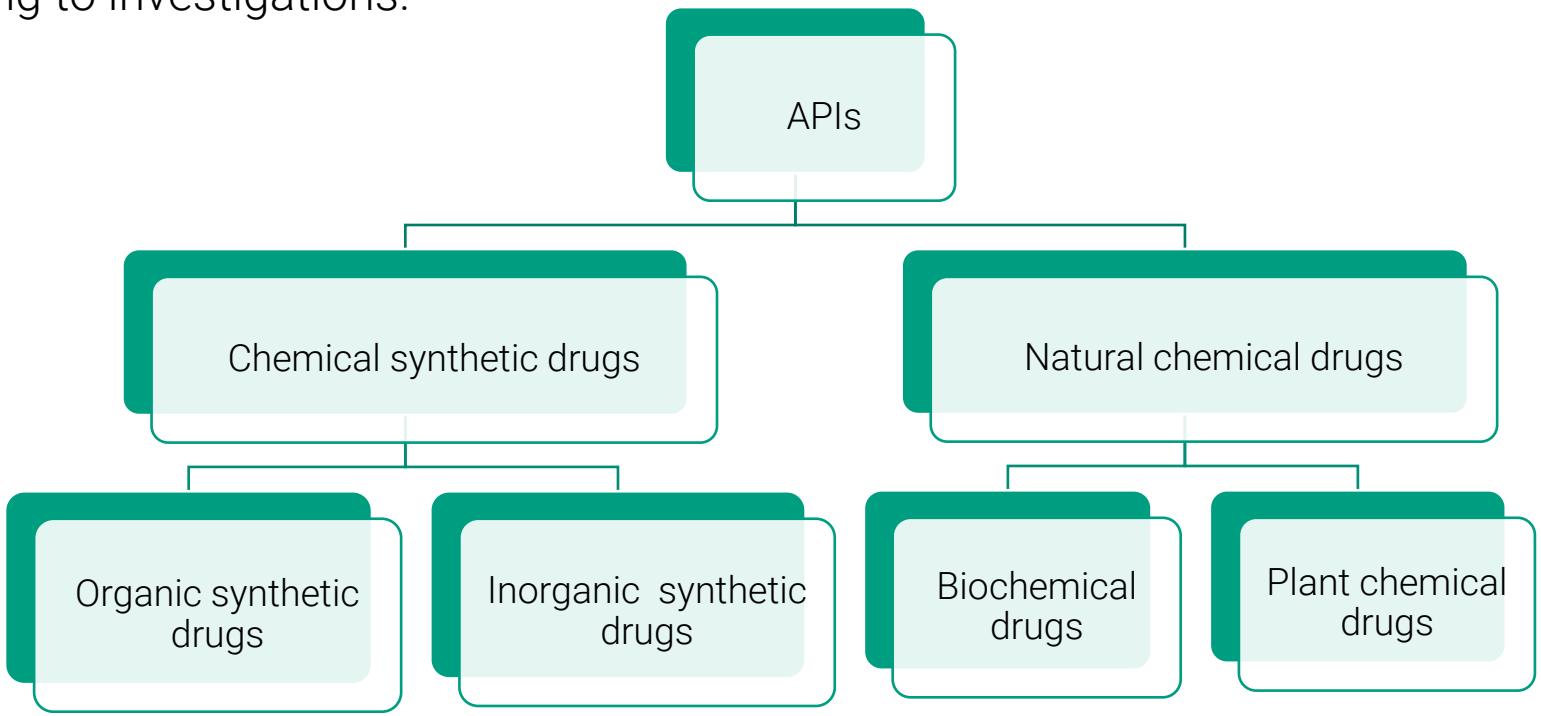
Innovative Drug Delivery Systems

GraftBio™ Technologies

API types

API is Active Pharmaceutical Ingredients, that are the raw materials used to design various types of complete drugs. They are in a diversity of states, such as crystals and powders. It has pharmacological activity or other direct effects in the diagnosis, treatment, symptom relief, or prevention of disease, or it can modify the function or structure of the body.

The main characteristic of the API is that it cannot be directly used for clinical use. It is a raw material and can only be used as a pharmaceutical preparation after processing, and then can be used as a medicine for clinical application according to investigations.



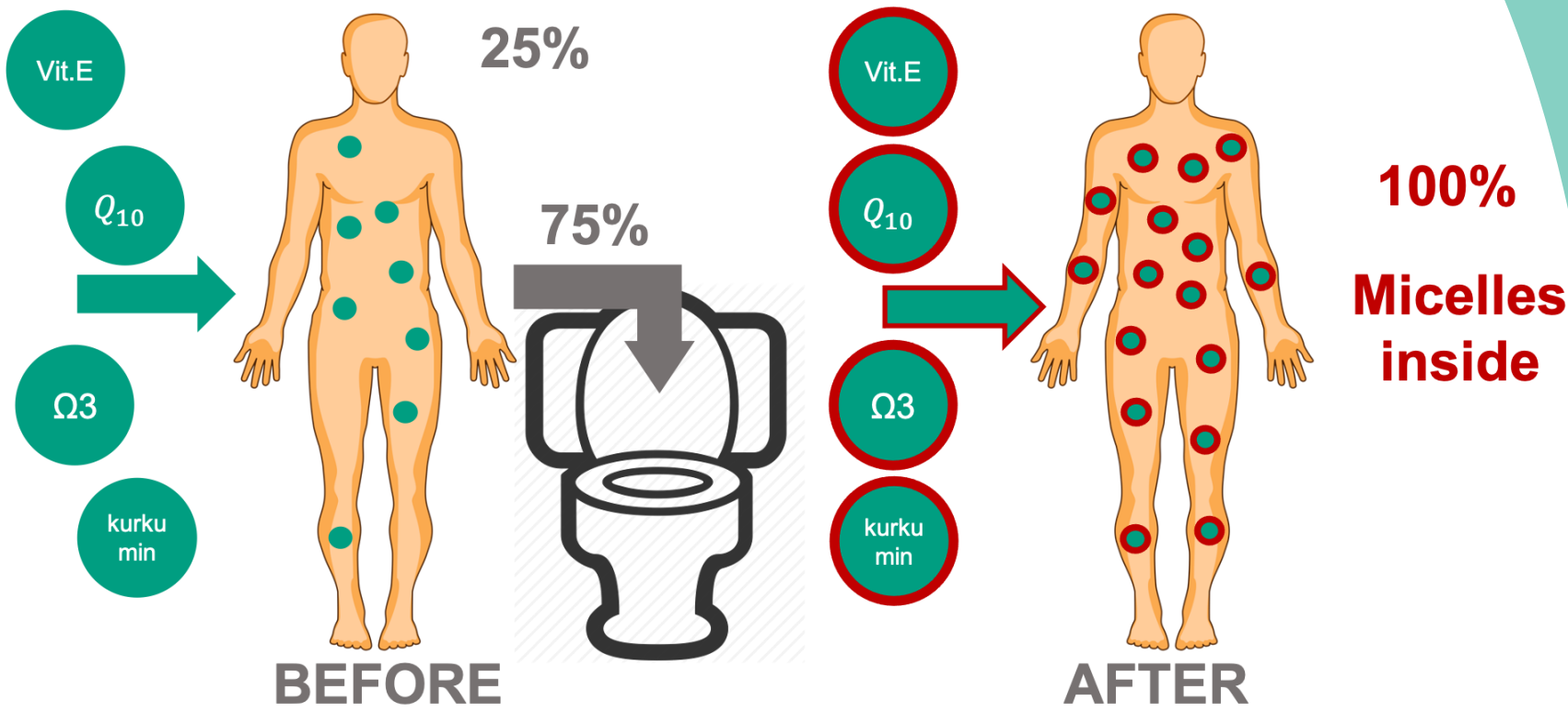
API examples and therapeutic applications

