美多秀™产品介绍及应用案例分析
-缓控释规格新产品质量标准和直压规格

The Development of Improved METHOCEL™
Controlled Release Grades and Direct Compression Grades

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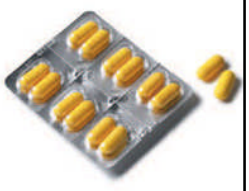
陶氏沃尔富纤维素事业部介绍 DWC Introduction

dowwolff CELLULOSICS Dow

- 陶氏沃尔富纤维素事业部是陶氏化学下属一个部门单元
  A business unit of The Dow Chemical Company
  - 提供用于医药，个人护理用品，食品，建筑，工业等多方面应用的高性能纤维素
    High performance cellulosics, specialty additives and dispersions for the pharmaceutical, personal care, food, construction, and industrial specialty sectors
- 医药级别产品包括 Focus on pharmaceuticals
  - 爱多秀™ 乙基纤维素 ETHOCEL™ Ethylcellulose Polymers
  - 美多秀™ 甲基纤维素及羟丙甲基纤维素METHOCEL™ Cellulose Ethers
  - 保益乐™ 聚乙烯氧化物 POLYOX™ Water Soluble Resins
  - 华洛赛™ 羧甲基纤维素钠 Walocel™ C
- 应用领域 Applications include:
  - 缓控释配方 Controlled-release formulations
  - 片剂及小丸包衣 Coatings for tablets and multiparticulates
  - HPMC硬胶囊 HPMC capsules
  - 薄膜剂和泡沫制粒 Films and foams
  - 液体制剂 Liquid formulations



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演讲内容 Agenda

- QbD 项目
  QbD innitiatives
- HPMC在亲水凝胶骨架片中的主要影响因素
  Key variables of HPMC that affect matrix formulations
  - 通过扑热息痛案例分析了解HPMC的主要影响因素
    Paracetamol study to understand most impactful factors
- 美多秀™ 缓控释规格新的质量标准
  The development of the new CR grades
  - 如何确定产品新的质量标准
    Insight on how the specifications were determined
- 美多秀™ 直压规
  METHOCEL™ DC Grade
  - 硝苯地平用于美多秀™ DC直压工艺案例分析
    Development of nifedipine sustained release tablet formulation by direct compression using METHOCEL™ DC in matrix

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FDA发起的QbD Quality by Design - FDA Initiative

- QbD是一项科学的，基于风险管理的，全面的，主动的行为，对医药行业的发展意义重大。
  Scientific, risk-based, holistic and proactive approach to pharmaceutical development
- 目的是要达到对于监管人，药品生产商和病人全都收益
  The desired state is a Win-Win-Win outcome for regulators, manufacturers, and patients
- QbD的工作贯穿产品定义初期到研发，生产，销售整个环节
  Deliberate design effort from product conception through commercialization
- QbD要求充分理解原材料的特性，以及生产工艺过程与最终产品的质量之间的关系
  Full understanding of how raw material attributes and manufacturing process relate to product performance
- QbD工作范围：全方位的综合评价原材料和生产工艺过程的变量会对最终产品质量的影响，以确保产品质量的稳定
  Design space: the multidimensional combination and interaction of input variables (like material attributes) and process parameters that have been demonstrated to provide assurance of quality

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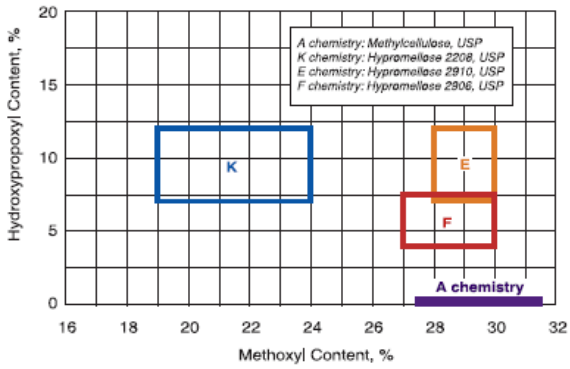
陶氏化学对QbD的承诺 DWC's commitment to QbD

- 帮助制药工业强化QbD的重要性
  Helping pharmaceutical industry address QbD
  - 提供QbD工作所需要的数据
    QbD technical data packages
  - 陶氏化学和卡乐康公司共同建立QbD样品库，以支持客户的配方研究
    Colorcon and DWC are gradually building a library of QbD samples to support formulation development
    - 样品库范围： 所有CR规格
      Scope: CR grades
    - 提供“极限”规格以配合客户配方研究，从而确定“配方空间”
      Proactively define formulation “design space” using “extremes”
- 作为辅料供应商希望能在配方研究初期，同研发人员频繁沟通交流，从而提供有效帮助
  Formulator, excipient manufacturer and supplier must collaborate early and often during development

