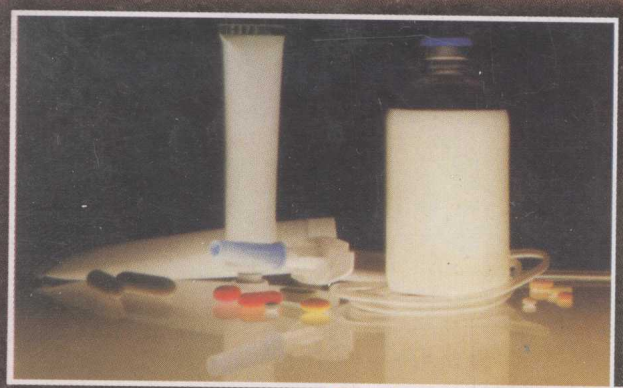
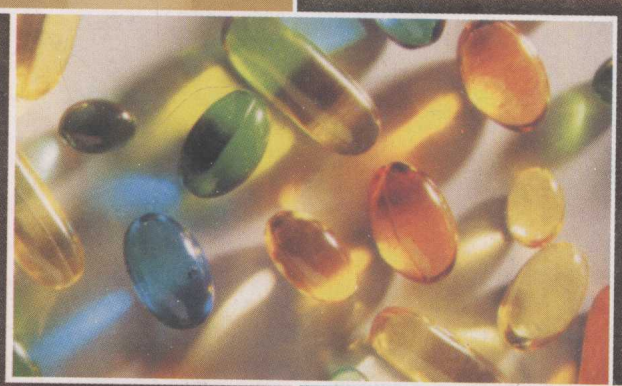
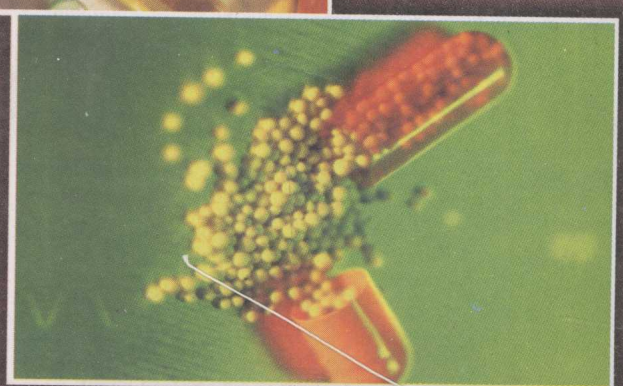
HANDBOOK OF PHARMACEUTICAL TECHNOLOGY







L.K. Ghosh

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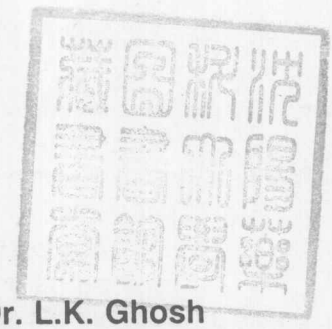

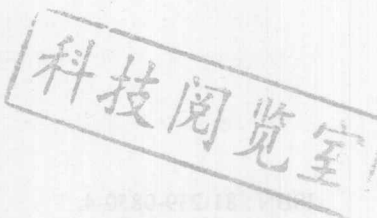

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Dedicated
to
My Mentor
Prof. B.K. Gupta

Preface

The personnel practising the noble profession of pharmacy are responsible for producing life-saving medicines, delivering the same to the patients in an effective condition and monitoring the dosage regimen during the entire course of therapy. The pharmaceutical science and technology has undergone revolutionary changes during the last few decades. A student of pharmacy, during the course of study, has to cover a huge syllabi. Before appearing in any competitive examination it is very difficult for them to have a quick look through these fast-changing syllabi. Keeping in view this problem, emphasis has been given to author this book in a most concise and exhaustive manner according to the syllabus approved by the Pharmacy Council of India.

This book encompasses four subjects, viz. Pharmaceutics I, Pharmaceutics II, Pharmacognosy and Pharmaceutical Jurisprudence (Forensic Pharmacy). Model questions are incorporated topic-wise, chapterwise or subjectwise in such a manner that in many cases informations provided through these are not included in the text to reduce the size of this book. It may be used as a textbook by both diploma and degree students and at the same time it will provide valuable and necessary information to all concerned appearing for any competitive examination in pharmacy including GATE.

I am grateful to my friend, philosopher and guide Prof. B.K. Gupta for his continuous guidance and encouragement; and to my students for their assistance during preparation of the manuscript.

