|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Table 1: Final screened bioactive compounds** | | | | | | | | | | | |
| **S.NO.** | **MOLECULE NO** | **PUBCHEM ID** | **BIOACTIVE COMPOUNDS** | **PREDICTED ORAL BIOAVALIBLITY#** | **PREDICTED DRUGLIKENESS$** | **CYP** | **P-GP SUBSTRATE** | **BBB PERMEABILITY** | **GI ABSORPTION** | **WATER SOLUBLITY** | **LOG Kp (CM/S)** |
| **1** | **Molecule 2** | **561497** | 2H-Indeno[1,2-b]oxirene, octahydro-, (1a.alpha.,1b.beta.,5a.alpha.,6a.alpha.)- | 0.55 | YES | NO | NO | YES | HIGH | SOLUBLE | -5.45 cm/s |
| **2** | **Molecule 3** | **600027** | 6,6-Dimethyl-2-(2-methyl-allyl)-1,6- dihydropyrimidine-4- carbonitrile | 0.55 | YES | NO | NO | YES | HIGH | SOLUBLE | -6.38 cm/s |
| **3** | **Molecule 4** | **76705** | Isoquinoline, 3,4-dihydro- | 0.55 | YES | NO | NO | YES | HIGH | SOLUBLE | -6.16 cm/s |
| **4** | **Molecule 5** | **111037** | 3-Cyclohexene-1-methanol, .alpha.,.alpha.,4-trimethyl-, acetate | 0.55 | YES | CYP2C9 inhibitor | NO | YES | HIGH | SOLUBLE | -4.69 cm/s |
| **5** | **Molecule 6** | **2966** | 2(1H)-Isoquinolinecarboximidamide, 3,4-dihydro- | 0.55 | YES | NO | NO | NO | HIGH | SOLUBLE | -6.84 cm/s |
| **6** | **Molecule 11** | **1742210** | Caryophyllene oxide | 0.55 | YES | CYP2C9 inhibitor,CYP2C19 inhibitor | NO | YES | HIGH | SOLUBLE | -5.12 cm/s |
| **7** | **Molecule 13** | **557046** | 4,8-Divinylbicyclo[3.3.1]nonane-2,6-dione | 0.55 | YES | NO | NO | YES | HIGH | SOLUBLE | -6.58 cm/s |
| **8** | **Molecule 14** | **546206** | 2-Azido-2,4,4,6,6,8,8-heptamethylnonane | 0.55 | YES | NO | NO | YES | HIGH | SOLUBLE | -6.58 cm/s |
| **9** | **Molecule 18** | **5365580** | 12-Hydroxy-14-methyl-oxa-cyclotetradec-6-en-2-one | 0.55 | YES | NO | NO | YES | HIGH | SOLUBLE | -5.64 cm/s |
| **10** | **Molecule 19** | **582989** | 1-(2-Vinylphenyl)propan-1-one | 0.55 | YES | NO | NO | YES | HIGH | SOLUBLE | -5.25 cm/s |
| **11** | **Molecule 20** | **590618** | 1,2,3,4-Tetrahydroisoquinolin-6-ol,1-[3-hydroxybenzyl]- | 0.55 | YES | CYP2D6 inhibitor | YES | YES | HIGH | SOLUBLE | -6.00 cm/s |
| **12** | **Molecule 26** | **31401** | Ursodeoxycholic acid | 0.55 | YES | NO | YES | NO | HIGH | SOLUBLE | -6.51 cm/s |

After applying Swiss ADME crieteria;-

# Oral bioavailability is predicted from the RADAR graph which explains whether the optimal ranges for all the properties of a molecule lie within the pink.

1. Lipophilicity (LIPO):

2. Size:

3. Polarity (POLAR):

4. Solubility (INSOLU):

5. Saturation (INSATU):

6. Flexibility (FLEX):

$ Drug-likeness is predicted from five drug-likeness models (Lipinski, Ghose, Veber, Egan, and Muegge) and were selected as bioactive with good bioavailability if three or more models among five met "yes".

