Fiscal Year:	FY 2017	**Task Last Updated:**	FY 04/13/2017
PI Name:	Wu, Lei Ph.D.		
Project Title:	Development of Predictive Degradation Models and Determination of Bioequivalence of Pharmaceutical Preparations Contained in the Medical Kits on Board the International Space Station		
Division Name:	Human Research		
Program/Discipline:	NSBRI		
Program/Discipline--Element/Subdiscipline:	NSBRI--Smart Medical Systems and Technology Team		
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **ExMC**:Exploration Medical Capabilities		
Human Research Program Risks:	None		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Comments:			
Project Type:	GROUND	**Solicitation / Funding Source:**	2015 NSBRI-RFA-15-01 First Award Fellowships
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No. of Post Docs:	1	**No. of PhD Degrees:**	0
No. of PhD Candidates:	0	**No. of Master' Degrees:**	0
No. of Master's Candidates:	0	**No. of Bachelor's Degrees:**	0
No. of Bachelor's Candidates:	0	**Monitoring Center:**	NSBRI
Contact Monitor:		**Contact Phone:**	
Contact Email:			
Flight Program:			
Flight Assignment:	NOTE: End date changed to 10/1/2016 to reflect actual end date of project (Ed., 4/12/17)		
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Chow, Diana Ph.D. (MENTOR/ University of Houston) Nair, Ajith Ph.D. (Bilcare Research Inc.)		
Grant/Contract No.:	NCC 9-58-PF04306		
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Task Description:	POSTDOCTORAL FELLOWSHIP The overall goal of the proposed research is to develop and validate predictive degradation models for select pharmaceutical preparations contained in the International Space Station (ISS) medical kits. A related objective of our research is to examine whether or not integrity and performance of degraded formulations is compromised as indicated by bioequivalence in ground-based animal model. The following specific aims will be pursued to accomplish our research goal: 1) Establish a validated HPLC-MS/MS assay method that can be used for the identification and quantification of active pharmaceutical ingredient (API) and degradation products of the selected formulations. 2) Characterize degradation profiles and API content of medications received from ISS and compare with existing data from ISS payload and irradiation studies. 3) Conduct ground-based accelerated stability studies with matching set of medications selected for the above aims to develop predictive degradation models. 4) Estimate bioequivalence between Earth-based control and Space X returned formulations in a small animal model (rat) to examine integrity and performance of medications stored on board the ISS. In the stability study, a rapid, sensitive and specific UPLC-MS/MS method was developed for the simultaneous determination of ibuprofen tablets and promethazine in tablets and injection solutions stored on board the ISS and on ground. Another rapid, sensitive, and specific UPLC-MS/MS method was developed for the identification and quantification of azithromycin tablets stored on board the ISS and on ground. With the LC-MS/MS approaches, the API of formulations was quantified. The three pharmaceuticals returned from ISS contain less API contents than their respective ground controls. Ibuprofen tablet has 14-17% less APT content than their ground controls; promethazine tablet has 14-23% less API content, while promethazine injection solution has 15-18% less API content, and azithromycin tablet has17-27% less API content. Results of this study provide important information for future identification of degradation profiles for ibuprofen and promethazine. These data will be also useful in understanding whether the degradation patterns of medications onboard space missions is the same or different from those on the ground. In the bioequivalence study, 24 Healthy Sprague-Dawley (SD) rats in 6 group were used for the estimation of bioequivalence of Ibuprofen (IBU) tablets, promethazine in tablets, and promethazine injection solution between Space X returned formulations and the Earth-based controls. After PK (pharmokinetics) study of IBU in rats, the results showed that IBU from ISS groups were not bioequivalent to the reference control in SD rats, based on systemic exposure of AUC and maximum observed concentration (Cmax). The drug exposure was decreased since the degradation of API of ibuprofen stored in ISS. The similar pharmacokinetic studies on promethazine products; however, did not demonstrate such bio-inequivalency. It warrants further investigation with a larger sample size. On the other hand, the study might indicate that the losses of drug content might or might not lead to the non-bioequivalence. The results from this study could identify the formulations that were sensitive and degraded in the space environment. The selection of future medications should take this observation into consideration, and the storage condition requires additional measure to protect, if it is still selected.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	This project addresses the long term goal of development of predictive degradation models that enable testing and validation of protective packaging and dispensing technologies for space pharmacy. This technology development project attempts to identify a standard protocol and a scientific scale/algorithm for evaluating and quantifying the pharmaceutical product integrity and activity as a function of specific space environmental factors. The results from our progress are the first successful step towards identifying appropriate packaging materials that can assure extended shelf life of pharmaceuticals in space. Results from the in vivo study of selected formulations provides information on formulation integrity and performance effects due to storage on board the ISS and impact on bioequivalence. The result of this study also enable selection and identification of both stable formulations as well as appropriate storage conditions for future missions. Finally, this project will provide validation of methods for future technology development and address an important Human Research Program (HRP) Gap Pharm02: We do not know how long medications may be safe and effective beyond their expiration dates.
Task Progress:	Stability study completed in April 2016. A rapid, sensitive, and specific UPLC-MS/MS method was developed for the simultaneous determination of ibuprofen and promethazine in tablets and injection solutions stored on ground and on the board the ISS. Another rapid, sensitive, and specific UPLC-MS/MS method was developed for identification and quantification of azithromycin tablets stored on ground and on the board the ISS. API content of medications received from ground control and ISS were quantitated and compared with existing data from ISS payload and irradiation studies. Bioequivalence study completed in October 2016. Healthy Sprague-Dawley (SD) rats were used for the estimation of bioequivalence between Earth-based control and Space X returned formulations. Ibuprofen, promethazine in tablets, and promethazine injection solution from ground-based reference control and ISS groups were administered to the animals in six groups (4 per group). Three groups of animals were dosed with ground-based reference control and other 3 groups were dosed with ISS returned samples. Pk study were finished and PK parameters were derived and compared between ground control group and ISS group.
Bibliography Type:	Description: (Last Updated:)