Idarubicin HCl Datasheet

Technical Data

<table>
<thead>
<tr>
<th>Molecular Weight (MW)</th>
<th>Solubility (25°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>533.95</td>
<td>DMSO 107 mg/mL</td>
</tr>
<tr>
<td></td>
<td>Water 10 mg/mL</td>
</tr>
<tr>
<td></td>
<td>Ethanol &lt;1 mg/mL</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Formula</th>
<th>Storage</th>
</tr>
</thead>
<tbody>
<tr>
<td>C_{26}H_{32}N_{12}O_{12}HCl</td>
<td>2 years -20°C Powder</td>
</tr>
<tr>
<td></td>
<td>2 weeks 4°C in DMSO</td>
</tr>
<tr>
<td></td>
<td>6 months -80°C in DMSO</td>
</tr>
</tbody>
</table>

Idarubicin HCl (Idamycin, Zavedos, 4-demethoxydaunorubicin) is a hydrochloride salt form of Idarubicin which is an anthracycline antibiotic and a DNA topoisomerase II (topo II) inhibitor for MCF-7 cells with an IC50 of 3.3 ng/mL.

Biological Activity

In vitro

Idarubicin has significant cytotoxic activity against multicellular spheroids, comparable to the antiproliferative effects on monolayer cells. \(^{(1)}\) Idarubicin inhibits CYP450 2D6. Idarubicin is much more effective than doxorubicin or epirubicin. \(^{(2)}\) Idarubicin is about 57.5-fold and 25-fold more active, respectively. Idarubicin is able to overcome P-glycoprotein-mediated multidrug resistance. \(^{(3)}\) Idarubicin inhibits P4N superoxide radical formation. \(^{(4)}\) Idarubicin could be coupled to the monoclonal antibodies (anti-Ly-2.1, anti-L3T4, or anti-Thy-1) with retention of protein solubility and antibody activity. \(^{(5)}\) Idarubicin inhibits the proliferation of NALM6 cells with an IC50 of 12 nM. \(^{(6)}\)

In vivo

Reduction of Idarubicin is dependent upon ketone reductases, and proceeds more stereoselectively than that of most ketones giving rise to the (13S)-epimer almost exclusively. The high stereospecificity in Idarubicin reduction might result from chiral induction due to the presence of asymmetric centres near to the carbonyl group in Idarubicin. \(^{(7)}\)

Clinical Trials

Idarubicin plus Decitabine and cytarabine has entered in a phase II clinical trial in the treatment of adult acute myeloid leukemia, and adult acute monoblastic leukemia, refractory anemia with excess blasts.

Features

Idarubicin is a substrate for CYP450 2D6 and 2C9.

Protocol (Only for Reference)

**Kinase Assay:**

Evaluation of Idarubicin metabolism by the CYP450 isoenzymes 3A4, 2D6, 2C8, 2C9, and 1A2 is completed using isolated human CYP450 proteins for each isoform. The high throughput P450 inhibition testing method is utilized for these evaluations. The metabolism experiments are designed to investigate the following properties of each drug: (1) if Idarubicin is a substrate of the CYP450 3A4, 2C8, 2C9, 1A2 or 2D6 isoenzymes; (2) if metabolism is affected by known inhibitors of each isoenzyme; (3) if Idarubicin is inhibitors of CYP450 isoenzymes; and (4) if caspofungin or itraconazole inhibit the CYP450 metabolism of Idarubicin. Dibenzylfluorescein (DBF) (CYP3A4, CYP2C8, CYP2C9), 3-cyano-7-ethoxycoumarin (Cyp1A2), and 7-methoxy-4-(aminomethyl)-coumarin (MAMC) (CYP2D6) are the known substrates utilized as controls to confirm the respective isoenzyme activity and evaluate the effects of Idarubicin on the isoenzyme activity. In addition, ketocoumarin, quercetin, sulfaphenazole, furafylline, and quinidine are utilized as control inhibitors of CYP450 isoenzymes; and (4) if caspofungin or itraconazole inhibit the CYP450 metabolism of Idarubicin. Dibenzylfluorescein (DBF) (CYP3A4, CYP2C8, CYP2C9), 3-cyano-7-ethoxycoumarin (Cyp1A2), and 7-methoxy-4-(aminomethyl)-coumarin (MAMC) (CYP2D6) are the known substrates utilized as controls to confirm the respective isoenzyme activity and evaluate the effects of Idarubicin on the isoenzyme activity. In addition, ketocoumarin, quercetin, sulfaphenazole, furafylline, and quinidine are utilized as control inhibitors of CYP450 isoenzymes; and (4) if caspofungin or itraconazole inhibit the CYP450 metabolism of Idarubicin.

**CYP450 metabolism experiments**

Idarubicin inhibits CYP450 2D6. Idarubicin is much more effective than doxorubicin or epirubicin. \(^{(2)}\) Idarubicin is about 57.5-fold and 25-fold more active, respectively. Idarubicin is able to overcome P-glycoprotein-mediated multidrug resistance. \(^{(3)}\) Idarubicin inhibits P4N superoxide radical formation. \(^{(4)}\) Idarubicin could be coupled to the monoclonal antibodies (anti-Ly-2.1, anti-L3T4, or anti-Thy-1) with retention of protein solubility and antibody activity. \(^{(5)}\) Idarubicin inhibits the proliferation of NALM6 cells with an IC50 of 12 nM. \(^{(6)}\)

**Cell Assay:**

**Cell Lines**

NALM6 cells

**Concentrations**

0.1 nM-10 μM

**Incubation Time**

24 hours

**Methods**

The anti-proliferative activity of the Idarubicin in the conjugate is compared to that of free drug by measuring the inhibition of \(^{3}H\)thymidine uptake. Briefly, NALM6 cells (1.5 × 10\(^{5}\) cells) are added to a flat-bottomed microtitre plate (100 μL/well) and incubated for 1 hours at 37°C. Free Idarubicin and Idarubicin-mAb conjugates are sterilised by filtration and diluted in sterile PBS; various concentrations are added to the wells (100 μL/well) in duplicate and the plates are incubated at 37°C, 7% CO\(_2\) for 24 hours. Following incubation, 50 μL medium containing 1 μCi \(^{3}H\)thymidine is added to each well and the plates are incubated for a further 4 hours. Cells are harvested onto glass-fibre filter-paper, dried and counted in a scintillation counter. Specificity studies are performed using the same technique where the ability of

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www.selleckchem.com/datasheet/Idarubicin-DataSheet.html
Animal Study:

Animal Models
- Rat, rabbit, mouse, dog

Formulation
- Saline

Doses
- 2 mg/kg, 0 mg/kg - 75 mg/kg, 3 mg/kg and 0 mg/kg - 75 mg/kg

Administration
- Administered via i.v.

References