Preliminary Evaluation of Commercial Off the Shelf (COTS) packing materials for Flight Medication Dispenser (FMD) Technology Development

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Aim

Evaluate COTS packing materials for Radiation Shielding and Moisture Protection of three susceptible medications from Space Flight Medication Kit (SFMK)

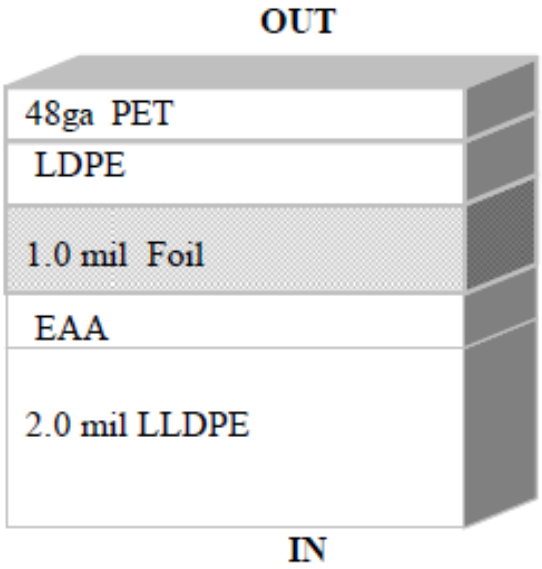
Introduction

- As NASA moved forward with exploration and longer duration missions, pharmaceutical use in space has increased.
- During the first 33 space shuttle missions, crew members took more than 500 individual doses of 31 different medications (Tietze and Putcha, 1994).
- Anecdotal reports from crew members described medications as generally “well tolerated” and “effective”. However, reports of increased medication doses and discrepancies in ground vs. flight efficacy were reported.
- One of the possible causes for reduced potency or altered bioavailability can be changes in chemical and/or physical parameters of pharmaceutical stability .

Background

- **Technology Development Goal –**

  Blister packs and FMD with special shielding material for protection against radiation, thermal degradation, oxidation, hydrolysis and shear effects



- **COTS Shielding Material –**

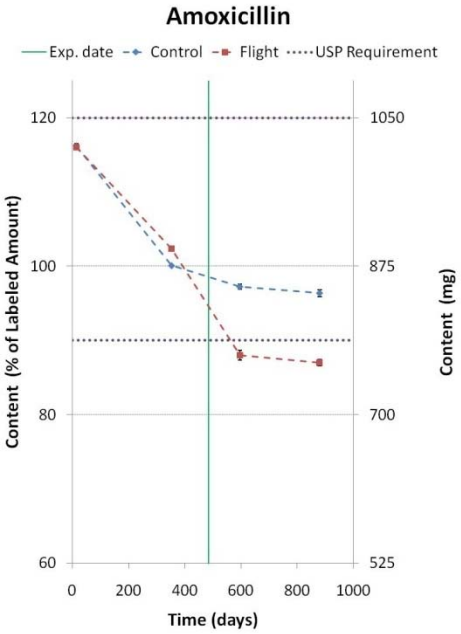
  Aluminum coated Mylar sheathing material coated with multifunctional nanocomposities based on polyethylene with dispersed boron-rich nanophases

