CAPSUGEL®

Robust Liquid-Filled Licaps® Capsules with LEMS® Technology

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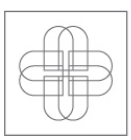

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PURPOSE

The work presented hereafter documents that the combination of new generation of Licaps® hard gelatin capsules and optimization of LEMS® sealing equipment[1] improves significantly mechanical resistance over time of filled and sealed capsules.

Photo 1: LEMS70® machine

Licaps® hard gelatin capsule is proposed in different sizes, colors, and from different gelatin origins (porcine, bovine, fish) for more than 15 years. In order to improve the seal zone coverage and to optimize sealed capsule elasticity, Capsugel improved the design of capsule shell[2] as presented in Photo 2.

The purpose of this study is to demonstrate the robustness of liquid-filled improved Licaps ® capsules sealed with Capsugel sealing technology and their suitability for transportation, storage and deblistering.

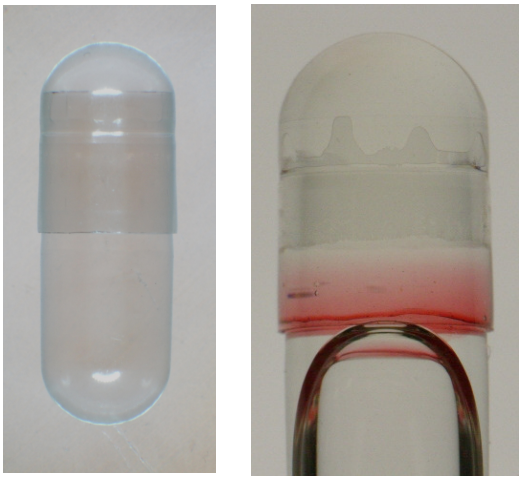

Photo 2: Licaps® New Design capsule natural transparent in closed position on the left, filled and sealed on the right.

METHODS

Product description

The natural transparent capsules considered are Licaps® capsules natural transparent and white opaque size #0, filled with various products: medium chain triglyceride (25-35cP), peanut oil (50-60cP), diluted lecithin (200-250cP), poloxamer mixture (>5,000cP) and sealed with LEMS®70 technology.

Testing protocol

Part 1: A design of experiments was performed using two factors at two levels: capsule color (natural transparent and white opaque) and filling conditions (22°C versus 60°C) to detect effect of sealing process on capsule robustness.

Part 2: Capsules from various gelatin origins and commercial productions were selected randomly, stored in room conditions and submitted to testing for 20 months

Measurement of mechanical resistance

During the stability study, capsules are submitted to:

Compression (Photo 3): 20 capsules are crushed between two disks; force at break is measured as well as water content in shell. Values of interest are: force at break average in Newtons and the ratio of capsules that breaks below 65N in percent, i.e. weak capsules which could be at risk for deblistering.

Tube test (Photo 3): 50 capsules are submitted each to the free fall of 50g from 8cm high. Result is expressed as the percentage of broken capsules.

Drop test (Photo 3): 50 capsules are packed in HDPE bottle and submitted to free fall from 1 meter high five times. Result is expressed as the percentage of broken capsules.

Deblistering test: 20 capsules are packed in PVC blister and submitted to manual de-blistering. Result is expressed as the percentage of broken capsules.

(a) (b) (c)

Photo 3: compression test (a), tube test (b) and drop test (c).

RESULTS

Part 1: The overall results are consistent between repeats (Fig.1). Whatever the sealing conditions and the capsule color, capsules are robust: we do not detect any weak capsule below 65N and force at break average equals or is greater than 200N.

The significant factor detected by compression is capsule color: natural transparent capsules are more robust than opaque capsules.

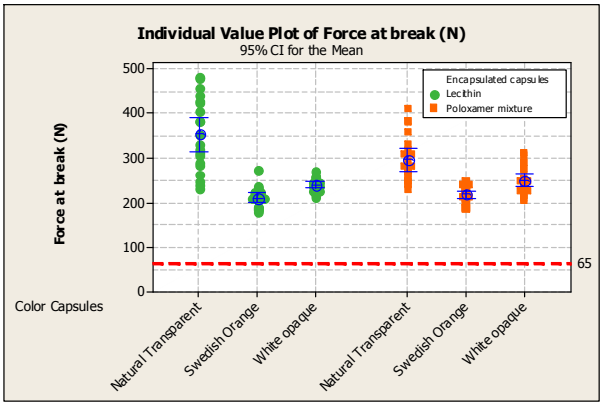

Fig. 1: Main effect detected in Design of Experiment is capsule color.

