Unit 1

Basic Concepts of Dispensing

General Introduction and Historical Background

History of Pharmacy Profession in India

In ancient India the sources of drugs were of vegetable, animal and mineral origin. They were prepared empirically by few experienced persons. Knowledge of that medical system was usually kept secret within a family.

There were no scientific methods of standardization of drugs.

Muslim rule in India

The Indian system of medicine declined during the Muslim rule while the Arabic or the Unani-Tibbi system flourished.

British rule in India

The western or the so-called Allopathic system came into India with the British traders who later become the rulers. Under British rule this system got state patronage. At that time it was meant for the ruling race only. Later it descended to the people and become popular by the close of 19th Century.

Before 1940

Initially all the drugs were imported from Europe. Later some drugs of this system began to be manufactured in this country.

1901: Establishment of the Bengal Chemical and Pharmaceutical Works, Calcutta by Acharya P.C. Ray.

1903: A small factory at Parel (Bombay) by Prof. T.K. Gujjar.

1907: Alembic Chemical Works at Baroda by Prof. T.K. Gujjar.

Drugs were mostly exported in crude form and imported in finished form. During World War-I (1914 – 1920) the imports of drugs were cut-off. Imports of drugs were resumed after the War. In absence of any restrictions

on quality of drugs imported, manufacturers abroad took advantage of the situation. The consequences were as follows:

(i) Foreign manufacturers dumped inferior quality medicines and adulterated drugs.

(ii) Markets were full of all sorts of useless and deleterious drugs which were sold by unqualified men.

Examples of maladies:

- Poisoning due to quinine.
- Putting of croton oil into eye instead of atropine solution.
- Selling of chalk powder tablets in place of quinine.
- Drug santonin was badly adulterated.
- Potent drugs like compounds of antimony and arsenic and preparations of digitalis were dispensed without any standard.

Few laws were promulgated, but they proved insufficient.

1878	Opium Act	Dealt with cultivation of poppy and the manufacture, transport, export, import and sale of opium.
1889	Indian Merchandise Act	Misbranding of goods in general
1894	Indian Tariff Act	Levy of customs duty on goods including foods, drinks, drugs, chemicals and medicines imported into India or exported there from.
1898	Sea Customs Act	Goods with 'false trade description' were prevented from importing under this act.
1860	Indian Penal Code	Some sections of IPC have mention of intentional adulterations as punishable offence.
1919	Poisons Act	Regulated the import, possession and sale of poisons.

Some state-level law had indirect references to drugs:

1884	Bengal Municipal Act	
1901	City of Bombay District Municipal Act	Concerned with food.
1909	Bengal Excise Act	
1911	Punjab Municipal Act	
1912	United Provinces (now Uttar Pradesh) Prevention of Adulteration Act	Refers to adulteration of foods and drugs.
1914	Pujab Excise Act	
1916	United Provinces Municipalities Act	Inspection of shops and seizure of adulterated substances.
1919	Bengal Food Adulteration Act	

Contd...

1919	Bihar and Orissa Prevention of Adulteration Act	
1919	Madras Prevention of Adulteration Act	Chiefly concerned with food adulteration
1922	Bihar and Orissa Municipal Act	
1922	Central Provinces Municipalities Act	
1925	Bombay Prevention of Adulteration Act	
1929	Punjab Pure Food Act	

The laws were too superficial and had indirect link to drugs.

Drug enquiry committee

Government of India on 11th August 1930, appointed a committee under the chairmanship of Late Col. R.N. Chopra to look into the problems of Pharmacy in India and recommend the measures to be taken. This committee published its report in 1931. It was reported that there was no recognized specialized profession of Pharmacy. A set of people known as compounders were filling the gap.

Just after the publication of the report Prof. Mahadeva Lal Schroff initiated pharmaceutical education at the university level in the Banaras Hindu University.

In 1935 United Province Pharmaceutical Association was established which later converted into Indian Pharmaceutical Association.

The Indian Journal of Pharmacy was started by Prof. M.L. Schroff in 1939. All India Pharmaceutical Congress Association was established in 1940. The Pharmaceutical Conference held its sessions at different places to publicize Pharmacy as a whole in India.

1937: Government of India brought 'Import of Drugs Bill'; later it was withdrawn.

1940: Govt. brought 'Drugs Bill' to regulate the import, manufacture, sale and distribution of drugs in British India. This Bill was finally adopted as 'Drugs Act of 1940'.

1941: The first Drugs Technical Advisory Board (D.T.A.B.) under this act was constituted.

Central Drugs Laboratory was established in Calcutta

1945: 'Drugs Rule under the Drugs Act of 1940' was established.

The Drugs Act has been modified from time to time and at present the provisions of the Act cover Cosmetics and Ayurvedic, Unani and Homeopathic medicines in some respects.

1945: Government brought the Pharmacy Bill to standardize the Pharmacy Education in India.

1946: The Indian Pharmacopoeial List was published under the chairmanship of late Col. R.N. Chopra. It contains lists of drugs in use in India at those times which were not included in British Pharmacopoeia.

1948: Pharmacy Act 1948 was enacted on 04-03-1948 with the following preamble- "An Act to regulate the profession of pharmacy.

1948: Indian Pharmacopoeial Committee was constituted under the chairmanship of late Dr. B.N. Ghosh.

1949: Pharmacy Council of India (P.C.I.) was established under Pharmacy Act 1948.

1954: Education Regulation came into force in some states, but many states lagged behind.

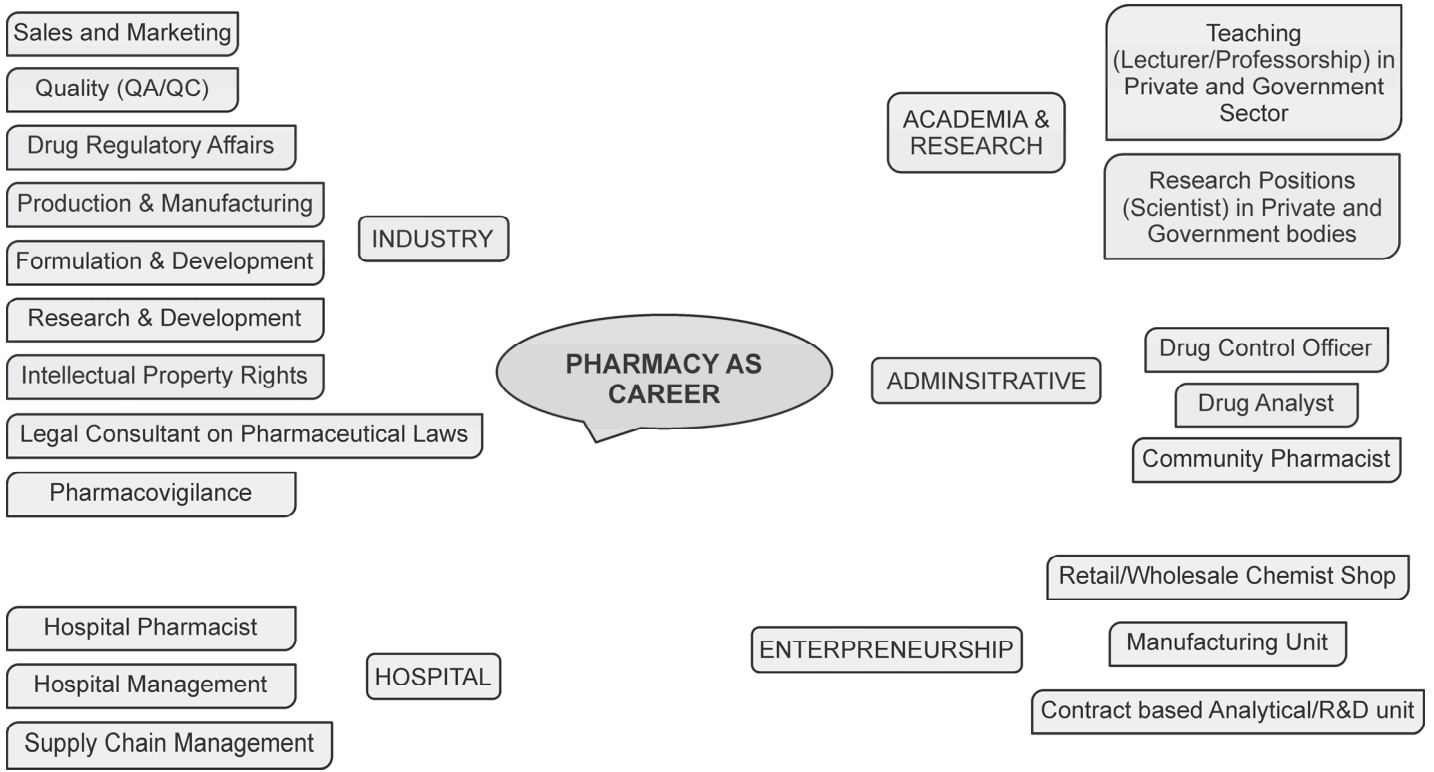
1954: Drugs and Magic Remedies (Objectionable Advertisements) Act 1954 was passed to stop misleading advertisements (e.g. Cure all pills)

1955: Medicinal and Toilet Preparations (Excise Duties) Act no. 16 of 1955 was introduced to enforce uniform collection of levy and duties of excise on medicinal and toilet preparation (alcohol products) in all states.

1955: First Edition of Indian Pharmacopoeia was published.

1985: Narcotic and Psychotropic Substances Act was enacted to protect society from the dangers of addictive drugs.

Government of India controls the price of drugs in India through Drugs Price Order changed from time to time.


PHARMACY AS CAREER
INDUSTRY
Sales and Marketing
Quality (QA/QC)
Drug Regulatory Affairs
Production & Manufacturing
Formulation & Development
Research & Development
Intellectual Property Rights
Legal Consultant on Pharmaceutical Laws
Pharmacovigilance
ACADEMIA & RESEARCH
Teaching (Lecturer/Professorship) in Private and Government Sector
Research Positions (Scientist) in Private and Government bodies
ADMINSITRATIVE
Drug Control Officer
Drug Analyst
Community Pharmacist
HOSPITAL
Hospital Pharmacist
Hospital Management
Supply Chain Management
ENTERPRENEURSHIP
Retail/Wholesale Chemist Shop
Manufacturing Unit
Contract based Analytical/R&D unit

Pharmacopoeia / Formularies / Compendia

The term "***pharmacopoeia***" is derived from the Greek language '*pharmacon'* meaning 'drug' and '*poieo'* means 'to make'.

Literally, it is the written compilation or list of standards for drugs/medicinal substances/crude drugs or other related substances with approval from the drug regulatory authorities of the respective government in the country and termed as ***pharmacopoeia*** and ***formularies*** - collectively these standard text/reference books are known as the ***drug compendia.***

Such drug compendia comprise a list of drugs and other related substances regarding their source, descriptions, standards, tests, formulae for concoting the same, action and uses, doses, storage conditions etc. These reference text books are revised and amended from time to time so as to incorporate the latest information regarding drugs or substances of therapeutic activity. For the preparation of these standard reference materials, expert reviews and opinions are taken from diverse segment of medical practitioners, teachers, pharmaceutical manufacturers and other stakeholders associated with the pharmaceutical field. Further, in order to keep the length and size of these reference books within the reasonable limit, some of the information regarding less frequently used drugs/ old monographs or substances which are not currently in practice is omitted in the new/revised editions of the book updated from time to time.

Classification

These standard text/drug-compendia can be classified into *Official compendia and Non-official compendia*

A. *Official Compendia*

Official compendia are the compilations of drugs and other related substances which are recognized as legal standards of purity, quality and strength by a government agency of respective countries of their origin. For example- British Pharmacopoeia (BP), British Pharmaceutical Codex (BPC), Indian Pharmacopoeia (IP), United States Pharmacopoeia (USP), National Formulary (NF), The State Pharmacopoeia of USSR and Pharmacopoeias of other countries

B. *Non-Official Compendia*

The book other than official drug compendia which are used as secondary reference sources for drugs and other related substances are known as non-official drug compendia. *For example*-Merck Index, Extra Pharmacopoeia (Martindale) and United States Dispensatory.

Indian Pharmacopoeial Commission (IPC)

IPC (an autonomous institution of the Ministry of health and family welfare, Government of India) was formed according to the Indian Drugs and Cosmetics Act of 1940 and established under the executive orders of the Government of India in 1956, primarily works in close coordination with all the stakeholders (including pharmaceutical industry, drug control laboratories, research and teaching institutions) of Indian Pharmacopoeia (IP) for the development of monographs.

IPC is mandated to set standards of drugs alongwith the updation of such standards of drugs commonly required for treatment of diseases prevailing in this country on regular basis.

IPC publishes official documents for improving quality of medicines by way of adding new and updating existing monographs (encompasses information related to chemical structures of drugs and their properties such as molecular weight, physical description, solubility, identification tests, standards, assay method, storage etc.) It further promotes rational use of generic medicines by publishing National Formulary of India (NFI). IP prescribes standards for identity, purity and strength of drugs essentially required from health care perspective of human beings and animals. IPC also provides IP Reference Substances (IPRS) which act as a finger print for identification of an article under test and its purity as prescribed in IP.

Recently, in 1st of July, 2022, IPC released the 9th edition of 'IP-2022' comprising 3152 monographs. A total of 92 new monographs for drugs have been added to IP 2022 edition. Monographs of *lorcaserin hydrochloride tablets and locraserin hydrochloride hemihydrate* have been omitted form the current IP edition vide IPC's Notice dated March 10, 2021. Further a general chapter on assay of Human Anti-D Immunoglobulin Methods B and C has also been omitted from IP 2022.

Objectives

- ✓ To develop comprehensive monographs for drugs to be included in the Indian Pharmacopoeia (IP), comprising of active pharmaceutical ingredients, pharmaceutical aids and dosage forms as well as medical devices and to keep them updated by revision on a regular basis.
- ✓ To develop monographs for herbal drugs, both raw drugs and extracts/formulations there from.
- ✓ To accord priority to monographs of drugs included in the National Essential Medicines List and their dosage forms.

- ✓ To take note of the different levels of sophistication in analytical testing/ instrumentation available while framing the monographs.
- ✓ To accelerate the process of preparation, certification and distribution of IP Reference Substances, including the related substances, impurities and degradation products.
- ✓ To collaborate with pharmacopoeias like the Ph Eur, BP, USP, JP, ChP and International Pharmacopoeia with a view to harmonizing with global standards.
- ✓ To review existing monographs periodically with a view to deleting obsolete ones and amending those requiring upgrading /revision.
- ✓ To organize educational programs and research activities for spreading and establishing awareness on the need and scope of quality standards for drugs and related articles /materials.
- ✓ To publish the NFI for updating medical practitioners and other healthcare professionals.
- ✓ To act as a National Coordination Centre for Pharma-covigilance Programme of India.

The Indian Pharmacopoeia

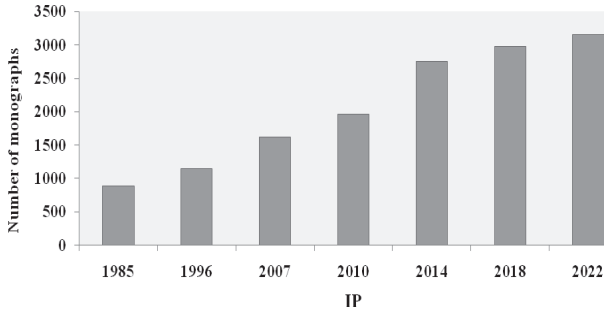
Some of the earliest reference to the development of pharmacopoeia in India dates back to 1563 and the credit goes to *Garcia da Orta* a Portugese physician-cum-teacher. The first raw form of IP was conceived in 1837 which got actual shape in the form of Bengal Pharmacopoeia and Conspectus of Drugs in 1841.

In 1946, Indian Pharmacopoeial list containing drugs both included (i.e. crude drugs, chemicals and their preparations) and not included (i.e. drugs of plant origin, drugs of animal origin, biological products, insecticides, colouring agents, synthetics, miscellaneous and drugs for veterinary use) in the British Pharmacopoeia along with standards to protect their usefulness, tests for identity and purity was released by Department of Health, Govt. of India under the chairmanship of Col. Sir R.N. Chopra along with other nine members. This Indian Pharmacopoeial list published in 1946 actually laid the foundation of official document in the form of first edition of Indian Pharmacopoeia published in 1955. Further, its draft preparation was initiated in 1944 with directions to Drugs Technical Advisory Board by the Government of India.

Historical Timeline of IP

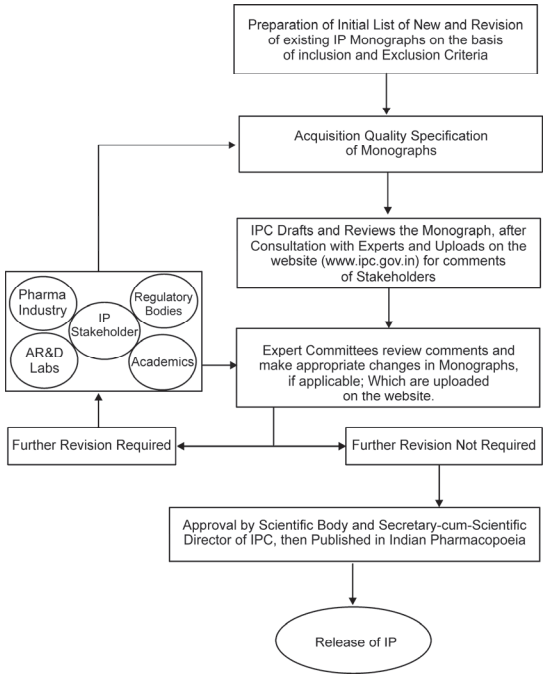
Published/ Released by	Time Line	Publication Events
IP Commiteee *(Under the chairmanship of Dr. B.N. Ghosh)*	1946	Release of *Indian Pharmacopoeial List* by GoI
	1948	The GoI constituted a permanent Indian Pharmacopoeia Committee (IPC). and tasked to formulate IP and to keep it up-to-date
	1955	The **1st edition ofIP**
	1960	Supplement of IP 1955 *(Note-The revision of IP as well as compilation of its new edition was taken up simultaneously by the committee. However, after the death of Dr. B.N..Ghosh in 1958, Dr. B. Mukherjee, the Director of CDRI was appointed as the chairman of IPC.)*
	1966	The **2nd edition of IP**
	1975	Supplement of IP 1966 *(Note- In 1978, The IPC was reconstituted by the GoI, MHFW, under the chairmanship of Dr. Nitya Nand, Director, CDRI, Lucknow)*
	1985	The **3rd edition of IP** in two volumes, Vol.-I & Vol.-II
	1989 &1991	Addendum (I) and (II) to IP 1985 respectively
	1996	The **4th edition of IP**
	2000	Veterinary Supplement
	2000 and 2002	Addendum to IP 1996 respectively
IP Commission	2005	Addendum to IP 1996 respectively
	2007	**The 5th edition of IP**
	2008	Addendum to IP
	2010	**The 6th edition of IP**
	2012	Addendum to IP
	2014	**The 7th edition of IP**
	2015 & 2016	Addendum (I) and (II) to IP 2014 respectively
	2018	**The 8th edition of IP with four volumes in DVD as well as hard form**
	2019 & 2021	Addendum (I) and (II) to IP, 2018 respectively
	2022	**The 9th edition of IP**

The yearwise addition in the number of new monographs from 1985 to 2022 being depicted in successive IPs indicates the continuous updation in the information related to drugs and medicinal substances.



