

**SMi 5th. Nutraceuticals & Functional Foods Conf.
January 26th. London, UK.**

Delivering Biological Effectiveness from Nutraceuticals

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Ceres Consulting
Canada**



Ceres Consulting

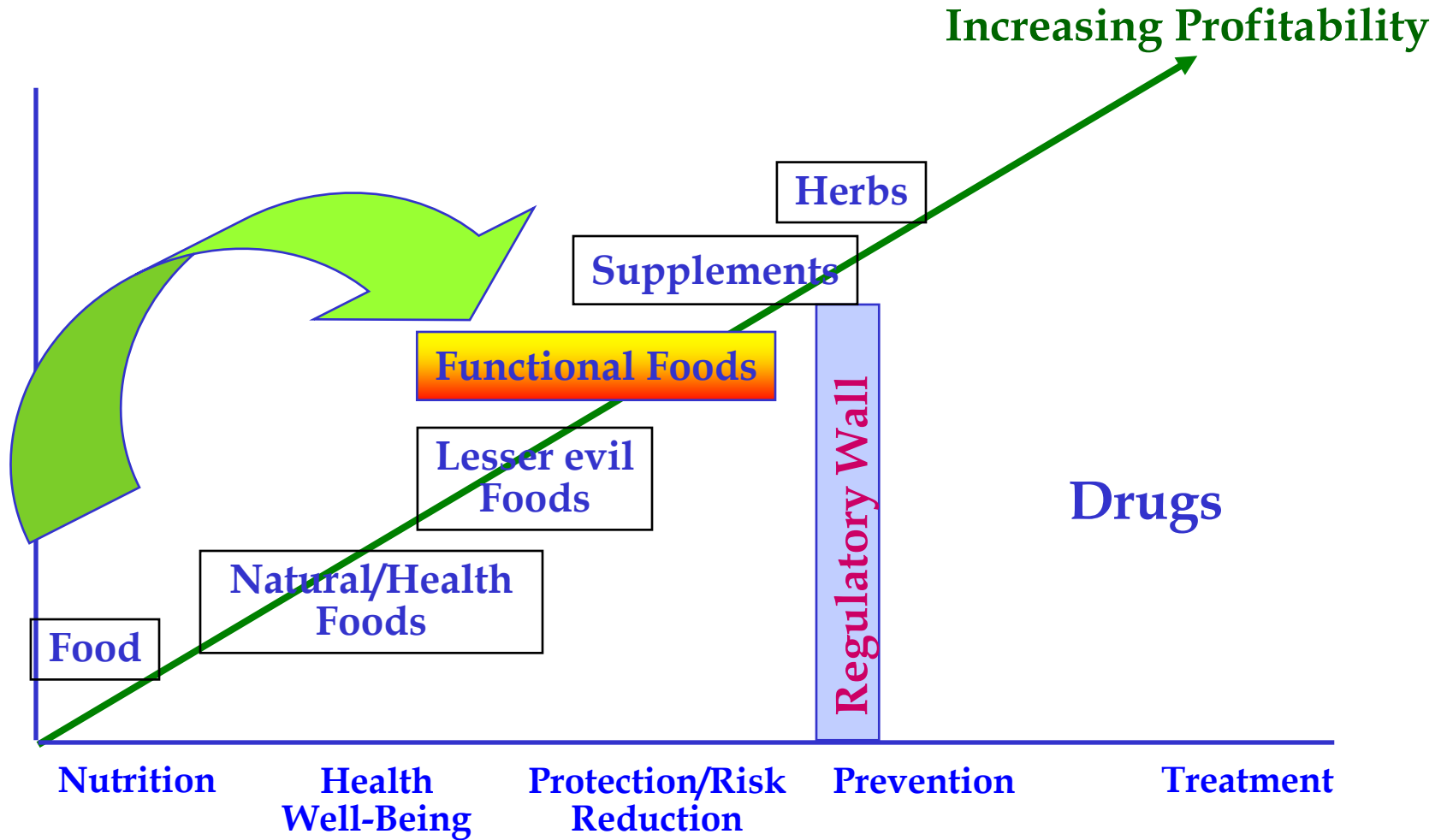
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The Basics for Nutraceutical actives

- Dried forms (herbs, plant parts, animal parts)
 - Extractions
 - Pressure
 - Solvent, organic or water
 - Super critical gases
 - Microwave assisted (solvent)
 - Refining (oils especially)
 - Synthetics
-
- Product form development
 - Powders (SD and adsorbates)
 - Agglomerations/aggregates
 - Emulsions
 - Liposomes
 - Non co-valent bond forms



Foods to Drugs....



Trends driving FF market

Consumers

- More health conscious
- 'Natural' self-medication
- Ageing population

Health Care Professionals(HCP)

- New discoveries in FF
- Promote healthy eating



Government

- Rising healthcare costs
- Regulatory framework

Retailer/Marketers

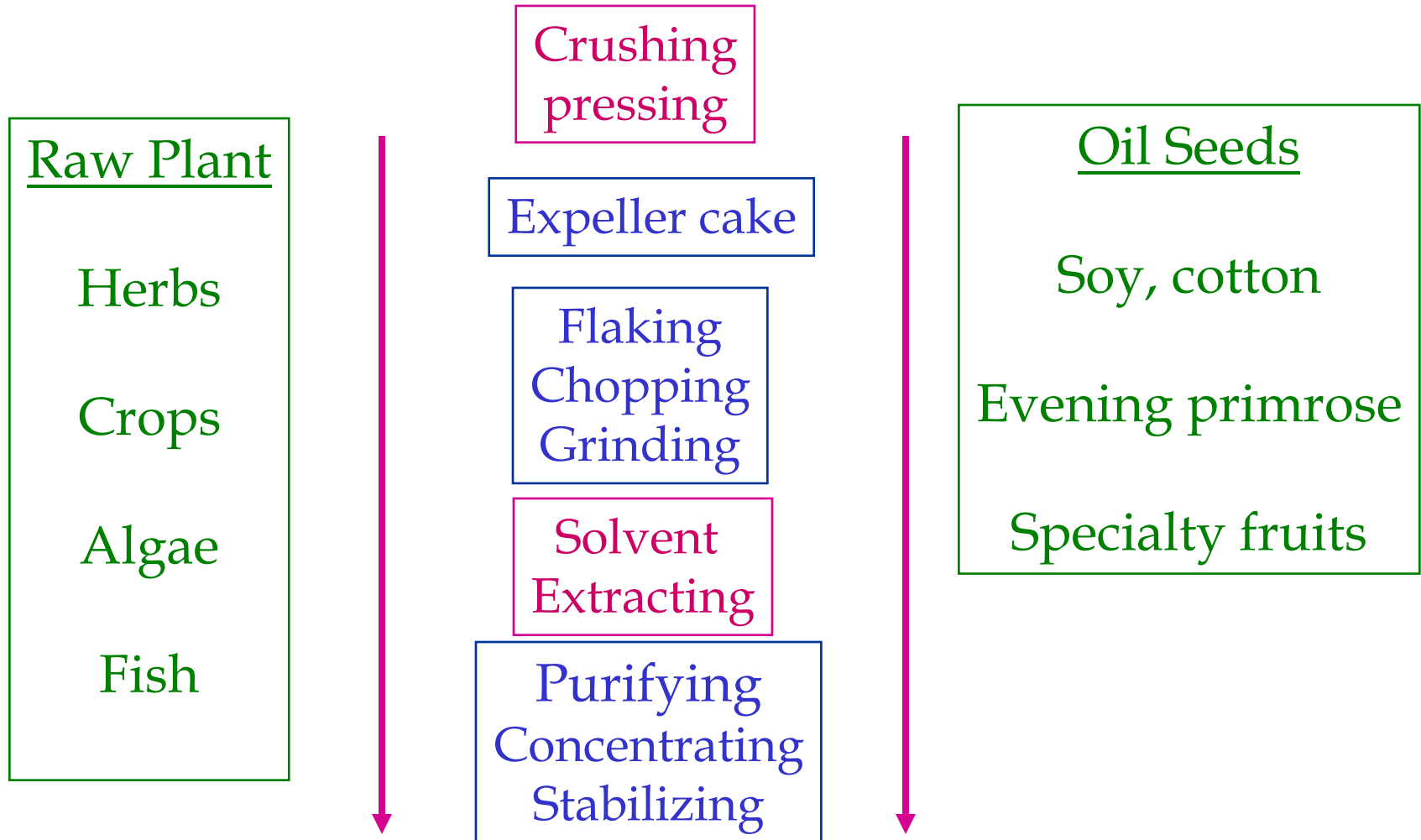
- Search for growth opportunities



Cost Effectiveness Cholesterol lowering Agents



Extraction and Refining



Pressing and solvent extraction

- Well established and cost effective
- Large scale plant equipment (capital)
- Large volumes of solvent and recovery required
- Reasonably efficient, diffusion process
- Solvent (VOC) volatiles concerns and regs.
- Often hazardous hot solvents



Supercritical Fluid Extraction

- Can be used in wide variety of applications
- High cost
- Useful for smaller high value actives
- Large uses due to specialized need, decaffeination (reduces hazardous solvent)
- Absence of any organic solvents (uses CO₂)
- Selective extraction/fractionation possible





Microwave Assisted Solvent Extraction of Phytochemicals (MAP)

Radiant Technologies

The Radiant MAP™ technology

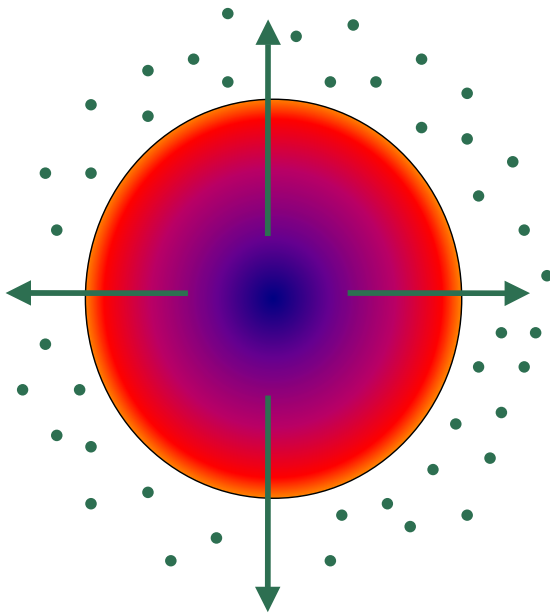
- Use of microwave energy to extract active ingredients from biomass
- Selective and localized heating of residual moisture in “target” organic matter
- Solvents are relatively microwave transparent and stay cool (reduced heat degradation - better product stability)
- Rapid temperature rise can cause cell membranes to rupture, resulting in a fast release of actives
- Normal diffusion-driven mechanism not important

Faster - Better - Cheaper - Cleaner



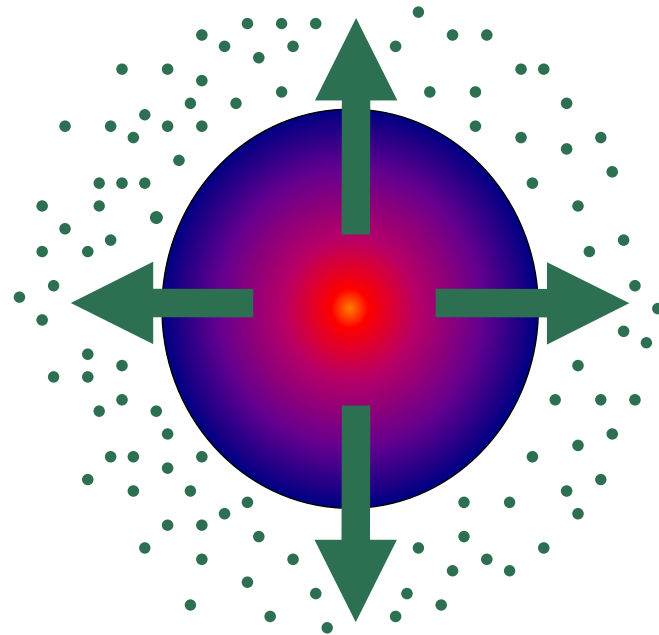
Novel Extraction Mechanism

Conventional Solvent Extraction



- Diffusion-driven process
- Driving force is concentration gradient

Microwave-Assisted Solvent Extraction

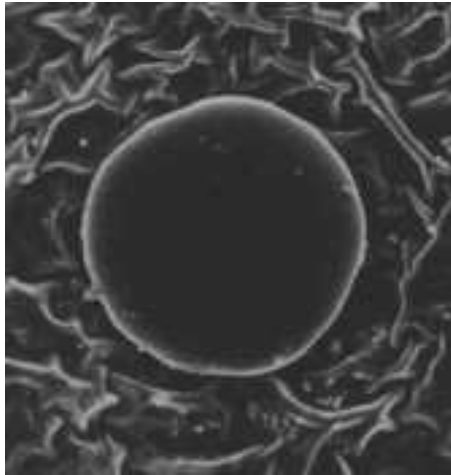


- Inverted thermal gradient
- Pressure-driven “direct” extraction

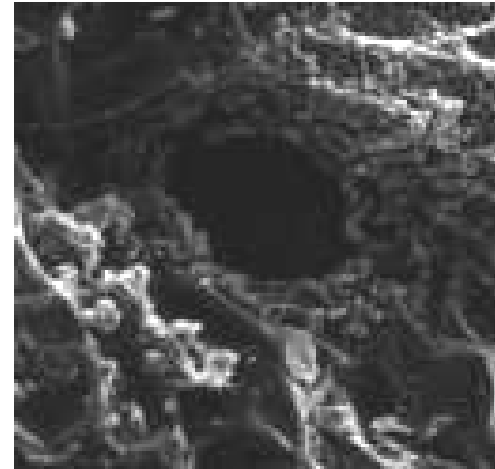


Cell Rupture Possible

- Rapid temperature rise can cause cell membranes to rupture, resulting in fast release of desired components



Mint gland before exposure to microwaves



Microwave-exploded gland



The Possibilities for MAPTM Extraction

Commodity Food Oils

Canola oil, soybean oil, corn oil,
World market \$30.9B in 1999

- Low value / high volume production
- Process economics important
- Emerging regulatory pressures
- Hexane now a US EPA HAP

Naturally-Derived Chemicals

Flavours, fragrances, colours,
nutraceuticals / pharma actives
World market \$7.8B in 1998

- Market growing by 9% per year
- Driven by desire for improved products
- Purity and yield are important



Value to Manufacturers

- **Reduced processing costs**
 - Increased recovery of marker/active compounds
 - Significantly faster, minutes vs. hours
 - Reduced energy usage
 - Reduced solvent usage
 - Uses existing plant, increases throughput
- **Improved Products**
 - Increased purity of crude extracts
 - Possibility to use less toxic solvents
 - Reduced heat degradation
 - Novel compositions

