Novel hybrids derived from aspirin and chalcones potently suppress colorectal cancer in vitro and in vivo

Shan Lu, a, * Obinna N Obianom, b Yong Ai b, **

a College of Pharmacy, Hubei University of Chinese Medicine, Hubei 430065, PR China
b Department of Pharmaceutical Sciences, University of Maryland School of Pharmacy, Baltimore, MD 21201, United States

* Corresponding author, College of Pharmacy, Hubei University of Chinese Medicine, Hubei 430065, PR China. E-mail address: lushan9805@163.com (S. Lu).
** Corresponding author, Department of Pharmaceutical Sciences, University of Maryland School of Pharmacy, Baltimore, MD 21201, United States. E-mail address: aiyong0508@126.com (Y. Ai).
1H NMR data of chalcones 6a-p.

(E)-3-(2-hydroxyphenyl)-1-(p-tolyl)prop-2-en-1-one (6a). The title compound was prepared according to the general procedure in 68% yield. 1H-NMR (400 MHz, DMSO-d6) δ 10.49 (s, 1H), 8.23-8.13 (m, 3H), 8.00-7.97 (m, 2H), 7.48 (d, J = 7.6 Hz, 2H), 7.41 (t, J = 6.8, 7.2 Hz, 1H), 7.10 (d, J = 7.6 Hz, 1H), 7.01 (t, J = 6.8, 7.2 Hz, 1H), 2.50 (s, 3H).

(E)-3-(2-hydroxyphenyl)-1-(4-methoxyphenyl)prop-2-en-1-one (6b). The title compound was prepared according to the general procedure in 60% yield. 1H-NMR (400 MHz, DMSO-d6) δ 10.25 (s, 1H), 8.11 (d, J = 8.0 Hz, 2H), 8.02 (d, J = 15.6 Hz, 1H), 7.88 (m, 2H), 7.26 (t, J = 8.0, 7.6 Hz, 1H), 7.08 (d, J = 8.0 Hz, 2H), 6.93 (d, J = 8.0 Hz, 1H), 6.87 (t, J = 6.8, 7.2 Hz, 1H), 3.85 (s, 3H).

(E)-1-(4-chlorophenyl)-3-(2-hydroxyphenyl)prop-2-en-1-one (6c). The title compound was prepared according to the general procedure in 65% yield. 1H-NMR (400 MHz, DMSO-d6) δ 10.39 (s, 1H), 8.10-8.07 (m, 3H), 7.86-7.80 (m, 2H), 7.58 (d, J = 8.4 Hz, 2H), 7.27 (t, J = 8.0, 6.8 Hz, 1H), 6.96 (d, J = 8.0 Hz, 1H), 6.86 (t, J = 7.2, 7.6 Hz, 1H).

(E)-1-(4-bromophenyl)-3-(2-hydroxyphenyl)prop-2-en-1-one (6d). The title compound was prepared according to the general procedure in 55% yield. 1H-NMR (400 MHz, DMSO-d6) δ 10.34 (s, 1H), 8.09-8.05 (m, 3H), 7.90-7.78 (m, 4H), 7.29 (t, J = 8.0 Hz, 1H), 6.95 (d, J = 8.0 Hz, 1H), 6.89 (t, J = 6.8 Hz, 1H).

(E)-4-(3-(2-hydroxyphenyl)acryloyl)benzonitrile (6e). The title compound was prepared according to the general procedure in 50% yield. 1H-NMR (400 MHz, DMSO-d6) δ 10.39 (s, 1H), 8.25 (d, J = 7.6 Hz, 2H), 8.12-8.05 (m, 3H), 7.92-7.85 (m, 2H), 7.31 (t, J = 7.6, 8.0 Hz, 1H), 6.95 (d, J = 8.0 Hz, 6.89 (7.6, 7.2 Hz, 1H).

(E)-3-(2-hydroxyphenyl)-1-(4-nitrophenyl)prop-2-en-1-one (6f). The title compound was prepared according to the general procedure in 44% yield. 1H-NMR (400 MHz,
DMSO-d$_6$ δ 10.44 (s, 1H), 8.35-8.26 (m, 4H), 8.08 (d, $J$ = 14.6 Hz, 1H), 7.86-7.82 (m, 2H), 7.29 (t, $J$ = 6.4 Hz, 1H), 6.96-6.88 (m, 2H).

(E)-1-(4-chlorophenyl)-3-(2-hydroxy-4-methoxyphenyl)prop-2-en-1-one (6g). The title compound was prepared according to the general procedure in 47% yield. $^1$H-NMR (400 MHz, DMSO-d$_6$) δ 10.43 (s, 1H), 8.08 (d, $J$ = 8.0 Hz, 2H), 8.0 (d, $J$ = 15.6 Hz, 1H), 7.82 (d, $J$ = 15.6 Hz, 1H), 7.64 (d, $J$ = 8.0 Hz, 2H), 6.93-6.91 (m, 2H), 3.78 (s, 3H).

(E)-1-(4-chlorophenyl)-3-(2-hydroxy-5-methoxyphenyl)prop-2-en-1-one (6h). The title compound was prepared according to the general procedure in 60% yield. $^1$H-NMR (400 MHz, DMSO-d$_6$) δ 9.87 (s, 1H), 8.16 (d, $J$ = 7.6 Hz, 2H), 8.07 (d, $J$ = 15.6 Hz, 1H), 7.87 (d, $J$ = 15.6 Hz, 1H), 7.64 (d, $J$ = 7.6 Hz, 2H), 7.45 (s, 1H), 6.93-6.86 (m, 2H), 3.78 (s, 3H).

