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Using Space Medicinal Chemistry Against SARS-CoV-2: SpaceMedChem Consortium– Project 1.

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1. Introduction

Research on drug stability has expanded over recent years investigating the effects of storage, transport, and repackaging on stability and more importantly for drug safety reasons in order to minimize the decomposition of the drug components leading to toxic agents. Microgravity, as a promising and emerging tool offers a novel approach to investigate drug stability and develop pharmaceutical compounds and processes with improved properties for applications either in space or on Earth.[1,2]

In the present study, the effect of microgravity was investigated on the complex formation of REM (Remdesivir) and SBECD (sulfobutyl etherbeta-cyclodextrin), that would potentially allow to optimize the formulation process leading to elevated drug efficiency for COVID-19 treatment and/or to improved characteristics such as higher stability of the active compound.

The present experiment was the very first event when anti-COVID-19 research was brought to space.[3]

2. Materials and methods (if necessary)

Physical mixtures of REM (20 mg) and SBECD (200 mg) were suspended either in 0.8 mL ultrapure water or in 0.8 mL HCl solution with concentration of 0.1 M (to obtain pH 3.5). Each suspension (0.4 mL) was transferred to polyethylene vials for microgravity and terrestrial (control) experiments. Two-two samples were kept at 20°C during the whole experiment of 30 days on the International Space Station (ISS) and on Earth. Following the experiment, samples on ground were separated to solid / liquid phases by centrifugation and analyzed by FE-SEM, XRD and Raman spectroscopy / HPLC, respectively.

3. Results

Morphological investigations showed that REM crystals in samples staying on the International Space Station (ISS) for 30 days consisted of particles with significantly smaller size, compared to REM crystals formed in the reference samples

Figure 1 *Experiments were carried out in ESA's Columbus laboratory on the ISS*

Figure 2 *The "KIRARA" cube platform with samples for microgravity testing*

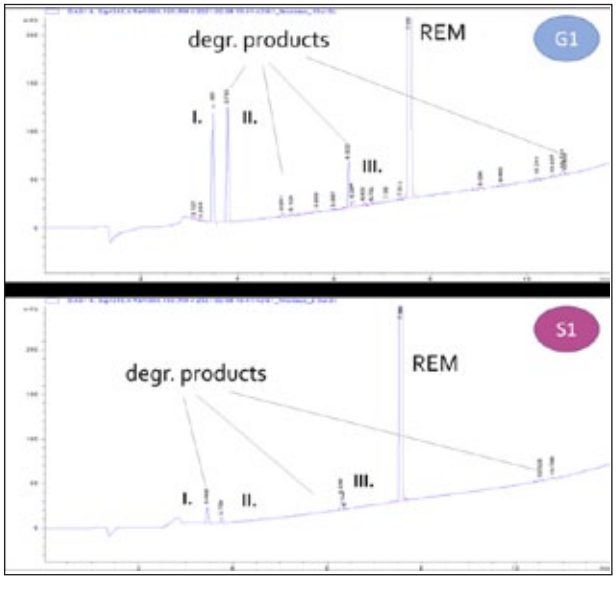

Figure 3 *Fingerprint HPLC chromatograms of the REM-SBECD complex prepared under under terrestrial (G1) and microgravity (G1) conditions.*

(kept on the ground). The highly unexpected major finding of the study is that samples formulated in space at neutral pH revealed significantly less degradation rate of REM in the REM-SBECD complex than observed in the ground sample. The results suggest that the complex formation, and perhaps REM degradation as well took place via different mechanism in space and on Earth. These findings may open new avenues to develop drug molecules with improved stability and efficiency in space, and contribute to the foundation of a new discipline 'space medicinal chemistry'.

4. Conclusions

While microgravity is generally known to diminish drug stability, it was unexpectedly observed that in case of REM/SBECD complex formation, the REM stability was increased in space relative to the reference samples on Earth. Complex formation, and perhaps REM degradation as well took place via different chemical mechanism in space and on Earth. Microgravity can affect morphologies of drugs (including anti-COVID agents) formulated in space. Microparticles with significantly smaller size could be formulated under microgravity.

Further, follow-up experiments are planned to run in frame of the International Consortium for Space Medicinal Chemistry.

It is assumed that the present results provide a promising, novel solution to cope with stability problems of new APIs emerging in the late phase of drug development pipelines. **A consultative/interactive webinar series on Drug Discovery in Space (4) will further discuss the proposed phenomena.**

References

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