Preparation and Characterization of Dithiocarbazate Loaded Mesoporous Silica Nanoparticles

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Introduction and Objectives

Dithiocarbazates comprise an important class of Schiff bases that have remarkable pharmacological applications due to the imine group present in their structure [1]. However, the lipophilic character of 1-(S-benzyldithiocarbazate)-3-methyl-5-phenyl-pyrazole (DTC) (figure 1) limits its gastrointestinal absorption leading to low oral bioavailability [2,3]. Using DTC-loaded nanoparticles, such as mesoporous silica nanoparticles (MSiNP), synthesized by the Stöber method, which allows controlling pores, walls, and surfaces, can be an excellent strategy to overcome these drawbacks [4].

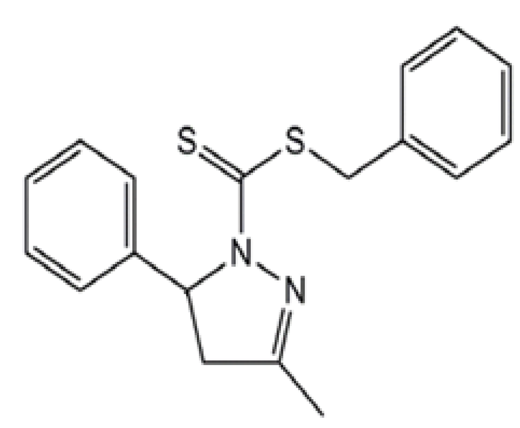
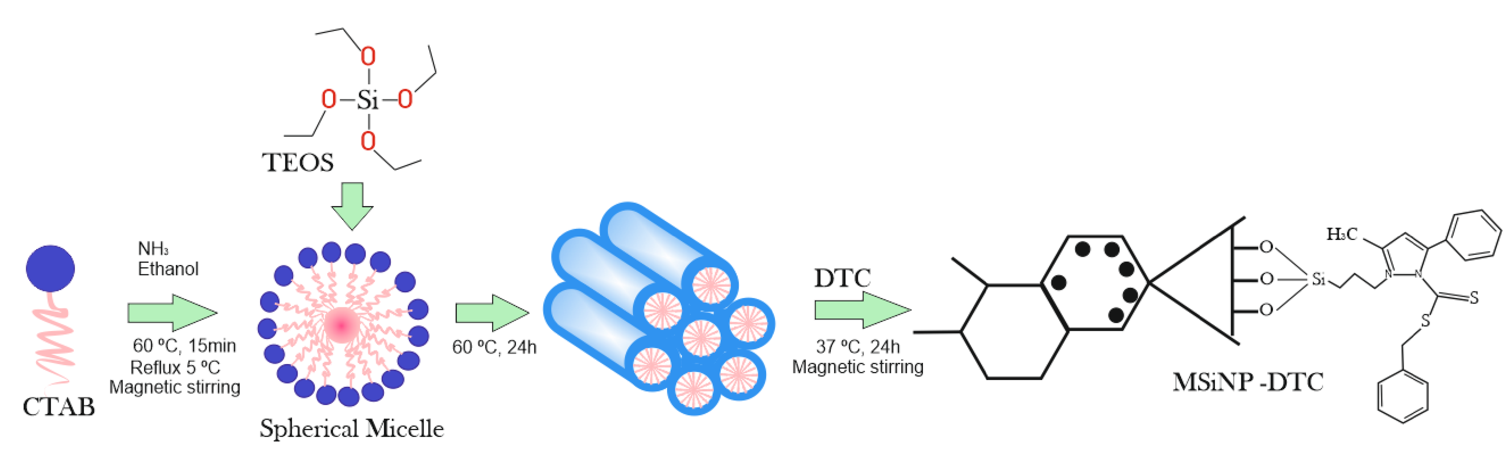


Figure 1: Structures of the 3-methyl-5-phenyl-pyrazoline-1- (S -benzyldithiocarbazate) (DTC).

In this sense, the present work aims at contributing to the understanding of several physicochemical characteristics related to the mean particle size (Z-Ave), polydispersity index (PDI), zeta potential (ZP), internal structure (Transmission Electron Microscope (TEM) analysis; Fourier-transform infra-red and Nitrogen Adsorption), Thermal analysis (Differential Scanning Calorimetry–DSC), drug load capacity (DL) and entrament efficiency (EE) of MSiNP proposed as a nanocarrier for DTC delivery.

