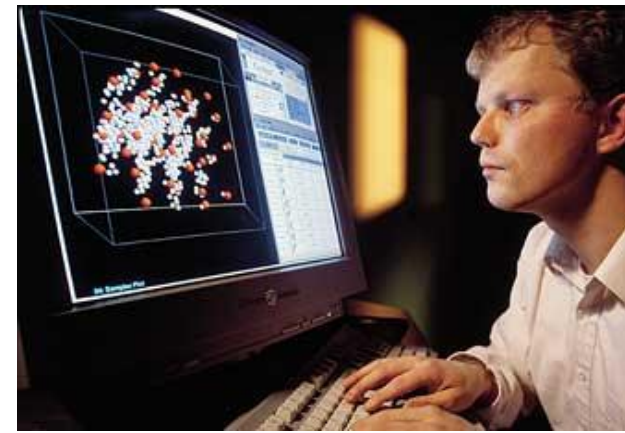


INTRODUCTION TO PHARMACEUTICAL CHEMISTRY

Prof. Dr. Esin AKI-YALÇIN

Department of Pharmaceutical
Chemistry

2021

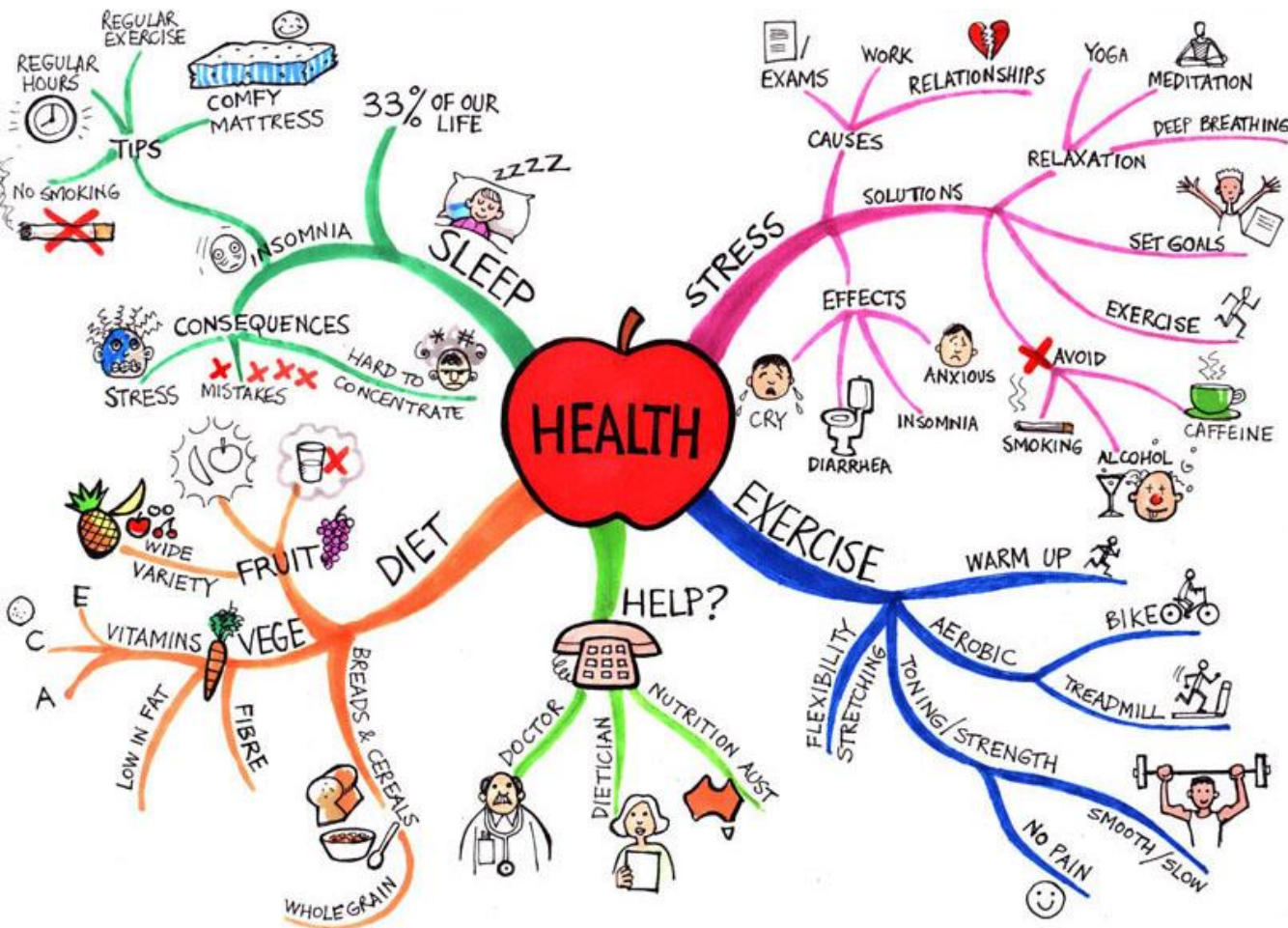


DRUGS ARE USED FOR:

Protect human health

Improve the quality of life

Create a healthy social life



DRUG THERAPY:

**Diagnosis,
Treatment
Prevention of Diseases**



Drugs

Their chemical structure and properties have been determined.

Obtained from chemical synthesis or natural sources.

Used in in humans and animals.

Drug Nomenclature

Code number

Generally, it is given by the laboratory, researcher or research group that discover or test the drug first.

It is used in patent application.

Ex: MK801

Drug Nomenclature

Chemical name

Chemical naming that explains the structure of the chemical compound fully.

(nomenclature according to IUPAC)



2-(acetyloxy)benzoic acid



IUPAC International Union of Pure and Applied Chemistry

Drug Nomenclature

Generic name



2-(acetyloxy)benzoic acid

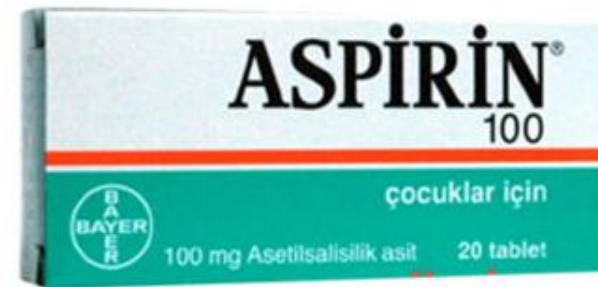
Acetylsalicylic acid +

Name given to a drug by official institutions to ensure standardization in national or international communications (It is coined by national official institutions in each country and WHO in the world.)

Drug Nomenclature

Trade (brand) name

It is a special name given by the manufacturer company to its product.

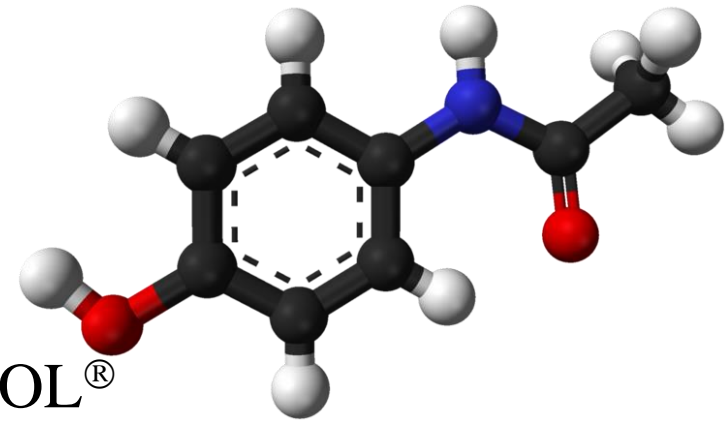


Generic name

Acetaminophen +

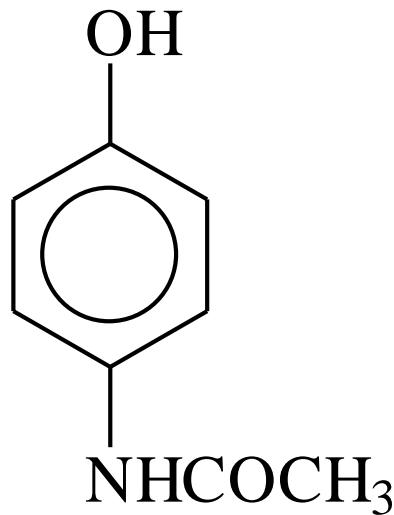
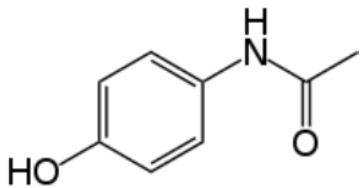
Trade name

PARASETAMOL[®]
ARBITUS[®]PANADOL[®]PAROL[®]
PIROFEN Supp[®]



Chemical name

p-acetylamino-phenol



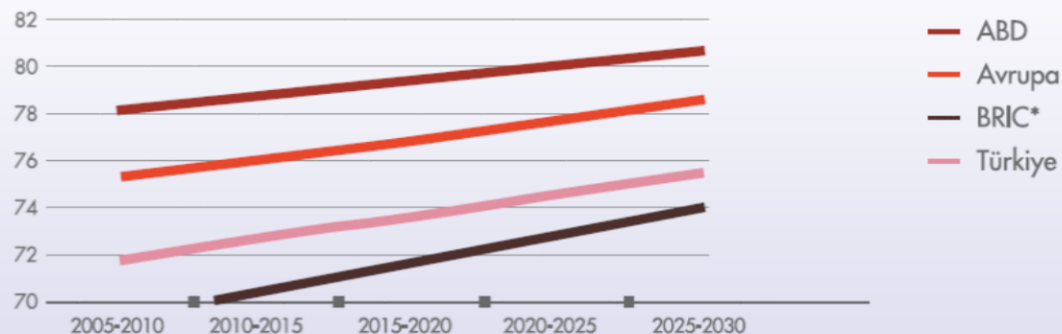
There are more than 5,000 drug as active substance.

