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Creatinine as a normalization factor to estimate the representativeness of urine sample - Intra-subject and inter-subject variability studies

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HIGHLIGHTS

- Standardization of chemical procedure for creatinine and creatinine co-efficient.
- Investigation of parameters affecting the absorbance using UV-vis spectrophotometer.
- Intra-subject and inter-subject variability study in daily creatinine excretion.
- Variation in creatinine conc. with age, volume & duration of sample was studied.
- The results would be more accurate if a true 24 h urine sample is submitted.

ARTICLE INFO

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Creatinine
Creatinine co-efficient
Daily urinary excretion rate
Intra-subject and inter-subject variability

ABSTRACT

In-vitro bioassay monitoring generally involves analysis of overnight urine samples (~12 h) collected from radiation workers to estimate the excretion rate of radionuclides from the body. The unknown duration of sample collection (10–16 h) adds to the overall uncertainty in computation of internal dose. In order to minimize this, IAEA recommends measurement of specific gravity or creatinine excretion rate in urine. Creatinine is excreted at a steady rate with normally functioning kidneys therefore, can be used as a normalization factor to infer the duration of collection and/or dilution of the sample, if any. The present study reports the chemical procedure standardized and its application for the estimation of creatinine as well as creatinine co-efficient in normal healthy individuals. Observations indicate higher inter-subject variability and lower constancy in daily excretion of creatinine for the same subject. Thus creatinine excretion rate may not be a useful indicator for extrapolating to 24 h sample collection.

1. Introduction

In-vitro bioassay monitoring is based on the determination of activity concentrations of radionuclides in biological samples excreted from the body and is most suitable for alpha and beta emitters such as $^{239+240}$Pu, ^{241}Am, U(nat.) etc.. Bioassay sample collection is avoided from workplace and is collected at home after taking bath. A true representative urine sample is the one having all the voids collected during a 24 h period. However, this being technically difficult, overnight urine samples are collected by the workers. These samples are usually collected overnight for 10–16 h duration. However, in the absence of any specific information, 12 h duration is assumed and the analysis results are then extrapolated accordingly to obtain the daily excretion rate. This unknown duration of sample collection adds to the overall uncertainty in computation of intake and internal dose. In order to minimize this uncertainty, IAEA (1999) has recommended measurement of specific gravity or creatinine excretion rate in urine samples collected from radiation workers (International Atomic Energy Agency (IAEA), 1999). Creatinine is a final metabolic product of a high energy storage compound creatine phosphate in the body. It is normally formed by an irreversible, non-enzymatic mechanism involving creatine dehydration and is excreted at a steady rate (1–1.8 g d^{-1}) for people with normally functioning kidneys (Cocchetto et al., 1983; Boeniger et al., 1993). It is often recommended as a normalization factor for estimation of duration of sample collection (Karpas et al., 1998; Duke, 1998). Following study was therefore, taken up to derive the reference values for creatinine excretion and creatinine co-efficient for individuals and to observe its usefulness as an indicator for completeness of 24 h urine collection. To estimate creatinine in urine samples all parameters in Jaffe's method (Husdan and Rapoport, 1968;

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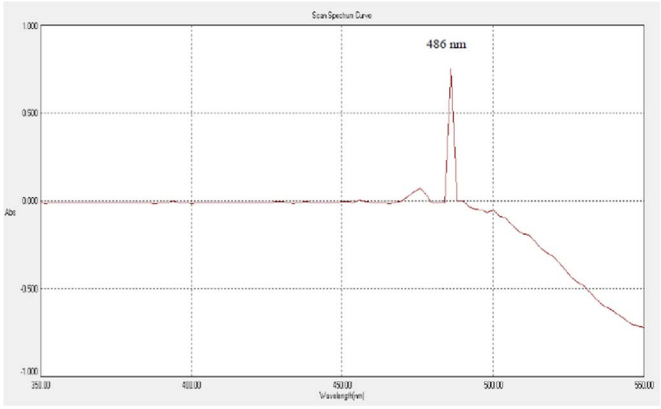

Fig. 1. Determination of λ_{max} for creatinine picrate.

Bonsnes and Taussky, 1945; Kroll et al., 1987) were standardized.

2. Experimental

2.1. Sample details

120 healthy individuals were provided with sample collection kit (1.2 L polythene bottle) and an instruction slip for collecting urine samples for known duration of time. The time duration varied from 2 h to 72 h. About 1100 analyses were carried out to estimate creatinine in these samples by standardized Jaffe's method.

