



## Challenges in Nutraceutical formulations

**Dr. D. N. Raut**

# **Content**

**What are nutraceuticals**

**Nutraceuticals and health**

**Therapeutic benefits**

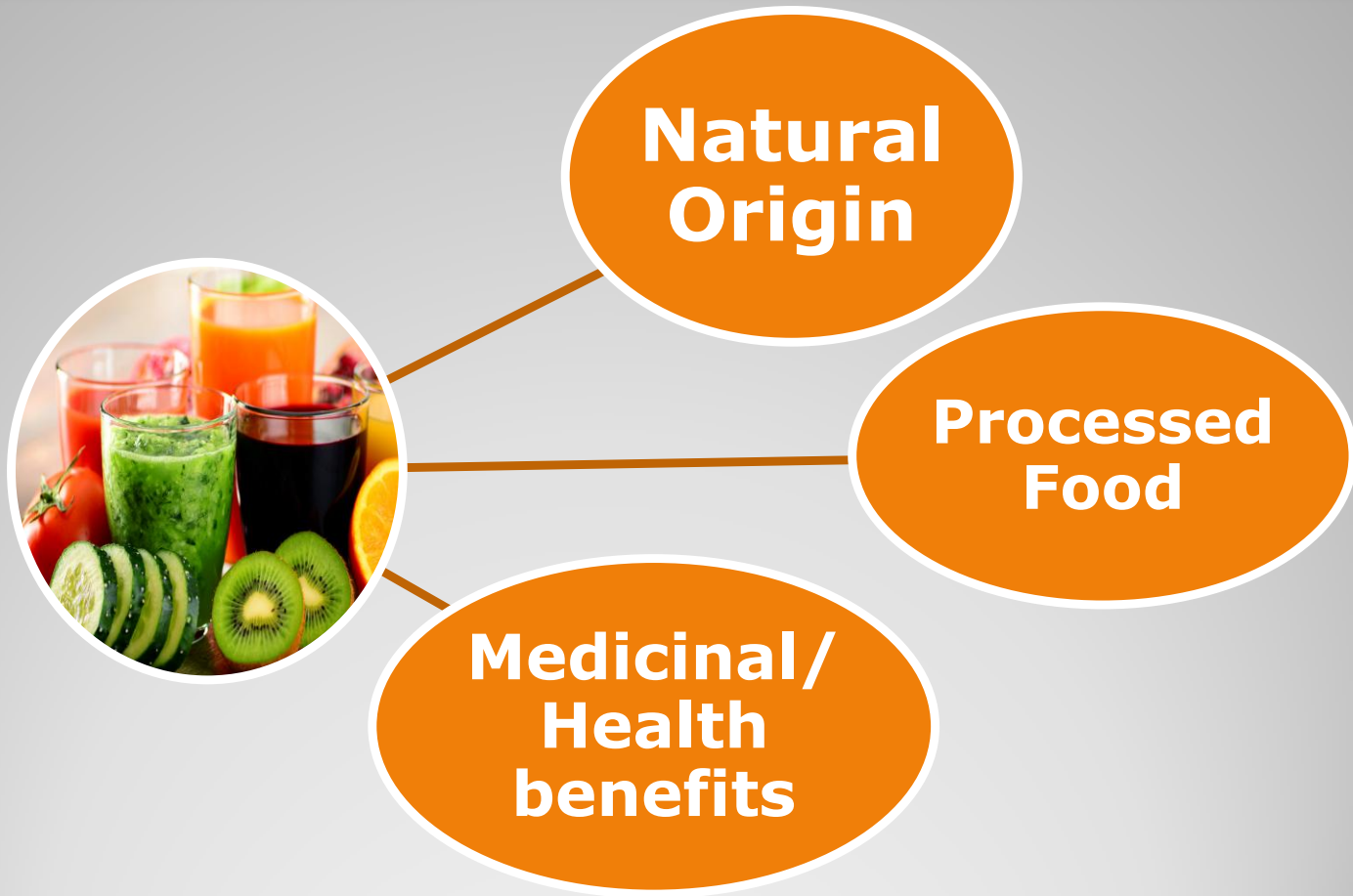
**Challenges**

**Strategies to overcome  
challenges**

**Nanotechnology to overcome  
challenges**

**Conclusion**

# Nutraceuticals



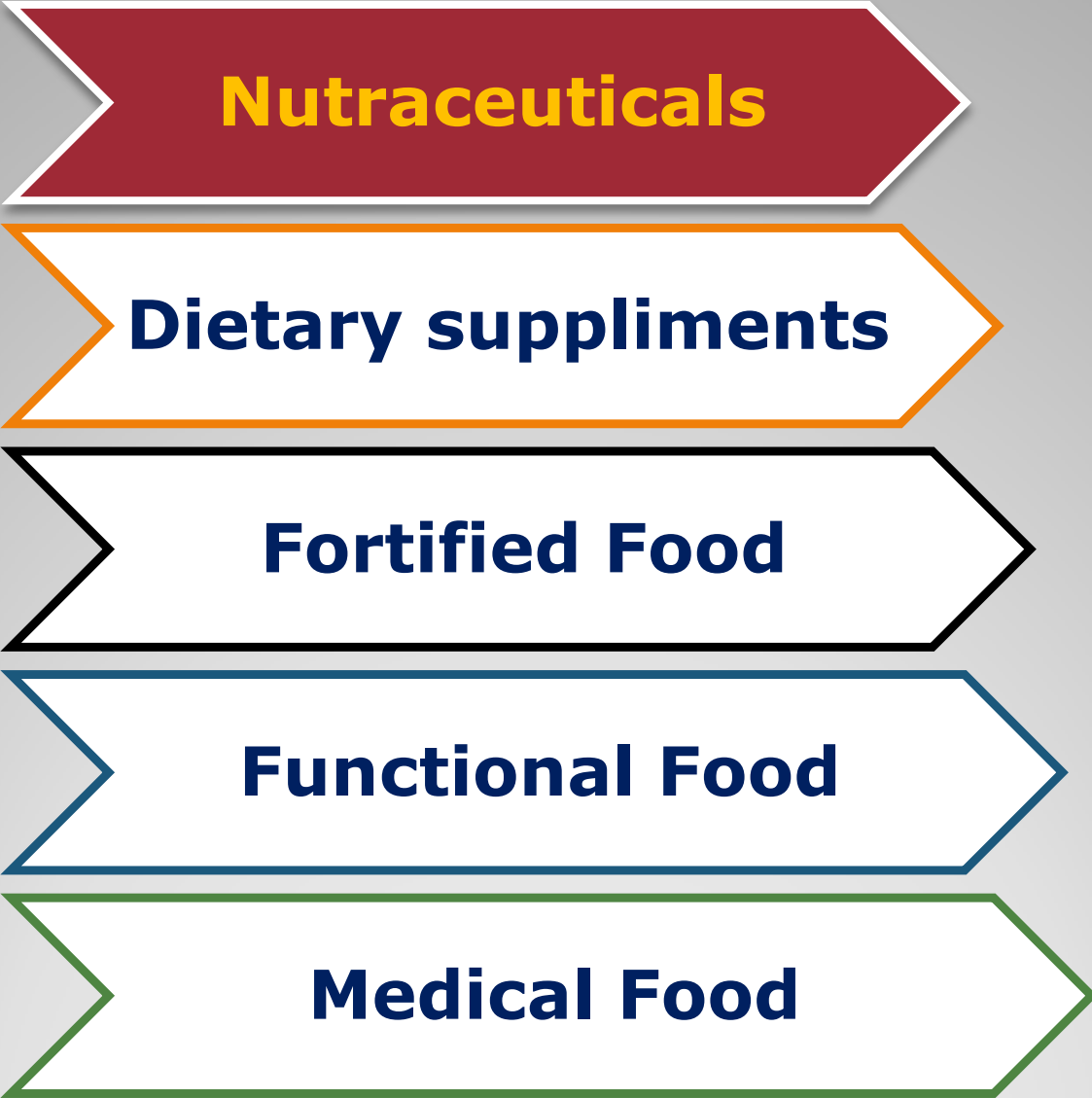
Nutraceuticals are **non-toxic food** components extracted from foods that has **scientifically established potential health benefits** for disease treatment and disease prevention.





