙星(盐酸)(CIP)^[115-116]、庆大霉素(硫酸)(GS)^[117-119]、万古霉素^[120-121]、阿莫西林^[122]等(见图 3)。然而，药物应用到镁及合金表面时面临着两个巨大的挑战：药物递送和药物缓释。

常用的抗菌药物按其水溶性可分为亲水性(盐酸二甲双胍)和疏水性(庆大霉素、万古霉素、环丙沙星等)两种，如果药物本身具有较高的亲水性，则不存在递送问题(存在的靶向识别问题本文不做赘述)。对于较多使用的疏水性药物，其疏水亲脂的特性使其在发挥功能时能够有效地识别细菌生物膜表面的标靶，起到针对性杀灭细菌的作用。同时，疏水性药物穿透磷脂双分子层组成的细胞膜，在细菌内部发挥作用。但是此类药物难以通过细胞液递送到目标位置。因此，制备一种用来递送疏水性药物的载体十分必要。另外，众所周知，伤口的愈合需要一定的周期，如果药物在植入伊始全部释放，不仅会对机体产生毒性，不利于伤口愈合，同时还不利于遏制后期感染。因此，控制药物以一定的速率在一定的周期内缓慢释放是极其重要的。

通常，药物的递送和缓释需要载体，如图 4 所

表 3 天然抗菌剂对镁合金抗菌与耐蚀性能的影响

Table 3 Effects of natural antibacterial agents on antibacterial and corrosion resistance of magnesium alloys

Antibacterial molecular	Antibacterial composition	Antibacterial ability	Corrosion resistance density, $J_{\text{corr}}/(\text{A} \cdot \text{cm}^{-2})$
CHI ^[91]	AZ31-DNA/CHI (LbL)	93.6% (<i>S.aureus</i>), 94.2% (<i>E.coil</i>)	Increase ($7.63 \times 10^{-5} \rightarrow 1.54 \times 10^{-7}$)
CHI ^[92]	AZ31-PGA/CHI (LbL)	97.32 %	Increase ($6.85 \times 10^{-6} \rightarrow 4.04 \times 10^{-7}$)
CHI ^[93]	MAO/CHI	85.39%	Increase ($2.48 \times 10^{-5} \rightarrow 6.71 \times 10^{-6}$)
TA ^[101]	MAO@TA	92.29% (<i>S.aureus</i>), 97.30% (<i>E.coil</i>)	Increase ($1.47 \times 10^{-5} \rightarrow 5.22 \times 10^{-7}$)
Curcumin ^[109]	MOF	100%	—
Tea polyphenols ^[114]	Mg ²⁺ multilayer conversion coating	—	Increase ($1.62 \times 10^{-5} \rightarrow 6.84 \times 10^{-7}$)