There are more than 20,000 pharmaceutical products.

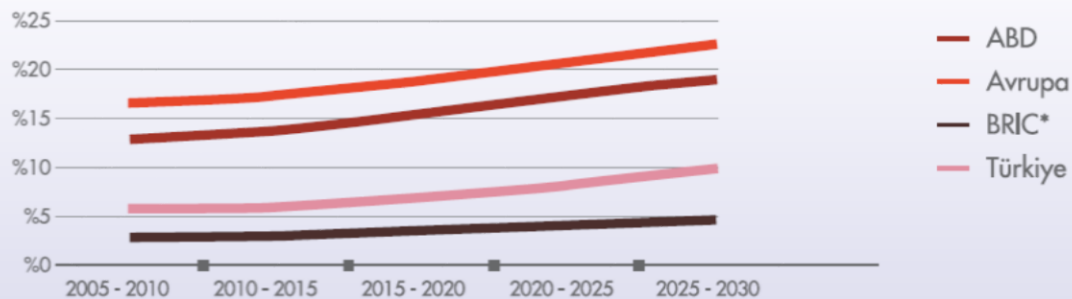
IMPORTANCE OF THE PHARMACEUTICAL SECTOR

The Importance of New Drugs and Treatments in Human Life

Ortalama Yaşam Süresi (Yıl)



65 Yaş Üzeri Nüfusun Toplam Nüfusa Oranı (%)



* BRIC: Brezilya, Rusya, Hindistan, Çin

Source: AİFD (Turkey Drug Sector Vision 2013 Report), August 2012.

Life expectancy increases.

World population is growing and aging.

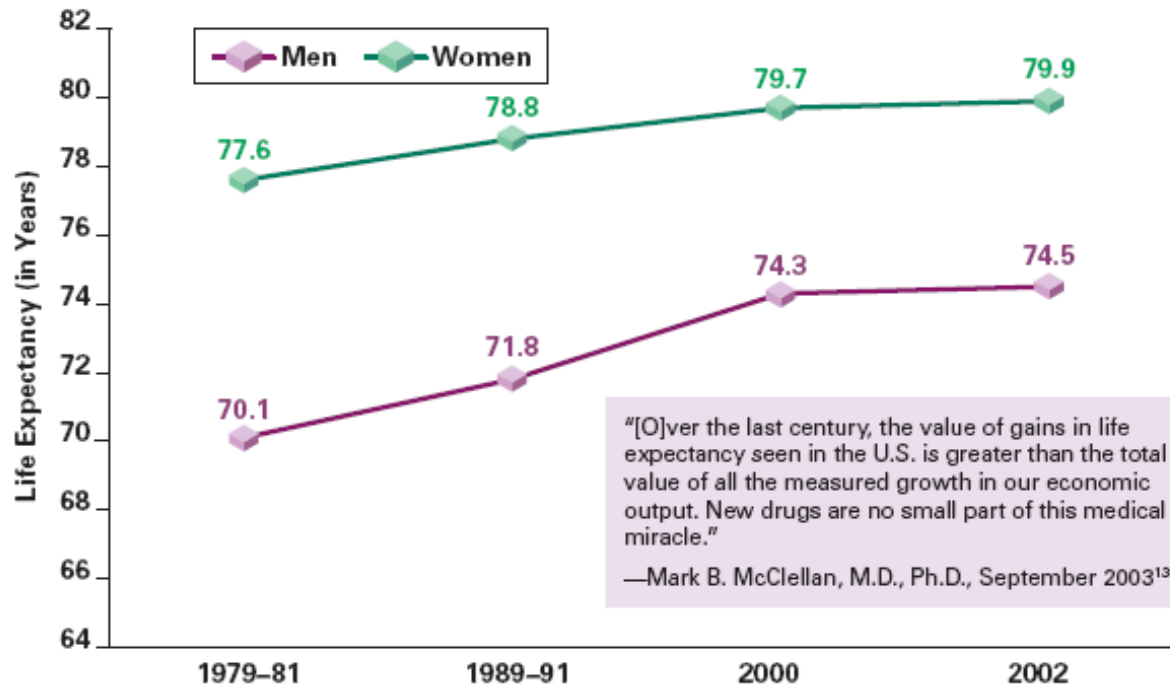
Exposure to chronic diseases is prolonged.

Urbanization and mobility are increasing.

Global warming

All These Changes Increase the Need for Health Care Services.

Prolongation of Life Expectancy in USA



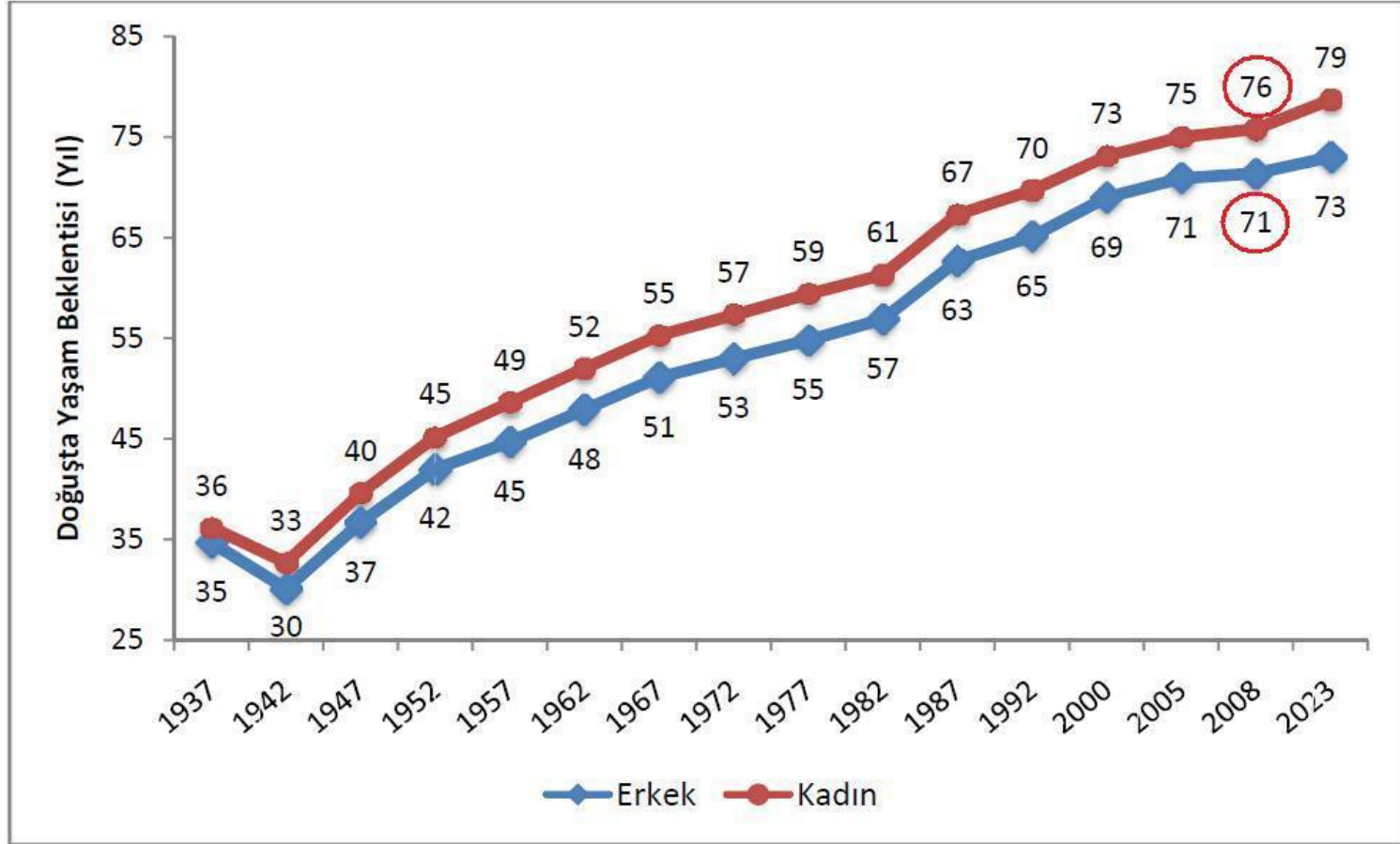
Data source: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics¹⁴

