The detection of cholestasis-inducing agents in cultured primary rat hepatocytes

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Organisation
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SCOPE OF THE METHOD

<table>
<thead>
<tr>
<th>The Method relates to</th>
<th>Human health</th>
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<tbody>
<tr>
<td>The Method is situated in</td>
<td>Basic Research, Translational - Applied Research</td>
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<tr>
<td>Type of method</td>
<td>In vitro - Ex vivo</td>
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<tr>
<td>Species from which cells/tissues/organs are derived</td>
<td>Rat</td>
</tr>
<tr>
<td>Type of cells/tissues/organs</td>
<td>Primary rat hepatocytes</td>
</tr>
</tbody>
</table>

DESCRIPTION

Method keywords
Sandwich cultures
Hepatocytes
Bile salt export pump (Bsep) inhibition
Cholyl-lysyl-fluorescein (CLF)
Cholestasis-inducing potential

Scientific area keywords
Toxicology
in vitro
Drug-induced liver injury (DILI)
cholestasis

Method description
The standard operating procedure describes a method to assess the cholestasis-inducing potential of chemicals, in casu in cultures of primary rat hepatocytes. The procedure relies on the accumulation of the fluorescent bile salt export pump (Bsep) substrate cholyl-lysyl-fluorescein (CLF) in the canalicular network of sandwich-cultured rat hepatocytes either in presence or the absence of Bsep inhibitors.

Lab equipment
Fluorescent microscope (Nikon Eclipse Ti-S, Belgium)

PROS, CONS & FUTURE POTENTIAL

Advantages
The standard operating procedure comprises an easy-to-apply method to detect cholestasis-inducing agents based on Bsep inhibition. Since sandwich cultures of hepatocytes, in contrast to conventional monolayer cultures, exhibit reformation of the canalicular network and polarized excretory functions, this culture systems forms an appropriate experimental setting for studying biliary excretion.

Challenges
Most Bsep substrates, including CLF, cannot undergo efficient cellular translocation without the support of an uptake transporter, such as sodium-dependent taurocholate cotransporting polypeptide (Ntcp). A number of drugs, known to inhibit Bsep activity, also possess the ability to interfere with the Ntcp-mediated uptake of
bile salts. This phenomenon should always be taken into account as it may complicate the interpretation of the experimental results.

REFERENCES, ASSOCIATED DOCUMENTS AND OTHER INFORMATION

References


Associated documents

BSEP inhibition.docx