

Medicines for Moon Outpost: Cosmic ray stability of space-developed of ibuprofen formulations on Earth and the International Space Station

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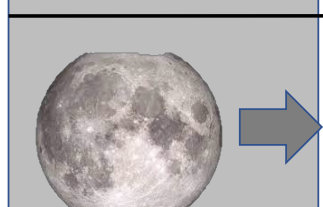






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Introduction

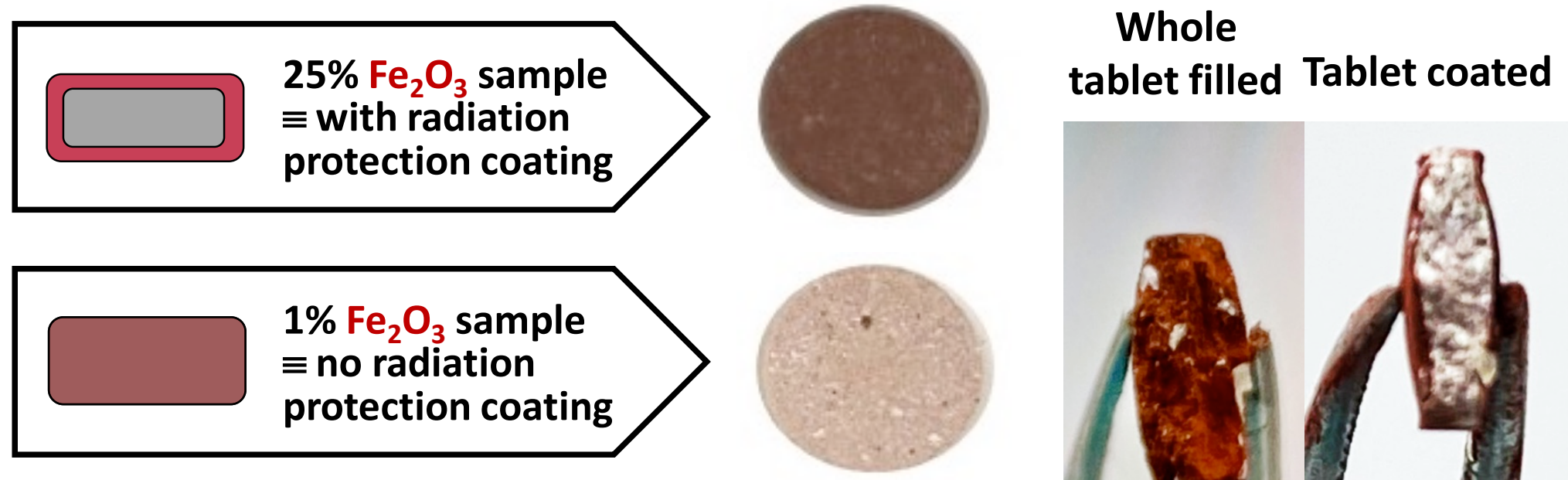
- Medicines in space have shorter shelf-life
- Cosmic ray is one of the underlying causes.
- Resupply of onboard medicines will not be feasible in extended human space missions
- Our proposed space medicine**
- Self-stabilize under cosmic radiation
- Utilized space resources as excipient analogues which allows future in-space manufacturing
- Current formulation uses Moon abundant materials, e.g., iron oxide and titania for coating

	Silica	Iron Oxide	Titania	Talc	CaH-Phosphate
					
Excipient function	Flowing agent, anti-caking, binder	Colourant, light protectant	Colourant, opacifier	Gildant, anti-adherent	Filler

Cosmic ray protection concepts

Space medicine can be stabilized under radiation via shielding concepts:

- Dilution of API in the excipient matrix
- Coating with high atomic number elements
- Molecular interaction between drug – excipients



