STIKES NOTOKUSUMO
YOGYAKARTA

KONTRAK PERKULIAHAN

PENGEMBANGAN PRODUK

TAHUN AJARAN 2024/2025

SISTEM PERKULIAHAN

1

TIM PENGAMPU

apt. Trifonia Rosa Kurniasih, M.Biotech (KOORDINATOR)
apt. Indrawati Kurnia Setyani., M.Pharm.Sci

2

JUMLAH PERTEMUAN

14 PERTEMUAN TEORI
UJIAN TENGAH SEMESTER
UJIAN AKHIR SEMESTER

3

JADWAL PERTEMUAN

Rabu, 10.00 – 11.40 WIB

KONTRAK PERKULIAHAN

Kehadiran

- HADIR TEPAT WAKTU, SESUAI JADWAL
- TOLERANSI KETERLAMBATAN 15 MENIT

Jumlah pertemuan

- JUMLAH KEHADIRAN MINIMAL **75%**
- BERHAK REMIDIAL (JIKA DIBUKA)
- JIKA KURANG, MAKA NILAI AKHIR TIDAK AKAN DIKELUARKAN DAN NILAI DEFAULT **E (TIDAK LULUS)**
  - TIDAK HADIR :
    - SAKIT (DENGAN SURAT KETERANGAN DOKTER)
    - IZIN : TUGAS KAMPUS
    - KEDUKAAN

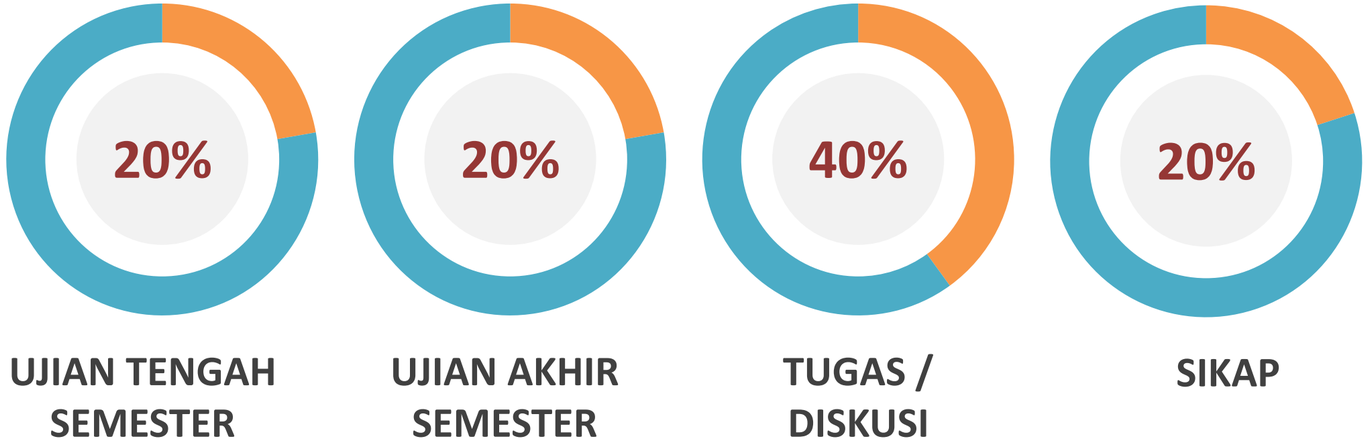
Sistem pembelajaran

- SELAMA KULIAH, MEDIA PEMBELAJARAN YANG DIGUNAKAN AKAN MENYESUAIKAN

Pembagian materi

- 7 TOPIK KULIAH : IBU ROSA
- 7 TOPIK KULIAH : IBU INDRAWATI

BOBOT NILAI



RENCANA EVALUASI			
BASIS EVALUASI	KOMPONEN EVALUASI	BOBOT (%)	DESKRIPSI
Aktivitas Partisipatif	Kehadiran	10	Kehadiran mahasiswa selama mengikuti perkuliahan (16 pertemuan) melalui SIAKAD
	Observasi aktivitas mahasiswa	10	Aktivitas partisipatif mahasiswa dalam diskusi di kelas dengan menjawab dan mengajukan pertanyaan
Hasil Proyek	Case-Based Learning	40	a.Penyelesaian kasus b.Pemaparan dan diskusi c.Pembuatan rancangan kemasan dan leaflet produk
Kognitif / Pengetahuan	a. UTS	20	Ujian tengah semester dilaksanakan secara bersama sesuai jadwal
	a. UAS	20	Ujian akhir semester dilaksanakan secara bersama sesuai jadwal
Jumlah Nilai		100	

MATERI KULIAH

MATERI UTS

1. Arti pengembangan produk obat
2. Pengembangan Obat
3. Preformulasi obat
4. Uji praklinis obat
5. Pengujian stabilitas obat dan kegunaannya
6. Studi kasus pengembangan obat
7. Studi kasus pengembangan obat

MATERI UAS

1. CPOB
2. Optimalisasi formulasi obat baru
3. Validasi analisis kuantitatif obat baru
4. Uji klinis untuk obat baru dan tahapannya
5. Teknologi pengemasan produk obat
6. Penetapan harga produk dan analisis keuangan
7. Registrasi/pendaftaran obat

REFERENSI

1. July Manurung. 2005. Pemastian Mutu Obat. Penerbit EGC: Jakarta.
2. Yogeshwar Bachhav. 2019. Innovative Dosage Forms : Design and Development at Early Stage. Wiley : Germany.
3. Yihong, Qiu, Yisheng, Chen, Geoff. G.Z, Zhang. 2009. Developing Solid Oral Dosage Forms : Pharmaceuitcal Theory and Practice. Elsevier : UK.
4. Bhavishya Mittal. 2017. How to Develop Robust Solid Oral Dosage Forms : From Conception to Post-Approval. Academic Press: London.
5. Curtis L. Meinert. 2013. Clinical Trials Handbook : Design and Conduct. Wiley: New Jersey.
6. International Conferenceon on Harmonisazion of Technical Requirements for Registation of Pharmaceutical for Human Use (ICH), Q8-Pharmaceutical Developtment. 2007
7. International Conference on Harmonisazion of Technical Requirements for Registation of Pharmaceutical for Human Use (ICH), Q9- Quality Risk Management. 2009.

STIKES NOTOKUSUMO YOGYAKARTA

PENGEMBANGAN PRODUK

Pertemuan 1

apt. Trifonia Rosa K., M.Biotech

Topik Bahasan

Definisi pengembangan produk

Penemuan vs pengembangan

Perkembangan sediaan Farmasi di indonesia

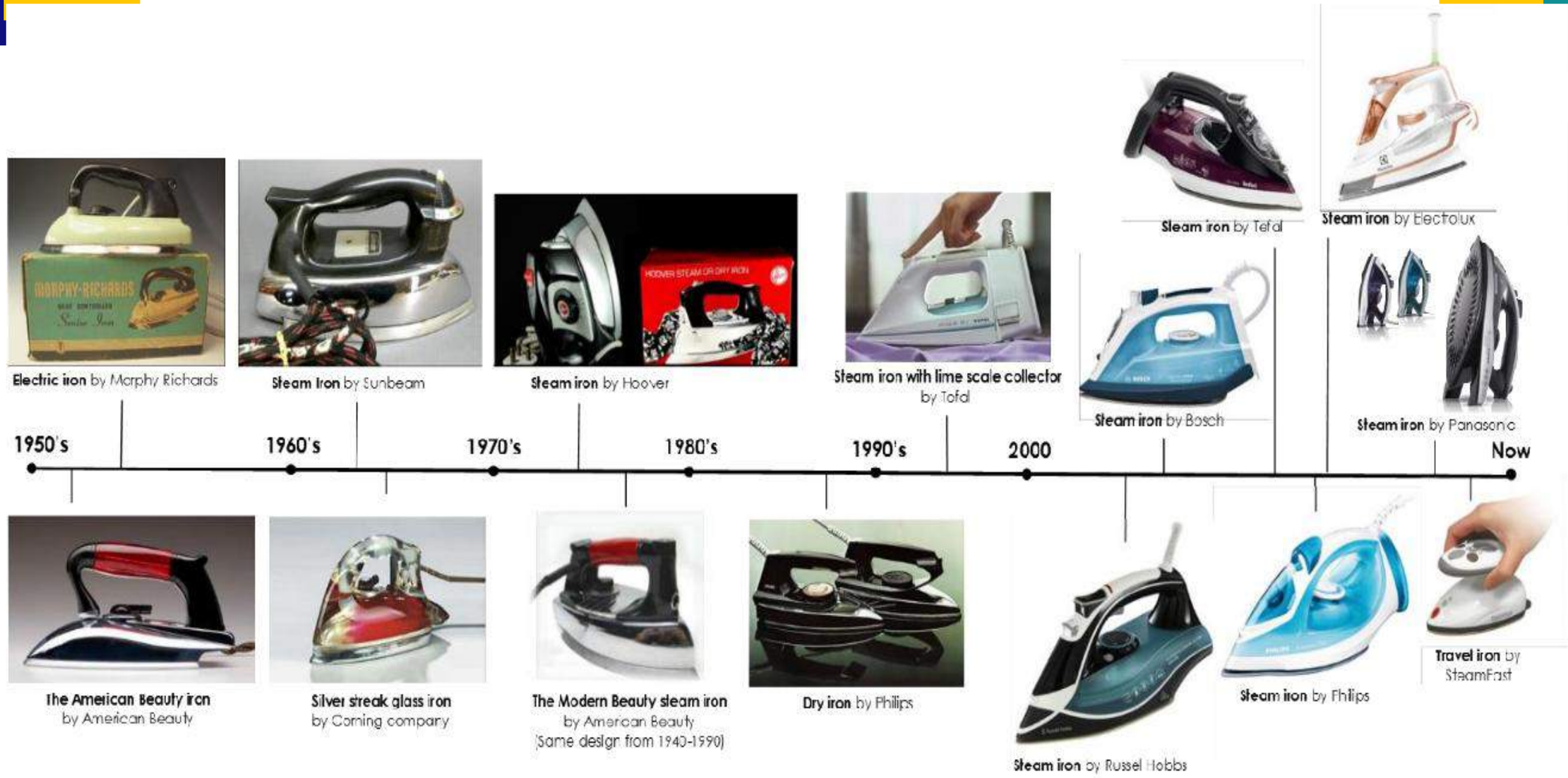
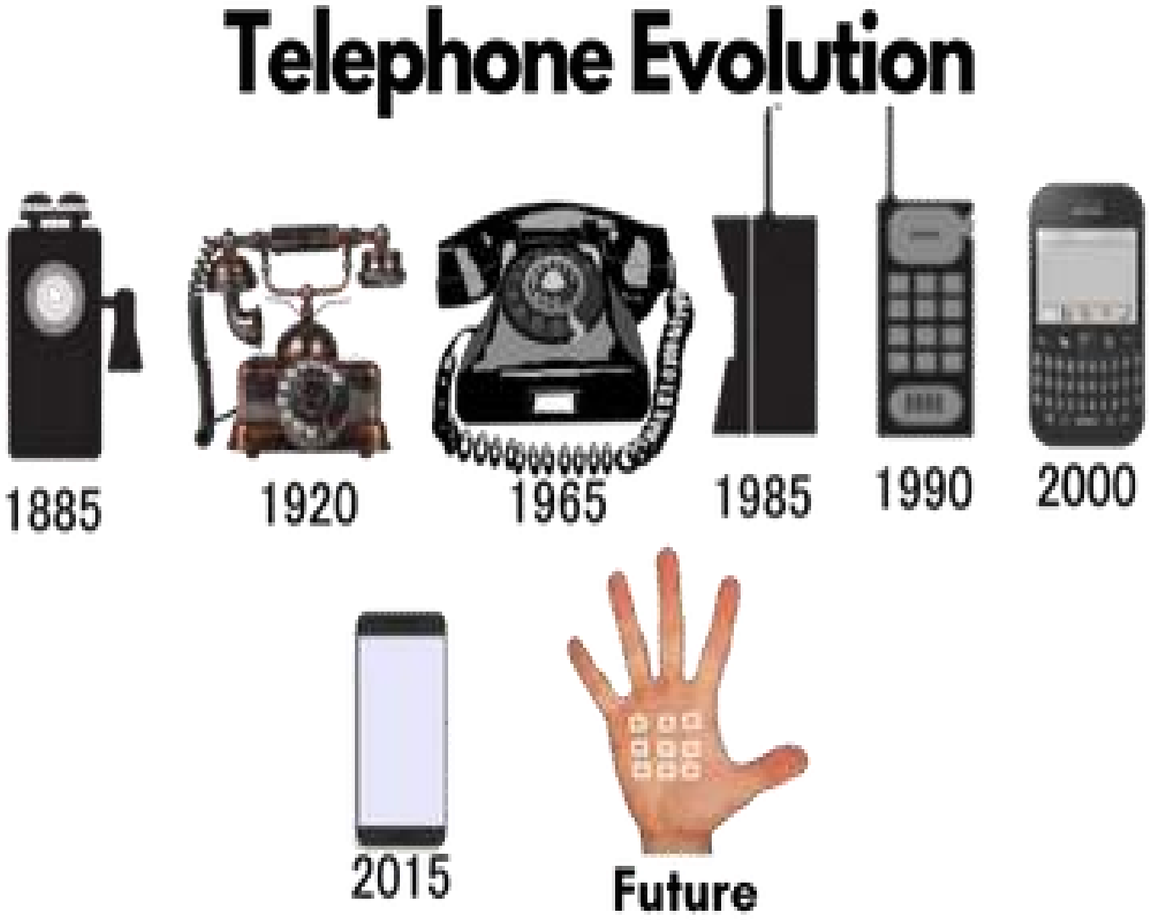
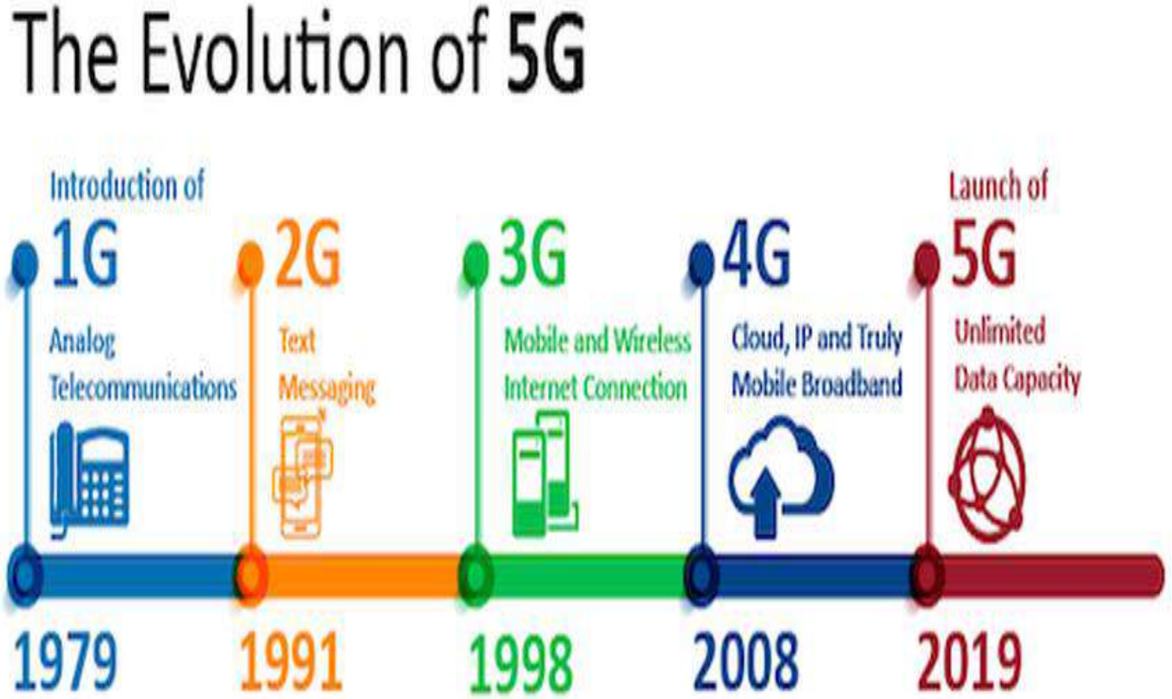


Figure 6. Design development of irons from 1950's to present time.


Telephone Evolution
1885
1920
1965
1985
1990
2000
2015
Future


The Evolution of 5G
Introduction of
1G
Analog
Telecommunications
2G
Text
Messaging
3G
Mobile and Wireless
Internet Connection
4G
Cloud, IP and Truly
Mobile Broadband
Launch of
5G
Unlimited
Data Capacity
1979
1991
1998
2008
2019

1984
Macintosh

1986
Macintosh Plus

1987
Macintosh II

1987
Macintosh SE

1989
Macintosh IIci

1989
Macintosh IIfx

1990
Macintosh Classic

1990
Macintosh IIsi

1990
Macintosh LC

1993
Macintosh Centris

1993
Macintosh TV

1995
Macintosh LC

1998
iMac

1999
iMac DV

2001
iMac Patterns

2002
iMac

2004
iMac G5

2006
iMac Slimmer Intel

2007
Novo iMac

1500 BCE

The first pill was developed by the ancient Egyptians.

100-200 AD

The Romans developed a form of tar pill.

1776

America starts contributing to medical advances as nation grows.

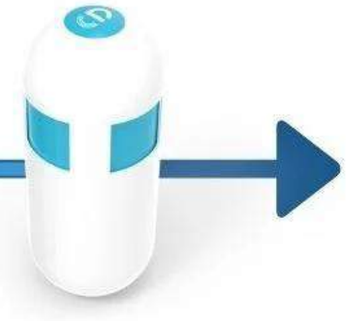
1853

The first needle was used to deliver medication.

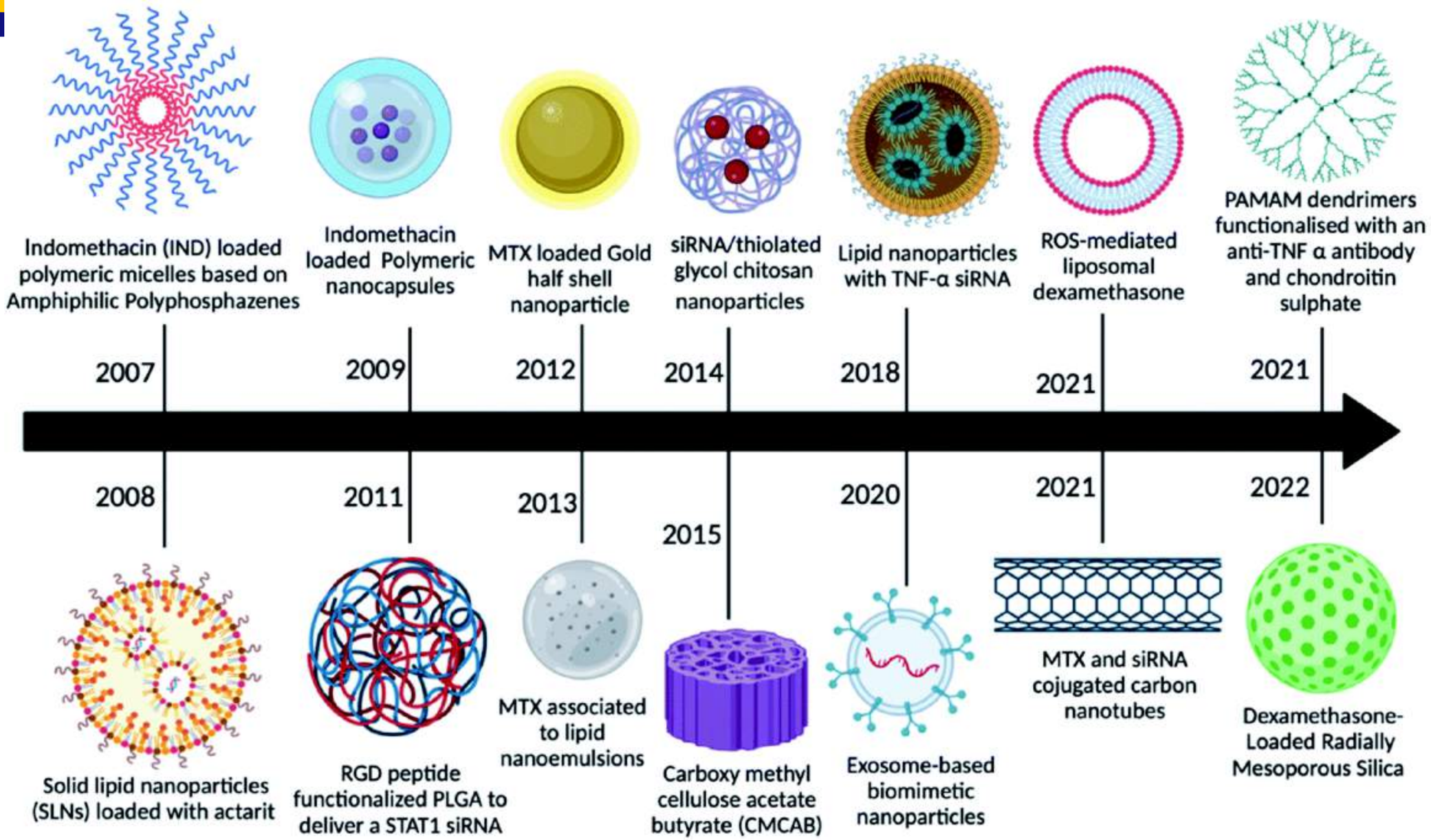
1940'S

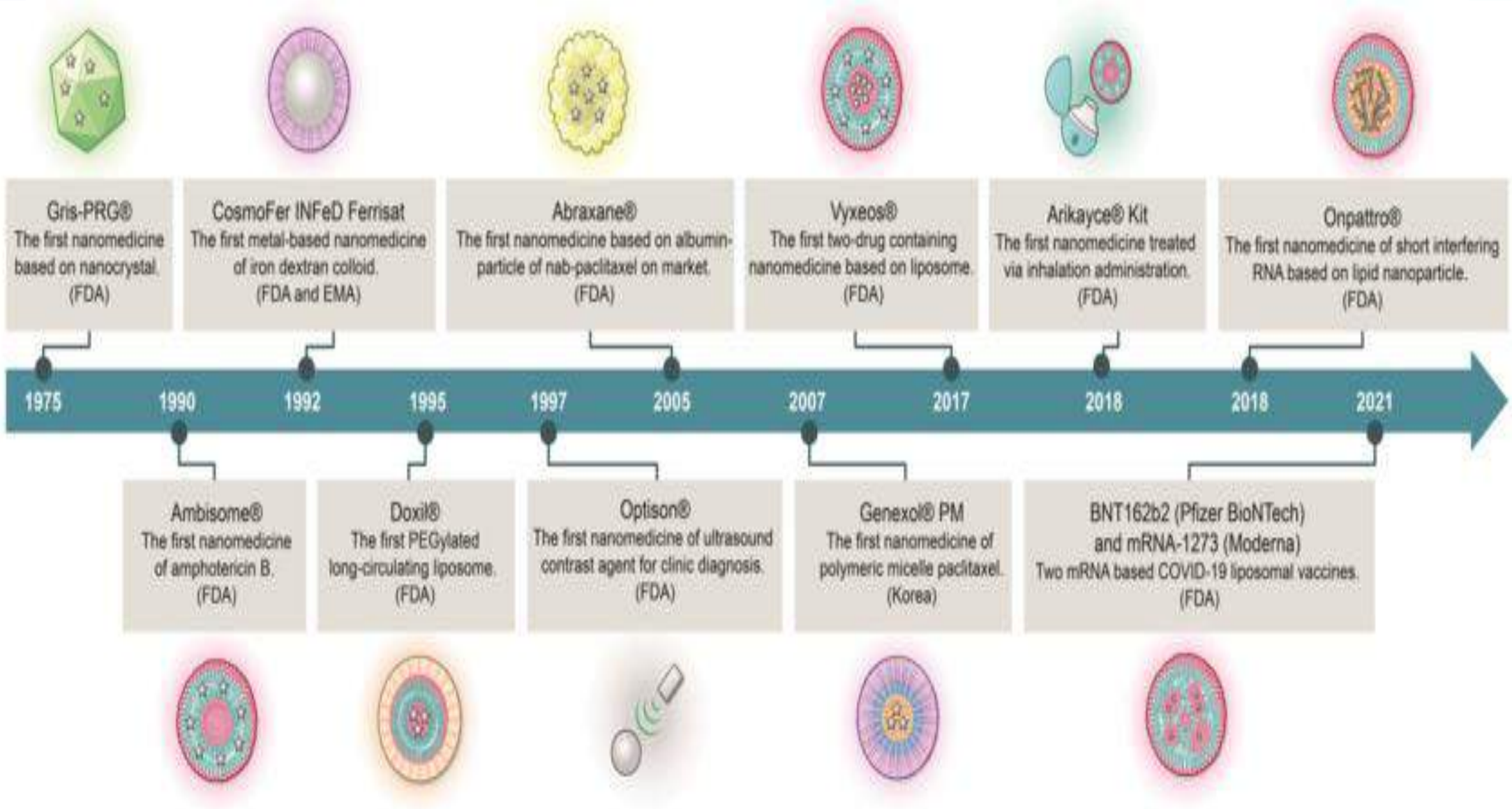
Delayed release pills were developed, optimizing delivery.

2020'S

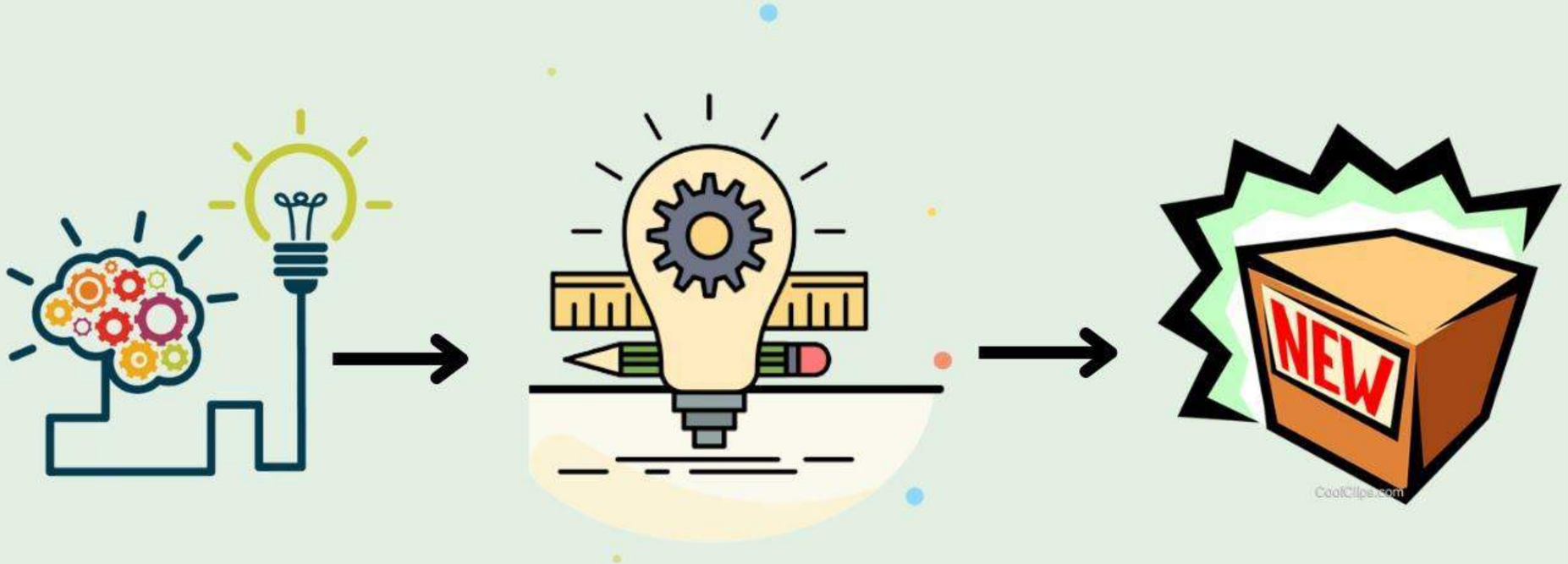


SmartTab is pioneering wireless drug delivery technology.


Indomethacin (IND) loaded polymeric micelles based on Amphiphilic Polyphosphazenes
2007
Indomethacin loaded Polymeric nanocapsules
2009
MTX loaded Gold half shell nanoparticle
2012
siRNA/thiolated glycol chitosan nanoparticles
2014
Lipid nanoparticles with TNF-α siRNA
2018
ROS-mediated liposomal dexamethasone
2021
PAMAM dendrimers functionalised with an anti-TNF α antibody and chondroitin sulphate
2021
Solid lipid nanoparticles (SLNs) loaded with actarit
2008
RGD peptide functionalized PLGA to deliver a STAT1 siRNA
2011
MTX associated to lipid nanoemulsions
2013
Carboxy methyl cellulose acetate butyrate (CMCAB)
2015
Exosome-based biomimetic nanoparticles
2020
MTX and siRNA cojugated carbon nanotubes
2021
Dexamethasone-Loaded Radially Mesoporous Silica
2022


Gris-PRG®
The first nanomedicine based on nanocrystal.
(FDA)
CosmoFer INFeD Ferrisat
The first metal-based nanomedicine of iron dextran colloid.
(FDA and EMA)
Abraxane®
The first nanomedicine based on albumin-particle of nab-paclitaxel on market.
(FDA)
Vyxeos®
The first two-drug containing nanomedicine based on liposome.
(FDA)
Arikayce® Kit
The first nanomedicine treated via inhalation administration.
(FDA)
Onpattro®
The first nanomedicine of short interfering RNA based on lipid nanoparticle.
(FDA)
1975
1990
1992
1995
1997
2005
2007
2017
2018
2018
2021
Ambisome®
The first nanomedicine of amphotericin B.
(FDA)
Doxil®
The first PEGylated long-circulating liposome.
(FDA)
Optison®
The first nanomedicine of ultrasound contrast agent for clinic diagnosis.
(FDA)
Genexol® PM
The first nanomedicine of polymeric micelle paclitaxel.
(Korea)
BNT162b2 (Pfizer BioNTech) and mRNA-1273 (Moderna)
Two mRNA based COVID-19 liposomal vaccines.
(FDA)

Product Development



educationleaves.com

Pengertian

Menurut Tjiptono (2008)

Pengembangan produk adalah **strategi untuk produk baru** meliputi produk orisinil, produk yang **disempurnakan,** produk yang **dimodifikasi,** dan merek baru yang **dikembangkan** melalui usaha **riset dan pengembangan**.

Menurut Kotler dan Amstrong (2008)

Pengembangan produk adalah **strategi untuk pertumbuhan perusahaan** dengan menawarkan produk **memodifikasi** atau produk baru ke segmen pasar yang ada sekarang pengembangan konsep produk menjadi produk fisik dalam upaya memastikan bahwa ide produk bisa diubah menjadi produk yang bisa diwujudkan secara efektif.

