study on 1mg per day rapamycin use in humans

Human studies using 1 mg per day of rapamycin have been conducted, mainly in older adults, with the majority showing that this low dose is generally well-tolerated but produces only mild metabolic changes and variable effects on aging biomarkers.[1] [2] [3] [4]

Study Findings Overview

- Several recent clinical trials have administered 1 mg/day rapamycin for periods ranging from 8 to 18 weeks to older adults and patients with mild cognitive impairment or neurodegenerative diseases.[2] [5] [4] [6]
- These studies consistently found that the daily 1 mg rapamycin regimen was safe and did not result in significant immunosuppression or serious adverse effects; most reported side effects were mild, such as increased triglycerides, HbA1c, and very-low-density lipoprotein (VLDL) levels.[5] [4] [2]
- In some studies, there was a mild increase in hemoglobin A1c and systolic blood pressure, along with minor hematological changes, but all remained within normal clinical ranges.[4] [5]
- No significant improvements were found in cognitive function or metabolic parameters in healthy older adults; however, there were signs of enhanced immune function and reduced infections in the elderly.[7] [1] [2]

Safety and Tolerability

- The 1 mg/day dose is considered low and generally avoids the immunosuppressive risks associated with higher doses used in transplant medicine.[3] [8] [2]
- Most adverse effects reported—such as mild diarrhea or urinary urgency—resolved without intervention and did not require discontinuation of therapy in pilot studies.[5] [4]
- The metabolic shifts observed, such as increased triglycerides or mild reductions in some blood count parameters, suggest that while generally tolerable, monitoring is essential for long-term use.[1] [4]

Dosing Considerations

- Rapamycin is sometimes given weekly in larger doses (5–7 mg), with some evidence suggesting intermittent dosing may have fewer side effects.[9] [8] [3]
- Studies have yet to decisively compare the efficacy of daily versus intermittent dosing for longevity or disease prevention in humans.[9]

Research Limitations

- Most clinical studies are pilot-sized (with around 10–40 participants) and short-term (typically ≤ 8 weeks), limiting conclusions about long-term efficacy or risks.[4] [1] [5]
- No strong evidence yet supports daily rapamycin at 1 mg as a broadly effective anti-aging intervention, though safety is encouraging.[7] [1] [4]

Key Study References

- Oxford study: 1 mg/day for 8 weeks reduced senescent immune cells without immunosuppression.[2]
- Alzheimer's and aging studies: 1 mg/day for 8 weeks safe, with mild metabolic effects and stable cognitive functions.[5] [4]
- General longevity: 1 mg/day appears safe in the short term, with negligible side effects in healthy elderly.[3] [9]

In summary, multiple human studies show 1 mg per day rapamycin is safe and well-tolerated for up to several months, producing mild metabolic effects but no substantial anti-aging or disease-modifying benefits in the short term. Long-term data and head-to-head studies of different dosing schedules are still needed.[1] [2] [4]

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what is a accumulation rate and peak accumulation over a 30 day period

Accumulation rate and peak accumulation for rapamycin refer to how the drug builds up in the blood with regular dosing and the highest concentration reached during this period. For oral rapamycin in humans, the half-life is long (ranging from 60–70 hours), so daily dosing leads to steady accumulation over time.[16] [17]

Accumulation Rate

- The accumulation rate is determined by the drug’s half-life and dosing interval.[16]
- With a half-life of roughly 62 hours, daily dosing means rapamycin accumulates and approaches a steady-state concentration after about 4–5 half-lives (roughly 10–14 days).[17] [16]
- After steady state, the plasma (or whole blood) concentration stays relatively consistent with ongoing daily dosing.[16]

Peak Accumulation Over 30 Days

- Peak accumulation is reached around days 14–21 when steady-state is established, considering rapamycin’s half-life.[17] [16]
- For a daily dose of 1 mg, trough concentrations (lowest levels before the next dose) range from approximately 0.5–6.4 ng/mL in clinical studies at different doses.[16]

- The peak blood concentration (Cmax) occurs a few hours after each dose, but cumulative buildup means average concentrations rise until steady state is achieved.[17] [16]

Example Calculation (for typical dosing)

- If starting daily 1 mg dosing, the accumulation causes concentrations to rise each day, peaking and plateauing by around day 14.[16]
- The highest average concentration (steady state) for 1 mg daily in humans is generally below 5 ng/mL whole blood, although individual variation is common.[17] [16]

In summary, daily 1 mg rapamycin dosing results in gradual accumulation, with blood levels peaking and stabilizing at steady state between days 14 and 21. The peak accumulation at steady state for this dose is typically below 5 ng/mL in whole blood.[17] [16]

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