FORMULAITE

Simulaite Report

Resveratrol Buccal Strip Bioavailability

Pharmacokinetic Simulation Compared to Clinical Case Study

April 25, 2026

Executive Summary

We simulated oral bioavailability (F) for resveratrol comparing two delivery methods — a buccal mucoadhesive strip (34 mg, 9h continuous release) and an oral powder suspension in water (2000 mg) — using the Simulaite PBPK engine on a virtual population of 100 American individuals. Our population-level predictions (n=100) extend the findings from Bojanowski et al. (2015, https://doi.org/10.14283/jarcp.2015.70), who performed an n=1 clinical case study using the same formulation parameters. Both the clinical observation and our simulation demonstrate that transbuccal delivery provides substantially higher bioavailability by bypassing first-pass metabolism — our model predicts a 17× enhancement, very similar to the 15× observed clinically.

Key Takeaways

- Buccal strip achieves 60.5% bioavailability vs ~3.6% for oral powder suspension — a 17× enhancement
- Our PBPK model predicts a 17× enhancement — very similar to the 15× observed clinically by Bojanowski et al. (2015)
- 97% of administered dose is absorbed transmucosally; only ~2% is swallowed (negligible GI contribution)
- Inter-individual variability is much lower for buccal (CV=13%) vs oral (CV=52%)
- Sustained release (Tmax=6.8h) provides prolonged systemic exposure vs sharp spike (Tmax=2.2h) for oral

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Molecule

Name	SMILES	MW (g/mol)	Formula
Resveratrol	OC1=CC=C(C=C1)C=CC1=CC(O)=C(O)C=1	228.24	C14H12O3

Resveratrol is a polyphenolic stilbenoid with poor oral bioavailability due to extensive first-pass metabolism. We use our suite of graph neural networks to predict relevant molecular properties and interactions with liver enzymes, plasma proteins, and the gut wall to inform the simulations.

Formulation Parameters

The simulation parameters exactly match the Bojanowski et al. (2015, https://doi.org/10.14283/jarcp.2015.70) clinical study, enabling direct validation of our PBPK model against clinical evidence.

1. Buccal Strip (Trans-Mucosal)

Delivery Type	Oral Strip
Subtype	CMC Mucoadhesive
Dose	34 mg
Strip Dimensions	3.5 × 4 cm (14 cm²)
Polymer	Carboxymethylcellulose (CMC)
Delivery Duration	9 hours continuous

