**Round robin experiment "Bead production technologies"**

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**Introduction**

The encapsulation of various materials and living cells inside beads for different purposes in the pharmaceutical, chemical or food industry as well as in agriculture, biotechnology or medicine is of great importance. Thus, a large number of papers deal with this topic. Despite the broad application of bead-encapsulated material the knowledge about the different technologies for bead production and their advantages and disadvantages is limited. From literature it is not easy to extract which might be the best technology available for the special encapsulation purpose as the different technologies have so far not been compared to each other with the same material.
In order to give a potential user comparable data about the different common bead production technologies, several members of the Working Group 3 within the COST 840 action carried out the round robin experiment "Bead production technologies" in which beads in a definite diameter range have been produced by the most common technologies using the same polymer solutions as starting material.

**Material and methods**

The bead production technologies used in the different labs are indicated in table 1:

| Lab | Bead production technology |
|---|---|
| Slovak Academy of Sciences, Bratislava | Coaxial air-flow dropping |
| University of Belgrade, Belgrade | Electrostatic dropping |
| Polish Academy of Science, Warsaw | Electrostatic dropping |
| Institute Meurice, Brussels | Vibration, JetCutter |
| University of Perugia, Perugia | Vibration |
| ENITIIA, Nantes | Vibration |
| FAL and geniaLab GmbH, Braunschweig | JetCutter |

**Table 1: Bead production technologies used in the different labs**

Each lab received sodium alginate powder (Protanal LF 20/40 supplied by FMC Biopolymer) which has been taken from the same batch. In each lab solutions with an alginate content of 0.5, 1, 2, 3, and 4 % w/w, respectively, have been prepared by dissolving the sodium alginate powder at room temperature in distilled/deionised water. In some labs, the dynamic viscosity η of the solutions has been measured at 30°C directly after preparation. The results are shown in table 2.

| **Na-alginate content, % w/w** | **Bratislava** | **Belgrade** | **Warsaw** | **Brussels** | **Nantes** |
|---|---|---|---|---|---|
| | **η in mPa·s at (shear rate in $s^{-1}$)** | | | | |
| 0.5 | 33 (100) | - | 24 (233) | 32 (12) | 26 (300) |
| 1 | 140 (10) | - | 92 (233) | 155 (11) | 83 (300) |
| 2 | 1232 (1) | 1129 (6.3) | 667 (129) | 1334 (1) | 424 (300) |
| 3 | 5501 (0.5) | 5236 (2.5) | 2008 (23) | 4632 (20) | - |
| 4 | 10516 (0.1) | 11251 (2.5) | 10560 (10) | 12187 (10) | - |

**Table 2: Dynamic viscosity η (in mPa·s at 30°C) of solutions with different sodium alginate contents measured in the different labs, the corresponding shear rate in $s^{-1}$ is given in brackets**

Beads with a resulting diameter of 800 ± 100 µm (600 ± 100 µm in Perugia) have been produced with the different technologies by gelation in a 2 % w/w $CaCl_2$ bath at room temperature. The production rate for each experiment has also been recorded to serve as criteria for the throughput of the technology. After bead preparation the size distribution has been determined by taking photographs of the beads under a microscope.

The JetCutter can be operated either in the "normal mode" or in the "soft-landing mode". Normal mode means that the JetCutter is placed somewhere at a definite height (e.g. about one meter from the floor) and the beads are collected in a $CaCl_2$ bath placed on the floor. Soft-landing mode means that the JetCutter is placed on the floor and the beads are collected at a height of about 2 meters. This reduces the velocity of the bead when entering the gelation bath, which otherwise would lead to a deformation of the beads. The two modes are schematically represented in figure 1.

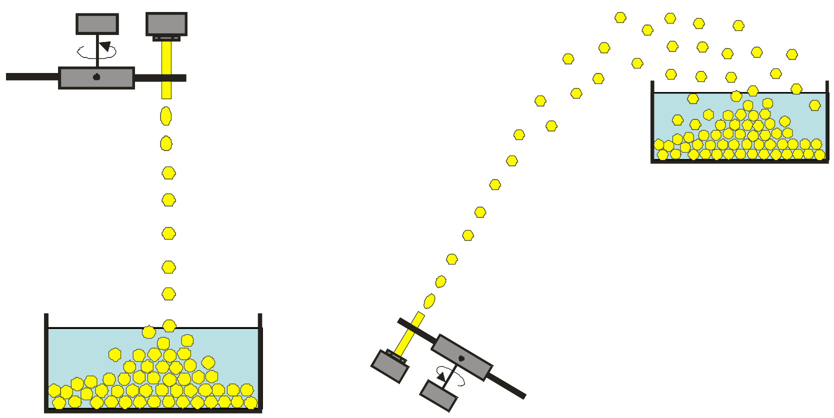


**Figure 1: Two modes to operate the JetCutter. Left: normal mode, right: soft-landing mode**

## Results and discussion

Photographs of the beads produced by the diverse technologies in the different labs are shown in table 3.