Thus, total 12 bioactive phytoconstituents were screened.

Supplementary Table 1 (Phytoconstituents and their targets targeting breast CA genes targets)

|  |  |  |
| --- | --- | --- |
| Phytoconstituents | PCID | TAR |
| 3-Cyclohexene-1-methanol, .alpha.,.alpha.,4-trimethyl-, acetate | 111037 | HSD11B1 |
| 3-Cyclohexene-1-methanol, .alpha.,.alpha.,4-trimethyl-, acetate | 111037 | HSD11B2 |
| 3-Cyclohexene-1-methanol, .alpha.,.alpha.,4-trimethyl-, acetate | 111037 | AR |
| 3-Cyclohexene-1-methanol, .alpha.,.alpha.,4-trimethyl-, acetate | 111037 | CYP19A1 |
| 3-Cyclohexene-1-methanol, .alpha.,.alpha.,4-trimethyl-, acetate | 111037 | F10 |
| 3-Cyclohexene-1-methanol, .alpha.,.alpha.,4-trimethyl-, acetate | 111037 | CES2 |
| 3-Cyclohexene-1-methanol, .alpha.,.alpha.,4-trimethyl-, acetate | 111037 | DHCR24 |
| 3-Cyclohexene-1-methanol, .alpha.,.alpha.,4-trimethyl-, acetate | 111037 | PLA2G1B |
| 3-Cyclohexene-1-methanol, .alpha.,.alpha.,4-trimethyl-, acetate | 111037 | PTGES |
| 3-Cyclohexene-1-methanol, .alpha.,.alpha.,4-trimethyl-, acetate | 111037 | PTGS2 |
| 3-Cyclohexene-1-methanol, .alpha.,.alpha.,4-trimethyl-, acetate | 111037 | CYP17A1 |
| 3-Cyclohexene-1-methanol, .alpha.,.alpha.,4-trimethyl-, acetate | 111037 | TRPM2 |
| 3-Cyclohexene-1-methanol, .alpha.,.alpha.,4-trimethyl-, acetate | 111037 | PTPN1 |
| 2(1H)-Isoquinolinecarboximidamide, 3,4-dihydro- | 2966 | MAOB |
| Caryophyllene oxide | 1742210 | HSP90AA1 |
| 4,8-Divinylbicyclo[3.3.1]nonane-2,6-dione | 557046 | DRD1 |
| 4,8-Divinylbicyclo[3.3.1]nonane-2,6-dione | 557046 | NR1I2 |
| 4,8-Divinylbicyclo[3.3.1]nonane-2,6-dione | 557046 | DLAT |
| 12-Hydroxy-14-methyl-oxa-cyclotetradec-6-en-2-one | 5365580 | PKD1 |
| 12-Hydroxy-14-methyl-oxa-cyclotetradec-6-en-2-one | 5365580 | PTGS2 |
| 12-Hydroxy-14-methyl-oxa-cyclotetradec-6-en-2-one | 5365580 | PRKCE |
| 1,2,3,4-Tetrahydroisoquinolin-6-ol,1-[3-hydroxybenzyl]- | 590618 | ADRB1 |
| 1,2,3,4-Tetrahydroisoquinolin-6-ol,1-[3-hydroxybenzyl]- | 590618 | ADRB3 |
| 1,2,3,4-Tetrahydroisoquinolin-6-ol,1-[3-hydroxybenzyl]- | 590618 | DRD1 |
| 1,2,3,4-Tetrahydroisoquinolin-6-ol,1-[3-hydroxybenzyl]- | 590618 | DRD5 |
| 1,2,3,4-Tetrahydroisoquinolin-6-ol,1-[3-hydroxybenzyl]- | 590618 | DRD2 |
| 1,2,3,4-Tetrahydroisoquinolin-6-ol,1-[3-hydroxybenzyl]- | 590618 | DRD3 |
| 1,2,3,4-Tetrahydroisoquinolin-6-ol,1-[3-hydroxybenzyl]- | 590618 | DRD4 |
| 1,2,3,4-Tetrahydroisoquinolin-6-ol,1-[3-hydroxybenzyl]- | 590618 | TBXA2R |
| Ursodeoxycholic acid | 31401 | AKR1B10 |
| Ursodeoxycholic acid | 31401 | AR |
| Ursodeoxycholic acid | 31401 | NR1H4 |
| Ursodeoxycholic acid | 31401 | FXR1 |
| Ursodeoxycholic acid | 31401 | HSD11B2 |
| Ursodeoxycholic acid | 31401 | ALB |
| Ursodeoxycholic acid | 31401 | CYP19A1 |
| Ursodeoxycholic acid | 31401 | F10 |
| Ursodeoxycholic acid | 31401 | ESR2 |
| Ursodeoxycholic acid | 31401 | GPBAR1 |
| Ursodeoxycholic acid | 31401 | GABRA4 |
| Ursodeoxycholic acid | 31401 | NR3C1 |
| Ursodeoxycholic acid | 31401 | PTGFR |
| Ursodeoxycholic acid | 31401 | SHBG |
| Ursodeoxycholic acid | 31401 | F3 |
| Ursodeoxycholic acid | 31401 | UGT2B7 |