美多秀产品规格及命名原则



美多秀™ A系列：甲基纤维素

羟丙甲纤维素：
美多秀™ K系列：USP 2208
美多秀™ E系列：USP 2910
美多秀™ F系列：USP 2906

美多秀™ K 4M CR

陶氏化学甲基纤维素，羟丙甲纤维素商品名

取代度：A, E, F, K

20度，2%水溶液中的粘度
4:4cps,
4C:400cps,
4M:4000cps

CR:缓控释规格
DC:直压规格
LV:低粘度规格
VLV:极低粘度规格

HPMC在亲水凝胶骨架片中的影响 HPMC Sustained Release Matrix Tablets

- HPMC在配方中的变量

  Key Hypromellose Formulation Variables:

  - HPMC用量 Level
  - HPMC分子量及粘度 Molecular weight/viscosity
  - HPMC取代类型 Substitution type
  - HPMC粒径分布 Particle size distribution

- 活性药物或者其他辅料的性质也可能导致配方对HPMC性质的变化更加敏感

  Actives and other excipients can cause the formulation to be more sensitive to HPMC properties

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HPMC用量 HPMC Level

- 对于选定好的HPMC，用量通常是影响药物释放的主要因素

  For a selected hypromellose product, polymer level is usually the major drug release rate controlling factor

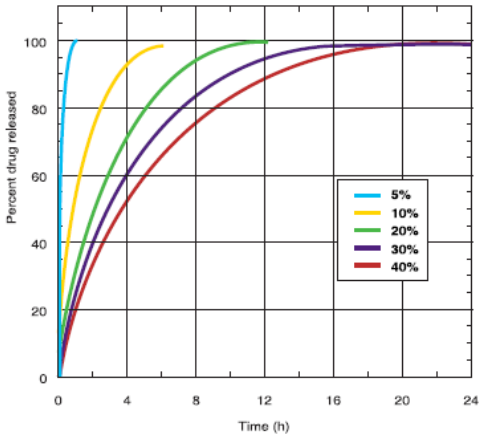
  - Ford *et al*. 1985. *IJP*, 24:327-338 and 339-350

- HPMC用量小于30%的情况下，药物释放行为会对HPMC的其他特性非常敏感

  Drug release may be more sensitive to variations in hypromellose properties at low hypromellose levels (< 30%)

10%盐酸普萘洛尔，美多秀™ K4M，乳糖，0.5%硬镁

10% propranolol HCl, METHOCEL™ K4M (as indicated)
balance lactose, 0.5% mag stearate



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HPMC粘度的影响 Viscosity Effect

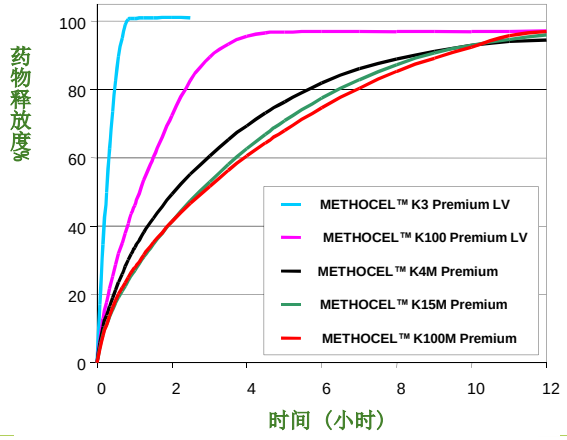
高粘度规格会使药物释放变慢

Higher polymer MW results in slower drug dissolution

5% 茶碱，20%HPMC， 74.5%乳糖，0.5%硬镁

5% theophylline, 20% hypromellose

74.5% lactose, 0.5% mag stearate



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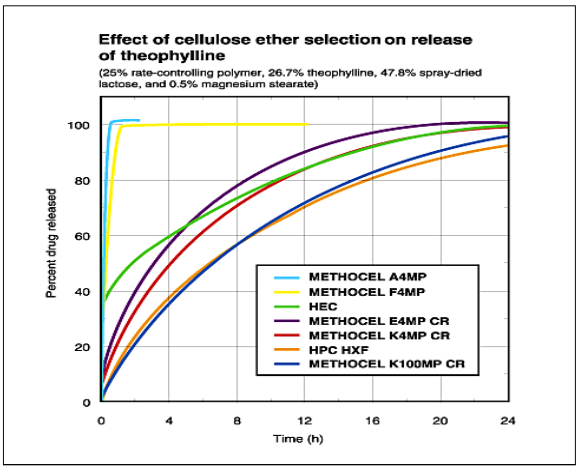
HPMC取代度的选择 Selection of Hypromellose substitution grade

