

Romina Nemecek<sup>1</sup>, Stefan Harmuth<sup>1</sup>, Rainer W. Schmid<sup>2</sup>

<sup>1</sup> Dept. Surgery, <sup>2</sup> Dept. Laboratory Medicine, University Hospital - Medical University of Vienna, Vienna, Austria

Email: rainer.schmid@meduniwien.ac.at

INTRODUCTION

In surgical patients gastric emptying is monitored by following the serum kinetic of acetaminophen after application of a test dose of the drug. To avoid the stress for patients and for medical staff due to repetitive blood drawings, it was studied, if collection of saliva samples could be a feasible and clinical valuable alternative.

METHODS

In 10 surgical patients up to 10 venous blood samples were drawn in period of 3 hours in a relative narrowly timed kinetic protocol.

Concomitantly oral fluid samples were collected using the commercially available GREINER saliva collection system (Saliva Extraction System, Greiner Bio-ONE Corp, Fig.1): It is based on a buffered and coloured liquid extraction (carrier) fluid ('SES') which the individual has to keep in the mouth for 2 minutes and which is then voided into a collection beaker. After collection into an evacuated collection tube and centrifugation it can be directly utilized for further analysis.

The volume of collected saliva ('Saliva fraction') was assessed by photometric quantification of the yellow dye in the SES-fluid using the GREINER Saliva Quantification Kit applied on a Olympus AU2700 Clinical Analyzer.

Acetaminophen in both samples matrices was analyzed using the DRI EMIT immune assay (Microgenics) using the manufacturer's protocol after minor modifications to increase the assay sensitivity, also applied on a Olympus AU2700 Clinical Analyzer. Oral fluid measurements were normalized by division with the measured Saliva Fraction to obtain the paracetamol values in saliva.



Fig.1: The GREINER Saliva Collection System (SCS)

