NATIONAL INSTITUTE FOR LASER, PLASMA AND RADIATION PHYSICS

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Laser-assisted Generated Nanoemulsions as Drug Delivery Systems

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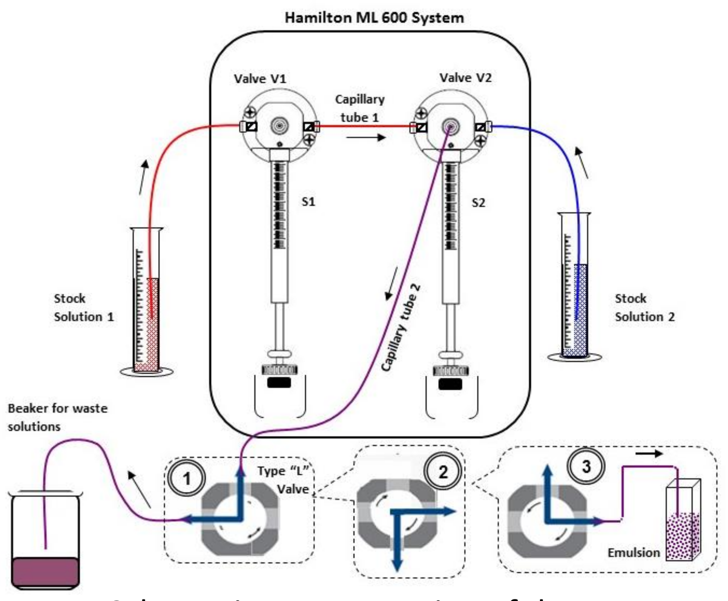
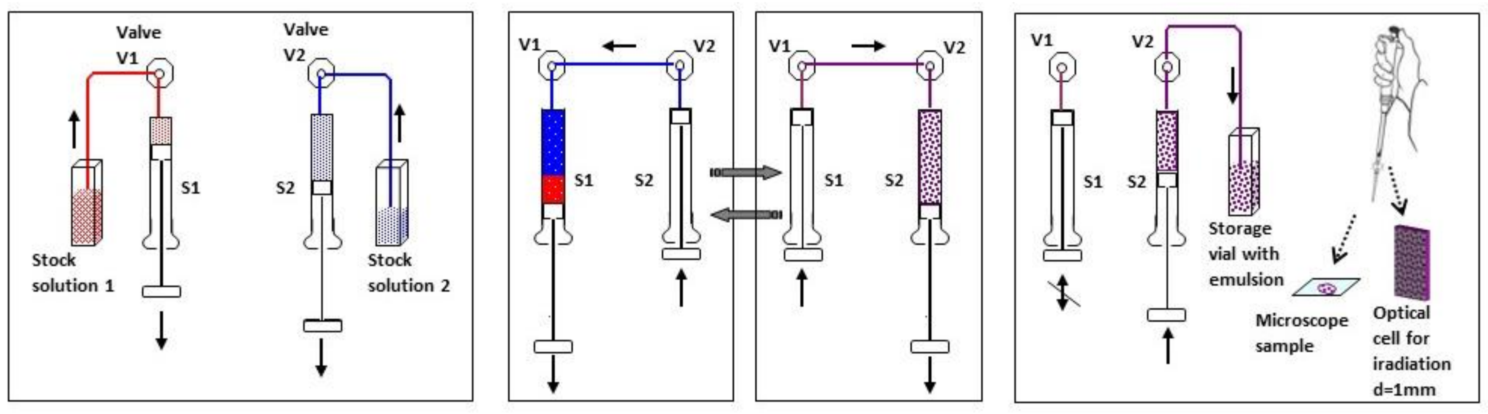
Outline

- Ongoing studies are focused on the development of new drug delivery systems (DDS) to combat the toxicity of cytostatics, minimize harm to healthy cells, and overcome multidrug resistance developed by cancer cells.
- A laser-assisted method of emulsification was developed.
- Spectroscopic, microfluidic, optical microscopy and DLS studies of the generated emulsions containing a sclerosing medicine (Sodium Tetradecyl Sulfate) and oily Vitamin A are presented, as well as the effect of laser radiation on these emulsions.

