NANOPARTICLES BASED ON FRUCTOSE AND ALKALY_EARTH HALOGENIDES WITH SECOND HARMONIC GENERATION PROPERTIES FOR APPLICATIONS AS BIO-SENSORS AND FOR RADIOTHERAPY

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In recent years, some Metal Organic Frameworks (MOFs) with Second Harmonic Generation (SHG) properties, based on fructose and alkali-earth alogenides, were investigated to understand the effect of cation size and anion polarizability on crucial quantities correlated to the non-linear optical (NLO) response, such as hyperpolarizability and optical susceptibility [1,2]. The compounds studied are interesting for biomedicine applications, as they combine high biocompatibility, due to their non-toxic components, and significant SH emission, that can permit exploitation for *in vitro* bio-imaging.

Results from our previous work [2] (figure 1) suggested that the SH efficiency is much influenced by the anion, the first static hyperpolarizability and second order susceptibility being higher for bromide compounds with respect to those with chloride.

In order to enhance the SH efficiency of our systems, we decided to synthetized three new MOFs with iodide as anion, instead of bromide and chloride. In particular we obtained three MOFs based on fructose and SrI_2 salts, of formula $[Sr(fructose)_2]I_2$, $[Sr_2(fructose)_3]I_4{\cdot}H_2O$ and $[Sr(fructose)(H_2O)_3I]I$ (figure 2), that contain quite the same building blocks but show different structural arrangements. The compounds were characterized by single-crystal and powder XRD, and the first static hyperpolarizability and second-order susceptibility were estimated from theoretical calculations, both in vacuo and in the solid state (table 1) [3], and measured with the Kurtz and Perry method.

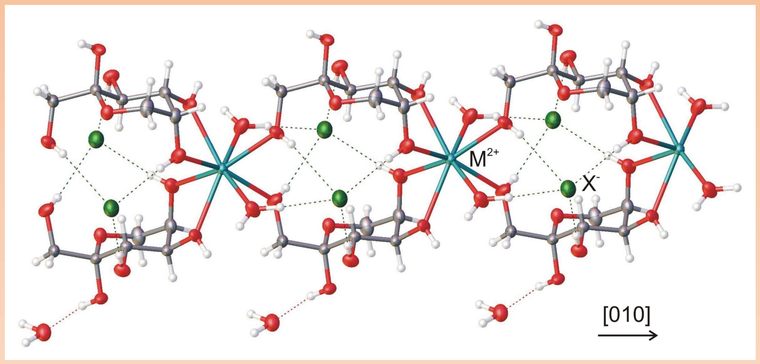


Figure 1: Isomorphous structure of the four compounds of formula $[M(fructose)_2(H_2O)_2]X_2{\cdot}H_2O$, M=Ca,Sr and X=Cl, Br [2].

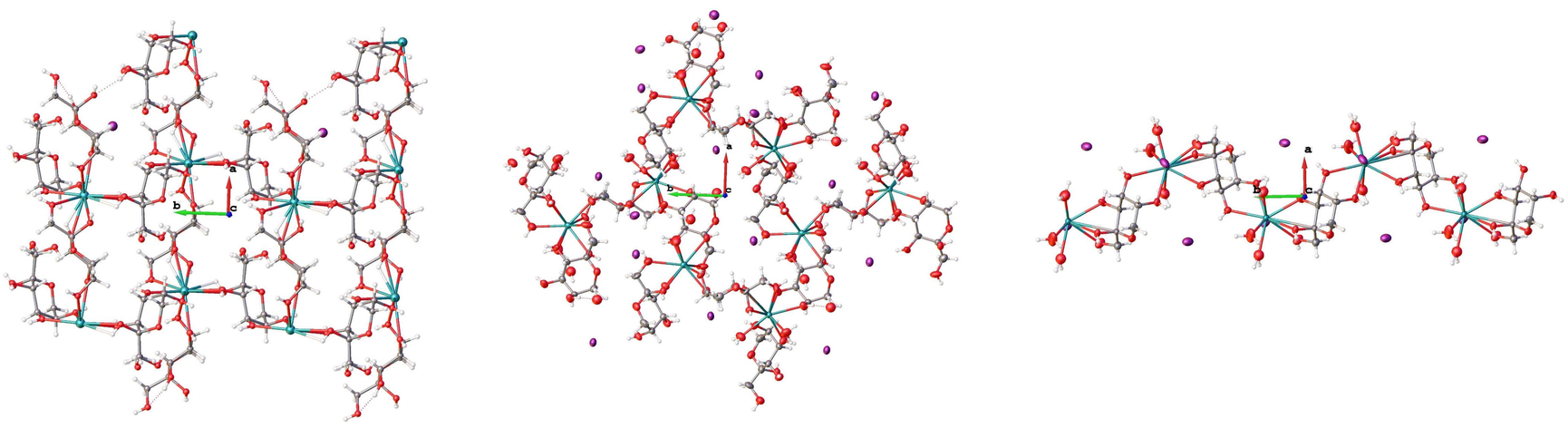


Figure 2. Structure arrangements of the three fructose-SrI_2 based MOFs.

