|  |
| --- |
|  |

Figure S1: Representative GC chromatogram of tamanu oil components

Figure S2: Graphical representation of % Wound Contraction

|  |  |  |  |
| --- | --- | --- | --- |
| **Groups** | **(H& E)** | **Masson’s trichome (MT)** | |
| **Control** |  |  | |
| **Tamanu oil** |  |  | |
| **Murivenna®** |  | **h** |
| **BG1** |  | **h** |
| **BG4** |  |  |
| **BG8** |  | **h** |

Figure S3: Photomicrographs (100x) showing H&E stain and MT stain section of skin tissues at day 15 for control, standard and formulation treated groups

(**Yellow**- re-epithelialization, **Green**- irregular connective tissue, **Blue**- epidermis, **Black**-collagen formation and **h**- healed area with multiple layers of fibrous connective tissue)

Table S1: Molecular properties of Ligands (constituents of Tamanu oil)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Properties/ Drugs** | **Molecular Weight** | **LogP** | **No. of Rotatable Bonds** | **No. of H-Bond Acceptors** | **No. of H- Bond Donors** | **Surface Area (m2)** |
| **Calophyllolide** | 416.473 | 5.8017 | 4 | 5 | 0 | 180.154 |
| **Inophyllum C** | 402.446 | 5.2439 | 1 | 5 | 0 | 173.473 |
| **Calanolide A** | ***370.445*** | ***4.3801*** | ***2*** | ***5*** | ***1*** | ***158.144*** |
| **4-Norlanosta-17(20),24-diene-11,16-diol-21-oic acid, 3-oxo-16,21-lactone** | 454.651 | 5.7834 | 3 | 4 | 1 | 198.78 |
| **Bleomycin** | 1415.576 | -7.70358 | 35 | 31 | 20 | 558.81 |

**Table S2:** Predicted ADMET properties of compounds

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Properties** | **Calophyllolide** | **Inophyllum C** | **Calanolide A** | **4-Norlanosta-17(20),24-diene-11,16-diol-21-oic acid, 3-oxo-16,21-lactone** | **Bleomycin** |
| **Water solubility (log mol/L)** | -5.699 | -4.952 | -4.982 | -5.716 | -2.892 |
| **Caco2 permeability (log Papp in 10-6 cm/s)** | 1.121 | 1.119 | 0.757 | 0.605 | -2.018 |
| **Skin Permeability (log Kp)** | -2.702 | -2.729 | -3.013 | -3.253 | -2.735 |
| **P-glycoprotein substrate** | No | No | Yes | No | Yes |
| **P-glycoprotein I inhibitor** | Yes | Yes | Yes | Yes | No |
| **P-glycoprotein II inhibitor** | Yes | Yes | Yes | Yes | No |
| **VDss (human)(log L/kg)** | 0.47 | 0.169 | 0.371 | -0.124 | -0.159 |
| **Fraction unbound (human)(Fu)** | 0.147 | 0.165 | 0.103 | 0 | 0.387 |
| **BBB permeability (log BB)** | -0.823 | -0.453 | -0.322 | -0.56 | -4.5 |
| **CNS permeability (log PS)** | -1.678 | -1.606 | -1.82 | -1.59 | -7.772 |
| **CYP2D6 substrate** | No | No | No | No | No |
| **CYP3A4 substrate** | Yes | Yes | Yes | Yes | No |
| **CYP1A2 inhibitor** | Yes | Yes | Yes | No | No |
| **CYP2C19 inhibitor** | Yes | Yes | Yes | No | No |
| **CYP2C9 inhibitor** | Yes | Yes | Yes | No | No |
| **CYP2D6 inhibitor** | No | No | No | No | No |
| **CYP3A4 inhibitor** | Yes | Yes | Yes | No | No |
| **Total Clearance(log ml/min/kg)** | 0.757 | 0.589 | 0.506 | 0.331 | 0.649 |
| **Renal OCT2 substrate** | No | No | No | No | No |
| **AMES toxicity** | No | No | No | No | Yes |
| **Max. tolerated dose (human)(log mg/kg/day)** | 0.255 | 0.11 | -0.315 | -0.535 | 0.438 |
| **hERG I inhibitor** | No | No | No | No | No |
| **hERG II inhibitor** | Yes | Yes | Yes | No | Yes |
| **Hepatotoxicity** | No | Yes | No | No | No |
| **Skin Sensitisation** | No | No | No | No | No |

Table S3: Period of epithelialization in all groups

|  |  |  |
| --- | --- | --- |
| **Sl. no.** | **Groups** | **Period of Epithelialization (days)** |
| **1.** | Control | 12.83±0.30 |
| **2.** | Tamanu oil | 10.16 ±0.47\*\* |
| **3.** | Murivenna® | 10.00±0.36\*\* |
| **4.** | BG1 | 11.50±0.42\* |
| **5.** | BG4 | 8.16±0.60\*\* |
| **6.** | BG8 | 6.66±0.66\*\* |

Data are expressed as Mean ± SEM (n=6) and analysed by one-way ANOVA method of variance followed by Dunnett test for multiple comparison. ns p>0.05, \* p<0.05, \*\* p<0.01, in comparison to control. (Where, ns= non-significant, \* moderately significant,

Table S4: Formulation of Bigels

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **BG1** | **BG2** | **BG3** | **BG4** | **BG5** | **BG6** | **BG7** | **BG8** |
| **OLEOGEL PHASE** | | | | | | | | |
| **Tween 20 (mL)** | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| **Tamanu oil (mL)** | 5 | 10 | 15 | 20 | 5 | 10 | 15 | 20 |
| **HYDROGEL PHASE** | | | | | | | | |
| **Micronized Xanthan gum (g)** | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 |
| **Geogard® ECT (mL)** | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| **Vanilla fragrance oil (mL)** | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 |
| **Water (mL)** | q.s 100mL | | | | | | | |