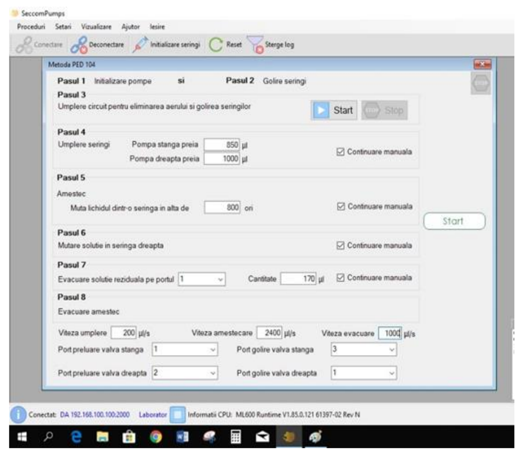
Materials & Methods



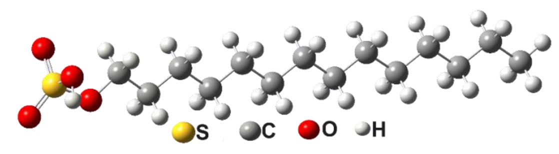
Schematic representation of the emulsifying system



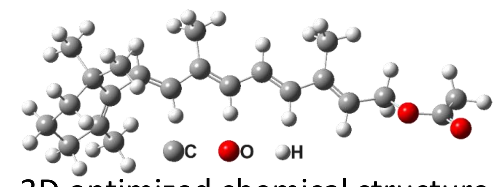
Principle of the method: 1) syringe loading with stock solutions; 2) mixing the solutions for *n* times; 3) ejecting and exposing the emulsion to laser radiation.



The developed software that controls the emulsifying system, allowing to set: volume of each syringe, number of pumping cycles, filling speed, mixing speed, ejecting speed.



3D optimized chemical structure of Sodium Tetradecyl Sulfate (STS)



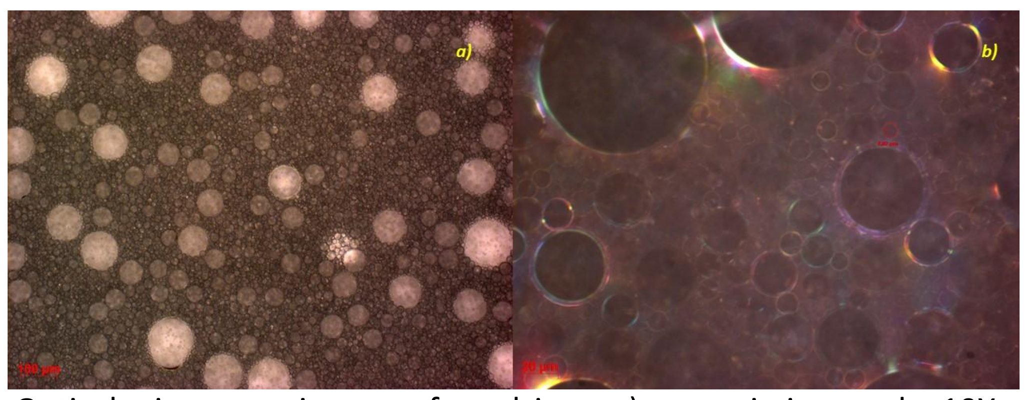
3D optimized chemical structure of Vitamin A

Experimental conditions:

