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Formulation Development Studies

Satyam Kumar Yadav[1], Mr. Jitendra Kumar Yadav[2]

[1] (B Pharm)
Gmail-satyamky2003@gmail.com
[2] (Assistant Professor)
University-AKTU College-S. N. College Of Pharmacy

ABSTRACT :

Formulation development is a crucial part of pharmaceutical development and offers an important part in the therapeutic and commercial acquisition of products by providing quality, safety, and efficacy. Product development techniques such as drug discovery are the primary component of formulation development. research, etc. Both the initial phase of medication development and the subsequent marketing success of the drug product depend on it. It connects the investigation of a novel medication ingredient to the effective creation of a pharmaceutical product. Formulation can affect a pharmaceutical product's lifespan and patentability.

Every pharmaceutical product requires a customized formulation because of the complexity of several pathways that could impact product stability, the unique properties of the therapeutic molecule, unique patient requirements, and even marketing concerns. Numerous methods can be used to approach formulation development, including logical design, reliance on scientific ideas, and application of these insights to thousands of components. This article reviews formulation development and explains pre-formulation and SOP management so that everyone can understand and appreciate the significance of the procedures.

INTRODUCTION

In the biotechnology and pharmaceutical sectors, drug development is a hot trend. The majority of pharmaceutical and biotech businesses are contributing to the development of their probable new pharmaceuticals, since the need to investigate drug candidates from discovery to human clinical trials as quickly as feasible has grown. Outsourcing is a more economical option and shortens the time needed for product development. Outsourcing offers a multiple cost structure, increasing resources and spending and decreasing when demand decreases. This allows the organization and individuals to quickly address changing needs. A pharmaceutical product's lifespan and patentability can be determined by its formulation.

In order to improve their product development, companies use these formulation development guidelines, regulations, and staff. Large pharmaceutical businesses may have specialized sections for things like formulation problems and the physical characterization of medication ingredients. Since various divisions frequently operate in different locations, it is crucial that they be handled by a single authority in order to speed up development and shorten the formulation development period. Around 1950, we became aware of the pre-formulation notion as a result of industrial pharmaceutical growth. The physical and chemical properties of the medication or drug material are described and established during this stage of pharmaceutical product development, and the psychochemical and biopharmaceutical qualities provide suitable formulation and delivery mechanisms.

Definition: Current good manufacturing practices (cGMP) are those that adhere to the guidelines established by the relevant authorities. Approval and licensing of medications, nutritional supplements, cosmetics, food and drink products, and medical equipment are the responsibilities of these institutions. cGMP systems involve several controls for operations that prioritize quality, including

1. Management system
2. Superior Raw Materials
3. . Managing protocols
4. Identifying deviations
5. Examining deviations
6. Dependable testing.

2. HISTORY

In Hindu legend, Dhanvantari, the gods' doctor, created Ayurveda after learning it from Brahma. The Vedas, also known as the Atharvaveda, contain the earliest information on it. German scientist Friedrich Sertürner created the first pharmacological drug in the modern era in 1804. The earliest pharmaceuticals were natural substances derived from plants, roots, fungus, herbs, and vines.

Nature's medicines were the only means of alleviating human suffering until the middle of the 1800s. Chloral hydrate, the first synthetic medicine, was created in 1869 and used as a sedative-hypnotic; in certain nations, it is still accessible today. Due in large part to the abundant supply of organic compounds obtained from the distillation of coal (coal-tar), the first pharmaceutical firms were a direct inverse of the textile and synthetic dye industries.

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The first analgesics and antipyretics were made from coal tar byproducts called phenacetin and acetanilide, which are chemical derivatives of aniline and p-nitrophenol. For generations, a white willow bark extract has been used to treat a variety of fevers and inflammations. A straightforward chemical change made acetylsalicylic acid, the first well-known medication, far more beneficial than the bitter salicin or salicylic acid found in white willow, which also inflamed the stomach mucosa. The first barbiturate drug listed in the pharmacopoeia was at the beginning of the twentieth century, and the rest is history.

4. STEPS IN FORMULATIONS

1. Identification and characterization of drug:

The identification of drug characterization is highly significant since it affects the end result and also the influence of numerous characters make the drug more potent or dangerous.

2. Excipients Compatibility Study:

The more compatible the excipient is with the drug, the greater the possibilities of drug formulation success and the drug's effect.

3. Formulation development:

The following step deals with formulation development so that witch chemicals go with witch and witch excipients are suitable for medications.

4. Formulation Optimization:

In this stage, formulations such as vaccines are produced. This type of formulation requires more studies than typical formulations and a significant quantity of knowledge.