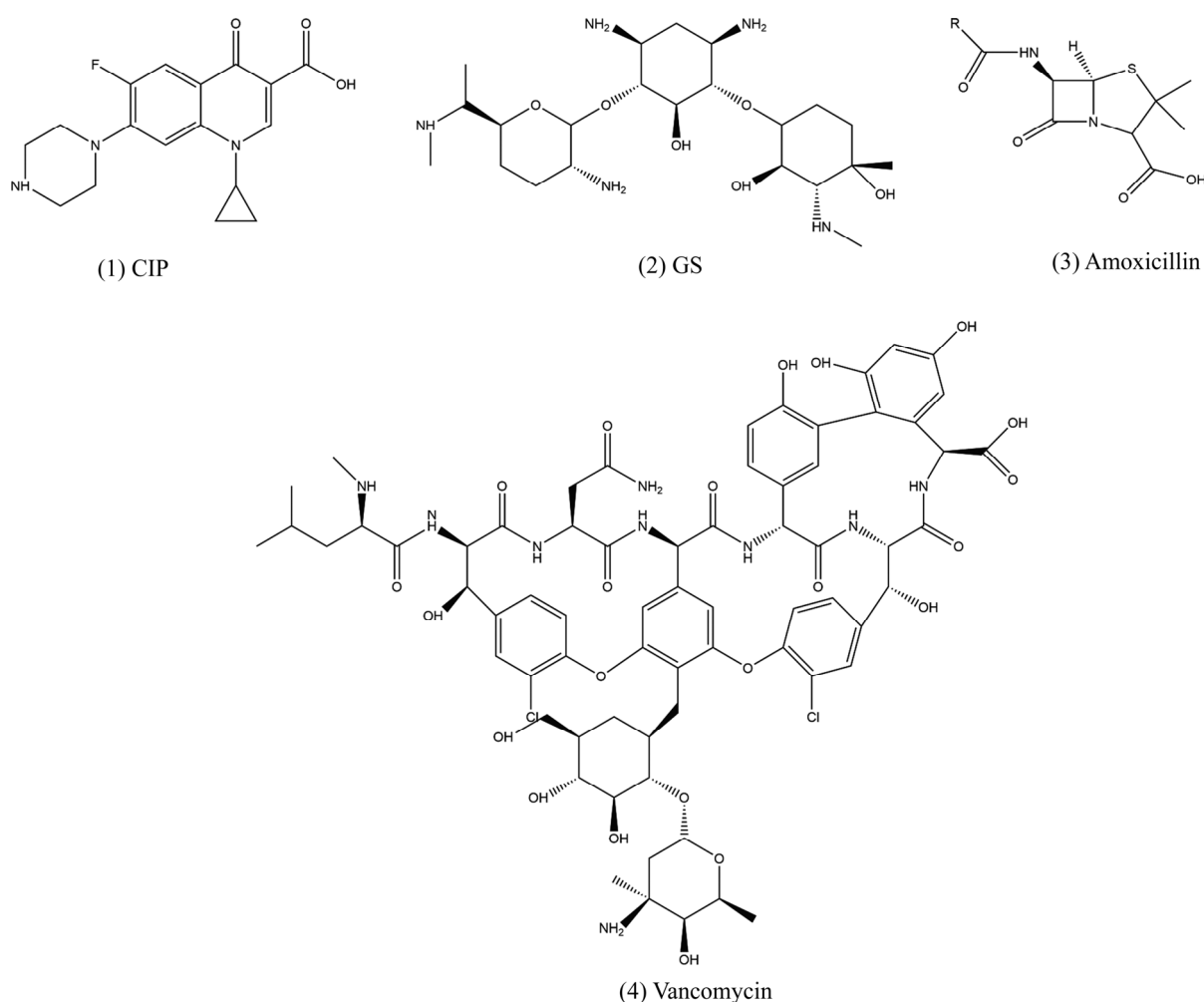


图 3 常用药物分子式

Fig. 3 Molecular formula of commonly used drugs

示, 纳米纤维^[123]、纳米颗粒^[124]、脂质^[125]、金属有机框架(MOF)结构、明胶^[126]、树枝状大分子^[127]等都是较好的载体。纳米颗粒的抗生物膜活性取决于它们比现有的游离药物分子在生物膜基质中具有增强的相互作用和穿透能力^[128-129]。同样的, 纳米颗粒与抗菌药物的结合也能够有效的提高药物的杀菌性能。ARAFA 等^[124]设计了一种聚乳酸(PLGA)-CHI 为基的纳米胶囊来递送不溶于水的环丙沙星有效提高了抗菌性能。同样的, PLGA 的微粒也被用来向皮肤炎症处递送环丙沙星和人参皂苷 Rh2, 用来治疗金黄色葡萄球菌的感染^[115]。

鉴于大量药物递送体系的逐渐完善, 把药物负载到镁及合金表面, 赋予合金功能化成为可能。ESCOBAR 等^[130]通过 LbL 的方法在玻璃表面制备了一种负载了硫酸庆大霉素(GS)的聚丙烯酸/聚赖氨酸(PAA/PLL)涂层, 有效地提高了基材抗菌性,

涂层在浸泡初期的 6 h 药物释放量达到 58%, 而后药物的释放速率保持稳定, 释放时间持续一周, 符合骨植入术后临床感染预防与治疗的特征。在此基础上, ZHAO 等^[119]采用 LbL 技术在镁合金表面制备了负载 GS 的聚丙烯胺盐酸盐(PAH)/PAA 涂层, 在提高镁合金耐蚀能力的同时, 赋予其良好的抗菌性能。除此之外, 聚电解质多层还表现出一定的自修复性能。与此同时, ZHAO 等^[131]发现利用旋转的剪切力能够提高涂层与合金的结合力。因此, 旋涂法成为镁合金表面 LbL 制备的耐蚀功能性涂层的常见方法, 避免了普通浸泡法对镁及合金基体或者内部陶瓷涂层的腐蚀^[132]。JI 等^[133]在镁合金表面通过旋涂法 LbL 制备了一种 GS 负载的聚电解质诱导羟基磷灰石涂层(HA), 药物释放周期达到了 400 h, 前期突释造成的药物释放占比减少到了 25%。