2010



81.5

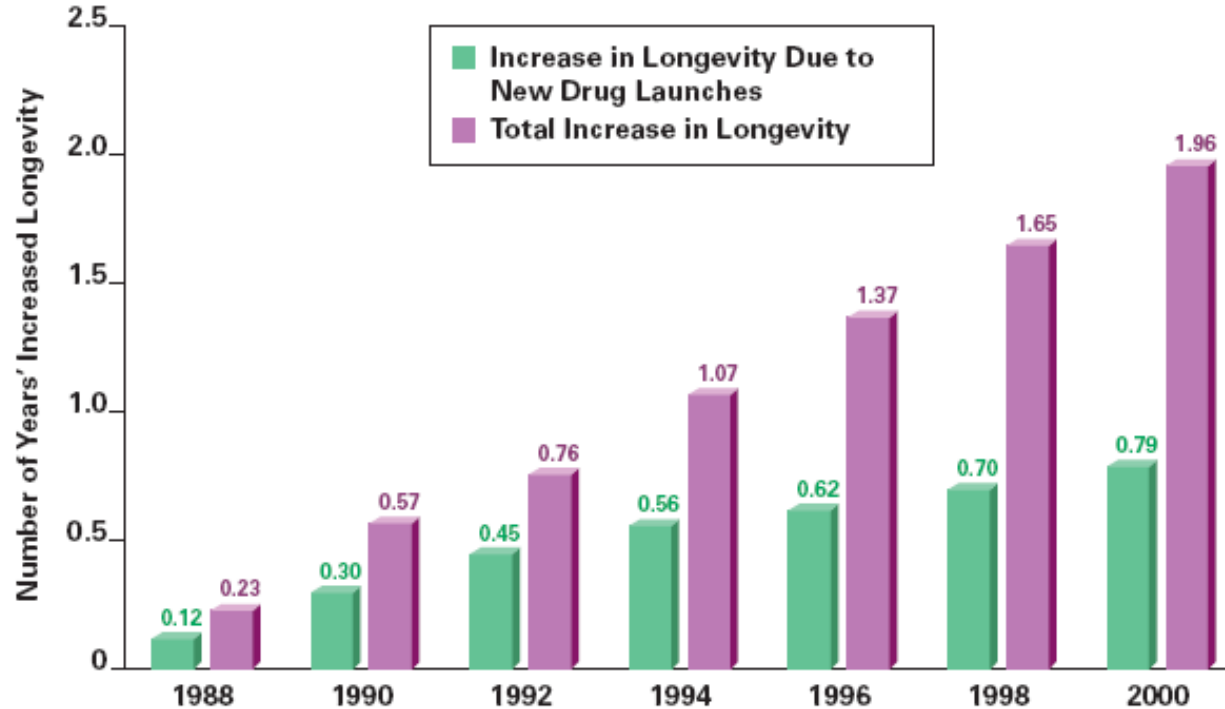
Life expectancy in Turkey



Kaynak: Fişek ve Shorter, 1968; TÜİK, 1995, 2009, 2010e; Ergöçmen, Hancıoğlu ve Ünalın, 1995

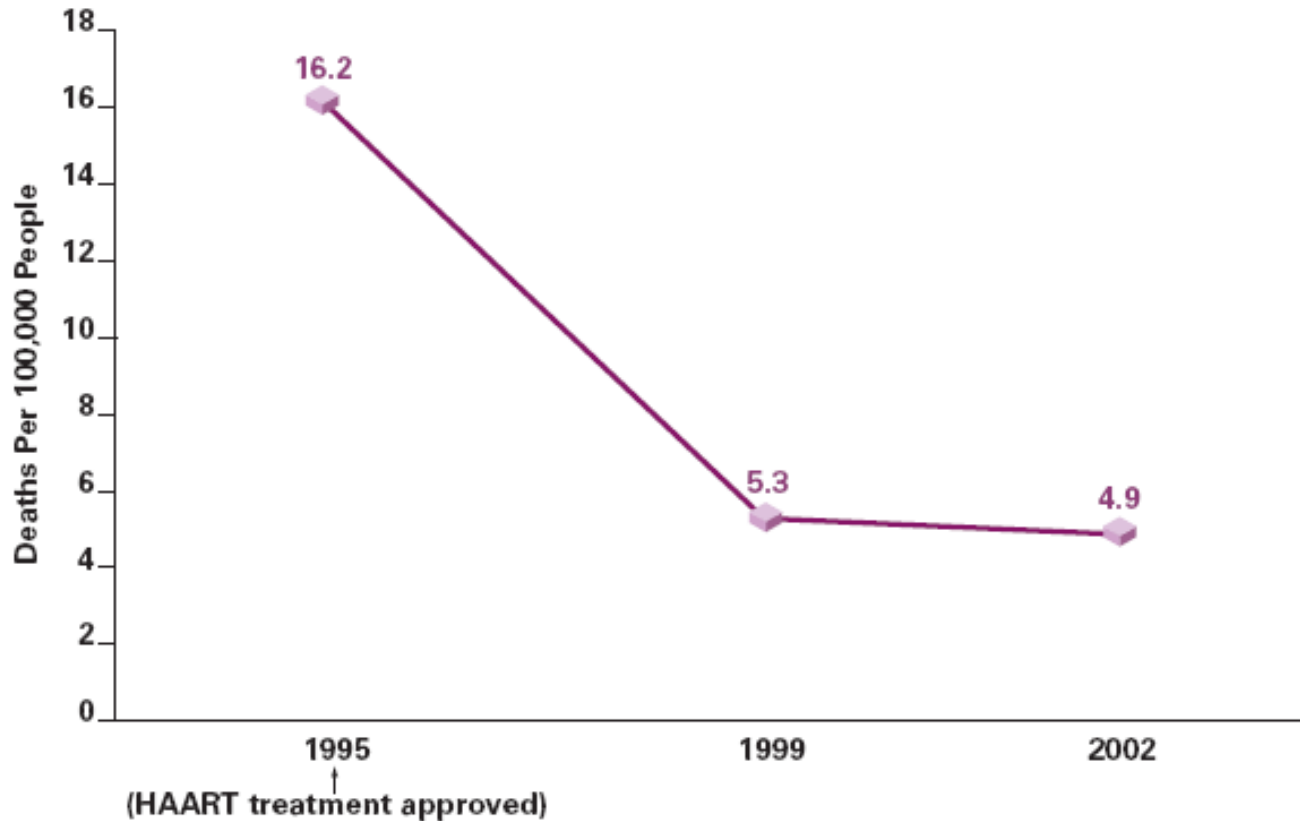
New Drugs Increase Life Expectancy

- Prolonging life is 40% due to new drugs



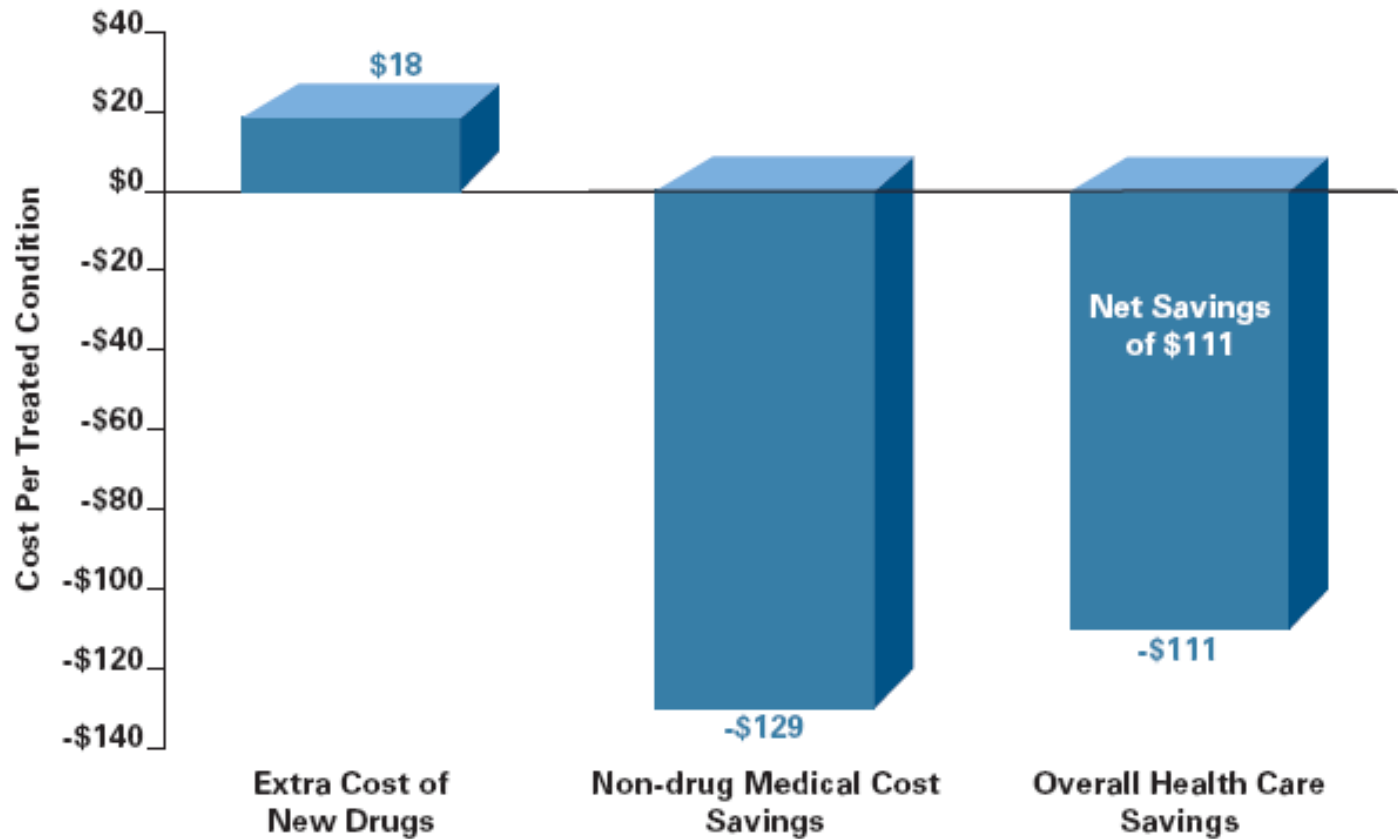
Data source: Lichtenberg⁸

AIDS mortality rate declines in USA



Data source: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics¹⁴

Using new drugs saves \$ 111 per case



Scope and Purpose of Pharmaceutical Chemistry

:

It covers all studies related to drug active substances.

