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Review on Formulation Development of Diclofenac Sodium

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ABSTRACT:

Formulation development is a key area of product development that can determine patentability, lifecycle and, ultimately, the success of a pharmaceutical product. Formulation development serves the purpose to determine the optimal dosage form, composition, and manufacturing route for pharmaceutical products. It is a process of utmost importance as it involves developing an adequate preparation and form of a drug, which is both stable and acceptable to the patient. Pharmaceutical formulation development links the discovery of a new drug substance to the successful development of commercial product formulation development scientists must determine the most appropriate route to achieving effective drug delivery based on patient need then optimize the formulations characteristics based on a knowledge of the drug products bioavailability and processing requiring.

Objectives:

1. To study the knowledge about formulation development.
2. To understand the preparation diclofenac sodium tablets.
3. To understand the different manufacturing process of diclofenac sodium tablets.
4. To study the evaluation of diclofenac sodium tablets.
5. To study about different equipment used for preparation of tablets.
6. To understands the uses of diclofenac sodium tablets.

Introduction to formulation development:

The process in which different chemical substances, drug(s) and excipients, are combined to fabricate a final medicinal product of a desired dosage form. Pharmaceutical products are formulated products with specific dosage forms for efficient delivery and product stability.Formulation development serves the purpose to determine the optimal dosage form, composition and manufacturing route for pharmaceutical products.

There are different kinds of pharmaceutical dosage forms such as:Oral tablets, Capsules, Solutions, Suspensions ,Topical ointments ,Gels, Injections for intravenous (IV), intramuscular (IM), or subcutaneous(SC) administration.A dosage form is the physical form of a dose of a drug intended for administration or consumption.

Concept of cGMP :

CGMP refers to Current Good Manufacturing Practice (CGMP) regulations enforced by US FDA. Current Good Manufacturing Practices are the methods to be used in, the facilities or controls to be used for, the manufacturing, processing, packaging or holding of a drug to assure that such drug meets the requirements of the act, and has the identity and strength and meets the quality and purity characteristics that is represented to possess.The regulations make sure that a product is safe for use, and that it has the ingredients and strength it claims to have.

"Good Manufacturing Practice is a part of Quality Assurance which ensures that medicinal products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorization or product specification".

The "C" in GMP means current - up to date technologies.

• cGMP Requirements:

A Quality System (change control, validation), qualified and trained personnel, Fit for use buildings and facilities to meet thepurpose Equipment that is suitable, clean, maintained and calibrated, Controls in place to prevent degradation or contamination of materials (raw, in process and final) ,Production and in-process controls for performance monitoring anddeviations, Proper packaging and labelling - ID and Protection ,Laboratory controls - specifications, samples, testing

Fig. no. 1: Good Manufacturing Practice

Steps in formulation development :

1. **Identification and characterization of drug :**

Identification:

Drug identification starts with isolating the function of a possible therapeutic target (gene/nucleic acid/protein) and its role in the disease. Identification of the drug is followed by characterization of the molecular mechanisms addressed by the drug. An ideal drug should be efficacious, safe, meet clinical and commercial requirements and be druggable. The techniques used for drug identification may be based on principles of molecular biology, biochemistry, genetics, biophysics, or other disciplines.

Characterization :

When any new drug molecule shows a promising therapeutic activity, then the molecule is characterized by its size, shape, strength, weakness, use, toxicity, and biological activity. Early stages of pharmacological studies are helpful to characterize the mechanism of action of the compound.

2. **Excipient compatibility study :**

Drug molecule contains various reactive functional groups which are susceptible to react with another reactive functional groups which might be excipients, excipient or drugs impurities formed during manufacturing or storage. These leads to formation of drug related impurities as well as excipient impurities reaction with active Pharmaceutical Ingredients.

3. **Formulation Development :**

Pharmaceutical formulation development links the discovery of a new drug substance to the successful development of a commercial drug product.

Development of a successful pharmaceutical formulation requires the combination of the active pharmaceutical ingredient (API) with inactive excipients.

4. **Formulation Optimization :**

Formulation optimization is done during the product design phase as the company believes this approach helps to bridge the gap between R&D and commercial production of the final drug product.

5. **Evaluation of formulation :**

Several pre-formulation evaluations may be performed to evaluatetheir bulk and tapped density from the values obtained, compressibility index and

Hausner-ratio were calculated.

And then post-formulation evaluation performed to evaluate tablet for weight variation, hardness, thickness, friability and content uniformity.

6. Stability study :

Stability means capacity of a drug or product to remain within established specifications of identity , quality, purity in a specific period of time.

Requirement listing and procurement :

1. Procurement of drug and excipients required for selected formulation :

It is a process of acquiring supplies of drugs and excipients through purchases from the manufacturer , their agents like distributors or from private or public suppliers .