5. Formulation Evaluation:

The assessment studies help to improve the already established formulation by modifying the parts of the formulation, such as the vehicle kinds.

6. Stability Studies:

The assessment studies help to improve the already established formulation by modifying the parts of the formulation, such as the vehicle varieties. It deals with the long-term stability of the formulation by completing various tests so that the stability of the formulation increases. It also helps to improve the shelf life of formulation.

5. PRE-FORMULATION STUDIES:

The concept of pre-formulation is based on emphasis industrial pharmaceutical development, in which the physicochemical properties of medicinal ingredients are established and characterized. Pre-formulation studies are laboratory investigations to evaluate the characteristics of active substances and excipients that may influence formulation, process design, and performance. Pre-formulations are a type of study that focuses on the physicochemical qualities of a novel drug candidate and how they interact with excipients to affect drug performance.

- **OBJECTIVES:**

1. To establish its compatibility with common excipients and determine product stability.
2. To provide insights into how drug products should be processed and stored to ensure their quality.
3. To generate useful information to design a drug delivery system with good Bioavailability
4. To develop the elegant, stable effective and safe dosage form by establishing kinetic rate profile and establish physicochemical parameter of new API
5. To generate useful data needed in developing safe dosage forms that can be manufactured on a commercial scale

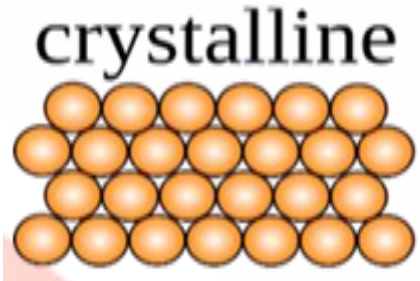
6. PROPERTIES AND PHYSICAL FORMS:

[1] PHYSICAL PROPERTIES:

The physical properties with organoleptic properties of the candidate drug molecule and excipients such as color odor taste by just analyzing them various properties of the drugs are shown like when analyzing odor the constituents present can be determine by checking colour one can determine the impurities.

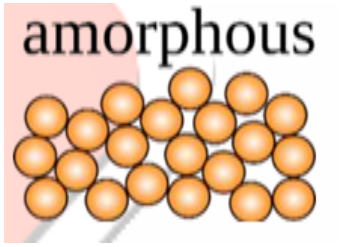
[2] PHYSICAL FORMS:

1. CRYSTALLINE :



It has repetitious spacing of constituents atom or molecules In dimensional array it is more stable than amorphous

2.AMORPHOUS:



Does not have any fixed internal shape

3.PARTIAL SIZE AND SHAPE:

It is the most essential property that affects the bulk qualities of the material such as teste color performance, efficiency, solubility, stability, homogeneity, and texture. The particle size is obtained using surface area equations.

[3]FLOW PROPERTIES:

It is critical in tablet orientation in case of large doses the powder should have proper flow properties it is found out by the cars index

7.FORMULATION OF NOVEL DRUG DELIVERY SYSTEMS

This innovative technique to medication delivery overcomes limitations of previous methods like as controlled drug administration, nano carriers, vesicular drug delivery, and gastro retention systems.

1. CONTROLLED DRUG DELIVERY SYSTEM:

A controlled medication delivery system is designed to provide the appropriate dose of a therapy directly to the intended zone and during the specified time period.

•TYPE: DIFFUSION CONTROLLED, DISSOLUTION CONTROLLED

•Mof: the fundamental principle for evaluation of the kinetics of drug release was offered by Noyes and Whitney in 1897 as the equation (10): dM/dt = KS (Cs ñ Ct)

2.VESICULAR DRUG DELIVERY SYSTEM:

Vesicular drug delivery systems are one type of technology that can increase medication bioavailability and reduce toxicity by delivering the molecule to a specific spot. Bingham pioneered the biologic genesis of vesicular systems in 1965, thus the term Bingham bodies.

3. NANO CARRIERS:

Nanocarriers are important in the drug delivery process because they may transport medications to site-specific targets. This allows pharmaceuticals to be administered in particular organs or cells but not in others.

•TYPE: liposomes, phytotosomes, nanoparticles, microsphere,

4.GASTRO RETENTIVE DRUG DELIVERY SYSTEM:

Gastro retentive delivery systems are designed to be retained in the stomach for a prolonged time and release their active ingredients, thereby enabling sustained and prolonged input of the drug to the upper part of the gastrointestinal (GI) tract. Examples include bio adhesive drugs, expandable drugs, floating drugs, and high density drug delivery.

