STABILITY INVESTIGATION OF GAMMA-RAY IRRADIATED ANTIBIOTICS

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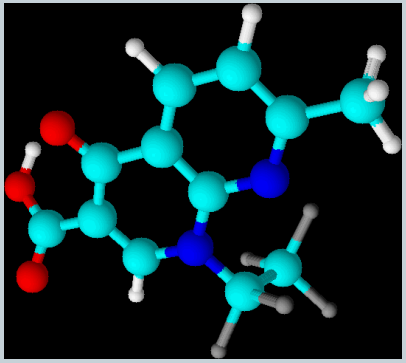
AIMS

- Evaluation of gamma radiation influence on selected antibiotics;
- Long time stability of medicines subsequent to their gamma irradiation exposure;
- Necessity: safety and effective multifunctional medicines for use during long-duration spaceflights.

MATERIALS

- **Nalidixic acid (NAL); $C_{12}H_{12}N_2O_3$**



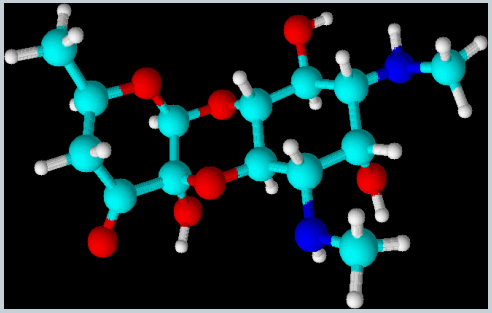
M=232.24 g/mol

White powder;

Colorless solution

(in deionized water);

- **Spectinomycin (SPEC); $C_{14}H_{24}N_2O_7$**



M=495.35 g/mol

Colorless solution

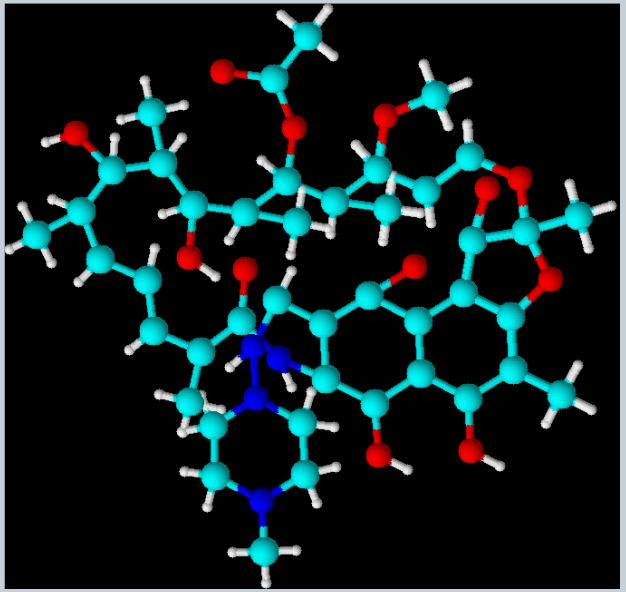
(in deionized water);

- **Rifampicin (RIF); $C_{43}H_{58}N_4O_{12}$**

M=823 g/mol

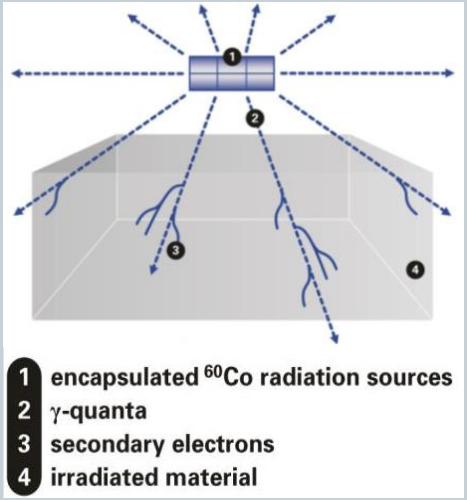
Red powder/solution

(in 50:50 deionized water /EtOH)