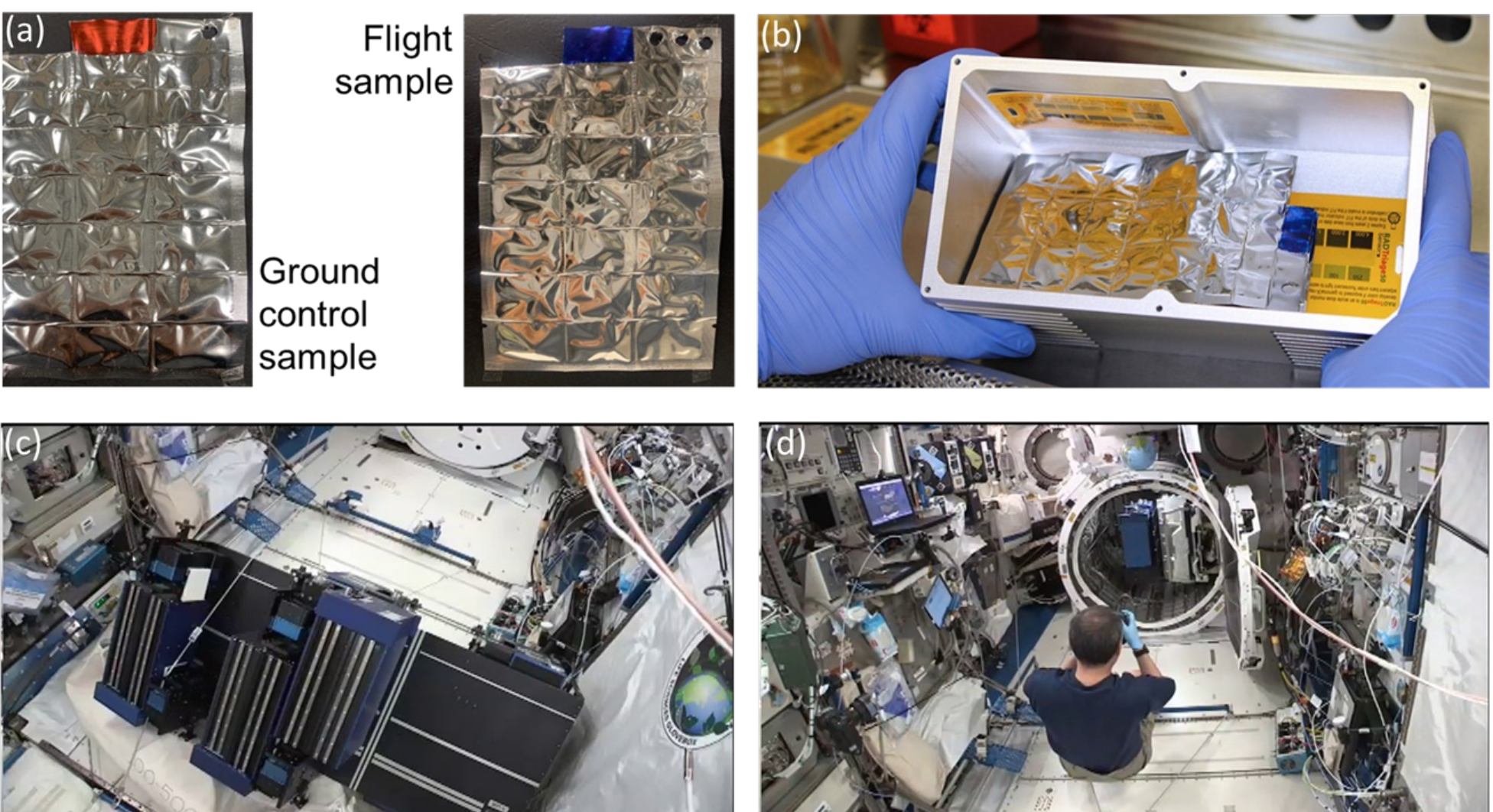
Space missions

NG-14 mission

- ☐ Stored inside ISS
- ☐ 60 tablets – 19 different compositions
- ☐ Moderate dose cosmic radiation

