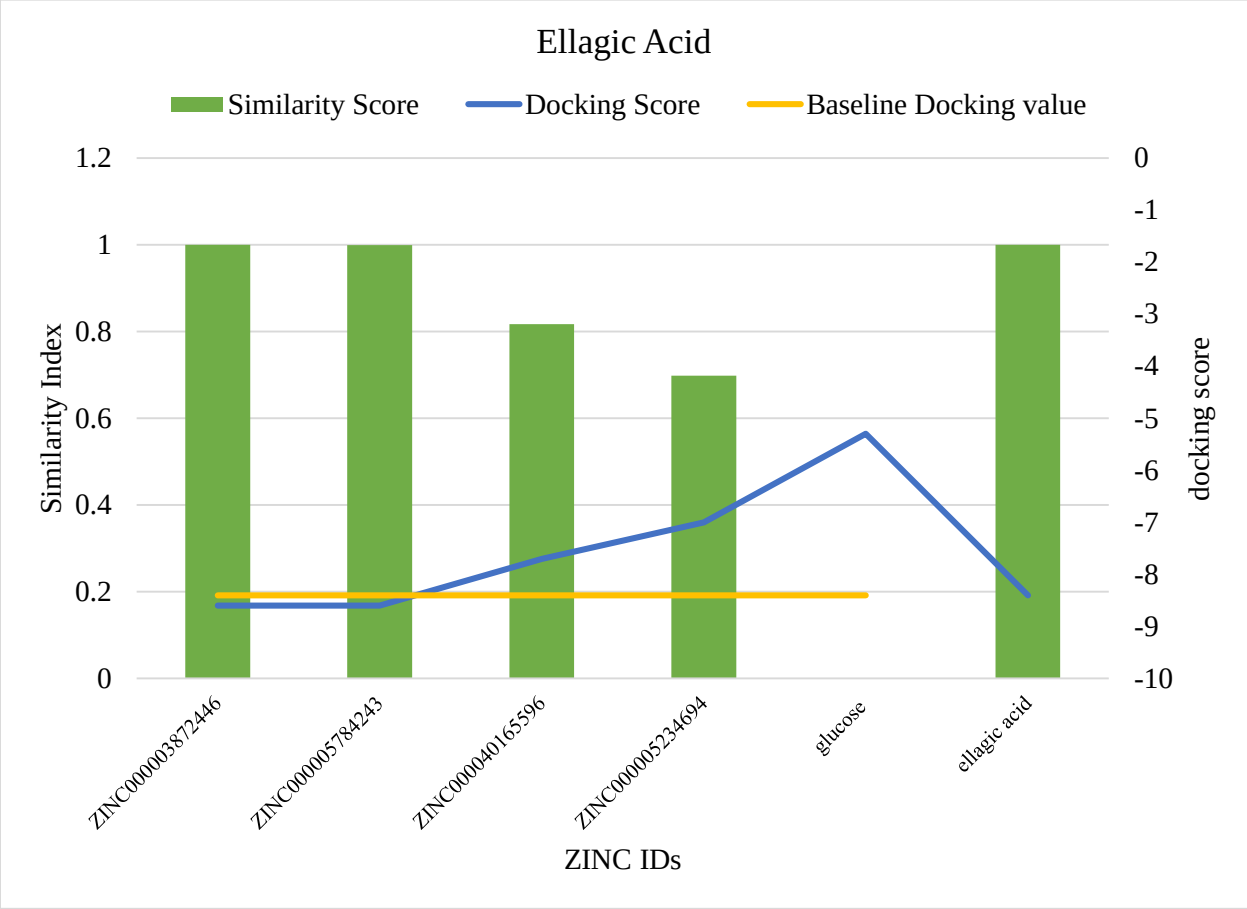
A. Docking Scores and Similarity Index of Phytochemical Analogs