METHODS

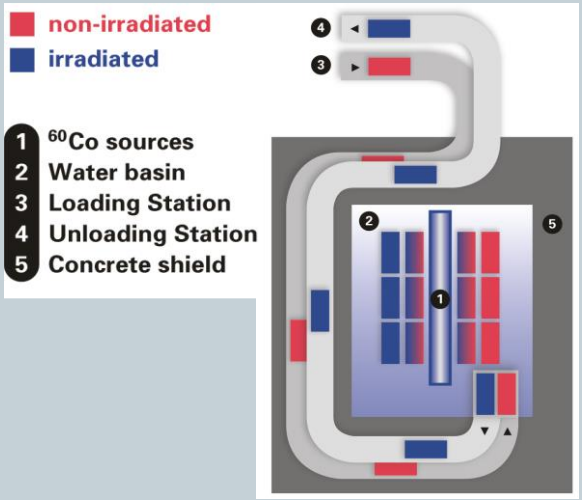
- Gamma Irradiation (BGS, Germany): ^{60}Co source



Antibiotics – solid samples

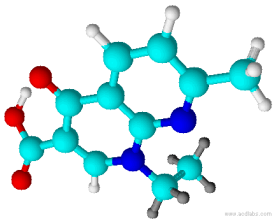
irradiation doses:

6-204 kGy

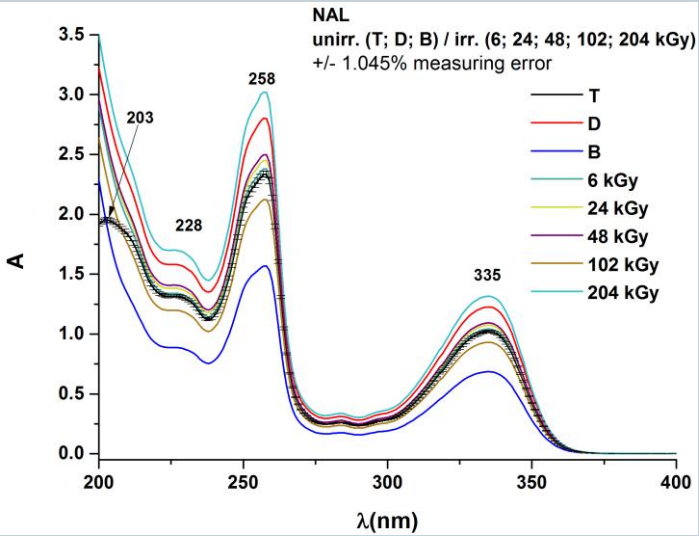


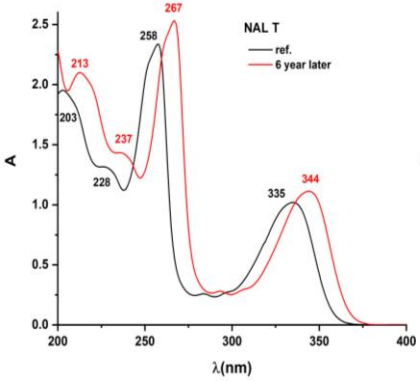
- Spectral measurements (SOL-INFLPR, Romania):
  - UV-VIS Absorption (Lambda 950, Perkin Elmer, U.S.A., rez. ≤0.05 nm)
  - FTIR Absorption (Nicolet IS50, Thermo Scientific, U.S.A., 4000-400 cm^{-1}, resolution 4 cm^{-1}, Omnic 9 Standard)