**Vitamins, carotenoids, flavonoids, curcuminoids, polyunsaturated fatty acids, proteins, peptides, dietary fibers, oligosaccharides, and minerals.**





**Nutraceuticals**

**Dietary suppliments**

**Fortified Food**

**Functional Food**

**Medical Food**

- Nutraceuticals: The term nutraceutical, is a portmanteau of the words “nutrition” and “pharmaceutical”, and was coined by Stephen DeFelice.
- It covers isolated nutrients, dietary supplements, fortified foods, functional foods and medical foods.
- Thus, nutraceuticals are more correctly defined as parts of a food or a whole food that have a medical or health benefit, including the prevention and treatment of disease.

## **Dietary supplements:**

- Any product (other than tobacco) that is intended to supplement the diet and contains one or more of –
  - Vitamin,
  - Mineral,
  - Herb or other botanical
  - An amino acid or metabolite
  - An extract; or any combination of the above.



## **Fortified foods:**

- Enriched with vitamins and minerals, usually at a range up to 100 percent of the Dietary Reference Intake (DRI) for that nutrient.
- It is mandated by law to be fortified to a level that replaces nutrients lost during processing, as in adding B vitamins to many baked goods.
- Breakfast cereals is a food category that has been fortified since the 1940s.

## **Functional foods:**

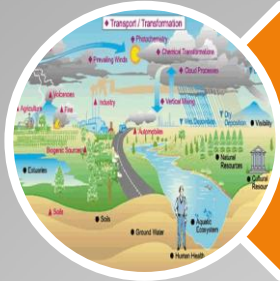
- Functional foods are any food or food ingredient that may provide a **health benefit** beyond the **traditional nutrients** it contains.
- “traditional nutrients” refers only to vitamins and minerals.

## **Medical foods:**

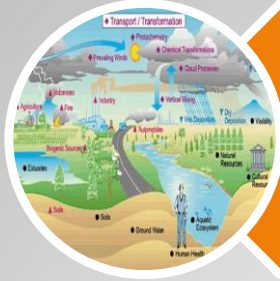
- Medical foods refer to a food formulated to be consumed or administered internally while under the supervision of a physician.



**Industrialization caused high levels of atmospheric pollution.**



**The extensive use of  
various harmful  
chemicals and products**



**Industrialization**



**Lifestyle**

- ❑ Dramatically increase in the cost of medical care.
- ❑ People have tried to achieve a better quality of life by consuming more vegetables, fruits, and other plant foods, taking dietary supplements or so called nutraceuticals.

- ❑ The nutraceuticals do possess multiple therapeutic benefits and have been claimed to have physiological benefits
- ❑ most nutraceuticals currently used are known vital nutrients for the human body,.
- ❑ however dose, drug interaction, nutraceutical - drug interaction, and their effects on individuals under certain health conditions remain indescribable.

A pink piggy bank is broken into several pieces on a light gray surface. The main body is cracked and split open, with a large piece missing. A smaller piece lies nearby. The background is a plain, light gray wall.

**Due to Relatively low  
and/or variable oral  
bioavailability as a  
result of various  
physicochemical  
and/or physiological  
processes.**

**Potential benefits of  
many nutraceuticals  
are not optimally  
realized**

**Relatively low and/or variable oral bioavailability as a result of -**

**formation of insoluble complexes with other components in the gastrointestinal tract (GIT)**

**low solubility in gastrointestinal fluids**

**low permeability across the mucus layer or epithelium cells**

**Molecular transformations in the GIT.**

**Restricted liberation from the food matrix**



- The **reduced bioavailability, stability and permeability** of the bioactive components in the gastrointestinal (GI) fluids leads to their partial absorption from the GI tract during their first pass metabolism.
- This results in their **reduced or almost no biological activity**, which is a major concern of the researchers today.