I am also thankful to the authority of Jadavpur University, particularly our Vice-Chancellor, Prof. A.N. Basu, and Finance Officer, Mr. G.K. Pattanayak for their moral support.

I am also grateful to all authors whose books I have consulted.

My thanks are also due to the CBS Publishers & Distributors for their keen interest in publishing this book. I would greatly appreciate if readers bring suggestions, criticisms, omissions and errors to my attention for further improvement of this book.

L.K. Ghosh

Contents

SECTION I

Pharmaceutics I

CHAPTER 1

Familiarization With New Drug Delivery Systems

- New Drug Delivery Systems

The main objective of sustained/controlled/prolonged release formulation

The formulation is designed in such a way that minimum effective plasma concentration (MEC) level of drug should attain quickly and thereafter the rate of entry of drug to the body should equal with the rate of total elimination or inactivation of drug from the body. As a result the plasma drug concentration curve will run parallel to the time axis just above the MEC level. Following are the examples of some of the advantages associated with sustained released formulations :

(i) Patient will get uninterrupted therapeutic response for a prolonged period.

(ii) Toxicity associated with peak plasma concentrations and chances of drug resistance associated with 'deep' ineffective plasma drug concentrations would be diminished.

(iii) Frequency of drug administration is reduced, therefore, compliance to the patient as well as nursing staffs.

(iv) Much lesser amount of drug is essential for the entire course of therapy. On the other hand multidose conventional delivery systems are wasteful.

Few Latest Delivery Systems

(i) Microencapsulation : In this technique the drug along with a suitable polymer(s) are transformed to numerous micro-capsules. Few hundreds of such solid microcapsules containing a definite amount of drug is then taken in a hard gelatin capsule shell or compressed into a quickly disintegrating tablet for administration to the patient. This formulation now-a-days is widely used as sustained release formulation as the entrapped drug releases slowly from the microcapsule.

(ii) Nano-particles : In this case also the entrapped or adsorbed drug is released slowly giving sustained action and the sizes of the particles permit i.v. administration.

(iii) Transdermal drug delivery system : Our skin can absorb a considerable amount of drug to initiate and continue physiological responses. The drug with moderate lipid-water partition co-efficient (not too hydrophilic or too lipophilic) can be delivered as transdermal patch alongwith pressure sensitive adhesive. The patient is directed to fix up the patch onto the particular area of skin and also remove the patch when the drug action is not required. Examples include :
   a. Transdermal scopolamine to control motion sickness.
   b. Transdermal testosterone.
   c. Transdermal oestrogen to female during post menopausai period.
   d. Transdermal antianginal preparation.

(iv) Liposomal drug delivery system.

(v) Multiple emulsions.

(vi) Monoclonal antibody tagged drug delivery system.

(vii) Drug loaded erythrocytes.

(viii) Iontophoretic techniques.

(ix) Controlled release suppository.

(x) Prodrug for sustained drug action.

MODEL QUESTIONS

1. In general, the various oral dosage forms can be ranked in which of the following expected order of availability (fastest to slowest)
   A. aqueous solution > capsule > tablet > powder > coated tablet > suspension
   B. capsule > tablet > coated tablet > powder > suspension > aqueous solution
   C. aqueous solution > suspension > powder > capsule > tablet > coated tablet
   D. suspension > aqueous solution > powder > capsule > coated tablet > tablet
   E. aqueous solution > suspension > capsule > powder > coated tablet > tablet
2. Whenever a drug is more rapidly and /or more completely absorbed from a solution than from a solid dosage form,
   A. it is due to the fact that the solid dosage form did not disintegrate
   B. it indicates that the solid dosage form is poorly formulated
   C. a solution is the only practical oral formulation
   D. it is likely that absorption is rate limited by the dissolution process
   E. none of the above.
3. The term "Prodrug" refers to a
   A. drug that is classified as being "probably effective"
   B. chemical substance that is part of the synthesis procedure in preparing a drug.

C. drug that has only prophylactic activity in the body
D. compound which may be therapeutically active but is still under clinical trials.
E. compound that liberates an active drug in the body.

