SHAMBHUNATH INSTITUTE OF PHARMACY, JHALWA, ALLAHABAD

LECTURE NOTES
ON

PHARMACEUTICS -I

UNIT -I

(BP-103T)

B. PHARM. 1st Year 1st Sem

BY

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UNIT I

HISTORY OF PHARMACY AND PHARMACOPOEIA

ORIGIN AND DEVELOPMENT OF PHARMACY:

In ancient times, people used to think that the diseases are caused due to evil forces or God's anger. Thus some magicians or religious persons were involved in the treatment of patients.

Ancient man learned from observation of birds and beasts. Eventually, he applied his knowledge for the benefit of others. As the time progressed, the human race used to depend up on the plant derivatives for the treatment of illness.

The pharmacy profession can be traced back to the Sumerian population, living in modern day Iraq. From around 4000 BC, they used medicinal plants such as liquorice, mustard, myrrh and opium. There were separate people who worked to prepare medicines as a separate role from diagnosis and treatment which was carried out by doctors. The Sumerians wrote the earliest surviving prescriptions from at least 2700 B.C. – so nearly 5000 years ago.

The Ancient Egyptians had specific preparers of medicine, known as *Pastophor*. Pharmacy was viewed as a high status branch of medicine.

From surviving papyrus scrolls, notably the Ebers Papyrus which dates from 1500 BC, we know that the Egyptians made and used infusions, ointments, lozenges, suppositories, lotions, enemas, and pills. The Ebers Papyrus includes 875 prescriptions and 700 drugs.

Meanwhile, in China in about the same era (2000 BC), a man called Shen Nung wrote the first *Pen T'sao* or native herbal, which contained descriptions of 365 plant-based drugs.

Stalls and shops selling medicinal goods existed around 1900 B.C. in the town of Sippara on the Euphrates river. However, the earliest recorded shop dealing with sales of medicines in London was opened in 1345.

Greeks were one of the first patrons of this profession. The word pharmacy originated from the Greek word "**PHARMAKON**".

It was in 9th century in the civilized world around Baghdad that the profession of pharmacy started acquiring shape.

It slowly spread to Europe as alchemy and finally developed into chemistry. The first known chemical process was carried out by the artisans of Mesopotamia, Egypt and China.

However in the 19th century it completely sprouted out from medicine and started developing as a separate profession.

This happened only when the role of pharmacist as a compounder of medicines were identified and differentiated from physician whose role was accepted as the therapist.

The practice in those times was restricted to compounding, dispensing medication and manufacturing medicaments in bulk lots not for general sale.

The medicament commonly produced was simple elixirs, spirits, and powders in contrast to the complex pharmaceutical remedies of the present era.

The 19th century witnessed various milestones being set in the field of pharmacy. In 1821, first school of pharmacy was established in U.S at Philadelphia.

The first U.S pharmacopoeia was published in 1820.

American pharmacist association was founded in 1852.

The first National formulary was published in 1888.

HISTORY OF PHARMACY 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. In our country, **Ayurveda** was the ancient science of life. Vedas and Upanishads provide information pertaining to medicinal plants. Next to Ayurvedic system, **Siddha system** was in practice in south India and with the advent of Mughals, **Unani system** came into practice. 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.

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 imoported, manufacturer abroad took advantage of the situation. The consequences were as follows:

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

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

Government of India on 11th August 1930 , appointed a committee under the chairmanship of Late Col. R.N.Chopra to see 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. M.L.Schroff (Prof. Mahadeva Lal Schroff) initiated pharmaceutical education at the university level in the Banaras Hindu University.

1940: Govt. brought 'Drugs Bill'to regulate the imort, 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.

1948: Pharmacy Act 1948 published.

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 have come in force in some states but other states lagged behind.

1955: First Edition of Indian Pharmacopoeia was published.

Govt. of India controls the price of drugs in India by Drugs Price Order changed from time to time.

The inception of **pharmacy profession in India** was marked by the first class of the chemist and druggist conducted at the Madras medical college in 1870s to train students to gain skills in pharmacy practice. Pharmacy education pattern was based on the instructions provided by the pharmaceutical society of Great Britain. A formal training of the compounders was started in 1881 in Bengal.