除了 LbL 技术, BAKHSHESHI-RAD 等^[134]利用明胶纳米纤维负载环丙沙星(CIP),有效延长了药物释放时间。QI 等^[135]同样以明胶(Gelatin)纳米团簇作为辛伐他汀(Simvastatin)的载体,结合 CHI 通过电沉积技术制备涂层,除了浸泡第一天存在突释现象外,涂层可以在 28 d 内实现有效的缓释。SUN 等^[136]利用聚谷氨酸和 7-羟基-4-甲基香豆素共聚获得胶体颗粒,实现了维他命 M 有效负载和缓慢释放。聚乳酸^[137-138]、羟基磷灰石^[139]等也是可在镁合金表面涂层中获得良好应用的载药纳米颗粒。

药物对镁合金抗菌与耐蚀性能的影响如表 4 所

示, 尽管镁合金表面载药涂层的抑菌率均保持在 99%以上, 有利于抑制植入术后初期易发生的感染问题或者赋予植入物特定的治疗功能, 但是药物释放时间、释放量与伤口愈合或者疾病治疗周期的匹配却是亟待解决的问题。一般来说, 正常骨折伤口的易感染期为 5~7 d, 但不同病症所对应的易感染周期是完全不同的, 糖尿病等慢性疾病会延长易感染期, 另外还有年龄、环境、突发情况以及伤口位置不同等其他因素的影响^[41, 140]。此外, 植入前期的突释问题以及细菌耐药性等仍制约着载药涂层的应用。

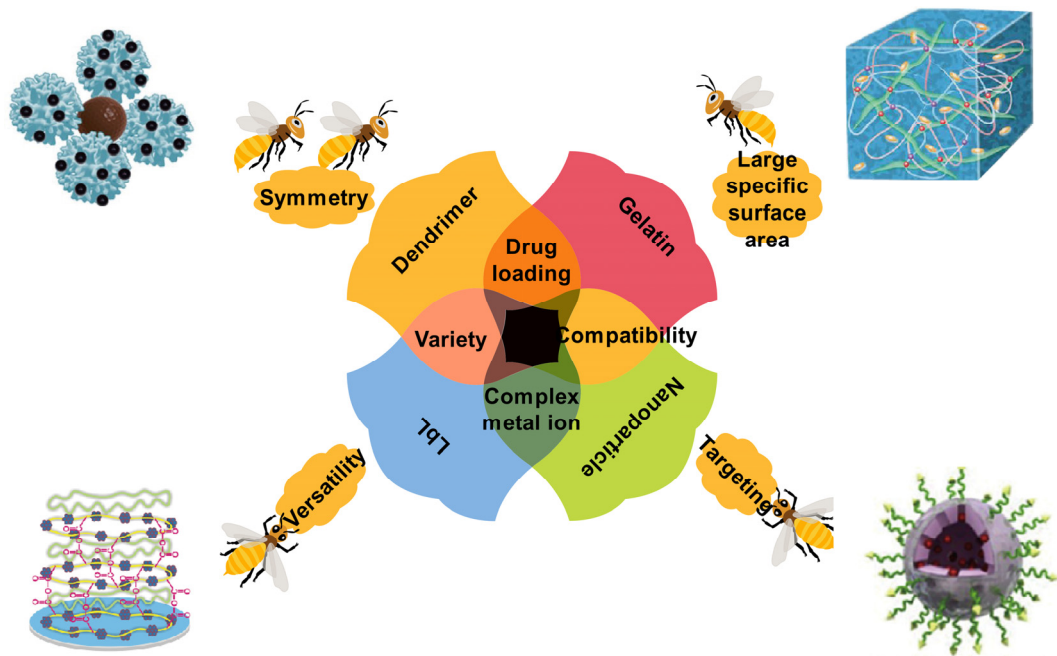


图 4 常见载药模型^[119, 123, 126-127]

Fig. 4 Common drug loading models^[119, 123, 126-127]

