

FALSELY ELEVATED SERUM DIGITOXIN CONCENTRATIONS MEASURED BY IMMUNOASSAY USING MURINE ANTIBODIES IN A CLINICALLY ASYMPTOMATIC PATIENT

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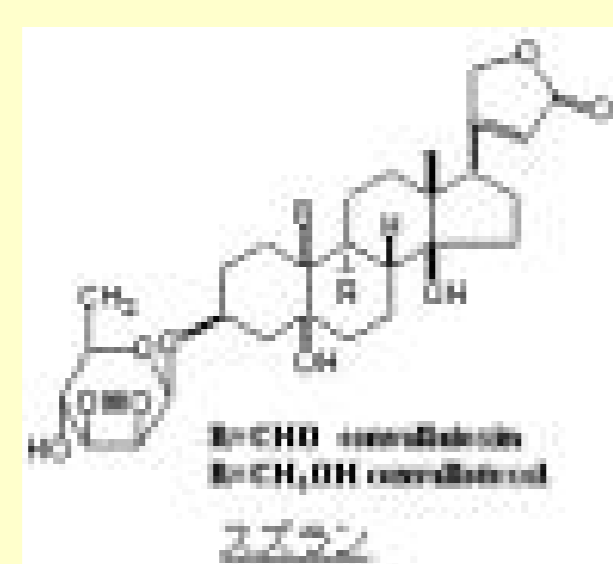
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Objective

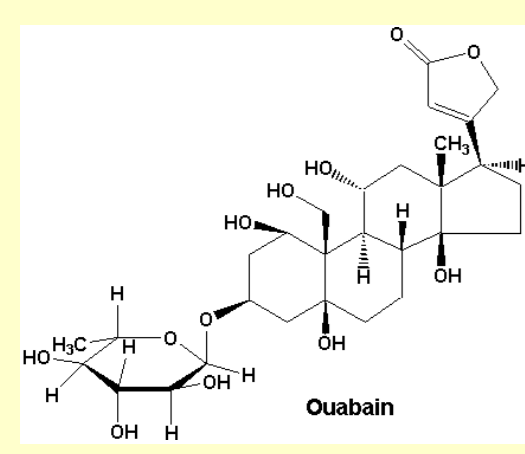
The low specificity of immunoassays compared to other analytical methods (HPLC, LC-MS) used for the routine Therapeutic Drug Monitoring of patients undergoing digitoxin therapy can lead to some pitfalls. We report about a highly elevated digitoxin serum concentration measured by an immunoassay method using murine antibodies (Advia, Bayer) in a clinically asymptomatic patient.