Menurut Alma (2002)

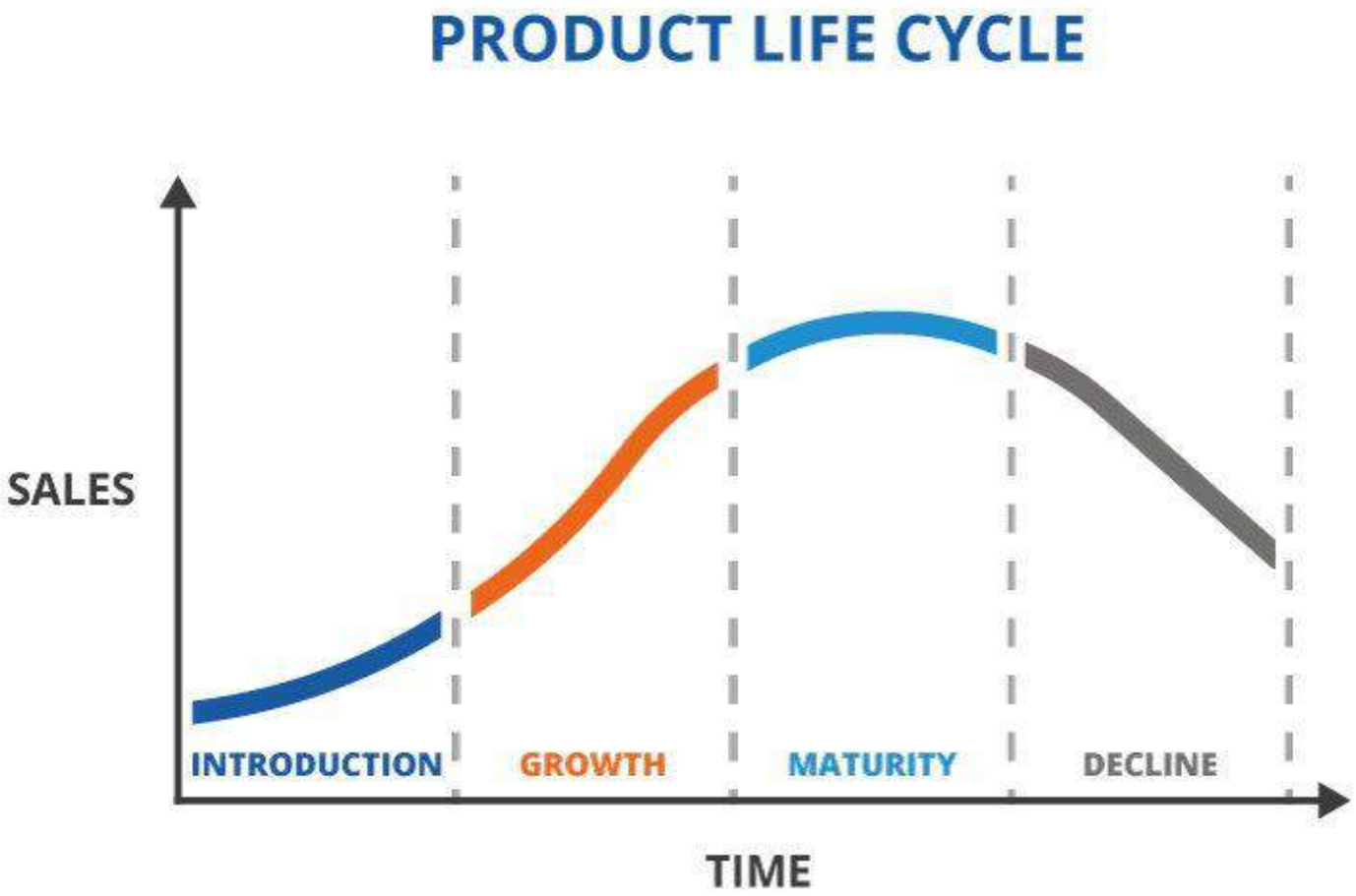
Pengembangan produk adalah semua kegiatan yang dilakukan oleh pabrikan atau produsen dalam **menentukan dan mengembangkan produknya**, **memperbaiki produk lama**, **memperbanyak kegunaan** dari produk yang sudah ada dan mengurangi biaya produksi dan biaya pengemas.

Menurut Simamora (2000)

Pengembangan produk adalah **proses pencarian gagasan untuk barang dan jasa baru** dan mengkonversikannya ke dalam tambahan lini produk yang berhasil secara komersial. Pencarian produk baru didasarkan pada asumsi bahwa para pelanggan menginginkan unsur-unsur baru dan pengenaan produk baru akan membantu mencapai tujuan perusahaan.

Menurut Ullman, 2009; Ulrich &Eppinger, 2004

Pengembangan produk adalah **penciptaan produk dengan karakteristik baru atau berbeda** yang menawarkan manfaat baru atau tambahan bagi pelanggan. Pengembangan produk mungkin **melibatkan modifikasi** produk yang sudah ada atau presentasi atau formulasi produk yang sama sekali baru yang memenuhi keinginan pelanggan atau kekosongan pasar yang baru ditentukan.



Introduction stage: maintenance cost is high at this stage, and profit is limited. Product needs to be sold immediately to earn profit

Growth: maintenance cost is lower than the introduction stage, and sales are increased. Competitors are appearing in the market, too.

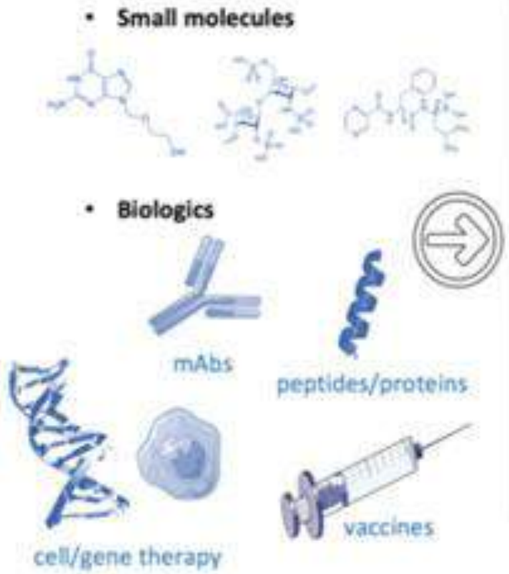
Maturity: this stage brings the most profit to the business, sales increase and maintenance cost gets much lower

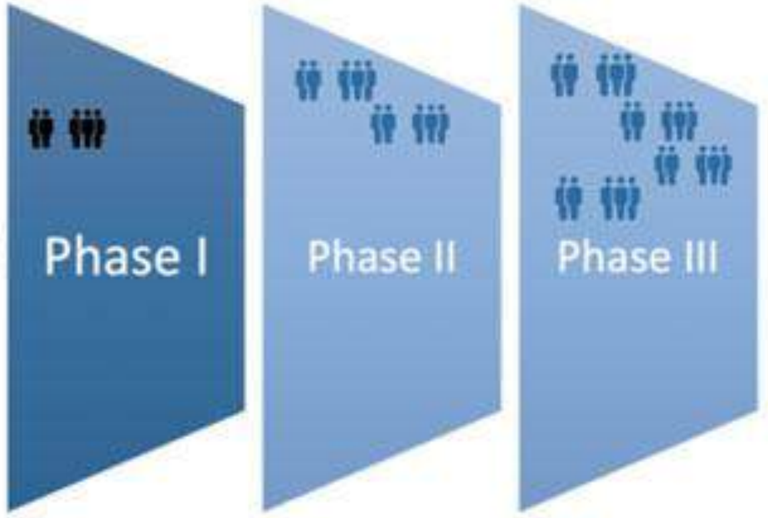
Decline and withdrawal: at this stage, products of competitors are preferred; therefore, profit decreases significantly

Stage 1	Stages 2 and 3	Stage 4	Stage 5	
"Pre-discovery"	Drug discovery & Preclinical studies	Clinical trials	Review & Approval	Phase IV

~12-15 years

Basic research
Clinical observations





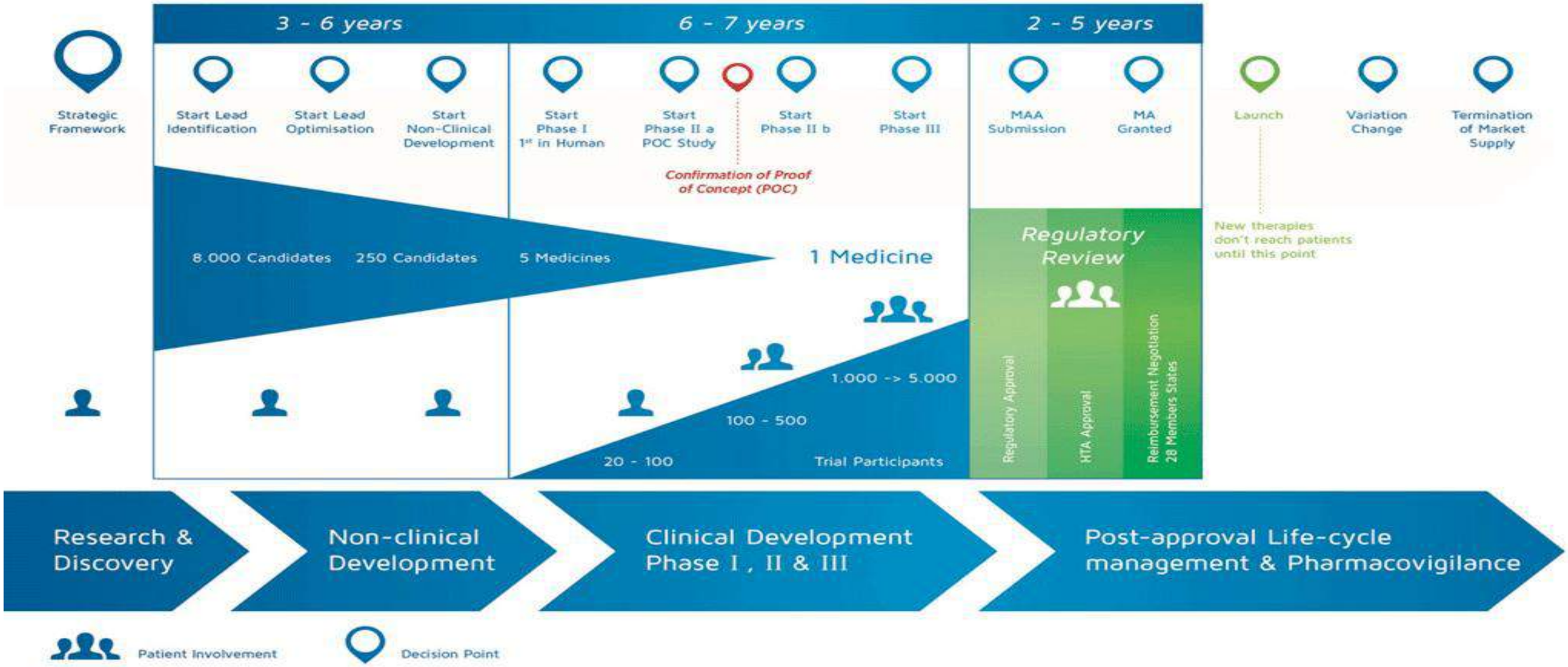
Molecular mechanisms involved in the disease state, identification of putative targets...

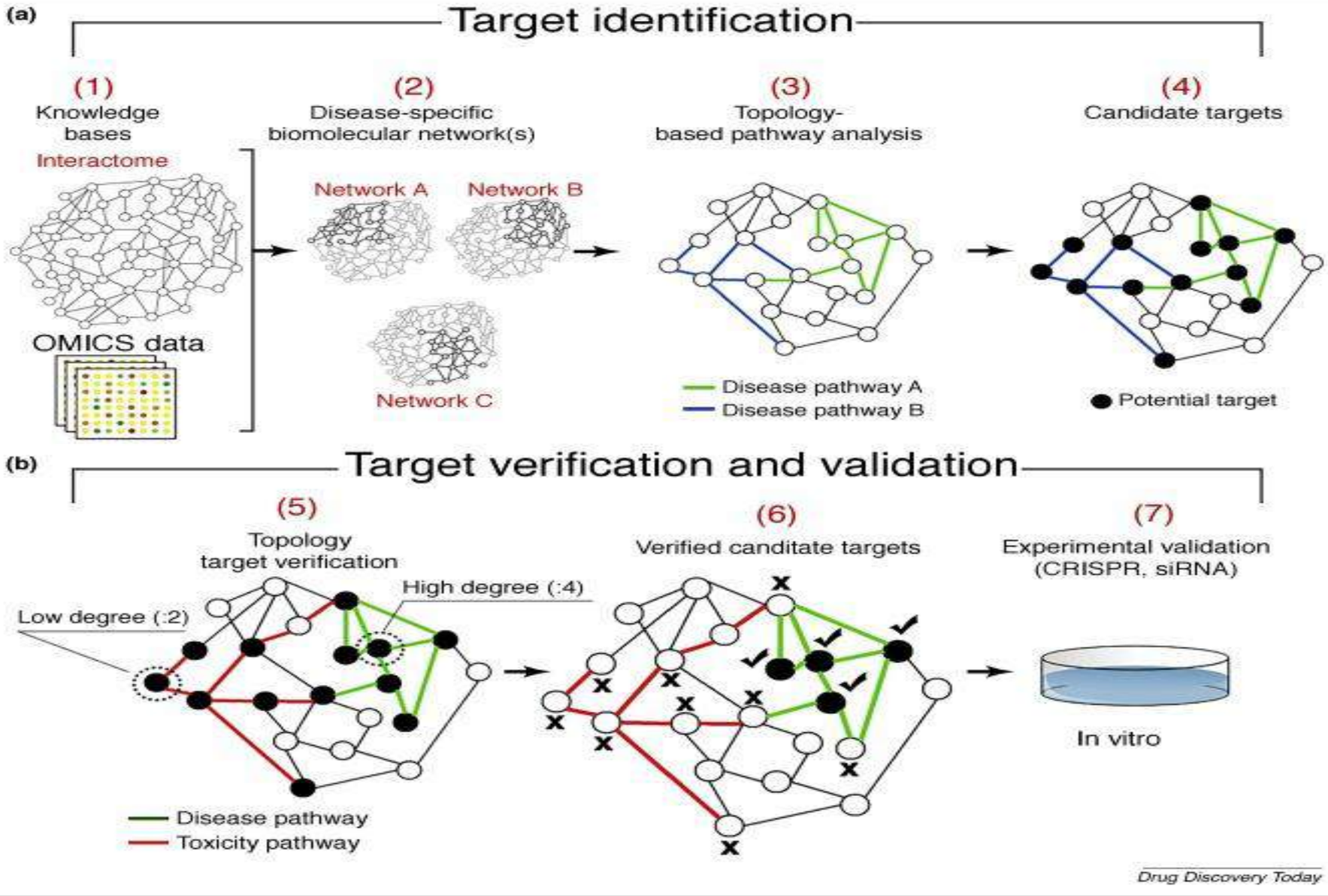
Identification of the therapeutic agents modulating the selected target(s), ADMET, efficacy,... first evaluations silico-vitro-vivo

Evaluations in humans
PK, dose, efficacy, toxicity...

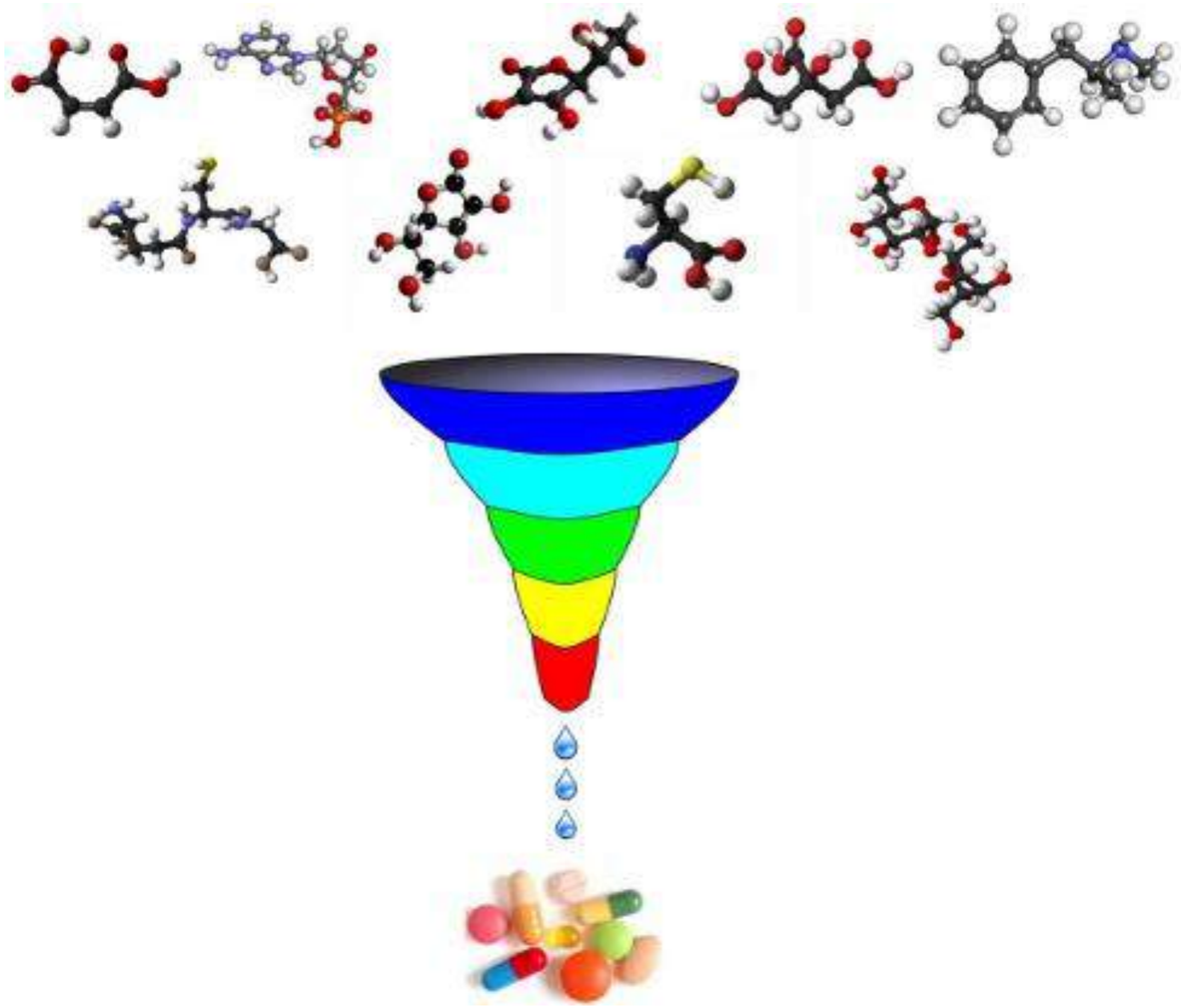
Reviewing, approval & post-market monitoring

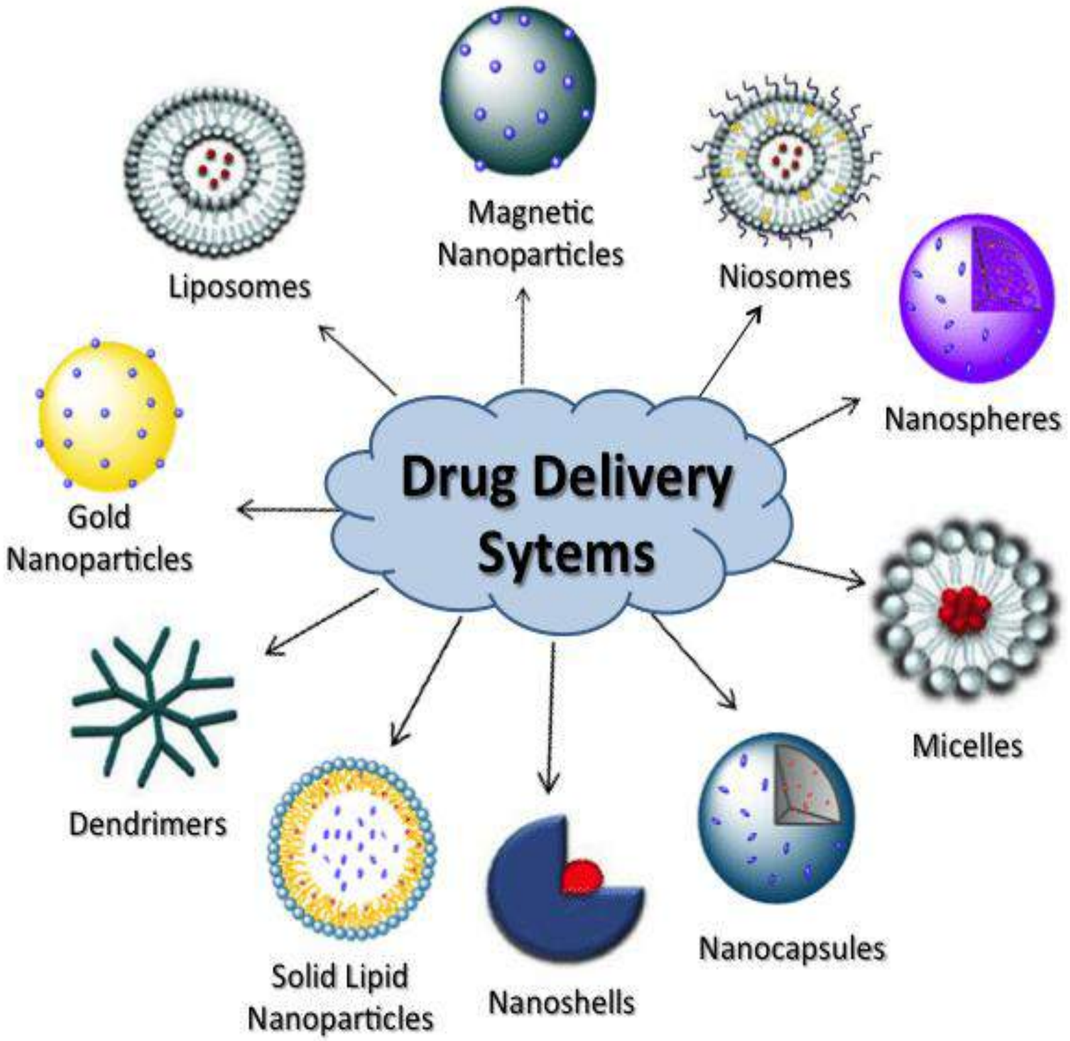
Overview of Decision Points and Development Steps in Medicines R&D





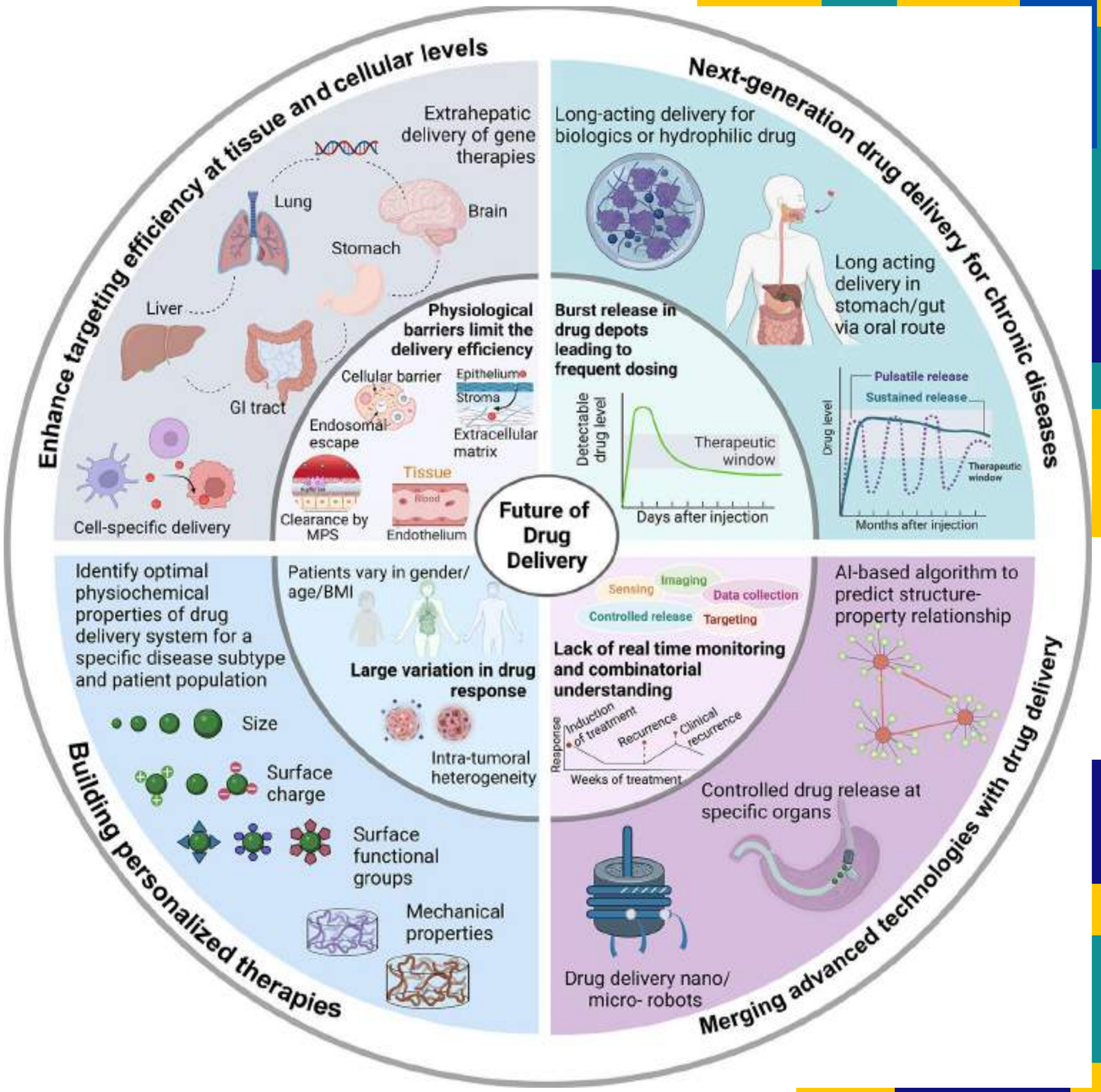
Network-based technologies for early drug discovery

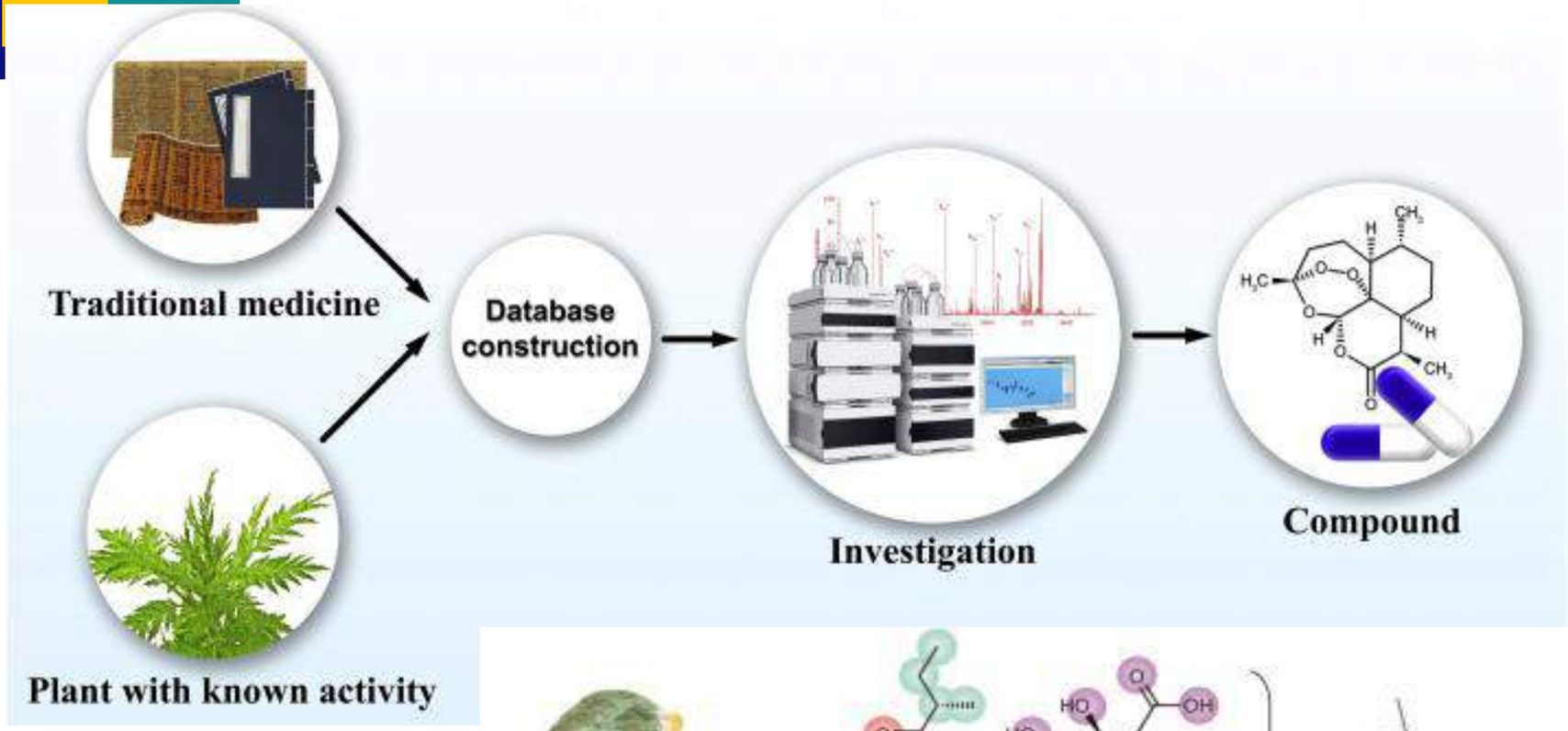


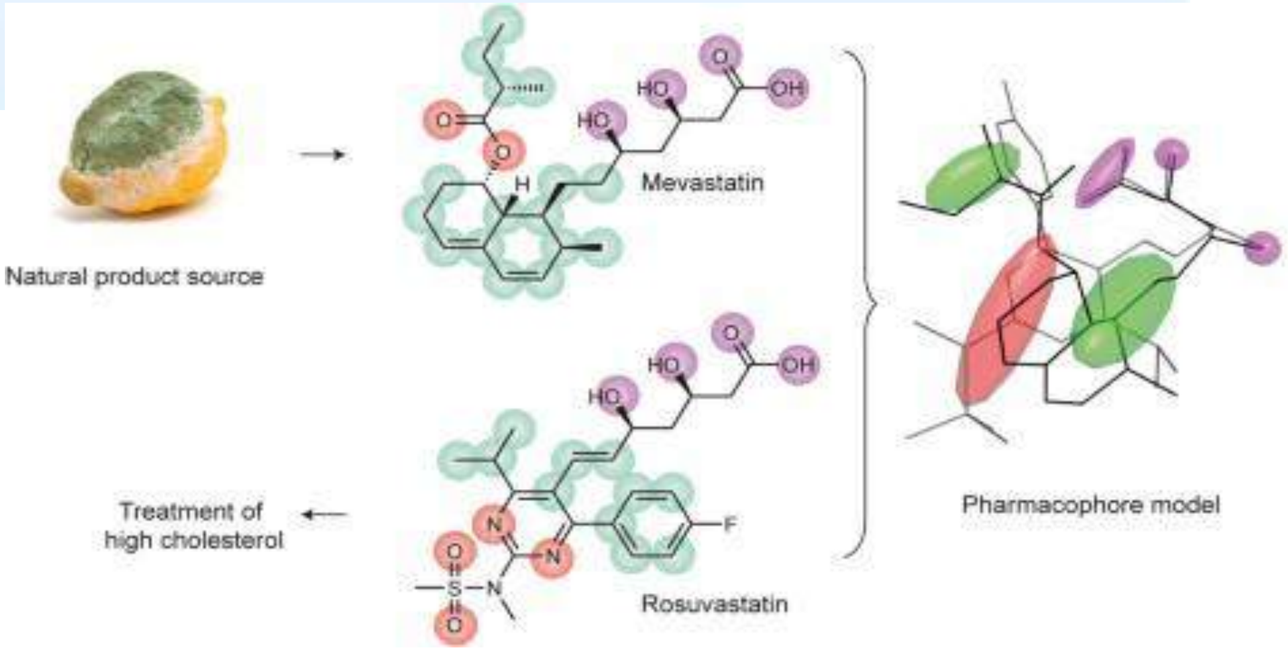


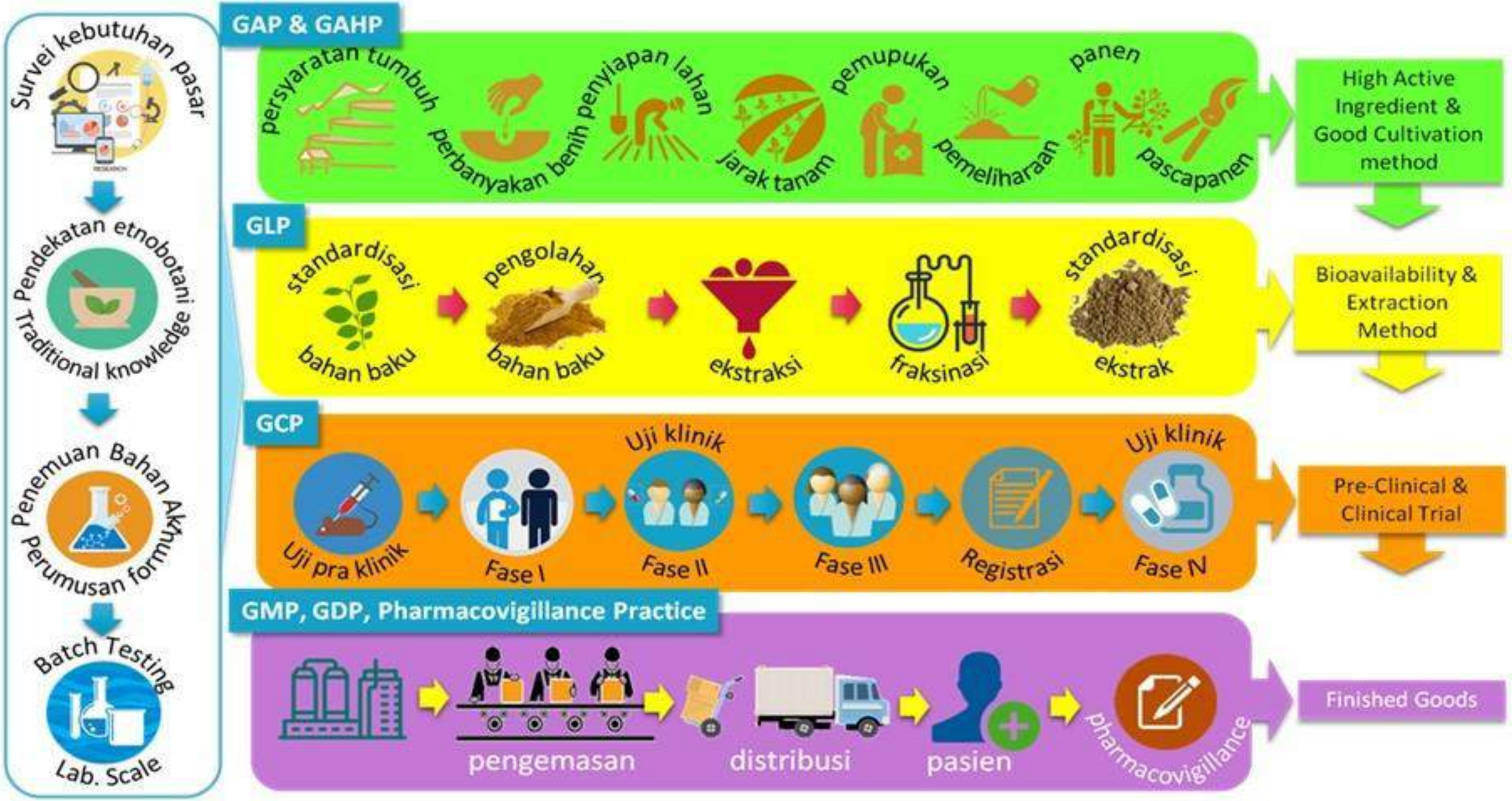
Drug discovery


Tablets
Capsules
Granules
Ointments
Syrups
Suppositories
Conventional Drug Delivery Systems
Limitations
Poor absorption from target site
Poor Bioavailability
High First-pass Metabolism
Fluctuations in Plasma drug level
Premature excretion from the body
Repeated dosing
High dose dumping