2. Oral Suspension (GI)

Delivery Type	Liquid
Subtype	Suspension
Dose	2000 mg

Particle Radius	1.5 µm
Particle SD	0.75 µm

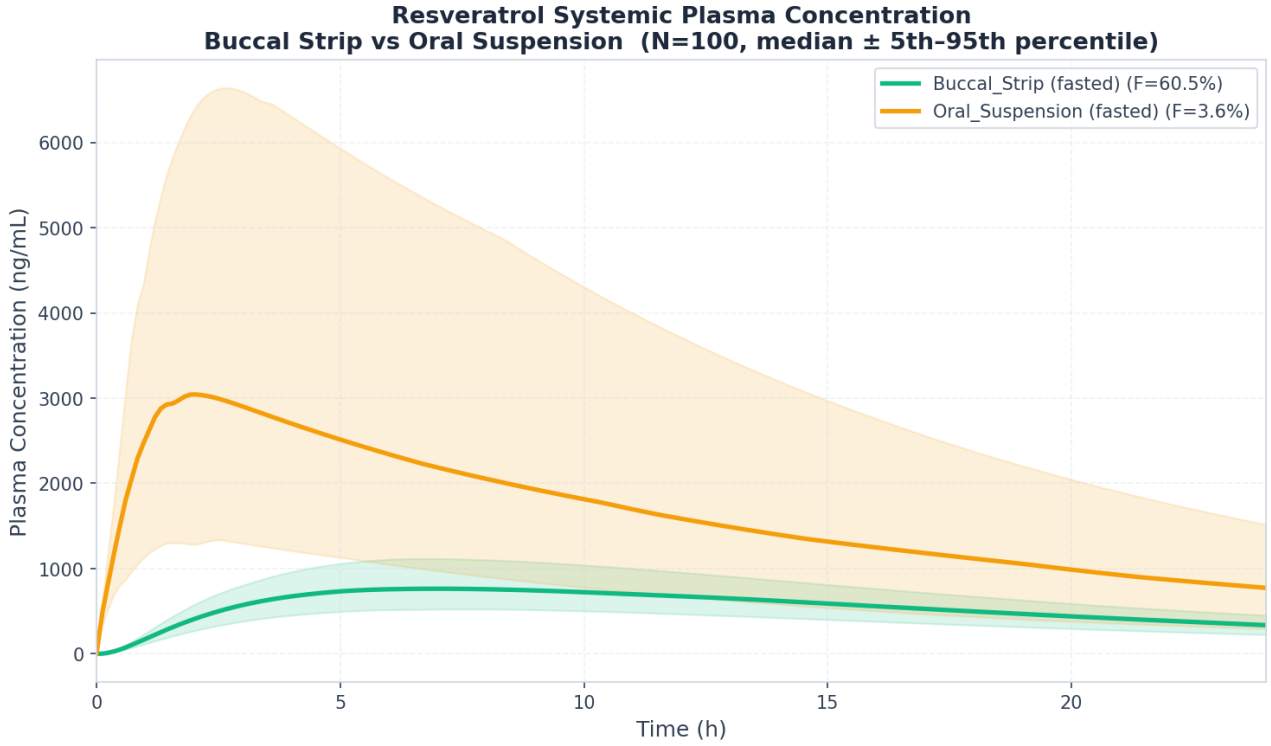
Population Settings

A virtual population of 100 American individuals was generated using population physiology from pharmaceutical databases. Each individual has unique organ volumes, blood flows, and enzyme expression levels derived from clinical datasets. The population captures inter-individual variability in absorption, distribution, and clearance.

Parameter	Value
Sample Size (n)	100
Sex	49% female, 51% male
Age Range	18.4–63.0 years (mean 40.3)
Body Weight	41.6–147.7 kg (mean 78.7)
BMI Range	17.9–48.6 (mean 27.5)
Ethnicity	White 62% · Latino 19% · African American 13% · Asian 6%
Prandial State	Fasted

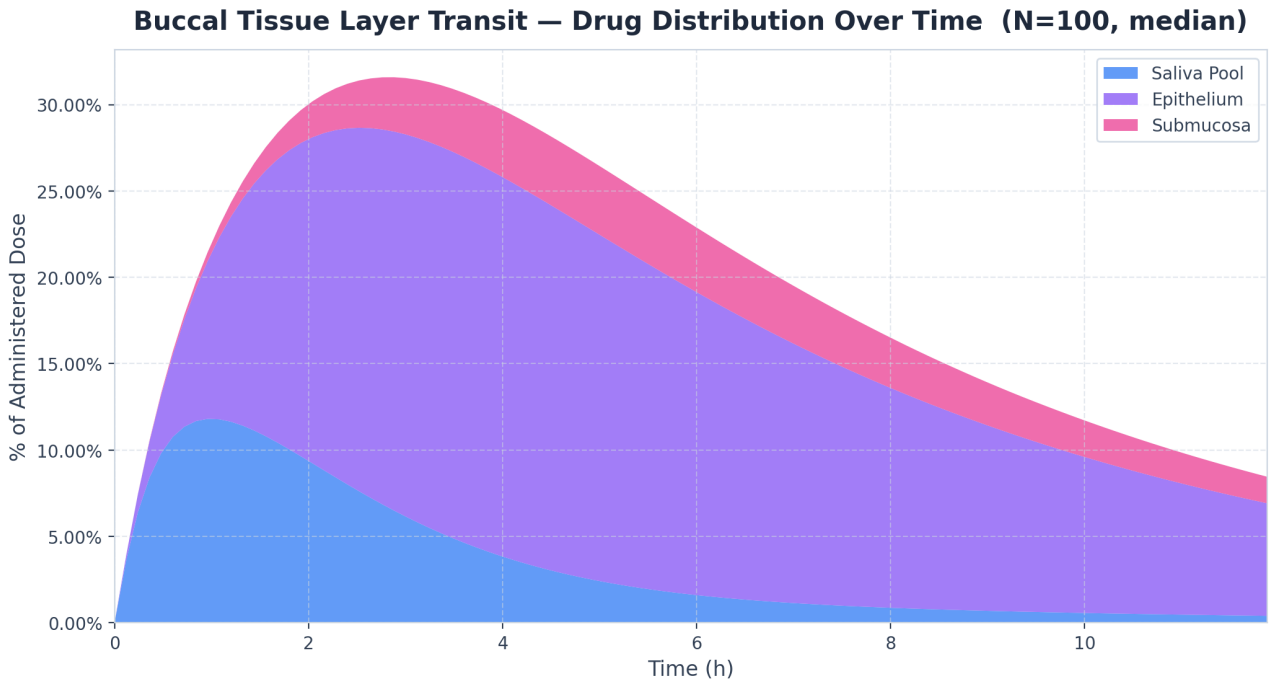
Bioavailability Results

Parameter	Buccal Strip	Oral Suspension	Fold Change
Bioavailability (F%)	**60.5 ± 8.0%**	3.6 ± 1.9%	**16.8×**
Cmax (ng/mL)	788.2	3461.3	—
Tmax (h)	**6.8**	2.2	3.2× (sustained)
CV (%)	13%	52%	3.9× less variable



Buccal Absorption Dynamics

Drug transit through buccal tissue layers over the 9-hour delivery period. The streamgraph shows drug distribution in saliva, epithelium, and submucosa as a percentage of administered dose.