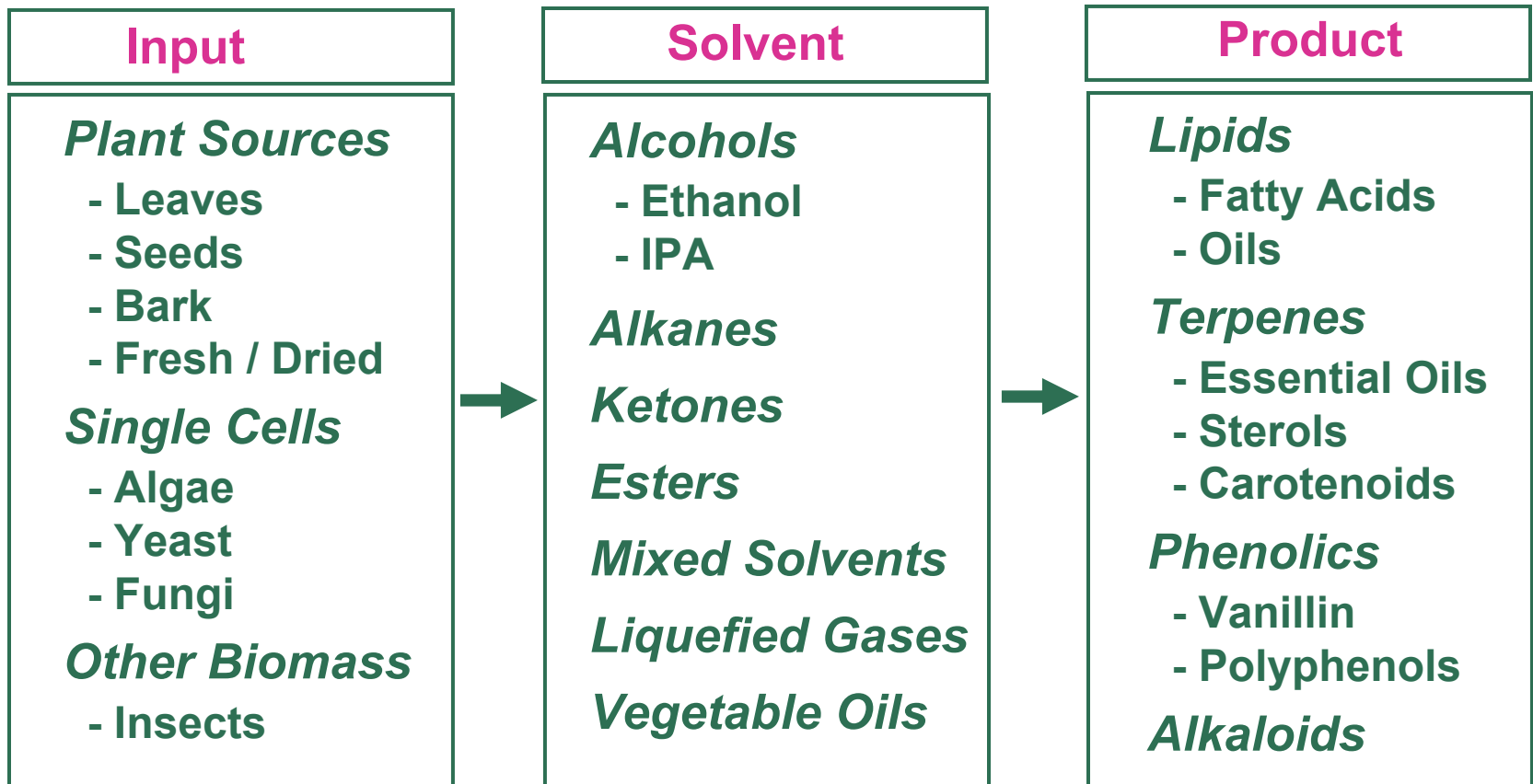


Greater Flexibility Drives Opportunities

- **Many levers:**
 - » microwave power / energy density
 - » post-microwave mixing
 - » solubility properties of mixed solvents
 - » raw material pre-treatments
- **Solvent flexibility:**
 - » diffusivity, viscosity not important
- **Efficient down-stream processing:**
 - » multiple extraction sequences
 - » further purification / isolation steps



Many Compelling Examples



Case Studies

- **Antioxidants from Rosemary Herb**
- **Alkaloids (piperine) from Black Pepper**
- **Fatty Acids from Oilseeds**
- **Polyphenols from Green Tea**



Antioxidants: Carnosic Acid from Rosemary

Commercial Goal: Maximize recovery and purity of main antioxidant marker, *carnosic acid* (CA)

	Purity (% CA)	Recovery (%)
Conventional Extraction	<i>Crude Extract</i>	15%
	<i>Refined Extract:</i>	40 - 50%
Radiant MAP Extraction	<i>Crude Extract</i>	29%
	<i>Refined Extract:</i>	58%

Recovery values for Radiant MAP Extraction: >95% (Crude), >90% (Refined)

- Reduced degradation of CA
- Low volatile oil content (low flavor)
- Similar results obtained using only EtOH

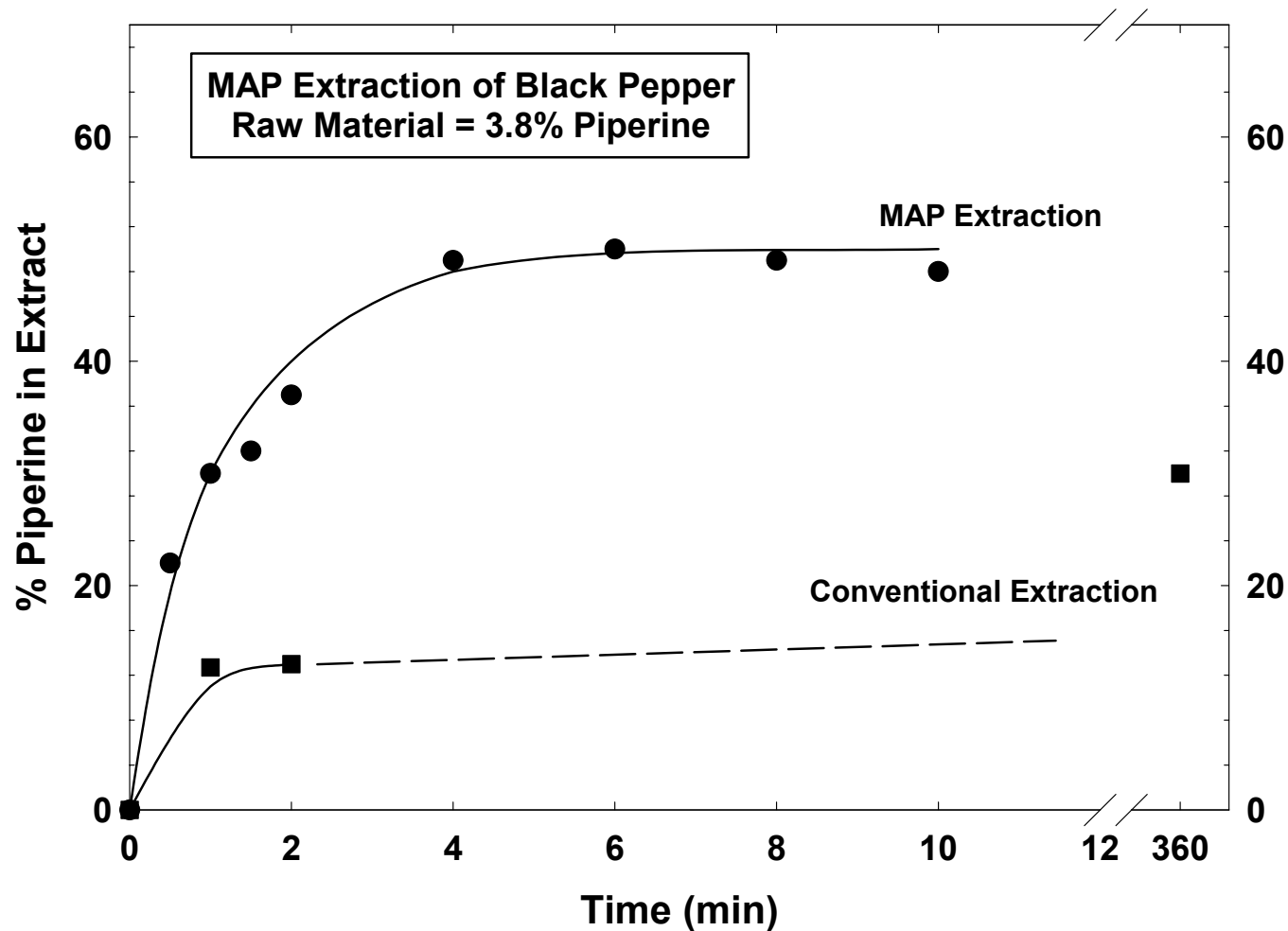


Alkaloids: Piperine from Black Pepper

- **Piperine responsible for pungency**
 - » Bacteriostatic, fungistatic and insecticidal activity
 - » Bio-availability enhancer
- **Conventional extraction takes 16 to 24 h**
 - » Non-selective
 - » Crude extracts typically contain 30 - 40% piperine
 - » SFE gives up to 60% piperine



Alkaloids: Piperine from Black Pepper



Piperine Extraction

Extraction Conditions	Extract Yield (%)	Extract Purity (% piperine)
Soxhlet MeOH / 2 days	11.5%	33%
MAP Hexane / 8 min	6.2%	58%* (95% recovery)

* Equivalent purity for 5% starting material = 70 - 75%

MAP enables fast, selective extraction of piperine



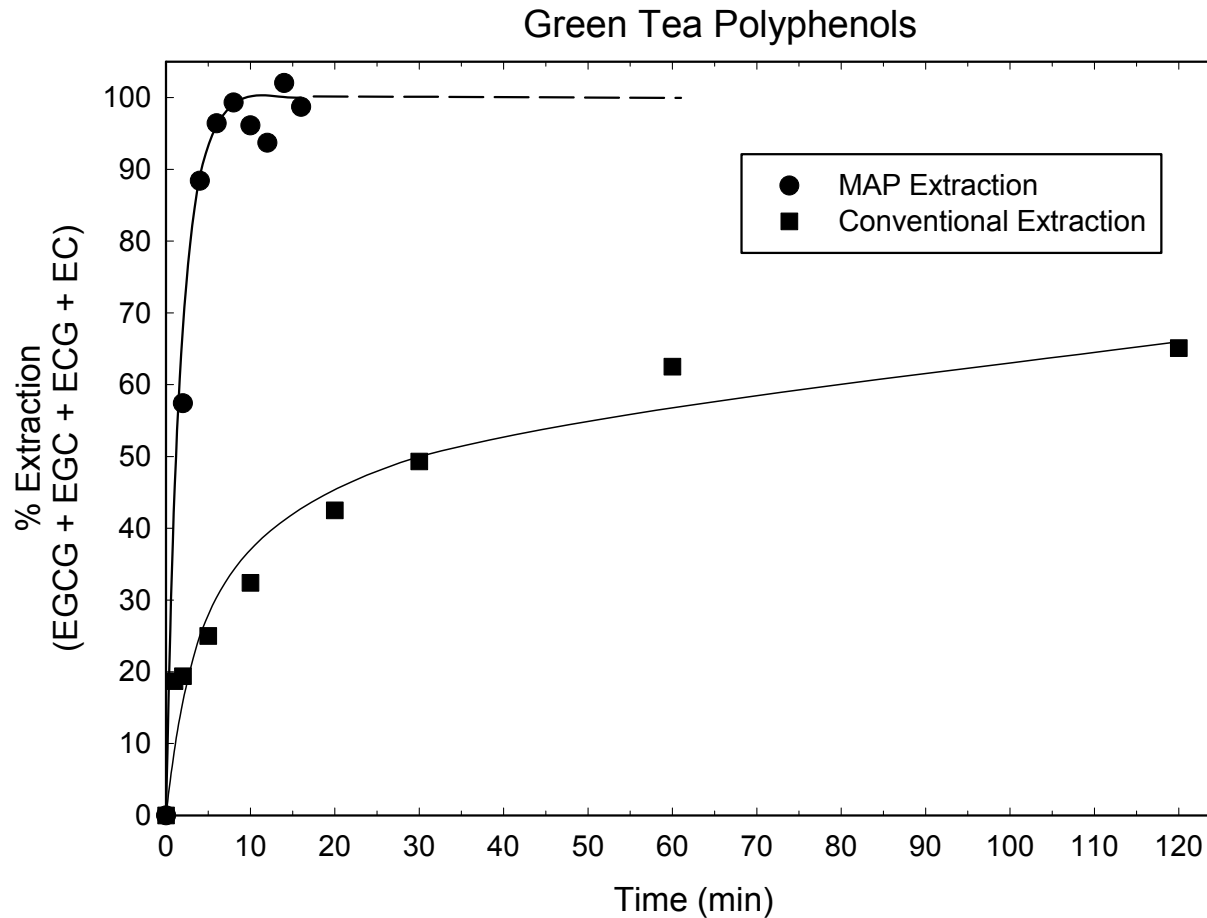
Lipids:Extraction of Oils from Oilseeds

(evening primrose, borage)

- **Fast and efficient**
 - » 99% extraction efficiency (<1% residual oil)
 - » 5 minutes total residence time
- **Flexible**
 - » Ability to extract with a range of solvents
- **Low Cost**
 - » Very low effective solvent ratios
- **Better Product**
 - » Possible to deactivate enzymes, reduce degradation



Antioxidants: Polyphenols from Green Tea



Antioxidants: Polyphenols from Green Tea

Key Dimension	Details	Potential for Optimization
Input Profile	Commercially-available green tea <u>Specs:</u> Polyphenol content: 10.8% (EGCG + EGC + ECG + EC)	Unknown
Marker Recovery:	>95% recovery of catechins	
Extract Profile:	70% polyphenols (EGCG+EGC+ECG+EC) (60% of total polyphenols as EGCG)	Possible



Other Examples

- **Extraction of PUFAs from microalgae**
 - » potential for crude fractionation
 - » short extraction times = >99% C18s
 - » concentration of LCPUFAs
- **Efficient extraction of carotenoids from paprika**
 - » direct fortification / pigmentation of oils
 - » “solvent free” extraction



