# UNIT-I

## HISTORY OF PHARMACY PROFESSION IN INDIA IN RELATED TO PHARMACY EDUCATION.

India, a developing nation that occupies the greater part of South Asia, is a sovereign, secular republic consisting of 28 states and 7 union territories.1 With a population of approximately 1.2 billion,2 India is the second most populous country on the planet. In India, formal pharmacy education leading to a degree began with the introduction of a 3-year bachelor of pharmacy (BPharm) at Banaras Hindu University in 1937. At that time, the curriculum was presented as a combination of pharmaceutical chemistry, analytical chemistry, and pharmacy, which prepared graduates to work as specialists in quality control and standardization of drugs for pharmaceutical companies,3 but not for pharmacy practice. Before India gained independence in 1947, there were 3 institutions offering pharmacy degree programs.4 In 1944, the Punjab University started a pharmacy department; in 1947 L.M. College was established in Ahmedabad (Table 1). At independence in 1947, India inherited a system for the pharmacy profession from the British rulers that was unorganized and there was no legal restriction on the practice of pharmacy. The concept of pharmacy practice was not realized until after independence was gained. In 1948, the Pharmacy Act5 was enacted as the nation's first minimum standard of educational qualification for pharmacy practice. to regulate the practice, education, and profession of pharmacy. Currently, one needs at least a diploma in pharmacy to practice as a pharmacist. Provisions of the Act are implemented through the Pharmacy Council of India (PCI).6 The Act requires individual states to establish state pharmacy councils that are responsible for controlling and registering pharmacists in their respective states. Throughout this paper the word ''institution'' has been used to describe both colleges/schools and universities. English is the only language of instruction for all pharmacy institutions.

**EDUCATIONAL PROGRAMS**:

A variety of pharmacy degree programs are offered in India: diploma in pharmacy (D Pharm), bachelor of pharmacy (BPharm), master of pharmacy (M Pharm), master of science in pharmacy [MS(Pharm)] and master of technology in pharmacy [MTech (Pharm)], doctor of pharmacy (PharmD), and doctor of philosophy in pharmacy (PhD). The entry point, for D Pharm, BPharm, and PharmD programs is 12 years of formal education in the sciences. The D Pharm program requires a minimum of 2 years of didactic coursework followed by 500 hours of required practical training anticipated to be completed within 3 months in either a hospital or community setting. The BPharm involves 4 years of study in colleges affiliated with universities or in a university department. Students holding a BPharm degree can earn an M Pharm degree in 2 years, of which the second year is devoted to research leading to a dissertation in pharmacology, pharmaceutical chemistry, or pharmacognosy. Recently, M Pharm programs on industrial pharmacy, quality assurance, and pharmaceutical biotechnology have been introduced. To train the graduate pharmacist to provide clinical-oriented services, the MPharm program in pharmacy practice was introduced at Jagadguru Sri Shivaratreeswara (JSS) College of pharmacy at Mysore in 1996 and at Ooty in 1997.7 There are 6 National Institutes of Pharmaceutical Education and Research

(NIPERs) in India offering MS (Pharm), MTech (Pharm), and higher-level degrees. The NIPERs were created with the vision of providing excellence in pharmacy and pharmacy-related education. Students with an MPharm degree in any discipline can work toward a PhD with an additional minimum 3 years of study and research. The PharmD program constitutes 6 years of full-time study. The PharmD (post-baccalaureate) program is a 3-year program. The PharmD program was introduced in 2008 with the aim of producing pharmacists who had undergone extensive training in practice sites and could provide pharmaceutical care to patients.

**Growth of Pharmacy Education** Prior to mid-1980s, the growth of publicly funded institutions of higher education (including pharmacy institutions) was very slow.8 Until early 1980s, there were 11 universities and 26 colleges offering pharmacy education at the bachelor's and master's levels.3 In addition, there was at least 1 government school in every Indian state offering the DPharm program. Since the late 1980s, due to rapid industrialization in the pharmaceutical sector, privatization, and economic growth, pharmacy education has been developing faster in India than anywhere in the world. In 2007, there were 854 institutions that admitted more than 52,000 students to the BPharm degree program and 583 institutions that trained more than 34,000 students in the DPharm degree program.9 Most of the institutions, however, are privately funded colleges or privately funded universities. The private sector, which accounted for about 10% of the students admitted in the 1980s, now accounts for 91% of all pharmacy students admitted.10 While there are a large number of DPharm and BPharm graduates each year, the number of students that has graduated in any state varies widely. A large number of privately funded institutions are located in states like Tamilnadu, Karnataka, Andhra Pradesh, Maharashtra, and Gujrat.11 In Tamilnadu, around 45 colleges and universities educate approximately 2,960 D Pharm and 2590 BPharm graduates per year (within a total state population of about 64 million).

**Admission Criteria**:

Entry qualifications for pharmacy programs vary across and within states, and most significantly, between private and public institutions. Entry requirements also vary depending on the degree program. The majority of privately funded institutions do not have a direct formal application process. There is no centralized data repository to indicate the number of applicants to private and public institutions in India.

**D Pharm Program:**

In India, higher secondary study is concluded by a terminal examination, the higher secondary examination, at the end of 12 years. Admission to the first year DPharm program in any government college is based on performance on the higher secondary examination. However, private colleges have their own admission procedures that comply with the education regulations of the PCI. Students generally may choose to undertake the DPharm program as their second or third choice, having been unable to obtain a place at the college in another degree program that was their first choice. The DPharm curriculum is framed through the education regulations of the Pharmacy Act. The present education regulations framed way back in 1991 (ER91). The curriculum is the same throughout the country. In the 1990s, the efforts of the pharmacy council

of India for upgrading the minimum qualification for registration from DPharm to BPharm failed due to lack of consensus.12 BPharm Program. Admission to the first-year BPharm program is made directly from higher secondary school on the basis of marks obtained in the higher secondary examination or on the basis of a merit list rank prepared based on scores on an entrance examination administered by a state or individual institution. Administering an entrance examination as an admissions requirement is used mainly by public institutions. For example, admission to the first-year BPharm of Banaras Hindu University (BHU) is made through the joint entrance examination (JEE) conducted by Indian Institutions of Technology (IITs), a group of 13 autonomous engineering and technology-oriented public institutes of higher education established and declared as institutes of national importance by the government of India. The selected students opt for more rewarding bachelor of technology (BTech) programs; therefore, most of the 40 seats open in the BPharm program at BHU remain vacant. The practice regarding preparing a merit list of applicants also differs. Some states and institutions place emphasis on entrance examination scores and use this as the only criterion in the selection process. A few private universities and at least 1 Indian state (Tamilnadu) have abandoned entrance examinations and use grades scored in the higher secondary examination instead. Many government institutions adopt a middle ground and use a combination of grades and entrance examination scores in their selection

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**M Pharm Program.**

The criterion for entry to an MPharm program is academic performance in the B Pharm or an entrance test or both. Currently, there is more demand for the MPharm program than the availability of places in the country. An important criterion, a high Graduate AptitudeTestfor Engineering(GATE)score, qualifies a student to receive government scholarship during the period of their MPharm study. This criterion is optional for admission to the first-year MPharm program. However, many public institutions require both past academic performance and GATE score for application to the MPharm program.

**Pharm D Program.**

Admission to a PharmD degree vprogram is on the basis of successful completion of the higher secondary examination or the DPharm program. Passing the higher secondary examination with physics,chemistry, and biology or mathematics entitles a student to enter the PharmD program. BPharm degree holders can join the PharmD program in the fourth year.

**REGULATIONS AND QUALITY ISSUES**

Pharmacy education in India is regulated by 2 organizations: the Pharmacy Council of India (PCI),6 under the Pharmacy Act of 1948, and the All India Council for Technical Education (AICTE),14 which was established under the AICTE Act of 1987. Asmentioned previously, the PCI makes regulations regarding the minimum standard of education required for qualification as a pharmacist. It is responsible for registration of persons fulfilling the prescribed eligibility criteria (minimum DPharm) and issuing a license permitting them to practice in an Indian state. Registration activity is decentralized and the state pharmacy councils are responsible for registering pharmacists in their respective states. Thus, the PCI regulates the DPharmprogramand the recently introduced PharmDprogram. The BPharm programneeds to be recognized by the PCI for the qualifications to be accepted for registration purpose only. The PCI has no jurisdiction over MPharm and other higher-level degree programs.

Pharmacy education at all levels excluding the PharmD is regulated by the AICTE and all these programs must be approved by it. The AICTE is primarily responsible for planning, formulating, and maintaining norms and standards in technical education, which include pharmacy. Beside the Pharmacy Act, pharmacy practice is also governed by theDrugs and CosmeticsAct of 1940,15 which stipulates the manufacture, distribution, and sale of drugs. Currently, there are no regulatory body and regulatory control for clinical pharmacy practice. TheAICTE is also responsible for quality assurance of pharmacy programs (DPharm, BPharm and MPharm) through accreditation by National Board of Accreditation (NBA) constituted by the AICTE. However, only 8% of pharmacy programs have been accredited.9 Accreditation is voluntary and also a stringent process; thus, few institutions have applied for accreditation on their own. The voluntary accreditation seems to serve little purpose for any of its stakeholders. Unlike other countries, the current regulations do not require any continuing education tomaintain licensure once they are conferred.

In addition, registered pharmacists do not have any established norms on competencies or standards of services. There is no categorizationof practicing and non-practicing pharmacists.

**INTRODUCTION:**

In the previous chapter, researcher has tried to emphasis an overall information about Pharma Industry in India which includes; basic information about bulk drugs and domestic formulations. At the same time the researcher has studied growth of domestic formulation & bulk drug in India for the study period. In addition to this the researcher has focused on pharmaceutical industries overview for the last five years as well as Indian Exports, framagentation in the domestic formulation. Chapter three also focued on comparative cost structures of Indian companies and MNCs in India to understand the various cost factors like material cost, marketing & selling expenses and employee cost against total sales of pharma companies in India. In this chapter, data of the present study have been collected from various Pharamaceutical Journals. It would faciliatate in better understanding the historical development and review of Pharma Industry in India. Efforts have been made in this chapter to provide a historical picture of the background covering as many factors as possible such as origin of the Pharma Industry, various pathies and the Pharma Industry scenario in India since its inception.

## HISTORY:

It was the incarnation of Lord Vishnu who invented the Science of Medicine in the Universe and it is he who quickly cures all ailments of the ever- diseased living being. According to the reference, the commonly worshiped Hindu God of Medicine, "DHANVANTARI" is the original exponent of the Indian medicine (raga Shrimad Bhagwatam 8/8/31-35). Ayurveda, the Historical and Developmantal Review of Pharma Industry in India. 43"Science of Life" practiced by the ancient Indians is based on Atharveda. It was one of the oldest scriptures of the Hindus, about 3,000 years old. 1/5th of the human race practices it even today.

## Origin of medicine :

Charaka has mentioned about how Bharadwaja learnt Ayurveda from Lord Indra and brought and propagated it on the earth to cure the diseased people. There are two schools of thoughts: I) Atreya Sampradaya, i.e. the school of medicine originated from the great sage Bharadwaja, and II) Dhanvantari Sampradaya, i.e. the school of surgery originated by Lord Dhanvantari. The philosophy of the Ayurveda lies in the theory of Panchamahabhutas (five basic entities) namely: Akash (space), Vayu (air), Agni/Tejas (fire), Apa (water) and Prithvi (earth), of which all the universe and living beings are made of the unions of these five elements are represented in the form of Tridosh (triad), e.g. Vata (ether+air), Pitta (fire) and Kapha (water + earth). The Pre-Vedic period comprises all the human communities in the sub-continent, from the Old Stone Age to the time written history begins, i.e. the Indus valley civilization. About 5000 years ago, the Aryans came to northern India from Central Asia and a new civilization began on the banks of river Ganga.

## DIFFERENT PATHIES OF MEDICINES:

## AYURVEDA:

## The Dravagun vigyan:

Liquid or Rasa extracted from herbs for curing diseases is called the Dravagun Vigyan. The Dravagun Vigyan is one of the modes of administration of medicine in Ayurveda. Liquid used for medicinal purpose is called "Rasa". In olden days, minerals and mercury were Historical and Developmantal Review of Pharma Industry in India. used for Rasa purposes. Prominent annotators of Ayurveda like Charak, Sushruta, Kashayap and Wagbhatta regarded the Dravagun Vigyan as a branch of Atherveda.

**Mantropchar Therepy:**

Ayurveda is the first medical faculty, which has considered mind as a part for treatment. The mind is profoundly reflected in Mantropchar therapy. Modern concept of placibo or concept of faith-healing has its origin in Ayurveda. In Charak Samhita, incatation therapy [mantropchar] was practiced. Repetition of Mantra or repetition of name of Gods results in positive results. At the time of administration of medicine, old generations used to chant shlokas. The logic was simple; shlokas were related with religion and people had strong faith in religion. Naturally, chanting of the shlokas were helpful to boost the confidence among the patients about the therapy, which has been resulted in faith healing processes.

**B. Homeopathy:**

Homeopathy is a 200-year-old medical science and art developed by the German physician, Samuel Hahnemann. It is an alternative, complementary medicine based on the Law of Similes. Homeopathy is a safe, effective, FDA regulated natural medicine that has been used for a wide range of illnesses including ADHD, depression anxiety, allergies, asthma, chronic fatigue, fibromyalgia, PMS, menopause and headaches. In 1854, Abraham Lincoln was retained to prepare a state legislative proposal to charter a homeopathic medical college in Chicago. This was a complex task in view of the deep-seated animosity between the allopathic or orthodox medical practitioners and the irregular healers. Homeopathy was regarded as a cult by the nascent American Medical Association. In addition, the poor reputation of medical education in the United States in general, further complicated the project. The origin of Homeopathy can be traced to the Germans in the 18th century. This pathy was invented and adopted by the German scientist Hahneman for treating diseases by prescribing minute doses of drugs which in maximum dose would produce similar symptoms of the disease.

**C Naturopathy :**

Reiki is a very ancient science, rediscovered by Dr. Mikao Usui in mid-1800's. Reiki in the Japanese language, means "Universal Life Force Energy". It is made up two parts, 'Rei'— meaning universal, transcendental spirit, and 'Ki'— meaning energy or power. In India, this energy is called 'Shakti' or 'Prana'. It is a technique for stress reduction and relaxation which allows everyone to tap the unlimited supply of 'life force energy' to improve health and enhance quality of life.

**E Acupuncture:**

This is an alternative system of medicine, which treats ailments by insertion of needles at acupoints. Specific sensation called Quichi or Teichi is elicited during needling.

**Unani:**

The Unani Medicine is based on the Greek philosophy. According to the basic principles of the Unani medicine, a body is made up of the four basic elements, i.e. Earth, Air, Water and Fire which have different temperaments i.e. Cold, Hot, Wet and Dry.

**G. Allopathy:**

Hippocratic is the founder of Allopathy. Allopathy is a very different kind of medical practice as compared to the above-mentioned pathies. The origin of Allopathy is in the Western countries. In this pathy, synthetic chemicals are used for treatment. presently, Allopathy is the most advanced science having world-wide recognition. In this pathy, different modes of operations are used for administrating medicines like oral, topical and injectable. The earliest records of medicinal plants and minerals could be found in the ancient Chinese, Hindus, and Mediterranean civilizations. In 2735 BC, the Chinese emperor Shen Nung wrote on herbs, in which he described the anti-fever and anti-malerial alkaloids capabilities, of substance known as "Chang shang".Practice of pharmacy was separated from medicine by legislation as early as 1224 by Fedric the Second the Holy Roman Emperor. Historians have proclaimed the Empire's legislation as the "Charter of Pharmacy." In 1617, "The Society of Apothecaries, (pharmacy) London", was founded, making the emergence of pharmacy as a distinct profession. King James authorized the separation of Apothecaries from grocers.

**DEVELOPMENT OF THE PHARMA INDUSTRY IN INDIA:**

It is a well-known fact that because of the British rule, pharmaceutical industry could not be developed significantly in India. After independence, the Government declared its industrial policy in the year 1950. The Government gave importance to the development of the pharmaceutical industry.During 1950, there were 65 domestic pharmaceutical units in India, while foreign units were 28 in number. In 1952, about 1,643 licenses were issued under the Drug Act. In 1989, the number had increased to 12,000. Of these, only 1,554 were manufacturing units. In the year 2003-04, it had increased to over 24,000 units. In 1952, total investment in the pharmaceutical industry was only Rs. 24 crores which increased to Rs. 1,175 corers in 1984-85. Now, in 2004-05, it has reached over Rs 15,000 crores. Due to development of the pharmaceutical industry, the average life expectancy of Indian increased from 32 years to 60 years. In fact, India has also made adequate research in this field. However, the multinationals have already entered the Indian market. These companies are competing with the Indian pharmaceutical companies. As there is a free entry in the Indian market, the foreign pharmaceutical companies with modern techniques for production are procuring raw materials and manufacturing products with the help of cheap labour. Therefore, these companies are likely to get more profit as compared to the Indian pharmaceutical companies. 405. Research/Expermentation on Indian Pharma Industry: To give a planned direction to all

industries, the Republic of India passed a bill known as the 'Industrial Development Regulation Act' in 1951.

**The Pharmaceutical industry is divided into two parts :**

1. Bulk Drugs [fermentation, synthetic and plant products] and

2. Formulations.

The whole pharmaceutical manufacturing industry is divided into three categories. Small scale, Medium scale, and Large scale depending upon the amount of the investment. Investments in the pharma industry were Rs.5,796 crores in the year 1994-95. The large-scale companies are required to obtain industrial license from the Director General of Technical Department.Presently, the multinational companies operating in India are keeping 40% of the shares with them and the rest with the public.

All the pharmaceutical companies are governed by the Drugs and Cosmetic Act, 1940 and the Rules of 1945 for the purpose of manufacturing, storage, marketing, quality control, etc.

Before starting the manufacturing and marketing of the pharmaceutical products, an industry is compelled to obtain license from the Food and Drug Department. The food and drug department is located in every part of the country. In every state, there is a Commissioner or a Director appointed by the Government. Their major task is to enforce the existing rules and regulations as well as the Bills passed by the Parliament and the State Assemblies, from time to time. To supervise the import of drugs, the office of the Drug Controller is in existence along with four major branch offices situated at Madras

(Chennai), Bombay (Mumbai), Cochin (Kochchi) and Calcutta (Kolkata). India desires to and aims at standing with importance on the map of the Pharmaceutical world. Self reliance is one of the mottos of India's pharmaceutical Industry. For this purpose, the Indian Government and the Pharmaceutical Industry are very cautious about quality control and research. The Intention of any research is to invent new drugs and design new formulations containing the drugs as per new trend and considering the need of the time. Most of the Indian companies are trying to develop research centers. Particularly the multinational companies operating in India are arranging major financial sources for research purpose. Considering all of the above facts, the pharma companies are not only required in the manufacturing field but also in the marketing and selling fields.

