FORMULAITE

Simulaite Report

Curcuminoid Formulation Comparison

Crystalline Powder vs Hydrophilic Carrier ASD vs Phytosome — Relative Bioavailability

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Executive Summary

We simulated oral bioavailability for three curcuminoid formulations — Crystalline Powder (1800 mg), Hydrophilic Carrier ASD (376 mg), and Phytosome (376 mg) — using the Simulaite PBPK engine on a virtual population of 12 individuals matched to the clinical study by Jäger et al. 2014 in formulation composition, dose, demographics, and prandial state. Predicted relative bioavailability is benchmarked against the published clinical data.

Key Simulation Results

- Hydrophilic Carrier ASD: 48.3× more bioavailable than Crystalline Powder (dose-normalized blend AUC) — clinical: 45.9×
- Phytosome: 5.5× more bioavailable than Crystalline Powder — clinical: 7.9×
- ASD vs Phytosome: 8.7× advantage for ASD at equal dose — clinical: 5.8×

Molecules

Curcuminoids are polyphenolic pigments extracted from turmeric (Curcuma longa). Three principal compounds are present in the 77:17:6 ratio. All molecular properties are predicted from SMILES by our GNN suite — no experimental measurements are required.

Compound	MW (g/mol)	Blend Ratio	SMILES
Curcumin	368.4	77%	COC1=C(C=CC(=C1)/C=C/C(=O)CC(=O)/C=C/C2=CC(=C(C=C2)O)OC)O
Demethoxycurcumin (DMC)	338.4	17%	COC1=C(C=CC(=C1)/C=C/C(=O)CC(=O)/C=C/C2=CC=C(C=C2)O)O
Bisdemethoxycurcumin (BDMC)	308.3	6%	C1=CC(=CC=C1/C=C/C(=O)CC(=O)/C=C/C2=CC=C(C=C2)O)O

All three curcuminoids display very low oral bioavailability from crystalline powder. Formulation technology is the primary lever for improving systemic exposure. 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.

Simulation Study Design

Parameter	Value
Prandial state	Fasted
Simulation window	12 hours
Curcuminoid ratio	77:17:6 (Curcumin:DMC:BDMC, C3 standard)
Validation reference	Jäger R et al. "Comparative absorption of curcumin formulations." *Nutr J* 2014, 13:11. PMID: 24461029. doi:10.1186/1475-2891-13-11
Branded ingredients†	*C3 Complex® (Sabinsa), CurcuWIN® (OmniActive), Meriva® (Indena)*

† Formulations modeled from publicly available patent and CoA data for branded ingredients — exact compositions are not published.

Virtual Population (matched to Jager 2014)

Parameter	Value
n	12
Sex	11 male, 1 female
Age	23 ± 2.4 years
Weight	86.2 ± 4.2 kg
Height	182.9 ± 6.1 cm
Race	11 Caucasian, 1 African American

1. Crystalline Powder

Delivery Type	Oral capsule
Route	Oral (swallowed)
Total dose	1800 mg curcuminoids
Particle size	Log-normal PSD: geomean=4.5 µm radius, GSD=2.44 (mass-weighted fit to CoA sieve data)

2. Hydrophilic Carrier ASD

Delivery Type	Oral capsule
Route	Oral (swallowed)
Total dose	376 mg curcuminoids
Polymer	HPMC (hydroxypropyl methylcellulose)
Lipid excipient	Hydrogenated soybean oil
Drug loading	~22.7% w/w curcuminoids

3. Phytosome

Delivery Type	Oral capsule
Route	Oral (swallowed)
Total dose	376 mg curcuminoids
Phospholipid	Soy lecithin (≥30% PC, pharmaceutical grade)
Ratio	1:2 curcuminoid:lecithin (w/w)

Bioavailability (F%) by Compound

Mean ± SD bioavailability for each curcuminoid across the three formulations (n=12, study-matched population).

Compound	Crystalline Powder (1800 mg)	Hydrophilic Carrier ASD (376 mg)	Phytosome (376 mg)
Curcumin	0.170% ± 0.090%	11.110% ± 5.590%	1.080% ± 0.590%
DMC	1.470% ± 0.750%	25.840% ± 10.160%	5.860% ± 2.910%
BDMC	2.440% ± 1.230%	25.790% ± 10.090%	8.090% ± 3.950%
Blend (77:17:6)	*0.527% ± 0.163%*	*14.495% ± 4.677%*	*2.313% ± 0.712%*

Relative Bioavailability — Blend (Dose-Normalized)

Dose-normalized blend AUC fold vs Crystalline Powder, weighted 77:17:6 (Curcumin:DMC:BDMC). Clinical values from Jager et al. 2014 (Relative Absorption column, already dose-normalized).

Comparison	Predicted Fold	Clinical Fold (Jager 2014)	Pred/Clin Ratio
ASD vs Crystalline Powder	**48.3×**	45.9×	1.05×

Comparison	Predicted Fold	Clinical Fold (Jager 2014)	Pred/Clin Ratio
Phytosome vs Crystalline Powder	5.5×	7.9×	0.70×
ASD vs Phytosome	8.7×	5.8×	1.51×

Metabolic Fingerprint

CYP and UGT enzyme contributions to total intrinsic clearance, plus P-glycoprotein efflux substrate status. Values are derived from our GNN suite predictions and integrated into the PBPK simulation. The GNN models predict substrate probability, intrinsic clearance per enzyme, and inhibition probability — all applied during simulation.

Substrate Profile — Enzymes & Transporters

Intrinsic clearance (CLint) fractions per compound, predicted by our GNN suite from molecular structure. Bold teal = dominant clearance enzyme.

Compound	CYP1A2	CYP3A4	CYP2D6	CYP2C9	CYP2C19	UGT1A1	SULT1A1	P-gp Efflux
Curcumin	—	6.2%	3.0%	2.8%	—	**49.8%**	38.2%	Yes
DMC	—	5.8%	3.1%	2.9%	—	**49.5%**	38.7%	Yes
BDMC	—	5.4%	3.1%	2.9%	—	**49.3%**	39.3%	—

Inhibition Profile — Enzymes & Transporters

Inhibition probabilities predicted by our GNN suite. Cross-compound DDI factors are computed from these values and applied during simulation.

Compound	CYP1A2	CYP3A4	CYP2D6	CYP2C9	CYP2C19	UGT1A1	P-gp
Curcumin	Yes	—	—	Yes	Yes	—	Yes
DMC	Yes	—	—	Yes	Yes	—	—
BDMC	Yes	—	—	Yes	Yes	—	—