TINY
TECHNOLOGIES

Human in vivo Study

TINY MELATONIN

CLINICAL STUDY REPORT

DETAILS 1/4

Study No: SLS-CT-0003-22-MELA
Protocol Version: 01
CTRI Number: CTRI/2022/06/043163
Report Date: 03 Sep 22
EMA- and FDA-certified Contract Research Organization

Project Title:

An Open Label, Balanced, Randomized, Single-Dose, Two-Treatment, Two-Sequence, Two-Period, Two-Way Crossover Oral Bioavailability Study of Melatonin 5 mg in 1 mL Nano Emulsion (liquid), in Healthy, Adult Human Subjects Under Fasting Conditions.

Conducted in accordance with the Good Clinical Practice guidelines as issued by the International Conference on Harmonization E6 (R2), Dated 9 November 2016, the New Drugs and Clinical Trials Rules 19th March 2019, ICMR 2017 guidelines and the Declaration of Helsinki (64th WMA General Assembly, Fortaleza, Brazil, October 2013)

STUDY OBJECTIVES

Primary Objective:

To determine the **Oral Bioavailability** of **Melatonin** 5 mg in 1 mL **Nano Emulsion** (liquid) Manufactured by Tiny Technologies, (...) with Melatonin 5 mg **Sublingual Tablets** Manufactured by (...) In Healthy, Adult Human Subjects Under Fasting Conditions.

Secondary Objective:

To monitor the **safety and tolerability** of a single dose administered in healthy human adult subjects under fasting conditions.

CLINICAL STUDY REPORT: DETAILS 2/4

Purpose:

The pineal gland hormone melatonin that is involved in the sleep-wake cycle has been extensively applied to alleviate sleep disturbances demanding the need for high bioavailability and easy administration. The aim of this study was to **investigate the pharmacokinetics of a sublingual melatonin nanoemulsion and an orally administered melatonin tablet** in healthy adults.

Furthermore, the bioavailability determined by this study was compared with two other melatonin products of the same melatonin dose from a previously reported clinical study by *Bartoli et al..**

Methods:

In this melatonin bioavailability study the subjects were exposed to two investigational products of 5 mg melatonin, a **sublingual nanoemulsion** and an **oral tablet**. The previously reported comparative study consisted of a **sublingual oral spray** and an oral tablet of the same 5 mg melatonin dose. In both studies blood samples were collected at different time points following administration of the products. The primary pharmacokinetic parameters assessed and compared were:

1) Maximum observed concentration (Cmax),
2) time of maximum concentration (Tmax), and
3) area under the curve (AUC0–t).

** Bartoli, A., 2013. Bioavailability of a New Oral Spray Melatonin Emulsion Compared with a Standard Oral Formulation in Healthy Volunteers. Journal of Bioequivalence & Bioavailability, 04(07).*

CLINICAL STUDY REPORT: DETAILS 3/4

Disposition of subjects

- 12 +01 (Standby A) subjects were enrolled
- 12 subjects were dosed in period-I
- 12 subjects were dosed in period-II
- Totally 12 subjects completed the study as per the protocol and their disposition

Laboratory Investigations :

- Haematology [Hb, RBC, WBC (TC and DC)
- platelet count
- ESR
- Blood Grouping/Rh typing]
- Biochemistry [Glucose (Random)
- Urea, Creatinine
- Total Cholesterol
- SGOT
- SGPT
- ALP
- Bilirubin (Total and direct)
- Protein (Total, albumin and globulin)]
- Urine Routine Analysis [Colour, Appearance, pH, Specific Gravity, Protein]
- Glucose
- Urobilinogen
- Bilirubin, Ketone and blood]
- Serology [HIV, HbsAg, HCV and RPR/VDRL]

Study Flow Chart

Screening Period (Day 0 - Day 21)

- Inclusion/ exclusion criteria and informed consent, demography, medical history and concomitant medication, physical examination and vital signs
- Laboratory investigation (haematology, biochemistry, serology, clinical pathology)
- 12-lead ECG, chest x-ray

Study Period-I (Day 1 - Day 4)