- **Antimicrobial**
  - Artemisinim
  - Caffeic acid
  - Capsaicin
  - Coumarin
  - Eugenol
  - Menthol
- **Anti-inflamatory**
  - Capsaicin
  - Colchicine
  - Curcumin
  - Epigallocatechin-3-gallate
  - Quercetin
  - Resveratrol
  - Cannabinoids
- **Neuroprotective**
  - Bacoside A
  - Bilobalide
  - Curcumin
  - Galantamine
  - Ginsenosides
  - Withaferin A
  - Cannabinoids
- **Antioxidants**
  - Curcumin
  - Cyanidin
  - Gingerol
  - *Ginkgo biloba*
  - Glycyrrhizin
  - Quercetin
- **Cardiovascular protection**
  - Berberine
  - Curcumin
  - Dihydrotanshinone
  - Quercetin
- **Anti-cancer**
  - Curcumin
  - Kaempferol
  - Paclitaxel
  - Resveratrol
  - Silamarin
  - Vancristine
  - Cannabinoids

GLOBAL PROBLEM and CHALLENGES

The traditional medicinal system used rich herbal sources either alone or in combination, together with other required ingredients to treat various conditions. Despite these uses of medicinal plants over the years there has been *a lag to deliver a therapeutically efficacious drug/nutraceutical from a plant source.*

Many of the plant molecules are hydrophobic in nature and hence are not water soluble. The poor bioavailability of these molecules reflects the lack of efficient natural drugs in the market, in spite of their traditionally known benefits. On the other hand, biopharmaceuticals have been suffering from instability and biological degradation before reaching the target site.



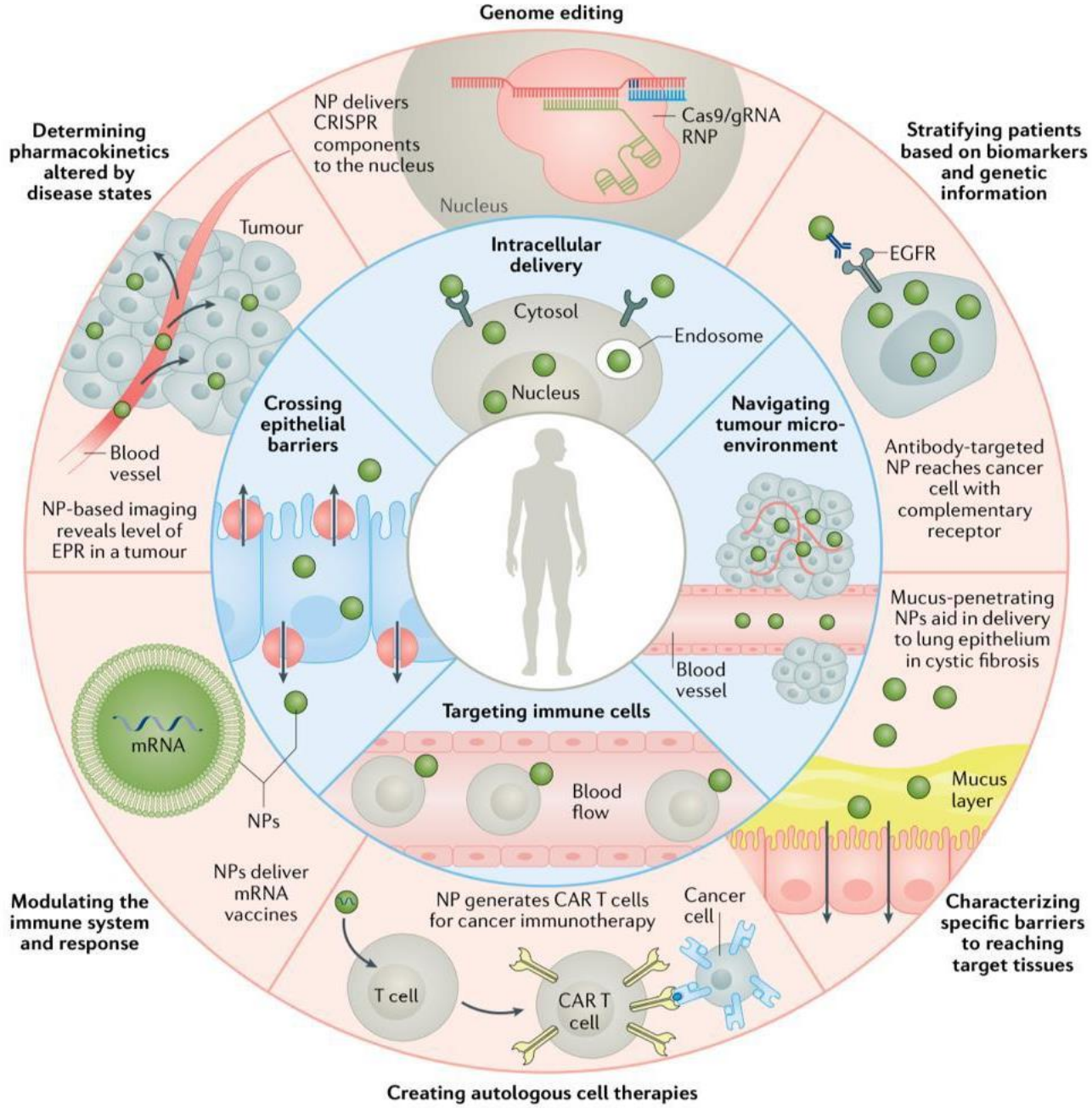
Human Biological Barriers

The improvement of the solubility of poorly water-soluble drugs is one of the principal current challenges to pharmaceutical sciences. The oral bioavailability of a drug depends on its solubility and dissolution rate, which is the rate-determining step for the onset of therapeutic action. Several techniques have been developed over the years to enhance the dissolution of the drug such as micronization, solubilization, salt formation, complexation with polymers, change in physical form, use of prodrugs, drug derivatization, alteration of pH, the addition of surfactants, etc.