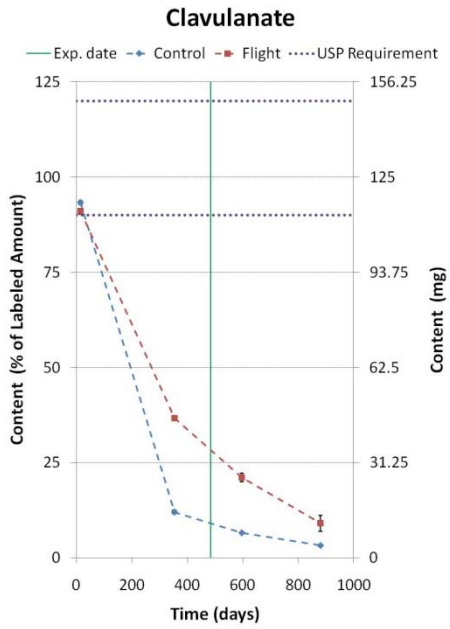
Related Research

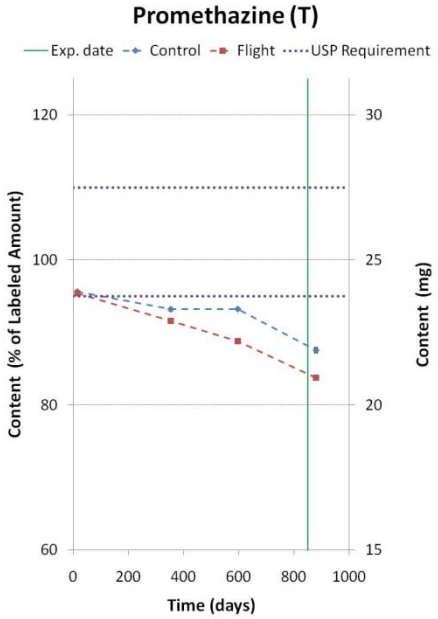
- **Stability of dosage forms in the pharmaceutical payload aboard space missions**

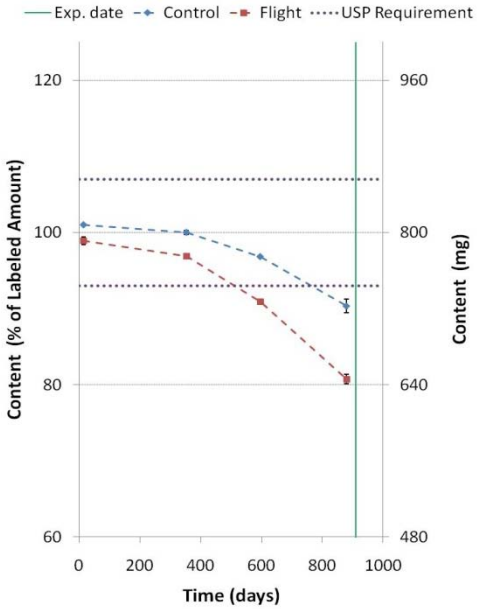
Results: Some medications are more sensitive than others to conditions of space flight.

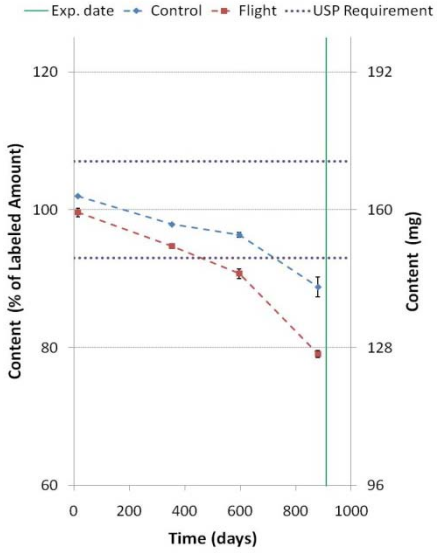
- Augmentin® tablets – sensitive to light and humidity
- Bactrim® tablets – sensitive to light
- Promethazine tablets – sensitive to light


Amoxicillin
Exp. date
Control
Flight
USP Requirement
Content (% of Labeled Amount)
Content (mg)
Time (days)
120
100
80
60
1050
875
700
525
0
200
400
600
800
1000


Clavulanate
Exp. date
Control
Flight
USP Requirement
Content (% of Labeled Amount)
Content (mg)
Time (days)
125
100
75
50
25
0
156.25
125
93.75
62.5
31.25
0
200
400
600
800
1000


Promethazine (T)
Exp. date
Control
Flight
USP Requirement
Content (% of Labeled Amount)
Content (mg)
Time (days)
120
100
80
60
30
25
20
15
0
200
400
600
800
1000


Sulfamethoxazole
Exp. date
Control
Flight
USP Requirement
Content (% of Labeled Amount)
Content (mg)
Time (days)
120
100
80
60
960
800
640
480
0
200
400
600
800
1000


Trimethoprim
Exp. date
Control
Flight
USP Requirement
Content (% of Labeled Amount)
Content (mg)
Time (days)
120
100
80
60
192
160
128
96
0
200
400
600
800
1000

Objective

Test Oliver-Tolas TPL-1475 and TPF-0599B bags for protection of medications against ionizing radiation and moisture effects

- **Augmentin®: Amoxicillin/Clavulanate combination antibiotic**
- **Bactrim® - Sulfamethoxazole/trimethoprim combination antibiotic**
- **Phenergan® - promethazine antihistamine**

