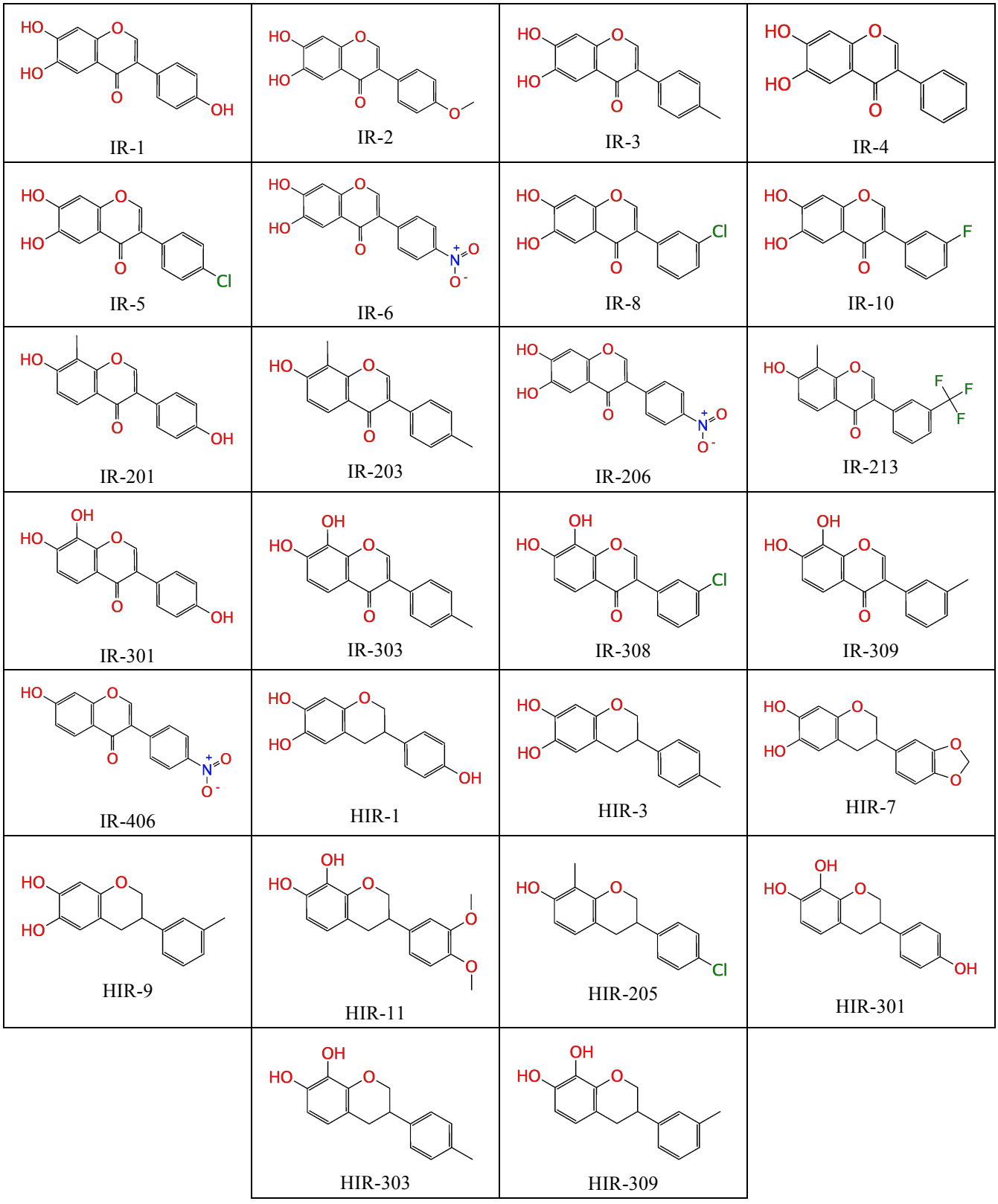

Figure S1. Isoflavonoids synthetized in laboratory for this study. IR are isoflavones and HIR are isoflavans.