INTRODUCTION

Pharmacy is the branch of science, which dealing with collection, preparation, and standardization of drugs, derives its name from the Greek root pharmakon, a drug and pharmaceutical words is related to drugs used in medical treatment and a company which makes and sell drug known as pharmaceutical industry.[1] The builder of the Indian pharmaceutical industry would be Acharya P.C. Ray. In the year 1901, Acharya P.C. Ray founded Bengal Chemicals and Pharmaceuticals

Works Ltd. It started by making drugs from indigenous materials and then went on to manufacture quality chemicals, drugs, pharmaceuticals and employed local technology, skills, and resources. The Indian pharmaceutical sector is highly fragmented with more than 20,000 registered units. It has expanded drastically in the last two decades. This industry plays an important role in promoting and sustaining development in the field of global medicine. The pharmaceutical and chemical industry in India is an extremely fragmented market with severe price competition and government price control. The Pharmaceutical industry in India meets around 70% of the country's demand for bulk drugs, drug intermediates, pharmaceutical formulations, chemicals, tablets, capsules, orals, and injectable. There are approximately 250 large units and about 8000 Small Scale Units, which form the core of the pharmaceutical industry in India (including 5 Central Public Sector Units). The government has also played a vital role in the development of the Indian pharmaceutical industry currently tops the chart among India's science-based industries with wide ranging capabilities in the complex field of drug manufacture and technology. A highly organized sector, the Indian pharmaceutical industry is estimated to be worth $4.5 billion, growing at about 8–9% annually.[4,5] Due to the presence of low-cost manufacturing facilities, educated and skilled manpower and cheap labor force among others, the industry is set to scale new heights in the fields of production, development, manufacturing and research that's why it ranks very high among all over the world, in terms of technology, quality and the vast range of medicines that are manufactured.[6] It ranges from simple headache pills to sophisticated antibiotics and complex cardiac compounds; almost every type of medicine is now made in the Indian pharmaceutical industry.

**CAREER OPPORTUNITY FOR PHARMACY PROFESSIONAL**

QUALITY CONTROL

Quality control is the part of quality management focused on fulfilling quality requirements. They are dealing with sampling, inspecting, testing, monitoring, releasing/rejecting of starting materials, packaging materials, intermediates, bulk products, under process product, finished products. Highly specialized and trained staff is required to handle sensitive analytical procedures and sophisticated equipment (such as gas chromatography–mass spectrometry, high-performance liquid chromatography (HPLC) UV-VIS spectroscopy, Fourier transform infrared spectroscopy, titrometer, NMR etc.).

A pharmacy professional holds various posts in QC department such as: • QC Chemist • QC Executive • Technical Manager – QC • QC Manager.

QUALITY ASSURANCE

Quality assurance is the part of the quality management focused on providing confidence that quality requirements will be fulfilled. QA is wide-ranging concept concerning all matters that individually or collectively influence the quality of the product. QA is the totality of the arrangements made with the object of ensuring that products are of the quality required for intended use. They ensure product quality starting from the procurement of raw materials up to the

marketing of manufactured product. Their role is to implement and maintain Total Quality Management System needed for building the confidence that manufactured products are of standard quality with minimum risk of rejection and maximum customer satisfaction.[19,20] Pharmacy professionals working on various positions in QA department such as:[21] • QA Inspector • QA Executive • Document Controller • QMS - coordinator • Validation - coordinator • QA Manager.

## RESEARCH AND DEVELOPMENT

Research and Development is the mind of the pharmaceutical industry, as it is the key to growth and nourishment of the industry. In R&D Pharmacy professional works in the following areas:[22] • New Drug Discovery Research • P and D of API-development of viable processes for the manufacture of drugs and intermediates for their commercial production • F and D of Conventional and Novel Drug Delivery Systems. Pharmacy professional give their services on various position such as: • R&D Chemist • R&D Executive • Research Scientist • Research Associates • Group Leader - R&D • Head - R&D • Vice President - R&D

## CLINICAL RESEARCH

Clinical research is a branch of healthcare science that determines the safety and effectiveness of medications, devices, diagnostic products and treatment regimens intended for human use. These may be used for prevention, treatment, diagnosis or for relieving symptoms of a disease. Clinical Research is different from clinical practice. In clinical practice, one uses established treatments while in clinical research evidence is collected to establish a treatment.

Pharmacy professionals have high job opportunity in the following area of clinical research: • Clinical trials • Bioequivalence study • Pharmacokinetics study and • Toxicological studies.

These are some of the areas of clinical research, which are in high demand as they are involved in the systematic evaluation of potential drug substances prior to getting them approved by the regulatory authorities.

Pharmacy professionals have job potential in the Clinical Research in the following position:• Clinical Training Analyst • Clinical Research Monitor • Clinical Research Associate • Clinical Affairs - Project Manager • Clinical Trials Manager • Clinical Research Coordinator • Clinical Research Manager • Patient Recruiter • QC Manager • QA Manager • Manager Clinical Operation.

## REGULATORY AFFAIRS AND INTELLECTUAL PROPERTY RIGHTS

With globalization process reaching out to India, the geographical barriers have become obsolete. Any country will have to compete and trade globally in order to progress and survive in the years to come. The major drugs and pharm companies have realized this fact and have stepped into the global area of competitive trade. If an Indian manufacturer wants to sell his drug or formulation to a foreign country, it is mandatory that he has to fulfill all the statutory requirements laid by the

regulatory authorities of that country. Also, his product needs to be perfectly as per the specifications laid down by the concerned regulatory authority. Thus, in order to enter into trade with the foreign countries, it is mandatory to get the necessary approvals and sanctions as per the formats given by local regulatory authorities such as approvals to be obtained from US FDA for USA, Therapeutic Goods Administration (TGA). for Australia

and N>Zeeland, MCA and MCM for UK and European countries and ICH guidelines going to be uniform for international levels.[28-30] At National level, the FDA (Foods and Drugs Control Administration) is the main regulatory body governing and implementing the rules and regulations for the Drug and Pharma industry. The FDA has state branches and subbranches all over the country. The job opportunities for Pharmacy graduates are excellent and range from the levels of a Drug Inspector (DI), Sr. DI, Deputy Drug Controller, Asst. Drug Controller, Drug Controller and finally Drug Controller of India. This is highly respected and sought after profession. A graduate in pharmacy is the minimum eligibility. Every Pharmaceutical Industry has now set up RA department that's why regulatory experts are thus in great demand. Since, the field is highly technical Pharmacy professionals again fit in these positions. Similarly, patents and trademarks, Intellectual property rights (IPRs) experts are also in high demand as far as the Pharma Industry is concerned. Pharmacy professionals are the pivotal people in this department at different level and position. RA offer a lot of job opportunities at different level:[31,32] • They are required for Interaction with all departments of the company and based on this cooperation prepare a variety of documents necessary for research, development and production of drugs/medical devices • Providing information and expertise in the latest changes in the regulatory requirements of national GMP, WHO - GMP, US FDA, TGA, ICH guidelines Preparing for regulatory inspection • Interaction with government to obtain regulatory approval (licensing) for production of therapeutics • Interaction with government to obtain regulatory approval for conducting clinical studies and for production of therapeutics • WHO certification • IPRs and Pharma Patents • Preparation of Drug Master Files (DMF), New Drug Application (NDA)/Abbreviated NDA (ANDA)/ Common Technical Document (CTD) • Preparation of registration dossier for export. These professionals will find employment in industry as: • RA Assistants • RA Associates • Documentation Administrators and Medical Information Associates • RA Consultants for Pharm/Biotechnology Industry • Regulatory Food Safety Scientist • Pharmaco-vigilance Manager • Drug Safety Specialist.

PRODUCTION MANAGEMENT

Pharmaceutical Production Management is a process that combines and transforms various resources (Raw material, Labour, Machine) used in the production subsystem of organization into value added product, in controlled manner, as per the policies of the organization. Therefore, it is that part of an organization that is concern with conversion a range of inputs into the required product having the required quality level. Production Manager is responsible for production schedule, staffing, procurement and maintenance of equipment and coordination of production activities among different departments. They also take care of economic efficiency and in-time

delivery of the products. They are also aware, recent market trends and the resultant change in the demand pattern. Pharmacy professional has very good career opportunity in Production Management.

A pharmacy professional works in the production of bulk drugs (API) and intermediates and formulation as: • Production Chemist • Production Officer • Production Executive • Production Planner • Production Manager • Vice President - Production.

SALES AND MARKETING

Medical sales representatives are a key link between pharmaceutical companies and medical and healthcare professionals. They work strategically to increase the awareness and usages of a company's pharmaceutical and medical products. They also promote products to the different organizations and government department as well.[37] Based on a specific geographical location, and they usually specialize in a particular product or medical area viz. Cardiovascular Division, Diabetes Division, Gynecological Division, Psychiatric Division, Ayurveda Division, Neuro Division, Dermatological Division, etc. They may also make presentations and organize group events for healthcare professionals, as well as work with contacts on a one-toone basis. Marketing is a result-oriented job, as the results Pharma sales and marketing are highly technical field and offers excellent opportunities for the pharmacy graduates. Pharmacy professional starts their career in sales and marketing career as MR and go up to the levels of:[38] • Sales Officer • Area Sales Manager • Regional Sales Manager • Zonal Sales Manager • General Marketing Manager • Manager - International Marketing and Exports.

BIOINFORMATICS

Bioinformatics is the application of information technology to the field of molecular biology. The primary goal of bioinformatics is to increase our understanding of biological processes. Major research efforts in the field include: • Sequence alignment • Genetic finding, genome assembly • Protein structure alignment • Protein structure prediction • Prediction of gene expressions • Protein-protein interactions • Modeling of evolution. Pharmacy professional with knowledge of computer application and software has job potential in the bioinformatics in the following position: • Bioinformatics trainee • Bioinformatics analyst • Scientist/senior scientist – Bioinformatics • Team leader – Bioinformatics • Bioinformatics – Trainer • Bioinformatics – Lecturer to professor.

MEDICAL TRANSCRIPTION

Medical transcription also known as MT is an allied health profession, which deals in the process of transcription, or converting voice-recorded reports as read out by physicians and/or other healthcare professionals, into electronic format. A medical transcriptionist is the person responsible for converting the patient's medical records into electronic format.[4,5] Due to the increasing demand to document medical records, countries particularly USA started to outsource the services of medical transcription. Since India is several hours ahead of America and Europe, Indian medical transcription industries can offer the natural advantage of quicker turnaround time.

That is why India is chosen as the one of the best source of outsourcing in MT. In Typical MT firm, the pharmacy professional gives their services on various posts:[3] • Trained medical transcriptionist • Senior medical transcriptionist • Proof readers • Sub editors • Editors • Supervisor • Manager.

HOSPITAL PHARMACY

Another opening for a pharmacy professional is as a “Registered Pharmacist” in the hospitals or drug stores. This is a very sought after professional especially in countries like the USA and Canada.[5] The trend is already set in many hospitals in the country. This is a key position, and the Pharmacist plays an important role form preparing prescription to the patient’s medical history after the Medical doctor has diagnosed the disease. The Pharmacist is the bestinformed qualified drug expert whose advice is sought by everybody regarding the dosage, incompatibilities and side effects of drugs.

A pharmacopoeia, pharmacopeia, or pharmacopoea (from the obsolete typography *pharmacopœia*, 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.

**History:**

Although older writings exist which deal with herbal medicine, the major initial works in the field are considered to be the Edwin Smith Papyrus in Egypt, Pliny’s pharmacopoeia and *De Materia Medica* a five-volume book originally written in Greek by Pedanius Dioscorides. The latter is considered to be precursor to all modern pharmacopoeias, and is one of the most influential herbal books in history. In fact it remained in use until about CE 1600.

A number of early pharmacopoeia books were written by Persian and Arab physicians. These included *The Canon of Medicine* of Avicenna in 1025, and works by Ibn Zuhr (Avenzoar) in the 12th century (and printed in 1491), and Ibn Baytar in the 14th century The Shen-nung pen ts'ao ching (Divine Husbandman's Materia Medica) is the earliest known Chinese pharmacopoeia. The text describes 365 medicines derived from plants, animals, and minerals; according to legend it was written by the Chinese god Shennong.

The ***British Pharmacopoeia*** (***BP***) is the national pharmacopoeia of the United Kingdom. It is an annually published collection of quality standards for UK medicinal substances. It is used by individuals and organisations involved in pharmaceutical research, development, manufacture and testing.

Pharmacopoeial standards are publicly available and legally enforceable standards of quality for medicinal products and their constituents. The *British Pharmacopoeia* is an important statutory component in the control of medicines which complements and assists the licensing and inspection processes of the Medicines and Healthcare products Regulatory Agency (MHRA) of the United Kingdom. Together with the *British National Formulary* (BNF), the *British Pharmacopoeia* defines the UK's pharmaceutical standards.

Pharmacopoeial standards are compliance requirements; that is, they provide the means for an independent judgement as to the overall quality of an article, and apply throughout the shelf-life of a product. Inclusion of a substance in a pharmacopoeia does not indicate that it is either safe or effective for the treatment of any disease.

he *British Pharmacopoeia* is published on behalf of the Health Ministers of the United Kingdom; on the recommendation of the Commission on Human Medicines, in accordance with section 99(6) of the Medicines Act 1968, and notified in draft to the European Commission (EC) in accordance with Directive 98/34/EEC.

The monographs of the European Pharmacopoeia (as amended by Supplements published by the Council of Europe) are reproduced either in the *British Pharmacopoeia*, or in the associated edition of the *British Pharmacopoeia (Veterinary)*.

In the pharmacopoeia, certain drugs and preparations are included regardless of the existence of actual or potential patent rights. Where substances are protected by letters patent, their inclusion in the pharmacopoeia neither conveys, nor implies, licence to manufacture.

The regulation of medicinal products by officials in the United Kingdom dates back to the reign of King Henry VIII (1491–1547). The Royal College of Physicians of London had the power to inspect apothecaries' products in the London area, and to destroy defective stock. The first list of approved drugs, with information on how they should be prepared, was the *London Pharmacopoeia*, published in 1618. The first edition of what is now known as the *British Pharmacopoeia* was published in 1864, and was one of the first attempts to harmonise pharmaceutical standards, through the merger of the *London*, *Edinburgh* and *Dublin Pharmacopoeias*. The New Latin name that had some currency at the time was *Pharmacopoeia Britannica* (Ph. Br.).

A commission was first appointed by the General Medical Council (GMC), when the body was made statutorily responsible under the Medical Act 1858 for producing a British pharmacopoeia on a national basis. In 1907, the *British Pharmacopoeia* was supplemented by the *British Pharmaceutical Codex*, which gave information on drugs and other pharmaceutical substances not included in the *BP*, and provided standards for these.

The Medicines Act 1968[1] established the legal status of the British Pharmacopoeia Commission, and of the *British Pharmacopoeia*, as the UK standard for medicinal products under section 4 of the Act. The British Pharmacopoeia Commission continues the work of the earlier Commissions appointed by the GMC, and is responsible for preparing new editions of the *British Pharmacopoeia* and the *British Pharmacopoeia (Veterinary)*, and for keeping them up to date. Under Section 100 of the Medicines Act, the British Pharmacopoeia Commission is also responsible for selecting and devising British Approved Names (BANs )

Since its first publication back in 1864, the distribution of the *British Pharmacopoeia* has grown throughout the world. It is now used in over 100 countries. Australia and Canada are two of the countries that have adopted the *BP* as their national standard alongside the UK; in other countries, e.g. South Korea, the *BP* is recognised as an acceptable reference standard The current edition of the *British Pharmacopoeia* comprises six volumes, which contain nearly 3,000 monographs for drug substances, excipients, and formulated preparation, together with supporting general notices, appendices (test methods, reagents etc.), and reference spectra, used in the practice of medicine, all comprehensively indexed and cross-referenced for easy reference. Items used exclusively in veterinary medicine in the UK are included in the *BP (Veterinary)*.

**Volumes I and II**

- Medicinal Substances

**Volume III**

- Formulated Preparations
- Blood related Preparations
- Immunological Products
- Radiopharmaceutical Preparations
- Surgical Materials
- Homeopathic Preparations

**Volume IV**

- Appendices
- Infrared Reference Spectra
- Index

**Volume V**

- British Pharmacopoeia (Veterinary)

**Volume VI**

(CD-ROM version)

- British Pharmacopoeia
- British Pharmacopoeia (Veterinary)
- British Approved Names

The *British Pharmacopoeia* is available as a printed volume and electronically in both on-line and CD-ROM versions; the electronic products use sophisticated search techniques to locate information quickly. For example, pharmacists referring to a monograph can immediately link to other related substances and appendices referenced in the content by using 130,000+ hypertext links within the text.

The *British Pharmacopoeia* is prepared by the Pharmacopoeial Secretariat, working in collaboration with the British Pharmacopoeia Laboratory, the British Pharmacopoeia Commission (BPC), and its Expert Advisory Groups (EAG) and Advisory Panels. The development of pharmacopoeial standards receives input from relevant industries, hospitals, academia, professional bodies and governmental sources, both within and outside the UK.

The British Pharmacopoeia Laboratory provides analytical and technical support to the *British Pharmacopoeia*. Its major functions are:

- Development of new pharmacopoeial monographs: the laboratory undertakes the development and validation of qualitative and quantitative test methods for new BP monograph specifications, and refines and revalidates test methods for existing British Pharmacopoeia monographs.
- British Pharmacopoeia Chemical Reference Substances (BPCRS): the laboratory is responsible for the procurement, establishment, maintenance and sale of BPCRS. The catalogue currently contains nearly 500 BPCRS, which are needed as standards for monograph tests in both the *British Pharmacopoeia* and the *British Pharmacopoeia (Veterinary)*.

**Indian Pharmacopoeia Commission** (**IPC**) is an autonomous institution of the Ministry of Health and Family Welfare which sets standards for all drugs that are manufactured, sold and consumed in India. The set of standards are published under the title **Indian Pharmacopoeia** (**IP**) which has been modelled over and historically follows from the British Pharmacopoeia. The standards that are in effect since 1 December 2010, is the *Indian Pharmacopoeia 2010 (IP 2010)*. The Pharmacopoeia 2014 was released by Health Minister Ghulam Nabi Azad on 4 November 2013.

**I.P.**, the abbreviation of 'Indian Pharmacopoeia' is familiar to the consumers in the Indian sub-continent as a mandatory drug name suffix. Drugs manufactured in India have to be labelled with the mandatory non-proprietary drug name with the suffix *I.P* This is similar to the *B.P.* suffix for British Pharmacopoeia and the *U.S.P.* suffix for the United States Pharmacopeia.

The IPC was formed according to the Indian *Drugs and Cosmetics Act* of 1940 and established by executive orders of the Government of India in 1956.

the actual process of publishing the first Pharmacopoeia started in the year 1944 under the chairmanship of Col. R. N. Chopra. The I. P. list was first published in the year 1946 and was put forth for approval. The titles are suffixed with the respective years of publication, e.g. IP 1996.

The first edition of IP was published in 1955, by the govt. Of India, Ministry of health and family welfare, under the chairmanship of Dr.B.N.Ghosh.It is written in English and official titles of monographs are in Latin.It covers 986 monographs.The supplement of IP 1955 was published in 1960.It consists of 1 volume. The second edition of the Indian pharmacopoeia was published in 1966 and later on it's supplement was published in 1975,under the chairmanship of Dr.B.Mukharjee.274 monographs from IP 1955 and their supplements were deleted, and 93 new monographs we're added.In this supplement 126 new monographs we're included and 250 monographs we're amended. Most importantly cholera vaccine were deleted. The third edition of IP was published in 1985 and presented in two volumes and nine appendices.In all total 261 new monographs we're added and 450 monographs we're deleted.It consists of 2 addendums .The addendum 1 was published in the year 1989 in which 46 new monographs we're added and 126 amended.Addendum 2 was published in the year 1991 in which 62 new monographs we're added and 110 we're amended. The fourth edition was published in the year 1996 and presented in two volumes, under the chairmanship of Dr.Nityanand.It has been made effective from 1st December 1996. It covered 1149 monographs and 123 appendices.It includes 294 new monographs and 110 monographs have been deleted.It consists of 3 addendums.The addendum 1 was published in 2000 wherein 42 monographs we're added.The addendum 2 was published in the year 2002 and 19 new monographs have been added. Addendum 3 was published in the year 2005.The veterinary supplement contains 208 monographs and four appendices.The fifth edition of IP was published in the year 2008 and was presented in 3 volumes, under the chairmanship of Dr. Nityanand.The supplement was published in the year 2008 containing 72 new monographs.

