《药剂学》教材比较研究

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一、美国、英国、日本药剂学教材的特点

- 深入浅出
- 适合拓展
- 强调基础

Aulton's Pharmaceutics: The Design and Manufacture of Medicines

- 药剂学是一门综合性科学，涉及药物制剂的研制、生产、质量控制、合理应用等。该书是一本对药物剂型有清晰描述的教材，作者为Michael E. Aulton，已经出版2次（1988、2002年），前身是Tutorial Pharmacy。本书重基础，是一本适合于本科教学的教材。本比较教材为第三版，由英国Chuchill Livingstone (Elsevier)公司出版。本教材对剂型的设计和生产的科学、技术问题进行了深入的探讨。
- 全书的结构和内容根据现代药剂学的特点进行了编排，考虑了全球各大学的课程设置。全书分五部分，共46章：

第一部分 剂型设计的科学原理

- 第一章 剂型设计
- 第二章 溶出度和溶解度
- 第三章 溶液性质
- 第四章 流变学
- 第五章 表面及界面现象
- 第六章 分散系统
- 第七章 药品稳定性动力学

第二部分 颗粒科学和粉末技术

- 第八章 固态性质
- 第九章 粒径分析
- 第十章 粒径降低技术（粉碎法）
- 第十一章 粒径分离法（筛分法）
- 第十二章 混合法
- 第十三章 粉末流动

第三部分 微生物学和灭菌法

- 第十四章　　微生物学基础
- 第十五章　　微生物技术在药剂学中的应用
- 第十六章　　物理手段和化学法对微生物的作用
- 第十七章　　灭菌原理
- 第十八章　　灭菌实践

Table 18.1 Examples of sterile preparations and devices

Preparation/product/item	Typical volume	Typical container	Sterilization process
Injections			
Intravenous infusion, e.g. blood products	0.5 L	Plastic, glass	Moist heat Filtration (e.g. addition of additives)
Total parenteral nutrition (TPN)	>3 L	Plastic, glass	Moist heat Filtration (e.g. addition of vitamins)
Small volume injections, e.g. insulin, vaccine	1–50 mL	Plastic, glass	Moist heat[a] Filtration
Small-volume oily injections		Glass	Dry heat
Non-injectable sterile fluids			
Non-injectable water, e.g. surgery, irrigation	0.5–1 L	Plastic (polyethylene or polypropylene)	Moist heat
Urological irrigation solution	>3 L	Plastic (rigid)	Moist heat Filtration
Peritoneal dialysis and haemodialysis solutions	2.5 L	Plastic	Moist heat
Inhaler solutions	Diluted in WFI[a]	Plastic (polyethylene nebulas)	Dry heat
Ophthalmic preparations			
Eye drops	0.3–0.5 mL	Plastic, glass	Moist heat[b] Filtration
Eye lotions	>0.1 L	Plastic, glass	Moist heat
Eye ointments	–	Plastic, aluminium	Dry heat Filtration
Contact lens solutions	Small	Plastic	Chemical disinfection
Dressings			
Chlorhexidine gauze dressing Polyurethane foam dressing Elastic adhesive dressing Plastic wound dressings	Different wrapping[c]	Moist heat[d] Dry heat Ethylene oxide Ionizing radiation Other effective method	
Implants	Small, sterile cylinders of drug	Dry heat Chemical (0.02% PMN, 12h 75°C)	
Absorbable haemostats			
Oxidized cellulose, human fibrin foam		Dry heat	
Surgical ligatures and sutures			
Sterilized surgical catgut		γ-radiation Chemical (96% ethanol + 0.002% PMN + formaldehyde in ethanol 24h prior use; naphthalene or toluene at 160°C for 2 h)	
Non-absorbable type		γ-radiation Moist heat	
Instruments and equipment			
Syringes	Glass, plastic	Dry heat Moist heat	