➢不同取代度的HPMC会对药物释放产生很大影响

Hypromellose grade has a significant effect on dissolution

➢甲基纤维素和HPMC 2906(即美多秀™A和F级别)通常不用做缓控释应用

Methylcellulose and Hypromellose 2906 (A and F Chemistry) typically are not used for CR applications



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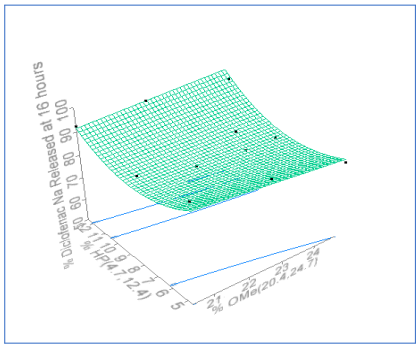
HPMC的取代度对配方的影响 Hypromellose Substitution

受配方中的活性药物或者其他辅料的影响，HPMC的取代度可能对配方产生重大影响，也可能影响很小

Some formulations show that HPMC substitution levels within a substitution type have little impact on drug release; some may show significant effects

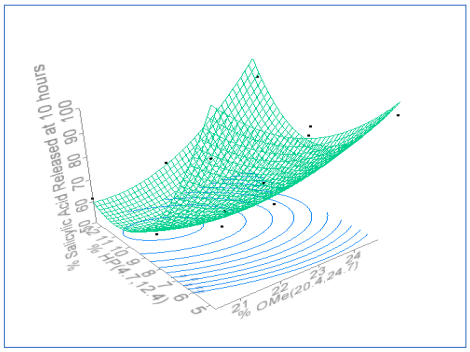
50%双氯芬酸钠，40%美多秀™ K15M，9.5%乳糖， 0.5%硬镁

50% diclofenac sodium, 40% METHOCEL™ K15M 9.5% lactose, 0.5% mag stearate



40%水杨酸，30%美多秀™ K15M，29%乳糖，1%硬镁

40% salicylic acid, 30% METHOCEL™ K15M 29% lactose, 1% mag stearate



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粒径的影响（案例分析） Particle Size (case study)

- 试验选取某一个美多秀™ 批次，通过筛分得到不同粒径规格

  Analysis involved taking a given lot of METHOCEL™ and using sieve cuts to generate specific particle size cuts

- 这些样品直接用于配方分析，或者同其他筛分出来的粒径规格组合出特定的粒径分布规格

  These cuts were used as is or blended with other cuts to obtain specific particle size distributions

- 美多秀™的粒径和粘度有共线性的特性

  There is a co-linearity within a given lot of METHOCEL™ between particle size and molecular weight (viscosity)

  - 比方说美多秀™ K系列，粒径降低，粘度降低

    For METHOCEL™ K Chemistry (USP 2208), as the particle size decreases the molecular weight (viscosity) decreases

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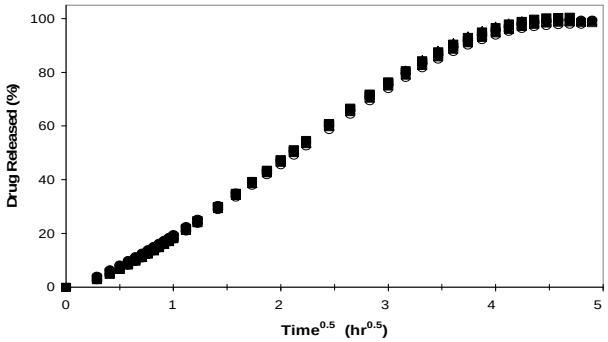
HPMC粒径影响因素 Hypromellose Particle Size

50%咖啡因，30%美多秀™ K15M，
19%乳糖， 1%硬镁

50% caffeine, 30% METHOCEL™ K15M
19% lactose, 1% mag stearate



HPMC	100 mesh (% thru)	230 mesh (%thru)	D1,0 (µm)	D4,3 (µm)	Viscosity (cps)
●>100 mesh	28.3	4.2	57.3	243.1	21,249
▲>100 mesh (50%) + 200-230 mesh (50%)	64.5	51.1	55.3	173.1	19,849
■>100 mesh (50%) + < 325 mesh (50%)	65.0	51.6	34.1	110.8	14,046
○unsieved	96.2	68.9	43.7	104.7	17,751
△< 325 mesh	99.8	99.3	34.5	47.4	9,869
□230-270 mesh	99.7	99.6	56.6	78.2	20,447