Methods

Synthesis of porous silica nanoparticles was carried out under a high concentration of precursors, which results in nanoparticles of highly uniform spherical shape (Scheme 1).



Scheme 1: Synthesis of MSiNP and MSiNP-DTC

Conclusions

- DTC compound was successfully loaded into the mesoporous matrix (MSiNP) by means of a simple and efficient synthesis;
- Z-Ave values corroborated that the immobilization of the DTC did not drastically change the particle size of MSiNP and PDI values indicate the formation of monodisperse suspensions;
- The ZP values changed from positive values to negative values, suggesting the modification of the MSiNP surface with DTC;
- From FTIR results, the main DTC band suffered displacement, by increasing the intensity of the bands related to MSiNP;
- There was a change between loaded and unloaded MSiNP in the BET results. Nevertheless, the pore size was larger after loading and thus, can be related to the presence of DTC on the matrix surface instead of the pores;
- Therefore, the data suggest that MSiNP-DTC have potential for the use in drug delivery applications, improving stability and overcoming the low water solubility of Schiff's dithiocarbazate bases.

References

1. Manan, M. A. F. A.; Tahir, M. I. M.; Crouse, K. a.; How, F. N.-F.; Watkin, D. J.J. Chem. Crystallogr. 2011, 42 (2), 173–179.
2. Costa, A. R.; de Menezes, T. I.; Nascimento, R. R.; dos Anjos, P. N. M.; Viana, R. B.; de Araujo Fernandes, A. G.; Santos, R. L. S. R. J. Therm. Anal. Calorim. 2019, 138,1683–1696.
3. de Menezes, T. I.; de Oliveira Costa, R.; Sanches, R. N. F.; de Oliveira Silva, D.; Santos, R. L. S. R. Colloid Polym. Sci. 2019, 297 (11–12), 1465–1475.
4. Paula, A. J.; Martinez, D. S. T.; Júnior, R. T. A.; Filho, A. G. S.; Alves, O. L. J. Braz. Chem. Soc. 2012, 23 (10), 1807–1814.

Acknowledgements

NORTE2020 through project Norte-08-5369-FSE-000050 for financial support of a PhD grant.
This work was partially supported by the FCT under Research Grant UIDB/00081/2020 – CIQUP

Results and Discussion

DYNAMIC LIGHT SCATTERING (DLS), ZETA POTENTIAL and ENTRAPMENT EFFICIENCY

Table 1. Z-Ave, PDI and ZP, EE and DL values of MSiNP/MSiNP-DTC. Results are expressed as mean ± standard deviation (SD) of three independent measurements)

Sample	Z-Ave ± SD (nm)	PDI ± SD	ZP ± SD (mV)	EE ± SD	DL ± SD
MSiNP	168.4 ± 3.9	0.29 ± 0.02	+ 14.6 ± 0.5	-	-
MSiNP-DTC	175.7 ± 1.0	0.38 ± 0.04	- 21.9 ± 0.3	95.77 ± 0.08%	4.79 ± 0.004%

