General information

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Project duration 3 years (1.10.2007-30.09.2010)
Research team:
    RODICA CUCIUREANU - project director
    MIHAI NECHIFOR - researcher
    LAURIAN VLASE - researcher
    DANA MUNTEAN- researcher
    MAGDALENA CUCIUREANU-researcher

Title of the project:

“PHARMACOKINETICS OF DRUG INTERACTIONS BETWEEN THE SOME ANTIBIOTICS (LINEZOLID, MOXIFLOXACIN), SOME NONSTEROIDAL ANTIINFLAMMATORY DRUGS (DICLOFENAC, CELECOXIB) AND THE GRAPEFRUIT JUICE”

Project summary:

MUCH REDUCED. THIS IS WHY WE CONSIDER THE NONCLINICAL AND CLINICAL STUDY OF PHARMACOKINETIC INTERACTIONS OF DICLOFENAC, CELECOXIB, MOXIFLOXACIN, LINEZOLID WITH GRAPEFRUIT JUICE ABSOLUTELY NECESSARY. THE RESULTS OF THE RESEARCHES MAY CONTRIBUTE TO THE OPTIMIZATION OF DRUG ADMINISTRATION DEPENDING ON THE GRAPEFRUIT JUICE INGESTION.

Objective 1:
Validation of the methods of quantitative analysis for the active compounds from the tested drugs.
Objectives 2, 3:

2. Establishment of the experimental model in order to emphasize the pharmacokinetic interactions between some NSAIDs or antibiotics and grapefruit juice.
3. Pharmacokinetic study regarding the interactions of Celecoxib, Diclofenac, Moxifloxacin, Linezolid with grapefruit juice

Pharmacokinetic parameters of diclofenac

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Diclofenac</th>
<th>Diclofenac + grapefruit juice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cmax (ng/ml)</td>
<td>1384.56</td>
<td>2262.59</td>
</tr>
<tr>
<td>Tmax (ore)</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>ASClast (ng/ml*ora)</td>
<td>7101.78</td>
<td>9233.88</td>
</tr>
<tr>
<td>ASCtot (ng/ml*ora)</td>
<td>7652.13</td>
<td>9527.67</td>
</tr>
<tr>
<td>%ASCextra</td>
<td>7.19</td>
<td>3.08</td>
</tr>
<tr>
<td>t1/2</td>
<td>2.33</td>
<td>2.35</td>
</tr>
<tr>
<td>Time of residence (h)</td>
<td>4.35</td>
<td>3.91</td>
</tr>
</tbody>
</table>

Mean plasma levels of celecoxib administered alone or after grapefruit juice, on rats
Pharmacokinetic parameters of linezolid

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Linezolid</th>
<th>Linezolid + grapefruit juice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cmax (ng/ml)</td>
<td>25755</td>
<td>39834</td>
</tr>
<tr>
<td>Tmax (h)</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>AUClast (ng/ml*ora)</td>
<td>133611</td>
<td>220973</td>
</tr>
<tr>
<td>AUCtot (ng/ml*h)</td>
<td>135579</td>
<td>224304</td>
</tr>
<tr>
<td>%ASCextra</td>
<td>1.45</td>
<td>1.48</td>
</tr>
<tr>
<td>t1/2(h)</td>
<td>1.73</td>
<td>1.69</td>
</tr>
<tr>
<td>Time of residence (h)</td>
<td>3.65</td>
<td>3.97</td>
</tr>
</tbody>
</table>

Objective 4:

Mean plasma levels of celecoxib administered alone or after grapefruit juice (clinical studies)
Mean plasma levels of celecoxib administered alone or after grapefruit juice (clinical studies)

**Publications:**


The involvement of young researchers in the activities of the project:

Cuciureanu Magdalena, MD in Clinical Pharmacology, PhD in Medicine, took part in:
- carrying out the clinical stages of the experiments on animals;
- conducting clinical trials (Diclogrep and Celegrep in 2009; Moxigrep and Linezogrep in 2010);
- editing the dossiers that have been submitted to the National Medicines Agency in order to obtain approvals for conducting clinical trials;
- editing scientific reports for all of the stages accomplished until present;
- editing the scientific papers, communicated or published, related to the theme of the grant;

Muntean Dana, Chemistry researcher, PhD in Chemistry, took part in:
- carrying out the analytical stages related to all of the objectives that have been accomplished until present (validation of analytical methods, determination of active substances from blood samples taken from rats and from the human volunteers that were included in the clinical trials;
- calculating the statistical parameters for the analytical data that has been obtained;
- editing the scientific reports for all of the stages accomplished until present;
- editing the scientific papers communicated or published, related to the theme of the grant.