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 µmol/L; fig. 5)
- Ascorbic acid (25 mg/L = 0.14 mmol/L; fig. 6)

Uric acid	Creatinine	Triacylglycerides	Cholesterol
[µmol/L]	[µmol/L]	[mmol/L]	[mmol/L]
290	81	1.26	4.8

Tab. 1: Pooled blood plasma original values

The second set of samples was prepared with unified concentration of 1 mmol/L drug per sample. The results of cholesterol, creatinine, triacylglycerides 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 triacylglycerides (TRIGL) by Roche company.

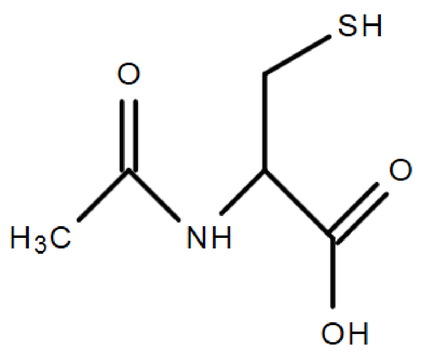

Fig. 1: N-acetylcysteine (ACC®)

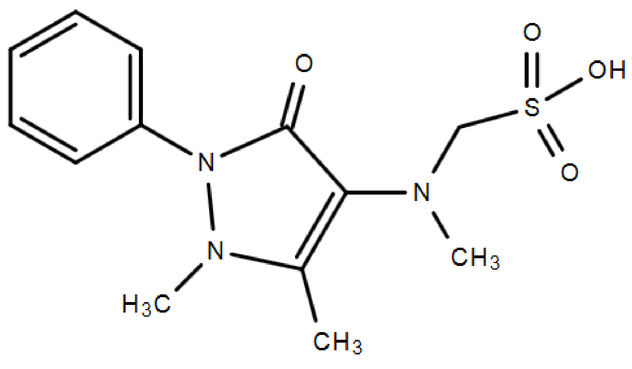

Fig. 2: Metamizole (Novalgin®)

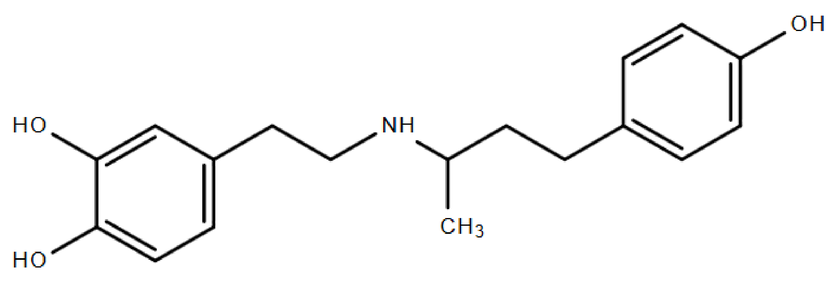

Fig. 3: Dobutamine (Dobutamine Admeda®)

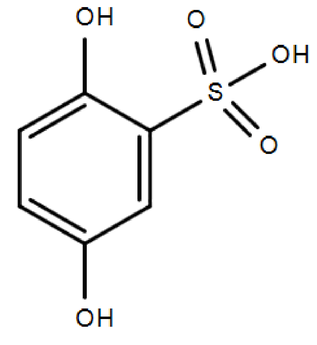

Fig. 4: Etamsylate (Dicynone®)

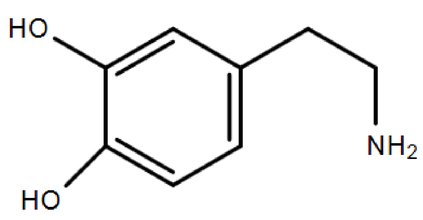

Fig. 5: Dopamine (Tensamin®)

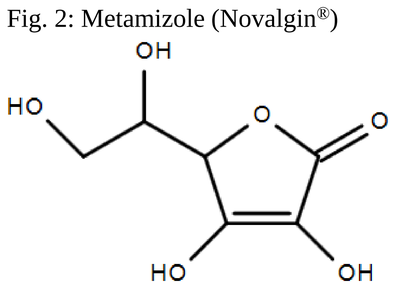

Fig. 6: Ascorbic acid

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%, triacylglycerides -83.3%, uric acid -22.1%), Dicynone® (creatinine -54.3%, triacylglycerides -24.6%, uric acid -21.0%) and Novalgin® (creatinine -28.4%, triacylglycerides -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 Dobutamine Admeda® (cholesterol -52.1%, creatinine -39.5%, triacylglycerides -89.7%, uric acid -83.0%), Tensamin® (cholesterol -39.6%, creatinine -85.2%, triacylglycerides -81.7%, uric acid -86.1%) and Dicynone® (cholesterol -16.7%, creatinine -81.5%, triacylglycerides -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.