**Effective  
solubilisation**

**Encapsulation**

**Delivery**

**Lead  
to**

**Based  
on**

**Excellent absorption  
in lower doses**

**Reduced frequency  
of administration**

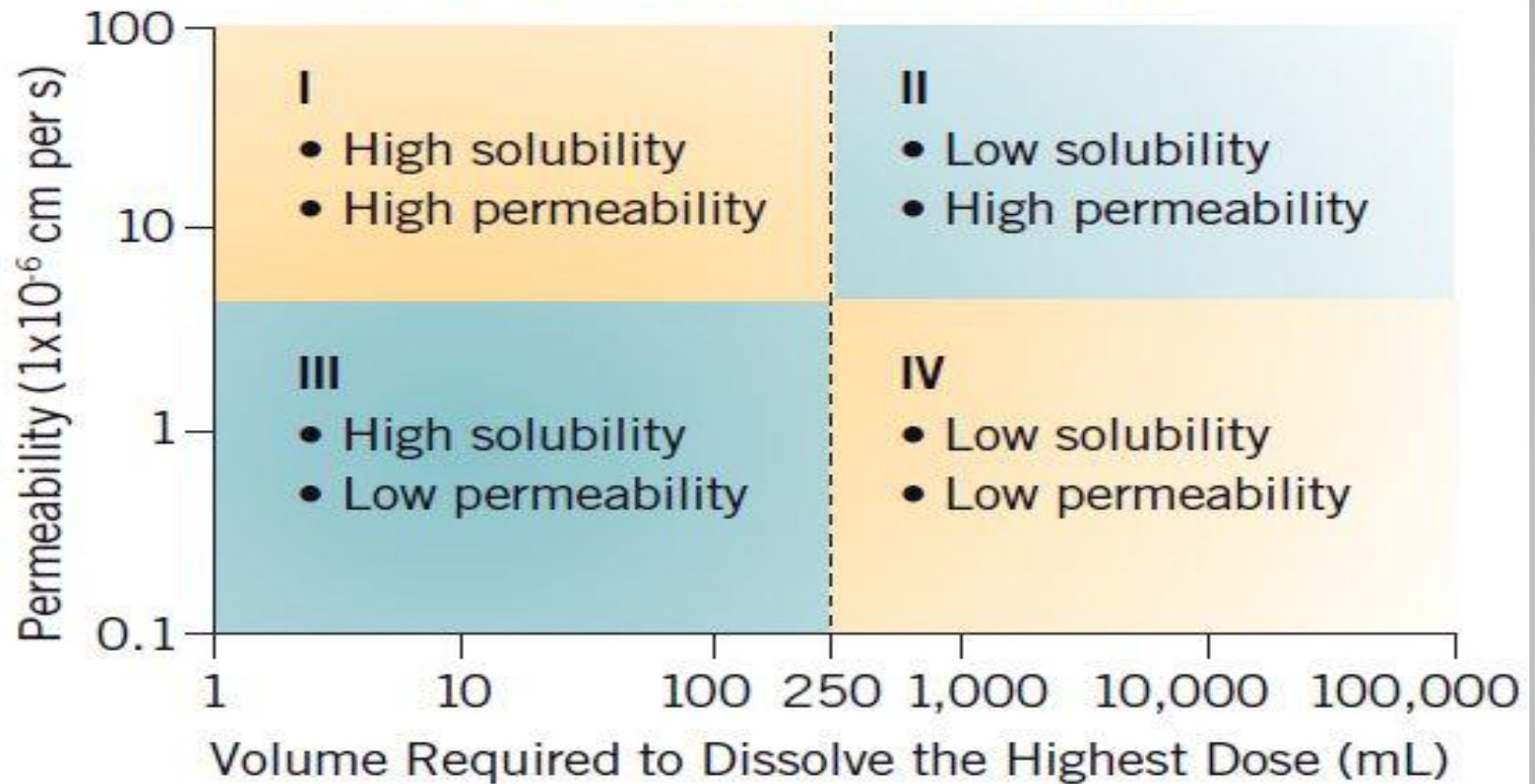
**Amended  
therapeutic index.**

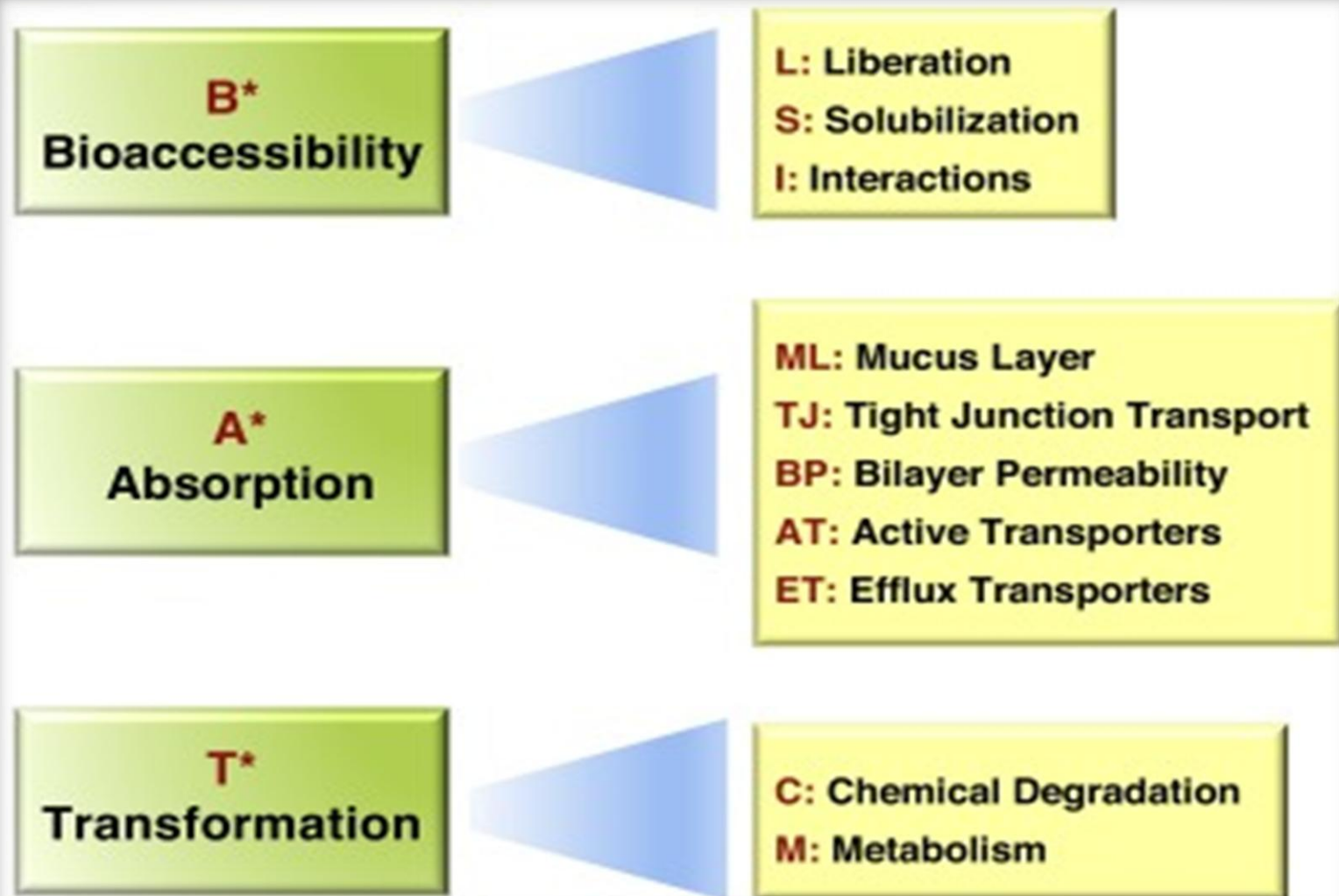
**In search of  
Drug Delivery  
Techniques for  
Nutraceuticals**

