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PHARMACEUTICS AND PREFORMULATION: THE DYNAMIC DUO OF PHARMACEUTICAL DEVELOPMENT

Ranitha R.*, Alka Eldos, Rifna Sherin C. K., Safvana P., Dr. Deepu S., Deborah Evangeline, Kanaka V. S., Neenu Anna Thomas, Srathika K.

Department of Pharmaceutics, Ahalia School of Pharmacy, Palakkad, India.

***Corresponding Author: Ranitha R.**

Department of Pharmaceutics, Ahalia School of Pharmacy, Palakkad, India.

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ABSTRACT

This article presents a comprehensive review of key foundational and advanced concepts in the pharmaceutical sciences. It outlines the scope of pharmaceutics and its critical role in ensuring drug efficacy, safety, and stability. A detailed exploration of the preformulation phase is provided, highlighting essential physicochemical considerations such as drug-excipient interactions, solubility, pH, partition coefficient, buffer capacity, salt forms, pKa, and lipophilicity. Patient-related factors like age and sex, which influence drug performance and safety, are also discussed. The review further elaborates on the sequential steps involved in pharmaceutical research and development, starting from drug discovery and preclinical research to clinical evaluation. Key preclinical processes such as toxicology testing, Investigational New Drug (IND) applications and product characterization are examined. It also discusses formulation and packaging development, labeling standards, and regulatory considerations. Additionally, pharmacokinetics and drug disposition are analyzed to understand the body's handling of pharmaceuticals. Finally, the stages of clinical research, including bio analytical testing and clinical trials are reviewed to emphasize their significance in ensuring therapeutic success and regulatory approval. This review serves as an essential resource for students, researchers, and professionals seeking a holistic understanding of the pharmaceutical research continuum.

KEYWORDS: Preformulation, Pharmaceutics, Pharmaceutical industry, Research, Evaluation.

INTRODUCTION

Pharmaceutical development is an intricate and multifaceted process that necessitates the harmonious convergence of diverse scientific disciplines, including chemistry, biology, pharmacology and engineering to transform promising molecular entities into safe, effective and commercially viable medicinal products that improve human health and quality of life. Within this complex framework, pharmaceutics and pre-formulation emerge as two intimately interconnected and interdependent fields. It plays a pivotal role in optimizing drug delivery systems, enhancing bioavailability and ensuring therapeutic efficacy, while also addressing critical considerations such as stability, scalability, and regulatory compliance. This dynamic duo forms the backbone of pharmaceutical development, working in tandem to overcome the challenges of drug development, from the initial discovery phase to the final commercialisation stage, and ultimately, to bring innovative, life-changing therapies to the patients in need. In this article, we will delve into the intricacies of pharmaceutics and pre-formulation, exploring their respective roles, synergies, and impact on the pharmaceutical industry, and examining the latest advances, trends, and best practices in these fields.

1. ROLE OF PHARMACEUTICS IN THE PHARMA INDUSTRY

1.1. PHARMA INDUSTRY[1]

Pharmaceutics is the overall process of developing a new chemical entity into an approved therapy that is safe and effective in treating or preventing disease. The focus areas include drug formulation, drug delivery system, pharmacokinetics and pharmacodynamics, stability and bioavailability, and pharmacovigilance. The pharmaceutical industry is a medical industry that

discovers, develops, produces and markets pharmaceutical goods such as medications and medical devices. It includes R&D, production, quality assurance, marketing and distribution, pharmacovigilance.

The pharmaceutical industry can be broadly categorized into two: generic industries and research-based industries. The generic industries include formulations, herbal formulations, ayurvedic formulations, nutraceuticals and bulk drug (APIs).

