SDRL Laboratory

TOXICOLOGY TIMES

SDRL Laboratory

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Technical Brief: Methadone and Methadone Metabolite (part 1)

Methadone (under the Trade Names of Dolophine and Methadose) was first synthesized as a morphine substitute in Germany during the course of World War II and has been clinically available in the United States since 1947. The drug is supplied as the hydrochloride salt in 5-40 mg tablets, 40 mg diskettes or solutions of 10 mg/ml.

Methadone is totally absorbed by the gastrointestinal tract and can be detected in plasma within 30 minutes of an oral dose. The dose reaches a peak plasma concentration within four hours of the dosing. The methadone dose is distributed throughout the body carried or bound by plasma proteins, and is stored primarily in the liver. Storage also occurs in tissue and with the proteins. Repeated daily administration stabilizes this storage in the tissue and also in brain. The basis of therapeutic monitoring of methadone in serum is to verify this stability with respect to concentration in the total biological system. The relative constant level with the appropriate dosing allows the desired secondary effects of the methadone to be relatively constant and the patient feel functional without the opiate craving. High plasma levels of methadone will result in the patient feeling sleepy and groggy while low values will result is withdrawal. Correct therapeutic levels will result in the patient feeling well and able to function in his daily life.

The metabolism of the methadone dose is rather extensive with the primary metabolite being 2-ethylidine-1, 5dimethyl-3, 3-diphenylpyrrolidine, noted for simplicity as EDDP. The amount of methadone and EDDP excreted for a daily dose begins with the majority being methadone after the dose is first consumed, to the end being primarily EDDP. The elimination curve for methadone is high initially and falls off at the end of the 24 hour period after the dose. The ratio of EDDP/ methadone is initially 0.5 and ends at about 1.8. The plasma values follow this same elimination type curve.

When administration of the daily dose stops, or when the patient skips a dose, the value of the methadone falls below the detectable limit in the urine while the EDDP is still seen, and continues to be eliminated. The half life of the methadone in the patient is on the order of 15 to 55 hours. The half life is the time in hours during which 50% of the dose is eliminated. The only active metabolite is methadol; all the rest of the metabolites are biologically inactive. These metabolites are EDDP, EDMP and the glucuronide, with the majority of the ingested sample being excreted as methadone and EDDP.

Part 2 of this Technical Brief will appear in the November issue of *Toxicology Times*.

??? Did You Know ???

That the acceptable temperature range for a urine drug screen is 90º - 100º Fahrenheit post void? If a patient's urine sample falls either below or above this range, it is likely that the patient has either supplied a completely substituted sample brought in from the outside or the sample is some type of full or partial urine substitute (mixed with toilet or tap water, as an example). Urine can cool quickly at room temperature, so it is recommended that a sample's temperature be taken within four minutes post void. Because temperature strips placed on collection devices can be manipulated, SDRL recommends using an infrared thermometer to measure a specimen's temperature. An infrared thermometer is inexpensive (many models can be purchased online for under $50), easy to use (the device is simply pointed at the collection bottle; no contact with urine is necessary), and provides results within seconds. If a patient's sample does not fall within 90º - 100ºF, per SAMHSA guidelines, the sample is to be rejected as unacceptable by the collection facility.

Question of the Month

Question: *When I call SDRL to order additional testing, what do I ask for?*

Answer: Many of our clients' initial panel is an immunoassay panel (class screen only). The most common request for additional testing from these clients is for a confirmation by TLC (Thin Layer Chromatography) or GC/MS (Gas Chromatography/Mass Spectrometry), in which they receive the result for the specific analyte found in a sample – for example, "Morphine" instead of "Opiates". (In California, a confirmation is required to be performed on the initial class abnormal results.) In addition to confirmations, clients can request a "retest", which simply tests the sample again exactly as it was tested before. If Opiates were the class in question, a *retest* of an immunoassay screen would be reported with a result of "Opiates" being Positive or Negative. A *confirmation* would be reported with a result of "Morphine, Codeine", etc. being Positive or Negative.