二茂铁及其衍生物在传感器上的应用进展

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摘 要 二茂铁是一类具有夹心结构的有机金属配合物,有良好的氧化-还原特性,可有效改善传感器电极上的电子传递效率。本文评述了近年来二茂铁及其衍生物在酶生物传感器、免疫传感器和离子传感器上的研究状况,并对其今后的发展方向做出展望。

关键词 二茂铁,电子传递介体,传感器,酶生物传感器,修饰电极
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二茂铁是最早被发现的一类夹心配合物,也是最重要的有机金属配合物之一[1]。其独特的夹心结构和芳香性,特有的氧化-还原性以及良好的生物相容性使其在生物功能材料[2-4]、光电磁等功能材料[5-6]、电化学传感器[7]、分子电器元件[8]以及生物医药[9-16]等高新技术领域具有广泛的应用前景[17]。

由于具有良好的电化学性质并易于被官能化,二茂铁在电化学方面的应用备受关注。但由于二茂铁不能在电极上形成稳定的吸附层,所以固定并防止其流失一直是个难点。此外,二茂铁与其它导电物质的有效结合也是研究人员最感兴趣的问题之一。本文介绍了二茂铁及其衍生物在电化学传感器方面的应用研究进展,并对今后的研究方向做出展望。

1 生物传感器

生物传感器是对生物物质敏感并将其浓度转换为电信号进行检测的仪器,由固定化的生物敏感材料作识别元件(包括酶、抗体和抗原等)与适当的理化换能器及信号放大装置构成,可检测生物分子,主要用于临床诊断检查[18-20]、发酵工业和食品工业[21-22]、环境监测等方面。根据敏感组分的不同,生物传感器分为酶传感器、免疫传感器、细胞传感器、微生物传感器以及组织传感器等。本文主要介绍二茂铁在酶生物传感器和免疫传感器中的应用。

1.1 酶生物传感器

氧化还原酶和电极间的电子转移是建立酶生物传感器的基本条件,但是酶的活性中心常被包埋在蛋白质外壳中,导致酶与电极间的电子传导速率较低,从而酶电极的效率较低。目前利用纳米结构材料,如金纳米粒子、碳纳米管和石墨烯等修饰电极,改善电极的电催化性质,增强电极的直接电子传导作用;或将电极表面用氧化-还原电子传递介体进行化学修饰,提高其间接电子传导效率[23-24]。间接电子传导是用氧化-还原电子传递介体接近酶的氧化还原中心,将酶反应过程中产生的电子从酶反应中心转移到电极表面,作为电荷载体加快电子传递,以改善检测性能[23,25-26]。二茂铁及其衍生物具有高的氧化-还原活性,快的电子转移速率,良好的生物相容性,相对低的分子质量,对 pH 独立,是良好的电子传递介体[19,27-28],在修饰电极中被用作生物分子和电极间电子转移的介体,广泛应用于介导型安培生物传感器[7,29]。

Şenel 等[28]将辣根过氧化物酶(HRP)用酰胺键共价固定在高分子膜上,建立无试剂生物传感器。其传导机理如 Scheme 1 所示。HRP 与过氧化氢反应,HRP 被氧化为 HRP(Ⅰ),同邻近的还原态二茂铁反应后 HRP 被还原为 HRP(Ⅱ),同时二茂铁被氧化,HRP(Ⅱ)进一步同还原态二茂铁反应,生成 HRP

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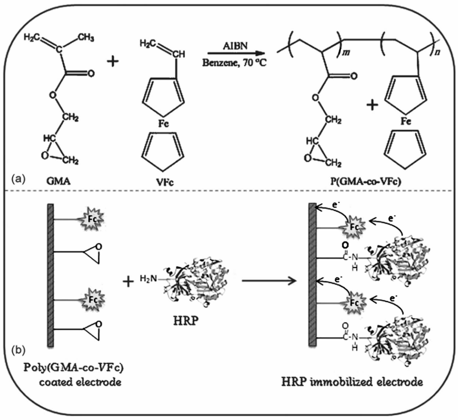
和氧化态二茂铁。生成的氧化二茂铁得到电子,恢复成还原态二茂铁,再次进行反应。整个过程中,HRP和过氧化物反应生成的电子,经由二茂铁的传导,进入电极,而非直接传入电极。