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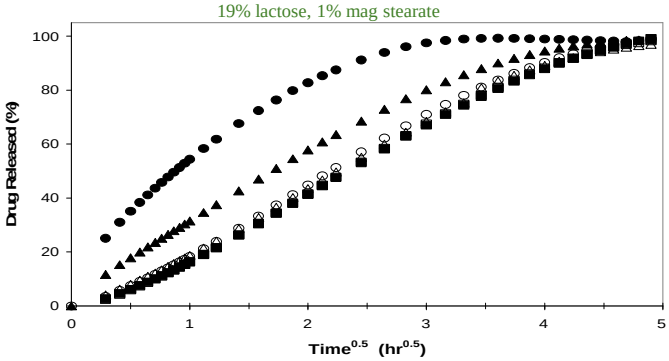
HPMC粒径影响因素 Hypromellose Particle Size

50%对乙酰氨基酚， 30%美多秀™ K100M，
19%乳糖，1%硬镁

50% acetaminophen,
30% METHOCEL™ K100M
19% lactose, 1% mag stearate



HPMC	100 mesh (% thru)	230 mesh (%thru)	D1,0 (µm)	D4,3 (µm)	Viscosity (cps)
●>170 mesh	84.5	9.0	82.0	177.4	142,260
▲100-200 mesh	99.6	32.9	66.4	131.5	122,675
■>100 mesh (50%) + < 325 mesh (50%)	69.5	50.6	36.2	153.2	69,895
○unsieved	96.2	68.3	44.1	100.3	81,792
△200-230 mesh	100.0	96.2	51.2	85.6	90,417
□< 325 mesh	99.9	99.5	34.9	50.5	43,855

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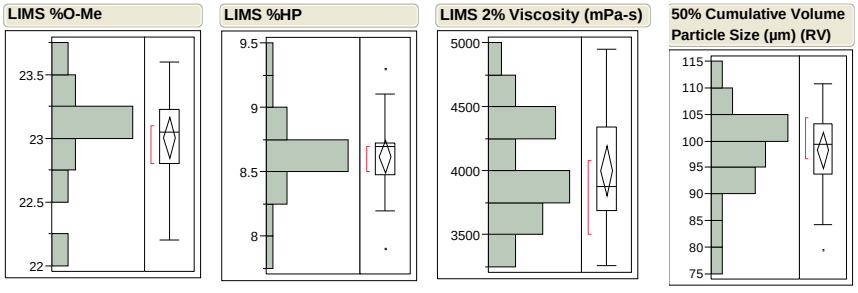
最有影响力的因素分析 Understanding the most impactful attribute

- **配方 Tablet formulation**
  - 扑热息痛 Paracetamol 50%
  - 美多秀™ K4M CR METHOCEL™ K4M CR 30%
  - 直压乳糖 Fast-flowing lactose 18%
  - 滑石粉 Talc 1%
  - 硬酯酸镁 Magnesium stearate 1%

- **片芯性质 Tablet properties**
  - 片重 ：500mg Total weight: 500 mg
  - 目标片硬度：90N target hardness: 90 N
  - 直径10.8mm， 厚度3.9mm 10.8-mm diameter by 3.9-mm thick
  - 压片冲模：13/32FFBE Tooling: 13/32 FFBE

- **考察22批美多秀™ K4M CR Twenty-two METHOCEL™ K4M CR batches investigated**

美多秀™ K4M CR 性质 METHOCEL™ K4M CR properties



K4M 影响骨架片释放的特性
K4M properties impacting matrix performance

K4M CR 性质	p-值
D50 (µm)	0.2154
%OMe	0.0245*
%HP	0.0014*
2% Viscosity	0.3834

基于本配方，取代度是最大的影响因素
Substitution is the most significant factor based on this formulation

美多秀™ CR规格新质量标准介绍 METHOCEL™ CR grades

- 通过生产工艺控制，以及关键质量参数对配方影响的了解，我们对以下影响配方的因素得以控制并缩小范围

  Process control and understanding of critical quality attribute impact on dosage form performance has led to tightening of the following criteria

  - 甲氧基取代度 Methoxyl content
  - 羟丙基取代度 Hydroxypropoxyl content
  - 粒径–通过230目标准筛 Particle size – percent through a 230 U.S. Std sieve
- 产品其他质量标准没有任何更改

  All other specifications remain unchanged
- 产品更改从2010年12月1日开始生效–对非CR规格没有影响

  Change effective December 1, 2010 - No impact to PREMIUM grades
- 减少美多秀™ CR规格产品的批间差异，提高稳定性

  Decreases variability, increases METHOCEL™ CR reliability
  - 能够提供更稳定的配方表现 Robust, consistent dosage form performance
  - 降低工艺操作过程中偏差对产品质量影响 Narrowed process capability window