Scope and Purpose of Pharmaceutical Chemistry:

I. Design and Development of Drugs

- Structure-Activity Relationships
- Quantitative Structure-Activity Relationships
- Molecular Modeling Methods

II. Synthesis and Analysis of Drugs

- Determination and Application of Synthesis Methods
- Elucidation of the Synthesized Drugs
- Determination of Physical, Chemical and Physicochemical

Properties of the Drugs

III. Evaluate the results of biological activities of the drugs through *in vitro* and *in vivo* Experiments.

Scope and Purpose of Pharmaceutical Chemistry:

IV. Determination of the metabolites.

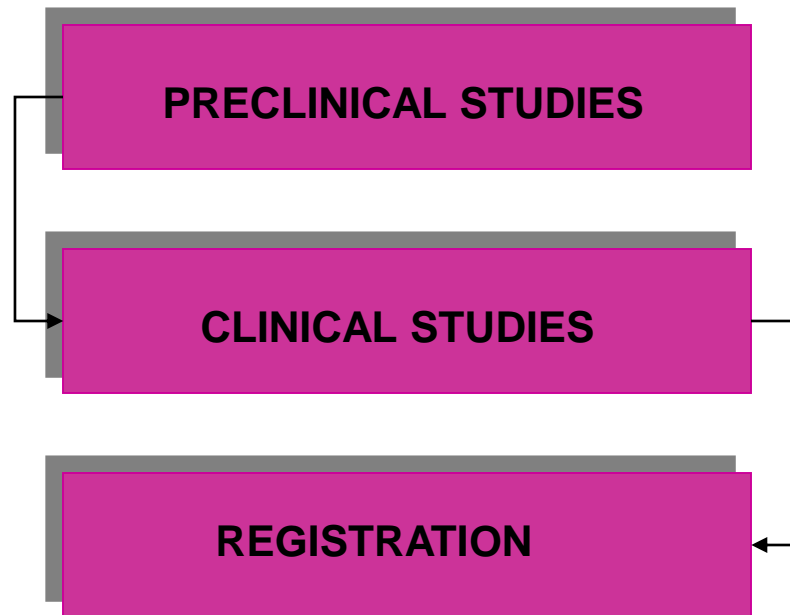
V. Determination of Quantity and Quality (Purity Control)

VI. Determine the stability (whether it degrades depending on storage conditions and time)

Ideal Drug:

- 1. More active (more broad-spectrum)**
- 2. Less toxic**
- 3. Less side effect (selectively active)**

STUDIES CONDUCTED TO TAKE AN ORIGINAL DRUG TO THE MARKET



STUDIES CONDUCTED TO TAKE AN ORIGINAL DRUG TO THE MARKET

1. Preclinical Process:

- Designing drugs
- Synthesis of the drugs
- Determination of biological activity of the drugs
- ADMET studies (Absorption-Distribution-Metabolism-Excretion-Toxicity)

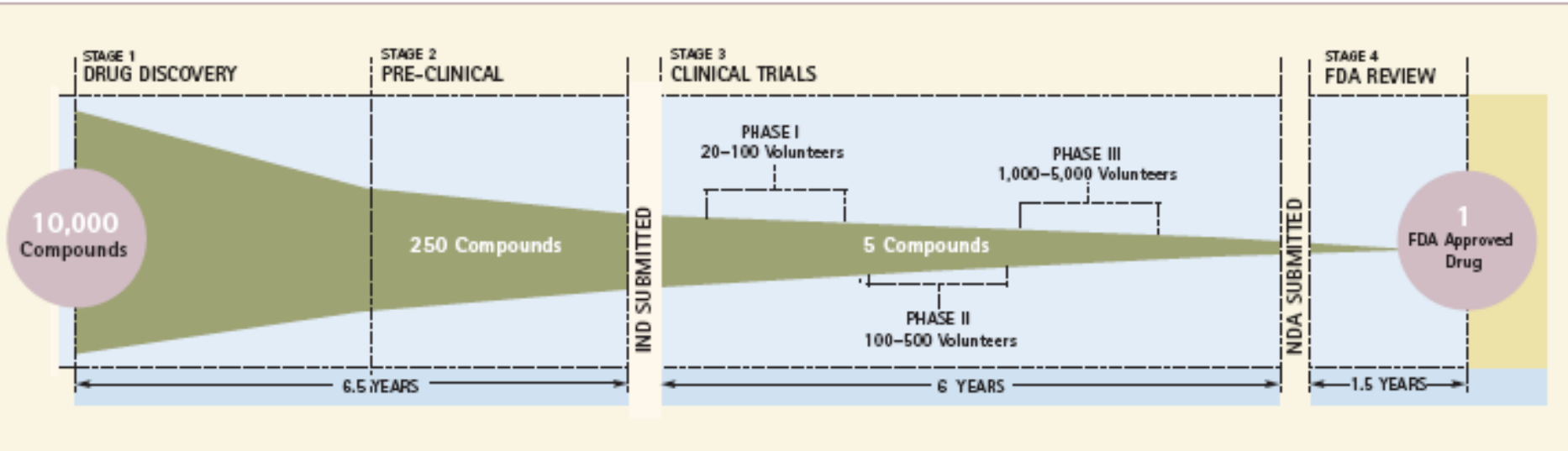
2. Clinical Process:

Execution of the clinical studies related to the drugs (Phase I-III).

3. Registration:

Approval and manufacturing the drugs

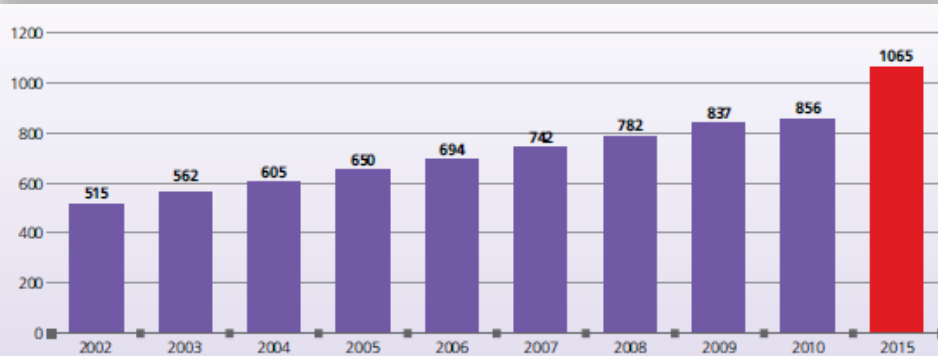
Yeni Bir İlaç Piyasaya Verilmesi



Source: www.innovation.org

IMPORTANCE OF THE DRUG SECTOR

The world pharmaceutical industry exceeded \$ 1 trillion by growing around 5% annually.



In terms of size, Turkish pharmaceutical industry ranks 16th.

Source: AİFD (Turkey Drug Sector Vision 2013 Report), August 2012.

The Size of Global Pharmaceutical Sector (Billion \$), 2011



Bringing a new drug to the market:

