

Remington's Pharmaceutical Sciences

EDITED BY THE EDITORIAL BOARD OF REMINGTON'S PHARMACEUTICAL SCIENCES

Eighteenth Edition

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Table of Contents

Part 1 Orientation			44	Cholinomimetic Drugs	889
1	Scope	3	45	Adrenergic and Adrenergic Neuron Blocking Drugs	898
2	Evolution of Pharmacy	8	46	Antimuscarinic and Antispasmodic Drugs	907
3	Ethics	20	47	Skeletal Muscle Relaxants	916
4	The Practice of Community Pharmacy	28	48	Diuretic Drugs	929
5	Opportunities for Pharmacists in the Pharmaceuti- cal Industry	33	49	Uterine and Antimigraine Drugs	943
6	Pharmacists in Government	38	50	Hormones	948
7	Drug Information	49	51	Vitamins and Other Nutrients	1002
8	Research	60	52	Enzymes	1035
Part 2 Pharmaceutics			53	General Anesthetics	1039
9	Metrology and Calculation	69	54	Local Anesthetics	1048
10	Statistics	104	55	Sedatives and Hypnotics	1057
11	Computer Science	108	56	Antiepileptics	1072
12	Calculus	145	57	Psychopharmacologic Agents	1082
13	Molecular Structure, Properties and States of Matter	158	58	Analgesics and Antipyretics	1097
14	Complex Formation	182	59	Histamine and Antihistamines	1123
15	Thermodynamics	197	60	Central Nervous System Stimulants	1132
16	Solutions and Phase Equilibria	207	61	Antineoplastic and Immunosuppressive Drugs ...	1138
17	Ionic Solutions and Electrolytic Equilibria	228	62	Antimicrobial Drugs	1163
18	Reaction Kinetics	247	63	Parasitocides	1242
19	Disperse Systems	257	64	Pesticides	1249
20	Rheology	310	65	Diagnostic Drugs	1272
Part 3 Pharmaceutical Chemistry			66	Pharmaceutical Necessities	1286
21	Inorganic Pharmaceutical Chemistry	329	67	Adverse Drug Reactions	1330
22	Organic Pharmaceutical Chemistry	356	68	Pharmacogenetics	1344
23	Natural Products	380	69	Pharmacological Aspects of Drug Abuse	1349
24	Drug Nomenclature—United States Adopted Names	412	70	Introduction of New Drugs	1365
25	Structure-Activity Relationship and Drug Design	422	Part 7 Biological Products		
Part 4 Testing and Analysis			71	Principles of Immunology	1379
26	Analysis of Medicinals	435	72	Immunizing Agents and Diagnostic Skin Antigens	1389
27	Biological Testing	464	73	Allergenic Extracts	1405
28	Clinical Analysis	495	74	Biotechnology and Drugs	1416
29	Chromatography	529	Part 8 Pharmaceutical Preparations and Their Manufacture		
30	Instrumental Methods of Analysis	555	75	Preformulation	1435
31	Dissolution	589	76	Bioavailability and Bioequivalency Testing	1451
Part 5 Radioisotopes in Pharmacy and Medicine			77	Separation	1459
32	Fundamentals of Radioisotopes	605	78	Sterilization	1470
33	Medical Applications of Radioisotopes	624	79	Tonicity, Osmoticity, Osmolality and Osmolarity ..	1481
Part 6 Pharmaceutical and Medicinal Agents			80	Plastic Packaging Materials	1499
34	Diseases: Manifestations and Patho- physiology	655	81	Stability of Pharmaceutical Products	1504
35	Drug Absorption, Action and Disposition	697	82	Quality Assurance and Control	1513
36	Basic Pharmacokinetics	725	83	Solutions, Emulsions, Suspensions and Extractives	1519
37	Clinical Pharmacokinetics	746	84	Parenteral Preparations	1545
38	Topical Drugs	757	85	Intravenous Admixtures	1570
39	Gastrointestinal Drugs	774	86	Ophthalmic Preparations	1581
40	Blood, Fluids, Electrolytes and Hematologic Drugs	800	87	Medicated Applications	1596
41	Cardiovascular Drugs	831	88	Powders	1615
42	Respiratory Drugs	860	89	Oral Solid Dosage Forms	1633
43	Sympathomimetic Drugs	870	90	Coating of Pharmaceutical Dosage Forms	1666
			91	Sustained-Release Drug Delivery Systems	1676
			92	Aerosols	1694
			Part 9 Pharmaceutical Practice		
			93	Ambulatory Patient Care	1715
			94	Institutional Patient Care	1737
			95	Long-Term Care Facilities	1758
			96	The Pharmacist and Public Health	1773

97	The Patient: Behavioral Determinants	1788	106	Poison Control	1905
98	Patient Communication	1796	107	Laws Governing Pharmacy	1914
99	Drug Education	1803	108	Community Pharmacy Economics and Management	1940
100	Patient Compliance	1813	109	Dental Services	1957
101	The Prescription	1828			
102	Drug Interactions	1842			
103	Clinical Drug Literature	1859			
104	Health Accessories	1864			
105	Surgical Supplies	1895			
			Index		
			Alphabetic Index		1967

pressure (eg, 3000 to 5000 psi) and then through the second stage at a greatly reduced pressure (eg, 1000 psi). This breaks down any clusters formed in the first step.

