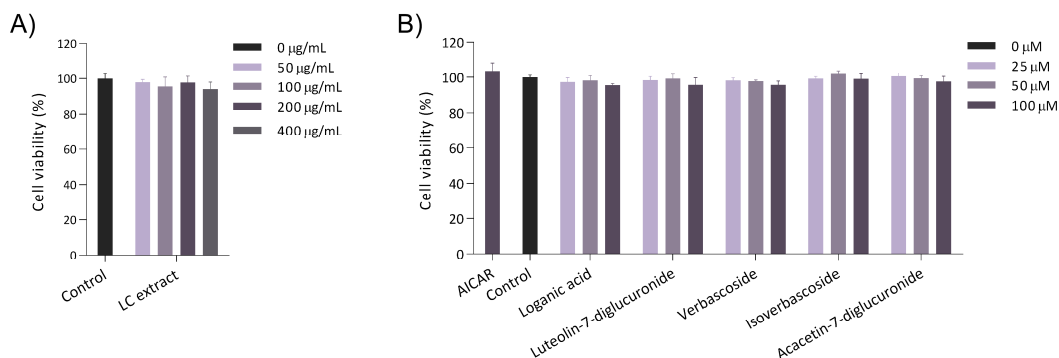


## Supplementary



**Supplementary Figure 1.** Cell viability of adipocytes 3T3-L1 after 24 h of incubation with LC extract (A) or individual compounds (B). Number of cells was counted by staining nuclei with Hoechst. AICAR was incubated at 100 µM for 24 h and represented in panels B. All the treatments are normalized to their respective controls in DMSO or water depending on the solubility of the compounds. The data are expressed as the mean  $\pm$  S.D (n = 5).

**Supplementary Table 1.** Details of the interaction of loganic acid docked to the human AMPK (see Figure 4C).

Cluster number	$\Delta G$ , [kcal/mol]	Dissoc. constant, [ $\mu$ M]	Members	Residues of the AMPK that contact loganic acid
1	-9.735 $\pm$ 1.015	0.073095	4.85%	ARG(A)-369, LYS(A)-399, ALA(A)-400, TRP(A)-402, ILE(B)-214, LEU(B)-215, ASN(B)-216, LYS(B)-217, ASP(B)-218, THR(B)-219, LEU(B)-228, LEU(B)-242, LEU(B)-265, TYR(B)-267, LYS(B)-47, THR(B)-66, ASN(B)-67
2	-9.626 $\pm$ 0.899	0.087846	6.06%	LYS(A)-364, PRO(A)-365, HIS(A)-366, PRO(A)-367, ARG(A)-369, MET(A)-370, PRO(A)-371, ILE(E)-240, PHE(E)-244, ASP(E)-245, ASN(E)-248, LEU(E)-266, HIS(E)-268, ARG(E)-269, TYR(E)-272, PHE(E)-273, GLU(E)-274, GLY(E)-275, VAL(E)-276, LEU(E)-277, VAL(E)-297
3	-9.603 $\pm$ 0.892	0.091275	2.12%	ARG(E)-70, LEU(E)-74, GLY(E)-84, MET(E)-85, LEU(E)-86, THR(E)-87, THR(E)-89, ASP(E)-90, ARG(E)-118, TYR(E)-121, LYS(E)-127, LEU(E)-129, VAL(E)-130, CYS(E)-131, LYS(E)-149, ILE(E)-150, HIS(E)-151, ARG(E)-152, LEU(E)-153, PRO(E)-154, LYS(E)-243
4	-9.340 $\pm$ 1.363	0.142345	3.83%	LEU(A)-373, LYS(A)-398, LYS(A)-399, ALA(A)-400, TRP(A)-402, LEU(B)-215, LEU(B)-242, LYS(B)-245, ASP(B)-246, VAL(B)-248, VAL(B)-250, LEU(B)-265, TYR(B)-267, LYS(E)-59, PHE(E)-62, ALA(E)-63, THR(E)-66, ASN(E)-67

5	-9.121±1.164	0.206011	2.02%	GLY(E)-199, THR(E)-200, ALA(E)-202, ASN(E)-203, ILE(E)-204, ALA(E)-205, HIS(E)-223, ARG(E)-224, VAL(E)-225, SER(E)-226, ALA(E)-227, LEU(E)-228, PRO(E)-229, ARG(E)-299, ILE(E)-312, VAL(E)-313, SER(E)-314, SER(E)-316, ASP(E)-317
---	--------------	----------	-------	--

**Supplementary Table 2. Details of the interaction of luteolin 7-diglucuronide docked to the human AMPK (see Figure 4D).**

