Drug interference in Trinder reaction
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Background
The Trinder reaction brought indisputable benefits to the clinical laboratory analysis providing specific and precise measurement of several clinical markers. However, multiple recent studies showed chemical interferences in Trinder reaction based analyses such as creatinine, triglycerides, uric acid and cholesterol tests, that significantly alter laboratory results. The aim of this study was to quantify interference effects of six widely prescribed drugs with analytical methods utilizing the Trinder chromogenic reaction.

Material and methods:
Samples were prepared by spiking a pooled blood plasma with the specific medical solution (original values listed in tab. 1). The first set of samples was prepared with therapeutic concentrations of six drugs:

- ACC® (N-acetylcysteine; 875 mg/L = 5.36 mmol/L; fig. 1)
- Novalgin® (metamizole; 150 mg/L = 0.48 mmol/L; fig. 2)
- Dobutamin Admeda® (dobutamine; 400 μg/L = 1.33 μmol/L; fig. 3)
- Dicynone® (etamsylate; 50 mg/L = 0.19 mmol/L; fig. 4)
- Tensamin® (dopamine; 75 μg/L = 0.49 mmol/L; fig. 5)
- Ascorbic acid (25 mg/L = 0.14 mmol/L; fig. 6)

The second set of samples was prepared with unified concentration of 1 mmol/L drug per sample. The results of cholesterol, creatinine, triglycerides and uric acid were compared to the values obtained from the pooled plasma with physiological solution addition. The analysis was performed in University Hospital Brno with the C8000 c702 (Roche) analyzer with the reagent sets of cholesterol (CHOL2), creatinine (CREP2), uric acid (UA2) and triglycerides (TRIGL) by Roche company.

Results
Significant interference occurred in three out of the six samples with therapeutic concentration of drugs (fig. 7). ACC® (cholesterol -54.2%, creatinine -33.3%, triglycerides -83.3%, uric acid -22.1%), Dicynone® (creatinine -54.3%, triglycerides -24.6%, uric acid -21.0%) and Novalgin® (creatinine -28.4%, triglycerides -15.9%, uric acid -10.7%). The interference in samples containing 1 mmol/L drug concentration showed in all of the samples (fig. 8) and most prominently in Dobutamin Admeda® (cholesterol -52.1%, creatinine -39.5%, triglycerides -89.7%, uric acid -83.0%), Tensamin® (cholesterol -39.6%, creatinine -85.2%, triglycerides -81.7%, uric acid -86.1%) and Dicynone® (cholesterol -16.7%, creatinine -81.5%, triglycerides -69.8%, uric acid -56.9%). The effective molecules have similar hydroquinone structure, which may enable us to predict the risk of interference in drugs of the same type.

Conclusions
This study shows how significantly are common medications able to alter the measurement results. Even though some information of these interferences were available in the past, their acknowledgement in the field of laboratory medicine is still low. This may be fixed by the application of sophisticated software informing doctors of a known interfering substance.

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<table>
<thead>
<tr>
<th>Drug</th>
<th>Uric acid [μmol/L]</th>
<th>Creatinine [μmol/L]</th>
<th>Triacylglycerides [mmol/L]</th>
<th>Cholesterol [mmol/L]</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACC®</td>
<td>290</td>
<td>81</td>
<td>1.26</td>
<td>4.8</td>
</tr>
</tbody>
</table>

Tab. 1. Pooled blood plasma original values

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Fig. 1: N-acetylcysteine (ACC®)
Fig. 2: Metamizole (Novalgin®)
Fig. 3: Dobutamine (Dobutamin Admeda®)
Fig. 4: Etamsylate (Dicynone®)
Fig. 5: Dopamine (Tensamin®)
Fig. 6: Ascorbic acid

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**Therapeutic drug concentration interference**

**1 mmol/L drug concentration interference**

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