i. Ellagic acid

Figure 1

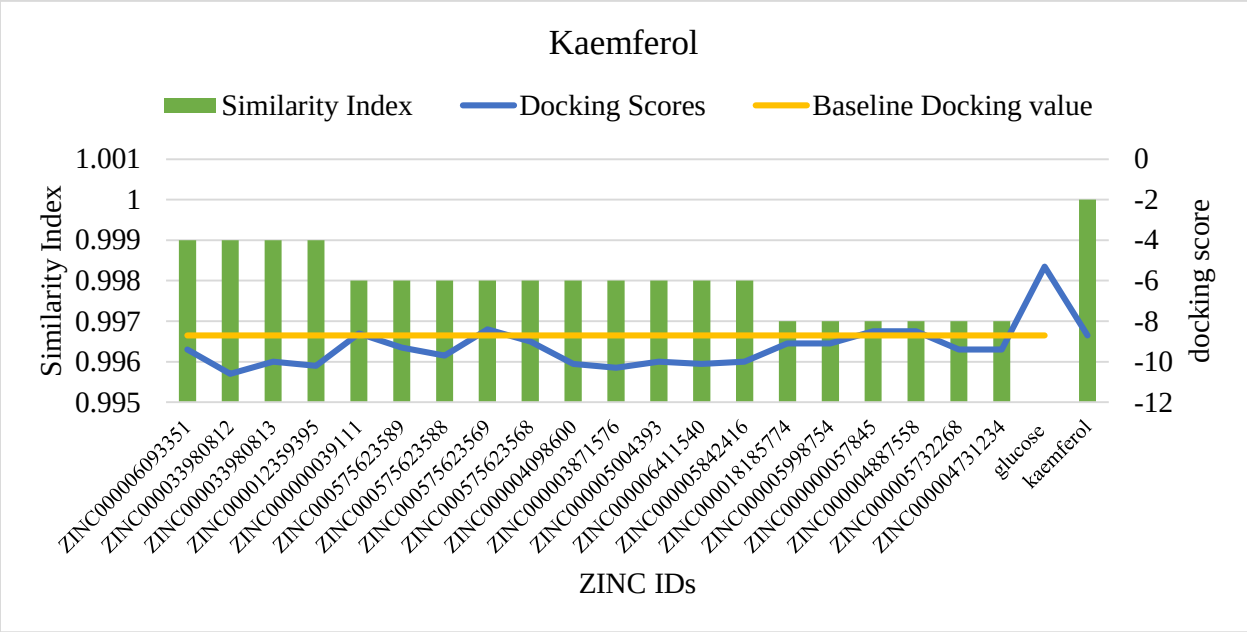
Docking and Similarity Scores of Chemical Analogs Compared to Glucose and Original Phytochemical (Ellagic Acid)



