**There are indeed clinical studies that call into question the superiority of NAD+ precursors over oral NAD+ supplementation, especially when combined with PQQ. However, the research in this area is still evolving, and the results are not entirely conclusive.**

## Recent studies have highlighted several important points:

1. **Conversion of precursors:** A substantial portion of orally administered NAD+ precursors like nicotinamide riboside (NR) and nicotinamide (NAM) is metabolized to nicotinic acid (NA) by the gut microbiome before being utilized for NAD+ synthesis in the liver[1].

2. **Biphasic absorption:** Oral administration of NR and NAM increases NAD+ levels in a biphasic manner. There's an early phase of direct uptake by the small intestine, followed by a later phase where conversion to NA by gut microbiota drives sustained NAD+ synthesis[1].

3. **Variable bioavailability:** The oral bioavailability of NAD+ precursors like NR is highly variable among individuals, potentially due to factors such as instability in blood samples, hydrophilicity, and variations in intestinal transport mechanisms[4].

4. **Tissue-specific effects:** Different NAD+ precursors show varying effectiveness in elevating NAD+ levels in different tissues. For example, NR was found to be superior in increasing liver NAD+ content compared to NAM and NA, but NR and NA were more effective in increasing muscle NAD+ content compared to NMN[4].

While these studies don't directly compare oral NAD+ with precursors, they suggest that the absorption and conversion of NAD+ precursors is complex and variable. The effectiveness of oral NAD+ supplementation, especially when combined with PQQ, has not been extensively studied in direct comparison to precursors.

## PQQ's potential role in enhancing NAD+ absorption and utilization is noteworthy:

1. PQQ promotes the oxidation of NADH to NAD+, potentially increasing cellular NAD+ levels[5].

2. It enhances mitochondrial function and biogenesis, which may indirectly support NAD+ production and utilization[5].

3. PQQ activates sirtuins, NAD+-dependent enzymes involved in various cellular processes[5].

However, clinical studies directly comparing the effectiveness of oral NAD+ with PQQ to NAD+ precursors are limited. More research is needed to definitively answer whether this combination is superior to precursor supplementation in terms of absorption and conversion to NAD+.

In conclusion, while there is evidence questioning the universal superiority of NAD+ precursors, there is also a lack of comprehensive clinical studies directly comparing oral NAD+ with PQQ to precursor supplementation. The complexity of NAD+ metabolism and the potential synergistic effects of PQQ warrant further investigation to draw definitive conclusions.

Citations:
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