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美多秀™ K系列CR规格新产品质量标准

	甲氧基	羟丙基	%粒径通过40目标准筛(420微米)	%粒径通过100目标准筛(149微米)	%粒径通过230目标准筛(63微米)
美多秀™ K100 LV CR	19.0-24.0% **22.0-24.0%**	7.0-12.0% **7.5-9.5%**	>99.0% **无变化**	>99.0% **无变化**	无要求 **50.0-80.0%**
美多秀™ K4M CR	19.0-24.0% **22.0-24.0%**	7.0-12.0% **7.5-9.5%**	>99.0% **无变化**	>99.0% **无变化**	无要求 **50.0-80.0%**
美多秀™ K15M CR	19.0-24.0% **22.0-24.0%**	7.0-12.0% **8.5-10.5%**	>99.0% **无变化**	>99.0% **无变化**	无要求 **50.0-80.0%**
美多秀™ K100M CR	19.0-24.0% **22.0-24.0%**	7.0-12.0% **9.5-11.5%**	>99.0% **无变化**	>99.0% **无变化**	无要求 **50.0-80.0%**

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关于美多秀™ K100M CR新质量规格的粘度范围

- 较宽的粘度范围 ，粘度分布为正态分布
  Broad, basically normal distribution of values
- 粘度范围中间值不在100000mPa·s,因为药典粘度范围也是不对称的(72750-135800 mPa·s)
  Distribution is not centered at 100,000 mPa·s, but note that the compendial viscosity limits are asymmetric around the nominal value (75,000-140,000 mPa·s)
  - 粘度质量标准中心点107500 mPa·s. 107500 mPa·s Center point of specification: 107,500 mPa·s
  - 中位值=110700 mPa·s, 平均值=110400 mPa·s. Median value = 110,700 mPa·s; mean value = 110,400 mPa·s
- 美多秀医药级别产品生产符合药典规定粘度范围
  Premium material production uses entire compendial range
- 为CR规格而缩小粘度质量标准是不可行的。
  Narrowing the viscosity specification for the CR Grade products is not feasible

关于美多秀™ K100M CR新质量规格的粒径范围

- 使用通过230目标准筛的百分比作为粒径的表征
  % of product that passes through 230 mesh (63μ) sieve used as indicator of particle size; this is at or near the center of a sieve analysis of particle size distribution
- 粒径呈正态分布
  Normal distribution of values
- 只有3.7%的产品有超过一半的粒径大于230目标准筛
  Only a small fraction (3.7%) of production had < 50.0% through 230 mesh
- 考虑到通常较细的颗粒会使配方更稳定，K系列CR规格新的粒径要求设定在50%-80%通过230目标准筛
  Given the generally more robust performance of finer particle size distributions of the polymer and the desire to be consistent with other METHOCEL K chemistry (USP substitution type 2208) products, this new, additional specification for CR Grades set at 50.0-80.0% through 230 mesh

关于美多秀™ K100M CR新质量规格的羟丙基范围

- K100M的羟丙基取代不是正态分布的
  In this case, the distribution of data is not normal
- 美国药典规定的范围是4-12%，原有的CR规格标准是7-12%
  Recall that USP limits are 4.0-12.0% and the METHOCEL Premium CR Grade specifications were 7.0-12.0%
- 只有1.5%的产品的羟丙基取代<9.5%
  Only 1.5% of production lots had <9.5 %HP
- 考虑到药典检测羟丙基方法的内在误差，我们将CR规格新的羟丙基范围定在±1%，即9.5-11.5%
  Given the experimental error inherent in the compendial method for determination of substitution levels, we consider a 2.0% specification range to be the minimum practical, therefore the upgraded CR Grade specification is set at 9.5-11.5 %HP

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关于美多秀™ K100M CR新质量规格的甲氧基范围

- K100M的甲氧基取代分布不是正态的
  In this case, the distribution of data is not normal (best fit: "Normal 3 mixture")
- 美国药典规定的范围是19.0-24.0%，原有的CR规格标准也是如此
  Recall that USP limits are 19.0-24.0%, as were METHOCEL Premium CR Grade specifications
- 只有0.7%的批次甲氧基含量<22.0%
  Only 0.7% of production lots had <22.0 %MeO
- 考虑到药典检测羟丙基方法的内在误差，我们将CR规格新的甲氧基范围定在±1%，即22.0-24.0%
  As was the case with %MeO, given the experimental error inherent in the compendial method for determination of substitution levels, we consider a 2.0% specification range to be the minimum practical, therefore the upgraded CR Grade specification set at 22.0-24.0 %MeO

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我们能为您做什么？

- 基于QbD试验的需要，我们从生产线上获得满足试验需要的样品

  For QbD purposes, what we desire to have is a set of samples from full-scale manufacturing lots that meet multiple parameters described by a given experimental design (for example, 1/1/1/1 for an orthogonal design)