Process for IP Monograph Development

People from all segments of pharmaceutical fraternity including public reviews and comments are given special attention while developing the IP standards. The principle of "*openness, justice and fairness*" is kept in mind during compiling and editing the contents of the Indian Pharmacopoeia. Figure below illustrates the methodology adopted for the development of a monograph in I.P.



The process of development of a monograph
(Courtesy: https://www.ipc.gov.in)

Some Other Official Publications Related to Pharmacy Profession in India

National Formulary of India (NFI)

'Formulary' is a manual containing clinically oriented summaries of pharmacological information about selected drugs which serve as a guidance for medical practitioners, medical students, pharmacists in hospitals and different sectors in sales departments. This manual may incorporate administrative and regulatory information pertaining to the prescribing and dispensing of drugs. It also contains information about drug interaction, resistance, cumulative effects, drug dependence, prescription writing etc.

In general, a national formulary focuses on available and cost effective medicines that are relevant to the treatment of diseases, native or endemic to a particular region or a country.

The first NFI was published in 1960 by the Ministry of Health. The second and third formularies were published in 1966 and 1979 respectively. To address the need of publication of an updated version of NFI, Ministry of Health and Family Welfare, Govt. of India vide their Notification No. F.No.X.11035/2/06- DFQC dated 8th May, 2008 assigned this mandatory responsibility to the Indian Pharmacopoeia Commission (IPC), Ghaziabad. Therefore, from 2008 the NFI is published by the Indian Pharmacopoeia Commission on behalf of the Health Ministry. The current edition of NFI-2021 (adopted from the WHO Model Formulary) is presently in use for reference which has been thoroughly updated for its content, especially keeping in view the end user in India and guidance to medical practitioners.

Pharmacist's Oath
(Courtesy: Pharmacy Council of India)

I swear by the code of ethics of Pharmacy Council of India, in relation to the community and shall act as an integral part of health care team.

I shall uphold the laws and standards governing my profession.

I shall strive to perfect and enlarge my knowledge to contribute to the advancement of pharmacy and public health.

I shall follow the system which I consider best for Pharmaceutical care and counseling of patients.

I shall endeavor to discover and manufacture drugs of quality to alleviate sufferings of humanity. I shall hold in confidence the knowledge gained about the patients in connection with my professional practice and never divulge unless compelled to do so by the law.

I shall associate with organizations having their objectives for betterment of the profession of Pharmacy and make contribution to carry out the work of those organizations.

While I continue to keep this oath unviolated, may it be granted to me to enjoy life and the practice of pharmacy respected by all, at all times!

Should I trespass and violate this oath, may the reverse be my lot !

Pharmacist's Code of Ethics

(As adopted by Pharmacy Council of India)

Ethics is defined as 'code of moral principles'. It emphasizes on the determination of right or wrong while doing one's duty. Code of Pharmaceutical Ethics as formulated by Pharmacy Council of India are meant to guide the pharmacist as to how he should conduct himself (or herself), in relation to himself (or herself), his / her patrons (owner of the pharmacy), general public, co-professionals etc. and patients.

Introduction

The profession of pharmacy is noble in its ideals and pious in its character. Apart from being a career for earning livelihood, it has inherent attitude of service and sacrifice in the interests of the suffering humanity. The lofty ideals set up by *Charaka,* the ancient Philosopher, Physician and Pharmacist in his enunciation: "*Even if your own life be in danger you should not betray or neglect the interests of your patients*" should be fondly cherished by all Pharmacists.

A Pharmacist must, above all be a good citizen and must uphold and defend the laws of the state and the Nation.

Government has restricted the practice of Pharmacy to only Professional Pharmacists i.e. Registered Pharmacist under the Pharmacy Act 1948. PCI framed the following ethics for Indian Pharmacists, which may be categorized under the following headings:

- ✓ Pharmacist in relation to his job.
- ✓ Pharmacist in relation to his trade.
- ✓ Pharmacist in relation to medical profession.
- ✓ Pharmacist in relation to his profession.

Pharmacist in Relation to His Job

A pharmacist should keep the following things in relation to his job.

(i) *Pharmaceutical services*

A Registered pharmacist should provide comprehensive pharmaceutical service (which involves the supply of commonly required medicines

without undue delay) and have a willingness to furnish emergency supplies at all times.

(ii) *Conduct of the Pharmacy*

The conditions in a pharmacy should be such as to preclude avoidable risk error of accidental contamination in the preparation, dispensing and supply of medicines. The appearance of the premises should reflect the professional character of the pharmacy. It should be clear to the public that the practice of pharmacy is carried out in the establishment.

(iii) *Handling of Prescription*

When a prescription is presented for dispensing, it should be received by a pharmacist without any discussion or comment over it regarding the merits and demerits of its therapeutic efficiency. In matter of refilling prescriptions, a pharmacist should solely be guided by the instructions of a prescriber and he should advise patients to use medicines or remedies strictly in accordance with the intention of the physician as noted on the prescription.

(iv) *Handling of drugs*

All possible care should be taken to dispense a prescription correctly by weighing and measuring all ingredients in correct proportions by the help of scale and measures. Further, a Pharmacist should always use drugs and medicinal preparations of standard quality available.

(v) *Apprentice Pharmacist*

While in-charge of a dispensary, drug store or hospital pharmacy where apprentice pharmacists are admitted for practical training, a pharmacist should see that the trainees are given full facilities for their work so that on the completion of their training they have acquired sufficient technique and skill to make themselves dependable pharmacists. No certificate or credentials should be granted unless the above criterion is attained and the recipient has proved himself worthy of the same.

Pharmacist in Relation to His Trade

Following are the provisions which pharmacist should keep in mind while dealing with his trade:

(i) *Price structure*

Prices charged from customers should be fair and in keeping with the quality and quantity of commodity supplied and the labor and skill required in making it ready for use, so as to ensure an adequate remuneration to the pharmacist taking into consideration his knowledge, skill, the time consumed and the great responsibility involved, but at the same time without unduly taxing the purchaser.

(ii) *Fair trade practice*

No attempt should be made to capture the business of a contemporary by cut-throat competition, that is, by offering any sort of prizes or gifts or any kind of allurement to patronizes or by knowingly charging lower prices for medical commodities than those charged by a fellow pharmacist if they be reasonable. In case any order or prescription genuinely intended to be served by some dispensary is brought by mistake to another, the latter should refuse to accept it and should direct the customer to the right place. Labels, trademarks and other signs and symbols of contemporaries should not be imitated or copied.

(iii) *Purchase of drugs*

Drugs should always be purchased from genuine and reputable sources and a pharmacist should always be on his guard not to aid or abet, directly or indirectly the manufacture, possession, distribution and sale of spurious or sub-standard drugs.

(iv) *Advertising and Displays*

No display material either on the premises, in the press or elsewhere should be used by a pharmacist in connection with the sale to the public of medicines or medical appliances which is undignified in style.

Pharmacist in Relation to Medical Profession

Following are the code of ethics of a pharmacist in relation to medical profession:

(i) *Limitation of professional activity*

The professional activity of the medical practitioner as well as the pharmacists should be confined to their own field only. Medical practitioners should not possess drugs stores and pharmacists should not diagnose diseases and prescribe remedies. A pharmacist may, however, can deliver first aid to the victim in case of accident or emergency.

(ii) *Cladenstine arrangement*

A pharmacist should not enter into a secret arrangement or contract with a physician by offering him any commission or any advantages.

(iii) *Liasion with public.*

A pharmacist should always maintain proper link between physicians and people. He should advise the physicians on pharmaceutical matters and should educate the people regarding health and hygiene. The pharmacist should be keeping himself / herself up-to-date with pharmaceutical knowledge from various journals or publications. Any information acquired by a pharmacist during his professional activities should not be disclosed to any third party until and unless required to do so by law.

Pharmacist in Relation to His Profession

Regarding to the profession the following code of ethics should be fulfilled.

(i) *Professional vigilance*

A pharmacist must abide by the pharmaceutical laws and he/she should see that other pharmacists are abiding it.

(ii) *Law-abiding citizens*

The pharmacists should have a fair knowledge of the laws of the country pertaining to food, drug, pharmacy, health, sanitation etc.

(iii) *Relationship with Professional Organizations*

A pharmacist should be actively involved in professional organization, should advance the cause of such organizations.

(iv) *Decorum and Propriety*

A pharmacist should not indulge in doing anything that goes against the decorum and propriety of Pharmacy Profession.

Regulatory Authorities of Different Regions/Countries

1. **INDIA –** CDSCO (Central drugs standard control organization)
2. **USA -** FDA (Food & Drug Administration)
3. **CANADA –** HPFB (Health products & food branch)
4. **Australia –** TGA (Therapeutic goods administration**)**
5. **JAPAN –** PFSB (Pharmaceutical & food safety bureau), PMDA (Pharmaceutical & medical devices agency)
6. **CHINA –** NMPA (National medical products administration)
7. **EUROPE –** EMA (European medicines agency)
8. **RUSSIA –** Ministry of health of the Russian federation

Good Dispensing Practice (GDP) Guidelines (As recommended by World Health Organization)

Good Dispensing Practice (GDP) warrants that the right medicines of desired quality are delivered fittingly to the right patient with the right dose, strength, frequency, dosage form and quantity, together with clear instructions, both written and verbal and with appropriate packaging suitable for maintaining the quality and efficacy of the medicine. A safe, clean and organized working environment provides the basis for GDP.

The dispensing environment includes:

- Qualified / trained staff Appropriate physical surroundings
- Adequate shelving and storage areas
- Proper work surfaces

- Suitable equipment
- Necessary packaging materials

Scope: The scope and application of GDP guidelines is pertinent to only:

- Poisons list of substances (as per WHO)
- Medicines for human use
- Public healthcare facilities
- Licensed private healthcare facilities (clinics, hospitals, community pharmacies, dental clinics)

Dispensing Process

Adherence to good dispensing procedures is vital in ensuring that medicines are dispensed correctly and any potential/ real errors which may occur during the dispensing process are detected and rectified before medicines reach the patient.

Who should be involved in the process of dispensing?

(a) Screening of Prescription: Healthcare professional (Registered medical practitioner/ registered dentist/ pharmacist)

(b) Preparation of Medicines: Pharmacist, registered medical practitioner or a person under immediate supervision of a pharmacist/ medical practitioner

(c) Supplying the Medicines: Registered medical practitioner, registered dentist or pharmacist

(d) Counseling: By healthcare professional

General instructions for Students in a Practical Dispensing Lab

- ✓ Each student is expected to work on his/her own. If advice is needed, it should be obtained only from the class teacher conducting practical lab or a lab technician.
- ✓ Each student should have a duster cloth or small hand towel, a pair of scissors, a pair of forceps, a pair of scapula, a set of pencil colours, a black/blue pen and red pen (fine point), a ruler and a calculator.
- ✓ Each student should possess a dispensable paper towels at the end of each bench/slab for mopping up wet spillage if occurs. All work for dispensing the dosage form should be conducted in a clean and tidy manner.
- ✓ Read the prescription/composition/formula for the dosage form or pill carefully, if necessary verify the composition from most recent editions of I.P. or B.P. or U.S.P. or Martindale.
- ✓ The student should work out the amount to be used from the formula and write them in ink after checking the calculations in two ways if possible.

- ✓ In pharmaceutical calculations, the student should always have the habit of protecting the decimal point with a '0' i.e. 0.1 not .1; since if the decimal point is not written distinctly, there is a risk of administrating/prescribing a ten times (×10) overdose.
- ✓ The student must always write down the details of every weighing and measurement.
- ✓ Every student should possess pre-calibrated weights before any manual weighing procedure with precision and accuracy and cross contamination of products or excipients should be avoided at any cost.
- ✓ The student should exercise care while considering approximations. In general, it should not be made when the amount is being weighed or measured with the weights. Unless it is unavoidable, try to add minimal approximations (or NMT 5%). Further, the student must write the correct amount first and show the approximation in brackets at the side – e.g. 12.678g (12.68g).
- ✓ The student must use a spatula for weighing solids. This avoids fouling the neck of the bottle. In order to keep out the dust, the student should hold the bottle as near to horizontal as possible with one hand and remove the stopper with the little finger and palm of the other. Unless the stopper is too large, keep it in the hand; the student will find that he/she can easily use the spatula with the same hand. If it is essential to put the stopper down, place it the right way up on a clean sheet of white paper.
- ✓ The student must look up for the storage requirements of the preparation or the medicaments if the preparation is a special formulation not prescribed in one of these standard books (i.e. I.P./U.S.P./B.P.). Choose the correct container for storage, protection from light, storage in a cool place, etc. may also be necessary.
- ✓ After finalizing the preparation, store the product into the container and the preparation must be protected from accidental contamination.
- ✓ For liquids to be transferred, the student should hold the bottle in such a way that the label is on the opposite side. This will prevent the label from getting spoilt while transferring the liquid.
- ✓ No ingredient should be transferred and kept on paper to ensure its identity till the end.
- ✓ ***Labelling:*** The student should cut the label to fit the container but do not trim off the name of the preparation or the supplier (the manufacturing group). Use the largest possible label on the dosage form.
- ✓ During the labelling procedure, if a wrong figure or unit is written, cross it out and write the correct one above of at the side. But don't overwrite it or alter the wrong one.

- ✓ The student must carefully observe the labels of the stock bottles while using and watch particularly for words such as Compound (e.g. Compound tragacanth powder is different from tragacanth powder); concentration (e.g. Concentrated compound infusion of Gentianis different from Compound Infusion of Gentian); Strong (Fort)(e.g. Strong Coal Tar Solution is different from Coal tar solution). Moreover, the student must be vigilant for medicaments that have similar names (e.g. Eucalyptol and Eucalyptus oil) or e.g. Terebone and Turpentine Oil (Oil Terebinth).
- ✓ The student should check the label of the stock bottle against the composition formula before and after using the prescription.
- ✓ The student should hold the bottle with the label uppermost so that it can be seen during use. As a result, an error may be detected. Also, liquid from the rim will not run down the label.
- ✓ ***Presentation of the Label after dosage form design:*** The student should receive or get issued the clean and polished glass or plastic containers from the store keeper. Polishing should be done after, as well as before labelling, to remove gum and finger- marks.
- ✓ Acacia-gum labels will not adhere to plastics or metal containers; self-adhesive labels must be used.

How to Write a Dosage Form Design Experiment in a Note Book
(Left Side Page of the Notebook)

Step 1: Write 'AIM OF THE EXPERIMENT' on the left side page of the practical note book and record the date on the right side of the note book

Step 2: Write the material/chemical and equipment requirements as per the requirement of the experiment.

Step 3: Write the exact 'CHEMICAL FORMULA' of the dosage form or prescription as written depicting all the names and record the quantity of each ingredient/substance in a tabular form opposite the name of the drug to which it refers.

Step 3: Check for the prescription/dosage form refers to I.P., NFI., U.S.P., B.P., B.P.C., or B.N.F. preparation, and record the official formula together with the official quantities, and record as in the quantities used.

Step 4: *Calculation of doses:* Calculate and Convert the prescription composition or chemical formula of the dosage form indicating all the ingredients as per the dispensing amount of the experiment and record the details of all calculations of doses and quantities for dilutions and trituration for each active ingredient.

Step 5: Design a 'SPECIMEN LABEL' using example as shown below on the left side page of your note book

SIMPLE SYRUP (I.P.) 30 g		
Composition: **Each 30 g contains:** Oil of peppermint- 0.1 ml Distilled water q.s.- 50 ml **Dose:** 10 to 40 ml **Storage:** Store in well-closed, light-resistant container cool place to volatilization of oil	**SHERRICOF®** (Simple Syrup) (Used as an antispasmodic and carminative in flatulence of the gastrointestinal tract, cramping and bloating, flatulent colic to relieve nausea and vomiting, and as a gentle aromatic stimulant) PROTECT FROM SUN LIGHT NOT FOR INJECTION	Mfg. Lic. No.- HAT/2018 Batch No.- AKH 4311 Mfg. Date- Jan. 2018 Exp. Date- Dec. 2019 M.R.P.- Rs. 49.00 (Inclusive of all taxes) Mfd. By: AKT PHARMA SADIQ ROAD, PATIALA PB-147002

Step 6: Affix a duplicate of the label applied to the product and include also any auxiliary labels used; e.g. shake the bottle well before use (if required).

Step 7: *Container:* Record details of the size and type of container used together with any special container specification for the product. E.g. test for the limit of alkalinity of glass (L.A.G.).

Step 8: *Storage Requirements:* Record the shelf life of the product and details of any special requirements for storage, e.g. Protect from light.

(Right Side Page of the Notebook)

Step 1: Write 'AIM OF THE EXPERIMENT' at the top as heading on the right side page of the practical note book and record the date on the right side of the note book.

Step 2: Write the 'REFERNCE' from a standard compendia or text book source or practical manual from where the composition or formula of the prescription/ dosage form was taken in a following manner:

(*Full surname with first name in abbreviated form, title of the chapter, In: (title of the book/journal), Editors name, Publishers name, Chapter number, issue and volume of the book, year of 0publication)*

Step 3: THEORY: *Main pharmaceutical actions of the active drug/ excipients:* Write a brief account on the main pharmaceutical actions of the active ingredients in the preparation, in the context of the dosage form supplied.

Clinical Conditions and Dose Regimen of Product: It has to be noted that this action refers to the final dispensed product only, and not to other dosage forms of the same drugs.