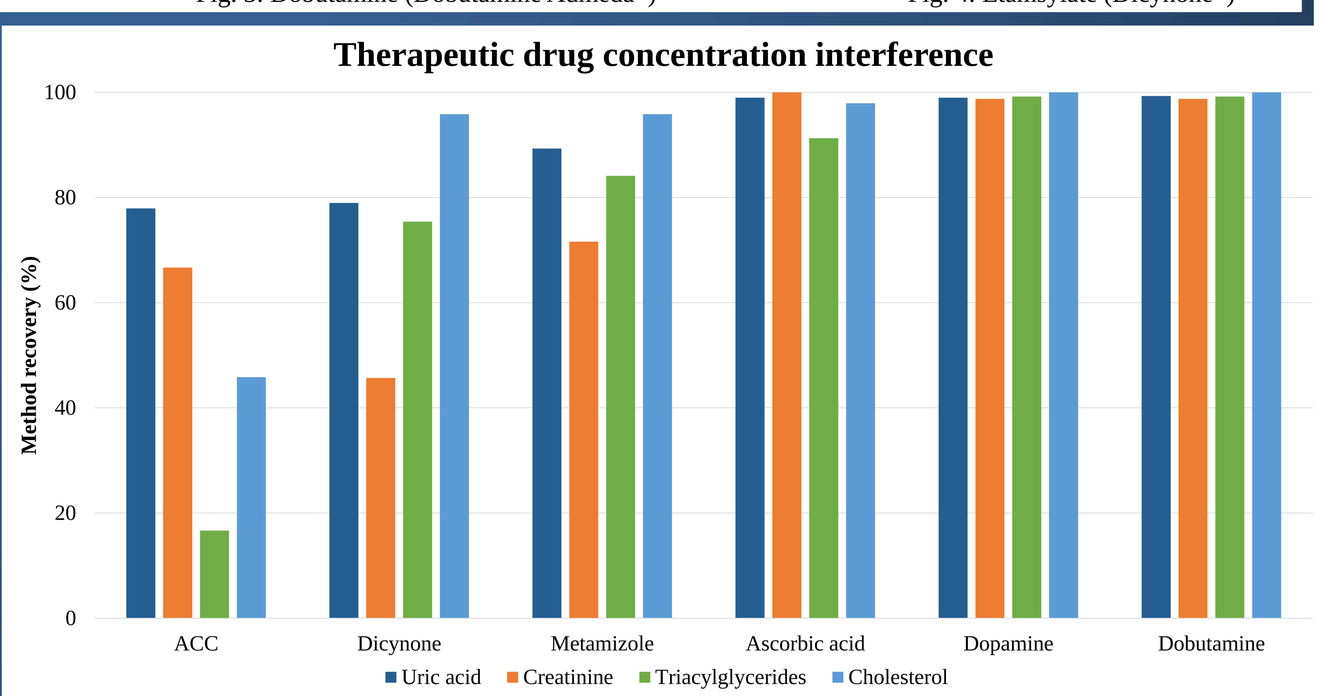

Fig. 7: Decrease of method recovery for individual analytes with each of six drugs in their therapeutic concentrations.

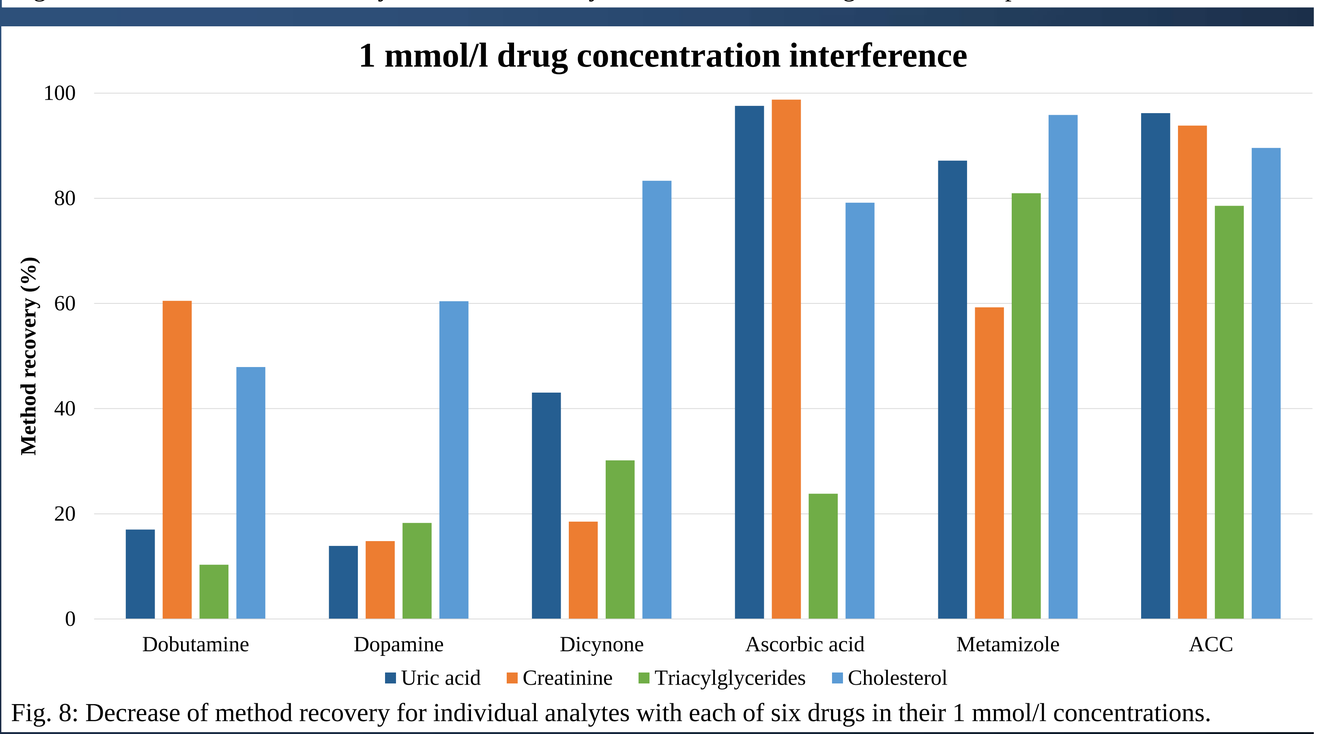

Fig. 8: Decrease of method recovery for individual analytes with each of six drugs in their 1 mmol/l concentrations.

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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