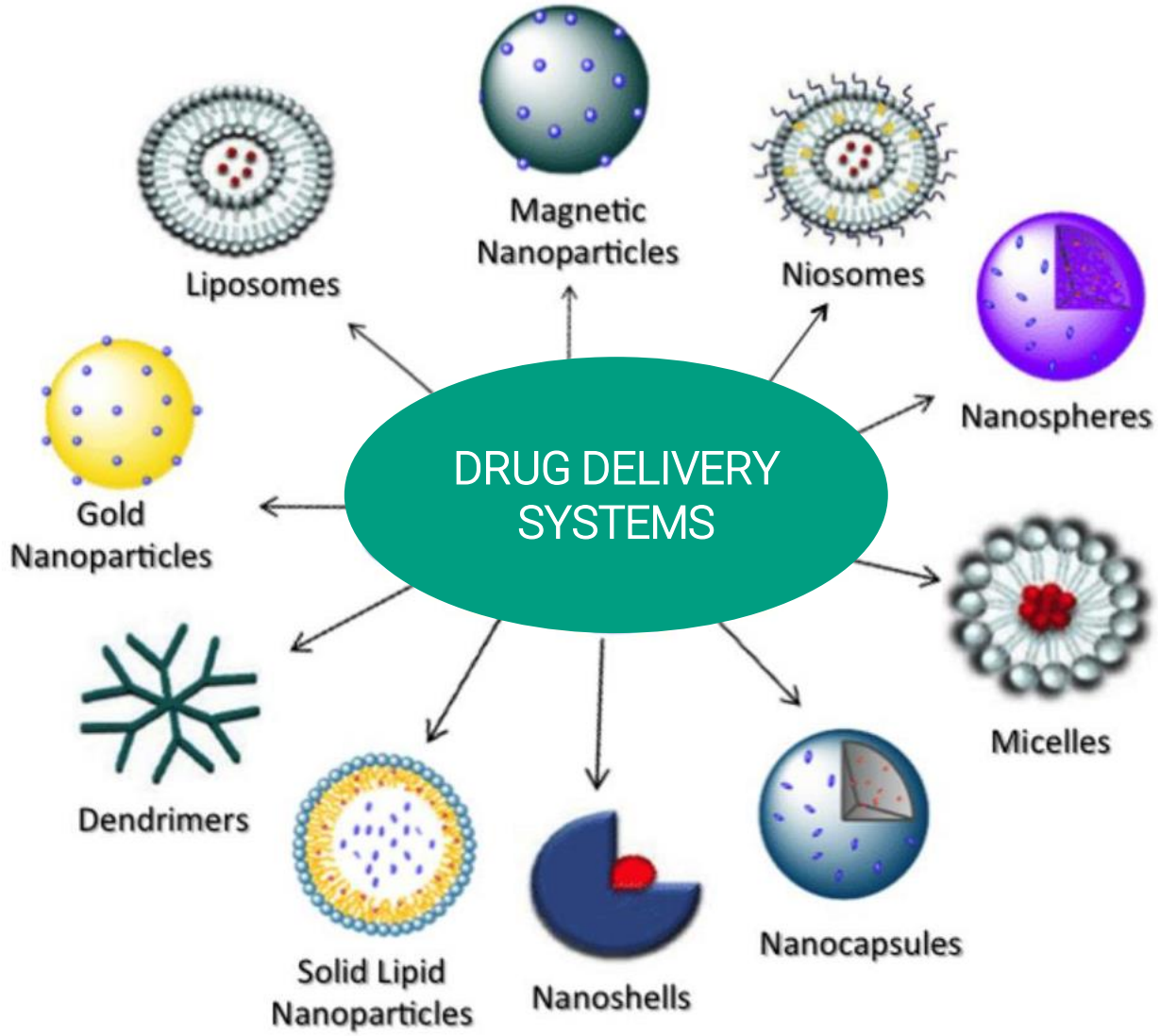
As noted, there are a variety of natural and synthetic APIs around the world. However, there is a need for the safe and effective delivery of APIs to the body, which is 80% water.

Thus, the main challenge is to increase bioavailability, stability and safety of Drug Delivery Systems.

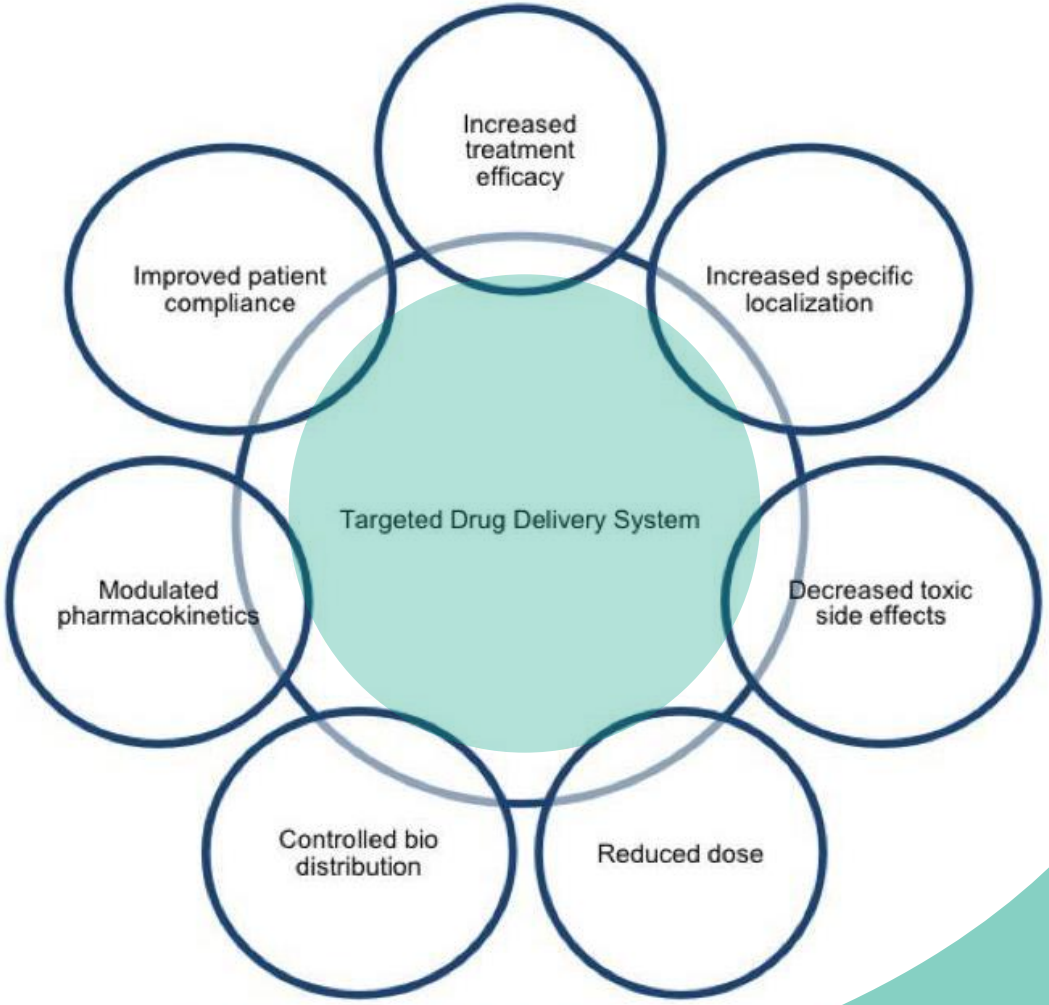
- ✓ Bioavailability
- ✓ Stability
- ✓ Safety of DDS