convallatoxin

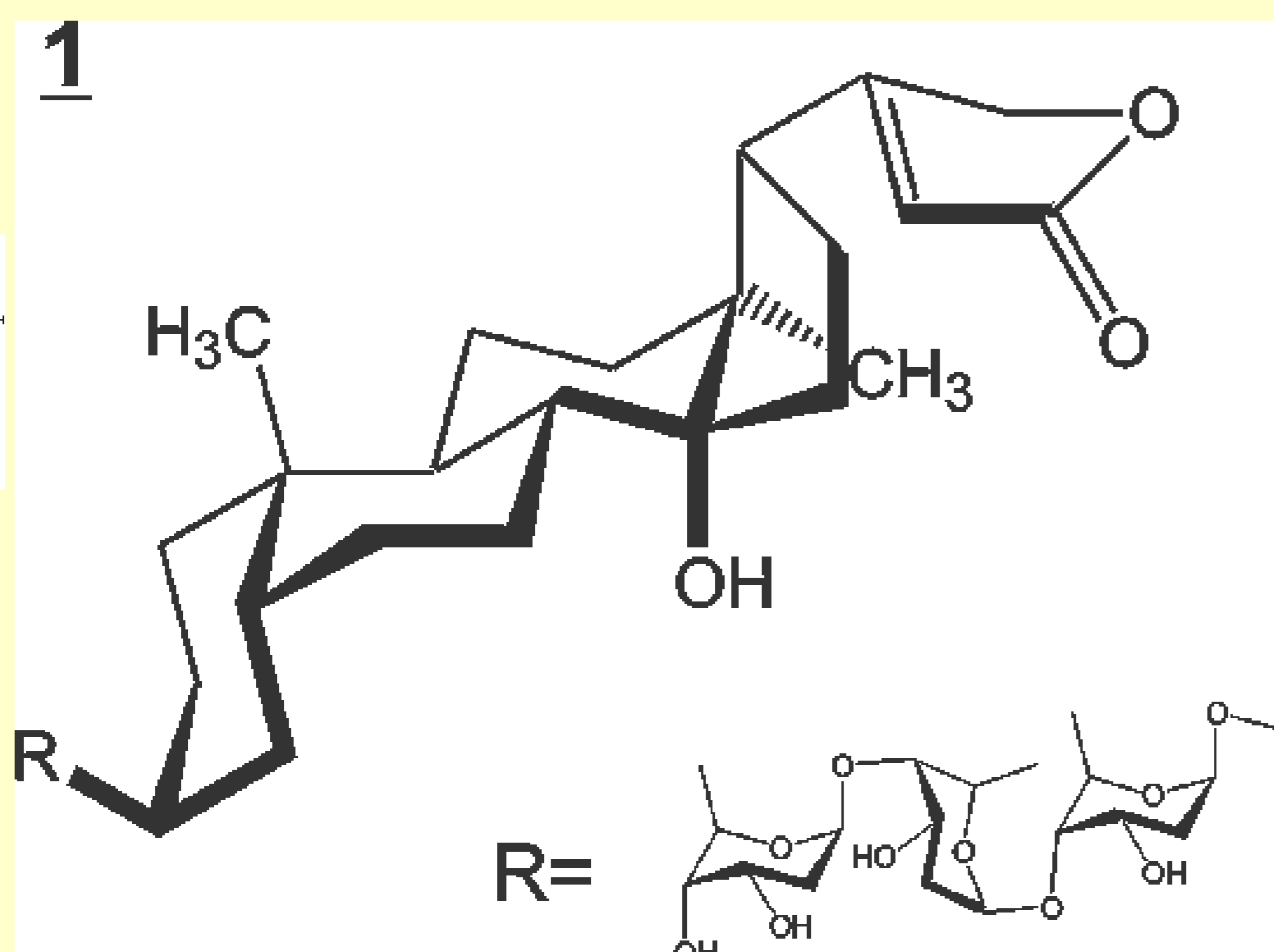
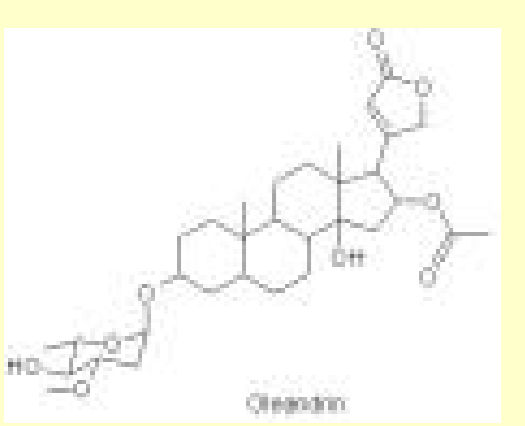