Step 4: METHODS OF PREPARATION: A detailed description of the step wise procedure or in a note form with every possible details used in the methods. (Note-*Clarification: Wherever applicable, specify the medium used; Sterlization: Wherever applicable, specify the record methods, time and temperature). Formulation notes*- Record the details of additives, excipients, colouring agents and aids used in the dosage form design. Mention also any incompatibilities encountered. If you have formulated the product, give the reasons for your choice of formulation.

Step 5: GENERAL PRECAUTIONS:

- Verify the doses of internal preparations (including suppositories and enemas) and take into account the directions for use.
- In case of any over dosage, report to the lab technician or class incharge.
- If any ingredient used in the chemical formula belongs to the category of a poison (or mentioned in the Poisons and T.S.A. Guide or mentioned on the label of the stock bottle/container) the weight or volume must be dispensed by the lab technician or Class incharge only.
- In order to confirm if there is no pharmaceutical or pharmacological incompatibility, use I.P., B.P., U.S.P or Extra Pharmacopoeia. In case of any doubt about the method of preparation, refer to previous dispensing schedules.
- Step 6: RESULTS: Report the inference or conclusion of the experiment in a one line only.*(*Note: The experiment should be reported on the index page of the note book and get it signed from the class incharge after the viva-voce of the experiment)*

General Packaging Instructions for Dispensing

Packaging Instructions:

The choice of container used for dispensing medicines for the packaging of individual preparations is made solely on technical grounds. Official recommendations on colours and changes of container for each type of medication should be adhered, so as to reduce the accidental misuse of medicines. The following points are to be noted in the packaging of dispensed products.

- All mixtures intended for oral use must be packed in plain bottles and covered with plastic screw-caps.
- All preparations intended for external use only (e.g. Gargles, lotions, etc.) must be packed in fluted or ribbed glass bottles.
- All preparations containing photo-labile (i.e. light-sensitive) ingredients are packed in amber coloured bottles.
- Any thick liquid preparations such as emulsion, liniments etc. are packed in wide-mouthed bottles to allow for easy pouring out of contents from the bottle.

Labeling Directions for Various Types of Preparations

Aim of the Labeling:

The primary aim of any label is to accurately direct the patient as to how and when the medicine should be taken or used. Therefore, a label is an important factor in the appearance of the final medicine and a high standard in label presentation that will do much to maintain confidence of the patient. Hence, every effort should be made to be competent on this point.

In nutshell, the mantra for an ideal label should be

'LEGIBLE, NEAT AND WELL-BALANCED'

General Instructions:

Choose the correct size of container for the product and match the label size to the container.

- ✓ Polish the bottles or containers before labeling.
- ✓ Affix labels symmetrically on the container.
- ✓ Never have more than one unlabelled product on the bench at the same time.
- ✓ Never place a fresh label over an old label which may pose dangerous hazards.
- ✓ Generally, labels for 'Internal Medicines' adopt black prints and those for 'External Medicines' adopt red prints.
- ✓ The main label should clearly state the quantity of the product, the type of preparation e.g. 'The Mixture' 'The Tablets', etc. or where so directed the actual name of the preparation.
- ✓ In a case if any official (I.P., N.F.I., U.S.P., B.P., or Extra Pharmacopoeia) dosage form is being dispensed, it is not necessary to declare on the label, the concentration of the active ingredients. It is for instance sufficient to

label the product as, 'AMMONIUM CHLORIDE AND MORPHINE MIXTURE BP 188. Vol.I.'

- ✓ Write precise instructions for use in minimum words. Add the date of dispensing and a reference number (if it is a private prescription),the name of the patient, the name and address of the pharmacy. (*Note- The word 'POISON' should not appear on the label of a dispensed medicine unless specifically requested*)

For some preparations, instructions which are specifically detailed on the prescription must be given on the container. Such instructions serve to amplify how the medicine is to be used or to guide the patient regarding the best storage conditions. Auxiliary labels should be sensibly positioned relative to the main label and should not be fixed on the main label.

Auxiliary label	Circumstances in which label is used	Examples of preparations for which the label is appropriate
SHAKE THE BOTTLE	Liquid preparations which are disperse systems	Emulsions and Suspensions
	Liquid preparations where precipitations or separation is considered possible	
FOR EXTERNAL USE ONLY	Liquid preparations for external application Solid and semi-solid preparations for external application	Lotions, liniments, skin paints Creams, dusting powders and ointments
NOT TO BE TAKEN ORALLY (A possible alternative label for these products)	Liquid preparation which are not administered orally and which are not applied to a skin surface	Ear Drops, eye Lotions, eye Drops, Inhalations, nasal drops, enemas
NOT TO BE TAKEN BY MOUTH	Solid dosage forms which might inadvertently be administered by oral route	Inhalation, pessaries, some solutions, tablets for external use, and suppositories

Some Important Pharmacopoeial Definitions

Temperature

STORAGE CONDITION (I.P)	TEMPERATURE (ºC)
Cold	2-8
Cool	8-25
Warm	30-40
Excess heat	> 40

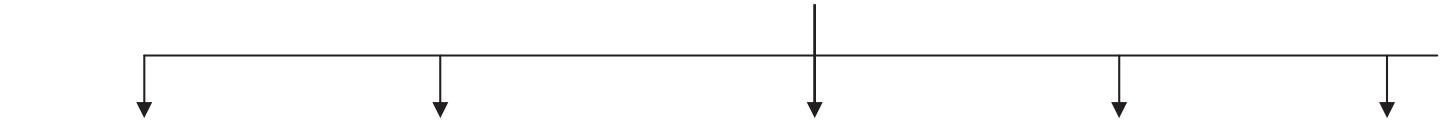
Volume Measure

MEASURE OF LIQUID TRANSFERRED (U.S.P)	VOLUME IN METRIC SYSTEM (ml)	VOLUME IN IMPERIAL SYSTEM
One drop	0.06	1 minim
One teaspoonful	5.0	1 fluid drachm
One dessertspoonful	8.0	2 fluid drachm
One tablespoonful	15.0	0.5 fluid ounce
One wineglassful	60.0	2 fluid ounce
One teacupful	120.0	4 fluid ounce
One tumblerful	240.0	8 fluid ounce

Powders (I.P.)

CLASSIFICATION	DESIGNATION	DEFINITION
Coarse powder	10/44	A powder of which all particles pass through a sieve no. 10 and not more than 40% by weight pass through sieve no. 44
Moderately coarse powder	22/60	A powder of which all particles pass through a sieve no. 22 and not more than 40% by weight pass through sieve no. 60
Moderately fine powder	44/85	A powder of which all particles pass through a sieve no. 44 and not more than 40% by weight pass through sieve no. 85
Fine powder	85/120	A powder of which all particles pass through a sieve no. 85 and not more than 40% by weight pass through sieve no. 120
Very fine powder	120/350	A powder of which all particles pass through a sieve no. 120 and not more than 40% by weight pass through sieve no. 350
Micro fine powder	350	A powder of which not less than 90% by weight of the particles pass through a sieve no. 350
Superfine powder	--	A powder of which not less than 90% by number of the particles are less than 10 micron in size

CLASSIFICATION OF DOSAGE FORMS



LIQUIDS

Monophasic systems

Aromatic Waters
Solutions
Glycerites
Mouth wash
Spirits
Elixirs
Mucilage
Milk/Magma
Gargles
Throat Paints
Syrups
Eye Drops
Nasal Drops

Biphasic Systems

- Suspensions
- Emulsions
- Lotions
- Liniments
- Applications
- Enemas

SOLIDS

Powders

- Dusting Powder
- Insufflations
- Dentifrice

Effervescent Granules

Tablets

- Lozenges
- Enteric Coated
- Non Enteric Coated
- Chewable
- Sublingual
- Time Release
- Sustained Release
- Extended Release

Suppositories

- Cocoa butter
- Glycero gelatin

Pessaries

- PEG
- Glycero gelatin

Capsules

Hard Gelatin Capsule
Soft Gelatin Capsule

Microcapsules

Microspheres

SEMISOLIDS

Ointments

Creams

- Vanishing Creams
- Cold Creams

Pastes

Gellies/Clear Gels

GASES

- Oxygen
- Hydrogen
- Helium
- Nitric Oxide

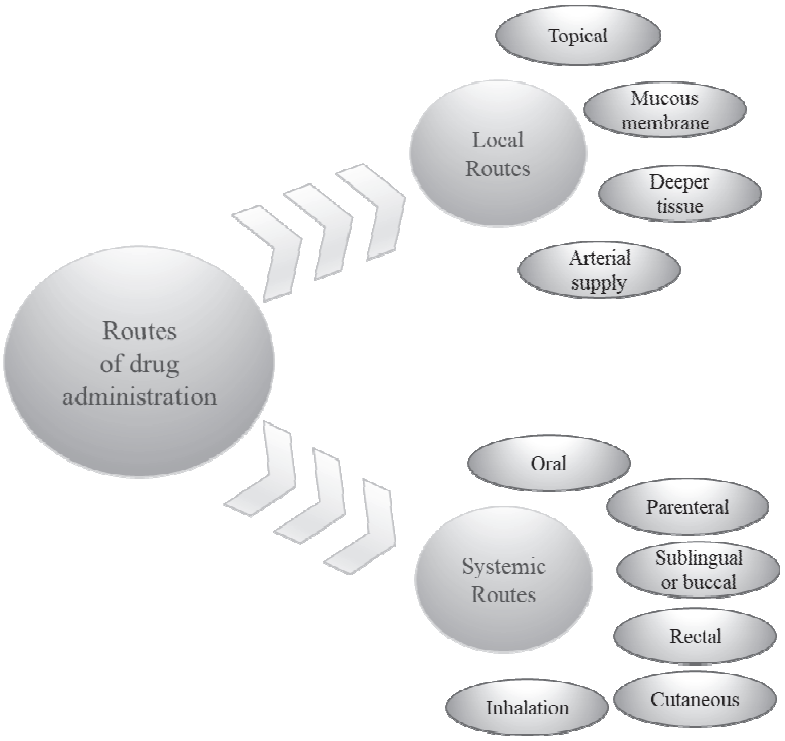
AEROSOLS

- Sprays
- Inhalants
- Foams

Routes of Drug Administration

A drug will produce its action only when it enters the body, tissue or cells (i.e. site of action). So the entrance through which a drug is delivered is called the route of drug administration.

Classification



Local Routes

These routes can only be used for localized lesions at accessible sites. Systemic absorption of the drug from these routes is minimal or absent. Thus, high concentrations are attained at the desired site without exposing the rest of the body.

Topical

This refers to external application of the drug to the surface for localized action.

(a) Skin: Drug is applied as ointment, cream, lotion, paste, powder, dressing etc.

(b) Mucous membrane: The dosage form depends on the site:

- ✓ *Mouth and pharynx:* Paints, lozenges, mouth washes, gargles.

- ✓ *Eyes, ears and nose:* Drops, ointments, irrigation, nasal spray.
- ✓ *Gastrointestinal tract:* Non-absorbable drugs given orally e.g. aluminum hydroxide, magnesium hydroxide, methyl polysiloxane etc.
- ✓ *Bronchi and lungs*: As inhalations, aerosols (nebulized solution or fine powder)- e.g. salbutamol, cromolyn sodium.
- ✓ *Urethra:* Jellies e.g. lidocaine, irrigating solutions.
- ✓ *Vagina:* Pessaries, vaginal tablets, inserts, cream, powders, douches.
- ✓ *Anal canal:* Ointment, suppositories.

Deeper Tissues

Certain deep areas can be approached by using a syringe and needle, but the drug should be such that systemic absorption is slow. e.g. intra-articular injection (hydrocortisone acetate), intra-thecal injection (lidocaine, amphotericin B) and retrobulbar injection (xylocaine).

Arterial Supply

Close intra-arterial injection is used for contrast media in femoral or bronchial artery for limb malignancies. In these cases, the drug is injected into the artery that is supplying the blood to the desired site (i.e., site for diagnosis or the cancerous tissues). The drug travels with the blood flow towards the tissue it is perfusing and not towards the heart. Thus, systemic action is avoided and localized action is achieved. (*Note - In case of vein the drug will be carried to the heart and from there to the system i.e. to the whole body*).

Systemic Routes

Parenteral

(*Par*- beyond, *enteral*- intestinal). Routes of drug administration other than oral route are known as parenteral route. This refers to administration by injection which takes the drug directly into the tissue fluid or blood without having to cross the intestinal mucosa and subsequently liver.

Advantages: Absorption is faster, hence drug can be administered rapidly and in accurate dose in time of emergencies.

- ✓ Gastric irritation and vomiting are avoided.
- ✓ It can be employed in unconscious, uncooperative or vomiting patients.
- ✓ There are no chances of interference by food or digestive juices.
- ✓ Liver is bypassed.

Diverse systemic routes which are intended for the administration of drug to be absorbed into blood and distributed all over, including the site of action, through circulation.

Systemic Routes	*Enteral*								*Parenteral*			
	Oral	***Sublingual /buccal***	***Rectal***	***Cutaneous***	***Inhala Tional***	***Intra-peritoneal***	***Intra--arterial***	***Nasal***	***IV***	***IM***	***SC***	***ID***
Mode	Dosage form is taken through the mouth and it is absorbed from the GIT	Dosage form is placed under the tongue (sublingual) or crushed in the mouth and spread over the buccal mucosa. The drug is absorbed through the buccal mucosa	Drug containing dosage form is either inserted or put into the rectum as suppositories or retention enema. One part of the absorbed drug passes to the liver, another part to the systemic circulation	Dosage form is applied or placed on the skin and the drug penetrates the skin to reach the blood i.e. cutaneous route is meant for systemic absorption.	The drug is administered through nose or mouth, carried by the air to reach the lung. The alveoli are rich with capillary vessels. The drug is diffused into the blood stream. Thus systemic action is obtained	Drug is injected into the peritoneal cavity.	Drug is injected into an artery. The effect of a drug can be localized in a particular organ or tissue by choosing the appropriate artery	Drug is administered as snuff or spray or nebulized solution in the nose; where the drug penetrates the nasal mucous membrane to reach the blood	Drug is injected as a bolus or infused slowly over hours in one of the superficial veins (generally brachial vein).	Drug is injected in one of the large skeletal muscles such as deltoid, triceps, gluteus maximus, rectus femoris	Drug is injected under the skin. The drug is deposited in the loose SC tissue which is richly supplied by nerves (irritant drugs cannot be injected but is less vascular (absorption is slower)	Drug is injected into the dermis of skin raising a bleb (e.g. BCG vaccine, sensitivity testing of drugs) or scarring / multiple puncture of the epidermis through a drop of the drug (small pox vaccine) is done. This route is employed for specific purpose only
Dosage forms	e.g. Solid dosage forms (e.g. tablets, capsules, powders) and liquid dosage forms (e.g elixirs, syrups, emulsions, mixtures)	e.g. Tablets or pellets of Nitroglycerine, isoprenaline, clonidine, nifedipine.	e.g. Aminophylline, indomethacin, paraldehyde, diazepam, ergotamine	e.g. Transdermal patches of nitroglycerin, hyoscine, clonidine and estradiol.E.g. Transdermal drug delivery systems of timolol, testosterone, nicotine and isosorbide dinitrite	e.g. Volatile liquids and gases are given by inhalation-such as general anaesthetics, amylnitrite	e.g. Fluids like glucose and saline can be given to children.	e.g. anti cancer drugs	e.g. Posterior pituitary powder and desmop-ressin powder		e.g. Low volume injections - Vitamin A, hydrocortisone acetate, tetanus toxoid, antibiotic etc.		

Contd….

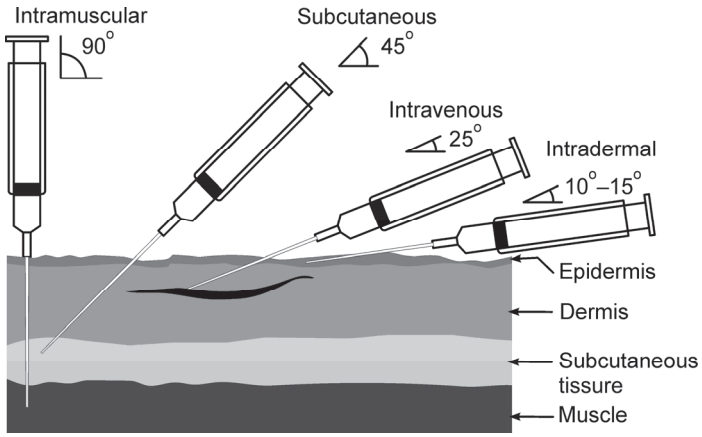
Systemic Routes	*Enteral*								*Parenteral*			
	Oral	***Sublingual /buccal***	***Rectal***	***Cutaneous***	***Inhala Tional***	***Intra-peritoneal***	***Intra--arterial***	***Nasal***	***IV***	***IM***	***SC***	***ID***
Pros	More safer, and convenient. No assistance is required for administration. It is painless. The medicament need not be sterile and so is cheaper.	Absorption is relatively rapid - action can be produced in a minute. One can spit the drug after the desired effect has been obtained. The liver is bypassed and drugs with high first-pass metabolism can be absorbed directly into the systemic circulation	Drugs having bad taste or odour can be given through this route. Drug that degrades in acidic pH of the gastric juice can be given through this route. This route can also be used when the patient is having recurrent vomiting.	Highly lipid soluble drugs can be applied over the skin for slow and prolonged absorption. The liver is bypassed through this route. The drug can be incorporated in an ointment and applied over specified area of skin. Transdermal drug delivery systems deliver the drug in a controlled manner and for a prolonged period. They provide smooth plasma concentration of drug.	Absorption takes place from the vast surface of alveoli - hence action is very rapid. When administration is discontinued the drug diffuses back and is rapidly eliminated in expired air. Thus controlled administration is possible with time to time adjustment. Bypasses the liver			The drug can avoid digestive juices and liver. Drugs are readily absorbed from this route.	The drug directly reaches the blood stream and effect is produced immediately, hence, this route can be used in emergencies. The inside of the veins is insensitive and drug gets diluted with blood quickly, therefore, even highly irritant drugs can be given by i.v route. Large volumes can be infused (e.g. normal saline). It is useful in unconscious patients.	Muscle is less richly supplied with sensory nerves, hence mild irritants can be injected. Muscle is more vascular hence absorption is faster than subcutaneous route. It is less painful. Depot preparations can be injected by this route and the action of the drug may be prolonged.	Self injection is possible because deep penetration is not required. Oily solutions or aqueous suspensions can form a depot which will release drug slowly for a prolonged period.	

