

冷冻干燥中升华界面的临界温度实验^{*}

左建国 李维仲 翁林峯

(大连理工大学能源与动力工程学院, 大连 116024)

【摘要】 利用冻干显微镜(FDM)研究了二元水溶液冷冻干燥过程中升华界面的临界温度,采用差示扫描量热法(DSC)测量了溶液的共晶熔融温度和最大冻结浓缩溶液的玻璃化转变温度。实验结果表明,对于降温时发生共晶的溶液,临界温度为共晶熔融温度,否则将发生融化;对于降温时发生玻璃化转变的溶液,临界温度为塌陷温度,否则将发生塌陷。对于质量分数为5%蔗糖、10%葡萄糖、10%麦芽糖、10%聚乙烯吡咯烷酮(PVP)二元水溶液,微塌陷温度与塌陷温度的差值在2℃以内,微塌陷温度比玻璃化转变温度高1~3℃。

关键词: 冷冻干燥 塌陷温度 冻干显微镜 差示扫描量热法 玻璃化转变

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Critical Temperature of Sublimation Interface in Freeze-drying

Zuo Jianguo Li Weizhong Weng Lindong

(School of Energy and Power Engineering, Dalian University of Technology, Dalian 116024, China)

Abstract

Freeze-drying microscopy (FDM) was used to investigate the critical temperature (T_{cr}) of sublimation interface during freeze-drying of binary aqueous solutions, and differential scanning calorimetry (DSC) was used to investigate the eutectic melting temperature (T_{em}) and the glass transition temperature of the maximally freeze concentrated solution (T'_g). The experimental results showed that if a solute crystallized from solution during freezing step, the critical temperature was the eutectic melting temperature, or else a meltback would occur. If the solute remained amorphous during the freezing process, the critical temperature was the collapse temperature, or else the amorphous phase would undergo viscous flow. For 5% Sucrose, 10% glucose, 10% maltose, 10% PVP binary aqueous solutions, the microcollapse temperature (T_{mc}) and the collapse temperature (T_c) differed by less than 2℃, and T_{mc} was 1~3℃ above T'_g .

Key words Freeze-drying, Collapse temperature, Freeze-drying microscopy, Differential scanning calorimetry, Glass transition

引言

目前,冷冻干燥广泛应用于热敏性食品及生物制品的保存^[1-2]。由于升华干燥速率低,整个冻干过程时间长,能耗大,优化和改进冻干过程是当前面临的重要问题^[3]。升华干燥阶段的样品温度是一个重要参数,温度每升高1℃,升华干燥时间将缩短13%^[4],因此控制产品升华界面的温度,使其尽量

接近并低于临界温度是优化冻干过程的有效方法^[5]。产品的临界温度是其升华时所允许的最高温度。通常认为,升华干燥过程中物料温度不能超过共晶熔融温度或者玻璃化转变温度,否则就会发生塌陷。塌陷将造成干燥层的多孔通道被堵塞,残余水分增多,复水时间延长,导致生物制品活性丧失^[6]。塌陷温度是冻干过程中玻璃体发生粘性流动时的温度,过去常常认为塌陷温度与玻璃化转变

温度是一致的^[7-8]。但实际上二者并不相等。目前,冻干文献中报道的绝大多数都是关于玻璃化转变温度的数据^[9-11],而关于塌陷温度的数据却甚少,而且即使是同一物料的塌陷温度值,不同文献的测量值也相差较大^[12-14]。鉴于升华干燥温度对提高干燥速率的重要性,本文利用差示扫描量热法和冻干显微镜研究常见冻干保护剂二元水溶液的升华界面临界温度,并重点观测冻干过程中的塌陷行为。

1 材料和方法

实验中用到的试剂均为分析纯(国药集团化学试剂有限公司),溶液均以质量分数表示。

差示扫描量热仪为功率补偿型(Diamond DSC, Perkin Elmer),冷却方式为机械制冷(Intracooler II, Perkin Elmer),样品冲洗气体为高纯度氮气(纯度大于 99.999%),流量 20 mL/min 并保持恒定。温度标定采用正癸烷和钢(熔点分别为 -29.66°C 和 156.60°C)。样品皿为标准液体铝皿,用液体压片机压制。样品质量取 5 mg 左右,精度为 0.1 mg。在参比侧放置与样品皿相同的空皿。样品以 5°C/min 从 25°C 降温至 -60°C,等温 5 min;然后以 10°C/min 升温至 25°C,在升温扫描时读取数据。玻璃化转变