**SUPPLEMENTARY TABLE:2 BIOACITVE COMPOUNDS TARGETS LIST**

|  |  |  |
| --- | --- | --- |
| S.No. | Bioactive compounds | Targets |
| 1. | 3-Cyclohexene-1-methanol, .alpha.,.alpha.,4-trimethyl-, acetate | HSD11B1, HSD11B2, AR, CYP19A1, F10, CES2, DHCR24, PLA2G1B, PTGES, PTGS2, CYP17A1, TRPM2, PTPN1 |
| 2. | 2(1H)-Isoquinolinecarboximidamide, 3,4-dihydro- | MAOB |
| 3. | Caryophyllene oxide | HSP90AA1 |
| 4. | 4,8-Divinylbicyclo[3.3.1]nonane-2,6-dione | DRD1, NR1I2, DLAT |
| 5. | 12-Hydroxy-14-methyl-oxa-cyclotetradec-6-en-2-one | PKD1, PTGS2, PRKCE |
| 6. | 1,2,3,4-Tetrahydroisoquinolin-6-ol,1-[3-hydroxybenzyl] | ADRB1, ADRB3, DRD1, DRD5, DRD2, DRD3, DRD4, TBXA2R |
| 7. | Ursodeoxycholic acid | AKR1B10, AR, NR1H4, FXR1, HSD11B2, ALB, CYP19A1, F10, ESR2, GPBAR1, GABRA4, NR3C1, PTGFR, SHBG, F3, UGT2B7 |
| 8. | 3-Cyclohexene-1-methanol, .alpha.,.alpha.,4-trimethyl-, acetate+ 12-Hydroxy-14-methyl-oxa-cyclotetradec-6-en-2-one | PTGS2 |
| 9. | 3-Cyclohexene-1-methanol, .alpha.,.alpha.,4-trimethyl-, acetate + Ursodeoxycholic acid | HSD11B2,AR,CYP19A1,F10 |
| 10. | 4,8-Divinylbicyclo[3.3.1]nonane-2,6-dione + 1,2,3,4-Tetrahydroisoquinolin-6-ol,1-[3-hydroxybenzyl] | DRD1 |