	5-LOX		12-LOX		15-LOX	
Molecule	Binding energy (kcal/mol)	IC_{50} (μM)	Binding energy (kcal/mol)	IC_{50} (μM)	Binding energy (kcal/mol)	IC_{50} (μM)
IR-1	-0.34 (35)*	>40	-1.27 (3)	8.7	-2.01 (1)	49
IR-2	-1.18 (21)	1.2	-0.56 (40)*	>100	-2.16 (16)*	>100
IR-3	-1.99 (31)*	0.36	-2.78 (6)	2.3	-2.85 (13)*	18
IR-4	-2.23 (16)	>40	-3.77 (33)*	>40	-2.6 (9)	>40
IR-5	-0.66 (32)*	31	-0.63 (4)	>100	-1.6 (17)*	>100
IR-6	-1.37 (32)*	1.5	-0.9 (1)	5.8	-2.61 (24)*	>100
IR-8	-2.38 (17)*	0.39	-2.56 (19)*	0.28	-2.55 (19)*	0.59
IR-10	-1.16 (16)*	0.49	-2.55 (31)*	4.2	-1.63 (12)	12
IR-201	-0.39 (26)*	12	-0.85 (30)*	>100	-0.82 (7)	>100
IR-203	-1.91 (32)*	1.5	-1.6 (6)	>100	-1.92 (14)	>100
IR-206	-1.27 (25)*	300	-0.55 (4)	>100	-0.28 (9)*	>100
IR-213	+0.27 (18)	600	-0.2 (12)	>100	-0.2 (29)*	>100
IR-301	-1.66 (48)*	0.9	-2.2 (22)	>100	-2.57 (16)*	50
IR-303	-3.2 (33)*	0.25	-3.29 (25)*	1.6	-3.76 (26)*	7.8
IR-308	-3.38 (19)*	0.3	-3.73 (17)*	0.78	-3.31 (15)	6.2
IR-309	-3.82 (19)*	0.3	-4.62 (29)*	3.6	-3.64 (15)*	11
IR-406	-0.52 (17)	5	No match	>100	-1.39 (24)*	>100
HIR-1	-2.35 (29)*	0.3	-3.71 (24)	17	-4.32 (28)*	0.5
HIR-3	-4.12 (34)*	0.28	5.22 (32)*	5.5	-4.41 (2)	2.3
HIR-7	-3.19 (29)*	0.4	-4.11 (17)*	11	-4.26 (10)	0.35
HIR-9	-4.66 (16)	0.5	-5.33 (23)*	15	-3.98 (3)	0.21
HIR-11	-3.0 (18)	0.69	-5.84 (19)	17	-6.4 (34)*	11
HIR-205	-2.28 (39)*	7.1	-2.76 (6)	>40	-3.43 (22)*	29
HIR-301	-3.25 (45)*	0.31	-4.8 (21)*	>40	-4.64 (4)	>40
HIR-303	-4.74 (36)*	0.18	-5.99 (28)*	7.7	-6.74 (32)*	34
HIR-309	-4.53 (10)	0.15	-6.35 (24)*	6.4	-6.68 (32)*	5.8
Baicalein	-1.81 (14)	0.85	-3.28 (13)	0.86	-2.43 (5)	9.1
Zileuton	-6.76 (40)	0.18				

Table S2. Docking of each of the isoflavonoids used in the study and the enzyme 5-. 12- and 15-lipoxygenase performed in duplicate. The analysis was based on clustering. which indicates the average binding energy and the number of conformations involving that result. which is shown in parentheses. The energy value was determined based on the conformation associated with the interaction that occurred at the active site. The asterisk indicates that the conformation is also the most likely analyzed by the size of the cluster. IC_{50} provided by Mascayano *et al*. 2014 except for Zileuton, provide by Berget *et al*, 2007.