Cluster number	$\Delta G$ , [kcal/mol]	Dissoc. constant, [ $\mu M$ ]	Members	Residues of the AMPK that contact luteolin 7-diglucuronide
1	-11.696±1.722	0.002669	1.11%	LEU(A)-373, VAL(A)-397, LYS(A)-398, LYS(A)-399, ALA(A)-400, LYS(A)-401, TRP(A)-402, LEU(B)-215, ASN(B)-216, LEU(B)-242, SER(B)-243, LYS(B)-245, ASP(B)-246, VAL(B)-248, VAL(B)-250, TYR(B)-267, LYS(E)-47, LYS(E)-59, PHE(E)-62, ALA(E)-63, THR(E)-66, ASN(E)-67
2	-10.279±1.223	0.029203	1.01%	ARG(A)-369, MET(A)-370, PRO(A)-371, PRO(A)-372, LEU(A)-373, VAL(A)-397, LYS(A)-398, LYS(A)-399, ALA(A)-400, TRP(A)-402, LEU(B)-215, LYS(B)-217, ASP(B)-218, THR(B)-219, ILE(B)-221, LEU(B)-242, LEU(B)-265, LYS(E)-47, VAL(E)-65, THR(E)-66, ASN(E)-67, GLY(E)-68
3	-11.485±1.304	0.00381	0.91%	ARG(E)-70, GLY(E)-84, MET(E)-85, LEU(E)-86, THR(E)-87, ILE(E)-88, THR(E)-89, ASP(E)-90, ASN(E)-93, TYR(E)-121, LYS(E)-127, PRO(E)-128, LEU(E)-129, VAL(E)-130, ASN(E)-148, LYS(E)-149, ILE(E)-150, HIS(E)-151, ARG(E)-152, PHE(E)-220, VAL(E)-221, ARG(E)-224, SER(E)-226, LYS(E)-243
4	10.427±1.529	0.022743	2.12%	LYS(A)-364, PRO(A)-365, HIS(A)-366, PRO(A)-367, GLU(A)-368, ARG(A)-369, MET(A)-370, PRO(A)-371, PHE(E)-244, ASP(E)-245, HIS(E)-268, ARG(E)-269, HIS(E)-271, TYR(E)-272, PHE(E)-273, GLU(E)-274, GLY(E)-275, LEU(E)-277

**Supplementary Table 3. Details of the interaction of verbascoside docked to the human AMPK (see Figure 4E).**

Cluster number	$\Delta G$ , [kcal/mol]	Dissoc. constant, [ $\mu M$ ]	Members	Residues of the AMPK that contact verbascoside
1	-10.500±1.226	0.020111	1.05%	ARG(A)-369, MET(A)-370, PRO(A)-371, PRO(A)-372, LEU(A)-373, LYS(A)-399, ALA(A)-400, TRP(A)-402, LYS(B)-217, ASP(B)-218, THR(B)-219, PRO(B)-225, LEU(B)-228, LEU(B)-242, VAL(B)-250, LEU(B)-265, TYR(B)-267, LYS(E)-47,

VAL(E)-65, THR(E)-66, ASN(E)-67, GLY(E)-68

2	-10.190±0.440	0.033937	2.50%	ASP(A)-128, HIS(A)-131, ARG(A)-132, MET(A)-164, ALA(A)-191, PRO(A)-193, GLU(A)-194, ILE(A)-197, THR(A)-258, ILE(A)-259, LYS(A)-260, GLU(A)-291, HIS(B)-209, GLU(B)-230, PRO(B)-231, ASN(B)-232, HIS(B)-233, LYS(B)-259, TYR(B)-261, THR(E)-44
3	-10.120±1.228	0.038193	3.61%	GLU(A)-295, GLU(A)-298, LYS(A)-299, PHE(A)-300, GLU(A)-301, ILE(A)-327, ASN(A)-330, ARG(A)-331, MET(A)-334, LYS(B)-258, SER(E)-35, HIS(E)-36, ARG(E)-37, TYR(E)-39, ASP(E)-40, ASN(E)-135
4	-9.700±0.540	0.077597	4.21%	TRP(B)-84, GLY(B)-86, GLY(B)-87, GLY(B)-88, LYS(B)-89, LYS(B)-126, VAL(B)-129, ASP(B)-130, GLN(B)-132, TRP(B)-133, THR(B)-134, HIS(B)-135, ASP(B)-136, PRO(B)-137, GLY(B)-147, THR(B)-148, VAL(B)-149
5	-9.540±0.362	0.101655	3.85%	GLY(A)-9, ARG(A)-10, VAL(A)-11, LYS(A)-12, LEU(B)-103, PRO(B)-104, LEU(B)-105, THR(B)-106, ARG(B)-107, VAL(B)-113, ALA(B)-114, ILE(B)-115, LEU(B)-116, ASP(B)-117
6	-11.777±1.159	0.002328	1.07%	LYS(A)-364, PRO(A)-365, HIS(A)-366, PRO(A)-367, GLU(A)-368, ARG(A)-369, MET(A)-370, PRO(A)-371, ILE(E)-240, PHE(E)-244, ASP(E)-245, HIS(E)-268, ARG(E)-269, TYR(E)-272, PHE(E)-273, GLU(E)-274, GLY(E)-275, VAL(E)-276, LEU(E)-277, LYS(E)-278, ARG(E)-291, ALA(E)-295, VAL(E)-297, ARG(E)-299
7	-10.240±0.232	0.031190	1.06%	VAL(E)-83, GLY(E)-84, MET(E)-85, THR(E)-89, ASN(E)-93, ARG(E)-118, TYR(E)-121, LEU(E)-122, GLN(E)-123, ASP(E)-124, SER(E)-125, LYS(E)-127, PRO(E)-128, LEU(E)-129, VAL(E)-130, ASN(E)-148, LYS(E)-149, ILE(E)-150, ARG(E)-152, PRO(E)-154, ARG(E)-224, LYS(E)-243
8	-9.880±0.142	0.057267	2.03%	ILE(E)-204, ALA(E)-205, MET(E)-206, VAL(E)-207, ARG(E)-208, THR(E)-209, THR(E)-210, THR(E)-211, PRO(E)-212, VAL(E)-215, ILE(E)-219, VAL(E)-231, ASP(E)-232, GLU(E)-233