digitoxin

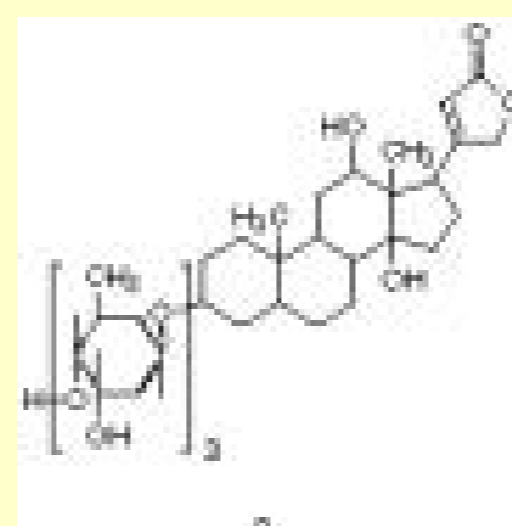
ouabain



oleandrin



digoxin



bufalin

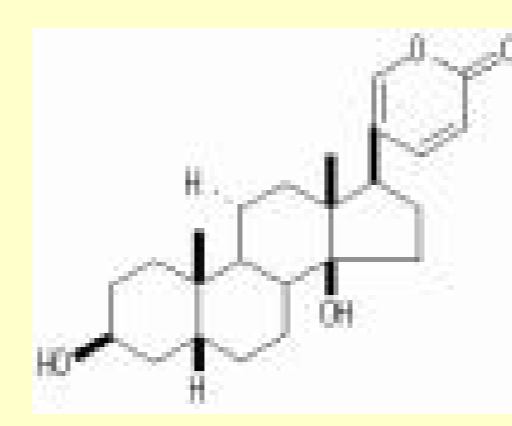


Figure 1. Chemical structure of digitoxin and similar molecules

Case report

PIC Erfurt 200400160

Patient: 70-year-old man

He stayed in hospital for treatment after a threefold coronary bypass operation. He received his last digitoxin medication in a therapeutic dose three weeks ago.

Clinical features:

➤ **ECG:**

In ECG a known normofrequent absolute arrhythmia was observed. Bloodpressure was 120/70 mm Hg and no clinical signs of digitoxin toxicity were seen in the patient during his stay in hospital over 3 weeks.

➤ **Laboratory findings:**

The digitoxin serum concentration was **83.6 nmol/l** although the patient had received his last digitoxin medication in a therapeutic dose 3 weeks ago. After remeasurement of the same serum samples by another immunoassay not using murine antibodies (Dimension, Behring) the digitoxin serum concentration was **6.06 and 7.2 nmol/l**, respectively.

➤ **Possible explanation:**

As possible explanation for this phenomenon of falsely elevated digitoxin serum levels the generation of autoantibodies against murine antibodies in the patient was discussed because he had received murine antibodies (Abiximab) to prevent aggregation of thrombocytes in 1998. However, other substances (endogenous and nutritional) causing crossreactivity due similar chemical structure (Figure 1) have to be considered, as well.

During 2000 and 2004 5 cases with discrepance between high digitoxin serum concentrations and no clinical symptoms of digitoxin intoxication were observed by our poisons information centre

Case series

PIC Erfurt 2000 - 2004

PIC Erfurt	Age	Sex	Symptoms	Digitoxin serum concentration	Method of determination
200004357	80	female	no symptoms of digitoxin intoxication; treatment of diabetes mellitus	200-605 nmol/l	unknown immunoassay
200311033	elderly	female	no symptoms of digitoxin intoxication	10 to 100 fold increase of therapeutic digitoxin serum concentration	FPIA-immunoassay, Integra, Roche; ECL-immunoassay, Elecsys, Boehringer; both with similar results
200400160	70	male	no symptoms of digitoxin intoxication; in ECG a known normofrequent absolute arrhythmia was observed; last digitoxin medication 3 weeks ago	83.6 nmol/l 6.06 and 7.2 nmol/l	immunoassay Advia, Bayer immunoassay dimension, Dade Behring
200403072	76	female	no symptoms of digitoxin intoxication	163.8 nmol/l 34.1 nmol/l	unknown immunoassay MEIA-immunoassay, unknown manufacturer
200403266	83	female	no symptoms of digitoxin intoxication	117.9 nmol/l 43.2 nmol/l	unknown immunoassay unknown immunoassay

Conclusion

- Because of low specificity of immunoassays falsely elevated digitoxin serum concentrations can be observed in asymptomatic patients.
- In these cases a remeasurement by a specific method (HPLC, LC-MS) and a treatment according to the clinical symptoms is recommended.

Literature:

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