The following table describes the publication history of the Indian Pharmacopoeia

| Edition | Year | Addendum/Supplement |
|---|---|---|
| 1st Edition | **1955** | Supplement 1960 |
| 2nd Edition | **1966** | Supplement 1975 |
| 3rd Edition | **1985** | Addendum 1989 |
| | | Addendum 1991 |
| 4th Edition | **1996** | Addendum 2000 |
| | | Vet Supplement 2000 |
| | | Addendum 2002 |
| | | Addendum 2005 |
| 5th Edition | **2007** | Addendum 2008 |
| 6th Edition | **2010** | Addendum 2012 |
| 7th Edition | **2014** | Addendum 2015 |
| | | Addendum 2016 |
| 8th Edition | **2018** | Addendum 2019 |

During the Revolutionary War a few local pharmacopeias were published. The Lititz Pharmacopoeia was the first in 1778, compiled by William Brown who was trained in Edinburgh. Another small pharmacopeia was published for the French military hospitals in North America, the Compendium Pharmaceuticum by Jean Francois Costé. After the war ended the use of these works diminished and for the most part American physicians went back to using British pharmacopoeias and dispensatories. Physicians began to emerge during these early years of the republic, and they practiced both medicine and pharmacy by diagnosing diseases, and compounded and dispensed medicines. But still there was no assurance that these medicines were composed of quality materials and even if they were potent. John Morgan, who established the first medical school in America in Philadelphia in 1765, proposed the "composing a pharmacopoeia for use by Physicians and Practitioners of Pennsylvania" at a meeting and on June 3, 1788 passed a motion to appoint a committee to "form a Pharmacopoeia for use of the College." But by 1789, the interest in a pharmacopoeia just for Pennsylvania had dwindled. Support grew, instead, for creating a national pharmacopoeia that would bring order to these preparationsthroughout the nation. Prominent national and medical figures such as Benjamin Franklin spoke not only about a formulary but of "some Standard amongst ourselves" for America. But this goal proved to be challenging in a country that was still undeveloped and sparsely populated, pharmacy could be practiced without a license, and the joint practice of medicine and pharmacy prevailed. This effort did not come to fruition and no pharmacopoeia was published at this time to support the nationalistic fervor of some of the leading physicians of the time who wanted the "full range of truly American medicinal plants" (Sonnedecker, A National Movement Emerges 1994) to be included.

The distinction of the first American Pharmacopoeia went to the Massachusetts Pharmacopoeia, published in 1808 by the Massachusetts Medical Society (Sonnedecker, A National Movement Emerges 1994). Two young physicians, James Jackson and John Collins Warren took on the responsibility to identify those articles that cured diseases and best methods of preparation, and named them using English versus Latin names. The Massachusetts Pharmacopoeia was intended to be a standard of uniformity for medicinal articles to be adopted by all "professional men" in the United States, although compliance with it was not required. It relied on "selfgovernment among independent and reliable practitioners, rather than government intervention" (Sonnedecker, A National Movement Emerges 1994). The New Hampshire Medical Society adopted it but South Carolina, although supportive of the idea of a national pharmacopeia did not see it as a "national" effort representing the differences between diseases and their treatment in different parts of the country. Nonetheless, it was a significant achievement and proved to be a model for future efforts. An American New Dispensatory based on the Massachusetts Pharmacopeia published by James Thacher, a Boston physician and Revolutionary veteran gave further credibility to the Massachusetts effort. Ten years later, in 1816, Samuel Latham Mitchill, along with Valentine Seaman, published the Pharmacopoeia of the New York Hospital, again for the use of hospital interns. But Mitchill had greater ambitions of breaking free of the 'colonial' yolk of Britain. Mitchill along with Lyman Spalding and Jacob Bigelow, who later became the founders of the USP, had their own motivations to start a 'national' pharmacopoeia. Spalding espoused uniformity, Mitchill, nationalism, and Bigelow saw a pharmacopoeia as supporting the native materia medica. Spalding drew the initial plan and coordinated the group. His goal was to fulfill the urgent need

for uniform standards for medicines that could be utilized across the country. Mitchill used his influencein medical and political arena (he was also a United States senator) to promote the idea. Bigelow with his expertise in plant drugs and the publication process, served as editor of the USP. On January 6, 1817, during a meeting of the New York County Medical Society, Lyman Spalding formally proposed the framework for the establishment of an American pharmacopoeia in the United States of America. It was proposed that four pharmacopeial conventions would be held in the four regional districts. Each would produce or select a pharmacopeia, and would send delegates to the national convention in Washington, January 1, 1820. The pharmacopeia would be revised every ten years. The state medical societies would adopt it thereby giving it authority. A committee of the State Medical Society of New York adopted the project of establishing a "uniform Pharmacopoeia throughout the United States" (Sonnedecker, A National Movement Emerges 1994) and named an influential implementation committee. The society sent a circular to other medical societies and schools around the nation marking the beginning of democratic participation in the revision of USP.

Less than three years later, on January 1, 1820, 11 of the 16 delegates - all physicians - gathered in Old Senate Chamber of the U.S. Capitol building to form the United States Pharmacopoeial Convention and create the first Pharmacopoeia of the United States. Holding the Convention at the U.S. Capitol underscored its national significance and democratic procedure although no government support or enforcement of the pharmacopeia was expected (Sonnedecker, A National Movement Emerges 1994). The first Pharmacopoeia of the United States of America containing 221 monographs was successfully published by the end of that year. It was made up of five sections, beginning with the front matter, the historical introduction and preface, followed by the materia medica, a list of 221 drugs; a secondary list of 71 drugs for substances of "doubtful efficacy"; a section on weights and measures; and an untitled section of 329 preparations and compositions (Anderson and Higby 1995). In terms of content, the pharmacopeia reflected the therapeutics of the time including tonics, strong laxatives, diuretics, and flavoring herbs. The preparations included cerates, confections, decoctions, extracts, honeys, infusions, liniments, mixtures, ointments, pills, plasters, powders, spirits, syrups, tinctures, troches, vinegars, washes, waters, and wines. No techniques were included, just recipes. There was nothing to address the purity of chemicals - chemical formula, identifications or assays which are hallmarks of a modernpharmacopeia. In 1828, a second printing of the pharmacopeia was released with corrigenda that corrected a number of errors in the first edition. By the time the first decennial revision, a schism had developed between two of the most influential medical centers of the day, New York and Philadelphia. There were different interpretations of a section of the founding convention plans for future revisions, with Mitchill interpreting it as three delegates from each district, and the Philadelphia medical leaders thinking that the local medical societies were to send three delegates to the convention and were also late in submitting the names to Mitchill. He used this fact to keep out the Philadelphians who had been very critical of the 1820 edition. Rival conventions were held in New York and Washington. Mitchill presided over the New York Convention and two sessions were held on January 1, 1830 and June 2, 1830 as there were not many delegates in the former session. The Washington Convention was held on January 1, 1830, as had been stipulated in the founding documents. Two separate first revisions were issued, one in 1830, the New York edition as a result of the New York Convention and the other in1831, the

Philadelphia edition out of the Washington Convention. The New York edition was revised in a hurry on the premise that if it was published earlier it would give it primacy. But there were a number of errors. The Washington Convention was more deliberate in its process. It appointed a Committee of Revision with two members from different states and once the contents were drafted, they solicited feedback from the Philadelphia College of Pharmacy thus marking the entry of organized pharmacy into the pharmacopeial revision process. The New York edition also lacked a detailed preface, robbing it of any authority or credibility. The Philadelphia edition gave an informative preface about how choices were made with regard to nomenclature and admission of new drugs and preparation, and included "many practical suggestions" made by pharmacists. In the preface of the Philadelphia edition, George Wood stressed the need for uniformity and that it was the pharmacopeia's most salient contribution to medical and pharmacy practice. The Philadelphia edition survived based on it being a more thoroughly revised pharmacopeia than the New York edition and the fact that Philadelphia College of Physicians supported and publicized it with pharmacists. Bigelow also threw his weight behind the 1830 Philadelphia edition. With the death of Mitchill in 1831, the New York medical establishment withdrew from pharmacopeial revision for the next 50 years. Throughout the nineteenth-century, members of the Convention continued to follow the guidelines laid out in the preface of the first pharmacopoeia, meeting every ten years in Washington, DC. Underthe stewardship of great leaders and physicians like George B. Wood and Franklin Bache for the next four decades, the United States Pharmacopoeia (U.S.Ph) achieved sustained prominence and gained further recognition as a national standard. Bache and Wood also authored the United States Dispensatory (USD) that provided fuller descriptions and explanations of preparations but deferred to the authority of the U.S.Ph. The 1840 U.S.Ph revision contained numerous changes and new features and was said to be a "completely revised pharmacopoeia" (Anderson and Higby 1995). In 1848, an important step toward solidifying U.S.Ph's role as a recognized national standard came with the passage of the Drug Import Act, which mandated that drugs imported into the country must comply with USP's quality standards for strength and purity. Pharmacists became an integral part of pharmacopeial revision process during the 1850 revision that continues to this day along with physicians and other scientists in related disciplines. The 1860 (USP IV) and 1870 editions were not structurally any different from the earlier editions, but did include newer remedies and processes as well as technical methods. The Civil War distracted professionals responsible for its revision and did not alter the content much to meet the war time needs. USP IV for the first time included potency standards for cinchona, opium and scammony and the committee wrestled with problems in measurement science (metrology). It was the most popular edition up to that time. The 1870 edition included metric weights and measures tables, after the US Congress made the metric system legal in 1866. At the close of the nineteenth-century, in 1880, pharmacist Charles Rice, the newly appointed Chair of the Committee of Revision, initiated a complete revision and modernization of the USP reflecting advances that had been made in pharmaceutical chemistry. Antiquated pharmaceutical recipes were replaced with specific chemical formulas and precise tests for purity. A single alphabetical listing replaced the separate lists; short descriptions of all crude drugs, common adulterants, as well as parts by weight were included in the monographs. This edition also broke free of the dominance of the nomenclature discussions in the preface and instead focused on pharmaceutical technology. There was a separate section of reagents and tables - various test solutions and volumetric solutions, specific gravity and solubility tables (Anderson and Higby

1995). In addition, Dr. Rice established the first subcommittees and pioneered the use of revision circulars to give each member of the Committee of Revision equal influence in the revision process by implementing a voting and commenting system, the framework of which is still in use today. Dr. Rice had also served as head of the Pharmacopeia Committee at the American Pharmacists Association (APhA), that later published the National Formulary (NF) in 1888. As early as 1856, the APhA promoted the "standardization of names and formulas for dosage forms of drugs not described elsewhere" (Powers 1946) . The first edition was named National Formulary of Unofficial Preparations. It included primarily formulas that pharmacist's could compound including elixirs, emulsions, fluid extracts, tinctures, solutions, syrups, and dosage forms of the time. Over time with the emergence of pharmaceutical manufacturing in the late 1800s and the lessening of pharmacist-compounded medications, the NF began to focus on drugs that were not included in the U.S.Ph. Thus, the U.S.Ph was to include "drugs of first choice therapeutically "and NF "for other drugs whose extent of use justified development of a monograph" (Sonnedecker, Changing character of the National Formulary 1890-1970 1989). Although there was no legal recognition of the NF it was well established by the time the 1906 Federal Food and Drug Laws provided a role for both the U.S.Ph and NF in defining whether a drug should be deemed adulterated under federal law. The NF along with the U.S.Ph went a long way in establishing uniformity in drugs, nomenclature and preparations. Once the work of NF was completed, Rice turned his attention to revising U.S.Ph for the next decennial revision in 1890. For this revision, Rice solicited the opinion of outside experts who were not members of the Committee of Revision. This has been the mainstay of USP's revision process ever since. In 1892, the Revision Committee voted to change the abbreviation of the compendium from "U.S. Ph" to "USP." USP VII completely switched from parts-by-weight to metric system. It also did not include patented and trademarked drugs. In Remington's words "One of the principal objectives of a Pharmacopoeia is to establish standards, to prove the identity and purity of the substances admitted; in order to make such operative, it is necessary to have more than one source of supply or manufacture" (Anderson and Higby 1995). This exclusion of patented drugs proved to be an ongoing matter of debate, as the changes in medicine, and pharmacy increasingly called for the scope of the pharmacopoeia also follow suit. But it wasn't until the 1940s that they were cleared for consideration into the pharmacopeia. Synthetic compounds began to replace "mineral and vegetable drugs." Federal regulations started intervening in the manufacture and marketing of drugs. These developments demanded more from the USP in terms of time, expertise, and financial obligations that led to major procedural and organizational changes. The next major turning point in USP's history was initiated during the Pharmacopeial

Convention of 1900, when then Convention President, Horatio C Wood, urged the Convention to create a written Constitution and Bylaws. "The new Constitution and Bylaws defined for the first time the institutions entitled to have representation at the Convention", (Anderson and Higby 1995) and called for the creation of USP's first Board of Trustees. Moreover, the members of the 1900 convention passed a resolution directing the Board of Trustees to officially incorporate the United States Pharmacopeia in the District of Columbia. The July 11, 1900 certificate of incorporation gave USP's newly created Board of Trustees power over the "management and control of the affairs, funds, and property" of the organization." (Anderson and Higby 1995) USP VIII became official in 1905 with significant changes. Average doses, allowable percentages of

impurities, specific assays for several drugs, and nomenclature of synthetic drugs and chemicals made their way into the pharmacopoeia. It included a disclaimer that the standards for purity and strength in the compendium are for substances used solely for medicinal purposes. It also included the first official biological product, diphtheria antitoxin. (Anderson and Higby 1995) Another significant event for USP at the turn of the century was the passage of the 1906 Food, Drug, and Cosmetic Act by the federal government. Although individual states had increasingly recognized USP, this legislation strengthened USP's role by mandating that drugs "sold under or by a name recognized in the United States Pharmacopeia or National Formulary," must meet the standards of strength, quality, or purity stipulated in these compendia. The impact that this legislation had on the USP and NF was significant and it elevated the position of the compendia. The 4th ed. of the NF, the first after the Act was passed, was published in 1916. It introduced standards for identity, strength quality and purity as well as distinctive titles and formulas. Official formulas for parenteral solutions, "Ampuls," were also included for the first time. Due to the passage of the 1906 Act, there was more scrutiny of the USP and more discrepancies and errors were brought to the attention of the Committee. 243 monographs were deleted; notable amongst them were standards for whiskey and brandy. Small pox vaccine was added to USP IX. The 9th revision of the USP also addressed the issue of scope. Remington remained steadfast in his stand on excluding patented drugs from USP IX. E. Fullerton Cook took over the reins of the Committee of Revision and USP X replaced Part 1 and II of USP IX with Monographs, and General Tests, Processes and Apparatus. Only preparations that had some claim to efficacy were included. As a result many common drugs used widely by 1906 FD&C Act 1938 FD&C Act USP Chinese Translation USP Vitamin Advisory Board physicians and patients ended up with no public standards. It wasn't until the next revision that proprietary or branded drugs were admitted into USP X. It was included in the USP only if the manufacturers had provided written consent, appropriate tests and standards, and admitted only under chemical or descriptive names. This was supported by the pharmaceutical industry and a closer working relationship was established between USP and industry. They participated more actively in the revision of the USP. Cook also reintroduced advisory panels so the best minds in science, pharmacy and medicine could participate in the revision of the pharmacopeia. The USP Vitamin Advisory Board included leading experts Lafayette Mendel and Elmer V. McCollum, and its work led to the first vitamin standard to be included in the USP. This period also saw closer cooperation between USP and government agencies with the importance of bioassay methods growing as also the developments in legislative (1902 Biologics Act) and scientific areas. The assays that determined the potency of digitalis led to the Bureau of Chemistry, the predecessor to the Food and Drug Administration (FDA) providing packaged, standardized product samples, or "reference standards", for industry to comply with methods in USP X. The 1920's marked the advent of the USP Reference Standards program with standards for Vitamin A and D content in cod liver oil. During the period 1900 and 1930, the USP was translated into Spanish and then Chinese, both being important contributions to international public health. There were other innovations in the publication of the USP such as the continuous revision in the 1930s to keep pace with rapid developments in medical and pharmaceutical science and industry. The NF also saw major revisions in the 1930s. The sixth edition of the NF included monographs on ampuls and tablets with standards for identity, strength, purity and quality and admissions into the NF were based on science. Obsolete drugs were discontinued and "additional chemical, biological and proximate assays were developed and introduced" (Powers 1946). The 11th revision of the