The pharmacy profession entered India almost simultaneously. For almost half a century not much progress was noticed, until B. Pharm. course was started in 1937 at Banaras Hindu University and in 1944 at the Punjab University, Lahore now in Pakistan. The B. Pharm. course at BHU was industry oriented while that at Punjab University was oriented towards Pharmacy practice. Though the profession was oriented towards pharmacy practice at the introductory stage but as it grew it became more industry oriented. This bend lead to the development of modern Indian pharmaceutical industry, which is now the 4th in terms of volume and 14th in terms of value. The future prediction for the Indian pharmaceutical industry is that it is expected to become the super power by the year 2020. The future of a pharmacy is in pharmacy practice. So, it is now observed that pharmacy in India is going back to from where it started: Pharmacy Practice.

CAREERS IN PHARMACY

SCOPE AND POTENTIAL OF PHARMACY

Business Drug Store Whole sale Repacking Bulk drug distribution Cosmetic manufacturing	D. PHARM	Service Hospital Pharmacy Chemist in Drug Store / Whole sale store Medical representative Packaging, store maintenance in Pharmaceutical Industry Secretary / PA to MD in Pharm. industry
Business Pharmaceutical industry Bulk Drug Manufacturing Pharmacist job abraod Cultivation of medicinal plants Public testing laboratories Consultancy	B.PHARM. M. PHARM. PhD	FDA job Teacher diploma courses Production Marketing Teacher for Graduate level courses Research and development

Career Scope for Pharmacy Professionals

A career in pharmacy, unfolds a vista full of opportunities leading to a golden future for a young career aspirant. The job opportunities, working conditions, job satisfaction and monetary benefits are excellent. The various vocations a pharmacy professional can opt, for, are discussed below

Production & Manufacturing

A pharmacy professional can work as a production person (chemist, officer, executive, manager, vice-president), involved in the production of bulk drug & intermediates or formulations and dosage forms. Industries manufacturing cosmetics, soaps, toiletries and dental products also hire pharmacy professionals. Blood and plasma products as well as biological & biotechnological products are other areas with immense potential worldwide.

Production of biological & biotechnological products, surgical dressings, medical devices, equipment, ayurvedic/ homeopathic / unani medicines, veterinary medicine, perfumery, fragrances, nutraceuticals also involve the presence of pharmacy professionals in their production.

Research & Development

This forms the heart of any industry, as it is the key to growth and sustenance. Mainly M. Pharms & Ph.Ds are in great demand in the various areas of Pharmaceutical Research &

Development such as New Drug Discovery Research, Process Development, Formulation & Development, Clinical Trials, Bio equivalence studies and Toxicological Studies.

Analysis & Testing
Quality control (QC) and Quality Assurance (QA) are the most integral areas of the drug & pharmaceutical industry. Highly specialized and trained staff are required to handle sensitive analytical procedures & sophisticated equipment. M.Pharms & Ph.Ds in Pharm. Analysis /Q. A. are highly preferred for this job.

Marketing
The Pharma. Sales & Marketing is a highly technical field & offers excellent opportunities for the pharmacy graduates. An aspirant of a highly bright future can enter through various openings like starting his own retail or wholesale drug store or becoming a professional sales representative (known as medical Sales Representative or M. R.) to the levels of International Marketing & Exports. The monetary rewards and perks are the best.

Hospital Pharmacy
Like U.S.A. & Canada, this trend is already set in many hospitals in our country. The Pharmacist is the best-informed qualified drug expert whose advice is sought by everybody regarding the dosage, incompatibilities and side effects of drugs.

Community Pharmacy
This concept is rapidly catching up the Healthcare service in our country. A pharmacist becomes a vital link between the patients and the products i.e., drugs.

Opportunities
Golden opportunities galore for qualified Pharmacy professionals in various countries. There are plenty of higher education and research opportunities in the developed western countries along with excellent job openings. The monetary job benefits abroad are highly exciting.

Academics
This is a profession associated with job satisfaction and social status as teaching is considered to be noble profession. The posts in the hierarchy are Lecturer, Sr. Lecturer, Reader, Asst. Professor, Professor, Principal etc. The emoluments are satisfactory. Besides teaching Academic related opportunities involve positions on Research Posts and Training programs.

Regulatory Affairs
Locally the F. D.A. (Foods & Drugs Control Administration) is the main regulatory body governing and implementing the rules and regulations for the Drug & Pharma industry. The job opportunities range from the levels of a Drug Inspector (D. I.), Sr. D. I., Asst. Drug Controller, Deputy Drug Controller, Drug Controller of state and finally D.C. I. (Drug Controller of India). A graduate in Pharmacy is the minimum eligibility. Since, the business involved is worth multibillion dollars, this branch has assumed tremendous significance and is bound to grow enormously, in the Post-GATT era. Regulatory experts are thus in great demand. Similarly, Patents and Trademarks, I.P.R. Experts are also in high demand as far as the pharma. industry is concerned.