1.2. GLOBAL MARKET

In 2023, the global pharmaceutical market was valued at over $1.60 trillion, a 4.4% increase, demonstrating its impressive growth. With 40% of the market share and revenues up 4.5% to $550 billion, the US continues to be the main growth centre. Europe and emerging markets contribute $210 billion and $211 billion, respectively, while China is the second-largest market with $190 billion. The biopharmaceutical sector, which is currently worth $321 billion and accounts for 24% of the global drug market, has made a substantial contribution to this expansion. Furthermore, between $150 and $160 billion is spent globally on research and development (R&D), demonstrating the industry's dedication to advancement and innovation.

2.1.

2.1.1.

As per 2024 reports, the top pharmaceutical companies in the world, based on total revenue Pfizer is leading company with $58.5 billion in revenue and followed closely by Johnson & Johnson at $54.76 billion. This reflects each company's strategic focus on therapeutic innovation, biologics, and global market influence.

1.3. INDIAN MARKET

The Indian pharmaceutical industry plays a crucial role in the global pharmaceutical market. The Indian pharmaceutical industry is growing in both domestic and international markets. 95% of the nation's domestic needs are met by the more than 400 Active Pharmaceutical Ingredients (APIs) and approximately 9,500 formulations are produced by Indian industry. India is one of the top five producers of bulk drugs worldwide, ranking fourth in terms of volume and thirteenth in terms of value. Supported by more than 1,000 research units, the industry encompasses manufacturing, contract research, and biosimilars. India's cost-effectiveness generates significant international opportunities because its production costs are almost 33% lower than those of the US. Additionally, it manufactures more than 2,500 FDA-approved medications and has the second-highest number of USFDA-approved manufacturing facilities outside of the US.

Indian pharma supplies over 50% of global demand for various vaccines, 20% of global generic demand. It acts as a major exporter of pharmaceuticals in Latin America (16%), North America (31%) and Africa (19%). Major Indian pharmaceutical industries are Sun Pharma, Cipla, Lupin, Abbott, and Mankind. Lots of opportunities in diverse functions for graduates and post-graduates. Opportunities for startups have increased with government support and funding.

2. DRUG DISCOVERY AND DEVELOPMENT[2]

Drug discovery is a process that aims at identifying a compound therapeutically useful in curing and treating disease. This process involves the identification of candidates, synthesis, characterization, validation, optimization, screening, and assays for therapeutic efficacy.

Once a compound has shown its significance in these investigations, it will initiate the drug development process earlier to clinical trials. The new drug development process must continue through several stages to make a safe, effective medicine that has approved all regulatory requirements. There are four stages of drug discovery and development;

- Drug Discovery
- Preclinical Development
- Clinical Development
- Regulatory Review and Approval

DRUG DISCOVERY

TARGET IDENTIFICATION

Target identification is a fundamental step in the drug development process, where researchers determine a specific biological molecule such as a protein, gene, or RNA that plays a crucial role in the development or progression of a disease.[2,3] The goal is to find a "target" that, when modulated by a drug, can correct or alter the disease state. This process involves extensive research into the molecular mechanisms of diseases using tools like genomics, proteomics, and bioinformatics.

Once a potential target is identified, it undergoes validation to ensure that its inhibition or activation will have a therapeutic effect without causing significant harm to normal biological functions. Successful target identification lays the groundwork for the entire drug discovery process, as it directs subsequent efforts toward finding or designing compounds that can specifically interact with the chosen target.

2.1.2. TARGET VALIDATION

Target validation is a critical step in drug development that follows target identification and ensures that a chosen biological target is directly involved in a disease process and that modulating it will produce a therapeutic effect. Validation involves a combination of experimental techniques, such as gene knockdown or knockout studies using technologies.

Target validation also includes analyzing the expression of the target in diseased versus healthy tissues to confirm its specificity. A thoroughly validated target increases the likelihood of success in subsequent stages of drug

development, making it a crucial foundation for selecting promising drug candidates.

2.1.3. LEAD COMPOUND IDENTIFICATION

Lead compound identification is a vital stage in drug development where researchers discover chemical or biological molecules that can interact effectively with the validated target to produce a desired therapeutic effect. These compounds, known as "lead compounds," serve as the starting point for the development of a new drug. The identification process typically involves screening large libraries of natural or synthetic compounds. In addition to HTS, computational approaches like molecular docking and structure-based drug design are also used to predict how well compounds might bind to the target. Once potential leads are found, they are evaluated for their potency, selectivity, and preliminary safety profile.