Contd….

Systemic Routes	*Enteral*								*Parenteral*			
	Oral	***Sublingual /buccal***	***Rectal***	***Cutaneous***	***Inhala Tional***	***Intra-peritoneal***	***Intra--arterial***	***Nasal***	***IV***	***IM***	***SC***	***ID***
Cons	Action is slower and not suitable for emergencies. Unpalatable drugs (e.g. paraldehyde) are difficult to administer. May cause nausea and vomiting (e.g. emetine). vomiting patients. Certain drugs are not absorbed (e.g. streptomycin). Some drugs are destroyed by digestive juices (e.g. penicillin G, insulin) or in liver (e.g., nitroglycerin, testosterone, lidocaine)	Only lipid soluble and non-irritating drugs can be administered in this way; Drugs with bad taste or objectionable odour are not possible to administer on the tongue.	Administration of drug through this route is rather inconvenient and embarrassing. Absorption is slower, irregular and often unpredictable. Drug absorbed into external haemorrhoidal veins (about 50%) bypasses liver, but not that absorbed into internal haemorrhoidal veins. Rectal inflammation ca results from highly irritant drugs.	Absorption is very slow. So it cannot be used in emergency situation. Water soluble drugs are minimally absorbed through the skin.	Irritant vapors (ether) cause inflammation of respiratory tract and increase secretion.			Not suitable for irritant drugs	Drugs that precipitate in the blood cannot be administered. Only aqueous solution can be administered. If the needle puncture the vessel (i.e. extra vasation) then thrombo-phlebitis of the injected vein and necrosis of the adjoining tissues may occur. No drug can be given in depot form - so the action is not prolonged compared to other parenteral administrations. Untoward reactions if occur are immediate. Once administered, withdrawal of the drug is not possible.	Since deep penetration is needed hence self-medication is not possible. Large volume cannot be given.	Since skin is richly supplied by nerve-endings hence irritant drugs cannot be injected. This route should be avoided in shock patients.e.g. Insulin injection.	

Disadvantages:

- ✓ The preparation has to be sterilized and is costlier.
- ✓ Injection are painful.
- ✓ Self medication is difficult - another trained person is required to give the injection.
- ✓ Abscess and inflammation at the site of injection may take place.



Pharmaceutical Terms

Pharmacokinetics is the subject that deals with 'what body does to the drug'.

This subject includes absorption, distribution, metabolism and excretion of the drugs. It determines the routes of administration, dose, onset of action, time of peak action, duration of action and frequency of administration.

Pharamcodynamics is the subject that deals with 'what drug does to the body'.

It is the study of the effect of drug on the body, its mechanism of action, dose-effect relationship, drug-drug interaction, and factors modifying drug action

Dose is the quantity of a drug to be administered at one time to achieve a therapeutic response.

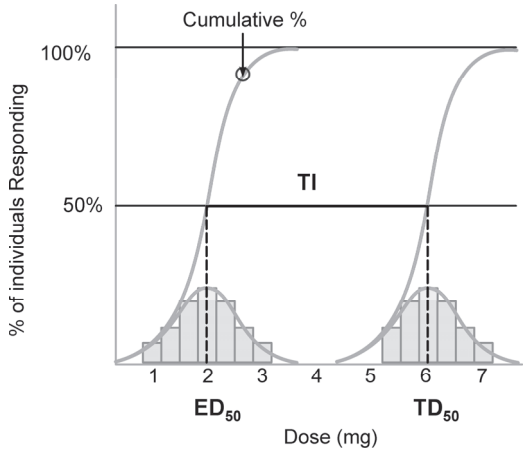
e.g. Oral adult dose of paracetamol is 325 mg.

Dosage is the determination and regulation of the size (dose), frequency, and number of doses.

e.g. Oral adult dosage of paracetamol is 325 mg thrice a day (t.i.d).

Therapeutic index (or Therapeutic ratio)

By this term the therapeutic effect and untoward effect of a drug is compared. The untoward effect is expressed by TD_{50} i.e toxic dose for 50% animals and the therapeutic effect by ED_{50} i.e. effective dose for 50% of animals.



The *therapeutic index* (T.I.) expressed as the ratio of TD_{50} / ED_{50} in humans.

(*Note- Therapeutic index (T.I.) is also expressed as the ratio of LD_{50} / ED_{50} in animals*).

When the therapeutic index is small the drug should be administered under careful observation because the probability of occurance of toxic effect is higher. When the therapeutic effect is large it is safer to administer the drug than with smaller therapeutic index.

The therapeutic index varies widely among substances, even within a related group. For instance, the opioid pain killer remifentanil is very forgiving, offering a therapeutic index of 33,000:1, while Diazepam, a benzodiazepine sedative-hypnotic and skeletal muscle relaxant, has a less forgiving therapeutic index of 100:1. Morphine is even less so with a therapeutic index of 70.

Less safe are cocaine (a stimulant and local anaesthetic) and ethanol (colloquially, the “alcohol” in alcoholic beverages, a widely available sedative consumed worldwide): the therapeutic indices for these substances are 15:1 and 10:1, respectively.

Even less safer drugs such as digoxin, a cardiac glycoside; its therapeutic index is approximately 2:1.

Other examples of drugs with a narrow therapeutic range, which may require drug monitoring both to achieve therapeutic levels and to minimise toxicity, include: paracetamol (acetaminophen), dimercaprol, theophylline, warfarin and lithium carbonate.

Some antibiotics and antifungals require monitoring to balance efficacy with minimising adverse effects, including: gentamicin, vancomycin, amphotericin B (nicknamed 'amphoterrible' for this very reason), and polymyxin B

E.g. benzodiazepines have greater therapeutic index than barbiturates, hence, are less likely to be fatal when taken in accidental overdose.

LD_{50}

Before any new drug molecule is approved for testing in man, extensive toxicity testing is done in various animal species. The crudest type of toxicity test is the LD_{50}.

LD_{50} is defined as the lethal dose for 50% of a group of animals. In other words, it is an individual dose required to kill 50% of test population (i.e. rat, fish, mice, cockroach). Therefore, lower is the LD_{50}, more will be the toxicity of drug/test chemical substance. (For example- A test compound with an LD_{50} value of 10 mg/kg is ten times more toxic than a chemical with LD_{50} value of 100 mg/kg).

Application:-It is used as a standard to compare the relative toxicities of the chemicals

Methods of determination

Various doses of drugs are administered to groups of 10 animals. The mortality (death) in each group within a fixed period of time (say 2 days) is determined and used to construct a curve relating fraction mortality to log (dose).

Significance: It is a parameter which defines (though not adequately) the chemical toxicity of a drug molecule.

Relation of Toxicity with LD_{50}

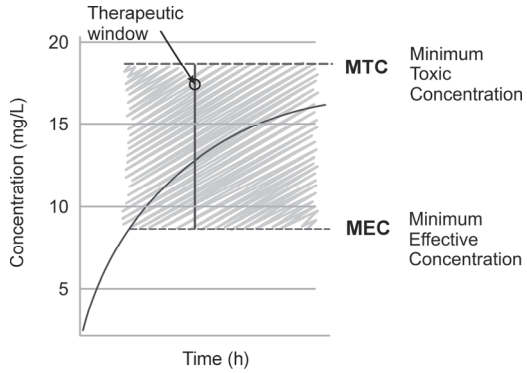
S.No.	Toxicity	LD_{50} (mg/kg/b.wt.)	Lethal dose	Examples
1.	Super	<0.01	Less than 1 drop	Dioxin; botulism; mushrooms
2.	Extreme	<5	Less than 7 drops	Heroin; nicotine
3.	Very	5-50	7 drops to 1 tsp.	Morphine; codeine
4.	Toxic	50-500	1tsp.	DDT, H_2SO_4; Caffeine
5.	Moderate	500-5K	1oz.-1pt.	Aspirin; wood alcohol
6.	Slightly	5K-15K	1pt.	Ethyl alcohol; soaps
7.	Non-toxic	>15K	>1qt.	Water; table sugar

Protective Index (P.I)

It is a similar concept, except that it uses TD_{50} (median toxic dose) in place of LD_{50}. For many substances, toxic effects can occur at levels far below those needed to cause death, and thus the P.I. (if toxicity is properly specified) is often more informative about a substance's relative safety. Nevertheless, the T.I. is still useful as it can be considered an upper bound for the protective index, and the former also has the advantages of objectivity and easier comprehension.

Therapeutic Window

Also known as pharmaceutical window of a drug, it is the range of drug dosages which can treat disease effectively without having toxic effects. Drugs with a small therapeutic window must be administered with care and control, frequently measuring blood concentration of the drug, to avoid harm. Drugs with narrow therapeutic windows include theophylline, digoxin, lithium, and warfarin.*(Note-Students must take care while using the terms therapeutic index and therapeutic window as both these terms are totally different from each other).*



Optimal biological dose (OBD)

The quantity of a drug that will most effectively produce the desired effect while remaining in the range of acceptable toxicity.

Some other terms which are commonly used in relation to expression of doses are:

- **Minimum dose**

  The lowest dose exerting the desired therapeutic effect in an average patient is said to be a minimum dose. The response of the patient will indicate whether in continuing treatment this dose should be maintained or increased.

- **Maximum dose**

  The highest dose usually tolerated without undesirable effects in the average patient. This dose is not the greatest amount that can be administered, as in certain specific treatments the official maximum dose may be exceeded.

❖ **Prophylactic dose**

The dose necessary to prevent the onset of a disease

❖ **Therapeutic dose**

The dose necessary to treat an established disease

❖ **Loading dose**

A dose higher than the maintenance, given on the initiation of therapy to give rapid drug plasma levels equivalent to that reached after multiple dosing. This higher dosage is used for a short period of time only; often it only involves a single dose.

❖ **Maintenance dose**

A dose given to maintain the therapeutic level of a drug in the body

❖ **Toxic dose**

The dose capable of producing marked functional derangement in the body.

❖ **Lethal dose**

The smallest dose known to have produced a human death

❖ **Maximum tolerated dose (MTD)**

This refers to the highest dose of a radiological or pharmacological treatment that will produce the desired effect without unacceptable toxicity. The purpose of administering MTD is to determine whether long-term exposure to a chemical might lead to unacceptable adverse health effects in a population, when the level of exposure is not sufficient to cause premature mortality due to short-term toxic effects. The maximum dose is used, rather than a lower dose, to reduce the number of test subjects (and, among other things, the cost of testing), to detect an effect that might occur only rarely. MTD is an essential aspect of a drug's profile and studies are also done in clinical trials. All modern healthcare systems dictate a maximum safe dose for each drug, and generally have numerous safeguards to prevent the prescription and dispensing of quantities exceeding the highest dosage which has been demonstrated to be safe for members of the general patient population.

ED_{50}

There are two type of ED_{50} with which normally the dose effect relationship of a drug is related.

(i) *50% Effective dose* or *Individual ED_{50}* and;

(ii) *Median effective dose*

(i) 50% Effective dose (ED_{50})

In order to have dose-effect relationship the *intensity* of biological effect of a drug is plotted against the *dose* [or log (dose)] of the drug.

Individual ED_{50} is the dose required to elicit 50% of the maximum intensity of the biological effect.

Individual ED_{50} is required to compare the effect between two drugs in an individual.

The *relative potency* of any drug may be obtained by dividing the ED_{50} of the standard, or prototype drug by the drug in question. Since dose-intensity curve varies from individual to individual, hence individual *ED_{50}* is not accurate enough.

(ii) Median effective dose

In this case % of animals showing a desired level of effect is plotted against log (dose) (i.e. *dose-frequency relationship*). The curves generally produced are sigmoidal in nature.

ED_{50} is the dose at which 50% of the animal shows the desired level of effect.

Safety Ratio

Sometimes the term safety ratio is used instead, particularly when referring to psychoactive drugs used for non-therapeutic purposes, e.g. recreational use. In such cases, the effective dose is the amount and frequency that produces the desired effect, which can vary, and can be greater or less than the therapeutically effective dose.

Certain Safety factor (CSF) or Margin of Safety (MOS)

It is the ratio of the lethal dose to 1% of population to the effective dose to 99% of the population (LD_1/ED_{99}). This is a better safety index than the LD_{50} for materials that have both desirable and undesirable effects, because it factors in the ends of the spectrum where doses may be necessary to produce a response in one person but can, at the same dose, be lethal in another.

Special Instructions for Particular Dosage Form

Dosage form	Latin term	Commonly used instructions
Capsules	*Capsula*	*Swallow with a draught of water.*
Creams	*Cremor*	*For external use only.* *Keep in a cool place.*
Dusting powder	*Pulvis*	*For external use only.* *Not to be applied to open wounds or weeping surfaces.*
Ear drops	*Auristillae*	*For external use only.*
Emulsions	*Emulsion*	*Shake the bottle before use.*

Contd…

Dosage form	Latin term	Commonly used instructions
Enemas	*Enema*	*For rectal use only.* *Warm to body temperature before use.*
Eye drops	*Guttae*	*To be used within 30 days after first opening.*
Gargles and mouthwashes	*Gargarisma and Collutrorium*	*Not to be swallowed in large amount.*
Linctuses	*Linctus*	*To be sipped and swallowed slowly without addition of water.*
Liniments and lotions	*Linimentum and Lotio*	*For external use only.* *Shake the bottle before use.* *Do not apply on broken skin.* (Because it will produce irritation)
Mixtures	*Mistura*	*Shake it well before use.*
Suspensions	*Suspensiō*	*Shake the bottle before use.*
Nasal drops	*Naristillae*	*For nasal use only*
Ointments, Pastes and Paints	*Unguentum, Pasta and pigmentum*	*For external use only.*
Pessaries	*Pessus*	*For vaginal use only*
Suppositories	*Suppositorum*	*For rectal use only.* *Store in a cool place.*

Selection of Containers for Dispensing Medicines

The aim should be to make a clear distinction between preparations that may be taken internally and those intended for external use. The container should also be selected which will best protect the life of the preparation.

Storage conditions and containers for internal or external use:

Preparation	Containers
Cachets	Air tight containers which give adequate physical protection. Containers made of glass, rigid plastics, or extruded aluminum are generally suitable. Use cardboard boxes, which are suitable for short storage periods
Capsules	Airtight containers which give adequate physical protection (Note: Containers made of glass rigid plastics, or extruded aluminum are generally suitable. Suitable internal wadding may be required).
Creams	Wide-mouthed, squat glass jars fitted with plastic screw caps and suitable liners. Certain plastic containers may also be suitable, provided they prevent evaporation of water vapour; plastic containers are unsuitable for those preparations containing plasticizers such as methylsalicylate or phthalate esters.
Draughts	White glass bottles fitted with plastic screw caps with plastic or other impervious liners. Such dose should be packed separately or the exact dose should be made on the label.
Dusting Powders	Cylindrical paper board boxes or plain white glass jars with sprinkler holes on the closure

Contd…

Preparation	Containers
Ear drops	Coloured fluted glass bottles fitted with suitable droppers. Plastic dropper bottles are also suitable provided that the plastic is compatible with the content.
Eye drops	Coloured, fluted glass dropper bottles which are capable of being sterilized by autoclaving. Plastic containers are suitable for some eye-drops provided that the plastic is compatible with the content. (*Note:* The glass must be neutral or soda treated screw-capped dropper bottles and must comply with Indian Pharmacopoeial Standards)
Eye Ointments	Sterile collapsible tubes.
Eye Lotions	Coloured, fluted glass bottles fitted with plastic screw caps with plastic or other impervious liners. Unprotected bulk closures should not be used for eye lotions.
Mouthwashes and gargles	Clear ribbed bottle, glass or plastic, or, amber if contents sensitive to light
Enemas	Coloured fluted glass bottles with plastic screw-caps with plastic or other impervious liners. Disposable flexible plastic containers are suitable for some enemas provided that the plastic is compatible with the content.
Elixirs	Plain white glass bottles fitted with plastic screw-caps with plastic or other impervious liners.
Gargles	White fluted glass bottles fitted with plastic screw-caps with plastic or other impervious liners.
Granules	Airtight containers which give adequate; physical protection containers made of glass, rigid plastics, or extruded aluminum; are generally suitable.
Inhalations	White fluted glass bottles fitted with plastic screw caps with plastic or impervious liners.
Linctuses	Plain white glass bottles fitted with plastic screw caps with plastic or other impervious liners
Liniments	Coloured fluted glass bottles fitted with plastic screw caps with plastic or other impervious liners
Lotions	Coloured fluted glass bottles fitted with plastic screw caps with plastic or other impervious liners.
Lozenges	Airtight containers which give adequate physical protection. Containers made of glass, rigid plastics, or extruded aluminum, are generally suitable.
Mixtures	Plain white non-graduated glass bottles fitted with plastic or other impervious liners
Mouthwashes	White fluted glass bottles fitted with plastic screw caps with plastic or other impervious liners
Nasal drops	Coloured fluted glass bottles with a dropper. Plastic dropper bottles are also suitable, provided that the plastic is compatible with the content.
Ointments	Wide-mouthed, screw-capped, plain squat glass jars or plastic jars metal or plastic flexible tubes with screw caps. Certain plastic containers containing plasticizers such as methyl salicylate ester are not suitable for some ointments

Contd…

Preparation	Containers
Paints	Coloured fluted glass bottles fitted with plastic screw caps with plastic or other impervious liners.
Pastes	Wide-mouthed, screw-capped, plain squat glass or plastic jar metal or; plastic flexible tubes with screw caps.
Pastilles	Airtight containers, which give adequate physical protection, containers made of glass, rigid plastics, or extruded aluminum, are generally suitable
Pessaries	They should be wrapped individually in waxed paper, in metal foil, or in some suitable form of strip packing. They should be dispensed in partitioned boxes or in suitable plastics containers (for 4 g pessaries use 120 g ointment jars).
Powders	Bulk powders should be dispensed in airtight containers, which give adequate physical protection. Containers made of glass, rigid plastics, or extruded Aluminium, are generally suitable. Individually wrapped powders should be dispensed in stout paperboard boxes with bonded plastic membrane, plastic boxes with bonded plastic membrane, plastic boxes or folding paperboard cartons, which give adequate physical protection. Powders containing deliquescent or volatile materials should be double wrapped in greaseproof paper.
Solution Tablets	Airtight containers, which give adequate physical protection. Containers made of glass, rigid plastics, or extruded aluminum, are generally suitable
Spray Solutions	White fluted glass bottles fitted with plastic screw-caps with plastic or other impervious liners
Suppositories	As for pessaries
Tablets	Airtight containers which give adequate physical protection. Containers made of glass, rigid plastics, or extruded aluminum are generally suitable. Foil or strip packed tablets should be packed in suitable paperboard boxes or folding paperboard cartons which give adequate physical protection. Internal wadding may be necessary

Important Conversions, Formulae and Equations

1. Relationship between Celsius degrees (°C) and Fahrenheit degrees (°F)
   $9(°C) = 5(°F)-160$
2. Density = Weight/Volume or Weight = Density× Volume
3. Various order of reactions:

Order of Reaction	Equation	Final Concentration	Half-life ($T^{1/2}$)
Zero order	$dc/dt= -k\times c^{\circ}$	$C=C_{\circ}-kt$	$0.5C_{\circ}/k$
First order	$dc/dt= -k\times c^{1}$	$\text{Log } C=\log C_{\circ}-kt/2.303$	0.693/k
Second order	$dc/dt= -k\times c^{2}$	$1/C=1/ C_{\circ}+ kt$	$1/ C_{\circ}/k$

Prescription and its Components

It is defined as a written order by a physician, dentist, veterinarian or a registered medical practitioner to a pharmacist to compound and dispense a specific medication for the patient. It comprises the directions which are provided to the pharmacist about what type of dosage form/preparation (such as powder mixture, syrup, tablet, emulsion or suspension etc.) has to be dispensed by the pharmacist for the patient. Further, it also directs to the pharmacist about the dose of the drug, dosing interval (dosage regimen) and route of administration which has to be followed by the patient. Earlier, prescriptions were written in Latin language so that the prescription content remains unknown to the patients to avoid self medication.

