

DRUG DISCOVERY AND PRECLINICAL EVALUATION OF DRUGS

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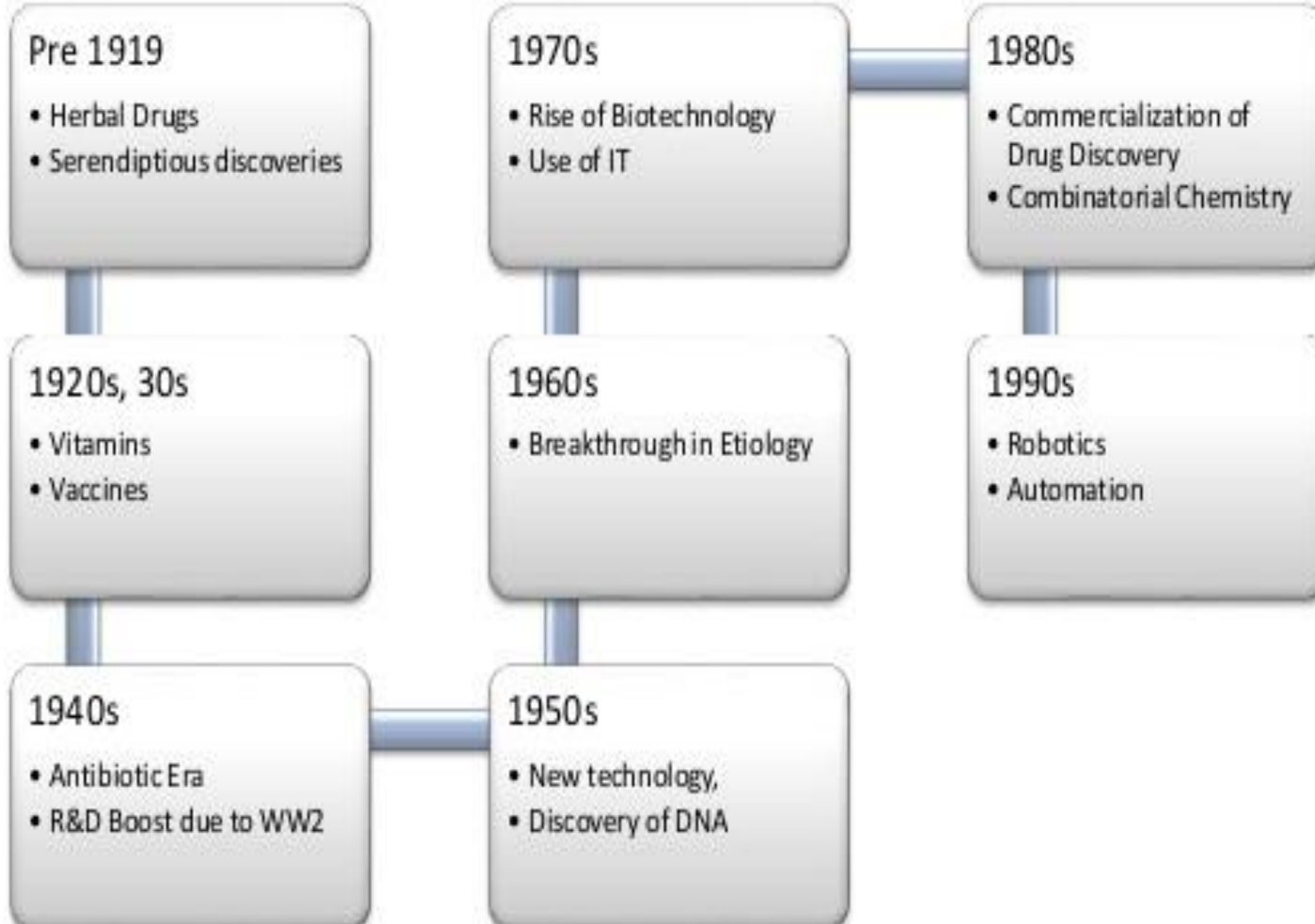
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DRUG DISCOVERY PROCESS

INTRODUCTION

- ▶ In the past most drugs have been discovered either by identifying the active ingredient from traditional remedies or by serendipitous discovery.
- ▶ But now we know diseases are controlled at molecular and physiological level.
- ▶ Also shape of an molecule at atomic level is well understood.
- ▶ Information of Human Genome

History of Drug Discovery :



