电化学传感器用于检测抗寄生虫药物的应用进展

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摘 要 随着抗寄生虫药物在医学、食品行业、环境卫生等方面的广泛应用,寄生虫的耐药性也随之增加,其中假劣伪制药物是导致寄生虫产生耐药性的重要原因之一.因此,开发灵敏快捷的抗寄生虫药物监测方法至关重要.在各类抗寄生虫药物检测技术中,电化学方法因操作简便,响应时间快,灵敏度高,成本低和仪器便携等优势展示出广阔的应用前景.评述了近年来用于抗寄生虫药物检测的电化学传感器研究进展及其在实际样品分析中的应用,并重点比较了不同复合传感界面及其检测性能.电化学传感器在抗寄生虫药物检测领域在未来的发展趋势是更高的灵敏度、更快的检测速度及更广泛的应用等.

关键词 抗寄生虫药物;电化学方法;传感器;电极

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Recent progress in electrochemical sensors for detecting antiparasitic drugs

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Abstract With the widespread use of antiparasitic drugs in medicine, food industry, environmental hygiene, and other fields, there has been an increase in parasite resistance. Counterfeit and substandard drugs are significant contributors to the development of this resistance. Therefore, it is crucial to develop sensitive and rapid antiparasitic drug monitoring methods. Compared with various anti-parasitic drug detection methods, electrochemical methods have demonstrated extensive potential due to their advantages of simple operation, fast response time, high sensitivity, low-cost and portable instrument. Herein, the research progress of electrochemical sensors in the detection of anti-parasitic drugs and their application in actual sample analysis in recent years are reviewed. Then, the sensing properties of different composite interfaces are compared. Finally, the future development trend of electrochemical sensors in the field of anti-parasitic drug detection is prospected, including higher sensitivity, faster detection speed and wider application range.

Keywords antiparasitic agents; electrochemical method; sensor; electrodes

寄生虫是生存于宿主体内或体外以获取食物、发育繁殖的生物,主要包括蠕虫和原生生物.世界卫生组织(WHO)指出,世界各地都有由寄生虫造成的感染和死亡案例,寄生虫严重危害人类健康[1].针对不同类型的寄生虫引起的疾病,目前已有各种抗寄生虫药物对其进行治疗,例如由恶性疟原虫引起的疟疾,临床上一线疗法是采用以青蒿素为基础药物的联合疗法(ACTs)[2],但是许多抗寄生虫药物的

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疗效受到耐药性的限制,研究表明寄生虫正在对最新的药物产生耐药性,原因由诸多因素引起,其中假劣伪制药物是导致寄生虫产生耐药性的重要原因之一[3-4],其次,在药物剂量不足以及频繁地使用抗寄生虫药物期间,会增加寄生虫的耐药性.对于不同的寄生虫类型,使用有效的抗寄生虫药物、遵循医嘱进行正确的给药、严格把控药物质量及采用标准化的检测方法是延缓抗寄生虫药物耐药性的非常重要的策略[5].

目前,各种分析方法中对抗寄生虫药物的定量分析方法有很多,例如TELLA等[6]使用紫外分光光度法(UV-Vis)测定片剂和混悬剂中的苯并咪唑类药物阿苯达唑(ABZ);RUYCK等[7]开发出了定量液相色谱-电喷雾串联质谱法(LC-MS/MS)定量测定驱肠虫药物甲苯咪唑(MBZ)及其在绵羊体内的水解和还原代谢产物;GATTI等[8]开发出了高效液相色谱-荧光法(RP-HPLC-FLD)同时测定四种主要的金鸡纳抗疟生物碱及其二氢衍生物;LIU等[9]使用改进的气相色谱法(GC)测定了青蒿单叶或单花中的青蒿素(ART);QUENNOZ等[10]使用薄层色谱法(TLC)对青蒿叶片中ART的总含量进行量化.然而,这些技术检测都有分析时间长和仪器操作复杂等困难.因此,迫切需要便携式、简单且经济的分析技术.与上述技术相比,电化学传感技术具有经济、快速及方便等优点.此外,电化学传感器可以根据检测目标的不同改变修饰材料,这些复合传感器通过协同效应优化纳米材料和其他组件的特性,有助于更精确地检测[11].

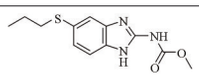
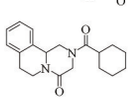
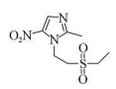
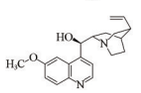
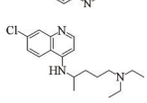
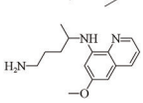
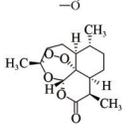
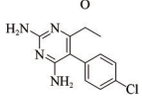
通过结合电化学原理和先进的传感技术,电化学传感器为抗寄生虫药物的检测提供了新的途径和解决方案.本文具体综述了近年来各类电化学传感器检测不同种类的抗寄生虫药物的应用进展,包括传感器修饰材料类型、电化学分析方法、检测效果等,探讨了其面临的困难与挑战,并展望了这一领域的未来发展前景.

1 抗寄生虫药物概述

对不同的寄生虫类别选择的药物也有所不同,可分为驱肠虫药、抗血吸虫病药和抗疟药.对其分类如表1所示.

表1 抗寄生虫药物概况[12-18]

Tab. 1 Overview of antiparasitic drugs[12-18]

抗寄生虫种类	药物种类	代表药物	化学结构	杀虫原理
驱肠虫	苯并咪唑类	ABZ		抑制葡萄糖吸收
抗血吸虫	非锑剂	PZQ		抑制二氢叶酸还原酶
抗阿米巴原虫	硝基咪唑类	TNZ		抑制DNA合成,产生有毒代谢产物
抗疟原虫	4-喹啉甲醇类	QN		抑制核酸合成
抗疟原虫	4-氨基喹啉类	CQ		抑制核酸合成
抗疟原虫	8-氨基喹啉类	PQ		抑制核酸合成
抗疟原虫	青蒿素类	ART		生成氧自由基,破坏代谢活动
抗疟原虫	嘧啶类	PMT		抑制二氢叶酸还原酶

注:TNZ(替硝唑);QN(奎宁);CQ(氯喹);PQ(伯氨喹);PMT(乙胺嘧啶).