For example: A typical prescription can be depicted as follows:

ABNISH HEALTHY BABY
Leela Bhawan, Patiala (PB.)

Ref: ..... *Date:* .....

Name: Mr. Vardhaan *Age*: 2 years *Sex*: Male

Address: #72, Hira Bagh, Patiala

℞ (Superscription)

Inscription	Sodium bicarbonate	3g	
	Compound tincture of cardamom		2ml
	Simple Syrup	6ml	
	Purified Water q.s.	90ml	

Fiat misture. (Subscription)

Sig. Cochleare magnum ter in die post cibos sumenda. (Signatura)

Refill: _____

Sd/-

Dr. Abnish Goyal, MD
(Pediatrics), GMC, Patiala
Regd. Lic. No.PB-15127

Parts of a Prescription

A typical prescription consists of the following parts:

1. **Date**

   Date on the prescription helps the pharmacists to know when the medicines were last dispensed if the prescription is brought for redispensing of the prescription. In case of habit forming drug the date prevents the misuse of the drug by the patient.

2. Name, age, sex and address of the patient

By name and address the patient and the prescription can be identified. Age and sex of the patient is especially required for child patient to check the prescribed dose.

3. Superscription

It is represented by a Latin symbol ℞, an abbreviation of Latin term '**recipe**' which means '**take thou**' or '**you take**'.

[N.B. In olden days, the symbol was considered to be originated from the sign of Jupiter, the Greek God of healing. This symbol was employed by the ancient in requesting God for the quick recovery of the patient.]

4. Inscription

This is the main part of the prescription. It contains the names and quantities of the prescribed medicaments. The medicament may be official preparation or nonofficial preparation. If is official preparation (i.e. from pharmacopoeia or formulary) then only the name of the preparation is written e.g. Piperazine Citrate Elixir IP.

If it is non-official preparation, then the quantity of each ingredient will be given. The type of preparation will also be given e.g.

Sodium bicarbonate	3 g
Simple Syrup	6 ml
Purified Water q.s.	100 ml

The inscription of prescriptions containing several ingredients are divided into the following parts:

(a) *Base*: The active medicaments those are intended to produce the therapeutic effect.

(b) *Adjuvants*: These are included either to enhance the action of the drug or to make the preparation more palatable.

(c) *Vehicle*: It is the main carrier of the drug. In liquid preparations drugs are either dissolved or dispersed in the vehicle.

5. Subscription

In this part the prescriber gives direction to the pharmacist regarding the dosage form to be prepared and the number of doses to be dispensed.

6. Signatura

It is usually written as '**Sig.**'. The instructions given in the prescription should be written in the label of the container so that the patient can follow them. The instructions may include:

(a) The quantity to be taken (b) The frequency and timing of administration of the preparation (c) The route of administration (d) The special instruction (if any).

7. Renewal instructions

The prescriber indicates in every prescription, whether it should be renewed, and if renewed, for how many times. It is very important particularly for habit forming drugs to prevent their misuse.

8. Signature, address and registration number of the prescriber

The prescription must be signed by the prescriber by his / her own hand. His/her address and registration number should be written in the case of dangerous and habit forming drugs.

Handling of Prescription

The following procedures should be adopted by the pharmacist while handling the prescription for compounding and dispensing:

(i) Receiving
(ii) Reading and checking
(iii) Collecting and weighing the materials
(iv) Compounding, labeling and packaging

(i) Receiving

- The prescription should be received by the pharmacist himself / herself.
- While receiving a prescription from a patient a pharmacist should bot change his/her facial expression that gives an impression to the patient that he/she is confused or surprised after seeing the prescription.

(ii) Reading and checking

- After receiving the prescription, it should be screened behind the counter.
- The prescription is a hospital slip or from a nursing home or from a private practitioner and their authenticity should be checked. The signature of the prescriber and the date of prescription is checked.
- The pharmacist should read all the lines and words of the prescription. He/she must not guess any word. If there is any doubt, the pharmacist should consult with the other pharmacist or the prescriber over telephone.

(iii) Collecting and weighing the material

Before compounding a prescription all the materials required should be collected from the shelves or drawers and kept at the left hand side of the balance. After measuring, each material should be kept on the right hand side of the balance. After compounding the prescription, the materials

are replaced back to the shelves / drawers where from they were collected.

While compounding the label of every container of material should be checked thrice in the following manner:

(i) When collected from the shelves/drawers.

(ii) When the materials are measured.

(iii) When the containers are replaced back to the shelves/drawers.

(iv) Compounding, labeling and packaging

- Only one prescription should be compounded at a time.
- Compounding should be done on a clean table.
- All equipment required should be clean and dry.
- The preparation should be prepared according to the direction of the prescriber or as per methods given in pharmacopoeia or formulary are according to established pharmaceutical art of compounding.

Errors in Prescription

1. Dispensing related errors
2. Prescribe related errors
3. Patient related errors

1. Dispensing related errors:

(a) Abbreviation: In most of the prescriptions abbreviated terms are used by the prescriber that leads to major errors during interpretation by the pharmacists. E.g. 'SSKI' is the abbreviated term of 'Saturated Solution of Potassium Iodide'. It is preferable to avoid this type of misleading abbreviations.

(b) Name of the drugs

Names of some drugs (especially the brand names) either looks or sounds alike. So any error in the name of a drug will lead to major danger to the patient.

e.g. Althrocin – Eltroxin, Acidin – Apidin etc.

(c) Strength of the preparation

Drugs are available in the market in various strengths. So a drug must not be dispensed if the strength is not written in the prescription. E.g. Paracetamol tablet 500mg should not be dispensed when no strength is mentioned in the prescription.

(d) Dosage form of the drug prescribed

Many drug are available in more than one dosage forms e.g. liquid, tablets, injections or suppositories. The dosage form intended for the patient must be mentioned in the prescription to reduce ambiguity.

(e) Dose

If unusually high or low dose is mentioned in the prescription, then it must be consulted with the prescriber. Some time a sustained release (SR) dosage form is prescribed thrice or more times daily. Actually, SR dosage forms should be given once or twice a day.

(f) Instructions to the patient

Some times the instruction for a certain preparation is either omitted of mentioned partially. The route of administration should be mentioned clearly.

(g) Incompatibilities

It is essential to check that there are no pharmaceutical or therapeutic incompatibilities in the prescription. If more than two medicines are prescribed, then it is the duty of the pharmacist to see whether their interactions will produce any harm to the patient or not. Certain drugs have interactions with food. The pharmacist has to advise the patient about it. e.g., Tetracycline should not be taken with milk or antacid.

2. Prescriber related errors:

(a) Misleading or erroneous references
(b) Ambiguity in handwriting and types documents
(c) Wrong patient errors
(d) Errors in dosage

3. Patient related errors:

(a) Unable to explain symptoms
(b) Hiding co-morbities
(c) Hiding co-medication being taken concomitantly
(d) Self alteration of dose
(e) Self alteration of time of drug administration
(f) Simultaneously consultations with another doctor

Care Required in Dispensing Prescription

Following precautions should be taken while dispensing a prescription.

1. The prescription must be carried with the pharmacist while taking the medicine out of the shelves. It will constantly remind the name and strength of the preparation required.
2. The dispensing balance should always be checked before weighing any ingredient.
3. All the chemicals and stock preparations should be replaced back in to their original positions in the shelf.

4. While pouring or measuring a liquid ingredient care must be taken to prevent surplus liquid running down of the bottle and staining the label.
5. Care should be taken to keep the balance clean after each measurement. The powders should be transferred by a clean spatula.
6. Liquid preparations for external use should be supplied in a fluted bottle and the label must display FOR EXTERNAL USE ONLY in red ink.
7. Before handing over the medicine to the patient, again the preparation should be checked that the correct preparation, in the correct strength, has been supplied and the correct direction has been stated on the label.

Labeling of Dispensed Medicines

After dispensing the medicine in a container, a label is attached by adhesive. The label on the dispensed medicines should provide the following information: –

1. **Name of the preparation**

   When the prescriber mentions the name in the prescription the same name must be displayed on the label.

   e.g. PIPERAZINE CITRATE ELIXIR IP

   If it is a non-official preparation, then the name of the dosage form should be given on the label.

   e.g. THE MIXTURE, THE EMULSION, THE DUSTING POWDER

2. **The strength of the medicine**

   The strength of the active ingredient in the preparation must be displayed if it is intended for internal (oral) purpose.

   The amount in each unit of dose should be mentioned.

   e.g. In case of oral liquids "Each 5ml contains 250 mg"

   e.g. In case of tablet "Each tablet contains 500 mg".

   The values must be written in whole numbers and if decimal is not avoidable then a zero is placed before the decimal point. E.g. instead of 0.1 g it should be 100 mg, and instead of .5% it should be 0.5%.

   In case of an official preparation the strength is not required to be given, because the name with reference to the pharmacopoeia is sufficient.

   e.g. Chloramphenicol Oral Suspension I.P.

3. **The quantity supplied in the container**

   The total quantity of the product dispensed in the container should be indicated on the label. E.g. 50 ml, 4tabs etc.

4. **Storage conditions and shelf life (expiry date) of the product**

   (a) *Temperature:* Many preparations are required to be kept below 15^0C. In these cases the label should indicate KEEP IN A COOL PLACE.

Suppositories and pessaries melts at 37^0C so the label should indicate KEEP IN A COOL PLACE.

Insulin injections should be stored at 2 to 8^0C so the label should indicate KEEP IN REFRIGERATOR.

(b) *Humidity*: Powders, tablets and capsules should be stored in an air-tight container. The label should indicate KEEP THE BOTTLE TIGHTLY CLOSED.

(c) *Light*: Drugs those degrade in presence of light should be stored in dark place. The label should indicate KEEP IN A DARK PLACE.

5. Instructions to the patient

(a) *Directions*

The directions are normally written by the prescriber. These include

(i) the quantity to be taken

(ii) the frequency or timing of administration

(iii) the route of administration

(iv) or the method of use

The phrases used are generally '*to be taken*', '*to be given*', or '*to be used*'.

e.g. One tablet to be taken thrice daily after meal.

(b) *Warning label*:

For external use only.	In case of external preparations like ointment, pastes, dusting powders etc.
Drowsiness warning.	*Warning*: May cause drowsiness. Do not drive or operate machinery or car.
Potential interactions with food or drink	(i) Drugs in which absorption improves if taken before food: *Warning*: To be taken an hour before meal or in empty stomach. (ii) Drugs causing gastrointestinal irritation *Warning*: To be taken with or after meal. (iii) In case of metronidazole *Warning*: Avoid alcoholic drink.
Interactions with other medicine	Tetracycline complexes with calcium, iron, magnesium and inhibits its absorption, *Warning*: Do not take milk, iron preparation or antacids with this medicine.
Special methods of administration	(i) The drug formulation that is required to be dissolved in the mouth *Warning*: To be sucked or chewed. (ii) Oral powders or granules are required to be dissolved in water *Warning*: To be dissolved in water before taking. (iii) Drugs causing gastro-intestinal irritation *Warning*: *To be taken with plenty of water.*

Contd…

Cautions	(i) Preparation that may produce photosensitization *Warning*: Avoid exposure of skin to direct sunlight. (ii) The preparation that may produce unusual effect. *Warning*: The preparation may color the urine or stool. (iii) In case of inflammable preparation *Warning*: Keep away from naked flame.

Common Latin Terms Used in Prescriptions

Latin term	Abbreviation	English meaning
Auristillae	Auristill.	Ear drops
Charta	Chart	Powder
Collutorium	Collut.	Mouthwash
Collyrium	Collyr.	Eye lotion
Cremor	Crem.	Cream
Emulsio	Emul.	Emulsion
Gargarisma	Garg.	Galgle
Guttae	Gtt.	Drops
Guttur pigmentum	Gtt. Pigm.	Drops
Haustus	Ht	Draught
Inhalatio	Inhal.	Inhalation
Insufflatio	Insuff	Insufflation
Linimentum	Lin.	Liniment
Liquor	Liq.	Solution
Lotio	Lot.	Lotion
Mistura	Mist.	Mixture
Oculus guttae	Ocul. Gtt.	Eye drops
Oculentum	Oculent.	Eye ointment
Pulvis	Pulv.	Powder
Pulvis consperus	Pulv. Consper	Dusting powder
Sternutamentum	Sternut	Snuff
Trochiscus	Troch.	Lozenge
Unguentum	Ung.	Ointment
Applicandus	Applicand.	To be applied
Ad usum externum	Ad. Us. Enter.	For eternal use
Capiendus	Capiend.	To be taken
Consperge	Consper.	Dust, sprinkle
Dolore urgente	Dol. Urg.	When pain is severe
Infricandus	Infricand	To be rubbed
Quantum libitum	q. lib.	As much as you wish

Contd…

Latin term	Abbreviation	English meaning
Quantum sufficiat	q.s.	As much as is sufficient
Sine	s	Without
Pro usu externo	Pro. Us. Exter.	For external use
Ut dictum	Ut. Dict.	As directed
More dicto	m.d.	As directed
Prorenata	p.r.n.	Occcasionally
Si opus sit	s.o.s	Whenever necessary or required
Statim	Stat.	Immediately
Semel in die	Sem in die	Once a day
Bis in die	b.i.d.	Twice a day
Ter in die	t.i.d.	Thrice a day
Quarter in die	q.i.d.	Four times a day
Sexies in die	Se i. d.	Six times a day
Bis terve die	b.t.i.d.	Two or three times a day
Ter quaterve die	t.q.d.	Three or four times a day
Quaque hora	qq.h.	Every hour
Singulis hora	Sing. Hor.	Every one hour
Cibos (cibum)	C	Meal
Hora decubitus	h.d.	At bed time
Quoties opus sit	Quot.o.s.	As often as necessary
Primo mane	Prim. M.	Early in the morning
Prima luce	Prim. Luc.	Early in the morning
Mane	M	In the morning
Omni mane	o. m.	Every morning
Omni nocte	o.n.	Every night
Inter nocte	Inter noct.	During the night
Jentaculum	Jentac.	Breakfast
Nocte manaque	n. m.	Night and morning
Omni quarta hora	o.q.h.	Every four hour
Quaaue secunda hora	qq. sec. h.	Every alternate hour
Alternis horis	Alt. hor.	Every two hours
Tertiis horis	Tert. Hor.	Every three hours
Ante cibos	a.c.	Before meals
Post		After
Post cibos	p. c.	After meals
Inter cibos	i.c.	Between meals
Cochleare amplum	Coch. Amp.	One tablespoonful
Cochleare magnum	Coch. Mag.	One tablespoonful
Cochleare maximum	Coch. Max.	One tablespoonful
Cochleare parvem	Coch. Parv.	One tea spoonful
Cochleare infans	Coch. Inf.	One tea spoonful
Cochleare minimum	Coch. Min.	One tea spoonful
Cochleare medium	Coch. Med.	One desertspoonful

Contd…

Latin term	Abbreviation	English meaning
Ex lacte	e. lact.	With milk
E aqua	Ex. Aq.	With water
Misce	m.	Mix
Partes aequalis	p.a.	Equal parts
Ad	Ad.	To, upto
Ana	Aa	F each
Ante	A	Before
Pro dosi		As a dose

Posology

'Posology' refers to calculation of doses for children.

Factors affecting posology: The factors which affect the posology are listed as hereunder:

1. **Age**: Human beings can be categorized into the following age groups:

Neonate	Up to 1 month from birth
Infant	Up to 1 year age
Child in between	*1 to 4 years*
Child in between	*5 to 12 years*
Adult	Up to 60 years from 16 years
Geriatric (elderly) patients	>60 years

In children the enzyme systems in the liver and renal excretion remain less developed. So all the dose should be less than that of an adult. In elderly patients the renal functions decline. Metabolism rate in the liver also decreases. Drug absorption from the intestine becomes slower in elderly patients. So in geriatric patients the dose is less and should be judiciously administered.

2. **Sex**: Special care should be taken while administering any drug to a woman during menstruation, pregnancy and lactation. Strong purgatives should not be given in menstruation and pregnancy. Antimalarials, ergot alkaloids should not be taken during pregnancy to avoid deformation of foetus. Antihistaminic and sedative drugs are not taken during breast feeding because these drugs are secreted in the milk and the child may be affected by consuming them.

3. **Body size**: It influences the concentration of drug in the body. The average adult dose is calculated for a person with 70 kg body weight (BW). For exceptionally obese (fat) or lean (thin) patient the dose may be calculated on body weight basis.

$$\text{Individual dose} = \frac{\text{Body Weight (kg)}}{70} \times \text{Average adult dose}$$

Another method of dose calculation is according to the *body surface area* (BSA). This method is more accurate than the body weight method.

$$\text{Individual dose} = \frac{\text{Body surface area } (m^2)}{1.7} \times \text{Average adult dose}$$

The body surface area (BSA) of an individual can be obtained from the following formula:

$BSA\ (m^2) = BW(kg)^{0.425} \times Height\ (cm)^{0.725} \times 0.007184$

4. Route of administration

In case of intravenous injection, the total drug reach immediately to the systemic circulation hence the dose is less in i.v. injection than through oral route or any other route.