2.1.4. LEAD OPTIMIZATION[2]

Lead optimization is a crucial phase in drug development that follows the identification of lead compounds. The main goals of lead optimization are to improve the compound's potency, selectivity, pharmacokinetics (absorption, distribution, metabolism, and excretion), and safety profile. Advanced techniques such as structure-activity relationship (SAR) analysis, computer-aided drug design, and in vitro and in vivo testing are commonly used in this process. Through multiple cycles of design, synthesis, and testing, the most promising optimized compounds often referred to as a "drug candidate" are selected for further evaluation in preclinical studies.

2.2. PRECLINICAL DEVELOPMENT[2,3]

Preclinical development is a critical phase in drug development that takes place before a new drug candidate is tested in humans. The primary goal of this stage is to assess the safety, efficacy, and pharmacological properties of the drug through laboratory and animal studies. During preclinical testing, researchers examine how the drug behaves in the body, how it is absorbed, distributed, metabolized, and excreted (pharmacokinetics) as well as its biological effects on target and non-target tissues (pharmacodynamics).

Toxicology studies are also conducted to identify potential harmful effects, determine safe dosage ranges, and evaluate the risk of long-term exposure. These studies are essential for predicting how the drug might behave in humans and for identifying any safety concerns that could prevent clinical trials.[4] Additionally, formulation development occurs during this stage, in which the drug is prepared in a suitable form for administration, such as a tablet, capsule, or injection. The results of preclinical development form the basis of the Investigational New Drug (IND) application submitted to regulatory authorities to obtain approval for human clinical trials.

Key Components of Preclinical Studies

2.2.1. PHARMACOLOGY STUDIES[5]

Pharmacology studies in preclinical development are essential for understanding both how a drug affects the body (pharmacodynamics) and how the body affects the drug (pharmacokinetics). Pharmacodynamics (PD) focuses on determining the drug's mechanism of action, dose-response relationship, and biological activity in target and non-target tissues. These effects are typically studied using receptor binding assays, functional assays, and disease-relevant animal models.

Pharmacokinetics (PK), in contrast, evaluates the drug's absorption, distribution, metabolism, and excretion (ADME). Important pharmacokinetic parameters include the peak plasma concentration (C_{max}), time to reach peak concentration (T_{max}), half-life ($t½$), bioavailability, clearance, and volume of distribution. Together PD and PK studies provide a comprehensive understanding of a drug's behavior in the body and are usually conducted in both rodents and non-rodents, such as rats, dogs, or monkeys, to support the transition to human clinical trials.

2.2.2. TOXICOLOGY STUDIES

Toxicology studies are an essential component of drug discovery and development, focusing on evaluating the safety and potential harmful effects of new drug candidates before they enter human trials.[5,6] These studies aim to identify toxic effects on various organs and biological systems, determine safe dosage levels, and provide critical data to support regulatory submissions such as the Investigational New Drug (IND) application.

Toxicology assessments include acute toxicity tests to evaluate immediate effects, sub-acute and sub-chronic studies for repeated dose toxicity, as well as long-term chronic toxicity studies to observe potential adverse effects over time. The results of toxicology studies are crucial for determining safe starting doses for clinical trials, guiding risk management strategies, and ensuring ethical compliance and regulatory approval. Ultimately, toxicology helps protect patient safety by ensuring that only drugs with acceptable safety profiles advance to human testing.

2.2.3. ADME STUDIES (Absorption, Distribution, Metabolism, Excretion)[7]

These are the key processes that determine a drug's behaviour inside the body. During drug discovery and development, understanding ADME is crucial to predict how well a drug is absorbed into the bloodstream, how it is distributed to tissues, how it is metabolized or broken down (mainly by the liver), and how it is ultimately excreted from the body. Studying ADME helps optimize drug efficacy, minimize toxicity, and determine appropriate dosing regimens before a candidate moves into clinical trials.