Radiant Technologies Fully Operational Plant



0.5 tonne / h, 6 kW system

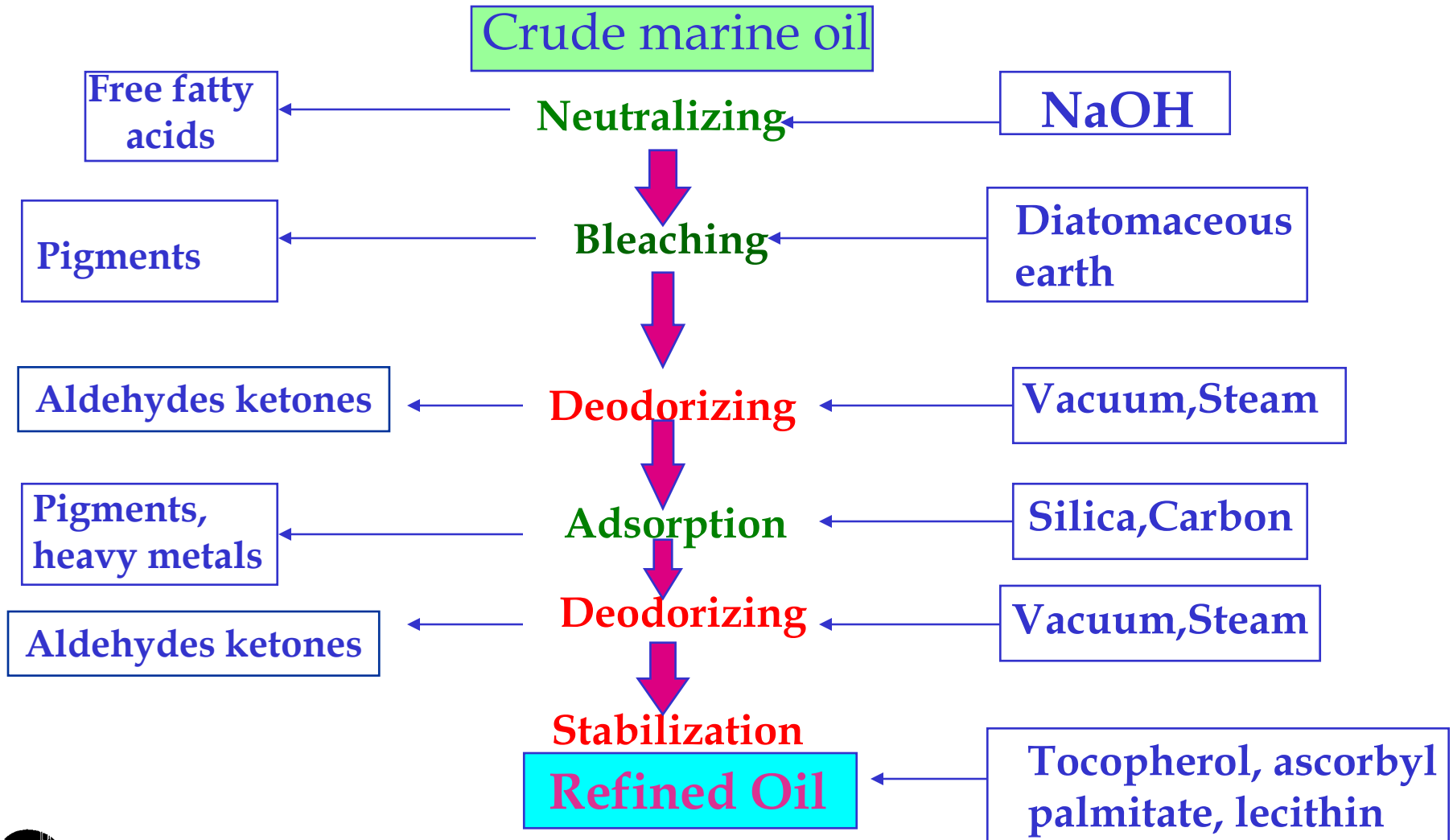


Next Generation “Liquefied-Gas” Pilot System

- Less toxic solvents
- Easier product / solvent separation (less energy)
- Less residual solvent in products



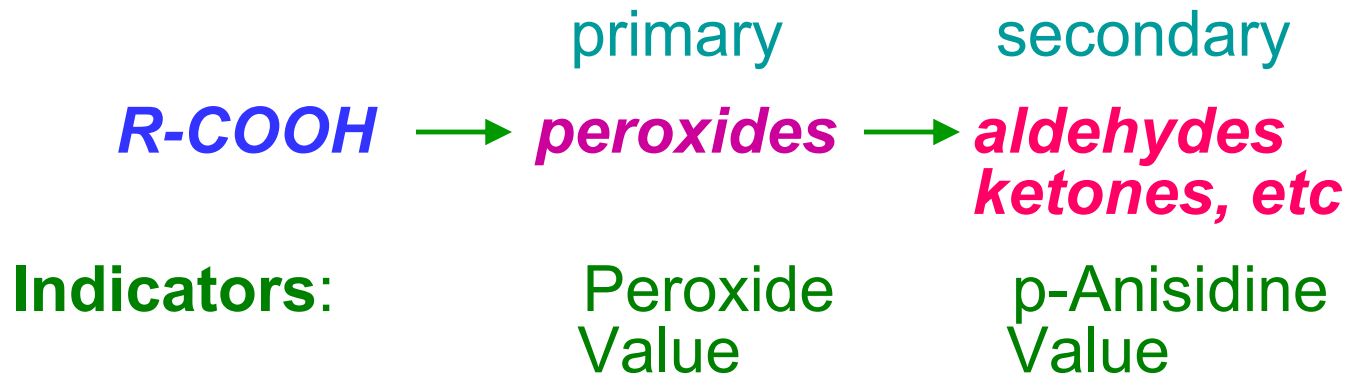
Refining Process for Long Chain OMEGA-3 Fish Oils



Instability of Omega-3 Oils

Conventionally refined marine oils possess unpleasant taste, smell and poor oxidative stability due to EPA and DHA (5 and 6 double bonds respectively)

- Prone to oxidation



- Oxidation results in:

- Loss of EPA% and DHA%
- Off fishy odor and/or taste



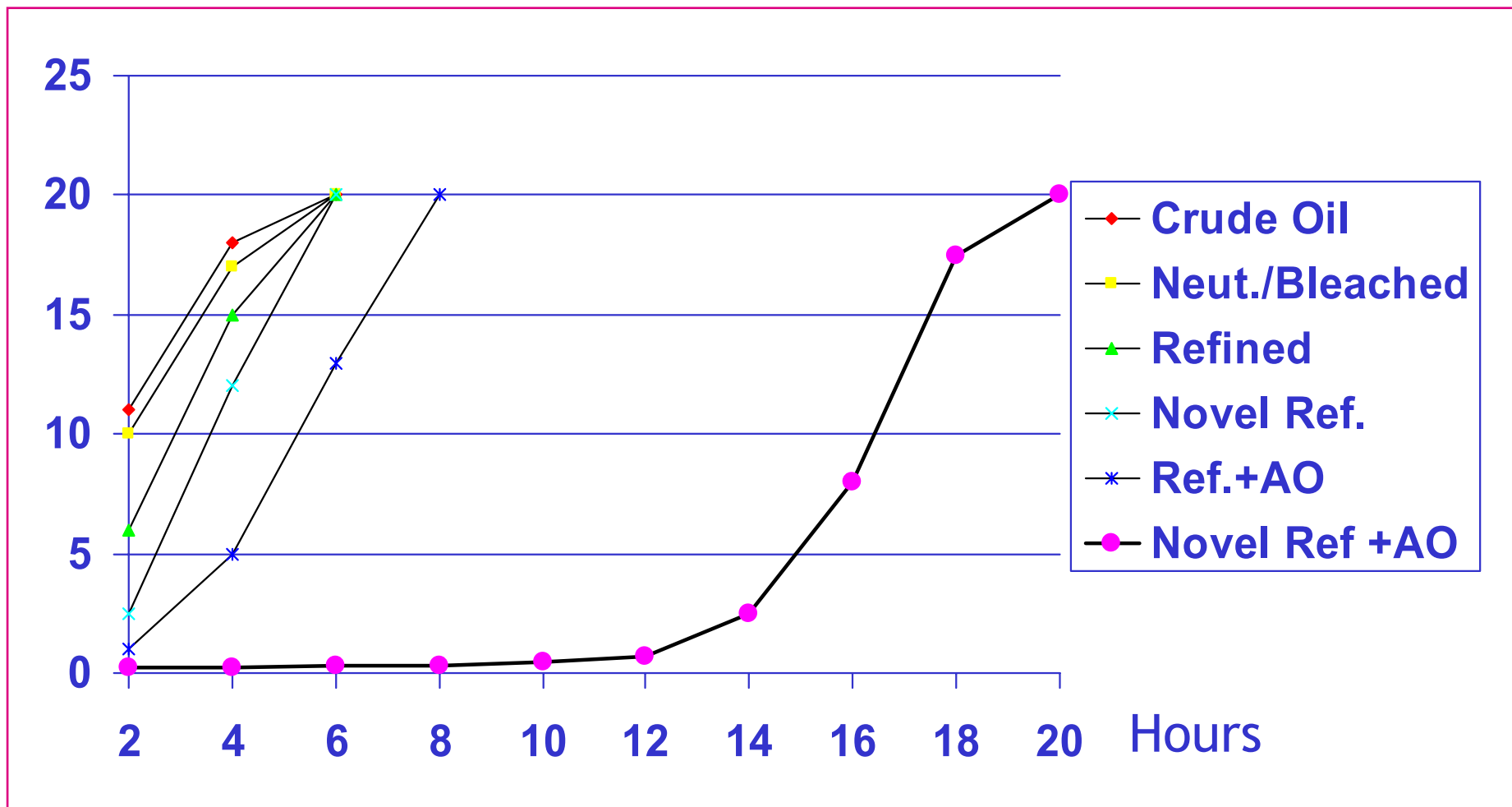
A Novel Two Fold Solution

- Reduction of Anisidine reactive aldehydes to improve organoleptic properties
- A powerful antioxidant system to prevent rapid build-up of new peroxides and aldehydes



Rancimat Stability of Marine Oils

(90C, 20l/Hr.)



Composition of the Headspace During Refining of Tuna Oil

Purification Step	Alkanals %	Alkenals %	Alkadienals %	Others %	Total Headspace ppb
Crude 1	30	9	46	14	40,000
Crude 2	30	10	46	13	
Crude 3	33	10	44	13	
Crude 4	31	9	47	13	
Crude 5	34	10	38	18	
Step 1/1	36	11	40	13	12,000
Step 1/2	30	12	46	13	
Step 1/3	30	10	46	13	
Step 1/4	30	14	44	12	
Step 1/5	35	11	37	17	
Step 2/1	58	0	13	30	1,000
Step 2/2	30	1	15	53	
Step 2/3	35	0	32	32	
Step 2/4	31	0	13	56	
Step 2/5	49	0	21	30	
Refined 1	37	0	5	58	300
Refined 2	35	0	6	59	
Refined 3	33	0	0	67	
Refined 4	32	1	10	58	
Refined 5	30	0	5	65	

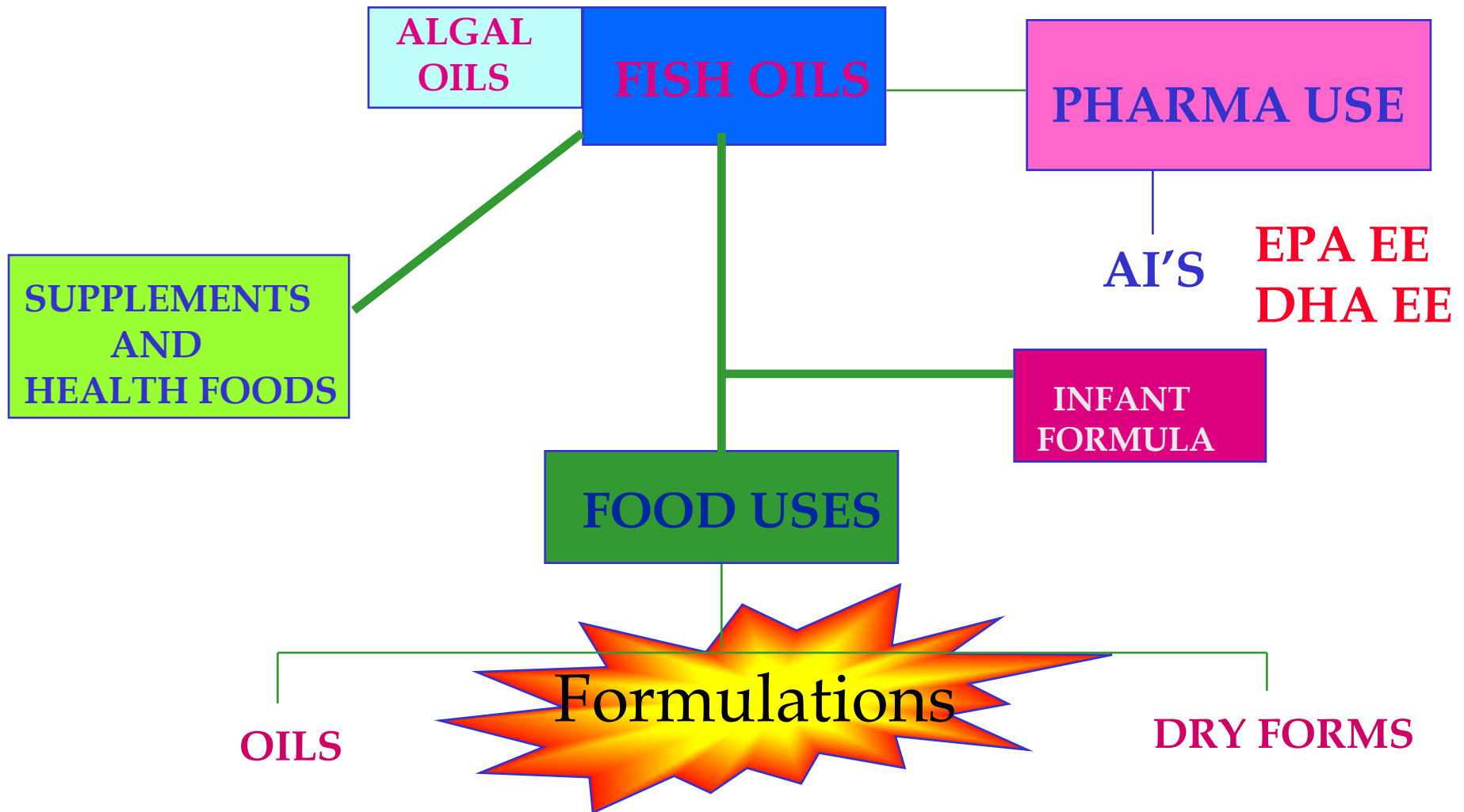


Enrichment of Foods with Omega -3 Oils/Powders

	Form	Addition Level	Use Direction	Shelf life
Cookies/Cakes	Oil	1.0 %	• Fat blend	6 - 9 mths
Bread	Oil	0.3 %	• Fat blend • Mixed with flour	Normal for bread
	Powder	1.0 %	• Flour premix/flour improver premix	
Fruit Juices	Oil	0.1 %	• Fruit concentrate before homogenisation	6 mths
Instant bev. powders (chocolate/malt based products)	Powder	1-1.5 %	• Dry mixing	12 mths



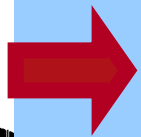
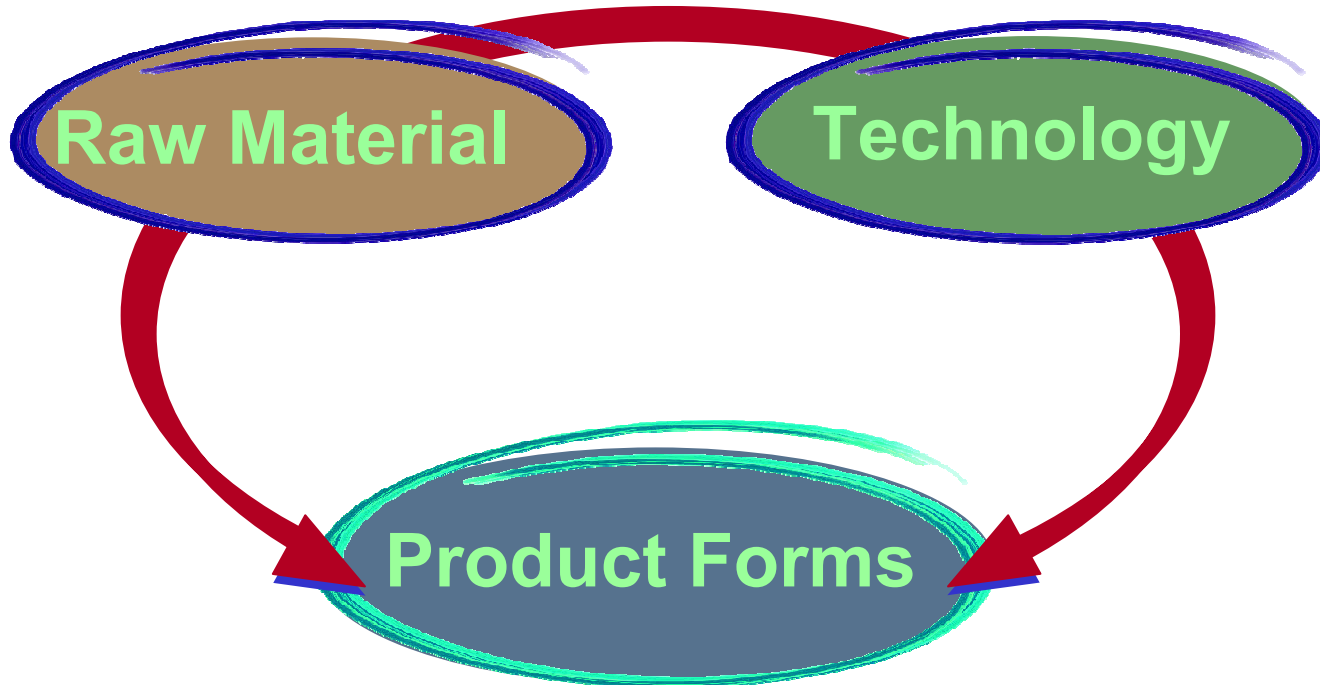
Long Chain Omega 3 PUFA Uses