USP in 1936 saw obsolete items such as fluidextracts and tinctures being removed. A number of biologicals were added such as the scarlet fever antitoxin, rabies and typhoid vaccines and ephedrine. The 1938 Food, Drug & Cosmetic ( FD&C Act) expanded the role of both the USP & NF in the adulteration and misbranding provisions of federal law, regarding naming, identity, and strength, quality and purity, and also provided a role for USP's and NF's packaging and USP XIV labeling requirements. The Act had far reaching effects on how the USP and NF worked. The USP evolved from 'continuous revision' to a five year publication cycle in the 1940s. The NF also included provisions to issue revision supplements and being published every five years instead of 10 years. The publication schedules were also synchronized and slowly the differences between USP and NF monographs became almost indistinguishable over the next few decades as the NF also started admitting drugs based on their therapeutic value as opposed to just extent of use. In contrast to the USP's reluctance to set up a laboratory in earlier revision cycles, the American Pharmaceutical Association, the publishers of NF, saw the need for a well equipped laboratory to research and test new methods and procedures. A laboratory was established in 1938 at the Association's headquarters. It also saw efforts to coordinate the scope of the two compendia. As a result of diagnostic agents being recognized as "drugs" in the 1938 Act, NF VII included a chapter on diagnostic substances. USP XII in 1942 was the first revision published under the five year schedule and it included monographs for injections for the first time, and compressed tablets finally were included although they were in use since Charles Rice's time. There were also some firsts for the FDA. Insulin in 1941 and increased production of Penicillin in 1944 during World War II led to the Congress of the United States adding sections to the 1938 FD&C Act requiring FDA to certify insulin and penicillin products in response to appeals from USP and AMA. USP XIII was the first revision to have monographs under English titles following the NF decision to switch to English titles earlier. Five of the oils that were official since the 1820 USP, were dropped from USP XIII and the first adrenal hormones and seven penicillin preparations were introduced. For the first time, the "unqualified admission of proprietary products without regard to patent status" (Anderson and Penningroth, Good Work and True 2000) were included. USP XIV saw the disappearance of the diphthong, the "œ" in the word Pharmacopeia on its title page. Patented drugs were indicated with an asterisk and there was also a warning against violating property rights of the patent and trademark holders. It included five antibiotics, and the first official monograph for antihistamine. Folic acid was first included in USP XIV, as also the first two official anticoagulants, heparin and bishydroxycoumarin, and amphetamine. With continued official legal recognition, USP grew and expanded its efforts to promote public health during the mid twentieth-century. In 1950 after years of working out of the homes of its volunteers, USP purchased its first permanent headquarters on Park Avenue in New York City, which was urgently needed to support USP's rapid expansion. To cultivate this growth, the USP Board of Trustees appointed Lloyd Miller to serve as Director of Revision in 1949, making him USP's first USP X-XVIII; NF 8-12 salaried employee. USP XV released in 1955, included new steroid products, combined diphtheria and tetanus toxoids and pertussis vaccine (DTP), and excluded several older remedies such as cascara sagrada extract and fluid extract, ephedrine, and estradiol. The General Tests section was extensively revised with modern tests and assays. The General Notices section was revised collaboratively with APhA's Revision Committee, so the two compendia were as close to conformance as possible. It also included detailed standards for official biologicals that previous revisions did not. Miller also insisted on clarity and consistency in style and a USP Style Guide

provided guidelines for the publication. Dosage ranges and the classification of drugs according to pharmacological category was introduced in USP XV and XVI. Due to the rapid introduction of new drugs into the market, the USP was to a certain extent outdated when a new revision was published so the Committee of Revision decided to include a list of "provisional admissions" in the XVI revision that were worthy of admission but did not have monographs at the time of publication. These would then be elaborated through Supplements. The XVI revision most notably included the first chemical assay for vitamin D; diuretics, human blood cells, and influenza virus and poliomyelitis vaccine were some others. During Miller's tenure the USP would also grapple with nomenclature issues, specifically in selecting nonproprietary names in the USP and the need for a USP research laboratory. In response to these challenges, USP took on its first auxiliary publication, the United States Adopted Names or USAN that was a combined effort of the AMA, USP and APhA. It also established the Drug Standards Laboratory with funding provided by the AMA, APhA, and USP in the 1960s thus supporting the expansion of the Reference Standards program. The 1962 Kefauver-Harris amendments to the FD&C Act introduced key changes affecting USP. FDA for the first time was given authority to require GMPs (current good manufacturing practices). Also for the first time drugs were required to be cleared by FDA for both safety, and efficacy, before marketing; this obviated the need for a USP committee on scope, since all newly marketed drugs were required to be deemed both safe and effective. Beginning with the XVII revision official antibiotic monographs included "only those aspects of identity, purity, potency, and packaging and storage that are of special interest to the physician and pharmacist" (United States Pharmacopeial Convention 1965) reflecting the requirement that FDA certify all antibiotics. USP XVII and XVII included several technical innovations such as standards for plastic prescription containers, content uniformity standards for some tablets and capsules, and caution statements for few dangerous drugs such as digoxin and methotrexate. Reference Standards (there had been only 37 in 1950) grew considerably in USP XVIII but did not include narcotic agents and radioactive agents. The most challenging problem of OTA Report USP-NF Merger this time was the bioavailability of solid dosage forms and setting practical bioavailability standards proved to be elusive. As a start USP XVIII included dissolution tests for six monographs replacing the disintegration tests. Another technical advance that was anticipated, Good Manufacturing Practices (GMP), was "monitoring potentially harmful bacteria" in the production process and chose "four index organisms" to serve as a warning signal (Anderson and Higby 1995, 359). The General Tests, Processes and Apparatus section included three chapters on effectiveness of antimicrobial agents in parenterals and ophthalmic solutions. The 1960s also saw drugs in the currently official USP and NF being included in third-party health care plans and those of the federal government drug coverage (Anderson and Higby 1995, 374). The USP maintained its headquarters in New York for nearly twenty years before relocating to Washington, DC area in 1969, a move that was prompted by the need for more space and a closer proximity to the FDA that had expanded its operations and authority as a result of the KefauverHarris Act. One of the major technical issues facing the Committee of Revision during the 1970s was that of bioequivalence. The OTA Drug Bioequivalence Study in 1974 criticized "current standards and regulatory practices" in assuring bioequivalence for drug products and did not spare either the FDA's Good Manufacturing Practices or compendial standards of USP and NF. It charged that the "physical tests and assay procedures of much greater sensitivity" (Anderson and Higby 1995, 465) than those specified by the compendia existed, objected to the initial dissolution test in USP XVIII

among other issues. It also called for a single compendial organization to "revise drug and drug product standards continuously on the basis of the best available technology." (Anderson and Higby 1995, 466). William Heller, the Executive Director, responded that organizational changes were already underway with the purchase of the NF and the drug standards laboratory. He also indicated that the panel failed to differentiate between manufacturing processes that were under FDA authority and "regulatory standards and tests for raw materials and finished drug products" (Anderson and Higby 1995, 466) that were in the compendia. After long and protracted negotiations, USP successfully purchased the NF, along with the Drug Standards Laboratory in the 1975 from the APhA. The USP released the first combined edition of the USP-NF in 1980. It also began publishing the Pharmacopeial Forum in 1975 to publicize revision proposals and to solicit public comments. The 1970s and 1980s were dominated by organizational and business issues with major reorganization of staff as well as the Committee of Revision. A major focus of the revision activity in the early 1970s was focused on drug selection and this was formally separated from standard- USP Reference Standards USP-NF Electronic setting providing expanded opportunities for USP. In 1973, the first edition of the USP Guide to Select Drugs was published. It was a listing of drugs admitted into USP XIX and arranged according to pharmacological/therapeutic categories based on the American Hospital Formulary Service classification. This was all in the hopes that a federal formulary would be established aimed at Medicare and Medicaid programs. This did not come to fruition due to a number of reasons such as physician opposition, drug efficacy requirement of the 1962 Act, acquisition of the NF and difficulty in the drug selection program, and as a result USP withdrew altogether from drug selection, which had been a part of USP's mission since 1820. The 1970 convention resolution had called for including therapeutic information in the USP. USP XIX included brief dispensing information and expanded the dosage section but these were "nonenforceable" information in the official monographs that concerned a number of stakeholders. Most supported a separate volume clearly identified as nonofficial and the FDA wanted no distinction between approved and nonapproved uses of drugs. USP Board endorsed the separate volume but wanted it to be an extension of USP. This led to the birth of the USP Dispensing Information (USP DI) in 1980. USP XIX in 1975 had 1284 monographs which was a substantial increase from USP XVIII. It also included complex tests and methods, partly in response to the OTA report. Liquid chromatography was introduced and was increasingly used in later revisions. The first excipient monograph also made its way into the pharmacopeia. System suitability tests were introduced in USP XIX. USP XX-NF XV was the first combined volume and it discontinued dispensing information that was published in a separate publication USP DI. The Reference Standard program took over the distribution of reference substances of controlled drugs from NIMH in 1972 and the antibiotic reference standards from the FDA in 1975. The number of reference standards grew from about 250 in 1970 to 700 in 1975 (Anderson and Penningroth, Good Work and True 2000) and about 1200 Reference Standards were available in 1988. Most of the innovations between 1970 and 1990 were in the areas of dissolution tests, microbial limit tests, and standards for particulate matter in parenterals. Setting excipient standards was challenging as traditional parameters of strength and purity were not as important as particle size or surface area. Another major technological advance was the public offering of the sixth supplement to the USP XXII-NF XVII in an electronic version in 1992. The growth in the number of monographs admitted into USPNF continued into the 1990s with USP XXII-NF XVI covering a majority of the top 2000 drug substances and products with

over 3,200 monographsBy the mid-eighties USP had once again outgrown its current space in Rockville, MD that it had purchased in 1970, and began construction on a new building for its headquarters, known today as Twinbrook II. At the time of this building's completion in 1989, USP was increasingly making efforts to improve its international activities, and promote public health around the world. In 1989, the USP along with representatives from the Japanese and European Pharmacopoeia formed the Pharmacopeial Discussion Group to support the international harmonization of pharmaceutical monographs. Most notable of the harmonization efforts at this time was the NF monograph on 'Lactose Monohydrate' which was the first monograph to be harmonized. USP 23-NF 18 published in 1995 included a new section on nutritional supplements that included four new general chapters, on disintegration-dissolution, manufacturing practices, microbial limits and weight variation. It also worked to replace, reduce and refine tests and assays that used live animals. 250 rabbit pyrogen tests were replaced by the Bacterial Endotoxin Test, an in vitro procedure. Mouse safety test was deleted from antibiotic monographs. Veterinary drugs also made their appearance in USP 23. Two new chapters dealing with bioavailability and bioequivalence were introduced. Apothecary units were deleted and metric units were used for prescription and dispensing. Computer generated graphic formulas was another first in this revision. In 1996, USP introduced its first web site. USP 24-NF 19, published in 2000, saw the deletion of federal and other texts that were based on federal regulations as now they were freely available from government websites. Along with a GMP general chapter, two other information chapters dealing with FD&C Act requirements and Controlled Substances Act (CAS) were deleted. The 1997 FDA Modernization Act (FDAMA) provided a role for USP-NF monographs related to compounding, including the USP chapter on compounding, as part of a Congressional initiative to address pharmacy compounding. FDAMA also included a special role for USP standards related to determining when Positron Emission Tomography (PET) drugs might be deemed adulterated. PET tracers were addressed in 11 monographs and a general chapter on radiopharmaceutical in PET compounding was developed. Three radiolabeled monoclonal antibodies were introduced, the first antibodies to be included in the USP. Microbiology was another area where the standards were extensively revised. A general chapter on biocompatibility of materials, and cell permeability was introduced although standards for biomaterials themselves were deferred to later revisions. Chapters on quality of biotechnology drug products were also prepared. USP-NF Recall Notice MC & HMC Online USP-NF Online FCC & USP DS The Bacterial Endotoxin test chapter was entirely harmonized and a single reference standard was developed. USP 25-NF 20 published in 2002 started the annual publication of the USPNF and also as an online product. Two Supplements were published between annual editions. This revision created safety criteria for admission of dietary supplement monographs and classes for these monographs. In USP 28-NF 23 published in 2005, chromatographic assays were developed for a number of drug substance monographs replacing titration assays as the FDA required stability-indicating assays for these articles. The process of continuous revision continued with standards for pharmaceutical waters, packaging and storage, labeling and of mutlidose and singe dose vials, cautionary statements on ferrule and cap overseals for neuromuscular agents, control of heavy metals, medical gases, heparin, glycerin, sterile compounding, elemental impurities being some of the significant revisions. A major initiative of redesigning monographs was initiated in 2009 with "~4,000 monographs in the USP 33–NF 28 were redesigned, encompassing more than 4,100 pages, over four million words, and many figures and tables" (United States Pharmacopeial Convention 2010), with the intent of not

changing any of the substantive monograph requirements. There were significant errors in this massive undertaking and for the first time in USP history, a revision was recalled and reissued in 2010. USP's international expansion and interests continued to grow into the twenty-first century, leading in 2005 to the establishment of USP's first international office in Basel, Switzerland. This was followed by the opening of international laboratories in India in 2006 and China in 2007 and soon after in Brazil in 2008. USP has also engaged in a number of global health initiatives that help support the efforts of under-resourced countries to build capacity to combat substandard and counterfeit medicines. During the first two decades of this century USP has also successfully launched several new publications including the Pharmacists Pharmacopeia; the USP Reference Standards USP Locations newly acquired Food Chemical Codex (FCC); Dietary Supplements Compendium (DSC); and two online only publications Medicines Compendium (MC) and Herbal Medicines Compendium (HMC). USP has also translated the USP-NF into Spanish, Russian and Chinese. USP34-NF29 Published inon in 2011. USP35-NF 30 is published as a combinaton of two official compendia the USP and NF and made officially applicable from 1st may 2012. The USP 36-NF31 is published in November 2012. The USP 37-NF32 is published in November 2014. The USP 38-NF33 is published in november 2015. The USP39-NF34 is published in February 2016. USP40-NF35 becomes official from may 1st 2017. USP41-NF36 becomes offcial from may 1st 2018. USP42-NF37 was published in 2019. The USP43-NF38 published in 2020.

***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* aims to cover drugs and related substances reported to be of clinical interest anywhere in the world. It provides a useful source of information for patients arriving from abroad to identify their existing medication. This may reveal that a currently taken proprietary preparation is available under another brand name. Alternatively if the drug is not available, the class of agent can be determined allowing a pharmacist or doctor to determine which alternative equivalent drugs can be substituted. Monographs include Chemical Abstracts Service (CAS), Anatomical Therapeutic Chemical Classification System (ATC) numbers and FDA Unique Ingredient Identifier (UNII) codes to help readers refer to other information systems.

*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.

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.

Dosage Form (DF) is defined as the physical form of a dose of a chemical compound used as a drug or medication intended for administration or consumption. Common dosage forms include pill, tablet, or capsule, drink or syrup, aerosol or inhaler, liquid injection, pure powder or solid crystal (e.g., via oral ingestion or freebase smoking), and natural or herbal form such as plant or food of sorts, among many others. The route of administration (ROA) for drug delivery is dependent on the dosage form of the substance.

**Importance of dosage forms:**

- To provide safe and helpful delivery of accurate dosage
- We can easily identify many dosage forms from their different shape, colour.
- To mask the bitter and salty taste and odour of the drug
- To provide maximum drug action through inhalation therapy. e.g. inhalants
- To provide for the insertion of the drug into the body cavities. e.g. rectal, vaginal
- To protect the drug from the adverse effect of gastric juice of the stomach after oral administration. e.g. enteric coated tablet
- To provide the maximum drug action through the skin by topical administration. e.g. creams, ointments etc.
- To provide the drug within the body tissues. e.g. injections

Solid Dosage Forms (Oral):

*Solid dosage form means of capsules or tablets or similar solid drug products that taken orally. Examples: Tablets, capsules, pills etc.*

**Merits(advantages) and demerits(disadvantages) of Solid dosage form:**

**Merits:**

1. Unit dose system
2. Simplicity in production
3. Rapid dissolution
4. Provides stability

**Demerits:**

1. Not useful for unconscious patients
2. Difficult to swallow by children

Tablets: Tablets are the solid dosage forms containing medicinal substances with or without diluents.
It is prepared either by compression or moulding.
They may be either circular, flat or biconvex in shape.
There are many types of tablets-

Oral tablets

- Lozenge tablets
- Buccal tablets
- Sublingual tablets
- Chewable tablets
- Effervescent tablets
- Enteric-coated tablets
- Vaginal tablets
- example: paracetamol tablets,aminophylline tablets

Implants: Implants are sterile small tablets meant for insertion under the skin by a small cutting.
They are used to provide slow and continuous release of the drug
for a long time( 3-6 months).
Generally, these tablets are used in animals than a human being.
examples: steroidal hormones like testosterone, stilbesterol etc.

Capsules: Capsule is the solid unit dosage form of medicament in which the drug is enclosed.

Two main types of capsules-

1. Hard gelatin capsules:

- It is composed of gelatin, water, and less % of plasticizer.
- It has two parts-body and cap
- It is cylindrical and hemispherical
- These capsules filled by hand-operated or semi-automatic device
- example: amoxicillin

2.Soft gelatin capsules:

- It is composed of gelatin, water and 100% plasticizer
- It has a unit body
- It has different shapes like oval or spherical
- These capsules filled by machine(rotary machine)
- example: progesterone soft gelatin capsule

**Cachets:** Cachets consists of a dry powder enclosed in a shell, usually prepared from a mixture of rice flour and water by moulding into a suitable shape.
example: sodium aminosalicylate cachets

Powder: Powders are solid dosage form which containing mixtures of drugs in a dry state.
Powders are classified as-

- Simple powder
- Compound powder
- Effervescent powder
- Bulk powder
- Compressed powder

Pills: Pills are small, round-shaped solid forms containing a medicament.

Dusting powders: Dusting powders are mixtures of two or more ingredients in the fine powder. They are used in the skin for antiseptic, protective and lubricant purposes.

Effervescent powder: These are specially prepared solid dosage form intended for internal use. They usually contain citric acid, tartaric acid. sodium bicarbonate, medicament and sweetening agent(sucrose or saccharin).
Before administration, the desired quantity of granules is added to water, acids react with sodium bicarbonate and produce effervescence.
This preparation acts as an antacid.

Dentifrices: These are preparations in the form of **tooth-paste** or tooth powder.
They are used for cleaning the teeth with the help of a toothbrush.

**Mono-phasic Liquid Dosage Forms**

Liniments: Liniments are liquid or semi-solid preparations meant for external application to the skin.
Liniments are applied by rubbing or friction but should not be applied to the broken skin.
example: white liniment, soap liniment etc.

Lotion: Lotions are liquid preparation meant for external application on the skin without friction.
They are applied directly to the skin with the help of some absorbent material like cotton wool or gauze.
They usually contain alcohol and glycerin because alcohol hastens to dry and produces cooling sensation where glycerin keeps the skin moist.
They are generally used for the antiseptic purpose.
example- calamine lotion

Syrups: Syrups are sweet, viscous concentrated solutions of sucrose.
Syrups are two groups-
Syrups are prepared by a *simple solution method*. e.g. simple syrup
Syrups made by the *extraction process*. e.g. tolu syrup

Elixir: Elixirs are clear, flavoured, sweetened hydroalcoholic liquid preparations for oral administration.
example-piperazine citrate elixir

Linctus: Linctus is sweet, viscous liquid preparations containing medicinal substances which have demulcent, sedative or expectorant properties.
example- linctus codeine phosphate
They are used for cough treatment.

Gargles: Gargles are aqueous solutions containing medicaments meant for throat infection.

example- phenol gargle

Mouthwashes: Mouthwash is an aqueous solution containing medicaments, used for rinsing, deodorant, antiseptic action.
example- compound sodium chloride mouthwash

Throatpaints: Throatpaints are viscous liquid preparation used for mouth and throat infections.
example- iodine paint compound B.P.C

Sprays: Sprays are simple solutions containing medicaments intended for spraying into the throat and nose.

Ear drops: These are solutions of drugs which are introduced into the ear cavity with the help of a dropper.
It is used to prevent ear infections.
example- hydrogen peroxide ear drops, phenol ear drops.

Eye drops: Eye drops are sterile aqueous or oily solutions or suspensions which are introduced into the eye.
example- chloramphenicol eye drops, pilocarpine eye drops etc.

**I. Biphasic Liquid Dosage forms**

Emulsions: Emulsion is a biphasic liquid dosage form which containing two immiscible liquids, one of which is dispersed as minute globules into the other liquid with the help of an emulsifying agent.

This is two types- (a) o/w type(oil in water) emulsion

(b) w/o type(water in oil) emulsion

Suspension: Suspensions are the biphasic liquid dosage form in which finely divided solid particles is dispersed in a liquid or semi-solid medium.

They are used for external applications.

*example*- Ampicillin for oral suspension I.P.

Ointments: Ointments are semi-solid preparations which are used for *skin and mucous membrane.*
The ointment is mainly used as protective or emollient for the skin.
Typesof ointments:

- Epidermic ointments
- Endodermic ointments

- Antibiotic ointments
- Antifungal ointments
- Protectant ointments

*examples*- Salicylic acid ointment I.P.

Creams: Creams are viscous semi-solid emulsions for external uses to the *skin or mucous membrane.*
*examples*- Hydrocortisone cream B.P.C.
This is two types- (a) o/w (oil in water) creams and (b) w/o (water in oil) creams
Oil-in-water creams are more used for cosmetic preparations.