Procurement of drug and excipients required for the Diclofenac sodium formulation.

a) Diclofenac Sodium

b) HPMC

c) Sodium bicarbonate

d) Isopropyl Alcohol

e) Mg. Stearate

f) Talc

g) Citric Acid

2. Procurement of equipment and instruments for formulation and analysis :

It is a process of acquiring supplies of equipment and instruments through purchases from the manufacturer , their agents like distributors or from private or public suppliers

Procurement of equipment and instrument for formuation :

a) Tablet Compression Machine

b) Friability Test apparatus

c) Monsato Hardness Tester

d) Hot air oven

SOP Handling :

(a) Preparation of SOPs for different instruments and equipment's :

A Standard Operating Procedure is a document which describes the regularly recurring operations relevant to the quality of the investigation. The purpose of the SOP (Standard Operating Procedure) is to describe the procedure of instrument maintenance and preventive maintenance. A SOP should be available at the place where the work is done.

Objectives :

1. The purpose of a SOP is to provide detailed instruction on how to carry out a task so that any employee can carry out a task correctly every time .
2. To maintained the quality control and quality assurance.
3. To serves as a training documents for teaching users about the process for which the SOP was written .
4. To facilitate consistent conformance to quality system requirements and to support data quality .
5. To provide guidelines for accurate and timely data collection.
6. Uniformity of performance.

Steps involved in preparation of SOPs:

1. Develop a list of processes that you believe need SOP creation. .
2. Plan the the process for developing and managing SOPs

3. Collect information for the content of your SOP
4. Write,review the SOP.
5. Maintained your SOP during handling of instruments and equipments.

Various equipment's and instruments handling :

Tablet compression machines :

The tablet press is a high-speed mechanical device. It compresses the ingredients into the required tablet shape with extreme precision.It can make the tablet in many shapes, although they are usually round or oval.

Principle:

▪The basic principle behind the tablet compression machine is hydraulic pressure. This pressure is transmitted unreduced through the static fluid. Any externally applied pressure is transmitted via static fluid to all the directions in the same proportion. It also makes it possible to multiply the force as needed.

Different stages of compression process :

1. Filling :

2. Metering:

3. Compression :

4. Ejection :

SOP for tablet compression machine (Rotary Press) :

1. Clean the dies and punches with spirit and fix the required set of it.
2. Switch on "mains knob"
3. Fill the powder blend in hopper
4. Switch on "start knob" and set speed by "speed knob"
5. Adjust the adequate hardness by adjusting "hardness adjustment knob"
6. After preparation of all tablets, switch off the machine by pressing "stop knob" and finally switch off "main switch" clean dies and punches

1. Preformulation studies and preparation of pre-formulation data sheet

a) Identification of Drug:

We identified the diclofenac sodium drug by it's colour, particle shape, odour ,physical form, particle size.

b) **Solubility:**

We check the solubility of diclofenac sodium by taking 1 gm of drug in solvent of choice in beaker then stired the solution for 10Minutes.After 10 minutes we checked either drug is soluble in that solvent or not.

c) **Melting Point:**

The melting point of diclofenac sodium was determined by introducing the small amount of diclofenac sodium in capillary tube and attached this to stem of thermometer and then placed in the thiele's tube and observed the temperature at which diclofenac sodium begins to melt.

d) Flow Properties:

1. Angle of Repose :

The angle of repose was determined by fixed funnel method in which containers are filled with sample and gradually lifted up then allowed the sample to accumulate and formed the conical heap on the surface .And then calculated the angle of repose by following formula:

$0 = \tan^{-1} (h/r)$

Where, 0= Angle of repose ,h = height of pile ,r = radius of circle

2. Tapped Density :

Tapped density was determined by mechanically tapping the graduated measuring cylinder containing diclofenac sodium powder. And calculated the tapped density by formula:

Tapped Density = Weight of sample (W) / Tapped Volume (V1)

3. Bulk Density:

Bulk density was determined by measuring volume of 100 g of powder in 250 ml graduated cylinder after exposure to compaction by standardized tapping . And then bulk density was calculated by formula :

Bulk density = Weight of sample (W) / Tapped density (V2)

4. Hausner Ratio :

Housner's Ratio calculated by following formula:

Hausner's Ratio = Tapped Density / Bulk Density

5. Carr's Index :

Carr's index calculated by formula:

Carr's Index = Tapped Density - Bulk Density / Tapped Density ×100

Outcome:

After the completion of the report on Formulation and Evaluation of Gastro-retentive Floating Tablet of Development of Diclofenac sodium understood:

- The knowledge about tablets preparation.
- Different types of manufacturing processes used in preparation of tablets.
- Understood the different type of instrument and apparatus used in manufacturing of tablets
- Understood the uses of Diclofenac Sodium tablet .

Conclusion:

After the completion of the report on formulation development we understood the introduction to formulation development, concepts of cGMP, steps in formulation development, requirements listing and procurement, SOP handling, various equipment's and instruments handling, pre-formulation studies and preparation of pre-formulation data sheet, formulation of novel drug delivery system, and its evaluation.

Gastro-retentive floating tablets of diclofenac sodium were successfully prepared by effervescence technology. Diclofenac floating tablets prepared were found to be good without sticking, capping, and chipping.