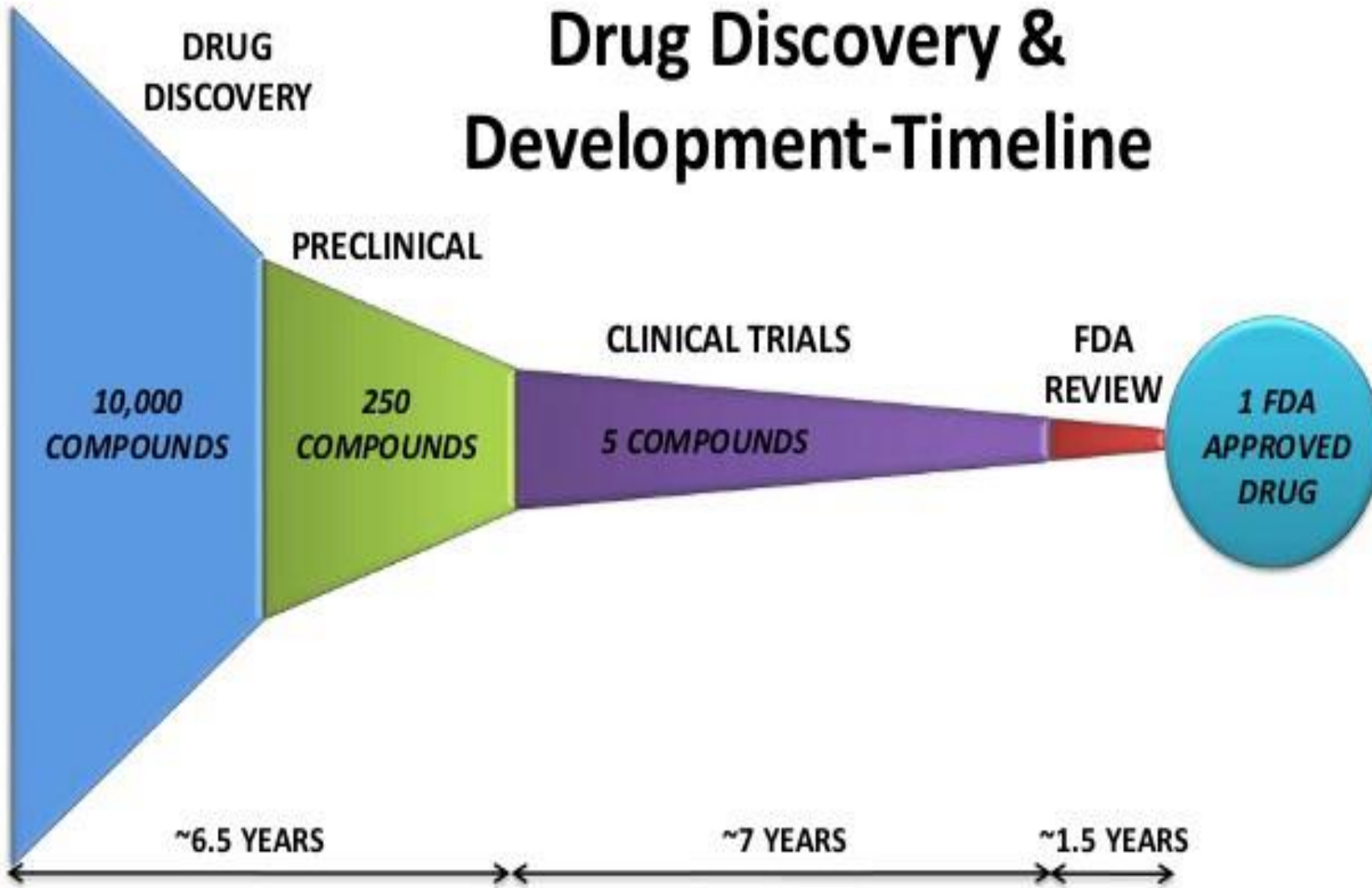
REGISTRATION

- ▶ The Ministry of health & Family Welfare and the Ministry of Chemicals & Fertilizers have major role in regulation of IPM.
- ▶ NDA must be submitted to DCGI
- ▶ Phase III study reported to CDL, Kolkata
- ▶ Package inserted approved by DCI
- ▶ Marketing approval from FDA

MARKET SCENARIO

- ▶ \$800 M spent to bring a new drug to market
- ▶ \$127 Billion spent on Pharma R&D in 2010
- ▶ Share of CROs in research operations is 27%
- ▶ World CRO market is 16.3 B (Indian share \$500 M)