Paste: Pastes are semi-solid preparations intended for external application to the skin. Paste differ from ointment as they contain a high proportion of finely powdered medications, such as Zinc oxide (ZnO), Calcium carbonate( $CaCO_3$) etc.

Suppositories: Suppositories are semi-solid dosage form of medicament, that is *inserted in the body cavities(vagina, urethra or rectum) other than the mouth*.
*examples:* aminophylline suppositories, glycerol suppositories etc.
Types of suppositories:

1. Rectal suppositories
2. Vaginal suppositories
3. Nasal suppositories
4. Urethral suppositories

Aerosols: Aerosols may be defined as the disperse phase system, in which very fine solid particles or liquid droplets get dispersed in the which acts as the continuous phase.

Inhalations**:** Inhalations are the solutions of the volatile substance administered by the nasal route in the form of vapour.

Introduction Definition: A prescription is a written order from Registered Medical Practitioner or a Physician to a Pharmacist to compound and dispense a specific medication for the patient.
What does prescription includes: Patient details Directions for the pharmacist to prepare and dispense the medicament. Directions for the patient regarding administration of drugs.

Parts of the prescription Prescription Date Name,age,sex and address of the patient Superscription Inscription Subscription Signatura Renewal instructions Signature, address and registration number of the prescriber

Date: Every prescription must bear the date on which the particular medicines are prescribed. This helps the pharmacist to keep day-day Patient's record in chronologic order which helps the pharmacist or a physician to refer the old case in future. To avoid misuse of the narcotic or other habitat forming drugs containing prescriptions by the patient a number of times for dispensing. Name, Age, Sex and Address of the patient: Name, Age, Sex and Address of the patient must be written on the prescription.

Name helps the pharmacist to identify the correct Patients avoiding any chance of giving the medicine to a person other than the one it is dispensed for. Note: patient's full name must be written instead of nicknames or surnames. Age of the patient becomes important in the case of the Pediatric(children) and Geriatric(old people) cases. Because the dose of drugs in such cases varies(due to their differences in ability to metabolize drugs). Hence dose of the drugs are calculated based on the age factor in such cases. Note: In some cases weight and height of the patients are also required.

Sex/Gender of the patient also plays major role in prescription because dose of drugs may also vary based on the sex/gender of the patient(as their abilities to metabolize/ response towards drugs may vary in many cases). Address of the patient is generally recorded to contact the person at the later stage or to deliver the medication personally.

Superscription: This part of the prescription is represented by the symbol RX. In the ancient times it is considered as a prayer to Jupiter the God of healing for the fast recovery of the patient. Now a days it is used as a abbreviation for the Latin term "Take Thou" which means "you take" Inscription: This is considered as the main part of the prescription order. It contains the names and quantities of the prescribed ingredients. The name of each ingredient is written on a separate along with its quantity.

In the complex prescription containing several ingredients the inscription can be divided into following parts: Base (active medicament of therapeutic action) Adjuvants(substances added to increase action of medicament/ its palatability) vehicle(substance used to dissolve medicament/increase volume of preparation) Base Adjuvant Vehicle

Subscription: This part of the prescription contains directions of the prescriber to the pharmacist regarding the type and compounding of dosage form along with number of doses to be dispensed. This is important because dose of drug also depends on the type of the dosage form. Signatura: This part of the prescription contains directions to the patient regarding the administration of the drugs.

It is generally represented as ‘Sig’ on the prescription.

The instructions may include: The quantity to be taken The frequency of administration The mode of administration The special instructions such as dilation direction Renewal instructions: In this part, the prescriber whether the prescription can be renewed or not. It also should include the specifications like how many times it can be renewed It is of utmost importance incase of narcotic/other habitat forming drugs.Signature, Address and Regd.no of the prescriber: The signature and Regd.no of the prescriber turns the prescription into legal and authentic order to the pharmacist. This helps in preventing the use of spurious drugs. Regd.no is of utmost importance in prescription containing narcotic drugs.

Terms used in prescription Meaning Teaspoon full 5ml Dessertspoon full 8ml Tablespoon full 15ml Wineglass full 60ml Teacup full 120ml Tumblerfull 240ml O.D Once in a day B.D Twice in a day T.D Thrice in a day Q.D Four times in a day

HANDLING OF A PRESCRIPTION

The following steps are to be followed during handling of a prescription for compounding and dispensing: Receiving Reading and checking Collecting and weighing the material Compounding, labeling and packing Receiving: ¬The prescription should be received by the pharmacist himself. ¬While receiving, he shouldn't change any facial expressions

Because it may cause a impression on the patient that he is surprised or confused after seeing the prescription. ϖ Reading and Checking: ¬ On receiving the prescription the pharmacist should check the prescription whether it is written in a proper format. ¬ The prescription should always be screened behind the counter. ¬ Any doubts in case of prescription ingredients or drugs and directions he should discuss with another senior pharmacist or physician but not with the patient.

What to check in a prescription… ? Error in dosage Wrong drug or dosage form, Contra indicated drugs , Synergistic and Antagonistic drugs ,Drug interactions

Collecting and weighing the material: ¬ Before compounding the prescription, all the materials required for it are collected on the left side of the balance. ¬ After weighing each material should be shifted on to the right side of the balance. Note: while compounding label of the stock bottle should be read at least three times to avoid any error: When taken from the shelf When the contents are removed for weighing/measuring When containers are returned back to its proper place

Compounding, labeling and packing: ¬ Compounding should be carried out in a neat place. All the equipment required are cleaned and dried thoroughly. Only one prescription should be compounded at a time. The compounded materials should be filled in a suitable container based

on quantity and use. The size of the label should be proportional to the size of the container. Label should contain the required suggestions/directions to the patient.

**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 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. 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.

**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. 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.

**11 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.

**12. 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.

*cquired 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.

*achyphylaxis*: (*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.

**Dose proportionate to age:**

**i).Youngs formula:**

Dose for the child = (Age in years/ age in years+12) Adult dose

The formula is used for calculationg the doses for children under 12 years of age.

**ii).Dillings formula:**

Dose for the child = (Age in years/ 20) Adult dose

The formula is used for calculationg the doses for children in between 4 to 20 years of age.

**iii).Frieds formula:**

Dose for the child = (Age in months / 150) Adult dose

**Dose proportionate to body weight:**

**Clarks formula:**

Dose for the child = (childs weight in Kg/ 70) Adult dose

**Dose proportionate to body surface area:**

Dose for the child = (Surface area of child / surface area of adult) Adult dose

The average body surface area of adult 1.73m2

# UNIT-II

## WEIGHTS AND MEASURES- IMPERIAL AND METRIC SYSTEM

The imperial system of units, imperial system or imperial units (also known as British Imperial or Exchequer Standards of 1825) is the system of units first defined in the British Weights and Measures Act 1824 and continued to be developed through a series of Weights and Measures Acts and amendments. The imperial units replaced the Winchester Standards, which were in effect from 1588 to 1825.[2] The system came into official use across the British Empire. By the late 20th century, most nations of the former empire had officially adopted the metric system as their main system of measurement but imperial units are still used in the United Kingdom, Canada and other countries formerly part of the British Empire. The imperial system developed from what were first known as English units, as did the related system of United States customary units.

Apothecaries units are mentioned neither in the act of 1824 nor 1825. At the time, apothecaries' weights and measures were regulated "in England, Wales, and Berwick-upon-Tweed" by the London College of Physicians, and in Ireland by the Dublin College of Physicians. In Scotland, apothecaries' units were unofficially regulated by the Edinburgh College of Physicians. The three colleges published, at infrequent intervals, pharmacopoeiae, the London and Dublin editions having the force of law.[6][7]

Imperial apothecaries' measures, based on the imperial pint of 20 fluid ounces, were introduced by the publication of the London Pharmacopoeia of 1836,[8][9] the Edinburgh Pharmacopoeia of 1839,[10] and the Dublin Pharmacopoeia of 1850.[11] The Medical Act of 1858 transferred to The Crown the right to publish the official pharmacopoeia and to regulate apothecaries' weights and measures.[12]

A metric system is a system of measurement that succeeded the decimalised system based on the metre introduced in France in the 1790s. The historical development of these systems culminated in the definition of the International System of Units (SI), under the oversight of an international standards body.

The historical evolution of metric systems has resulted in the recognition of several principles. Each of the fundamental dimensions of nature is expressed by a single base unit of measure. The definition of base units has increasingly been realised from natural principles, rather than by copies of physical artefacts. For quantities derived from the fundamental base units of the system, units derived from the base units are used–e.g., the square metre is the derived unit for area, a quantity derived from length. These derived units are coherent, which means that they involve only products of powers of the base units, without empirical factors. For any given quantity whose unit has a special name and symbol, an extended set of smaller and larger units is defined that are related in a systematic system of factors of powers of ten. The unit of time should be the second; the unit of length should be either the metre or a decimal multiple of it; and the unit of mass should be the gram or a decimal multiple of it.

Metric systems have evolved since the 1790s, as science and technology have evolved, in providing a single universal measuring system. Before and in addition to the SI, some other examples of metric systems are the following: the MKS system of units and the MKSA systems, which are the direct forerunners of the SI; the centimetre–gram–second (CGS) system and its subtypes, the CGS electrostatic (cgs-esu) system, the CGS electromagnetic (cgs-emu) system, and their still-popular blend, the Gaussian system; the metre–tonne–second (MTS) system; and the gravitational metric systems, which can be based on either the metre or the centimetre, and either the gram(-force) or the kilogram(-force).

In the metric system, multiples and sub multiples of units follow a decimal pattern.

| Metric prefixes in everyday use | | | |
|---|---|---|---|
| **Text** | **Symbol** | **Factor** | **Power** |
| tera | T | 1000000000000 | $10^{12}$ |
| giga | G | 1000000000 | $10^{9}$ |
| mega | M | 1000000 | $10^{6}$ |
| kilo | k | 1000 | $10^{3}$ |
| hecto | h | 100 | $10^{2}$ |
| deca | da | 10 | $10^{1}$ |
| (none) | (none) | 1 | $10^{0}$ |
| deci | d | 0.1 | $10^{-1}$ |
| centi | c | 0.01 | $10^{-2}$ |
| milli | m | 0.001 | $10^{-3}$ |
| micro | μ | 0.000001 | $10^{-6}$ |
| nano | n | 0.000000001 | $10^{-9}$ |

| | | | |
|---|---|---|---|
| pico | p | 0.000000000001 | $10^{-12}$ |

- v
- t
- e

A common set of decimal-based prefixes that have the effect of multiplication or division by an integer power of ten can be applied to units that are themselves too large or too small for practical use. The concept of using consistent classical (Latin or Greek) names for the prefixes was first proposed in a report by the French Revolutionary Commission on Weights and Measures in May 1793. The prefix *kilo*, for example, is used to multiply the unit by 1000, and the prefix *milli* is to indicate a one-thousandth part of the unit. Thus the *kilogram* and *kilometre* are a housand grams and metres respectively, and a *milligram* and *millimetre* are one thousandth of a gram and metre respectively. These relations can be written symbolically as:[6]

1 mg = 0.001 g

1 km = 1000 m

In the early days, multipliers that were positive powers of ten were given Greek-derived prefixes such as *kilo-* and *mega-*, and those that were negative powers of ten were given Latin-derived prefixes such as *centi-* and *milli-*. However, 1935 extensions to the prefix system did not follow this convention: the prefixes *nano-* and *micro-*, for example have Greek roots. During the 19th century the

prefix *myria-*, derived from the Greek word μύριοι (*mýrioi*), was used as a multiplier for 10000.

When applying prefixes to derived units of area and volume that are expressed in terms of units of length squared or cubed, the square and cube operators are applied to the unit of length including the prefix, as illustrated below.

1 $mm^2$ (square millimetre) = $(1\ mm)^2$ = $(0.001\ m)^2$ = 0.000001 $m^2$

1 $km^2$ (square kilometre) = $(1\ km)^2$ = $(1000\ m)^2$ = 1000000 $m^2$

1 $mm^3$ (cubic millimetre) = $(1\ mm)^3$ = $(0.001\ m)^3$ = 0.000000001 $m^3$

1 $km^3$ (cubic kilometre) = $(1\ km)^3$ = $(1000\ m)^3$ = 1000000000 $m^3$

Prefixes are not usually used to indicate multiples of a second greater than 1; the non-SI units of minute, hour and day are used instead. On the other hand, prefixes are used for multiples of the non-SI unit of volume, the litre (l, L) such as millilitres (ml).

Often, a worker will need to change the concentration of a solution by changing the amount of solvent. Dilution is the addition of solvent, which decreases the concentration of the solute in the solution. Concentration is the removal of solvent, which increases the concentration of the solute in the solution. (Do not confuse the two uses of the word *concentration* here!)

In both dilution and concentration, the amount of solute stays the same. This gives us a way to calculate what the new solution volume must be for the desired concentration of solute. From the definition of molarity,

molarity = moles of solute / liters of solution

we can solve for the number of moles of solute:

moles of solute = (molarity)(liters of solution)

A simpler way of writing this is to use $M$ to represent molarity and $V$ to represent volume. So the equation becomes

moles of solute = $MV$

Because this quantity does not change before and after the change in concentration, the product $MV$ must be the same before and after the concentration change. Using numbers to represent the initial and final conditions, we have

$M_1V_1 = M_2V_2$

as the dilution equation. The volumes must be expressed in the same units. Note that this equation gives only the initial and final conditions, not the amount of the change. The amount of change is determined by subtraction.

Example 9

If 25.0 mL of a 2.19 M solution are diluted to 72.8 mL, what is the final concentration?

Solution

It does not matter which set of conditions is labelled 1 or 2, as long as the conditions are paired together properly. Using the dilution equation, we have

(2.19 M)(25.0 mL) = M2(72.8 mL)

Solving for the second concentration (noting that the milliliter units cancel),

M2 = 0.752 M

The concentration of the solution has decreased. In going from 25.0 mL to 72.8 mL, 72.8 − 25.0 = 47.8 mL of solvent must be added.

Test Yourself

A 0.885 M solution of KBr whose initial volume is 76.5 mL has more water added until its concentration is 0.500 M. What is the new volume of the solution?

Answer

135.4 mL

Concentrating solutions involves removing solvent. Usually this is done by evapourating or boiling, assuming that the heat of boiling does not affect the solute. The dilution equation is used in these circumstances as well.

# UNIT-III

## MONOPHASIC AND BIPHASIC LIQUID DOSAGE FORMS

**Chapter Objectives**

**At the conclusion of this chapter the student should be able to:**

1. Classify and define monophasic and biphasic liquid dosage forms along with their advantages and disadvantages.
2. Discuss the desirable qualities of pharmaceutical suspensions.
3. Formulation of suspensions
4. Discuss the factors that affect the stability of suspensions and explain flocculation.
5. Describe settling and sedimentation theory and calculate sedimentation rates.
6. Define and calculate the two useful sedimentation parameters, sedimentation volume and degree of flocculation.
7. Define pharmaceutical emulsion and emulsifying agent and identify the type of emulsion.
8. Discuss the formulation of pharmaceutical emulsion, stability problem and methods to overcome it.

**Monophasic liquids**: Definitions and preparations of Gargles, Mouthwashes, Throat Paint, Eardrops, Nasal drops, Enemas, Syrups, Elixirs, Liniments and Lotions.

**Biphasic liquids:**

**Suspensions:** Definition, advantages and disadvantages, classifications, Preparation of suspensions; Flocculated and Deflocculated suspension & stability problems and methods to overcome.

**Emulsions:** Definition, classification, emulsifying agent, test for the identification of type ofEmulsion, Methods of preparation & stability problems and methods to overcome.

## LIQUID DOSAGE FORMS

Liquid dosage forms are either monophasic or biphasic. A monophasic liquid dosage form is one which contains only one phase. That is, it is a true solution. A true solution is a homogenous mixture of solid, liquid or gas in a liquid. A biphasic liquid dosage form contains two phases.

**Advantages of Liquid Dosage Forms**

i) They are the most suitable dosage form for infants, children and geriatric patients.

ii) The unpleasant taste of the drugs can be masked by adding sweetening and flavouring agents.

iii) It is attractive in appearance and gives beneficial psychological effects.

iv) The drug is rapidly available for absorption.

**Disadvantages of Liquid Dosage Forms**

i) The liquid dosage forms have less stability when compared to solid dosage forms.

ii) It is bulky to carry.

iii) A spoon is needed to administer a dose.

iv) Accidental breakage of the container results in loss of whole dosage form.

**Classification of Liquid Dosage Forms**

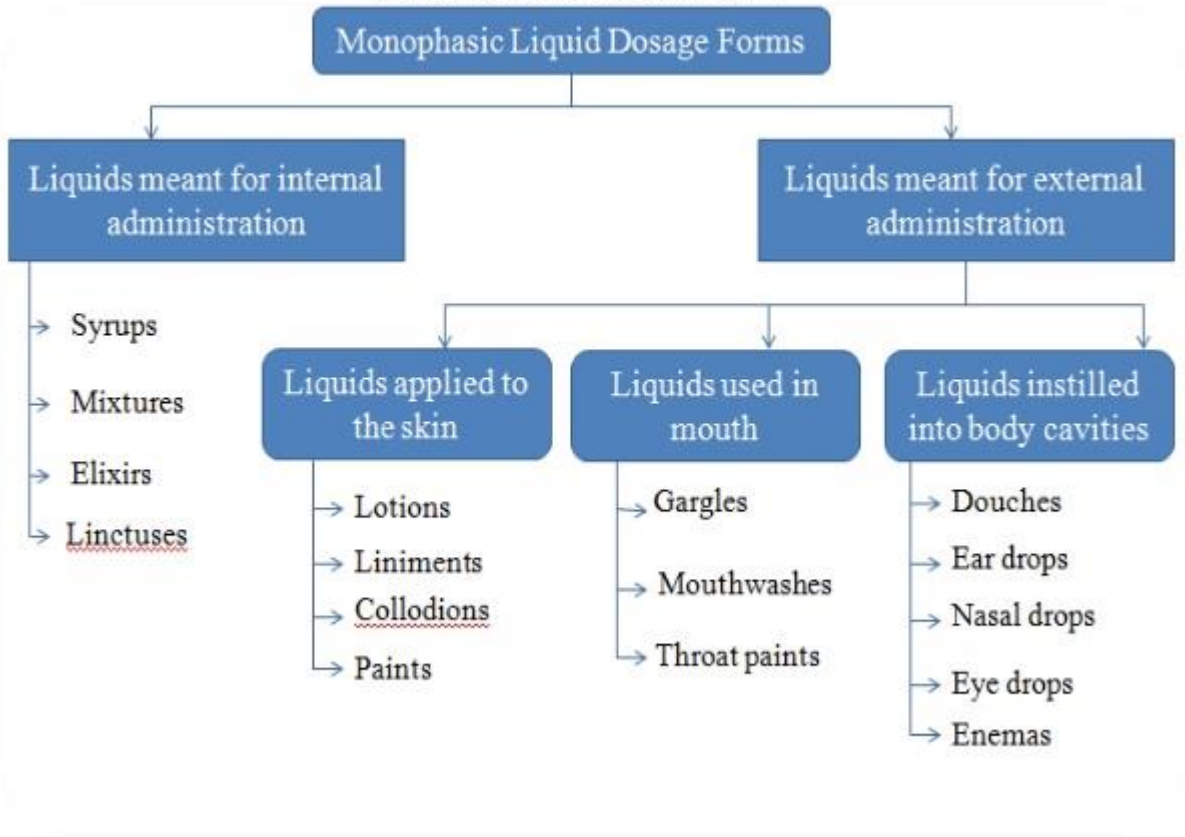
Liquid dosage forms are broadly classified into two groups:

a) Monophasic liquid dosage forms

b) Biphasic liquid dosage forms

## Monophasic Liquid Dosage Forms

Monophasic dosage form refers to liquid preparation containing two or more components in one phase system, it is represent by true solution. A true solution is a clear homogenous mixture that is prepared by dissolving solute in a suitable solvent. The component of the solution which is present in a large quantity is known as “SOLVENT” where as the component present in small quantity is termed as “SOLUTE”. The monophasic liquid dosage form are broadly classified into four groups. Each one can be further classified into different groups as shown below:




## MIXTURES

A mixture is a liquid preparation meant for oral administration in which a medicament or medicaments are dissolved or suspended in a suitable liquid. They should be freshly or recently prepared and used fairly quickly, usually within a month. They are mainly prescribed for short term therapy like cough, diarrhoea, constipation etc. Mixtures are further classified into five different groups. They are

**a] Simple mixtures containing soluble substances**: It contains only soluble ingredients.

Eg., carminative mixture, diarrhea mixture and expectorant mixture.