- The biopharmaceutical classification scheme (BCS) that is widely used in the pharmaceuticals to characterize the major factors limiting the oral bioavailability of drugs, such as their low solubility and/or permeability.
- There are various complicating factors that impact the bioavailability of nutraceuticals present within food matrices, which limits the usefulness of the BCS for food components.

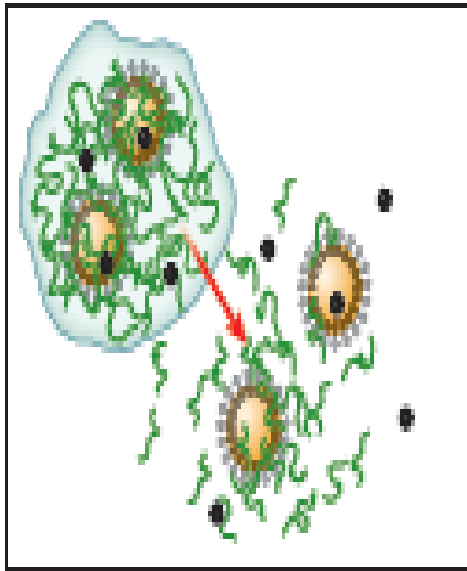
Ref.: Amidon et al. 1995, Dahan et al. 2009.

# BIOPHARMACEUTICAL CLASSIFICATION SYSTEM

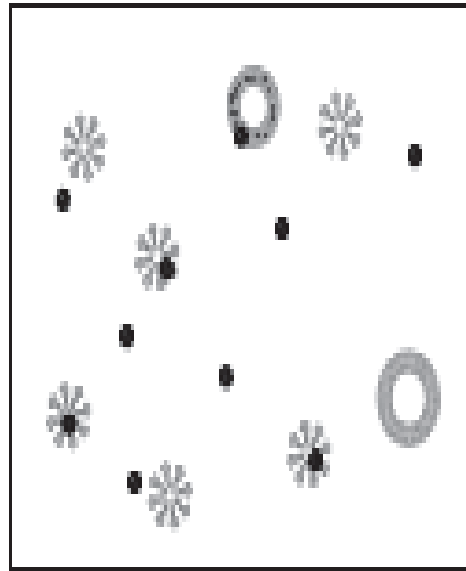




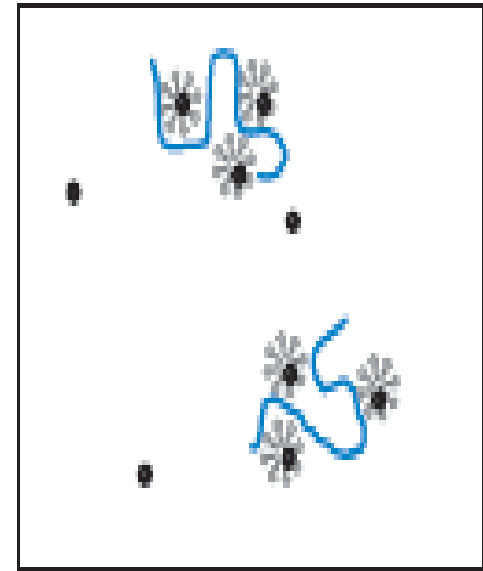
Classification scheme for Nutraceuticals Bioavailability developed by **McClements et al**