Transmission Electron Microscope (TEM) analysis

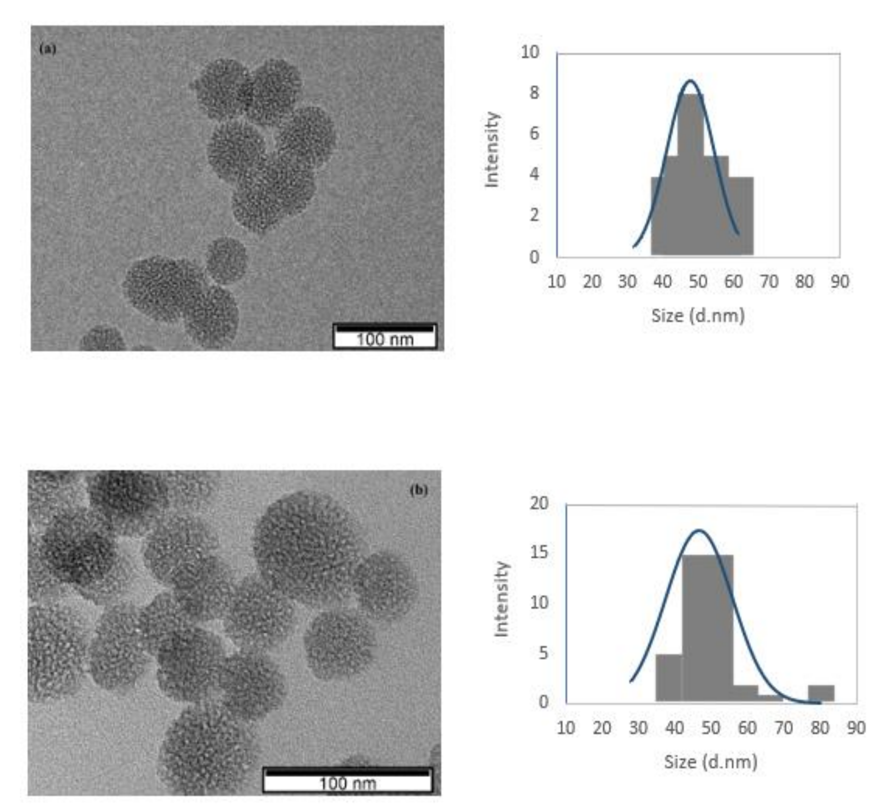


Figure 1. TEM images of MSiNP (a) and MSiNP-DTC (b) and their Histograms (size distributions) calculated by ImageJ.

FOURIER TRANSFORM INFRARED (FTIR)

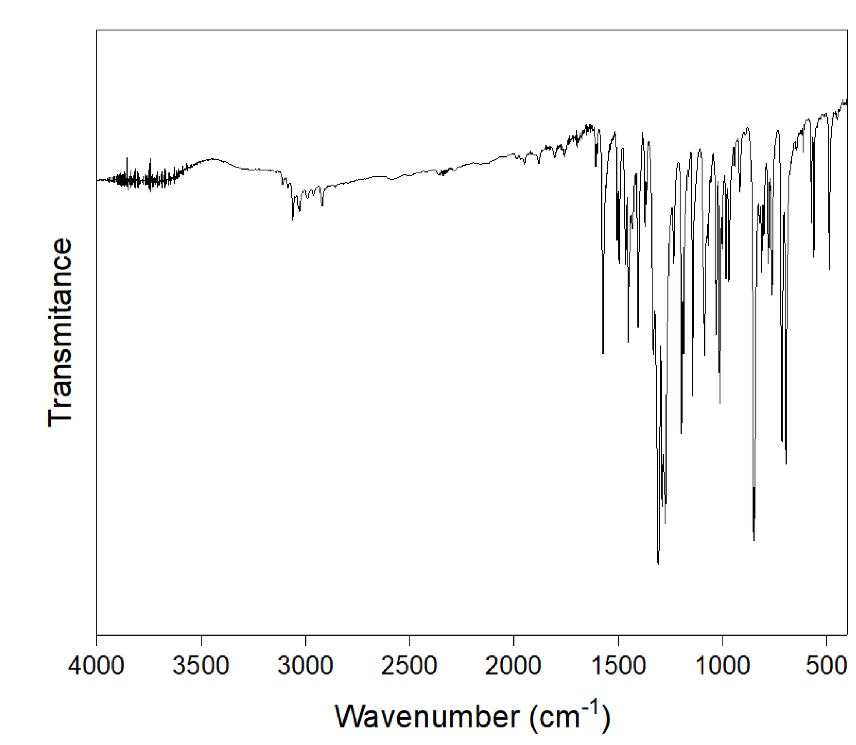


Figure 2. Vibrational spectrum in the infrared region of the compound DTC in KBr.