ii. Kaemferol

Figure 2

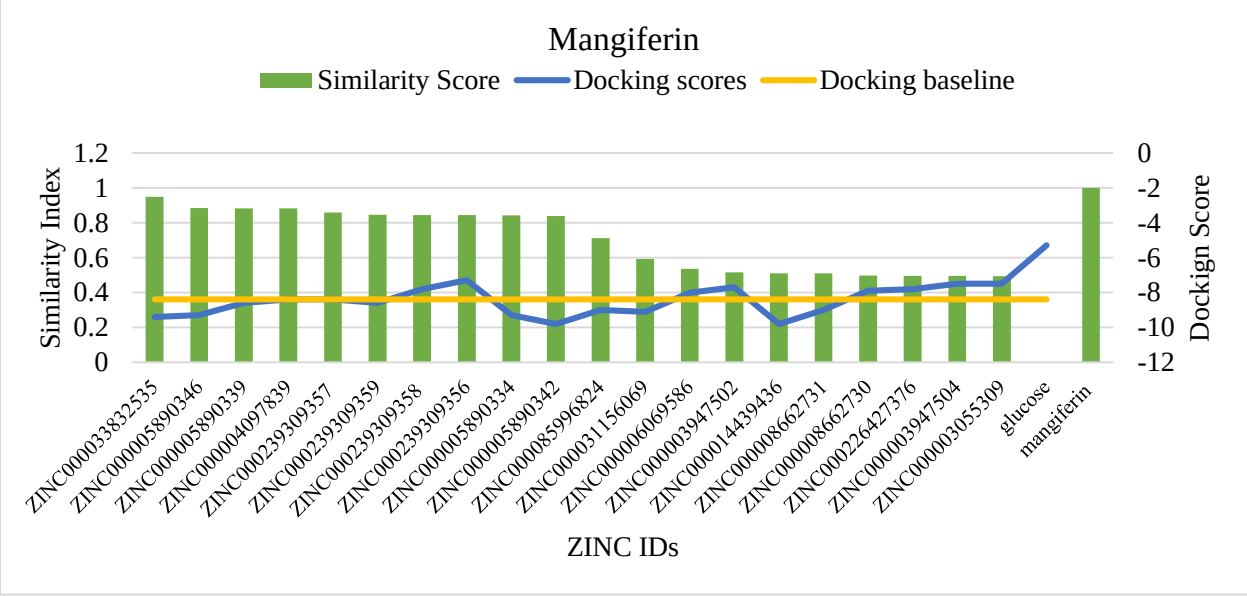
Docking and Similarity Scores of Chemical Analogs Compared to Glucose and Original Phytochemical (Kaemferol)



iii. Mangiferin

Figure 3

Docking and Similarity Scores of Chemical Analogs Compared to Glucose and Original Phytochemical (Mangiferin)



B. Pharmacokinetic Profile of Selected Phytochemical Analogs

i. Ellagic acid

Table 1

Predicted Pharmacokinetic Profile of Ellagic Acid Analogs

ZINC IDs	Log P	Log Kp (cm/s)	Limpinski rule of 5	GI absorption	Pgp substrate	BBB permeation	CYP enzyme inhibition					BA score	PAINS alert	Leadlikedness violation	Synthetic accessibility
							1A2	2C19	2C9	2D6	3A4				
ZINC000003872446	1.06	-7.36	0	High	No	No	Yes	No	No	No	No	0.55	1	0	3.17
ZINC000005784243	0.84	-7.32	0	Low	No	No	Yes	No	No	No	No	0.55	1	0	3.25
ZINC000040165596	1.47	-6.41	0	High	No	Yes	Yes	No	No	No	Yes	0.55	1	1	2.56
ZINC000005234694	0.64	-7.59	0	High	No	No	No	No	No	No	No	0.56	0	1	2.59