8. Various equipment and instrument handling:

1) Tablet Compression machine: A mechanical device that works quickly is the tablet press. It accurately compresses the ingredients into the desired shape of a tablet. It can make tablets in different shapes, though most are oval or round. The basic idea behind the tablet compression machine is hydraulic pressure. This pressure is passed through a stationary fluid without losing strength. The stationary fluid spreads the pressure equally in all directions. It also allows the force to be increased as needed.

FIG1: Tablet Compression Machine.

Tablet coating machines

Tablet coating machines operate on a simple principle. Coating material is applied to a moving bed of tablets while heated air is simultaneously used to encourage the evaporation of the solvent. To apply the coating, the tablets are moved either perpendicularly (coating pan) or vertically (air suspension). The working principles of tablet coating machines involve applying coating ingredients in the form of a solution to a group of tablets in a bed that may move horizontally or vertically. A concurrent flow of heated air facilitates the evaporation of the solvents.

FIG 2: Tablet Coater.

5) Extruder and Spheronizer:

The most commonly used process for making pellets is extrusion-spheronization. The following steps are involved: (i)granulation, which prepares the wet mass; (ii) extrusion, which shapes the wet mass into cylinders; (iii) spheronization, which breaks up the extrudate and rounds the particles into spheres; and (iv) drying of the pellets. Extrusion is a process that creates extrudates by applying pressure to a repaired plastic mass until it flows out through an aperture. Plastic deformation causes the extruded, cylindrical particles to break into uniform lengths and progressively change into spherical shapes throughout the spheronization process.

FIG 3: Extruder and Spheronizer.

9. Evaluation:

a) Solid dosage form:

I. Dissolution test:

The assembly includes a motor, a drive shaft, a cylindrical basket (which is the stirring element), and a tank.The tank can be covered and made of glass or another transparent, inert material that does not absorb, react with, or block the preparation being tested. The vessel is heated using a heating jacket or can be partially submerged in a water bath of any suitable size. The temperature inside the vessel is maintained at 37 ± 0.5 ºC throughout the test using a water bath or other heating equipment.

Dissolution Time: 6 solid dosage forms are placed in each tube. For coated ones, the time is 15 minutes; for uncoated, it's 30 minutes; for plain, it's 60 minutes. For capsules, the time is 30 minutes. If the dosage form does not disintegrate, repeat the test using 12 and 16.

2.Weight variation:

The weight variation calculation is a in-process quality control technique is used to determine the uniformity of dosage unit in pharmaceutical dosage form. Only certain unit dosages can be used for the weight variation (WV) test. Formula= W average – W initial/W average 8*1000

3.Hardness test:

The test is also referred to as the "crushing strength test" measures the force needed to crush a tablet, which is called tablet hardness. This is measured in kg/cm². For regular tablets, the hardness range is from 2.5-5 kg/cm², while for dispersible and chewable tablets, the range is 2.25-2.5 kg/cm². Extended release tablets have higher hardness, ranging from 5-7.5 kg/cm².

b). LIQUIDE DOSAGE FORM:

The liquid dosage for needs various test of evaluation so that it shows popper properties of drugs

I. I. Leakage Test: Ten containers filled with liquid medicine are turned upside down for 24 hours. Check if any liquid leaks out, especially if the containers have rubber seals.

II. Clarity Test: Mix the ingredients with water and use clean water as a reference. Look for cloudiness. When viewed against a white background, black or dark particles are visible. When viewed against a black background, transparent or white particles are seen.

III. Sterility Test: This test checks for bacteria, fungi, and yeast in medicines given directly into the body. The test must be done in a clean, controlled environment to prevent accidental contamination. There are two main methods: direct transfer and membrane filtration.

- Direct transfer method: non filterable product test by this method test sample 10% →culture medium 9 ml tubes to 75 ml bottles →direct inoculum → incubate 14 days → M. growth
- Membrane filtration method: sample →0.22 to 0.4 um pore size 47 mm diameter filter→ membrane cut into 2 halves → 100 ml culture medium →incubated 30 to 35 ºC 7 days →anther halve 20 to 25 ºC for 7 days

IV. Pyrogen Test: Pyrogens are substances made by microbes that can cause fever.

V. LAL Test: Limulus Amoebocyte Lysate (LAL) is taken from the blood of horseshoe crabs. A 0.1 ml sample is mixed with LAL reagent and kept at 37°C for one hour. Then, check for clot formation.

10. LABELLING AND PACKAGING:

DEFINITION: Pharmaceutical packaging refers to the packages and the processes used to handle pharmaceutical preparations. It covers all activities from the production stage through the distribution channels until the product reaches the end user. It includes containers or devices that hold the drugs, ensuring easy, safe, and proper assembly of the product.