Scheme 1 Mechanism of indirect electron transfer mediated by ferrocene

为提高酶电极的敏感性,Yilmaz等[30]将纳米材料填入壳聚糖-二茂铁基质中,可以更有效地提高酶电极的电子传导性。此外,Fan等[31]将二茂铁电子传递介体与氨基化的氧化石墨烯等导电物质相结合,用二茂铁功能化的石墨烯修饰电极并制备酶传感器。其中,接枝在石墨烯上的二茂铁保持了电化学活性,有良好的电子转移特性。该电极具有高的敏感性、良好的选择性及高的稳定性。Goff等[32]用二茂铁功能化的多壁碳纳米管制备了良好的生物传感器。而Pepi等[24]将二茂铁"软着陆"在具有羧基的多壁碳纳米管上,也可应用在生物传感器和生物燃料电池中。Qiu等[33]用醛基二茂铁修饰带有氨基的多壁碳纳米管,然后固定在玻碳电极上,用来检测葡萄糖。二茂铁-多壁碳纳米管综合了碳纳米管的直接电子传导和二茂铁的间接电子传导作用,加快了电极上电子转移效率,可以用于构建特殊的生物传感器[34]。有报道证明,双壁碳纳米管可作为分子导线使电子在电极和双壁碳纳米管中的氧化还原性的二茂铁之间传输[35]。Liu等[23]用二茂铁和乙酰基硫醇封端固定在金纳米粒子表面,形成稳定的电活性层,再结合在覆盖石墨烯-壳聚糖薄膜的玻碳电极上,二茂铁、纳米材料及石墨烯的协同作用提高了电子转移效率,这样构建的高敏感、低检出限和稳定性良好的电极用于检测芸香苷。该电极虽没有酶的参与,却为酶电极提供了直接电子传导与间接电子传导机制相结合的思路。

以上所述说明,二茂铁作为酶生物传感器的电极修饰材料,能直接与被蛋白质包覆的酶活性中心相连,将反应产生的电子从不导电的蛋白质外壳中转移,直接导入电极表面。此外,将二茂铁与纳米贵金属、石墨烯和碳纳米管等导电物质相结合,还可更好地改善电极电子的传导,可作为今后的研究方向。

小分子电子传递介体通常容易从电极上流失。为此,有人用主客体包合的方法,将二茂铁包合在环糊精、杯芳烃等主体中,以防止二茂铁电介质的泄漏[36]。Şenel等[28-29]将乙烯基二茂铁直接共价结合在甲基丙烯酸缩水甘油酯(GMA)高分子膜上,也可良好保留二茂铁。此外,二茂铁固定在电极材料上还有多种方法,如自组装膜[37-39]、酰胺链接[25]和点击化学[40]等方法。

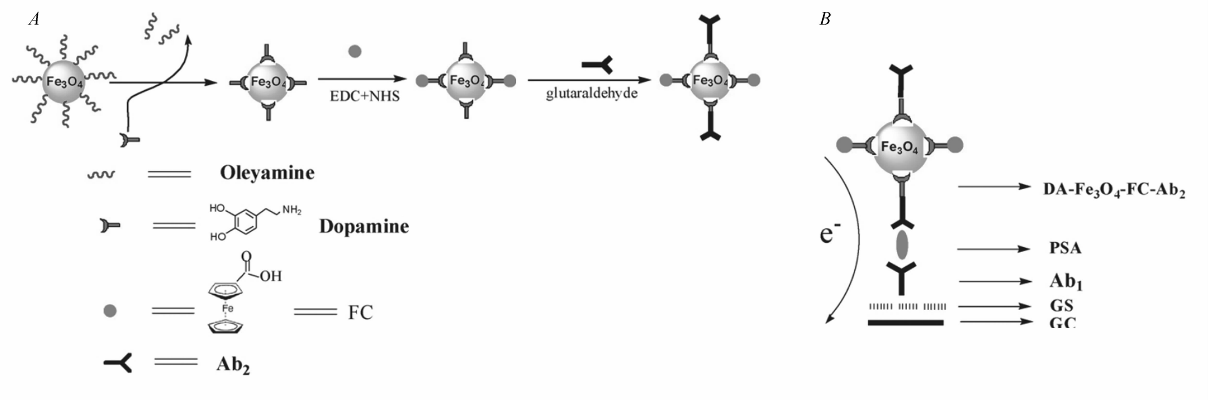
Huang等[41]用含叠氮的烷烃长链将二茂铁单分子层覆盖在硅表面,连接在二茂铁与硅表面间较长的链阻碍了电子传递,使得导电性能下降。可见,在设计用二茂铁共价修饰电极时,连接二茂铁与电极的链结构也是需要考虑的因素。