ii. Kaemferol

Table 2

Predicted Pharmacokinetic Profile of Kaemferol Analogs

ZINC IDs	Log P	Log Kp (cm/s)	Limpinski rule of 5	GI absorption	Pgp substrate	BBB permeation	CYP enzyme inhibition					BA score	PAINS alert	Leadlikedness violation	Synthetic accessibility
							1A2	2C19	2C9	2D6	3A4				
ZINC000006093351	2.01	-6.04	0	High	No	No	Yes	No	No	Yes	Yes	0.55	0	0	3.08
ZINC000033980812	1.23	-7.05	0	High	No	No	Yes	No	No	Yes	Yes	0.55	1	0	3.23
ZINC000033980813	1.23	-7.05	0	High	No	No	Yes	No	No	Yes	Yes	0.55	1	0	3.23
ZINC000012359395	1.54	-6.65	0	High	No	No	Yes	No	No	Yes	Yes	0.55	1	0	3.15
ZINC000000039111	1.55	-6.65	0	High	No	No	Yes	No	No	Yes	Yes	0.55	1	0	3.16
ZINC000575623589	1.55	-6.65	0	High	No	No	Yes	No	No	Yes	Yes	0.55	1	0	3.16
ZINC000575623588	1.55	-6.65	0	High	No	No	Yes	No	No	Yes	Yes	0.55	1	0	3.16
ZINC000575623569	1.99	-6.35	0	High	No	No	Yes	No	No	Yes	Yes	0.55	0	0	3.12
ZINC000575623568	1.99	-6.35	0	High	No	No	Yes	No	No	Yes	Yes	0.55	0	0	3.12
ZINC000004098600	1.12	-7	0	High	No	No	Yes	No	No	Yes	Yes	0.55	1	0	3.21
ZINC000003871576	2.11	-5.8	0	High	No	No	Yes	No	No	Yes	Yes	0.55	0	0	2.96
ZINC000005004393	1.3	-6.4	0	High	No	No	Yes	No	No	Yes	Yes	0.55	0	0	3.09
ZINC000006411540	2	-6.56	0	High	No	No	Yes	No	No	Yes	Yes	0.55	0	0	3.16
ZINC000005842416	1.81	-6.16	0	High	No	No	Yes	No	No	Yes	Yes	0.55	1	0	3.04
ZINC000018185774	1.73	-6.25	0	High	No	No	Yes	No	No	Yes	Yes	0.55	1	0	3.02
ZINC000005998754	1.98	-6.56	0	High	No	No	Yes	No	No	Yes	Yes	0.55	0	0	3.21
ZINC000000057845	1.93	-6.3	0	High	No	No	Yes	No	No	Yes	Yes	0.55	0	0	3.14
ZINC000004887558	1.37	-6.75	0	High	No	No	Yes	No	No	Yes	Yes	0.55	1	0	3.16
ZINC000005732268	1.94	-6.56	0	High	No	No	Yes	No	No	Yes	Yes	0.55	0	0	3.2
ZINC000004731234	1.66	-6.43	0	High	No	No	Yes	No	No	Yes	Yes	0.55	1	0	3.42

iii. Mangiferin

Table 3

Predicted Pharmacokinetic Profile of Mangiferin Analogs

ZINC IDs	Log P	Log Kp (cm/s)	Limpinski rule of 5	GI absorption	Pgp substrate	BBB permeation	CYP enzyme activity					BA score	PAINS alert	Leadlikedness violation	Synthetic accessibility
							1A2	2C19	2C9	2D6	3A4				
ZINC000033832535	0.55	-8.68	0	Low	No	No	No	No	No	No	No	0.55	0	1	5.05
ZINC000005890346	-0.4	-9.61	0	Low	No	No	No	No	No	No	No	0.55	0	1	5.07
ZINC000005890339	-0.28	-9.61	0	Low	No	No	No	No	No	No	No	0.55	0	1	5.07
ZINC000004097839	-0.45	-9.61	0	Low	No	No	No	No	No	No	No	0.55	0	1	5.07
ZINC000239309357	-0.26	-9.61	0	Low	No	No	No	No	No	No	No	0.55	0	1	5.07
ZINC000239309359	-0.34	-9.61	0	Low	No	No	No	No	No	No	No	0.55	0	1	5.07
ZINC000239309358	-0.63	-9.61	0	Low	No	No	No	No	No	No	No	0.55	0	1	5.07
ZINC000239309356	-0.38	-9.61	0	Low	No	No	No	No	No	No	No	0.55	0	1	5.07
ZINC000005890334	-0.14	-9.61	0	Low	No	No	No	No	No	No	No	0.55	0	1	5.07
ZINC000005890342	-0.28	-9.61	0	Low	No	No	No	No	No	No	No	0.55	0	1	5.07
ZINC000085996824	2.31	-6.91	0	High	Yes	No	No	No	No	No	Yes	0.55	0	1	4.41
ZINC000031156069	-0.12	-7.82	0	Low	No	No	No	No	No	No	No	0.55	0	1	4.8
ZINC000006069586	0.64	-7.91	0	Low	No	No	No	No	No	No	No	0.55	0	1	4.96
ZINC000003947502	0.67	-8.18	0	Low	Yes	No	No	No	No	No	Yes	0.55	0	1	5.23
ZINC000014439436	1.21	-8.13	1	Low	Yes	No	No	No	No	No	No	0.11	1	1	5.15
ZINC000008662731	0.72	-8.18	0	Low	Yes	No	No	No	No	No	Yes	0.55	0	1	5.15
ZINC000008662730	0.75	-8.18	0	Low	Yes	No	No	No	No	No	Yes	0.55	0	1	5.15
ZINC000226427376	0.83	-8.18	0	Low	Yes	No	No	No	No	No	Yes	0.55	0	1	5.15
ZINC000003947504	0.77	-8.18	0	Low	Yes	No	No	No	No	No	Yes	0.55	0	1	5.23
ZINC000003055309	0.78	-8.18	0	Low	Yes	No	No	No	No	No	Yes	0.55	0	1	5.15