**Liberation from  
food matrix**

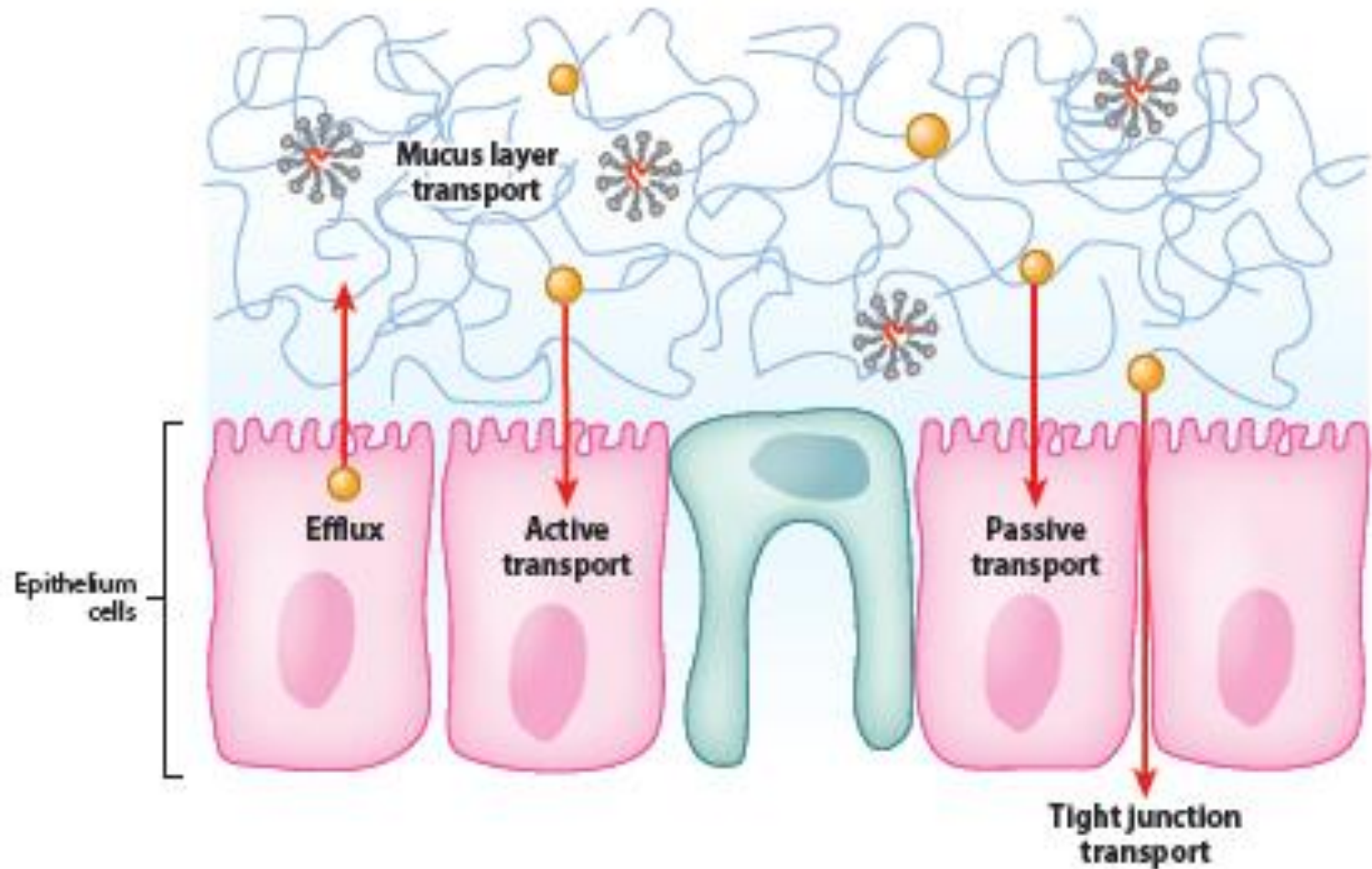


**Solubilization in  
intestinal fluids**



**Interactions and  
insoluble complex  
formation**





**Factors limiting absorption of nutraceuticals by epithelium i.e transport across mucous layer.**



| Major Class      | Sub Classes                   |                          |                               |                  |                  |
|------------------|-------------------------------|--------------------------|-------------------------------|------------------|------------------|
| Bioaccessibility | Liberation Limited            | Solubality limited       | Interaction limited           |                  |                  |
| Absorption       | Mucin layer transport limited | Tight Junction transport | Membrane Permeability limited | Active Transport | Efflux transport |
| Transformation   | Chemical degradation limited  | Metabolism limited       |                               |                  |                  |

Factors limiting bioavailability

## Bioaccessibility:

*It is related to the bioaccessibility of the nutraceutical within the intestinal fluids of the GIT.*

Before ingested nutraceuticals can be efficiently taken up by the body, they must be present within a physical form that is suitable for absorption.

For hydrophilic nutraceuticals, this may simply be the fraction of the nutraceutical that is fully dissolved within the intestinal fluids (rather than present in an insoluble, complexed, or crystalline form).

For hydrophobic nutraceuticals, this may be the fraction of the nutraceutical that is solubilized within mixed micelles in the small intestinal fluids.

***Liberation limited:***

***The bioaccessibility of a nutraceutical may be limited by its ability to be released from the food matrix.***

**E.g.** carotenoid trapped within the cellular structure of a raw vegetable that is not fully released in the GIT after the vegetable is ingested

Increasing the release of these kinds of nutraceuticals from the food matrix would be an **effective strategy** to increase their bioavailability.

**This may be achieved**

By **altering food processing conditions** (such as cooking, shearing, or homogenization),

By **changing eating habits** (such as duration of mastication), or

By **altering food matrix properties** (such as composition&structure).

### ***Solubility limited:***

*The bioaccessibility of a nutraceutical may also be limited by its ability to be solubilized within intestinal fluids.*

hydrophobic nutraceuticals have low solubility in water, and therefore need to be incorporated into mixed micelles in the small intestine before they can be absorbed.

The bioavailability may therefore be improved by utilizing food compositions or structures that enhance their intestinal solubility.

### **Interaction limited:**

It is limited by its interaction with other components in the gastrointestinal fluids.

It may arise from the ingested food matrix, or they may be naturally present within the GIT.

A nutraceutical in this class may form **an insoluble complex** that is not easily absorbed. E.g. anionic long chain saturated fatty acids may interact with cationic calcium ions in the intestinal fluids and form an insoluble complex that has low bioaccessibility.

It can be limited by the **presence of particular components** within ingested food matrices, such as ionic biopolymers or chelating agents. E.g. **chelating agent** may decrease the bioaccessibility of a mineral io, or a cationic biopolymer (such as chitosan) may decrease the bioavailability of anionic fatty acids due to the formation of insoluble electrostatic complexes .

(Wydro et al. 2007).

## **Absorption:**

This is related to the absorption of the nutraceutical from the gastrointestinal fluids.

The fraction that travels through the mucus layer, across the epithelium cells, and into the systemic circulation.

- *Mucin layer transport limited*
- *Bilayer permeability limited*
- *Tight junction transport limited*
- *Active transport limited*
- *Efflux transporter limited*

***Overall factors limiting absorption***

## Transformation:

- The bioavailability of many nutraceuticals is limited because they are transformed into an inactive form within the GIT.

