FORMULAITE

Simulaite Report

Bioavailability Simulation — Kalmegh (Andrographis paniculata) Extract Capsule

March 11, 2026

Executive Summary

We simulated oral bioavailability (F) for diterpene lactone compounds in a standardized Kalmegh (Andrographis paniculata) extract capsule using our Simulaite engine with AI-powered pharmacokinetic modeling on a virtual population of 100 individuals (Asian demographics). Four scenarios were compared: fed state with full extract, fasted state with full extract, fed state with full extract plus piperine bioenhancer, and fed state with andrographolide alone (to quantify the extract's synergistic bioenhancement effect).

Key Takeaways

- Synergistic extract bioenhancement is the dominant mechanism: andrographolide alone achieves only 10.0% F, but within the full extract reaches 29.2% F — a 2.9× boost from co-extracted flavonoids inhibiting CYP3A4 and reducing P-gp efflux
- Piperine provides only a modest additional lift of 1.05× on top of the extract's own bioenhancement (29.2% to 30.6%)
- Food effect is minimal for andrographolide (1.03×) but significant for 14-Deoxy-DHA (1.3×), attributed to bile salt solubilization of the less water-soluble dehydro compound
- Population variability ranges from CV 36–49% for the diterpene lactones in the full extract, but rises to CV 53% when andrographolide is administered alone — the synergistic enhancement stabilizes inter-individual variability

Molecules

Name	SMILES
Andrographolide	C[C@@]12CC[C@H]([C@@]([C@H]1CCC(=C)[C@H]2C/C=C/3\[C@@H](COC3=O)O)(C)CO)O
Neoandrographolide	C[C@]1(CCC[C@@]2([C@@H]1CCC(=C)[C@H]2CCC3=CCOC3=O)C)CO[C@H]4[C@@H]([C@H]([C@@H]([C@H](O4)CO)O)O)O
14-Deoxy-11,12-didehydroandrographolide	C[C@@]12CC[C@H]([C@@]([C@H]1CCC(=C)[C@H]2/C=C/C3=CCOC3=O)(C)CO)O
14-Deoxyandrographolide	C[C@@]12CC[C@H]([C@@]([C@H]1CCC(=C)[C@H]2CCC3=CCOC3=O)(C)CO)O
7-O-Methylwogonin	COC1=C(C2=C(C(=C1)O)C(=O)C=C(O2)C3=CC=CC=C3)OC

Name	SMILES
Skullcapflavone I	COC1=C(C2=C(C(=C1)O)C(=O)C=C(O2)C3=CC=CC=C3O)OC
Piperine	C1CCN(CC1)C(=O)/C=C/C=C/C2=CC3=C(C=C2)OCO3

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.

Extracts

Kalmegh Extract (Standardized Andrographis paniculata)

Composition represents a generic representative A. paniculata stem/leaf extract based on published phytochemical profiles, not HPLC analysis of a specific commercial product.

Molecule	Percentage (%)	Role
Andrographolide	10%	*primary diterpene lactone*
Neoandrographolide	4.5%	–
14-Deoxy-11,12-didehydroandrographolide	2.5%	–
14-Deoxyandrographolide	3.5%	–
7-O-Methylwogonin	0.6%	*flavonoid*
Skullcapflavone I	0.6%	*flavonoid*

Black Pepper Extract

Molecule	Percentage (%)	Role
Piperine	95%	–

Recipes

Kalmegh Extract Capsule (no Piperine)

Ingredient	Type	Dose (mg)
Kalmegh Extract	extract	250 mg

Kalmegh Extract + Piperine Capsule

Ingredient	Type	Dose (mg)
Kalmegh Extract	extract	250 mg
Black Pepper Extract	extract	5.26 mg

Andrographolide Capsule (isolated compound)

Ingredient	Type	Dose (mg)
Andrographolide	pure compound	25 mg

Formulations

1. Kalmegh Extract Capsule (no Piperine)

Recipe	Kalmegh Extract Capsule (no Piperine)
Delivery Type	Capsule
Subtype	Powder
Extract Particle Radius Mean	50 µm
Capsule Shell Lag Time	10 min