1. TYPES OF PACKAGING :

- PRIMARY PACKAGING: they have direct contact with drugs ex. cap cap liner label
- .SECONDARY PACKAGING: external to the primary packaging add additional physical protection , leaflets cartons etc
- TERRITORY PACKAGING: provides protection handling Wearhouse storage and transportation ex brown cardboard boxes wood pallets etc
- Ampoules. Vials. Containers. Strip package. Blister Packaging. Syringe. Dosing Doppler. Sachet Packaging Containers. Aluminium foil.
- Injectables / Vials .Bottles . Cartons. Paper Board. Latitudes. Paper etc
- Airtight containers. These containers prevent the contents from dust, moisture, and air.

- Light resistant containers. Multi-dose containers. Single-dose containers. Well closed containers. Aerosol containers. Child-proof containers etc

PACKAGING MATERIAL :

GLASS: They are most commonly used for storing pharmaceutical products because they offer excellent protection.

- Borosilicate glass type 1: 80% silica, 10% boric acid, and a small amount of sodium oxide.
- Soda lime glass: treated with sulfur, which makes it more resistant than type 3.
- Regular soda lime glass: 75% silica, 15% sodium oxide, and 10% calcium oxide.
- Products: coloured glass ampules, bottles, etc.

PLASTIC: They are made from one or more polymers along with additives, which allows them to be shaped easily into the desired form.
Materials used: polyethylene, polystyrene, polycarbonate, polyvinyl chloride, polyvinylidene chloride, polypropylene, etc.
METALS: Metals are the most versatile of all the materials used.
Materials used: aluminium, tin, etc.
PAPER PAPERBOARD : they are traditional material used ever since ex boxes sachets etc
RUBBER: They are used for closures, stoppers, caps, liners, and bulbs.
TYPE 1: most preferred strictest requirement
type 2 ; mechanical properties
Materials: natural, neoprene, nitryl, butyl, Chornobyl , silicon
COTTON : It is employed to prevent collisions by wadding solid preparations.
FILMS FOILS LAMINATIONS : They utilized to support the barrier heat sealing decoration.
ADESSIVE LINKS: they used for labelling adhesion

EVALUATION TEST FOR PACKAGING MATERIALS :

•**IDENTIFICATION:** appearance of packaging material alone and combination of the product content is checked
•**PHYSICAL TEST:** Light absorption, pH, non-volatile matter, residue on ignition, heavy metals, buffering ability, and oxidizable compounds are all checked.
•**CHEMICAL TEST:** Tests include ph. materials chloride sulphates, paper or board, alkalinity of glass, compatibility test for containers.
•**MECHANICAL TESTs:** to check working and strength
•**BIOLOGICAL TEST**:USP includes procedures for it implantation, systemic injection, and intracutaneous tests.
•**ENVIRONMENTAL TEST** : materials test in environment
•**TESTS AS FOLLOWS**: LEAKAGE TEST, COLLAPSIBILITY, CLARITY , TRANSPARENCY, WATER VAPOUR PERMEABILITY, TEST FOR METALLIC ADDITIVES , NON VOLATILE RESIDUAL ,METALLIC ADDITIVES, SURFACE RESISTANCE ,HYDRAULIC RESISTANCE ,ETCHING, LIGHTTRNSMMISION,STHERSOLUBLE,THERMALSHOCK,INTE NALBURSTING, PENETRABILITY TEST,FRAGMENTATION,SELFSEALABILITY,EXTRACTIVE,COMPATIBILITY,LIGH TABSOTBTION

LABELLING OF DIFFERENT DOSAGE FORM:

DEFINITION

The word "labelling" refers to all the labels and other written, printed, or graphic information that appears on the container of a product or on any package or wrapper that holds it, except for the outer box used for shipping. Drug labelling, also called prescription labelling, is any written, printed, or graphic information found on a drug or on the container that holds it, or that comes with the drug. The purpose of drug labels is to tell what the drug contains and to provide instructions or warnings about how to use it, how to store it, and how to dispose of it. When labelling a dosage form, it is important to include all the necessary details. These include the product name, drug facts, a table, active ingredients, purpose and use, warnings, directions, information about allergic reactions, the expiry date, the manufacturing date, and details about different types of drugs. The first label was introduced in 1800, and many changes have taken place since then. It is important to keep all the details included on the label up to date.

Conclusion:

Formulation development, pre-formulation studies, tests, and sop handling are crucial aspects of the pharmaceutical industry. Without them, the industry cannot function properly or solve problems effectively. Formulation development requires significant effort and knowledge, as even minor mistakes can have serious consequences. Formulation development is a dynamic process that converts APIs into useful pharmaceutical products. Scientists use design of experiments to examine formulation parameters in a systematic and timely manner, optimizing the production process.

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