驱肠虫药是用以控制和治疗动物或人体寄生蛔虫、钩虫、绦虫等肠道寄生虫感染的药物，临床上广泛使用的是ABZ[19]. 血吸虫病是一种传染性疾病，主要通过接触含有血吸虫幼虫的水体导致感染. 吡喹酮（PZQ）为控制及治疗血吸虫病中不可或缺的一种药物[20]. ART衍生物以其抗疟活性而闻名，也有抗血吸虫活性的报道[21-22]. 疟疾是由疟原虫属的原生动物寄生虫引起的，通过蚊子进行传播，有高发病率和死亡率，抗疟药物主要是通过消除疟原虫在人体的红细胞阶段而产生疗效，ACTs是由一种强效ART成分外加一种作用较长的伴侣药物组成，可快速清除大多数寄生虫[4].

根据一项针对学龄前儿童对驱肠虫药物耐药性测试，ABZ对卢旺达学龄儿童蛔虫的疗效降低，肠道寄生虫的耐药性正在增加[23]. 另一项研究显示，埃及尼罗河三角洲地区的五个村庄1.6%的肠血吸虫病患者在使用PZQ后未能治愈，并从这些患者体中分离出了耐受株，证明抗血吸虫的耐药性正在增加[24]. 来自柬埔寨的报告显示，部分ACTs的疗效正在下降，疟原虫对ART耐药性的增长日益显著[25].

2　电化学传感器及其在抗寄生虫药物检测中的应用

电化学分析方法基于目标分析物和电化学传感器之间的相互作用产生电流、电位、电阻或阻抗形式的电化学信号. 运用循环伏安法（CV）、差分脉冲伏安法（DPV）、交流伏安法（ACV）、方波伏安法（SWV）和线性扫描伏安法（LSV）等检测手段可直接或间接分析电化学信号从而检测出溶液中待测物的含量. 电化学传感器按照传感元件的类型划分，可以分为无机材料基传感器和生物材料基传感器，这两类传感器均在抗寄生虫药物检测中有着广泛的应用（图1）.

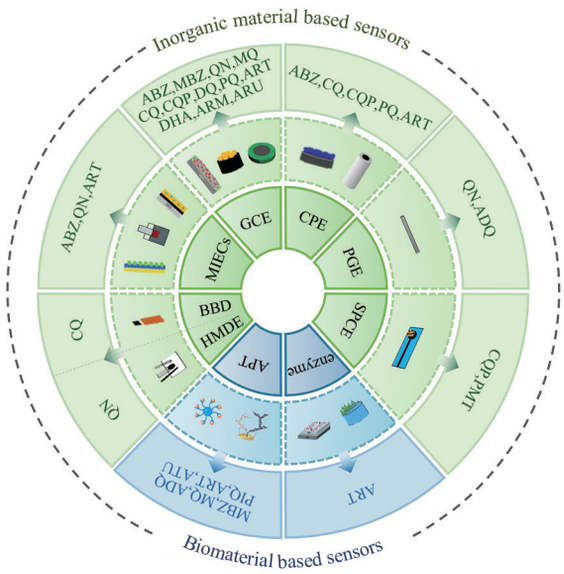


图1　用于抗寄生虫药物检测的不同电化学传感器类型及示意图

Fig. 1　Schematic diagram of different types of electrochemical sensors used for the detection of antiparasitic drugs

2.1　无机材料基传感器

无机材料基传感器是一种利用物理、化学材料作为传感元件的传感器. 这些材料通常具有良好的电导性和表面活性，能够与目标物质发生吸附、表面反应或电子传导等相互作用，从而产生电化学信号. 由于材料的多样性和可调性，该类传感器可以实现高度选择性和灵敏度，能够针对不同的目标物质改变材料类型. 在无机材料基传感器检测抗寄生虫药物方面，以碳材料为传感元件的碳材料电化学传感器应用最为广泛，也有其他电化学传感器如分子印迹传感器、硼掺杂金刚石电极、悬挂式汞滴电极的报道.

基底电极可以被制成浸入溶液的形式，电化学信号在基底电极上产生. 碳材料具有相对惰性、可加工性、经济成本、优良的物理和化学特性等优点，使其成为最受欢迎的电化学基底材料[26]. 以碳材料为基底电极的电化学传感器主要包括玻碳电极传感器、碳糊电极传感器、铅笔石墨电极传感器、丝网印刷碳电极传感器. 碳材料电化学传感器对抗寄生虫药物检测如表2所示.

表2　用于检测抗寄生虫药物的碳材料电化学传感器

Tab. 2　Carbon material electrochemical sensors for detecting antiparasitic drugs

序号	修饰材料	基底电极	检测方法	检测限	线性范围	目标药物
1	Pt-Pd	GCE	DPV/CV	0.08 μmol/L	3.12×10^{-6}~2.26×10^{-5} mol/L	ABZ[27]
2	CTAB@g-C_3N_4	CPE	CV/SWV	1.1×10^{-8} mol/L	0.2×10^{-6}~10×10^{-6} mol/L	ABZ[28]
3	GaN-PANI-PPy	GCE	DPV/CV	2.581×10^{-8} mol/L	3×10^{-7}~9×10^{-8} mol/L	MBZ[29]
4	POA/CNTs	GCE	DPV/CV/CA	0.4 μmol/L	1.0~35.0 μmol/L	MBZ[30]
5	GNS-CNS/CS	GCE	DPV/CV/AdSDPV	10.5 nmol/L	0.02~1.0 μmol/L	MBZ[31]
6	MnO_2-ErGO	GCE	LS-AdCSV/EIS	0.33 μmol/L	1~20 μmol/L	TNZ[32]
7	PLA	CPE	CV/EIS/ DPV	0.0841 μmol/L	0.2~9.0 μmol/L	TNZ[33]