C. Toxicology Results

i. Ellagic acid

Table 4

Toxicity Results for Selected Compounds Similar to Ellagic Acid

ZINC ID	Predicted LD50	Toxicology class	Hepatotoxicity	Carcinogenicity	Immunotoxicity	Mutagenicity	Cytotoxicity
ZINC000003872446	2991mg/kg	4	inactive	active (0.59)	inactive	inactive	inactive
ZINC000005784243	3200mg/kg	5	inactive	active (0.54)	inactive (0.68)	inactive	inactive
ZINC000040165596	5370mg/kg	6	inactive	active (0.84)	inactive	inactive (0.53)	inactive
ZINC000005234694	3200mg/kg	5	inactive	inactive (0.62)	inactive	inactive (0.67)	inactive

ZINC ID	Nuclear receptor signaling pathways							Stress response pathways				
	AHR	AR	ARLBD	Aromatase	ERα	ERLBD	PPARδ	ARE	HSFRE	MMP	TS-P53	ATAD5
ZINC000003872446	Inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive
ZINC000005784243	Inactive (0.67)	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive (0.69)	inactive	inactive
ZINC000040165596	Active (0.65)	inactive	inactive (0.69)	inactive	inactive	Inactive (0.69)	inactive	inactive (0.62)	inactive (0.62)	Active (0.7)	inactive (0.62)	inactive
ZINC000005234694	inactive	inactive	inactive	inactive	inactive (0.64)	inactive	inactive (0.65)	inactive	inactive	Active (0.6)	inactive (0.64)	inactive

Values in bracket represent probability of activity or inactivity; those without probability represent a 70% or more chance of activity or inactivity
AHR; Aryl hydrocarbon Receptor
AR; Androgen Receptor
ARLBD; Androgen Receptor Ligand Binding Domain
ERα; Estrogen Receptor Alpha

ERLBD; Estrogen Receptor Ligand Binding Domain
PPARδ; Peroxisome Proliferator Activated Receptor Gamma
ARE; Nuclear factor (erythroid-derived 2)-like 2/antioxidant responsive element
HSFRE; Heat shock factor response element
MMP; Mitochondrial Membrane Potential
TS-P53; Phosphoprotein (Tumor Supressor) p53
ATPase family AAA domain-containing protein 5 (ATAD5)