Self employment
Self employment - can establish his own manufacturing facilities and register the same.

Documentation, Library Information Services & Pharma. Journalism
Most of the major Indian Pharma. companies have established separate Documentation Departments with a highly technical & skilled staff for this purpose. Similarly, the R & D & Q. C. Departments of the Pharma. Companies need Library Information services. Pharma-Journalism is already a very lucrative business in this field.

Consultancy
This is an ideal opportunity for highly technical and experienced pharmacy professionals to earn handsomely as self-employed entrepreneurs, even after the age of retirement.

PHARMACIST IN GOVERNMENT SERVICE

- **Pharmacist in Army, Navy, Air force & Govt. Hospitals**
- **Drug Inspectors**
- **Scientists- Food and Drugs laboratories**
- **Forensic Scientists**
- **Research on tropical diseases, public health**
- **Toxicologist microbiologist**
- **Govt. Approved Chemist**
- **Consultants (mental health, family planning, pollution, poisons, self-medication, immunization)**

INTRODUCTION TO PHARMACOPOEIAS

PHARMACOPOEIA / FORMULARIES / COMPENDIA

Pharmacopoeia, pharmacopeia, or pharmacopoea (literally, "drug-making"), in its modern technical sense, is a book containing directions for the identification of compound medicines, and published by the authority of a government or a medical or pharmaceutical society.

Descriptions of preparations are called monographs. In a broader sense it is a reference work for pharmaceutical drug specifications.

The books containing the standards for drugs and other related substances are known as pharmacopoeia and formularies - collectively these books are known as the drug compendia. The pharmacopoeias or formularies contain a list of drugs and other related substances regarding their source, descriptions, standards, tests, formulae for preparing the same, action and uses, doses, storage conditions etc.

These books are prepared under the authority of the Government of the respective countries. The word "pharmacopoeia" is derived from the Greek words '*pharmacon'* meaning 'drug' and '*poieo'* means 'make'. Literally it means that it is a list of medicinal substances, crude drugs and formulae for making preparations from them.

These books are revised from time to time so as to introduce the latest information available as early as possible after they become established. In order to keep the size of book within reasonable limit it becomes necessary to omit certain less frequently used drugs and pharmaceutical adjuvants from each new edition of the book. Therefore, in each new edition of these books certain new monographs are added while the older ones are deleted.

For the preparation of these books the expert opinion of medical practitioners, teachers and pharmaceutical manufacturers are obtained.

CLASSIFICATION

The drug-compendia are classified as:

(i) Official compendia
(ii) 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.

e.g. 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.

e.g. Merck Index
Extra Pharmacopoeia (Martindale)
United States Dispensatory etc.

NATIONAL PHARMACOPOEIAS

Pharmacopoeias are generally prepared under the authority of the government of the respective countries - these pharmacopoeias are known as national pharmacopoeias.
Example of some national pharmacopoeias are as follows:-
Indian Pharmacopoeia, British Pharmacopoeia, united States Pharmacopoeia etc.

The drugs used may vary from nation to nation so, the respective pharmacopoeia includes those drugs or dosage forms which are frequently used in that very country at that time.

The national pharmacopoeia is recognized as the reference book by the legislative authority (by law) of the respective country, Whenever a conflict arises regarding drugs these books will be referred.

IMPORTANCE OF PHARMACOPOEIA

The importance of Pharmacopoeia can be discussed from the following three angles:

(i) Drug industry
(ii) Administration
(iii) Academic

From the point of view of drug industries

To market a new drug molecule stupendous amount of money is required for the research and development. Very few companies can bear this cost, especially the drug industries in developing countries (like India) are unable to bear the expenditure. In that case the drugs of products mentioned in the pharmacopoeias can be marketed without any further research on it, because only the tested, safe and efficacious drugs and pharmaceuticals are included in the pharmacopoeias.

Drugs and pharmaceuticals products are prepared from some raw materials, the standards of which should rigorously be met with that of pharmacopoeia. Though there are several other sources of information about the standard of drugs and pharmaceuticals, the pharmacopoeia is the most reliable one.