续表

序号	修饰材料	基底电极	检测方法	检测限	线性范围	目标药物
8	poly(DPASA)	GCE	CV/EIS/DPV	4.27×10^{-9} μmol/L	0.05~300 μmol/L	TNZ[34]
9	poly (BBPDRRuC)	GCE	CV/SWV/EIS	2.5 nmol/L	10^{-8}~3.0×10^{-4} mol/L	TNZ[35]
10	Chit@alumina	GCE	CV/EIS/DPV	16 nmol/L	0.6×10^{-9}~36×10^{-8} mol/L	TNZ[36]
11	GR/Fe_3O_4 NPs	GCE	DPV/CV	0.23 μmol/L	0.05~120 μmol/L	MNZ[37]
12	f-Co@rGO	GCE	DPV/CV	0.015 nmol/L	0.025~500 nmol/L	MNZ[38]
13	Au-MWCNTs	GCE	DPV/CV	0.005 μmol/L	0.005~250 μmol/L	MNZ[39]
14	MoS_2 /gCN	GCE	DPV	0.099 μmol/L	2~125 μmol/L	MNZ[40]
15	-	PGE	DPV/CV	0.2 μmol/L	0.5~100 μmol/L	QN[41]
16	p-(AHNSA)	GCE	CV/SWV	1.42×10^{-8} μmol/L	1.0×10^{-7}~1.0×10^{-5} μmol/L	QN[42]
17	MIPs	GCE	EIS/CV	2.0×10^{-8} mol/L	8.0×10^{-7}~2.6×10^{-4} mol/L	QN[43]
18	MWCNTs-RTIL	GCE	CV/SWV	0.44 μmol/L	3.0×10^{-3}~0.10 mmol/L	QS[44]
19	AuNUs	GCE	EIS/SWV/CV	1.42×10^{-9} mol/L	2.0×10^{-9}~1.0×10^{-6} mol/L	MQ[45]
20	poly([Cu(Bip)$_2$OH]I)	GCE	CV/EIS/SWV	4.22×10^{-3} μmol/L	0.5~250 μmol/L	CQ[46]
21	rGO@WS	GCE	DPV/CV	80 nmol/L	0.5~82.4 μmol/L	CQ[47]
22	Cu(OH)$_2$-NW	CPE	DPV	0.01 μg/mL	0.068~6.88 μg/mL	CQ[48]
23	dsDNA	CPE	DPV/CV	3.0×10^{-8} mol/L	1.0×10^{-7}~1.0×10^{-5} mol/L	CQ[49]
24	TiO_2-NPs@rGO	GCE	CV/EIS/DPV	10^{-8} mol/L	10^{-7}~10 mol/L	CQ[50]
25	SnO_2	CPE	CV/EIS/DPV	0.01 μmol/L	0.1~23.3 μmol/L	CQP[51]
26	rGO-CuNPs	GCE	CV/SWV	0.23 μmol/L	0.5~110 μmol/L	CQP[52]
27	Poly(DHRPCo)	GCE	CV/EIS/AdSSWV	0.00039 μmol/L	0.005~300.0 μmol/L	CQP[53]
28	ZnSe/rGO-ODA	SPCE	DPV/CV	0.00143 μmol/L	0.199~250.06 μmol/L	CQP[54]
29	MWCNT/PMO	GCE	DPV/CV	8.9×10^{-8} mol/L	1.0×10^{-7}~3.5×10^{-6} mol/L	ADQ[55]
30	-	PGE	DPV/CV	0.30 nmol/L	1.0~200 nmol/L	ADQ[56]
31	poly(CCN)	PGE	DPV/CV	0.16 μmol/L	0.50~25 μmol/L	ADQ[57]
32	Dy-MOF@MWCNT	GCE	DPV/CV	0.377 μmol/L	0.4~20 μmol/L	ADQ[58]
33	PANI-Co_3O_4	GCE	DPV/CV	2.07×10^{-9} mol/L	2×10^{-5}~3.6×10^{-5} mol/L	PQ[59]
34	MWCNT	GCE	CV/SWV	28 nmol/L	0.1~5.0 μmol/L	PQ[60]
35	AuNUs	GCE	EIS/SWV/CV/DPV	3.52×10^{-9} mol/L	1.0×10^{-8}~1.0×10^{-6} mol/L	PQ[61]
36	Cu(OH)$_2$-NW	CPE	DPV	0.25 μg/mL	0.58~5.89 μg/mL	PQ[48]
37	CoPc	CPE	DPV/CV	6.5×10^{-6} mol/L	2.1×10^{-5}~5.3×10^{-4} mol/L	ART[62]
38	MWNT-DHP	GCE	LSV	3.5×10^{-7} mol/L	0.4~40 mg/mL	ART[63]
39	AgNPs/Gr	GCE	CV/EIS/DPV	1.2×10^{-9} mol/L	1.1×10^{-8}~3.0×10^{-6} mol/L	ART[64]
40	AgNPs/GN/PTH	GCE	CV/EIS/DPV	1.2×10^{-9} mol/L	3.2×10^{-8}~1.0×10^{-6} mol/L	ART[65]
41	CoS/rGO	GCE	DPV	0.015 μmol/L	30~100 μmol/L	ART[66]
42	GNP-MWCNT-IL/CoPc	GCE	DPV/CV	0.55 μmol/L	1.5~60 μmol/L 60~600 μmol/L	ART[67]
43	[FeT(oglu)PPCl]/AuNPs	GCE	CV	1.7×10^{-9} mol/L	1.8×10^{-7}~1.7×10^{-9} mol/L	ART[68]
44	SWCNT	GCE	EIS/CV/LSV	3.0×10^{-7} mol/L	5.0×10^{-7}~5.0×10^{-4} mol/L	DHA[69]
45	SWCNTs	GCE	EIS/CV/CC/CA	4.02×10^{-7} mol/L	6.71×10^{-7}~2.45×10^{-4} mol/L	ARM[70]
46	-	GCE	SWV/CV/DPV	0.491 μg/mL	4.0~40 μg/mL	ARU[71]
47	Ppy@ZnO/Fe_3O_4	CPS	CV/AdSDPV	0.24 pmol/L	0.8~15.0 pmol/L	ARU[72]
48	dsDNA	SPCE	DPV/CV	1.0×10^{-8} mol/L	1.0×10^{-7}~5.0×10^{-5} mol/L	PMT[18]
49	BLSO NPs	SPCE	DPV/CV	4 nmol/L	0.01~172 μmol/L	NTZ[73]
50	Mo-$MnWO_4$ NCs	GCE	CV/i-t	3.7 nmol/L	0.014~170.2 μmol/L	NTZ[74]

