6. Summary:

Examination of NADH pharmacokinetic in vivo and in vitro

NADH is one of the most important coenzymes of the intermediary metabolism. During the processes ranging from digestion to the eventual synthesis of ATP, it is in charge of capturing free electrons and transporting them to the site of reaction. The critical role of NADH as the primary source of reducing equivalents is most prominent in the Krebs cycle and in oxidative phosphorylation.

In light of the central role of NADH within energy metabolism, in recent decades many research approaches have emerged examining its influence on pathogenic and symptomatic parameters (Mitochondrial diseases: Alzheimer's disease, Parkinson's disease) as well as its use as a diagnostic tool (tumor diagnosis).

The present study aims at analyzing certain aspects of NADH pharmacokinetic. First, we investigated whether NADH is indeed absorbed by the intestine. In a second step we focused on the question whether sublingually administered NADH is able to influence NADH concentration within the cerebral cortex of the rat.
In addition, changes in cortical NADH fluorescence were examined prior to administration of the oxidized analogue NAD^+.

The preliminary experiment was undertaken *in vitro* using the everted gut sack model.
The absorption rate of NADH was compared to Diazepam, a substance that is absorbed well through the intestinal wall, and Strophantine, known to be poorly absorbed by the intestine. The data obtained for NADH was in all cases below the Strophantine absorption rate. Statistical analysis of the absorption rates of the three NADH doses (NADH 10, 50 and 100mg/kg) studied revealed no significant differences.

$NADH/NAD^+$ redox-system is endowed with properties ideally suited for spectroscopic detection, such as laser-induced fluorescence spectroscopy. Only the reduced form NADH reacts to radiation (λ = 340nm) with the emission of a characteristic fluorescence spectrum (maximum at λ = 464nm). The signal emitted is proportional to intracellular NADH concentration.

Employing a laser-induced fluorescence spectroscopic detection technique, we studied the central bioavailability of NADH in the cortex of anaesthetized rats following sublingual administration of three different NADH dosages (10mg/kg, 50mg/kg and 100mg/kg).

The data collected revealed that central bioavailabiliy of NADH was only considerably influenced by a dose of NADH 100mg/kg, showing a significant increase in cortical NADH fluorescent signal.

The fact that the administration of NAD^+, a non-fluorescent compound, also induces a rise in cortical NADH fluorescence, is consistent with the notion that there is an equilibrium between the low-energy form NAD^+ and the high-energy form NADH.

On the basis of the data obtained, we conclude that absorption and central bioavailability of NADH in rat is possible when applied sublingually at a dose of 100mg/kg or above.