COX Inhibitor Pack
Item No. 10186

Laboratory Procedures
For long term storage, we suggest that COX Inhibitor Pack be stored as supplied at -20°C. It should be stable for at least one year.

The Cayman COX Inhibitor Pack contains a combination of frequently used cyclooxygenase (COX) inhibitors. Each kit contains aspirin, the archetype nonselective, irreversible COX inhibitor.1 As series of COX-2 selective inhibitors are available in the COX Inhibitor Pack, including NS-398, one of the first reported and most widely used. 2 Another COX-2-selective inhibitor included is CAY10404, with nearly 500,000-fold COX-2 selectivity.3

The potent COX-1-selective inhibitor SC-560 is an example of a reversible, diaryl heterocycle COX-1 inhibitor with low nM activity.4 Also included is valeroyl salicylate, an irreversible alkylation of COX enzymes with some selectivity toward COX-1.5 trans-Resveratrol is also included in the COX Inhibitor Pack due to its complex activities, which include COX inhibition, peroxidase inhibition, antioxidant activity, and gene regulation.6,7

<table>
<thead>
<tr>
<th>Component</th>
<th>Amount</th>
<th>Solubility</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAY10404</td>
<td>5 mg</td>
<td>&gt;0.5 mg/ml in DMF:PBS (pH 7.2) (1:1)</td>
</tr>
<tr>
<td>Aspirin</td>
<td>50 mg</td>
<td>&gt;2.7 mg/ml in PBS (pH 7.2)</td>
</tr>
<tr>
<td>APHS</td>
<td>5 mg</td>
<td>N/A</td>
</tr>
<tr>
<td>SC-560</td>
<td>5 mg</td>
<td>&gt;1.2 mg/ml in DMF:PBS (pH 7.2) (1:1)</td>
</tr>
<tr>
<td>NS-398</td>
<td>5 mg</td>
<td>&gt;0.4 mg/ml in DMSO:PBS (pH 7.2) (1:3)</td>
</tr>
<tr>
<td>SC-58125</td>
<td>5 mg</td>
<td>&gt;0.25 mg/ml in DMF:PBS (pH 7.2) (1:3)</td>
</tr>
<tr>
<td>Valeroyl Salicylate</td>
<td>50 mg</td>
<td>&gt;6 mg/ml in PBS (pH 7.2)</td>
</tr>
<tr>
<td>trans-Resveratrol</td>
<td>10 mg</td>
<td>&gt;0.1 mg/ml in PBS (pH 7.2)</td>
</tr>
<tr>
<td>Valdecoxib</td>
<td>5 mg</td>
<td>&gt;0.5 mg/ml in DMSO:PBS (pH 7.2) (1:8)</td>
</tr>
<tr>
<td>Licofelone</td>
<td>5 mg</td>
<td>&gt;0.5 mg/ml in DMSO:PBS (pH 7.2) (1:8)</td>
</tr>
</tbody>
</table>

References
CAY10404
Item No. 70210

CAS Registry No.: 340267-36-9
Formal Name: 3-[4-(methylsulfonyl)phenyl]-4-phenyl-5-(trifluoromethyl)-isoxazole
MF: C₁₇H₁₂F₃NO₅S
FW: 367.4
Purity: ≥98%
UV/Vis.: λ_max: 239 nm
Supplied as: A crystalline solid
Storage: -20°C
Stability: ≥2 years

Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

CAY10404 is supplied as a crystalline solid. A stock solution may be made by dissolving the CAY10404 in the solvent of choice. CAY10404 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF), which should be purged with an inert gas. The solubility of CAY10404 in ethanol and DMSO is approximately 17 mg/ml and approximately 21 mg/ml in DMF.