1989

One from 10,000 compounds

12-16 years

1999

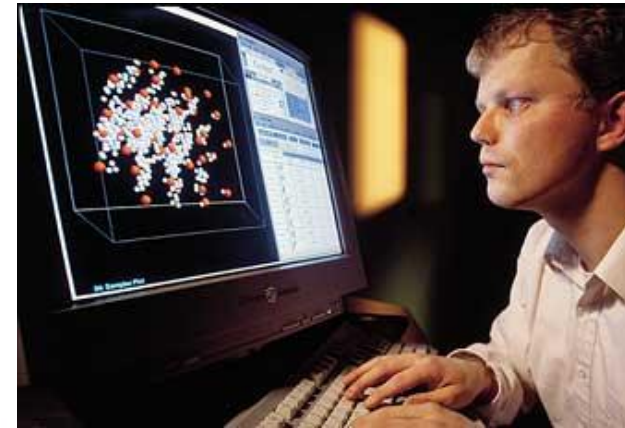
One from 5,000 compounds

12-16 years

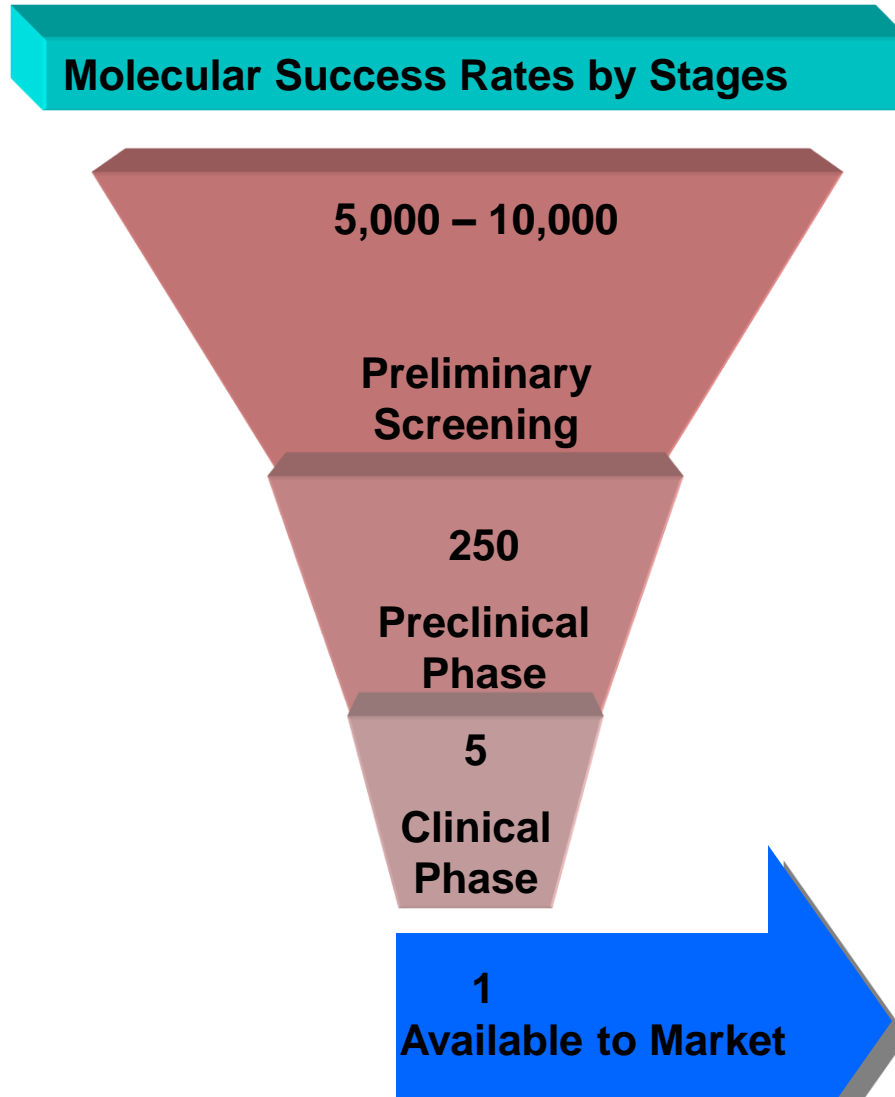
2000-

8-10 years

Cost 500 million \$

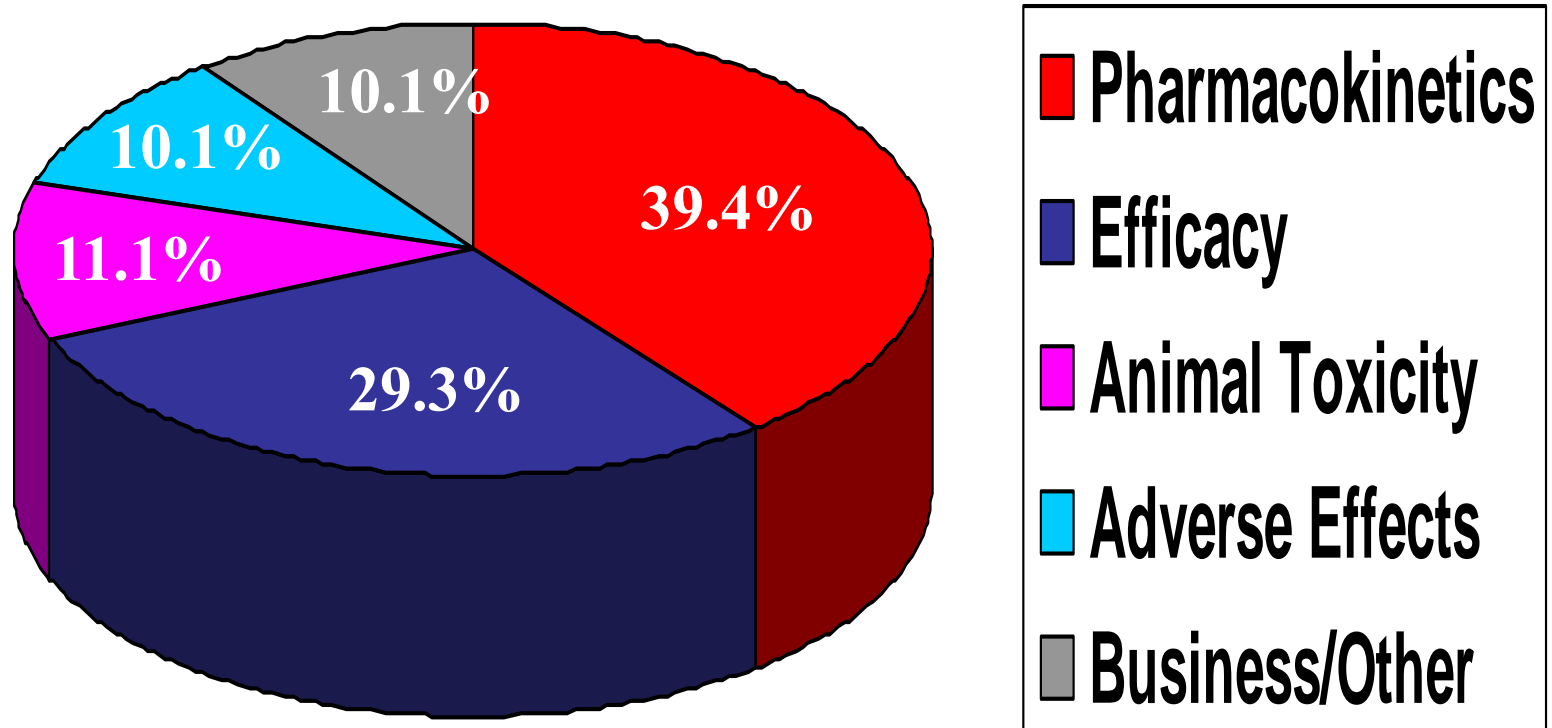


RATE OF DRUGS TO REACH THE MARKET (CLASSICAL DEFINITION)

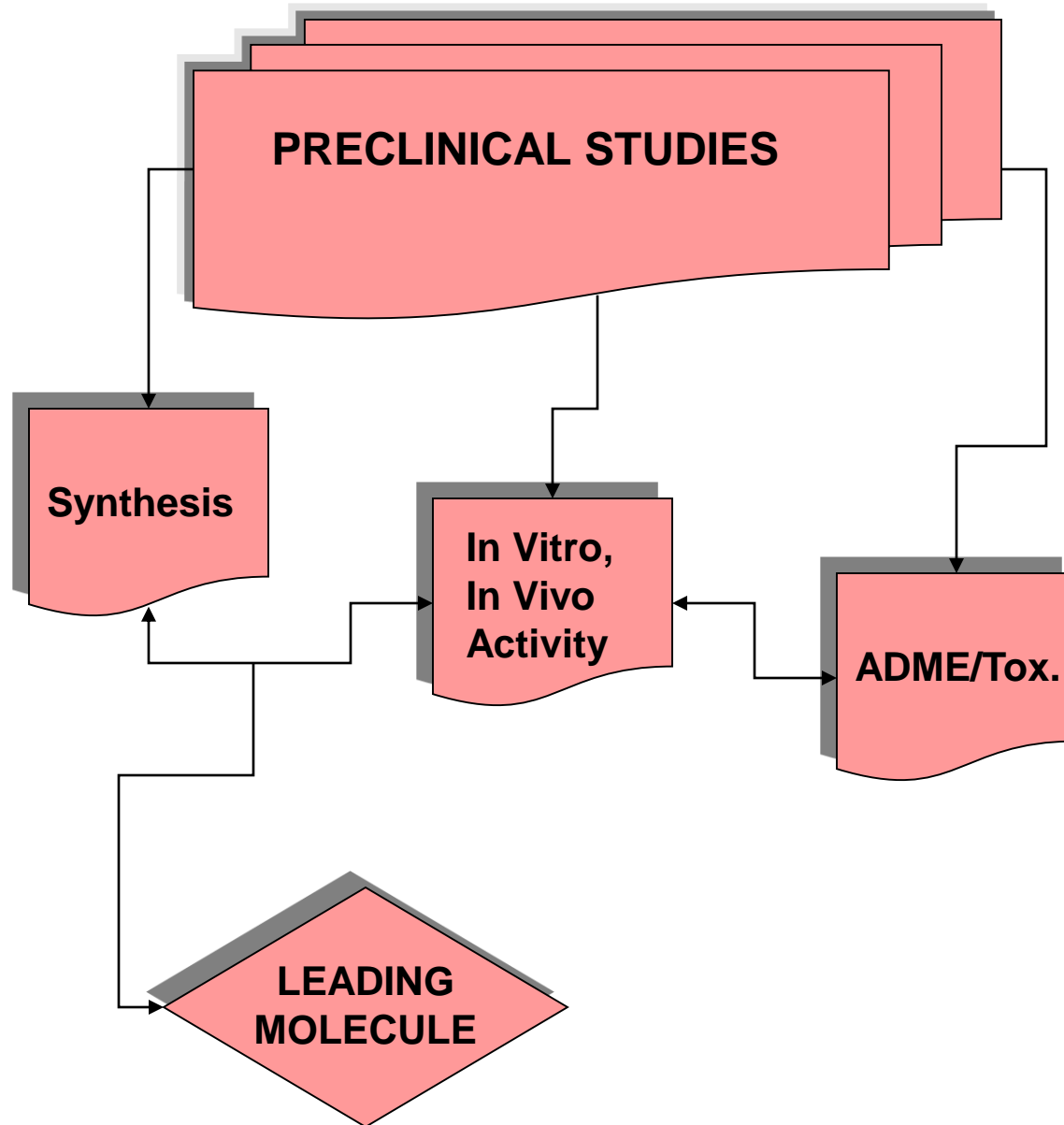


- FDA approved 28 drugs in 2005.
- Only 3 out of 10 drugs have achieved or exceeded the calculated profit rate.

