NEW AND EMERGING FOOD APPLICATIONS OF POLYMERIC NANOPARTICLES FOR IMPROVED HEALTH

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NANOTECHNOLOGY

• Nanotechnology: “The understanding and control of matter at dimensions of roughly 1 to 100 nanometers, where unique phenomena enable novel applications” (NSF, 2004)

• “Nanoparticles are submicronic colloidal systems, ranging in size from a few nanometers to 1 µm, made of artificial or natural polymers” (Nakache et al., 2000)
**Delivery Systems at the Nano Scale**

- Micelles
- Emulsions
- Liposomes
- Stabilized emulsions
- Polymeric nanoparticles
- Solid lipid nanoparticles

- Enhanced quality
- Improved functionality
- Targeting
- Controlled release
POLYMERIC NANOPARTICLES FOR FOOD APPLICATIONS- CONSIDERATIONS

- Method selection
  - Bottom-up techniques (monomer)
  - Top-down techniques (polymer)
  - Synthesis parameters

- Materials used
  - Biodegradable and biocompatible polymers
  - Organic solvents, surfactants, and other additives

- Nanoparticle characterization
  - Size and size distribution
  - Surface properties
  - Stability
  - Functionality
TOP-DOWN TECHNIQUES

- Emulsion evaporation and nanoprecipitation

[Diagram showing mixing, homogenization, sonication, and evaporation processes leading to nanoparticles]
MATERIAL SELECTION- POLYMERS

Alginic acid
- Polysaccharide with mannuronic and guluronic acid
- Negative charges from carboxylic groups
- Thickening agent

PLGA
- Poly(lactic-co-glycolic) acid
- Biocompatible and biodegradable
- Mostly used for biomedical applications

Chitosan
- N-deacetylated derivative of chitin
- Degrades to non-toxic compounds
- Positively charged
MATERIAL SELECTION - SURFACTANTS

70 nm PLGA/SDS

200 nm PLGA/PVA

280 nm PLGA/Chi/Lecithin

Graphs showing the size and polydispersity index of nanoparticles as a function of SDS and Span 80 concentration.
IMPROVED DELIVERY OF ANTIOXIDANT LIPOPHILIC VITAMIN

Imola Zigoneanu, Carlos Astete, and Abitha Murugeshu

Vitamin E

- Antioxidant lipophilic vitamin
  - Prevents damage from chemical reactions related to cancer, diabetes, cardiovascular disease, inflammatory responses, degenerative diseases, aging, liver injury, cataract, etc.

- Vitamin E = tocopherols + tocotrienols

- α-tocopherol is the most biologically active form
  - ~ 36% absorption of Vit. E recorded in subjects
  - 64% of the dose is lost
PLGA NPs with entrapped α-tocopherol made with SDS and PVA

<table>
<thead>
<tr>
<th>αT theoretical loading (%)</th>
<th>SDS</th>
<th>PVA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Size (nm)</td>
<td>PDI (au)</td>
</tr>
<tr>
<td>0</td>
<td>71.2 ± 0.33a</td>
<td>0.096 ± 0.012a</td>
</tr>
<tr>
<td>8</td>
<td>57.2 ± 0.28b</td>
<td>0.136 ± 0.015b</td>
</tr>
<tr>
<td>16</td>
<td>53.6 ± 0.30c</td>
<td>0.150 ± 0.003b</td>
</tr>
</tbody>
</table>

-Surfactant: SDS and PVA with different effects on NP size
-Release: lower initial loading, faster release
-Processing: no effect on size but significant effect on PDI by freeze-drying
## Particle Characterization

<table>
<thead>
<tr>
<th>αT theoretical loading (% w/w relative to PLGA)</th>
<th>PLGA/Lecithin/a-TOC</th>
<th>Chi/ PLGA/Lecithin/a-TOC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Size (nm)</td>
<td>PDI (au)</td>
</tr>
<tr>
<td>0</td>
<td>111.1 ± 15.4</td>
<td>0.210 ± 0.0178</td>
</tr>
<tr>
<td>8</td>
<td>97.7 ± 3.0</td>
<td>0.256 ± 0.0288</td>
</tr>
<tr>
<td>16</td>
<td>83.2 ± 3.0</td>
<td>0.160 ± 0.0155</td>
</tr>
<tr>
<td>24</td>
<td>87.4 ± 2.3</td>
<td>0.146 ± 0.0196</td>
</tr>
</tbody>
</table>
PH CHANGES DURING FOOD TRANSIT AFTER A MEAL

- Basal (Fasted) pH
  - Gastric = 1.3 – 1.7
  - Duodenal = 5.9 – 6.4
- During Meal pH
  - Gastric = can rise to ~ 5.0
  - Duodenal = drop to ~5.5

**pH Effect on the Surface Charge and Size of Chitosan/PLGA Particles**

**pH Effect on the Surface Charge**

- Zeta Potential (mV) vs. Time (hrs)
- Time: 0 to 7 hrs
- pH 1.5 and pH 6.5

**pH Effect on Size**

- Average Diameter (nm) vs. Time (Hrs)
- Time: 0 to 4 Hrs
- pH 1.5 and pH 6.5
**PH EFFECT ON MORPHOLOGY OF CHITOSAN/PLGA PARTICLES**