Enhance targeting efficiency at tissue and cellular levels
Extrahepatic delivery of gene therapies
Lung
Brain
Stomach
Liver
GI tract
Physiological barriers limit the delivery efficiency
Cellular barrier
Epithelium
Stroma
Extracellular matrix
Endosomal escape
Tissue
Endothelium
Clearance by MPS
Cell-specific delivery
Next-generation drug delivery for chronic diseases
Long-acting delivery for biologics or hydrophilic drug
Long acting delivery in stomach/gut via oral route
Burst release in drug depots leading to frequent dosing
Detectable drug level
Therapeutic window
Days after injection
Pulsatile release
Sustained release
Drug level
Therapeutic window
Months after injection
Future of Drug Delivery
Identify optimal physiochemical properties of drug delivery system for a specific disease subtype and patient population
Size
Surface charge
Surface functional groups
Mechanical properties
Patients vary in gender/ age/BMI
Large variation in drug response
Intra-tumoral heterogeneity
Building personalized therapies
Sensing
Imaging
Data collection
Controlled release
Targeting
Lack of real time monitoring and combinatorial understanding
Response
Induction of treatment
Recurrence
Clinical recurrence
Weeks of treatment
AI-based algorithm to predict structure-property relationship
Controlled drug release at specific organs
Drug delivery nano/ micro- robots
Merging advanced technologies with drug delivery


Traditional medicine
Database construction
Investigation
Compound
Plant with known activity


Natural product source
Mevastatin
Treatment of high cholesterol
Rosuvastatin
Pharmacophore model
Superimposed crystal structures


Survei kebutuhan pasar
Pendekatan etnobotani
Traditional knowledge
Penemuan Bahan Aktif
Perumusan formulasi
Batch Testing
Lab. Scale
GAP & GAHP
persyaratan tumbuh
perbanyakan benih
penyiapan lahan
jarak tanam
pemupukan
pemeliharaan
panen
pascapanen
High Active Ingredient & Good Cultivation method
GLP
standardisasi
bahan baku
pengolahan
bahan baku
ekstraksi
fraksinasi
standardisasi
ekstrak
Bioavailability & Extraction Method
GCP
Uji pra klinik
Fase I
Uji klinik
Fase II
Fase III
Registrasi
Uji klinik
Fase IV
Pre-Clinical & Clinical Trial
GMP, GDP, Pharmacovigillance Practice
pengemasan
distribusi
pasien
pharmacovigillance
Finished Goods

OMAI

Jamu

> 8000

Kriteria :

- Aman
- Memenuhi persyaratan mutu
- Khasiat dibuktikan secara empiris

Obat Herbal Terstandar (45)

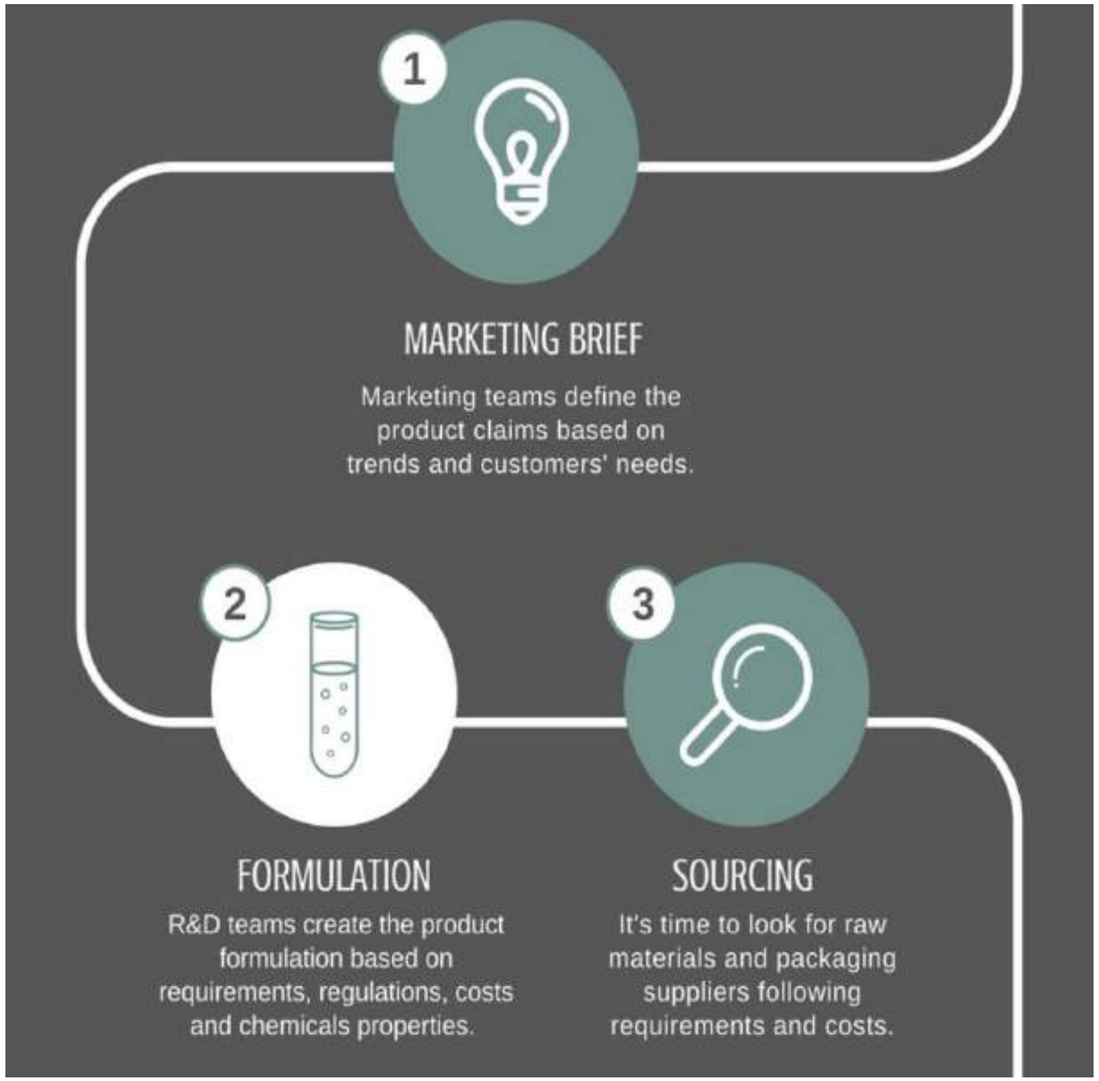
Kriteria :

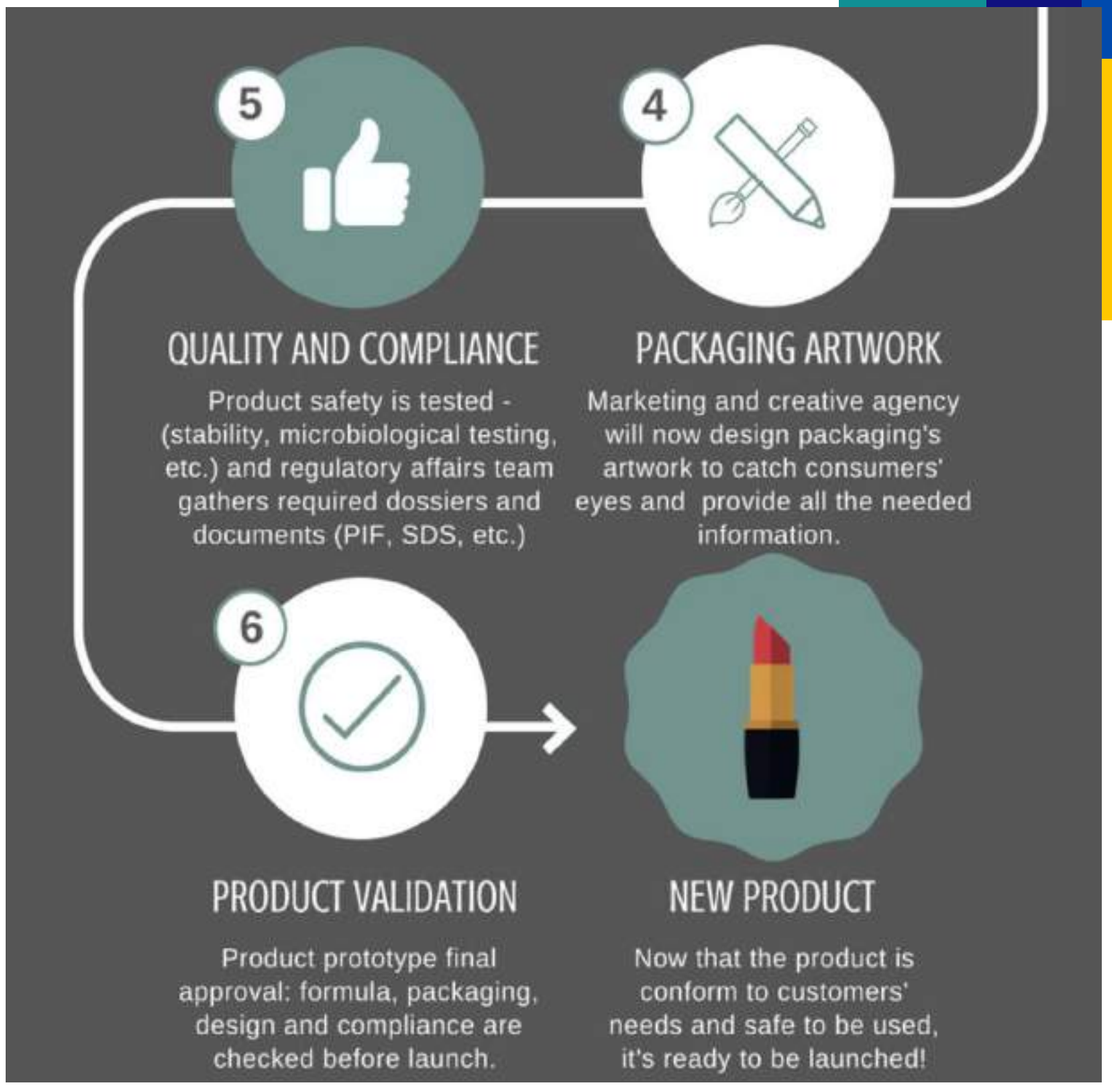
- Aman
- Memenuhi persyaratan mutu
- Khasiat dibuktikan secara ilmiah atau praklinik
- Bahan baku yang digunakan terstandar

Fitofarmaka (21)

Kriteria :

- Aman
- Memenuhi persyaratan mutu
- Khasiat dibuktikan secara klinis
- Bahan baku yang digunakan terstandar





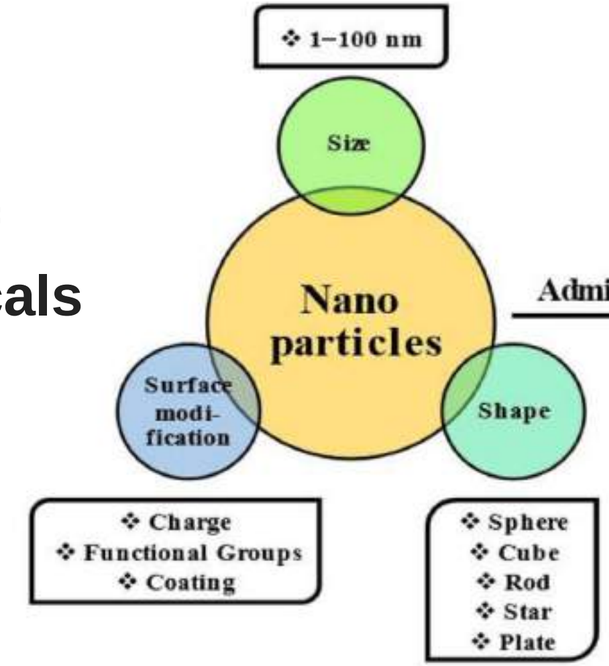
PENGEMBANGAN KOSMETIK

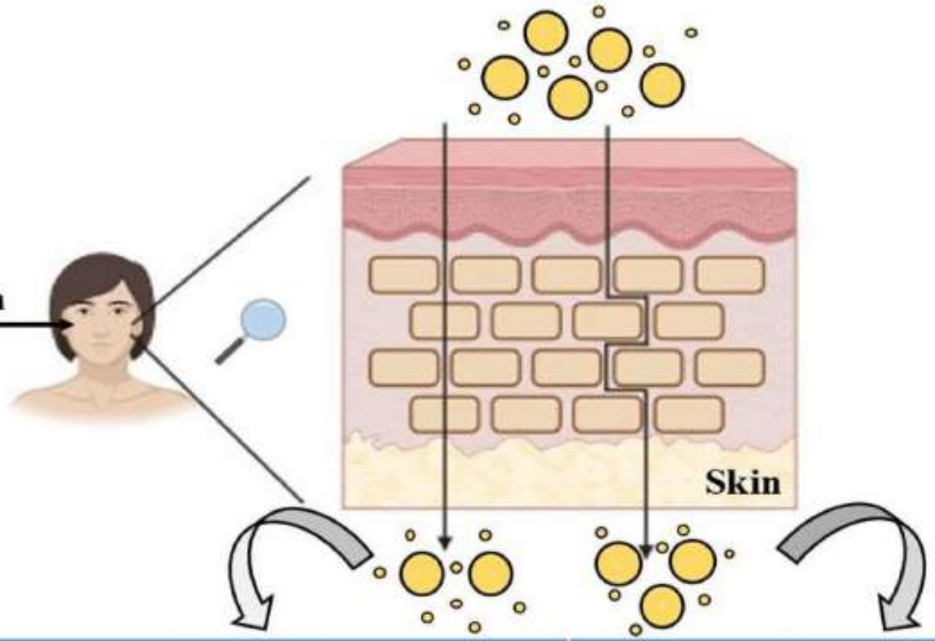
Table 1. Main effects of cosmetic vehicles on the skin.

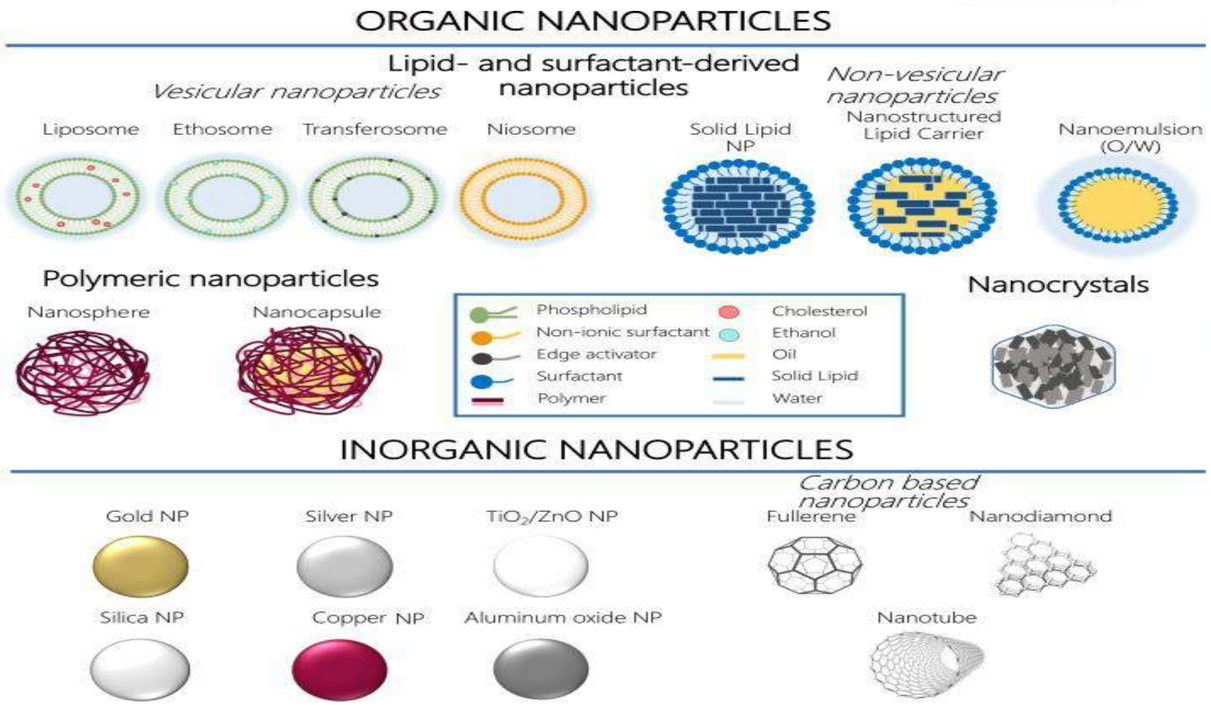
Effect	Definition
Protective	Protects the skin from external harmful factors (dry air, pollution, UV light)
Cleansing	Eliminates dirt and microorganisms from the skin
Hydrating	Provides water in order to restore or maintain fluid balance
Moisturizing	Establishes an effective barrier that prevents water loss through the epidermis
Soothing	Provides a gently calming effect
Firming	Makes the skin more toned and smoother

PENGEMBANGAN KOSMETIK

Advantages of nanocosmeceuticals

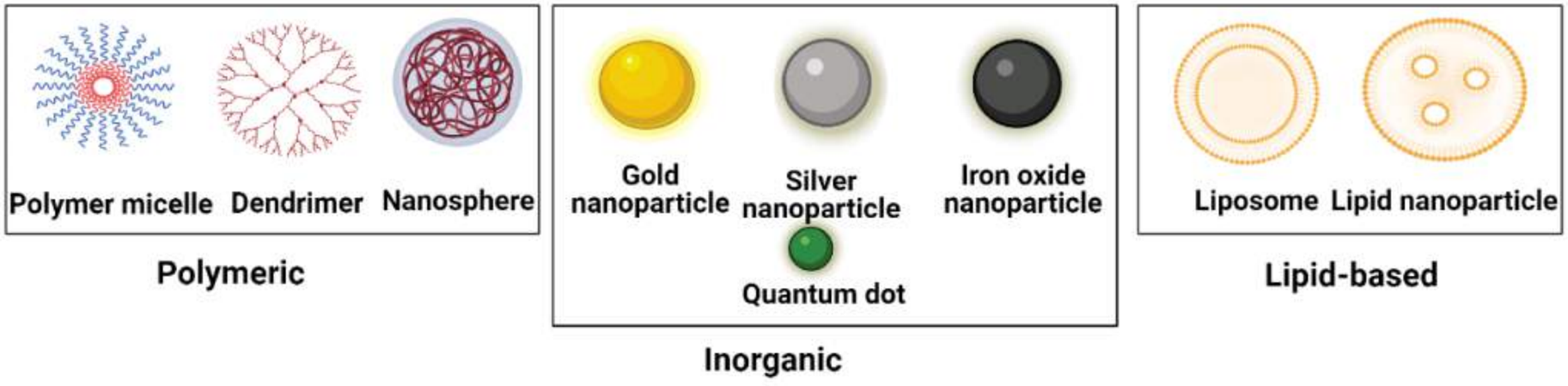


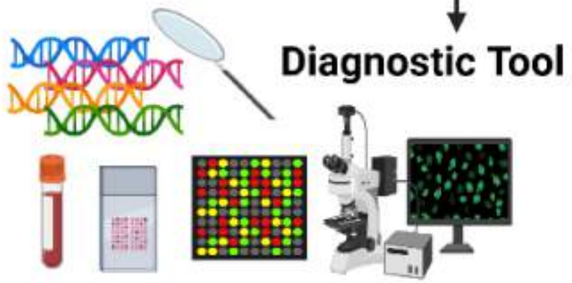




Advantages	Disadvantages
Control & targeted delivery	Nanoparticle toxicity may lead to inflammation, oxidative stress, & consequent damage to membranes & proteins
↑ Texture & transparency of the cosmetic formulation	Require sophisticated equipment for manufacturing
↑ Dermal penetration & bioavailability	↑ Cost of production
↑ Appearance, covering power, aesthetic appeal & adherence over the skin	↑ Environmental concern
↑ Stability & efficacy to the cosmetic formulation	Teratogenic in nature, due to easy placenta penetration
Better drug holding capacity	May damage DNA & lead to malignancy

Nanoparticles





Diagnostic Tool

Therapeutic Approach

Personalized Medicine

Tujuan Pengembangan Produk Baru

1. Untuk memberikan nilai maksimal bagi konsumen
2. Memenangkan persaingan perusahaan dengan memilih produk yang inovatif, produk yang dimodifikasi serta mempunyai nilai yang tinggi baik dalam desain warna, ukuran, kemasan, merek, dan ciri-ciri lain.

REFERENSI

1. Liu, Q., Zou, J., Chen, Z., He, W., & Wu, W. (2023). Current research trends of nanomedicines. Acta Pharmaceutica Sinica B, 13(11), 4391–4416. https://doi.org/10.1016/J.APSB.2023.05.018
2. Fotis, C., Antoranz, A., Hatziavramidis, D., Sakellaropoulos, T., & Alexopoulos, L. G. (2018). Network-based technologies for early drug discovery. Drug Discovery Today, 23(3), 626–635. https://doi.org/10.1016/J.DRUDIS.2017.12.001
3. Vargason, A. M., Anselmo, A. C., & Mitragotri, S. (2021). The evolution of commercial drug delivery technologies. Nature Biomedical Engineering 2021 5:9, 5(9), 951–967. https://doi.org/10.1038/s41551-021-00698-w
4. Gupta, V., Mohapatra, S., Mishra, H., Farooq, U., Kumar, K., Ansari, M. J., Aldawsari, M. F., Alalaiwe, A. S., Mirza, M. A., & Iqbal, Z. (2022). Nanotechnology in Cosmetics and Cosmeceuticals—A Review of Latest Advancements. Gels 2022, Vol. 8, Page 173, 8(3), 173. https://doi.org/10.3390/GELS8030173
5. Salvioni, L., Morelli, L., Ochoa, E., Labra, M., Fiandra, L., Palugan, L., Prosperi, D., & Colombo, M. (2021). The emerging role of nanotechnology in skincare. Advances in Colloid and Interface Science, 293, 102437. https://doi.org/10.1016/J.CIS.2021.102437

THANK YOU

STIKES NOTOKUSUMO YOGYAKARTA

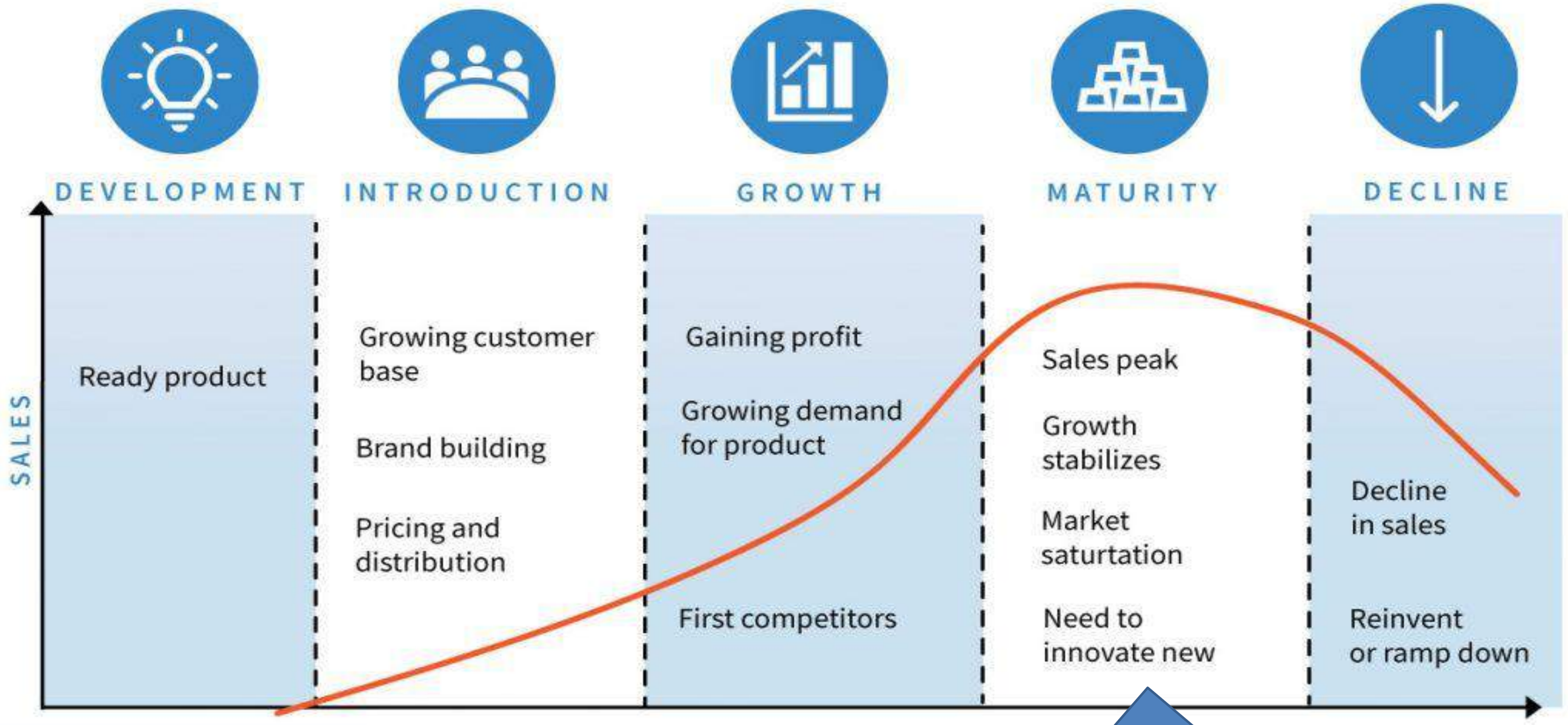
Pertemuan 2

PENGEMBANGAN PRODUK

apt. Trifonia Rosa K., M.Biotech

Topik pembahasan

- Tahapan pengembangan produk
- Strategi pemasaran produk



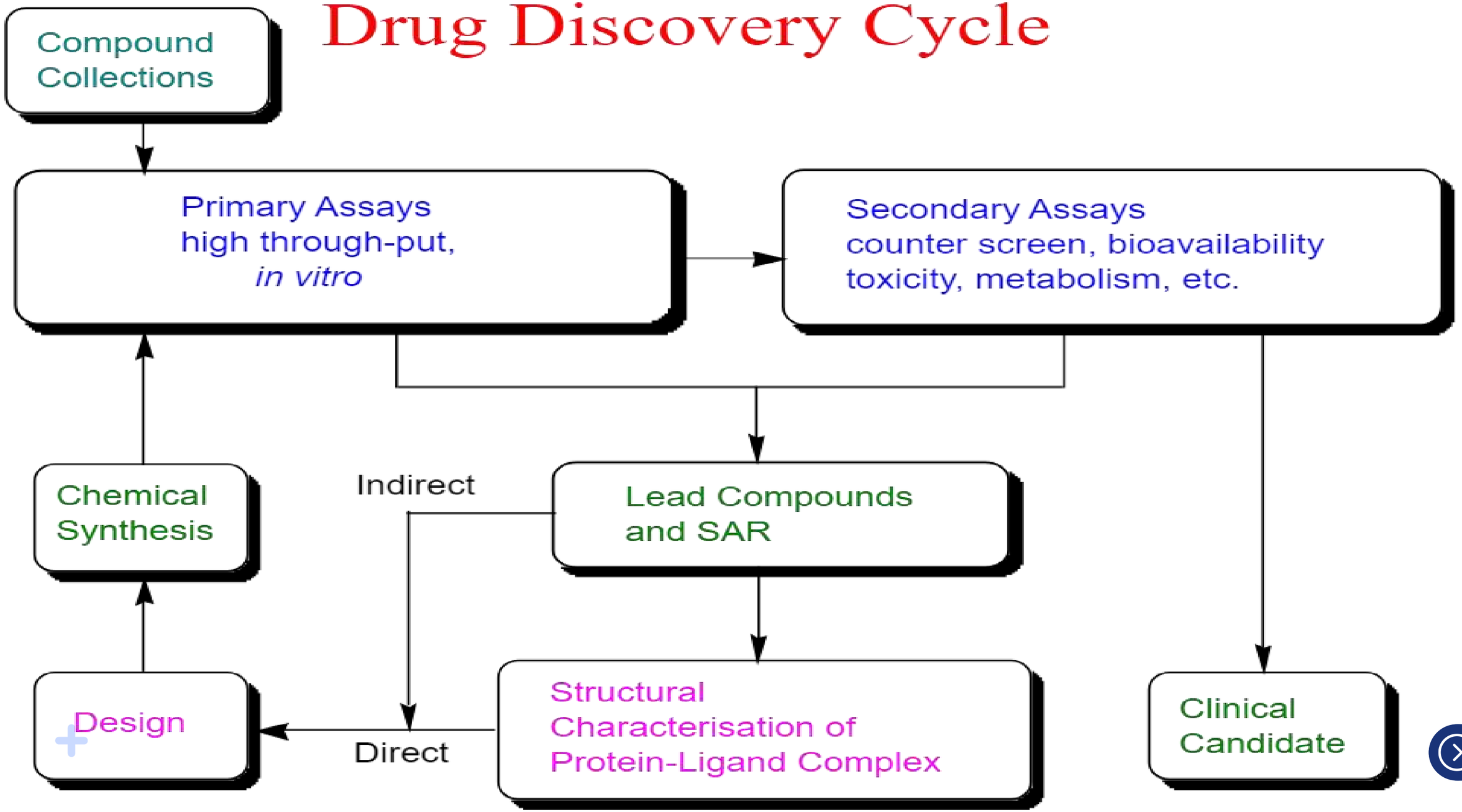
Expand to new markets or expand product capabilities

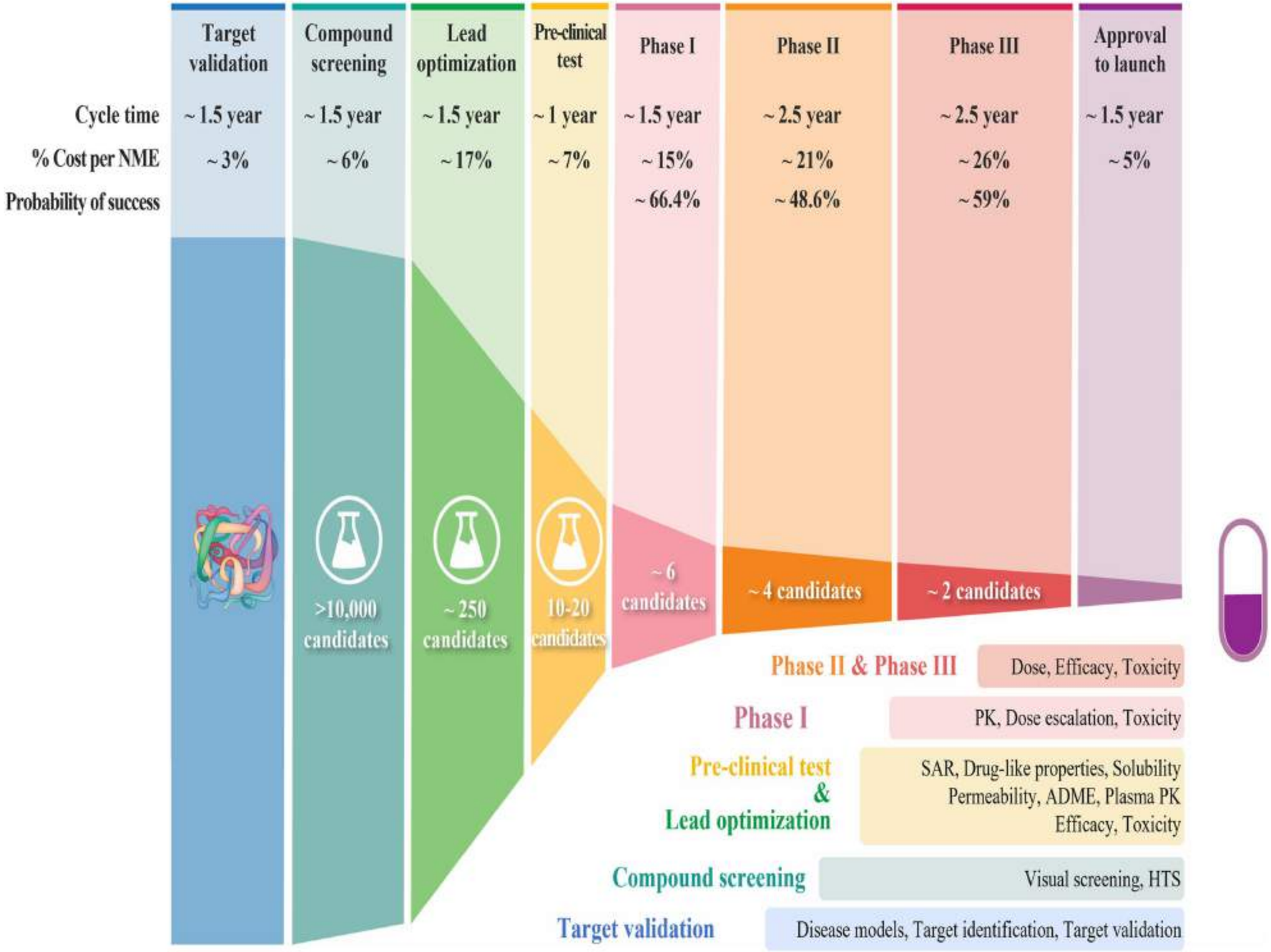
PENGEMBANGAN PRODUK

Kriteria Produk Baru

- **Inovasi besar** : produk baru dengan pasar baru
- **Peningkatan produk** : produk baru dengan pasar yang sama
- **Penambahan produk** : produk imitasi yang menggunakan pasar yang dibuat oleh produsen produk asli.
- **Produk yang diposisikan ulang** : Produk yang diposisikan ulang dipromosikan dengan cara baru untuk menarik berbagai jenis pelanggan.