ii. Kaemferol

Table 5

Toxicity Results for Selected Compounds Similar to Kaemferol

ZINC ID	Predicted LD50	Toxicology class	Hepatotoxicity	Carcinogenicity	Immunotoxicity	Mutagenicity	Cytotoxicity
ZINC000006093351	4000mg/kg	5	inactive (0.69)	inactive (0.62)	inactive	inactive (0.65)	inactive
ZINC000033980812	159mg/kg	3	inactive (0.69)	active (0.68)	inactive	active (0.51)	inactive
ZINC000033980813	159mg/kg	3	inactive (0.69)	active (0.68)	inactive	active (0.51)	inactive
ZINC000012359395	3919mg/kg	5	inactive	active (0.71)	inactive	inactive (0.53)	inactive
ZINC000000039111	159mg/kg	3	inactive	active (0.71)	inactive (0.51)	inactive (0.53)	inactive
ZINC000575623589	159mg/kg	3	inactive	active (0.71)	inactive (0.51)	inactive (0.53)	inactive
ZINC000575623588	159mg/kg	3	inactive	active (0.71)	inactive (0.51)	inactive (0.53)	inactive
ZINC000575623569	3919mg/kg	5	inactive (0.68)	inactive	inactive	inactive (0.52)	inactive
ZINC000575623568	3919mg/kg	5	inactive (0.68)	inactive	inactive	inactive (0.52)	inactive
ZINC000004098600	159mg/kg	3	inactive (0.69)	active (0.68)	active (0.55)	active (0.51)	inactive
ZINC000003871576	2500mg/kg	5	inactive (0.68)	inactive (0.62)	inactive	inactive (0.57)	inactive
ZINC000005004393	3919mg/kg	5	inactive (0.69)	inactive (0.69)	inactive	inactive	inactive
ZINC000006411540	3919mg/kg	5	inactive (0.72)	inactive (0.68)	inactive (0.69)	inactive	inactive
ZINC000005842416	3919mg/kg	5	inactive (0.69)	active (0.68)	inactive	active (0.51)	inactive
ZINC000018185774	3919mg/kg	5	inactive (0.69)	active (0.68)	inactive	active (0.51)	inactive
ZINC000005998754	4000mg/kg	5	inactive	inactive (0.72)	inactive	inactive	inactive
ZINC000000057845	4000mg/kg	5	inactive (0.69)	inactive (0.62)	inactive (0.60)	inactive (0.65)	inactive
ZINC000004887558	3919mg/kg	5	inactive (0.69)	active (0.68)	inactive	active (0.51)	inactive
ZINC000005732268	3919mg/kg	5	inactive	inactive (0.68)	inactive	inactive	inactive
ZINC000004731234	5000mg/kg	5	inactive (0.69)	active (0.60)	inactive (0.57)	inactive (0.51)	inactive