(E)-1-(4-chlorophenyl)-3-(5-fluoro-2-hydroxyphenyl)prop-2-en-1-one (6i). The title compound was prepared according to the general procedure in 65% yield. $^1$H-NMR (400 MHz, DMSO-d$_6$) δ 10.30 (s, 1H), 8.17 (d, $J$ = 7.6 Hz, 2H), 8.02 (d, $J$ = 15.6 Hz, 1H), 7.91 (d, $J$ = 15.6 Hz, 1H), 7.84 (m, 1H), 7.64 (d, $J$ = 8.0 Hz, 2H), 7.14 (t, $J$ = 8.0 Hz, 1H), 6.94-6.91 (m, 1H).

(E)-3-(5-chloro-2-hydroxyphenyl)-1-(4-chlorophenyl)prop-2-en-1-one (6j). The title compound was prepared according to the general procedure in 70% yield. $^1$H-NMR (400 MHz, DMSO-d$_6$) δ 10.61 (s, 1H), 8.20-8.18 (m, 3H), 8.02-7.92 (m, 2H), 7.64 (d, $J$ = 8.0 Hz, 1H).

(E)-3-(5-bromo-2-hydroxyphenyl)-1-(4-chlorophenyl)prop-2-en-1-one (6k). The title compound was prepared according to the general procedure in 59% yield. $^1$H-NMR (400 MHz, DMSO-d$_6$) δ 10.63 (s, 1H), 8.20-8.18 (m, 3H), 8.02-7.92 (m, 2H), 7.64 (d,
$J = 8.0 \text{ Hz, 2H}), 7.42 \text{ (d, } J = 8.0 \text{ Hz, 1H}), 6.99 \text{ (d, } J = 8.0 \text{ Hz, 1H}).$

$(E)$-1-(4-chlorophenyl)-3-(2-hydroxy-3-methoxyphenyl)prop-2-en-1-one (6l). The title compound was prepared according to the general procedure in 67% yield. $^1$H-NMR (400 MHz, DMSO-d$_6$) $\delta$ 9.51 (s, 1H), 8.13-8.07 (m, 3H), 7.82 (d, $J = 15.6$ Hz, 1H), 7.62 (d, $J = 8.0$ Hz, 2H), 7.49 (d, $J = 8.0$ Hz, 1H), 7.04 (d, $J = 8.0$ Hz, 2H), 6.84 (t, $J = 8.0$ Hz, 1H), 3.83 (s, 3H).

$(E)$-1-(4-chlorophenyl)-3-(2-hydroxy-5-methylphenyl)prop-2-en-1-one (6m). The title compound was prepared according to the general procedure in 65% yield. $^1$H-NMR (400 MHz, DMSO-d$_6$) $\delta$ 10.11 (s, 1H), 8.12 (d, $J = 8.4$ Hz, 2H), 8.04 (d, $J = 15.6$ Hz, 1H), 7.80 (d, $J = 15.6$ Hz, 1H), 7.69 (s, 1H), 7.62 (d, $J = 8.4$ Hz, 2H), 7.08 (d, $J = 8.0$ Hz, 1H), 6.83 (d, $J = 8.0$ Hz, 1H), 2.23 (s, 3H).

$(E)$-3-(2-hydroxy-5-methoxyphenyl)-1-(4-methoxyphenyl)prop-2-en-1-one (6n). The title compound was prepared according to the general procedure in 70% yield. $^1$H-NMR (400 MHz, DMSO-d$_6$) $\delta$ 9.81 (s, 1H), 8.13 (d, $J = 8.8$ Hz, 2H), 8.00 (d, $J = 16.0$ Hz, 1H), 7.85 (d, $J = 16.0$ Hz, 1H), 7.41 (s, 1H), 7.07 (d, $J = 8.0$ Hz, 2H), 6.90-6.84 (m, 2H), 3.85 (s, 3H), 3.75 (s, 3H).

$(E)$-3-(5-bromo-2-hydroxyphenyl)-1-(4-methoxyphenyl)prop-2-en-1-one (6o). The title compound was prepared according to the general procedure in 70% yield. $^1$H-NMR (400 MHz, DMSO-d$_6$) $\delta$ 10.61 (s, 1H), 8.15-8.10 (m, 3H), 7.99-7.90 (m, 2H), 7.37 (d, $J = 8.8$ Hz, 1H), 7.03 (d, $J = 8.4$ Hz, 2H), 6.90 (d, $J = 8.4$ Hz, 1H), 3.82 (s, 3H).

$(E)$-3-(5-chloro-2-hydroxyphenyl)-1-(4-methoxyphenyl)prop-2-en-1-one (6p). The title compound was prepared according to the general procedure in 70% yield. $^1$H-NMR (400 MHz, DMSO-d$_6$) $\delta$ 10.56 (s, 1H), 8.13 (d, $J = 8.8$ Hz, 2H), 8.00-7.89 (m, 3H), 7.24 (d, $J = 8.4$ Hz, 1H), 7.02 (d, $J = 8.4$ Hz, 2H), 6.94 (d, $J = 8.8$ Hz, 1H), 3.81 (s, 3H).
Spectral copies of $^1$H NMR, and $^{13}$C NMR of compounds 7a-p