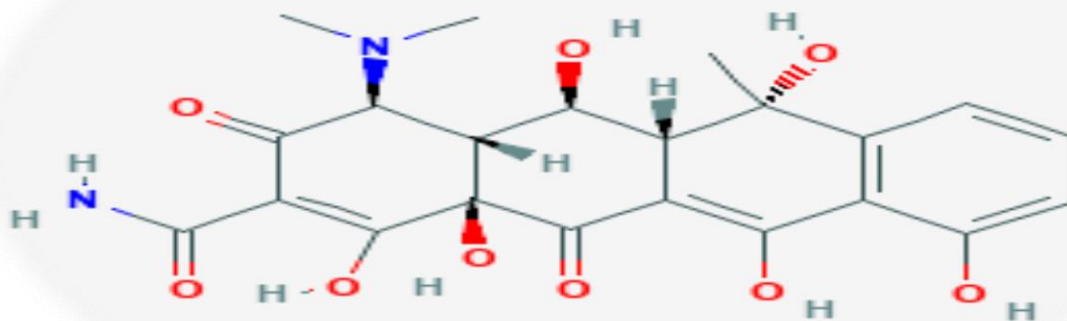


# Drug formulation in aquaculture



# Introduction

- **Drug formulation:** It is the processes in which different chemical substances i.e., active chemical substances will combined together to produce a drug compound.
- **Drug design:** It is the process of producing or invention of novel and/ or new medical product, the design of this new product completely based on the knowledge of biological target.
- **Drug:** a chemical substance used in the treatment, cure, prevention, or used to enhance physical or mental well-being.

- Drug formulation can affect the absorption of drug in two way:
  1. Rate at which the drug goes into solution (dissolution), or
  2. Rate of absorption of the drug across biological membranes.
- **Absorption of drug:** Movement of drugs from Gastrointestinal tract(GIT) to Systemic circulation(SC) or blood.
- **Dissolution:** It is the process in which a drug form a solution.

# Drug Design

- There are two major types or classifications of drug design.
- The first is called as (1) **ligand-based drug design** and the second, (2) **structure-based drug design**.

**1. Ligand-based drug design-** In this branch or type of pharmaceutical formulation the design of the drug will be made or built depends on the knowledge of what binds to it.

**2. Structure-based-** while this type drug design will depend on the information related with the three dimensional structure of the biological target these information will be gotten by using methods like X-ray or Drug design software.

Software and computer based programs used during new drug discovery and development.

Sr. No.	Software name	Major use
<i>1. Pharmacokinetic parameters</i>		
1	DDDPlus	Dissolution and disintegration study
2	GastroPlus	In-vitro and in vivo correlation for various formulations
3	MapCheck	Compare dose or fluency measurement
<i>2. Ligand interactions and molecular dynamic</i>		
4	AutoDock	Evaluate the ligand-protein interaction
5	Schrodinger	Ligand-receptor docking
6	GOLD	Protein-ligand docking
7	BioSuite	Genome analyzing and sequence analyzing
<i>3. Molecular modeling and structural activity relationship</i>		
8	Maestro	Molecular modeling analysis
9	ArgusLab	Molecular docking calculations and molecular modeling package
10	GRAMM	Protein-protein docking and protein-ligand docking
11	SYBYL-X Suite	Molecular modeling and ligand based design
12	Sanjeevini	Predict protein-ligand binding affinity
13	PASS	Create and analysis of SAR models
<i>4. Image analysis and Visualizers</i>		
14	AMIDE (A Medical Image Data Examiner)	Medical image analysis in molecular imaging
15	Discovery Studio® Visualizer	Viewing and analyzing protein data
16	Imaging Software Scge-Pro	Cytogenetic and DNA damage analysis
17	Xenogen Living Image Software	In vivo imaging display and analysis
<i>5. Data analysis</i>		
18	GeneSpring	Identify variation across set of sample and for correction method in samples
19	QSARPro	Protein-protein interaction study
20	REST 2009 Software	Analysis of gene expression data
<i>6. Behavioral study</i>		
21	Ethowatcher	Behavior analysis
22	MARS (Multimodal Animal Rotation System)	Animal activity tracking, enzyme activity, nanoparticle tracking and delivery study

# Factors affecting Drug formulation

- Particle size
- Polymorphism
- pH
- Solubility
- Stability
- Drug concentration

# The Drug development process

Step-1: Discovery and Development of active drug element or compound

Step 2: Preclinical Research

Step 3: Clinical Research

Step 4: FDA Drug Review

Step 5: FDA Post-Market Drug Safety Monitoring

# The Drug development process

- **Step 1: Discovery and Development**

- **Discovery**

- Researchers discover new drugs through:
- New insights into a disease process that allow researchers to design a product to stop or reverse the effects of the disease.
- Many tests of molecular compounds to find possible beneficial effects against any of a large number of diseases.
- New technologies, such as those that provide new ways to target medical products to specific sites within the body.



- At this stage in the process, thousands of compounds may be potential candidates for development as a medical treatment.
- After early testing, only a small number of compounds look promising and call for further study.
- **Development**
  - Once researchers identify a promising compound for development, they conduct experiments to gather information on:
    - ✓ How it is absorbed, distributed, metabolized, and excreted.
    - ✓ Its potential benefits and mechanisms of action.

