

Supporting Information Table 2. The following sub-tables contain the output for the population estimates as provided by Monolix. All results in Monolix reported here are calculated for (A) Genistein 4'-glucuronide (G-4'G), (B) Genistein 7-glucuronide (G-7G), (C) Genistein 4'-sulfate-7-glucuronide (G-4'S-7G), (D) Genistein 7-sulfate (G-7S) and (E) Genistein diglucuronide (G-4',7-diG).

A. G-4'G

	parameter	s.e.	r.s.e.(%)	p-value
tlag	2.8	0.37	13	
beta_tlag(TREAT_2)	0.0934	0.16	169	0.55
beta_tlag(TREAT_3)	-0.129	0.15	119	0.4
ka	0.75	0.33	44	
beta_ka(TREAT_2)	0.708	0.69	98	0.31
beta_ka(TREAT_3)	-0.658	0.47	71	0.16
V	0.00132	0.00031	23	
beta_V(TREAT_2)	-0.382	0.19	50	0.044
beta_V(TREAT_3)	-0.122	0.22	181	0.58
k	0.306	0.094	31	
beta_k(TREAT_2)	0.0603	0.18	307	0.74
beta_k(TREAT_3)	0.0299	0.22	738	0.89
omega_tlag	0.171	0.086	50	
omega_ka	0.682	0.31	45	
omega_V	0.447	0.15	33	
omega_k	0.744	0.2	27	
gamma_tlag	0.212	0.058	27	
gamma_ka	0.602	0.22	36	
gamma_V	0.247	0.067	27	
gamma_k	0.201	0.082	41	
a	1.28e+003		84	7
b	0	-	-	
c	1	-	-	
r	0	-	-	

correlation matrix of the estimates

tlag	1												
beta_tlag(TREAT_2)	-0.65	1											
beta_tlag(TREAT_3)	-0.7	0.54	1										
ka	0.29	-0.18	-0.26	1									
beta_ka(TREAT_2)	-0.15	0.44	0.08	-0.35	1								
beta_ka(TREAT_3)	-0.26	0.19	0.31	-0.63	0.34	1							
V	0.15	-0.04	-0.15	0.37	-0.05	-0.27	1						
beta_V(TREAT_2)	-0.15	0.28	0.13	-0.32	0.44	0.29	-0.48	1					
beta_V(TREAT_3)	-0.13	0.11	0.15	-0.23	0.14	0.51	-0.39	0.48	1				
k	-0.01	-0.05	0.03	-0.24	0.01	0.17	-0.32	0.21	0.16	1			
beta_k(TREAT_2)	0.01	-0.06	0	0.26	-0.39	-0.23	0.29	-0.52	-0.27	-0.37	1		
beta_k(TREAT_3)	-0.01	0.01	0	0.18	-0.11	-0.42	0.23	-0.27	-0.66	-0.3	0.49	1	
Eigenvalues	(min,	max,	max/min):	0.17	3.9	23							
omega_tlag	1												
omega_ka	-0.02	1											
omega_V	0	-0.07	1										
omega_k	0	-0.01	-0.05	1									
gamma_tlag	-0.35	0.02	0	0	1								
gamma_ka	0.02	-0.29	0.01	0	-0.11	1							
gamma_V	-0.01	0.01	-0.09	0.01	-0.02	-0.05	1						
gamma_k	0.01	0.01	0.01	-0.04	-0.03	-0.05	-0.22	1					

a	-0.01	-0.01	-0.01	-0.01	-0.03	-0.07	-0.02	-0.08	1
Eigenvalues	(min,	max,	max/min):	0.59	1.4	2.4			

Estimation	by	linearization		
			log-likelihood:	3441.74
Akaike	-2 x	Information	Criteria	(AIC): 3483.74
Bayesian		Information	Criteria	(BIC): 3510.96

Categorical	covariates				
	TREAT				
	Reference	group:	1		
	Other	groups:	2	3	
	S-TREAT				
	Reference	group:	01.02.2003		
	Other	groups:	2-1-3,	2-3-1,	3-1-2, 3-2-1,
	OCC				
	Reference	group:	1		
	Other	groups:	2	3	

Elapsed	time	is	21.2	seconds.
CPU	time	is	35.3	seconds.