ZINC ID	Nuclear receptor signaling pathways							Stress response pathways				
	AHR	AR	ARLBD	Aromatase	ERα	ERLBD	PPARδ	ARE	HSFRE	MMP	TS-P53	ATAD5
ZINC000006093351	active (0.95)	inactive	inactive	active (0.8)	active (0.85)	active (0.91)	inactive	inactive	inactive	active (0.86)	inactive	inactive (0.56)
ZINC000033980812	active (0.91)	inactive	inactive	inactive	active (0.87)	active (0.95)	inactive	inactive	inactive	active (1.0)	inactive	inactive
ZINC000033980813	active (0.91)	inactive	inactive	inactive	active (0.87)	active (0.95)	inactive	inactive	inactive	active (1.0)	inactive	inactive
ZINC000012359395	active (0.84)	inactive	inactive	inactive	active (0.69)	active (0.86)	inactive	inactive	inactive	active (0.82)	inactive	inactive
ZINC000000039111	active (0.84)	inactive	inactive	inactive	active (0.69)	active (0.86)	inactive	inactive	inactive	active (0.82)	inactive	inactive
ZINC000575623589	active (0.84)	inactive	inactive	inactive	active (0.69)	active (0.86)	inactive	inactive	inactive	active (0.82)	inactive	inactive
ZINC000575623588	active (0.84)	inactive	inactive	inactive	Active (0.69)	active (0.86)	inactive	inactive	inactive	active (0.82)	inactive	inactive
ZINC000575623569	active (1.0)	inactive	inactive	active (0.96)	active (1.0)	active (0.95)	inactive	inactive	inactive	active (1.0)	inactive	inactive
ZINC000575623568	active (1.0)	inactive	inactive	active (0.96)	active (1.0)	active (0.95)	inactive	inactive	inactive	active (1.0)	inactive	inactive
ZINC000004098600	active (0.91)	inactive	inactive	inactive	active (0.87)	active (0.95)	inactive	inactive	inactive	active (1.0)	inactive	inactive
ZINC000003871576	active (1.0)	inactive	inactive	active (0.61)	active (1.0)	active (1.0)	active (1.0)	inactive	inactive	active (1.0)	active (1.0)	active (0.96)
ZINC000005004393	active (1.0)	inactive	inactive	active (0.82)	active (1.0)	active (1.0)	inactive	inactive	inactive	active (0.99)	active (1.0)	active (1.0)
ZINC000006411540	active (0.97)	inactive	inactive	active (0.58)	active (0.88)	active (0.89)	inactive	inactive	inactive	active (0.92)	inactive	active (0.65)
ZINC000005842416	active (0.91)	inactive	inactive	inactive	active (0.87)	active (0.95)	inactive	inactive	inactive	active (1.0)	inactive	inactive
ZINC000018185774	active (0.91)	inactive	inactive	inactive	active (0.87)	active (0.95)	inactive	inactive	inactive	active (1.0)	inactive	inactive
ZINC000005998754	active (0.94)	inactive	inactive	active (0.5)	active (0.78)	active (0.85)	inactive	inactive	inactive	active (0.89)	inactive	active (0.70)
ZINC000000057845	active (0.95)	inactive	inactive	active (0.8)	active (0.85)	active (0.91)	inactive	inactive	inactive	active (0.86)	inactive	inactive (0.56)
ZINC000004887558	active (0.91)	inactive	inactive	inactive	active (0.87)	active (0.95)	inactive	inactive	inactive	active (1.0)	inactive	inactive
ZINC000005732268	active (0.97)	inactive	inactive	active (0.58)	active (0.88)	active (0.89)	inactive	inactive	inactive	active (0.92)	inactive	active (0.65)
ZINC000004731234	active (0.90)	inactive	inactive	inactive	active (0.84)	active (0.88)	inactive	inactive	inactive	active (0.98)	inactive	inactive

Values in bracket represent probability of activity or inactivity; those without probability represent a 70% or more chance of activity or inactivity
AHR; Aryl hydrocarbon Receptor
AR; Androgen Receptor
ARLBD; Androgen Receptor Ligand Binding Domain
ERα; Estrogen Receptor Alpha

ERLBD; Estrogen Receptor Ligand Binding Domain
PPARδ; Peroxisome Proliferator Activated Receptor Gamma
ARE; Nuclear factor (erythroid-derived 2)-like 2/antioxidant responsive element
HSFRE; Heat shock factor response element
MMP; Mitochondrial Membrane Potential
TS-P53; Phosphoprotein (Tumor Supressor) p53
ATPase family AAA domain-containing protein 5 (ATAD5)