- ✓ The best dosage.
- ✓ The best way to give the drug (Drug delivery methods).
- ✓ Side effects or adverse events that can often be referred to as toxicity.
- ✓ How it affects different groups of people (such as by gender, race, or ethnicity) differently.
- ✓ How it interacts with other drugs and treatments.

# Step 2: Preclinical Research

- Before testing a drug in people, researchers must find out whether it has the potential to cause serious harm, also called toxicity.
- The two types of preclinical research are:
  - In Vitro
  - In Vivo
- These studies must provide detailed information on dosing and toxicity levels.
- After preclinical testing, researchers review their findings and decide whether the drug should be tested in people.

# Step 3: Clinical Research

- “Clinical research” refers to studies, or trials, that are done in people.
- In this step researchers design the clinical study, different Clinical Research Phases(0-IV) and begin the Investigational New Drug Process (IND).
- Designing Clinical Trials
- Clinical Research Phase Studies
- The Investigational New Drug Process
- FDA IND Review Team
- Approval

# Designing Clinical Trials

- These trials follow a specific study plan, called a protocol, that is developed by the researcher or manufacturer.
- Before a clinical trial begins, researchers review prior information about the drug to develop research questions and objectives.
- Then, they decide:
  - Who qualifies to participate (selection criteria)
  - How many people will be part of the study
  - How long the study will last

# Contd-

- Whether there will be a control group and other ways to limit research bias.
- How the drug will be given to patients and at what dosage
- What assessments will be conducted, when, and what data will be collected.
- How the data will be reviewed and analyzed.

# The Investigational New Drug Process

- In the IND application, developers must include:
- Animal study data and toxicity (side effects that cause great harm) data.
- Manufacturing information.
- Clinical protocols (study plans) for studies to be conducted.
- Data from any prior human research.
- Information about the investigator.

## Step 4: FDA Drug Review

- If a drug developer has evidence from its early tests and preclinical and clinical research that a drug is safe and effective for its intended use, the company can file an application to market the drug.
- The FDA review team thoroughly examines all submitted data on the drug and makes a decision to approve or not to approve it.



- **New Drug Application**

- A New Drug Application (NDA) tells the full story of a drug.
- Its purpose is to demonstrate that a drug is safe and effective for its intended use in the population studied.
- A drug developer must include everything about a drug—from preclinical data to Phase 3 trial data—in an NDA.

- Developers must include reports on all studies, data, and analyses. Along with clinical results, developers must include:

- ✓ Proposed labeling
- ✓ Safety updates
- ✓ Drug abuse information
- ✓ Patent information
- ✓ Institutional review board compliance information
- ✓ Directions for use

- **FDA Review**

- Once FDA receives an NDA, the review team decides if it is complete.
- If it is not complete, the review team can refuse to file the NDA.
- If it is complete, the review team has 6 to 10 months to make a decision on whether to approve the drug.

# Step 5: FDA Post-Market Drug Safety Monitoring

- Even though clinical trials provide important information on a drug's efficacy and safety, it is impossible to have complete information about the safety of a drug at the time of approval.
- Despite the rigorous steps in the process of drug development, limitations exist.
- Therefore, the true picture of a product's safety actually evolves over the months and even years that make up a product's lifetime in the marketplace.

# Phases of Clinical trials

## Phase-0

- Phase 0 trials are the first clinical trials done among people.
- They aim to learn how a drug is processed in the body and how it affects the body.
- In these trials, a very small dose of a drug is given to about 10 to 15 people.

# Phase I

- Phase I trials aim to find the best dose of a new drug with the fewest side effects.
- Study Participants: 20 to 100 healthy volunteers or people with the disease/condition.
- Length of Study: Several months.
- **Purpose:** Safety and dosage.
- Approximately 70% of drugs move to the next phase.
- The Central Drugs Standard Control Organization (CDSCO) is the national regulatory body for Indian pharmaceuticals and medical devices.

# Phase II

- Phase II trials further assess safety as well as if a drug works.
- Study Participants: Up to several hundred people with the disease/condition.
- Length of Study: Several months to 2 years.
- **Purpose:** Efficacy and side effects.
- Approximately 33% of drugs move to the next phase

# Phase III

- Study Participants: 300 to 3,000 volunteers who have the disease or condition.
- Length of Study: 1 to 4 years.
- **Purpose:** Efficacy and monitoring of adverse reactions.
- Approximately 25-30% of drugs move to the next phase.



# Phase IV

- Study Participants: Several thousand volunteers who have the disease/condition.
- Purpose: Safety and efficacy.

## Approval

- The FDA review team has 30 days to review the original IND submission.
- The process protects volunteers who participate in clinical trials from unreasonable and significant risk in clinical trials.
-

## FDA responds to IND applications in one of two ways:

1. Approval to begin clinical trials.
  2. Clinical hold to delay or stop the investigation.
- FDA can place a clinical hold for specific reasons, including:
    - Participants are exposed to unreasonable or significant risk.
    - Investigators are not qualified.
    - Materials for the volunteer participants are misleading.
    - The IND application does not include enough information about the trial's risks.