2.2.4. *IN-VITRO* AND *IN-VIVO* STUDIES

In vitro studies are experiments conducted outside a living organism, typically using cells, tissues, or biochemical assays in a controlled lab environment. These studies help identify a drug's biological activity, toxicity, and mechanism of action early in the discovery process with high efficiency and lower cost.

In vivo studies involve testing drug candidates in living organisms, usually animal models, to evaluate the drug's overall effects, including pharmacokinetics, efficacy, and safety in a complex biological system. These studies provide crucial data on how the drug behaves in a whole organism, helping to predict its potential performance in humans before clinical trials.

2.3. CLINICAL DEVELOPMENT[8,9]

Clinical development is the critical phase in drug development where a drug candidate is tested in humans to evaluate its safety, efficacy, dosage, and overall benefit-to-risk profile. This phase follows successful preclinical studies and regulatory approval to initiate human trials.

Clinical development is typically divided into four phases

- **Phase I** trials involve a small number of healthy volunteers (20–100) and focus primarily on assessing the drug's safety, tolerability, pharmacokinetics (how the drug is absorbed, distributed, metabolized, and excreted), and determining appropriate dosage ranges. These trials help establish the maximum tolerated dose and identify any immediate adverse effects.
- **Phase II** trials include a larger group of patients (100–500) who have the target disease or condition. The goal is to evaluate the drug's efficacy while continuing to monitor safety. These trials help refine the dose, assess short-term side effects, and provide preliminary evidence of therapeutic benefits.
- **Phase III** trials are large-scale studies involving hundreds to thousands of patients. They are designed to confirm the drug's effectiveness, monitor adverse reactions, compare it to standard treatments or a placebo, and gather comprehensive safety data. Successful Phase III trials are essential for regulatory approval.
- **Phase IV** trials, also known as post-marketing surveillance studies, take place after the drug is approved and marketed. These studies continue to monitor long-term safety, effectiveness, and any rare or delayed adverse effects in the broader patient population.

Clinical development is highly regulated to ensure patient safety and robust data collection, and it represents one of the most resource-intensive stages of drug development. The insights gained during this phase are critical for gaining regulatory approval and ultimately making new therapies available to patients.[10]

2.4. REGULATORY REVIEW AND APPROVAL[11]

Regulatory review and approval are a vital stage in the drug development process where regulatory authorities evaluate all the scientific data collected from preclinical and clinical studies to determine whether a drug is safe, effective, and of high quality for public use.

After successful completion of clinical trials, the drug sponsor submits a comprehensive application commonly called a New Drug Application (NDA) or Biologics License Application (BLA), which includes detailed data on pharmacology, toxicology, manufacturing processes, clinical trial results, and proposed labelling.

During the review, regulators thoroughly assess

- Safety and efficacy data to ensure the benefits outweigh risks
- Quality and consistency of drug manufacturing
- Accuracy of labelling and instructions for use
- Risk management plans for monitoring adverse effects post-approval

The review process can take several months to years, depending on the drug type and regulatory pathway. Approval is granted only if the evidence convincingly demonstrates that the drug is safe and effective for its intended use. Once approved, the drug can be marketed and prescribed to patients, but regulatory oversight continues through post-marketing surveillance to detect any long-term or rare side effects and ensure ongoing safety.