5. Time of administration

The drugs are most quickly absorbed from empty stomach. The presence of food in the stomach delays the absorption of drugs. Hence a potent drug is given before meal. Drug irritant to the stomach is given after meal so that the drug is diluted with food and thus produces less irritation.

6. Environmental factors

Stimulant types of drug are taken at day time and sedative types of drugs are taken at night. So the dose of a sedative required in day time will be much higher than at night.

7. Psychological state

Psychological state of mind can affect the response of a drug, e.g. a nervous and anxious patient requires more general anaesthetics. *Placebo* is an inert substance that does not contain any drug. Commonly used placebos are *lactose tablets and distilled water injections.* Some time patients often get some psychological effects from this *placebo*. Placebos are more often used in clinical trials of drugs.

8. Pathological states (i.e. Presence of disease)

Several diseases may affect the dose of drugs:

In *gastrointestinal disease* like *achlorhydria* (reduced secretion of HCl acid in the stomach) the absorption of aspirin decreases.

In *liver disease* (like liver cirrhosis) metabolism of some drugs (like morphine, pentobarbitone etc.) decreases.

In *kidney diseases* excretion of drugs (like aminoglycosides, digoxin, phenobarbitone) is reduced, so less dose of the drugs should be administered.

9. Accumulation

Any drug will accumulate in the body if the rate of absorption is more than the rate of elimination. Slowly eliminated drugs are often accumulated in the body and often causes toxicity e.g. prolonged use of chloroquin causes damage to retina.

10. Drug interactions

Simultaneous administration of two drugs may result in same or increased or decrease effects.

Drug administration with dose	Pharmacological effect
Drug A	Effect A
Drug B	Effect B
Drug A + Drug B	Effect AB

Relationship	Name of the effect	Examples
Effect AB = Effect A + Effect B	Additive effect	Aspirin + Paracetamol
Effect AB > Effect A + Effect B	Synergistic (or potentiation)	Sulfamethaxazole + Trimethoprim
Effect AB < Effect A + Effect B	Antagonism	Histamine + Adrenaline

11. Idiosyncrasy

This an exceptional response to a drug in few individual patients. For example, in some patients, aspirin may cause asthma, penicillin causes irritating rashes on the skin etc.

12. Genetic diseases

Some patients may have genetic defects. They lack some enzymes. In those cases some drugs are contraindicated.

e.g. Patients lacking *Glucose-6-phosphate dehydrogenase* enzyme should not be given *primaquine* (an antimalarial drug) because it will cause hemolysis.

13. Tolerance

Some time higher dose of a drug is required to produce a given response (*previously less dose was required*).

Natural Tolerance: Some races are inherently less sensitive to some drugs, e.g. rabbits and black race (Africans) are more tolerant to atropine.

Acquired Tolerance: By repeated use of a drug in an individual for a long time require larger dose to produce the same effect that was obtained with normal dose previously.

Cross tolerance: It is the development of tolerance to pharmacologically related drugs e.g. alcoholics are relatively more tolerant to sedative drugs.

Tachyphylaxis: (*Tachy* = fast, *phylaxis* = protection) is rapid development of tolerance. When a dose of a drug is repeated in quick succession a reduction in response occurs – this is called *tachyphylaxis*. This is usually seen in ephedrine, nicotine.

Drug resistance: It refers to tolerance of microorganisms to inhibitory action of antimicrobials e.g. *Staphylococci* to penicillin.

Pediatric Dose Calculations

Various Formulas for Calculation of Doses

Based on Age

1. Young's Formula

$$\text{Dose of Child} = \frac{\text{Age of child (years)}}{\text{Age of child (years)} + 12} \times \text{Adult dose}$$

2. Dilling's Formula

$$\text{Dose of Child} = \frac{\text{Age of child (years)}}{20} \times \text{Adult dose}$$

3. Cowling's Formula

$$\text{Dose of Child} = \frac{\text{Age of child (years)} + 1}{24} \times \text{Adult dose}$$

4. Fried's Formula

$$\text{Dose of Child} = \frac{\text{Age of child (months)}}{150} \times \text{Adult dose}$$

5. Bastedo's Formula

$$\text{Dose of Child} = \frac{\text{Age of child (years)} + 3}{30} \times \text{Adult dose}$$

Based on Body Weight

Clark's Formula

$$\text{Dose of Child} = \frac{\text{Weight of child (pounds)}}{150 \text{ (pounds)}} \times \text{Adult dose}$$

$$\text{Dose of Child} = \frac{\text{Weight of child (kilograms)}}{70} \times \text{Adult dose}$$

Based on Body Surface Area Method

Nomogram based on Dubois method:

$$\text{BSA } (m^2) = \frac{(\text{Height})\text{cm} \times \text{Weight}(\text{kg})^{1/2}}{60}$$

Catzel's Rule

$$\text{Dose of Child} = \frac{\text{Body surface area of child}}{\text{Body surface area of adult } (1.73M^2)} \times \text{Adult dose}$$

Mosteller's Rule: A most accurate method commonly used in oncology settings.

$$\text{BSA } (M^2) = \sqrt{\frac{\text{ht(cm)} \times \text{wt(kg)}}{3600}}$$

Calculation of Child Doses

Age	Weight (kg)	Height (cm)	BSA (m^2)	Fraction of adult dose		
				Young's rule	Clark's Rule	BSA method
Birth	3.5	50.5	0.21	–	0.05	0.12
3 mos	5.7	59.9	0.29	0.02	0.08	0.17
6 mos	7.5	65.8	0.35	0.04	0.11	0.20
1 yr	9.9	74.7	0.44	0.08	0.15	0.25
2 yrs	12.5	86.9	0.54	0.14	0.18	0.31
3 yrs	14.5	96.0	0.61	0.20	0.21	0.35
4 yrs	16.5	103.4	0.68	0.25	0.24	0.39
5 yrs	19.1	110.5	0.76	0.29	0.28	0.44
6 yrs	21.5	116.8	0.84	0.33	0.32	0.49
7 yrs	24.2	123.2	0.91	0.37	0.35	0.53
8 yrs	26.9	129.0	0.98	0.40	0.39	0.57
9 yrs	29.5	134.1	1.04	0.43	0.43	0.60
10 yrs	32.3	139.4	1.12	0.45	0.47	0.65
11 yrs	35.5	144.5	1.20	0.48	0.52	0.69
12 yrs	39.1	150.9	1.28	0.60	0.57	0.74

Practice Example: What will be the dose for a child of 6 years if the adult dose is 500 mg.

Reducing and enlarging formulae (recipe)

In order to prepare any pharmaceutical product, it is necessary to make it from a *master formula* or *official formula*. This master formula may be scaled down or scaled up depending on the requirement.

Rules for conversion of the formula

1. Determine the total weight or volume of the whole preparation.

2. Calculate the ratio of $\frac{\text{amount to be prepared}}{\text{total amount of the preparation}}$.

   This is called *conversion factor*.

3. Multiply the *conversion factor* with the quantity of each ingredient. The unit should be unchanged.

Example of reducing the recipe

The master formula: Give the working formula for 100 ml preparation.

Ingredient	Quantity required
Drug X	120 g
Sucrose	480 g
Purified water q.s.	1000 ml

The total volume of the preparation is 1000 ml. Required volume of the preparation is 100 ml.

So the conversion factor is $\frac{100}{1000} = 0.1$

The reduced formula

Ingredient	Quantity required for 1000 ml	Conversion factor	Quantity required for 100 ml
Drug X	120 g	100/1000 = 0.1	12.0 g
Sucrose	480 g		48.0 g
Purified water q.s.	1000 ml		100 ml

Example of enlarging the recipe

The master formula: Give the working formula for 2.5 L

Ingredient	Quantity required
Liquid P	35 ml
Solid A	9 g
Liquid R	2.5 ml
Liquid S	20 ml
Purified water q.s.	100 ml

Total volume of the preparation is 100 ml. Required volume of the preparation is 2.5 L i.e. 2500 ml.

So the conversion factor is $\frac{2500}{100} = 25$

The enlarged formula

Ingredient	Quantity required for 1000 ml	Conversion factor	Quantity required for 100 ml
Liquid P	35 ml	2500/100 = 25	875 ml
Solid A	9 g		225 g
Liquid R	2.5 ml		62.5 ml
Liquid S	20 ml		500 ml
Purified water q.s.	100 ml		2500 ml

Exercise: Calculate the amount of ingredients required for preparing 30g of ointment.

Ingredient	Quantity required for 1000 g	Conversion factor	Quantity required for 30 g
Wool fat	50 g	30/1000 = 0.03	1.5 g
Hard Paraffin	50 g		1.5 g
Cetostearyl alcohol	50 g		1.5 g
White soft paraffin	850 g		25.5 g
	Total = 1000 g		

Typical Label for a Formulation

CALAMINE LOTION I.P. 40 ml	
INGREDIENTS	
Calamine	06.0 g
Zinc Oxide	02.0 g
Bentonite	01.2 g
Sodium Citrate	00.2 g
Liquefied Phenol	00.2 ml
Glycerin	02.0 ml
Rose Water q.s.	40.0 ml
MANUFACTURED BY: ABC Pharmaceuticals ***MFG. DATE:*** ***EXP. DATE:***	
USE: Use on skin rashes, minor burns and infections ***DOSE:*** ***STORAGE: Keep in cool place***	
FOR EXTERNAL USE ONLY	
Dispensed By:	

Adult Doses of Few Important Drugs

Category	Drug	Dose	Dosage regimen
ANALGESICS	Metamizole Sodium	500 mg	3-4 times a day
	Aspirin(Dispersible)	350 mg	3 times a day
	Ibuprofen	400 mg	4 times a day
	Rofecoxib	12.5/25/50 mg	Once Daily
	Celecoxib	50/100/200 mg	Twice Daily
	Etoricoxib	30/60/90/120 mg	Once Daily
ANTI PYRETICS	Paracetamol	500 mg	Three times daily
	Nimesulide	100 mg	2 times a day
ANTIBIOTICS	Amoxicillin	500 mg	Every 8 to 12 h
	Ciprofloxacin	500 mg	2 times a day
	Azithromycin	250/500 mg	Once daily
	Roxithromycin	200/400 mg	Twice daily
	Ofloxacin	200/400 mg	Twice daily
ANTIHYPERTENSIVES	Clonidine	100/150/300 µg	1 or 2 times a day as
	Atenolol	50 mg	prescribed
	Lisinopril	7.5/15 mg	Once daily
	Amlodipine	10/20 mg	Once daily
	Valsartan	40/80/120 mg	Once daily
	Candesartan	4/8/16/32 mg	Twice daily
	Telmisartan	20/40/80 mg	Once daily
	Olmesartan	5/20/40 mg	Once daily
			Once daily
ANTI DIABETICS	Glipizide	5 mg	1 or 2 times a day as
	Metformin	500/1000 mg	prescribed
	Canagliflozin	100 mg	Twice daily
			Once daily
ANTI VIRALS	Acyclovir	400 mg	Thrice daily (10 days)
	Rimantidine	100 mg	Once daily
	Zidovudine(HIV)	300 mg	Twice daily
ANTI HISTAMINIC	Cetirizine	10 mg tab	Once daily
	Levoctirizine	5 mg tab	Once daily
	Diphenhydramine	25/50 mg	Once daily
	Fexofinadine	60/180 mg	Once daily
ANTI AMOEBIC	Metronidazole	700 mg	Thrice daily for 5-7 days
	Tinidazole	2 g	Once daily for 3-6 days
	Paromomycin	500 mg	Thrice daily for 7 days
	Ornidazole	500-1000 mg	Once /Twice Daily

Contd…

Category	Drug	Dose	Dosage regimen
ANTI ASTHEMATICS	Noscapine Salbutamol Montelukast Zafirlukast	1.4 mg/ml syrup 2/4 mg 10 mg 10/20 mg	Twice daily Once daily Once daily 20 mg (Twice daily)
STEROIDAL DRUGS	Prednisolone Betamethasone Fludrocortisone		5-60 mg/day 0.5-5 mg /day 50-200 µg daily
ANTI MIGRAINE	Sumatriptan Ergotamine Rizatriptan	50,100 mg tab 2 mg 5/10 mg	Once daily Once daily Once daily
ANTI LIPIDEMIC	Atorvastatin Fluvastatin	10/20/40/80 mg 20/40/80 mg	Once daily Once daily

Pharmaceutical Calculations

Weights and measures:

There are two systems of weights and measurements- Imperial and Metric system. The imperial system is traditional system of weight and measures categorized into systems- Avoirdupois and Apothecaries (also known as Troy System). In Avoidupois system, pound (lb) is the standard unit of weight and all measures of mass is derived from it whereas in Apothecaries system, grain is the standard unit of weight and all measures of mass is derived from it.

Measurements of weights in imperial system

Weight is a measure of the gravitational force acting on a body and is directly proportional to its mass.

(a) Avoirdupois system

In this system **pound (lb)** is taken as the standard of weight (mass).

1 pound avoir (lb)	= 16 oz avoir	**oz** is pronounced as *ounce*.
1 pound avoir (lb)	= 7000 grains (gr)	

(b) Apothecary or Troy system

In this system **grain (gr)** is taken as the standard of weight (mass).

1 pound apoth (lb)	= 12 ounces ($\overline{\overline{\text{ʒ}}}$)	1 pound apoth (lb) = 5760 grains (gr)
1 ounce ($\overline{\overline{\text{ʒ}}}$)	= 8 drachms ($\overline{\text{ʒ}}$)	
1 drachm ($\overline{\text{ʒ}}$)	= 3 scruples (ɜ)	
1 scruple (ɜ)	= 20 grains (gr)	

In summary, the conversion of various units between Avoirdupois and Apothecaries systems has been listed hereunder:

Apothecaries system	Avoidupois system
1 Lb	16 oz or 7000 gr
1oz	437.5 gr
20 grains (gr)	1 scruple
60 grains	1 drachm
480 grains	1 ounce (apothe)
12 ounces	1 pound (apothe)
5760 grains	1 pound (apothe)

Weights in metric system: This system is used in Indian pharmacopoeia (I.P) for measurements of weights and volume and was implemented in India w.e.f. 01.04.1964 in pharmacy profession. A kilogram is the standard unit of weight and all measures of mass are derived from it.

Units	Abbreviated symbols	Equivalent to grams (g)
1 microgram	µg or mcg	0.000,001
1 milligram	Mg	0.001
1 centigram	Cg	0.01
1 decigram	Dg	0.1
1 gram	G	1.0
1 dekagram	Dag	10.0
1 hectogram	Hg	100.0
1 kilogram	Kg	1000.0

Linear measurements in metric system:

Units	Abbreviated symbols	Equivalent to meter(m)
1 inch	In	0.0254
1 nanometer	Nm	1e-9
1 A (angstrom unit)	Å	1e-10
1 micrometer	µm	1e-6
1 millimeter	Mm	0.001
1 centimeter	Cm	0.01
1 decimeter	Dm	0.1
1 meter	M	1.0
1 dekameter	Dam	10
1 hectometer	Hm	100
1 kilometer	Km	1000.0

Measurements of Volumes in Imperical System

1 gallon (c)	= 4 quarts = 160 fl. ounces = 8 pints
1 quart	= 2 pint (o)= 40 fl. ounces
1 pint (o)	= 20 fluid ounce
1 fluid ounce	= 8 fluid drachm= 480 minims
1 fluid drachm	= 3 fluid scruple
1 fluid scruple	= 20 minims

Example:

Convert (i) *quart to minim*

1 quart = 2 pint

= 2 × (20 fluid ounce)

= 2× 20 × (8 fluid drachm)

= 2 × 20 × 8 × (3 fluid scruple)

= 2 × 20 × 8 × 3 × (20 minims)

= 19200 minims

(ii) pint to fluid ounce, (iii) fluid ounce to minim, fluid drachm = minim

Measurements of volumes in metric system

Units	Abbreviated symbols	Equivalent to litres (L)
1 microlitre	µL	0.000,001
1 millilitre	mL	0.001
1 centilitre	cL	0.01
1 decilitre	dL	0.1
1 litre	L	1.0
1 dekalitre	daL	10.0
1 hectolitre	hL	100.0
1 kilolitre	kL	1000.0

Percentage Calculations

Percentages are also commonly used to express the strength of solutions. Usually these solutions are not intended for the oral route of administration. As a percentage this can have four different meanings and in order to make clear the intention the following terms are used:

- **% w/w percentage weight in weight.** This expresses the amount in grams of solute in 100 g of product.

- **% w/v percentage weight in volume.** This expresses the amount in grams of solute in 100 ml of product.
- **% v/v percentage volume in volume.** This expresses the number of millilitres of solute in 100 ml of product.
- **% v/w percentage volume in weight.** This expresses the number of millilitres of solute in 100 g of product.

The strength of solutions of solids in liquids is usually expressed as % w/v, whereas that of liquids in liquids is expressed as % v/v. When the type of percentage is not specified by convention the above rule will apply. For example, % solid in liquid is interpreted as % w/v.

Weight in volume (w/v)

In this case the general formula for 1% (w/v) is:

		The formula is actually:	
Solute	1part by weight	Solute	1 g
Solvent upto	100 parts by volume	Solvent upto	100 ml

Exercise 1: Calculate the quantity of sodium chloride required for 500ml of 0.9% solution.

Ans: 0.9%w/v solution of sodium chloride = $\frac{0.9\text{g Sodium chloride}}{100\text{ml solution}}$

So 500ml solution will contain

$$\frac{0.9\text{g Sodium chloride}}{100\text{ml solution}} \text{ x } 500\text{ml} = \frac{0.9\text{g x } 500\text{ml}}{100\text{ml}} = \frac{0.9 \text{ x } 500}{100}\text{g} = 4.5\text{ g sodium chloride}$$

Exercise 2: Send 100ml of a solution of potassium permanganate of which one part diluted with seven parts of water makes a 1 in 8000 solutions.

Ans. The planning of calculation is as follows:

Original solution	Dilution of the solution	*Final solution* after dilution
Solution of potassium permanganate, x % w/v, 100ml	Solution, x % w/v = 1ml Water = 7ml Volume of solution = 8ml	Potassium permanganate = 1g Volume of solution= 8000ml

So, we have to calculate x. Let us start from final solution.

