

IMPACT OF MASKING ON METHYLPHENIDATE DISSOLUTION FOR OVER ENCAPSULATED CAPSULES OF RITALIN LA 10 MG

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Background

- Drug development for a double-blind clinical trial
- Over-encapsulated capsules** + backfilled excipient for masking
- Ritalin LA (Extended release) containing 10 mg Methylphenidate (MH) - **Bimodal release of RITALIN** (SODAS[®] technology)

1st release :

- Immediately
- 50% dose
- Acidic pH

2nd release :

- After 2h
- 50% dose
- pH > 6

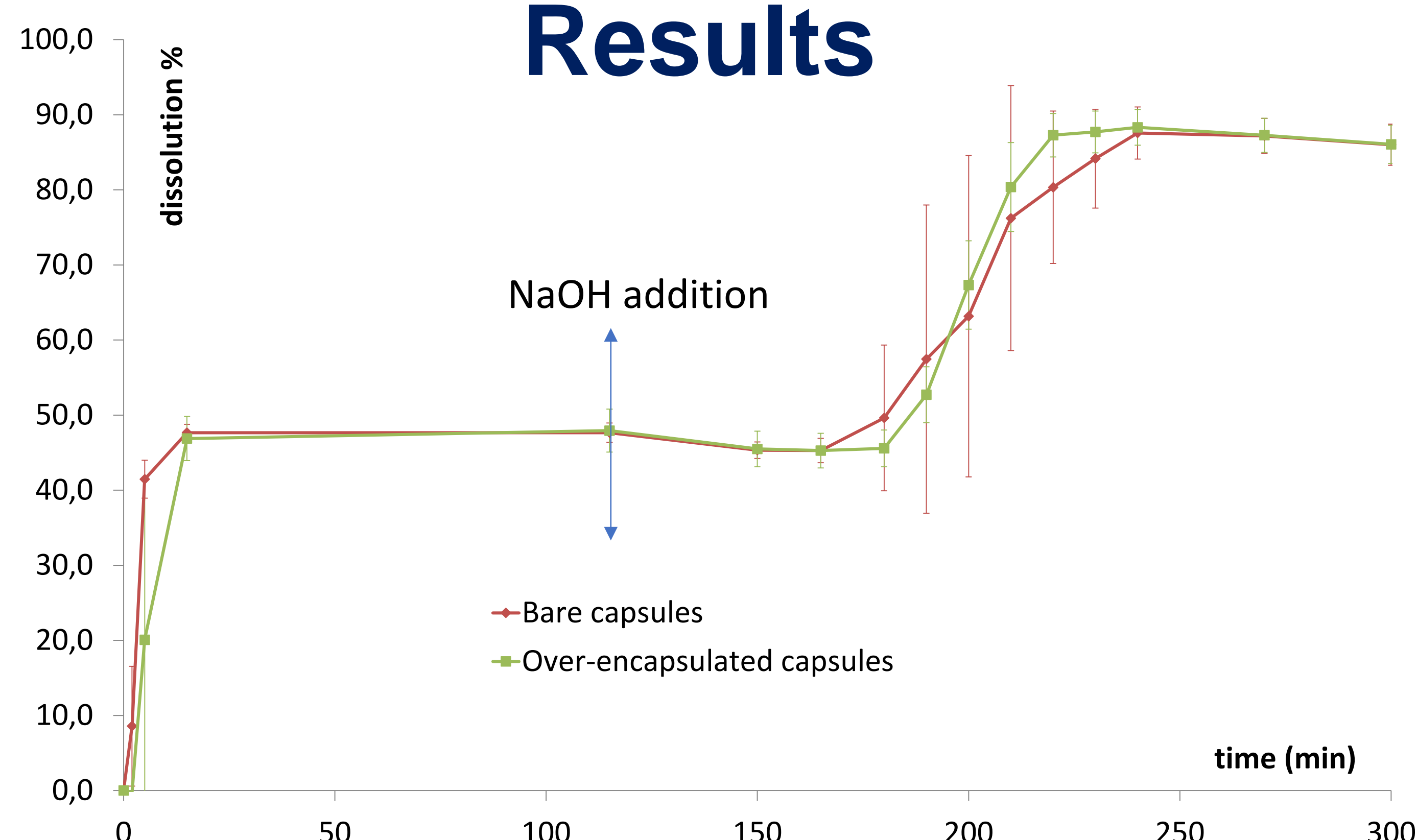
Objective

- To study the potential impact of masking in over-encapsulated capsules on MH dissolution compared with bare capsules, thanks to *in vitro* biopharmaceutical parameters.

Methods

- MH dissolution study : - **bare capsules** (n=6)
- **over-encapsulated** (n=6)
Backfilled excipient = microcrystalline cellulose (MC)
- 2 release phases : 1 unique dissolution medium = a Britton-Robinson buffer at 37°C
→ pH 2 for 2h → adjusting by NaOH addition
→ pH 6.8 for 3h
- Basket dissolution apparatus (EurPh 2.9.3) at 50 rpm
- 15 samples/capsule → HPLC-UV-DAD (stability-indicating)
- ➔ 2 dissolution profiles compared with :
 - fit factors* $f_1 < 15\%$ $f_2 > 50\%$ for similarity
 - Rescigno index* $\xi_1, \xi_2 \rightarrow 0$ for similarity
- Desintegration test (EurPh 2.9.1)

Results



- On the whole of dissolution profile:

$$f_1 = 2.2\%$$

fit factors

$$f_2 = 96.0\%$$

$$\xi_1 = 0.012$$

Rescigno index

$$\xi_2 = 0.025$$

NaOH addition

| Time (min) | Dissolution % | | | |
|------------|---------------|------|----------------------------|------|
| | Bare capsules | | Over-encapsulated capsules | |
| | Average | Sd | Average | Sd |
| 2 | 8,6 | 8,0 | 0,0 | 0,0 |
| 5 | 41,5 | 2,5 | 20,2 | 21,4 |
| 15 | 47,7 | 1,1 | 46,9 | 2,9 |
| 115 | 47,7 | 1,3 | 47,9 | 2,9 |
| 150 | 45,3 | 1,1 | 45,5 | 2,4 |
| 165 | 45,3 | 1,6 | 45,3 | 2,3 |
| 180 | 49,6 | 9,7 | 45,6 | 2,4 |
| 190 | 57,4 | 20,5 | 52,7 | 3,7 |
| 200 | 63,2 | 21,4 | 67,3 | 5,9 |
| 210 | 76,2 | 17,6 | 80,4 | 5,9 |
| 220 | 80,3 | 10,1 | 87,3 | 2,9 |
| 230 | 84,2 | 6,6 | 87,7 | 2,8 |
| 240 | 87,6 | 3,5 | 88,3 | 2,4 |
| 270 | 87,2 | 2,3 | 87,3 | 2,3 |
| 300 | 86,0 | 2,7 | 86,1 | 2,5 |

- Lag time of few minutes in the beginning of dissolution for over-encapsulated capsules = in part explained by delay due to capsules desintegration (103s vs 170s)
- MH progressive degradation was highlighted in buffer after NaOH addition → could explain maximum < 100%

Conclusions

- A similarity between over-encapsulated and bare capsules is demonstrated by using MC.