2. FORMULATION AND DEVELOPMENT (F&D)[12]

Formulation and development in pharmaceutics is the process of converting active pharmaceutical ingredients into stable and bioavailable dosage forms like tablets. Formulation is the process of combining active pharmaceutical ingredients with excipients that leads to formulation of a new dosage form, and development is the process of designing, testing and optimizing a formulation to ensure its safety, efficacy and quality. It starts with thorough preformulation studies to analyze the physicochemical properties of the drug. By analyzing this data, appropriate types of tablets and excipients are selected. It plays a crucial role in the pharmaceutical industry by ensuring product efficacy and safety. F&D helps in minimizing risk associated with medication. The activities under F&D should comply with the regulatory requirements set by the FDA, EMA and other authorities. Also, F&D helps in ensuring the product is stable throughout its shelf life. Optimizing the production cost, reducing waste and improving resource allocation are also a function of this organization. Successful F&D can lead to business growth as new products and technologies are developed. The tools and technologies involved in the process of F&D are quality by design (Q_bD), process analytical technology (PAT) and Design of Experiments (D_oE). After getting a satisfactory

product it is scaled up for industrial production with thorough validation in each step.

3. PREFORMULATION[13,14]

It is defined as the investigation of physico-chemical properties of a drug substance, either alone or when combined with excipients, that could affect the drug performance and development of an efficacious dosage form. It is a critical step in selection of excipients, manufacturing process, selection of container, selection of packaging material and to select optimum storage conditions.

★ **OBJECTIVES**

➔ To determine physico-chemical properties of new drugs.
➔ To determine kinetic rate profile.
➔ To determine compatibility of new drugs.
➔ To develop an optimal drug delivery system.
➔ It is an initial step in rational development of a dosage form.

★ **GENERAL ASPECTS**

4.1. DRUG EXCIPIENT INTERACTION[15,16,17]

An excipient is a pharmacologically inert substance formulated with active pharmaceutical ingredients to provide specific attributes to a dosage form. Excipients provide bulkiness to the formulations and also enhance the bioavailability of drugs. Though the excipients are pharmacologically inert under certain circumstances they interact with other formulations and cause physical and chemical changes. This interaction leads to instability of the formulations. Thus the selection of excipients and concentration should be based on drug excipient interactions. It can be broadly classified as physical interaction, chemical interaction and biopharmaceutical interaction. Physical interactions are very common and challenging to detect. It involves change in dosage uniformity, color, odour, dissolution, stability and sedimentation rate. Interaction between drugs and excipients or drugs and impurities of formulations comes under chemical interaction. This interaction causes degradation of products and it is classified as chemical interaction between drug and excipients, interaction between drug and impurities. The biopharmaceutical interaction is the interaction that takes place after the intake of a medicine. This takes place between medicine and the body fluid. Also have a lean to affect the absorption rate of the drug. Premature breakdown of an enteric coated tablet is an example for this type of interaction. Differential scanning calorimeter, differential thermal analysis, self-interaction chromatography, TLC and HPTLC are different analytical techniques used to detect drug excipient interactions. Understanding and evaluating these interactions is essential to ensure the development of an effective, stable and regulatory compliant pharmaceutical product.

4.2. BUFFER CAPACITY[17]

Buffers are solutions that can resist changes in pH upon addition of small amounts of acids or base. Buffer mixtures usually contain a conjugate acid and conjugate base; these together can resist large changes in pH on absorption of H^+ or OH^- ions added to the system. That is, buffer capacity is equal to resistance. Buffers act by adding by H+ ions or OH- ions to the buffer system and react with the conjugate base and conjugate acid respectively.

Buffer capacity is the number of moles of acid or base that must be added to 1L of the -9buffer solution to change its pH by one unit. It is the quantitative measure of a buffer's ability to withstand the changes in pH upon the addition of strong acid or base. The H+ ions cause a decrease in the pH and OH- ions cause an increase in the pH of the solution. Buffer capacity designated by the term Buffer index (β) which is also called Buffer Value or Buffer Efficiency.

According to Koppel, Spiro and Slyke buffer capacity is given as;
Buffer capacity, $\beta = \Delta B/\Delta pH$ where, C= total buffer concentration. ΔB= the increment of strong base or acid in gram equivalents per litre and ΔpH= small change in pH.

A buffer with a higher buffer capacity is more effective in resisting changes in pH. Buffer capacity reaches its maximum value when the concentration of the acid and its conjugate base or the base and its conjugate acid is equal.

