Supplementary Table

Table S1. Predicted biological activity of Gmelofuran

Predicted Biological Activity	**Pi [a] (%)**	**Pa [b] (%)**
Ubiquinol-cytochrome-c reductase inhibitor	0.901	0.005
Histidine kinase inhibitor	0.858	0.003
CYP2H substrate	0.824	0.014
Carminative	0.758	0.005
HIF1A expression inhibitor	0.765	0.014
CF transmembrane conductance regulator agonist	0.706	0.003
Membrane permeability inhibitor	0.656	0.059
Apoptosis agonist	0.612	0.025
Anti-inflammatory	0.608	0.030
Immunosuppressant	0.582	0.031

[a]Pa represents the probability of active

[b]Pi represents the probability of inactive

Table S2. Predicted biological activity of Agarol

Predicted Biological Activity	**Pi [a] (%)**	**Pa [b] (%)**
Anti-inflammatory	0.884	0.005
Ubiquinol-cytochrome-c reductase inhibitor	0.870	0.011
Histidine kinase inhibitor	0.851	0.003
Carminative	0.808	0.004
Membrane permeability inhibitor	0.612	0.081
Antineoplastic	0.602	0.044
Vaso protector	0.578	0.023
Antimetastatic	0.513	0.017
Immunosuppressant	0.502	0.042
Apoptosis agonist	0.471	0.046

[a]Pa represents the probability of active

[b]Pi represents the probability of inactive

Table S3. Predicted biological activity of Aquillochin

Predicted Biological Activity	**Pi** [a] **(%)**	**Pa** [b] **(%)**
Monophenol monooxygenase inhibitor	0.963	0.001
Free radical scavenger	0.949	0.001
Hepato-protectant	0.913	0.002
TP53 expression enhancer	0.873	0.006
Hepatic disorders treatment	0.805	0.004
CYP2A11 substrate	0.787	0.004
Chemo-preventive	0.773	0.004
Caspase 3 stimulant	0.772	0.007
Anti-inflammatory	0.726	0.013
Apoptosis agonist	0.707	0.014

[a]Pa represents the probability of active

[b]Pi represents the probability of inactive

Table S4. Predicted biological activity of Agarospirol

Predicted Biological Activity	**Pi [a] (%)**	**Pa [b] (%)**
Immunosuppressant	0.756	0.010
Testosterone 17beta-dehydrogenase (NADP+) inhibitor	0.735	0.044
Carminative	0.679	0.008
Ubiquinol-cytochrome-c reductase inhibitor	0.705	0.067
CYP2J substrate	0.672	0.060
Alkylacetylglycerophosphatase inhibitor	0.631	0.029
Acylcarnitine hydrolase inhibitor	0.616	0.040
Adenomatous polyposis treatment	0.584	0.024
Alkenylglycerophosphocholine hydrolase inhibitor	0.603	0.045
Antitussive	0.559	0.008

[a]Pa represents the probability of active

[b]Pi represents the probability of inactive

Table S5. Parameters evaluated for drug-likeness of Grewin and the control drug BDA - 366

Compound	MCE-18	SA score	Fsp^3	PAINS	NP Score	Pfizer	Lipinski
Grewin	73.000	3.458	0.211	1	1.899	Accepted	Accepted
BDA - 366	71.788	3.314	0.375	0	-0.327	Accepted	Accepted

Table S6. Parameters evaluated for absorption of Grewin and the control drug BDA - 366

Compound	Caco-2 permeability	MDCK permeability	Pgp-inhibitor	Pgp-substrate	HIA	F (20%)	F (30%)
Grewin	-5.269	1.7e-05	0.266	0.004	0.085	0.025	0.994
BDA - 366	-5.694	4e-06	0.01	0.974	0.689	0.816	0.827

Table S7. Parameters evaluated for distribution of Grewin and the control drug BDA - 366

Compound	PPB (%)	VD (L/kg)	BBB (log BB)	Fu (%)
Grewin	89.849%	0.617	0.045	12.846%
BDA - 366	96.76%	0.961	0.053	3.982%

Table S8. Parameters evaluated for metabolism of Grewin and the control drug BDA - 366.

Compound	CYP1A2 inhibitor	CYP1A2 substrate	CYP2C19 inhibitor	CYP2C19 substrate	CYP2C9 inhibitor	CYP2C9 substrate	CYP2D6 inhibitor	CYP2D6 substrate	CYP3A4 inhibitor	CYP3A4 substrate
Grewin	0.136	0.625	0.053	0.083	0.334	0.461	0.309	0.48	0.553	0.552
BDA - 366	0.855	0.888	0.089	0.065	0.112	0.125	0.051	0.52	0.083	0.107

Table S9. Parameters evaluated for excretion of Grewin and the control drug BDA - 366.

Compound	CL	$T_{1/2}$
Grewin	12.275	0.716
BDA - 366	13.582	0.793

Table S10. Parameters evaluated for toxicity of Grewin and the control drug BDA - 366.

Compound	hERG Blockers	H-HT	DILI	AMES Toxicity	ROA	Skin Sensitization	Carcinogenicity	Eye Corrosion	Respiratory Toxicity
Grewin	0.168	0.356	0.805	0.062	0.12	0.652	0.552	0.003	0.157
BDA - 366	0.621	0.438	0.924	0.901	0.135	0.949	0.313	0.003	0.013

Table S11. Sequences of primers used for mRNA gene expression analysis by qRT-PCR

Gene	Primer Sequences (5′-3′)
p53	**F:** TCT TGGGCC TGT GTT ATC TCC **R:** CGC CCA TGC AGG AAC TGT TA
bcl2	**F:** GAA GGG CAG CCG TTA GGAAA **R:** GCG CCC AAT ACG ACC AAA TC
BAX	**F:** GGT TGC CCT CTT CTA CTT T **R:** AGC CAC CCT GGT CTT G
CASPASE 3	**F:** GAA GGA ACA CGC CAG GAA AC **R:** GCA AAG TGA AAT GTA GCA CCA A
CASPASE 9	**F:** GCC CGA GTT TGA GAG GAA AA **R:** CAC AGC CAG ACC AGG AC
COX-2	F: CCT GAG CAT CTA CGG TTT GC R: ACT GCT CAT CAC CCC ATT CA
iNOS	F: CCT GAG CAT CTA CGG TTT GC R: ACT GCT CAT CAC CCC ATT CA
TNF-	**F:** GCCAGAATGCTGCAGGACTT **R:** GGCCTAAGGTCCACTTGTGTCA
IL-6	**F:** AGGGTTGCCAGATGCAATAC **R:** AAACCAAGGCACAGTGGAAC
IL-8	**F:** CCGGAGAGGAGACTTCACAG **R:** GGAAATTGGGGTAGGAAGGA
GAPDH	**F:** CAA GGT CAT CCA TGA CAA CTT TG **R:** GTC CAC CAC CCT GTT GCT GTA G