***Method of dispensing:***

- Dissolve the solid substances in three-fourth of vehicle.
- Examine the solution critically by holdin it against the light. If foreign particles are visible, strain it through a cotton wool.

- Add any liquid ingredients.
- Add the remaining vehicle to produce final volume.
- Transfer the mixture into the bottle. Cork it thoroughly and ten polish the bottle to remove the finger prints. Attach the label, wrap the bottle and dispense.

Example: Dispense 9O ml of the mixture

Rx

Potassium Bromide 4g

Tincture nux vomica 4ml

Chloroform water add upto 9Oml

Prepare a mixture

Direction: One table spoon full to be taken three times after meals

Method: Dissolve potassium bromide in three fourth of chloroform water. Filter the solution to remove foreign particles. Add tincture nux vomica. Add more chloroform water to make upto the required volume. Transfer the mixture to a bottle. Cork, label and dispense.

**b] Mixtures containing diffusible solids:** Diffusible solids are those which do not dissolve in water, but may be mixed by shaking. As a result it is evenly distributed throughout the liquid for sufficient time for uniform dose distribution. Examples are bismuth carbonate, bismuth subnitrate, magnesium carconate, quinine sulphate, light kaolin etc,.

***Method of Dispensing:***

- Finely powder the drug in a mortar. Add any soluble drug and mix.
- Measure three fourth of vehicle and make a smooth cream
- Transfer the content of mortar into a measure. Rinse the mortar with little amount of vehicle and transfer into a measure.
- Add any liquid ingredient.
- Add the remaining vehicle to make upto the required volume.
- Transfer the mixture into the dispensing bottle, cork, label and dispense. Label as "SHAKE THE BOTTLE WELL BEFORE USE"

Example

Rx

Magnesium sulphate 15g

Magnesium carbonate 2g

Peppermint water ad upto 9Oml

Prepare a mixture

Direction: One table spoonful to be taken two hours before breakfast

Method: Mix the required quantity of magnesium sulphate and magnesium carbonate in amortar. Add small quantity of water to make smooth cream and then add remaining amount of vehicle. Strain through muslin piece to remove foreign particles. Transfer the mixture to a bottle, cork and label.

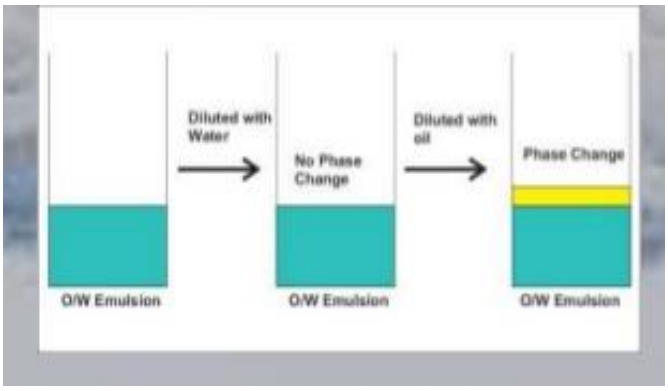
**c] Mixtures containing indiffusible solids:** Indiffusible solids are those which are not soluble in water and do not remain uniformly distributed in the solvent for sufficiently long time. So we have to add a substance to suspend (suspending agent) these particles in the solvent. Examples are acetyl salicylic acid, calomel, phenacetin, benzoic acid etc,. The suspending agents which are commonly used in mixture containing indiffusible solids are:

- Compound tragacanth powder[CTP]: in proportion of 2g/1OO ml of the mixture, it is used when the vehicle is other than water or chloroform water.
- Tragacanth mucilage: in proportion of $1/4^{th}$ volume of the mixture, it is used when the vehicle is water or chloroform water.

## METHODS TO IDENTIFY THE TYPE OF EMULSIONS

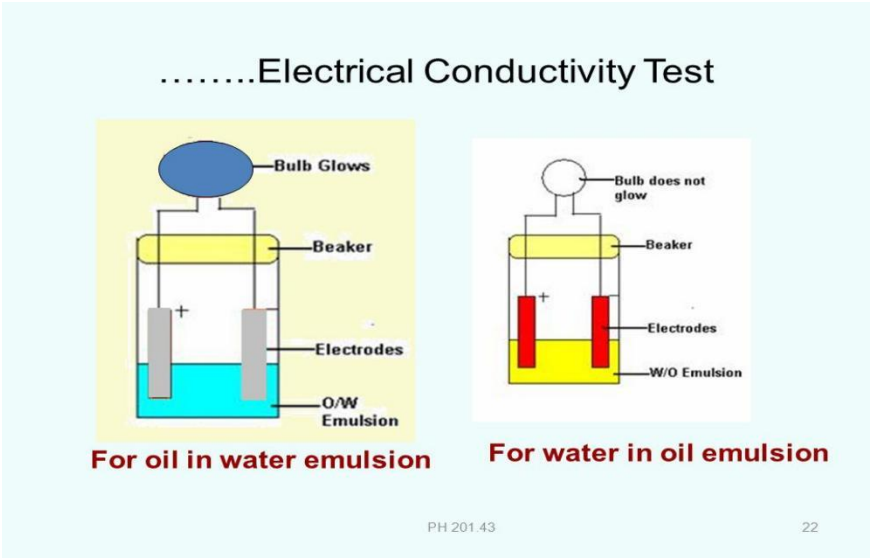
### 1) Dilution test

On adding water to an o/w emulsion, it will still remain stable as water is the dispersion medium, but on adding oil it will get destabilised as oil & water are immiscible. Similarly, w/o emulsion can be diluted with oil & would still be stable, but would get destabilised on the addition of water.



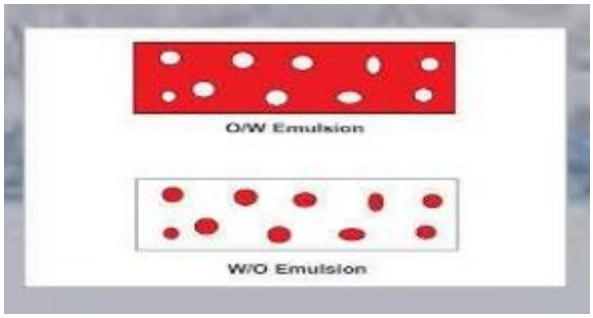

**2) Conductivity test**

In this test the emulsion is kept between 2 electrodes and a bulb is connected in the circuit as shown in the diagram. An o/w emulsion will conduct electricity as water conducts electricity, but a w/o will not conduct electricity.



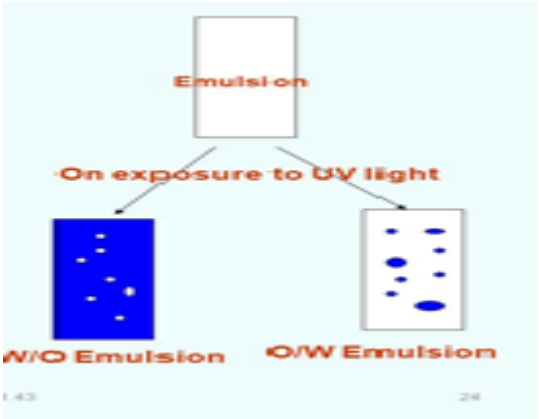

**3) Dye test:**

In this, a water-soluble dye is added to the emulsion. If it is an o/w emulsion, the dispersion medium appears red and the dispersed phase colourless and vice-versa.




**4) Fluorescent Test**:

Based on the fluorescence of oils under ultraviolet light, the emulsion is examined under the light in the microscope. If the whole fluid is fluorescent, it is water in oil w/o but in case of oil in water o/w spotty fluorescence will appear.




**5) Cobalt Chloride Test**:

When a filter paper soaked in cobalt chloride solution is dipped in to an emulsion and dried, it turns from blue to pink, indicating that the emulsion is o/w type.

## METHODS OF EMULSION PREPARATION

On small scale extemporaneous preparation of emulsions, three methods may be used which are continental or dry gum method, English or wet gum method, and the bottle or Forbes bottle method. .

**A] Continental or dry gum method:**

- It also referred to as the 4:2:1 method because for every 4 parts by volume of oil , 2 parts of water and 1 part of gum are added in preparing the initial or primary emulsion.

- In this method, the acacia or other emulsifier is triturated with oil in dry Wedgwood or porcelain mortar until thoroughly mixed.

- A mortar with a rough surface rather than a smooth surface must be used to ensure proper grinding and reduction of particle size.

- After the oil and gum have been mixed, the two parts of water are added all at once and the mixture triturated immediately, rapidly and continuously until the primary emulsion is creamy white and produces a crackling sound to the movement of pestle.

- Generally about 3 minutes of mixing is required to produce a primary emulsion.

- Other liquid formulative ingredients that are soluble in or miscible with the external phase may then be mixed into primary emulsion.

- Solid substances such as preservatives, stabilizers, colorants and flavoring agents are usually dissolved in a suitable volume of water and adds as a solution to the primary emulsion.

Based on the following table oil, water and gum ratios are used for different types of oil.

| **Type Of Oil** | **Example** | **Quantities For Primary Emulsion** | | |
|---|---|---|---|---|
| | | **OIL** | **WATER** | **GUM** |
| Fixed Oil | Almond oil Arachis Oil Castor oil Codliver oil | 4 | 2 | 1 |
| Mineral oil | Liquid Paraffin | 3 | 2 | 1 |

| | | | | |
|---|---|---|---|---|
| Volatile oil | Turpentine oil Cinnamon oil Pepperment oil | 2 | 2 | 1 |
| Oleo-Resin | Male Fern Extract | 1 | 2 | 1 |

**B] English or Wet gum method:**

- The same proportions of oil, water and gum which are used in dry gum method but the order of mixing is different and the proportions of ingredients may be varied during preparation of the primary emulsion.

- The mucilage of gum is prepared by triturating in a mortar acacia with twice its weight of water.

- Oil is then added slowly in portions and the mixture is triturated to emulsify the oil 7 • After all oil has been added , the mixture is thoroughly mixed for several minutes to ensure uniformity • Finally, other formulative materials are added and the emulsion is transferred to graduate and brought to volume with water.

**C] Bottle or Forbes bottle method**

- The bottle method is useful for preparation of emulsions from volatile oils and oleaginous substances of low viscosities.

- Powdered acacia is placed in a dry bottle, two parts of oil are added and the mixture is thoroughly shaken in the container.

- A volume of water approximately equal to that of oil is then added in portions and the mixture is shaken after each addition.

- When all of the water has been added, the primary emulsion has formed may be diluted to the proper volume with water or an aqueous solution of other formulative agents.

## APPLICATIONS AND USES OF EMULSION

Emulsions are very much famous in various fields of science. It is utilized in the tanning and dyeing industries, used in the manufacturing process of plastics and synthetic rubber.

- Usually used in cosmetics, pharmaceuticals, personal hygiene.
- Microemulsions are used to deliver vaccines to kill various microbes.
- It is used in chemical synthesis mainly in the manufacture of polymer dispersions.
- It is used in fire fighting.
- Nanoemulsions such as soybean oil are used to kill microbes.
- Mayonnaise is an oil in water emulsion with egg yolk or sodium stearyl lactylate.

# UNIT-IV

## SUPPOSITORIES AND PHARMACEUTICAL INCOMPATIBILITIES

**Chapter Objectives**

**At the conclusion of this chapter the student should be able to:**

1. Classify and define suppositories along with their advantages and disadvantages.
2. Discuss the importance of displacement value and its calculation in preparation of suppositories.
3. Formulation of suppositories
4. Discuss the different types of bases used in preparation of suppositories.
5. Define incompatibility and explain the types of incompatibilities.
6. Discuss how the incompatibilities will arise and how to overcome them

**Suppositories:** Definition, types, advantages and disadvantages, types of bases, methods of preparations. Displacement value & its calculations, evaluation of suppositories.

**Pharmaceutical incompatibilities:** Definition, classification, physical, chemical and therapeutic incompatibilities with examples.

## SUPPOSITORIES

***Suppositories*** are solid dosage forms intended for insertion into body orifices where they melt, soften, or dissolve and exert localized or systemic effects.

***-British Pharmacopoeia (BP) definition:***

"Suppositories are solid, single-dose preparations. The shape, volume and consistency of suppositories are suitable for rectal administration."

***Pessaries***

Pessaries are a type of suppository intended for vaginal use. The larger size moulds are usually used in the preparation of pessaries such as 4 g and 8 g moulds. Pessaries are used almost exclusively for local medication, the exception being prostaglandin pessaries that do exert a systemic effect.

***-British Pharmacopoeia (BP) definition:*** " Pessaries are solid, single-dose preparations. They have various shapes, usually ovoid, with a volume and consistency suitable for insertion into the vagina. They contain one or more active substances dispersed or dissolved in a suitable bases that may be soluble or dispersible in water or may melt at body temperature. Excipients such as diluents, adsorbents, surface-active agents, lubricants, antimicrobial preservatives and colouring matter, authorised by the competent authority, may be added, if necessary."

Common ingredients for inclusion in pessaries for local action include:

- Antiseptics
- contraceptive agents
- local anaesthetics
- various therapeutic agents to treat trichomonal, bacterial and monilial infections.

**Types of Suppositories:**

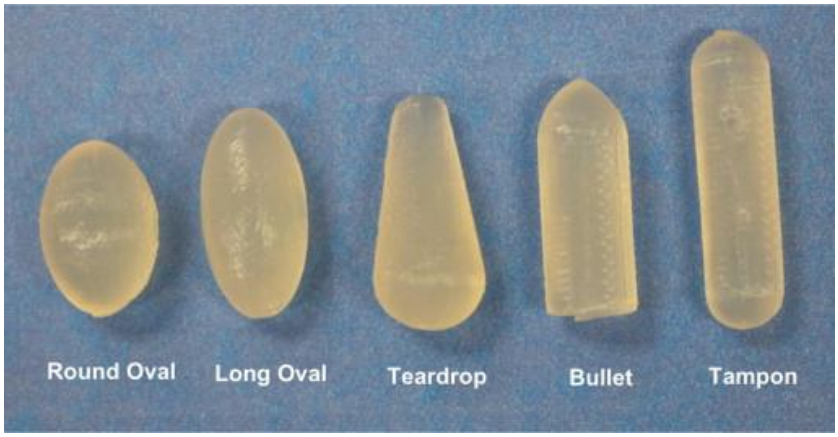
**a. *Rectal suppositories:*** for adults weigh 2 gm and are torpedo shape. Children's suppositories weigh about 1 gm.

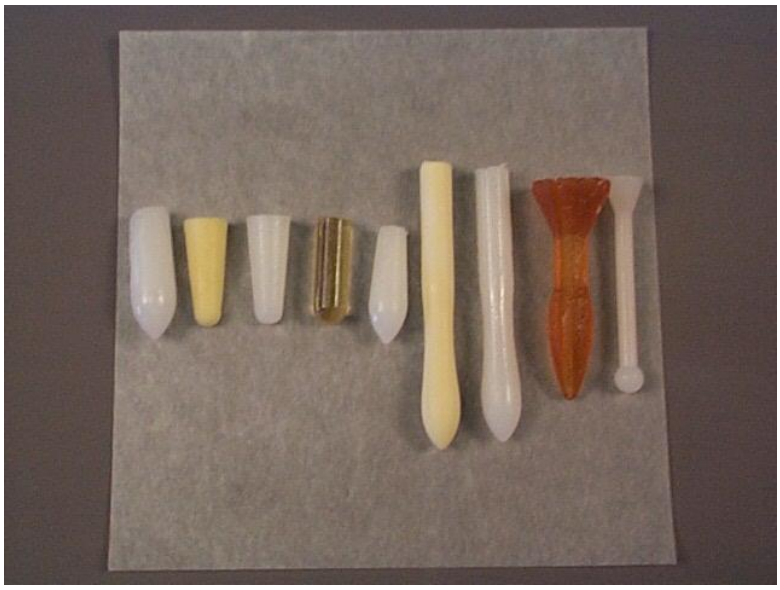
b. ***Vaginal suppositories or Pessaries:*** weigh about 3- 5gm and are molded in globular or oviform shape or compressed on a tablet press into conical shapes.

**c. *Urethral suppositories:*** called bougies are pencil shape. Those intended for males weigh 4 gm each and are 100-150 mm long. those for females are 2 gm each and 60-75 mm in length.

**d. *Nasal suppositories:*** called nasal bougies or buginaria meant for introduction in to nasal cavity. They are prepared with glycerogelatin base. They weigh about 1 gm and length 9-10 cm.

***e. Ear cones:*** Aurinaria and meant for introduction into ear.Rarely used. Theobroma oil is used as base. Prepared in urethral bougies mould and cut according to size.



***New trends of Suppositories:***

a. ***Tablet Suppositories:*** Suppositories and pessaries are prepared by compression just like compressed tablets. The compressed pessaries are generally almond shape for ease in insertion and to provide a large surface area for disintegration and absorption. The rectal tablets are generally coated with polyethylene glycol for protection and its easy insertion into the rectum.
b. ***Layered Suppositories:*** They contain different drugs in different layers to avoid incompatibility between them. The drugs having different melting point or dissolution rate can be incorporated to control the rate of release of medicament. These types of

suppositories can be prepared by partially filling the mould with one type of material. When it gets solidified, then the other materials are added one after other as a separate layer.

c. ***Capsule Suppositories:*** The soft gelatin capsules of different sizes and shapes are used for insertion into the rectum or the vagina. The liquids, semi solids or solids can be filled into soft gelatin capsules. They has great demand.

d. ***Coated Suppositories:*** Suppositories are coated by dipping in the solution of the coated materials such as polyethylene glycols and cetyl alcohol etc. until the coats of desired thickeness have been obtained. These are then dried. These suppositories impart lubricant properties or to provide protection action during storage. They also helps to control The release of mediacament.

e. ***Disposable Moulds:*** These are made up of plastic materials or tin foils.. the suppository material is poured into the disposable moulds and cooled. The excess of mass is trimmed off with the help of sharp knife or blade and moulds are sealed. These are the packed into cartons. These are cheap and elegant. Their shapes can be changed at alower cost. Moreover, when suppositories mass melts during storage, it will remain in themould itself and can be reconverted into suppositories after cooling.