B. G-7G

	parameter	s.e.	r.s.e.(%)	p-value
tlag	3.07	0.56	18	
beta_tlag(TREAT_2)	0.152	0.19	122	0.41
beta_tlag(TREAT_3)	0.00441	0.21	4.8e+003	0.98
ka	0.751	0.44	58	
beta_ka(TREAT_2)	1.27	1.1	88	0.26
beta_ka(TREAT_3)	-0.662	0.61	93	0.28
V	0.00241	0.00063	26	
beta_V(TREAT_2)	-0.55	0.21	39	0.01
beta_V(TREAT_3)	-0.239	0.39	162	0.54
k	0.64	0.28	43	
beta_k(TREAT_2)	0.182	0.22	119	0.4
beta_k(TREAT_3)	0.11	0.38	346	0.77
omega_tlag	0.253	0.12	47	
omega_ka	0.983	0.39	39	
omega_V	0.384	0.17	44	
omega_k	1.09	0.3	27	
gamma_tlag	0.25	0.071	29	
gamma_ka	0.667	0.26	40	
gamma_V	0.165	0.086	52	
gamma_k	0.122	0.12	98	
a	567		35	6
b	0	-	-	
c	1	-	-	
r	0	-	-	

correlation	matrix	of	the	estimates								
tlag		1										
beta_tlag(TREAT_2)	-0.68		1									
beta_tlag(TREAT_3)	-0.6	0.61		1								
ka	0.31	-0.25	-0.28	1								
beta_ka(TREAT_2)	-0.13	0.39	0.15	-0.25	1							
beta_ka(TREAT_3)	-0.22	0.2	0.3	-0.52	0.2	1						
V	0.28	-0.2	-0.2	0.36	-0.05	-0.29	1					
beta_V(TREAT_2)	-0.24	0.37	0.26	-0.32	0.38	0.29	-0.54	1				
beta_V(TREAT_3)	-0.11	0.07	0.15	-0.11	0.02	0.62	-0.36	0.34	1			
k	0.04		0	0.03	-0.14	0.01	0.15	-0.33	0.24	0.16	1	
beta_k(TREAT_2)	0.02	-0.1	-0.03	0.22	-0.5	-0.16	0.35	-0.62	-0.2	-0.29	1	
beta_k(TREAT_3)	-0.04	0.08	0.07	0.05	0.02	-0.53	0.27	-0.22	-0.88	-0.21	0.3	1
Eigenvalues	(min,	max,	max/min):	0.063	3.8	61						
omega_tlag		1										
omega_ka	-0.03		1									
omega_V	-0.05	-0.03		1								
omega_k	-0.04		0	-0.05		1						
gamma_tlag	-0.29		0	0		0	1					
gamma_ka	0.01	-0.23	-0.02			0	-0.09	1				
gamma_V	0.01	-0.01	-0.1	0.01		-0.07	-0.02	1				
gamma_k	0.02		0	0.04	-0.02	-0.06	-0.05	-0.46	1			

a	0	-0.01	-0.01	-0.01	-0.03	-0.04	0	-0.08	1
Eigenvalues	(min,	max,	max/min):	0.49	1.5	3.1			

Estimation	by	linearization		
		log-		
		likelihood:	3092.27	
Akaike	-2 x	Criteria	(AIC):	3134.27
Bayesian	Information	Criteria	(BIC):	3161.48

Categorical	covariates						
	TREAT						
	Reference	group:	1				
	Other	groups:	2	3			
	S-TREAT						
	Reference	group:	01.02.2003				
	Other	groups:	2-1-3,	2-3-1,	3-1-2,	3-2-1,	
	OCC						
	Reference	group:	1				
	Other	groups:	2	3			

Elapsed	time	is	22.1	seconds.
CPU	time	is	39.1	seconds.