These molecular transformations can be divided into-

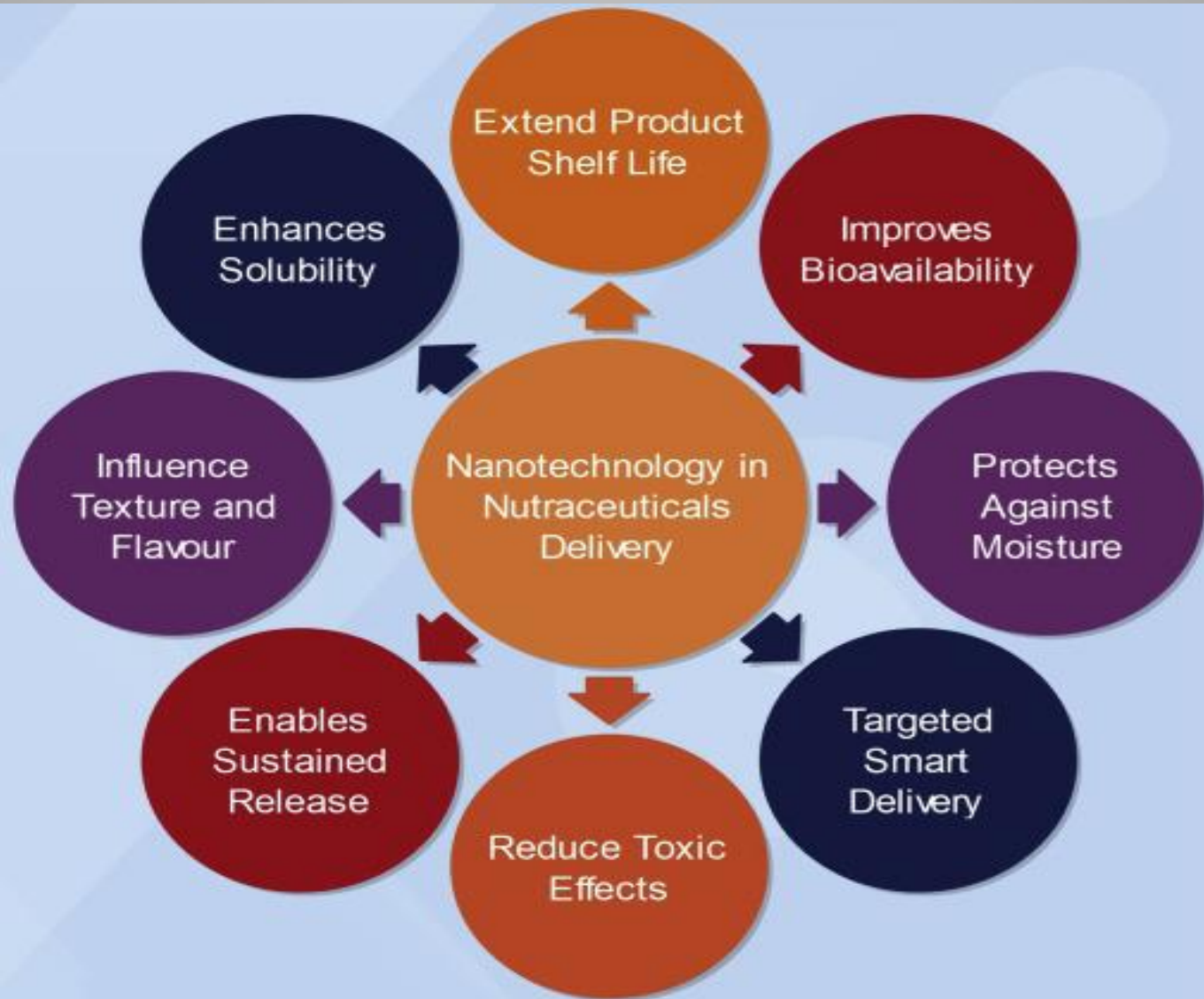
- **Chemical degradation limited**

E.g., polyunsaturated lipids (such as  $\omega$ -3 fatty acids or carotenoids) may be oxidized due to the presence of pro-oxidants in the GIT, whereas proteins or peptides may be hydrolyzed by the highly acidic and enzyme-active environment of the stomach.

- **Metabolism limited**

Some nutraceuticals are metabolized by specific enzyme systems within the GIT, e.g., resveratrol, quercetin and epicatechin.

Many important nutraceuticals are susceptible to phase I and phase II metabolism within the GI.



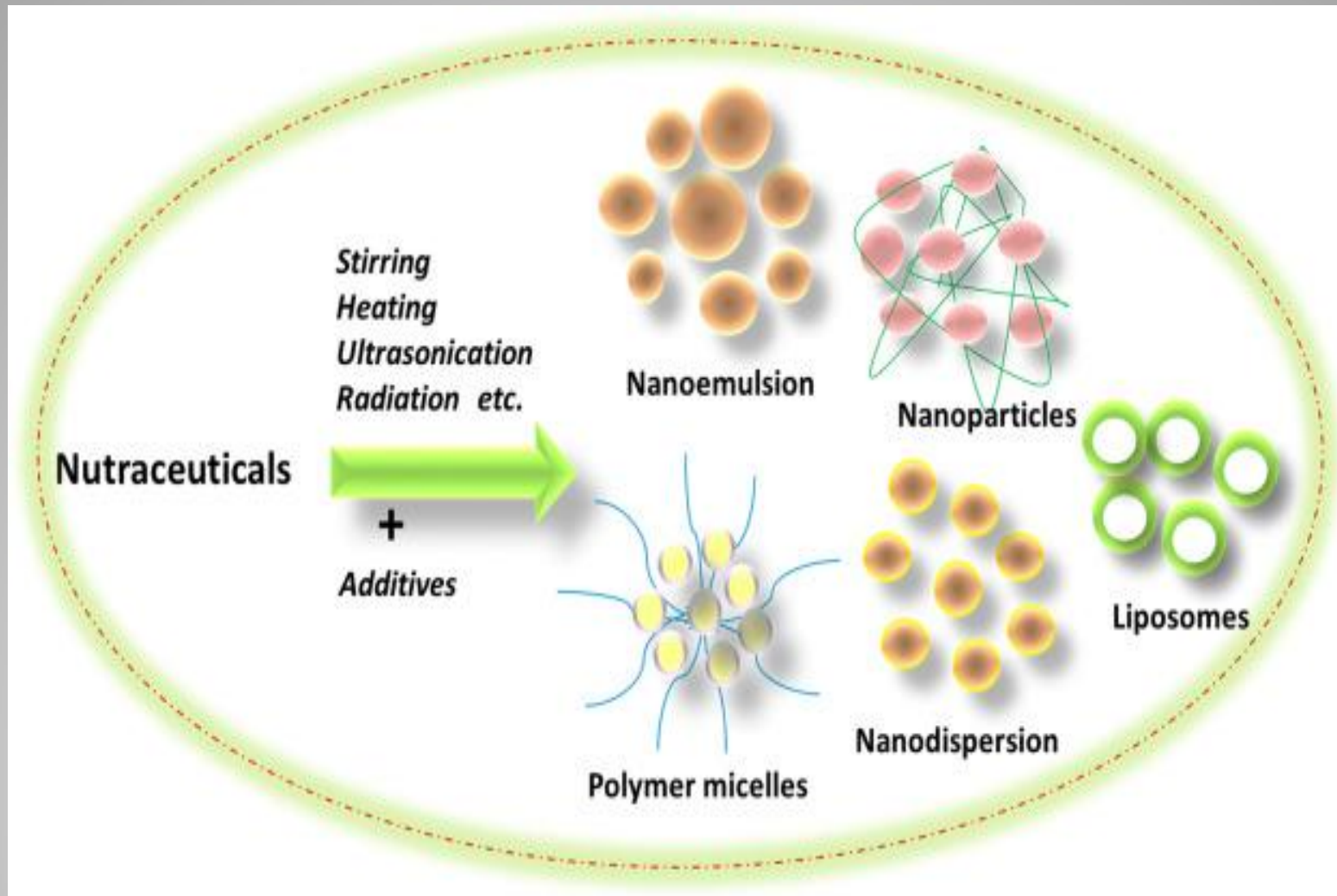


```
graph LR; A((Nutrients, and other natural compounds)) --- B((Can be loaded into biocompatible & biodegradable nanoparticles)); A --- C((which will improve their aqueous solubility, stability, bioavailability, circulation time and target specificity));
```