As predicted by compression test, we did not detect any broken capsule at de-blistering (Table 1). We confirmed also the robustness of gelatin capsules at tube test and drop test: capsules will be stored and transported without damage, except for the swedish orange opaque capsules which are less robust due to the large quantity of pigments in shell.

Color capsules	Natural Transparent	White opaque	Swedish Orange	Natural Transparent	White opaque	Swedish Orange
Product encapsulated	Lecithin			Poloxamer mixture		
Compression	359 +/- 81	241 +/- 15	212 +/- 23	298 +/- 53	250 +/- 32	220 +/- 18
Tube Test Broken capsules (%)	4%	0%	28%	0%	0%	10%
Drop Test Broken capsules (%)	2%	2%	4%	2%	4%	2%
Blister (% Broken caps)	0%	0%	0%	0%	0%	0%
LOD	12.9	12.7	12.5	13.3	13.1	13.2

Table 1: Robustness of Licaps size 0 capsules stored at 22°C/50%RH for 3 months: filled at room temperature with fluid lecithin (200cP) and filled at 60°C with poloxamer mixture (>5,000cP)

Part 2: We confirmed that all capsules filled with various products and sealed with LEMS® technology are robust over time when stored in room conditions: 50%RH+/-15% and 22°C +/-2°C (Fig.2). Furthermore, we confirmed that transparent capsules are even more robust than opaque capsules.

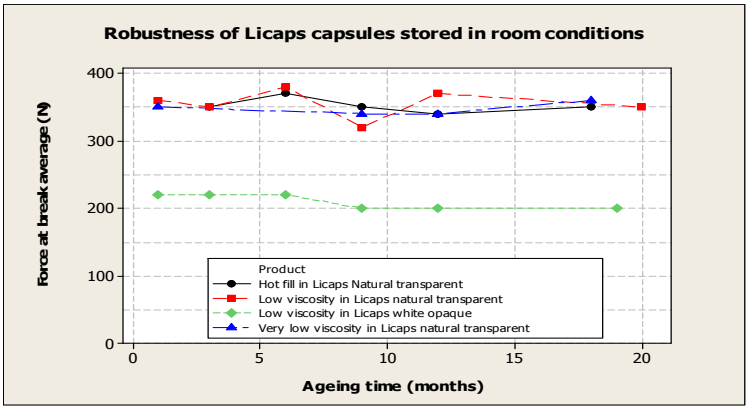

Fig. 2: Evolution of mechanical resistance of sealed capsules over time

The difference between opaque and transparent capsules is explained by the presence of pigments. All capsules tested exhibited stable robust performance (Table 2).

Color of capsules New Design size #0	Product Encapsulated	Ageing (Months)	% Weak capsules (<65N)	LOD (%)
White opaque	Fish oil & MCT 40cP	9M	0	13.0
White opaque	Fish oil & MCT 40cP	12M	0	13.0
White opaque	Fish oil & MCT 40cP	20M	0	12.8
Natural transparent	Fish oil & MCT 40cP	9M	0	13.1
Natural transparent	Fish oil & MCT 40cP	12M	0	13.0
Natural transparent	Fish oil & MCT 40cP	20M	0	12.9
Natural transparent	Fish oil & beeswax HOTFILL	9M	0	14.4
Natural transparent	Fish oil & beeswax HOTFILL	12M	0	13.4
Natural transparent	Fish oil & beeswax HOTFILL	20M	0	13.1
Natural transparent	MCT 25cP	9M	0	12.8
Natural transparent	MCT 25cP	12M	0	13.0
Natural transparent	MCT 25cP	20M	0	12.8
Red opaque	MCT 25cP	9M	0	12.3
White opaque	MCT 25cP	9M	0	12.9

Table 2: Confirmation of robustness after 20 months storage in the presence of various products of increasing viscosity at room temperature

CONCLUSIONS

The Capsugel LEMS®70 sealing machine produces robustly sealed Licaps® hard gelatin capsules filled with products of various viscosity from 25cP to solid, filled either at room temperature or 60°C. The quality obtained is consistent over time and at least equivalent to banded capsules from the market[3]. When environment is under control, we guarantee safe transportation, packing and de-blistering stages.

REFERENCES

[1] LEMS®70 brochure references 13771_ v 21_11-12-2008
[2] Patent EP06795209
[3] With our compression test, we measured 90 to 350N in average and 0 to 60% weak capsules.

ACKNOWLEDGEMENT

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