- 更有挑战性的是除了满足QbD的设计要求，产品的其他性质也要满足设计的要求

  To make this even more challenging, all of the other parameters must then meet the values defined for them within a multivariate experimental design

  - 因为HPMC的理化参数是相对独立的，所以要找到一个满足四方面要求的产品的可能性是很小的 Since the physicochemical parameters of hypromellose tend to be independent, the probability of finding a batch simultaneously meeting four criteria is the product of the four individual criteria – and therefore likely to be a very small value

- 同陶氏和卡乐康公司一道，通过QbD的样品确定配方设计空间，从而达到更稳定配方表现

  Drive improved and reproducible robust formulation performance by working with Dow and Colorcon on QbD samples and design formulation space

陶氏化学其他关于QbD的技术信息 More to come from Dow

- Controlled Release Society 2011: 2011年7月30日–8月3日
- “将QbD应用于亲水凝胶骨架片 Application of QbD to Hydrophilic Matrix Tablets: Given the Realities, Are Our Ambitions too Ambitious?”
  - Presenter: Dr. Tim Cabelka, Dow Wolff Cellulosics Pharmaceutical R&D
- 2011 IPEC-美国 网络培训：2011年6月21日
- “IPEC关于生产过程，分析方法以及清场的验证的指导意见。 Validation - Learn about IPEC's needed validation guideline on manufacturing processes, analytic methods and cleaning.”
  - Presenter: Ann Van Meter, Dow Wolff Cellulosics Quality
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硝苯地平用于美多秀™ DC直压工艺案例分析

Development of Nifedipine Sustained Release Tablet Formulation by Direct Compression Using METHOCEL™ DC as Matrix

直压工艺 Direct Compression Processing

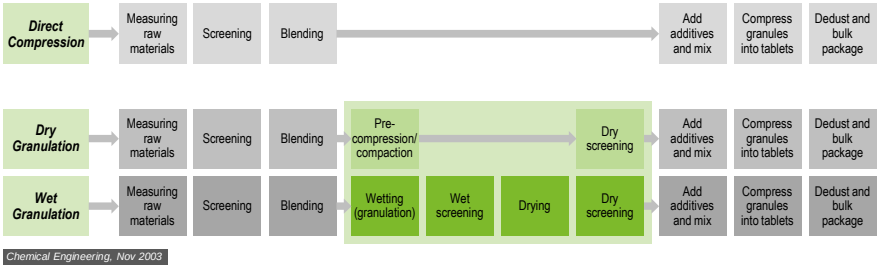
dowwolff CELLULOSICS

直压工艺就是处方中所有成分（主药+辅料）经干混后直接在压片机上压制成型的工艺

A tableting process in which a dry blend of ingredients (API + various excipients) is fed into a tablet press and compressed into tablets

采用这个方式可以省去制粒及相应后续工艺

Granulation steps are eliminated through Direct Compression



Chemical Engineering, Nov 2003

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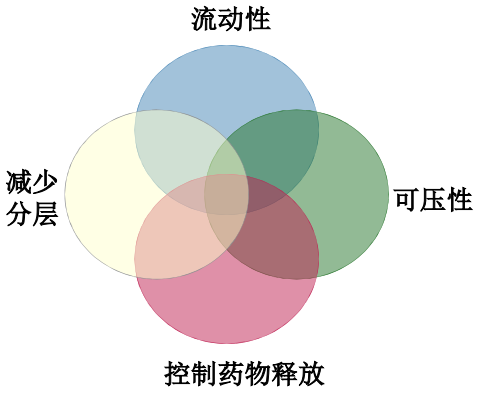
美多秀™ DC级别产品 METHOCEL™ DC Grade

美多秀DC级别产品在保留原有CR级别产品缓控释要求的同时，平衡了粉末的流动性，可压性，降低了配方的分层。

The product attributes for a DC grade HPMC for controlled release applications require balancing several, sometimes conflicting, performance dimensions.