温度 T'_g 取半比热外推温度(half Cp extrapolated),熔融温度取起始温度(onset)。

临界温度的测量采用冻干显微镜(FDCS196, Linkam),配有液氮冷却系统和真空泵。加热和冷却速率可控制在 0.01 ~ 130°C/min,压力最低可达 0.5 Pa。温度标定采用氯化镁、氯化钠和氯化钾(共晶熔融温度分别为 -33.6°C、-21.1°C 和 -11.1°C)。样品以 5°C/min 从 25°C 降温至玻璃化转变温度或共晶温度以下,抽真空,并调节电动阀使压力保持在 1 Pa,等温 5 min,然后以 0.5°C/min 升温。图像采集使用彩色高敏感度冷 CCD (Retiga 2000R, QImaging)。

2 结果与讨论

DSC 实验表明,5% 蔗糖、10% 麦芽糖、10% 葡萄糖、10% 聚乙烯吡咯烷酮(PVP)二元水溶液降温时发生玻璃化转变。氯化钠、甘氨酸本身易结晶,其二元水溶液在 5°C/min 降温时发生共晶转变。玻璃化转变温度、共晶熔融温度如表 1 所示。其中,10% 甘氨酸水溶液的共晶熔融温度与水的熔融温度非常接近,采用更低的扫描速率,可测得共晶熔融温度为 -3.4°C。

表 1 二元水溶液的玻璃化转变温度 T'_g 、共晶熔融温度 T_{em} 和临界温度 T_{cr}

Tab. 1 Glass transition temperature (T'_g), eutectic melting temperature (T_{em}) and critical temperature (T_{cr}) of binary aqueous solutions

样品	分子量 $M/g \cdot mol^{-1}$	玻璃化转变温度 $T'_g/^\circ C$	共晶熔融温度 $T_{em}/^\circ C$	临界温度 $T_{cr}/^\circ C$
5% 蔗糖	342.3	-32.6	—	-31.6 (MC) -29.9 (C)
10% 葡萄糖	180.2	-44.2	—	-41.2 (MC) -39.8 (C)
10% 麦芽糖	342.3	-30.2	—	-28.3 (MC) -26.8 (C)
10% PVP	~40 000	-21.1	—	-19.8 (MC) -18.7 (C)
10% 氯化钠	58.4	—	-21.1	-21.1 (EM)
10% 甘氨酸	75.1	—	-3.4	-3.4 (EM)

注:“—”表示不存在;MC:微塌陷;C:塌陷;EM:共晶熔融。

冻干显微实验表明,对于降温时发生玻璃化转变的样品,如蔗糖、麦芽糖、葡萄糖、PVP,其二元水溶液升温时均发生塌陷,表明临界温度为塌陷温度(表 1)。塌陷温度可分为微塌陷温度 T_{mc} 和塌陷温度 T_c 。前者对应样品结构的局部丧失,干燥区靠近升华界面处出现小的孔洞或裂缝;后者对应样品结构的整体丧失,干燥区靠近升华界面处出现大的孔洞或裂缝,干燥区与升华界面已不再相连。从表 1 中可以看出,所有样品的微塌陷温度与塌陷温度的差值均在 2°C 以内。图 1 为 5% 蔗糖水溶液的冻干显微图像。蔗糖溶液在 -33.5°C 时,干燥区和冻结区结构都保持完好,没有塌陷发生(图 1a);当样品

温度升高到 -31.6°C 时发生微塌陷(图 1b),干燥区贴近升华界面处局部出现了小的孔洞,孔洞之间并不相连;随着温度的不断升高,孔洞逐渐变大,并连成一片,当温度升高到 -29.9°C 时,干燥区靠近升华界面处整体发生了塌陷(图 1c),此时升华界面移动速度明显降低,表明干燥层的粘性流动堵塞了水蒸气逸出的通道。有些样品在发生微塌陷后,对产品最终性能影响不大,因此究竟以微塌陷温度 T_{mc} 还是以塌陷温度 T_c 作为临界温度,应视具体样品而定。从表 1 中可以看出,无论是单糖(葡萄糖)、二糖(蔗糖、麦芽糖)还是 PVP,其微塌陷温度 T_{mc} 均比玻璃化转变温度 T'_g 略高些,差值在 1 ~ 3°C 之间。因此,