**Advantages of Suppositories:**

- Can exert local effect on rectal mucosa.
- Used to promote evacuation of bowel.
- Avoid any gastrointestinal irritation.
- Can be used in unconscious patients (e.g. during fitting).
- Can be used for systemic absorption of drugs and avoid first-pass metabolism.
- Babies or old people who cannot swallow oral medication.
- Post operative people who cannot be administered oral medication.
- People suffering from severe nausea or vomiting.

**Disadvantages Of Suppositories:**

- The problem of patient acceptability.
- Suppositories are not suitable for patients suffering from diarrhea.
- In some cases the total amount of the drug must be given will be either too irritating or in greater amount than reasonably can be placed into suppository.
- Incomplete absorption may be obtained because suppository usually promotes evacuation of the bowel.

**Characteristics of Ideal Suppository Base:**

The ideal properties of a suppository base may be described as follows.

1) Having reached equilibrium crystallinity, the majority of component melts at rectal temperature but bases with higher melting ranges may be employed for eutectic mixtures.

2) The base must be completely nontoxic and nonirritant to sensitive and inflamed tissues.

3) Suppository base should be adaptable with broad variety of drugs.

4) Bases should not have meta stable forms

5) Suppository bases should shrink sufficiently on cooling to release itself from the mold without the need of mold lubricant

6) It must be non sensitizing, Non-toxic and non-irritant.

7) Suppository base should have good wetting and emulsifying effects

8) It must have water number so that high percentage of water can be incorporated in the suppository

9) Selected suppository base should be durable when stores for a long span of time and should not change colour, odour and drug release forms.

1O)Should melt at body temperature or dissolves in bodyfluids.

11]Compatible with any medicament.

12) Releases any medicament readily.

13)Easily moulded and removed from the mould.

14)Stable to heating above the melting point.

15)Easy to handle.

**Types of Bases**

**A] Fatty Bases:** designed to melt at body temperature.

- **Theobroma oil (Cocoa butter)**

` It is a yellowish-white solid obtained from crushed and roasted seeds of theobroma cocoa. It has butter like consistency with an odour of chocolate and is a mixture of glyceryl esters of different unsaturated fatty acids.

**Advantages:**

- A melting range of 30 - 36°C (solid at room temperature but melts in the body).
- Readily melted on warming, rapid setting on cooling.
- Miscible with many ingredients.
- Non-irritating.

**Disadvantages:**

- Polymorphism:

- When melted and cooled it solidifies in different crystalline forms, depending on the temperature of melting, rate of cooling and the size of the mass.

- If melted at not more than 36°C and slowly cooled it forms stable beta crystals with normal melting point.

- If over-heated then cooled it produce unstable gamma crystals which melt at about 15°C or alpha crystals melting at 20°C.

- Cocoa butter must be slowly melted over a warm water bath to avoid the formation of the unstable crystalline form.

- Adherence to the mould:
- Softening point too low for hot climates.
- Melting point reduced by soluble ingredients: Phenol and chloral hydrate have a tendency to lower the melting point of cocoa butter.So, solidifying agents like beeswax (4%) may be incorporated to compensate for the softening effect of the added substance.
- Rancidity on storage:
- Poor water-absorbing ability: Improved by the addition of emulsifying agents.
- Leakage from the body:
- Expensive

- ***Emulsified Theobromo oil:***

This may be used as a base when large uantities of aqueous solutions are to be incorporated. The use of 5% glyceryl monostearate, 1O% lenette wax, 2-3% cetyl alcohol, 4% beeswax, 12% spermaceti is recommended to prepare emulsified theobromo oil suppositories.

- ***Hydrogentaed oils:***

These are obtained by hydrogenation of various vegetable oils, such as arachis oil, cotton seed oil, coconut oil, palm oil etc. It is used as a substitute for theobromo oil because it has a number of advantages over theobromo oil. They are:

- They are resistant to oxidation
- Lubrication of the mould is required
- Overheating does not effect the solidifying point
- They produce colorless, odourless and elegant suppositories
- The emulsifying and water absorbing capacities are good.

**B] Water-soluble and water-miscible bases:**

- ***Glycero-gelatin Base:***

The commonest is Glycerol Suppositories Base B.P. It is a mixture of 14% w/w gelatin, and 70% w/w glycerol & water Q.S. to 100%. The glycerol-gelatin base U.S.P. consisted of 20% w/w gelatin, and 70% w/w glycerol & water Q.S. to 100%. [ glycerol +water + gelati = glycerol gelatin]. Glycerin and water are mixed and the mixture is made stiff by adding gelatin. The suppositories prepared by using this base are translucent, which tend to issolve or disperse slowly in the body cavity and release the medicament. Hence it is preferred over fatty base.

This base is used for preparing all types of suppositories particularly pessaries. Glycero-gelatin base is well suited for suppositories containing boric acid, chloral hydrate, bromides, iodides, iodoform, opium etc.

## THERAPEUTIC INCOMPATIBILITY

It is the modification of the therapeutic effect of one drug by the prior concomitant administration of another. It may be as a result of prescribing certain drugs to a patient with the intention to produce a specific degree of pharmacological action, but have restore or intensity of the action produced is different from that intended by the prescriber.

**MECHANISM:**

It is divided into two groups. They are

**Pharmacokinetic:** It involves the effect of a drug on another that includes changes in absorption, distribution, metabolism and excretion.

**Pharmacodynamics:** These are related to the pharmacological activity of the inter-acing drugs. E.g., Synergism, antagonism, altered cellular transport, effect on the receptor site.

Therapeutic incompatibilities occurs due to following reasons

a. Error in dosage

b. Wrong dose or dosage form

c. Contra-indicated drugs

d. Synergistic and antagonistic drugs

e. Drug interactions

- **Error In Dosage**

Many therapeutic incompatibilities result from errors in writing or interpreting the prescription order. The most serious type of the dosage error in the dispensing is overdose of a medication.

**E.g., Atropine sulphate capsules**

Rx

Atropine sulphate - 0.005g

Phenobarbitone - 0.015g

Aspirin - 0.300g

**Causes:-** In this prescription, the quantity of the atropine sulphate in each capsule is more than its recommended dose.

**Remedy:-** The prescription is referred back to the prescriber to correct the overdose of the atropine sulphate. The recommended dose of atropine for a single capsule is 0.25 to 2mg.

- **Wrong Dose Or Dosage Form**

There are certain drugs which have quite similar names and there is always a danger of dispensing the wrong drug2.

E.g., Prednisone and Prednisolone

Digoxin and Digitoxin

Sometimes many drugs are available in the different dosage forms and hence, if the dosage form is not clearly mentioned on the prescription, it becomes necessary to seek clarification from the prescriber. The responsibility of the pharmacist becomes to check the prescription intensively and if he finds these types of errors he should immediately consult the prescriber for the clarification.

- **Prescribing Contra-Indicated Drugs**

There are certain drugs which may be contra-indicated in a particular disease or a particular patient who is allergic to it.

- Corticosteroids are contra-indicated in the patients having peptic ulcers.
- The penicillin and sulphur drugs are contra-indicated in the patients who are allergic.
- Vasoconstrictors are contra-indicated in hypertensive patients.
- Barbiturates and morphine should not be given to the asthmatic patients.

**E.g., Sulphadiazine capsules**

**Causes:-**Ammonium chloride is a urinary acidifier. It causes the deposition of the sulphonamide crystals in the kidney.

**Remedy: -** Before prescribing such substances a doctor must be careful. If he does not, a pharmacist shows his caliber to point out such type of the doctor's error. It must immediately be referred back to the concerned doctor and get corrected.

- **Prescribing Synergistic Or Antagonistic Drugs**

When two drugs are prescribed together, they tend to increase the activity of each other which is known as "SYNERGISM". When two drugs are prescribed together, they tend to decrease the activity of each other which is known as "ANTAGONISM"

**E.g.,**

1. A combination of aspirin and paracetamol increases the analgesic activity.
2. A combination of penicillin and streptomycin increases the antibacterial activity.
3. Amphetamines show its antagonists effect with the barbiturates.

**E.g., Amphetamine sulphate syrup**

**Causes:-**In this prescription, there is a combination of two sympathomimetic drugs There by causing additive effect.

**Remedy:-** The prescription is referred back to the prescriber for necessary corrections.

- **Drug Interactions**

The effect of one drug is altered by the prior or simultaneous administration of another drug. The drug interaction can usually be corrected by the proper adjustment of dosage if the suspected interaction is detected30. **E.g., Tetracycline capsule - 250mg capsules**

Direction: Take one capsule every 6 hours with milk.

**Causes:-**Tetracycline is inactivated by calcium present in milk. So, it should not be taken with milk.

**Remedy:** In this prescription, the therapeutic incompatibility is unintentional. So, the prescription is referred back to the prescriber to change the direction.

# UNIT-V

## SEMISOLID DOSAGE FORMS

**Chapter Objectives**

**At the conclusion of this chapter the student should be able to:**

1. Classify and define semisolid dosage forms along with their advantages and disadvantages.
2. Discuss the bses that are suitable for preparation of ointments along with examples.
3. Discuss the factors influencing dermal penetration of drugs.
4. Preparation of semisolid dosage forms such as ointments, pastes , creams and gels.
5. Discuss the factors that affect the formulation of semisolid dosage forms.
6. Discuss the evaluation tests for semisolid dosage forms.

**Semisolid dosage forms:** Definitions, classification, mechanisms and factors influencing dermal penetration of drugs. Preparation of ointments, pastes, creams and gels. Excipients used in semi solid dosage forms. Evaluation of semi solid dosages forms.

### SEMISOLID DOSAGE FORMS

Ointments, creams and gels are semisolid dosage forms intended for topical application. They may be applied to the skin, placed onto the surface of the eye or used nasally, vaginally or rectally.

The majority of these preparations are used for the effects of the therapeutic agents they contain. Those which are non-medicated are used for their physical effects as protectants or lubricants. Topical preparations are used for the localised effects produced at the site of their application, although some unintended systemic drug absorption may occur, it is usually in sub-therapeutic quantities. However, systemic drug absorption can be an important consideration in certain instances, as when the patient is pregnant or nursing because drugs can enter the fetal blood supply and breast milk and be transferred to the fetus or nursing infant.

### OINTMENTS

Ointments are semisolid preparations intended for external application to the skin or mucous membranes. Ointments may be medicated or non-medicated. Non-medicated ointments are used for the physical effects that they provide as protectants, emollients or lubricants.

**Classification of Ointments:**

- ***Based on penetration***

1. Epidermic ointments – meant for action on epidermis and exert local action. Not absorbed.
2. Used as protective, antiseptics, local anti infectives, parasiticides.
3. Endodermic ointments – Meant for action into deeper layersof cutaneous tissues. Prtially absorbed. Acts as emollients, stimulants and local irritants.
4. Diadermic ointments – Meant for deeper penetration and release the mediacaments that passes through the skin and produce systemic effects.

- ***Based on therapeutic uses:***

1. Antibiotic ointments: used to kill microbes. [ neomycin, bacitracin]
2. Antifungal ointments: inhibit or kill fungi [benzoic acid, nystatin]
3. Anti-inflammatory ointments: relieve inflammatory allergic, pruritic conditions [Betamethasone valerate, hydrocortisone]
4. Antipruritic ointments: relieve itching [ benzocaine, coal tar]
5. Astringent ointments: contraction of skin an decreases discharges [ calamine, zinc oxide]
6. Antieczematous ointments: prevent oozing and excretion from vesicles on the skin [cortisones, ichthammol, coal tar]
7. Keratolytic ointments: remove or soften the horny layer of skin. [resorcinol, sulfur]
8. Counter-irritant ointments: applied locally to irritate the skin , thus reducing irritation or deep seated pain. Capsicum, methyl cellulose, oleoresin, iodine]
9. Anti-dandruff ointments: applied locally to get relief from dandruff. [salicylic acid, cetrimide]
10. Ointments for psoriasis treatment: treats psoriasis. [ coal tar, corticosteroid, dithranol]
11. Parasiticide ointments: destroy or inhibit living infestation such as lice and ticks. [ benzyl benzoate, hexachloride, sulfur]

**Advantages**:

¬ Handling of ointments is easier than bulky liquid dosage forms.

¬ They are chemically more stable than liquid dosage forms.

¬ They facilitate application of the directly to the effected body part and avoid exposure of other parts to the drug.

¬ They are suitable for patients who find it difficult to take the drugs by parenteral and oral routes.

¬ They prolong the contact time between the drug and effected area.

¬ The bioavailability of drugs administered as ointments is more since it prevents passage through liver.

**Disadvantages**

¬They are bulkier than solid dosage forms.

¬When applications of an exact quantity of ointment to the affected area is required, it is difficult to ascertain the same.

¬They are less stable than solid dosage forms.

**Ointment Bases:**

Ointment bases may be used for their physical effects or as vehicles in the preparation of medicated ointments.

**Selection of appropriate ointment base:**

The selection of the base to be used in the formula of an ointment depends on a number of factors:

1. Desired release rate of the drug substance from the ointment base.
2. Desirability of occlusion of moisture from the skin.
3. Stability of the drug in the ointment base.
4. Effect of the drug on the consistency of the ointment base.
5. The desire for a base that is easily removed by washing with water.

**Ideal ointment base should possess are:**

1. Does not retard wound healing.

2. Low sensitization index.
3. Pharmaceutical elegance.
4. A low index of irritation.
5. Non dehydrating.
6. Non greasy.
7. Neutral in reaction.
8. Good keeping qualities.

**Classification of Ointment Bases:**

Ointment bases are classified into four general groups:

1. Hydrocarbon bases (oleaginous bases)
2. Absorption bases
3. Water-removable bases
4. Water-soluble bases

**1. Hydrocarbon Bases:**

Hydrocarbon bases are also termed oleaginous bases, on application to the skin they have an emollient effect, protect against the escape of moisture, effective as occlusive dressing and can remain on the skin for prolonged periods of time without drying out and because of their immiscibility with water are difficult to wash off.

Water and aqueous preparations may be incorporated into them but only in small amounts and with some difficulty.

Petrolatum, white petrolatum, white ointment and yellow ointment are examples of hydrocarbon ointment bases.

When powdered substances are to be incorporated into hydrocarbon bases, liquid petrolatum (mineral oil) may be used as levigating agent.

- ***Petrolatum, USP [ Soft Paraffin]:***

- Petrolatum, USP is a purified mixture of semisolid hydrocarbons obtained from petroleum.
- It is an oily mass, varying in colour from yellowish to light amber.
- It melts at temperature between (38-60 °C) and may be used alone or in combination with other agents as an ointment base.

- Petrolatum is also known as 'Yellow Petrolatum' and 'Petroleum Jelly'. A commercial product is 'Vaseline'.

***Yellow ointment, USP [ Yellow soft paraffin]:***

This ointment has the following formula for the preparation of 1000 g:

Yellow wax 50 g

Petrolatum 950 g

Yellow wax is the purified wax obtained from the honey comb of the bee.

The ointment is prepared by melting the yellow wax on a water bath, adding the petrolatum until the mixture is uniform, then cooling with stirring until congealed.

***White ointment, USP[ White soft paraffin]:***

This ointment differs from yellow ointment by substituting white wax (bleached and purified yellow wax) and white petrolatum in the formula.

It is used when the medicament is white or colorless.

It is never used in ophthalmic preparations because it contains traces of bleaching agent left over after after bleaching of yellow soft paraffin. So, it may causes irritation to the eye.

- ***Hard Paraffin***

- It is a purified mixture of solid hydrocarbons obtained from petrolatum.
- It is colorless or white translucent, odourless, tasteless wax like substance.
- Used to harden or soften the ointment base.

- ***Liquid Paraffin***

- It consists of a mixture of liquid hydrocarbons obtained from petroleum by distillation.
- It is also known as white mineral oil or liquid petrolatum.
- It is colorless, odourless, tasteless and transparent oily liquid.
- It is soluble in ether and chloroform and insoluble in water and alcohol.
- Used along with hard paraffin and soft paraffin to get a desired consistency of the ointment.

***Properties of oleogenous bases:***

- ✓ They are greasy, sticky and are difficult to remove both from skin and clothing.
- ✓ They retain body heat which may produce an uncomfortable feeling of warmth.
- ✓ They do not help in absorption of medicaments.

- ✓ They prevent drainage on oozing areas and also prevent evaporation of cutaneous secretions along with perspiration.

**2. Absorption Bases:**

These are anhydrous substances which have the property of absorbing considerable quantities of water but still retains ointment like consistency.

Absorption bases are of two types:

1. Non-emulsified bases - Those that permit the incorporation of aqueous solutions resulting in the formation of w/o emulsions e.g. Hydrophilic petrolatum.

2. W/O emulsions (emulsion bases) - permit the incorporation of additional quantities of aqueous solutions. e.g. Lanolin

- ✓ These bases may be used as emollients although they don't provide the degree of occlusion afforded by the hydrocarbon bases.
- ✓ Absorption bases are greasy but can be easily removed from the skin, as compared to oleogenous bases.
- ✓ They are relatively heat stable.
- ✓ They are used in their anhydrous form or in emulsified form.
- ✓ Compatible with large number of ingredients.
- ✓ Absorption bases are useful as pharmaceutical adjuncts to incorporate small volumes of aqueous solutions into hydrocarbon bases. This is accomplished by incorporating the aqueous solution into the absorption base and then incorporating this mixture into the hydrocarbon base.

- ➢ ***Hydrophilic Petrolatum, USP:***

Hydrophilic petrolatum, USP has the following formula for the preparation of 1000 g:
Cholesterol 30 g
Stearyl alcohol 30 g
White wax 80 g
White petrolatum 860 g

It is prepared by melting stearyl alcohol and the white wax on a steam bath, adding the cholesterol with stirring until dissolved, then adding the white petrolatum and allowing the mixture to cool while being stirred until congealed.

- ***Hydrous wool fat [Lanolin], USP:***

- Lanolin, USP obtained from the wool of sheep.
- It is a purified wax like substance that has been cleaned, deodorised and decolourised. It contains not more than 0.25% water.
- It is a mixture of 7O% w/w wool fat and 3O % w/w purified water. Additional water may be incorporated into lanolin by mixing.
- It is insoluble in water but soluble in ether and chloroform.
- It is used alone as alone as emollient and an ingredient for several other ointments.

- ***Wool fat [ Anhydrous Lanolin]:***

- It is a purified fat like susbstance obtained from wool of sheep.
- It absorbs about 5O% of its weight of water. So, it is used in ointments where the proportion of water or aqueous liquids to be incorporated in hydrocarbon base is too large.
- It is an important constituent of simple ointment base and eye ointment base.

- ***Wool alcohol:***

- It is obtained from wool fat by treating it with alkali and separating the fraction containing cholesterol and other alcohols.
- It contains less than 3O% of cholesterol.
- It is used as an emulsifying agent for the preparation of w/o emulsions. It is also used to improve the texture, stability and emollient properties of O/W emulsions.

- ***Bees wax:***

It is purified wax obtained from honey comb of bees. It is available as yellow and white bees wax. White is produced from bleaching of yellow. It is used in stiffening of pastes and ointments.