Assay methods and identifications of drug of pharmaceuticals are given very clearly in the pharmacopoeias so it becomes easy for the drug industry to design the tests and follow the methods confidently because the assay and identification methods are tested and approved by the authority.

2. From the point of view of drug-administration

In every country there are drug industries with varied intentions - among which the major one is 'to make profit'. While making the profit some industries ignore the quality of the drugs and pharmaceuticals. Since drugs are related to the health of human beings and animals, this negligence is unpardonable. So every nation made their own Drugs and Acts and Rules. Whenever a conflict surfaces between a drug industry and Government the first reference book that is consulted, regarding the quality if the product, is the pharmacopoeia.

3. In academics

The pharmacopoeias are mines of information regarding drugs and pharmaceuticals. The researchers always consult it in first hand for developing an assay method of certain drug, for testing the quality of a dosage form. The microbiological and bioassays are given in details in the appendices with statistical quality controls. The usage of the drug, the adverse reaction, if any, and many more information are provided in the pharmacopoeias. The reason for the popularity of pharmacopoeias among the students, researchers, teachers is for the reliability of the information provided in it.

Indian Pharmacopoeia (I.P.)

The historical developments of Pharmacopoeia in India traces back to 1563 and the credit goes to Garcia da Orta a Portugese physician-cum-teacher.

The idea of indigeneous Indian Pharmacopoeia was conceived in 1837 which bore fruits in 1841 in the shape of **Bengal Pharmacopoeia** and **Conspectus of Drugs**.

The Bengali and Hindi version of **London Pharmacopoeia** was made available in India from 1901 onwards.

The **Indian Pharmacopoeial List**, published in 1946 formed the seeding for the true **Official Indian Pharmacopoeia** published in 1955.

The first edition of Indian Pharmacopoeia was published in 1955, but actually the process was started as early as 1944. In 1944 Government of India asked the Drugs Technical Advisory Board to prepare the list of drugs used, in India, having sufficient medicinal value to justify their inclusion in official pharmacopoeia.

The Indian Pharmacopoeial List, 1946.

The list of drugs both included and not included in the British Pharmacopoeia along with standards to secure their usefulness, tests for identity and purity was prepared by the committee and was published by the Government of India under the name '*The Indian Pharmacopoeial List 1946*'.

The committee constituted under the ch airmanship of Col. Sir R.N.Chopra along with other nine members, prepared the list of drugs with the following details:

Substances included in the British Pharmacopoeia for crude drugs, chemicals and their preparations.

Substances not included in the British pharmacopoeia

a) Drugs of plant origin
b) Drugs of animal origin
c) Biological products
d) Insecticides
e) Colouring agents
f) Synthetics
g) Miscellaneous
h) Drugs for veterinary use.

The Indian Pharmacopoeial List 1946 was prepared by Department of Health, Govt. of India in 1946.

The history of development of Indian Pharmacopoeia:

Year	Events
1946	The Govt. of India published the *Indian Pharmacopoeial List*.
1948	The Govt. of India constituted a permanent Indian Pharmacopoeia Committee. This committee was assigned the task of preparing Indian Pharmacopoeia and to keep it up-to-date.
1955	The **first** edition of **Indian Pharmacopoeia** (IP) was published.

1960* Supplement of IP 1955 was published.
N.B. The work of revision of the Indian Pharmacopoeia as well as compilation of new edition was taken up simultaneously under the chairmanship of Dr. B.N.Ghosh, who died in 1958. After Dr. B.N.Ghosh, Dr. B.Mukherjee, the Director of Central Drug Research Institute was appointed as the chairman of Indian Pharmacopoeia committee.

1966* The **second** edition of IP was published.

1975 A supplement of IP 1966 was published.

1978 The Indian Pharmacopoeia Committee was reconstituted by the Govt. of India, Ministry of Health and Family Welfare, under the chairmanship of Dr. Nitya Nand, Director, Central Drug Research Institute, Lucknow.

1985 The **third** edition of IP was published in two volumes, Volume-I and Volume-II by the Controller of Publications, on behalf of Govt. of India, Ministry of Health and Family Welfare.

1989 Addendum (I) to IP 1985 was published.

1991 Addendum (II) to IP 1985 was published.

1996* The **fourth** edition of IP was published.
Volume-I contains:
Legal Notices, Preface, Acknowledgments, Introduction, General Notices, and Monographs from A to O.
Volume-II contains:
Monographs from P to Z, Appendices, Contents of Appendices and Index.