Table 1. Crystal data and preliminary theoretical results on the fructose-SrI_2 based MOFs.

	$[Sr(fructose)_2]I_2$	$[Sr_2(fructose)_3]I_4{\cdot}H_2O$	$[Sr(fructose)(H_2O)_3I]I$
Lattice	Monoclinic	Ortorhombic	Ortorhombic
Space group	$P2_1$	$P2_12_12_1$	$P2_12_12_1$
Cell dimensions	7.8592 12.9355 9.9504 90 92.803 90	12.371685 17.435172 17.660701 90 90 90	9.119233 13.090843 13.550428 90 90 90
Cell volume	1010.37	3809.46	1617.63
Density calc (g cm^{-3})	2.307	2.225	2.364
μ (mm^{-1})	28.24	29.80	7.179
Asymmetric unit content	Sr^{2+} 2 FRU 2 I^-	2 Sr^{2+} 3 FRU 3 H_2O 4I^- 1 H_2O_{crist}	Sr^{2+} FRU 3 H_2O 2 I^-
β_{tot} (1) (10^{-30} cm^5 esu^{-1})	27.0	18.0	14.7
$\chi^{(2)}$ pmV^{-1}	5.6	3.2	ND
I/I_{sucr} (measured)(2)	0.7	0.05	

(1) Calculated at the B3LYP/631G(d) level of theory with Gaussian09.
(2) Measured values obtained from powders, with the Kurtz and Perry method.

Periodic LCGTF calculations (CRYSTAL14)

@Marconi 'Knights Landing' partition, 1 x 68-cores Intel Xeon Phi 7250 *CPU @1.4 GHz – Simulations either on 4 or 6 nodes*

Theoretical calculation has been obtained at the PBE0 level with 3-21G split valence basis set. [4]

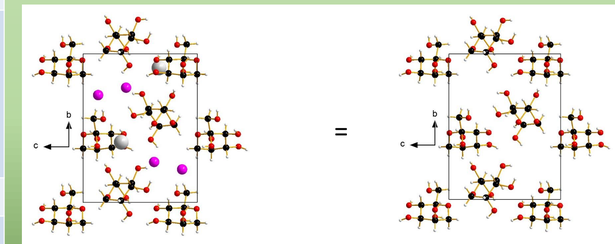
Exploiting symmetry in solid-state simulations $(\hat{i}\cdot\mathbf{S}^{\dagger})\cdot\boldsymbol{\chi}^{(2)}:(\mathbf{S}\cdot\hat{j})(\mathbf{S}\cdot\hat{k}) = \chi^{(2)}_{ijk}$.

Orthorhombic 222		Monoclinic 2	
	xyz, xzy, yzx, yxz, zxy, zyx		*xyz, xzy, xxy, xyx, yxx, yyy, yzz, yzx, yxz, zyz, zzy, zxy, zyx* (two fold axis parallel to $\hat{y}$)

$[Sr(fructose)_2]I_2$				
COMPONENT	BETA	CHI(2)	d(MKS)	d(cgs)
XXY	569.3482	0.5247	0.5102	0.0122
XYZ	-422.3184	-0.3892	-0.3784	-0.009
YYY	-760.5659	-0.7009	-0.6815	-0.016
YZZ	-167.1856	-0.1541	-0.1498	-0.004

$[Sr_2(fructose)_3]I_4{\cdot}H_2O$				
COMPONENT	BETA	CHI(2)	d(MKS)	d(cgs)
XYZ	280.4013	0.0685	0.0666	0.0016

$[Sr(fructose)(H_2O)_3I]I$				
COMPONENT	BETA	CHI(2)	d(MKS)	d(cgs)
XYZ	-178.0043	-0.1025	-0.0996	-0.002



COMPONENT	BETA	CHI(2)	d(MKS)	d(cgs)
XXY	140.061	0.1291	0.1255	0.003
XYZ	-16.3986	-0.0151	-0.0147	-0.0004
YYY	370.3652	0.3413	0.3319	0.0079
YZZ	-321.518	-0.2963	-0.2881	-0.0069

COMPONENT	BETA	CHI(2)	d(MKS)	d(cgs)
XXY	-0.4875	-0.0004	-0.0004	0
XYZ	0.5208	0.0005	0.0005	0
YYY	4.6095	0.0042	0.0041	0.0001
YZZ	-0.1603	-0.0001	-0.0001	0