```
ESTIMATED NORMALIZED LINEAR MODEL (SD = Standard Deviation)

ln IC50 / SD(ln IC50) =
       -36.96214
        +0.00243 * AM1_HOMO / SD(AM1_HOMO)
        -2.04609 * ASA_P / SD(ASA_P)
        +0.02382 * a_heavy / SD(a_heavy)
        +0.01178 * a_nO / SD(a_nO)
        +0.01743 * b_heavy / SD(b_heavy)
        +0.01972 * chi0 / SD(chi0)
        +0.00475 * chi1 / SD(chi1)
        -0.01530 * dipoleY / SD(dipoleY)
        +0.00014 * FASA_H / SD(FASA_H)
        +0.02122 * lip_acc / SD(lip_acc)
        +2.12027 * PEOE_VSA+2 / SD(PEOE_VSA+2)
        -0.54065 * PEOE_VSA+3 / SD(PEOE_VSA+3)
        +1.08139 * PEOE_VSA_HYD / SD(PEOE_VSA_HYD)
        -0.00266 * PM3_LUMO / SD(PM3_LUMO)
        -0.00000 * VAdjEq / SD(VAdjEq)
        +0.00003 * VAdjMa / SD(VAdjMa)
        +0.77222 * vsa_other / SD(vsa_other)
        +0.00004 * vsurf_CW5 / SD(vsurf_CW5)
        -0.00000 * vsurf_CW6 / SD(vsurf_CW6)
        -0.81295 * vsurf_D1 / SD(vsurf_D1)
        -0.00001 * vsurf_G / SD(vsurf_G)
        +1.27714 * vsurf_HB5 / SD(vsurf_HB5)
        -0.12067 * vsurf_HB6 / SD(vsurf_HB6)
        +0.00007 * vsurf_HL1 / SD(vsurf_HL1)
        +0.00000 * vsurf_HL2 / SD(vsurf_HL2)
        +0.00181 * vsurf_ID8 / SD(vsurf_ID8)
        +1.50662 * vsurf_W1 / SD(vsurf_W1)
        +0.17301 * vsurf_W2 / SD(vsurf_W2)
        -5.46695 * vsurf_W4 / SD(vsurf_W4)
        +1.38678 * vsurf_W5 / SD(vsurf_W5)
        -0.25022 * vsurf_W6 / SD(vsurf_W6)
        -1.11588 * vsurf_Wp1 / SD(vsurf_Wp1)
        +1.28045 * PEOE_VSA+1 / SD(PEOE_VSA+1)
        -0.57034 * PEOE_VSA-1 / SD(PEOE_VSA-1)
        +2.39731 * SlogP_VSA0 / SD(SlogP_VSA0)
        -0.95689 * SlogP_VSA5 / SD(SlogP_VSA5)
        +1.09782 * SlogP_VSA9 / SD(SlogP_VSA9)
        +2.14035 * SMR_VSA1 / SD(SMR_VSA1)
        +2.64307 * SMR_VSA2 / SD(SMR_VSA2)
        +1.76413 * SMR_VSA5 / SD(SMR_VSA5)
        -2.03528 * SMR_VSA6 / SD(SMR_VSA6)
        +0.92844 * SMR_VSA7 / SD(SMR_VSA7)
```

Figure S3-1. QSAR equation of isoflavonoids and 5-LOX of 41 descriptors (R2 96.8%) by MOE software.