NG-15 mission

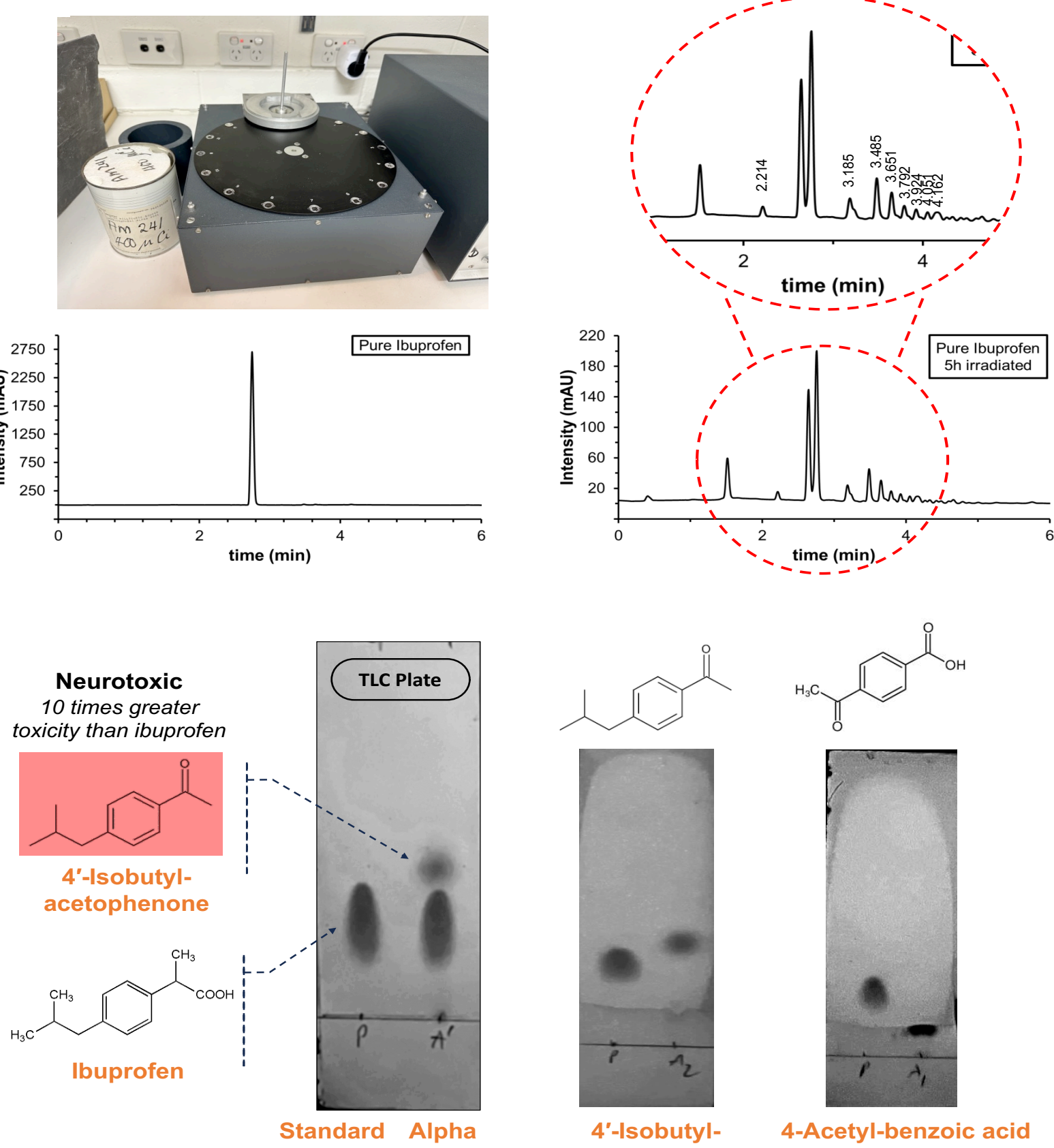
- ☐ Stored outside ISS – mounted on MISSE unit
- ☐ 6 tablet compositions
- ☐ High dose cosmic radiation