4.3. PARTITION CO-EFFICIENT[17,18]

Partition coefficient is defined as the ratio of a concentration of a compound in a mixture of two immiscible solvents at equilibrium. Partition coefficient is denoted as log P. Usually in experiments octanol is used as organic phase and water is used as aqueous phase. It is also called the distribution coefficient. It is the measure of hydrophilicity or lipophilicity of a compound. Partition coefficient helps in predicting how easily a drug can be absorbed into the bloodstream and to know the movement of pollutants in the environment. It acts as a key factor in preformulation studies by helping to design stable and effective dosage forms. Lipophilicity, solubility, temperature, ionization may affect partition coefficient adversely.

Partition coefficient, log $P = C_{org} / C_{aq}$, where C_{org} is the concentration of drug in organic phase and C_{aq} is the concentration of drug in aqueous phase.

Higher log P indicates more lipophilicity and poor solubility and vice versa. The method used to study partition coefficient is the shake flask method. The partition coefficient must be considered in developing a dosage form.

4.4. SALT FORM OF DRUG[17,19]

The salt form of the drug is the easiest way to improve the solubility as well as dissolution rate of drugs which are weak acids or weak base. A strong base salt like sodium and potassium salts of barbiturates and sulfonamides are prepared with weakly acidic drugs and for weakly basic drugs strong acid salt like hydrochloride or sulphate salts of alkaloidal drugs are prepared. The salt forms of drugs have higher aqueous solubility than their parent acids or bases forms, this character are important for absorption and bioavailability of drugs. It can protect the drug from chemical degradation such as oxidation and hydrolysis thus improving the drug stability. The salt form of a drug is more efficient for drug production because the salts can crystallize and purify easily. Hence salt form of a drug improves the general performance of medications. So it is very important to elect the right salt form.

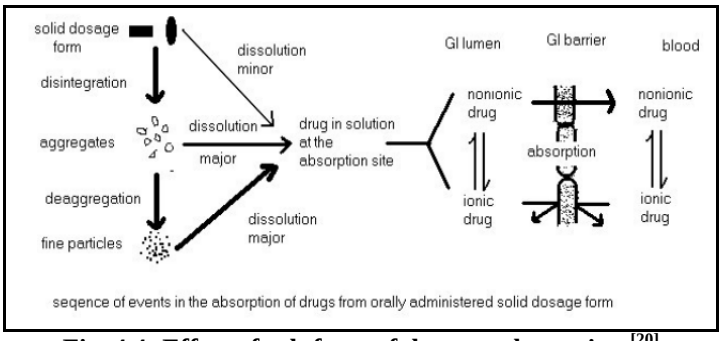

Fig. 4.4: Effect of salt form of drug on absorption.[20]

The mechanism involved in the salt form of a drug is explained by considering a diffusion layer around the drug which can be a weak acid or a weak base. While considering the salt of weak acid, at any pH of the bulk of solution, the pH in the diffusive layer is higher than free form of drug. This increased pH facilitates the solubility and dissolution of a drug. Hence the bioavailability of a drug can be improved.

If: [H+]d = hydrogen ion concentration of the diffusion layer and

[H+]b = hydrogen ion concentration of the bulk of the solution, then,

For salts of weak acids, [H+]d < [H+]b

For salts of weak bases, [H+]d > [H+]b

4.5. PH OF DRUG[17,21,22]

PH is the concentration of H+ ions of a solution. pH influences the absorption and bioavailability of a drug by affecting its dissolution in body fluids. Prolonged pH level causes degradation or neutralisation of drugs. In the stomach or intestine weakly acidic or basic drugs are easily absorbed at specific pH level and pH ensures that the drug is stable and effective throughout the shelf life. pH also plays a role in selecting the administration routes and it affects the drug interaction with the protein, enzymes and other molecules in our body. The pH of drug and site of administration or body should be compatible to minimize the irritation. Weakly acidic drugs are more soluble in alkaline environments that are at a high pH, whereas weakly basic drugs are more soluble in acidic environments that are at low pH. Strong acids and bases are