```
ESTIMATED NORMALIZED LINEAR MODEL (SD = Standard Deviation)

ln IC50 / SD(ln IC50) =
       -24.24517
        +0.56491 * AM1_HF / SD(AM1_HF)
        +0.00008 * AM1_IP / SD(AM1_IP)
        +1.07257 * ASA+ / SD(ASA+)
        +1.57510 * ASA_P / SD(ASA_P)
        -0.00003 * BCUT_SLOGP_1 / SD(BCUT_SLOGP_1)
        +0.12787 * CASA+ / SD(CASA+)
        -0.39724 * CASA- / SD(CASA-)
        -0.48939 * DASA / SD(DASA)
        +0.00071 * dipoleX / SD(dipoleX)
        +0.00041 * dipoleY / SD(dipoleY)
        +0.00094 * dipoleZ / SD(dipoleZ)
        -0.28216 * E / SD(E)
        -0.82894 * E_sol / SD(E_sol)
        +0.00001 * FASA+ / SD(FASA+)
        -0.00002 * FASA_H / SD(FASA_H)
        +0.00002 * FASA_P / SD(FASA_P)
        +0.00014 * FCASA+ / SD(FCASA+)
        +0.00022 * FCASA- / SD(FCASA-)
        +0.00115 * KierA1 / SD(KierA1)
        -2.29769 * MNDO_HF / SD(MNDO_HF)
        -0.00001 * npr2 / SD(npr2)
        -0.07775 * PEOE_VSA+1 / SD(PEOE_VSA+1)
        -0.00901 * PEOE_VSA-4 / SD(PEOE_VSA-4)
        -0.05346 * PEOE_VSA-6 / SD(PEOE_VSA-6)
        -0.06146 * PEOE_VSA_PPOS / SD(PEOE_VSA_PPOS)
        +0.40336 * PM3_HF / SD(PM3_HF)
        -0.00104 * PM3_LUMO / SD(PM3_LUMO)
        -0.49224 * pmiX / SD(pmiX)
        +0.00001 * Q_VSA_FHYD / SD(Q_VSA_FHYD)
        +0.00001 * Q_VSA_FNEG / SD(Q_VSA_FNEG)
        -0.00001 * Q_VSA_FPOL / SD(Q_VSA_FPOL)
        -0.00001 * Q_VSA_FPOS / SD(Q_VSA_FPOS)
        +0.82613 * Q_VSA_HYD / SD(Q_VSA_HYD)
        +0.35206 * Q_VSA_NEG / SD(Q_VSA_NEG)
        -0.19808 * Q_VSA_PNEG / SD(Q_VSA_PNEG)
        -0.79663 * Q_VSA_POL / SD(Q_VSA_POL)
        -0.36763 * Q_VSA_POS / SD(Q_VSA_POS)
        -0.33456 * Q_VSA_PPOS / SD(Q_VSA_PPOS)
        +0.05435 * SlogP_VSA1 / SD(SlogP_VSA1)
        -0.00529 * SlogP_VSA2 / SD(SlogP_VSA2)
        -0.33920 * SMR_VSA1 / SD(SMR_VSA1)
        -0.08338 * SMR_VSA3 / SD(SMR_VSA3)
        +0.00029 * vsurf_CW2 / SD(vsurf_CW2)
        +1.23373 * vsurf_D3 / SD(vsurf_D3)
        -0.00213 * vsurf_ID8 / SD(vsurf_ID8)
        -0.00033 * vsurf_IW1 / SD(vsurf_IW1)
        -0.00105 * vsurf_IW2 / SD(vsurf_IW2)
        +0.00413 * vsurf_IW3 / SD(vsurf_IW3)
        +0.33425 * PEOE_VSA-0 / SD(PEOE_VSA-0)
        -0.65369 * SlogP_VSA3 / SD(SlogP_VSA3)
        -0.79907 * SlogP_VSA9 / SD(SlogP_VSA9)
        -0.31249 * SMR_VSA7 / SD(SMR_VSA7)
```

Figure S3-2. QSAR equation of isoflavonoids and 12-LOX of 51 descriptors (R2 96.0%) by MOE software.

