Supplementary Information

The Table S1 highlights the overall absorption and disposition characteristics of BI and BE. The Pharmacokinetics of BI is characterized with poor oral absorption, high plasma protein binding, extensive metabolism, and enterohepatic recycling, prolonged oral half-life but low systemic levels poor in contrast to that of BE which shows better absorption, faster distribution, and clearance; lower dependence on microbiota but shorter systemic retention.

Table S1: Comparative Pharmacokinetics of Baicalin and Baicalein

Parameter	**Baicalin**	**Baicalein**	**References**
Chemical nature	Glucuronide form (glycoside)	Aglycone (non-glycoside)	(1)
Lipophilicity (log P)	Low (0.316) – poor membrane permeability	High (2.59) – good membrane permeability	(2)
Cell membrane permeability (P_{app})	0.037×10^{-6} cm/s (very low)	7.29 ± 0.70 × 10^-6 cm/s (high)	(2,3)
Primary absorption site	Colon (~2.32%/h); poor absorption in small intestine (~0.94%/h)	Efficient absorption throughout GI tract	(4-6), (15)
Bioavailability	Very low; dependent on microbial conversion	Low (~2.2% in rats) but higher than baicalin	(6-8)
Absorption mechanism	Passive diffusion; partially dissociates under acidic pH	Passive diffusion; high lipophilicity enhances uptake	(9,10) (2), (4,5)
Distribution	High binding to HSA; low CNS penetration; highest tissue levels in kidneys; moderate in liver, heart, lungs, spleen, and	Strong HSA binding; broader tissue distribution including CNS	(11-13)

	brain		
BBB permeability	Can cross BBB via OATP1A2 and OATP2B1; potential CNS protective role	Also penetrates BBB but less studied compared to baicalin	(14)
Metabolism	Extensive in liver and kidney: glucuronidation, methylation, sulfation, hydroxylation; excreted in bile, urine, and feces	Metabolized mainly to glucuronide conjugates; faster clearance than baicalin	(6), (13), (15,16)
Half-life (t½)	IV: 0.1–4 h; Oral: up to 12.1 h	Shorter t½; rapid systemic clearance	(6),(15)
Excretion	Mainly via bile and urine; significant enterohepatic recycling	Faster renal and biliary excretion; less recycling	(13), (15)

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