- Eligibility check
- Urine alcohol test & urine screen for drug abuse
- Subject check-in
- Vital signs, physical examination, randomisation, IP dispensing
- IP dosing
- Meal distribution
- Blood samples collection for pharmacological parameter analysis
- Safety assessment of adverse events
- Subject check-out
- wash out on day 5

Study Period-II (Day 8 - Day 11)

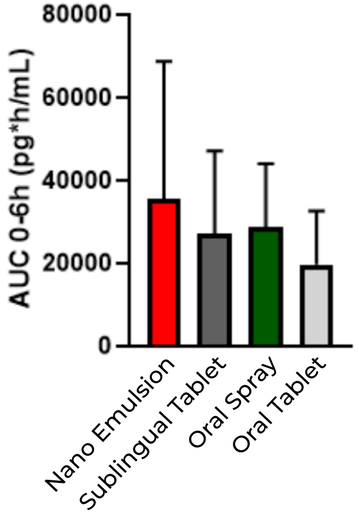
- Urine alcohol test & urine screen for drug abuse
- Subject check-in
- Vital signs, physical examination, randomisation, IP dispensing
- IP dosing
- Meal distribution
- Blood samples collection for pharmacological parameter analysis
- Post study safety sample collection
- Safety assessment of adverse events
- Subject check-out

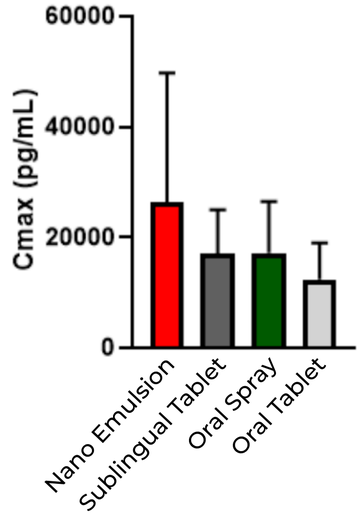
CLINICAL STUDY REPORT: DETAILS 4/4

Results and Conclusion

Primary Objective

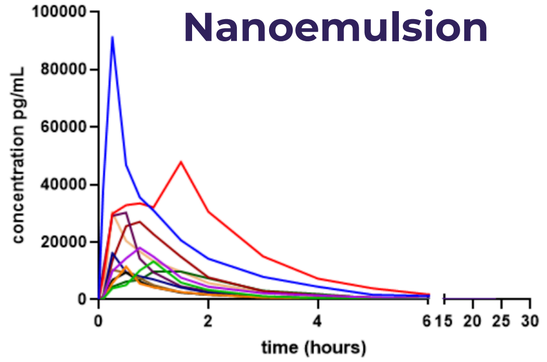
The study revealed considerable differences in the mean maximum concentration (Cmax), the time of the maximum concentration (Tmax), and the area under the curve (AUC0–24h) between the nanoemulsion and the reference products. The clearest results were obtained for the time of the maximum melatonin blood concentration (Tmax). Taken together, the **nanoemulsion resulted in higher blood melatonin levels in a shorter time** compared to the reference products, arguing for a better bioavailability.

