Supporting information

Exploring the cytotoxic effects of the extracts and bioactive triterpenoids from *Dillenia indica* against oral squamous cell carcinoma: A scientific interpretation and validation of indigenous knowledge.

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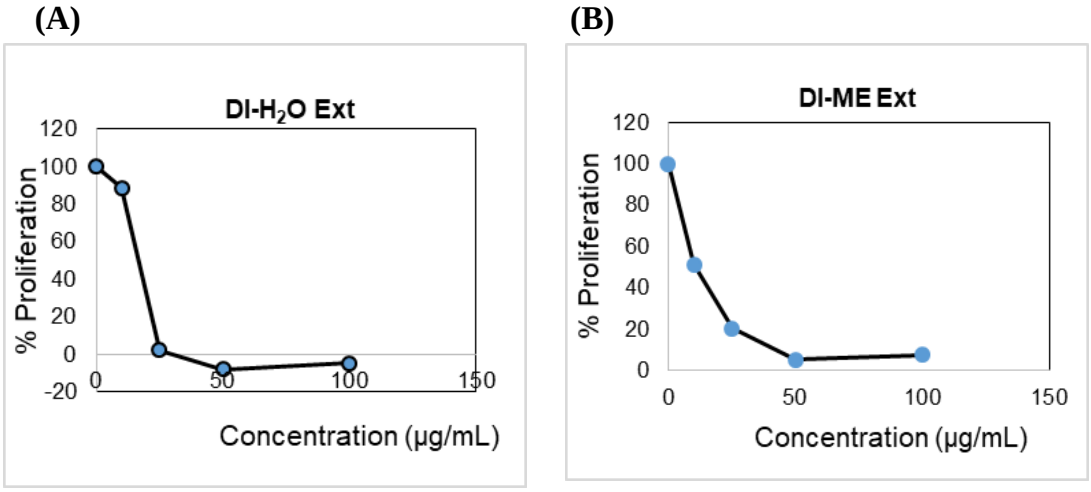

Figure S1: Inhibition of the proliferation of SAS cells by: (A) DI-H_2O Ext, with IC_{50} of 14 µg/mL (B) DI-ME Ext. with IC_{50} of 12 µg/mL.