注:QS(硫酸奎宁);MQ(甲氟喹); DHA(双氢青蒿素);ARM(蒿甲醚);ARU(青蒿琥酯); Pt-Pd(铂-钯);CTAB@g-C_3N_4(十六烷基三甲基溴化铵-石墨氮化碳);GaN-PANI-PPy(氮化镓-聚苯胺-聚吡咯);POA/CNTs(邻苯甲醚-多壁碳纳米管);MnO_2-ErGO(氧化锰/电化学还原氧化石墨烯); poly(DPASA)(聚二苯胺磺酸);poly (BBPDRRuC)(聚二(2,2′-联吡啶)二间苯二酚合钌(Ⅲ));f-Co@rGO(花状钴);MoS_2/gCN(二硫化钼-石墨氮化碳);p-(AHNSA)(聚4-氨基-3-羟基萘磺酸);MIPs(分子印迹聚合物); RTIL(离子液体凝胶); AuNUs(金纳米海胆);poly([Cu(Bip)$_2$OH]I)(聚(双(2,2′-联吡啶)羟基碘化铜(Ⅱ));rGO@WS(还原氧化石墨烯量子点);Cu(OH)$_2$-NW(氢氧化钠纳米线);dsDNA(小牛胸腺脱氧核糖核酸);TiO_2(二氧化钛);SnO_2(氧化锡);rGO-CuNPs(还原氧化石墨烯-铜纳米颗粒);Poly(DHRPCo)(二羟基-1,10-菲咯啉钴(Ⅱ)); PMO(甲基橙聚合物);poly(CCN)(聚钙黄绿);Dy-MOF(镝基金属有机框架);PANI-Co_3O_4(聚苯胺-氧化钴);CoPc(钴酞菁);MWNT-DHP(多壁碳纳米管膜);AgNPs/Gr(纳米银/石墨烯);PTH(聚硫堇);CoS(硫化钴);GNP-IL(石墨烯纳米片-离子液体);[FeT(oglu)PPCl](卟啉金属配合物);SWCNT(单壁碳纳米管);Ppy@ZnO/Fe_3O_4(核壳纳米复合材料);Bi-doped BLSO NPs(掺铋锡酸镧烧绿石); CPS(碳浆电极);DPV(差分脉冲伏安法);CV(循环伏安法);SWV(方波伏安法); CA(计时电流法);AdSDPV(吸附剥离差分脉冲伏安法);EIS(电化学阻抗谱);AdSSWV(吸附剥离方波伏安法);LSV(线性扫描伏安法);CC(计时库仑法);i-t(安培法).

2.1.1　玻碳电极传感器

玻碳电极(glassy carbon electrode,GCE)是由玻璃纤维和碳材料组成,通常在高温下将玻璃纤维烧结成坚硬的结构,然后在表面涂覆高度石墨化碳材料制成的电极,GCE比较稳定,不易崩解,是电化学传感器构建中使用频率最高的基底电极[27].在GCE上负载石墨烯纳米片和碳纳米球/壳聚糖(GNS-CNS/CS)[31],构建纳米复合材料修饰的玻碳电极传感器,该电极灵敏度高,对MBZ进行测定(图2(a)),表现出优异的电化学响应,有望用于测定临床制剂中的痕量MBZ.将电化学传感器与液相微萃取相结合[39],使用二丙胺(DPA)作为萃取溶剂,使用金多壁碳纳米管复合材料(Au-MWCNTs)修饰的GCE测量甲硝唑(MNZ)(图2(b)),该方法使溶剂消耗最小化,减少了分析过程中产生的废物和污染物.硝唑尼特(NTZ)是硝基噻唑的水杨酰胺衍生物,被用于治疗厌氧肠道寄生虫及细菌感染人类和动物的各种疾病.SUKANYA等[74]采用一锅水热合成法制备了钼掺杂钨酸锰(Mo-$MnWO_4$ NCs),使用Mo-$MnWO_4$ NCs/GCE在最佳条件下检测人血清和尿液样品中的NTZ(图2(c)),分别在94%~99.2%和95.3%~99.6%的范围内实现了高回收率.

2.1.2　铅笔石墨电极传感器

铅笔石墨电极(pencil graphite electrode,PGE)是由不同直径的石墨引线组成,石墨铅笔芯通常用于书写工具,容易获取且价格低廉,将铅笔芯表面涂覆石墨粉末后连接至电化学系统可构建铅笔石墨电极传感器.在电化学分析中,PGE具有机械刚度、化学惰性、便携性等特性[75].使用PGE对抗疟药物阿莫地喹(ADQ)进行超灵敏电化学测定[56],PGE为每次测量提供了可再生的传感表面(图2(d)).该传感器对饮用水、人造血液、母乳和人尿液基质中的ADQ测定中均显示出良好的适用性.

2.1.3　碳糊电极传感器

碳糊电极(carbon paste electrode, CPE)是将导电碳粉和粘合剂混合覆在电极表面制成的一种新型电极,CPE制作简单,可以轻松地制成不同形状和尺寸的电极,CPE的残余电流比GCE或贵金属电极的残余电流低10倍,因此CPE被广泛应用于各种分析领域.PATIL等[28]使用十六烷基三甲基溴化铵固定在石墨氮化碳上形成复合材料(CTAB@g-C_3N_4)改性CPE(图3(a)),与裸CPE相比,改性CPE在pH为3的磷酸盐缓冲溶液中对ABZ的电化学氧化表现出显著的电催化作用,该方法可用于药物制剂的临床诊断、质量控制和药物筛选.通过使用CV技术在BCPE表面聚合L-精氨酸(PLA)[33],制备PLAMCPE,与CPE相比,PLAMCPE对TNZ还原的电化学敏感性显著增强(图3(b)),DPV方法在0.2~9.0 μmol/L的线性范围内达到的检测限为0.0841 μmol/L,定量限为0.2803 μmol/L,该电极在检测TNZ时具有很高的灵敏度和选择性.