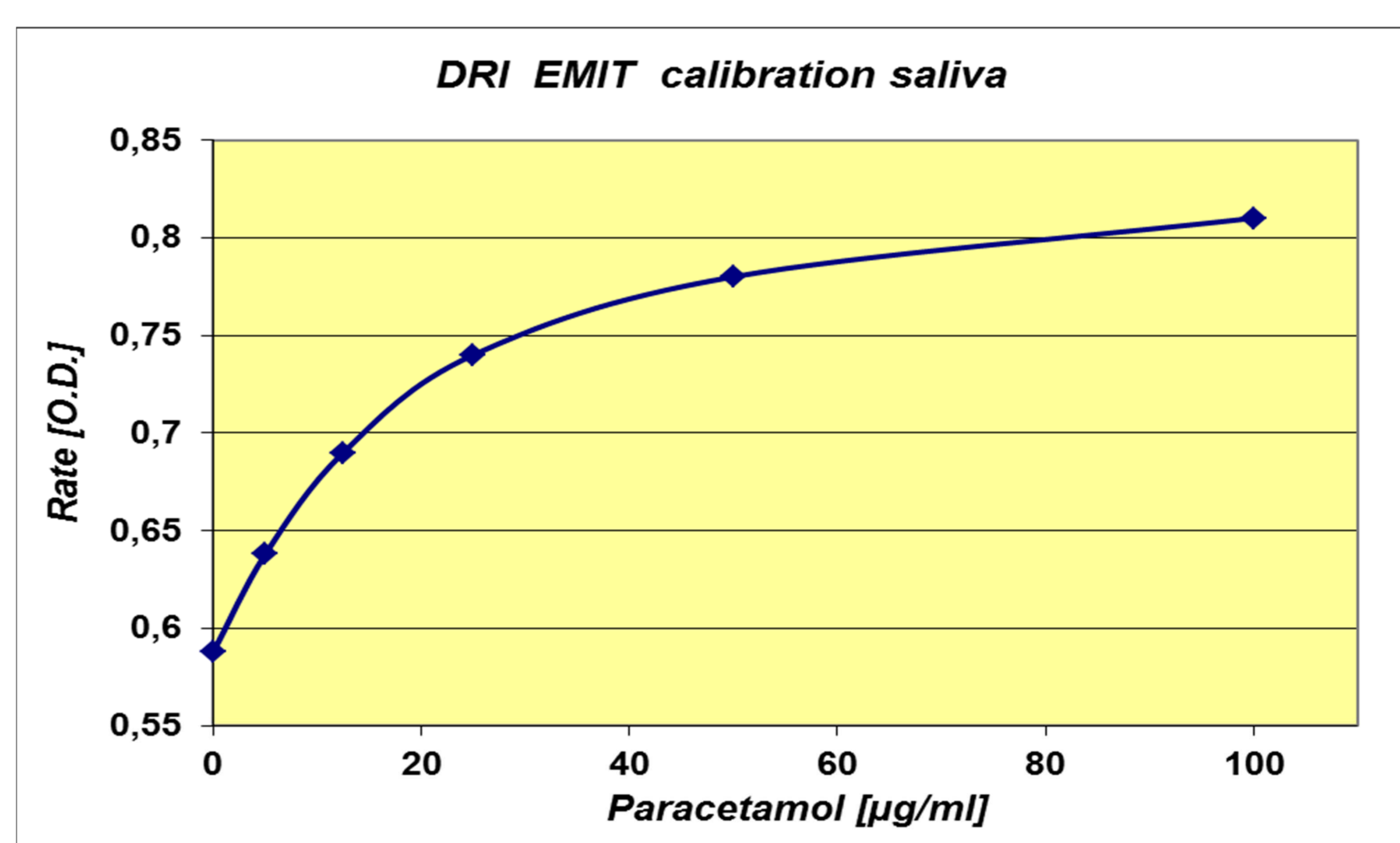


Fig.2: Calibration curve (modified DRI EMIT paracetamol assay)

RESULTS

Using the Microgenics EMIT immune assay acetaminophen can be determined in serum with good linearity and sensitivity down to the high microgram/L range by increasing the sample volume and scaling down calibration standards (Fig.2). The same assay protocol without further modifications gave as well good results for the oral fluid solutions as sample matrix.

Comparison of acetaminophen serum with saliva values (collected at the same time) showed an good agreement: As example, the mean kinetic curves of all patients, who underwent different gastric surgery strategies (Fig 3a and b). They display nearly identical paracetamol values in serum and oral fluid, besides of a consistent aberration at the first time points, which could not be explained and might be due to patho-physiological reasons (altered saliva production rate). Saliva/serum ratios were found to be consistently close to one, which was expected from the polarity of the molecule.