第四部分　药物传递的生物药剂学原理

- 第十九章　　生物药剂学概论
- 第二十章　　胃肠道——生理学和药物吸收
- 第二十一章　生物利用度——物理化学和剂型因素
- 第二十二章　生物药剂学性质的测定
- 第二十三章　给药方案

第五部分　剂型设计和生产

- 第二十四章　处方前工作
- 第二十五章　溶液剂
- 第二十六章　澄明度保证技术
- 第二十七章　混悬剂和乳剂
- 第二十八章　散剂和颗粒剂
- 第二十九章　制粒
- 第三十章　　干燥
- 第三十一章　片剂和压片法
- 第三十二章　调释制剂

- 第三十三章　　包衣技术（片剂和颗粒）
- 第三十四章　　硬胶囊
- 第三十五章　　软胶囊
- 第三十六章　　肺部给药制剂
- 第三十七章　　鼻腔给药制剂
- 第三十八章　　经皮吸收制剂
- 第三十九章　　伤口敷药制剂
- 第四十章　　直肠和阴道用制剂
- 第四十一章　　蛋白类药物制剂
- 第四十二章　　包装
- 第四十三章　　染菌、渗漏和防腐
- 第四十四章　　药品稳定性和稳定性试验
- 第四十五章　　车间设计
- 第四十六章　　热传递技术（蒸汽性质和应用）

Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems

- 第一部分 药物、药物剂型、和药物传递系统引论
- 第一章 药物和药学概论
- 第二章 新药开发和审批程序
- 第三章 现行药品生产质量管理规范和药品调剂质量管理规范

第二部分 药物剂型和药物传递系统设计

- 剂型设计：药剂学和处方设计考虑
- 剂型设计：生物药剂学和药动学考虑

PHYSICAL PHARMACY CAPSULE 5.1

Particle Size, Surface Area, and Dissolution Rate

Particle size has an effect on dissolution rate and solubility. As shown in the Noyes–Whitney equation,