2000: Addendum to Fourth Edition.
2000: Veterinary Supplement.
2002: Addendum to Fourth Edition.
2005: Addendum to Fourth Edition.
2007: Fifth Edition followed by its addendum in 2008.
2010: Sixth Edition followed by its addendum in 2012. Its DVD was also available.
2014: Seventh edition along with a DVD. Addendum Published in 2015 and 2016.
2018: Eighth edition in four volumes. Addendum in 2019.

Published by: The Controller of Publications, Delhi, on behalf of Govt. of India, Ministry of Health and Family Welfare.

- For the preparation of Pharmacopoeia of India, the pharmacopoeias of other countries, like British, Europe, United States, USSR, Japan, the National Formulary (USA) and Merck Index were consulted. The persons working in pharmaceutical industry, drug control laboratories, research and teaching institutions also actively participated.
- Under the Drugs and Cosmetics Act 1940, the Indian Pharmacopoeia is an official book that contains the standards for drugs and other related substances included in the pharmacopoeia. The drugs and other related substances prepared by pharmaceutical manufacturers must comply with these standards.

Highlights of I.P. 2018:

IP 2018 released on 29th September, 2017 by Sh. C. K. Mishra, Secretary Health & Family Welfare, Govt. of India is effective from 1st January, 2014

- 220 New Monographs included in this edition
- 366 revised monographs and 7 omissions.
- Presented in 4 hard bound volumes with DVD.
- Veterinary products monographs are the integral part of this edition
- Obsolete monographs have been omitted
- More herbal drugs monographs has been added
- 53 New Fixed Dose Combination (FDC's) combination monographs have been included, out of which 25 FDC monographs are not available in any Pharmacopoeia.

British Pharmacopoeia (B.P.)

The first British pharmacopoeia was published as a result of the fusion of the Pharmacopoeia Londinensis (first published in 1684), the Edinburgh Pharmacopoeia (first published in 1699) and the Dublin Pharmacopoeia (first published in 1807). The earlier versions of the B.P. generally contained monographs on crude drugs but the newer versions have more comprehensive coverage of medicinal substances. The current edition has six volumes and is published annually in August every year and becomes effective from the First of January of the next year.

History
1964: First edition of BP
1968: British Pharmacopoeia Committee was constituted.
1980: 13th Edition of BP was published
1988: 14th Edition of BP was published. Contains two volumes with 2100 monographs.
1993: 15th Edition of BP was published
1998: A consolidated edition is published.

Salient features of BP 1998

- Three volumes.
- All monographs of the European Pharmacopoeia (third edition) included
- Includes British Pharmacopoeia (Veterinary)
- CD-ROM included in the package for easy search.

Annual publication from 1998 onwards. In every year a new edition is published.
The version for each year takes effect on 1st January of that year.
The latest version is B.P. 2019, effective from 1st January 2019.(Thirty Sixth Edition)

Meant for The pharmaceutical and chemical industries, quality control personnel, analysts, government regulators, academics and students of pharmacy.

Published by The British Pharmacopoeia Commission The Stationary Office

United States Pharamcopoeia (U.S.P.)

The USP was originally published in 1820 under the authority of United States Pharmacopoeial Convention. The National Formulary (NF) was published in 1888 under the guidance of American Pharmaceutical Association.
In 1974 the NF was purchased by the United States Pharmacopoeial Convention and from 1980 onwards only one official book of drug standards was published under the heading The United States Pharmacopoeia and The National Formulary (USP-NF).
The title USP VIII was adopted for the ninth edition and the sequence goes on.

Some salient improvements in various editions include:

USP published in 1905 adopted average doses.

USP IX added biological assays, biological products and a chapter on analytical determination.

USP XVIII included dissolution test and microbial limit test.

From 1820-1942 the USP was published at 10 year intervals, from 1942-2000 at 5 year intervals and since 2002 it is also published annually.

Thus the latest version is USP 2019. USP-42 NF-37, effective from 1st May 2019.

International Pharmacopoeia

The International Pharmacopoeia (Pharmacopoeia Internationalis, Ph. Int.) is a pharmacopoeia issued by the World Health Organization as a recommendation, with the aim to achieve a wide global uniformity of quality specifications for selected pharmaceutical drugs, excipients, and dosage forms.