Methods

- **Radiation testing:**
  - **Packed 8 bags each of Oliver-Tolas TPC-1475(Clear) and Oliver-Tolas TPF-0599B (Foil) material containing 9 tablets in each bag of one of the three medications – total of 24 bags of 3 medications. Of the 8 bags,**
  - **2 bags served as control (no irradiation) .**
  - **2 bags of each medication were irradiated for different time intervals with 14.6 rad/min using Hopwell BX35 PS137 at 35 cm distance in a cardboard box to achieve 0.1 Gy, 1 Gy and 10 Gy of cumulative dose.**
- **Humidity testing:**
  - **Augmentin® tablets (9) were packaged in 4 TPC-1475 and 4 TPF-0599B bags.**
  - **2 bags served as control and 2 were stored at 25°C & 75%RH for 6 days for accelerated humidity testing.**
  - **Chemical content of all medications was analyzed using Waters UPLC system. All analyses were done according to standard United States Pharmacopeia (USP) methods verified and validated in the JSC Pharmaceutical Analysis Lab.**

Results

Augmentin® Tablets

Active	Amoxicillin		Clavulanate	
Condition	Content (%)	SD	Content (%)	SD
0 Time	107.9	0.77	98.4	0.35
Control	106.7	1.14	98.6	1.32
0.1Gy Clear	106.1	1.19	98.6	1.04
0.1Gy Foil	106.4	1.50	96.5	0.31
1Gy Clear	105.1	1.59	97.4	1.99
1Gy Foil	105.4	0.96	96.3	0.92
10 Gy Clear	106.6	0.43	96.5	0.44
10 Gy Foil	105.8	0.92	96.7	1.38
25oC&75%RH Clear	106.4	0.60	96.5	1.43
25oC&75%RH Foil	106.8	1.30	97.1	1.58

Bactrim® Tablets

Active	Sulfamethoxazole		Trimethoprim	
Condition	Content (%)	SD	Content (%)	SD
0 Time	101.5	0.64	100.5	1.05
Control	100.4	0.74	99.9	1.22
0.1Gy Clear	101.2	1.02	100.2	1.48
0.1Gy Foil	99.9	1.45	99.7	1.25
1Gy Clear	100.0	1.01	99.7	0.91
1Gy Foil	99.7	0.66	99.2	0.69
10 Gy Clear	99.4	0.78	98.6	1.29
10 Gy Foil	98.6	1.40	98.0	1.99

Promethazine Tablets

Condition	Content (%)	SD
0 Time	98.8	0.38
Control	98.3	0.83
0.1Gy Clear	95.9	0.74
0.1Gy Foil	96.0	0.58
1Gy Clear	96.0	0.78
1Gy Foil	95.8	1.08
10 Gy Clear	95.8	0.50
10 Gy Foil	95.3	0.54

Discussion

- No significant difference in content between control and irradiated samples was noticed for Bactrim® and Augmentin® tablets suggesting both COTS materials may offer protection against radiation (γ).

- Preliminary results from this study are insufficient to determine effectiveness of COTS materials for Phenergan® tablets.

- RH test results indicate no significant difference in content between control and test condition for Augmentin® tablets (6 days of storage in high RH of 75%).

Condition	Time (d)	% Content Amoxicillin	% Content Clavulanic Acid
25°C 75%RH SFMK Pill Bottle	0	110.5	95.7
	1	107.0	94.2
	3	100.9	88.1
	7	99.4	70.6
25°C 75%RH Commercial Package	0	110.5	95.7
	1	108.1	94.7
	3	105.2	93.2
	7	104.0	89.0

Experimental Artifacts

- Compromised experimental design
- Insufficient samples and controls
- Inadequate technology streamlining and validation procedures

Conclusion

- **Oliver-Tolas TPL-1475 and TPF-0599B bags materials may be suitable for protection of clavulanate against humidity.**

- **Both materials may have characteristics suitable for protection against ionizing radiation and high RH and may be candidates for further testing separately and in combination.**

Forward Plan

- Compare both materials for relative efficiency separately and in combination
- Investigate Nanoparticle coating technology for environmental protection (Rice Nanotechnology Center)
- Identify and develop FMD design options with the materials – unit dose pop-up packing (COTS redesign)
- special design multi dose dispenser bags (COTS)
- Investigate kit design options using the new materials for Space hardy storage and dispensing

Explore funding resources

Acknowledgements

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