```
ESTIMATED NORMALIZED LINEAR MODEL (SD = Standard Deviation)

log IC50 / SD(log IC50) =
        -3.93341
       -62.11923 * AM1_Eele / SD(AM1_Eele)
        -0.00021 * AM1_HF / SD(AM1_HF)
        +1.41758 * MNDO_E / SD(MNDO_E)
       +45.97849 * MNDO_Eele / SD(MNDO_Eele)
        +0.00046 * MNDO_HF / SD(MNDO_HF)
        +0.00001 * PC+ / SD(PC+)
        -0.00001 * PC- / SD(PC-)
        +0.00125 * PEOE_VSA+0 / SD(PEOE_VSA+0)
        +0.00209 * PEOE_VSA+1 / SD(PEOE_VSA+1)
        -0.00237 * PEOE_VSA+2 / SD(PEOE_VSA+2)
        -0.00048 * PEOE_VSA+3 / SD(PEOE_VSA+3)
        +0.00034 * PEOE_VSA+4 / SD(PEOE_VSA+4)
        +0.00001 * PEOE_VSA+5 / SD(PEOE_VSA+5)
        +0.00001 * PEOE_VSA+6 / SD(PEOE_VSA+6)
        +0.00138 * PEOE_VSA-0 / SD(PEOE_VSA-0)
        -0.00263 * PEOE_VSA-1 / SD(PEOE_VSA-1)
        +0.00008 * PEOE_VSA-3 / SD(PEOE_VSA-3)
        -0.00004 * PEOE_VSA-4 / SD(PEOE_VSA-4)
        +0.00099 * PEOE_VSA-5 / SD(PEOE_VSA-5)
        +0.00009 * PEOE_VSA-6 / SD(PEOE_VSA-6)
        +0.00080 * PEOE_VSA_NEG / SD(PEOE_VSA_NEG)
        -1.67829 * PM3_E / SD(PM3_E)
       +15.44930 * PM3_Eele / SD(PM3_Eele)
        -0.00044 * PM3_HF / SD(PM3_HF)
        +0.00003 * PM3_dipole / SD(PM3_dipole)
        +0.01147 * Q_VSA_POL / SD(Q_VSA_POL)
        +0.00107 * SMR_VSA0 / SD(SMR_VSA0)
        +0.00038 * SMR_VSA1 / SD(SMR_VSA1)
        +0.00039 * SMR_VSA2 / SD(SMR_VSA2)
        -0.00012 * SMR_VSA3 / SD(SMR_VSA3)
        +0.00002 * SMR_VSA4 / SD(SMR_VSA4)
        +0.00032 * SMR_VSA5 / SD(SMR_VSA5)
        -0.00181 * SMR_VSA6 / SD(SMR_VSA6)
        +0.00419 * SMR_VSA7 / SD(SMR_VSA7)
        +0.00053 * SlogP_VSA0 / SD(SlogP_VSA0)
        +0.00010 * SlogP_VSA1 / SD(SlogP_VSA1)
        -0.00002 * SlogP_VSA2 / SD(SlogP_VSA2)
        -0.00312 * SlogP_VSA3 / SD(SlogP_VSA3)
        +0.00112 * SlogP_VSA4 / SD(SlogP_VSA4)
        +0.00089 * SlogP_VSA5 / SD(SlogP_VSA5)
        -0.00005 * SlogP_VSA6 / SD(SlogP_VSA6)
        +0.00182 * SlogP_VSA7 / SD(SlogP_VSA7)
        +0.00044 * SlogP_VSA9 / SD(SlogP_VSA9)
        +0.00001 * b_double / SD(b_double)
        +0.00002 * diameter / SD(diameter)
        -0.15497 * pmi1 / SD(pmi1)
        -0.99740 * pmiZ / SD(pmiZ)
        +0.06512 * weinerPath / SD(weinerPath)
        -0.00013 * zagreb / SD(zagreb)
```

Figure S3-3. QSAR equation of isoflavonoids and 15-LOX of 49 descriptors (R2 79.4%) by MOE software.