导数分光光度法在药物分析中的应用

肖 艳 韩 娟 冯霞光 王怀友①
(山东师范大学化学化工与材料科学学院 济南市文化东路 88 号 250014)

摘 要 本文综述了导数分光光度法在药物分析中的应用及展望。

关键词 紫外–可见导数分光光度法, 荧光导数分光光度法, 药物分析。
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1 引言

19 世纪 50 年代, Morrison 等人提出导数分光光度法[1], 它是作为分辨波长相近的谱线的方法而提出来的, 利用光吸收(透过) 对波长的导数曲线来确定和分析吸收峰的位置和强度。该方法仪器简单, 操作简便, 准确度高, 可有效消除背景的干扰, 特别是它克服了样品烦琐的预处理过程, 达到不经分离就可测定的目的。随着计算机的使用和仪器的改进, 使导数分光光度法迅猛发展, 从一阶导数发展至二阶、三阶直至八阶、九阶导数。导数分光光度法已广泛应用于医药、环境、化工、临床、生物以及食品等众多领域, 可用来测定无机物和有机物, 气体、液体及固体, 一元及多元体系。导数分光光度法的原理及应用[2—7]已有综述, 本文拟就近几年来导数分光光度法在药物分析方面的研究工作进行综述。

2 紫外–可见导数分光光度法

2.1 一阶导数紫外–可见(UV–VIS)分光光度法

一阶导数 UV–VIS 分光光度法具有简单、快速的特点, 广泛应用于血浆、血清、尿样及药物测定。一阶导数 UV–VIS 分光光度法既可用于一元体系的直接测定, 也可用于二元混合体系的同时测定, 还可用于多种混合物中某一组分的测定。Rodenas 等[8]用此方法同时测定了扑热息痛(paracetamol) 及丙帕他莫(propacetamol), 并测定了乙醇、葡萄糖及盐溶液中丙帕他莫(propacetamol) 的稳定性。Ivanovic 等[9]应用一阶导数 UV–VIS 分光光度法成功地测定了阿司匹林和芬那露(安定药)。Uslu 等[10]测定了二元体系中的抗病毒药齐多夫定和拉米夫定。Pappano 等[11]测定了马来酸氯苯吡胺(扑尔敏) –诺司卡品和马来酸氯苯吡胺–愈创木酚甘油醚(祛痰药)。Berzas 等[12]测定了口服液中炔雌醇和左旋 18–甲基炔诺酮的含量。Abdellatef 等[13]测定了磺胺醋酰、磺胺二甲嘧啶和磺胺硫脲在降解产物中的含量。近十年来一阶导数 UV–VIS 分光光度法在药物分析中的应用, 如表 1 所示。可见, 一阶导数 UV–VIS 分光光度法在药物分析中的应用十分广泛。

2.2 二阶导数 UV–VIS 分光光度法

二阶导数 UV–VIS 分光光度法与一阶导数 UV–VIS 分光光度法相比, 可提供更多的信息和精细结构, 可用于测定一阶导数 UV–VIS 分光光度法无法测定的复杂体系。Baranowska 等[56]利用二阶导数方法分别测定三个黄酮类化合物体系, 栎精–山柰酚、栎精–杨梅黄酮及栎精–木犀草素。Prasad 等[57]测定了复合药片中的苯巴比妥和苯妥英钠。Morelli[58]建立的测定氨苄青霉素和邻氯青

① 联系人, 电话: (0531) 86619466; E-mail: wanghuaiyou@sdnu.edu.cn
作者简介: 肖艳(1976—), 女, 重庆市铜梁县人, 硕士研究生, 研究方向光分析化学。
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霉素的二阶导数方法可用于测定注射液和胶囊的含量。Kitamura 等[59]在背景干扰下利用二阶导数方法测定了药片中的异烟肼。Fuke 和 Kuo 等[60,61]在血清及尿液中测定了农药百草枯和敌草快的浓度。文献[62—82]也是有关二阶导数 UV-VIS 分光光度法在药物分析中的应用, 由于二阶导数分辨率高的特点, 二阶导数 UV-VIS 分光光度法在药物分析中将发挥更加重要的作用。

