Manufacturing Microcapsules for Advanced Materials

Dr. Thorsten Brandau, BRACE GmbH
Problem: Pure active agents have many disadvantages

- difficult application
- instable in air/in the digestive system
- „Burst“-effect
- difficult dosage
- difficult handling

Solution: Microencapsulation with chemoxide Microspheres

- Microspheres: Solid sphere with matrix-encapsulated active agent
- Microcapsules: Core-Shell principle
Release profiles

- small sphere
- large sphere
- thin shell
- thick shell

Release [%] vs Time
The BRACE-Processes

- Vibrating Nozzle processes
- Monomodale size distribution
- Very small size distribution, $d_{\text{max}}/d_{\text{min}} \leq 1.10, 1.05, 1.01$
- Microspheres and Microcapsules
- Wide product diameter range: 50 – 6000µm
- Patented processes
- Tradename „chemOxide“
Size Distribution in Process (150µm Nozzle)
The BRACE-Processes

- Wide range of shell materials
- GMP/GLP, FDA, Pharma-, Food-, Chemistry-, Industrial-Standards
- High scalability (10ml/h → 1000l/h)
- Low space and energy consumption
- Independent of the pre- and postprocessing
- Installations „Customer tailored“
free flowing
embedded agents
high porosity
precisely fitting diameters
high precision
coated
high density
activated
doped
Example:
Fusion Process

Applications

- Wax
- PEG
- Thermoplastics
- Pharmaceuticals
- Electronic alloys

Example:
Fusion Process

Microsphere Production Facility

BRACE Fusion Process

1. Control Cabinet
2. Vibrator Unit
3. Feed Tank
4. Fine Pressure Adjustment
5. Nozzleplate
6. Heating Cabinet
7. Stroboscope
8. TV Camera
9. Connection Device
10. Coagulation Line
Example:

Process scheme **Binder Process**

- Oils
- Liposomes
- Active Agents
- Caffeine
- Colourants, Pigments
- Food
- Cosmetics
- Encapsulation
- Textiles
Throughput and # of Microspheres with 500µm Nozzle
[Wax, Density = 0.8 g/cc]
Suitable Materials and Properties

- Liquid feed
- Viscosity < 10000 mPa·s
- Dispersed particles should be < ¼ diameter of the nozzle
- Emulsions/Dispersions have to be stable
- Presolidification has to be fast
Materials for the shell/matrix-Microcapsules

- Alginate
- Gelatine
- Agar-Agar
- Cellulose sulfate
- Wax/Thermoplastics
- Oxides: Si-, Al-, Ti-, Zr-, Hf-, Ce-, In-, Y-Oxid, mixtures
- Sols
- Polyethylenimine
- Polyethersulfone
- PEG, PVA
- Polyacrylate, -methacrylate
- Polyamide
- Polystyrene
Active agents for microencapsulation in matrix (Microsphere)

- Active agents that can be dispersed (Oxides, Colors, Pharmaceuticals, Cells, Liposomes, [...])
- Soluble materials (Vitamines, Oil, Flavors, Colors, [...])
- (stable) emulsified materials (Oils, Flavors, Fats, [...])

Core materials for Microcapsules

- Solutions
- Emulsions
- Dispersions
- Fusions/Melts
Postprocessing

- Drying: Circulating air, Fluidized bed, Beltdryer, Drumdryer [...]
- Calcining, sintering
- Coating: Spray-/rotation disc coating [...]
- Impregnation
- Sorting [...]
- Chemical treatment
Types of installations

- Continuous or batchwise
- GMP/GLP, FDA, CIP, WIP, sterilizable [...] 
- Fully- or semi-automatic
- Production, pilot or lab scale
- Adaptation for existing production facilities
- Machinery in stainless steel, glass, plastics [...]

