Physico-chemical and microbiological stability studies of a melatonin oral suspension for pediatric use.

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Background and Objective

Melatonin (MT) is commonly prescribed for sleep impairment in child psychiatry practice for diseases such as neurodevelopmental disabilities, autism spectrum disorders or attention-deficit/hyperactivity disorder. Children form a population of patients for which oral suspension is the most appropriate dosage form.

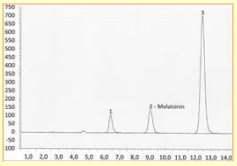
The liquid vehicle **Inorpha®** (Inresa) is a commercially available vehicle for oral solution or suspension, with sucralose as sweetener, and without paraben.
The aim of this study was to evaluate the **physico-chemical and microbiological stabilities** of **melatonin suspension (2mg/mL)** in Inorpha.

Setting and Method

Physico-chemical

The suspension of melatonin was divided into one hundred and twenty 5mL-tinted glass vials

- Half stored at **4°C**
- Half stored at **25°C**



For each temperature, melatonin concentration of three vials was assessed, in duplicate, by a validated method using HPLC with UV detection. The stability-indicating capability of the method was verified by forced degradation study.

Measurement every weeks, during 18 weeks, plus a final measurement after 6 months at 25°C

Microbiological

Two packagings were tested:

- 10mL-vials in order to evaluate the microbiological stability before opening
- 200mL-bottle opened at regular intervals in order to evaluate the stability under conditions of use.

Microbiological control used a membrane filtration of sample followed by culture on solid media allowing bacteria and fungi growth:

- Tryptic Soy Agars placed 5 days in incubator at 30°C
- Sabouraud Dextrose Agars put 7 days at 25°C

The media fertility and the counting method applicability were validated.

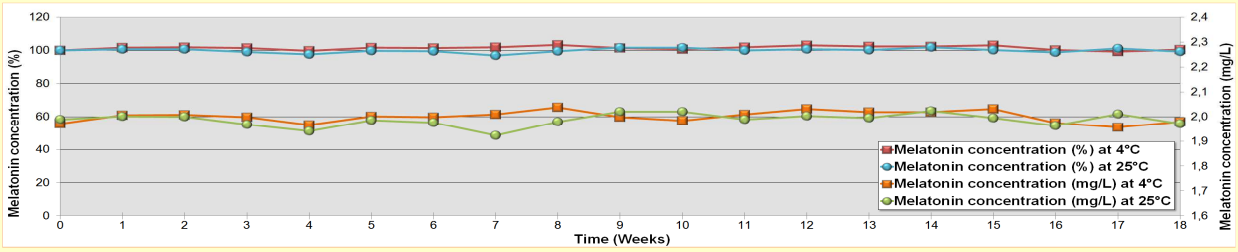
The microbiological study was performed over a period of 4 months (7 analyses)

Main Outcome Measures

Physico-chemical stability was defined by a concentration **above 95% of the initial concentration**. Suspensions were considered microbiologically stable if Total Aerobic Microbial Count (TAMC) was **less than 200 CFU/mL without any E.coli** and if total combined yeasts and molds count was **less than 20 CFU/mL**.

Results

Physico-chemical



97.7% of MT initial conc. was maintained after 18 week (95.5% after 6 months).

No significant difference between the 2 temperatures tested ($p < 0.001$).

Microbiological

Total Aerobic Microbial Count (CFU/mL) [Presence of E. coli]							
Analyse time (days)	J0	J7	J15	J30	J45	J75	J120
10mL-vials (n = 6)	**<10** [No]	**<10** [No]	**<10** [No]	**<10** [No]	**<10** [No]	**<10** [No]	**<10** [No]
200 mL-bottle	**<10** [No]	**<10** [No]	**<10** [No]	**<10** [No]	**<10** [No]	**<10** [No]	**<10** [No]

No yeast or mold growth was noted throughout the study period.

The highest TAMC obtained during the 4-month microbiological study was 0.3 CFU/mL (no E.coli).

Conclusions

Results of this stability study led to set the shelf life of melatonin suspension to 3 months at 25°C.
The microbiological quality was not altered by repeated openings of the bottle over the study period allowing production of multidose vials.

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