CAY10404 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, CAY10404 should first be dissolved in DMF and then diluted with the aqueous buffer of choice. CAY10404 has a solubility of approximately 0.5 mg/ml in a 1:1 solution of DMF:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

Many non-steroidal anti-inflammatory drugs (NSAIDs) are potent but non-selective inhibitors of both COX-1 and COX-2 in humans.¹ CAY10404 is one of the most selective inhibitors of COX-2 which has been reported to date, with a selectivity index (SI; SI = IC₅₀ COX-1/IC₅₀ COX-2) of >500,000, the COX-1 IC₅₀ is >500 μM, and COX-2 IC₅₀ is <1 nM.² As a reference point, the SI of celecoxib is about 400. Thus, CAY10404 has an SI which is several logs greater than the first generation of selective COX-2 inhibitors, and is comparable to the SI of second generation selective COX-2 inhibitors, such as valdecoxib and etoricoxib.³

References

Aspirin
Item No. 70260

CAS Registry No.: 50-78-2
Formal Name: 2-(acetyloxy)-benzoic acid
Synonym: Acetylsalicylic Acid
MF: C9H8O4
FW: 180.2
Purity: ≥99%
UV/Vis.: λmax: 226, 275 nm
Supplied as: A crystalline solid
Storage: Room temperature
Stability: ≥2 years

Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

Aspirin is supplied as a crystalline solid. A stock solution may be made by dissolving the aspirin in the solvent of choice. Aspirin is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide, which should be purged with an inert gas. The solubility of aspirin in these solvents is approximately 80, 41, and 30 mg/ml, respectively.

Further dilutions of the stock solution into aqueous buffers or isotonic saline should be made prior to performing biological experiments. Ensure that the residual amount of organic solvent is insignificant, since organic solvents may have physiological effects at low concentrations. Organic solvent-free aqueous solutions of aspirin can be prepared by directly dissolving the crystalline solid in aqueous buffers. The solubility of aspirin in PBS, pH 7.2, is approximately 2.7 mg/ml. Avoid adding aspirin to basic solutions (pH > 7.4), since base treatment will hydrolyze aspirin to salicylic acid. Store aqueous solutions of aspirin on ice and use within 30 minutes of preparation.

Description

Aspirin is a non-selective, irreversible COX inhibitor. The IC50 values for ovine COX-1 and -2 are 0.75 and 1.25 mM, respectively.1 Aspirin acetylates COX-1 at Ser530 and COX-2 at Ser516 resulting in irreversible enzyme inhibition.

Reference

APHS
Item No. 70330

CAS Registry No.: 209125-28-0
Formal Name: 2-(2-heptynylthio)-phenol acetate
MF: C_{15}H_{18}O_{2}S
FW: 262.4
Purity: ≥98%
UV/Vis.: λ_{max}: 249 nm
Supplied as: A solution in methyl acetate
Storage: -20°C
Stability: ≥1 year

Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

APHS is supplied as a solution in methyl acetate. To change the solvent, simply evaporate the methyl acetate under a gentle stream of nitrogen and immediately add the solvent of choice. Solvents such as ethanol, DMSO, and dimethyl formamide purged with an inert gas can be used. The solubility of APHS in these solvents is approximately 12.5, 11.1, and 14.3 mg/ml, respectively.

Further dilutions of the stock solution into aqueous buffers or isotonic saline should be made prior to performing biological experiments. Ensure that the residual amount of organic solvent is insignificant, since organic solvents may have physiological effects at low concentrations. If an organic solvent-free solution of APHS is needed, it can be prepared by evaporating the methyl acetate and directly dissolving the neat oil in aqueous buffers. The solubility of APHS in PBS, pH 7.2, is approximately 0.02 mg/ml. We do not recommend storing the aqueous solution for more than one day.

Description

APHS is an O-acetyl, S-alkyl ether of 2-thio phenol and a selective, irreversible inhibitor of COX-2. APHS is a potent inhibitor of both COX-1 and COX-2, with IC_{50} values of 17 and 0.8 μM for human recombinant COX-1 and COX-2, respectively.\(^1\) APHS exhibits 20-fold selectivity toward the inhibition of COX-2, yet it is still more potent than aspirin in the inhibition of COX-1. APHS acetylates COX-1 at Ser\(^{530}\) and COX-2 at Ser\(^{516}\) resulting in irreversible enzyme inhibition.\(^1\)