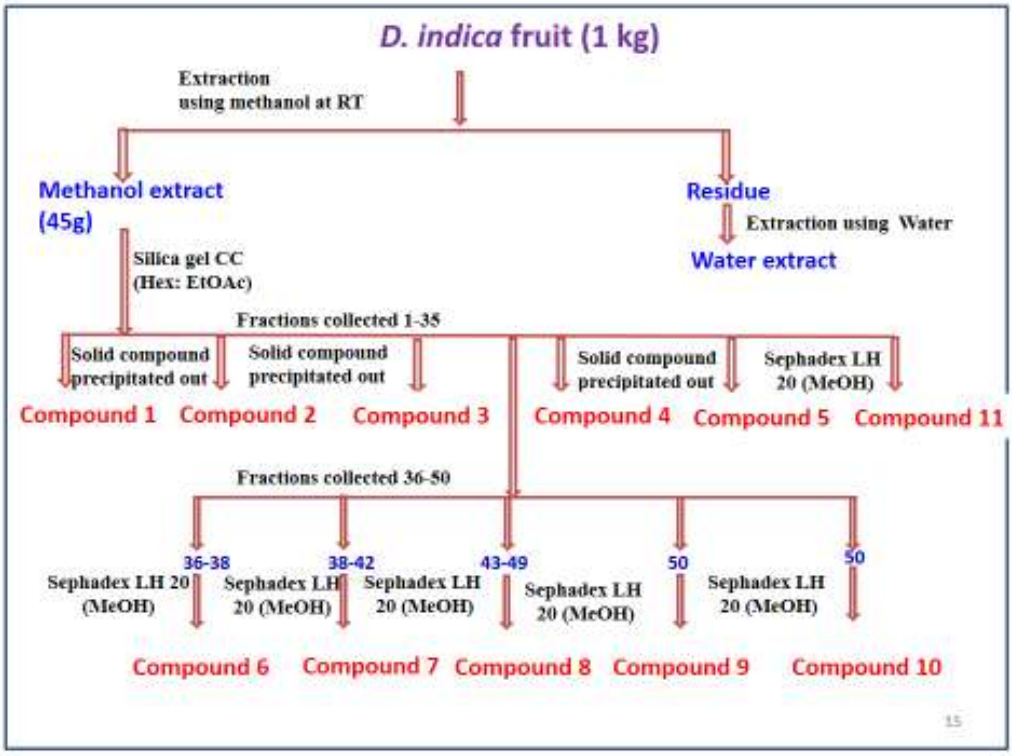

Figure S2: Extraction strategy and Isolation procedure from DI-ME Ext

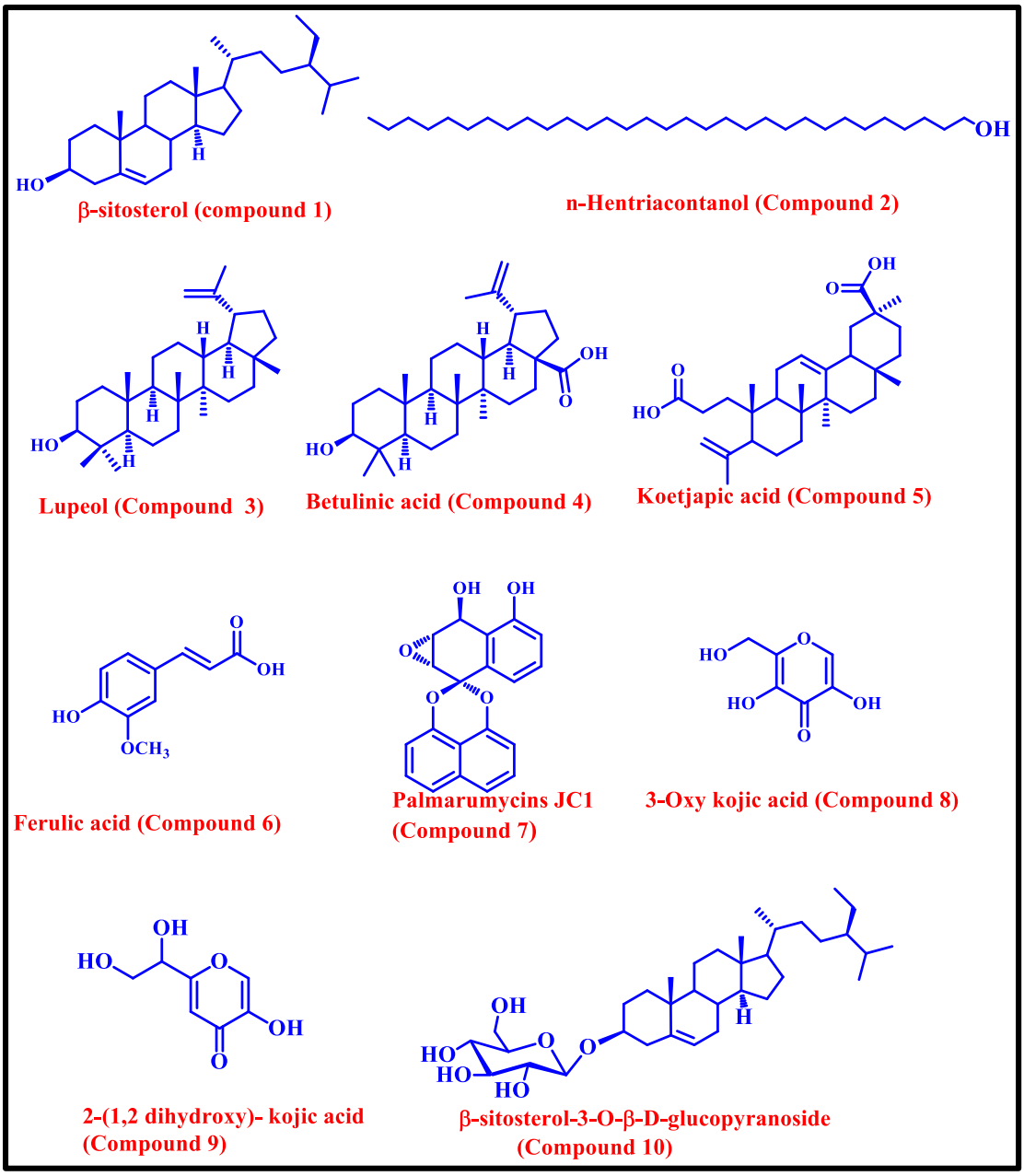

Figure S3: Structure of the molecules isolated from DI-ME Ext

Effect of isolated compounds on the proliferation of SAS cells.