Drug Discovery Cycle

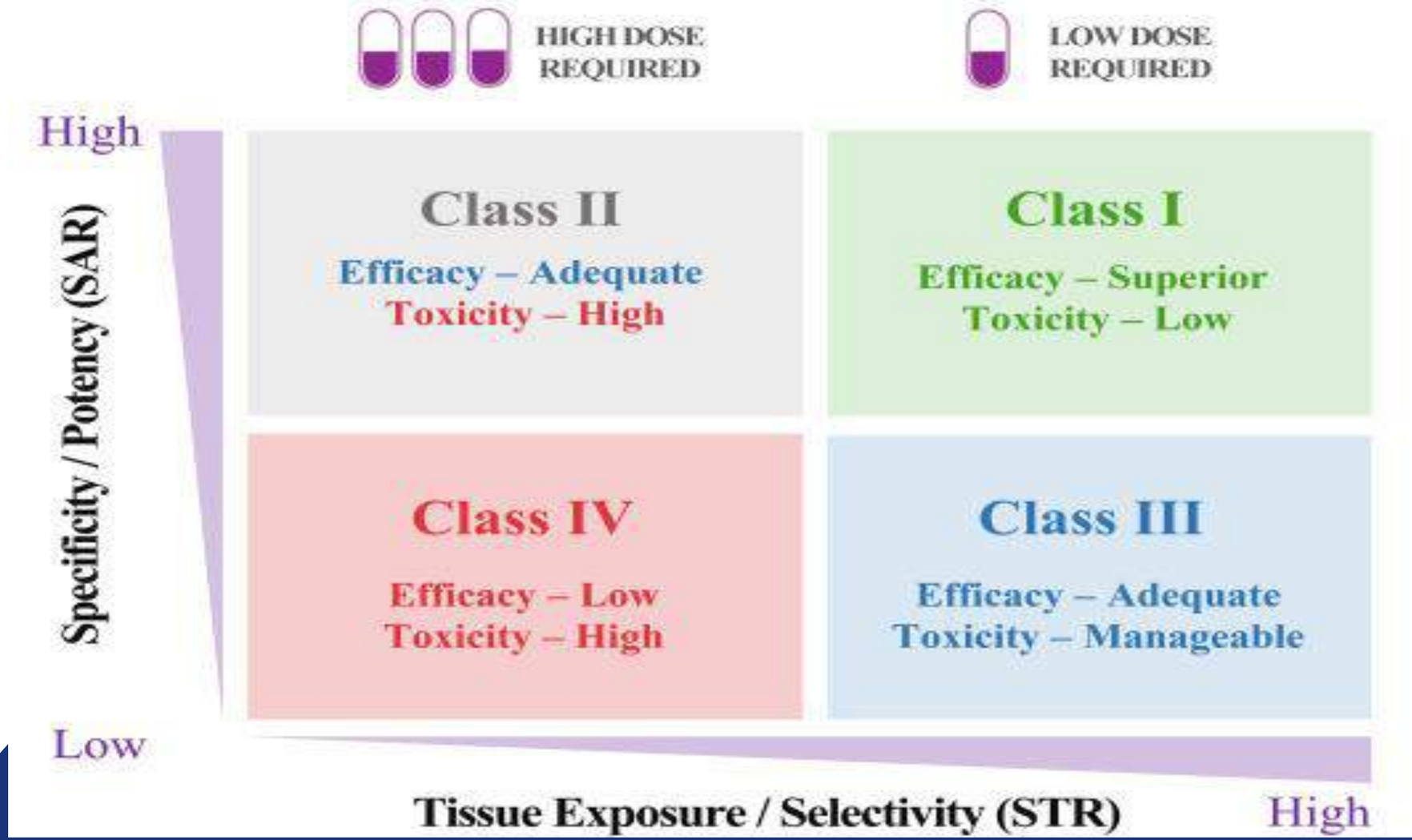




Analyses of clinical trial data from 2010 to 2017 show four possible reasons attributed to the 90% clinical failures of drug development:

- Lack of clinical efficacy (40% - 50%),
- Unmanageable toxicity (30%),
- Poor drug-like properties(10%-15%),
- Lack of commercial needs and poor strategic planning (10%)

Structure-Tissue Exposure/Selectivity-Activity Relationship (STAR)
Selects Drug Candidates and Balances Clinical Dose/Efficacy/Toxicity



What are the successful strategies to improve each aspect of drug development process in the past decades?

Select best lead drug candidate to achieve **adequate clinical efficacy**

Select best lead drug candidate to **minimize clinical toxicity**

Select best lead drug candidate with **optimal drug-like properties**

- Drug-like properties, such as solubility, permeability, metabolic stability and transporter effects are of critical importance for the success of drug candidates. They affect oral bioavailability, metabolism, clearance, toxicity, as well as in vitro pharmacology.

Optimize strategic planning in **drug development**

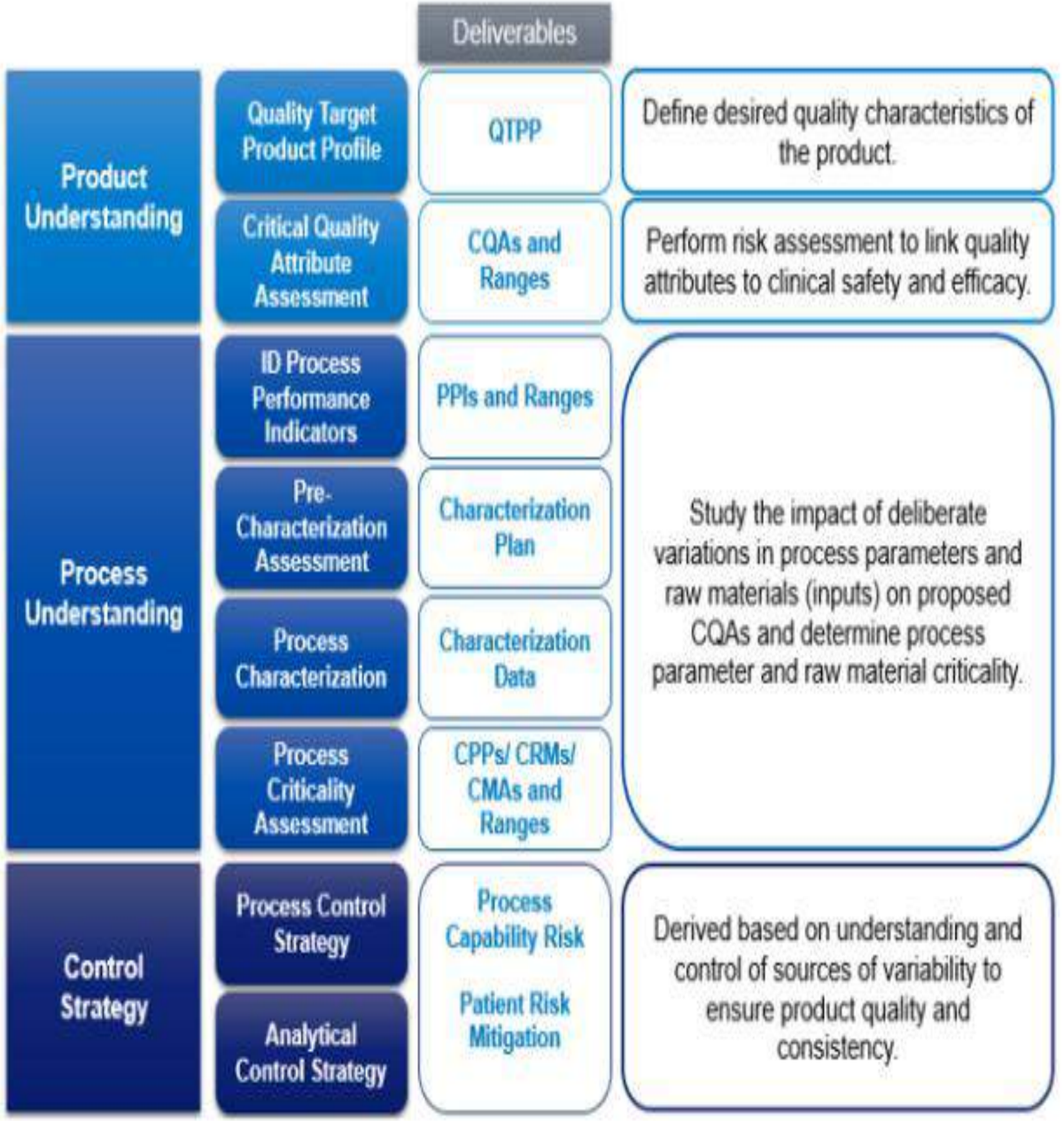
PHARMACEUTICAL DEVELOPMENT

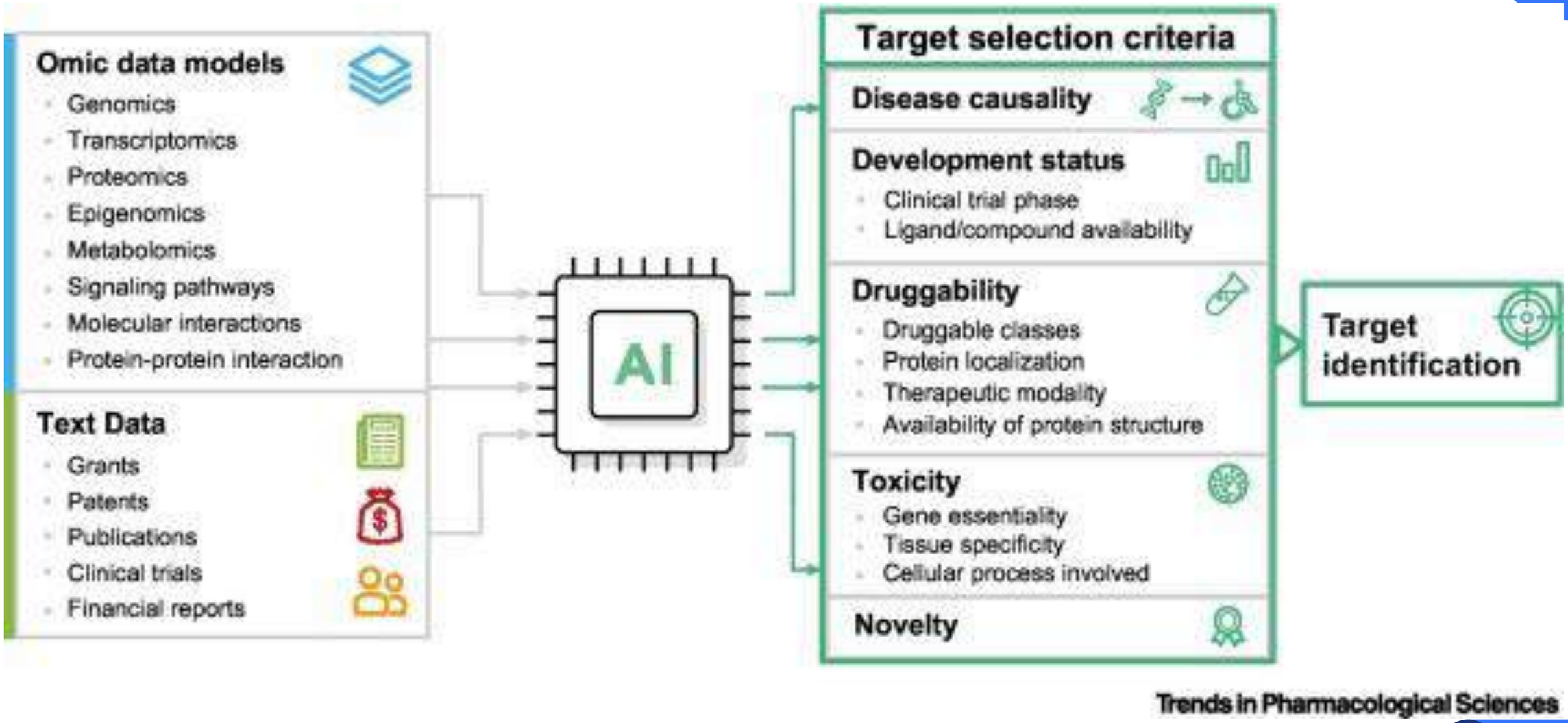
Quality-by-Design (QbD)

Pharmaceutical QbD is a **systematic approach to development** that begins with **predefined objectives** and **emphasizes product** and process understanding and **control based** on sound science and **quality risk** management .

The goals of pharmaceutical QbD may include the following:

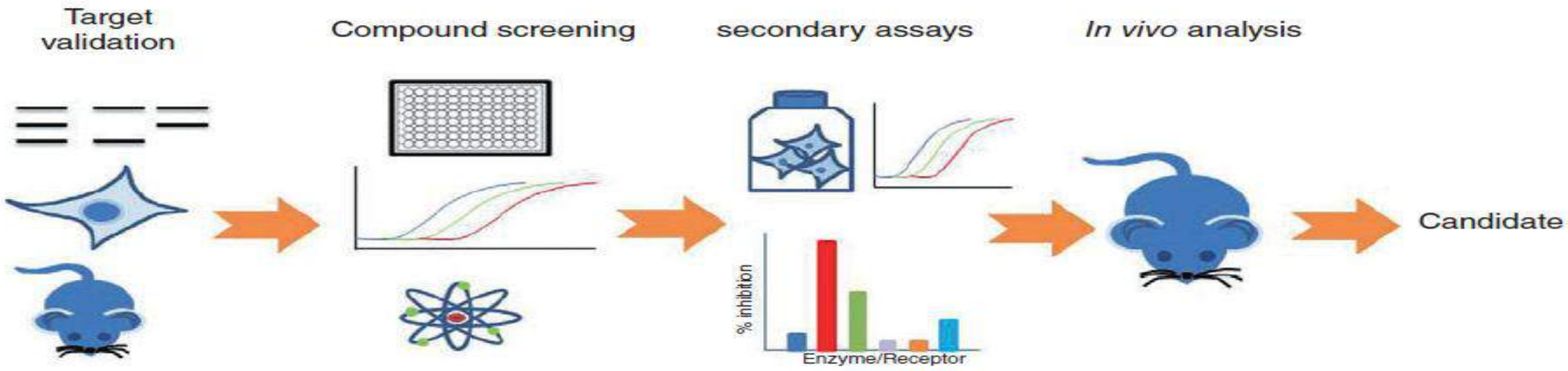
- To achieve **meaningful product** quality specifications that are based on **clinical performance**
- To **increase process capability** and reduce product variability and defects by enhancing product and process design, understanding, and control
- To **increase product development and manufacturing efficiencies**
- To enhance root cause analysis and postapproval change management





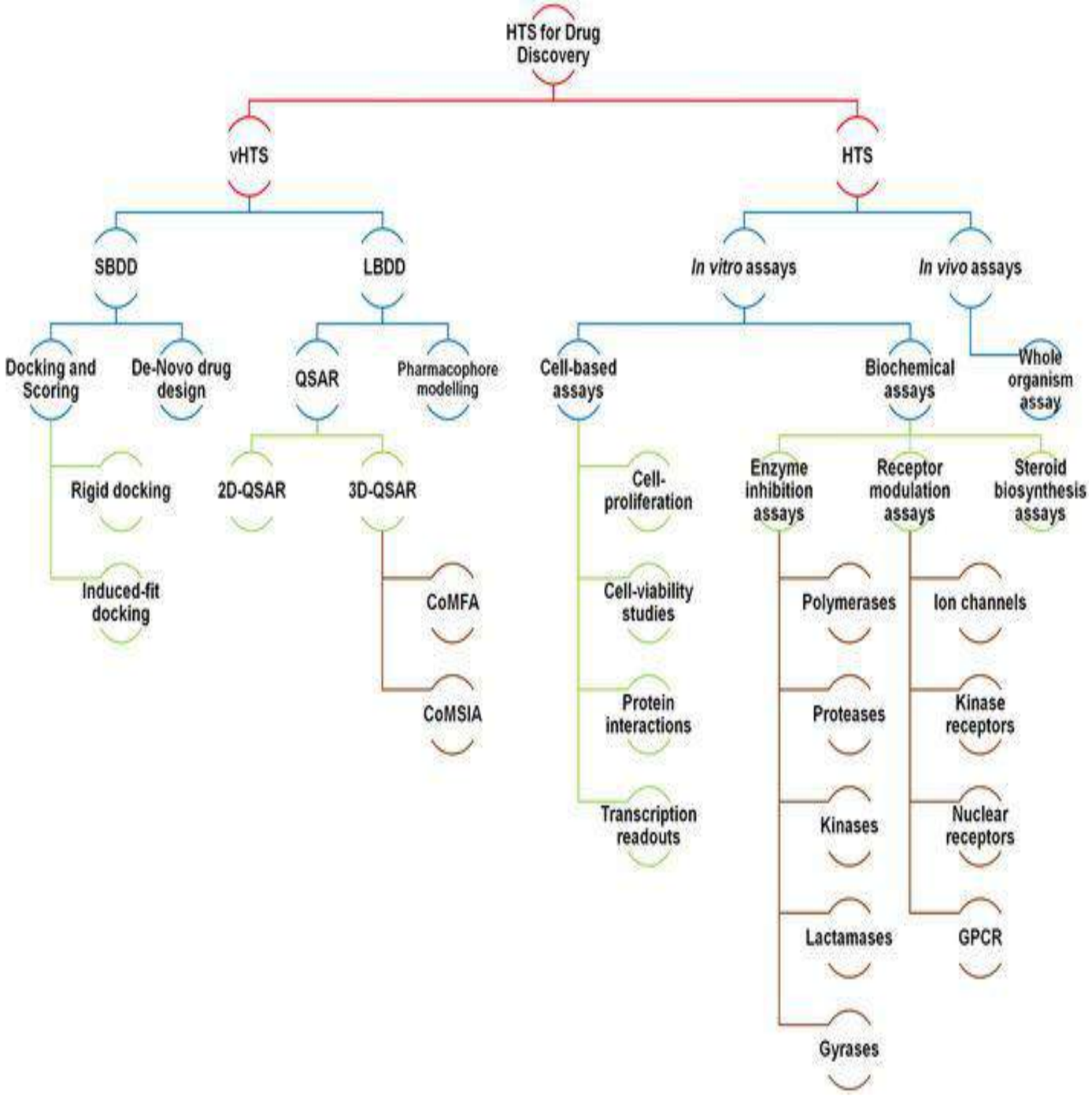
Trends in Pharmacological Sciences

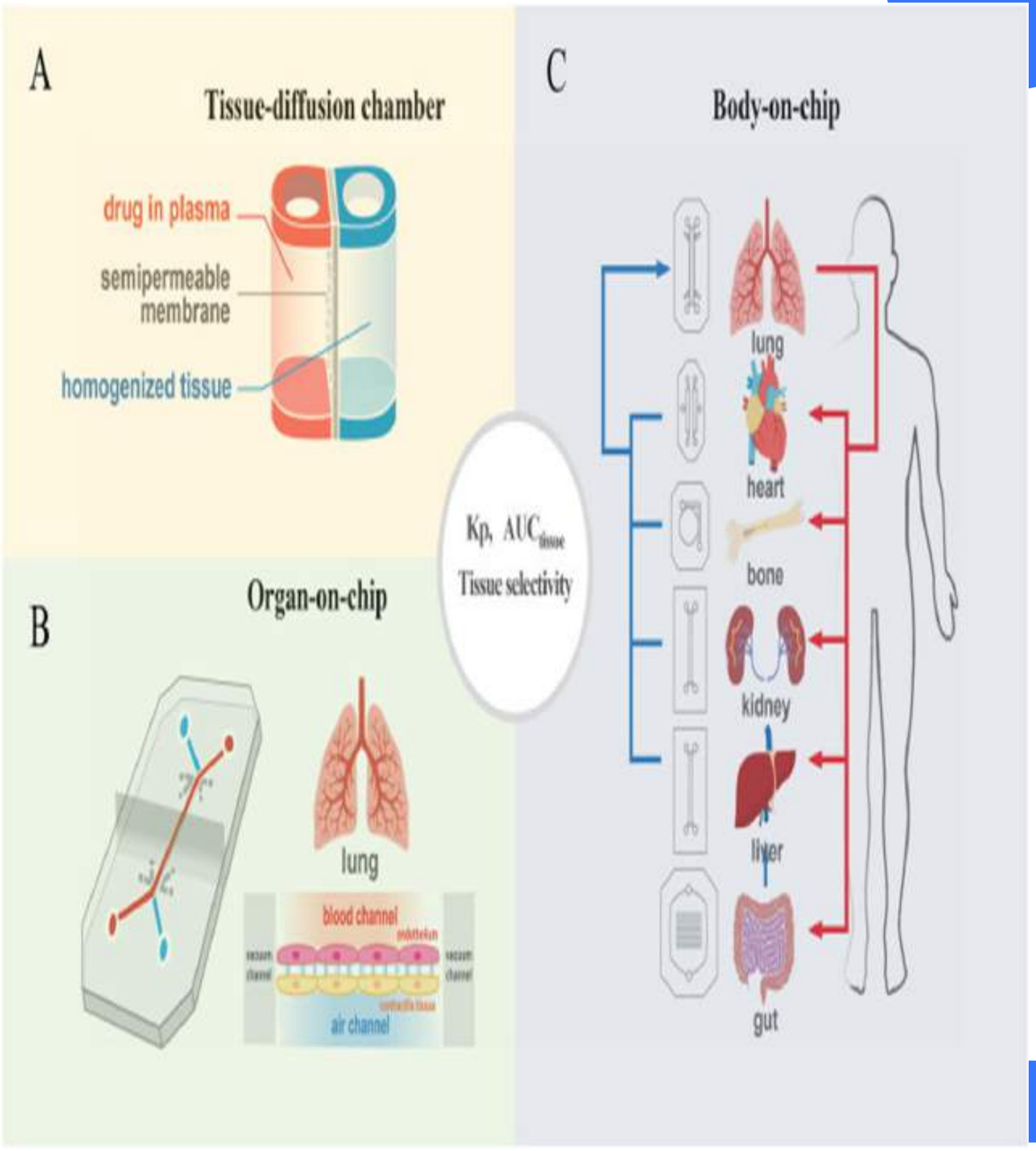
Phase	Target Discovery	Target Validation	Lead Generation & Refinement	Preclinical Development	
Goal	Find All Targets	Eliminate Wrong Targets	Generate Molecules	Eliminate Molecules	Advance Molecules



- Genetic, cellular and *in vivo* experimental models to identify and validate target
- HTS & selective library screens; structure based design
- Reiterative directed compound synthesis to improve compound properties
- *in vitro* & *ex vivo* secondary assays (mechanistic)
- Selectivity & liability assays
- Compound pharmacology
- Disease efficacy models
- Early safety & toxicity studies
- Preclinical safety & toxicity package

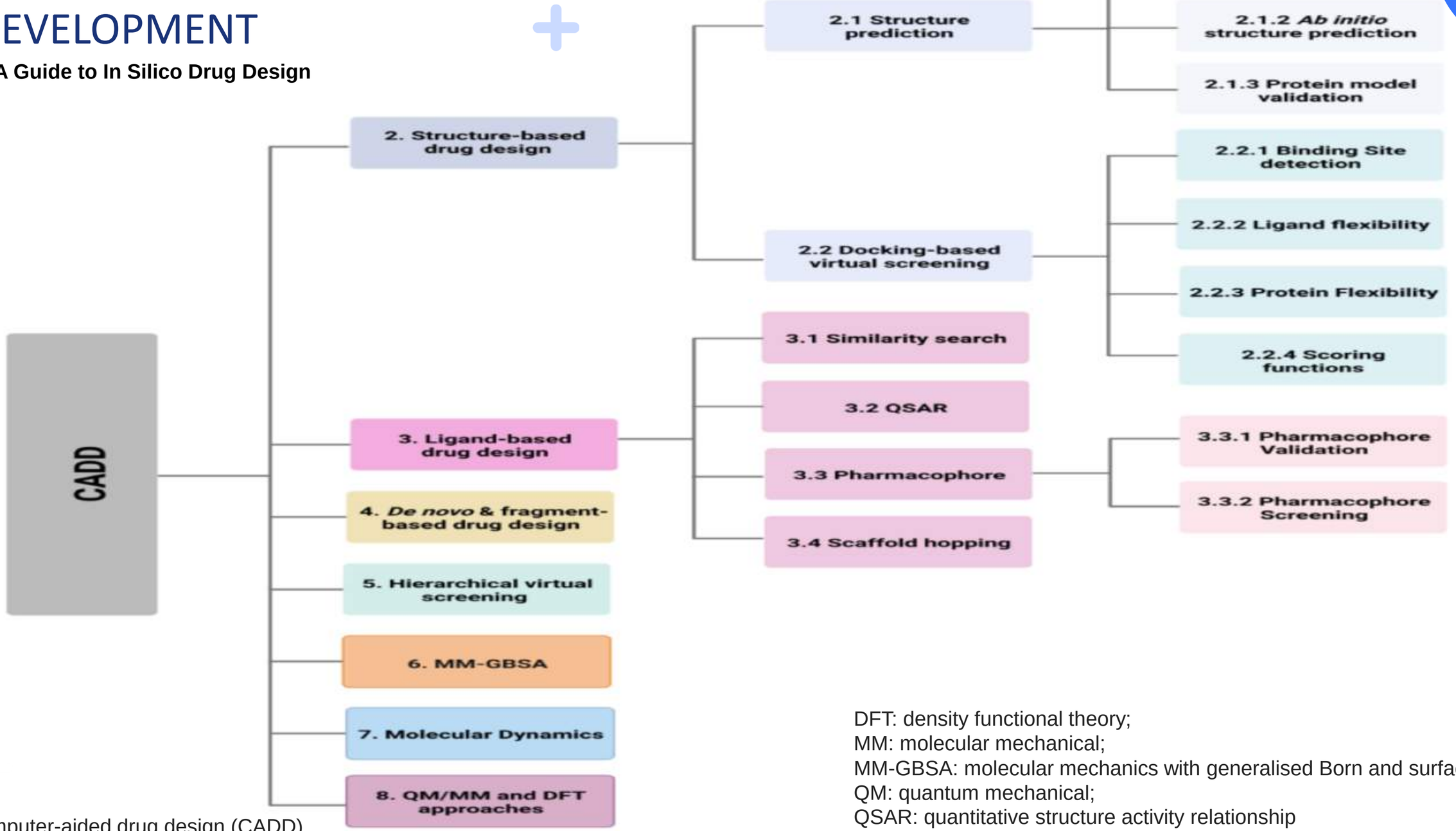
High throughput screening (HTS)


HTS for Drug Discovery
vHTS
HTS
SBDD
LBDD
In vitro assays
In vivo assays
Docking and Scoring
De-Novo drug design
QSAR
Pharmacophore modelling
Cell-based assays
Biochemical assays
Whole organism assay
Rigid docking
Induced-fit docking
2D-QSAR
3D-QSAR
Cell-proliferation
Enzyme inhibition assays
Receptor modulation assays
Steroid biosynthesis assays
CoMFA
CoMSIA
Cell-viability studies
Protein interactions
Transcription readouts
Polymerases
Proteases
Kinases
Lactamases
Gyrases
Ion channels
Kinase receptors
Nuclear receptors
GPCR


A
Tissue-diffusion chamber
drug in plasma
semipermeable membrane
homogenized tissue
B
Organ-on-chip
lung
blood channel
air channel
Kp, AUC tissue
Tissue selectivity
C
Body-on-chip
lung
heart
bone
kidney
liver
gut