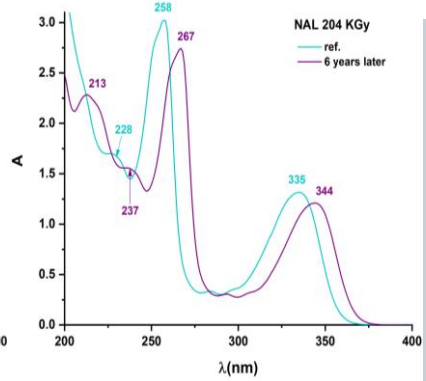
UV-VIS STABILITY

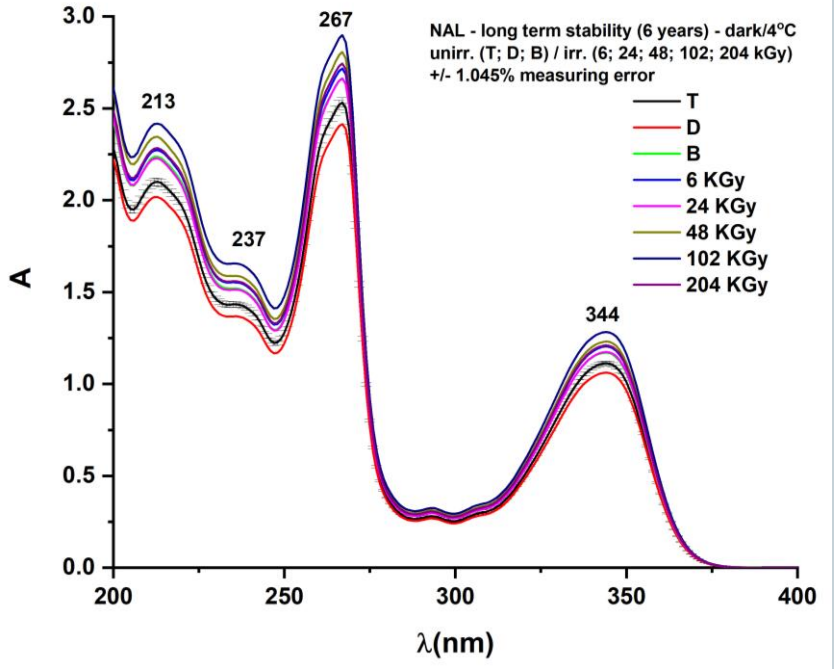


NAL



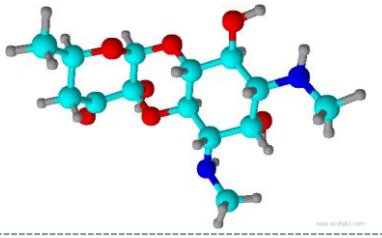




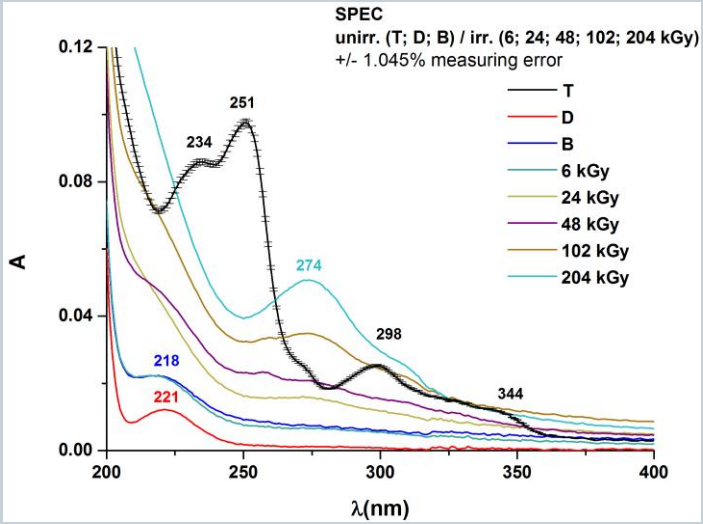


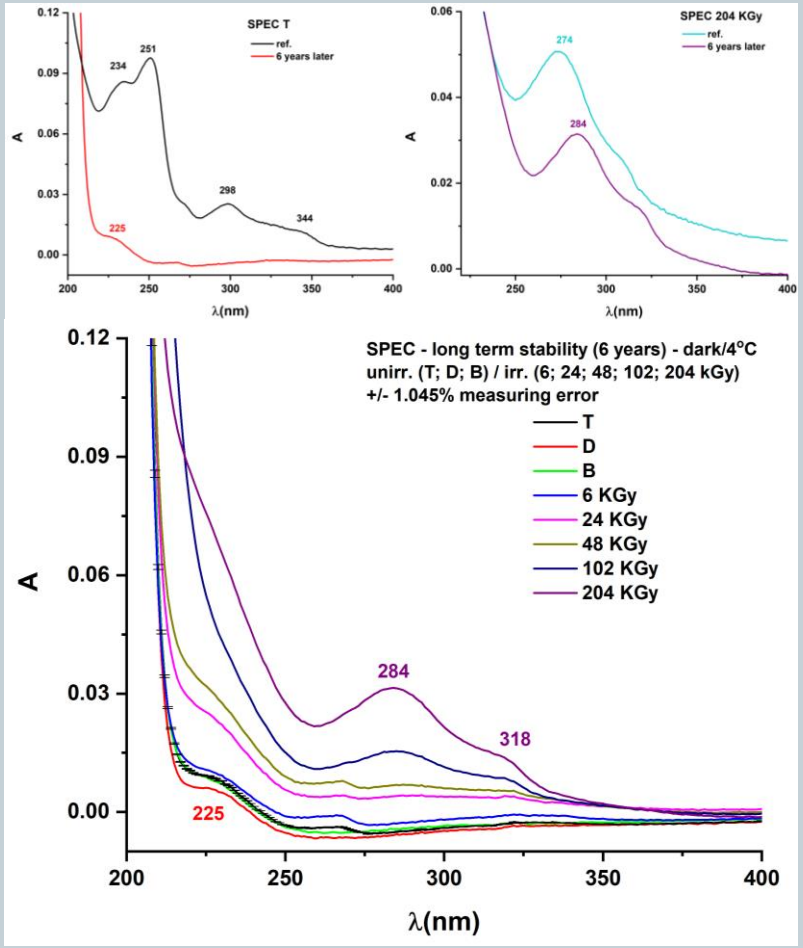
- Degradation of the irradiated solutions; exception the 6 kGy gamma-ray exposed sample;
- Degradation of the unirradiated solutions;
- Red shift along with hyperchromic effect in the characteristic absorption spectra of long term stored NAL unirradiated;
- Red shift along with hypochromic effect in the characteristic absorption spectra of long term stored NAL gamma irradiated.