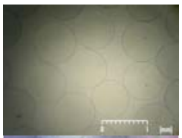
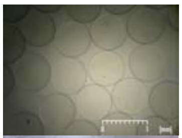
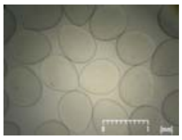
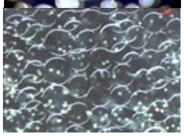
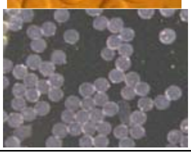
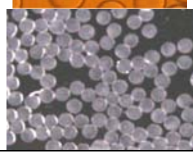
| technology (lab) | beads from solutions with alginate w/w content of | | | | |
|---|---|---|---|---|---|
| | **0.5 %** | **1 %** | **2 %** | **3 %** | **4 %** |
| coaxial air-flow (Bratislava) |  |  |  |  |  |
| electrostatic (Belgrade) |  |  |  | solution is too viscous | |
| electrostatic (Warsaw) |  |  |  |  |  |
| vibration (Brussels) |  |  |  | solution is too viscous | |
| vibration (Perugia) |  |  |  | solution is too viscous | |
| vibration (Nantes) |  |  | solution is too viscous | | |
| JetCutter – normal (Brussels) |  |  |  |  |  |
| JetCutter – soft-landing (Braunschweig) |  |  |  |  |  |

**Table 3: Photos of the beads produced from the different alginate solutions by the diverse technologies**

According to table 3 the ability of the different technologies for the processing of alginate solutions with diverse viscosities can be summarised as follows:

- *Coaxial air-flow*: very nice spherical beads up to 2 % alginate, lower roundness at higher viscosities, very good size distribution for all alginate solutions
- *electrostatic*: very nice spherical beads up to 4 % alginate possible, very good size distribution for all alginate contents
- *vibration*: very nice spherical beads up to 1 % alginate, medium shape and size distribution at 2 % alginate, no bead formation possible for alginate contents ≥ 3 %, very good size distribution up to 1 % alginate
- *JetCutter – normal mode*: no bead formation possible at 0.5 % alginate, poor shape and size distribution at 1 % alginate, very nice spherical beads for 2 – 3 % alginate, lower roundness at 4 % alginate, very good size distribution if beads can be produced
- *JetCutter – soft-landing mode*: good shape and size distribution at 0.5 % alginate, very nice spherical beads with very good size distribution from 1 – 4 % alginate

The throughput or the range of throughputs if more than one group performed experiments, respectively, corresponding to the production of the beads shown in table 3 are displayed in table 4:

| Alginate content | throughput, g/(s · nozzle) | | | | |
|---|---|---|---|---|---|
| | coaxial air-flow | electrostatic | vibration | JetCutter (normal) | JetCutter (soft-landing) |
| 0.5 % | 0.4 | 0.007 - 0.009 | 0.1 - 0.16 | 2.0 | 1.1 |
| 1 % | 0.4 | 0.004 - 0.005 | 0.12 - 0.21 | 2.0 | 1.5 |
| 2 % | 0.4 | 0.0008 - 0.007 | 0.15 - 0.21 | 2.0 | 1.4 |
| 3 % | 0.05 | 0.0014 | - | 2.0 | 1.4 |
| 4 % | 0.02 | 0.00013 | - | 2.2 | 1.3 |

**Table 4: Throughputs for the different bead production technologies**

It can be taken from table 4 that the throughput of the electrostatic device is by far the lowest. In fact, it is about one up to two orders of magnitude lower than the throughput of the vibration system, which itself has a throughput of about one order of magnitude lower than the JetCutter. In between the vibrating system and the JetCutter lies the coaxial air-flow system.

## Conclusions

From the results of this round robin experiment it can be concluded that each of the bead production technologies is suitable to produce spherical beads in a narrow size distribution from low viscous fluids ($\eta \leq 200$ mPa·s, alginate contents up to 1 %), with the restriction to use the JetCutter in the soft-landing mode. For medium viscous fluids (200 mPa·s $\leq \eta \leq$ 1000 mPa·s) the vibration system reaches its limitation - shape and size distribution become worse with increasing viscosity – whereas all other technologies still allow the production of nice beads. For higher viscosities ($\eta \geq$ 1000 – 2000 mPa·s, alginate contents higher than 2 %) the vibration system cannot be used anymore. The coaxial air-flow system reaches its limitations with regard to the shape of the beads – poorer roundness with increasing viscosity – and the throughput, which decreases about one order of magnitude. Only the electrostatic system and the JetCutter can be used for the production of beads from such high viscous fluids. In this connection, it has to be pointed out that the throughput of the JetCutter is about 1000 – 10000 times higher than the throughput of the electrostatic device.
For lab-scale applications, in which the throughput of a technology is of minor importance, each technology can, in principle, be used for bead production. If only very small amounts (< 10 g) of beads shall be prepared, which sometimes might be the fact in research, coaxial air-flow, electrostatic or vibration techniques might be more suited than the JetCutter as these techniques can be easily run with low throughputs, which is not easily achievable with the JetCutter. On the other hand, if high throughputs are necessary, e.g. for pilot or industrial scale applications, the JetCutter is the best choice.