PHARMACEUTICAL DEVELOPMENT

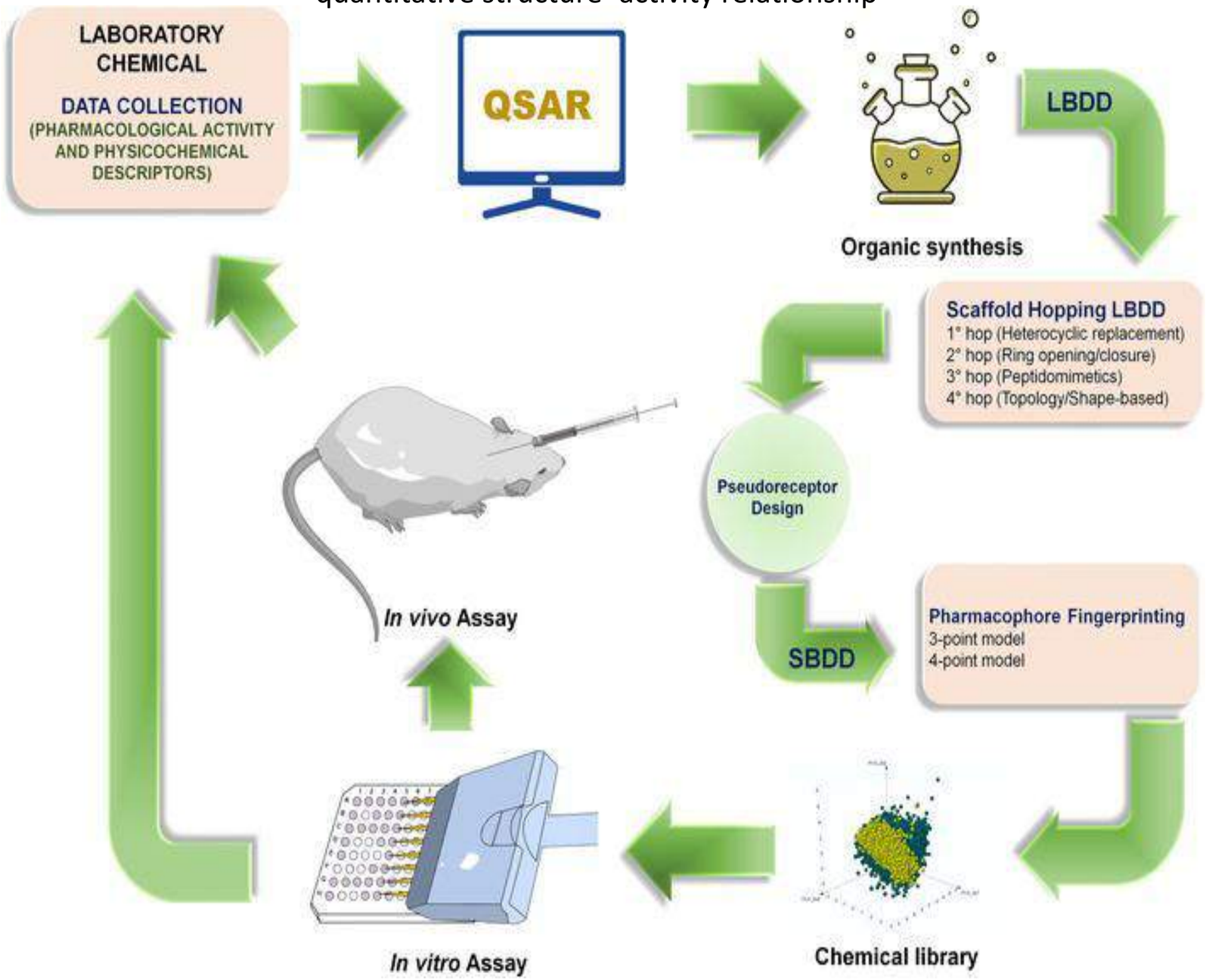
A Guide to In Silico Drug Design



Computer-aided drug design (CADD)

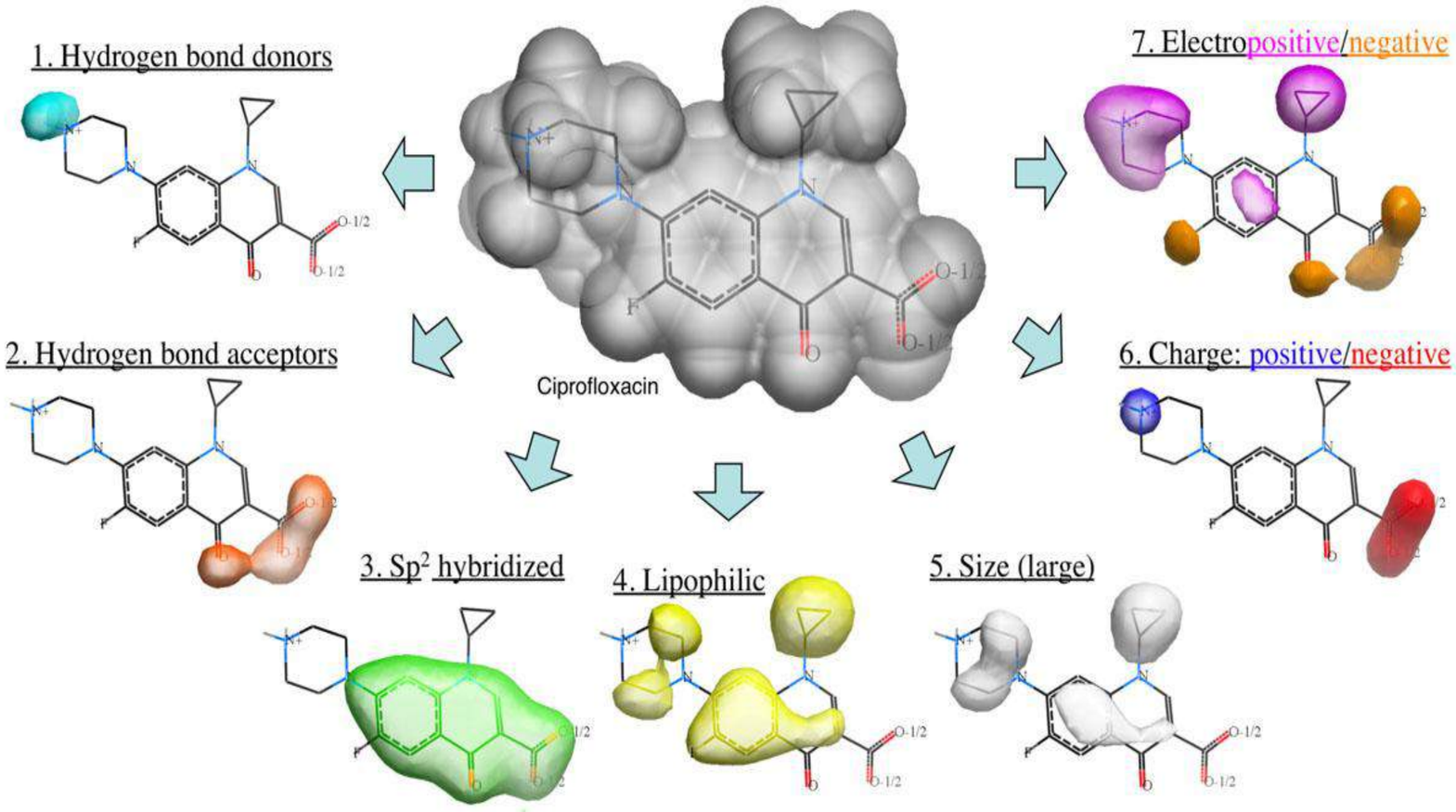
DFT: density functional theory;
MM: molecular mechanical;
MM-GBSA: molecular mechanics with generalised Born and surface area;
QM: quantum mechanical;
QSAR: quantitative structure activity relationship

quantitative structure–activity relationship



- **Pharmacophore fingerprinting** is a method to identify a common “pharmacophore feature” among a set of active drug or lead molecules that may be used in SBDD and/or LBDD.
- The pharmacophore feature is an essential chemical portion of lead/drug molecules which is required for biological functions and may include hydrogen bond donors/acceptors, aromatic rings, hydrophilic/hydrophobic attachments, or any possible combinations.
- These features are enumerated in terms of three-point and four-point sets of varied pharmacophores to measure the distance in terms of bonds.
- Pharmacophore fingerprints thus generated are utilized for developing novel lead molecules in combination with SBDD

LIGAND-BASED DRUG DESIGN



- **A ligand is a molecule that binds to a receptor.**
- **LBDD → Explores the chemical and structural features of known ligands (molecules that bind to a target) to understand the interactions that lead to biological activity.**

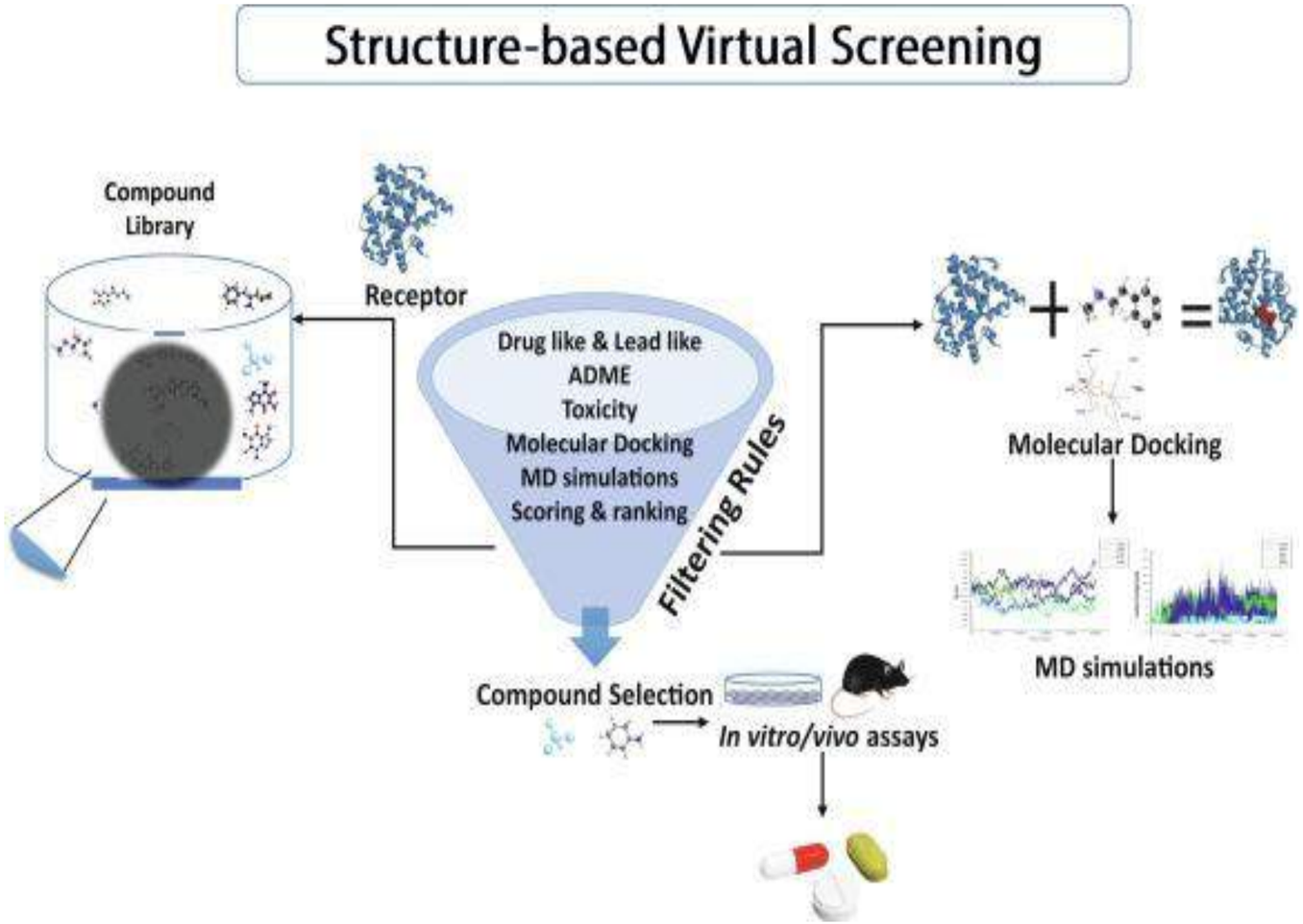
Ligand-based virtual screening can be performed using the Atomic Property Field (APF) method developed by MolSoft

STRUCTURE-BASED DRUG DESIGN

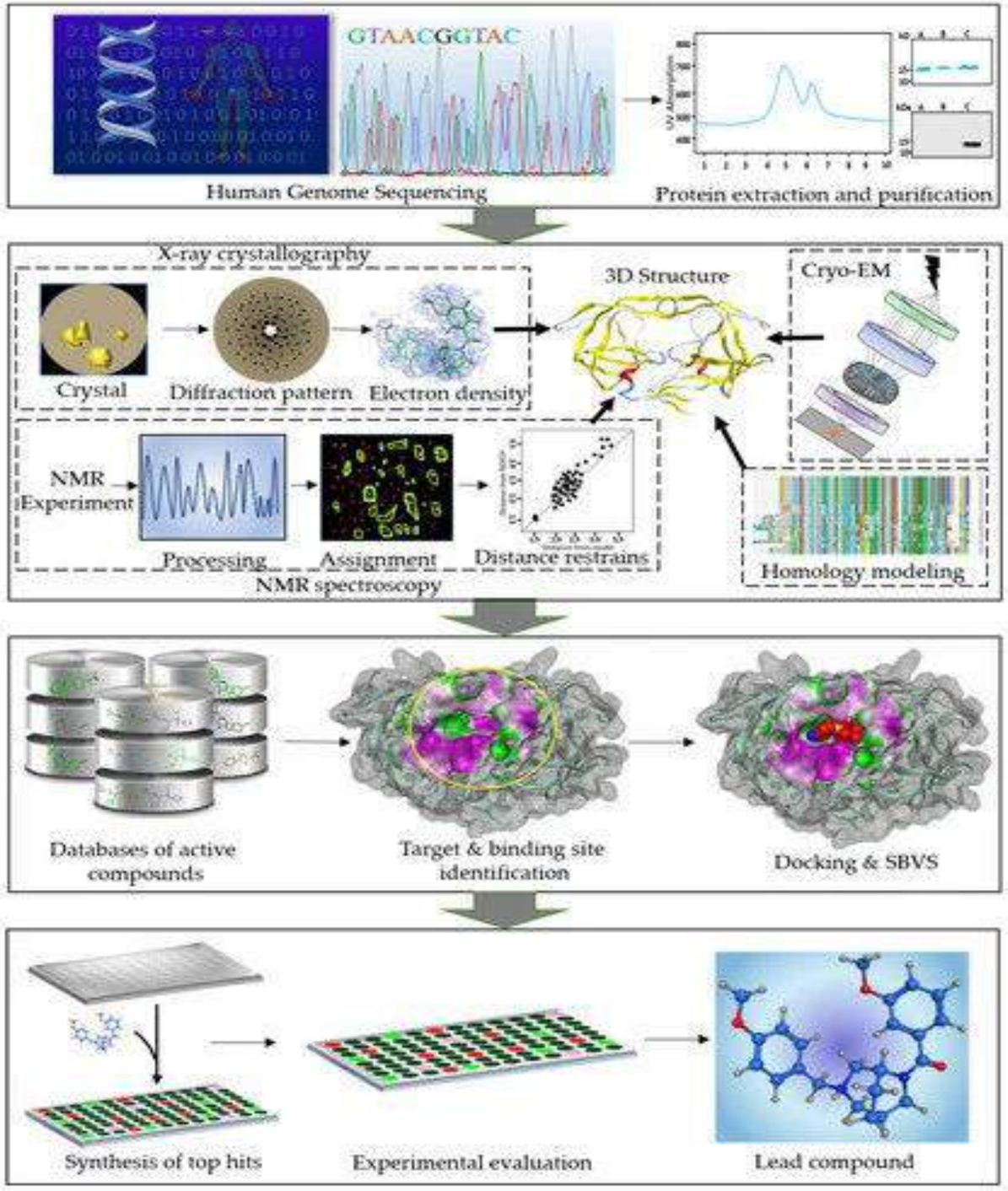
Uses the 3D structure of the target protein (e.g., enzyme, receptor) to design new ligands that bind specifically and effectively.

Among the relevant computational techniques, structure-based virtual screening (SBVS), molecular docking, and molecular dynamics (MD) simulations are the most common methods used in SBDD.

These methods have numerous applications in the analysis of binding energetics, ligand–protein interactions, and evaluation of the conformational changes occurring during the docking process



STRUCTURE-BASED DRUG DESIGN

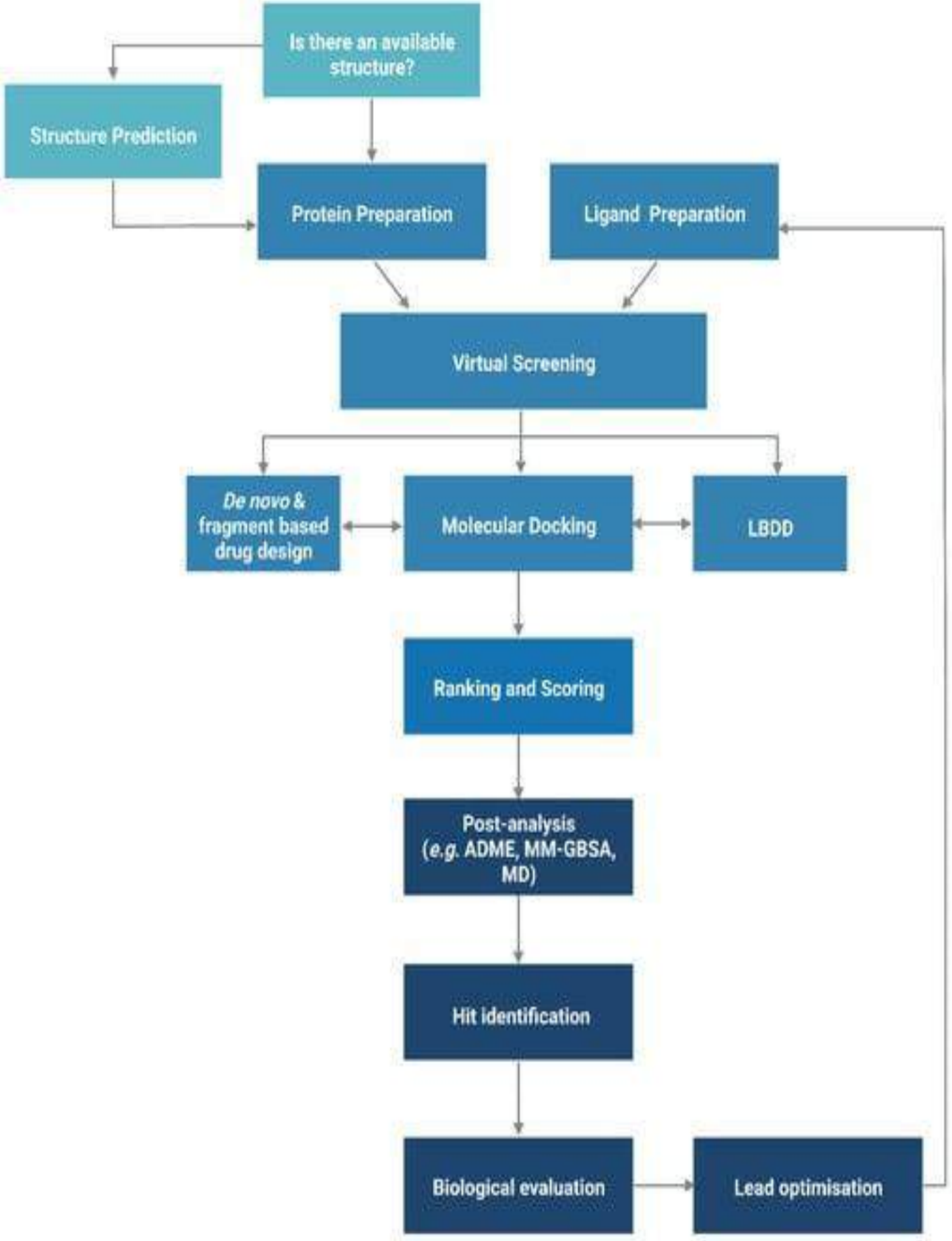


In conjunction with the storage of (and organizing) such data, there has been much hype about the development of sophisticated and robust computational techniques.

Completion of the Human Genome Project and advances in bioinformatics increased the pace of drug development because of the availability of a huge number of target proteins.

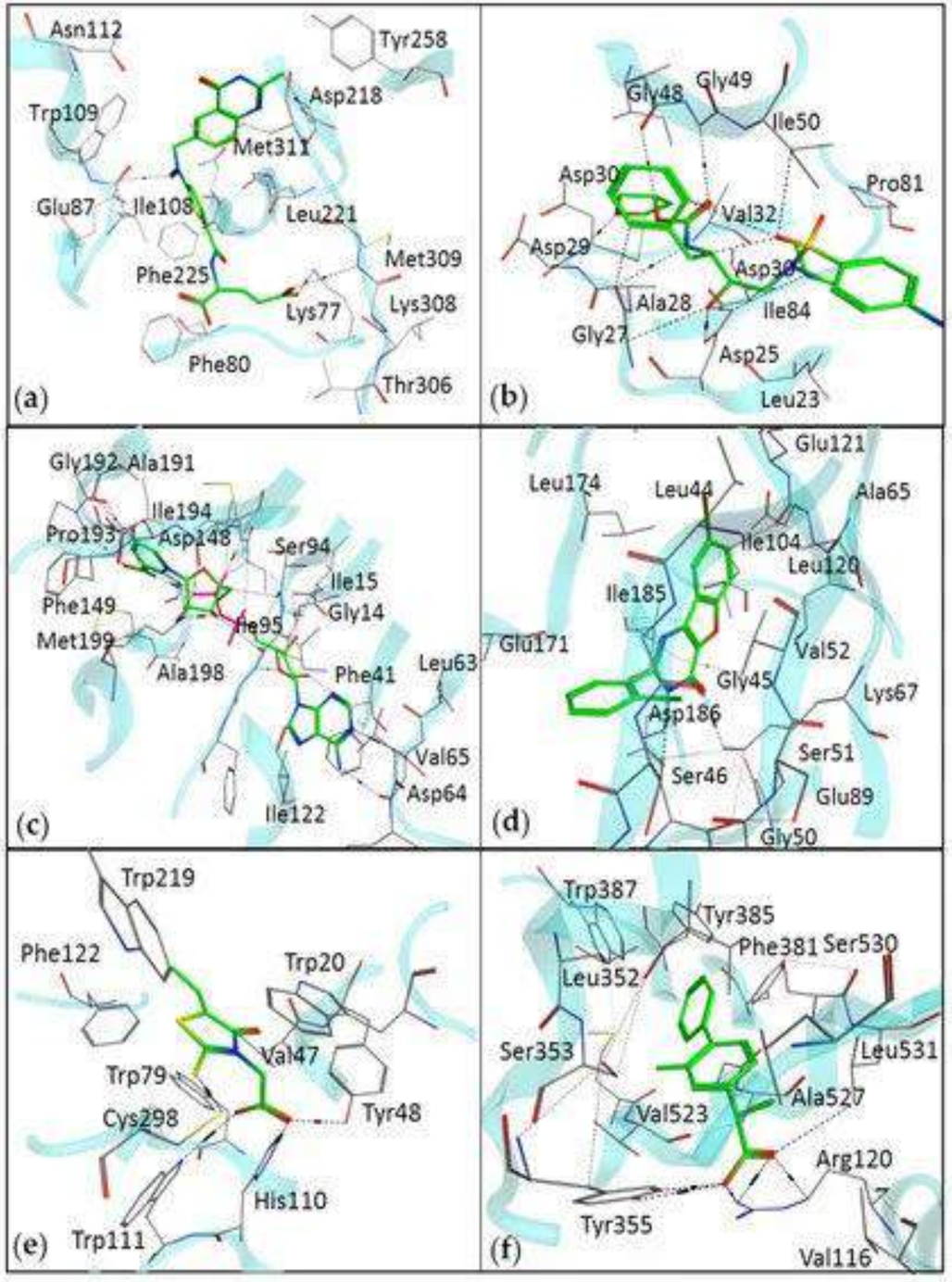
The availability of 3D structures of therapeutically important proteins favors identification of binding cavities and has laid the foundation for structure-based drug design (SBDD).

SBDD is a more specific, efficient, and rapid process for lead discovery and optimization because it deals with the 3D structure of a target protein and knowledge about the disease at the molecular level.



https://youtu.be/TTtrk0Ue-Cg?t=46

STRUCTURE-BASED DRUG DESIGN



The interaction diagram of drugs identified by SBDD methods, with their respective therapeutic targets.

- (**a**) An interaction of raltitrexed with thymidylate synthase (Protein Data Bank (PDB) ID: 5X5Q).
- (**b**) An interaction of amprenavir with HIV protease (PDB ID: 3EKV).
- (**c**) Isoniazid, a drug for tuberculosis, identified by the SBVS method (PDB ID: 1ENY).
- (**d**) Pim-1 kinase inhibitor, benzofuropyrimidine, for the treatment of various types of cancers (PDB ID: 4ALU).
- (**e**) Epalrestat is an aldose reductase inhibitor (PDB ID: 4JIR).
- (**f**) Flurbiprofen is a cyclooxygenase 2 inhibitor (PDB ID: 3PGH).

PHARMACEUTICAL DEVELOPMENT

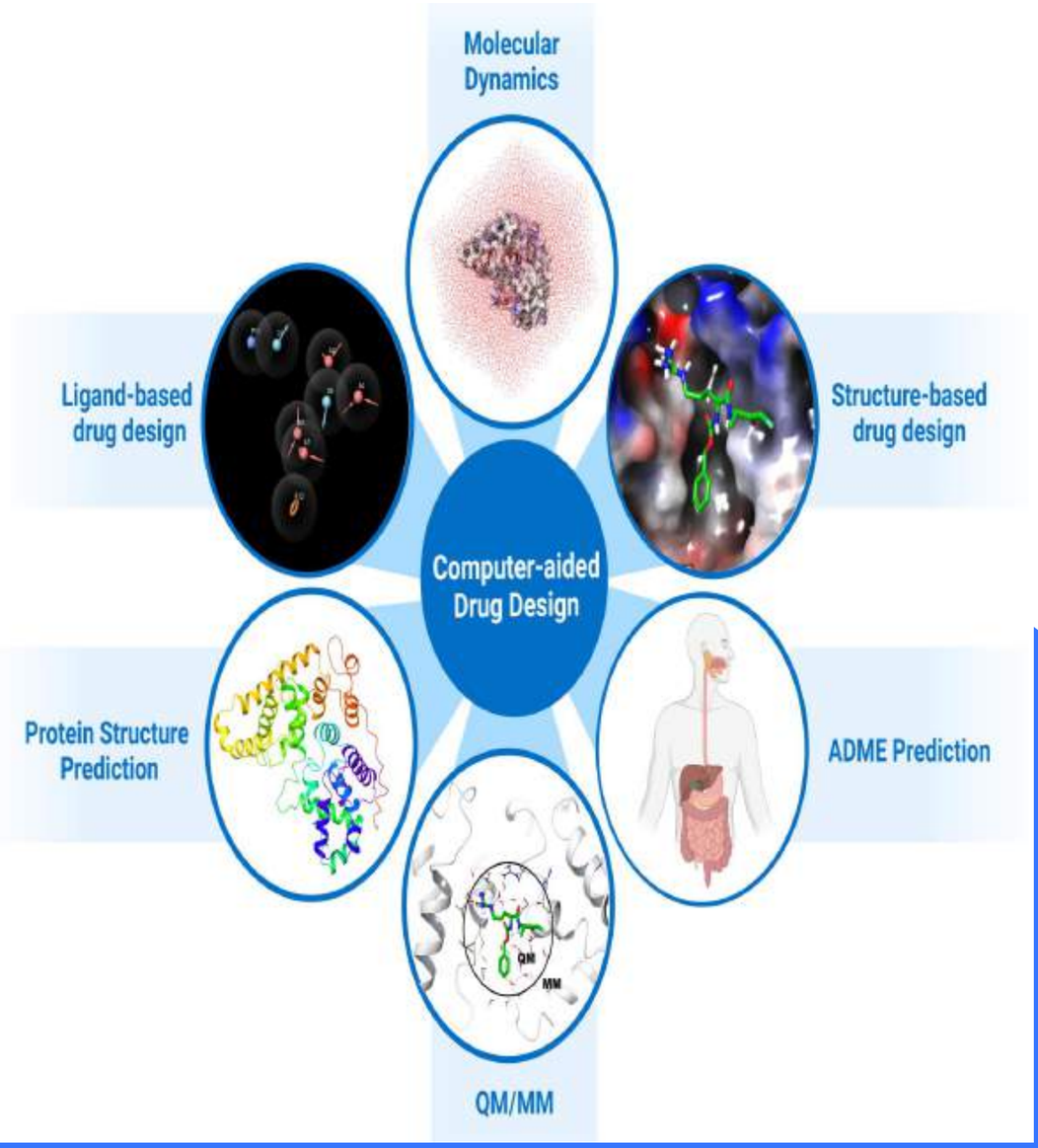


Table 1. The success cases of drug discovery by SBDD methods.

Drug	Drug Target	Target Disease	Technique
Raltitrexed	Thymidylate synthase	Human immunodeficiency virus (HIV)	SBDD
Amprenavir	Antiretroviral protease	HIV	Protein modeling and molecular dynamics (MD)
Isoniazid	InhA	Tuberculosis	Structure-based virtual screening (SBVS) and pharmacophore modeling
Pim-1 Kinase Inhibitors	Pim-1 Kinase	Cancer	Hierarchical multistage virtual screening (VS)
Epalrestat [2]	Aldose Reductase	Diabetic neuropathy	MD and SBVS
Flurbiprofen	Cyclooxygenase-2	Rheumatoid arthritis, Osteoarthritis	Molecular docking
STX-0119	STAT3 [1]	Lymphoma	SBVS
Norfloxacin	Topoisomerase II, IV	Urinary tract infection	SBVS
Dorzolamide	Carbonic anhydrase	Glaucoma, cystoid macular edema	Fragment-based screening

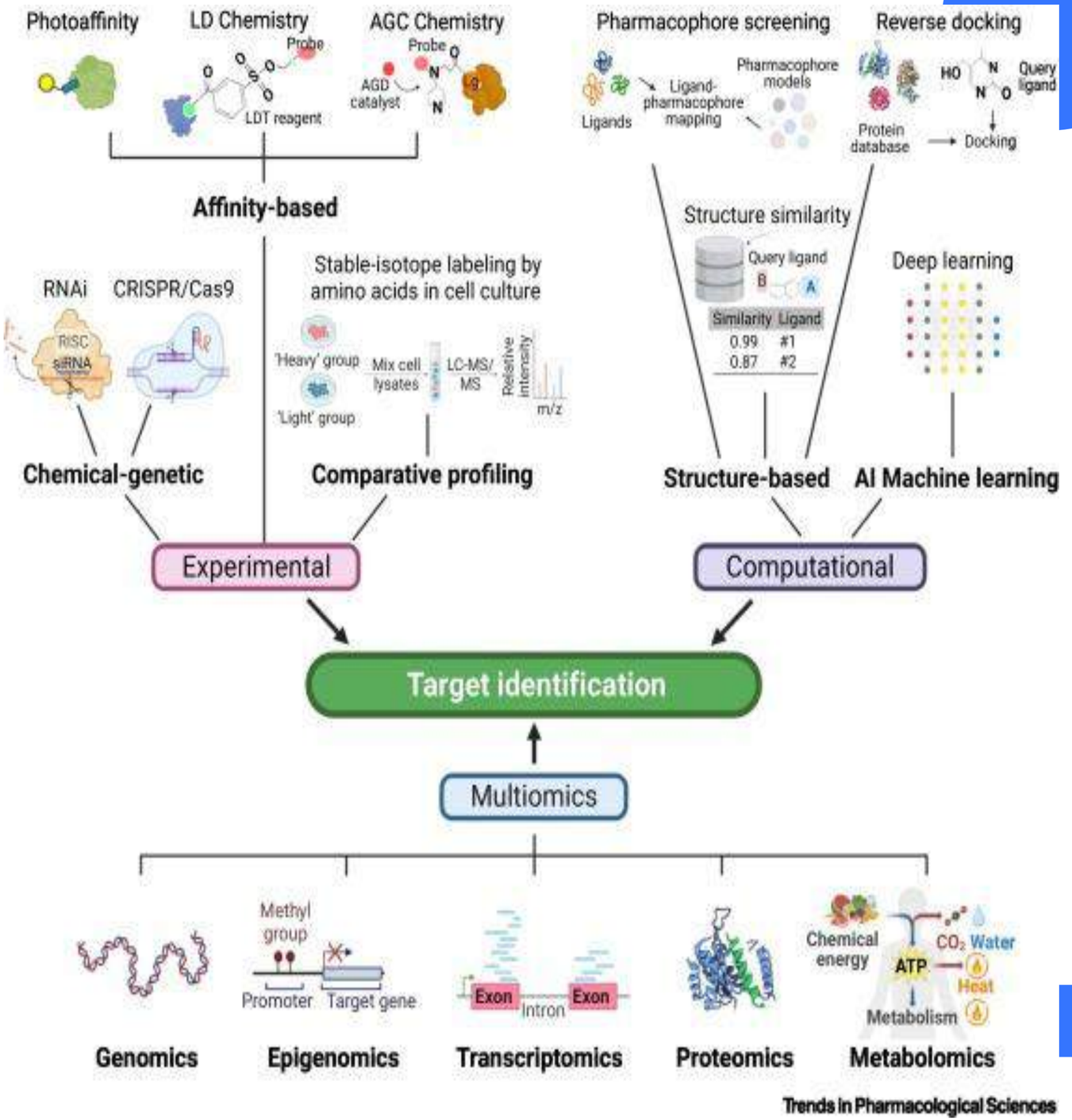
[1] Signal transducers and transcription activators (STATs). [2] Currently being sold in Japan under the brand name Kinedak®.