表 1　一阶导数 **UV-VIS** 分光光度法在药物分析中的应用

药名	特点	参考文献
1. 假麻黄碱硫酸盐-右旋溴苯吡胺马来酸假麻黄碱硫酸盐-氯雷他定	可用于药物合成	14
2. 甲萘威-毒死蜱(农药)	简单	15
3. 羟氨苄青霉素-克拉维酸	准确、直接、重现性好	16
4. 盐酸特比萘芬-去炎松-A	可用于药物合成	17
5. 盐酸多佐拉明-噻吗心安马来酸	用于合成混合药物的测定及药物合成	18
6. 氨氯吡脒-利尿磺胺	药方中二者不干扰	19
7. 头孢氨呋肟-头孢羟氨苄	尿液、药片及胶囊中二者测定	20
8. 扑尔敏-盐酸苯福林	鼻剂、纯药中测定	21
9. 培哚普利-茚磺苯酰胺	药物制剂中测定	22
10. 福辛普利-氢氯噻嗪	回收率高、简单、用于药物合成	23
11. 美沙芬-必消痰	线形方程相关系数 0.9999、检出限低	24
12. 对氨苯甲酸乙酯-氯化十六烷基吡啶	简单、灵敏度高、重现性好	25
13. 甲氧苯氧甲　唑啉酮-对乙酰氨基酚	结果准确	26
14. 米氮平	用于药物制备	27
15. 褪黑激素-吡哆醇	标准偏差小, 可用于实验室中药物制备	28
16. 盐酸麻黄碱-茶碱	结果准确、线性、重现性好	29
17. 茚磺苯酰胺	用于药物测定	30
18. 甲地妊娠素-环丙氯地孕酮	用于原材料及药剂中二者的测定	31
19. 氨苄青霉素钠盐-舒巴坦钠	用于针剂中的二者测定	32
20. 盐酸地布卡因	用于其酸降解产物及膏状药中的测定	33
21. 对乙酰基酚-可待因	简单、快速、准确	34
22. 氟罗沙星	用于血清、药剂中的测定	35
23. 利眠宁-溴奎环二苯酯	用于药片中二者的测定	36
24. 丁氧普鲁卡因	用于其酸降解产物中的测定及动力研究	37
25. 溴化异丙托品	用于瓶剂药物测定	38
26. 盐酸醋丁酰心安	用于其酸降解产物中的测定及动力研究	39
27. 头孢噻吩-头孢甲氧霉素	用于生物体血清及注射液的测定	40
28. 缬沙坦-氢氧噻嗪	用于实验制备混合物及药片的测定	41
29. 奥美拉唑	灵敏度是高效液相色谱的 2.59 倍	42
30. 美洛昔康	用于药片中含量的测定	43
31. 炎痛喜康	测定范围比高效液相色谱宽	44
32. 盐酸甲苯凡林-消旋宁	线性相关系数为 0.9999	45
33. 心痛定	用于稳定性研究	46
34. 甘氨苯唑-氟唑氨苯酯	用于原料及药片的测定	47
35. 噻嗪类利尿剂	用于光稳定性研究	48
36. 头孢磺吡苄-克拉维酸	用于静脉注射液的测定	49
37. 马来酸依那普利-氢氯噻嗪	用于实验制备混合物及药片的测定	50
38. 头孢哌酮-舒巴坦	用于注射液的测定	51
39. 亚胺培南-西斯他丁钠	方法选择性好、稳定	52
40. 灭菌丹-苯线磷(农药)	用于地下水及商品配方的测定	53
41. 愈创木酚甘油醚-美沙芬	选择性好、准确	54
42. 卤吡醇	在安息香酸酚酯存在时可测定	55

2.3　二阶以上导数 UV-VIS 分光光度法

二阶以上导数 UV-VIS 光谱分析技术提供了分光光度法新的发展方向, 扩大了应用范围。这种方法具有的高再现性、线形和双极性等性质, 显示了很大的应用潜力, 三阶到五阶导数可达到滤去干扰信号, 从而获得好的再现性。Saglik 等[83]建立的四阶导数法同时测福辛普利和双氢氯噻嗪; Morelli[84]利用三阶导数测定了三元混合体系(青霉素 G 钠盐, 普鲁卡因青霉素 G 盐和硫酸双氢链