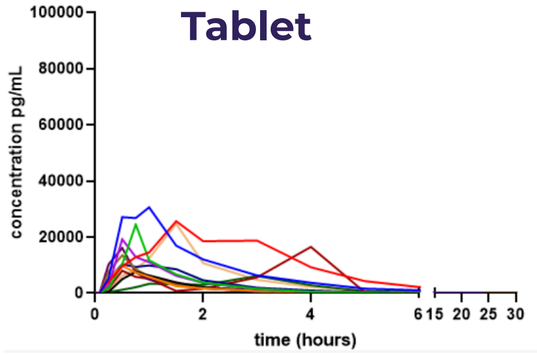




Secondary Objective

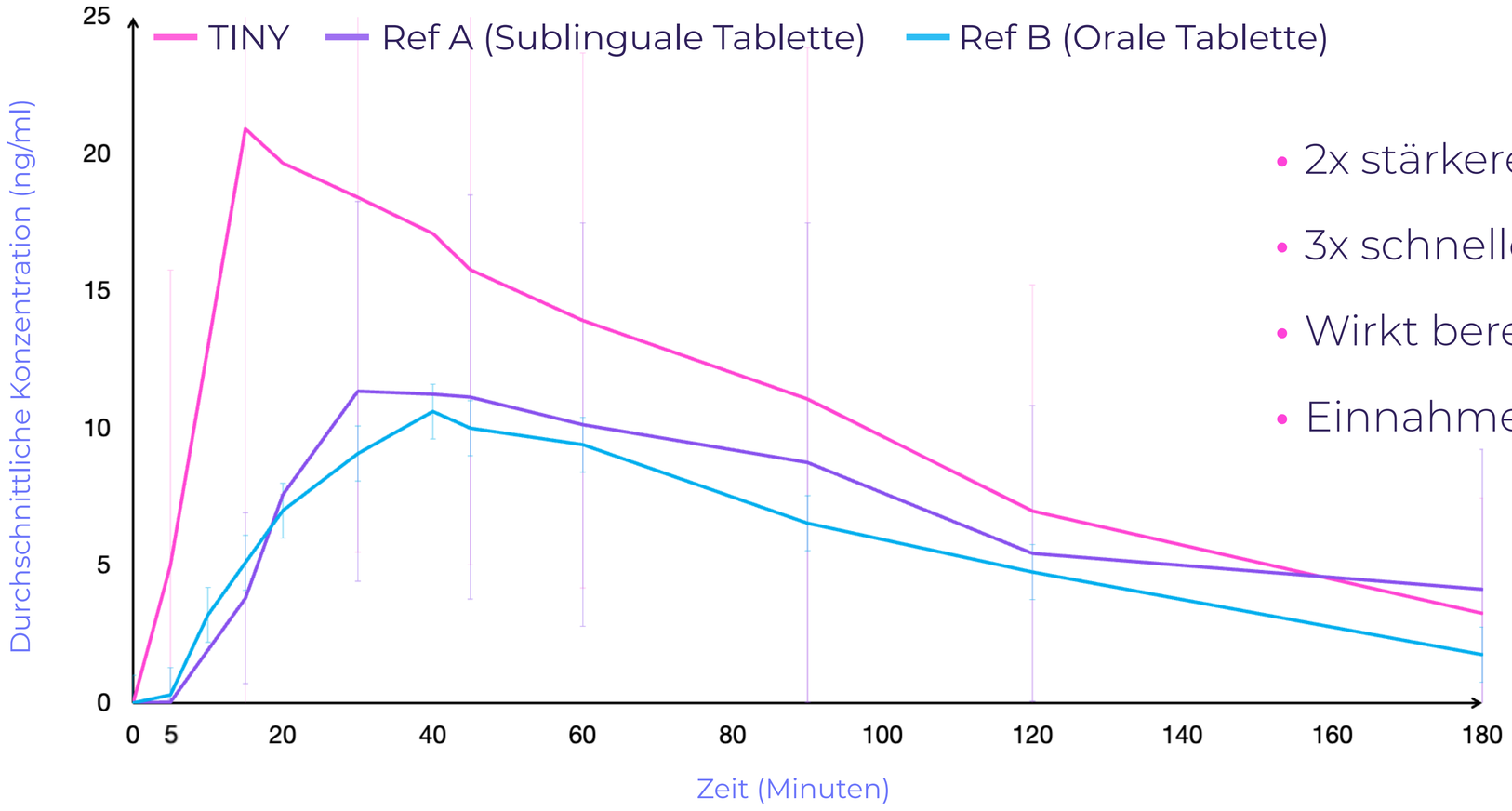
TINYs Melatonin Nano Emulsion performed **absolutely safe and tolerable** in all of the 12 subjects.





WISSENSCHAFTLICHE ÜBERLEGENHEIT

IN VIVO STUDIE MIT MELATONIN



- 2x stärkere Wirkung
- 3x schneller als Standard Melatonin
- Wirkt bereits in unter 5 Minuten
- Einnahme unmittelbar zum Einschlafen