From the raw material to the product manufacturer and the consumer



Focus of Product Form Development

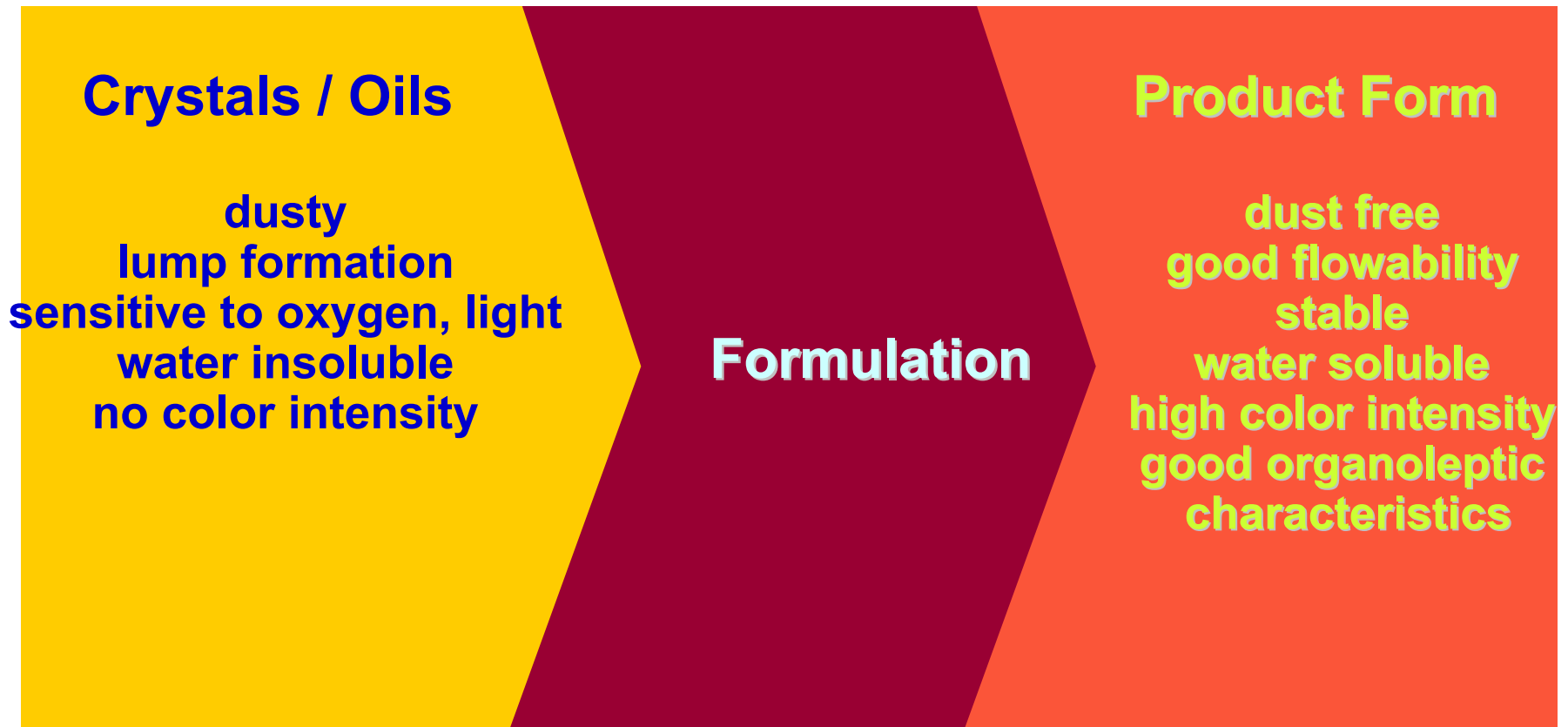


... to differentiate, meet manufacturers requirements, use new technology and raw materials



Formulation

From Crystals/Oils/Actives to a Product Form



Formulation of lipophilic actives

I. Preparation of Solutions

Fat Soluble Active
Ingredient + Stabilizers

Matrix (Gelatin) +
Sugar + Water

Emulsification

II. Preparation of Emulsion

O/W Emulsion

III. Drying of Emulsion

Spray drying

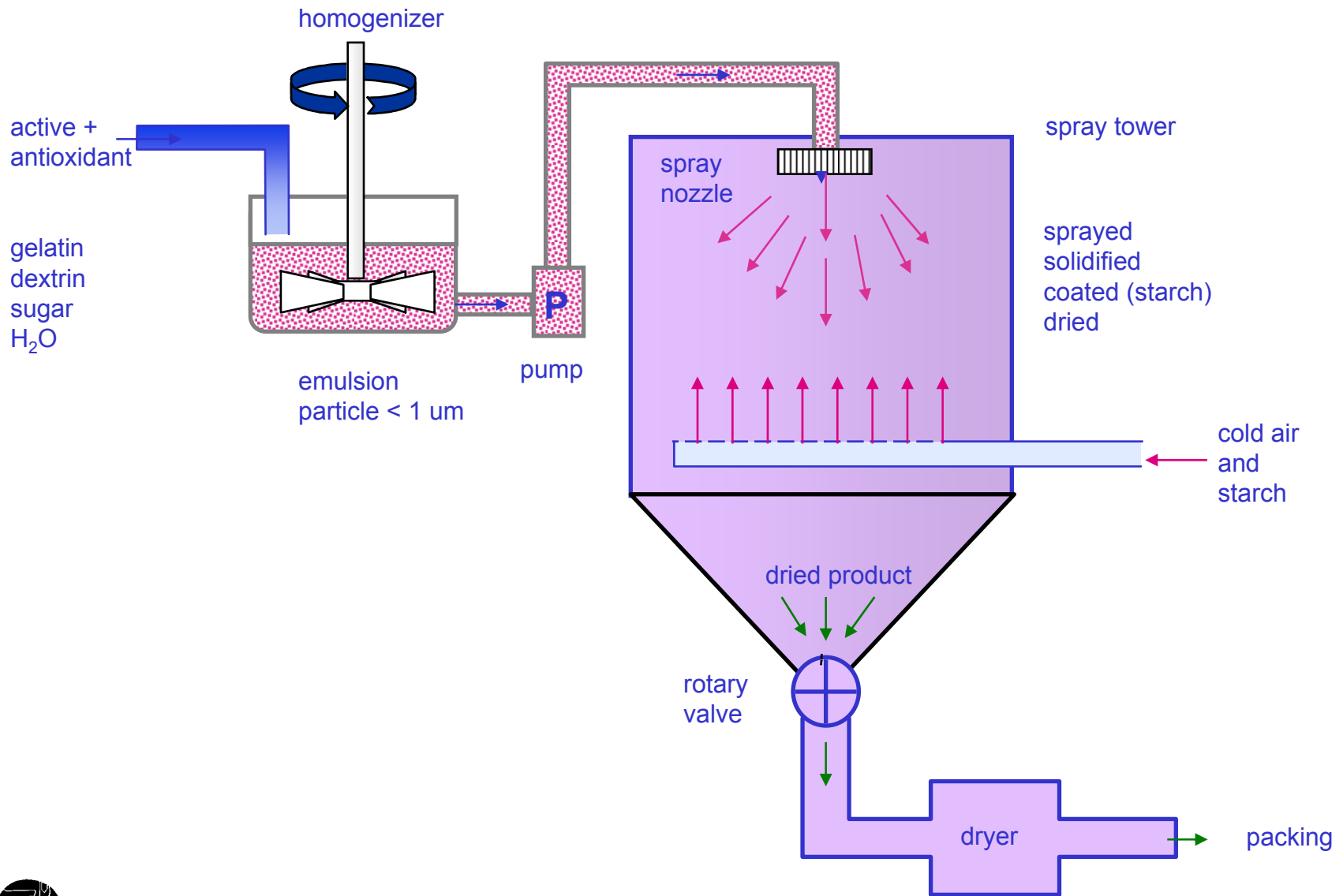
Powder Catch

Solid SD Form

Solid PC Form



Procedure of the Manufacturing of “Beadlet” Products

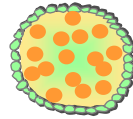


Spraying Technologies

Advantages and Disadvantages

- +: good stability, good flowability, dustfree spherical particle shape
- : slow dispersibility

Big Powder Catch



- +: good stability, good flowability, dustfree spherical particle shape
- : slow dispersibility, gelling matrix only

No Catch

Spray Drying (SD)

- +: good for premix
- : reduced flowability, dusty or clogging, slow dispersibility



Spray Drying Tall Tower (TT)

- +: good flowability, less dust, spherical particle shape



Fluidized Spray Drying (FSD)

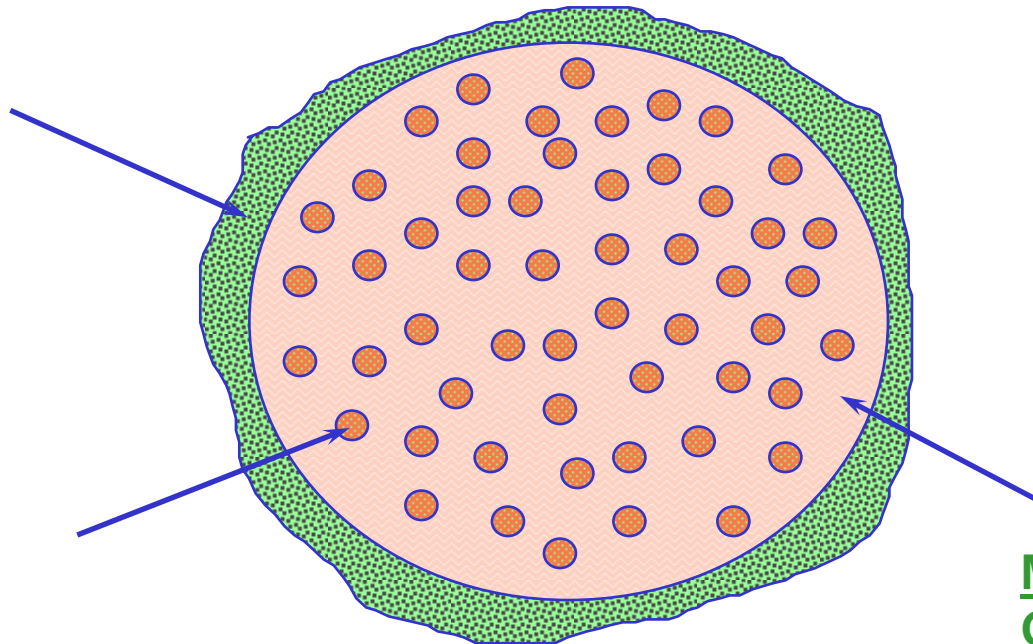
- +: good flowability, less dust, fast dispersibility



Microencapsulation (fish oils)

Beadlet Cross section

maize starch



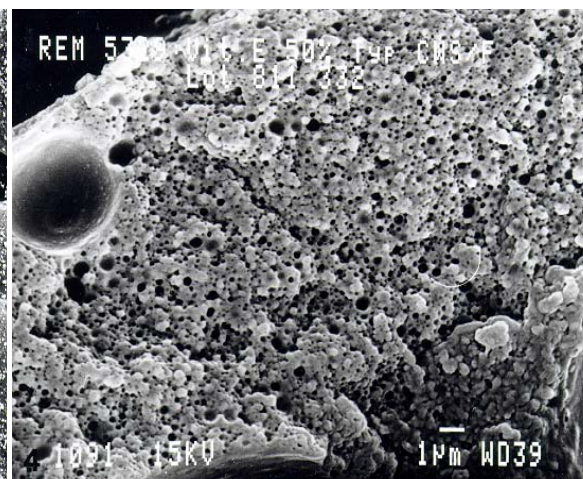
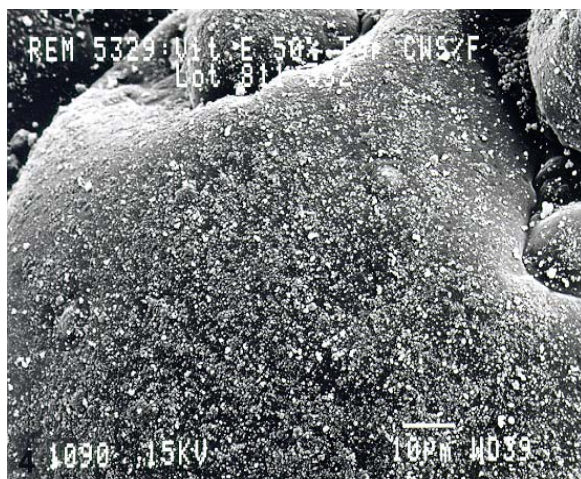
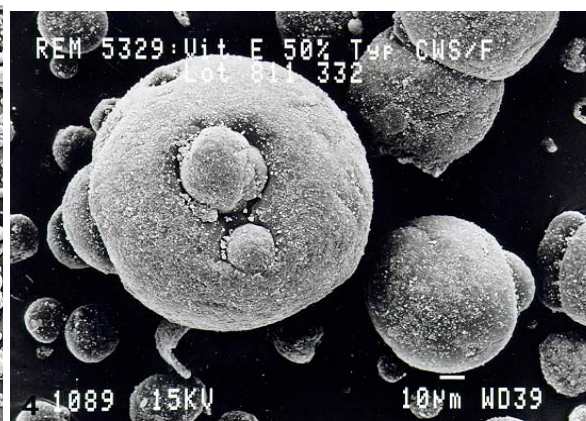
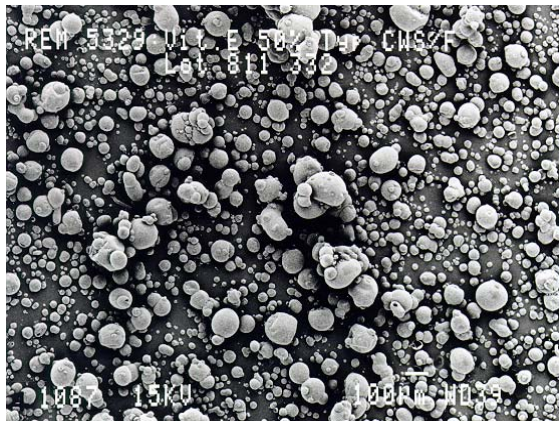
Inner phase
(0.2 - 0.4 μm)
with stabilizer (Tocopherols,
Rosemary Extract)