美多秀™ DC级别产品 METHOCEL™ DC Grade

美多秀DC产品是可以应用于口服固体缓控释制剂直压过程的辅料，产品符合USP/EP/JP要求，产品为100%HPMC,无其他添加剂。

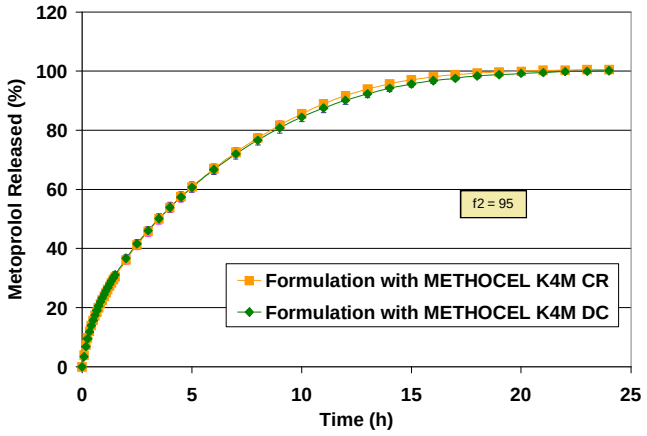
	K4M Premium DC	K100M Premium DC
*Methoxyl %	19.0 - 24.0	19.0 - 24.0
*Hydroxypropyl %	7.0 - 12.0	7.0 - 12.0
Substitution Type	2208	2208
Viscosity (cP)	2663 - 4970[1]	72,750 – 135,800[2]
*Moisture (%)	5% max	5% max

*Typical values, not to be construed as sales specifications
1. “Pre-harmonized” range: 3000-5600 cP
2. “Pre-harmonized” range: 75,000-140,000 cP

配方药物溶出

- 结果表明美多秀™ DC规格和CR规格可以达到同样的控制药物释放的目的

Results suggest the DC grade provides the same level of controlled drug release as the CR grade in this formulation。 The f2 factor measures the similarity between release profiles.



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酒石酸美托洛尔含量均匀性测试

- 实验全过程每间隔2分钟取样

Tablets collected at 2 minute intervals throughout trial

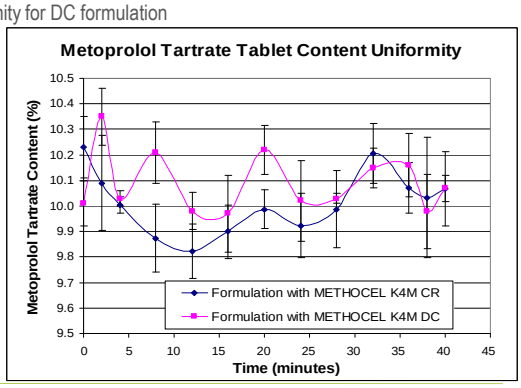
- 采用HPLC分析每个取样点酒石酸美托洛尔含量（3份进样）

Metoprolol Tartrate content determined via HPLC (in triplicate) for every time point

- 结果显示采用DC规格的处方含量均匀性更好的

Results indicate improved content uniformity for DC formulation

Metoprolol Tartrate Content含量	CR	DC
Average (%)平均值	10.01	10.09
Standard Deviation 标准偏差	0.16	0.10
Relative Standard Deviation 相对标准偏差	1.61	1.03



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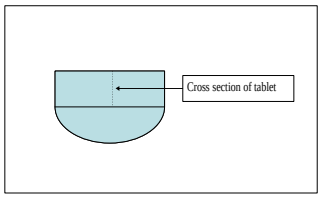
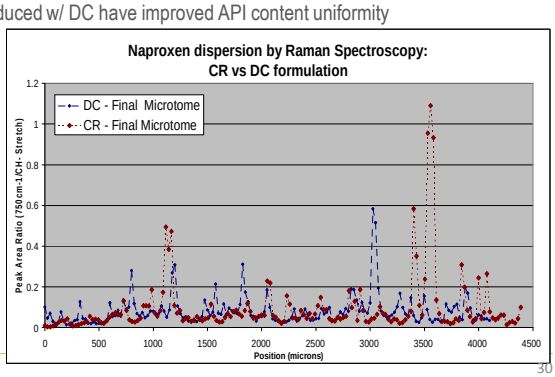
萘普生钠片剂内部含量均匀性测试

- 样片经横切后用切片刀处理得到一表面适合于分析
  Representative tablets were cross sectioned and microtomed to produce a surface suitable for analysis
- 采用拉曼光谱法测定这一表面含量均匀性
  Raman spectroscopy used to determine content uniformity across this surface
- 结果显示含DC规格的片子含量均匀性更好

Results indicate that tablets produced w/ DC have improved API content uniformity





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硝苯地平配方 Formulation

- 硝苯地平配方 Formulation
  - 20.0 % 硝苯地平 Nifedipine
    - 水不溶性药物 *Water in-soluble*
    - 光敏型药物，特别在溶液状态下 *Light-sensitive especially when moisture exists*
  - 17.7 % HPMC (DC 或者 CR 规格)
  - 40.9 % 直压乳糖 316 fast-flow Lactose 316
  - 20.4 % 微晶纤维素 Avicel PH 102
  - 1.0 % 硬脂酸镁 magnesium stearate