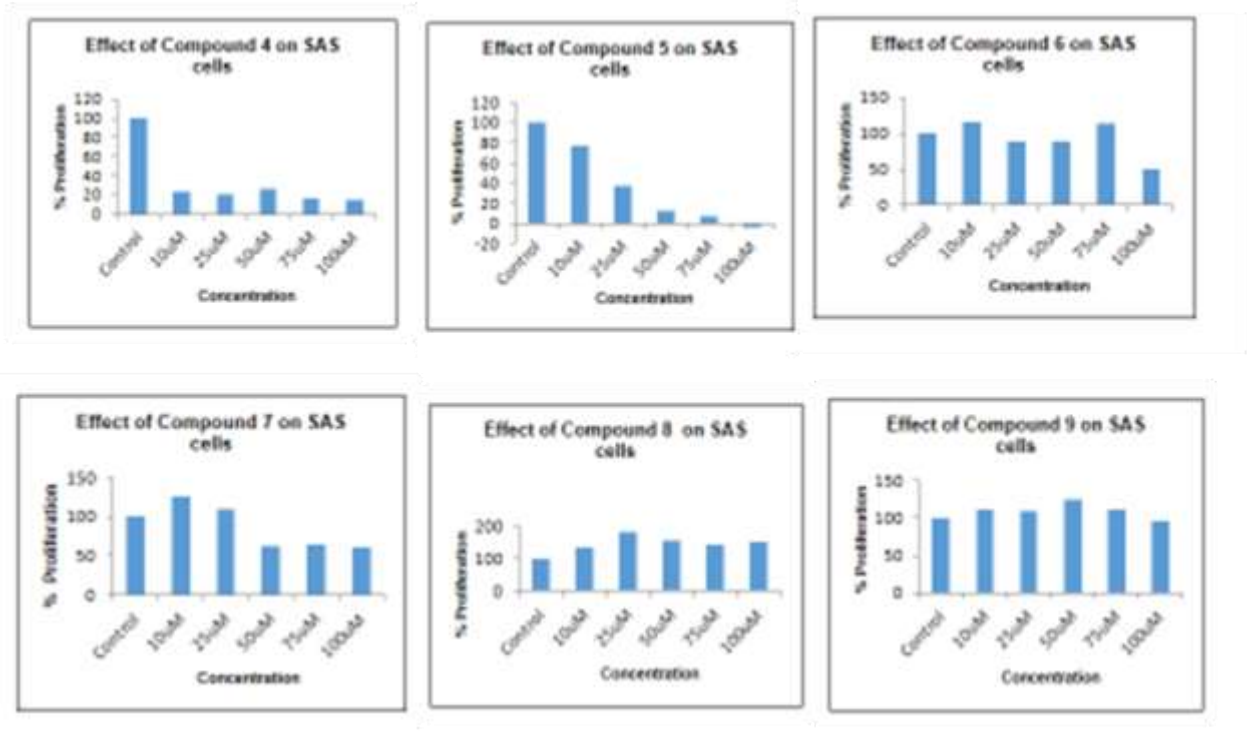

Figure S4: MTT assay of isolated molecules

Tables

Melting point	:	128-130 ^{o}C
Molecular formula	:	$C_{29}H_{50}O$
FT-IR (Neat) ν_{max}	:	3408, 3272, 2935, 2863, 1645, 1459, 1374, 1316, 1257, 1190, 1099, 1054, 1024, 958, 802 cm^{-1}
^{1}H NMR (500 MHz, $CDCl_3$)	:	δ5.37(d, 1H, *J*=5Hz), 3.53-3.54(m, 1H), 2.30-2.29(m, 2H), 2.04-1.87 (m, 2H), 1.87-1.84(m, 3H), 1.68-1.66 (m, 2H), 1.60-1.45 (m, 7H), 1.32-1.23 (m, 6H), 1.20-1.10 (m, 3H), 1.09-1.96 (m, 3H), 1.02 (s, 5H), 0.94- 0.93 (m, 3H), 0.87-0.71 (m 9H), 0.69 (s, 3H) ppm.
^{13}C NMR (125 MHz,$CDCl_3$)	:	δ140.8,121.7, 71.8, 56.8, 56.0, 50.1, 45.8, 42.3, 42.3, 39.8, 37.2, 36.5, 36.2, 33.9, 31.9, 31.7, 29.1, 28.3, 26.0, 24.3, 23.0, 21.1, 19.8, 19.4, 19.0, 18.8, 11.9, 11.9 ppm.