0.4 mm

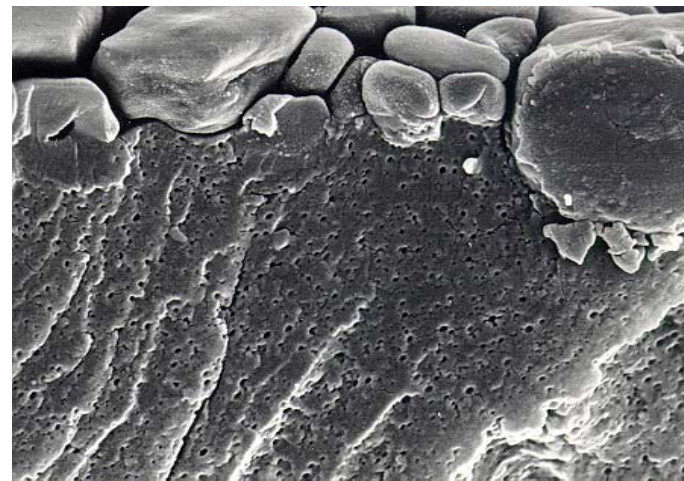
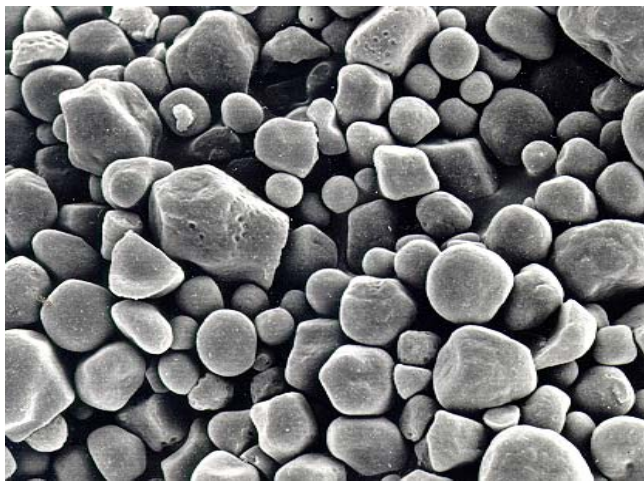
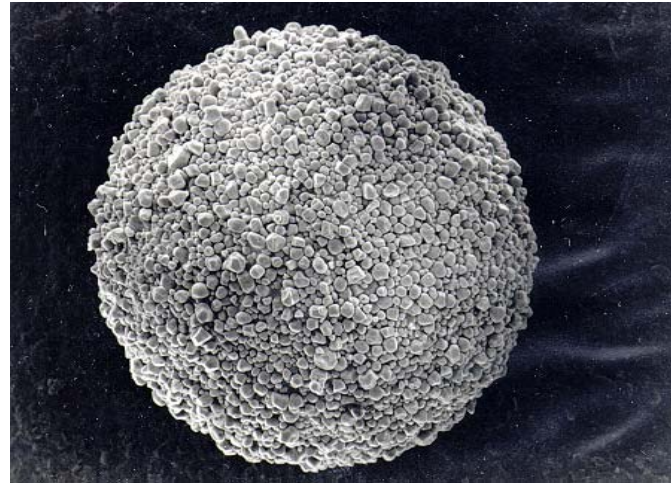
Matrix:
Gelatin
Carbohydrate
Sodium Ascorbate



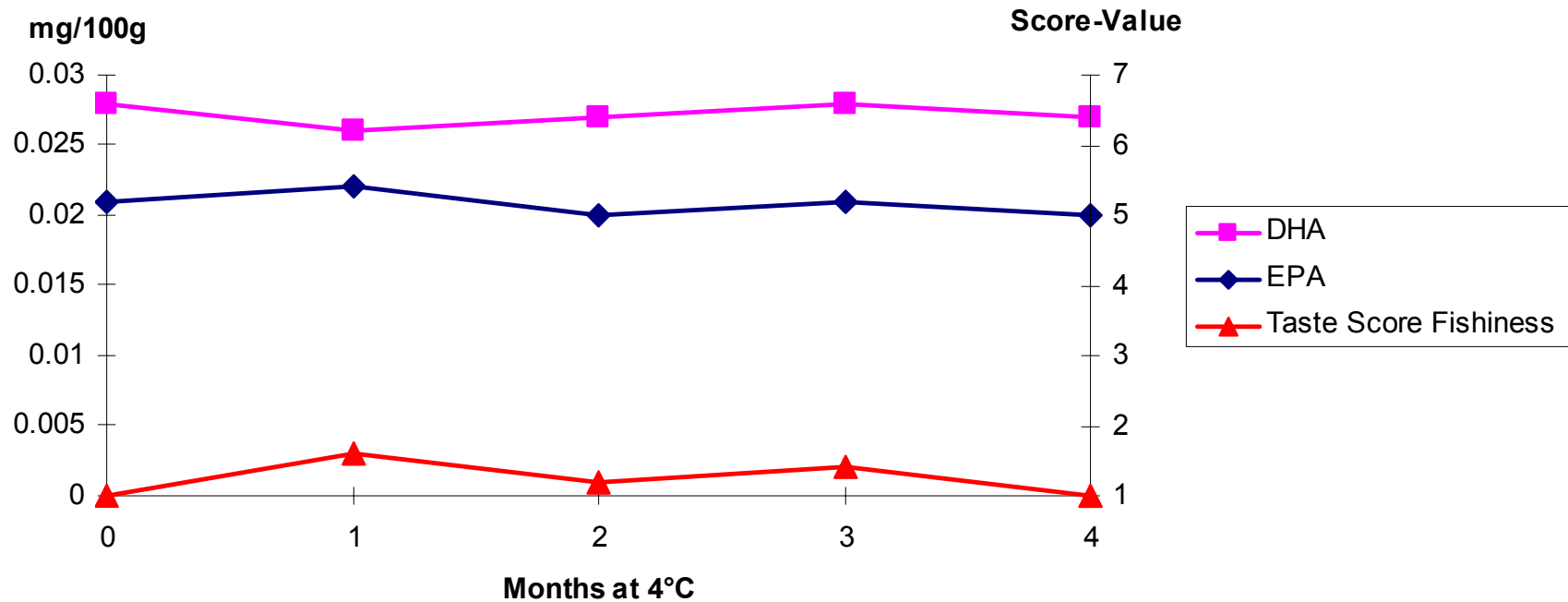
Microencapsulation - Spray Dried Form



Microencapsulation - Powder Catch Form



Stability of Chocolate Milk with 0.2% LC Omega-3 Oil



Microencapsulation of Omega-3 Oils

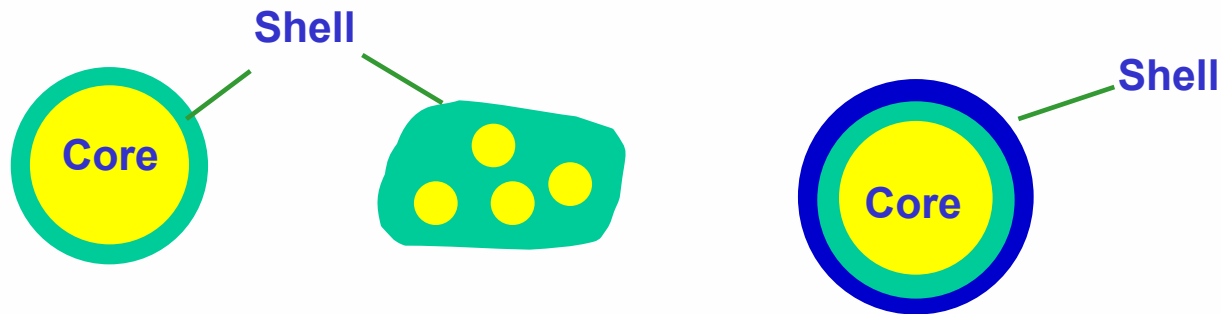
Microcapsules are membrane-coated small particles.
(Provides improved storage life, taste masking and handling)