表 4 不同药物对镁合金抗菌与耐蚀性能的影响

Table 4 Effects of different drugs on antibacterial and corrosion resistance of magnesium alloys				
Antibacterial drug	Antibacterial composition	Antibacterial ability	Corrosion resistance density, $J_{\text{corr}}/(\text{A}\cdot\text{cm}^{-2})$	Release time
CIP ^[124]	PLGA-CHI@CIP	Inhibition circle ($d=(32\pm0.5)$ mm)	—	24 h (68%)
CIP ^[115]	PLGA	100% (MRSA, 48 h)	—	24 h (55%)
GS ^[130]	GS/PAA/PLL	4 orders lower than substrate	—	6 h (58%)
GS ^[119]	GS/PAH/PAA	99.49%	Increase ($8.01\times10^{-6}\rightarrow3.69\times10^{-7}$)	12 h (18%), 288 h (100%)
GS ^[133]	GS-HA	99.99%	Increase ($3.52\times10^{-5}\rightarrow8.58\times10^{-8}$)	24h (23.1%)
Simvastatin ^[135]	Gelatin@Simvastatin	—	Increase ($6.05\times10^{-6}\rightarrow2.15\times10^{-6}$)	24 h (25%), 672 h (100%)

1.5 光热和光动力抗菌

近年来, 由于副作用小、效果明显、作用条件可控制等优点, 光热和光动力抗菌成为一种新型高效可循环利用的抗菌方法。光热疗法(PTT)通过光热剂将光能转化为热能进而导致细胞生物膜通透性改变、破坏细胞结构起到抗菌效果^[141]。光动力疗法(PDA)的作用原理为材料在接受特定波长的光激发后能产生杀死细菌的活性氧(ROS)^[142]。

目前, 具有光敏效果的物质大致可分为无机物和有机物两大类。一些金属氧化物(TiO_2 ^[143]等)、金属硫化物(CuS ^[144]、 MoS_2 ^[145]等)、金属离子(Au^{2+} ^[146]、 Zn^{2+} ^[147]等)在受光刺激后能将光能转化为热能或者产生活性氧杀死细菌, 但是这些无机物往往生物相容性低、造价高、难控制。有机物相对于无机物来说, 结构容易控制、制备涂层简单, 在光热、光动力抗菌领域已经得到广泛应用, 例如聚吡咯^[148]、菁染料^[149]、聚多巴胺^[150]、卟啉^[151-152]等。其特点在于结构中的大 π 键容易吸收光能转化为热量释放, 从而起到光热效果。同样的, 有机分子 π 键从光子中吸收能量后从基态跃迁到单线态, 不稳定的状态下快速释放能量达到低能量的稳定状态, 释放的能量会产生 ROS 抗菌。

HUANG 等^[148]在镁合金 AZ31 表面通过旋涂 LbL 法制备了一种聚几内酯/聚吡咯多层, 涂层不仅具有耐腐蚀、自愈合功能, 同时利用了物质的光热

性能。LOCATELLI 等^[153]则合成了一种 PLGA/聚乙二醇(PEG)包裹的锂-萘还原 Mg 纳米颗粒, 以还原 Mg 为核, 以有机物为壳的结构在 810 nm 近红外光的照射下表面温度能够至少提高 4~5 °C, 对镁合金表面制备光热涂层具有启示意义。但总体来说, 具有光热、光动力抗菌能力的涂层在镁合金表面的应用还比较少见, 需要研究者们进一步开发和研究。

2 可降解镁合金表面抗菌涂层制备方法

基于上述不同抗菌物质的不同特性, 为了更好地解决镁及合金降解速率过快的问题, 同时赋予表面抗菌功能, 研究者们重点关注以下几种涂层制备方法(见图 5)。

2.1 自组合法

利用有机涂层的物理屏障作用提高镁及合金的耐蚀性, 同时通过交联、共聚等反应机制负载抗菌物质, 赋予表面抗菌活性是一种常见的抗菌涂层设计思路。自组装(Self-assembly)法则是在镁合金表面制备有机涂层的常用方法。当然, 现今的涂层设计与制备已经不仅仅限于单一涂层, 对于有机涂层而言, 其往往会与内部无机涂层相结合, 进一步提高涂层的结合力。CHEN 等^[154]利用自组合法辅以高