C. G-4'S-7G

	parameter	s.e.	r.s.e.(%)	p-value
tlag	2.53	0.26	10	
beta_tlag(TREAT_2)	0.0434	0.12	271	0.71
beta_tlag(TREAT_3)	-0.171	0.15	85	0.24
ka	0.66	0.2	31	
beta_ka(TREAT_2)	-0.101	0.39	387	0.8
beta_ka(TREAT_3)	-0.679	0.43	63	0.11
V	0.000517	7.4e-005	14	
beta_V(TREAT_2)	-0.548	0.14	26	0.00012
beta_V(TREAT_3)	0.0639	0.18	288	0.73
k	0.0994	0.016	16	
beta_k(TREAT_2)	0.16	0.14	88	0.26
beta_k(TREAT_3)	-0.0359	0.21	571	0.86
omega_tlag	0.155	0.071	46	
omega_ka	0.18	0.31	172	
omega_V	0.276	0.088	32	
omega_k	0.316	0.095	30	
gamma_tlag	0.178	0.053	30	
gamma_ka	0.487	0.13	27	
gamma_V	0.208	0.046	22	
gamma_k	0.0475	0.17	355	
a	5.2e+003	3.5e+002	7	
b	0	-	-	
c	1	-	-	
r	0	-	-	

correlation	matrix	of	the	estimates								
tlag	1											
beta_tlag(TREAT_2)	-0.64		1									
beta_tlag(TREAT_3)	-0.52	0.46		1								
ka	0.39	-0.33	-0.27	1								
beta_ka(TREAT_2)	-0.3	0.43	0.21	-0.73	1							
beta_ka(TREAT_3)	-0.28	0.24	0.48	-0.67	0.52	1						
V	0.17	-0.14	-0.11	0.39	0.29	0.27	1					
beta_V(TREAT_2)	-0.16	0.23	0.11	-0.37	0.47	0.27	0.56	1				
beta_V(TREAT_3)	-0.12	0.11	0.3	-0.28	0.22	0.6	0.43	0.44	1			
k	-0.17	0.14	0.11	-0.43	0.31	0.29	0.39	0.36	0.27	1		
beta_k(TREAT_2)	0.19	-0.26	-0.13	0.46	0.57	0.33	0.41	0.63	0.32	0.58	1	
beta_k(TREAT_3)	0.13	-0.11	-0.3	0.32	0.24	0.64	0.28	0.28	0.77	-0.4	0.46	1
Eigenvalues	(min,	max,	max/min):	0.13	4.9	38						
omega_tlag	1											
omega_ka	-0.07		1									

omega_V	0	-0.05		1						
omega_k	0	-0.06	-0.02		1					
gamma_tlag	-0.33	0.04		0	0	1				
gamma_ka	0.04	-0.41		0	0.01	0.11	1			
gamma_V	0		0	-0.13	0.03	0	0	1		
gamma_k	0	0.05	0.03		-0.11	0.03	0.11	0.26	1	
a	0	-0.03	-0.01		-0.01	0.09	0.06	0.01	0.19	1
Eigenvalues	(min,	max,	max/min):	0.52	1.6	3				

Estimation	by	linearization		
	-2	x	log-likelihood:	3915.72
Akaike	Information	Criteria	(AIC):	3957.72
Bayesian	Information	Criteria	(BIC):	3984.94

Categorical	covariates					
	TREAT					
	Reference	group:	1			
	Other	groups:	2	3		
	S-TREAT					
	Reference	group:	01.02.2003			
	Other	groups:	2-1-3,	2-3-1,	3-1-2,	3-2-1,
	OCC					
	Reference	group:	1			
	Other	groups:	2	3		
Elapsed	time	is	17.9	seconds.		
CPU	time	is	28.5	seconds.		

