**S1 Table**: List of Mixtures with information about Compounds

| **Mixture No.** | **Compound Name** |
|---|---|
| Mixture 1 | 2-(carboxymethyl)benzoic acid<br>catechin hydrate (compound **1**). |
| Mixture 2 | Tetrahydroxy-1,4-quinone monohydrate<br>sodium (4-(*N*-thiazol-2-ylsulfamoyl) phenyl) amide<br>Indanol<br>Thymol |
| Mixture 3 | D, *L*-Camphene<br>(+)-Menthofuran<br>Plumbagin<br>Sclareol |
| Mixture 4 | 3,4-dihydroxy-L-phenylalanine, 2-benzylphenol, and 4-(phenyl amino)phenol (compound **2**) |
| Mixture 5 | 2,2,6,6-tetramethyl-4-piperidinol<br>3-hydroxypyridine<br>3-Hydroxy-4-methoxybenzyl alcohol<br>sodium (4-aminophenylsulfonyl) (quinoxalin-2-yl) amide |
| Mixture 6 | Troxerutin; 3', 4', 7-Tris[O-(2-hydroxyethyl) rutin<br>2,2,6-trimethylpiperidin-4-one hydrochloride<br>3-ethoxy-4-hydroxybenzaldehyde |
| Mixture 7 | bromofenac sodium,<br>2,3,4-trihydroxybenzophenone (Compound **3**). |
| Mixture 8 | 1-Hydroxy-2-naphthoic acid<br>8-hydroxyquinoline-5-sulfonic acid mono hydrate<br>3-hydroxypyridine<br>2,2,6,6-tetramethyl-4-piperidinol |
| Mixture 9 | sitagliptin and 4-hydroxynaphthalene-1,2-dione (Compound **4**)**.** |
| Mixture 10 | 3-hydroxy-4-nitrobenzoic acid<br>(2,2,6-trimethylpiperidin-4-one hydrochloride<br>(Ethoxymethylene-malononitrile<br>Cholesteryl acetate |
| Mixture 11 | desloratadine and *N*-(4-amino-2,5-diethoxyphenyl)benzamide (compound **5**) |
| Mixture 12 | Nimesulide<br>(*p*-Toluidine hydrochloride |
| Mixture 13 | (+)-Bicuculline<br>Baicalein |

| | |
|---|---|
| | Sesamol<br>(-)-Nicotine pestanal |
| Mixture 14 | 5-Chloro salicylic acid, (Compound **6**)<br>4-Hexylresorcinol |
| Mixture 15 | Salicylaldehyde hydrazine<br>*Bis* (*m*-nitro phenyl) Disulfide |
| Mixture 16 | Biphenyl-2-carboxylic acid<br>3,5-dimethoxy-4-hydroxy benzaldehyde<br>m-methoxycinnamic acid<br>(4-biphenylyl)-2-propanol |
| Mixture 17 | (4-(trifluoromethyl)phenyl) methanol,<br>compound **7,**<br>4-methylbenzenesulfonamide, compound **8,**<br>*p*-tolyl acetic acid,<br>5-indanol. |
| Mixture 18 | 1-Amino-2-naphthol-4-sulfonic Acid<br>3-Amino-4-methoxybenzamide<br>Alizarin(1,2-Dihydroxy-anthraquinone)<br>Anisic Acid (4-Methoxybenzoic acid) |
| Mixture 19 | 3-Bromo-4-chlorobenzotrifluoride<br>5-Bromo-3-hydroxyoxindole<br>2-Bromo-4,5-methylenedioxycinnamic Acid<br>(5(4)-amino-4(5)- (amino carbonyl)-imidazole hydrochloride |
| Mixture 20 | 2,4,6-tribromoaniline<br>4,4' BiPiperidyldihydrochloride<br>*p*-Thiocresol<br>2-Mercaptopyridine N-oxide-sodium salt hydrate |
| Mixture 21 | Benzyl Carbamate<br>Salicylaldehyde hydrazine<br>Methyl gallate |
| Mixture 23 | (-)-*N*, *N*, *N*-Tetramethyl-D-tartaramide (*L* (-)-thiazolidine-4-carboxylic acid:<br>(2-oxo-2*H*-chromene-3-carboxylic acid |
| Mixture 24 | 4-Hydroxy-3-methoxybenzyl alcohol:<br>3,7-dimethyl-1*H*-purine-2,6(3*H*,7*H*)-dione: |
| Mixture 25 | Cresol red<br>(*E*)-2-hydroxy-5-((4-(*N*-pyridin-2-ylsulfamoyl) phenyl) diazenyl) benzoic acid:<br>(*L* (-) Menthol : |
| Mixture 26 | 5-hydroxy-2-nitrobenzaldehyde, compound **9**, 2,3,5,6-tetramethyl pyrazine, 3-(trifluoromethyl) phenyl acetic acid, and 2,3,5,6-tetramethylbenzene-1,4-diamine. |
| Mixture 27 | 2-mercaptopyrimidine<br>1,3,5-triazine-2,4,6-triamine<br>1-napthol-3,6-disulfonic acid, disodium salt<br>5-chloro-8-hydroxyquinoline |