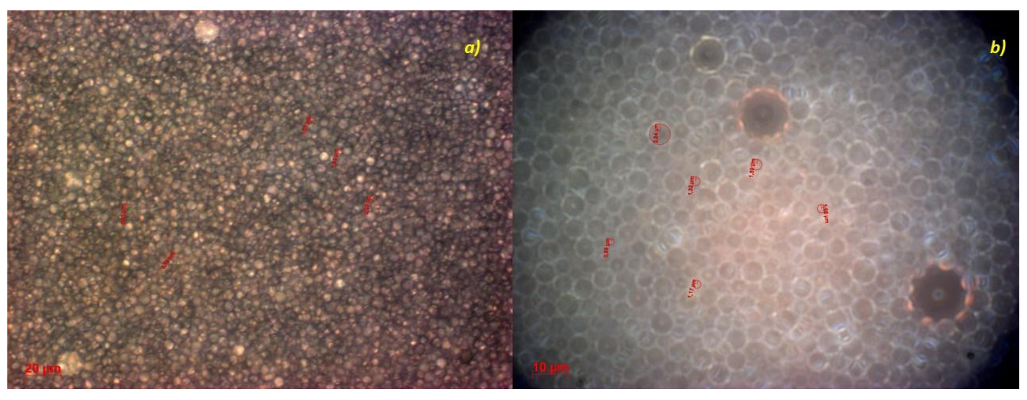
***Emulsions were prepared with STS 10% in ultrapure water and Vitamin A oily solution (1:1), mixing speed 2400 µl/s, 800 mixing cycles.**

***Emulsions were exposed to laser radiation provided by the second harmonic generation (λ = 532 nm) of a Nd:YAG laser (Surelite II, Continuum, Excel Technology), 10 Hz frequency, 6 ns pulse duration, E = 35 mJ, t = 1 hour.**

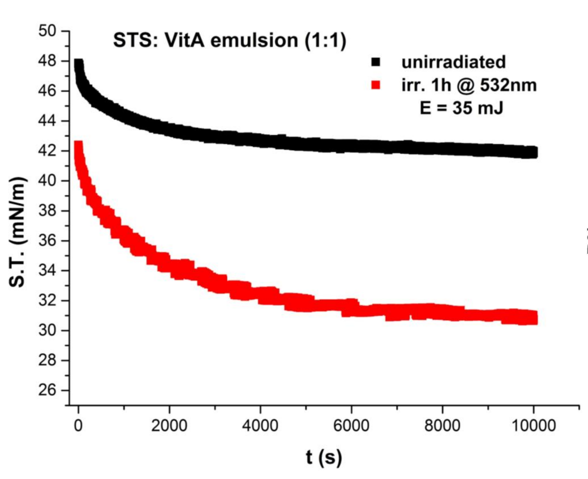
Results



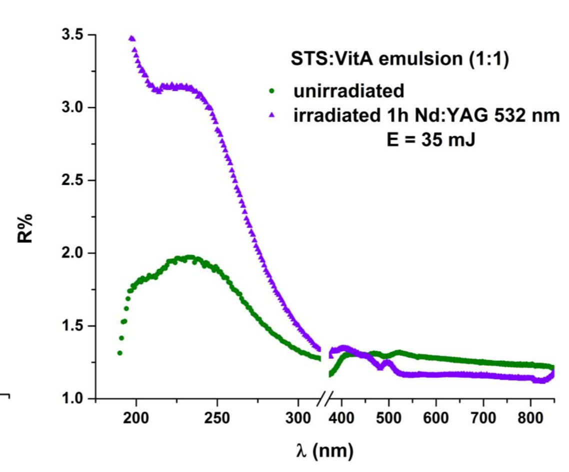
Optical microscopy images of emulsions: a) transmission mode, 10X; b) reflexion mode, 50X.



Optical microscopy images of irradiated emulsions: : a) transmission mode, 50X; b) reflexion mode, 100X.