Size: average of 50 μM

Core: omega-3 oil

Shell: food grade polymer

Shape: single core, multiple cores, multiple shells



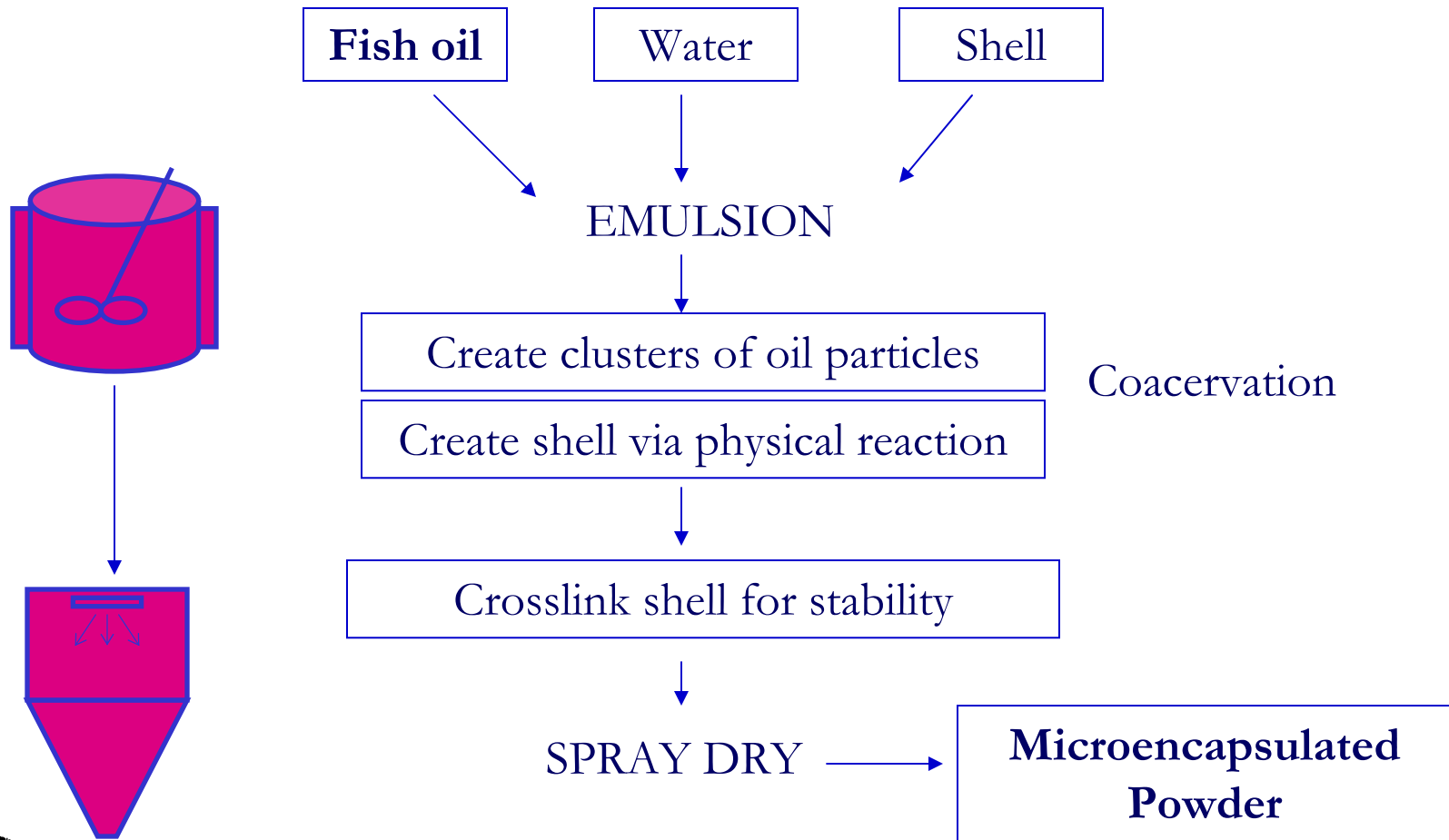
Single Core

Multiple Cores

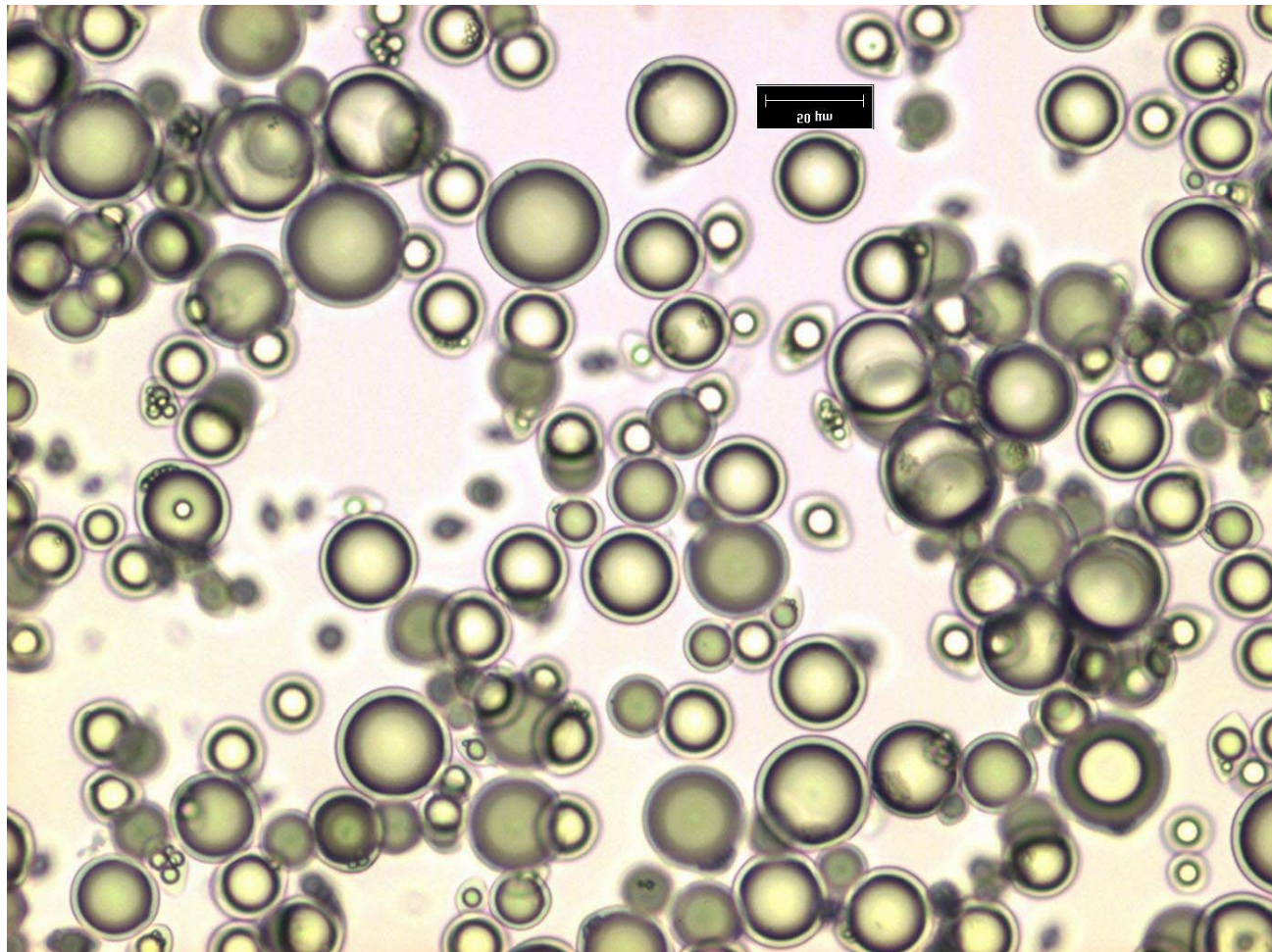
Multiple Shells



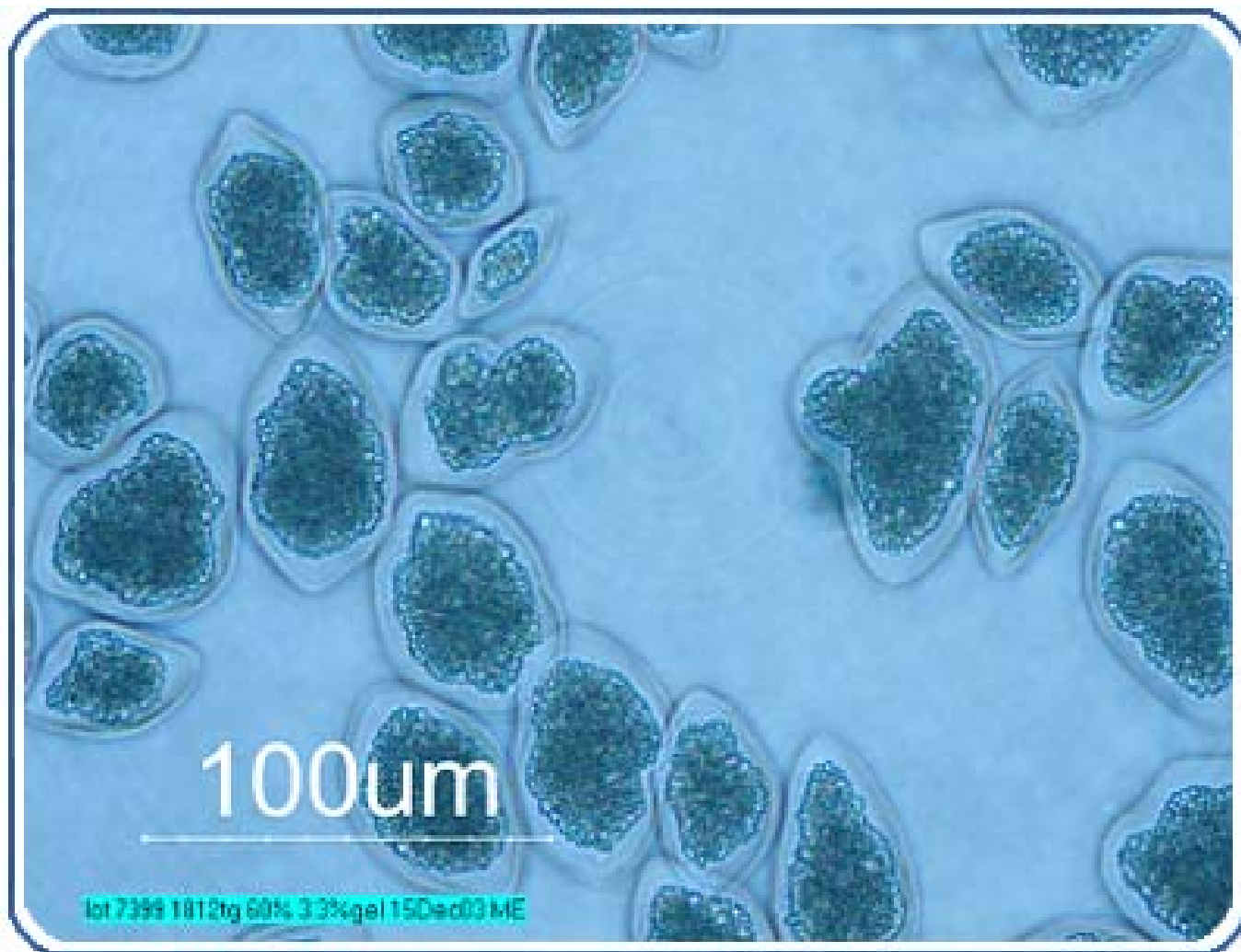
ONC Microencapsulation Technology



ONC Omega-3 Powder Type 1

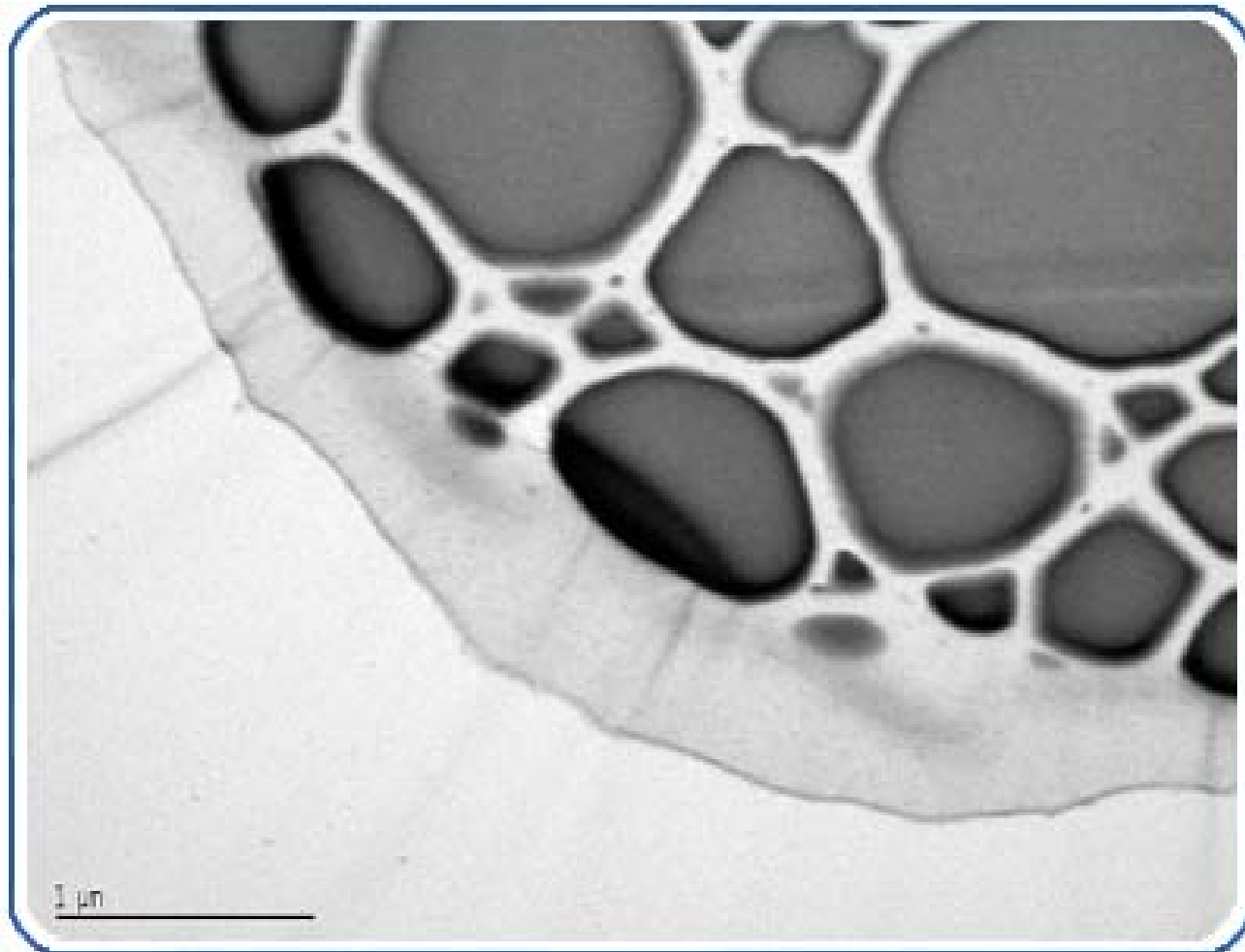


ONC Omega-3 Powder Type 2



ONC Omega-3 Powder Type 2

EM Figure



Bioavailability of ONC Omega-3 Powder

Group 1:



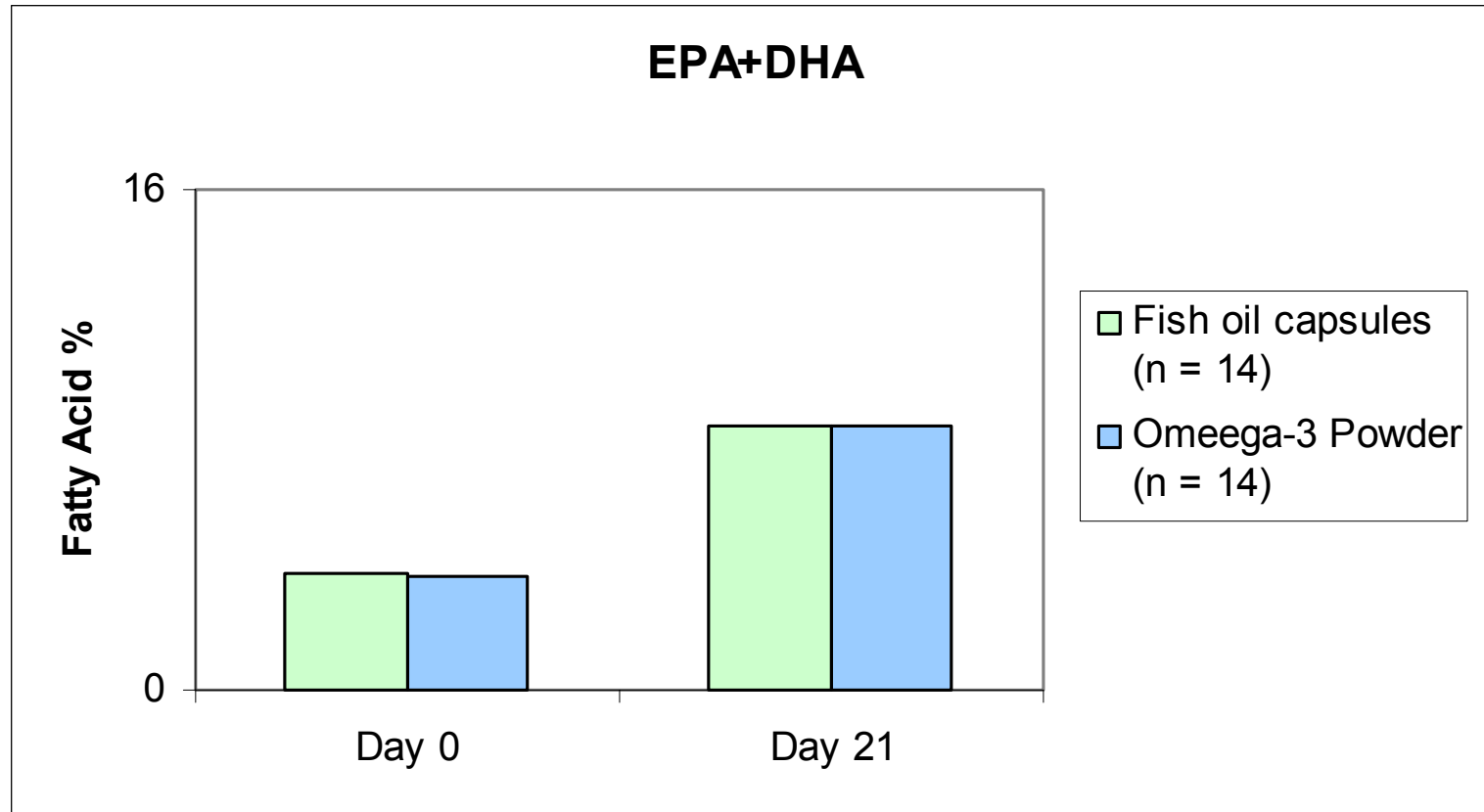
Group 2:



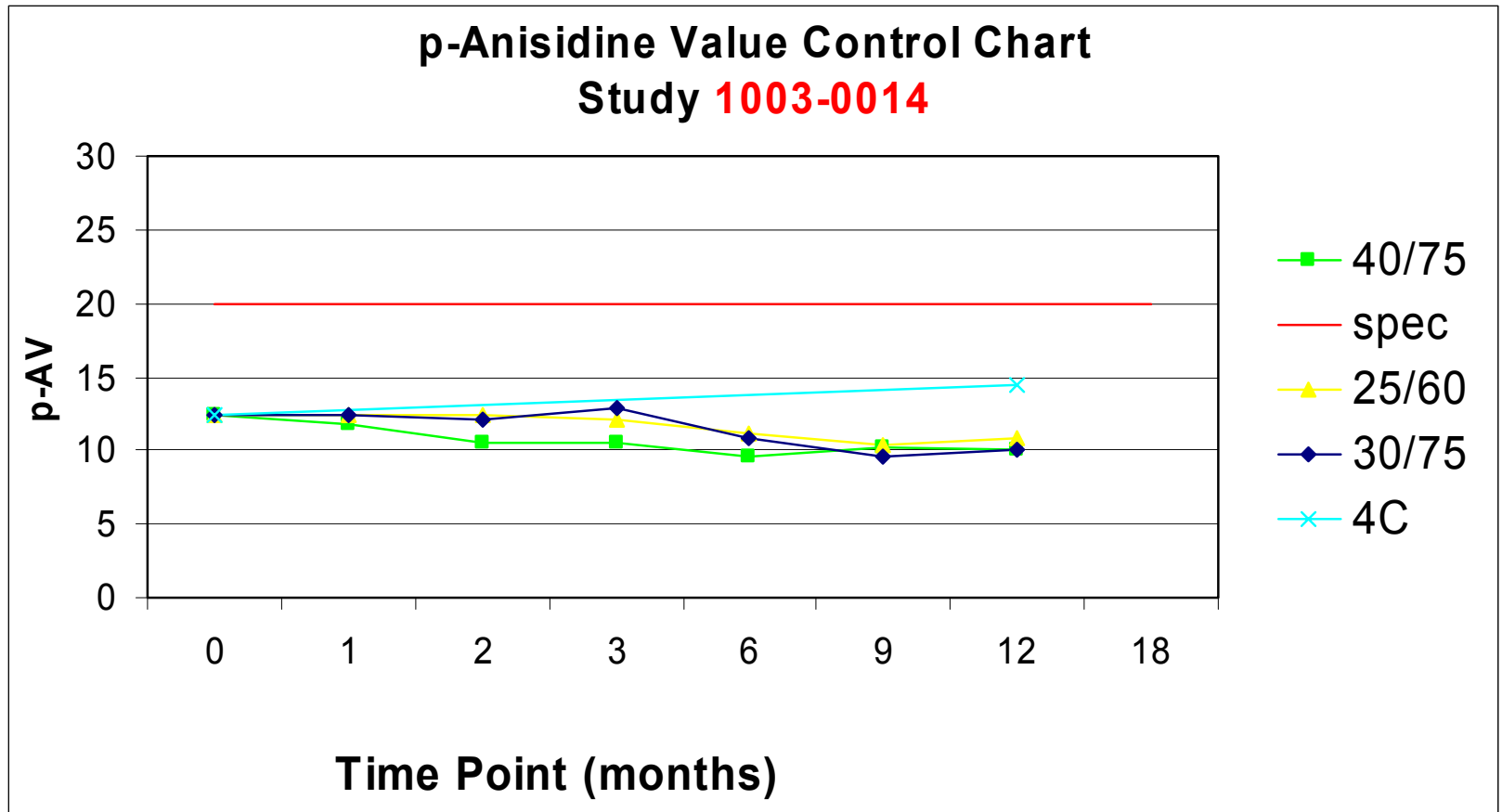
- 14 subjects, cross-over design.
- 2g EPA/DHA as capsule + milkshake or omega-3 powder.
- Blood lipid analysis at start and end of each period



