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HPMC Capsules Sealing with Capsugel CFS1200 Equipment for Small Scale Laboratory Development

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Key words: Hypromellose capsule, encapsulation, sealing, small scale development

PURPOSE

The work presented hereafter demonstrates that capsules made of hydroxypropylmethyl cellulose (HPMC) can be sealed on Capsugel CFS1200 equipment (Photo 1) to accelerate early stages of development of new medicines.

Photo 1: CFS 1200 machine

HPMC capsule is the non-animal alternative to gelatin capsule, which presents the same machinability, appearance, dissolution profile and better robustness regards to brittleness. As HPMC material equilibrates in standard conditions with lower content of water, it may be an advantage in case of hygroscopic products.

Capsugel provides two types of HPMC capsules (Photo 2):

- L-Vcaps™ capsules (natural aspect), with good dissolution in demineralized water and Japanese alkaline media, well appreciated in DS market.

- Vcaps® Plus capsules (glossy aspect), with excellent dissolution behavior whatever the dissolution media, designed for pharmaceutical products.

Photo 2: empty L-Vcaps™ capsule (left) and Vcaps® Plus capsule (right)

The purpose of this study is to evaluate the consistency of the sealing process of HMPC capsules filled with oily fluid material and sealed on CFS1200 equipment.

METHODS

Product description

The natural transparent capsules studied are L-Vcaps™ capsules size #0 and Vcaps®

Plus capsules size #0. The lecithin solution encapsulated is sunflower lecithin diluted at 40% in sunflower oil to obtain 250cP viscosity at room temperature. The sealing fluid compositions tested here are mixtures of pure alcohol (isopropanol or ethanol) and water 80/20 w/w.

Encapsulation conditions

A design of experiment was performed using three factors at two levels: capsules (L-Vcaps™/Vcaps® Plus), sealing fluid composition (isopropanol/ethanol) and sealing temperature (35°C/55°C). The eight runs of 500 capsules were repeated to access reproducibility. Each HPMC capsule was filled with 500mg lecithin, closed and sealed in the presence of 30µL sealing fluid on CFS1200. After
encapsulation, capsules are stored on trays in standard room conditions (22°C, 50%RH).

Measurement of sealing performances

During the sealing trial, capsules are inspected regarding to:
Visual quality of the sealed zone (Photo 3): capsules are ranked as "good" (>80% surface covered), "medium" (>50% surface covered) and "poor" (risk of leaker because sealing does not cover 360° of the seal zone).
Peel test: the cap is cut and peeled off the body after sealing and 1 week after sealing; if peel is easy, score is "0" whereas score equals "5" when peeling is not possible.
Leaker rate: capsules are submitted to depression (-0.8bars for 20minutes), then greasy spots are counted and the corresponding capsules are removed for inspection. Same sorting is done 4 hours later to confirm all leakers were removed.

Photo 3: Filled and sealed L-VcapsTM (left) and Vcaps® Plus (right) capsules.

RESULTS

The overall results are consistent between repeats (Fig.1). The impact of the 3 factors depends on the response considered. For instance, visual quality and peel test have opposite optimums:
- 35°C is better for visual quality, it is worse for peel test.
- Ethanol is better for peel test and worse for visual quality.

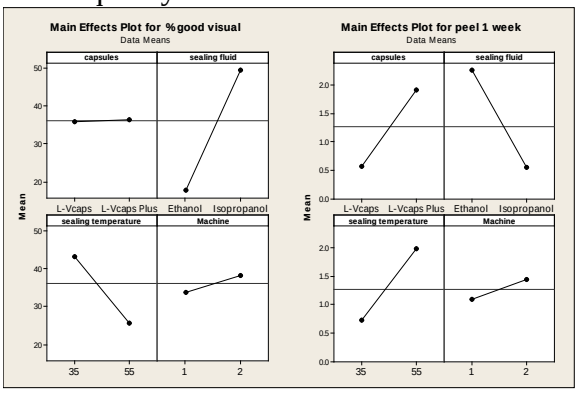

Fig. 1: Main effects of factors considered in Design of Experiment

The detailed results confirm that the optimal conditions depend on the response considered. Capsule type appears important

regards to peel test whereas visual quality is relative to sealing fluid composition.
L-VcapsTM capsules are ideally sealed with isopropanol at 35°C: visual quality is acceptable and leaker rate is less than 1% in the presence of fluid product (250cP viscosity at room temperature), whereas seal strength remains poor whatever the conditions.
Vcaps® Plus capsules can be sealed in the same conditions as L-Vcaps™ capsules with equivalent performances. Ethanol is a good option to favor seal strength and to lower the risk of leakers over time as a consequence.

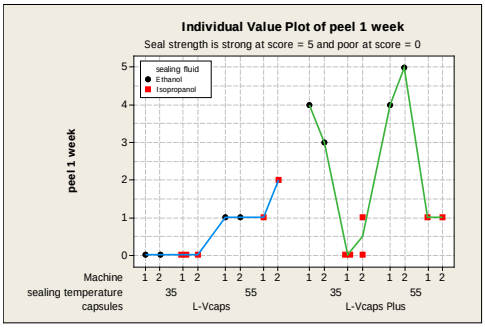

Fig.2: Evolution of visual quality

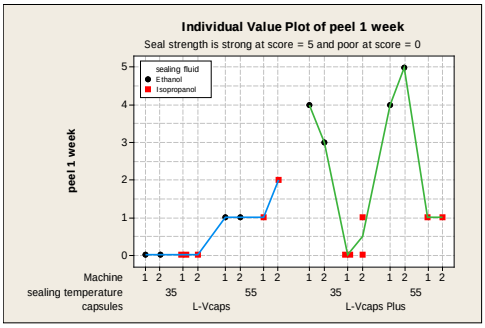

Fig.3: Evolution of seal strength

We confirmed the optimal conditions for both capsules types at larger scale (2,000 capsules instead of 500 per run). We also included the latest generation of Vcaps® Plus capsules designed to favor visual quality and peel test: Vcaps® Plus 2nd generation (Table 1).

Runs	Capsule	Conditions	Acceptable visual quality (%)	Peel test (score)	Leaker rate (%)
1	**L-Vcaps™**	Isopropanol 35°C	80	0	0.7
2	**Vcaps Plus®** (1st generation)	Ethanol 50°C	20	5	0.9
3	**Vcaps Plus®** (2ndgeneration)	Ethanol 50°C	70	5	0.8
4	**Vcaps Plus®** (2ndgeneration)	Ethanol 35°C	86	5	0

Table 1: Confirmation trial of optimal conditions

L-Vcaps™ and Vcaps® Plus capsules demonstrate good behavior on CFS1200 sealing machine. The quality of capsules sealed is equivalent or slightly inferior to the quality obtained on large scale sealing equipment LEMS®70.

CONCLUSION

The Capsugel laboratory sealing machine CFS1200 is able to process both types of HPMC capsules manufactured by Capsugel. The quality obtained is suitable for early stages of development of new active molecules (>99% yield). It accelerates the development time by providing rapidly samples ready for pre-clinical batches.

REFERENCES

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