2. Kalmegh Extract + Piperine Capsule

Recipe	Kalmegh Extract + Piperine Capsule
Delivery Type	Capsule
Subtype	Powder
Extract Particle Radius Mean	50 µm
Piperine Particle Radius Mean	40 µm
Capsule Shell Lag Time	10 min

3. Andrographolide Capsule (isolated compound)

Recipe	Andrographolide Capsule (isolated compound)
Delivery Type	Capsule
Subtype	Powder

Particle Radius Mean	50 µm
Capsule Shell Lag Time	10 min

Population Settings

Population	Asian
Sample Size (n)	100
Age Range	18–60
Female %	50%
Weight Range	38.8–87.3 kg
BMI Range	16.4–38.3 (mean 21.9)

Per-Compound Bioavailability (F%)

Bioavailability targets: the 3 primary diterpene lactones. All 6 kalmegh compounds + piperine (when present) are included in the formulation throughout all organs simulated for synergistic interaction modeling.

Scenario	Andrographolide	Neoandrographolide	14-Deoxy-DHA
Asian Population — Fed — Full Extract	**29.22 ± 10.62%**	**16.59 ± 7.43%**	**9.57 ± 4.69%**
Asian Population — Fasted — Full Extract	**28.29 ± 10.37%**	**16.10 ± 7.22%**	**7.41 ± 3.66%**
Asian Population — Fed — Extract + Piperine	**30.57 ± 10.84%**	**18.35 ± 7.98%**	**9.82 ± 4.79%**
Asian Population — Fed — Andrographolide Only	**10.04 ± 5.30%**	—	—

Key Comparisons

Synergistic Extract Enhancement (Andrographolide Alone vs Full Extract, Fed)

Condition	Andro F%	± SD	vs Alone
Andrographolide alone (25 mg)	**10.04%**	5.30%	**Baseline**
In Full Extract (no piperine)	**29.22%**	10.62%	**2.9×**
In Full Extract + Piperine	**30.57%**	10.84%	**3.0×**

Mechanism: The flavonoids 7-O-Methylwogonin and Skullcapflavone I in the extract inhibit CYP3A4 and CYP1A2, and reduce P-glycoprotein efflux, dramatically increasing andrographolide's oral bioavailability. This explains why whole-herb Kalmegh extracts are traditionally more effective than isolated andrographolide.

Piperine Enhancement (Fed State, Full Extract)

Compound	No Piperine	+ Piperine	Enhancement
Andrographolide	29.22%	**30.57%**	**1.05×**
Neoandrographolide	16.59%	**18.35%**	**1.11×**
14-Deoxy-DHA	9.57%	**9.82%**	**1.03×**

Piperine (5 mg) provides additional CYP3A4 inhibition and P-gp efflux reduction beyond what the extract already achieves. The marginal gain is modest because the extract's own flavonoids already provide substantial enzyme inhibition.

Fed vs Fasted (Full Extract, No Piperine)

Compound	Fed	Fasted	Food Effect
Andrographolide	**29.22%**	28.29%	1.03×
Neoandrographolide	**16.59%**	16.10%	1.03×
14-Deoxy-DHA	**9.57%**	7.41%	**1.29×**

Population Variability (Asian Population, n=100, Fed, Full Extract)

Compound	F% Mean	± SD	CV%	n
Andrographolide	**29.22%**	10.62%	36%	100
Neoandrographolide	**16.59%**	7.43%	45%	100
14-Deoxy-DHA	**9.57%**	4.69%	49%	100
Andro. (alone, no extract)	**10.04%**	5.30%	53%	100

Note: Andrographolide alone (no extract) shows higher inter-individual variability (CV 53%) than in the full extract (CV 36%), suggesting that the synergistic enhancement from co-extracted flavonoids not only boosts mean bioavailability but also reduces population variability — a desirable quality for consistent clinical response.