m/z	:	415.1097$(M+H)^+$

Table S1: NMR characterization data of compound 1

Melting point	:	97-99 ^oC
Molecular formula	:	$C_{31}H_{64}O$
FT-IR (Neat) ν_{max}	:	3318, 2927, 1046 cm^{-1}
^1H NMR (500 MHz, $CDCl_3$)	:	δ3.65 (t, *J*= 6.5 Hz, 2H), 1.60 – 1.55 (m, 5H), 1.36 – 1.22 (m, 54H), 0.88 (t, *J* = 6.5 Hz, 3H) ppm.
^{13}C NMR (125 MHz,$CDCl_3$)	:	δ63.1, 32.8, 31.9, 29.7, 29.6, 29.6, 29.5, 29.4, 25.7, 22.70, 14.1 ppm.
m/z	:	453.5035 $(M+H)^+$

Table S2: NMR characterization data of compound 2

Melting point	:	215-217 ^oC
Molecular formula	:	$C_{30}H_{50}O$
FT-IR (Neat) ν_{max}	:	3408, 3272, 2935, 2863, 1645, 1459, 1374, 1316, 1257, 1190, 1099 cm^{-1}
^1H NMR (500 MHz, $CDCl_3$)	:	δ 4.74 (s, 1H), 4.61 (s, 1H), 3.19 (dd, J_1 = 11.5, J_2= 4.4 Hz, 2H), 2.28-2.17 (m, 2H), 2.03-1.94 (m, 2H), 1.69-1.66 (m, 9H), 1.63 – 1.61 (m, 10H), 1.59-1.37 (m, 20H), 1.25 (s, 3H), 0.97 (s, 3H), 0.96 (s, 3H), 0.93 (s, 3H), 0.82 (S, 3H), 0.75 (s, 3H) ppm.
^{13}C NMR (125 MHz,$CDCl_3$)	:	δ150.7, 109.9, 79.1, 56.3, 55.3, 53.2, 50.5, 46.9, 42.4, 38.9, 38.3, 37.2, 37.1, 32.2, 29.5, 27.9, 25.4, 22.7, 18.3, 16.1, 16.0, 15.3, 14.6, 14.2 ppm.
m/z	:	427.3939 $(M + H)^+$

Table S3: NMR characterization data of compound 3

Melting point	:	312-314 ^{o}C
Molecular formula	:	$C_{30}H_{48}O_3$
FT-IR (Neat) ν_{max}	:	3428, 3075, 2944, 2671, 1693, 1454, 1440, 1379, 1143 cm^{-1}
^{1}H NMR (500 MHz, DMSO d6)	:	δ12.08 (s, 1H), 4.69 (d, J = 2Hz, 1H), 4.56 (s, 1H), 4.28 (s, 1H), 3.02 – 2.93 (m, 2H), 2.25 – 2.19 (m, 1H), 2.12-2.09 (M, 1H), 1.84 – 1.77 (m, 2H), 1.65 (s, 3H), 1.54 – 1.08 (m, 20H), 0.93 (s, 3H), 0.87 (s, 6H), 0.77 (s, 3H), 0.65 (s, 3H) ppm.
^{13}C NMR (125 MHz, DMSO d6)	:	δ177.7, 150.8, 110.1, 77.2, 55.9, 55.4, 50.4, 48.9, 47.1, 42.5, 38.9, 38.7, 38.0, 37.2, 36.8, 34.4, 32.2, 30.6, 29.7, 28.6, 27.6, 25.5, 20.9, 19.4, 18.4, 16.4, 16.3, 16.2, 14.8 ppm.
m/z	:	455.3525$(M-H)^{+}$