TYPES of DDS

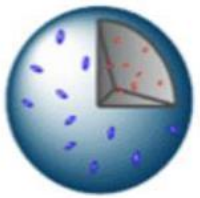


ADTANTAGES of TARGETED DDS



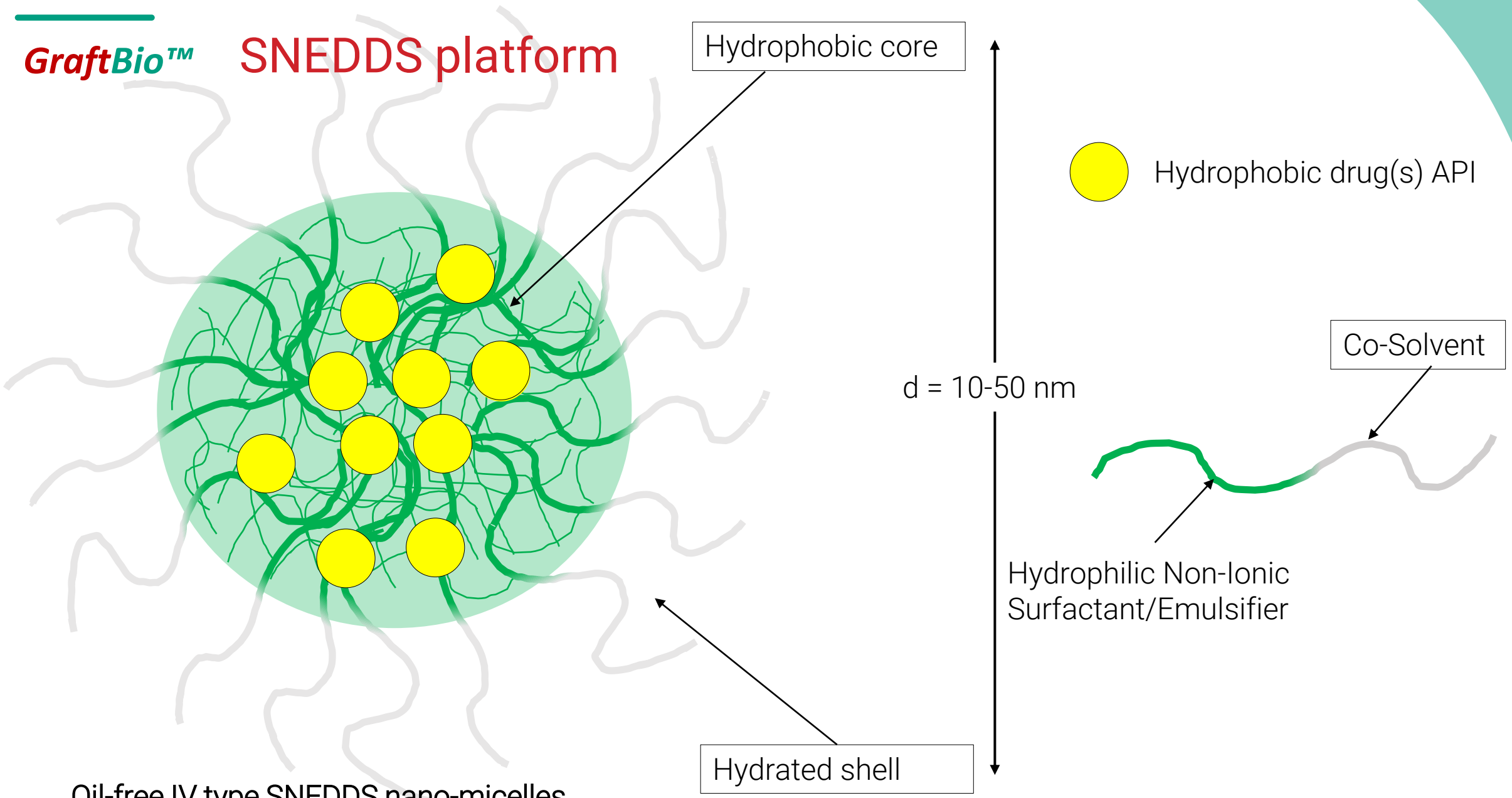
GRAFT POLYMER BUSINESS MODEL in DDS

GP Drug Delivery Platforms
GraftBio™

- **Nano-micellar**
  - ***GraftBio™ SNEDDS Nano-emulsion plarform*** *for various API*
  - 
- **Nano-capsule**
  - *Grafted PCL nano particles (solvent evaporation - W/O emulsion method)*
  - 
- **Porous nano-reservoir**
  - *SYNTETIC biodegradable porous reservoir*
  - 
  - *NATURAL organic biodegradable porous reservoir*
  - 
- **Bio-gel**
  - *Bio-material for substitution of human tissue*
  - 
- **Dendrimers**
  - *Hyper Branched Polymers*
  - 