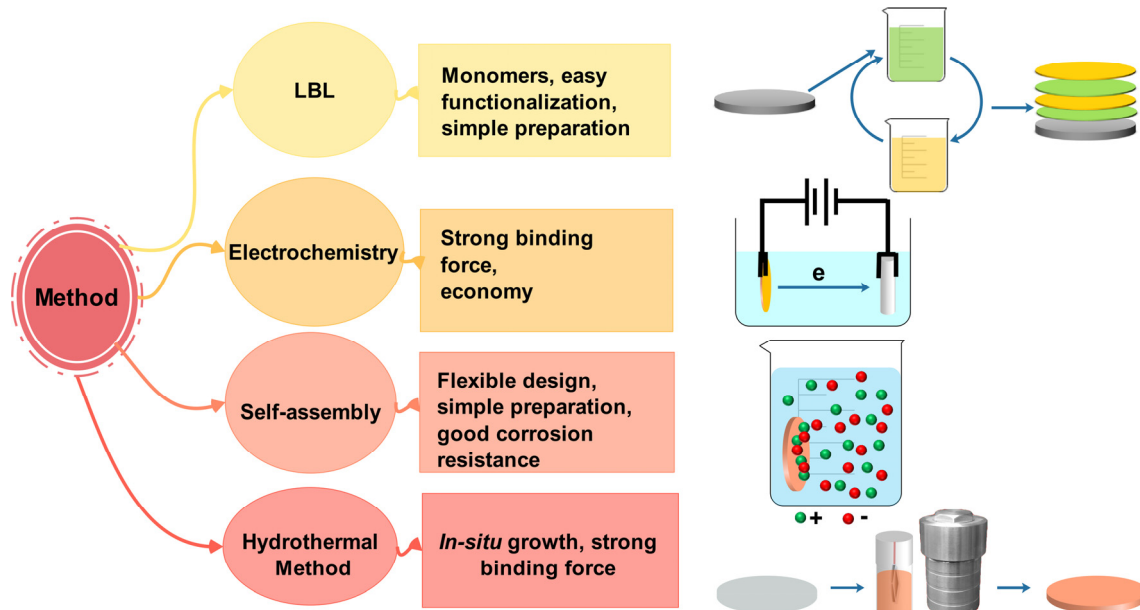


图5 可降解镁合金表面抗菌涂层制备过程示意图

Fig. 5 Schematic diagram of preparation process for antibacterial coating on Mg alloy surface

温,通过交联反应在纯镁表面构建了具有良好耐蚀性、pH 稳定性、抗菌活性、细胞相容性、光致发光和成骨分化能力的聚柠檬酸硅有机涂层,该涂层可以通过—COO—Mg 离子键实现与镁基体的良好结合。WANG 等^[155]和 YU 等^[93]则均以 MAO 涂层作为复合涂层内层,分别利用聚乙烯亚胺负载纳米 Ag 和 CHI,改善了镁合金的耐蚀性,同时赋予其较好的抗菌性,特别是 MAO 涂层特殊的多孔状形貌为外部有机涂层的成功制备提供了机械咬合作用,更有利于提高外部有机涂层与基材的结合。

2.2 层层组合法

层层组装(LbL)技术是通过利用不同离子之间的静电引力、共价键、氢键等分子间作用力,将聚电解质、聚合物、蛋白质、多肽、脂质、核酸、纳米颗粒和超结构等逐层交替制备涂层的一种方法,所得涂层往往为分子膜且质地均匀,这为制备复杂的功能化涂层提供了一种简单有效、环境友好的方式^[156]。自 2012 年,镁合金表面制备 LbL 涂层的技术逐渐成熟,组装前通常需要将镁合金表面进行碱处理,而后利用聚乙烯亚胺等作为前驱体,为后续涂层的制备提供条件^[157-159]。另外,组装单体和结合方式的多样性使得镁合金表面负载金属纳米粒子、金属氧化物、天然抗菌剂、药物等变得更为灵活。ZHANG 等^[160]利用 LbL 技术将纳米银载入共聚物多层中,从而改善了镁合金的耐蚀抗菌性。同时,组装单体官能团的多样性对涂层降解过程中控制腐蚀速率也十分关键。CUI 等^[91]通过 LbL 的方式,以 DNA 和 CHI 为组装单体,在氢氧化镁涂覆的镁合金表面制备复合涂层,涂层表现出良好的抗腐蚀性能和抗菌性能,复合涂层降解过程中, DNA 的磷酸基团和 CHI 的氨基可以通过诱导形成钙磷沉积产物进一步保护镁基体。但是, LbL 制备的涂层往往太薄,无法对镁合金提供长效的保护。在 LbL 技术实施过程中,浸泡法往往会损伤内部无机涂层或基体,旋涂或喷涂法则无法实现对形状复杂试样的制备。