**3. Water-removable Bases [ Emulsion bases]:**

Water-removable bases are o/w emulsions resembling creams in appearance and because the external phase of the emulsion is aqueous, they are easily washed from the skin and are often called ‘water-washable bases’. w/o type bases are greasy and sticky

They may be diluted with water or aqueous solutions. They have the ability to absorb serous discharge.

The emulsifying ointment is prepared from emulsifying wax, white soft paraffin and liquid paraffin.

Hydrophilic ointment USP, is an example of this type of base.

- ***Hydrophilic ointment, USP:***

Hydrophilic ointment has the following formula for the preparation of about 1000 g:

Methyl paraben 0.25 g

Propyl paraben 0.15 g

Sodium lauryl sulfate 10 g

Propylene glycol 120 g

Stearyl alcohol 250 g

White petrolatum 250 g

Purified water 370 g

In preparing this ointment, the stearyl alcohol and white petrolatum are melted together at about 75 °C. The other agents are dissolved in the purified water and then added with stirring until the mixture congeals.

• Sodium lauryl sulphate (SLS) is the emulsifying agent.

• Stearyl alcohol and white petrolatum comprising the oleaginous phase of the emulsion and the other ingredients form the aqueous phase.

• Methyl paraben and propyl paraben are antimicrobial preservatives.

**4. Water-soluble Bases [Greaseless ointment bases]:**

- Water-soluble bases don't contain oleaginous components, they are completely water-washable and often referred to as 'greaseless'. Since they soften greatly with the addition of water, large amounts of aqueous solutions are not effectively incorporated into these bases.
- They consists of PEG polymers popularly known as "Carbowaxes". Tragacanth, gelatin, pectin, cellulose derivatives, bentonite, magnesium aluminum silicate and sodium alginate are also used as water soluble bases.
- Polyethylene glycol ointment, NF is an example of water-soluble base.

- ***Polyethylene Glycol ointment, NF:***

Polyethylene glycol (PEG) is a polymer of ethylene oxide and water represented by the formula H(OCH2CH2 )nOH in which (n) represents the average number of oxyethylene groups. The numerical designations associated with PEG refer to the average molecular weight of the

polymer. PEG having average molecular weights below 600 are clear, colourless liquids and those with molecular weights above 1000 are wax-like materials and those with molecular weights in between are semisolids. The greater the molecular weight, the greater the viscosity. The general formula for the preparation of 1000 g of PEG ointment is:

Polyethylene Glycol 3350- 400 g

Polyethylene Glycol 400 -600 g

The combining of PEG 3350, a solid, with PEG 400, a liquid, results in a very pliable (flexible) semisolid ointment. If a firmer ointment is desired, the formula may be altered to contain up to equal parts of the two ingredients. When aqueous solutions are to be incorporated into the base, the substitution of 50 g of PEG 3350 with an equal amount of stearyl alcohol is advantageous in rendering the final product more firm.

| | Oleaginous Ointment Bases | Absorption Oint. Bases **Water-absorption** | Oil/Water Emulsion Oint. Bases **Water-misicble** | Water-miscible Ointment Bases **Water soluble** |
|---|---|---|---|---|
| Composition | oleaginous compounds | oleaginous base + w/o surfactant | oleaginous base + water (> 45% w/w) + o/w surfactant (HLB ≥9) | Polyethylene Glycols (PEGs) |
| Water Content | **anhydrous** | **anhydrous** | hydrous | **anhydrous**, hydrous |
| Affinity for Water | **hydrophobic** | hydrophilic | hydrophilic | hydrophilic |
| Spreadability | difficult | difficult | easy | moderate to easy |
| Washability | nonwashable | nonwashable | washable | washable |

## PASTES

Pastes are semisolid preparations intended for application to the skin, they generally contain a larger proportion of solid material (such as 25%) than ointments and therefore they are stiffer.

Pastes can be prepared in the same manner as ointments by direct mixing or the use of heat to soften the base prior to incorporating the solids. However, when a levigating agent is to be used to render the powdered component smooth, a portion of the base is often used rather than a liquid which would soften the paste. Because of the stiffness of the paste, they remain in place after application and they are effectively employed to absorb serous secretions.

Because of their stiffness and impermeability, pastes are not suitable for application to hairy parts of the body. e.g. zinc oxide paste, prepared by mixing 25% each of zinc oxide and starch with white petrolatum. The product is very firm and is able to protect the skin and absorb secretions than is zinc oxide ointment.

**Bases used for pastes:**

- ***Hydrocarbon bases:***

Soft and liquid paraffin are used

Example: prepare and dispense 1OOg of compound zinc paste B.P.C

Rx

| | |
|---|---|
| Zinc oxide, finely sifted | 25g |
| Starch, finely sifted | 25g |
| White, soft paraffin | 5Og |

Make a paste

Method: Melt the white soft paraffin on water baath. Seperately pass the zinc oxide and starch through sieve no 120. Mix the required weight of powder in a warm water. Add small amount of melted base with continuous trituration until smooth paste is obtained. Add the remaining part of the base and mix until cold and uniform paste is obtained. Transfer to suitable container, label and dispense.

- ***Water miscible bases***

Emulsifying ointment, glycerin are used as a water miscible base.

Example: Prepare and dispense 5Og of resorcinol an sulfurpaste B.P.C

Rx

| | |
|---|---|
| Resorcinol, finely sifted | 2.5g |
| Precipitated sulfur | 2.5g |

| | |
|---|---|
| Zinc oxide, finely sifted | 2Og |
| Emulsifying ointment | 25g |

Make a paste

Direction: To be applied on the affected area where dandruff is severe.

Method: Triturate the zinc oxide, resorcinol and precipitated sulfur with a portion of emulsifying ointment until smooth and gradually incorporate the remaining part of the emulsifying ointment, Transfer to a suitable container, label and dispense.

Water soluble bases:

Suitable containers of high and low molecular weight polyethylene glycols are mixed together to get product of desired consistency which soften or melt when applied to the skin. These bases are water soluble. Water soluble dental paste containing neomycin sulfate is prepared with macrogol base.

## Excipients in semisolid dosage forms

| Ointment | Paste | Cream | Gel |
|---|---|---|---|
| Ointment base | Paste base | Penetration enhancer | Gelling agent |
| Preservatives | Preservatives | Oil/oleaginous substances | Preservative |
| Anti-oxidant | Anti-oxidant | Emulgents | Hygroscopic substances |
| Chelating agent | perfume | Co-emulsifiers | Chelating agents. |
| Humectant | | Emulsion stabilizers | |
| perfume | | Mixed emulsifier systems | |
| | | Humectants | |
| | | Stabilizers | |
| | | perfumes | |

## Summary of Ointment & Cream

| Parameter | Ointment | Cream |
|---|---|---|
| Absorption | Not easily absorbed | Quickly absorbed by the skin |
| Consistencies | Have thicker consistencies | Have lighter consistencies |
| Greasiness | More greasy | Less greasy |
| Transparency | Clear | White |
| Conc. Of oil | Have a higher concentration of oil | Have a lower concentration of oil than ointment |
| Spreading ability | Low | High |
| Stability on skin | Stay longer on the surface | Stay short time on the surface |
| Healing power | Slow | Fast |

***Storage:***

- Should be stored in well closed container and in a cool place to prevent evaporation of moisture present in paste.
- Shoulb be stored and supplied in containers made of materials which do not allow absorption or diffusion of the contents.

## CREAMS

Pharmaceutical creams are semisolid preparations containing one or more medicinal agents dissolved in either an o/w or w/o emulsion. Creams find primary application in topical skin products and also in products used rectally and vaginally. Many patients and physicians prefer creams to ointments because they are easier to spread and remove than ointments. Pharmaceutical

manufacturers frequently manufacture topical preparations of a drug in both ointment and cream bases to satisfy the preference of the patient and physician.

Creams have a relatively soft, spreadable consistency. An example of an o/w cream is hydrophilic ointment and an example of a w/o cream is cold cream. When the term “cream” is used a water washable formulation is generally inferred.

**Preparation of creams:**

Creams may be formulated from a variety of oils (both mineral and vegetable) and from fatty alcohols, fatty acids and fatty esters. Emulsifying agents include non-ionic surfactants and soaps.

- Preparation involves separating the formula components into two portions: lipid and aqueous.
- The lipid portion contains all water-insoluble components and the aqueous portion the water-soluble components.
- Both phases are heated to a temperature above the melting point of the highest melting component.
- The phases then are mixed, and the mixture is stirred until reaching ambient temperature or the mixture has congealed. Mixing is continued during the cooling process to promote uniformity.
- High Preparation of creams Steps - Preparation of oil phase :flack/powder ingredient are dispersed in mineral oil or silicone oil ) heating may required for melting - Hydration of aqueous phase: emulsifiers, stabilizer, thickener are dispersed in water heating may required for hydrating - Forming the emulsion: two phases are blended under vigorous agitation - Dispersion of active ingredient

**Evaluation of creams:**

***A- Rheology:***

The rheology or viscosity should remain constant. Rheologic measurements are utilized to characterize the ease of pouring from a bottle, squeezing from a tube or container - maintaining

product shape in a jar or after extrusion, rubbing the product onto the skin • The viscosity can be measured using viscometers used for such liquids.

***B- Sensitivity:***

As various types of ingredients are used with occasional use of antiseptic, hormones. etc., there is a possibility of sensitization or photosensitization of the skin. This should be tested before hand. This test is normally done by patch test on skin and can be either open or occlusive. The test sample is applied along with a standard market product at different places and effect is compared after a period of time.

***C- Effect of thermal stresses:***

It is usual to evaluate the stability of an emulsion by subjecting it too high and low temperatures in alternating cycles. The samples are first exposed to 60 C for a few$^0$ hours and then to o to 40 C. Such exposures are repeated a number of times and emulsion stability assessed after each cycle.

***D- Phase separation:***

The rate and degree of phase separation in an emulsion can be easily determined by keeping a certain amount in a graduated cylinder and measuring the volume of separated phase after definite time intervals. The phase separation may result from creaming or coalescence of globules. The phase separation test can be accelerated by centrifugation at low/moderate speeds.

-

## GELS

Gels are usually clear, transparent non-greasy semisolids containing solubilised active substances in an aqueous liquid vehicle rendered jelly-like by the addition of a gelling agent. Among the gelling agents used are synthetic macromolecules such as carbomer, cellulose derivatives as carboxymethyl cellulose or hydroxypropyl cellulose and natural gums as tragacanth.

Vanishing creams are o/w emulsions containing large percentage of water and stearic acid. After application of the cream, the water evaporates leaving behind a thin residue film of stearic acid or other oleaginous components.

Gels may be used as lubricants or medicated gels administered by various routes including the skin, the eye, the nose, the vagina and the rectum. In addition to the gelling agent and water, gels may be formulated to contain a drug substance, solvents such as alcohol and/or propylene glycol, antimicrobial preservatives such as methyl and propyl parabens and stabilisers such as edetate disodium.

***Carbomers:***

Carbomers are high molecular weight water-soluble polymers of acrylic acid cross-linked with allyl ethers of sucrose and depending on their polymeric composition different viscosities result, for example carbomer 910, 934 and 940. They are used as gelling agents at concentrations of 0.5-2% in water.

Carbomer 940 yields the highest viscosity (40,000 – 60,000 centipoises) as a 0.5% aqueous dispersion. Single-phase gels are gels in which the macromolecules are uniformly distributed throughout a liquid with no apparent boundaries between the dispersed macromolecules and the liquid. A gel mass consisting of floccules of small distinct particles is termed a two-phase system often referred to as a magma.

**Types Of Gels:**

***Medicated gels:*** Used on mucous membrane and skin for spermicidal local anesthetic properties. Contain sufficient water which upon evaporation produces cooling effect and protective residual film. [Ephedrine sulphate gel]

***Lubricating gels:*** Used for lubrication of diagnostic equipment such as surgical gloves, cystoscopies, catheters, rectal thermometers. These should be thin, transparent and water soluble. Should be sterile, since to be inserted into body cavities.

***Miscellaneous gels:***

Patch testing - used as vehicle for allergens applied on skin to check sensitivity.

Electro cardiography - applied on the electrode to reduce electrical resistance between patient's skin and electrode. [sodium chloride, pumice powder, glycerin].

***Kind of gels:***

- Controlled release gels
- Bioadhesive gels
- Organogels

• Extended release gel

• Amphiphilic gels

• Hydrophilic gel

• Complexation gels

• Thermosensitive sol-gel resevesible hydrogel

**Formulation of gels:**

- ***Gelling agents:***

  usually organic hydrocolloids some inorganic.

***Tragacanth:*** used for lubricating, medicated and contraceptive gels. 2-5% gum is required. It forms lumps and can be avoided using dispersing agents like alcohol, glycerin and volatile oil.

Tragacanth gels:

- cannot be stored for long time, prone to microbial growth
- vary in viscosity because the gum is obtained from natural sources
- residual film formed after evaporation of jelly tends to flake.
- Lose viscosity blend pH range 4.5 to 7.O.

Example: Prepare and dispense 1OOg of ichthammol jelly

| | |
|---|---|
| Ichthammol | 2g |
| Tragacanth, in powder | 5g |
| Alcohol,9O% | 1Og |
| Glycerin | 2g |
| Water, add to | 1OOg |

Make a jelly

Direction: To be spread in a thin layer over the affected area.

Method: Prepare tragacanth mucilage in a wide mouth ar. Mix ichthammol and glycerin with small quantity of water. Add it to the mucilage and shake well. Add remaining quantity of water to adjust the final weight and reshake. Pack in a well closed container, label and dispense.

***Sodium alginate jellies***: used as lubricants and dermatological vehicles. The viscosity of sodium alginate jellies can be increase by adding traces of calcium salt.

***Pectin jellies:*** Gelling agent for acid products. It is more prone to microbial growth so preservatives must be added. Should b packed in well closed containers to prevent loss of moisture by evaporation.

***Gelatin:*** 2% gelatin soluble in hot water forms a jelly on cooling. 15% produce stiff mediacted jelly which should be melted before use and then dresses on the affected area.

***Cellulose derivatives:*** Methyl cellulose and sodium carboxymethyl cellulose prouces neutral llies of stable viscosity and good resistance.

**Preparation of jellies:**

Prepared by adding thickening agent to an aqueous solution of drug. The mass is triturated in a mortar until a uniform product is obtained. The glass pestle an mortar in case of dark colored drug.. The whole gum should be preferred over the powdered gum to prepare jelly because it produces a clear preparation of uniform consistency.

**Preservation:**

Jellies contain large amount of water and prone to bacterial and fungal growth. Preservatives sucha s methyl, propyl para hydroxyl benzoates, chlorocresol, phenyl mercuric nitrate, benzoic acid, benzalkonium chloride.

**Storage:** In well filled and well closed containers, store in a cool place, sterile jellies packed in collapsible tubes.

**Evaluation of gels**:

***A] Drug content***:

1gm of gel was accurately weighed in a 50ml of volumetric flask to which 20ml purified water was added with continuous shaking. Volume was adjusted with a mixture of 10% methanol in water. Absorbance of the solution with the blank was measured at 360nm using UV-spectrophotometer. - Measurement of pH -The pH of gels were determined by digital pH meter. One gram of gel was dissolved in 100ml of distilled water and stored at 4°C for two hours.

***B] Viscosity:***

Brookfield viscometer is used for determination of viscosity. Gels were filled in jar and spindle was lowered perpendicularly taking care that spindle do not touch bottom of the jar. The spindle was rotated in the gel at increasing shear rates 0.5, 1, 2.5 and 5rpm. At each speed, the corresponding dial reading was noted.

***C] Spreadability:***

A modified apparatus consisting of two glass slides containing gel in between with the lower slide fixed to a wooden plate and the upper one attached to a balance by a hook was used to determine spreadability.

***D] Extrudability:***

A simple method was adopted for determination of extrudability in terms of weight in grams required to extrude a 0.5cm ribbon of gel in 10 seconds

**Official requirements for semisolids**:

Ointments and other semisolid dosage forms must meet the USP tests for microbial content, minimum fill, packaging, storage and labelling.

Ophthalmic ointments must meet tests for sterility and metal particle content.

***Microbial content*** **-** With the exception of ophthalmic preparations, topical applications are not required to be sterile, they must however meet acceptable standards for microbial content and preparations which are prone to microbial growth must be preserved with antimicrobial preservatives. e.g. methyl and propyl parabens and quaternary ammonium salts.

For example, Betamethasone valerate ointment USP, must meet the requirements of the tests for the absence of staphylococcus aureus and Pseudomonas aeruginosa.

Preparations that contain water tend to support microbial growth to a greater extent than preparations which are water-free. These microbes are of special importance in dermatological preparations because of their capacity to infect the skin.

Semisolids intended for rectal and vaginal use should be tested for the presence of yeasts and moulds.

***Minimum fill*** **-** The USP minimum fill test involves the determination of the net weight or volume of the contents of the filled containers to assure proper contents compared with the labelled amount.

**Packaging and storage:**

Ointments and other semisolid preparations are packaged in metal or plastic tubes.

The tubes are first tested for compatibility and stability for the intended product.

Tubes used to package topical products are light in weight, relatively inexpensive, convenient for use by the patient, compatible with most formulative components and provide greater protection against external contamination and environmental conditions than jars.

Ointment tubes are made of aluminium or plastic. Tubes of aluminium generally are coated with epoxy resin to eliminate any interactions between the contents and the tube.

Plastic tubes are made of high or low density polyethylene (HDPE or LDPE) or blend of them, polypropylene (PP) and plastic-foil paper laminates. Laminates provide an excellent moisture barrier due to foil content, high durability and product compatibility. These qualities and flexibility make plastic and plastic laminate tubes preferred over metal tubes for the packaging of pharmaceuticals.

Topical dermatological preparations most frequently are packaged in 5, 15 and 30 g tubes.

Ophthalmic ointments are packaged in small aluminium or collapsible plastic tubes holding 3.5 g. The tubes are sterilised before being filled.

Semisolids must be stored in well-closed containers to protect against contamination and in a cool place to protect against product separation due to heat. When required, light-sensitive preparations are packaged in light resistant containers

**Evaluation of Semisoild Dosage Forms:**

- ***Test for rate of absorption:***

¬The diadermatic ointment should be evaluated for the rate of absorption of drug into the blood stream.

¬This test can be done in-vivo only

¬The ointment should be applied over a definite area of the skin by rubbing.

¬At regular intervals of time, serum and urine samples should be analyzed for the quantity of drug absorbed. The rate of absorption i.e., the amount of drug absorbed per unit time should be more.

- ***Test of Non-irritancy:***

¬ The bases used in the formulation of ointments may cause irritation or allergic reactions.

¬ Non-irritancy of the preparation is evaluated by patch test. ¬ In this test 24 human volunteers are selected.

¬ Daily the type of pharmacological action observed is noted. No visible reaction or erythema or intense erythema with edema and vesicular erosion should occur.

¬ A good ointment base shows no visible reaction.

- ***Test of rate of penetration:***

¬ The difference between the initial and the final weights of the preparation gives the amount of preparation penetrated through the skin and this when divided by the area and time period of application gives the rate of penetration of the preparation. The test should be repeated twice or thrice. The rate of penetration of a semisolid dosage form is crucial in the onset and duration of action of the drug.

¬Weighed quantity of the preparation should be applied over selected area of the skin for a definite period of time.

¬Then the preparation left over is collected and weighed