Results & Discussions

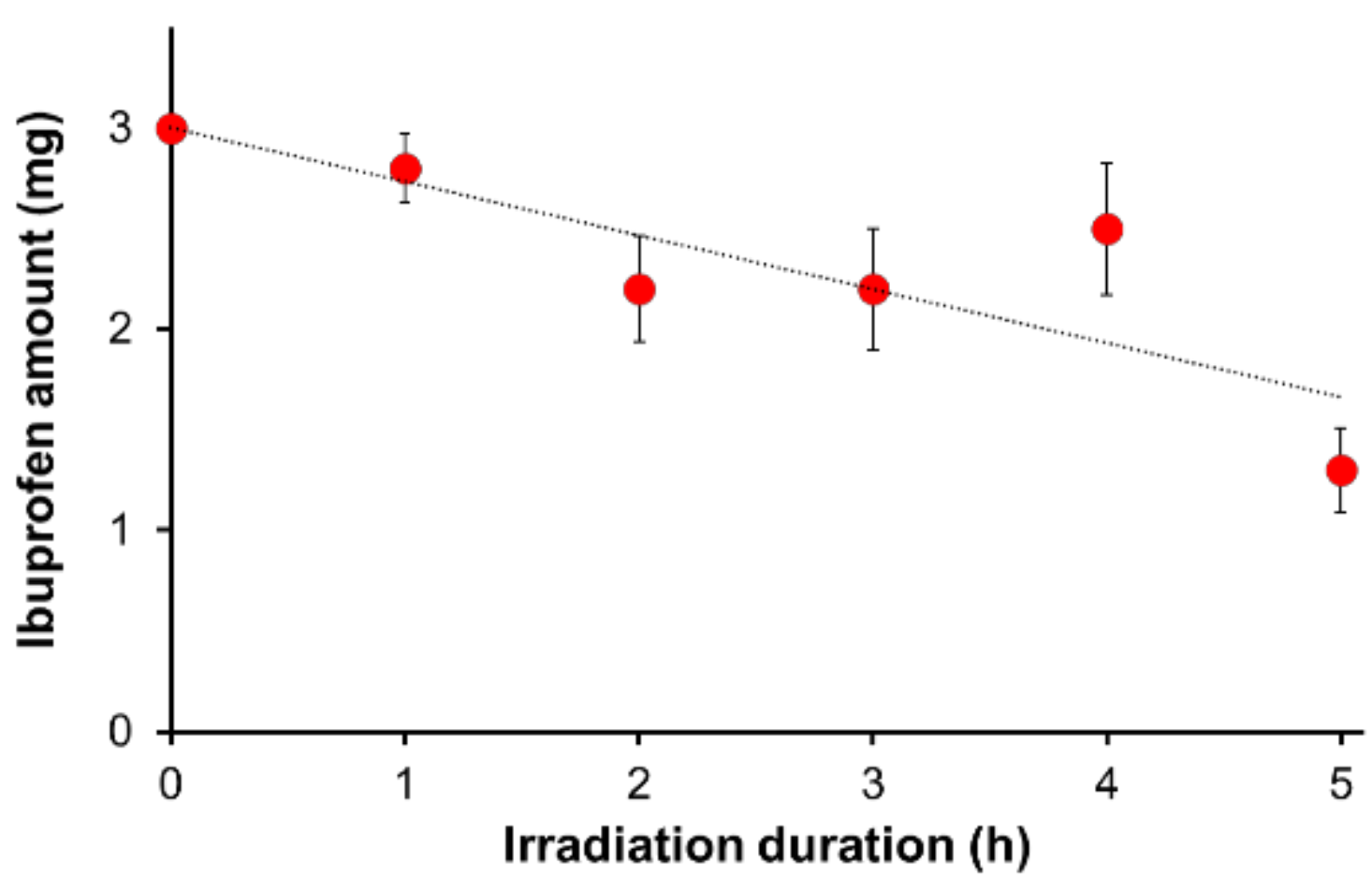
Earth-simulated space condition

Alpha radiation

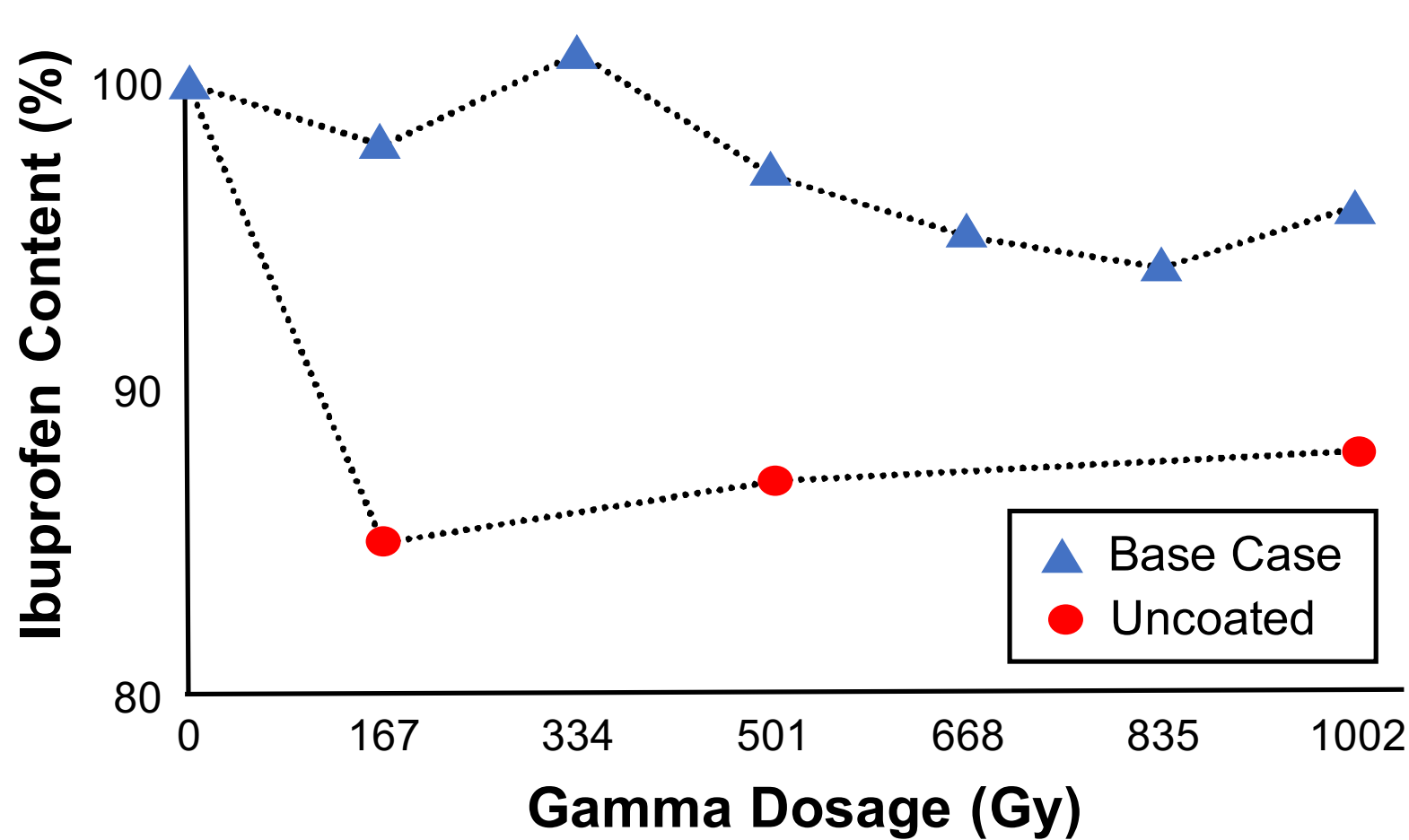


- **Alpha radiation** decomposes pure ibuprofen after 5hr of exposure
- 4'-isobutylacetophenone was identified, confirming that decarboxylation and oxidation occurred.
- 4'-isobutylacetophenone is a neurotoxin with 10 times greater toxicity than ibuprofen