UV-VIS STABILITY



SPEC

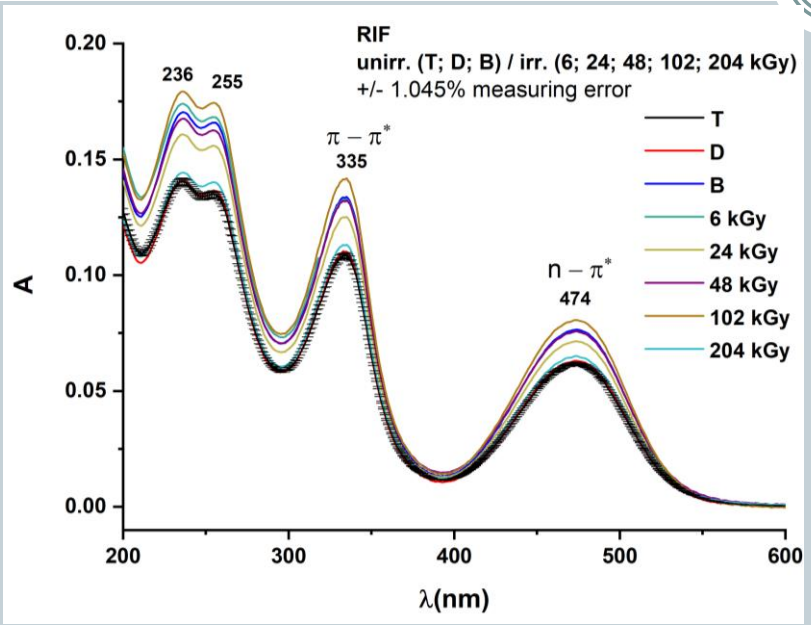


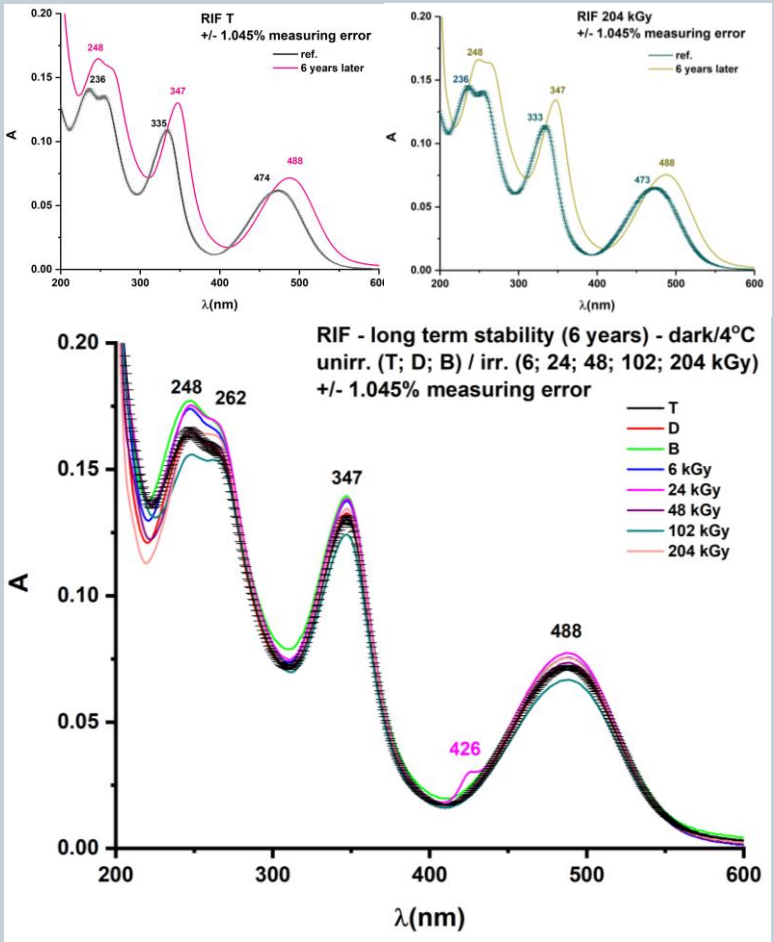


- Degradation of the unirradiated solutions;
- Similar behavior for the sample exposed at 6 kGy dose;
- Radiolytic degradation and appearance of secondary products due to the increase of the irradiation dose;
- Strong degradation of long term stored unirradiated samples;
- Red shift along with hypochromic effect shown by the absorption spectra of long term stored SPEC gamma irradiated.