BRACE GmbH
The Microsphere Company
Scalability

- Installations between 10ml/h and >1000l/h available
- Upscaling lab/pilot scale to production scale is very easy
- Upgrading for larger capacities possible
- Different products with different diameters in the same installation producable
# Thermoplastic Microspheres: Manufacturing costs in EURO

<table>
<thead>
<tr>
<th>Investment, Description</th>
<th>Tons per year</th>
<th>kg per hour</th>
<th># Nozzles</th>
<th>Feed preparation</th>
<th>Microsphere Unit</th>
<th>Storage and Packing</th>
<th>Total I</th>
<th>Laboratory, Quality control</th>
<th>Total II</th>
<th>Building (rent)</th>
<th>Raw material 1€/kg</th>
<th>Operators per shift</th>
<th>Operator costs per shift</th>
<th>Maintenance 5% of Total II</th>
<th>Amortisation 5a, 8% (0,2505)</th>
<th>Amortisation 10 a, 8% (0,14903)</th>
<th>Manufacturing costs per kg (5a)</th>
<th>Costs including material</th>
<th>Manufacturing costs per kg (10a)</th>
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</table>
Cosmetic waxes

- Peeling
- Esthétique
- Enhancement by Design
Agar-Agar

- Oily ingredients
- Optical Enhancement
- Stabilising of volatile ingredients
Microcapsules

- Oily ingredients
- Optical enhancement
- Stabilisation of volatile components
- Olfactorian and sensorical enhancement due to the „Burst“
- Shellmaterials like Gelatine, Alginate, Agar-Agar etc.
Microcapsules

- Many different sizes possible
- Shell thickness 10–90%
- Diameter 500 – 8000 µm
Metal Spheres

- Solder Alloys for BGA Chips or
- Silicon for Solar Cells
- Effect Colorants
Microcapsules

- Dried or humid applicable
- Drying by BRACE-Drumdrier
- Taste masking
- „Health-Food“ (Vitamines, \( \Omega_3 \)-Fatty acid, Lecithin, Probiotic ingredients etc.)
Polymer Beads

- Monomodale grain distribution
- Defined binding capacity
- Combinatorical Synthesis
Pharmaceuticals

- Controlled Release
- Adjustable release profiles
- Tastemasking of bitter agents
- Stabilising
- GMP/GLP/FDA production
Inorganic Carriers

- Vitamines
- Flavors
- Tooth paste
- Bone cement
- Catalysts
- Catalyst carriers
- Grinding balls
Small Pilot Production

- Exchangeable Plates
- Min. 15 Nozzles
- Max. 180 Nozzles
- Capacity 30-600 L/h
- Continuous Production
- Cosmetic Application
Pilot Nozzle Head

- 70fold Nozzle Plate
- Titanium
- 300-500 L/h
- Medium and High Viscosity
- up to 5000 mPas
- Overflow Funnel System
- Continous Production
Spherisator S

- Desktop Unit
- Recipe Development, Testing
- Small Scale Tests
- For Microspheres, Microcapsules etc.
- GMP/GLP-conform
Spherisator 2002 Mark II

- Desktop Unit
- Recipe Development, Testing
- Small Scale Tests
- Easy Scalable
- Same Options as Production Unit
- For Microspheres, Microcapsules etc.
- GMP/GLP-conform
Heating Chamber for Spherisator

- Fully Equipped
- Easy to Use
- Including Stand
- Option: Cooling Reaction Bath
- Option: Flow Reactor
- 150°C, 200°C, 500°C Available
- Spherisator L
- Up to 100kg/h
- Modular System
- Automated System
- Continuous and Batch Operation
- Production scale unit
- Capacity 10,000 kg/h
- Turnkey unit – Powder in – Spheres out
- Fully automatic
- 2 People per shift
- 24 h/day
- 7 days a week
- 360 day/year
Roundness Sorting

- Vibrational Sorting Tables
- 1-3 kg/h
- Very High Sorting Quality
- Continuous Operation
- Fully Automatic
Roundness Sorting

- High Quality Ceramics
- Bone Cement
- Ball Pen Tips
- Vitamin Capsules
- Pharmaceutical Microspheres
BRACE GmbH

- 1984 Company name BRACE
- Since 1992 GmbH
- ISO9001:2000 and HACCP certified
- GMP Planned for 2010
- Own laboratories, pilot installations, analysis
- Mission „idea to production“
- Development of recipes, manufacturing (up to ca. 300 t/a), engineering and construction of installations and machinery from desktop to large scale facilities
- Global operating specialist for microencapsulation
- Representatives in the Americas (North-, Middle-, South), Japan, Korea, Vietnam, China, Taiwan

Spherisator S  Large Scale Production  Drum Sieving Machine  Shape Sorter

Karlstein Facilities (QI/2010)