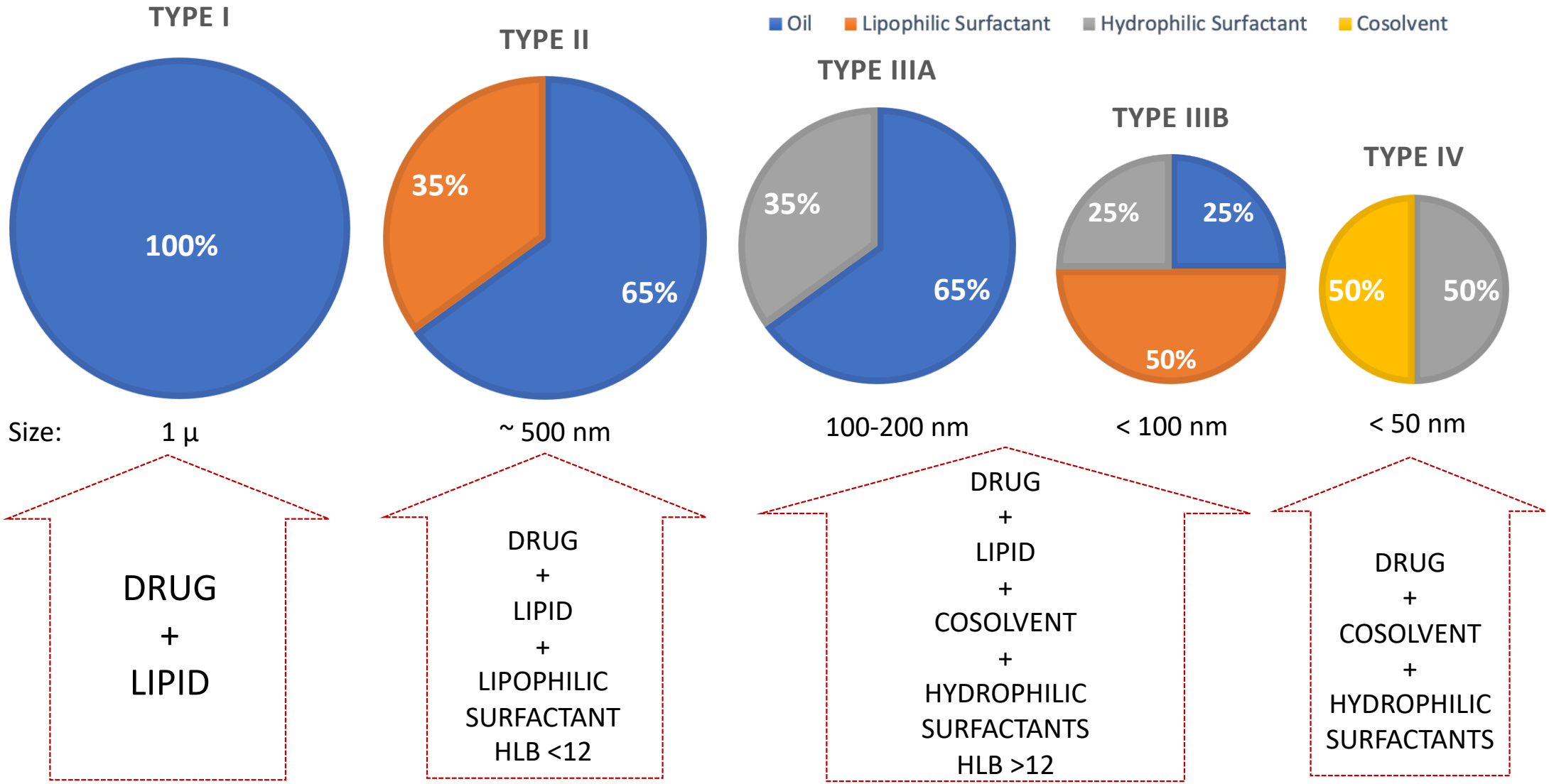
GraftBio™

SNEDDS platform



Oil-free IV type SNEDDS nano-micelles

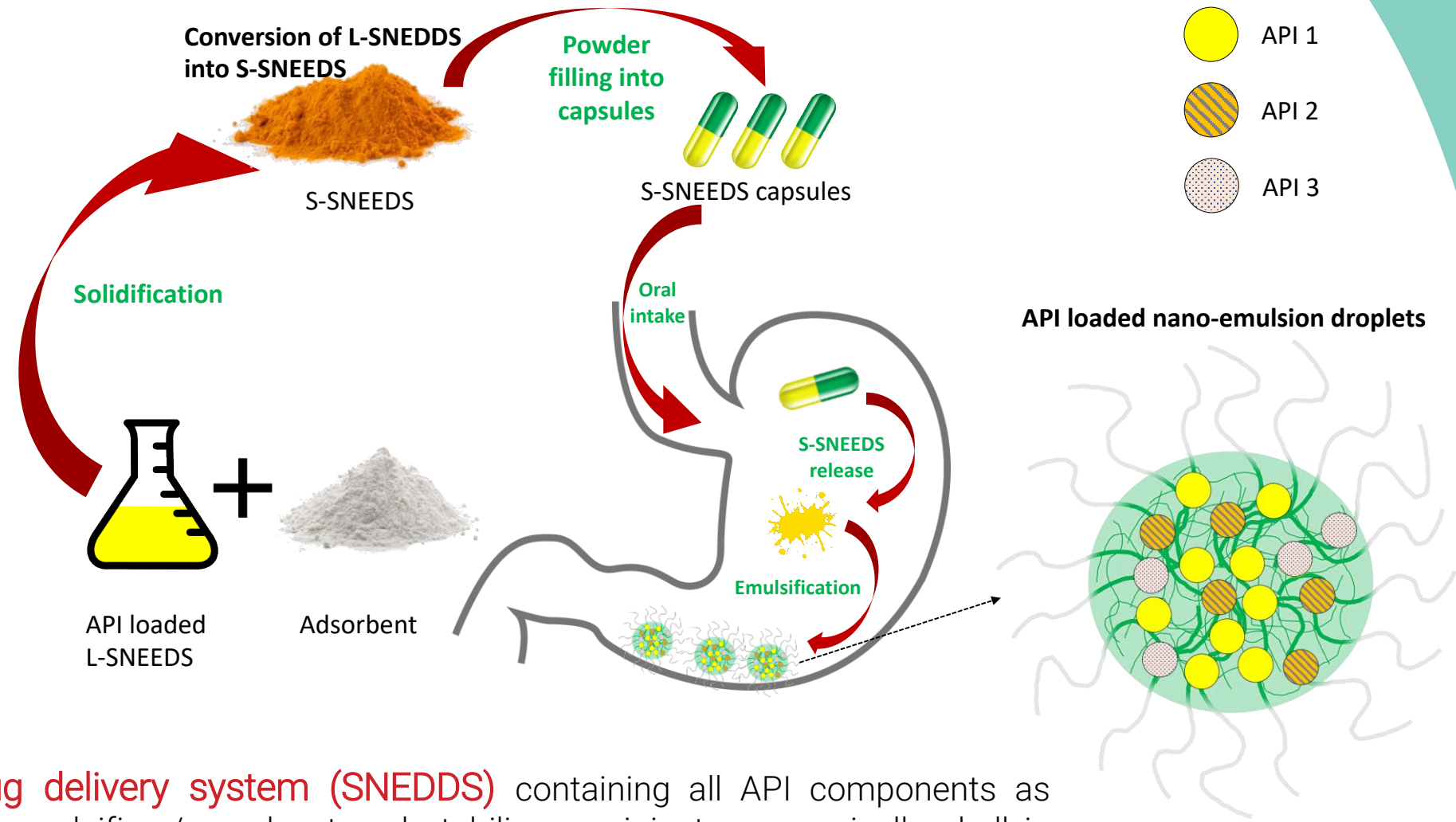
TYPES OF ORAL LIPID FORMULATIONS LFCS



GraftBio™ SNEDDS platform

Graft Polymer's novel and patented micelle technology encapsulate the particular substances in the tiniest, completely homogeneous individual parts in the shape of product micelles. Important agents are no longer discharged broadly unused but release their complete and planned effect by making active agents water-soluble.

