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DRIED URINE SPOT ANALYSIS FOR ASSESSING CARDIOVASCULAR DRUGS EXPOSURE IN
SPACEFLIGHT CONDITIONS**Abstract**

Background: Long-term spaceflights (> 6 months) induce an early arterial aging (EVA) of the astronauts, which can lead later to cardiovascular diseases. There is no preventive drug treatment yet validated. Moreover, the lack of pharmacokinetic data in astronauts justifies the development of a sampling method adapted to space constraints for performing pharmacokinetic/pharmacodynamic (PK/PD) studies on space induced EVA.

Method: We identified a medium, the dried urine spot (DUS), and validated its application coupled to liquid chromatography-mass spectrometry (LC-MS/MS) in the simultaneous detection of five antihypertensive drugs likely to be embarked in space mission. Transfer of urine was done before and during parabolic flight microgravity.

Results: The DUS method coupled to LC-MS/MS to detect these drugs in a single analysis on Alhstrom® paper card with a simple and fast preparation. Linearity was validated over a range of 10 to 300 ng/mL with satisfactory accuracy and precision. Drugs on DUS are stable at room temperature for up to 6 months. Transportation of samples by mail in envelopes presents a low risk of bias on the controls measured concentrations. The feasibility of DUS in microgravity was demonstrated during the CNES (National Centre for Space Studies) parabolic flight campaign in March 2022. The urine transfer was successful in 100% of cases during microgravity. We were able to perform more deposits than scheduled. Indeed, both experienced and novice operators could deposit twice or more per parabola (22 seconds), especially after day1 (D1). During these flights, we also tested the deposition of blood drops onto the dedicated paper card (dried blood spot, DBS) to extend the method of dosage to other drugs and study their metabolism.

Perspective: The feasibility of biological sampling by the DBS method during parabolic flights (March 2023) will be evaluated in flyers through a pharmacokinetic study of caffeine. Self-sampling, self-management and acceptability of DBS and DUS sampling will also be studied at Mars Desert Research Station in Utah (May 2023) by crew 261.

Conclusions: Operational advantages of the DUS in space research are the following: delivery and prolonged preservation of samples at lower cost, implementation of a safety pharmacokinetic study in flight, drug elimination monitoring in urine (biologic fluid). Dried matrices samples would allow to widen the field of application of urine collection in clinical practice for the optimization of therapeutic adherence at home in hypertensive patients.