For small-scale extemporaneous preparation of emulsions, the inexpensive *hand homogenizer* (available from *Med Times*) is particularly useful. It is probably the most efficient emulsifying apparatus available to the prescription pharmacist. The two phases, previously mixed in a bottle, are hand pumped through the apparatus. Recirculation of the emulsion through the apparatus will improve its quality.

A homogenizer does not incorporate air into the final product. Air may ruin an emulsion because the emulsifying agent is adsorbed preferentially at the air/water interface, followed by an irreversible precipitation termed *denaturation*. This is particularly prone to occur with protein emulsifying agents.

Homogenization may spoil an emulsion if the concentration of the emulsifying agent in the formulation is less than that required to take care of the increase in surface area produced by the process.

The temperature rise during homogenization is not very large. However, temperature does play an important role in the emulsification process. An increase in temperature will reduce the viscosity and, in certain instances, the interfacial tension between the oil and the water. There are, however, many instances, particularly in the manufacturing of cosmetic creams and ointments, where the ingredients will fail to emulsify properly if they are processed at too high a temperature. Emulsions of this type are processed first at an elevated temperature and then homogenized at a temperature not exceeding 40°.

Figure 83-6 shows the flow through the homogenizing valve, the heart of the high-pressure APV Gaulin homogenizer. The product enters the valve seat at high pressure, flows through the region between the valve and the seat at high velocity with a rapid pressure drop and then is discharged as a homogenized product. It is postulated that circulation and turbulence are responsible mainly for the homogenization that takes place. Different valve assemblies, two stage valve assemblies and equipment with a wide range of capacities are available.

The Macro Flow-Master *Kom-bi-nator* employs a number of different actions, each of which takes the ingredients a little further along in the process of subdividing droplets, until complete homogenization results. The machine is equipped with a pump which carries the liquid through the various stages of the process. In the first stage, the ingredients are forced between two specially designed rotors (gears) which shoot the liquid in opposite directions in a small chamber and, in this way, are mixed thoroughly. These rotors also set up a swirling action in the next chamber into

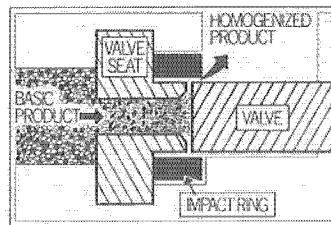


Fig 83-6. Operation of the homogenizer valve assembly (Courtesy APV Gaulin).

which the liquid is forced and swirled back and forth in eddies and crosscurrents. The second stage is a pulsing or vibrating action at rapid frequency. The product then leaves this chamber, goes through a small valve opening and is dashed against the wall of the homogenizing chamber. Pressure is applied, but it is not as great as that used in other types of homogenizers. Pressure is controlled accurately by adjusting devices on the front of the machine, and temperature is controlled by passing coolants through the stators.

Ultrasonic Devices—The preparation of emulsions by the use of ultrasonic vibrations also is possible. An oscillator of high frequency (100 to 500 kHz) is connected to two electrodes between which is placed a piezoelectric quartz plate. The quartz plate and electrodes are immersed in an oil bath and, when the oscillator is operating, high-frequency waves flow through the fluid. Emulsification is accomplished by simply immersing a tube containing the emulsion ingredients into this oil bath. Considerable research has been done on ultrasonic emulsification, particularly with regard to the mechanism of emulsion formation by this method. Limited data indicate that these devices will produce stable emulsions only with liquids of low viscosity. The method is not practical, however, for large-scale production of emulsions.

Special techniques and equipment in certain instances, will produce superior emulsions, including rapid cooling, reduction in particle size or ultrasonic devices. A wide selection of equipment for processing both emulsions and suspensions has been described by Eisberg.²² A number of improvements have been made to make the various processes more effective and energy-efficient.

General methods are available for testing the instability of emulsions including bulk changes, centrifugal and ultracentrifugal studies, dielectric measurement, surface-area measurement and accelerated-motion studies. Low-shear rheological studies measuring viscoelasticity are suggested as the optimal method of stability testing.

Suspensions

The physical chemist defines the word "suspension" as a two-phase system consisting of a finely divided solid dispersed in a solid, liquid or gas. The pharmacist accepts this definition and can show that a variety of dosage forms fall within the scope of the preceding statement. There is, however, a reluctance to be all-inclusive, and it is for this reason that the main emphasis is placed on solids dispersed in liquids. In addition, and because there is a need for more specific terminology, the pharmaceutical scientist differentiates between such preparations as suspensions, mixtures, magmas, gels and lotions. In a general sense, each of these preparations represents a suspension, but the state of subdivision of the insoluble solid varies from particles which settle gradually on standing to particles which are colloidal in nature. The lower limit of particle size is approximately 0.1

μm , and it is the preparations containing dispersed solids of this magnitude or greater that are defined pharmaceutically as suspensions.

Certain authors also include liniments, and the newer sustained-release suspensions, in any discussion of this particular subject. The former preparations now usually are considered as solutions although a number of older liniments were, in fact, suspensions. The sustained-release suspensions represent a very specialized class of preparation and, as such, are discussed in more detail in Chapter 91. Some insoluble drugs also are administered in aerosol form; one example is dexamethasone phosphate suspended in a propellant mixture of fluorochlorocarbons. More detail on aerosols is available in Chapter 92.

Suspension formulation and control is based on the prin-

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