Reference

SC-560
Item No. 70340

CAS Registry No.: 188817-13-2
Formal Name: 5-(4-chlorophenyl)-1-(4-methoxyphenyl)-3-(trifluoromethyl)-1H-pyrazole
MF: C_{17}H_{12}ClF_{3}N_{2}O
FW: 352.7
Purity: ≥98%
UV/Vis.: λ_{max}: 232, 251 nm
Supplied as: A crystalline solid
Storage: -20°C
Stability: ≥2 years

Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

SC-560 is supplied as a crystalline solid. A stock solution may be made by dissolving the SC-560 in the solvent of choice. SC-560 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF), which should be purged with an inert gas. The solubility of SC-560 in these solvents is approximately 22, 24, and 150 mg/ml, respectively.

SC-560 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, SC-560 should first be dissolved in DMF and then diluted with the aqueous buffer of choice. SC-560 has a solubility of approximately 1.2 mg/ml in a 1:1 solution of DMF:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

SC-560 is a member of the diaryl heterocycle class of cyclooxygenasase (COX) inhibitors which includes celecoxib (Celebrex™) and rofecoxib (Vioxx™). However, unlike these selective COX-2 inhibitors, SC-560 is a selective inhibitor of COX-1. Using human recombinant enzymes, the IC_{50} value for SC-560 with respect to COX-1 is 9 nM, while the corresponding IC_{50} value for COX-2 is 6.3 μM. Thus, SC-560 shows 700-fold selectivity for the COX-1 enzyme. SC-560 is orally active in the rat, where 10 mg/kg completely abolishes the ionophore-induced production of thromboxane B\textsubscript{2} in whole blood. However, SC-560 is ineffective in the treatment of inflammation in models, such as the LPS-induced rat air-pouch model, in which COX-2-generated prostaglandins play a significant role in the inflammatory process. In whole cells, however, SC-560 appears to act as a non-selective COX inhibitor. The mechanism of the selective versus non-selective effects of SC-560 in a cell-free environment compared whole cells has not been elucidated.

References

PRODUCT INFORMATION

NS-398
Item No. 70590

CAS Registry No.: 123653-11-2
Formal Name: N-[2-(cyclohexyloxy)-4-nitrophenyl]-methanesulfonamide
MF: C_{13}H_{18}N_{2}O_{5}S
FW: 314.4
Purity: ≥98%
UV/Vis.: λ_{max}: 238, 296, 337 nm
Supplied as: A crystalline solid
Storage: Room temperature
Stability: ≥2 years

Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

NS-398 is supplied as a crystalline solid. A stock solution may be made by dissolving the NS-398 in the solvent of choice. NS-398 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide, which should be purged with an inert gas. The solubility of NS-398 in these solvents is approximately 0.5, 25, and 30 mg/ml, respectively.

NS-398 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, NS-398 should first be dissolved in DMSO and then diluted with the aqueous buffer of choice. NS-398 has a solubility of approximately 0.4 mg/ml in a 1:3 solution of DMSO:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

NS-398 is a selective inhibitor of cyclooxygenase-2 (COX-2). The IC_{50} values for human recombinant COX-1 and -2 are 75 and 1.77 μM, respectively.\(^1\) The IC_{50} values for ovine COX-1 and -2 are 220 and 0.15 μM, respectively.\(^2\)

References

SC-58125
Item No. 70655

CAS Registry No.: 162054-19-5
Formal Name: 5-(4-fluorophenyl)-1-[4-(methylsulfonyl)phenyl]-3-(trifluoromethyl)-1H-pyrazole
MF: C_{17}H_{12}N_2SO_2F_4
FW: 384.3
Purity: ≥98%
UV/Vis.: λ_{max}: 255 nm
Supplied as: A crystalline solid
Storage: -20°C
Stability: ≥1 year

Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

SC-58125 is supplied as a crystalline solid. A stock solution may be made by dissolving the SC-58125 in the solvent of choice. SC-58125 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF), which should be purged with an inert gas. The solubility of SC-58125 in ethanol and DMSO is approximately 10 mg/ml and approximately 30 mg/ml in DMF.