UV-VIS STABILITY

RIF

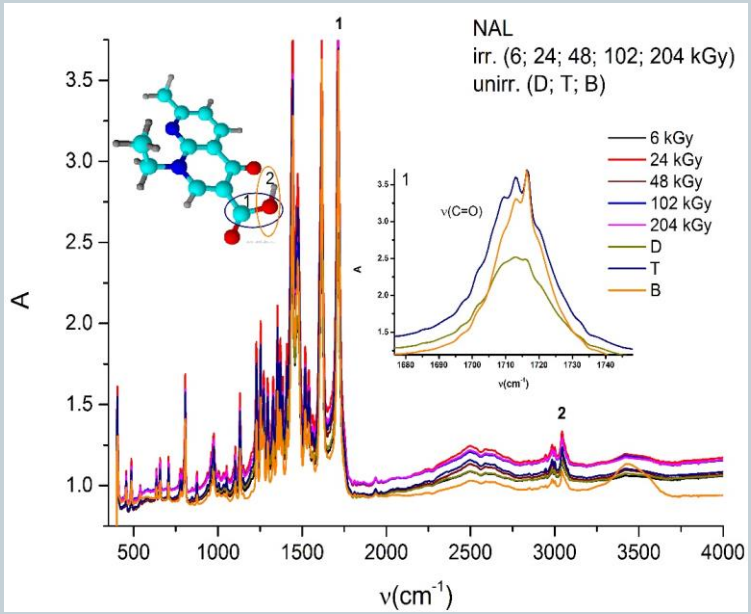


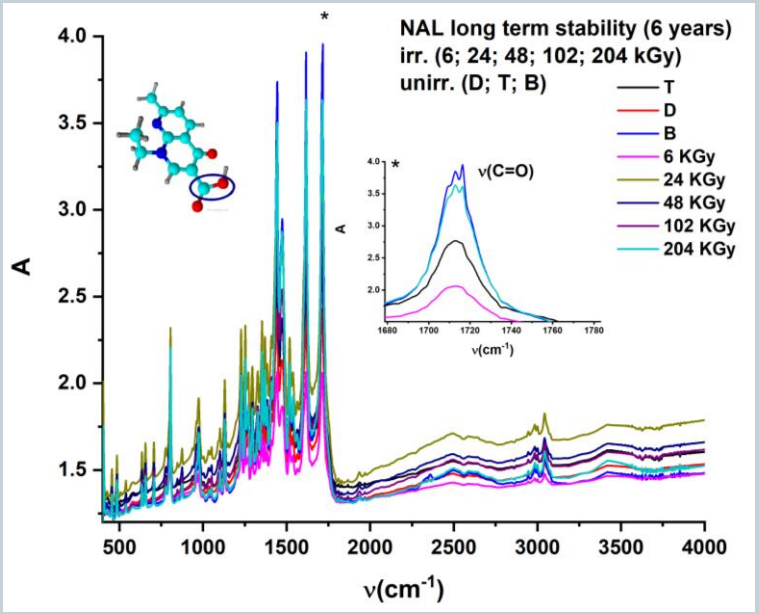


- Instability of the unirradiated solution kept at room temperature in the dark in the BGS irradiation facility lab;
- Increase of the absorbance intensity along with the irradiation dose;
- Bathochromic shift complemented with a hyperchromic effect of absorption spectra after long term storing.

FTIR STABILITY

NAL

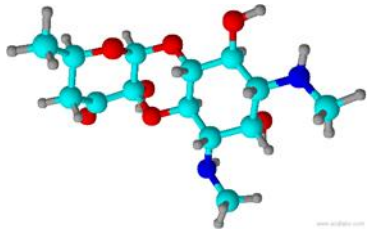