Beta radiation

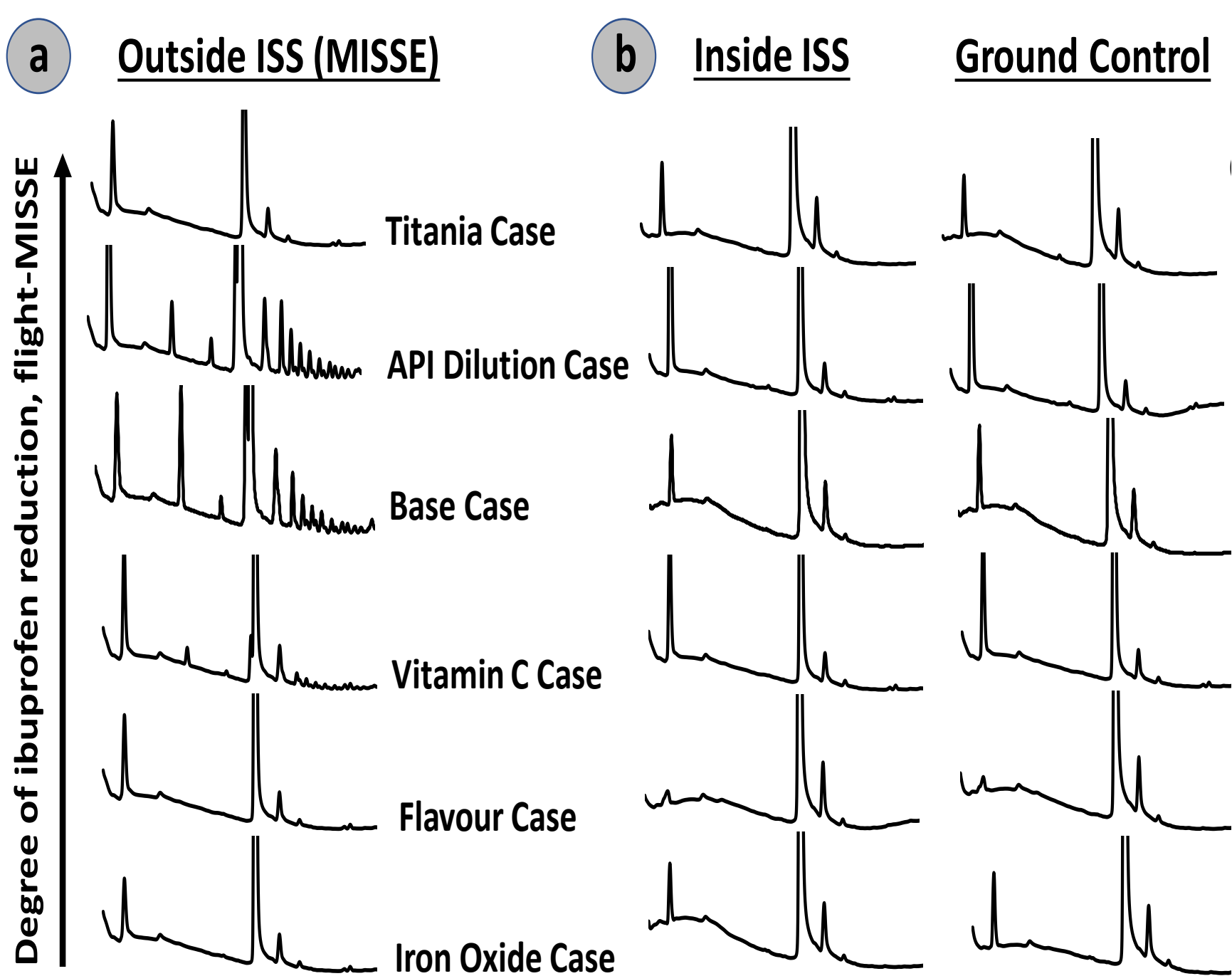


Gamma radiation



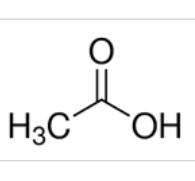
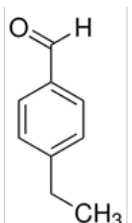
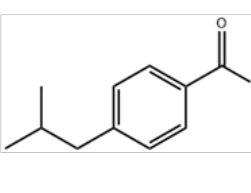
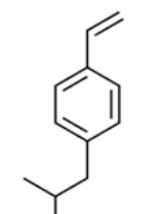
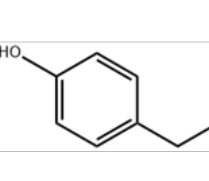
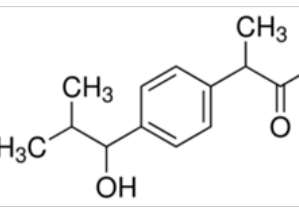
















































- **Beta radiation** was set to reflect ca. 5-year space radiation at ISS.
- Half of the ibuprofen was degraded after tested period
- **Gamma radiation** cause greater decompose effect on tablets with no shielding materials.
- This shows that iron oxide is also relevant to protect from Gamma rays.

Real space investigation



- **ISS tablets** 10-fold reduction in ibuprofen found in low iron oxide samples.
- Other cases show similar reduction in flight and control samples
- **MISSE tablets** help to reconfirm the role of iron oxide content in radiation protection.
- Titania sample shows the greatest reduction of ibuprofen content.
- Terpenes flavonoids support the stabilization of ibuprofen under exposure.

Space decomposition products

						
	Acetic acid	4-Ethylbenzaldehyde	4-Isobutylbenzoic acid	4-Isobutylstyrene	4-Isobutylphenol	2-(4-(1-Hydroxy-2-methylpropyl)phenyl)propanoic acid
Safety classification		Irritant	Irritant	Not reported	Irritant, corrosive	Irritant
GHS hazard rating		Skin, eye, organ	Skin, eye, organ	Not reported	Toxic, corrosive	H302 (100%)