以玻璃化转变温度 T'_g 作为临界温度的做法有些保守,而应以塌陷温度作为临界温度。更重要的是,玻璃化转变温度与塌陷温度的测试环境不同,前者通常是在封闭环境下测得的;而后者是在真正的冷冻干燥过程中测得的,更能真实地反映产品特性。

另外,无论是玻璃化转变温度还是塌陷温度,均随样品分子量的增大而呈增长趋势(表1),因此选用冻干保护剂时,在保证产品品质的情况下,应优先选用大分子保护剂,以提高升华干燥温度,缩短干燥时间。

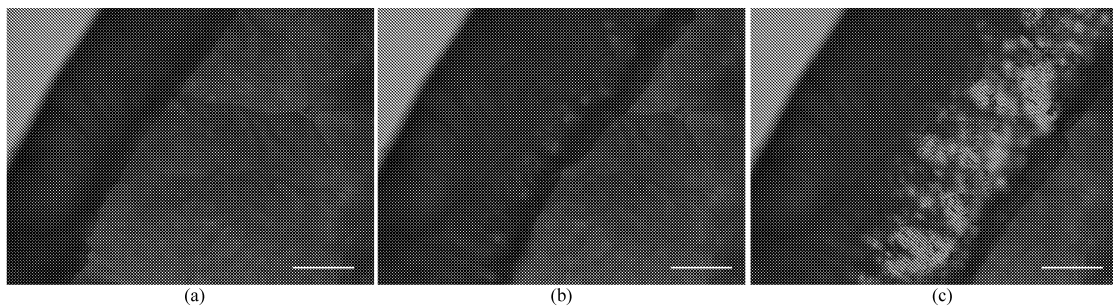


图1 5%蔗糖水溶液的冻干显微图像(标尺:100 μm)

Fig.1 Microscopic observations of freeze-drying of 5% sucrose aqueous solution (scale:100 μm)

(a) -33.5°C (b) -31.6°C (c) -29.9°C

对于降温时发生共晶的样品,如氯化钠、甘氨酸,其二元水溶液升温到共晶熔融温度时,冻结层和干燥层整体发生了融化,因此临界温度为共晶熔融温度(表1)。图2为10%甘氨酸水溶液的冻干显微

图像。甘氨酸溶液在 -3.6°C 时,干燥区和冻结区结构完整,没有融化发生(图2a);而到达共晶熔融温度 -3.4°C 时,整体发生了融化(图2b)。

3 结束语

氯化钠、甘氨酸二元水溶液降温时发生共晶,升华干燥过程中的临界温度为共晶熔融温度;蔗糖、麦芽糖、葡萄糖、PVP二元水溶液降温时发生玻璃化转变,临界温度为塌陷温度。微塌陷温度 T_{mc} 与塌陷温度 T_c 的差值在 2°C 以内,微塌陷温度 T_{mc} 比玻璃化转变温度 T'_g 高 $1 \sim 3^\circ\text{C}$ 。因此,对于降温时发生玻璃化转变的物料,以塌陷温度作为临界温度,能够在保证产品品质的前提下,提高升华干燥速率,缩短冻干时间。

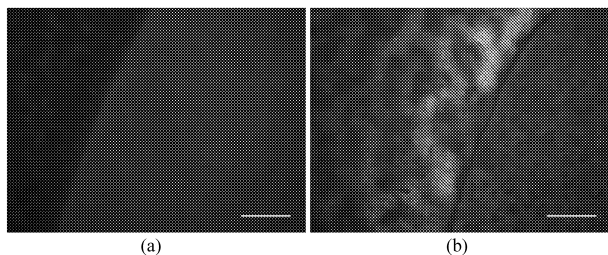


图2 10%甘氨酸水溶液的冻干显微图像(标尺:100 μm)

Fig.2 Microscopic observations of freeze-drying of 10% glycine aqueous solution (scale: 100 μm)

(a) -3.6°C (b) -3.4°C

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