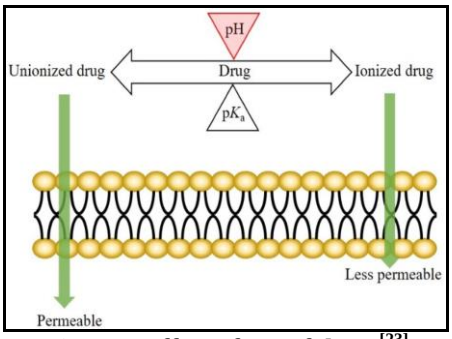

Fig. 4.5: Effect of pH of drug.[23]

Corrosive at extreme pH levels. Certain pH meters are used to measure the pH using electrodes that respond to hydrogen ion concentration. In general the pH of a drug affects the behavior and effectiveness of a drug so pH should be considered in the development and formulation stages of a dosage form.

4.6. DRUG pKa AND LIPOPHILICITY[24]

Ka is defined as the dissociation constant for a substance that dissociates into ions. pKa is the negative logarithm of base10 dissociation constant(Ka). Since the majority of drugs are weak acids or bases the measurements of pKa or ionization constant having an important role in drug preformulation. Ionization is the process in which atoms or molecules get negative or positive charge by gaining or losing electrons. The ionization constant is dependent upon the pH of the medium. That is, ion formation from weak acidic or basic compounds is pH dependent. The ionized and unionized form of a drug depends upon the pH. Ionized form is hydrophilic and it decreases absorption whereas unionized form is lipophilic and it increases absorption. Lower pKa indicates stronger acid and higher pH indicates stronger base.

Ionization constant, pKa = −logKa

When pKa is equal to pH there is a balance between ionized and ionized form of drug. When the pH is lower than the pKa of a drug, it tends to be mostly in its unionized form and when the pH is higher than the pKa the drug tends to be generally in its ionized form. Unionized form of a drug can cross the barriers. The methods used for determination of drug pKa are conductivity method solubility method, potentiometric method, spectroscopic method and HPLC. Lipophilicity is the drug's ability to dissolve in lipids or fats. Since the barrier membranes, skin or cell walls are made up of phospholipid bilayer the drug should have definite lipophilic characteristics. Hexane and toluene are examples for highly lipophilic compounds. If a drug has poor lipid solubility it will be poorly absorbed even though it is in unionized form. For optimum bioavailability a hydrophilic-lipophilic balance (HLB) should be present in the drug structure. Lipophilicity has significance in absorption, distribution, metabolism, excretion and toxicity.

4.7. PATIENT RELATED FACTORS[17,25, 26]

4.7.1. AGE

Age is a crucial factor in preformulation, as changes in age can significantly impact drug absorption, leading to variations in pharmacokinetics and efficacy across different age groups. In infants, the gastric pH is higher and intestinal surface area and blood flow to the gastrointestinal tract are lower, resulting in varied absorption factors compared to adults. Total body water both intracellular and extracellular is greater in infants whereas the fact content is higher in both infants and elderly persons. The blood brain barrier is not well developed in infants and the cerebral blood flow is high, it causes greater penetration of drugs into the brain. The low albumin content in neonates causes the concentration of unbound drugs to be high. While in elderly persons more albumin content causes increased concentration of free drugs.

4.7.2. SEX[27]

Sex can affect absorption, distribution, metabolism, excretion and pharmacodynamics of a new formulation. It is important to identify the effect of sex in preformulation stage favors in selecting drug design and ensuring therapeutic effectiveness. Typically females have high body fat and lower muscle mass than males, it is an important factor in distribution drugs. The volume of distribution is also sex specific. Hormonal fluctuations and enzymatic activity determines the absorption and metabolism of drugs. Since the females have slower gastric emptying and intestinal transit times the dissolution and absorption of orally administered drugs is also a sex specific. Using a combination of in vitro studies using sex specific biological media, preclinical studies in both sexes, liver microsomal studies, computational modelling, data mining and retrospective studies preformulation studies can effectively determine the consequences of sex on drug development.