**Nutrients,  
and other  
natural  
compounds**

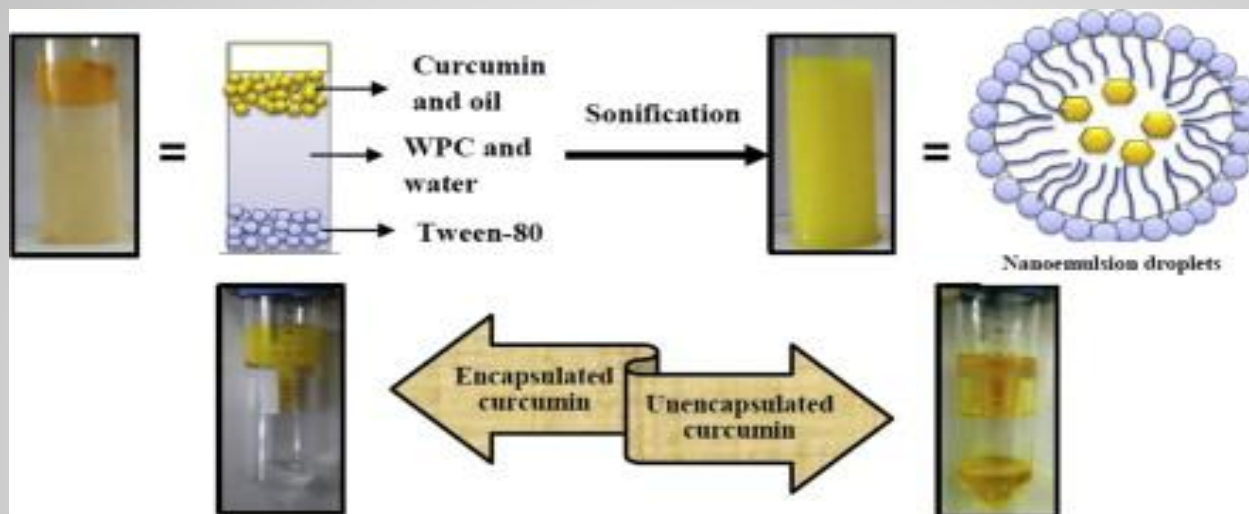
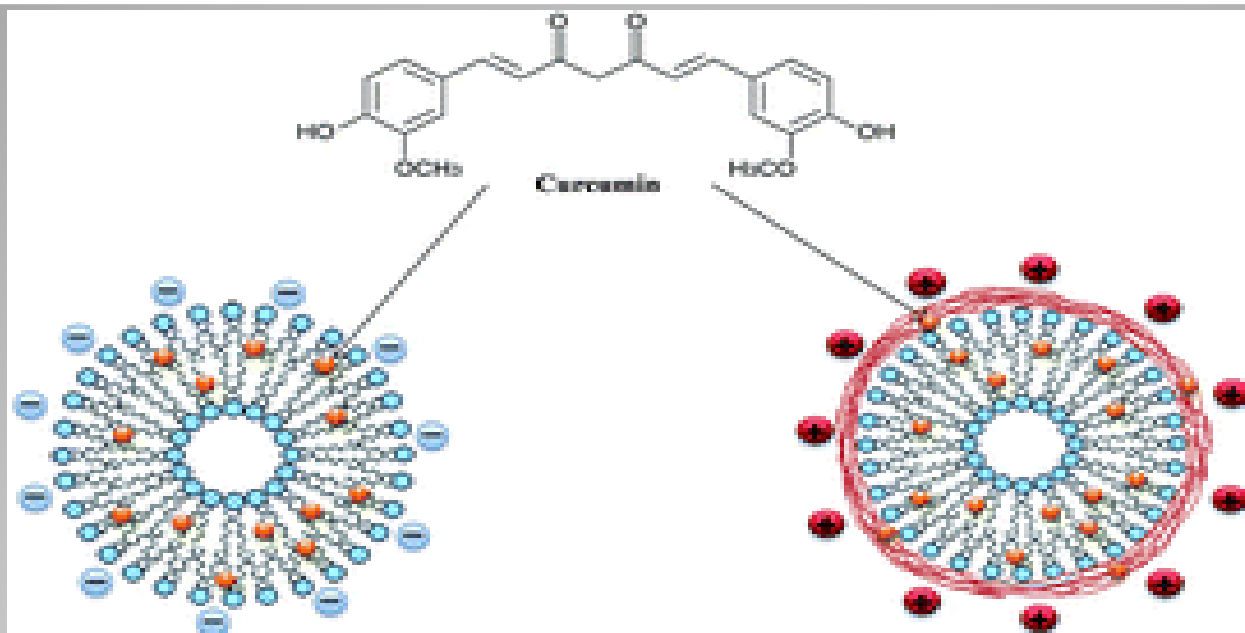
**Can be loaded  
into  
biocompatible &  
biodegradable  
nanoparticles**