- Long term vibrational changes of NAL molecules' carboxyl bonds

Nr crt	ν [cm^{-1}]	Assign.	Comments
1	1710-1720	ν(C=O)	- Molecular changes of 6/24 kGy irradiated samples - Molecular changes of the sample kept at BGS irradiation facility
2	3440	ν(O-H)	Molecular changes of the sample kept at BGS irradiation facility

FTIR STABILITY



SPEC

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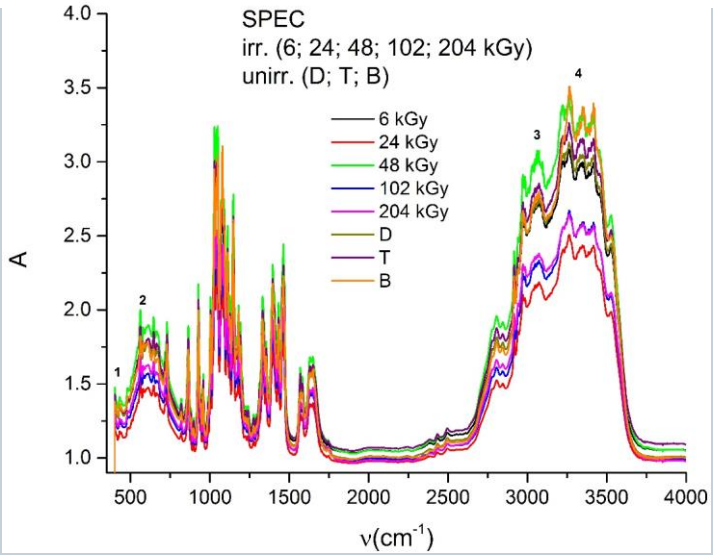
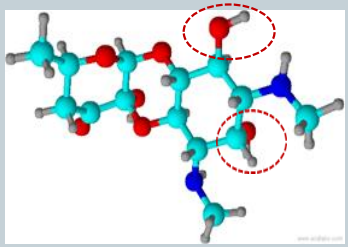
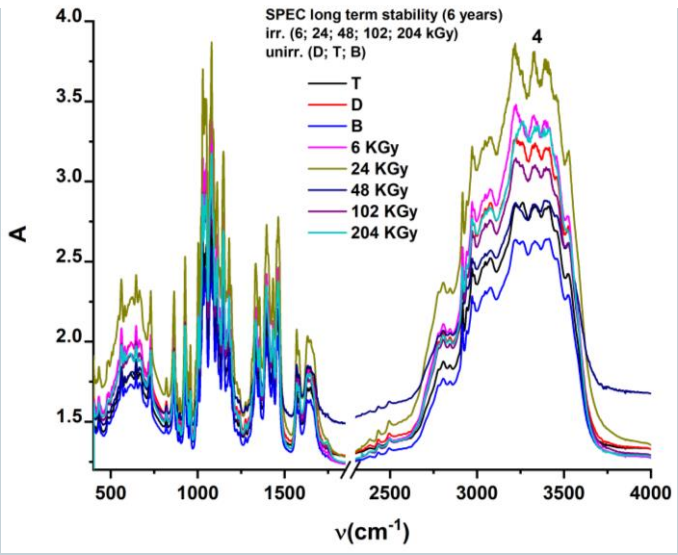