The information published in the International Pharmacopoeia is collated via a consultative procedure and is based on international experience, the monographs being established in an independent manner.

Priority is given to medicines that are widely used throughout the world. High priority is accorded to medicines that are important to WHO health programs, and which may not appear in any other pharmacopoeias, e.g., new antimalarial drugs.

List of the editions

S. No.	Edition number	Year	Medium	Notes
1	First Edition	1951 (Volume 1) 1955 (Volume 2)	Print	2 volumes plus supplement
2	Second Edition	1967	Print	
3	Third Edition	1979	Print	5 volumes
4	Fourth Edition	2006	Print or CD-ROM	2 volumes
5	Fifth Edition	2015	Online	
6	Sixth Edition	2016	Online	
7	Seventh Edition	2017	Online	

EXTRA PHARMACOPOEIA

Martindale: The Complete Drug Reference is a reference book published by Pharmaceutical Press listing some 6,000 drugs and medicines used throughout the world, including details of over 180,000 proprietary preparations. It also includes almost 700 disease treatment reviews. It was first published in 1883 under the title **Martindale: The Extra Pharmacopoeia**. Martindale contains information on drugs in clinical use worldwide, as well as selected investigational and veterinary drugs, herbal and complementary medicines, pharmaceutical excipients, vitamins and nutritional agents, vaccines, radiopharmaceuticals, contrast media and diagnostic agents, medicinal gases, drugs of abuse and recreational drugs, toxic substances, disinfectants, and pesticides.

Martindale is arranged into two main parts followed by three extensive indexes:

- **Monographs on drugs and ancillary substances**, listing over 6,000 monographs arranged in 49 chapters based on clinical use with the corresponding disease treatment reviews. Monographs summarize the nomenclature, properties, and actions of each substance. A chapter on supplementary drugs and other substances covers some 1190 monographs on new drugs, those not easily classified, herbals, and drugs no longer clinically used but still of interest. Monographs of some toxic substances are also included.

- **Preparations** - including over 180,000 items from 43 countries and regions, including China.
- **Directory of Manufacturers** listing some 20,000 entries.
- **Pharmaceutical Terms in Various Languages**: this index lists nearly 5,600 pharmaceutical terms and routes of administration in 13 major European languages as an aid to the non-native speaker in interpreting packaging, product information, or prescriptions written in another language.
- **General index**: prepared from 175,000 entries it includes approved names, synonyms and chemical names; a separate Cyrillic section lists nonproprietary and proprietary names in Russian and Ukrainian.

The Digital versions include an additional 1,000 drug monographs, 60,000 preparation names, and 5,000 manufacturers.

To date there have been 39 editions of Martindale: The Complete Drug Reference. The 39th edition was published in June 2017.

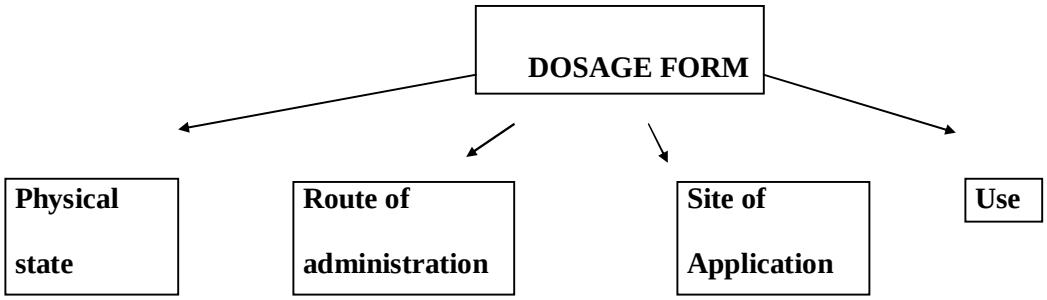
INTRODUCTION TO PHARMACEUTICAL DOSAGE FORMS

DOSAGE FORM

Drugs are rarely administered in their original pure state. They are converted into suitable formulations which are called **dosage forms**. Every dosage form is a combination of the drug and other non-drug components.

The non-drug components are known as "**additives**". The additives are used to give a particular shape to the formulation, to increase its stability and also to increase its palatability as well as to give more elegance to the preparation.