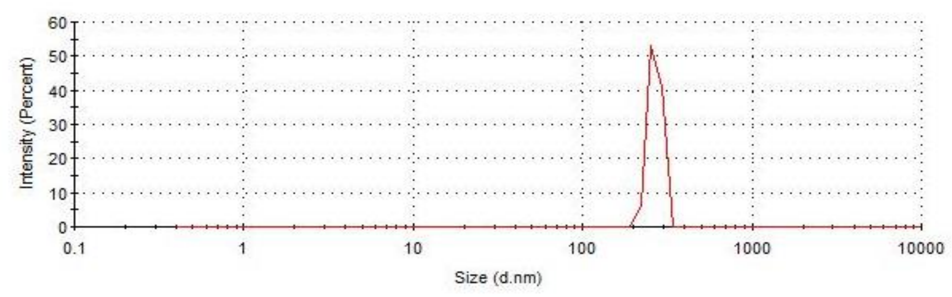
Surface tension comparison of unirradiated and irradiated emulsions



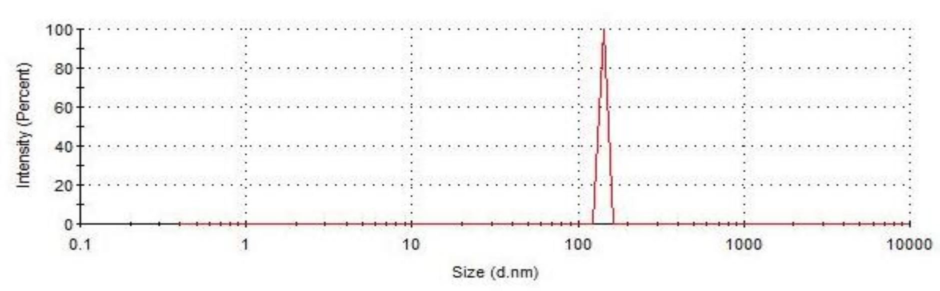
UV-Vis-NIR reflexion spectra of unirradiated and irradiated emulsions

Dynamic Light Scattering Analysis:

Sample Type	Dimension (nm)	Zeta Potential ζ (mV)
Unirradiated emulsion	269.5	- 42.2
Irradiated emulsion	141.8	- 54.6



Distribution of droplets function of dimension for the unirradiated emulsion: monomodal distribution at 269.5 nm

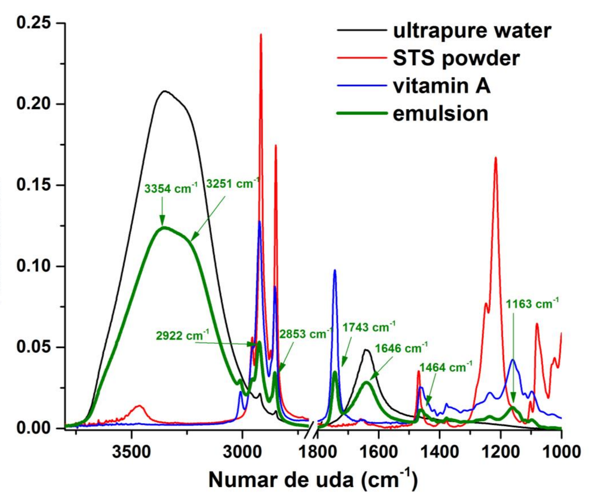


Distribution of droplets function of dimension for the irradiated emulsion: monomodal distribution at 141.8 nm

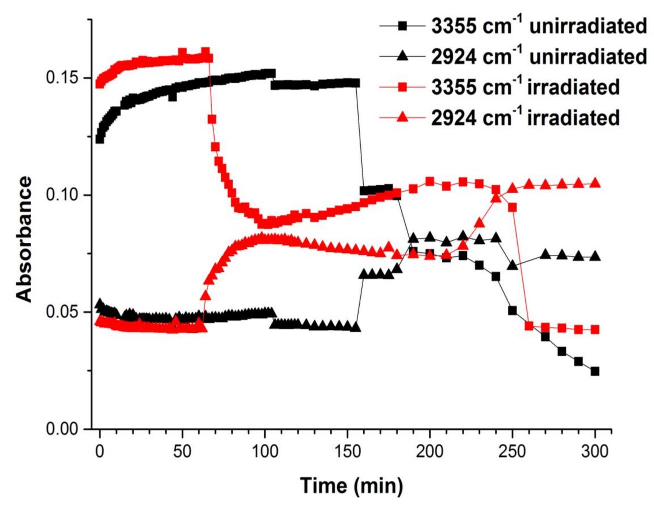
*Analysis of ζ gives info about stability of colloidal solutions: ζ >-30mV shows good physical stability of emulsions