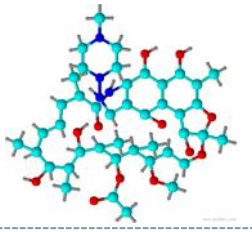


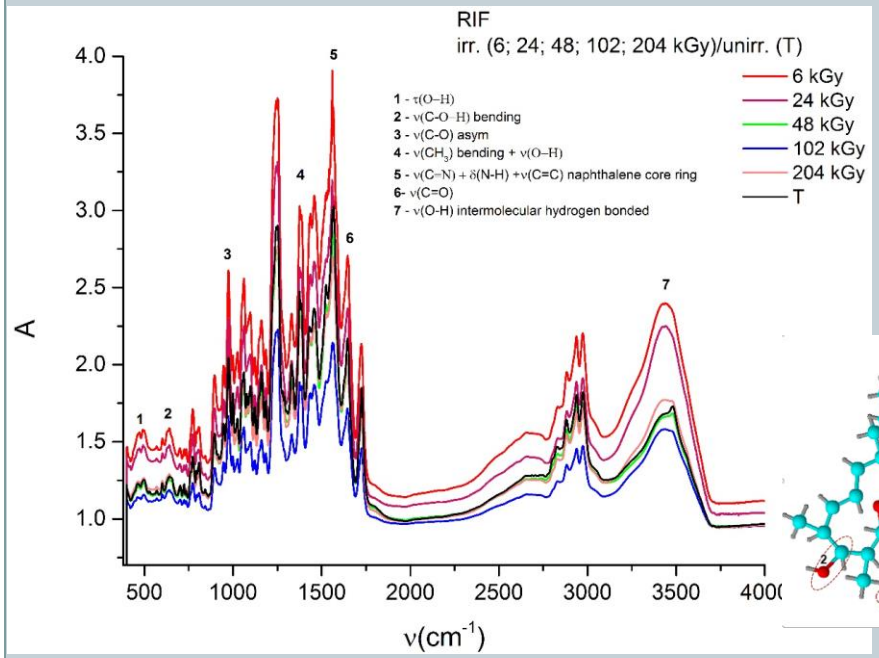
- Radiolytic degradation and appearance of byproducts produced by the increase in the irradiation dose;
- Long term molecular changes of all samples

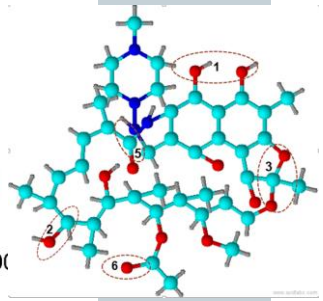
Nr crt	ν [cm^{-1}]	Assign.	Comments
1	418-440	τ(O-H)+ν (O-H)	Vibrational changes to all the irradiated samples
2	645-670	ν_{bend}(C-H) + τ (O-H)	Vibrational changes to all the irradiated samples
3	3020-3100	ν (O-H)	Vibrational changes of the 48 kGy irradiated sample
4	3200-3450	ν (O-H)	Molecular changes of the sample kept at BGS irradiation facility Long term molecular changes of all samples