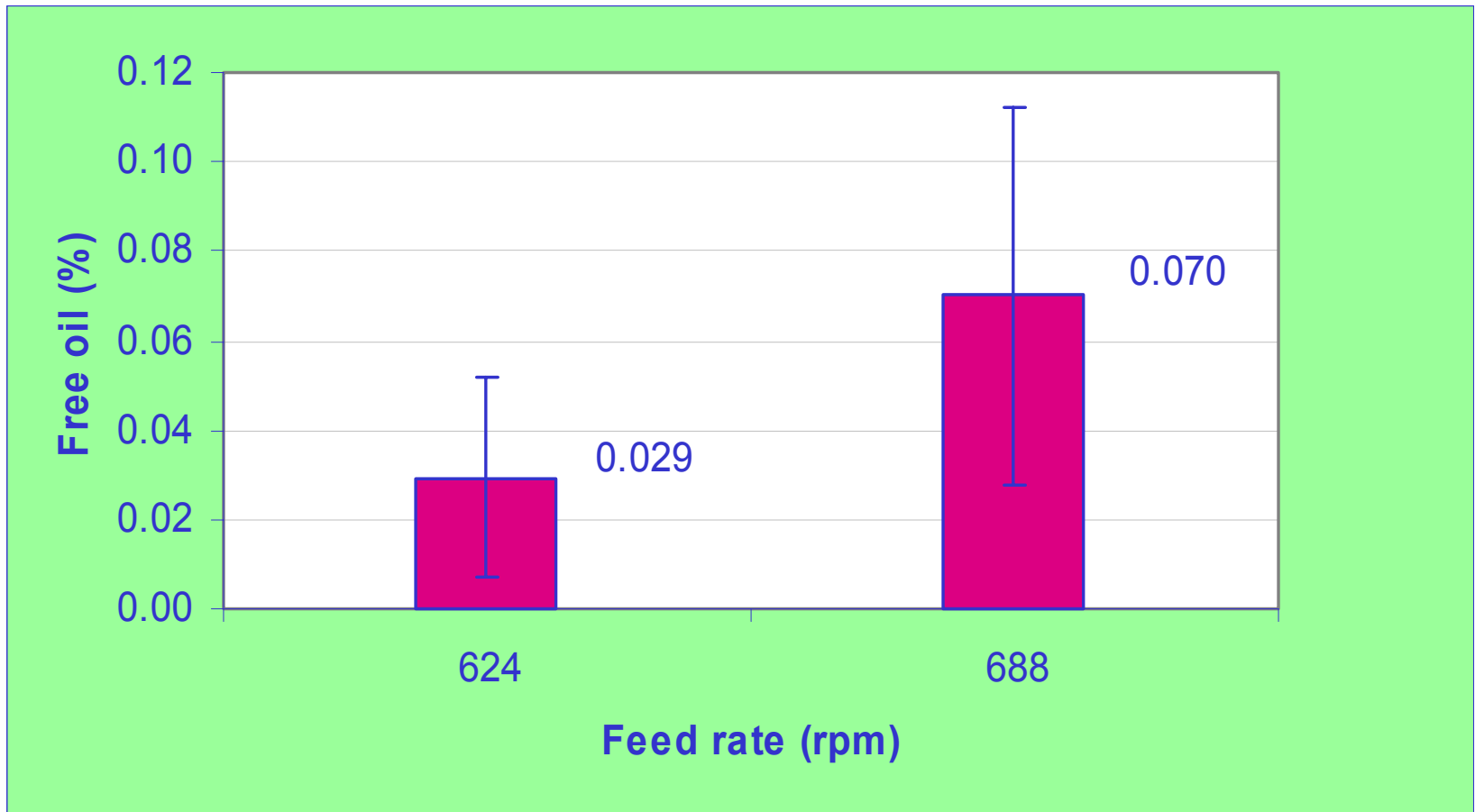
Gelcaps and ONC Omega-3 Powder: Fatty acids of serum phospholipid



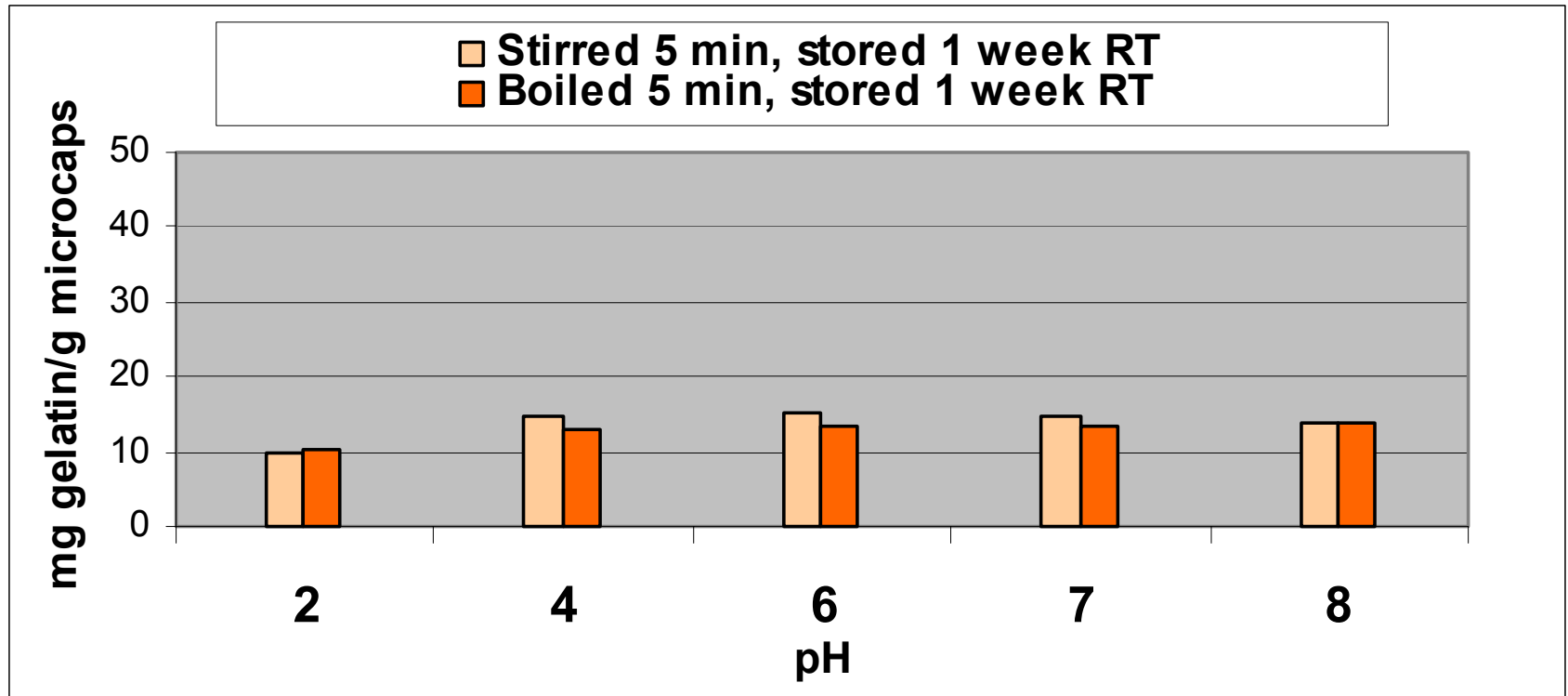
Real-Time Stability Required



ONC Free Oil in Production Batches



pH Stability of ONC Omega-3 Powder in Water



NPRI O2P (Oil to Powder) Process

- High loading of powder with active >50%
- Difficult actives possible in powder form
- Maltodextrin carrier base
- Fish oils and other actives commercial
- Tolling capabilities

"Winner" of the

O2P Oil Powders

Add benefits to your product without compromising taste, aroma or formulation.

Now you can add an antioxidant, help strengthen immune response or rejuvenate the body by providing a nutritional or therapeutic advantage to your customer and a unique product position with improved margins for your bottom line.

- Create a functional food
- Provide added fortification
- Turn cosmetics into skin care
- Add nutrition to your body care line

O2P oil powders help you create innovative products with distinct health or performance benefits. Each are:

- Unique - create proprietary blends with distinct health or performance benefits
- More appealing - powders offer flexibility in formulation and blending
- Easier to process - free-flowing 80-mesh powders vs. bulk oils
- Consumer-friendly - offer your customer a two-piece hard shell versus a softgel
- Versatile - powders can be encapsulated or blended easily

W W W

Basil Oil	Cod Liver Oil	Flax Seed Oil
Borage Oil	Corn Oil	Grape Seed Oil
CLA	Fish Oil (18:12)	Lecithin Oil

TM

Nutri Pharmaceuticals Research, Inc.



The O2P Powder Process

- Converts edible oils, gels or pastes into a free-flowing powder without altering the molecular structure, isomeric profile or the nutritional value of the base oil.

- Uses a patented gravity flow process without sprayers, blenders, other equipment that generate heat and destabilize the oil. Operates at room temperature,

- Offers range of oil loads from 10% to 70%, based on oil viscosity or end-use application.

- Retains a nitrogen head throughout the process, preserving original oil profile and limiting oxidation problems.

- Currently, offers more than forty O2P™ Powders such as Apricot Oil Powder, Vitamin E Oil Powder, Fish oil, each powder carries a minimum two year stability guarantee.



Ideal Carriers for Formulations

Properties of an ideal matrix :

- Good rheological properties at high concentration and ease of manipulation during the process of encapsulation.
- Ability to disperse or emulsify the active and stabilize the emulsion produced.
- Non-reactivity with the active both during processing and on prolonged storage.
- Ability to seal and hold the active within its structure during processing or during storage.
- Ability to provide maximum protection to the active against environmental conditions (e.g. heat, light, humidity).
- Ability to meet specified or desired product properties (solubility, active material release).
- Cost effective food grade substance (regulatory aspects)
- Good, reliable supply chain
- Constant product quality.



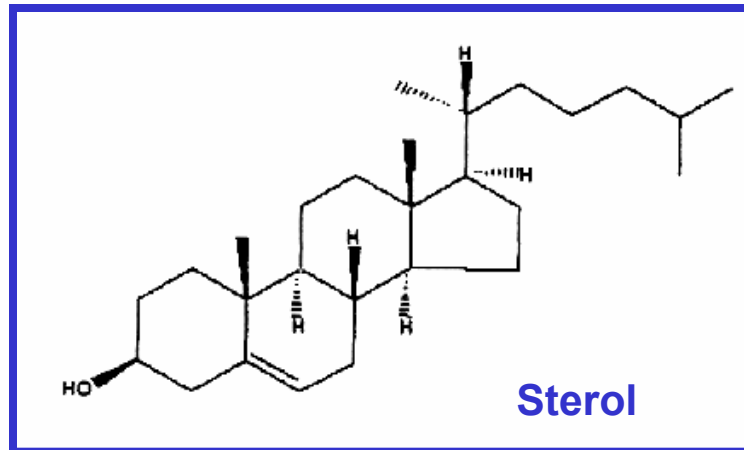
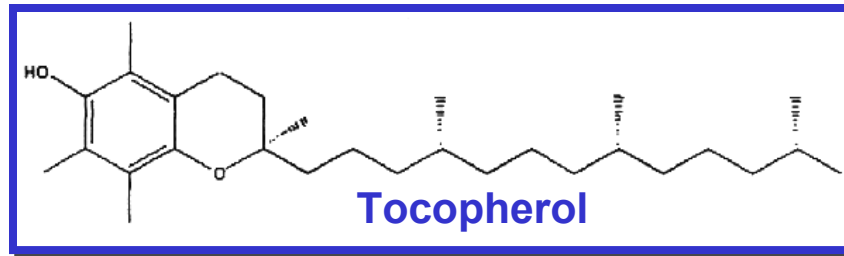
Any Raw Material Excipients

- Need to be in compliance with EC legislation surrounding source materials and processing of BSE/TSE related risk material.
- Compliance with GRAS as a food additive for USA
- Need to be compliant for religious/ethnic reasons
- Need to be compliant for contaminants



UbiSol Technology

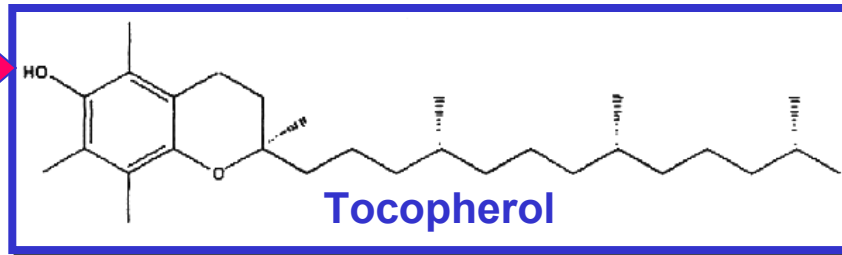
The solubilization is achieved through the application of a carrier system. The carriers are derived from naturally occurring compounds, mainly sterols and tocopherols.



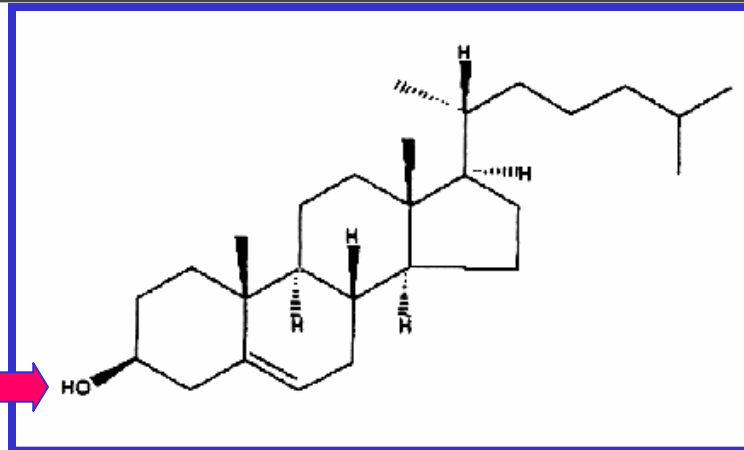
UbiSol Technology

The structure of the carrier molecule is chemically modified to increase its affinity for water (hydrophilicity).

esterification

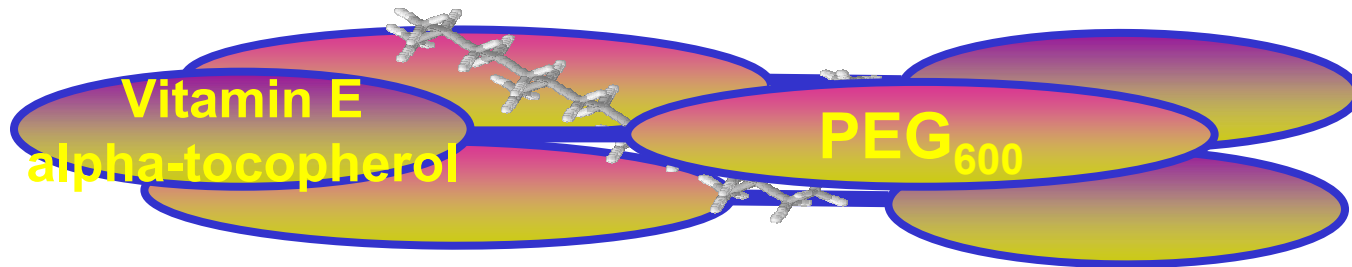


esterification



UbiSol Technology

Under certain conditions the carrier and the active form a stable non-covalent complex consisting of 2-4 molecules of carrier per 1 molecule of active.



The properties of these complexes are such that they remain stable, both water- and lipid-soluble for extended periods of time, even after exposure to extreme conditions such as a broad range of pH, high and low temperatures.