2.1.4　丝网印刷碳电极传感器

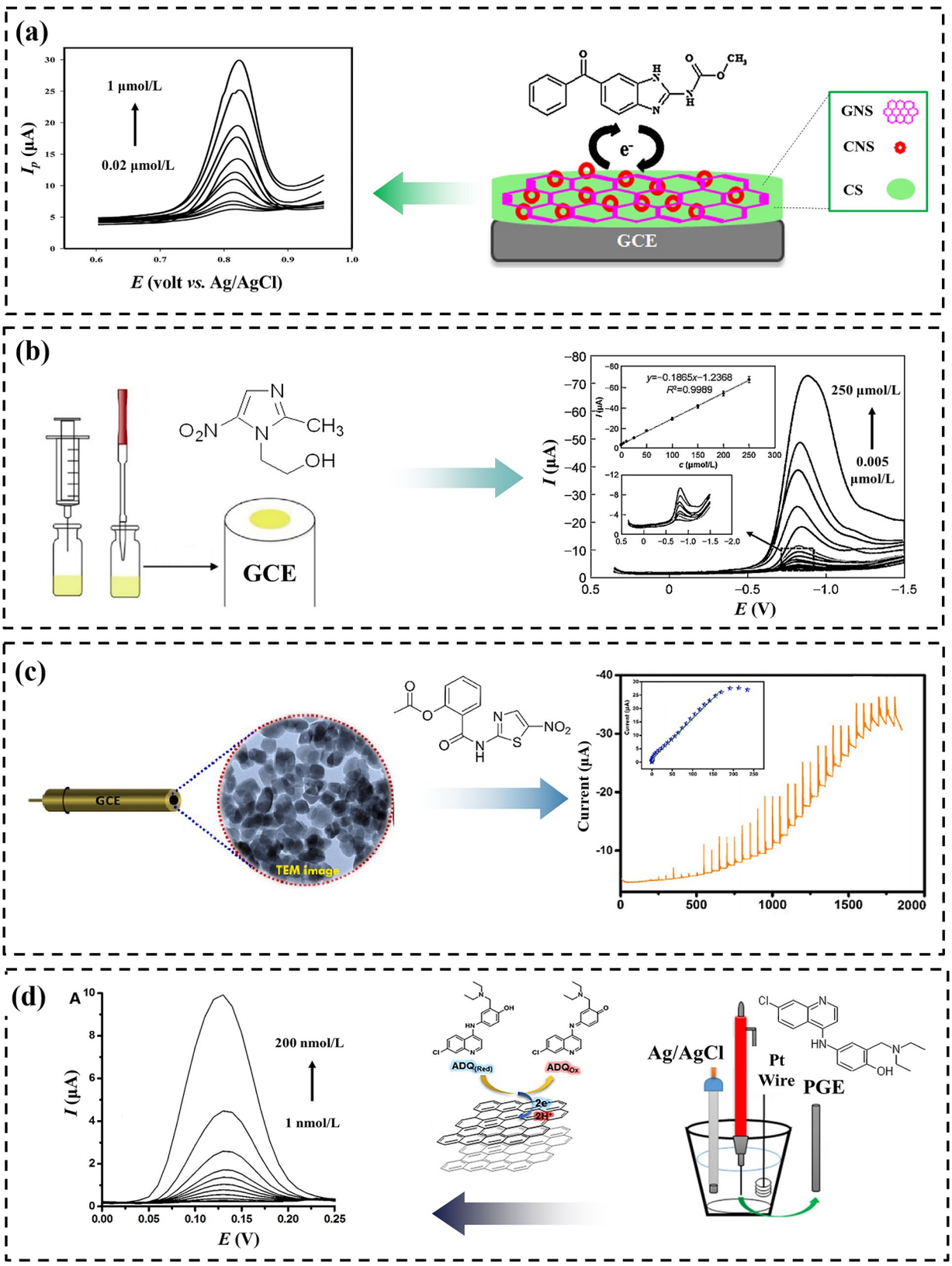
丝网印刷碳电极(screen-printed carbon electrode,SPCE)是在基底表面使用丝网印刷技术,将石墨粉基质和有机粘合剂沉积在基底上,形成电极结构,与传统电极相比,SPCE具有粗糙和多孔的结构,可产生较大的表面积,因此具有更高的电导率[76].GANGULY等[54]合成了硒化锌/还原氧化石墨烯-十八胺微球(ZnSe/rGO-ODA),并将微球悬浮液滴铸在基底电极SPCE上构建双模传感器(图3(c)),该传感器结合了各个组件的协同效应,有较高的比表面积和高效的催化活性,该传感器能实现对抗疟药物磷酸氯喹(CQP)的灵敏检测.用共沉淀法和热煅烧法相结合制备杂化结构的铋掺杂锡酸镧纳米粒子(BLSO NPs)[73],用BLSO NPs/SPCE测定NTZ(图3(d)),CV结果表明,由于BLSO纳米粒子的协同效应,铋掺杂后NTZ的电化学还原得到增强,BLSO NPs修饰的SPCE具有较低的电荷转移电阻、较高的电化学活性表面积、优异的灵敏度和对NTZ的选择性.

2.1.5　分子印迹传感器

分子印迹聚合物(MIPs)是一种合成聚合物材料,对目标分子具有高亲和力和选择性.印迹过程为在模板分子与功能单体混合物聚合之后,将其与一个固定电极表面接触,形成印迹膜,然后将模板分子从聚合物基质中去除,从而产生识别位点.分子印迹电化学传感器(MIECs)对抗寄生虫药物检测如表3所示.采用MIPs的MIECs具有制备成本低、对特定分子的高度选择性检测和灵敏度检测等特点[77].SRIVASTAVA等[78]通过ABZ模板分子存在下电沉积生物聚合物壳聚糖纳米颗粒,在金电极表面形成聚合物膜,并通过电化学方法优化各种参数,控制分子印迹聚合物修饰传感器的性能(图4).该分子印迹电化学传感器具有简单、廉价、环保、快速等优点,可有效测定ABZ.