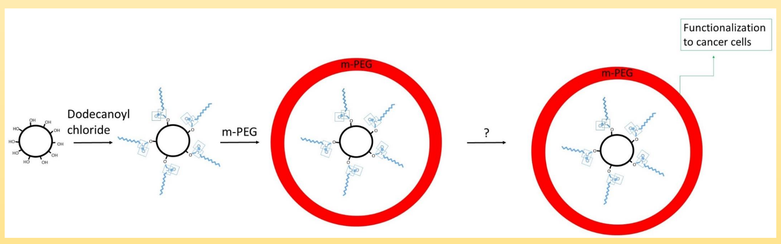
Substructure decomposition of Srfrui1

- beta terms are not pairwise additive
- if estimated tensor components are high for a given specie, it is reasonable to assume that the contribution to BETA of that specie will be relevant as well in the whole structure
- Results the sugar provides the largest contribution

Applications

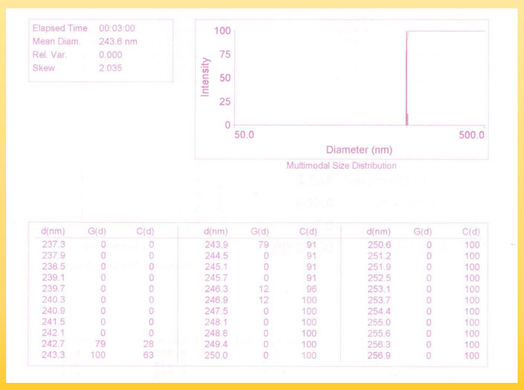
Synthesys of nanoparticles.

Nanoparticles of $[Sr(fructose)_2(H_2O)_2]Cl_2{\cdot}H_2O$ were obtained by fast precipitation of crystals from isobutanol solution, dryed in a stove at 70°C and grinded in a bill mill. Then the nanoparticles were proofed through reaction of the –OH groups on surface with dodecanoyl chloride and encapsulated in a phospholipidic m-PEG shell. They were characterized by Dynamic light scattering technique (DLS), showing a narrow band centered at ca. 245 nm (polidispersity 0.005).



Next step provide for the functionalization of the nanoparticles surfice in order to direct them towards specific cancer cells.

Table 2. Mean diameter (nm) and multimodal size distribution of nanoparticles determined by DLS.



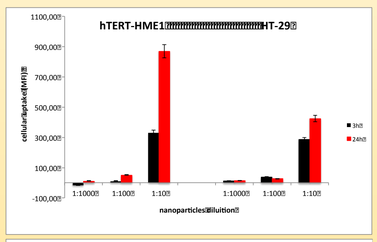
Cell uptake and viability tests.

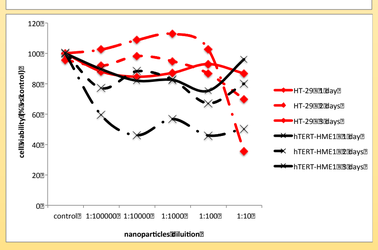
Preliminary activity studies on target cells are in progress. Nanoparticles were tested on two cell lines, hTERT-HME1 (breast epithelial cells immortalized with hTERT) and HT-29 (colorectal adenocarcinoma) to evaluate cellular uptake and viability.

To study cellular uptake, nanoparticles were loaded with fluorescein (1 mg/20 mg of the compound) before treatment with dodecanoyl chloride and their internalization was expressed as median fluorescence intensity. Preliminary data suggested that cellular uptake was dose- and time-dependent.

Cell viability was evaluated after 1, 2 and 5 days of treatment and was measured as ATP production.

Nanoparticles inhibited the growth of cells by about 50% at the maximum concentration after 5 days of treatment.





Radiotherapy applications.

Applications in radiotherapy of MOFs based on the co-crystallization of fructose and salts containing various radionuclides are presently under investigation. For example, ^{89}Sr, is a β emitter with a half-life of 50.57 d obtained by nuclear fission and used in the form of chloride for metastasized bone cancer.

The average energy of the β emitted by ^{89}Sr is 0.58 MeV. Based on a linear energy transfer in water of 1.75 MeV cm^{-1}, we calculate an average range of 3.3 mm and we assume a tumor size at least one order of magnitude larger. Under this hypothesis, the estimated dose delivered by functionalized particles of $[Sr(fructose)_2(H_2O)_2]Cl_2{\cdot}H_2O$ of radius 0.5 μm prepared with commercial strontium chloride with specific activity 4.57 MBq/mg would be 23.7 Gy. However, the selectivity towards tumor cells would be greatly enhanced with respect to strontium chloride itself.

References

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