Drug Discovery & Development-Timeline



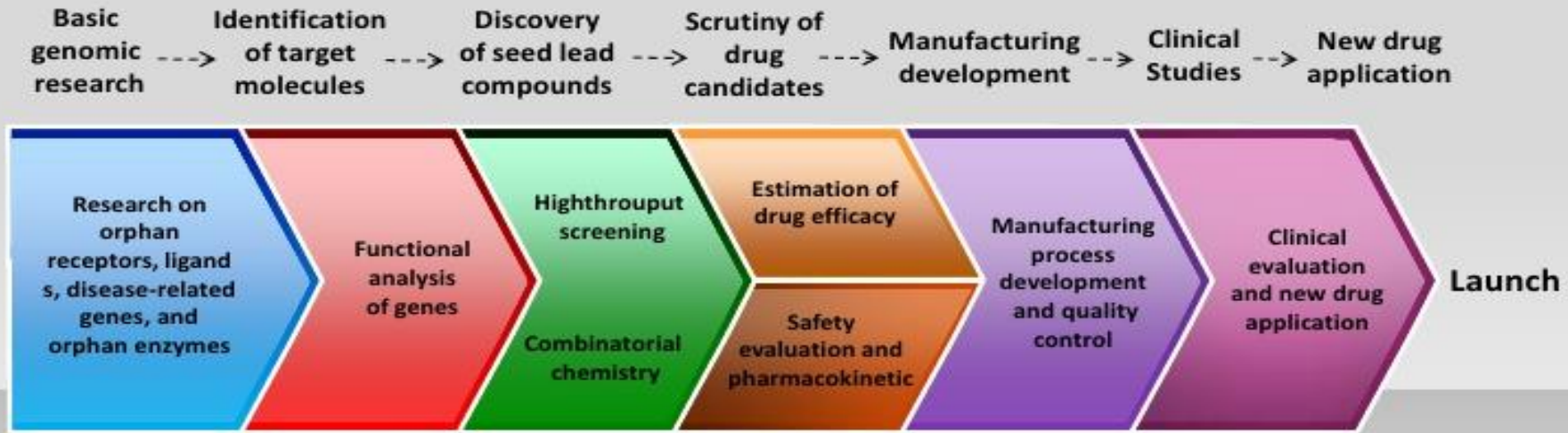
DRUG DISCOVERY METHODS

- ▶ Random Screening
- ▶ Molecular Manipulation
- ▶ Molecular Designing
- ▶ Drug Metabolites
- ▶ Serendipity

DRUG DISCOVERY PROCESS

- ▶ Target selection
- ▶ Lead discovery
- ▶ Medicinal chemistry
- ▶ In-vitro studies
- ▶ In-vivo studies
- ▶ Clinical trials and therapeutics

Drug Discovery Process – Style 3



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PRE-CLINICAL EVALUATION OF DRUGS

OBJECTIVE

- ▶ To determine the product's ultimate safety profile
- ▶ To decide whether it is reasonably safe to proceed with the human trials of the drug.

FOR DRUGS ACTING ON CENTRAL NERVOUS SYSTEM

1) MUSCLE CO-ORDINATION

- Grip strength in mice
- Rota-rod testing in mice

2) HYPNOTIC ACTIVITY

- Potentiation of Hexobarbitone-induced sleeping time
- Experimentally induced insomnia in rats

3) OTHERS : Anxiolytics, Antiepileptics etc.

FOR DRUGS ACTING ON PERIPHERAL NERVOUS SYSTEM

1) LOCAL ANAESTHETIC ACTIVITY

- Conduction anaesthesia in the sciatic nerve of rats and frogs
- Conduction anaesthesia on the mouse tail
- Corneal anaesthesia in rabbits

2) NEUROMUSCULAR BLOCKING ACTIVITY

- Rabbit head drop method
- Isolated phrenic nerve diaphragm preparation

FOR DRUGS ACTING ON THE CARDIOVASCULAR SYSTEM

1) ANTI-HYPERTENSIVE ACTIVITY

- Acute renal hypertension in rats
- Chronic renal hypertension in rats
- Salt-induced hypertension

2) ANTI-ARRHYTHMIC ACTIVITY

- Chemically-induced arrhythmias
- Electrically-induced arrhythmias
- Mechanically-induced arrhythmias

3) OTHERS : Cardiotonics, Cardiprotectives etc.

FOR DRUGS ACTING ON RESPIRATORY SYSTEM

1) BRONCHODILATOR AND ANTI-ASTHMATIC ACTIVITY

- Spasmolytic activity on guinea pigs
- Isolated tracheal chain and lung strip
- Bronchial perfusion of the isolated lung

2) ANTI-TUSSIVE AND EXPECTORANT ACTIVITY

- Citric acid inhalation-induced cough in guinea pigs
- Acute study of mucus secretion in rabbits

FOR ANALGESICS, ANTI-INFLAMMATORY AND ANTI-PYRETIC DRUGS

1) INFLAMMATORY ACTIONS

- Carrageenin-induced paw oedema
- UV erythema in guinea pigs

2) PYRETIC ACTIVITIES

- Antipyretic testing in rats
- Antipyretic testing in rabbits

3) ANALGESIC ACTIVITIES

- Chemically induced nociception
- Writhing tests
- Formalin tests in rats
- Electrical stimulation methods
- Flinch-jump test in mice
- Tail-flick test
- Tail-immersion test

STATISTICAL METHODS

- ▶ Collection of data and calculation of means
- ▶ Experimental designs
- ▶ Errors
- ▶ Variables
- ▶ Analysis of variance
- ▶ Tests of hypothesis
- ▶ Statistical tests : T-test, F-test etc.

THANK YOU !!