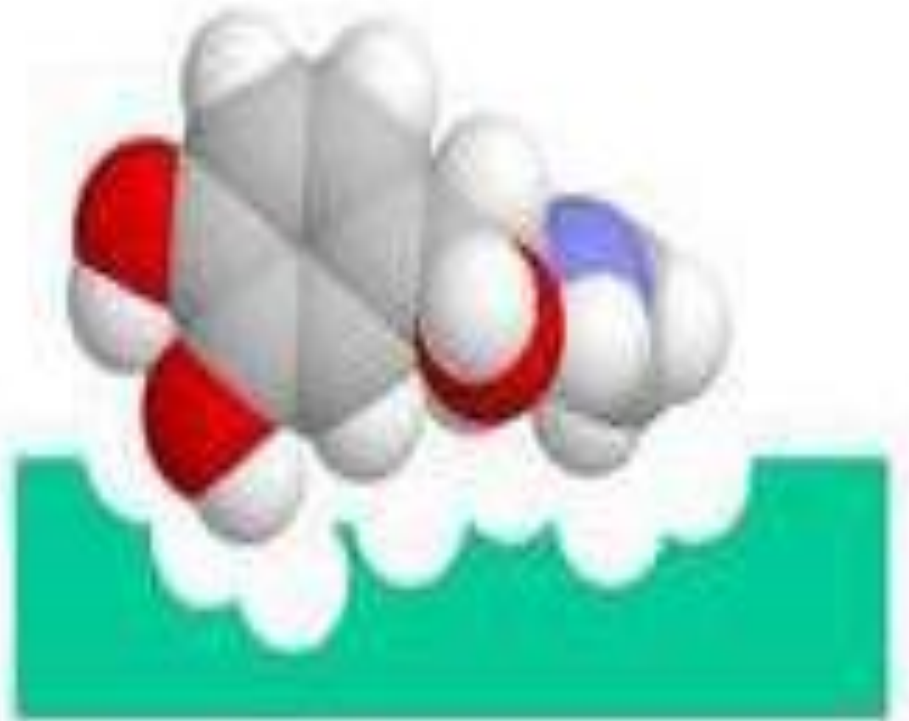
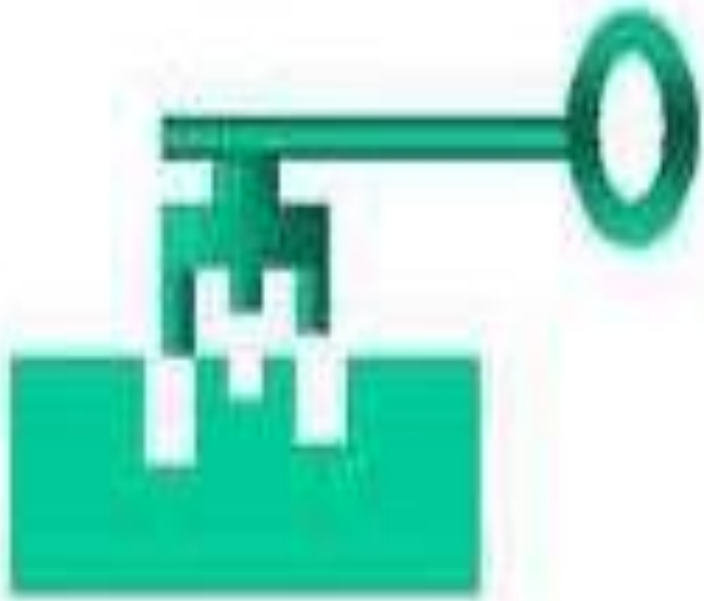
Causes for the failure of drugs according to a study conducted in UK in 1964-85.



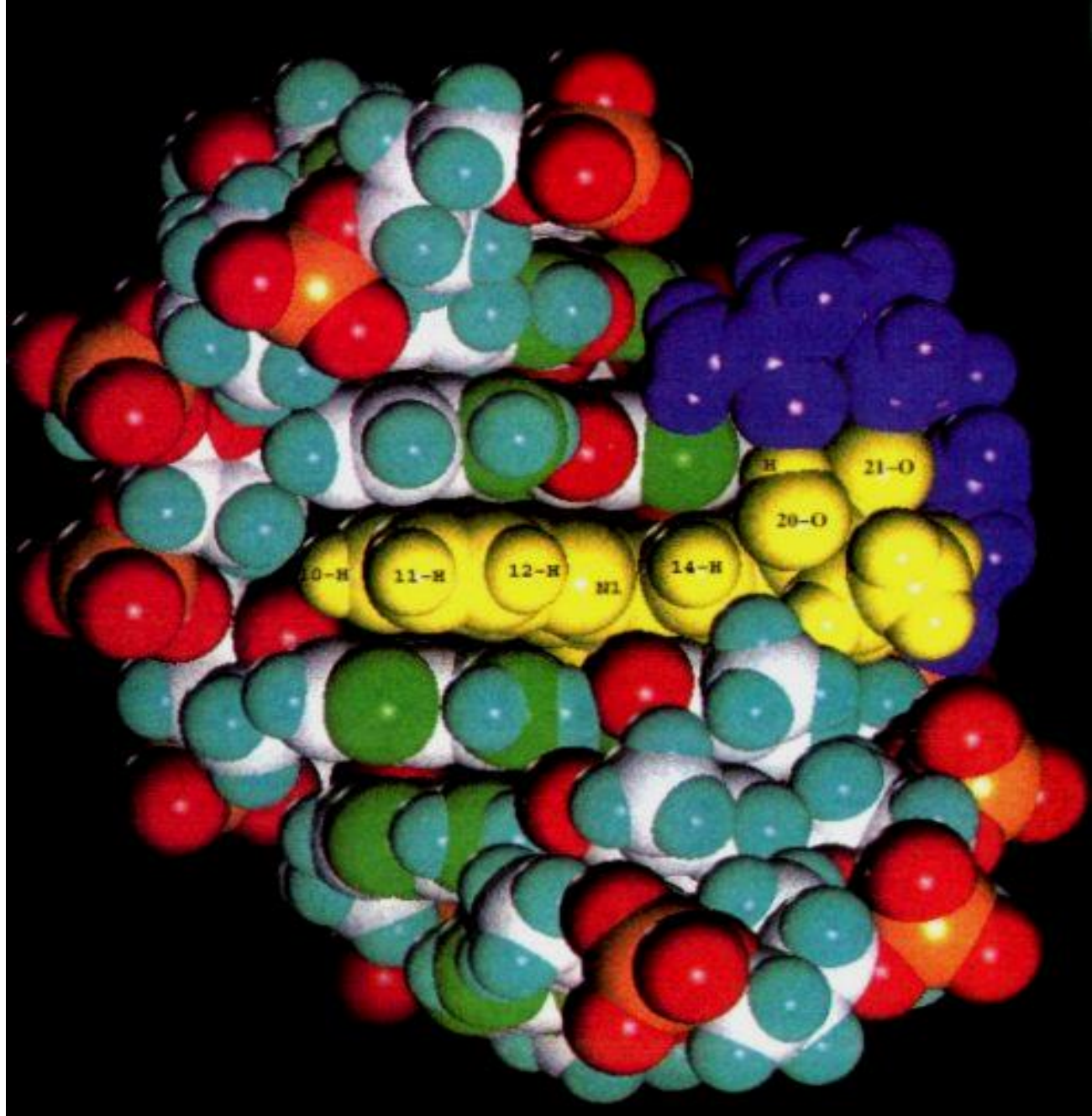
- Prentis, et al., *Br. J. Clin. Pharmac.* **1988**, *25*, 387-396



