2.2 搅拌速度和搅拌时间的影响 搅拌速度和时间的改变对微粒的粉体学性质的影响不同。球晶造粒技术的 SA法又可以分为溶剂置换法、反应法、盐析法和温度下降法。如采用反应法进行球晶制粒时,颗粒的平均粒径随搅拌时间的延长和搅拌速度增大而增大。如氨茶碱进行球晶造粒时,发现球晶颗粒的平均粒径随搅拌时间的延长而增大,直至达到平衡状态;同时还发现调节搅拌速度可以控制球晶的平均粒径,搅拌速度增大,粒径减小[27]。使用盐析法制备茶碱钠颗粒过程中,将茶碱的乙二胺溶液加入氯仿和乙醇的混合溶液中发生反应,再加入氯化钠溶液搅拌,此时颗粒粒径随搅拌速度的增加而减小[28]。当药物粒子集中增大时,更高的搅拌速度会导致聚集体孔隙率减小、更加紧实,从而抗压能力更强[29]。

2.3 搅拌方式和容器形状的影响 在制粒过程中,除溶剂系统对球晶造粒物的形成有较大影响外,搅拌方式和反应容器选择也不容忽视。Smith和 Pudding ton[30]发现不同的搅拌或振摇方式对球晶颗粒的形成有很大的影响。水平往复的运动可产生致密的、粒度分布较窄的颗粒;滚动式得到的颗粒粒径较小;纵向震动几乎不能产生球形颗粒。Kawashima等[2]采用推进式搅拌器得到的颗粒球形度较好,粒度分布窄而均匀。在造粒过程中,应尽量使用圆柱形或具有半圆形底的容器,可防止颗粒于某些边角沉积,增加架桥剂与微粒间及粒子间的接触,得到较均匀的球形颗粒。

3 展望

球晶造粒技术制备的球形微粒具有卓越的第二性质。微粒拥有极佳的流动性,使其更易被填充进冲模,这是因为微粒所拥有的球形形态、光滑的表面。此外,微粒有着优秀的填充性,是因为聚集体更加的密实和拥有优良的强度,这意味着其在压缩力作用下更易发生塑性形变,使其应用于直接压片具有出色的潜能,这也给在现代医药工业上很多流动性和可压性差的活性药物(如:扑热息痛、萘普生、苯甲酸等)应用于直接压片一个有益的借鉴。

相信通过药剂科研工作者对辅料的不断深入研究,将更多功能辅料引入到球晶造粒的过程中,一定能够研制出具有各种释放特性的片剂,这为解决像布洛芬这类半衰期短的药物制备具有缓控释效果,尼群地平这种极难溶药物制备具有速释效果,又可直接用于压片的一个成功处方提供机会和可能。

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具体操作如 3.3有效期检测实验部分。将各组所得数据综合,进行有效期计算。将 pH对稳定性影响实验得学生分成 5组,分别进行 pH为 1、3、5、7、9条件下的实验,具体操作如 3.4 pH对稳定性影响实验部分。将各组所得数据综合,绘制 pH速率图。

4 讨论

本次实验方法简便安全可行,实验时间适中,数据准确,完全可以替代维生素 C和青霉素 G钾盐,进行学生实验的设计。

本次实验设计在原有实验基础上,加入了 pH对药物有效期的影响实验,更加全面的与基础知识相结合。同时运用先进的检测方法,使学生熟悉现代仪器的操作,为今后科学研究打下良好的基础。

由于实验可操作性好,可以帮助学生巩固书本上的基础知识,提高实验操作技能、动手能力,逐步形成综合、归纳、分析和解决问题的能力,以培养学生的学科探究精神和良好的专业素质。因此,本实验可用于药剂学药物有效期预测及稳定性影响因素的学生教学实验。

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[收稿日期] 2009-09-16
[修回日期] 2009-10-14

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[收稿日期] 2009-06-19
[修回日期] 2009-10-26