Table S4: NMR characterization data of compound 4

Melting point	:	296-298 ^{o}C
Molecular formula	:	$C_{30}H_{46}O_4$
FT-IR (Neat) ν_{max}	:	3440, 2978, 2860, 1706, 1702, 1698, 1694, 1454, 1387, 1281, 1230, 1192, 906 cm^{-1}
^{1}H NMR (500 MHz, DMSO)	:	δ5.17 (s, 1H), 4.40 (d, J = 4.5 Hz, 21H), 4.31 (d, J = 4.5 Hz, 1H), 2.74 (dd, J_1 = 9.5, J_2= 4 Hz, 2H), 1.96 – 1.83 (m, 4H), 1.78 – 1.57 (m, 1H), 1.57 – 1.39 (m, 6H), 1.32-1.30 (m, 2H), 1.23- 1.18 (m, 4H), 1.15-0.98 (m, 7H), 0.92 (s, 3H), 0.90 (s, 3H), 0.88 (s, 6H), 0.79-0.75 (m, 2H), 0.71 (s,3H), 0.70 (s, 3H) ppm.
^{13}C NMR (125 MHz,DMSO)	:	δ 177.8, 176.9, 146.9, 144.4, 121.8, 107.9, 82.8, 67.6, 55.2, 47.7, 47.5, 46.3, 46.1, 39.6, 39.4, 38.2, 33.3, 32.7, 32.6, 31.2, 30.2, 29.3, 27.6, 26.0, 23.9, 23.6, 23.09, 18.5, 17.6, 17.4, 16.7 ppm.

m/z	:	469.3317(M-H)$^+$

Table S5: NMR characterization data of compound 5

Melting point	:	170-172 ^{o}C
Molecular formula	:	$C_{10}H_{10}O_4$
FT-IR (Neat) ν_{max}	:	3436, 2961, 2933, 2872, 1692, 1128, 1074, 1001cm^{-1}
^{1}H NMR (500 MHz, CD_3COCD_3)	:	δ8.27 (bs, 1H), 7.62 (d, J = 16 Hz, 1H), 7.35 (d, J = 2 Hz, 1H), 7.20 (dd, J_1 = 8.5, J_2=2 Hz, 1H), 6.90 (d, J = 8.5 Hz, 1H), 6.74 (d, J = 16 Hz, 1H), 3.94 (s, 3H) ppm.
^{13}C NMR (125 MHz, CD_3COCD_3)	:	δ 183.7, 149.2, 147.9, 140.5, 130.0, 122.9, 121.4, 115.4, 110.6, 55.4 ppm.
m/z	:	193.0500 (M-H)$^+$

Table S6: NMR characterization data of compound 6

Melting point	:	210-212 ^{o}C
Molecular formula	:	$C_{20}H_{14}O_5$
FT-IR (Neat) ν_{max}	:	3050, 1605, 1455, 1409 cm^{-1}
^{1}H NMR (500 MHz, DMSO)	:	δ9.90 (s, 1H), 7.63 (dd, J_1 = 12.5, J_2= 8.5 Hz, 2H), 7.56 (t, J = 7.5 Hz, 1H), 7.51 (t, J = 7.5 Hz, 1H), 7.25 (t, J = 7.5 Hz, 1H), 7.15 – 7.12 (m, 2H), 6.98 – 6.96 (m, 2H), 5.54 (bs, 1H), 5.32 (s, 1H), 3.61 (d, J = 3.5 Hz, 1H), 3.50 (dd, J_1 = 4.5, J_2= 2.5 Hz, 1H) ppm.
^{13}C NMR (125 MHz, DMSO)	:	δ 156.2, 147.7, 147.7, 134.2, 132.5, 129.5, 128.34, 128.3, 122.9, 121.2, 121.0, 117.6, 116.8, 112.9, 109.8, 109.4, 98.1, 59.5, 53.7, 50.2 ppm.
m/z	:	357.0691 (M+Na)$^+$

Table S7: NMR characterization data of compound 7

Melting point	:	153-155 ^{o}C
Molecular formula	:	$C_6H_6O_5$
FT-IR (Neat) ν_{max}	:	3271, 3175, 2948, 2668, 1706, 1697 cm^{-1}
^{1}H NMR (500 MHz, DMSO)	:	δ9.05 (s, 1H), 9.01 (s, 1H), 8.05 (s, 1H), 5.38 (t, J = 5.5 Hz, 1H), 4.40 (d, J = 5.5 Hz, 2H) ppm.
^{13}C NMR (125 MHz,DMSO)	:	δ169.6, 150.7, 144.8, 141.7, 139.8, 55.8 ppm.
m/z	:	157.0137$(M-H)^{+}$