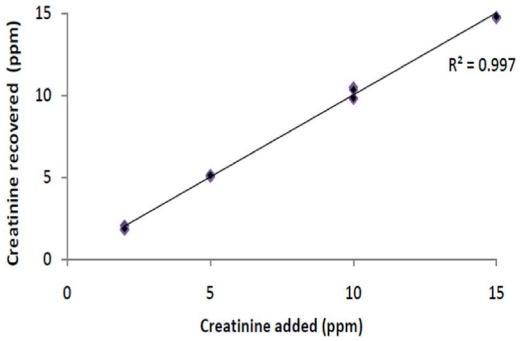

Fig. 3. Recovery of creatinine conc. by Jaffe's method.

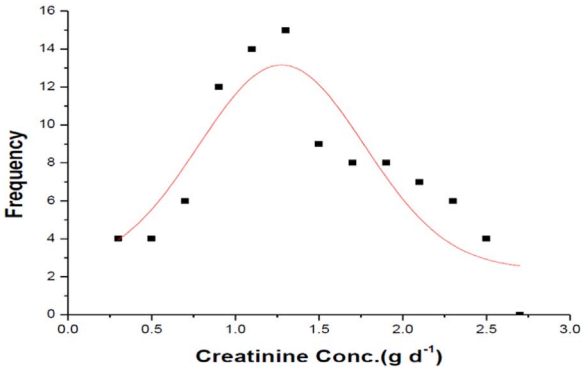

Fig. 4. Daily excretion of creatinine observed in individuals.

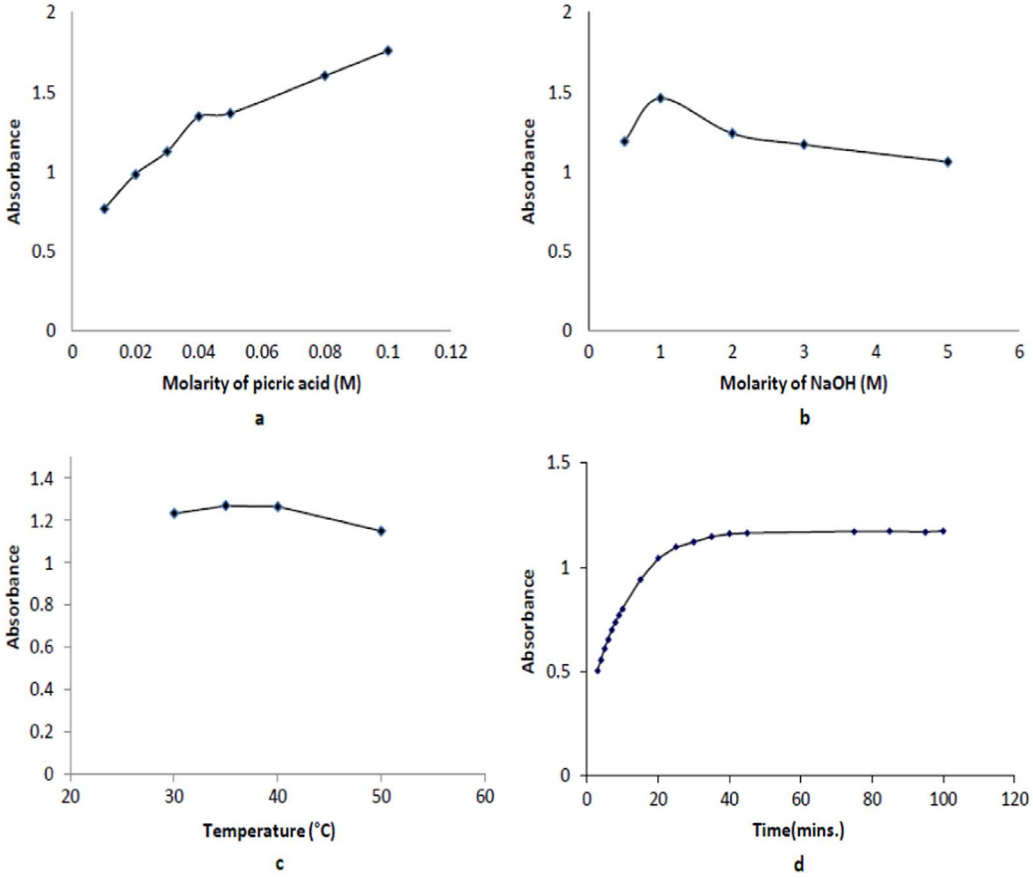

Fig. 2. Variation in absorbance with (a) molarity of picric acid (M) (b) molarity of NaOH (M) (c) temperature (°C) (d) time (mins).