Concentration of $KMnO_4$ is the final solution = $\frac{1\text{g}}{8000\text{ml}} \text{x } 100\text{ml}\,\%(\text{w}/\text{v})$ = 0.0125 %w/v

Method-1

Let us restructure the problem:

1 ml of x% w/v solution is diluted to a solution of 0.0125%w/v and the final volume is 8ml.

V1 = 1mlV2 = 8ml

S1 = x%w/v S2 = 0.0125%w/v

V1 x S1 = V2 x S2

Or, 1ml x X% = 8ml x 0.0125%

Or, $X\% = \frac{8\text{ml x } 0.0125\%}{1\text{ml}}$

Or, X% = 0.1%

Or, X = 0.1

Method-2

Concentration of initial solution = ?

Concentration of diluted solution = 0.0125% (w/v)

1 ml diluted to 8ml, so dilution factor = 8, i.e. the solution is diluted 8 times

Concentration of initial solution = Concentration of diluted solution × 8 = 0.0125% w/v × 8 = 0.1%w/v

Ans. A 0.1%w/v potassium permanganate solution is to be prepared.

Exercise 3: Send 250ml of 4 percent potassium permanganate solution and label with directions for preparing 1 liter quantities of a 1 in 2500 solution.

Ans. The planning of calculation is as follows:

Original solution	Dilution of the solution	*Final solution* after dilution
Solution of potassium permanganate, 4 % w/v, 250ml	Solution, 4 % w/v = 1ml Water = ?	Potassium permanganate = 1g Volume of solution = 2500ml

Now do it yourself. Do it by Method-2.

Ans: *100 times dilution i.e. 1 ml is diluted with 99ml water to obtain 100ml solution.*

Weight in weight (w/w)

In this case the general formula for 1%(w/w) is:

		The formula is actually:	
Solute	1part by weight	Solute	1 g
Solvent upto	100 parts by weight	Solvent up to	100 g

Problem: Prepare 100ml Phenol Glycerin BPC. It contains 16%w/w phenol in glycerol. Sp.gr. of glycerol = 1.26

Let us assume that phenol is not increasing the volume of the solution.

So the final solution: Volume = 100ml

Volume of glycerol = 100ml

Weight of glycerol = 100ml × 1.26 g/ml = 100 × 1.26 g = 126g

So the working formula will be:

Ingredient	Quantity for 100g	Quantity required for 100ml
Glycerol	84g	126g
Phenol	16g	$\frac{16g}{84g} \times 126g$ = 24g

Volume in volume (v/v)

In this case the general formula for 1%(w/w) is:

		The formula is actually:	
Solute	1part by volume	Solute	1 ml
Solvent upto	100 parts by volume	Solvent upto	100 ml

Problem: Prepare 600ml of 60%v/v alcohol from 95% v/v alcohol.

In this problem: V1 = ? S1 = 95% V2 = 600ml S2 = 60%

V1 x S1 = V2 x S2 or, $V1 = \frac{V2 \times S2}{S1} = \frac{600ml \times 60\%}{95\%} = 379ml$

Ans: 379 ml of 95% alcohol is diluted to 600ml to obtain 60% alcohol.

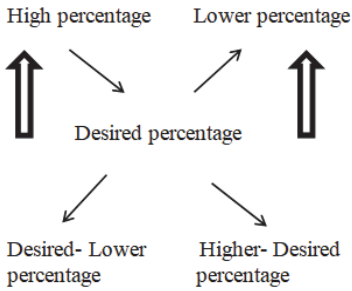
Alligation Method

This method is used to calculate the exact proportions in which substances of different strength or concentration are added to yield a mixture of desired strength or concentration.

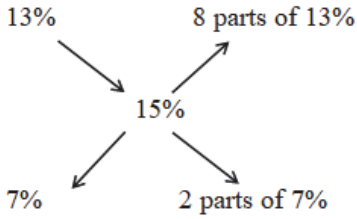
Rules 1- The desired percent (%) or concentration is placed in central position.

Rule 2-The lower percent (%) or concentration is placed on the left side below the center.

Rule 3- The higher percent (%) or concentration is placed on the left side above the center.



Example: In what proportion must a preparation containing 13% of drug be mixed with one 7% of drug to produce a mixture of 15% desired strength?

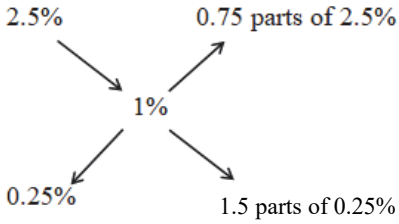


10 parts of 15%

The desired proportion is obtained by subtracting the 7% from 13% and is placed opposite the 13% on the right side and that obtained by subtracting the 15% from 13% is placed opposite the 7% figure on the right side.

Hence, 8 parts of 13% drug mixed with 2 parts of 7% drug shall produce drug mixture of desired strength.

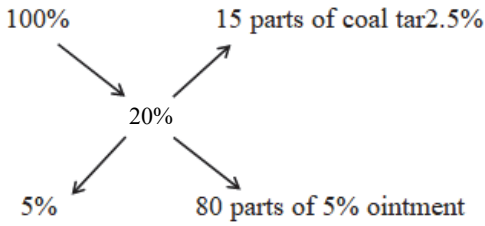
Example: How many grams of 2.5% hydrocortisone cream should be mixed with 360gm of 0.25% cream to make a 1% hydrocortisone cream?



For 2gm of 0.25% = 1gm of 2.5% cream is used

Therefore, for 360gm of 0.25% = 180gm of 2.5% cream is used.

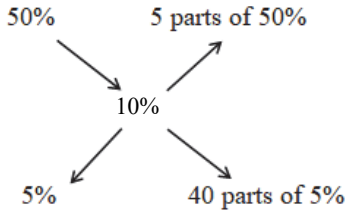
Example: How many grams of coal tar should be added to 3200gm of 5% coal tar ointment to prepare an ointment containing 20% coal tar?



For 16gm of 5% ointment = 3gm of 100% coal tar is needed

Therefore, for 3200gm of 5% ointment= $\frac{3200\times3}{16}$ = 600gm of coal tar is needed.

Example: How many ml of 50% (w/v) dextrose solution and how many ml of 5% (w/v) dextrose solution are required to prepare 4500ml of a 10% (w/v) solution.



For 9 parts = 1 part of 50% is needed

Therefore, for 4500ml = $\frac{4500\times1}{9}$ = 500ml of 50% solution is required.

For 9 parts = 8 part of 5% solution is needed

Therefore, for 4500ml = $\frac{4500\times8}{9}$ 4500 x 8 = 4000ml of 5% solution is required.

Millimolar calculations

The strength of active ingredient within a pharmaceutical preparation can be expressed as the number of millimoles per unit volume or mass of product. The mole is the unit of amount of substance and there are 1000 millimoles in a mole.

To calculate the number of millimoles of an ingredient in a medicinal product, you will firstly need to know the molecular weight of the ingredient. The number of moles of ingredient is the mass of ingredient divided by the molecular mass:

$$\text{Number of moles} = \frac{\text{Mass in grams}}{\text{Molecular Mass}}$$

For example, the molecular weight quoted for Sodium Chloride BP is 58.44. Therefore a molar solution of Sodium Chloride BP would contain 58.44 g of Sodium Chloride BP in a litre.

Example: Prepare 100 ml of Sodium Chloride BP solution containing 1.5 mmol per ml.

Answer:

1 ml contains 1.5 mmol or 100 ml contains 150 mmol

1 mole (1000 mmol) of Sodium Chloride BP weighs = 58.44 g

1 mmol of Sodium Chloride BP weighs =58.44/1000 g

150 mmol of Sodium Chloride BP weighs =58.44/1000 g × 150 g **= 8.766 g**

Proof Spirits:

In the United States Pharmacopoeia, all alcohol concentrations are expressed as volume-in-volume, based on the quantity of absolute alcohol present, as determined at 15.56 °C. Proof spirit was official in B.P. 1885. London Proof spirit means that mixture of ethyl alcohol and water which weighs exactly $12/13^{th}$ part of an equal volume of distilled water at 51°F.

As per Indian standards, strength of alcohol is measured in proof degrees. Proof spirit has a sp. gr. of 091976 at 15.5 °C and contains 57.1% v/v of ethyl alcohol is said to be 100 volume of proof spirit or 100° Proof. Proof spirit is therefore an aqueous solution containing 57.1% v/v of absolute alcohol.

In India the rates of excise duty are prescribed in terms of rupees per litre of proof alcohol. Thus, any %v/v of alcohol can be converted into proof strength and vice versa using the following method.

1. Multiply the percent strength of alcohol by 1.753 and deduct 100 from the product.
2. If the result is positive, it is termed as over proof (°O/P) means strength of alcohol above the proof strength.
3. If the result is negative, it is termed as under proof (°U/P) means strength of alcohol below proof strength.

Therefore, 25 (°U/P) mean that 100 volume of such alcohol are equivalent to 100-25 = 75 volume of proof sprit. 35 (°O/P) mean that 100 volume of such alcohol are equivalent to 100 + 35 = 135 volume of proof spirit.

In summary,

Proof spirit is that mixture of alcohol and water, which at 51^0F weighs $12/13^{th}$ of an equal volume of water.

[N.B. Density of proof spirit = 12/13 of density of water at 51^0F = 0.923 g/ml]

The US System: **Proof spirit** is 50% alcohol by volume (or 42.49% by weight).

The British / Indian system: **Proof spirit** is 57.1% ethanol by volume (or 48.24% by weight.

This means that any alcoholic solution that contains 57.1%v/v alcohol is a proof spirit and is said to be 100 proof.

100 degree proof alcohol = 57.1% v/v alcohol

If the strength of the alcohol is above 57.1%v/v alcohol, then the solution is called "*over proof*" (O.P).

If the strength of the alcohol is below 57.1%v/v alcohol, then the solution is called "*under proof*" (U.P).

Conversion factors: *Conversion of strength of alcohol from %**v/v** to **degrees proof** as per Indian system*

$$\text{Strength of alcohol} = \frac{\%\text{v / v strength}}{57.1\%\text{v / v}} \times 100$$

*Conversion of strength of alcohol from **degrees proof** to **%v/v** as per Indian system*

$$\text{Strength of alcohol in \%v/v} = \frac{\text{Strength of alcohol in degree proof} \times 57.1}{100}$$

Practice Examples

Example 1: Find the strength of 95%v/v alcohol in terms of proof spirit.

Strength of alcohol = $\frac{95\%\text{v / v}}{57.1\%\text{v / v}} \times 100 = 166.34$ degree proof = (166.34-100) degrees over proof = $66.34^{\ 0}$ op

Example 2: Find the strength of 20%v/v alcohol in terms of proof spirit.

Strength of alcohol = $\frac{20\%\text{v / v}}{57.1\%\text{v / v}} \times 100 = 35.03$ degree proof = (100-35.03) degrees under proof = $64.97^{\ 0}$ up

Example 3: Calculate the real strength of 30^0op and 40^0up.

30^0op = (100 + 30) = 130 deg proof

Therefore the strength of alcohol = $\frac{130 \text{ x } 57.1}{100}$ = 74.23%v/v

40^0op = (100 – 40) = 60 deg proof

Therefore the strength of alcohol = $\frac{60 \text{ x } 57.1}{100}$ = 34.26%v/v

Example 4: How many proof gallons are contained in 5 gallon of 70%v/v alcohol?

1 proof gallon = 1 gallon proof alcohol = 1 gallon of 100 degrees proof alcohol

70% v/v alcohol = $\frac{70\%}{57.1\%}$ × 100 degrees proof alcohol

= 122.59 degrees proof alcohol

= $\frac{122.59}{100}$ proof alcohol = 1.226 proof alcohol

5 gallons 70%v/v alcohol = 5 gallons of 1.226 proof alcohol

= 6.13 proof gallon

Example 5: Convert 90%v/v alcohol into proof spirit

As 57.1 volume of ethyl alcohol = 100 volume of proof spirit

1 volume of ethyl alcohol = 100/57.1 = 1.7513 volume of proof spirit

90 volume of ethyl alcohol = 90 × 1.7513 volume of proof spirit

Hence Proof strength of 90% v/v alcohol = (90 × 1.7513) - 100 = 57.6°0/P

Similarly, Proof strength of 30% v/v alcohol can be calculated as follows.

Proof strength of 30%v/v alcohol = (30 × 1.7513) - 100 = -47.5 or 47.5°U/P

Thus 70 °0/P = 100 + 70/ 1.7513 =97% v/v of ethyl alcohol, and

70 °U/P = 100 - 70 / 1.7513 = 17.13% v/v of ethyl alcohol.

Iso-Osmotic and Isotonic Solutions

Iso-Osmotic: If a solution is placed in contact with membrane that is permeable to molecules of the solvent but not permeable to the molecules of the solute, the movement of the molecules of the solvent through the membrane is called ***osmosis***. This type of membrane is called *semi-permeable* membrane. If a solution of a solute having higher concentration of the solute is placed on one side and solution of the same solute having low concentration of the same

solute is placed on the other side of such a membrane, the solvent will tend to pass from the side containing lower solute concentration to the side containing higher solute concentration. This process will continue till an equilibrium with respect to solute concentration is established on both sides of the semi-permeable membrane.

Iso-osmotic: Body fluids like blood, lacrimal fluid, sebum etc. normally has an osmotic pressure that corresponds to the osmotic pressure exerted by 0.9% w/v solution of sodium chloride. Therefore, 0.9% w/v solution of sodium chloride is said to be iso-osmotic with physiologic fluids.

Isotonic: Isotonic means having the same tone. This term has reference to physiological compatibility. For example, a solution of boric acid that is iso-osmotic with both blood and lacrimal fluid is isotonic only with lacrimal fluid. This is because boric acid readily crosses the RBC membrane and causes hemolysis of these cells.

Iso-osmotic is a physical term that compares the osmotic pressure or other colligative properties of two liquids neither of which may be a physiologic fluid or which may behave as a physiologic fluid under a given set of conditions. A solution can be isotonic with a living cell only when there is no net gain or loss of water by the cell, or another change in the cell. Physiologic solutions with an osmotic pressure lower than that of body fluids, or 0.9% w/v sodium chloride solution are referred to as being *hypotonic*. Physiologic solutions having a greater pressure than the body fluids or 0.9% w/v sodium chloride solution are termed *hypertonic*.

Isotonicity: A solution is isotonic with a living cell if there is no net gain or loss of water by the cell, when it is in contact with this solution.

If a living cell is kept in contact with a solution and there is no loss or gain of water by the cell then the solution is said to be *isotonic* with the *cell*.

- It is found that the osmotic pressure of 0.9%w/v NaCl solution is same as blood plasma. So 0.9%w/v NaCl solution is *isotonic* with plasma.

  Tonicity– A. Isotonic – When a solution has same osmotic pressure as that of 0.9%w/v NaCl solution.

  B. Paratonic – Not isotonic

  (a) Hypotonic – The osmotic pressure of the solution is higher than 0.9% w/v NaCl solution

  (b) Hypertonic – The osmotic pressure of the solution is lower than 0.9% w/v NaCl solution

Test of tonicity

A red blood corpuscle is placed in a solution and after some time it is viewed under microscope.

Observation	Conclusion	Mechanism
The shape and size of the cell remained unchanged	The solution is isotonic	Osmotic pressure of the cell fluid and the solution are same. No movement of water occurs across the cell membrane.
The size of the cell increased and may burst.	The solution is hypotonic.	Osmotic pressure of the cell fluid is more than the solution. Water molecules moved from the solution to the interior of the cell, so the cell swelled.
The size of the cell is reduced or shrinked.	The solution is hypertonic.	Osmotic pressure of the cell fluid is less than the solution outside. Water molecule moved from the interior of the cell to the solution.

N.B. If the red blood cell bursts then the hemoglobin comes out of the cell and the plasma become red in color. This phenomenon is called haemolysis.

Importance of adjustment of tonicity in pharmaceutical dosage forms

1. *Solution for intravenous injection*: The injection must be isotonic with plasma, otherwise the red blood corpuscle may be haemolysed.
2. *Solution for subcutaneous injection*: Isotonicity is required but not essential, because the solution is coming in contact with fatty tissue and not in contact with blood.
3. *Solution for intramuscular injection*: The aqueous solution may be slightly hypertonic. This will draw water from the adjoining tissue and increase the absorption of the drug.
4. *Solution for intracutaneous injection*: Diagnostic preparations must be isotonic, because a paratonic solution may cause a false reaction.
5. *Solutions for intrathecal injection*: Intrathecal injections are introduced in the cavities of brain and spinal chord. It mixes with the cerebrospinal fluid (CSF). The volume of CSF is only 60 to 80ml. So a small volume of paratonic injection may change the osmotic pressure of the CSF, which may lead to vomiting and other side effects.
6. *Solutions for nasal drops*: Aqueous solutions applied within the nostril may produce irritation if it is paratonic. So nasal drops must be isotonic with plasma.
7. *Solutions for ophthalmic use*: Only one or two drops of ophthalmic solutions are generally used. So it is not essential for eyedrops to be isotonic. Slight paratonicity will not produce great irritation because the eyedrops will be diluted with the lachrymal fluid.

Calculations for adjustment of tonicity

N.B. It is difficult and time consuming to determine the osmotic pressure of a solution. So some indirect methods are adopted to compare between two isotonic solutions. Two solutions will produce same osmotic pressure if both contain the same numbers of *ultimate units*. These units may be as follows:

- ✓ These units may be molecules in case of substances those do not ionize.
- ✓ These units may be ions in case of substances those ionize.
- ✓ These units may be both ions and unionized molecules in case of weak electrolytes.

Some physical properties of these solutions depend on this number (or, collection) of units, such as osmotic pressure, freezing point depression (ΔT_f), vapor pressure etc. – these physical properties are called *colligative properties* of the solutions.

Since these colligative properties are inter-dependent, so osmotic pressures of two solutions can be compared from their colligative properties like freezing point depression.

Tonicity of a solution can be adjusted by the following methods:

1. Freezing point depression method (ΔT_f)
2. Sodium chloride equivalent method (*E*)
3. Isotonic solution V-Value method

OSMOL: It is the weight in grams of a solute existing in a solution as molecules (and / or ions, macromolecules, aggregates, etc), which is osmotically equivalent to a mole of an ideally behaving nonelectrolyte. Hence, the osmol weight of a nonelectrolyte in a dilute solution is equal to its gram molecular weight. Therefore, 1 osmol will be the amount of solute that will provide 1 Avogardo's number (6.023×10^{23}) particles in solution. It is also the amount of solute that on dissolution in 1 Kg water will produce an osmotic pressure increase of 17,000 torr at 0ºC or 19,300 torr at 37ºC.