2.3 电化学法

电化学方法制备复合涂层是镁合金表面改性的一种较为简单便捷的方法。通常使用的方法有阳极氧化^[161]、MAO^[162]、电沉积等。阳极氧化是把镁

合金作为阳极,在低电压下制备氧化物涂层的方式。而 MAO 是在阳极氧化基础上的升级,通过提高电压在样品表面产生微电弧,促进基体与电解质溶液反应生成陶瓷涂层。常用的 MAO 电解液有植酸系、硅酸系和磷酸系。通过调整电解液的配方,可以直接制备抗菌 MAO 涂层。CUI 等^[101]通过在植酸系电解液中添加 TA 的方法制备了改性 MAO 涂层,减少了涂层表面的孔径和孔隙率,并且赋予了涂层一定的抗菌性能。另外, MAO 涂层往往表现为典型的多孔结构,这种结构一方面在降解过程中会成为离子交换的通道,导致电偶腐蚀,同时,也为构建复合涂层提供了有利条件(此处参见自组合法)。

电沉积法是通过电荷移动,把溶液中的带电离子或分子沉积到样品表面,从而制备出具有特定功能的涂层,涂层性能依赖于电解液的成分、pH、温度、电流密度等条件。SUN 等^[98]将丙烯酸异冰片酯和甲基丙烯酸二甲氨基乙酯共聚物 P(ISA-co-DMA)与 TA 制备的胶体颗粒电沉积在镁合金表面,提高了镁合金耐蚀性,同时赋予了镁合金良好的抗炎和细胞黏附能力。

2.4 水热法

水热处理法主要是指在密闭的容器中,涂层的有效成分经过不断的沉淀、粉碎、再结晶,形成一系列晶粒细小、分布均匀且颗粒团聚较轻的纳米颗粒的过程^[163]。目前,利用水热处理法制备抗菌涂层主要是包括直接原位生长抗菌无机涂层或者在自组装/LbL 的基础上诱导钙磷、水滑石等无机涂层,进而控制药物的缓慢释放。ZHAO 等^[59]和 ZOU 等^[78]均通过一步法分别在镁合金表面原位生长纳米银-水滑石涂层和载锌蒙脱石涂层,在提高耐蚀性的同时,赋予镁合金良好的抗菌能力。JI 等^[133, 164]则通过层层组装 GS、环丙沙星等药物诱导钙磷涂层,在赋予镁合金抗菌性的同时,实现了药物的缓慢释放。

2.5 几种制备方法的性能比较

不同制备方法和抑菌因子对不同种类镁合金耐蚀抗菌能力的影响如表 5 所示,自组装、LbL、电化学、水热法等均可导致镁合金自腐蚀电流密度降低 2~3 个数量级,即镁合金耐蚀性的提升与制备方法关系不大,而主要取决于合金种类、涂层结构

表 5 不同制备方法和抑菌因子对不同种类镁合金耐蚀抗菌能力的影响

Table 5 Effects of different preparation methods and antibacterial factors on corrosion and antibacterial ability of different kinds of magnesium alloys

Method	Alloy	Antibacterial composition	Antibacterial ability	Corrosion resistance density, $J_{\text{corr}}/(\text{A}\cdot\text{cm}^{-2})$
Self-assembly ^[155]	AZ31	Ag nanoparticle	98.72%	Increase ($6.97\times10^{-4}\rightarrow1.42\times10^{-7}$)
Self-assembly ^[93]	Mg-4Li-1Ca	CHI	85.39%	Increase ($2.48\times10^{-5}\rightarrow6.71\times10^{-6}$)
LbL ^[160]	AZ31D	Ag nanoparticle	Inhibition circle ($d=18\text{ mm}$)	Increase ($5.64\times10^{-4}\rightarrow1.79\times10^{-6}$)
LbL ^[91]	AZ31	CHI	93.6% (<i>S.aureus</i>), 94.2% (<i>E.coil</i>)	Increase ($7.63\times10^{-5}\rightarrow1.54\times10^{-7}$)
Electrochemistry ^[101]	AZ31	TA	92.29% (<i>S.aureus</i>), 97.30% (<i>E.coil</i>)	Increase ($1.47\times10^{-5}\rightarrow5.22\times10^{-7}$)
Electrochemistry ^[99]	Mg	TA	Weak	—
Hydrothermal method ^[59]	Mg-3Zn-0.5Zr-0.5Sr	Ag nanoparticle	Weak	Increase ($2.56\times10^{-5}\rightarrow2.09\times10^{-6}$)
Hydrothermal method ^[78]	AZ31	Zn	Inhibition circle ($d=(32\pm0.5)\text{ mm}$)	Increase ($2.81\times10^{-5}\rightarrow2.86\times10^{-7}$)
Hydrothermal method ^[133]	AZ31	GS	99.99%	Increase ($3.52\times10^{-5}\rightarrow8.58\times10^{-8}$)
Hydrothermal method ^[164]	AZ31	CIP	95.24% (<i>S.aureus</i>) 98.65% (<i>E.coil</i>)	Increase ($1.34\times10^{-4}\rightarrow1.59\times10^{-6}$)