The described method clears a particular potential in both the nutritional supplement and pharmaceutical market.



The self-nanoemulsifying drug delivery system (SNEDDS) containing all API components as lipophilic core of a micelle and emulsifiers/co-solvent and stabilizer excipients as a micelle shell in aqueous phase, with a globular micelle size below 50 nm.

METHODS for *GraftBio™* **Solid-SNEDDS** PREPARATION

Liquid SNEDDS

Addition of solidifying excepients

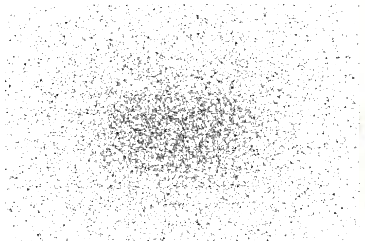
Physical adsorption using porous carriers

Direct compression

Extrusion spheronisation

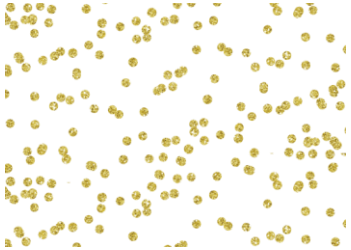
Melt extrusion

SE powders

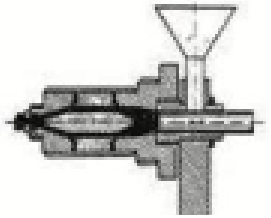


SE tablets

SE granules



SE pellets



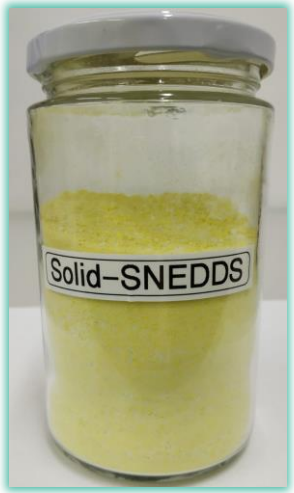
Food Supplements Product Pipeline based on ***GraftBio™*** SNEDDS platform (Examples)

- ***GraftBio™*** Q10 (water-soluble Co-enzyme)
- ***GraftBio™*** Gold (water-soluble Curcumin)
- ***GraftBio™*** Immune (water-soluble Cu + Vitamin C)
- ***GraftBio™*** CBD (water-soluble CBD)
- ***GraftBio™*** CimetrA (supplement against COVID-19)
- ***GraftBio™*** BSO (water-soluble Black Seed)
- ***GraftBio™*** Pro (water-soluble Propolis)
- ***GraftBio™*** GS (water-soluble Ginseng)
- ***GraftBio™*** Gin (water-soluble Ginger)

GP DEVELOPMENTS

GraftBio™ CimetrA

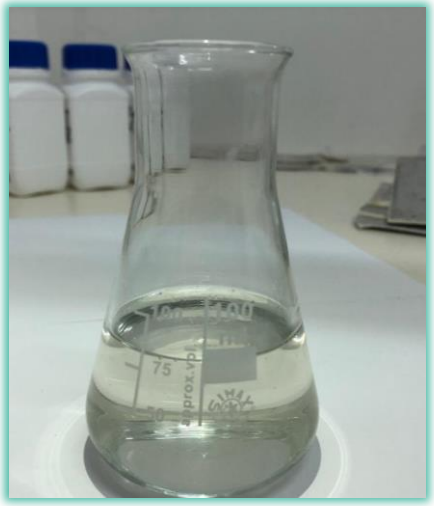
GraftBio™ S-SNEDDS



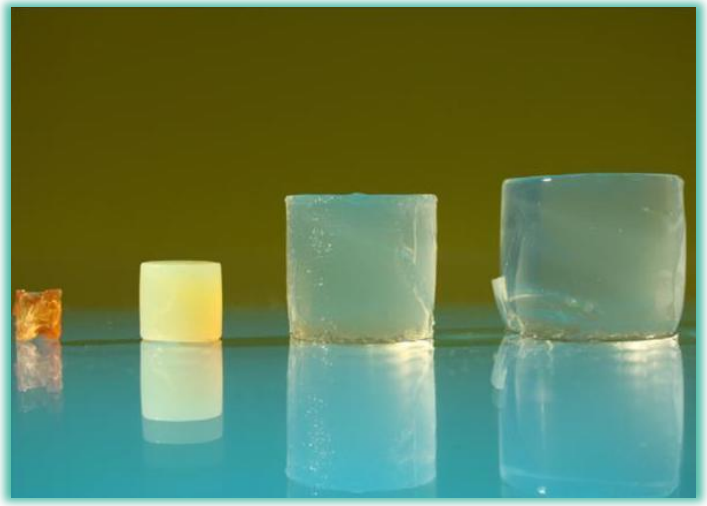
GraftBio™ CBD

GraftBio™ Boswellia

GraftBio™ Q 10



GraftBio™ Dendrimer



GraftBio™ Gel

GraftBio™ PLA Porous

GraftBio™ PCL-PVP

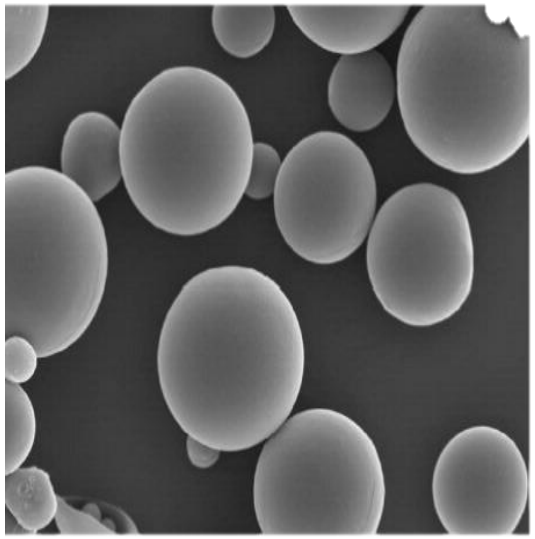
GP DEVELOPMENT EXAMPLES

GraftBio™ BIODEGRADABLE CORE-SHELL MICROCAPSULE

MP = Microparticle

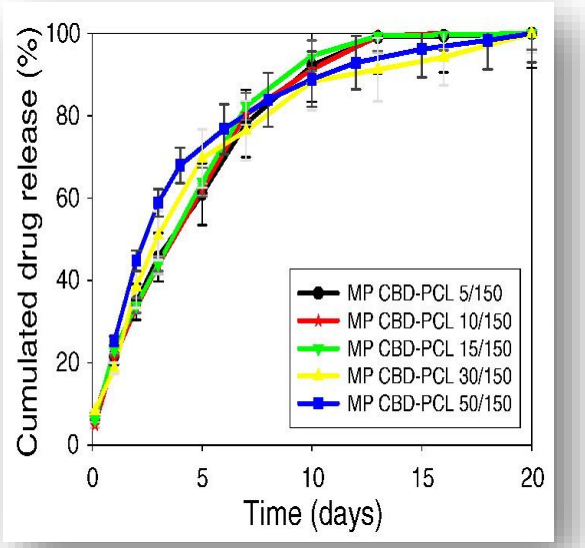
Cannabinoids
High Therapeutic potential,
but highly lipophillic
compounds