2.1.6　硼掺杂金刚石电极

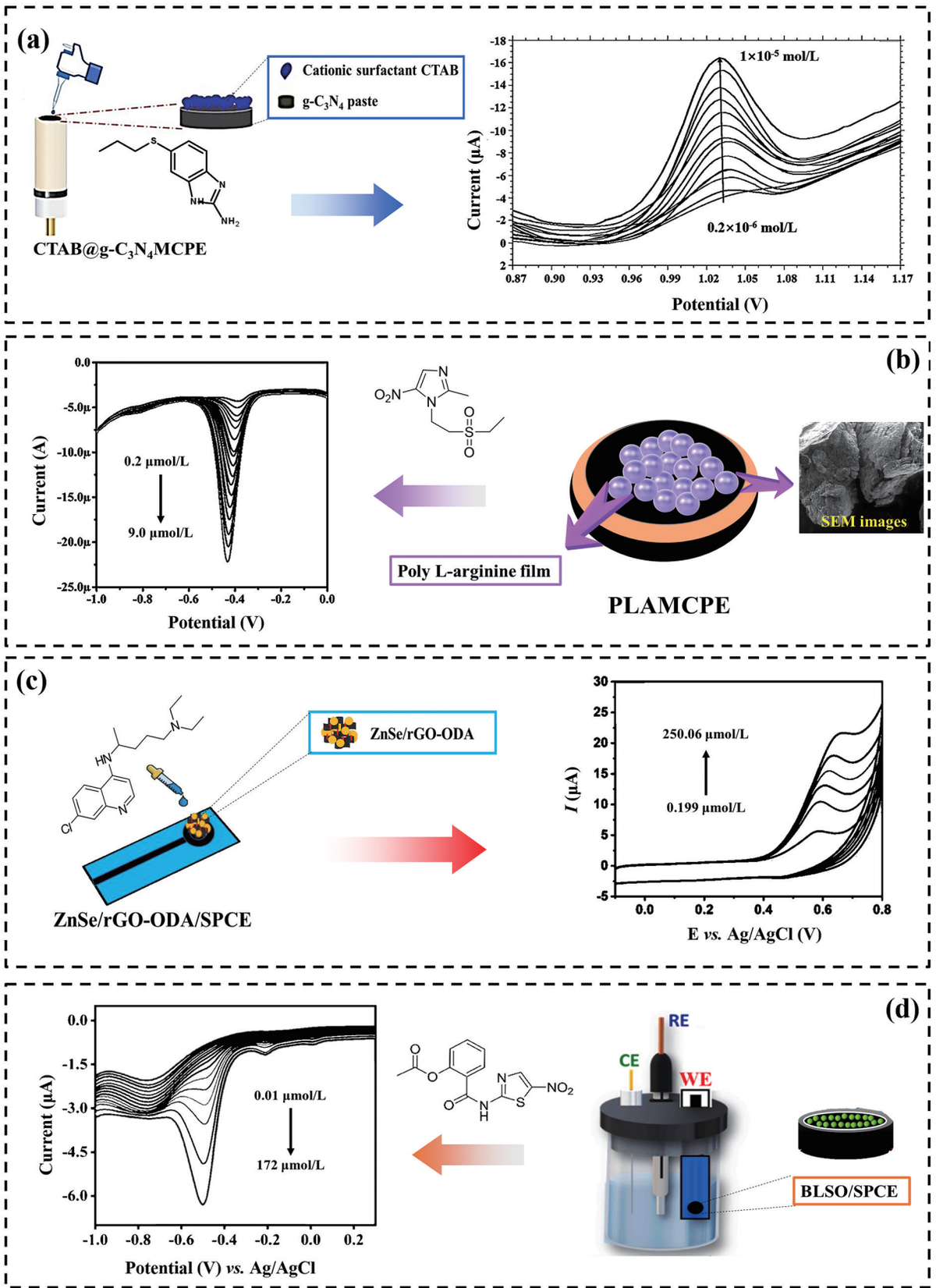
掺硼金刚石(BDD)薄膜是一类特殊的电极,也属于物理材料基传感器,这种传感器利用硼掺杂的



(a) GNS-CNS/CS/GCE 的 MBZ 检测示意图[31]；(b) Au-MWCNTs/GCE 的 MNZ 检测示意图[39]；(c) Mo-$MnWO_4$ NCs/GCE 的 NTZ 检测示意图[74]；(d) PGE 的 ADQ 检测示意图[56]

图 2　玻碳电极传感器和铅笔石墨电极传感器检测示意图

Fig. 2　Schematic diagram of glass carbon electrode sensor and pencil graphite electrode sensor



(a) CTAB@g-C3N4MCPE 的 ABZ 检测示意图[28];(b) PLAMCPE 的 TNZ 检测示意图[33];(c) ZnSe/rGO-ODA/SPCE 检测真实样品中的 CQP 示意图[54];(d) BLSO NPs/SPCE 的 NTZ 检测示意图[73]

图 3　碳糊电极传感器丝和网印刷碳电极传感器检测示意图

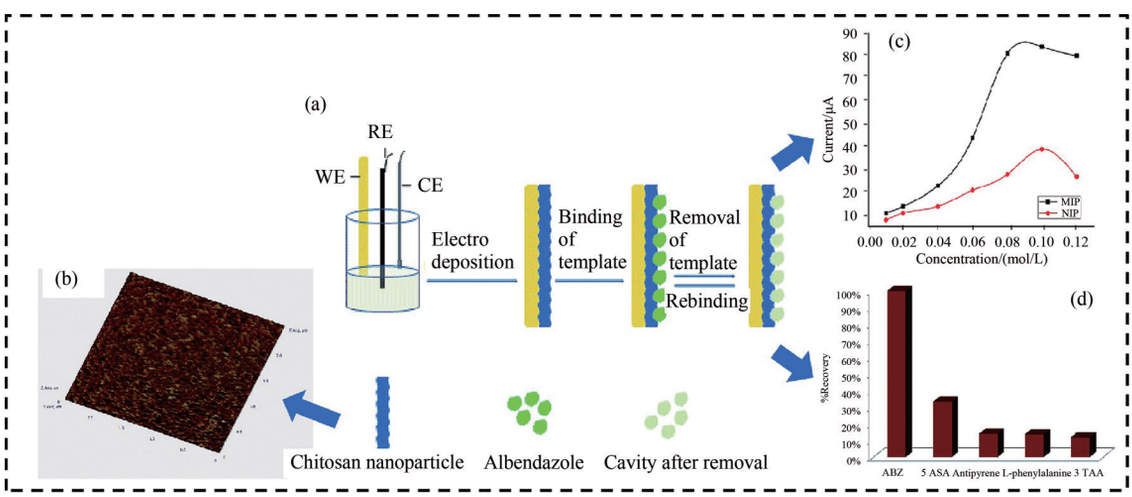
Fig. 3　Schematic diagram of carbon paste electrode sensor wire and mesh printing carbon electrode sensor detection schematic