- 规模：
  - 30g
  - 1.5kg

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工艺过程 Nifedipine Formulation

- 工艺过程以及检测方法 Formulation preparation and testing
  - 配方在V型混合器中混合，直接填入料斗 formulation was V-blended and transferred directly to hopper
  - 8冲旋转压片机 8 station Rimek, Mini Press-II S/F
    - 旋转 速度 *10-30rpm Speed 10 ~30 RPM*
    - 压片力 2300kg-2700kg *Target compression force 2300 kg ~ 2700 kg*
    - 操作时间-1小时 *Run time ~ 1 hr*
  - 流动性测试 Flowability test
    - 粉体流动性测试 *Granular test*
    - 压片机上的表现 *Behavior on the press*
  - 药物溶出 Drug release
    - SOTAX 溶出仪 *SOTAX AT7 Smart dissolution system*
    - 岛津 紫外分光仪 *Shimadzu, UV2450*

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配方流动性分析 Flowability Test for Blends

评价各种配方的粉体流动性

Parameters of flowability were tested for the intermediate and final blends (n=3)

评价项目	硝苯地平 乳糖 MCC	硝苯地平 乳糖 MCC 美多秀™ CR	硝苯地平 乳糖 MCC 美多秀™ DC	硝苯地平 乳糖 MCC 美多秀™ CR 硬镁	硝苯地平 乳糖 MCC 美多秀™ DC 硬镁
休止角(°)	46	47.5	46.4	48.5	46
Hausner Ratio	1.36	1.43	1.46	1.44	1.37
可压缩指数	26	30	31	30.5	26
粉体流动率 (cm^3/10 s)	160	128	133	148	155

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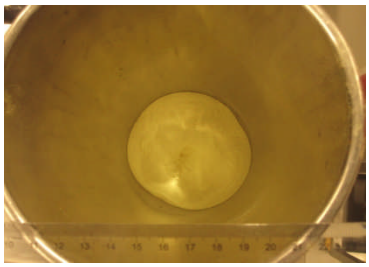
压片机上的表现 Flowability Test for Blends

配方整体粉体流动速率表现不同- 美多秀™DC配方流动速率一致，
美多秀™ CR配方在料斗中间流动速率快，靠近料斗壁流动速率慢



美多秀™DC配方

美多秀™CR配方

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转速对工艺的影响 Evaluation of Tableting Process

- 调节压片机转速为10rpm, 20rpm, 30rpm。
  Tablets collected at 10 rpm, 20 rpm, 30 rpm for compression rate throughout trial respectively
- 随机在压片过程中取样品，测试片重，片硬度和片厚度
  Tablet weight, hardness and thickness were determined for tablets manufactured at each compression rate
- 结果显示美多秀DC配方在各项检测指标中差异最小
  Results indicate less variables for DC formulation

配方	片重差异(mg)	片厚差异(mm)	片硬度差异(kp)
美多秀™DC	2.54	0.06	0.54
美多秀™CR	3.53	0.7	1.01

n=30

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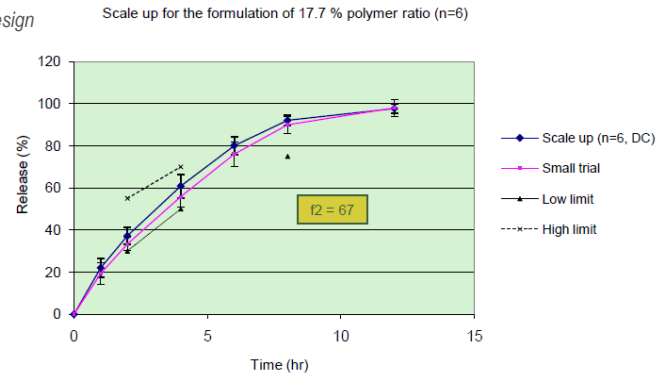
药物溶出 Release Testing with Small Trial & Scale up for Optimal Formulation

- **30g规模和1.5kg规模 药物溶出**

  Evaluation of final formulations for small trial and scale up also achieved similar drug release.

- **30g规模 Small trial**
  - 100片 *Formulation design*
    - *100 units (30 g)*
- **1.5kg规模 Scale up**
  - 1.5 kg *batch size (5000片)*



总结 Summary

- **美多秀缓控释规格缩小产品质量标准，从而能够提高配方稳定性**

  Improved METHOCEL™ CR grade provides robust formulations and release profiles.

- **陶氏化学致力于QbD的工作，同客户一道开发新的产品和规格**

  Dow's commitments on QbD initiatives will be benefit for pharmaceutical industry

- **美多秀直压规格在硝苯地平骨架片的应用能够获得目标释放行为，配方稳定，配方流动性和片剂性能得以改善。**

  The case study provided a good example for water insoluble drug using METHOCEL DC as matrix material to achieve desirable sustained release behavior. The current formulation is very robust and DC polymer contributed a lot to good flowability and satisfied release profile.