霉素); Walily 等[85] 采用三阶导数测定维生素 A 和维生素 E 的方法, 可用来测定胶囊和咀嚼片中二者的含量; Altuntas 等[86] 利用四阶导数技术测定了阿代斯汀和盐酸假麻黄碱; Randez-Gila 等[87] 同时采用五阶、六阶导数法测定了血浆中的硝基安定和氯硝安定; Claudio 等[88] 采用三阶、四阶导数分别测定了在不同溶剂中的四环素及其代谢产物。随着仪器的改进, 克服了高阶导数信噪比降低的缺点, 使二阶以上导数 UV-VIS 分光光度法保持了良好的发展趋势。

3 荧光导数分光光度法

荧光导数分光光度法自 20 世纪 70 年代提出后, 在解决了荧光的背景干扰和谱带重叠等问题并取得了良好的效果, 在药物分析中发挥着重要作用。导数与同步扫描技术相结合, 既改善了分辨能力, 消除了基体干扰, 并提高了灵敏度, 是一种用于混合物分析快速、简便、有效的方法。Ruiz 等[89] 利用二阶导数同步荧光技术分别测定了血清和药物制剂中的氟灭酸-甲氯灭酸和甲氯灭酸-甲灭酸。Fernandez-González 等[90] 通过二阶导数同步荧光技术, 利用土霉素与钙离子反应形成的荧光络合物来测定土霉素, 该方法不受磺胺二甲嘧啶和黏菌素硫酸盐存在的影响。Nevado 等[91] 利用一阶导数-能量同步扫描荧光法同时测定了吡哆醛和吡哆胺。Wang 等[92] 采用一阶导数同步荧光方法, 利用庆大霉素与乙酰丙酮和甲醛的反应, 测定了庆大霉素, 获得低的检测限。文献[93—107] 报道了导数荧光分光光度法在药物测定中的应用。随着导数荧光分光光度法研究的深入, 药物痕量分析将有进一步发展。

4 导数分光光度法在药物动力学研究中的应用

导数分光光度法除了用于药物的含量测定之外, 在药物动力学过程研究中也被广泛应用, 解决了传统分光光度法干扰严重的问题。Popovi 等[108] 利用二阶导数 UV-VIS 方法研究了氯羟去甲安定和氟胺安定的酸碱平衡过程, 测定了二者的酸碱平衡常数。Archontaki 等[109] 利用一阶导数 UV-VIS 法, 测定了氯羟去甲安定的稳定时间, 半衰期等动力学参数; 利用四阶导数 UV-VIS 法研究了环丙安定在其酸性水溶液中的降解过程[110]。Kitamura 等[111] 利用二阶导数 UV-VIS 法, 测得了吩噻嗪在人体的红细胞血影膜与水中的分配系数。文献[112—115] 也有报道, 在这方面的研究前景广阔。

此外, 在导数分光光度法的基础上, 出现的比光谱-导数分光光度法, 结合经典最小二乘法(CLS)、偏最小二乘法(PLS)、主成分回归法(PCR)、多元线形回归法(MLR)等, 可以更有效地获得高准确度和选择性, 被广泛应用于多组分药物分析。Salem 等[116] 利用比光谱-导数分光光度法和经典最小二乘法同时测定了脑益嗪和哌双咪酮马来酸, 回收率令人满意。El-Gindy 等[117] 用比光谱-二阶导数分光光度法, 结合主成分回归法, 测定了盐酸贝那普利和氢氯噻嗪。文献[118—132] 有过在此方面的报道。

5 展望

随着科学的发展, 导数分光光度法的应用范围不断扩大, 在药物纯度试验、质量控制、含量测定、药物动力学研究以及药物的制备过程中有效成分不经分离即可检测等方面有广阔的应用前景。导数分光光度法与高效液相色谱法、数学统计法及同步扫描技术等其他方法结合, 正成为药物分析中不可替代的测定手段。

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Application of Derivative Spectrophotometry in Drug Analysis

XIAO Yan　HAN Juan　FENG Xia-Guang　WANG Huai-You
(*College of Chemistry, Chemical Engineering and Materials Science, Shandong Normal University, Jinan* 250014, *P. R. China*)

Abstract　This paper reviews the application and prospect of derivative spectrophotometry in drug analysis in recent years.

Key words　Ultraviolet-Visible Derivative Spectrophotometry, Fluorescence Derivative Spectrophotometry, Drug Analysis.