*ζ values (-42.2 mV and -54.6 mV) show that the nanodroplets will not coalesce due to electrostatic rejection

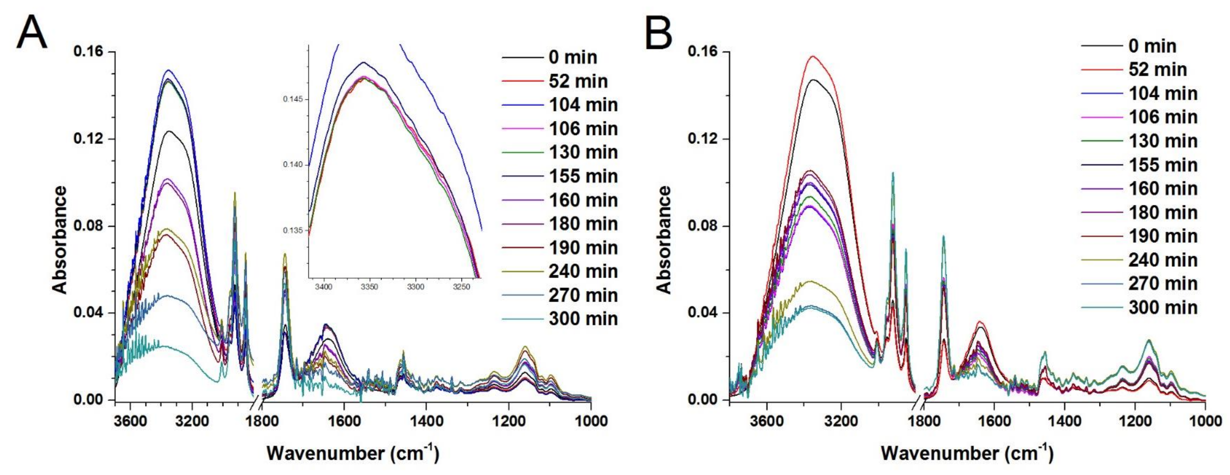
*Nanodroplets produced in emulsion by exposure to laser radiation have smaller dimensions and are more stable in time in comparison with the unirradiated emulsion



FTIR spectra of the ultrapure water, STS powder, vitamin A and unirradiated emulsion



Time stability of unirradiated and irradiated emulsions analyzing the absorbance of the peaks at 3354 cm^{-1} and 2924 cm^{-1}



FTIR spectra of the unirradiated (A) and irradiated emulsion(B)

- 3254 cm^{-1} – O–H stretching vibrations from water molecules
- 2924 cm^{-1} and 2853 cm^{-1} – CH_2 symetrical and asymetrical stretching vibrations from CH_3 group
- 1741 cm^{-1} – C=O stretching vibrations from vitamin A
- 1634 cm^{-1} – H–O–H bending vibrations from water molecules

Conclusions

- This type of laser-assisted device that generates emulsions with micro- and nano- structures is a novel emulsifying system, to the best of our knowledge, and has the advantage to allow the use of small quantities of solutions, as low as a few hundreds of µl.
- Dynamic light scattering (DLS) technique showed that the dimensions of the nanodroplets in emulsion was 269.5 nm before exposure to laser radiation and 141.8 nm after the emulsion was irradiated for 1 hour. Zeta potential values were -42.2 mV before exposure and -54.6 mV after exposure to laser beam.
- Optical microscopy images combined with DLS technique and with microfluidic and spectroscopic studies revealed that laser radiation (λ=532 nm) has a mechanical effect on emulsion, influencing the stability of the emulsion by decreasing and homogenizing the size of the droplets.
- FTIR-ATR spectroscopy indicated that the stability of the generated emulsions improved after irradiation.
- These findings substantiate the suitability of the laser-assisted method for producing nanoemulsions that can be used as DDS.

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