Key-Lock Model



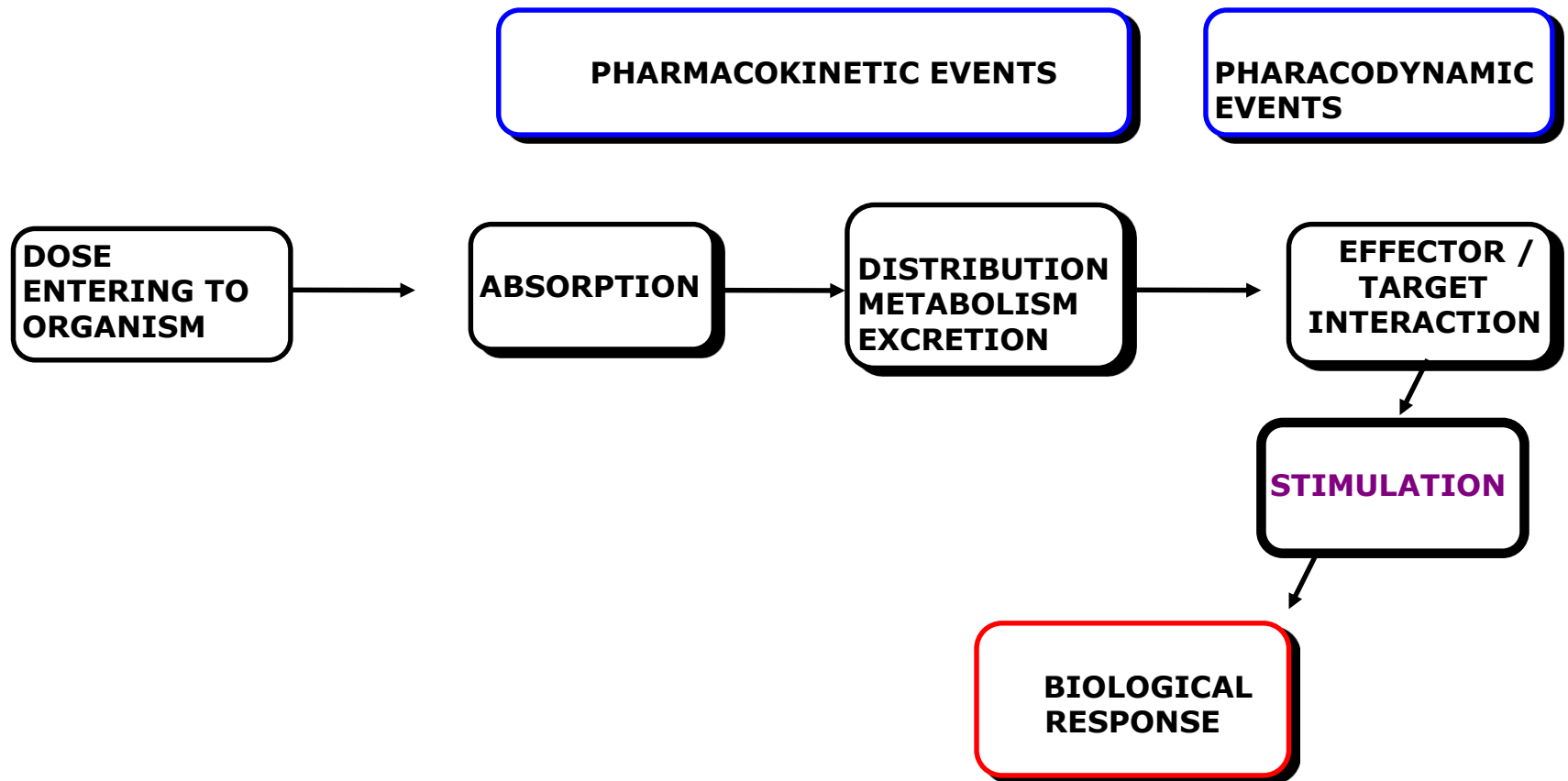
Key-Lock Model

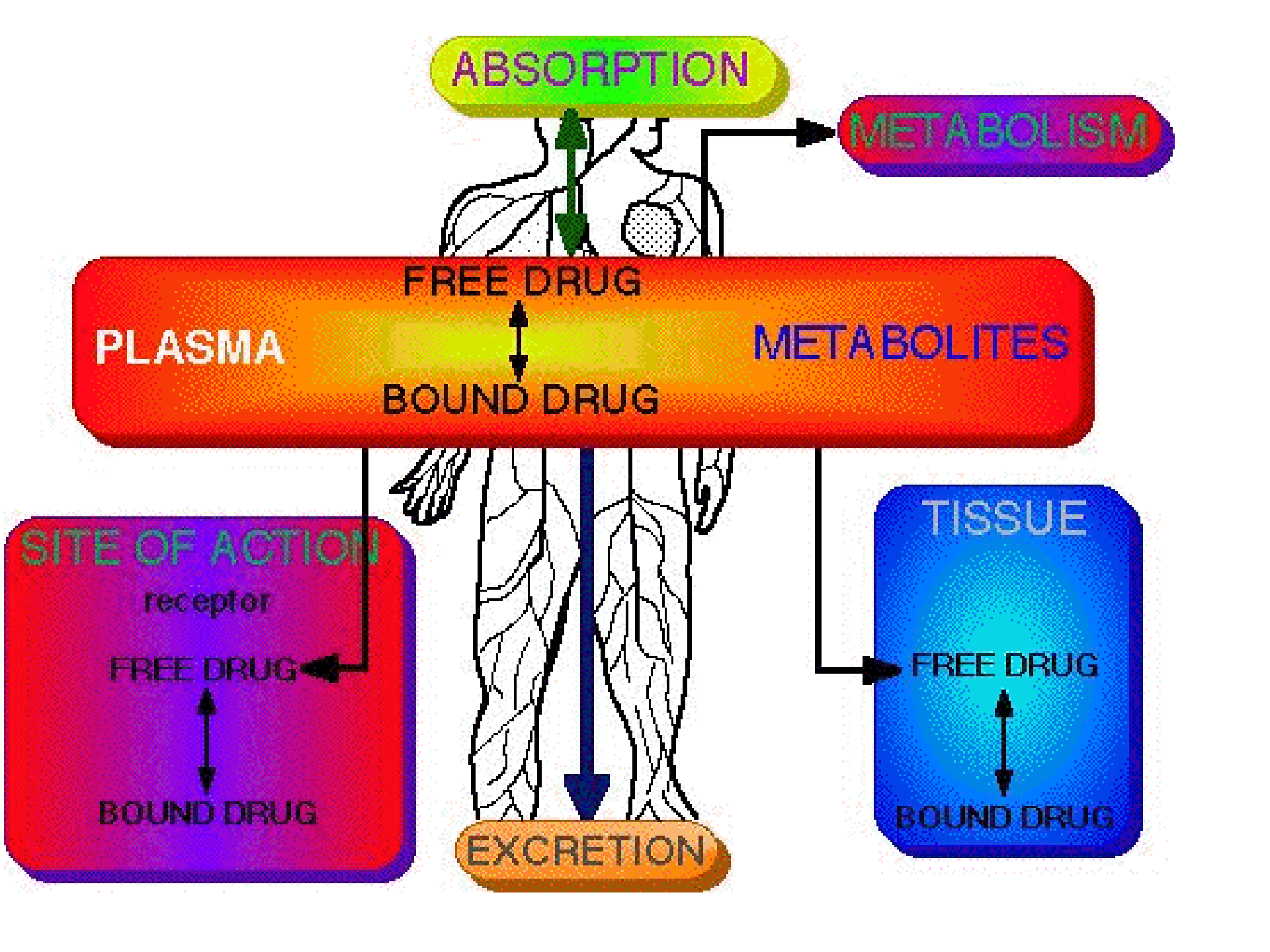




PHARMACOKINETIC- PHARACODYNAMIC EVENTS

PHARMACOKINETIC-PHARMACODYNAMIC EVENTS





1. Pharmacokinetic Phase (ADME)

- **A**bsorption
- **D**istribution
- **M**etabolism (Biotransformation)
- **E**limination (Excretion)

*** Physicochemical properties**

1. Pharmacokinetic Phase (Absorption)

Ionization:

Henderson- Hasselbach equation :

For acids :

$$pK_a - pH = \text{Log} [\text{nonionized drug conc.}] / [\text{ionized drug conc.}]$$

For bases :

$$pH - pK_a = \text{Log} [(\text{nonionized drug conc.}) / [\text{ionized drug conc.}]]$$

Weak acidic compounds are absorbed more from the stomach environment, weak basic compounds are absorbed more from the intestines.

The drugs should be nonionized to be absorbed.

Acidic drugs are nonionic in acid medium (stomach)

1. Pharmacokinetic Phase (Absorption)

Drug concentration : If the concentration of a drug at the place of application is high, its absorption is usually rapid.

Pharmacokinetic property of a drug : The pharmacological properties of a certain number of drugs affect the rate of absorption.

Example. vasoconstrictor drugs reduce their absorption by reducing the blood flow passing through the place of application.

2. Pharmacodynamic Phase

- **Pharmacological Activities**
- **Therapeutic Activities**
- **Toxic Effects**

Pharmacodynamic interactions:

- **Effector-Target Interaction**

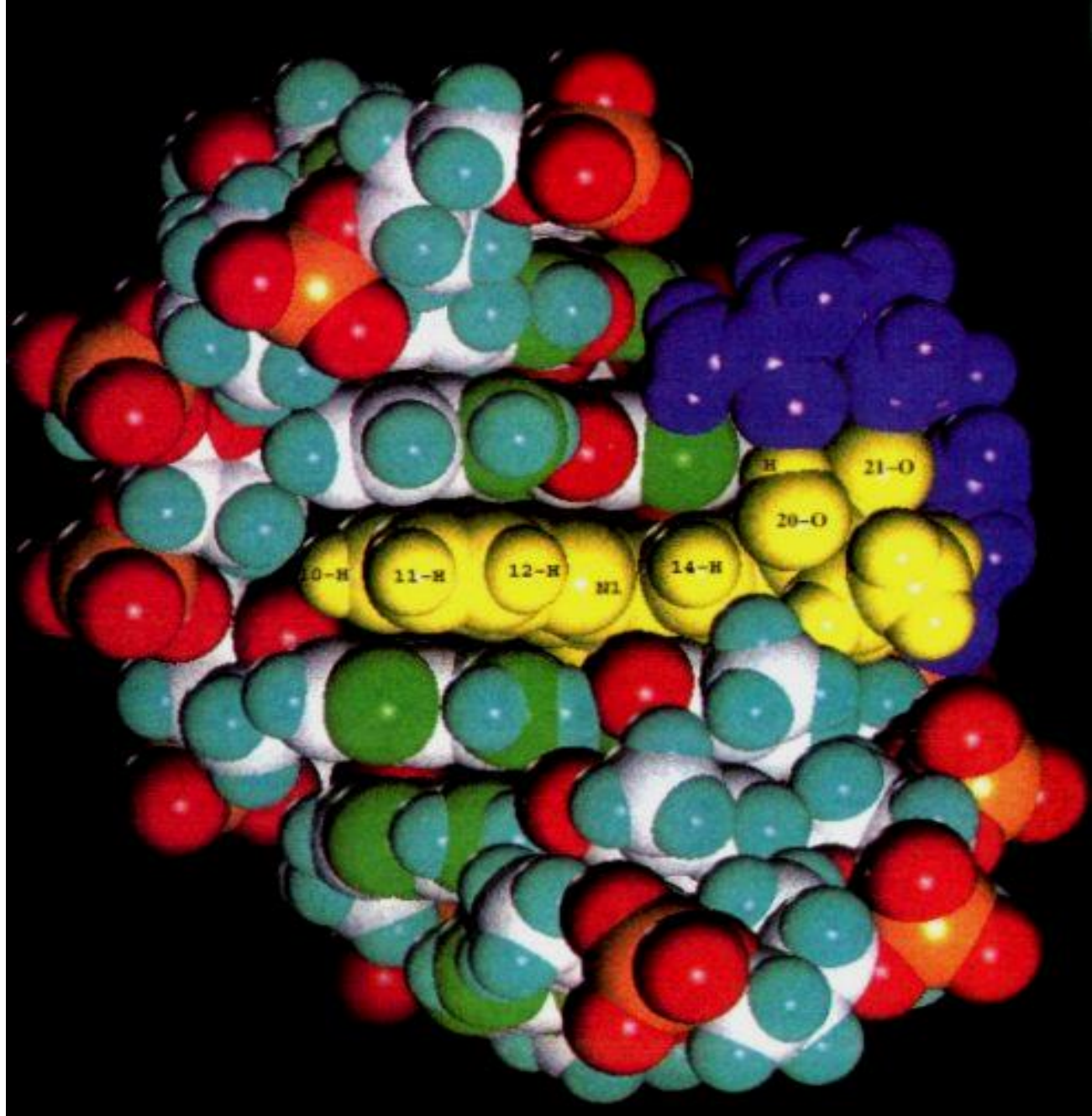
Effector: Natural endogenous substances in the organism.