表3 用于检测抗寄生虫药物的分子印迹传感器

Tab. 3 Molecular imprinting sensors for detecting antiparasitic drugs

序号	MIPs材料	检测方法	洗脱液	检测限	线性范围	目标药物
1	chitosan nanoparticles/ABZ	DPV/CV	乙酸:甲醇 1:4	0.119 μg/mL	-	ABZ[78]
2	MIC-AuNPs/MWCNT-chitosan/PGE	CV/EIS/DPV	乙醇:水 7:3	5.0×10^{-8} μmol/L	1.0×10^{-7}~1.0×10^{-3} μmol/L	QN[79]
3	ART/AM EGDMA/AIBN	DPV/CV	甲醇:乙酸 1:1	2.0×10^{-9} mol/L	1.0×10^{-8}~4.0×10^{-5} mol/L	ART[80]

注:chitosan nanoparticles(壳聚糖纳米颗粒);MIC(l-酪氨酸和3-甲基-4-硝基苯酚复合材料);AM(丙烯酰胺);EGDMA(乙二醇二甲基丙烯酸酯);AIBN(2,2-偶氮二异丁腈).



(a) 金电极上制备分子印迹传感器的示意图;(b) 壳聚糖纳米颗粒的原子力显微镜图像;(c) 分子印迹传感器和非分子印迹传感器对阿苯达唑药物再结合的比较研究;(d) 分子印迹传感器电流变化响应阿苯达唑的各种结构类似物的回收率百分比[78]

图4 金电极上制备分子印迹传感器

Fig. 4 Schematic diagram of preparing molecular imprinting sensor on gold electrodes

金刚石材料作为传感元件,其工作原理涉及目标物质与电极表面之间的电化学反应,从而产生电势信号用于测量目标物质的浓度或活性.基于BDD薄膜的工作电极具有化学惰性、在腐蚀性介质中的物理和化学稳定性、宽电位窗口、低背景电流和弱吸附等特点.与其他电极相比,在水性电解质中分解水之前,导电金刚石可以氧化几种分析物,氧气和氢气的析出不会干扰分析,BBD电极扩展到了传统电极材料无法实现的检测范围[81]. OLIVEIRA等[82]开发了一种BDD电极用于检测CQ,检测限为2.0 nmol/L,该检测限是迄今为止使用修饰和未修饰电极检测CQ的最低限,BDD电极体现出其作为电极材料在有机化合物伏安测定中的优越性.

2.1.7 悬挂式汞滴电极

悬挂式汞滴电极(HMDE)是利用悬挂在电解质溶液中的汞滴来进行分析.在这种传感器中,汞滴充当传感元件,通常与参考电极和计数电极一起构成电化学电池.HMDE具有析氢反应的高过电位,在电化学分析待测样品中,HMDE提供了一个理想的疏水表面,可以在受控条件下监测吸附和氧化还原情况,确定溶液中的目标物质的浓度或其他性质[83].利用CTAB在HMDE上的增强作用[84],开发了一种快速灵敏测定金鸡纳树皮及其药物制剂中QN的SWV,该方法灵敏度极高,检测限低至0.132 ng/mL,可用于QN在药代动力学、药效学、生物利用度等方面的研究.

2.2 生物材料基传感器

生物材料基传感器能将生物相互作用转化为可检测的电化学信号,酶和适配体等生物识别标记物可以固定在电化学界面上介导传感过程[85-86],具有操作简单、响应速度快、灵敏度高、成本低等特点.生物电化学传感器对抗寄生虫药物检测如表4所示.

2.2.1 适配体传感器

在各种电化学生物传感器中,基于适配体(aptamer,APT)的生物传感器在药物分析领域引起了广泛关注,APT是生物技术中使用的生物分子,通

表4　用于检测抗寄生虫药物的生物材料基传感器

Tab. 4　Biomaterial based sensors for detecting antiparasitic drugs

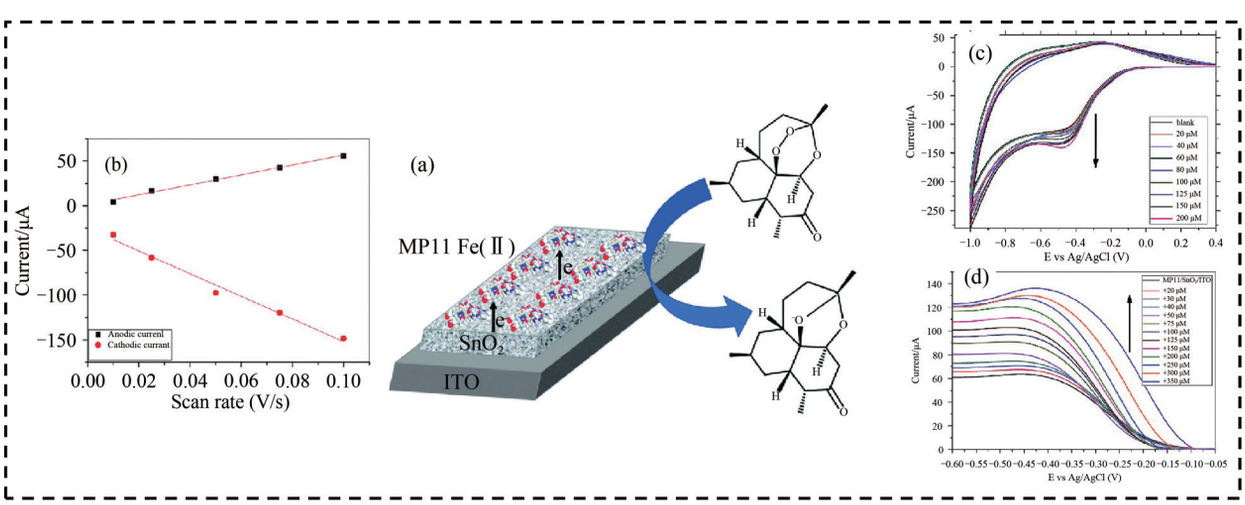
序号	生物传感界面	传感方法	检测限	线性范围	目标药物
1	SiNWs	DPV/CV	0.01 nmol/L	1~20 nmol/L	MBZ[86]
2	Apt	SWV	0.17 ng/mL	1~500 ng/mL	MQ[87]
3	Hb	DPV/SWV	3.30 mg/L	8.90~48.8 mg/L	ADQ[88]
4	Apt	SWV	0.061 ng/mL	0.1~500 ng/mL	PiQ[87]
5	PHA/AuNPs/HRP/ITO	CV/EIS/DPV	50 ng/mL	0.01~0.08 ng/mL	ART[89]
6	DNA-SWCNTs	CV	-	-	ART[90]
7	MP11/DDAB/SnO_2/ITO	DPV/CV	17 μmol/L	0~350 μmol/L	ART[91]
8	GC/CNF/Hb	CV	-	0~200 μmol/L	ART[92]
9	CPE/STH	CV	15 nmol/L	50~1000 nmol/L	ART[93]
10	GrO/PANI/HRP/ITO	CV/EIS	0.012 ng/mL	0.05~0.40 ng/mL	ARU[94]

