# Resveratrol for Intracranial Aneurysm Rupture Prevention

## Preclinical Studies

- **Mouse models of cerebral aneurysm**:
  - In hypertensive mice with induced aneurysms, resveratrol significantly reduced both the number and size of aneurysms.
  - Histological findings: reduced macrophage infiltration and healthier arterial wall thickness.
  - Proposed mechanism: inhibition of the NF-κB pathway and downregulation of MMP-2 and MMP-9.
- **Subarachnoid hemorrhage (SAH) models**:
  - In rodent SAH models, resveratrol reduced early brain injury, blood–brain barrier disruption, and cerebral edema.

## Human Evidence

- As of now, **no clinical trials** have evaluated resveratrol for preventing intracranial aneurysm rupture in humans.
- Existing human studies on resveratrol focus on other diseases (e.g., cardiovascular, metabolic) with **mixed or limited efficacy**.

## Summary Table

| Evidence Level | Findings |
|---|---|
| Animal studies | ↓ Aneurysm formation, ↓ inflammation, ↓ MMPs, ↓ NF-κB activity |
| SAH rodent models | ↓ Brain edema and injury, improved barrier integrity |
| Human data | No trials in aneurysms; low bioavailability limits systemic benefit |

## ⚠ Clinical Implications

- Resveratrol shows **promise in animal models** but is **not currently supported** as a preventive treatment for aneurysm rupture in humans.
- Oral resveratrol has **low bioavailability** (~0.5%) and is rapidly metabolized.
- Potential side effects at high doses include nausea and diarrhea.

## Conclusion

- Although preclinical data are encouraging, resveratrol **cannot yet be recommended** for intracranial aneurysm prevention.
- Patients should continue to follow established medical advice:

- Control hypertension
- Avoid tobacco
- Monitor known aneurysms regularly
- Discuss aspirin or statin use with a physician

# Recommendations

- Stay informed about emerging research and possible clinical trials.
- Consider resveratrol only as a research compound—not a clinical solution—for aneurysm prevention.

# In vivo animal studies

**Type of study**:: In vivo animal study (murine intracranial aneurysm model) **First author**:: Dang et al. **Author affiliations**::

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**Journal**:: Journal of Neuroscience Research **Purpose**:: To evaluate whether dietary resveratrol prevents formation or rupture of intracranial aneurysms via anti-inflammatory mechanisms. **Conclusions**::

- No significant reduction in aneurysm formation incidence
- Marked reduction in rupture rate (88 % → 40 %, p=0.026)
- Modulation of inflammatory markers: ↑Sirt1, ↓Nfkb1, ↓Tnf

**Citation**:: [1)]

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## Critical Review

**1. Model limitations** The elastase + DOCA-salt murine model poorly reflects human aneurysm pathophysiology, lacking hemodynamic fidelity. No histological validation of aneurysm similarity or wall integrity is presented.

**2. Statistical fragility** Sample size is small (N not disclosed), likely underpowered. The significant reduction in rupture risk may result from chance due to low event counts. No power analysis provided.

**3. Incomplete inflammatory profiling** Only mRNA (not protein) levels of Sirt1, Nfkb1, and Tnf were analyzed. No IHC, ELISA, or time-course experiments to demonstrate functional effects or causality.

**4. Intervention timing** Resveratrol was administered preventively—3 weeks before aneurysm induction. This limits translational relevance as human patients typically present after aneurysm formation.

**5. Lacking pharmacokinetics/pharmacodynamics** No measurement of serum/tissue levels of resveratrol. Effective concentrations in cerebral vasculature remain speculative.

**6. Uncontrolled confounders** No report of blood pressure differences between groups, despite using a DOCA-salt model of induced hypertension.

**7. Limited novelty** Anti-inflammatory vascular effects of resveratrol are well-documented. This work offers incremental rather than groundbreaking insight.

## Final Verdict

**Flawed design and lack of translational rigor** render the study hypothesis-generating at best. The purported protective role of resveratrol lacks mechanistic depth and clinical relevance.

## Takeaway for Neurosurgeons

Resveratrol may reduce rupture risk in an artificial murine model, but this does not justify clinical application. Future research must explore post-formation interventions, robust models, and PK/PD validation.

## Bottom Line

Encouraging data in mice—yet insufficient to warrant human trials.

## Rating

**3/10** – Preliminary and biologically plausible, but weak in methodology and translational relevance.

1)

Dang DNP, Kamio Y, Kawakatsu T, Makino H, Hokamura K, Imai R, Suzuki Y, Hiramatsu H, Zhitong L, Umemura K, Kurozumi K. Protective Effect of Resveratrol Against Intracranial Aneurysm Rupture in Mice. *J Neurosci Res*. 2025 Jun;103(6):e70059. doi:10.1002/jnr.70059. PMID: 40546125.