TUJUAN DAN TARGET

Several types of biomolecules can serve as therapeutic targets, including enzymes, cellular receptors, ion channels, DNA, and transcription factors

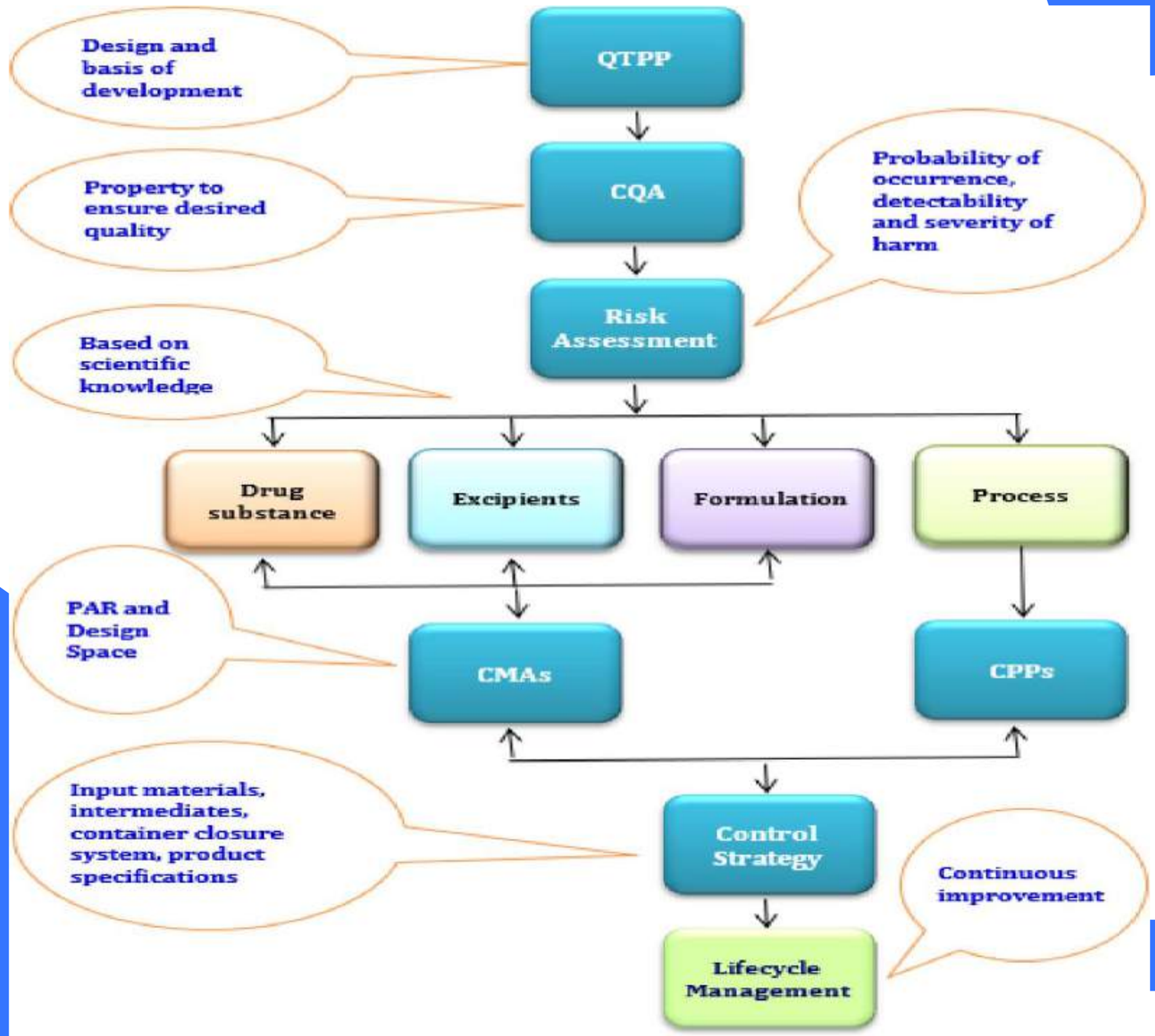
Due to this vast diversity of proteins and other chemicals present in a cell, identifying a specific biological target for a given drug can be extremely difficult.

The machine-based and biological experimental-based approaches facilitate the identification of probable drug targets.



PHARMACEUTICAL DEVELOPMENT

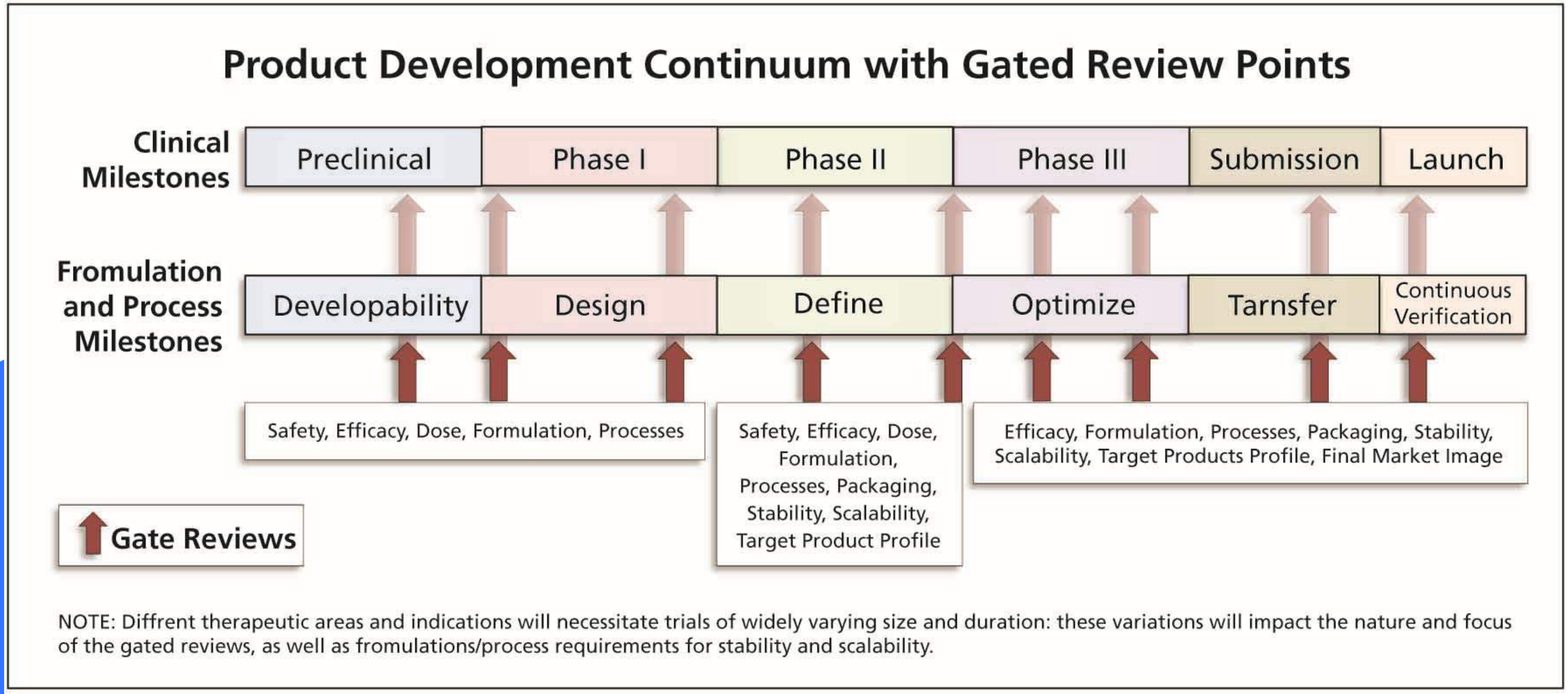
Quality-by-Design (QbD)



PHARMACEUTICAL DEVELOPMENT

+

Quality-by-Design (QbD)



At pre-specified pivot points in clinical and formulation development, a host of product features must be thoroughly reviewed to minimize risks and prepare for efficient scale up/feasibility.

PHARMACEUTICAL DEVELOPMENT

Quality-by-Design (QbD)

Tablet dosage form

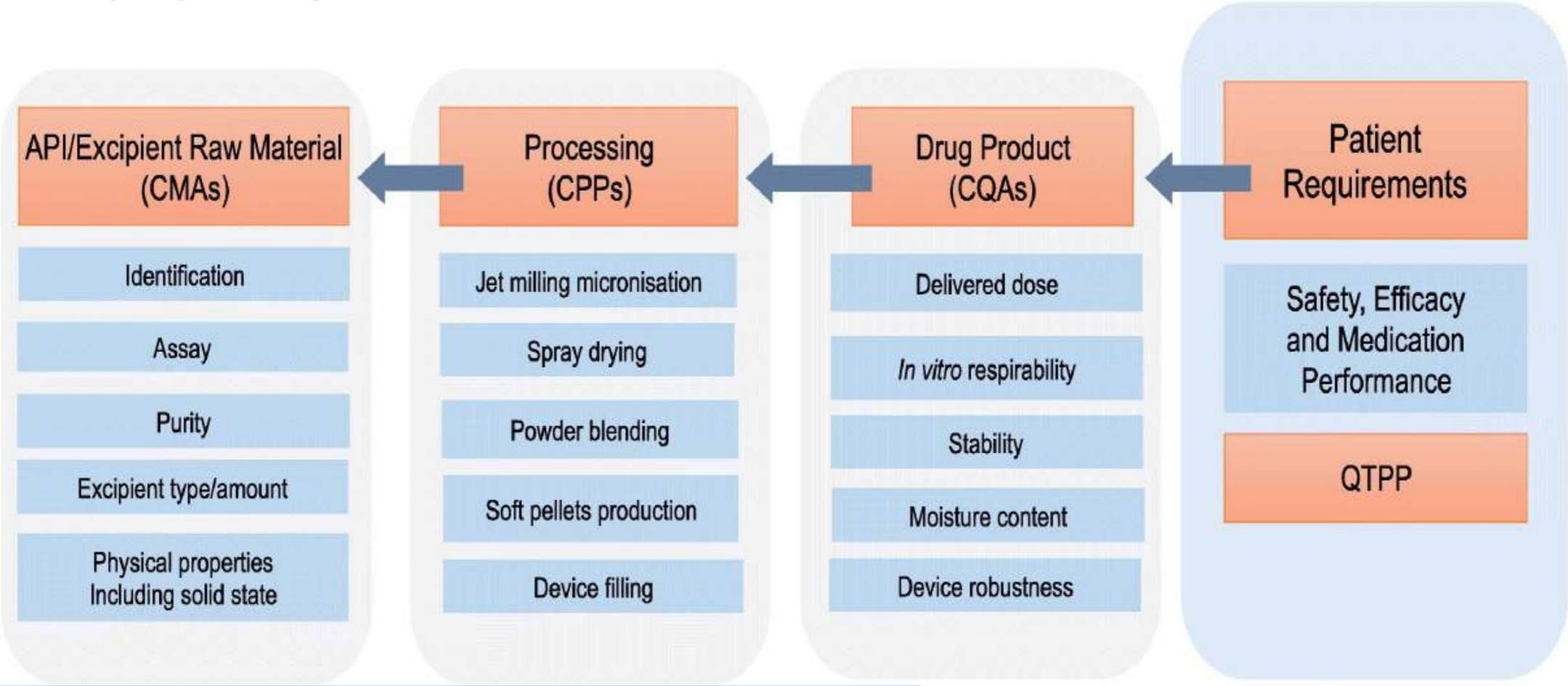
Table 1: Outline of Quality Target Product Profile

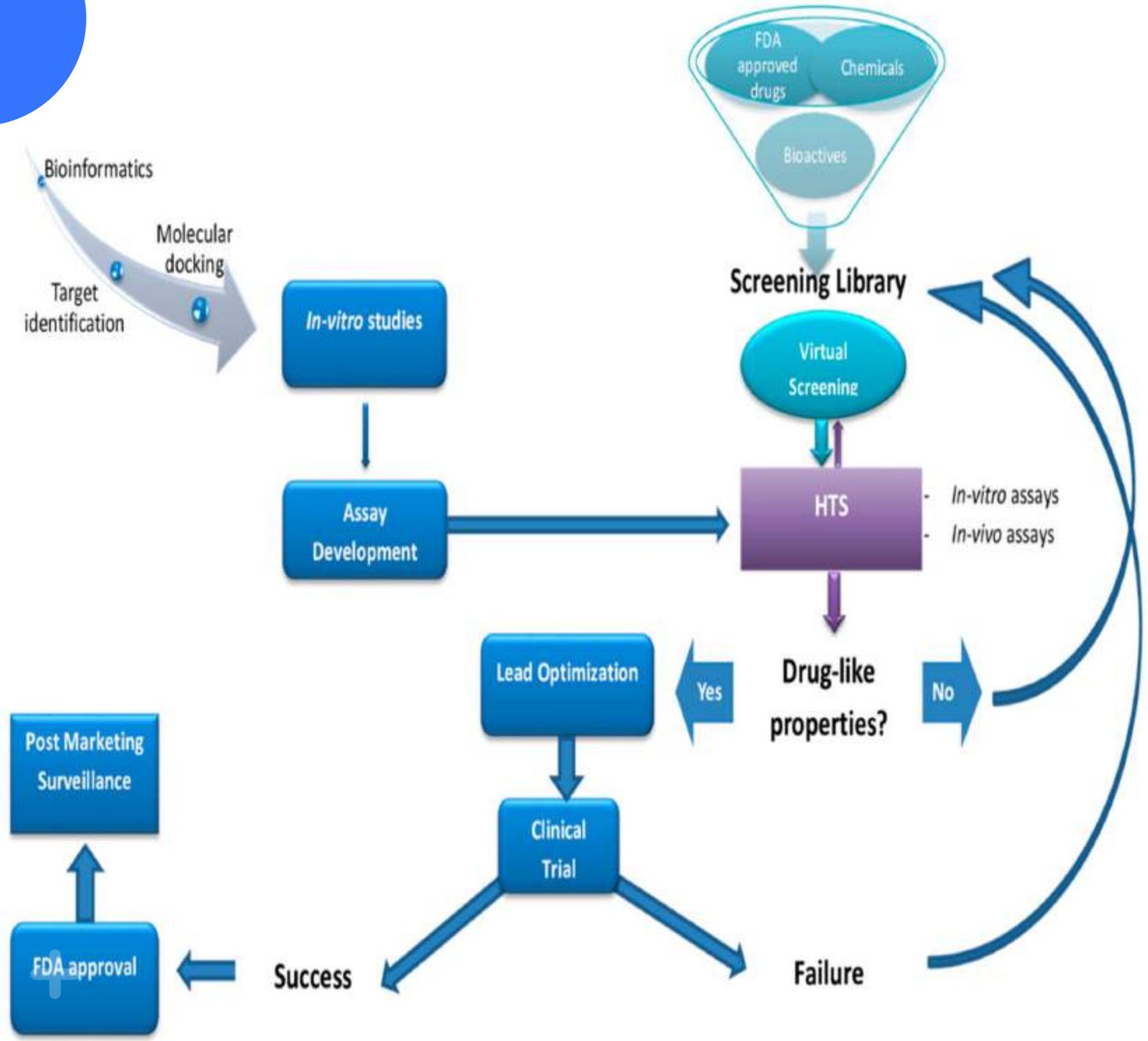
Elements		Target	Rationale
Dosage form		Immediate - release tablets or capsules Delayed –release tablets Extended - release tablets or capsules Dispersible Tablets Chewable tablets	Dosage form should be same as a requirement of Pharmaceutical Equivalence.
Administration		Oral route	Route of administration should be same as a requirement of Pharmaceutical Equivalence.
Alternative methods of administration		Administration via enteral tube	If labeling of reference product indicates drug product's suitability for administration via enteral tube.
Dose strengths		Strength as per reference product label.	Strength should be same as a requirement of Pharmaceutical Equivalence.
Pharmacokinetics		Bioequivalent to the reference product	Bioequivalence requirement.
Stability		Mention desired or expected shelf life and storage condition for your proposed drug product.	Equivalent to or better than reference product shelf-life. Preferably, can be stored at room temperature.
Drug product quality attributes	Physical attributes	Must meet the applicable quality standards for solid oral dosage forms.	
	Identification		
	Assay		
	Uniformity of dosage units		
	Dissolution		
	Organic impurity		
	Elemental impurity		
	Nitrosamine impurity		
	Water content		
	Residual solvents		
Container closure system		Mention desired or intended packaging system (bottle, blister, strip packaging etc.)	Drug product stability shall be ensured in proposed packaging system.

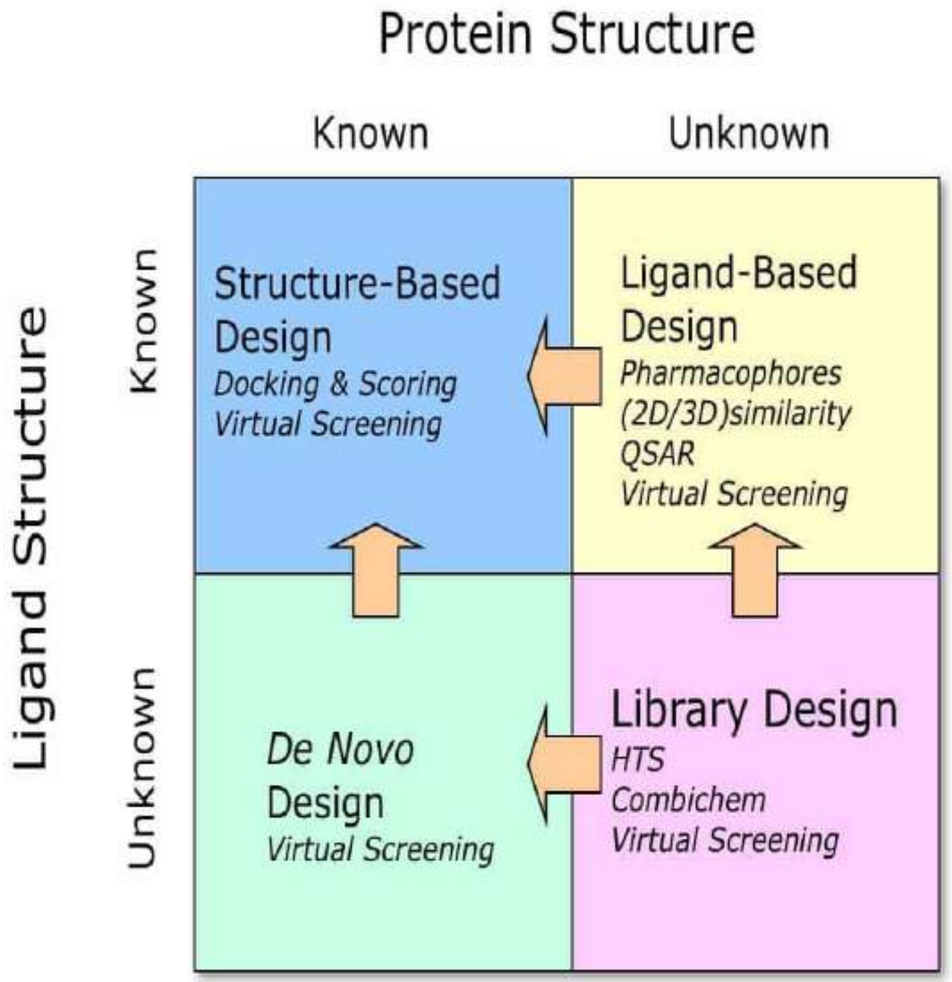
PHARMACEUTICAL DEVELOPMENT

Quality-by-Design (QbD)

Powder dosage form

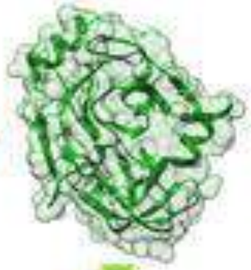



FDA approved drugs
Chemicals
Bioactives
Screening Library
Bioinformatics
Molecular docking
Target identification
In-vitro studies
Virtual Screening
Assay Development
HTS
In-vitro assays
In-vivo assays
Drug-like properties?
Yes
No
Lead Optimization
Clinical Trial
Success
Failure
FDA approval
Post Marketing Surveillance


Protein Structure
Known
Unknown
Ligand Structure
Known
Unknown
Structure-Based Design
Docking & Scoring
Virtual Screening
Ligand-Based Design
Pharmacophores
(2D/3D)similarity
QSAR
Virtual Screening
De Novo Design
Virtual Screening
Library Design
HTS
Combichem
Virtual Screening

Genome sequence analysis

Protein expression analysis



Protein isolation

Structure Determination (NMR/Crystallography)

Target Identification

Target Optimization

In vitro Assay Development

Post marketing surveillance

FDA Approval

Success

Preclinical/ clinical trails

Lead optimization

YES

Drug like properties

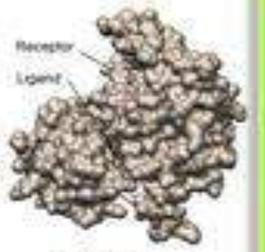
NO

Chemical Library generation

- Combinatorial Library
- Isolated Natural Products Library
- FDA Approved Drugs
- Chemicals (Fragment Based Drug Design)
- Virtually Structure Based Designed Chemical Libraries

Herbal extract

Bioassay Guided Isolation



Virtual High Throughput Screening (vHTS)

Lead like molecules

Toxicity

ADME

Shortlist

Ligand

High throughput screening

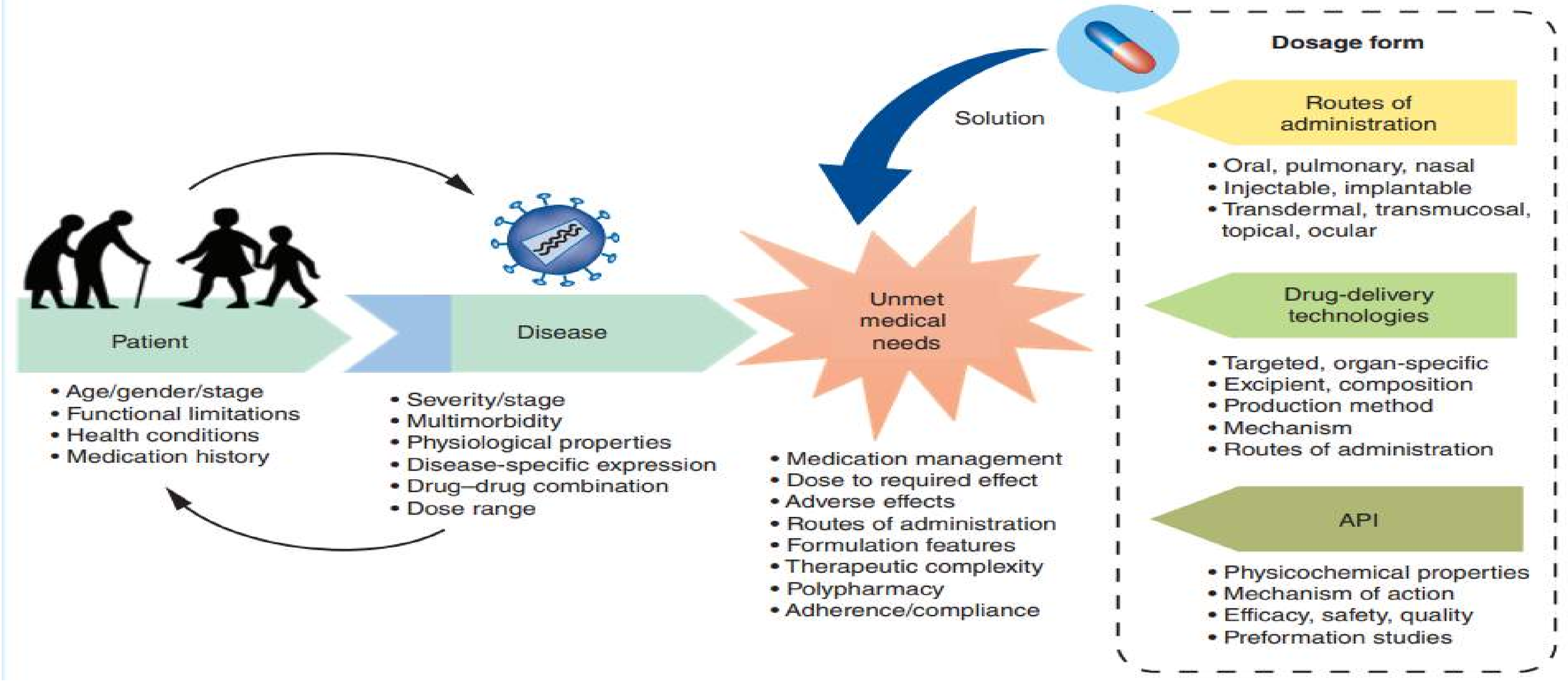
In vitro and *In vivo* assay

Bioassay guided isolation

Isolation and characterization of natural products

HTS guided chromatography

DDS


Patient
• Age/gender/stage
• Functional limitations
• Health conditions
• Medication history
Disease
• Severity/stage
• Multimorbidity
• Physiological properties
• Disease-specific expression
• Drug–drug combination
• Dose range
Unmet medical needs
• Medication management
• Dose to required effect
• Adverse effects
• Routes of administration
• Formulation features
• Therapeutic complexity
• Polypharmacy
• Adherence/compliance
Solution
Dosage form
Routes of administration
• Oral, pulmonary, nasal
• Injectable, implantable
• Transdermal, transmucosal, topical, ocular
Drug-delivery technologies
• Targeted, organ-specific
• Excipient, composition
• Production method
• Mechanism
• Routes of administration
API
• Physicochemical properties
• Mechanism of action
• Efficacy, safety, quality
• Preformation studies

DDS

Conventional Drug Delivery Systems

Limitations

- Poor absorption from target site
- Poor Bioavailability
- High First-pass Metabolism
- Fluctuations in Plasma drug level
- Premature excretion from the body
- Repeated dosing
- High dose dumping

Delivery

Conventional Delivery → Targeted Delivery → Site Specific Intracellular Delivery → Tissue Engineering

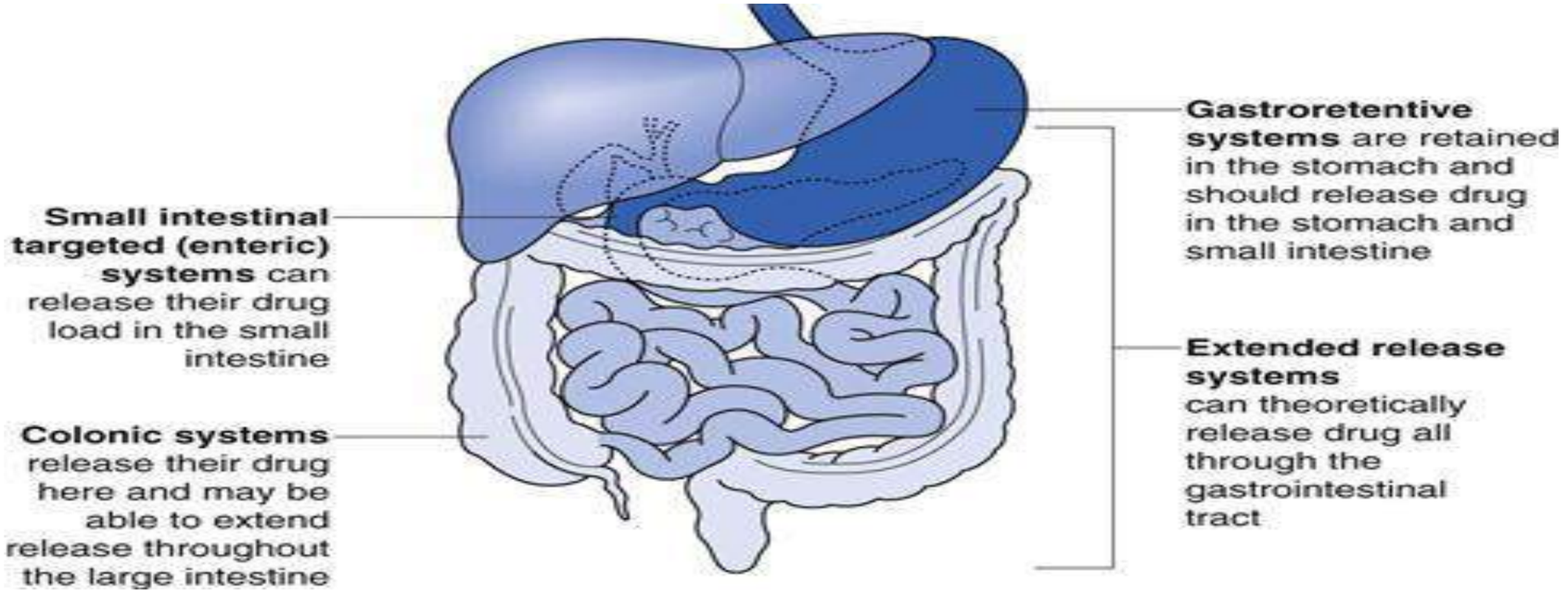
Therapeutic Modality

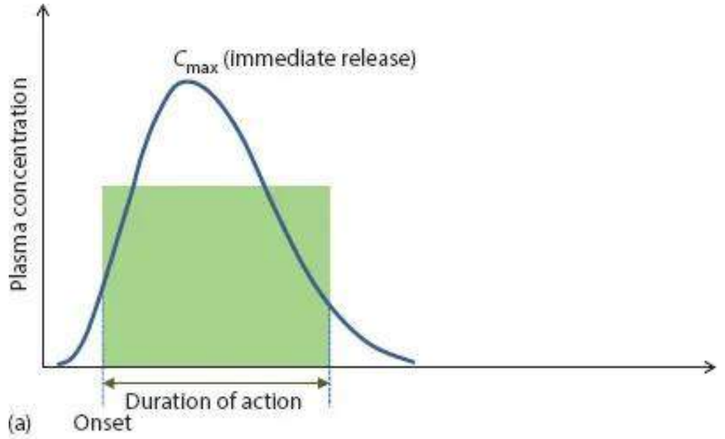
Small molecules Antibodies Peptides for extracellular targets Antisense oligonucleotides	**Nanoparticles** Antibody Drug Conjugates Ligand targeted	ASO siRNA mRNA saRNA CRISPR/Cas9	Stem cells Engineered T cells Engineered Macrophages Engineered NK cells

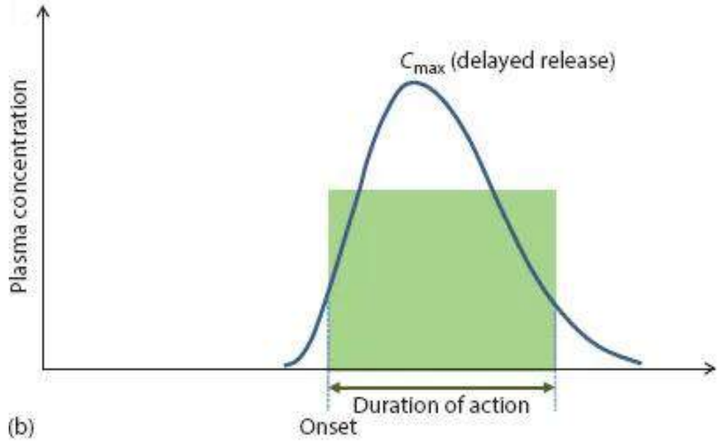
First generation → Second generation → Third generation → Fourth generation

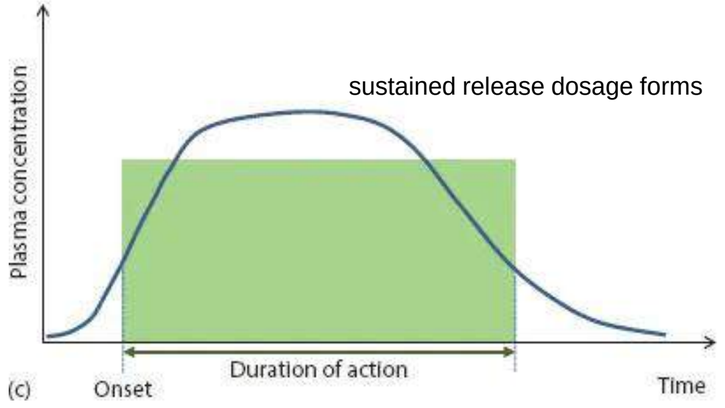
DDS

- Modified release DDS
  - Controlled release
    - Sustained release
    - Extended release
  - Delayed release
    - Prolonged release



