Protocol Title:

An open label, pilot study to evaluate the effects of a novel sublingual NAD+ wafer (SL-NAD+) in healthy individuals.

Aim:

Primary objective: To determine the effect of SL-NAD+ wafers on the NAD+ (nicotinamide adenine dinucleotide) levels in whole blood.

Secondary objectives: (i) To evaluate the effects of SL-NAD+ wafers on energy levels, mood, sleep, mental clarity and physical strength, (ii) To assess the safety and tolerability of SL-NAD+ wafers administered via sublingual route.

Method:

This is an open-label, pilot study in 9 healthy individuals (5 female, 4 male) with 7 included in the whole blood NAD+ analysis. Each participant self-administered SL-NAD+ wafers over a six week treatment period, 200mg NAD+ per day for the first 2 weeks (2 wafers a day), then 100mg NAD+ for the remaining 4 weeks period (1 wafer per day). Venous blood samples were collected at week 0 (baseline), week 2 and week 6 to determine whole blood NAD+ levels in plasma and within red blood cells by colorimetric assay.

Questionnaires captured data on lifestyle factors, modalities of special interest (energy levels, mood, sleep, mental clarity and physical strength) and adverse events at baseline, week 2, and week 6.

(SL-NAD+ uses a patented wafer matrix technology as the NAD+ carrier. The wafers were prepared by freeze-drying an aqueous dispersion of NAD+ in a patented matrix formulation, producing a highly porous, amorphous, non-ionic and non-crystalline solid dosage form. When placed under the tongue, the wafers disintegrate rapidly in contact with saliva, fully releasing NAD+ from the matrix to the sublingual mucosal membrane, enabling direct and increased sublingual uptake.)

Results and Discussions:

Figures 1 & 2 show the increase/ improvement in whole blood NAD+ concentration after taking sublingual NAD+ (SL-NAD+) for 6 weeks.

Figure 1 shows the average increase in whole blood NAD+ level after 6 weeks of sublingual administration. Figure 2 shows the blood NAD+ level for the seven individuals included in the whole blood NAD+ analysis

The graphs illustrate a significant elevation in whole blood NAD+ levels following sublingual administration of NAD+, with an average rise of 59% in the first two weeks and an increase of 76% over six weeks.

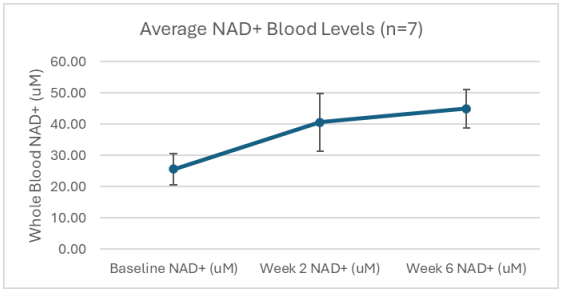

Figure 1: Average NAD+ Blood Levels (n=7)

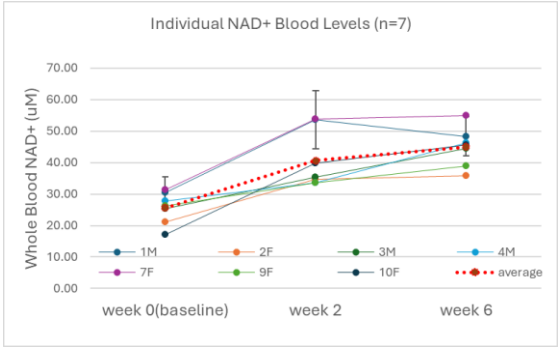

Figure 2: Individual NAD+ Blood Levels (n=7)

Figure 3 is the bar-graph version of both Figures 1 & 2. The horizontal lines reveal the average increase in whole blood NAD+ levels to 40.70 uM (after 2 weeks sublingual administration) and 45.00 uM (after 6 weeks sublingual administration) from a baseline whole blood NAD+ level of 25.60 uM.

The study confirms that NAD+ is absorbed sublingually into the bloodstream and subsequently intracellularly into the red blood cells.

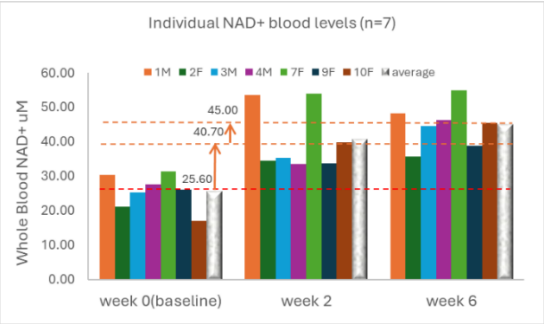

Figure 3: Individual NAD+ Blood Levels (n=7)

Figure 4 shows the differences between whole blood NAD+ levels between individuals who were younger than 50 years old (n=4) and those who were older than 50 years old (n=3). Despite a lower baseline NAD+ in the older age group, both groups reached a NAD+ whole blood level of approximately 45 uM after 6 weeks of daily supplementation.