Microencapsulation

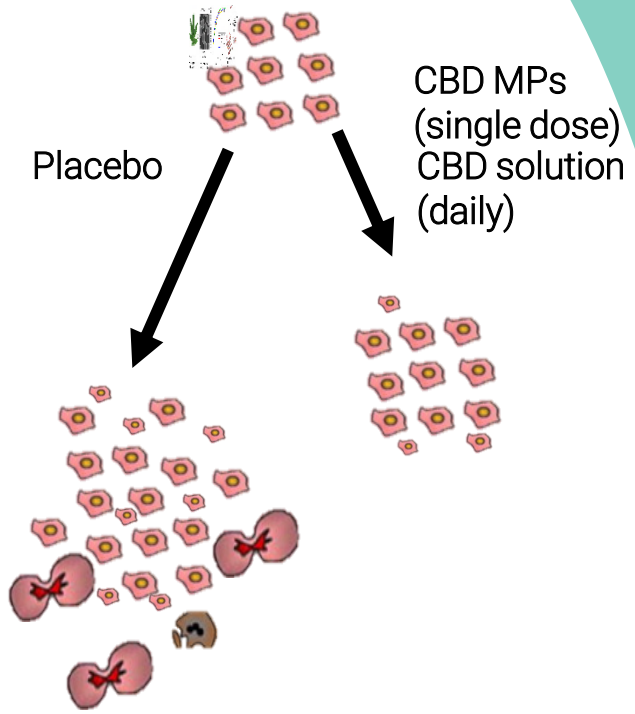


<100µm
sc administration

-Free Flowing particles
-Easy to weigh and handle

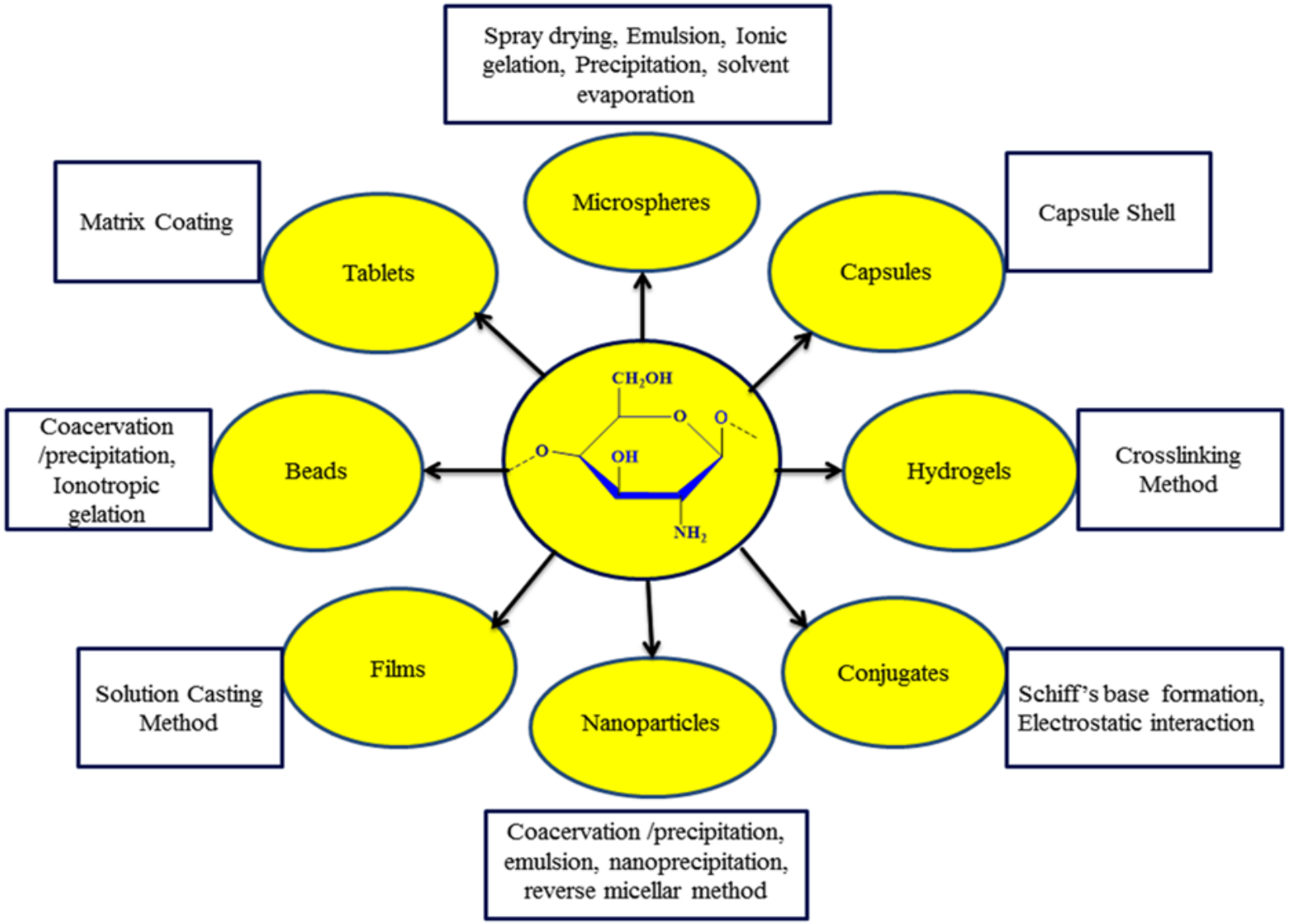


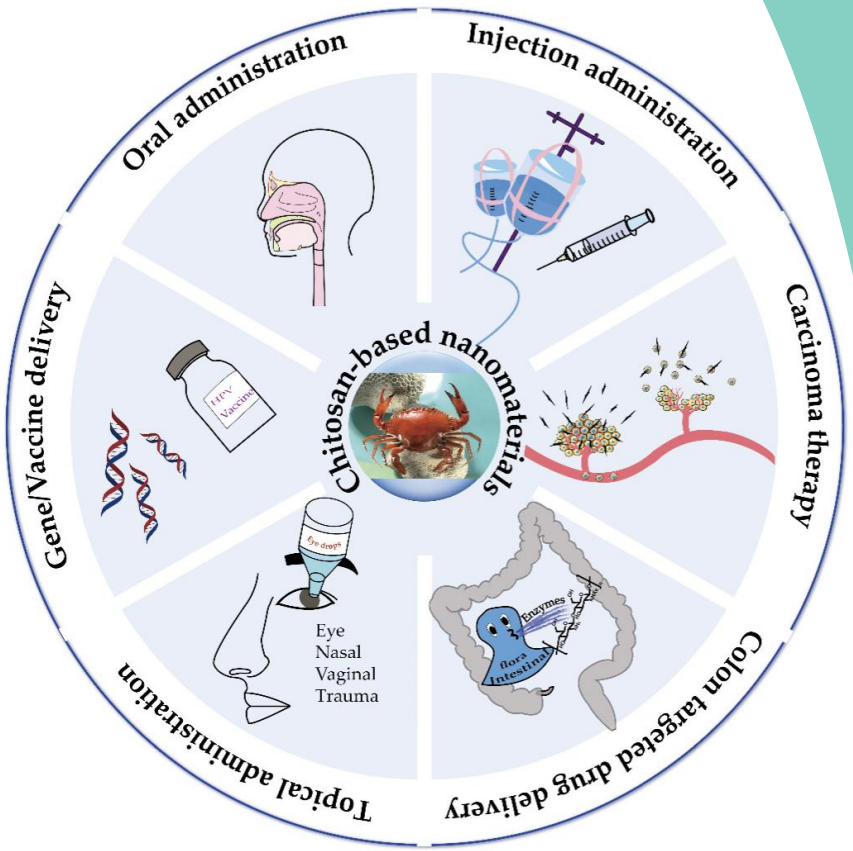
Prolonged Release



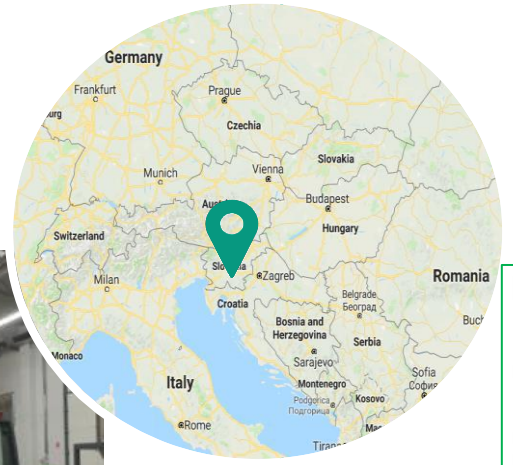
Antitumoral properties:
-MP: single dose
-CBD in solution: daily dose

GraftBio™ CHITOSAN FOR DRUG DELIVERY





IP DEVELOPMENT HISTORY



Since 2000, our team has been developing innovative polymer modification technologies and product applications to satisfy very specific market requirements across many polymer fields to provide the best solution.

Patent Applications for several grafting technologies already applied and additional patent applications will be made during 2021

Super-saturable self-nanoemulsifying drug delivery system (SNEDDS) for poorly water-soluble pharmaceutical compositions and method of its preparation

Inventors: **Victor Bolduev**, Pod Bukvami 7 ap.0017, 1000 Ljubljana, Slovenia
Aleksei Morozov, Kamnica 70, 1262 Dol pri Ljubljani, Slovenia
Ekaterina Kulevskaia, Resljeva cesta 28, 1000 Ljubljana, Slovenia

Method for industrial production of modified polymers and device for its realization

Inventors: **Victor Bolduev**, Pod Bukvami 7 ap.0017, 1000 Ljubljana, Slovenia
Ekaterina Kulevskaia, Resljeva cesta 28, 1000 Ljubljana, Slovenia

Assignees: **GRAFT POLYMER IP LIMITED,** Company Number 13155105, Eccleston Yards, 25 Eccleston Place, London SW1W 9NF

Method for production of modified polyolefin

Inventors: **Victor Bolduev**, Pod Bukvami 7 ap.0017, 1000 Ljubljana, Slovenia
Ekaterina Kulevskaia, Resljeva cesta 28, 1000 Ljubljana, Slovenia

Assignees: **GRAFT POLYMER IP LIMITED**, Company Number 13155105, Eccleston Yards, 25 Eccleston Place, London SW1W 9NF

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SWISS APPRAISAL
We Value Your Success