$$\frac{dC}{dT} = kS(C_s - C_t)$$

where

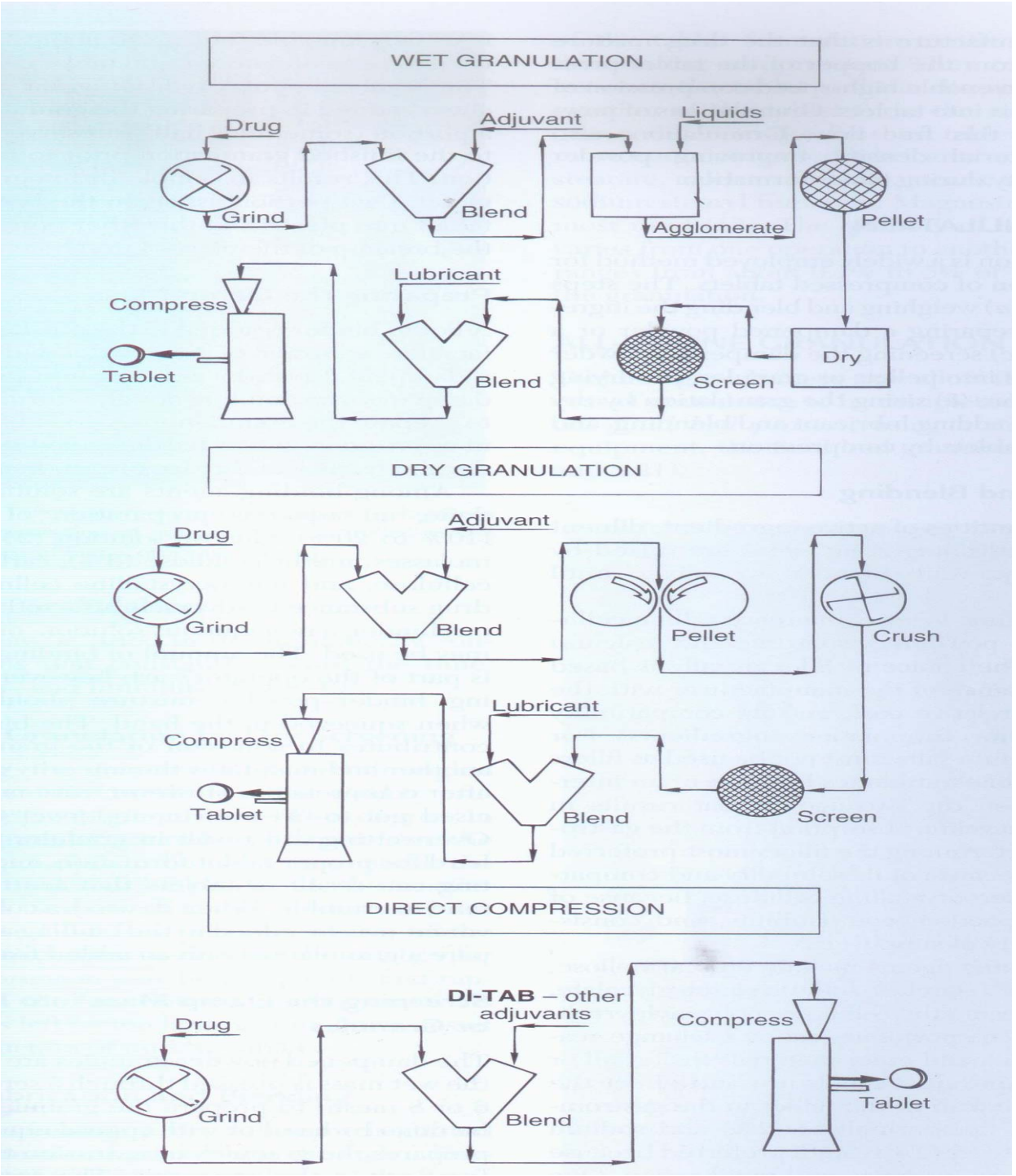
dC/dT is the rate of dissolution (concentration with respect to time),
k is the dissolution rate constant
S is the surface area of the particles,
C_s is the concentration of the drug in the immediate proximity of the dissolving particle, that is, the solubility of the drug, and
C_t is the concentration of the drug in the bulk fluid.

It is evident that C_s cannot be significantly changed, C_t is often under sink conditions (an amount of the drug is used that is < 20% of its solubility) and k comprises many factors, such as agitation and temperature. This leaves the S, surface area, as a factor that can affect the rate of dissolution.

An increase in the surface area of a drug will, within reason, increase the dissolution rate. Circumstances in which it may decrease the rate include a decrease in the effective surface area, that is, a condition in which the dissolving fluid cannot wet the particles. Wetting is the first step in dissolution. This can be demonstrated by visualizing a tablet of diameter 0.75 in. by thickness 0.25 in. The surface area of the tablet can be increased by drilling a series of 0.0625-in. holes in the tablet. However, even though the surface area has been increased, the dissolution fluid—water—because of surface tension and so on cannot necessarily penetrate the new holes and displace the air. Adsorbed air and other factors can decrease the effective surface area of a dosage form, including powders. This is the reason that particle size reduction does not always raise the dissolution rate. One can also visualize a powder that has been comminuted to a very fine state of subdivision; when it is placed in a beaker of water, the powder floats because of the entrapped and adsorbed air. The effective surface area is not the same as the actual surface area of the powder.