1.2 免疫传感器

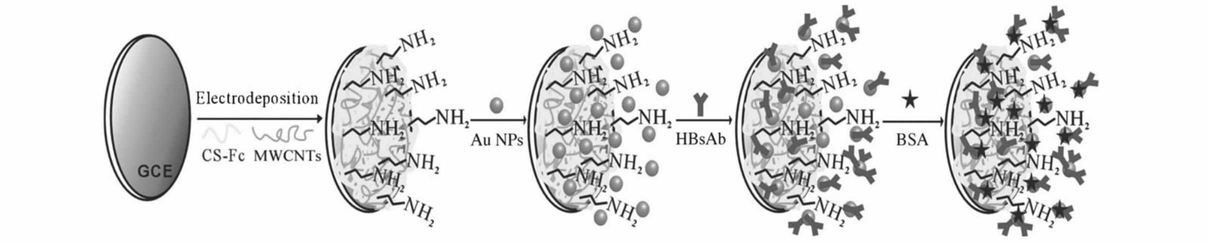
在免疫传感器中,抗原和抗体无电活性,无法产生电流,需要对其进行复杂的标记以制备安培型传感器。二茂铁可作为免疫传感器中的标记物[19-20,22,42]或作为电极上的电子传递介体[43-44]。如Li等[19]以含二茂铁的复合物作标记建立免疫传感器,其电信号由二茂铁产生氧化-还原电流提供,该传感器可用于检测前列腺特异抗原(PSA),以诊断前列腺癌(Scheme 2)。

Liang等[44]用壳聚糖-二茂铁/多壁碳纳米管修饰电极,增强二茂铁的电化学活性,同时为肝炎B表面抗原提供活性结合位点,当抗原抗体结合时,电信号经由二茂铁介导传入电极,检测过程中无标记物

(Scheme 3)。二茂铁免疫传感器可用来诊断癌症[19-20]、肝炎[44],检测蛋白质[42]和大肠杆菌[22]等。



Scheme 2　Detection of PSA with ferrocene as a label of sensor

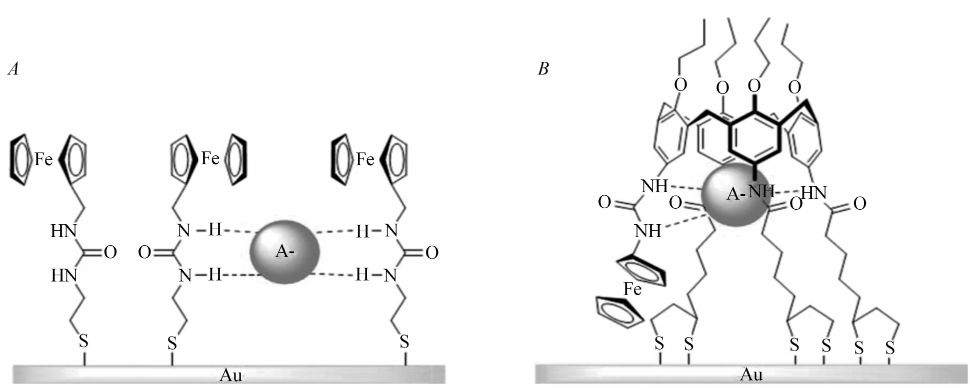


Scheme 3　Label-free detection of HBsAb with ferrocene

2　离子传感器

二茂铁独特的氧化-还原电化学特性和易官能化的性质,可将其应用在重金属和过渡金属离子的化学传感器中。二茂铁离子传感器的原理是基于其与被检测离子结合时所发生电势的转变[45],以及伴随着的溶液颜色、吸收光谱和荧光的改变,据此可建立一个多通道的离子检测传感器[45-50]。二茂铁基的阴离子传感器一般包括胺基,而阳离子传感器则含吡啶、聚吡啶或氮杂二烯、连氮、环醚和杂芳环等基团[46,51]。