SC-58125 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, SC-58125 should first be dissolved in DMF and then diluted with the aqueous buffer of choice. SC-58125 has a solubility of approximately 0.25 mg/ml in a 1:3 solution of DMF:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

SC-58125 is a member of the diaryl heterocycle group of selective COX-2 inhibitors which includes MK 966 (rofecoxib), DUP-697, and celecoxib. SC-58125 is a potent and time-dependent inhibitor of COX-2.\(^1\) When tested on the isolated recombinant enzymes, SC-58125 is at least 150 times more potent in the inhibition of COX-2 as COX-1.\(^2\) In cultured HUVEC cells, SC-58125 inhibits COX-2 with an IC_{50} value of 70 nM.\(^3\) It also inhibits the growth of the COX-2 expressing cell line HCA-7 in nude mice at 5-10 mg/kg when given intraperitoneally.\(^4\)

References

Valeroyl Salicylate

CAS Registry No.: 64206-54-8
Formal Name: 2-[(1-oxopentyl)oxy]-benzoic acid
Synonym: 2-Valeryloxybenzoic Acid
MF: C_{12}H_{14}O_{4}
FW: 222.2
Purity: ≥99%
Supplied as: A crystalline solid
Storage: Room temperature
Stability: ≥2 years

Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

Valeroyl salicylate is supplied as a crystalline solid. A stock solution may be made by dissolving the valeroyl salicylate in the solvent of choice. Valeroyl salicylate is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide, which should be purged with an inert gas. The solubility of valeroyl salicylate in these solvents is approximately 95, 43, and 70 mg/ml, respectively.

Further dilutions of the stock solution into aqueous buffers or isotonic saline should be made prior to performing biological experiments. Ensure that the residual amount of organic solvent is insignificant, since organic solvents may have physiological effects at low concentrations. Organic solvent-free aqueous solutions of valeroyl salicylate can be prepared by directly dissolving the crystalline solid in aqueous buffers. The solubility of valeroyl salicylate in PBS, pH 7.2, is approximately 6 mg/ml. We do not recommend storing the aqueous solution for more than one day.

Description

Valeroyl salicylate is a selective, irreversible inhibitor of COX-1. The IC_{50} values for ovine COX-1 and -2 are 0.8 mM and 15 mM, respectively. The half-lives for inactivation of human recombinant and ovine COX-1 in the presence of 500 μM valeroyl salicylate are 12 and 45 minutes, respectively.\(^1,2\)

References

trans-Resveratrol
Item No. 70675

CAS Registry No.: 501-36-0
Formal Name: 5-[(1E)-2-(4-hydroxyphenyl) ethenyl]-1,3-benzenediol
Synonym: (E)-Resveratrol
MF: C₁₄H₁₂O₃
FW: 228.2
Purity: ≥98%
UV/Vis.: λ<sub>max</sub>: 218, 307, 321 nm
Supplied as: A crystalline solid
Storage: -20°C
Stability: ≥2 years

Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

trans-Resveratrol is supplied as a crystalline solid. A stock solution may be made by dissolving the trans-Resveratrol in the solvent of choice. trans-Resveratrol is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF), which should be purged with an inert gas. The solubility of trans-Resveratrol in ethanol and DMSO is approximately 50 mg/ml and approximately 100 mg/ml in DMF.

Further dilutions of the stock solution into aqueous buffers or isotonic saline should be made prior to performing biological experiments. Ensure that the residual amount of organic solvent is insignificant, since organic solvents may have physiological effects at low concentrations. Organic solvent-free aqueous solutions of trans-Resveratrol can be prepared by directly dissolving the crystalline solid in aqueous buffers. The solubility of trans-Resveratrol in PBS, pH 7.2, is approximately 0.1 mg/ml. We do not recommend storing the aqueous solution for more than one day.