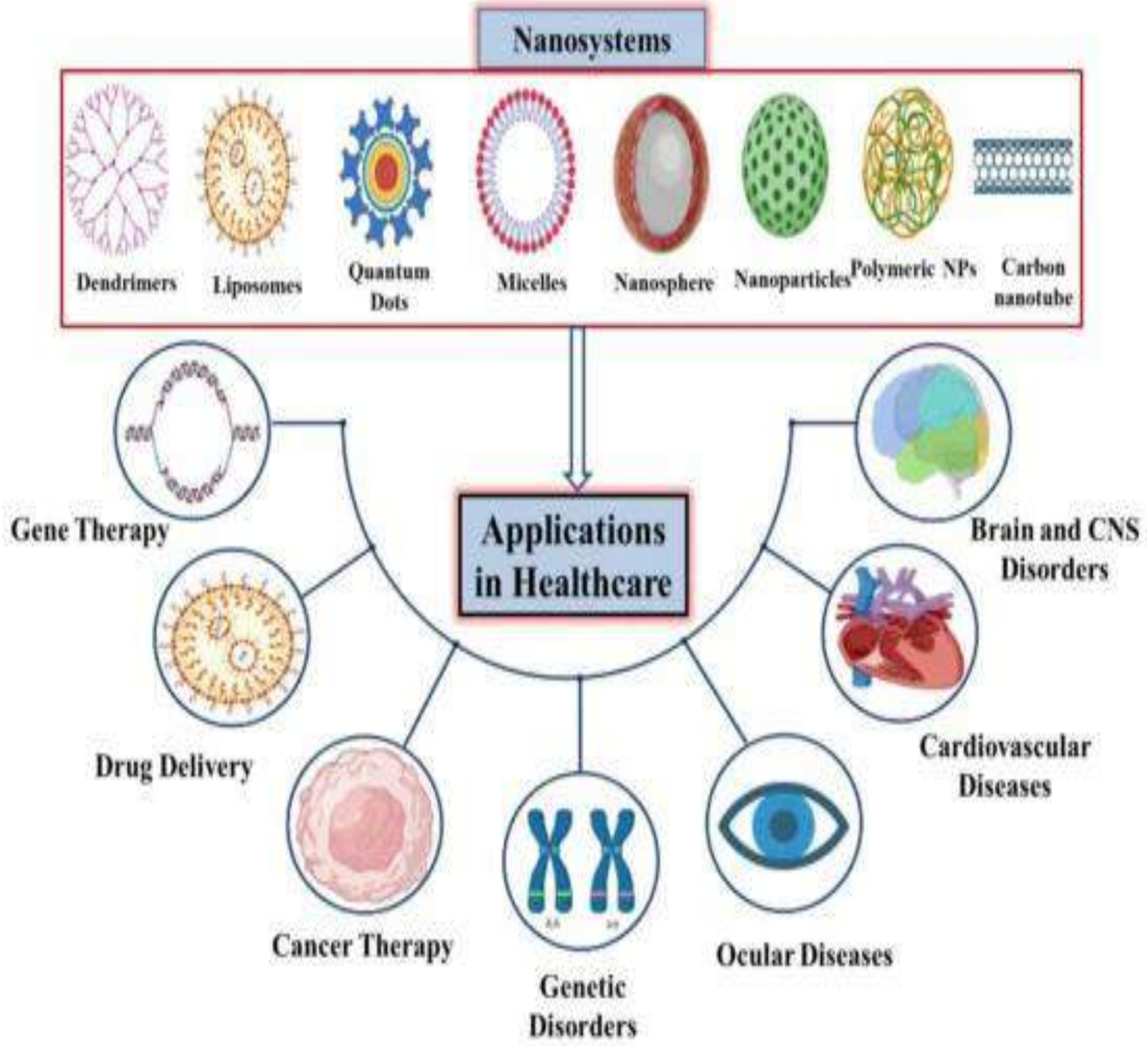


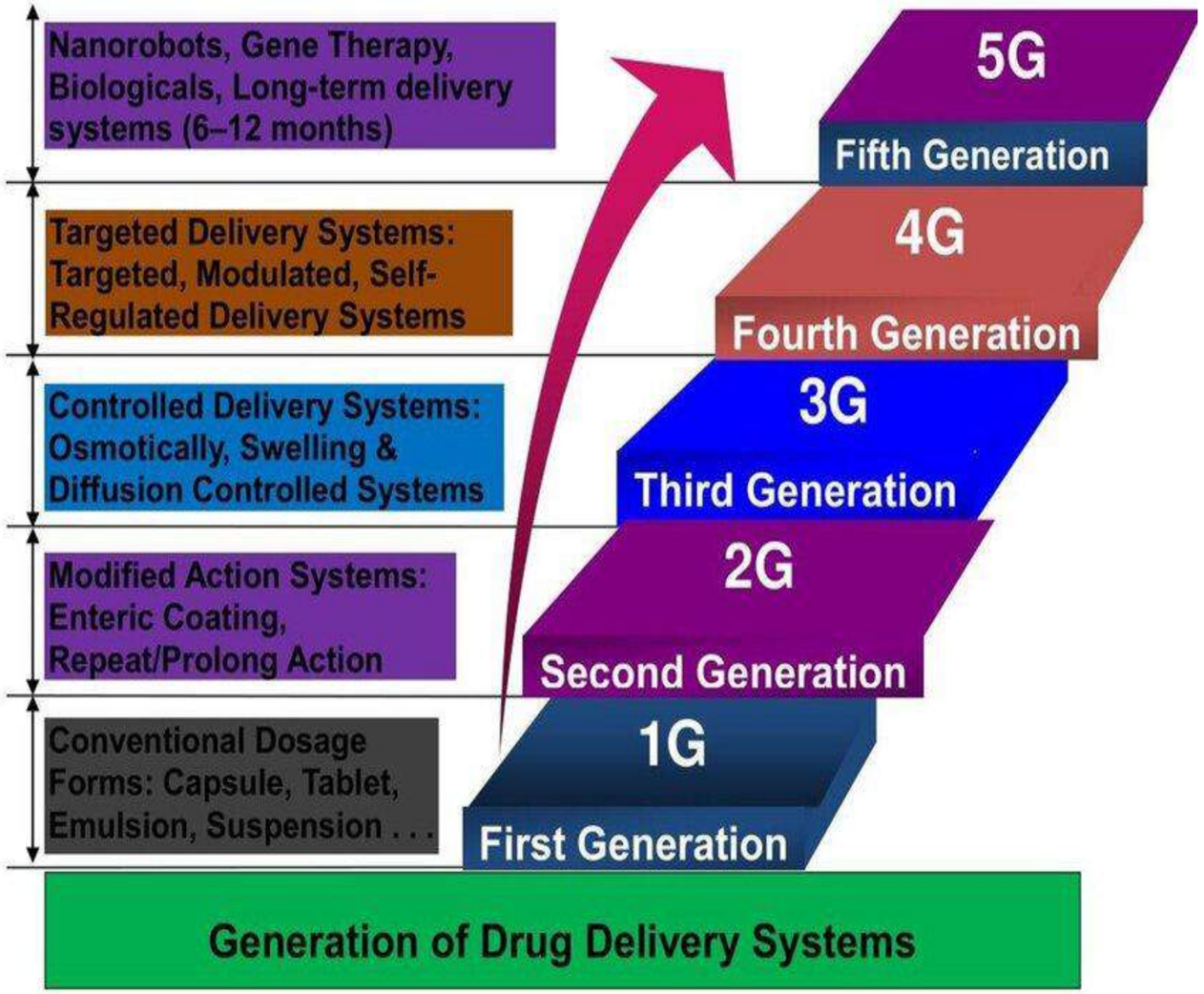




DDS

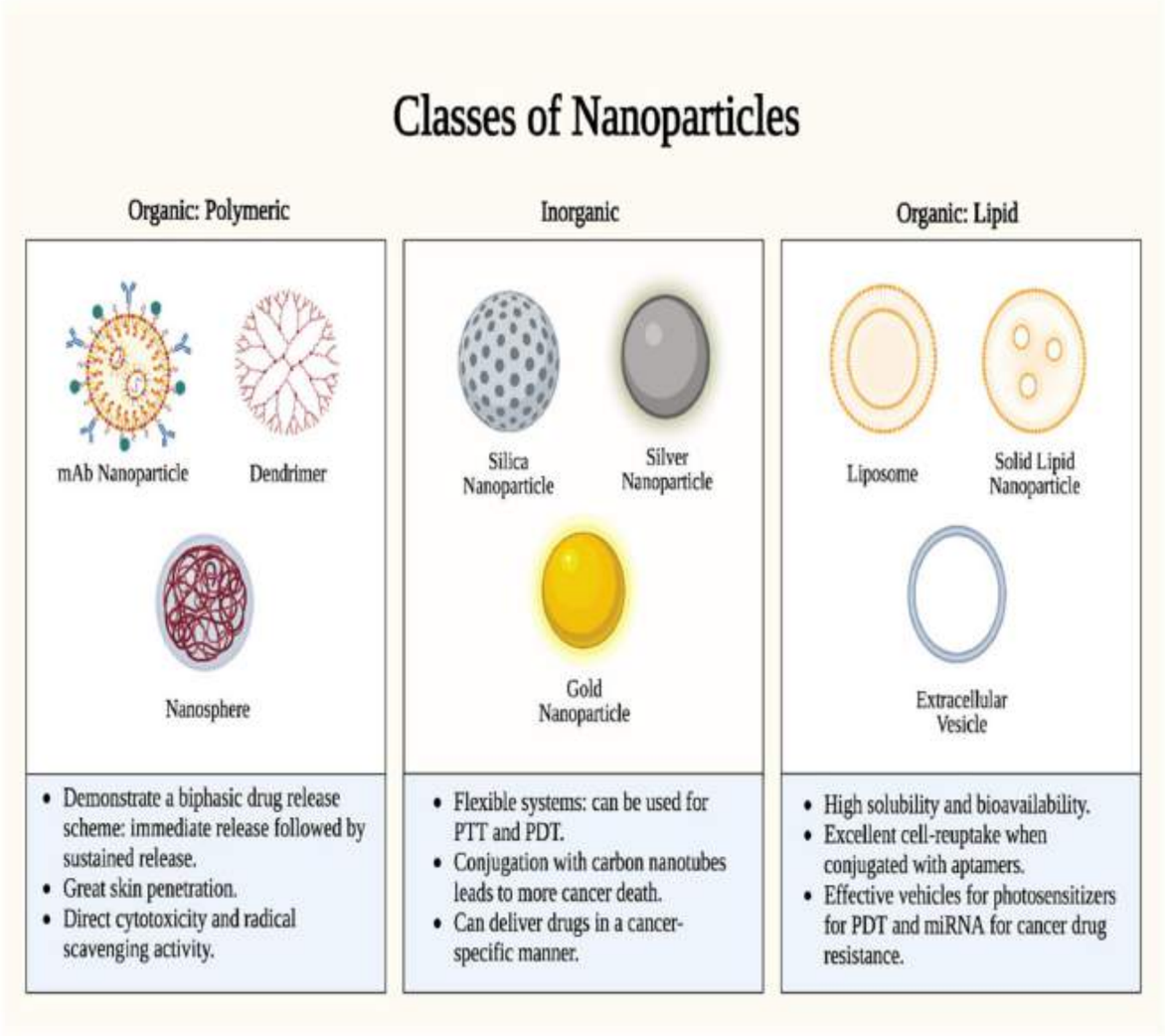
Next-generation drug delivery focuses on precise, targeted, and controlled release of therapeutics, utilizing nanotechnology, biomaterials, and advanced technologies to enhance efficacy and minimize side effects

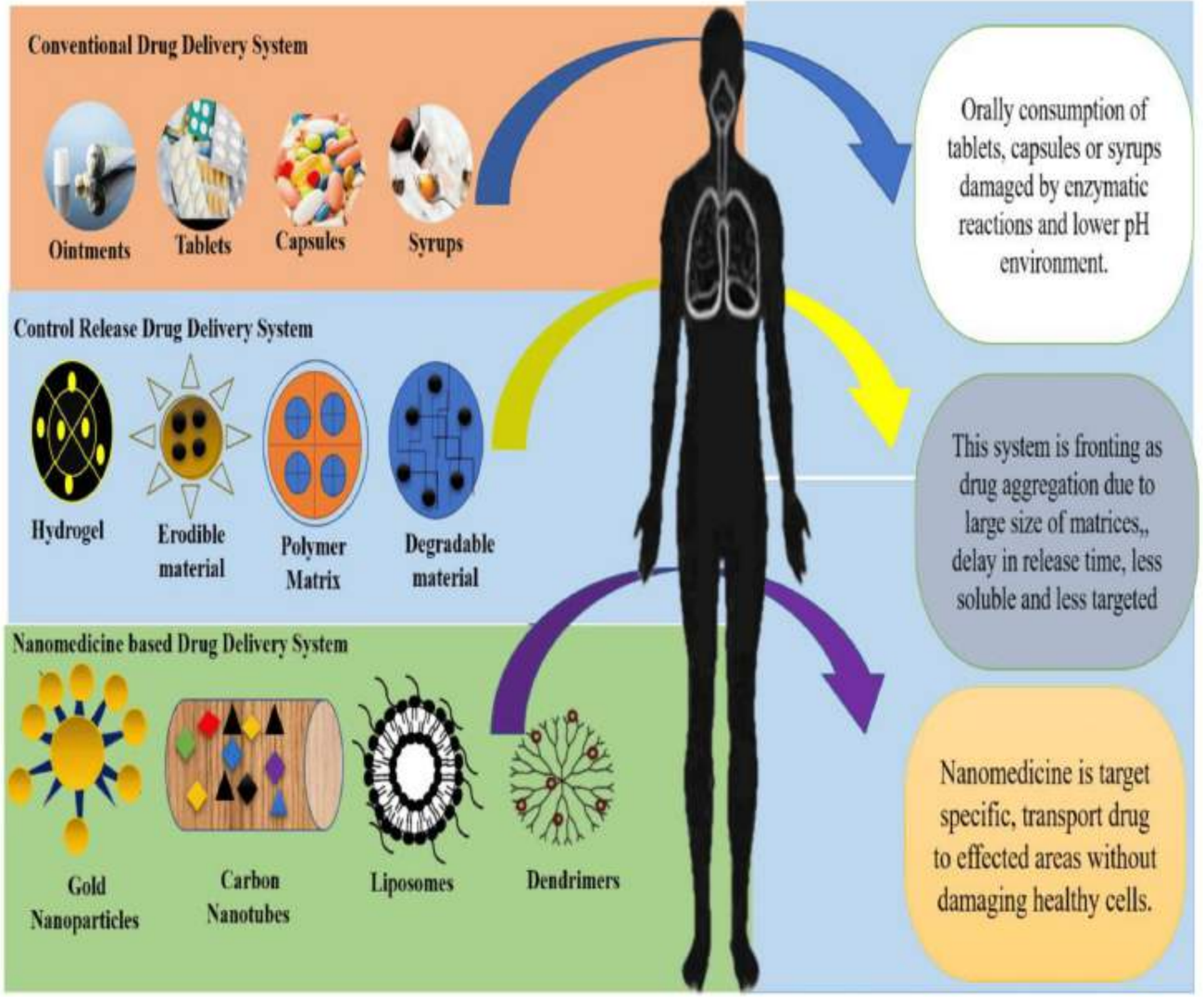




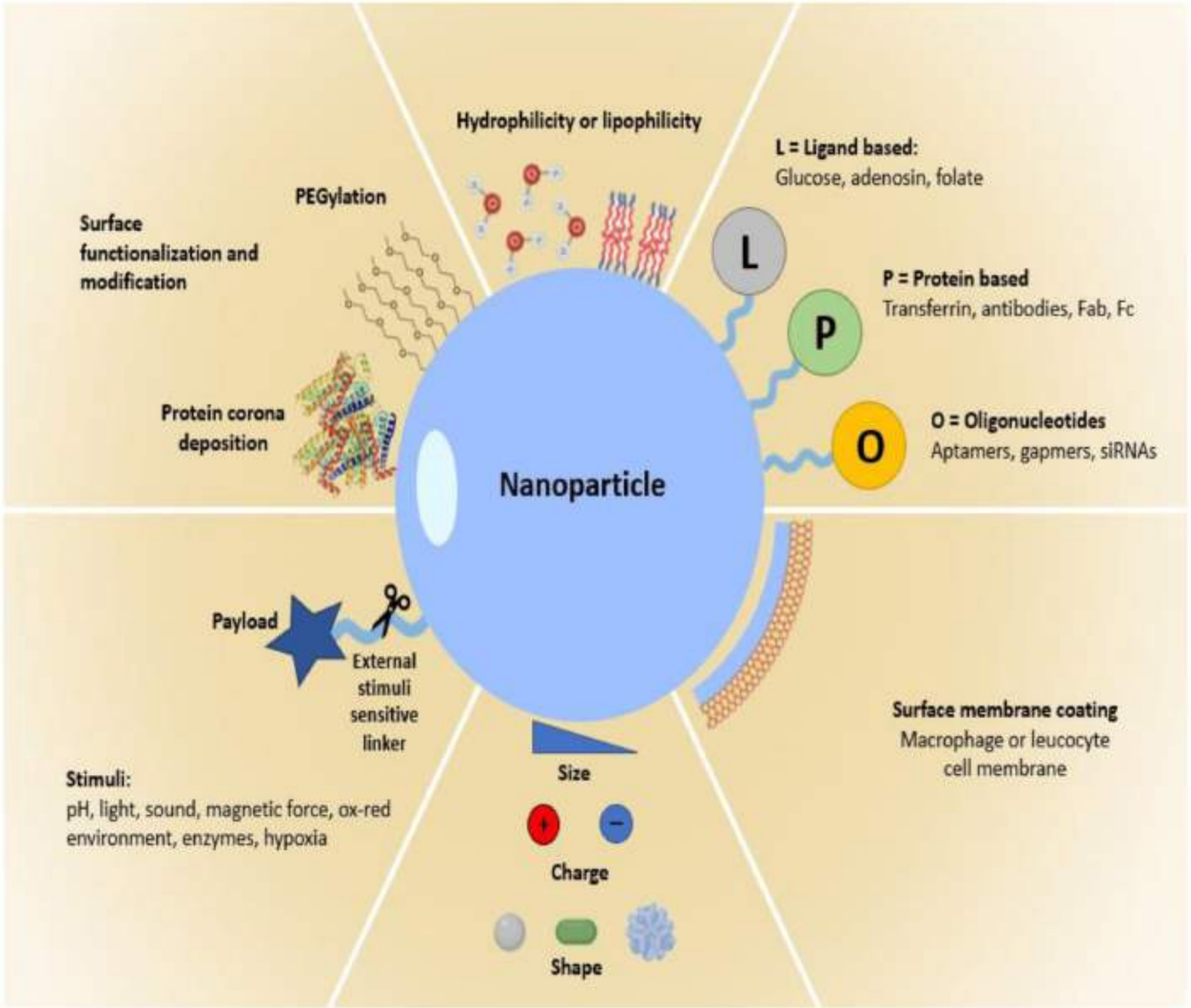
DDS

Next-generation drug delivery focuses on precise, targeted, and controlled release of therapeutics, utilizing **nanotechnology**, biomaterials, and advanced technologies to enhance efficacy and minimize side effects.



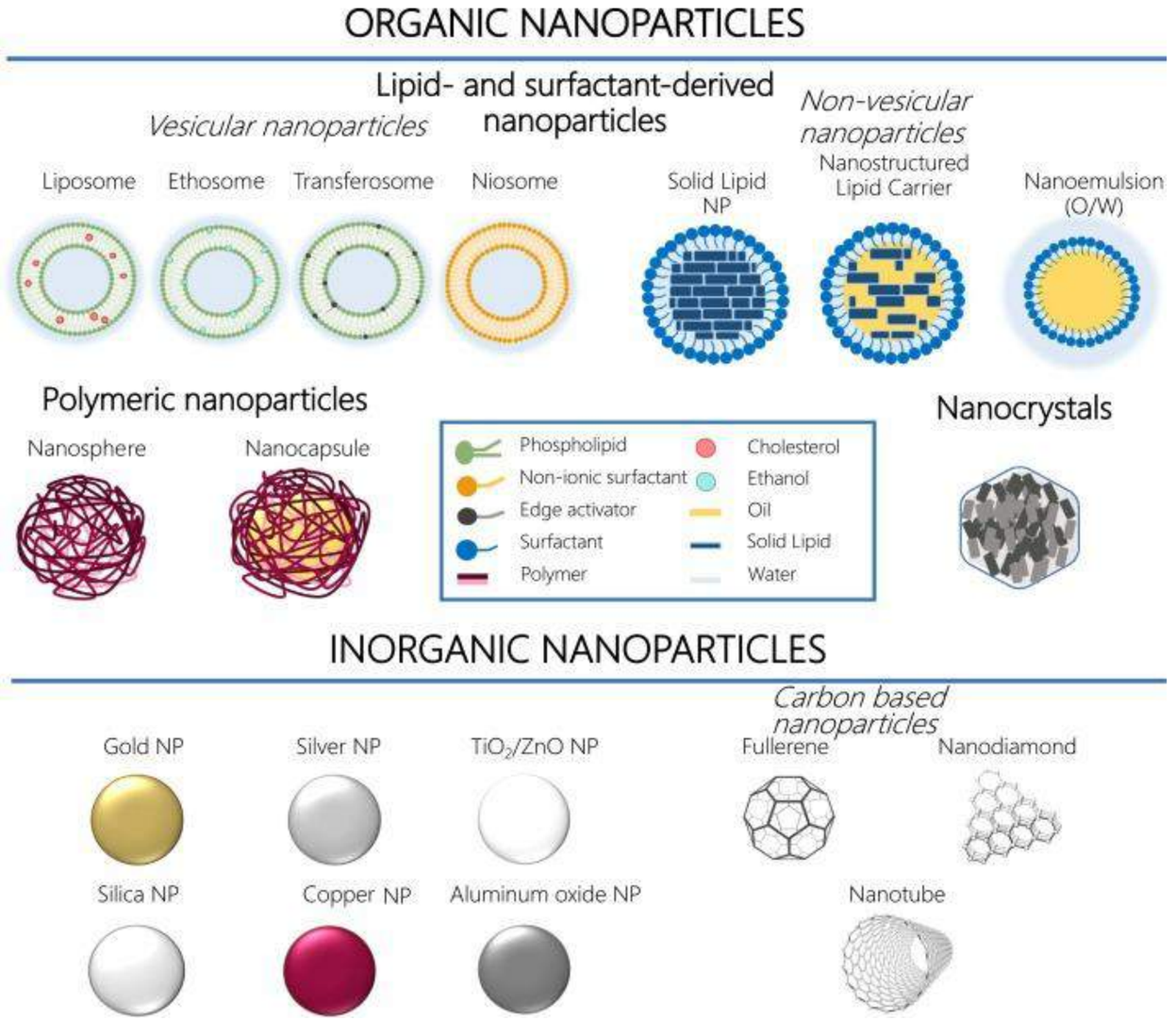


DDS

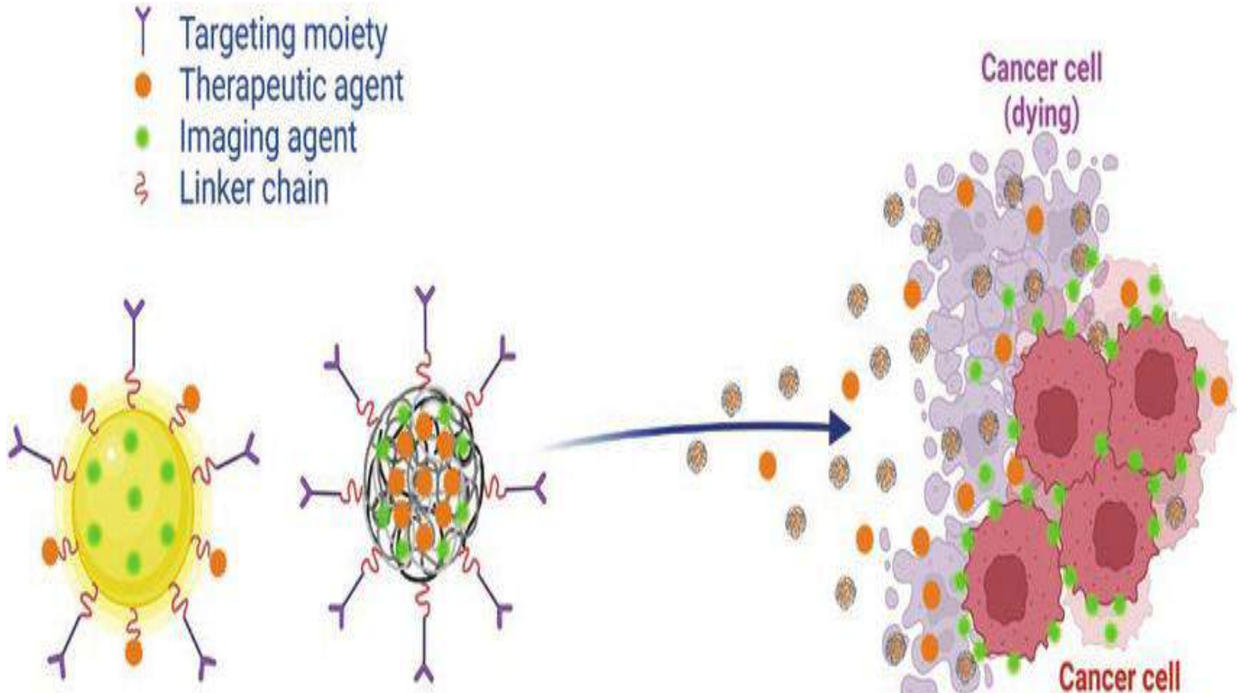


NANOTECHNOLOGY

Smart drug delivery systems

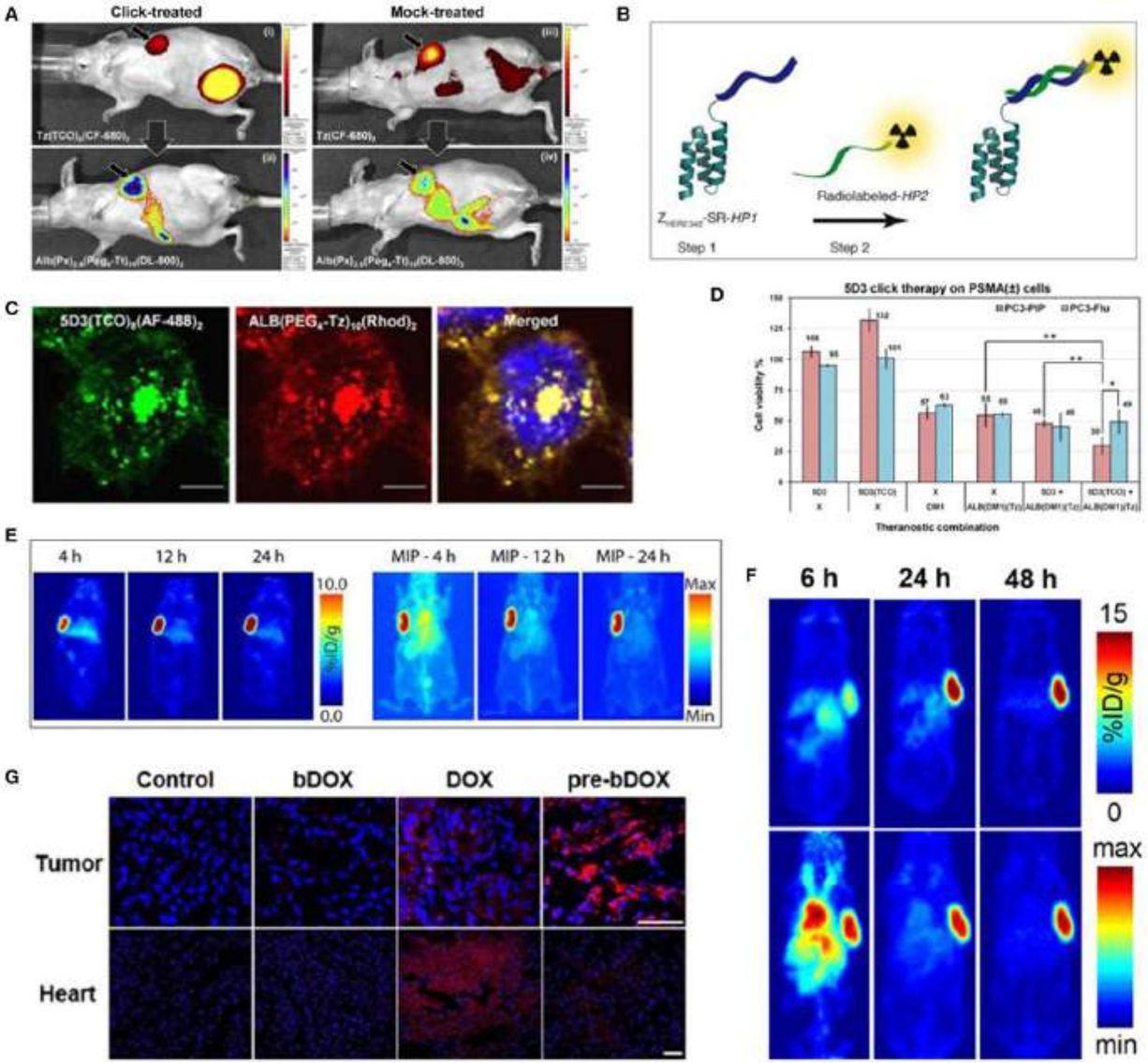


NANOTECHNOLOGY : CANCER

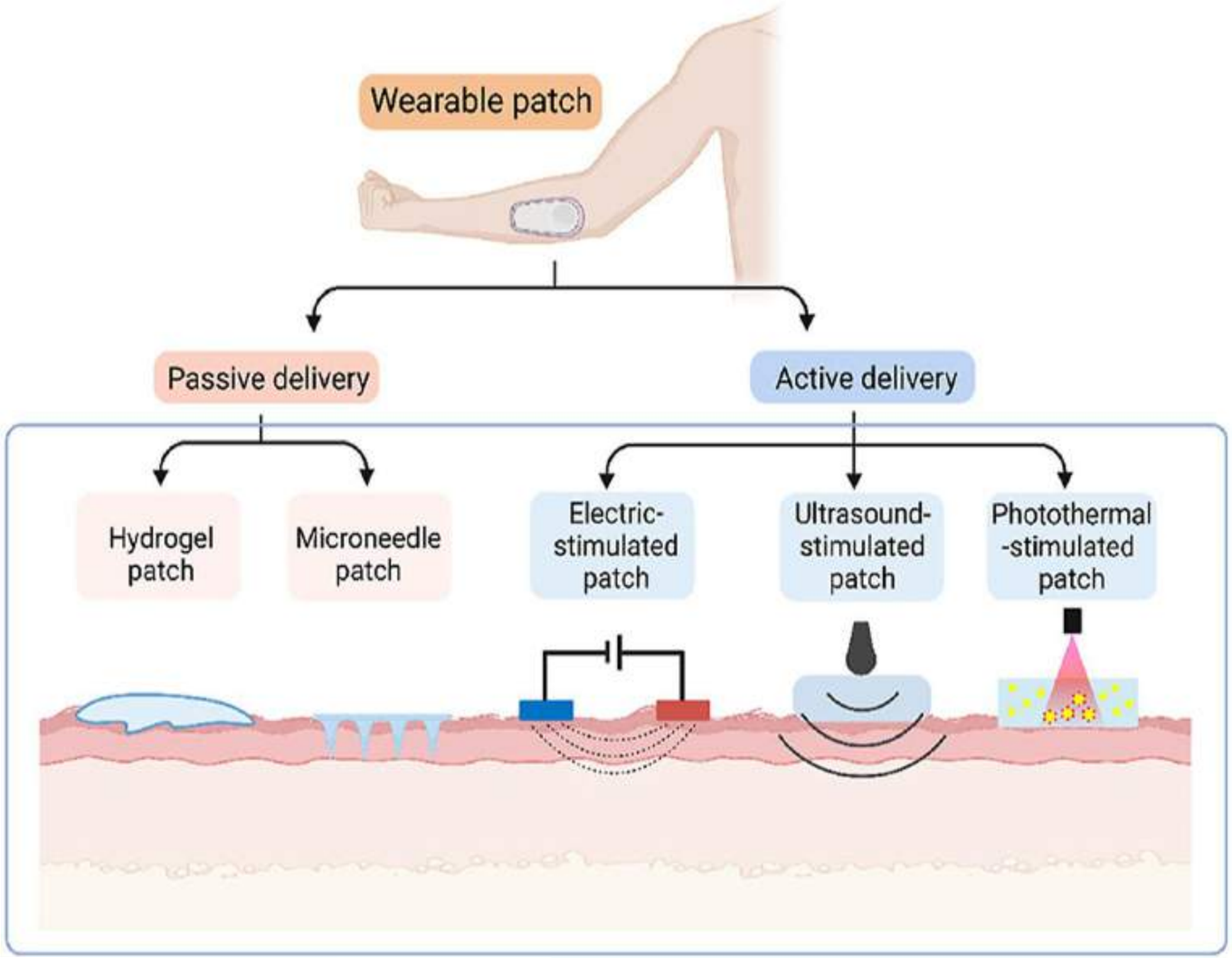


Two exemplar theranostic nanoparticles comprising therapeutic and imaging agents

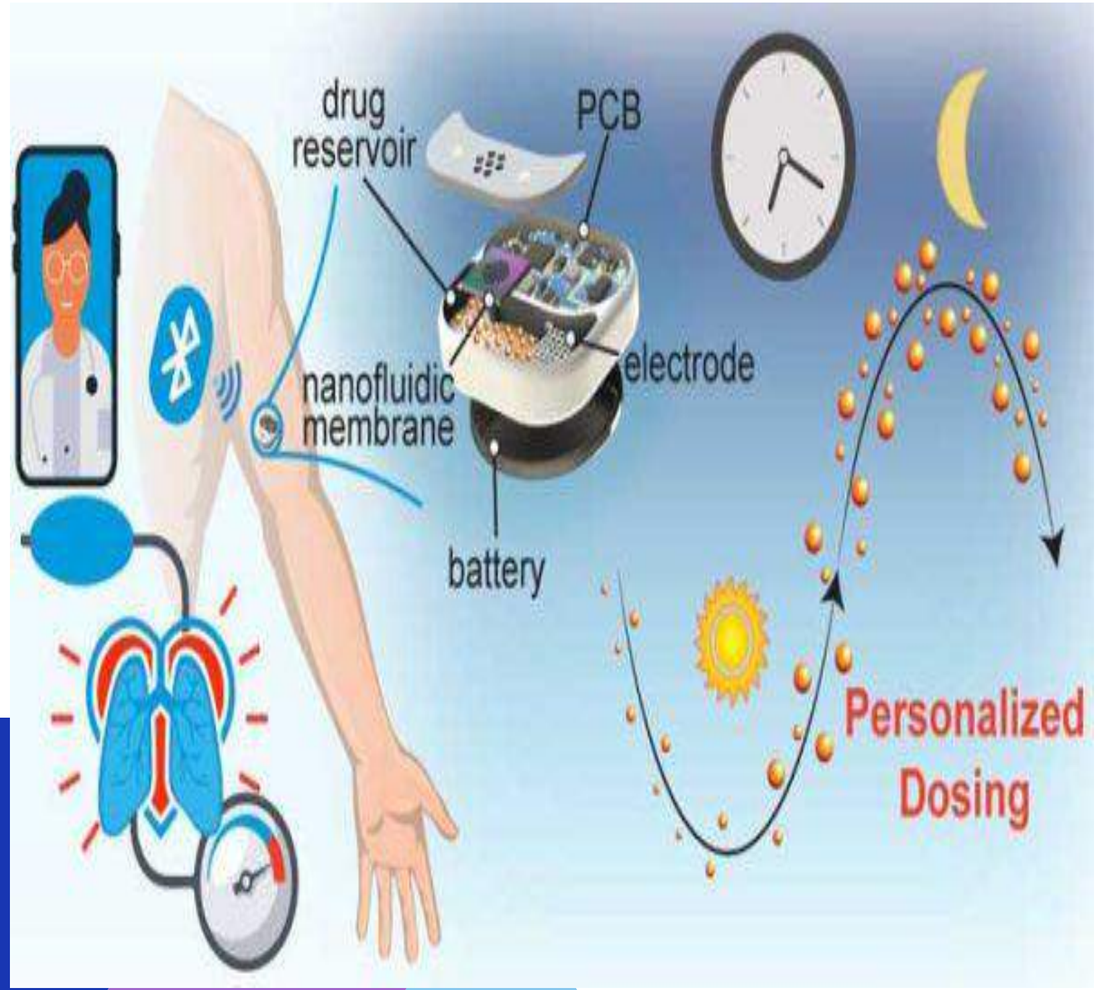
Tumourous tissue receiving therapeutic and imaging agents