4. Transdermal applications are popular for the administration of
   A. antidiabetic drugs
   B. cardiac stimulants
   C. tranquilisers
   D. coronary vasodilators.
5. Liposomes are
   A. uni or multilayered vesicles of phospholipids
   B. type of enzymes
   C. fibrinopeptides
   D. red blood cells
   E. none of the above.
6. The term bioavailability refers to the
   A. relationship between the physical & chemical properties of a drug and the systemic absorption of the drug.
   B. measurement of the rate and amount of therapeutically active drug that reaches the systemic circulation
   C. movement of drug into the body tissues over time.
   D. dissolution of a drug in the G.I. tract.
   E. all the above.
7. Match the following dosage forms with a primary advantage of each

(i)	Sublingual tablets	A.	Sustained action
(ii)	Kapseals	B.	Rapid solubility
(iii)	Repetabs	C.	Tamper proof
(iv)	Medihaler	D.	Metered dose
(v)	Effervescent salts	E.	Improved.

ANSWERS

1. C; 2. D; 3. E [Sometimes biologically active drugs are chemically modified in order to improve the pharmacodynamic or pharmaceutical qualities. These modified molecules (prodrug) are not active in *in vitro* but in *in vivo* condition. Upon biotransformation, the metabolite becomes active]; 4. D; 5. A [Liposome is defined as structure consisting of one or more concentric spheres of lipid bilayers separated by water or aqueous buffer compartments. If other conditions (such as sterility, homogeneity, pyrogen free etc.) are fulfilled this delivery system can be directly administered intravenously. Phospholipids and other derivatives of phosphatidic acid are used to produce liposomal vesicles]; 6. B; 7. i - B; ii - C; iii - A; iv - D; v - E.

CHAPTER 2

Introduction to Pharmacopoeias With Special Reference to the Indian Pharmacopoeia

- Introduction to Pharmacopoeias

Pharmacopoeia is an official book consisting of monographs of different drugs and their formulations which are official in that pharmacopoeia. Monograph of a drug may include its name, formulas etc., category, dose, description, solubility, storage, standards, identification, pH, clarity and color of soluion, specific optical rotation, related substances, sulfated ash, loss on drying, assay etc. In case of individual dosage forms monographs may include other requirements. As for example, in case of tablet dosage form it may include disintegration test, dissolution test etc.

The first pharmacopoeia of India was published in 1868. It was prepared under the authority of the Secretary of State for India in Council by an Indian Pharmacopoeia Committee constituted in 1865. It was edited by Edward John Waring. After independence an Indian Pharmacopoeia Committee was constituted in 1948, which prepared the Pharmacopoeia of India (The Indian Pharmacopoeia) 1955. A supplement to the first edition of I.P. was published in 1960. This pharmacopoeia contained western & also traditional drugs. The second edition of I.P. was published in 1966 and its supplement in 1975. Similarly, the third edition of I.P. was published in two volumes in 1985 and its Addenda in 1989 & 1991. In this edition traditional drugs were not included as publication of pharmacopoeia of traditional system drugs was taken up separately and only those herbal drugs were included which had supporting definite quality control standards. Finally the latest i.e., 4th edition of I.P. was published in two volumes in 1996 by the Ministry of Health and Family Welfare, Govt. of India.

I.P. = The Pharmacopoeia of India
B.P. = The British Pharmacopoeia
B.P.C. = British Pharmaceutical Codex
USP = The United States Pharmacopoeia
N.F. = National Formulary
] Combined

CHAPTER 3

Metrology and Pharmaceutical Calculations

- Systems of Weights and Measures
- Pharmaceutical Calculations including Conversion from One to Another System
- Percentage Calculations and Adjustments of Products
- Use of Alligation Method in Calculations
- Isotonic Solutions
- Proof Spirit, Denatured Alcohol and Alcohol Dilutions

Sensitivity of an analytical balance : The smallest weight to which the balance responds when loaded to capacity (the capacity is marked on the instrument).

Minimum Weighable Amounts : It is generally accepted that the error in the amount of any ingredients in a dispensed preparation should not be more than ± 5%. The percentage of error would be much more if weighable amount is very less. In order to avoid this, the minimum weighable amount should not be less than 100 mg (or 2 gr.). In some country like Sweden, the minimum weighable amount is 300 mg. In the USA a minimum of 200 mg is recommended in the National Formulary (N.F) for prescription balances with a sensitivity ratio of 10 mg. This is a wise precaution in case of weighing potent drugs (i.e., one with a maximum dose of 50 mg or less).

Percentage Calculations

Problem 1

Calculate the quantity of sodium chloride required for 500 ml of a 0.9% solution.

Ans. 100 ml solution contains 0.9 g sodium chloride.
500 ml solution contains $(0.9 \times 500/100) = 4.5$ g of NaCl.

Problem 2

Send 100 ml of a solution of potassium permanganate of which 1 part diluted with seven parts of water makes a 1 in 8000 solution.