**pH 1.5**
- 0 hr
- 1 hr
- 2 hrs

**pH 6.5**
- 0 hr
- 6 hrs
- 24 hrs
CONCLUSIONS-IMPROVED DELIVERY

- Particles of different characteristics (size, surface charge, morphology) with entrapped alpha-tocopherol were synthesized from PLGA and PLGA/Chitosan
  - Processing conditions
- Polymer and surfactants affected the properties of the particles
  - Materials used
- Freeze-drying and washing did not affect significantly particle size
  - Particle fate under other processing conditions
- Release of alpha-tocopherol can be controlled by initial loading
  - Interaction between particles and other food components
- PLGA/Chitosan particles were stable at acidic pHs (stomach), but aggregated at pHs> 5.5 (intestine)
  - Release and vitamin uptake under these conditions
IMPROVED ANTIMICROBIAL ACTIVITY

Nipur Patel
PLGA NPs WITH ENTTRAPPED ITRACONAZOLE

<table>
<thead>
<tr>
<th>NP Type</th>
<th>Theoretical Loading (% w/w)</th>
<th>Size (nm)</th>
<th>Pdi (au)</th>
<th>Zeta (mV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empty</td>
<td>0</td>
<td>201.32±5.33</td>
<td>0.010±0.031</td>
<td>-33.14±8.40</td>
</tr>
<tr>
<td>PLGA1</td>
<td>12.5</td>
<td>232.11±1.76</td>
<td>0.213±0.035</td>
<td>-31.89±5.30</td>
</tr>
<tr>
<td>PLGA2</td>
<td>25</td>
<td>199.75±4.66</td>
<td>0.114±0.042</td>
<td>-24.28±2.49</td>
</tr>
</tbody>
</table>

Unloaded PLGA NPs

Sporanox/PLGA NPs

Time (Hrs) vs. % Released

- 12%
- 24%
IMPROVED ANTIMICROBIAL ACTIVITY

Itraconazole/water

Itraconazole/NP conc. x

Itraconazole/Triton X sol.

Itraconazole/NP conc. 10x

Day 5

Day 5

Day 5

Day 5
Antifungal particles measuring ~200 nm were synthesized from PLGA with entrapped Itraconazole
- Other antifungals or antibacterials can be entrapped and studied
Release of the antifungal was sustained over 100 hrs
- Release can be modulated by choice of polymers, surfactants, etc.
Antifungal properties of the PLGA NPs were superior to those of free Itraconazole or emulsified antifungal
- Studies needed to identify mechanism of action
IMPROVED FUNCTIONALITY OF HYDROPHOBIC COLORANT

Carlos Astete

Components used are GRAS

<table>
<thead>
<tr>
<th>Alginic acid</th>
<th>Lecithin</th>
<th>β-carotene</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polysaccharide with mannuronic and guluronic acid</td>
<td>Phophatidyl choline</td>
<td>Natural pigment</td>
</tr>
<tr>
<td>Negative charges from carboxylic groups</td>
<td>Surfactant</td>
<td>Lipophilic</td>
</tr>
<tr>
<td>Thickening agent</td>
<td>Emulsions</td>
<td>Antioxidant</td>
</tr>
<tr>
<td></td>
<td>Extracted from egg yolk and soybeans</td>
<td></td>
</tr>
</tbody>
</table>
Approach
Nanoparticle synthesis

Organic Phase: Ethyl acetate/Chloroform

Aqueous Phase: Water Lecithin

Emulsion Sonication
Time: 6 min
Temperature 4-8 °C in an ice bath

Stabilization

Evaporation under vacuum

Pigment nanoparticles (suspension or dry)

CaCl₂
Alginic acid
No CaCl₂
Alginic acid: 0.35 mg/ml

CaCl₂: 0.29 mg/ml, Alginic acid: 0.35 mg/ml
Nanoparticle stability

Solvent: Ethyl acetate

Alginic acid (mg/ml) vs. Size (nm)

- a1
- a2
- a3

Solvent: Chloroform

Alginic acid (mg/ml) vs. Size (nm)

- b1
- b2
- b3

Particle precipitation
Antioxidant and pH stability

![Graphs showing antioxidant and pH stability](image)

- **Absorbance vs. Time (Hours)**
  - Different concentrations of CaCl2 (0%, 0.15%, 0.29%)
  - Emission of fluorescence

- **Ratio absorbance (C/C0)**
  - Linear relationship with time

- **Alginic acid: 0 mg/ml**
  - Graphs showing size and zeta potential vs. pH

- **Alginic acid: 0.07 mg/ml**
  - Graphs showing size and zeta potential vs. pH

- **Zeta potential (mV)**
  - Stability across pH range

- **Size (nm)**
  - Stability across pH range

- **pH**
  - Range from 1 to 7
CONCLUSIONS-IMPROVED FUNCTIONALITY

✓ Water-soluble nanostructures for entrapment of β-carotene were formed with the proposed method
✓ The nanostructures were capable of solubilizing natural pigments (β-carotene) in water to deliver an uniform color distribution
✓ The organic solvent used in the synthesis significantly affected the size and stability of the structures by precipitation
✓ Ca\(^{2+}\) and polymer concentration affected drastically the morphology and functionality of the system, not as much size and size distribution
✓ The nanostructures were stable between pH 3 and 7
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