注：SiNWs（硅纳米线）；Hb（血红素）；PHA/AuNPs/HRP/ITO（天然聚合物聚羟基链烷酸酯-金纳米颗粒复合生物传感器）；MP11/DDAB/SnO_2/ITO（玻璃基板上制备微过氧化物酶修饰的介孔氧化锡膜）；CNF/Hb（血红蛋白吸附在碳纳米纤维上）；STH（固定在氧化钛改性二氧化硅上的血红素）；GrO/PANI/HRP/ITO（石墨烯-聚苯胺纳米复合材料）.

常与目标分子特异性的结合以进行检测，对靶点具有很高的选择性和亲和力[95]. 通过物理吸附、共价结合、包埋等方法使 APT 与传感器结合，利用 APT 的选择性可以使传感器针对特定的生物分子形成 APT-目标物质复合物从而引起电化学信号变化，证明目标物质的存在. LI 等[87]利用分枝状 DNA 纳米结构组装能使信号放大的原理，让靶向药物哌喹（PiQ）、MQ 与 APT 结合后改变其构象，释放出 ssDNA 来触发辅助信号序列，使辅助信号序列在传感器上自组装形成分枝状纳米组装体从而放大电流信号，该传感器的构建成功实现了 PiQ 和 MQ 的同时监测.

2.2.2　酶传感器

酶是生化反应中有效的催化剂，并且对催化特定反应具有高度选择性和高度的灵敏度，酶还能在生物测定中用于放大响应信号. 因此，酶生物传感器广泛应用于疾病诊断、生物和生物医学研究等的各种靶点分析[96]. 微过氧化物酶-11（microperoxidase-11，MP-11）是一种小尺寸氧化还原酶，可用于开发酶生物传感器. 使用介孔 DDAB/SnO_2/ITO 薄膜电极成功固定 MP-11[91]，实现了 MP-11 的高负载，当 ART 与 DDAB/SnO_2/ITO 薄膜电极接触时，ART 会吸附到电极表面，MP-11 开始对青蒿素进行催化氧化，在 MP-11 的催化作用下，ART 发生氧化反应释放出电子，产生可检测的电流信号. 该传感器在磷酸盐缓冲液（pH=7）中实现对 ART 的检测，具有检测限较低，灵敏度、重复性和稳定性良好等优点（图 5）.



（a）SnO_2 膜上的 MP11 引起青蒿素的电催化还原的示意图；（b）电极在 10 mmol/L NaH_2PO_4（pH=7）中氧化还原峰值电流与扫描速率的关系图；（c）扫速为 0.05 V/s 时的 MP11/DDAB/SnO_2/ITO 薄膜电极在青蒿素浓度增加和不存在情况下的循环伏安图；（d）MP11/DDAB/SnO_2/ITO 薄膜电极在扫描速率为 0.01 V/s 的 10 mmol/L NaH_2PO_4（pH=7）缓冲液中添加增加青蒿素浓度后的差分伏安脉冲图[91]

图 5　SnO_2 膜上的 MP11 引起青蒿素的电催化还原的示意图

Fig. 5　Schematic diagram of MP11 on SnO_2 membrane causing electrocatalytic reduction of artemisinin

3 结语

近年来微型电化学传感器已成为电分析化学研究中极具发展前景的一个领域[97].电化学传感器在抗寄生虫药物检测的应用方面取得了显著的进展,为抗寄生虫药物的分析提供了快速、灵敏且可靠的新方法.通过对电化学传感器的研发和改进,在提升检测灵敏度、选择性、降低成本以及简化操作流程方面均取得了突破,逐步成为检测和分析抗寄生虫药物的重要工具.

尽管现有的研究取得了一定进展,但电化学传感器在抗寄生虫药物检测领域仍面临一些挑战.例如,许多电化学传感器在实际样品分析中还存在一定的干扰,需要进一步优化传感器的选择性和稳定性等关键参数.此外,针对不同寄生虫药物的多重检测问题,如何设计出具有广泛适用性、能同时检测多种药物的传感器,也是值得深入研究的课题.未来的研究可致力于开发多功能传感器,探索新型材料以提升对目标分子的选择性,从而应对复杂多变的实际样品矩阵.同时,研发出能够在现场快速检测抗寄生虫药物残留的便携式电化学传感器检测系统,对于实现实时、高效检测具有重要意义.

虽然电化学传感器在抗寄生虫药物检测领域发展前景广阔,但未来的发展需要面对多重技术与应用挑战.因此,在展望未来时需要保持谨慎,逐步解决技术难题,推动这一领域的持续发展.

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