第三部分 固体制剂和固体调释制剂

- 第六章 散剂和颗粒剂
- 第七章 胶囊剂
- 第八章 片剂
- 第九章 固体调释制剂


WET GRANULATION
Drug
Grind
Adjuvant
Blend
Liquids
Agglomerate
Pellet
Compress
Tablet
Lubricant
Blend
Screen
Dry
DRY GRANULATION
Drug
Grind
Adjuvant
Blend
Pellet
Crush
Compress
Tablet
Lubricant
Blend
Screen
DIRECT COMPRESSION
Drug
Grind
DI-TAB – other adjuvants
Blend
Compress
Tablet

第四部分 半固体制剂和透皮给药系统

- 软膏剂、乳膏剂和凝胶剂
- 透皮给药系统

第五部分 插入剂

- 第十二章　　栓剂和插入剂

第六部分 液体制剂

- 第十三章　　溶液剂
- 第十四章　　分散系统

CLINICAL CASE STUDY

Subjective Information

CC: K. F. is a 9-year-old WM who arrives at the pediatric clinic with his mother. The mother states that K. F. talks excessively, interrupts others when they speak, rarely follows her directions, and frequently runs around the house. The mother also states that she has heard from the teacher that he leaves the classroom in the middle of the class, often blurts out answers before questions have been completed, has a difficult time waiting his turn (e.g., in the lunchroom), is "fidgety," rarely follows directions or pays attention, and turns in incomplete homework assignments. His teacher has also told the mother that he frequently distracts the other students at school. The mother states, "I would like your help. But I do not want him to be put on a medicine where he has to take it more than once a day because I might forget to give it to him. Also, I do not want him taking any medicine to school."

HPI: The mother states that K. F. has been "this way" since he was 6 years old. However, it is now at the point where does not complete any of his tasks (e.g., making his bed, doing his homework) and his grades are "slipping." His latest report card showed "many Cs and Ds."

PMH: Otitis media, 4 weeks ago.

Meds: Zithromax Suspension, finished it about 3 weeks ago.

OTC Meds: K. F. (and his mother) deny K. F.'s use of vitamins, herbals, or any other supplements

PSH: None

FH: Mother, DM type II since age 29

SH: (per K. F.)
(–) Tobacco
(–) EtOH
(–) Illicit drugs
(+) Caffeine: Loves Mountain Dew, drinks a couple of cans (~2–3) per day

Exercise, daily activities: Goes to school from 8 A.M. to 3 P.M., after school likes to watch TV, in-line skate, and play basketball.

Timing of meals: Breakfast at 7:30 A.M, lunch at noon, snack at 3:30 P.M., and dinner at 6:30 P.M.

Diet: Chips, candy, peanut butter and jelly sandwiches, pasta, and two or three cans of Mountain Dew per day

Bedtime: 9:30 to 10:30 P.M.

Siblings: None

Mother and father are both accountants and each work ~40 hours per week. They have been married for 11 years.

ALL: NKDA

Objective Information

9-year-old WM

Ht: 4'2" **Wt:** 71 pounds

BP: 119/75 **P:** 70 **T:** 98.6°F **RR:** 15

Pain: none

The mother presents K. F.'s last report card with grades Cs and Ds along with notes from K. F.'s teacher about his behavior.

Assessment

ADHD: Combined type

Plan

Recommend extended-release methylphenidate HCl (i.e., Concerta) 18 mg by mouth once a day with breakfast and a full glass of water, milk, or juice at 7:30 A.M. (to aid with adherence). Inform the mother that the prescription has to be dispensed to her within 7 days after the date it is issued. Concerta has a rapid onset of action to help K. F. focus in the morning at school and a long duration of action, which will be useful during and after school for homework.

Counsel the mother on possible side effects, such as insomnia, loss of appetite, and weight loss. Inform K. F.'s mother also about a possible decrease in rate of height growth (not final height). Advise her that if her son misses a dose of the drug in the morning, not to administer it after school. Wait until the next morning for the next dose. Do not double the dose the next day. Inform the mother that this product is prepared in a nonabsorbable shell, which means that the empty shell may or may not be observed in the stool. So if K. F. notices something that resembles a tablet in the stool and mentions it to his mother, she can tell

(*continued*)

第七部分 无菌制剂和无菌给药系统

- 第十五章　　注射剂
- 第十六章　　疫苗
- 第十七章　　特殊溶液剂和混悬剂

FIGURE 15.11 Monovial safety guard system. (Courtesy of Becton-Dickinson.)

imes to transfer the fluid into the Monovial. The Monovial is shaken a few times to reconstitute he drug and inverted. Then the minibag is squeezed and released to transfer the drug back nto the infusion bag. This process is repeated ntil the vial is empty.