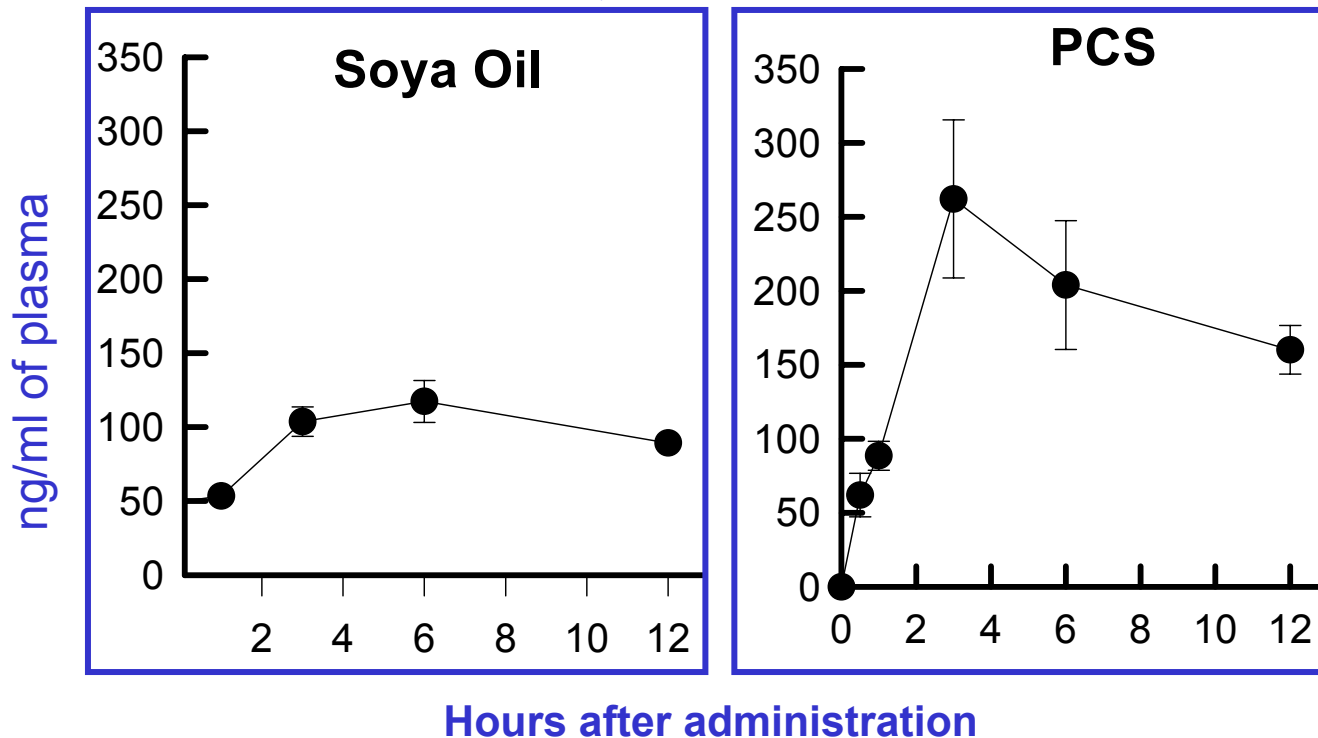
UbiSol Technology

- Using this technology it is able to achieve water solubility of several natural bioactive compounds, including:
 - ◆ Natural antioxidants
 - ◆ Vitamins
 - ◆ Lipids
 - ◆ Carotenoids
 - ◆ Terpenoids
 - ◆ Certain drug molecules



Improved bioavailability of water-soluble Coenzyme Q10

Plasma content of CoQ10 after oral administration

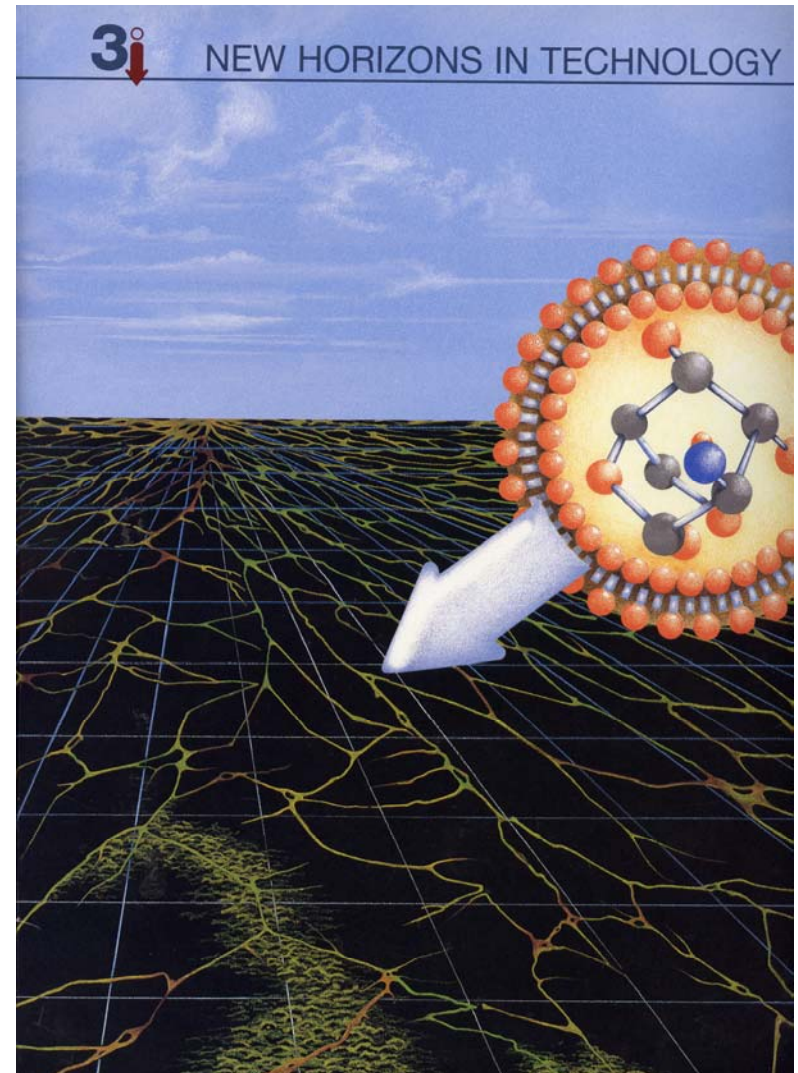


3 rats/time point were given orally (by gavage) 6 mg CoQ10/kg b.w. dissolved either in soya oil or formulated in PCS and dissolved in water



3i technology in Liposomes

- Manufactures ingredients for Human Health & Wellness products
- Oil-based products such as fish oil, CoQ10, Vitamins A & E
- Powders that are difficult to dissolve such as Lycopene and Lutein
- Patented nanotechnology to improve / change the characteristics of an ingredient
- Uses Liposome and Nanoparticle technology

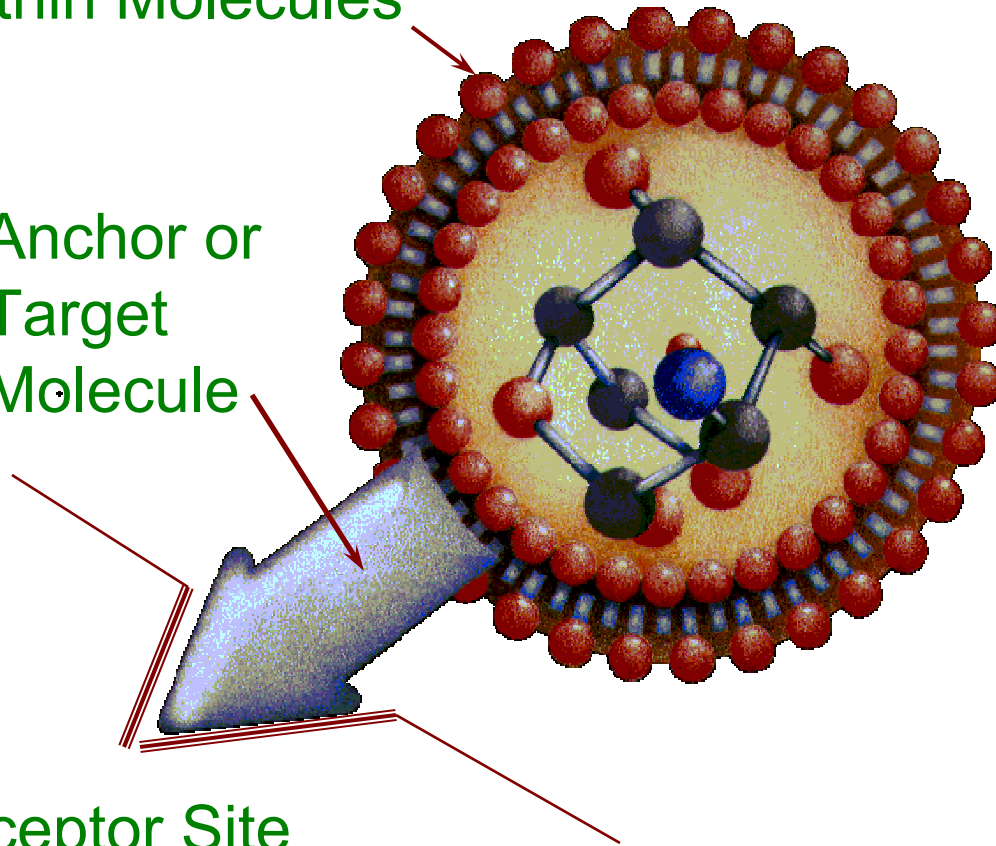


Liposomes

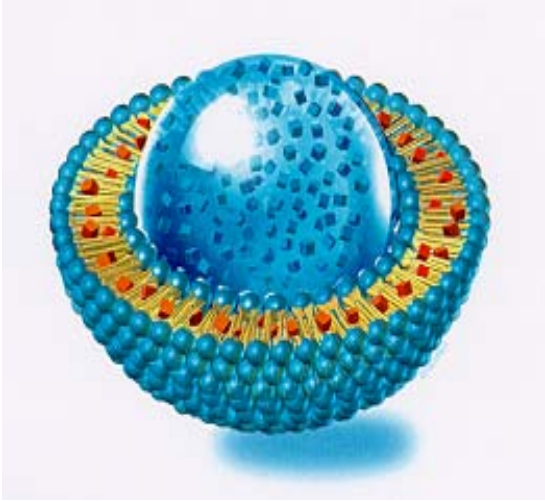
Soy Lecithin Molecules

Anchor or
Target
Molecule

Receptor Site



Liposomes and nanocolloids to Improve Bioavailability



Liposome



Nanocolloid



Liposomes and Nanodispersions

❁ Liposomes

- ❁ Carrier for hydrophilic or lipophilic compounds.
- ❁ Small size (100 nm).
- ❁ Stable, infinitely diluteable.
- ❁ Relatively low “loading” of lipophilic compounds
- ❁ Slow release of actives, via diffusion possible

❁ Nanodispersions

- ❁ Carrier for lipophilic compounds.
- ❁ Similar properties to liposomes.
- ❁ Relatively high “loading” possible.

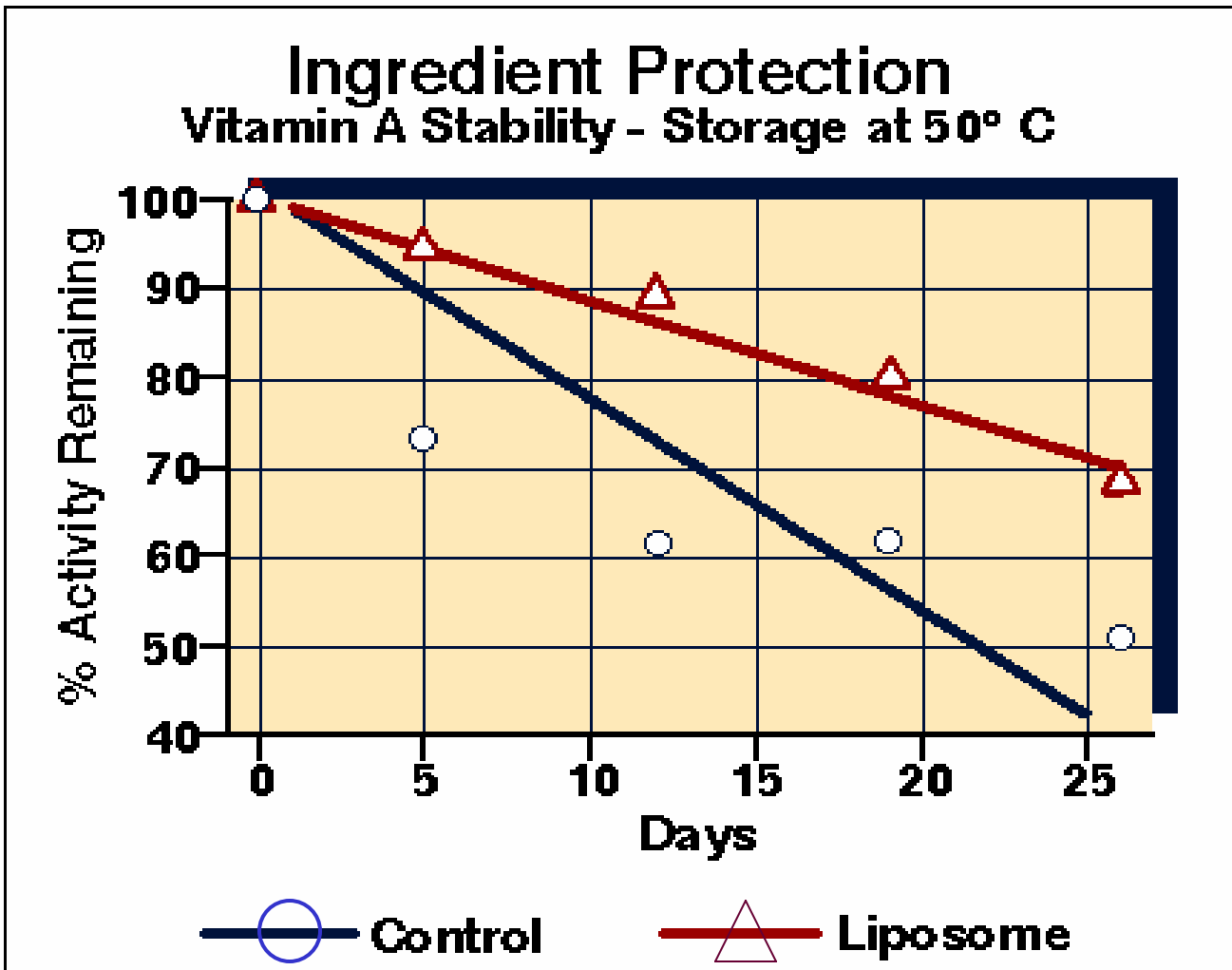


Benefits of Liposome Technology

- Can provide protection for ingredients.
- Reduced oxidation.
- Reduced interaction between ingredients.
- Improved bioavailability from high surface area and mucin binding properties
- Oily actives and lipophilic crystals can be uniformly dispersed in liquids
- Commercially viable; high value actives?



Ingredient protection example (Liposomes)



Summary

- New extraction technologies can lead to improved efficiencies, higher quality, cost effective extracts/actives
- Carrier selection and forms innovation can improve bioavailability, stability and wider use of actives in the food and supplement area
- Patents can extend life of the active and maintain a profit stream for the company



Thank You

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