| | |
|---|---|
| Mixture 28 | 4-hydroxy-3-nitrosonaphthalene-1-sulfonic acid tetra hydrate:<br>(4-hexylbenzene-1,3-diol:<br>(Sodium (*E*)-4,5-dihydroxy-3-((4-sulfonatophenyl) diazenyl) naphthalene-2,7-disulfonate: |
| Mixture 29 | guaifenesin, clioquiniol, nicotinic acid<br>compound **10**, and serotinin HCl. |
| Mixture 30 | (*p*-Tolyl-hydrazine hydrochloride:<br>(3-Bromo-5-chloro Salicylaldehyde:<br>(2-Bromo-5-fluorobenzaldehyde: |
| Mixture 31 | (3-(4-hydroxyphenyl)-propionic acid<br>(4-Ethyl benzoic acid |
| Mixture 32 | Salicin<br>(4-[4-(trifluoromethyl)-phenoxy] phenol:<br>2-mercaptonicotinic acid<br>*p*-Methoxycinnamic acid (Compound **11**) |
| Mixture 33 | (2-(4-biphenylyl)-2-propanol:<br>(Nicotinic acid: |
| Mixture 34 | (4-Amino-2,6-dibromophenol<br>(2-n-propylphenol |
| Mixture 35 | (*N*-(Benzyloxycarbonyloxy) succinimide<br>(2. 2-amino-p-cresol |
| Mixture 36 | (Bis(4-hydroxyphenyl)sulfide<br>(Phloroglucinol dehydrate |
| Mixture 37 | (Benzoin<br>(Anisic Acid (4-Methoxybenzoic acid |
| Mixture 38 | hydroquinone compound **12**)<br>Vitamin A Palmitate |

**S2 Table**: Cytotoxic activity of compounds towards BJ and HCT116 Cells

| **Compound** | **BJ Cell line** | **HCT-116** | **$IC_{50}$ ± SEM (µM)** |
|---|---|---|---|
| Compound **1** | NC* | NC | - |
| Compound **2** | NC | Cytotoxic | 81.9 ± 0.39 |
| Compound **3** | NC | Cytotoxic | 222.5 ± 8.1 |
| Compound **4** | NC | NC | - |
| Compound **5** | NC | Cytotoxic | 143 ± 1.94 |
| Compound **6** | NC | NC | - |
| Compound **7** | NC | NC | - |
| Compound **8** | NC | NC | - |
| Compound **9** | NC | NC | - |
| Compound **10** | NC | NC | - |
| Compound **11** | NC | NC | - |
| Compound **12** | NC | Cytotoxic | 31.11 ± 9.9 |
| **Tunicamycin** | - | Cytotoxic | **0.22 ± 0.78** |
| **Cyclohexamide** | Cytotoxic | - | **0.20 ± 0.10** |

Tunicamycin was used as a reference compound against HCT116 cells while Cyclohexamide was used as reference compound against BJ cells,

(NC*= non- cytotoxic).

S3 Table: Sequence of genes studied for the RT-PCR

| **Primer for gene** | **Sequence** |
|---|---|
| GAPDH-forward | 5'-cacatggcctccaaggagtaa-3' |
| GAPDH-reverse | 5' cttcaaggggtctacatggca-3' |
| MDM2- forward | 5'-gaacttggtagtagtcaatcagc-3' |
| MDM2-reverse | 5'-gcctgatacacagtaacttgata-3' |
| p53-forward | 5'-ctcctggcccctgtcatcttc3' |
| p53-reverse | 5'-agcgcctcacaacctccgtca-3' |
| c-Myc- forward | 5'-cttctctccgtcctcggattct-3' |
| c-Myc-reverse | 5'-gaaggtgatccagactctgacctt-3' |

| | |
|---|---|
| USP7-forward | 5'-ctctcagaccatgggatttccac-3' |
| USP7-reverse | 5'-attggtgtgtagatatgcccacag-3' |

S4 Table **:** Reported biological activities of compounds that interact USP7 enzyme.

| **Compound Code** | **Biological Activity** |
|---|---|
| Compound **1 (ss075)** | Anti-oxidant, anti-cancer, and in-vitro anti-epileptic activities |
| Compound **2 (Ss043)** | *In-vitro* anti-microbial activity |
| Compound **3 (ss046)** | Negatively modulate the activity of p8 subunit of transcription factor |
| Compound **4 (ss054)** | *In-vitro* anti-microbial activity |
| Compound **5 (SS039)** | Anti-microbial, analgesic, and anti-inflamatory activities |
| Compound **6 (AAB407)** | *In-vitro* anti-microbial activity |
| Compound **7 (AAB431)** | Anti-bacterial, anti-cancer, anti-oxidant activities |
| Compound **8 (AAB430)** | *In-vitro* anti-microbial activity |
| Compound **9 (AAB438)** | Xanthine oxidase inhibitory activity |
| Compound **10 (DB075)** | For curing pellagra disease |
| Compound **11 (AAB422)** | *In-vitro* anti-microbial activity |
| Compound **12 (DB190)** | For curing hyper-pigmentation |