ECHA hazard rating		Acute Tox. 4 (85%)	Irrit. 2 (100%)	Not reported	Acute Tox. 4 (100%)	Acute Tox. 4 (100%)
Base Case _{decomp}						
High Dilution _{decomp}						
Iron Case _{decomp}						
Vitamin-C _{decomp}						
Flavour _{decomp}						
Titania _{decomp}						
Base _{decomp}						
Standard _{decomp}						
Max. intensity _{decomp}	1.2 × 10 ⁹	6.5 × 10 ⁷	2.0 × 10 ⁷	1.3 × 10 ⁸	1.5 × 10 ⁸	6.0 × 10 ⁸

- 60 decomposition products were found in LC-MS, however, only 6 matches to ibuprofen decomposition database.
- Space decomposed ibuprofen follows photo-catalytic chemically oxidative, thermal oxidative, enzymatic, cavitation, and environmental degradative pathways.
- Acetic acid is rarely mentioned in the context of ibuprofen degradation; however, it is an essential component in our flavor mixtures.

Conclusions

- The first systematic investigation of ibuprofen tablet for cosmic-ray protection in space.
- An excipient matrix is a potent concept for enhancing medicines shelf-life in space
- Inorganic excipients have similar chemical identity with Moon resources, which open up potential in space manufacturing.
- Iron oxide coating and terpene flavours excipients stabilise ibuprofen in and outside ISS
- Titania destabilises ibuprofen as photocatalyst

References

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- Tran, Hessel et al. *In-Space Manufacturing and Resources: Earth and Planetary Exploration Applications* (2022) 47
- Nijhuis, Hessel et al. *Frontiers Space Technol* 2 (2022) 779696