D. G-7S

	parameter	s.e.	r.s.e.(%)	p-value
tlag	1.93	0.33	17	
beta_tlag(TREAT_2)	0.244	0.21	86	0.25
beta_tlag(TREAT_3)	-0.0138	0.2	1.47e+003	0.95
ka	0.884	0.48	55	
beta_ka(TREAT_2)	0.153	0.86	559	0.86
beta_ka(TREAT_3)	-0.738	0.69	93	0.28
V	0.00146	0.00052	36	
beta_V(TREAT_2)	0.101	0.35	344	0.77
beta_V(TREAT_3)	-0.6	0.43	71	0.16
k	0.59	0.18	30	
beta_k(TREAT_2)	-0.339	0.36	107	0.35
beta_k(TREAT_3)	0.221	0.43	196	0.61
omega_tlag	0.161	0.11	67	
omega_ka	0.0349	3.8	1.08e+004	
omega_V	0.689	0.19	27	
omega_k	0.321	0.16	51	
gamma_tlag	0.199	0.078	39	
gamma_ka	0.791	0.2	25	
gamma_V	0.159	0.12	78	
gamma_k	0.264	0.11	40	
a	1.33e+003		84	6
b	0	-	-	
c	1	-	-	
r	0	-	-	

correlation	matrix	of	the	estimates								
tlag		1										
beta_tlag(TREAT_2)	-0.69		1									
beta_tlag(TREAT_3)	-0.68	0.57		1								
ka	0.42	-0.28	-0.31	1								
beta_ka(TREAT_2)	-0.22	0.55	0.22	-0.53	1							
beta_ka(TREAT_3)	-0.34	0.23	0.25	-0.78	0.41	1						
V	0.29	-0.19	-0.22	0.6	0.29	0.45	1					
beta_V(TREAT_2)	-0.27	0.53	0.25	-0.49	0.79	0.37	0.49	1				
beta_V(TREAT_3)	-0.27	0.16	0.09	-0.48	0.2	0.73	0.46	0.36	1			
k	-0.14	0.07	0.1	-0.62	0.3	0.47	0.61	0.5	0.47	1		
beta_k(TREAT_2)	0.09	-0.31	-0.11	0.41	0.68	0.31	0.41	0.84	0.29	0.61	1	
beta_k(TREAT_3)	0.14	-0.05	0.07	0.43	0.17	0.64	0.41	-0.3	0.89	0.57	0.37	1
Eigenvalues	(min,	max,	max/min):	0.048	5.4	1.1e+002						
omega_tlag		1										
omega_ka	-0.1		1									

omega_V	0.01	-0.05		1								
omega_k		0	-0.18	-0.05		1						
gamma_tlag	-0.36		0.02		0	0.01		1				
gamma_ka	0.01	-0.47	0.01		-0.01		0.05		1			
gamma_V	-0.01	0.08	-0.06		0.06		0.05	0.16		1		
gamma_k	0.03	-0.04	0.03		-0.15		0.06	0.07	0.55		1	
a	-0.02	-0.01		0	-0.02		0.05	0.04	0.01	0.05		1
Eigenvalues	(min,	max,	max/min):		0.39		1.7	4.4				

Estimation	by	linearization		
	-2	x	log-likelihood:	3366.13
Akaike	Information	Criteria	(AIC):	3408.13
Bayesian	Information	Criteria	(BIC):	3435.35

Categorical	covariates			
	TREAT			
Reference	group:		1	
Other	groups:		2	3
	S-TREAT			
Reference	group:	01.02.2003		
Other	groups:	2-1-3,	2-3-1,	3-1-2, 3-2-1,
	OCC			
Reference	group:		1	
Other	groups:		2	3
Elapsed	time	is	24.7	seconds.
CPU	time	is	40.4	seconds.