In this above table it was found that bioactive compound 3-Cyclohexene-1-methanol, .alpha.,.alpha.,4-trimethyl-, acetate, 2(1H)-Isoquinolinecarboximidamide, 3,4-dihydro, Caryophyllene oxide, 4,8-Divinylbicyclo[3.3.1]nonane-2,6-dione, 12-Hydroxy-14-methyl-oxa-cyclotetradec-6-en-2-one, 1,2,3,4-Tetrahydroisoquinolin-6-ol,1-[3-hydroxybenzyl, Ursodeoxycholic acid have 13, 01, 01, 03, 03, 08, 16 targets respectively. Further we checked for the compound’s having more than one targets and it was found that 3-Cyclohexene-1-methanol, .alpha.,.alpha and 12-Hydroxy-14-methyl-oxa-cyclotetradec-6-en-2-one have one common target 3-Cyclohexene-1-methanol, .alpha.,.alpha.,4-trimethyl and Ursodeoxycholic acid have four common targets. Further we have also looked for more than three atgers and four targets but there were no any common targets were found.

|  |  |  |
| --- | --- | --- |
| S.No. | Bioactive compounds | Targets |
| 1. | 3-Cyclohexene-1-methanol, .alpha.,.alpha.,4-trimethyl-, acetate | HSD11B1, HSD11B2, AR, CYP19A1, F10, CES2, DHCR24, PLA2G1B, PTGES, PTGS2, CYP17A1, TRPM2, PTPN1 |
| 2. | 2(1H)-Isoquinolinecarboximidamide, 3,4-dihydro- | MAOB |
| 3. | Caryophyllene oxide | HSP90AA1 |
| 4. | 4,8-Divinylbicyclo[3.3.1]nonane-2,6-dione | DRD1, NR1I2, DLAT |
| 5. | 12-Hydroxy-14-methyl-oxa-cyclotetradec-6-en-2-one | PKD1, PTGS2, PRKCE |
| 6. | 1,2,3,4-Tetrahydroisoquinolin-6-ol,1-[3-hydroxybenzyl] | ADRB1, ADRB3, DRD1, DRD5, DRD2, DRD3, DRD4, TBXA2R |
| 7. | Ursodeoxycholic acid | AKR1B10, AR, NR1H4, FXR1, HSD11B2, ALB, CYP19A1, F10, ESR2, GPBAR1, GABRA4, NR3C1, PTGFR, SHBG, F3, UGT2B7 |
| 8. | 3-Cyclohexene-1-methanol, .alpha.,.alpha.,4-trimethyl-, acetate+ 12-Hydroxy-14-methyl-oxa-cyclotetradec-6-en-2-one | PTGS2 |
| 9. | 3-Cyclohexene-1-methanol, .alpha.,.alpha.,4-trimethyl-, acetate + Ursodeoxycholic acid | HSD11B2,AR,CYP19A1,F10 |
| 10. | 4,8-Divinylbicyclo[3.3.1]nonane-2,6-dione + 1,2,3,4-Tetrahydroisoquinolin-6-ol,1-[3-hydroxybenzyl] | DRD1 |

In this above table it was found that bioactive compound 3-Cyclohexene-1-methanol, .alpha.,.alpha.,4-trimethyl-, acetate, 2(1H)-Isoquinolinecarboximidamide, 3,4-dihydro, Caryophyllene oxide, 4,8-Divinylbicyclo[3.3.1]nonane-2,6-dione, 12-Hydroxy-14-methyl-oxa-cyclotetradec-6-en-2-one, 1,2,3,4-Tetrahydroisoquinolin-6-ol,1-[3-hydroxybenzyl, Ursodeoxycholic acid have 13, 01, 01, 03, 03, 08, 16 targets respectively. Further we checked for the compound’s having more than one targets and it was found that 3-Cyclohexene-1-methanol, .alpha.,.alpha and 12-Hydroxy-14-methyl-oxa-cyclotetradec-6-en-2-one have one common target 3-Cyclohexene-1-methanol, .alpha.,.alpha.,4-trimethyl and Ursodeoxycholic acid have four common targets. Further we have also looked for more than three atgers and four targets but there were no any common targets were found.