iii. Mangiferin

Table 6

Toxicity Results for Selected Compounds Similar to Mangiferin

ZINC ID	Predicted LD50	Toxicology class	Hepatotoxicity	Carcinogenicity	Immunotoxicity	Mutagenicity	Cytotoxicity
ZINC000033832535	832mg/kg	4	inactive	inactive	active (0.5)	inactive (0.59)	inactive (0.69)
ZINC000005890346	832mg/kg	4	inactive	inactive	inactive	active (0.54)	inactive
ZINC000005890339	832mg/kg	4	inactive	inactive	inactive	active (0.54)	inactive
ZINC000004097839	832mg/kg	4	inactive	inactive	inactive	active (0.54)	inactive
ZINC000239309357	832mg/kg	4	inactive	inactive	inactive	active (0.54)	inactive
ZINC000239309359	832mg/kg	4	inactive	inactive	inactive	active (0.54)	inactive
ZINC000239309358	832mg/kg	4	inactive	inactive	inactive	active (0.54)	inactive
ZINC000239309356	832mg/kg	4	inactive	inactive	inactive	active (0.54)	inactive
ZINC000005890334	832mg/kg	4	inactive	inactive	inactive	active (0.54)	inactive
ZINC000005890342	832mg/kg	4	inactive	inactive	inactive	active (0.54)	inactive
ZINC000085996824	1213mg/kg	4	inactive	active (0.52)	active (0.80)	inactive (0.65)	inactive
ZINC000031156069	5000mg/kg	5	inactive	inactive	inactive	active (0.75)	inactive (0.69)
ZINC000006069586	5000mg/kg	5	inactive	inactive	inactive (0.63)	active (0.75)	inactive (0.69)
ZINC000003947502	2500mg/kg	5	inactive	inactive	active (0.66)	inactive (0.65)	inactive (0.58)
ZINC000014439436	7mg/kg	2	inactive	inactive (0.64)	active (0.99)	inactive (0.60)	inactive
ZINC000008662731	5000mg/kg	5	inactive	inactive	active (0.82)	inactive (0.65)	inactive (0.58)
ZINC000008662730	5000mg/kg	5	inactive	inactive	active (0.82)	inactive (0.65)	inactive (0.58)
ZINC000226427376	5000mg/kg	5	inactive	inactive	active (0.82)	inactive (0.65)	inactive (0.58)
ZINC000003947504	2500mg/kg	5	inactive	inactive	active (0.66)	inactive (0.65)	inactive (0.58)
ZINC000003055309	5000mg/kg	5	inactive	inactive	active (0.82)	inactive (0.65)	inactive (0.58)

ZINC ID	Nuclear receptor signaling pathways							Stress response pathways				
	AHR	AR	ARLBD	Aromatase	ERα	ERLBD	PPARδ	ARE	HSFRE	MMP	TS-P53	ATAD5
ZINC000033832535	active (0.5)	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive
ZINC000005890346	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive
ZINC000005890339	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive
ZINC000004097839	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive
ZINC000239309357	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive
ZINC000239309359	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive
ZINC000239309358	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive
ZINC000239309356	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive
ZINC000005890334	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive
ZINC000005890342	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive
ZINC000085996824	inactive (0.53)	inactive	inactive	inactive	inactive (0.68)	inactive	inactive	inactive	inactive	active (0.62)	active (0.51)	inactive (0.65)
ZINC000031156069	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	active (0.5)	inactive
ZINC000006069586	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	active (0.5)	inactive
ZINC000003947502	inactive (0.62)	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive
ZINC000014439436	inactive	inactive	inactive	inactive (0.57)	inactive	inactive	inactive	inactive	inactive	active (0.67)	active (0.51)	inactive
ZINC000008662731	inactive (0.62)	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive
ZINC000008662730	inactive (0.62)	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive
ZINC000226427376	inactive (0.62)	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive
ZINC000003947504	inactive (0.62)	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive
ZINC000003055309	inactive (0.62)	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive	inactive

Values in bracket represent probability of activity or inactivity; those without probability represent a 70% or more chance of activity or inactivity
AHR; Aryl hydrocarbon Receptor
AR; Androgen Receptor
ARLBD; Androgen Receptor Ligand Binding Domain
ERα; Estrogen Receptor Alpha
ERLBD; Estrogen Receptor Ligand Binding Domain
PPARδ; Peroxisome Proliferator Activated Receptor Gamma
ARE; Nuclear factor (erythroid-derived 2)-like 2/antioxidant responsive element
HSFRE; Heat shock factor response element
MMP; Mitochondrial Membrane Potential
TS-P53; Phosphoprotein (Tumor Supressor) p53

ATPase family AAA domain-containing protein 5 (ATAD5)