In a published study, the plasma NAD+ level decreased from approximately 50 nM in young individuals (20–40 years) to approximately 10 nM in elderly subjects (60–87 years)[1].

The decline in NAD+ levels with age is associated with several factors[2] including metabolic changes, lifestyle factors (sedentary lifestyles, high fat/sugar diets, excessive alcohol intake, and immune challenges) and changes in cellular energy metabolism with dysregulation of cellular energy metabolism underpinning chronic age-related diseases, including dementia, cardiovascular disease, and cancer.

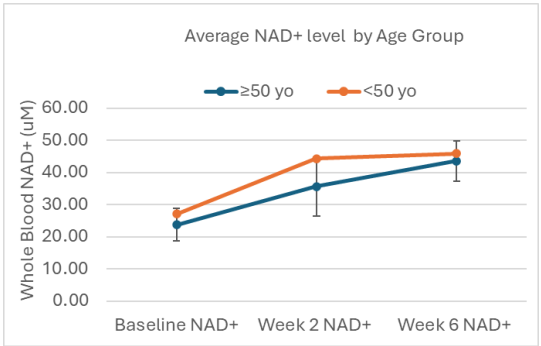

Figure 4: Average NAD+ level by Age Group

Figure 5 shows the differences between male and female whole blood NAD+ levels. The female participants (n=4) have lower baseline NAD+ whole blood level compared to the male participants (n=3). After 2 weeks and 6 weeks of sublingual administration of NAD+, both females and males had improved NAD+ whole blood concentrations to a similar average level.

There is a difference in NAD+ blood levels between men and women as shown in some studies. One study found that the whole blood NAD+ contents in men were significantly higher than that in women (34.5 vs. 31.3 μmol/L)[1]. This finding suggests that sex can influence NAD+ levels.

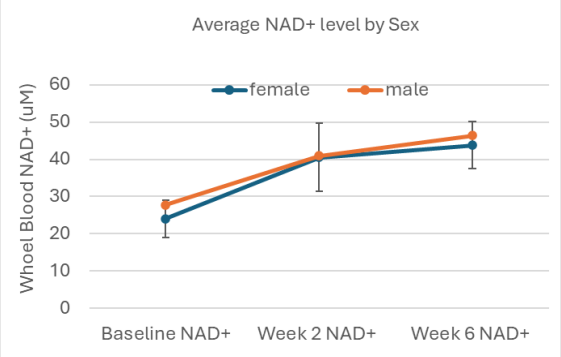

Figure 5: Average NAD+ level by Sex

Self-reported Questionnaire:

All 9 participants reported improvement in at least one modality of interest. Improvements were reported in the following modalities at week 2 and maintained throughout the study to week 6: Energy levels (6 out of 9 participants), mood (5 out of 9 participants), sleep quality (4 out of 9 participants), mental clarity (4 out of 9 participant) and physical strength (3 out of 9 participants).

Safety and Tolerability:

SL-NAD+ wafers were safe and well tolerated by all participants. Only one adverse event (mild headache) was reported by one participant during the 6 week period and was considered only possibly related to wafer administration. It resolved without intervention.

Conclusion:

This study demonstrated that sublingual administration of SL-NAD+ wafers significantly increased whole blood NAD+ levels (combined plasma and intracellular red blood cell levels) in healthy individuals, with an average increase of 59% after 2 weeks and 76% after 6 weeks. The study aligned with published data showing that NAD+ levels decrease with age, highlighting the potential of SL-NAD+ wafers to counteract this decline. This study also observed lower baseline NAD+ whole blood levels in female volunteers compared to males, suggesting that sex can influence NAD+ levels.

The SL-NAD+ wafers were found to be safe and well-tolerated by the participants over the 6-week treatment period.

The findings of this study highlight the high bioavailability of SL-NAD+ wafers through sublingual administration and support the potential benefits of NAD+ supplementation.

References:

1. Fan Yang et al. Association of Human Whole Blood NAD+ Contents With Aging. Frontiers in Endocrinology. March 2022 | Volume 13.

2. Hassina Massudi et al. Age-Associated Changes In Oxidative Stress and NAD metabolism In Human Tissue. PLoS ONE 7(7): e42357. https://doi.org/10.1371/journal.pone.0042357.