Example: **For Nonelectrolyte - Dextrose**

1 mol of anhydrous dextrose = 180 g

1 osmol of anhydrous dextrose (nonelectrolyte) = 180 g

Therefore, 180 mg of anhydrous dextrose dissolved in 1 Kg water will produce an increase in osmotic pressure of 19.3 torr at 37ºC (body temperature).

For electrolyte – Sodium chloride

1 molecule of sodium chloride will produce one sodium and one chloride ion.

Therefore, 1 mol represents 2 osmol of sodium chloride.

Hence, 1 osmol Sodium chloride = 58.5 g / 2 = 29.25 g

Therefore, 29.25 = 6.023 x 10^{23} ions (particles)

Osmolality & Osmolarity

Osmolality:

1 osmolal concentration = 1 osmol of solute / Kg of water

Osmolal solutions represent a w/w relationship between the solute and solvent.

Example: **For nonelectrolyte - Dextrose**

An osmol of any nonelectrolyte is equivalent to 1 mol of that compound, therefore, 1 osmolal solution of a nonelectrolyte is equal to its 1 molal solution.

For ionizing electrolyte – Sodium chloride

1 osmol = 0.5 mol of sodium chloride

Therefore, 1 osmolal solution of sodium chloride = 0.5 molal solution

Osmolarity:

1 osmolar solution = 1 osmol of solute per 1 L of solution.

Osmolar solutions represent a w/v relationship between solute and solvent.

Example: **For nonelectrolyte - Dextrose**

1 osmolar = 1 molar solution

For ionizing electrolyte – Sodium chloride

1 osmolar solution will contain 1 osmol of sodium chloride per liter which will be a 0.5 molar solution.

NOTE: A 1 osmolar solution of a solute will always be more concentrated than a 1 osmolal solution.

Calculation of Osmolarity

$$\textbf{Osmolarity}\left(\frac{mOsmol}{L}\right)=\frac{g}{L}\times\frac{mols}{g}\times\frac{osmol}{mol}\times\frac{1000mOsmol}{osmol}$$

The number of osmol / mol is equal to 1 for nonelectrolytes and is equal to number of ions per molecule for strong electrolytes.

0.9% sodium chloride has an osmolar concentration of 308 mOsmol/L and a concentration of 154 mOsmol/L in either sodium or chloride ion.

2. $$\frac{gwater}{mLsolution} = \frac{gsolution}{mLsolution} - \frac{gsolute}{mLsolution}$$

Then, Osmolarity

$$\left(\frac{mOsmol}{Lsolution}\right) = osmolality\left(\frac{mOsmol}{1000gwater}\right) \times \left(\frac{gwater}{mLsolution}\right)$$

Osmolality depends on the number of particles in the solution. The number of particles, in turn, influence the colligative properties of a solution namely osmotic pressure elevation, boiling point elevation, vapor pressure depression and freezing point depression.

Methods of Adjusting Tonicity

1. Freezing point depression method

The freezing point of normal, healthy human blood is – 0.52ºC. This means that in water as medium, any suspended or dissolved solute that freezes at – 0.52ºC will be isotonic with blood. Also, it is known that 0.9% w/v solution produces freezing point depression of 0.52 ºC. Therefore, a 0.9% w/v solution of sodium chloride is isotonic with human blood, serum, lacrimal fluid etc.

The Tables available in the literature list "D" values of many solutes. The "D" value has units of ºC/y% drug. For example, a "D" value of 0.05º/ 0.5% drug means that the drug will produce a freezing point depression of 0.05ºC when used at a concentration of 0.5% w/v. "D" value is nearly proportional to concentration.

Example 1	Dexamethasone sodium phosphate	0.1%
	Purified water qs	30 mL
	"D" value given is 0.050º / 0.5%	

A. Contribution of 0.1% drug towards freezing point depression will be:

(0.050 x 0.1) / 0.5 = 0.010ºC

Freezing point depression of human blood = 0.52ºC

Freezing point depression remaining to be contributed by adding sodium chloride = 0.52 – 0.010 = 0.51 ºC

0.9% w/v sodium chloride provides freezing point depression of 0.52ºC

Therefore, 0.51ºC depression in freezing point will be provided by (0.9 x 0.51) / 0.52 = 0.883% sodium chloride

For 30 mL solution the amount of sodium chloride needed will be (0.883 x 30) / 100 = 0.265 g sodium chloride

(B) If this solution has to be made isotonic by adding dextrose ("D" value = 0.091ºC/1%)

Then, 0.091 ºC freezing point depression will be provided by 1% dextrose

Therefore, 0.51ºC depression will be provided by: (0.51 x 1) / 0.091 = 5.6% dextrose

For 100 mL the quantity of dextrose required is 5.6g

Therefore, for 30 mL solution, the quantity of dextrose required will be: (5.6 x 30) / 100 = 1.68g dextrose

Hence, 1.68g dextrose can be added instead of 0.265g sodium chloride to make this solution isotonic.

2. Sodium chloride equivalent method

This method uses "E" value listed in the literature. "E" value is the weight of sodium chloride that will produce the same osmotic effect as 1g of the drug. For example, a "E" value of 0.18 means 0.18g of sodium chloride can produce the same osmotic effect as 1g of drug.

Example 1	Dexamethasone sodium phosphate	0.1%
	Purified water qs	30 mL
	"E" value given is 0.18	

A. Total quantity of drug in formulation will be: (30 x 0.1) / 100 = 0.03g

Total quantity of sodium chloride required for 30 mL if there was no drug = (30 x 0.9) / 100 = 0.27g

Contribution of drug in terms of sodium chloride: (0.18 x 0.03) / 1 = 0.0054g

Therefore, quantity of sodium chloride required to make 30 mL solution isotonic = 0.27 – 0.0054 = 0.265g

B. If this solution has to be made isotonic by adding dextrose ("E" value = 0.16)

0.16g sodium chloride is equivalent to 1g drug in terms of isotonicity

0.265g sodium chloride will be equivalent to: (0.265 x 1) / 0.16 = 1.66 dextrose

Hence, 1.66g dextrose can be added instead of 0.265g sodium chloride to make this solution isotonic.

3. Molecular concentration method

At normal temperature and pressure a solution containing 1 g molecule of a non-ionizing solute in 22.4 L has an osmotic pressure of 1 atmosphere.

This means that a solution containing 1 g molecule in 1 L (molar solution) will have an osmotic pressure of 22.4 atmosphere.

Osmotic pressure of blood plasma is 6.7 atmosphere

Therefore, molarity of plasma = 6.7 / 22.4 = 0.3M

Hence, 0.3M solution of any non-ionizing solute will be iso-osmotic with plasma.

For ionizing solutes, iso-osmoticity can be calculated by 0.3M / N, where 'N' is the number of ions.

pH AND BUFFER SOLUTIONS

A proton binds with a molecule of water to produce a hydronium ion, i.e. $H_2O + H^+ = H_3O^+$.

Mathematically the pH of a solution is defined as the negative logarithm of hydrogen ion (more appropriately hydronium $H_3O^{+)}$ concentration in **molarity**.

$$pH = - \log [H_3O^+]$$

Buffer / buffer solution / buffered solution refer to the ability of an aqueous solution to resist a change of pH on adding acid or alkali, or on dilution with a solvent.

N.B. Distilled water has very little buffer action, hence carbon dioxide of air, when equilibrated with distilled water (pH = 7.0), the pH of the water changes to 5.7.

A solution will show buffer action if a conjugate acid-base pair is present in the solution.

e.g. $CH_3COOH + H_2O \rightleftharpoons CH_3COO^{--} + H_3O^+$

Weak acid	Weak base	Strong base	Strong acid

The dissociation constant, $Ka = \frac{[CH_3COO^-][H_3O^+]}{[CH_3COOH]}$

Taking logarithm of both hand sides we get,

$$\log Ka = \log [CH_3COO^-] + \log [H_3O^+] - \log [CH_3COOH]$$

Multiplying –1 with both hand sides yield:

$$- \log Ka = - \log [H_3O^+] + \log [CH_3COOH] - \log [CH_3COO^-]$$

or, $$pKa = pH + \log [CH_3COOH] - \log [CH_3COO^-]$$

or, $$pH = pKa - \log [CH_3COOH] + \log [CH_3COO^-]$$

or, $$pH = pKa + \log \frac{[CH_3COO^-]}{[CH_3COOH]}$$

or, $$pH = pKa + \log \frac{[base]}{[acid]}$$

This equation is called **Henderson-Hasselbalch equation.**

This ratio of $\frac{[base]}{[acid]}$ and Ka determines the pH of the solution. For a certain weak acid or base Ka is constant, so if the ratio of concentrations of the [base] / [acid] is changed the pH of the buffer solution can be changed.

This equation can be used in the following buffer systems:

Name of the buffer system	Conjugate acid	Conjugate base
Acetic acid – Sodium acetate buffer	Acetic acid (CH_3COOH)	Acetate ion (CH_3COO^-)
Ammonia – Ammonium chloride buffer	Ammonium ion (NH_4^+)	Ammonia (NH_3)
Monosodium phosphate – Disodium phosphate	Monosodium phosphate (NaH_2PO_4)	Disodium phosphate (Na_2HPO_4)
Phenobarbital – Sodium phenobarbital	Phenobarbital	Sodium phenobarbital

Use of Henderson – Hasselbalch equation

1. The pH of a buffer solution can be calculated if the pKa, concentration of the base and acid are known.
2. During preparation of a buffer solution the ratio of the concentration of the conjugate acid and base pair can be calculated.
3. To calculate the buffer capacity of a buffer solution.

Example 1: *What will be the pH of a solution containing acetic acid and sodium acetate, each in 0.1M concentration? Ka of acetic acid is 1.8 x 10^{-5} at 25^0C.*

Ans: pKa = – log Ka = – log 1.8 x 10^{-5}. = – (log 1.8 + log $^{10-5}$) = – (0.26 – 5) = – (–4.74) = 4.74

Concentration of acid = [acid] = $[CH_3COOH]$ = 0.1M

Concentration of base = [base] = $[CH_3COO^-]$ = 0.1 M

From Hender- Hasselbalch equation we get

$$pH = pKa + \log \frac{[base]}{[acid]} = 4.74 + \log \frac{0.1}{0.1} = 4.74 + \log 1 = 4.74 + 0 = 4.74$$ *Ans.*

Example 2: *An acetic acid- acetate buffer is to be prepared having pH 4.5. What will be the ratio of the molar concentration of the acid base pair. Given pKa of acetic acid = 4.74.*

Ans: Using Henderson – Hasselbalch equation we get:

$$pH = pKa + \log\frac{[base]}{[acid]} \qquad \text{or,} \quad pH - pKa = \log\frac{[base]}{[acid]}$$

$$\text{or,} \quad \frac{[base]}{[acid]} = \text{antilog}\,(pH - pKa) = 10^{(pH - pKa)} = 10^{(4.5 - 4.74)} = 10^{-0.24} = 0.575$$

The answer is [sodium acetate]:[acetic acid] = 0.575: 1

Buffer Capacity

The ability of a buffer solution to resist changes in pH upon addition of acid or alkali is measured in terms of *buffer capacity* of the solution.

Van Slyke has defined the *buffer capacity* as follows:

The amount (gm-equivalent) of strong acid or strong base, required to be added to a solution to change its pH by 1 unit.

In mathematical form: *Buffer capacity of a solution* =

$$\frac{\text{gm eq of a strong acid or strong alkali added}}{\text{change of pH}}$$

Example 3: *(a) What is the change of pH on adding 0.01mol of NaOH to 1 L of 0.10 M acetic acid? (b)Calculate the buffer capacity of the acetic solution. Ka = 1.75 x 10^{-4}.*

Ans:

(a) Calculation of pH of 0.1 M solution of acetic acid

$$[H_3O^+] = \sqrt{Ka[CH_3COOH]} = \sqrt{1.75 \times 10^{-4} \times 0.1} = 4.18 \times 10^{-3}.$$

Therefore pH = – log (4.18 x 10^{-3}) = – (–2.38) = 2.38

(b) On adding 0.01moles of NaOH, 0.01 mol of acetic acid will be converted to form 0.01 mol of acetic acid.

So after addition of NaOH $[CH_3COO^-]$ = 0.01mol/ L = 0.01M

$[CH_3COOH]$ = (0.10mol – 0.01mol)/L = 0.09 mol / L = 0.09 M

Applying Henderson – Hasselbalch equation to calculate the pH of the final solution we get:

$$pH = pKa + \log\frac{[base]}{[acid]} = 4.76 + \log\frac{[0.01]}{[0.09]} = 4.76 + (-0.954) = 3.81$$

Therefore the change in pH after addition of NaOH = final pH – initial pH = 3.81 – 2.38 = 1.43

So, from definition the

Buffer capacity of the solution =

$$\frac{\text{eqwt of NaOH added}}{\text{change in pH}} = \frac{\text{mols of NaOH added}}{\text{change in pH}} = \frac{0.01}{1.43} = 0.007\ \textit{Ans.}$$

Example 4: *(a) What is the change of pH on adding 0.01mol of NaOH to 1 L of buffer solution of 0.10 M acetic acid 0.1M of sodium acetate? (b)Calculate the buffer capacity of the solution. Ka = 1.75 x 10^{-4}.*

Ans:

(a) The pH of the buffer solution before addition of NaOH is

$[base] = [CH_3COO^-] = 0.1M$

$[acid] = [CH_3COOH] = 0.1\ M$

$$pH = pKa + \log\frac{[base]}{[acid]} = 4.76 + \log\frac{[0.1]}{[0.1]} = 4.76 + \log(1) = 4.76 + 0 = 4.76$$

(b) On adding 0.01mol of NaOH per litre to this buffer solution 0.01mol aicd will be converted to base:

$[base] = [CH_3COO^-] = (0.10mol + 0.01mol) / L = 0.11mol / L = 0.11\ M$

$[acid] = [CH_3COOH] = (0.10mol – 0.01mol) / L = 0.09\ mol/L = 0.09\ M$

$$pH = pKa + \log\frac{[base]}{[acid]} = 4.76 + \log\frac{[0.11]}{[0.09]} = 4.76 + \log(1.22) = 4.76 + 0.09 = 4.85$$

Therefore the change in pH after addition of NaOH = final pH – initial pH = 4.85 – 4.76 = 0.09

So, from definition the

Buffer capacity of the solution =

$$\frac{\text{eqwt of NaOH added}}{\text{change in pH}} = \frac{\text{mols of NaOH added}}{\text{change in pH}} = \frac{0.01}{0.09} = 0.111\ \textit{Ans.}$$

So, this buffer solution has greater buffer capacity (0.111) than the solution in problem-3 (0.007).

Calculations Based on Radioisotopes

Disintegration Rate of a Radioisotope

Radioisotope nucleus → Daughter nucleus

The rate at which the radio-isotopes are degrading = $\frac{dN}{dt}$	where, N is the number of radioactive nuclei left to be disintegrated at time t
It is found that the degradation follows first order kinetics, i.e. $\frac{dN}{dt} = \lambda N$,	where λ = decay constant of the radionucleide

So, $\frac{dN}{dt} = \lambda N$ or, $\frac{dN}{N} = \lambda\, dt$

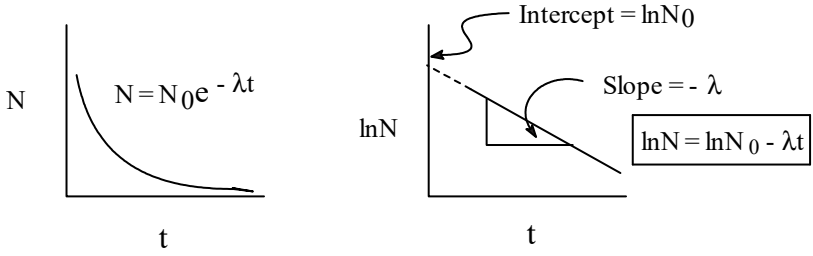
Integrating both sides we get

$$\int_{N_0}^{N} \frac{dN}{N} = \lambda \int_{0}^{t} dt \quad \text{or, } [\ln N]_{N_0}^{N} = \lambda (t - 0) \text{ or, } \ln N = \ln N_0 - \lambda t \text{ or, } \ln \frac{N}{N_0} = -\lambda t$$

or, $N/N_0 = e^{-\lambda t}$ or, $N = N_0 e^{-\lambda t}$

N_0 = initial number of radioactive nuclei

N = number of radioactive nuclei at time t



Half-life of radioactive nuclei

The time taken for half of the radioactive nuclei to disintegrate (i.e. for the activity to fall to half of its original value) is known as the half-life ($t_{1/2}$)

At time, t = 0 $N = N_0$.

At time, $t = t_{1/2}$ $N = N_0/2$

Therefore, $\ln \frac{N}{N_0} = -\lambda t$, or, $\ln \frac{N_0/2}{N_0} = -\lambda t_{1/2}$

or, $\ln (1/2) = -\lambda t_{1/2}$. or, $-\ln 2 = -\lambda t_{1/2}$. or, $t_{1/2} = \frac{0.693}{\lambda}$

Units of radioactivity

One g of radium was selected as the unit of radioactivity and was called *Curie*.

From 1 *curie* (Ci) radium 3.7 x 10^{10} numbers of nuclei disintegrates per second.

So 1 Ci = 3.7 x 10^{10}*dnps* *dnps* = disintegrating nucleus per second

Example:

The activity of a sample solution of ^{131}I was 500 μCi (microcurie) /ml at noon on Monday. Calculate its activity at 4.0 p.m. on Thursday. (Half-life of ^{131}I = 8days)

***Solution*:** $t_{1/2}$ = 8 days = 8 x 24 hours = 192 hours

From equation, $t_{1/2} = \frac{0.693}{\lambda}$, we get $\lambda = \frac{0.693}{t_{1/2}} = \frac{0.693}{192\,\text{hr}} = 0.00361\ \text{hr}^{-1}$.

From equation $\ln N = \ln N_0 - \lambda t$

In this problem N_0 = 500 μCi /ml

t = the time from 12 noon Monday to 4 p.m. Thursday = 3 × 24 + 4 = 76 hrs

$\therefore \ln N = \ln 500 - 0.00361 \times 76$

$= 6.218 - 0.2743$

$= 5.994$

or, $N = e^{5.994} = 381..1$

Ans. At 4 p.m. Thursday the radioactivity will be 381.1 μCi / ml.