Description

Phenolic compounds, particularly flavonoids, from plant sources have long been observed to have antioxidant activity with potential benefits for human health.¹ ³ trans-Resveratrol is a potent phenolic antioxidant found in grapes and red wine that also has antiproliferative and anti-inflammatory activity.⁴ trans-Resveratrol is also a selective inhibitor of cyclooxygenase 1 (COX-1).² It inhibits COX and peroxidase activities of COX-1 with ED<sub>50</sub> values of 15 and 3.7 µM, respectively; with essentially no inhibition of the COX activity of COX-2. Resveratrol also activates sirtuins⁶ and, in C. elegans, extends lifespan.⁷

References

**PRODUCT INFORMATION**

Valdecoxib  
*Item No. 10006120*

CAS Registry No.: 181695-72-7  
Formal Name: 4-(5-methyl-3-phenyl-4-isoxazolyl)-benzenesulfonamide  
Synonym: Bextra  
MF: C₁₆H₁₄N₂O₃S  
FW: 314.4  
Purity: ≥98%  
UV/Vis.: λₘₐₓ: 202, 235 nm  
Supplied as: A crystalline solid  
Storage: -20°C  
Stability: ≥2 years

Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

**Laboratory Procedures**

Valdecoxib is supplied as a crystalline solid. A stock solution may be made by dissolving the valdecoxib in the solvent of choice. Valdecoxib is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF), which should be purged with an inert gas. The solubility of valdecoxib in ethanol is approximately 5 mg/ml and approximately 20 mg/ml in DMSO and DMF.

Valdecoxib is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, valdecoxib should first be dissolved in DMSO and then diluted with the aqueous buffer of choice. Valdecoxib has a solubility of approximately 0.5 mg/ml in a 1:8 solution of DMSO:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

**Description**

Valdecoxib is a non-steroidal anti-inflammatory drug that selectively inhibits COX-2 activity, exhibiting IC₅₀ values of 26.1 and 0.87 µM for COX-1 and COX-2, respectively, in a human whole blood assay. The COX-2 selectivity ratio of 30 for valdecoxib in this assay is similar to the ratio of 35 observed for rofecoxib (Item No. 10010260). COX-2 selective inhibitors, including this compound, have been implicated as risk factors in acute atherothrombotic events.

**References**

Licofelone
Item No. 10007692

CAS No.: 156897-06-2
Formal Name: 6-(4-chlorophenyl)-2,3-dihydro-2,2-dimethyl-7-phenyl-1H-pyrrolizine-5-acetic acid
Synonym: ML 3000
MF: C_{23}H_{22}ClNO_{2}
FW: 379.9
Purity: ≥98%
UV/Vis.: \( \lambda_{\text{max}} \): 248, 278 nm
Supplied as: A crystalline solid
Storage: -20°C
Stability: ≥2 years

Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

Licofelone is supplied as a crystalline solid. A stock solution may be made by dissolving the licofelone in the solvent of choice. Licofelone is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF), which should be purged with an inert gas. The solubility of licofelone in ethanol is approximately 5 mg/ml and approximately 20 mg/ml in DMSO and DMF.

Licofelone is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, licofelone should first be dissolved in DMSO and then diluted with the aqueous buffer of choice. Licofelone has a solubility of approximately 0.5 mg/ml in a 1:8 solution of DMSO:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

Cross-talk between lipoxygenase (LO) and cyclooxygenase (COX) pathways has been observed in human osteoarthritic synovial explants which creates an arachidonic acid shunting phenomenon, stimulating interleukin-1β (IL-1β) synthesis. Licofelone is a dual inhibitor of COX and LO pathways, that decreases levels of prostaglandin E_{2}, leukotriene B_{4}, and lipoxins and prevents lipopolysaccharide-stimulated IL-1β expression.\(^1\) The IC_{50} values for inhibition of human thrombocyte COX and human 5-LO are 0.16 μM and 0.23 μM, respectively.\(^2\) Unlike other non-steroidal anti-inflammatory drugs, licofelone causes little or no damage to the gastric mucosa in rabbit parietal cells. This is presumably the result of licofelone’s affects on acid-secretory mechanisms, mediated by the inhibition of 5-LO activity.\(^3\)

References