Several manufacturers ship to the hospital pharmacy reconstituted IV antibiotic solutions, for example, cefazolin sodium, in the frozen state. When thawed, these nonpyrogenic solutions are stable for a finite period. Reconstituted cefazolin is stable for 48 hours at room temperature and for 10 days when refrigerated (5°C or 41°F). The product is packaged in a small plastic bag for piggyback use in IV administration.

PACKAGING, LABELING, AND STORAGE OF INJECTIONS

Containers for injections, including the closures, must not interact physically or chemically with the preparation so as to alter its strength or efficacy (Fig. 15.12). If the container is made of glass, it must be clear and colorless or light amber to permit inspection of its contents. The type of glass suitable for each parenteral preparation is usually stated in the individual

FIGURE 15.12 Testing compatibility of rubber closures with a solution. (Courtesy of Abbott Laboratories.)

第八部分　新剂型、给药系统和器械

- 第十八章　　放射药剂
- 第十九章　　生物制剂
- 第二十章　　新剂型和药物给药技术

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- 第一章　物质溶解
- 第二章　分散系统
- 第三章　制剂材料物性
- 第四章　制剂各论
- 第五章　制剂工艺
- 第六章　制剂检查法
- 第七章　药物传递系统的必要性
- 第八章　调释制剂
- 第九章　靶向制剂
- 第十章　前体药物