4. PACKAGING[28]

A pharmaceutical packaging is defined as the process of enclosing pharmaceutical preparations in a physical container on a package for distribution and storage. Packaging is responsible for multifaceted functions such as handling, protection, convenience, presentation, identification and information. Customization on packing is important in protecting factors such as environmental issues including sustainability, light, moisture and air. The packaging should be designed to provide optimal convenience, ease of use and accessibility for consumers enabling them to effortlessly open, handle and utilize the product thereby ensuring safe and effective use of the medication. Packaging also helps in attracting people during purchasing. Packaging of pharmaceutical products can be classified into primary, secondary and tertiary. In primary packaging the material gets direct contact with the product by enveloping it. Aerosol spray can, blister packs and bottles are examples for primary packaging. Secondary packaging refers to outer or external packaging that encloses and protects primary packaging so that an additional layer of security will be obtained for the products. Cartons, boxes, cases, and overwrapping are examples for secondary packaging. Tertiary packaging acts as the outermost layer of packaging that contains multiple units of secondary packaging. Mainly used in bulk handling and shipping.

This packaging provides more protection and efficiency for the products during storage, transportation and distribution. Pallet, barrel, container are some examples for this type of packaging.

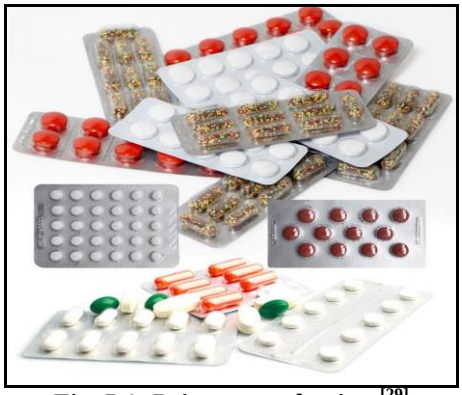

Fig. 5.1: Primary packaging.[29]

Fig. 5.2: Secondary packaging.[30]

Fig. 5.3: Tertiary packaging.[31]

LABELING

A label is defined as any display of written, printed, or graphic matter on the immediate container of any article, or any such matter affixed to any consumer commodity or affixed to or appearing upon a package containing any consumer commodity. The primary purpose of labeling as per FDA is to ensure patient safety by giving a short description on drugs safety and efficacy of a drug. Product name, date of manufacturing and expiry, indication and usage, dosage and administration, dosage forms and strength, contraindications, warnings and precautions are major requirements in a drug labeling. The labeling and selection of packaging should be selected by pharmacists for maintaining drug integrity. For assurance of labeling, the drug labeling is regulated by different bodies like federal regulations and state regulations. It is mainly regulated by US policy under 21 CFR 201.56(D) and 201.57 for human prescription drug and biological products.

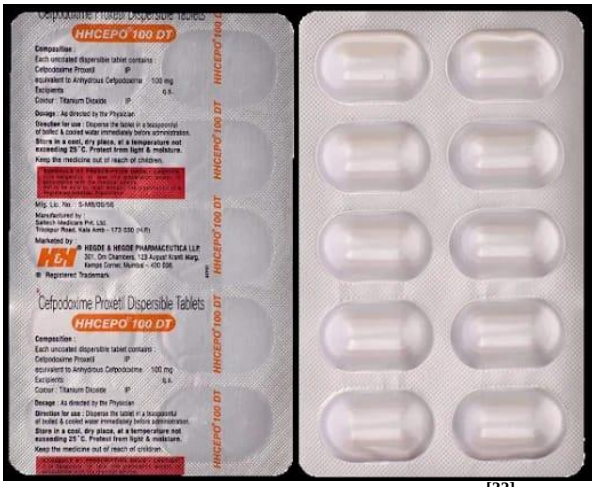

Fig. 06: Example for drug labelling.[32]

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