

Valentová J., Horáková R., Okruhlica L., Devínsky F.: **Stereoselective determination of methadone and its main metabolite in serum and urine from methadone maintenance patients.** Neuroendocrinology Letter, 2006, Vol. 27, Supplement 2, p. 130 – 133.

*Objectives:* A stereoselective HPLC method was developed to separate and quantify both enantiomers of methadone and its metabolite EDDP in serum and urine. The method was used to establish that there is a relationship between the dose of methadone prescribed and its serum concentration as well as urine excretion of methadone and its metabolite enantiomers. *Methods:* The chiral  $\alpha_1$ -glycoprotein stationary phase was used for enantioseparation of (R)-methadone, (S)-methadone and (R)-EDDP (S)-EDDS. The enantiomers of methadone and EDDP were extracted from urine and serum by a simple solid-phase procedure. *Results:* The validated method was applied to the analysis of 31 serum and urine samples obtained from methadone-maintained outpatients (65 % male, age  $28.8 \pm 4$ ; methadone dose  $146 \pm 47$ mg). A significant correlation (Pearson)  $r = 0.67$  ( $p < 0.001$ ) between methadone dose and serum concentration of (R)-methadone was found. Due to the large variation in results obtained from analysis of the subjects' urine specimens, no statistically significant relationship between methadone dose and urine excretion of methadone and EDDP enantiomers was established. The rate of R/S methadone (1.38 in serum, 2.43 in urine) and R/S EDDP (0.83 in urine) confirmed stereoselectivity in methadone metabolism with high individual variability. *Conclusions:* The enantioselective evaluation of serum methadone concentration might be an interesting tool in methadone maintenance programme. On the other hand, the urinary excretion of methadone and EEDP enantiomers is not reliable as marker of methadone compliance but could be useful for monitoring individual metabolism or studying the stereoselectivity in pharmacokinetics and metabolism of methadone.

**Key words:** methadone enantiomers – EEDP – stereoselective analysis – clinical application.