二茂铁在阴离子结合系统中常用作电化学受体单元,不仅是因为其稳定的氧化-还原性,还由于二茂铁容易官能化,经过设计可与阴离子强结合[52-53]。如 Cormode 等[54]用新型二茂铁杯芳烃受体(Scheme 4*B*),构建了单分子膜电化学阴离子传感器。将受体自组装在金电极上形成氧化-还原活性单分子膜,对阴离子有强的结合性,产生的复合物在金电极上引起阴极电位的改变,据此检测溶液中的离子(Scheme 4)。



Scheme 4　Ferrocene-immobilized electrode for anion sensoring

二茂铁-甘氨酸复合物具有选择性氧化-还原特性及很强的变色性,可作为荧光化学传感器在水环

境中用肉眼直接检测出 Hg^{2+}[55-56]。据最近报道[50],已合成得到了基于二茂铁-五元杂环(二茂铁-咪唑二苯吩嗪)分子的新型电化学传感器,可高效识别水溶液中过渡金属阳离子。二茂铁基受体作为对 Hg^{2+} 的选择性分子探针,在水环境中可通过电化学、比色法和荧光法等3种不同的方法检测 Hg^{2+}。

由于咪唑含有氮和亚氨基,与阴阳离子均可选择性反应,用二茂铁-咪唑苯酚建立的传感器既可检测阴离子又可检测阳离子,称为电荷中性化学传感器。Sathyaraj 等[51]用二茂铁-咪唑苯酚传感器成功检测了 Fe^{2+}、Cd^{2+}、Co^{2+}、Cu^{2+}、Ni^{2+} 和 Pb^{2+} 等阳离子和 HSO_4^-、F^-、Br^-、I^-、OAc^- 和 OH^- 等阴离子。

此外,还有人合成了一种蒽醌-二茂铁,将其结合在电极上用作 pH 和氧的传感器[57]。由于其特殊的荧光性质和离子选择性,二茂铁吡唑复合物不仅可用于检测 Cu^{2+} 和 Hg^{2+},还可用来设计复杂逻辑门控,建造分子水平上的集成逻辑电路[58]。

3 结论和展望

鉴于二茂铁具有上述优良性质,使得二茂铁及其衍生物作为传感器的电极修饰材料在近年来备受关注。此外,二茂铁在电极上的良好表现,也可以作为酶生物燃料电池电极的组分[59],与石墨烯、纳米贵金属及环糊精等相结合,在加快电子传递速率的同时也可为酶、生物活性物质等创造良好的生物环境,提高酶电池的工作效率与寿命。

未来还应继续寻求在电极上稳定固定二茂铁的方法,如与环糊精进行主客体包合,防止电介质渗漏的同时还可调节电极的导电性能,在增强电极效率的同时还保证了电极的稳定性和使用寿命;探索二茂铁与其它导电物质(如石墨烯等)的相互结合,以期实现电极上直接传导和间接传导电子机制的有机结合,更有效地提高电子转移的效率,以期拓展二茂铁及其衍生物的应用范围。

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Research Progress in the Sensor Application of Ferrocene and Its Derivatives

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Abstract Ferrocene(Fc), a metallorganic sandwich-structured compound, can improve the electron transfer efficiency of sensor electrode effectively, due to its excellent redox property. In this review, we summarized the recent development of ferrocene and its derivatives in enzyme biosensors, immunosensors and chemical ion sensors, and then prospected a further development outlook.

Keywords ferrocene, electron transfer mediator, sensor, enzyme biosensor, modified electrode