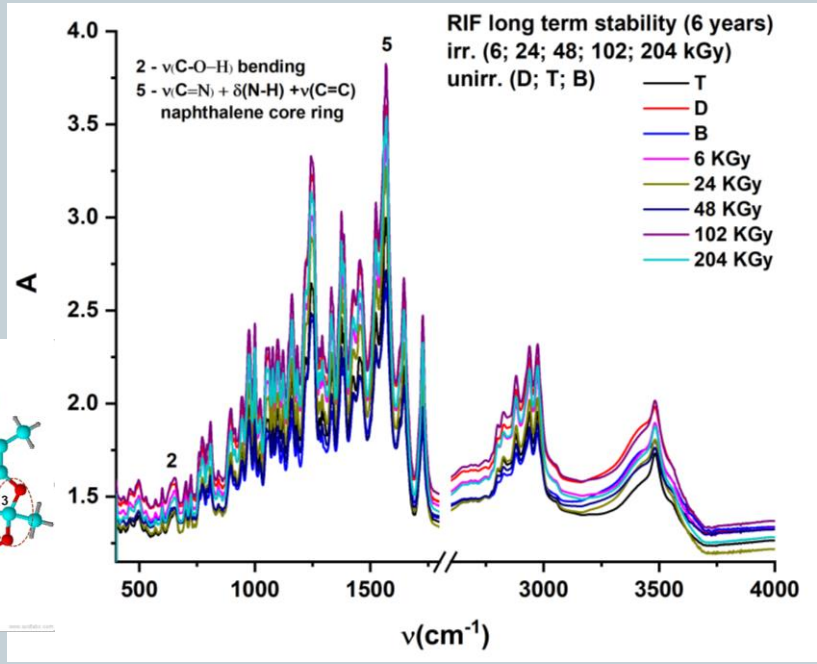
FTIR STABILITY

RIF



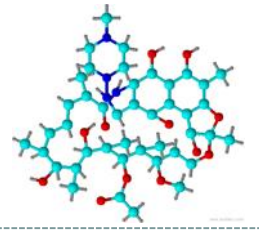






- Vibrational changes of the RIF molecules
- Long term vibrational changes of all samples

FTIR STABILITY



Nr crt	ν [cm^{-1}]	Assign.	Comments
1	492	τ(O-H)	Vibrational changes of the 6/24 kGy irradiated samples
2	626-660	ν_{bend}(C-O-H)	Vibrational changes of the 6/24 kGy irradiated samples Long term vibrational changes of all samples
3	1078	ν_{asym}(C-O)	Vibrational changes of the 24 kGy irradiated sample
4	1330-1340	$\nu_{bend}(CH_3)$ + ν(O-H)	Vibrational changes of the 6/24 kGy irradiated samples
5	1559	ν(C=N)+ δ(N-H) +ν(C=C) of naphthalene core ring	Vibrational changes of the 102 kGy irradiated sample Long term vibrational changes of the gamma irradiated samples
6	1726	ν(C=O)	Vibrational changes of the 6/24 kGy irradiated samples
7	3480	Intermolecular ν(O-H)	Vibrational changes of the 6/24 kGy irradiated samples

CONCLUSIONS & OUTLOOKS

- Investigating the long-term stability of medicines is useful in providing a set of basic multifunctional medicines to be used during long-term spaceflights;
- All the three antibiotics show variations in absorption intensity in UV-Vis spectral range, long term stability included;
- Molecular modifications of control samples (NAL and SPEC) stored in the BGS irradiation facility laboratory;
- All three antibiotics are particularly sensitive to irradiation doses up to 24 kGy;
- Occurrence of SPEC byproducts that absorb at 274 nm; their concentration in irradiated samples increases with the irradiation dose;
- Long term degradation of NAL due to protonation of carboxylic groups;
- The effect of hydroxyl groups on long time stability of SPEC is evidenced by both UV-Vis and FTIR spectroscopy.
- Further investigation on secondary products identification, as well as their antibacterial/antifungal/antiviral activity in spaceflight environment are necessary.

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