CLASSIFICATION OF DOSAGE FORMS



Physical state	Route of administration	Site of Application	Use
(i) Solid	(i) Oral	(i) Skin	(i) Internal
(ii) Semisolid	(ii) Parenteral	(ii) Eye	(ii)External
(iii) Liquid	(iii) Rectal	(iii) Tooth	
(iv) Gaseous	(iv) Nasal	(iv) Hand	
		(v) Foot	
		(vi) Hair	
		(vii) Nose	

Route of administration	Dosage forms
Oral	Powders, tablets, capsules, solutions, emulsions, syrups, elixirs, magmas, gels, cachets, pills.
Parenteral	Solutions, suspensions, emulsions.
Transdermal	Ointments, creams, powders, pastes, lotions, plaster
Rectal	Suppositories, tablets, ointments, creams, douches, foams.
Urethral	suppositories
Sublingual	Lozenges, tablets
Intranasal	Solutions, sprays, inhalations.
Conjunctival	Ointments
Intra-ocular	Solutions
Intra-respiratory	Aerosols

Classification according to physical state:

DOSAGE FORM

SOLID	SEMISOLID	LIQUID	GAS	MISCELLANEOUS
Cachets	Creams	Applications	Aerosols	Transdermal drug
Capsules	Jellies	Aromatic water	inhalation	delivery systems
Powders	Ointments	Collodion		
Insufflations	Pastes	Draught		Sustained release drug
Dentrifices	Ophthalmic	Ear drops		delivery system
Effervescent	ointments	eye drops		
granules		Nasal drops		Ophthalmic drug
Lozenges		Elixirs		delivery systems.
Pessaries		Mixtures		
Tablets		Emulsions		Implants
Suppositories		Suspensions		
		Enemas		
		Gargles		
		Gels		
		injections		
		Irrigations		
		Linctuses		
		Liniments		
		Lotions		
		Mouthwashes		
		Spirits		
		Sprays		
		Syrups		
		Tinctures		
		Paints		

PRESCRIPTION

DEFINITION

Prescription is an order written by a physician, dentist, veterinarian or a registered medical practitioner to a pharmacist to compound and dispense a specific medication for the patient.
Important features of a prescription:

- Directions are given to the pharmacist about what type of preparation (tablet, power, mixture etc.) is to be prepared.
- It contains directions for the patients, the dose of the drug and the dose interval, and how it is to be taken.

Prescriptions are generally written in Latin language, so that the prescription remains unknown to the patients to avoid self-medication.

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 nonofficial preparation then the quantity of each ingredient will be given. The type of preparation will also be given e.g.

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

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 the case of habit forming drugs to prevent its 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.

An example of a typical prescription is given as follows:

SHARMA NURSING HOME
New Delhi

Name: Mr. N. Anand *Age*: 42 years *Sex*: Male
Address: 32, Azad Nagar, new Delhi

℞ (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. Aswini Sharma
Regn. No. 14328

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 not 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 prescriptions authenticity should always 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.

3. Collecting and weighing the material

Before compounding a prescription all the materials required for it should be collected from the shelves or drawers and kept in 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.

4. 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 cleaned and dried.
- 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.
- The compounded preparations should be filled in suitable containers.

Round vials	For tablets and capsules
Oval prescription bottles Narrow mouthed	For liquid of low viscosity e.g. mixtures, oral emulsions etc.
Wide mouthed bottles	For filling liquids of high viscosity, large quantities of tablets or capsules and bulk powders.
Colored fluted bottles	For external preparations e.g. liniment and lotions.
Ointment jars and collapsible tubes	For ointments, creams or any other semisolid dosage forms.
Paper wrappers and envelops	For oral powders in divided doses.
Dropper bottles	For eye drops and ear drops.
Sifter top containers	For dusting powders.

- The containers are labeled as per the prescriber. If required some additional instructions may also be given.
  The following information should be written on the label:

Type of preparation:	The Emulsion, The Mixture, The Powder etc. Its quantity should also be mentioned.
For:	Name, Age and Sex of the patient.
Date of dispensing:	Date on which the prescription is dispensed.
Expiry date if any:	e.g. 'Must be taken within 7 days of dispensing.'
Directions for use:	e.g 'One teaspoonful thrice daily.'
Storage condition:	e.g. 'Keep in a cool place'
Secondary labeling:	e.g. 'SHAKE THE BOTTLE BEFORE USE' 'FOR EXTERNAL USE ONLY' etc.
Name and signature	of the pharmacist who dispensed
Name and Address	of the Pharmacy

- The container should be polished to remove any finger print.
- While delivering the preparation to the patient the pharmacist should explain the mode of administration, direction for use and storage.