E. G-4',7-diG

	parameter	s.e.	r.s.e.(%)	p-value
tlag	0.909	0.47	51	
beta_tlag(TREAT_2)	0.142	0.24	169	0.55
beta_tlag(TREAT_3)	-0.333	0.39	118	0.4
ka	0.164	0.072	44	
beta_ka(TREAT_2)	1.45	0.45	31	0.0012
beta_ka(TREAT_3)	-0.298	0.72	240	0.68
V	0.00149	0.00054	36	
beta_V(TREAT_2)	-0.551	0.32	58	0.082
beta_V(TREAT_3)	-0.0441	0.59	1.34e+003	0.94
k	0.0945	0.035	38	
beta_k(TREAT_2)	-0.184	0.37	203	0.62
beta_k(TREAT_3)	-0.0531	0.67	1.25e+003	0.94
omega_tlag	0.862	0.34	40	
omega_ka	0.102	0.27	269	
omega_V	0.492	0.12	24	
omega_k	0.188	0.087	46	
gamma_tlag	0.0432	0.49	1.14e+003	
gamma_ka	0.334	0.092	27	
gamma_V	0.0231	0.19	812	
gamma_k	0.169	0.061	36	
a	2.08e+003	1.3e+002	6	
b	0	-	-	
c	1	-	-	
r	0	-	-	

correlation	matrix	of	the	estimates								
tlag	1											
beta_tlag(TREAT_2)	-0.38		1									
beta_tlag(TREAT_3)	-0.27	0.55		1								
ka	0.38	-0.34	-0.23	1								
beta_ka(TREAT_2)	-0.18	0.41	0.22	-0.87	1							
beta_ka(TREAT_3)	-0.12	0.23	0.35	-0.55	0.54	1						
V	0.26	-0.23	-0.16	0.83	0.73	0.46	1					
beta_V(TREAT_2)	-0.26	0.28	0.18	-0.92	0.86	0.53	0.88	1				
beta_V(TREAT_3)	-0.06	0.16	0.27	-0.44	0.45	0.95	0.43	0.5	1			
k	-0.26	0.22	0.16	-0.88	0.79	0.5	0.85	0.95	0.47	1		
beta_k(TREAT_2)	0.24	-0.24	-0.16	0.87	0.82	-0.5	0.84	0.96	0.48	0.96	1	
beta_k(TREAT_3)	0.05	-0.15	-0.24	0.44	0.45	0.93	0.44	-0.5	0.98	0.51	0.51	1
Eigenvalues	(min,	max,	max/min):	0.0067	6.8	####						
omega_tlag	1											
omega_ka	-0.14		1									
omega_V	0	-0.01		1								
omega_k	0	-0.06	-0.01		1							

gamma_tlag	-0.04	0.02	0	0	1				
gamma_ka	-0.01	-0.35	0.01	-0.01	0.08	1			
gamma_V	0.02	-0.05	-0.05	0.01	0.03	0.25	1		
gamma_k	-0.01	0.02	0.03	-0.16	0.01	0.14	0.54	1	
a	-0.02	-0.03	0	-0.03	0.12	0.08	0.02	-0.1	1
Eigenvalues	(min,	max,	max/min):	0.39	1.7	4.4			

Estimation	by	linearization		
	-2 x	log-likelihood:	3522.35	
Akaike	Information	Criteria	(AIC):	3564.35
Bayesian	Information	Criteria	(BIC):	3591.56

Categorical	covariates				
	TREAT				
	Reference	group:	1		
	Other	groups:	2	3	
	S-TREAT				
	Reference	group:	#####		
	Other	groups:	2-1-3,	2-3-1,	3-1-2, 3-2-1,
	OCC				
	Reference	group:	1		
	Other	groups:	2	3	
Elapsed	time	is	25.3	seconds.	
CPU	time	is	41.1	seconds.	