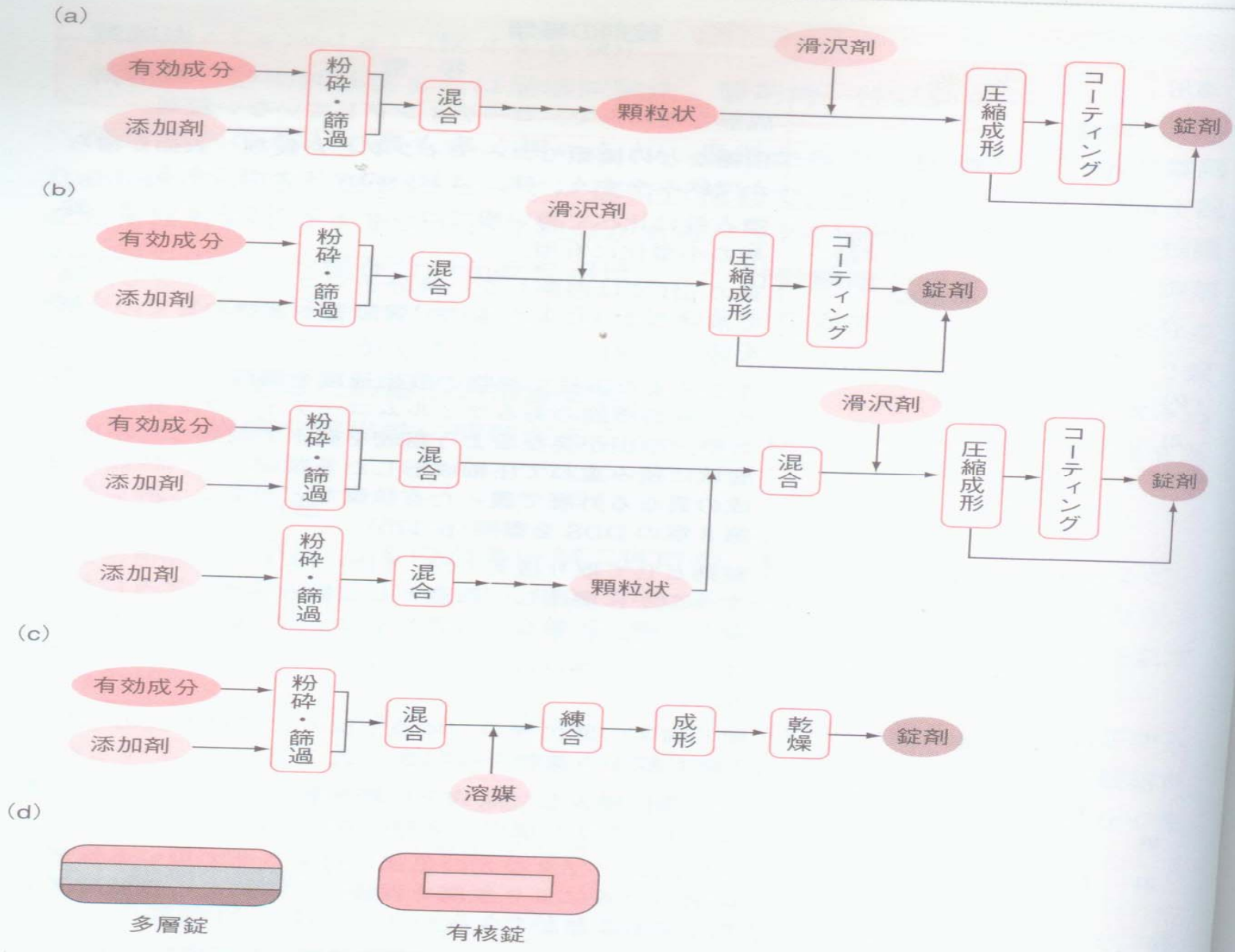

図 4.4 錠剤の製法

（a）間接打錠法，（b）直接打錠法・半直接打錠法，（c）湿式錠，（d）特殊な錠剤．

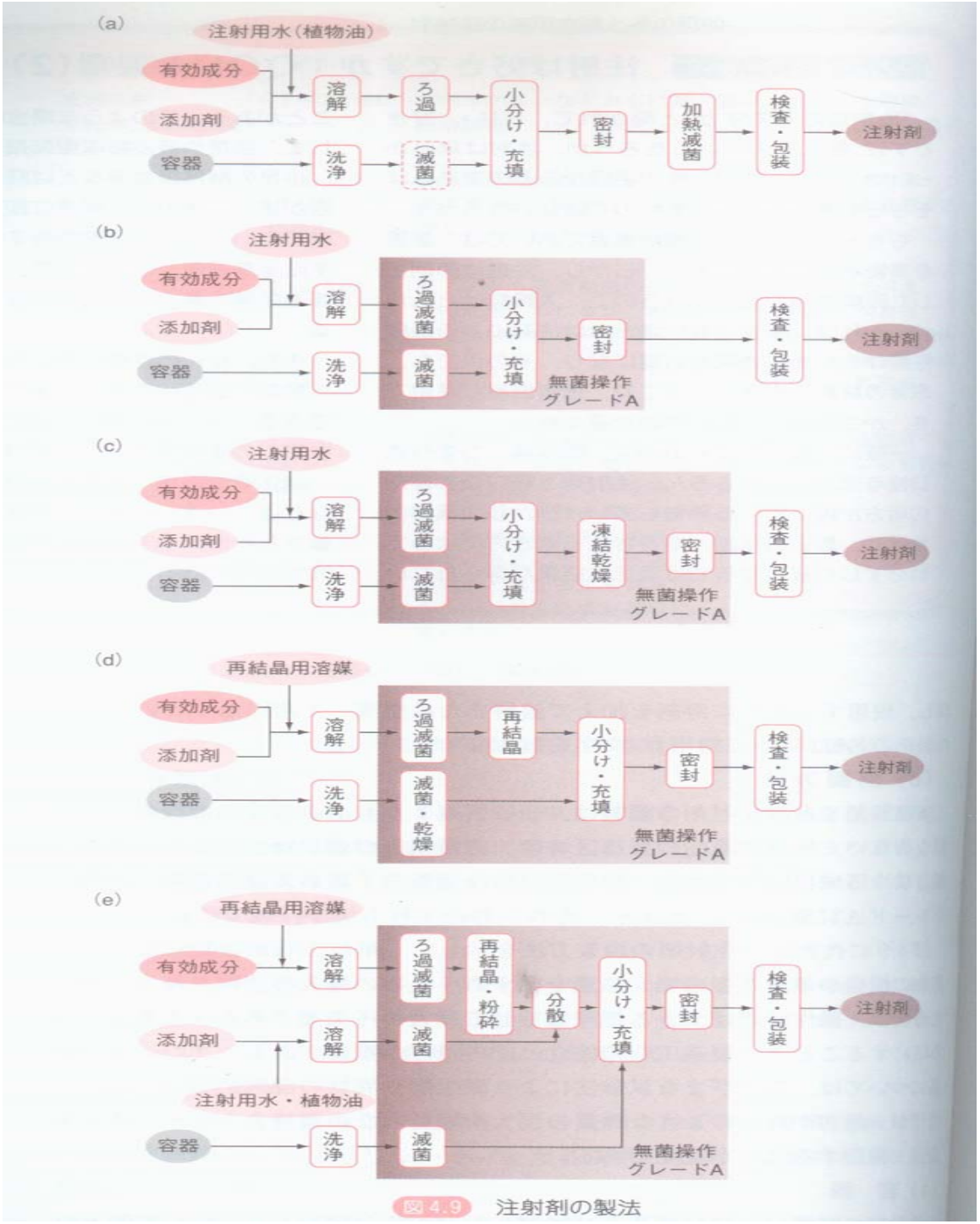
(a)
注射用水（植物油）
有効成分
添加剤
容器
溶解
洗浄
ろ過
（滅菌）
小分け・充填
密封
加熱滅菌
検査・包装
注射剤
(b)
注射用水
有効成分
添加剤
容器
溶解
洗浄
ろ過滅菌
滅菌
小分け・充填
密封
無菌操作
グレードA
検査・包装
注射剤
(c)
注射用水
有効成分
添加剤
容器
溶解
洗浄
ろ過滅菌
滅菌
小分け・充填
凍結乾燥
密封
無菌操作
グレードA
検査・包装
注射剤
(d)
再結晶用溶媒
有効成分
添加剤
容器
溶解
洗浄
ろ過滅菌
滅菌・乾燥
再結晶
小分け・充填
密封
無菌操作
グレードA
検査・包装
注射剤
(e)
再結晶用溶媒
有効成分
添加剤
注射用水・植物油
容器
溶解
溶解
洗浄
ろ過滅菌
滅菌
滅菌
再結晶・粉砕
分散
小分け・充填
密封
無菌操作
グレードA
検査・包装
注射剤

図 4.9　注射剤の製法

我国同类教材的特点和不足

- 我国目前统编教材为第六版《药剂学》，主编为崔福德教授，该书针对药学、药剂学专门化的学生，内容较全面。其优点是传统的内容叙述全面，学生易于学习。但缺点是理论部分显单薄，现代药剂学的内容不够完整，例如，灭菌法尚有流通蒸汽灭菌法，难以达到目前的要求。

比较中国与美国、英国、日本同类教材的区别

- （1）结构的比较
- 目前，除日本外，各国教材均为单元式介绍，这样便于老师讲述、学生学习。
- （2）内容的比较
- 英国教材内容最全面，包含了包装材料和相应的说明。美国的教材还包括了临床药学的内容。日本的教材包含了靶向制剂的等内容。我国统编教材内容较全，但在与新要求一致方面尚需要加强。

国外同类教材对我国教材编写、出版的借鉴意义

- 1. 内容应与现代要求一致；
- 2. 多采用表格；
- 3. 应增加机械、设备、制剂等彩图、实物图；
- 4. 物理药剂学内容应有助于学生拓展。

- 谢谢