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.

SOURCES OF ERRORS IN PRESCRIPTION

Following are the sources of errors which arise in prescription:

1) Abbreviation: Abbreviation presents a problem in understanding parts of the prescription order. Extreme care should be taken by a pharmacist in interpreting the abbreviation.

2) Name of the Drug: There are certain drugs whose name look or sound like those of other

drugs. Some of the examples of such drugs are as under:

Examples of Drugs often Confused
Digitoxin Digoxin
Prednisone Prednisolone
Indocin Lincocin
Doridon Doxidan
Pabalate Robalate
Ananase Orinase

Name of the pharmaceutical products have been changed on certain occasion due to the possible confusion with the name of the other products, e.g., the name of potassium supplement was changed from Kalyum to Kolyum because of the possible confusion of the former designation with valium.

3) Strength of the Preparation: The strength of the preparation should be stated by the prescriber. For example, it will be a wrong decision on the part of a pharmacist to dispense paracetamol tablet 500 mg when prescription for paracetamol tablet is received with no specific strength.

4) Dosage Form of the Drug Prescribed: Many medicines are available in more than one dosage form. For example, liquid, tablet, capsule and suppository. The pharmaceutical form of the product should be written on the prescription in order to avoid ambiguity.

5) Dose: Unusually high or low doses should be discussed with the prescriber. For example, a prescription for sustained release formulation to be administered after every four hours should be thoroughly checked because such dosage forms are usually administered only two or three times a day.

6) Instructions for the Patient: The quantity of the drug to be taken, the frequency and timing of administration, and route of administration should be clearly given in the prescription so as to avoid any confusion.

7) Incompatibilities: It is essential to check that there are no pharmaceutical or therapeutic incompatibilities in a prescribed preparation and that different medicines prescribed for the same patient do not interact with each other to produce any harm to the patient.

POSOLOGY

POSOLOGY is derived from the Greek word *posos* meaning *how much* and *logos* meaning *science*. So *posology* is the branch of medicine dealing with doses.
The optimum dose of a drug varies from patient to patient.

FACTORS AFFECTING POSOLOGY:
The following are some of the factors that influence the dose of a drug.
1. Age: Human beings can be categorized into the following age groups:

1. *Neonate*: From birth up to 30days.
2. *Infant*: Up to 1 year age
3. *Child in between 1 to 4 years*
4. *Child in between 5 to 12 years.*
5. *Adult*
6. *Geriatric (elderly) patients*

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

$$\text{Individual dose} = \frac{\text{BodyWeight (kg)}}{70} \text{ x Average adult dose}$$

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

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

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

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

4. Route of administration
In case of intravenous injection the total drugs reaches 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. An irritant drug is given after meal so that the drug is diluted with food and thus produce 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.

Alcohol is better tolerated in winter than in summer.

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 g*astrointestinal 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) are 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 *primaquin* (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 doses of a drug is repeated in quick succession an 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.

CALCULATIONS OF DOSES FOR CHILDREN

A number of methods have been used to relate doses for children to their ages.

1. Dose proportionate to age

Young's formula: This formula is used for children having age below 12 years.

$$\text{Dose for the child} = \frac{\text{Age in years}}{\text{Age} + 12} \times \text{Adult dose}$$

Dilling's formula: This formula is used for children having age from 4 to 20 years. This formula is better because it is easier to calculate the dose.

$$\text{Dose for the child} = \frac{\text{Age in years}}{20} \times \text{Adult dose}$$

Cowling's formula:

$$\text{Dose for the child} = \frac{\text{Age in years} + 1}{24} \times \text{Adult dose}$$

Fried's formula: For less than 12 months of age

$$\text{Dose for the child} = \frac{\text{Age in months}}{150} \times \text{Adult dose}$$

Bastedo's Formula:

$$\text{Dose for the child} = \frac{\text{Age in years} + 3}{30} \; x \; \textit{Adult dose}$$

2. Doses proportionate to body weight

Clark's formula:

$$\text{Dose for the child} = \frac{\text{Weight in pound}}{150} \times \text{Adult dose}$$

$$\text{Dose for the child} = \frac{\text{Weight in kg}}{68.2} \times \text{Adult dose}$$

3. Doses proportionate to body surface area (BSA)

$$\text{Dose of a child} = \frac{\text{Body surface area of the child } (m^2)}{1.7} \times \text{Average adult dose}$$

TABLE: 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

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