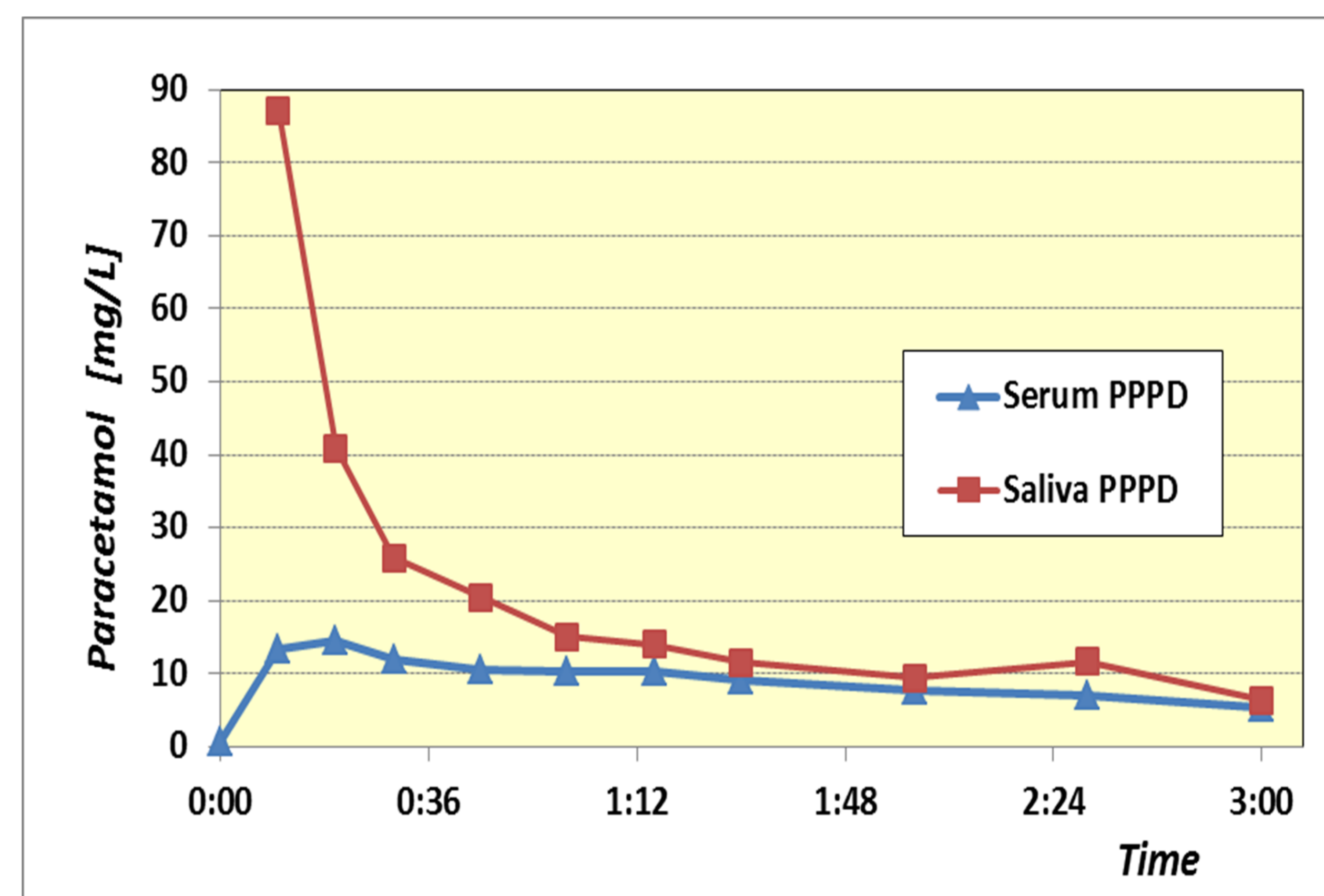
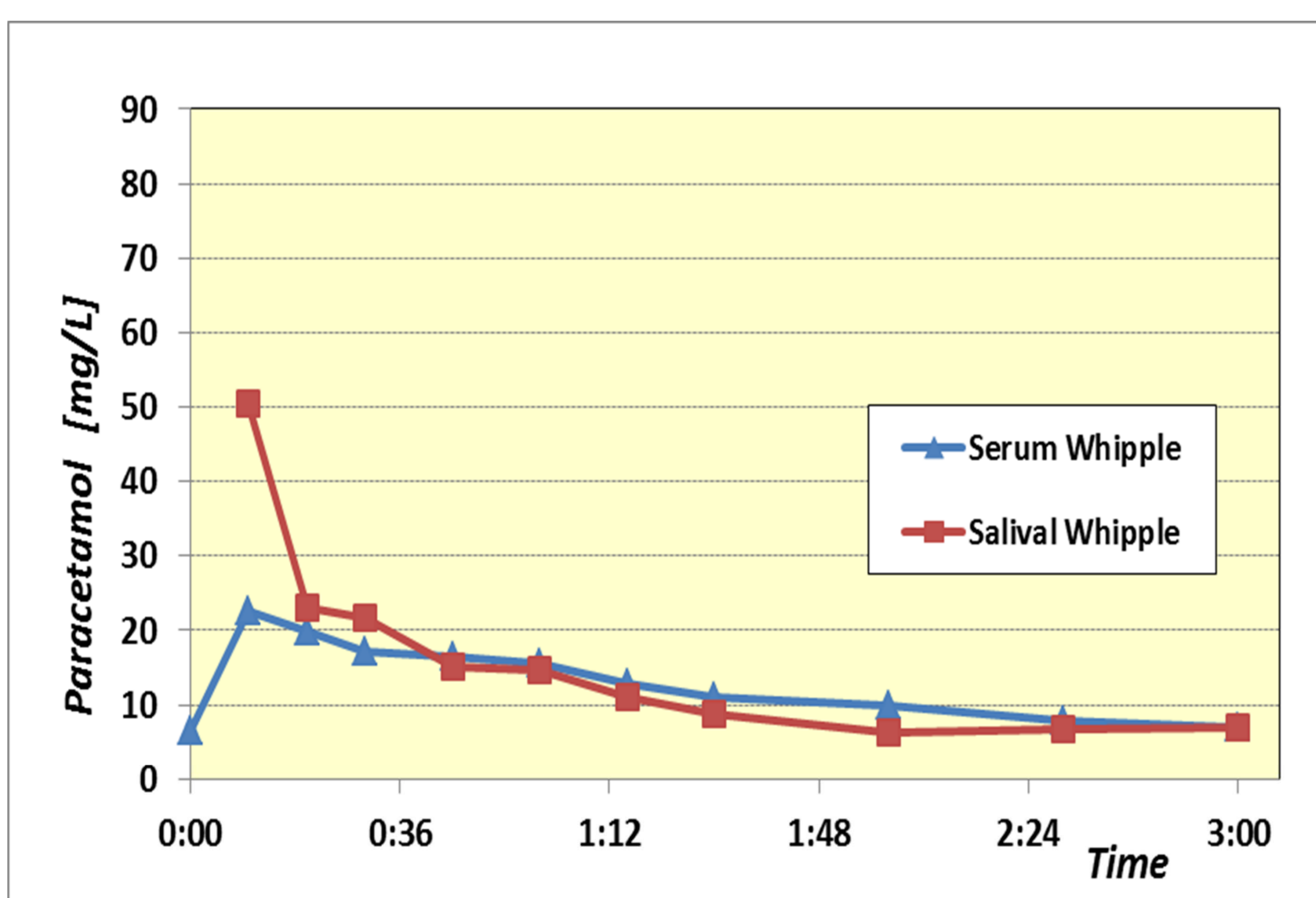


Fig.3 a and b: Mean Kinetic of paracetamol in serum and respective oral fluid of the two patient groups of gastric surgery.

CONCLUSIONS

The extended kinetic measurements of paracetamol demonstrate that oral fluid collection with the GREINER SCS collection system can be considered as a clinically equivalent alternative to serum for drug monitoring in selected clinical pharmacokinetic studies: This procedure gives much less stress to patients and medical staff and can facilitate the whole sample collection process significantly, especially in a tight time protocol.