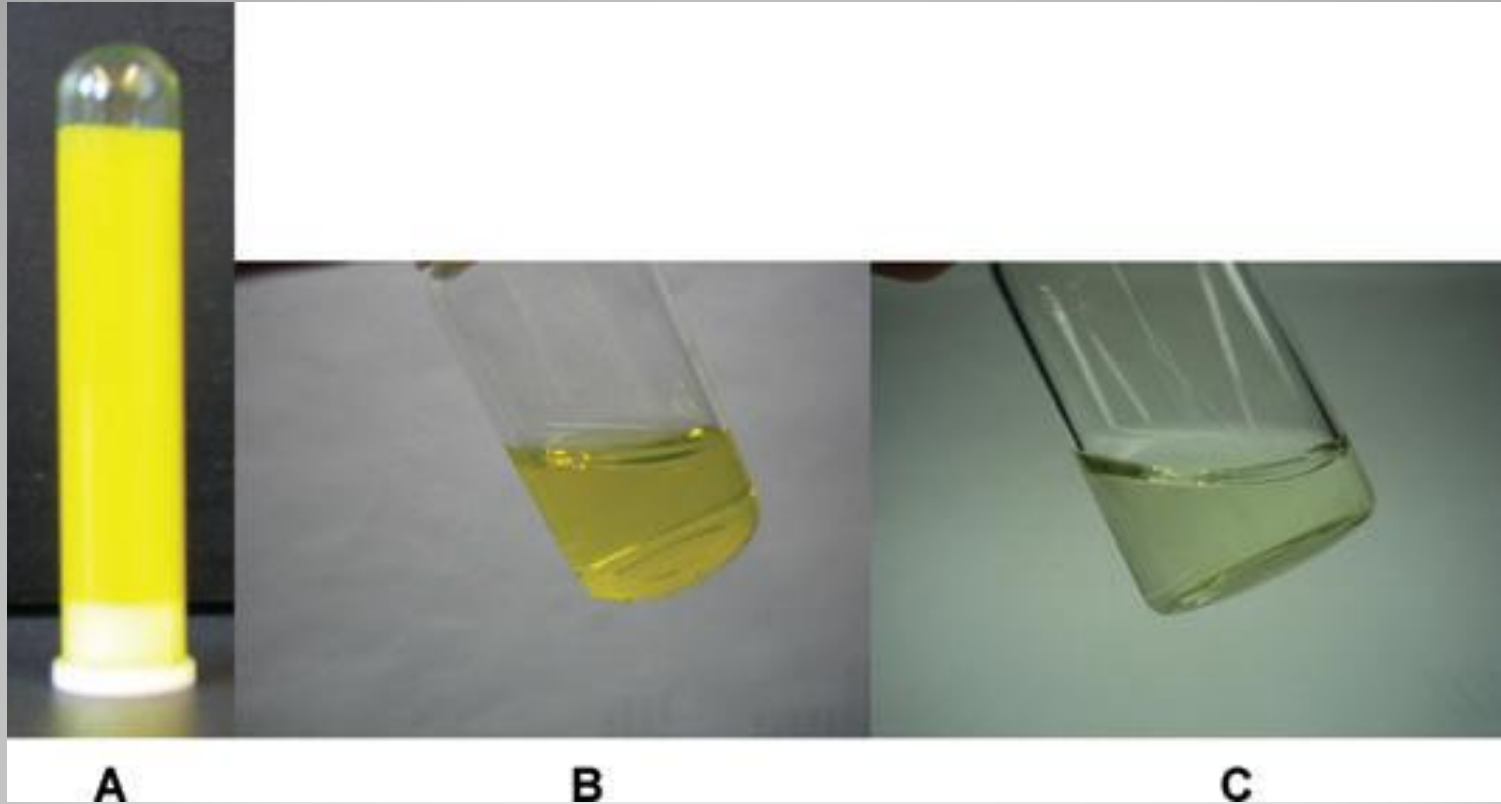
**which will improve  
their aqueous  
solubility, stability,  
bioavailability,  
circulation time  
and target  
specificity**



Reference: <https://doi.org/10.1016/B978-0-12-811942-6.00003-0>

- An excellent example to demonstrate the advent of nanotechnology for the incredible **enhancement in the solubility and the bioavailability of curcumin**, a potential nutraceutical with several significant properties including anti-cancer potential, has been evidenced by various *in vitro and in vivo studies, by the development of various nano-formulations*.
- The **encapsulation of curcumin along with magnetic nanoparticles** exhibited excellent reduction in cancer cells *in vitro in the synergistic with that of magnetic hyperthermia are demonstrated* .
- **Encapsulated lutein**, which is a potential nutraceutical, incorporated into **polymeric nanoparticles**, thus **enhancing the solubility** of the same.
- A cream using **nano-lutein and curcumin** for **cosmetic applications** was also studied





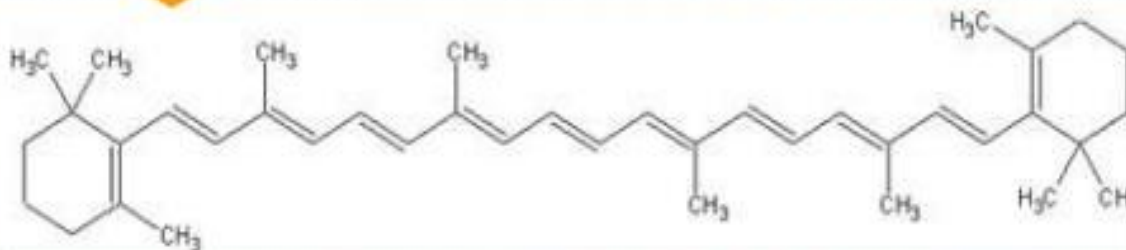
**Nanoemulsion based delivery of Curcumin.**

Main source: Carrots



$C_{40}H_{56}$

Apolar

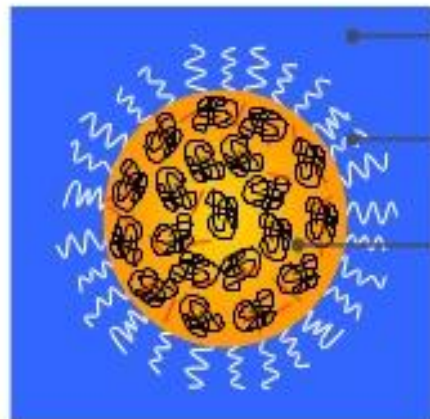


11 conjugated double bonds

Susceptible to oxidation and isomerisation

National food research institute, Japan

# $\beta$ -Carotene-enriched nanoparticles



Continuous phase: Water

Emulsifier

Dispersed phase: - Dissolved active compound  
- Polymer



- ✓ Spontaneous nanoparticles formation
- ✓ Water dispersible formulation
- ✓ High entrapment efficiency
- ✓ High reproducibility

# Conclusion

- ❑ Development of nutraceuticals and functional foods with distinctive traits would be a potential to deliver unique products to the world at large.
- ❑ Development of better characterized and research proven products will help to enhance consumer confidence in nutraceutical and functional food products in the rest of the world.





**Have a delicious and healthy food**



*Thank  
you*



**Your patience is highly appreciated!!!**