和成分。同一种抑菌因子, 通过不同制备方法实现负载时, 其抑菌性能不同, 这主要是由于抑菌因子在涂层中的分布与释放形式不同。因此, 涂层设计过程中, 需要研究者们根据需求, 选择适宜的抑菌因子和涂层制备方法, 平衡涂层可控降解与抗菌性之间的关系。

3 结语

近年来, 尽管可降解抗菌镁合金及其表面抗菌涂层越来越多样化, 但仍无法解决复杂的感染问题, 特别是兼顾镁基体的降解可控、顽固多样的菌种和多变的感染周期。突出的问题以及未来的发展方向体现如下:

1) 引入抗菌因子导致的腐蚀问题

对于引入金属离子导致的电偶腐蚀问题可以通过构建镁基体与抗菌涂层之间的物理屏障, 控制金属离子单向往溶液扩散来解决。而对于层层组装等由于制备过程导致的腐蚀问题, 则应通过调控 pH 值、浓度、温度等参数, 创造更为温和的制备条件。

2) 抑菌有效性问题

多肽、酶、CHI 等天然抑菌剂可利用其分子结构, 结合光动力疗法、光热疗法等新型抗菌机制改善其抗菌能力。对于载药涂层, 则应遵循感染规律, 通过选取适宜的药物载体, 通过控制载药量、降解速率等条件实现药物的可控释放。另外, 多数涂层的抑菌机制依靠与细菌的直接接触, 通过涂层结构设计, 实现逐层降解来移除黏附死细菌, 同时抑制细菌生物被膜形成十分关键。

3) 抗菌涂层的多功能化

作为骨固定材料, 在赋予镁合金抗菌能力的同时, 改善其促骨生长能力或者赋予其治疗特异性疾病(如骨髓炎等)的能力值得广大研究者们关注。

4) 抗菌涂层的智能化与适配化

不同年龄段、不同身体状态的个体的感染周期、伤口愈合周期各不相同, 通过涂层结构设计、设置可供调整的涂层制备参数或者利用微环境变化(如 pH 值、离子浓度、温度等)使得抗菌涂层智能化, 从而提高镁合金表面抗菌涂层在植入术后的适配性将是未来抗菌涂层设计需要解决的问题。

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Research progress of antibacterial coating on surface of biodegradable bone implant magnesium alloys

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Abstract: In recent years, the application of biodegradable implant materials has a fast development. Magnesium (Mg) and its alloys have become a new generation of biodegradable metal materials with broad prospects due to their good biocompatibility and biodegradability. However, the contradiction between the antibacterial properties, resulted from the releasing of Mg^{2+} ions and the alkalization of the surrounding environment in the process of rapid corrosion, and the long-term mechanical properties as the bone implants needs to be resolved urgently. This paper summarized the research progress of various metals and its oxides, biologically active substances, natural antibacterial substances and photothermal and photodynamic therapy on antibacterial Mg alloys and antibacterial coatings on the surface of Mg alloys. The preparation methods of various corrosion-resistant and antibacterial coatings on the surface of Mg alloys were studied, and the influence of different antibacterial carriers on the corrosion resistance and antibacterial activity of Mg alloys was discussed. The results show that the evolution of antibacterial Mg alloys and antibacterial coatings on the surface of Mg alloys are gradually matured, but there still are some problems need to be solved. Finally, the way forward of the antibacterial coating on the surface of biomedical degradable Mg alloys is elaborated.

Key words: magnesium alloys; antibacterial property; coating; biomaterials

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