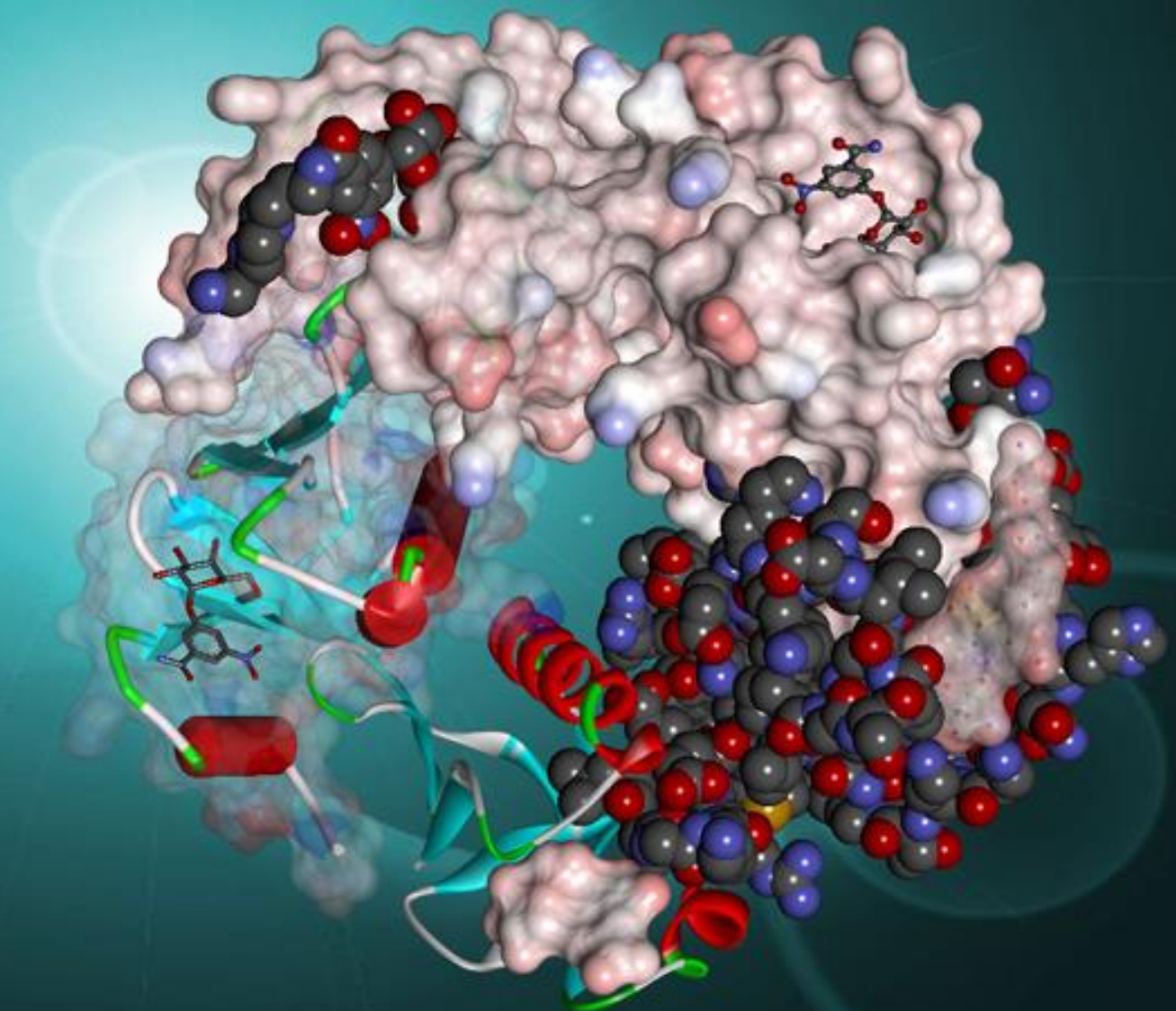
Ex: Ligands.

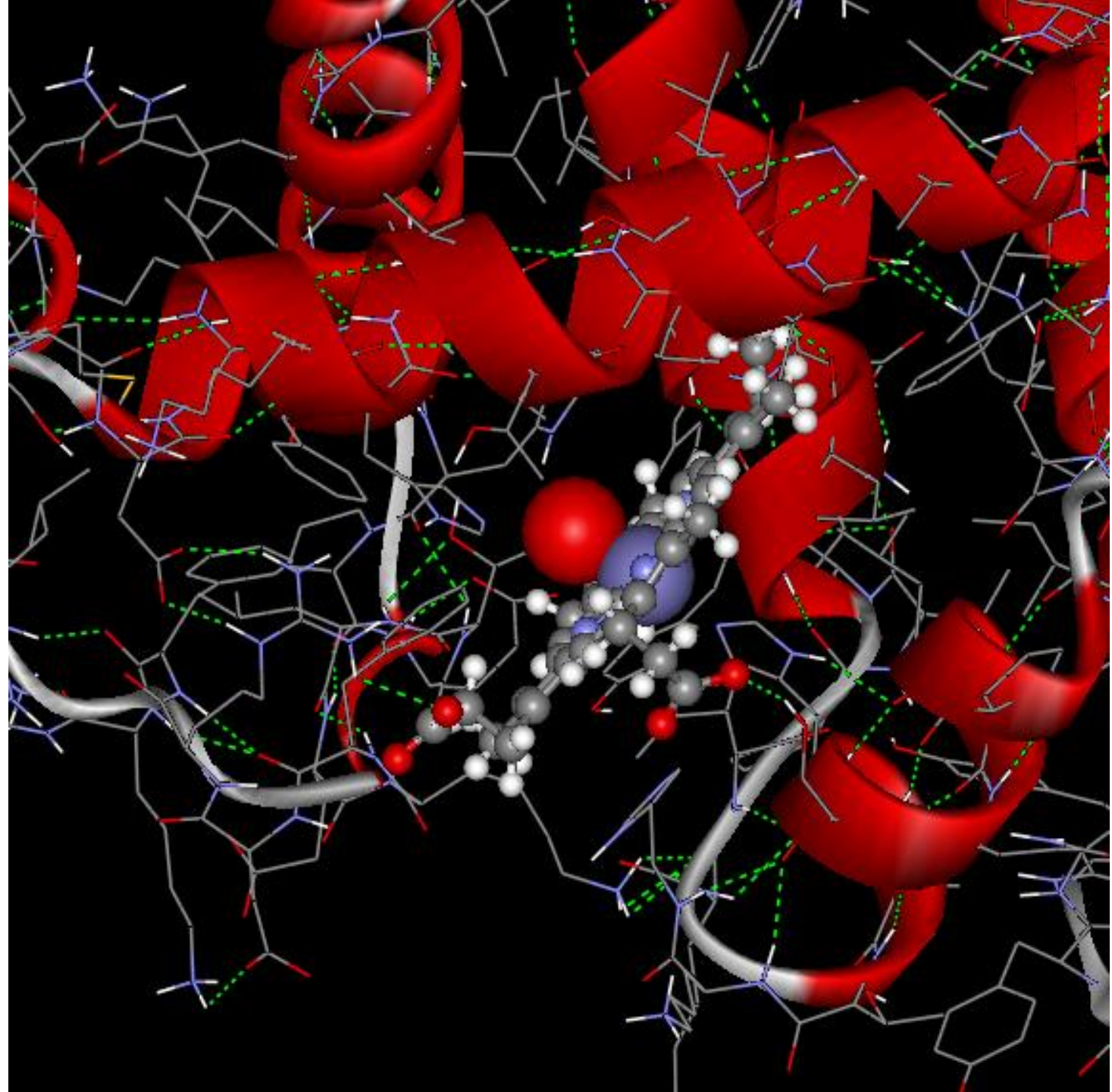
Drug Active Ingredients

Target: Biopolymers and macromolecules in the organism that ligands produce a response by impacting them.

Key-Lock Model









RECEPTOR, DEFINITION:

- It is defined as a protein located on the surface of the cell membrane, or in the cytoplasm and / or nucleus that can generate a specific biological response as a result of a series of events.



Receptor  Target