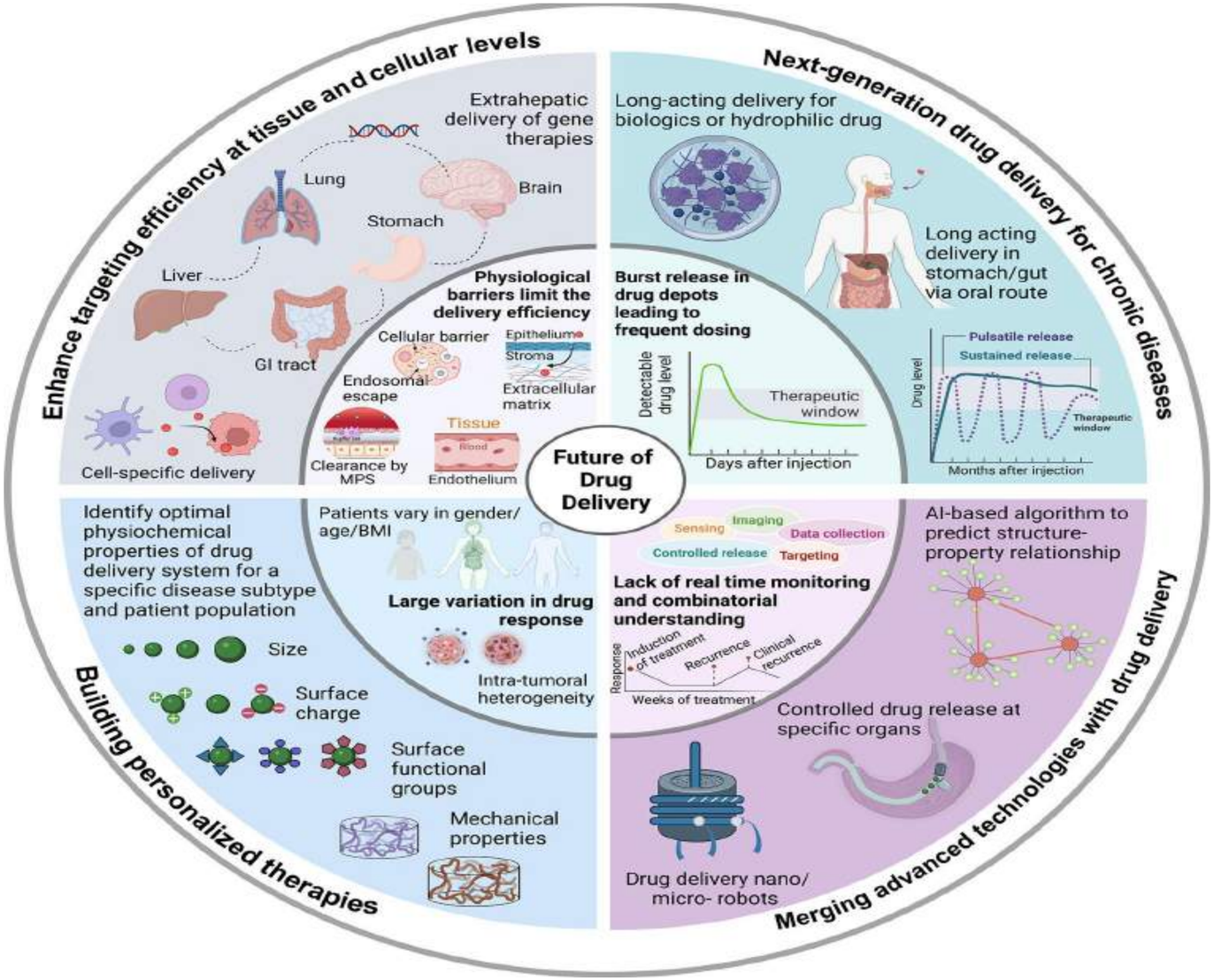


TRANSDERMAL DDS



FUTURE DDS


drug reservoir
PCB
electrode
nanofluidic membrane
battery
Personalized Dosing


Enhance targeting efficiency at tissue and cellular levels
Extrahepatic delivery of gene therapies
Lung
Brain
Stomach
Liver
GI tract
Cell-specific delivery
Physiological barriers limit the delivery efficiency
Cellular barrier
Epithelium
Stroma
Extracellular matrix
Endosomal escape
Tissue
Blood
Clearance by MPS
Endothelium
Future of Drug Delivery
Next-generation drug delivery for chronic diseases
Long-acting delivery for biologics or hydrophilic drug
Long acting delivery in stomach/gut via oral route
Burst release in drug depots leading to frequent dosing
Detectable drug level
Therapeutic window
Days after injection
Pulsatile release
Sustained release
Drug level
Therapeutic window
Months after injection
Building personalized therapies
Identify optimal physiochemical properties of drug delivery system for a specific disease subtype and patient population
Size
Surface charge
Surface functional groups
Mechanical properties
Patients vary in gender/ age/BMI
Large variation in drug response
Intra-tumoral heterogeneity
Merging advanced technologies with drug delivery
Sensing
Imaging
Data collection
Controlled release
Targeting
Lack of real time monitoring and combinatorial understanding
Response
Induction of treatment
Recurrence
Clinical recurrence
Weeks of treatment
AI-based algorithm to predict structure-property relationship
Controlled drug release at specific organs
Drug delivery nano/ micro- robots

Pharmaceutical Marketing Strategy

01 Identify Target Audience

02 Understand Audience Needs

03 Choose Marketing Channels

04 Content Creation

05 Targeted Messaging

06 Engagement with Healthcare Professionals

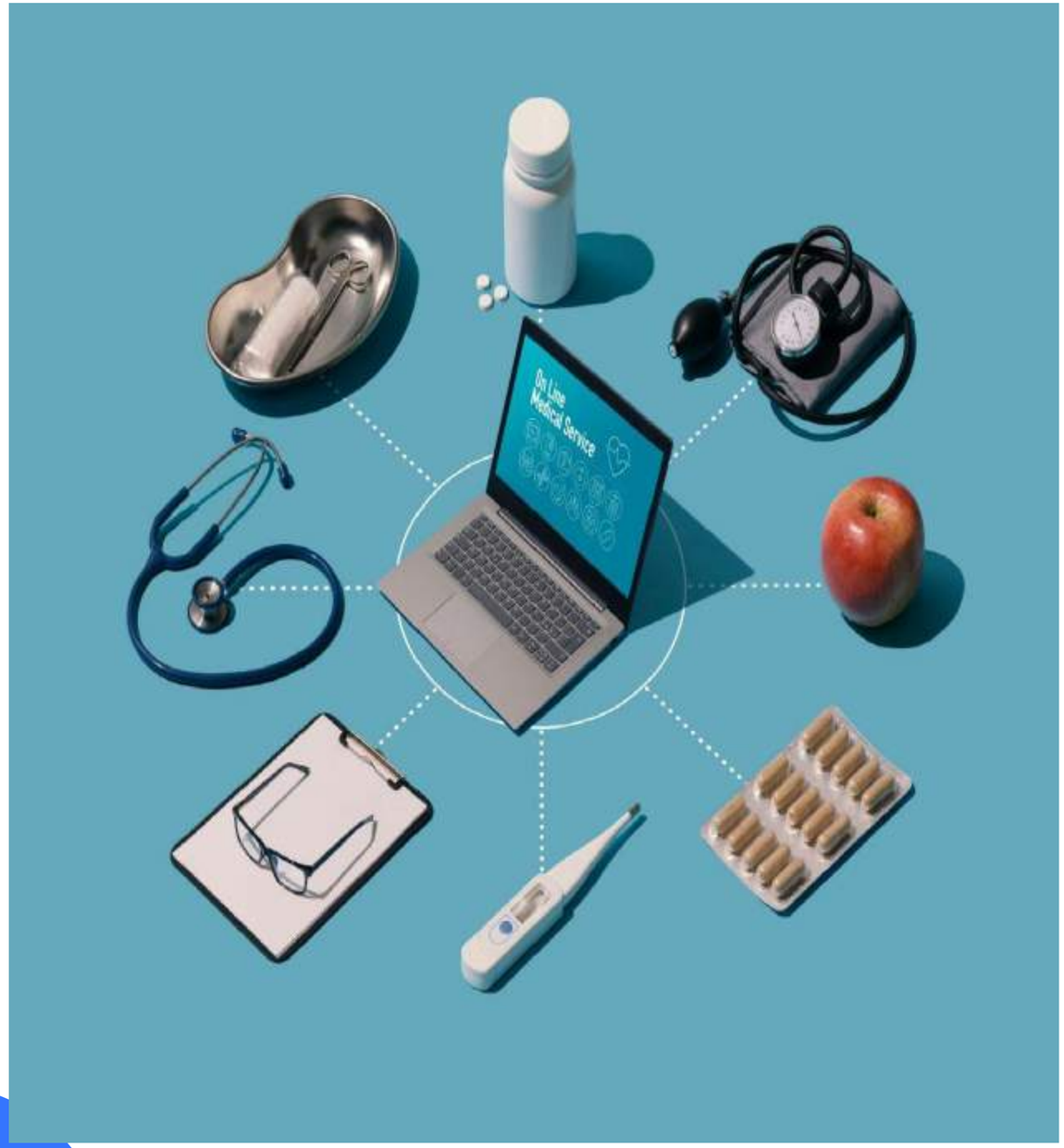
07 Compliance and Regulation

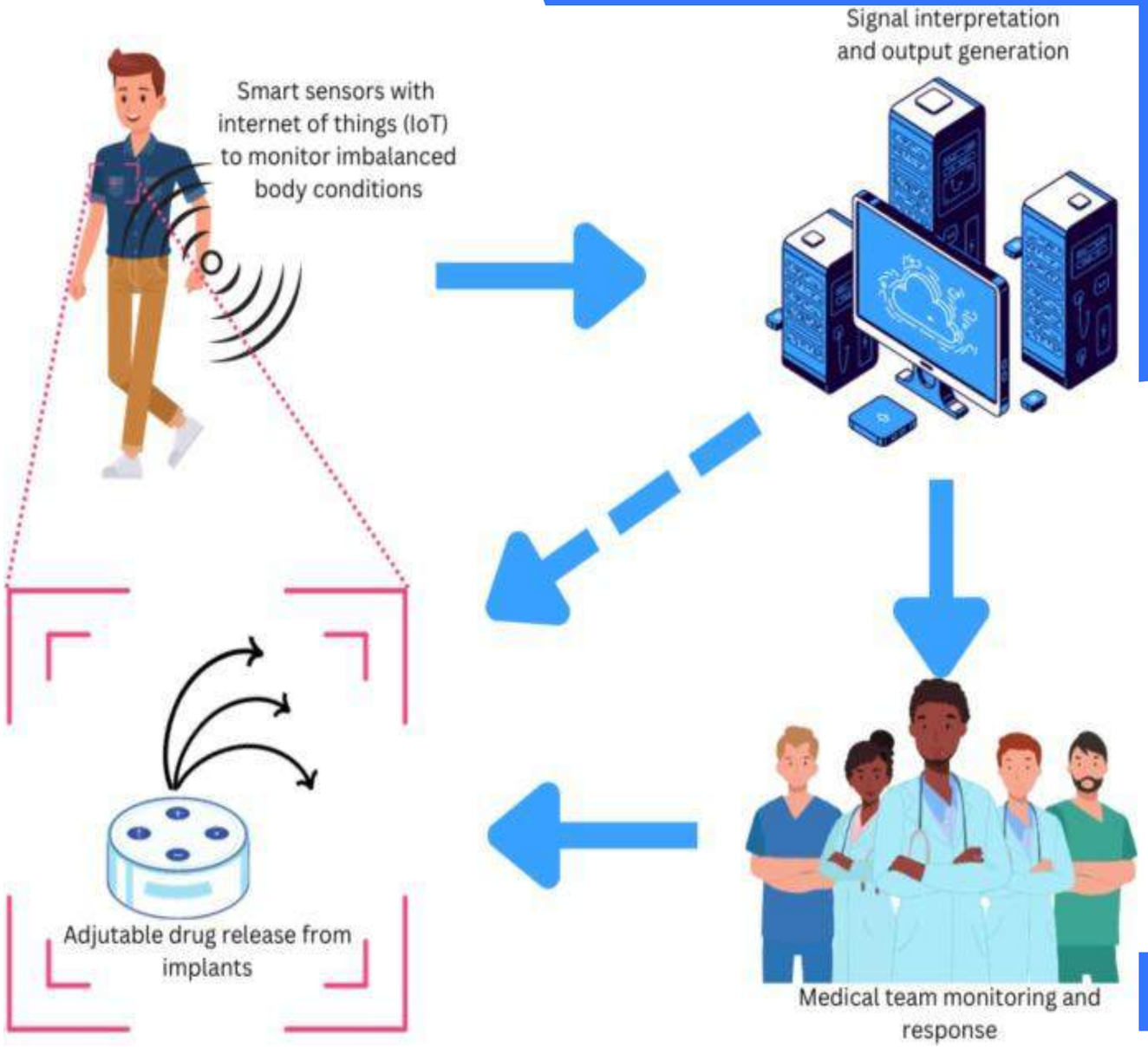
08 Track and Analyze Performance

09 Adaptation to Industry Changes

10 Ethical Considerations

Customers of Pharmaceutical Marketing


On Line
Medical Service


Smart sensors with internet of things (IoT) to monitor imbalanced body conditions
Signal interpretation and output generation
Adjutable drug release from implants
Medical team monitoring and response

Drug Delivery Systems Market

Market Drivers

- Introduction of advanced technologies
- Growth in incidence of chronic diseases

US$ 40.1 Bn

In 2022 (A)

Market Revenue

CAGR (2023–2031)

6.8%

Key Players

- Novartis AG
- Amgen Inc.
- F. Hoffmann-La Roche Ltd.
- Pfizer Inc.
- Johnson & Johnson Services, Ltd.
- Becton, Dickinson and Company
- AstraZeneca plc
- Baxter International, Inc.
- Bayer AG
- Boston Scientific Corporation

By Route of Administration

- Oral
- Injectable
- Inhalation
- Ocular
- Nasal
- Topical

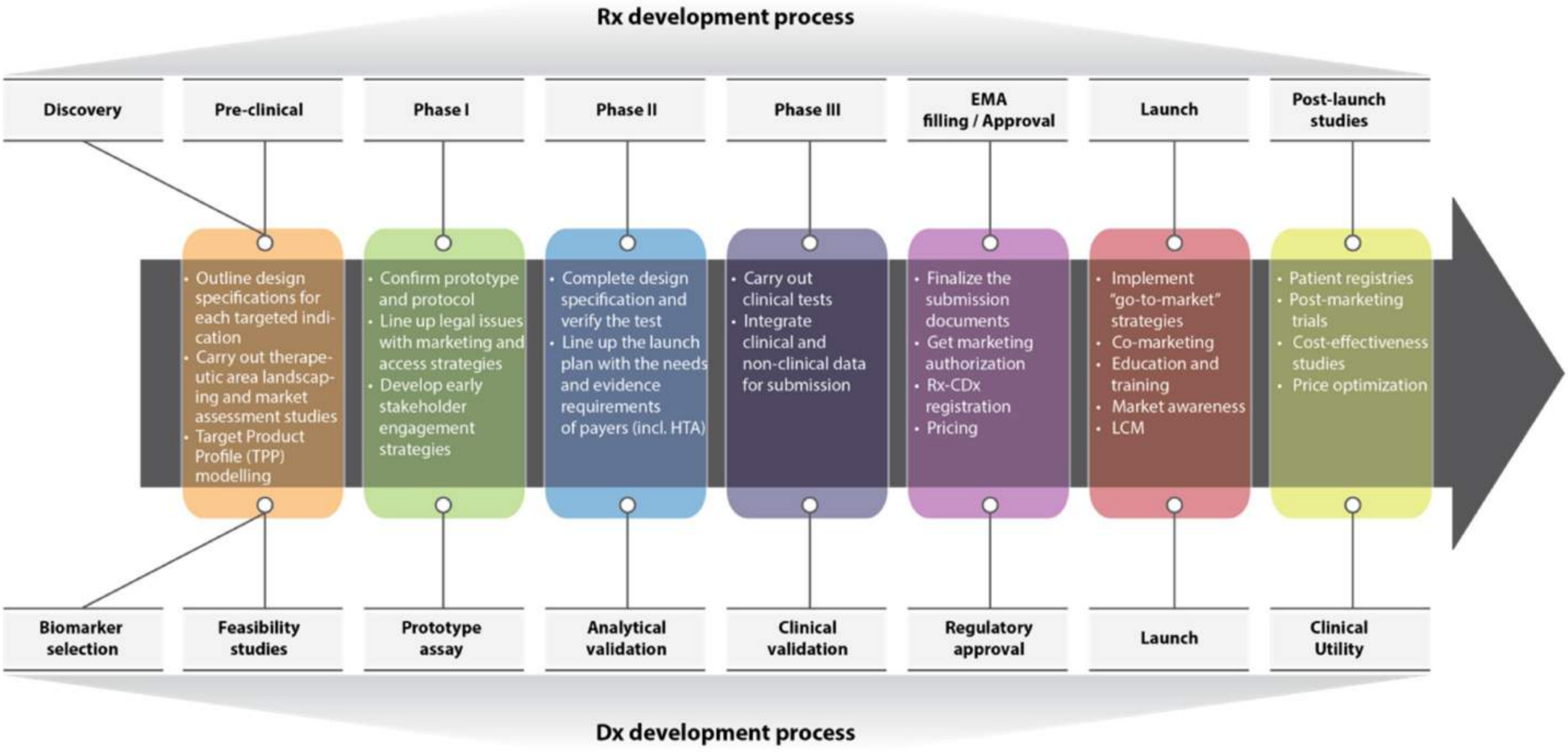
By Type of Delivery System

By Region

- North America
  - Largest market share in 2022

TRANSPARENCY MARKET RESEARCH

www.transparencymarketreserach.com


Rx development process
Discovery
Pre-clinical
Phase I
Phase II
Phase III
EMA filling / Approval
Launch
Post-launch studies
• Outline design specifications for each targeted indication
• Carry out therapeutic area landscaping and market assessment studies
• Target Product Profile (TPP) modelling
• Confirm prototype and protocol
• Line up legal issues with marketing and access strategies
• Develop early stakeholder engagement strategies
• Complete design specification and verify the test
• Line up the launch plan with the needs and evidence requirements of payers (incl. HTA)
• Carry out clinical tests
• Integrate clinical and non-clinical data for submission
• Finalize the submission documents
• Get marketing authorization
• Rx-CDx registration
• Pricing
• Implement "go-to-market" strategies
• Co-marketing
• Education and training
• Market awareness
• LCM
• Patient registries
• Post-marketing trials
• Cost-effectiveness studies
• Price optimization
Biomarker selection
Feasibility studies
Prototype assay
Analytical validation
Clinical validation
Regulatory approval
Launch
Clinical Utility
Dx development process

TUGAS

Strategi pengembangan obat analgetik : Opioid

Strategi pengembangan obat antibiotika : Penisilin

Strategi pengembangan obat antikolinergik : Atropin

Kamu harus tahu mengenai mekanisme aksi obat tersebut?

Permasalahan apa yang muncul akibat penggunaan senyawa obat tersebut?

Kaitannya dengan pengembangan obat, strategi apa yang perlu dilakukan ?

Referensi

1. Aldewachi, H., Al-Zidan, R. N., Conner, M. T., & Salman, M. M. (2021). High-Throughput Screening Platforms in the Discovery of Novel Drugs for Neurodegenerative Diseases. Bioengineering 2021, Vol. 8, Page 30, 8(2), 30. https://doi.org/10.3390/BIOENGINEERING8020030
2. Sun, D., Gao, W., Hu, H., & Zhou, S. (2022). Why 90% of clinical drug development fails and how to improve it? Acta Pharmaceutica Sinica B, 12(7), 3049–3062. https://doi.org/10.1016/J.APSB.2022.02.002
3. Gupta, A., Kumar, S., Maurya, V. K., Puri, B., Saxena, S. K., Gupta, A., Kumar, S., Maurya, V. K., Puri, B., & Saxena, S. K. (2022). High-Throughput Screening for Drug Discovery toward Infectious Diseases: Options and Challenges. High-Throughput Screening for Drug Discovery. https://doi.org/10.5772/INTECHOPEN.102936
4. Di, L., Kerns, E., & Carter, G. (2009). Drug-like property concepts in pharmaceutical design. Current Pharmaceutical Design, 15(19), 2184–2194. https://doi.org/10.2174/138161209788682479
5. Yu, L. X., Amidon, G., Khan, M. A., Hoag, S. W., Polli, J., Raju, G. K., & Woodcock, J. (2014). Understanding Pharmaceutical Quality by Design. The AAPS Journal, 16(4), 771. https://doi.org/10.1208/S12248-014-9598-3
6. Chang, Y. ;, Hawkins, B. A. ;, Du, J. J. ;, Groundwater, P. W. ;, Hibbs, D. E. ;, Lai, F., Chang, Y., Hawkins, B. A., Du, J. J., Groundwater, P. W., Hibbs, D. E., & Lai, F. (2022). A Guide to In Silico Drug Design. Pharmaceutics 2023, Vol. 15, Page 49, 15(1), 49. https://doi.org/10.3390/PHARMACEUTICS15010049
7. Parshuramkar, P., Khobragade, D., & Kashyap, P. (2023). Comprehension of Quality by Design in the Development of Oral Solid Dosage Forms. Journal of Young Pharmacists, 15(3), 406–418. https://doi.org/10.5530/JYP.2023.15.56
8. Akhmetov, I., Ramaswamy, R., Akhmetov, I., & Thimmaraju, P. K. (2015). Market Access Advancements and Challenges in “Drug-Companion Diagnostic Test” Co-Development in Europe. Journal of Personalized Medicine 2015, Vol. 5, Pages 213-228, 5(2), 213–228. https://doi.org/10.3390/JPM5020213

Referensi

1. Bajad, N. G., Rayala, S., Gutti, G., Sharma, A., Singh, M., Kumar, A., & Singh, S. K. (2021). Systematic review on role of structure based drug design (SBDD) in the identification of anti-viral leads against SARS-Cov-2. Current Research in Pharmacology and Drug Discovery, 2. https://doi.org/10.1016/J.CRPHAR.2021.100026
2. Batool, M., Ahmad, B., & Choi, S. (2019). A Structure-Based Drug Discovery Paradigm. International Journal of Molecular Sciences 2019, Vol. 20, Page 2783, 20(11), 2783. https://doi.org/10.3390/IJMS20112783
3. March-Vila, E., Pinzi, L., Sturm, N., Tinivella, A., Engkvist, O., Chen, H., & Rastelli, G. (2017). On the integration of in silico drug design methods for drug repurposing. Frontiers in Pharmacology, 8(MAY), 272508. https://doi.org/10.3389/FPHAR.2017.00298/BIBTEX
4. Göller, A. H., Kuhnke, L., Montanari, F., Bonin, A., Schneckener, S., ter Laak, A., Wichard, J., Lobell, M., & Hillisch, A. (2020). Bayer's in silico ADMET platform: a journey of machine learning over the past two decades. Drug Discovery Today, 25(9), 1702–1709. https://doi.org/10.1016/j.drudis.2020.07.001
5. Pun, F. W., Ozerov, I. v., & Zhavoronkov, A. (2023). AI-powered therapeutic target discovery. Trends in Pharmacological Sciences, 44(9), 561–572. https://doi.org/10.1016/j.tips.2023.06.010
6. Drug Delivery Systems. (n.d.). Retrieved March 14, 2024, from https://www.nibib.nih.gov/science-education/science-topics/drug-delivery-systems-getting-drugs-their-targets-controlled-manner
7. Zhang, X., Chen, G., Zhang, H., Shang, L., & Zhao, Y. (2023). Bioinspired oral delivery devices. Nature Reviews Bioengineering 2023 1:3, 1(3), 208–225. https://doi.org/10.1038/s44222-022-00006-4
8. Lou, J., Duan, H., Qin, Q., Teng, Z., Gan, F., Zhou, X., & Zhou, X. (2023). Advances in Oral Drug Delivery Systems: Challenges and Opportunities. Pharmaceutics 2023, Vol. 15, Page 484, 15(2), 484. https://doi.org/10.3390/PHARMACEUTICS15020484
9. Ouyang, J., Zhang, Z., Deng, B., Liu, J., Wang, L., Liu, H., Koo, S., Chen, S., Li, Y., Yaremenko, A. v., Huang, X., Chen, W., Lee, Y., & Tao, W. (2023). Oral drug delivery platforms for biomedical applications. Materials Today, 62, 296–326. https://doi.org/10.1016/J.MATTOD.2023.01.002
10. Adepu, S., & Ramakrishna, S. (2021). Controlled Drug Delivery Systems: Current Status and Future Directions. Molecules 2021, Vol. 26, Page 5905, 26(19), 5905. https://doi.org/10.3390/MOLECULES26195905

Referensi

1. Vargason, A. M., Anselmo, A. C., & Mitragotri, S. (2021). The evolution of commercial drug delivery technologies. Nature Biomedical Engineering 2021 5:9, 5(9), 951–967. https://doi.org/10.1038/s41551-021-00698-w
2. Sharma, A., Shambhwani, D., Pandey, S., Singh, J., Lalhlenmawia, H., Kumarasamy, M., Singh, S. K., Chellappan, D. K., Gupta, G., Prasher, P., Dua, K., & Kumar, D. (2023). Advances in Lung Cancer Treatment Using Nanomedicines. ACS Omega, 8(1), 10–41. https://doi.org/10.1021/ACSOMEGA.2C04078/ASSET/IMAGES/LARGE/AO2C04078_0010.JPEG
3. Diaz, M. J., Natarelli, N., Aflatooni, S., Aleman, S. J., Neelam, S., Tran, J. T., Taneja, K., Lucke-Wold, B., & Forouzandeh, M. (2023). Nanoparticle-Based Treatment Approaches for Skin Cancer: A Systematic Review. Current Oncology 2023, Vol. 30, Pages 7112-7131, 30(8), 7112–7131. https://doi.org/10.3390/CURRONCOL30080516
4. Wu, D., Chen, Q., Chen, X., Han, F., Chen, Z., & Wang, Y. (2023). The blood–brain barrier: structure, regulation, and drug delivery. Signal Transduction and Targeted Therapy 2023 8:1, 8(1), 1–27. https://doi.org/10.1038/s41392-023-01481-w
5. Afzal, O., Altamimi, A. S. A., Nadeem, M. S., Alzarea, S. I., Almalki, W. H., Tariq, A., Mubeen, B., Murtaza, B. N., Iftikhar, S., Riaz, N., & Kazmi, I. (2022). Nanoparticles in Drug Delivery: From History to Therapeutic Applications. Nanomaterials 2022, Vol. 12, Page 4494, 12(24), 4494. https://doi.org/10.3390/NANO12244494
6. Palmer, B. C., & DeLouise, L. A. (2016). Nanoparticle-Enabled Transdermal Drug Delivery Systems for Enhanced Dose Control and Tissue Targeting. Molecules 2016, Vol. 21, Page 1719, 21(12), 1719. https://doi.org/10.3390/MOLECULES21121719
7. Gao, J., Karp, J. M., Langer, R., & Joshi, N. (2023). The Future of Drug Delivery. Chemistry of Materials, 35(2), 359–363. https://doi.org/10.1021/ACS.CHEMMATER.2C03003/ASSET/IMAGES/LARGE/CM2C03003_0001.JPEG
8. Ramadon, D., McCrudden, M. T. C., Courtenay, A. J., & Donnelly, R. F. (2022). Enhancement strategies for transdermal drug delivery systems: current trends and applications. Drug Delivery and Translational Research, 12(4), 758–791. https://doi.org/10.1007/S13346-021-00909-6/FIGURES/22

Daftar singkatan

- SAR : Structure-Activity Relationship
- STR : Structure-Tissue Relationship
- HTS : *High throughput screening*
- CQAs : critical quality attributes
- PPIs : process performance indicators
- CMAs : critical material attributes
- CPP : critical process parameters
- vHTS : Virtual high-throughput screening
- SBDD : Structure-based drug design
- LBDD : Ligand-based drug design
- QSAR : quantitative structure–activity relationship
- CoMSIA : (Comparative Molecular Similarity Indices Analysis) is a method for analyzing structure-activity relationships and predicting the activity of new compounds based on their similarity to known active compounds.
- CoMFA : (Comparative Molecular Field Analysis) is a computational method for predicting the activity of molecules based on their 3D structure

Thank You.

For Your Attention