Ans. 8000 ml dilute solution contains 1 g of $KMnO_4$

$\therefore$ 1 ml dilute solution contains 1/8000 g of $KMnO_4$

$\therefore$ (1 + 7 = 8) ml dilute solution contains $1 \times 8/8000$ g of $KMnO_4$

This 8 ml dilute solution is actually produced by diluting 1 ml stock solution.

$\therefore$ 1 ml of stock solution contains 0.001 g of $KMnO_4$

$\therefore$ 100 ml of stock solution contains 0.001×100 g = 0.1 g of $KMnO_4$

Therefore, the strength of the stock solution/concentrate

= 0.1% (w/v).

Problem 3

Supply 10 capsules each containing 600 µg of hyoscine hydrobromide.

Ans. Total amount of hyosine hydrobromide in 10 capsules is 6000 µg = 6 mg.

But the minimum weighable amount should be at least 100 mg. This 100 mg of hyoscine hydrobromide to be mixed up with sufficient amount of an inert diluent such as lactose by way of geometric dilution process. The weighable amount of this final mixture also should not be less than 100 mg containing 600 µg of hyoscine hydrobromide, to be encapsulated in hard gelatin capsule.

Parts Per Million (ppm)

1 ppm = 1 part solute per 1 million parts of solution.

similarly, 5 ppm = 5 parts solute per 1 million parts of solution.

i.e., 10,00000 parts solution contain 5 parts solute

100 parts solution contain $5 \times 100/10,00000$ parts solute

= 0.0005% (w/v)

i.e., 5 ppm solution = 0.0005% (w/v) solution.

Mixing Different Strengths

What is the percent of alcohol in a mixture made by mixing 5 lit of 25% (v/v), 1 lit of 50% (v/v) and 1 lit of 95% (v/v) alcohol?

Ans. Determine the total amount of alcohol in the 3 solutions and the total amount of solution (1 lit = 1000 ml).

Assume additivity of volumes on mixing.

$25\% \times 5000$ ml = 1250 ml 100% alcohol

$50\% \times 1000$ ml = 500 ml 100% alcohol

$95\% \times 1000$ ml = 950 ml 100% alcohol

Total volume = 7000 ml $\equiv$ 2700 ml 100% alcohol

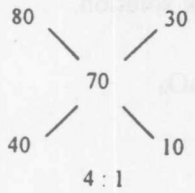
i.e., 7000 ml mixture contains 2700 ml pure alcohol

100 ml mixture contains $2700 \times 100/7000 = 38.57$ ml pure alcohol.

Therefore, the strength of the final solution be 38.57% (v/v)

Alligation Alternate :

How much ml of 80% alcohol to be mixed with 200 ml of 30% alcohol to produce 70% alcohol.



i.e., 4 parts of 80% alcohol and 1 part of 30% alcohol if mixed up then the final strength would be 70%.

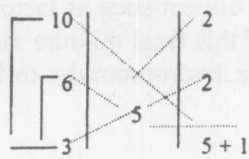
Now 1 part of 30% alcohol to be mixed up with 4 parts of 80% alcohol

∴ 200 parts of 30% alcohol to be mixed up with 4×200 parts of 80% alcohol

= 800 ml

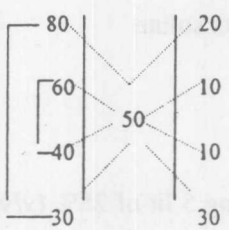
Calculation by Alligation Alternate or by The Method of Rectangles

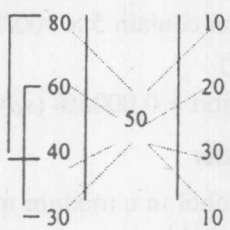
Example 1 : In what proportion 10%, 6% and 3% alcohol be mixed to get 5% alcohol?



∴ Thus, the proportion for mixing would be 2 : 2 : 6 to get 5% alcohol.

Example 2 : How many parts of 80%, 60%, 40% and 30% alcohol be mixed together to get 50% alcohol?





Thus, the proportion for mixing of 80%, 60%, 40% and 30% alcohol would be

(i) 20 : 10 : 10 : 30 or 2 : 1 : 1 : 3

(ii) 10 : 20 : 30 : 10 or 1 : 2 : 3 : 1

(iii) 30 : 30 : 40 : 40 or 3 : 3 : 4 : 4

Relationships of Weights and of Measures

1 fluidounce	=	30 ml (29.57 ml)
1 pint	=	473 ml
1 gallon	=	8 pint = 3785 ml
1 kilogram	=	2.2 lb.