Table S8: NMR characterization data of compound 8

Melting point	:	163-167 ^{o}C
Molecular formula	:	$C_7H_8O_5$
FT-IR (Neat) ν_{max}	:	3270, 3175, 3099, 2948, 2668, 1706, 1697 cm^{-1}
^{1}H NMR (500 MHz, DMSO)	:	δ9.07 (bs, 1H), 8.03 (s, 1H), 6.34 (s, 1H), 5.69 (s, 1H), 4.29 (d, J = 3 Hz, 2H), 4.13 (d, J = 5.0 Hz, 1H), 3.17 (d, J = 4.3 Hz, 1H) ppm.
^{13}C NMR (125 MHz, DMSO)	:	δ174.4, 168.5, 146.1, 139.7, 110.1, 59.9, 49.2 ppm.
m/z	:	171.0293$(M-H)^{+}$

Table S9: NMR characterization data of compound 9

Melting point	:	275-284 ^{o}C
Molecular formula	:	$C_{35}H_{60}O_6$
FT-IR (Neat) ν_{max}	:	3400, 2900 cm^{-1}.
^{1}H NMR (500 MHz, DMSO-d_6)	:	δ 5.34 (d, 1H, *J*=5Hz), 4.90-4-87 (m, 3H), 4.46-4.44(m, 1H), 4.23 (d, 1H, *J*=8Hz), 3.64-3.63 (m, 1H), 3.47-3.43 (m,

		2H), 3.13-3.12 (m, 1H), 3.10-3.07 (m, 1H), 3.02-3.01 (m, 1H), 2.90-2.89 (m, 1H), 2.36-2.35 (m, 1H), 2.13-2.10 (m, 1H), 1.95-1.94 (m, 2H), 1.81-1.79 (m, 3H), 1.53-1.51 (m, 1H), 1.51-1.40 (m, 6H), 1.28-1.23 (m, 6H), 1.21-1.19 (m, 4H), 0.96 (s, 3H), 0.91 (s, 5H), 0.82 (m, 9H), 0.66 (s, 3H) ppm.
^{13}C NMR (125 MHz, DMSO-d_6)	:	δ 140.4, 121.2, 100.7, 99.5, 76.9, 76.7, 73.4, 70.1, 61.1, 56.1, 55.4, 49.6, 45.1, 41.8, 38.3, 36.8, 36.2, 35.4, 33.3, 31.4, 31.3, 29.2, 28.7, 27.8, 25.4, 23.8, 22.6, 20.6, 19.7, 19.1, 18.9, 18.6, 11.8, 11.6 ppm
m/z	:	577.4013$(M+1)^+$

Table S10: NMR characterization data of compound 10

Computational screening of BA and KA

QikProp analysis

Inorder to check the druggability of the ligands-BA and KA, we carried out the QikProp anlaysis (~~Table 1~~ Table S11), which predict the ADME/T properties of the ligands based on the parameters already defined by the software. The important parameters we selected are: #stars (few stars-more drug-like): 0 to 5; M.W.(Molecular Weight):130.0 to 725.0; HBA (Hydrogen bond acceptor): 2.0 to 20.0; HBD(hydrogen bond donor): 0.0 to 6.0; CNS (Central Nervous System activity): -2 to +2; FISA (hydrophilic component of the SASA on N, O, and H on heteroatoms) 7.0 to 330.0; QPlogS (Aqueous solubility): -6.5 to 0.5; QPlogPo/w(octanol/water partition coefficient): -2.0 to 6.5; QPlogKhsa(binding to human serum albumin): -1.5 to 1.5; % HOA (%human oral absorption): >70, good and Ro5(Number of violations of Lipinski's rule of five): maximum is 4. From the output values, it is very clear that both the ligands are druggable with few #stars, 2 hydrogen bond donors and 4 hydrogen bond acceptors. The low CNS value and high %HOA indicate their high oral availability with less central nervous system toxicity. The octanol/water partition coefficient and binding to human serum albumin are also indicated the effectiveness of these drugs with only one violation from the Lipinski's rule of five (Ro5).

Table S11. Predicted ADME/T properties of BA and KA

Compound	*#stars*	*M.W.*	*HBA*	*HBD*	*CNS*	*FISA*	*QPlogS*	*QPlogPo/w*	*QPlogKhsa*	*%HOA*	*Ro5*

BA	*0*	*456.71*	*3.7*	*2*	*-1*	*95.96*	*-6.50*	*6.09*	*1.31*	*94.20*	*1*
KA	*0*	*470.69*	*4*	*2*	*-2*	*160.68*	*-6.09*	*6.286*	*1.11*	*73.69*	*1*