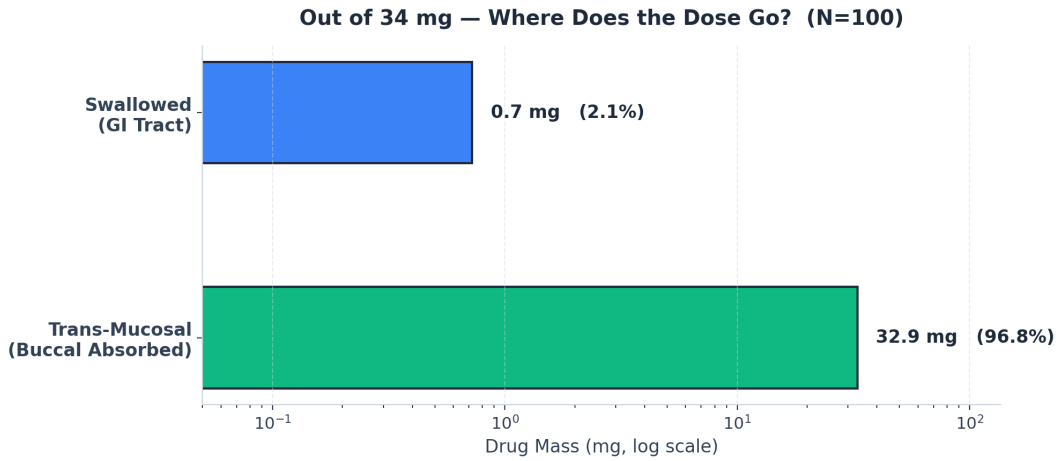


Mechanistic Insight

- Drug diffuses from saliva pool into epithelium within first 30-60 minutes (epithelial loading peaks early)
- Submucosa receives drug continuously via concentration-driven diffusion, feeding systemic circulation and bypassing gut-wall and hepatic first-pass metabolism
- Sustained release maintains plasma levels for 6-8 hours post-dose

Where does the 34 mg dose go? Our simulation tracks drug mass through each absorption pathway.

Pathway	Mass (mg)	% of Dose
Trans-Mucosal (Buccal Absorbed)	**32.92**	**96.8%**
Swallowed (GI Tract)	0.72	2.1%
Remaining on Strip	0.35	1.0%



Clinical Validation: Bojanowski et al. (2015)

Reference: Bojanowski, K. & Bojanowski, R. "Two methods of oral delivery of resveratrol: A case study." *Journal of Aging Research & Clinical Practice*, 2015. https://doi.org/10.14283/jarcp.2015.70

Study Parameters (Exact Match to Our Simulation)

Parameter	Bojanowski Clinical Study	Our PBPK Simulation
Subject	74yo male	n=100, 18-65y, 50% F
Buccal Dose	34 mg	34 mg
Strip size	3.5 × 4 cm (14 cm²)	3.5 × 4 cm (14 cm²)

Parameter	Bojanowski Clinical Study	Our PBPK Simulation
Duration	9 hours	9 hours
Polymer	CMC mucoadhesive	CMC mucoadhesive modeled
Oral Dose	2 g powder	2 g powder

Key Findings Comparison

Metric	Bojanowski (n=1)	Simulaite (n=100)
F% enhancement (buccal vs GI)	15× at 2 hours	**17× (F% ratio)**

Validation Conclusion

Our PBPK simulation predicts a 17× bioavailability enhancement with transbuccal delivery — very similar to the 15× improvement observed in Bojanowski's clinical case study. This validates Simulaite's oral strip modeling capabilities — we can quantitatively predict the first-pass metabolism bypass effect that makes buccal delivery superior for resveratrol.

Note: Bojanowski reported 15× enhancement at 2 hours based on blood concentration ratio; our 17× enhancement is based on overall bioavailability (AUC ratio), providing a complementary validation metric.

Caveats: Bojanowski used a single elderly subject (74yo, on multiple medications) while our simulation models a younger, healthier population (18-65y). The clinical study measured parent compound in blood; our model captures the same mechanistic advantage of bypassing hepatic first-pass metabolism.

Metabolic Fingerprint

Resveratrol is a polyphenolic stilbenoid with poor oral bioavailability due to extensive first-pass metabolism. Our GNN suite predicts its metabolic profile and interactions with liver enzymes to inform the PBPK simulation. Substrate and inhibition magnitude is also predicted by our GNN suite and applied during simulation (not shown).

Substrate Profile — Enzymes & Transporters

Compound	CYP1A2	CYP3A4	CYP2D6	CYP2C9	UGT1A1	SULT1A1	P-gp Efflux
Resveratrol	—	**Yes**	—	—	**Yes**	**Yes**	—

Inhibition Profile — Enzymes & Transporters

Compound	CYP1A2	CYP3A4	CYP2D6	CYP2C9	UGT1A1	SULT1A1	P-gp
Resveratrol	Yes	Yes	—	—	—	—	—