EXECUTIVE SUMMARY

In accordance with the Consulting Service Contract No.17-20448 dated February 14, 2017, Swiss Appraisal Russia, LLC (hereinafter referred to as the Expert) determined the fair value of the Valuation Object. For the purposes of the present Expert Opinion, the Valuation Object is defined as the use right for a know-how:

- Solid Phase Grafting Technology;
- Technology of Melt-Processible Ultra High Molecular Weight PE production;
- Surface-modified polymer particles (hot ozonolysis (plasma) modification);
- Self-Reinforced Polymers Flow – Induced Crystallization;
- Polymer Alloys (compatibilised);
- Thermoreversible Cross-linking.

The Valuation Date: March 1, 2017.

The purpose of the Expert Opinion is to determine the Valuation Object's fair value. In accordance with the Consulting Service Contract, the valuation results intended use is for the purposes of disclosure of an asset at fair value for contribution to an authorized capital

The fair value was defined in accordance with the International Valuation Standards (IVS) 2017 developed by the International Valuation Standards Council (IVSC).

Having analyzed the available information, the Expert is able to conclude that, with a view of the assumptions admitted and the restrictions stated, the Valuation Object's fair value as at the Valuation Date (March 1, 2017) approximately amounts to (VAT exclusive)

189 564 000

(One hundred eighty nine million five hundred sixty four thousand) USD

DDS Production Facility and R&D Laboratory

Feed Safety
GMP+
Assurance

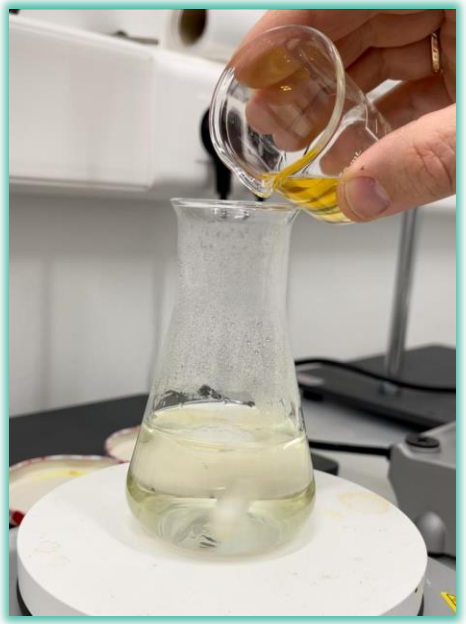
PROPOSALS to CLIENTS

Licensing ***GraftBio™*** DDS Technologies

Joint R&D Developments for DDS

Development of a Drug Delivery System at a Customer order

White Label for GP Food Supplement Products



GRAFT POLYMER
COMBINE INCOMPATIBLE

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