**Introduction**

Direct injection of urine samples for drug determinations is complicated by matrix constituents including phosphates at levels normally around 10 mmol in healthy adults. These matrix constituents and salts accumulate in inlets of mass spectrometers reducing or destroying response. Additionally, the formation of analyte ions in electrospray ion sources (ESI) can be suppressed by salts at these levels. In our experiments the mass spectrometer is protected by a curtain gas filter (CGF), a mobility-based device which allows only gaseous ions from the spray of an ESI source to enter the mass spectrometer. The CGF moves analyte ions to the capillary inlet through a stream of purified gas and sends all neutral contaminants including solvents, dissolved silica, and phosphate to an exhaust. A schematic representation of the CGF is presented below in figure 1 and an actual CGF is shown in figure 2.

A Shimadzu 2020 LC/MS was equipped with a curtain gas filter developed at NMSU and Rheodyne switching valve without an analytical column for flow injection analysis. Promethazine (a drug in the phenothiazines group of compounds) is used to treat nausea, vomiting and motion sickness after surgery. Promethazine was chosen for initial studies due to the excretion of its metabolites promethazine sulphoxide and dimethylpromazine in urine, and its availability in the lab. The focus of this work is not in detection of the metabolites but whether or not it is possible to detect a compound or compounds of interest (promethazine) in untreated urine. A common complication that arises with electrospray of untreated urine is the ion suppression within the ion source. The high salt content along with excretion of proteins and lipids makes urine analysis without preparation a very complicated process. Salt concentrations within urine in the range from 10 – 150 mM depending on the salt. The following elements/minerals are found in human urine: phosphorous, potassium, sodium, sulfur, magnesium, calcium, nitrogen (total), iron citrate along with a few trace elements. These high salt concentrations require some form of preparation for analysis with a mass spectrometer otherwise the risk of fouling the instrument after a few samples is high. Here no sample preparation has been provided only the CGF to protect the mass spectrometer from the high salt content of urine.

A calibration curve of promethazine in MeOH was prepared and experimental samples were prepared by spiking human urine with promethazine at 1, 10, 20, 50, 80, 100 ppm. Solvent parameters were kept simple at 50/50 MeOH/H2O at a flow rate of 1.4 ml/min. ESI voltage and nebulizing flow of the electrospray ion source were set to 4.5 kV and 1.5 L/min. Signal was recorded for multiple 5.0 μL injections and runs over the course of 2 weeks without having to clean the mass spectrometer. CGF operating parameters were set to optimized values previously recorded: 750 ml/min clean gas and 2.0 L/min exhaust flow rate with the counter electrode voltage set to 40 V. Figure 3 below is a picture of the CGF setup on the Shimadzu LCMS-2020.

**Method**

A Shimadzu 2020 LC/MS was equipped with a curtain gas filter developed at NMSU and Rheodyne switching valve without an analytical column for flow injection analysis. Promethazine (a drug in the phenothiazines group of compounds) is used to treat nausea, vomiting and motion sickness after surgery. Promethazine was chosen for initial studies due to the excretion of its metabolites promethazine sulphoxide and dimethylpromazine in urine, and its availability in the lab. The focus of this work is not in detection of the metabolites but whether or not it is possible to detect a compound or compounds of interest (promethazine) in untreated urine. A common complication that arises with electrospray of untreated urine is the ion suppression within the ion source. The high salt content along with excretion of proteins and lipids makes urine analysis without preparation a very complicated process. Salt concentrations within urine in the range from 10 – 150 mM depending on the salt. The following elements/minerals are found in human urine: phosphorous, potassium, sodium, sulfur, magnesium, calcium, nitrogen (total), iron citrate along with a few trace elements. These high salt concentrations require some form of preparation for analysis with a mass spectrometer otherwise the risk of fouling the instrument after a few samples is high. Here no sample preparation has been provided only the CGF to protect the mass spectrometer from the high salt content of urine.

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**Data**

The mass spectrometer coupled with the CGF was able to withstand repeated injections of human urine without any deterioration of its operation. It must be noted that the LCMS-2020 without a CGF resulted in clogging of the capillary transfer line after 3 injections of urine. Figure 4 shows the extracted ion chromatogram for m/z 285 as well as the mass spectrums for 50, 80, 100, and 500 ppm injections. The overall ion signal was low, due to ion suppression from salts in excess of 100 mM for some salts. However, even though ion suppression was occurring, the limit of detection for direct injection of urine with promethazine was 50 ppm, with studies in progress and through future development of the CGF lower detection limits seem very well achievable.

Future Work

The detection limit of promethazine in an untreated human urine standard was accomplished. The lower limit of detection for this particular study and matrix was 50 ppm or higher. Through the use of alternative techniques such as centrifuging and or filtering it is possible to lower the detection limit. Alternatively one is able to lower the detection limit to 10 ppm by simply injecting ACN following the urine injection. The CGF allows high sample throughput to the MS of unprepared samples that contain complex matrices and or high concentration salts without having to continuously clean the interface and or instrument.

**References**


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