Thermal Analysis

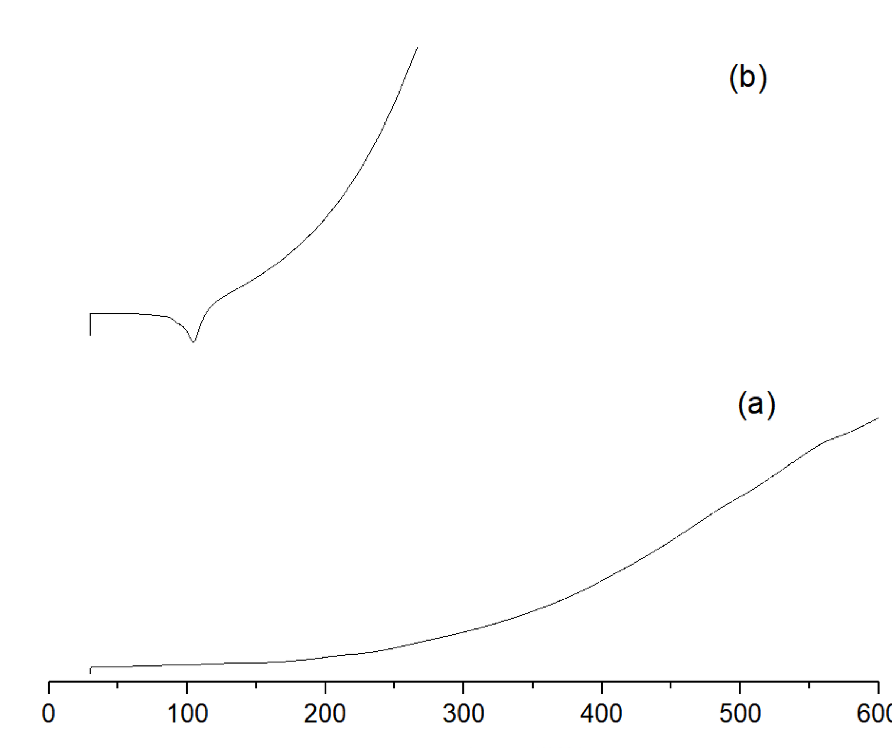


Figure 4. DSC profiles of MSiNP (a) and MSiNP-DTC (b).

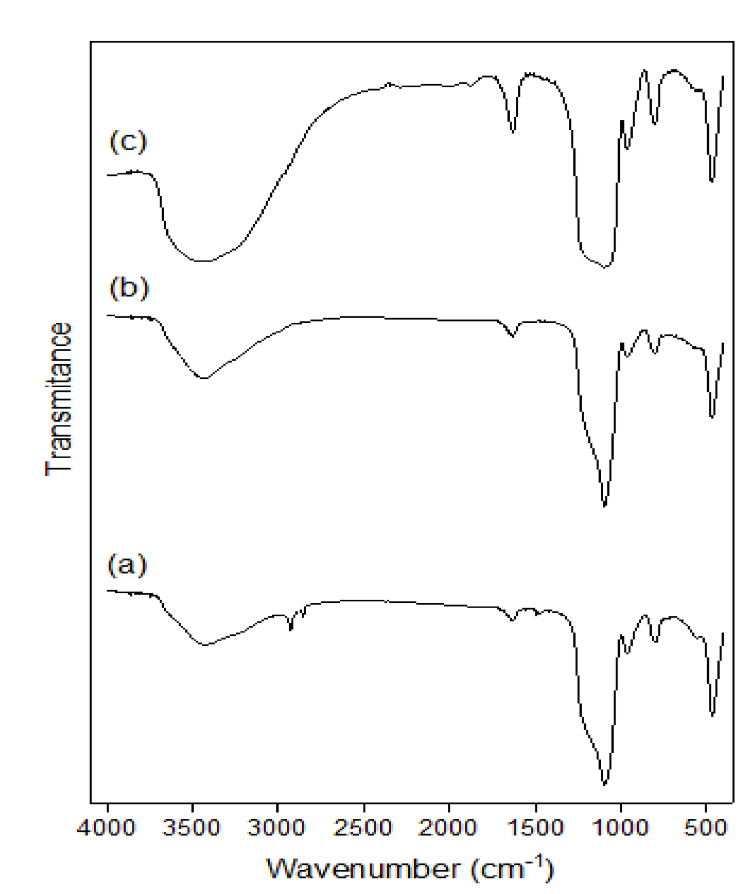


Figure 3. Vibrational Spectrum in the Infrared region of the MSiNP (a), MSiNP calcined (b) and MSiNP-DTC (c).

NITROGEN ADSORPTION

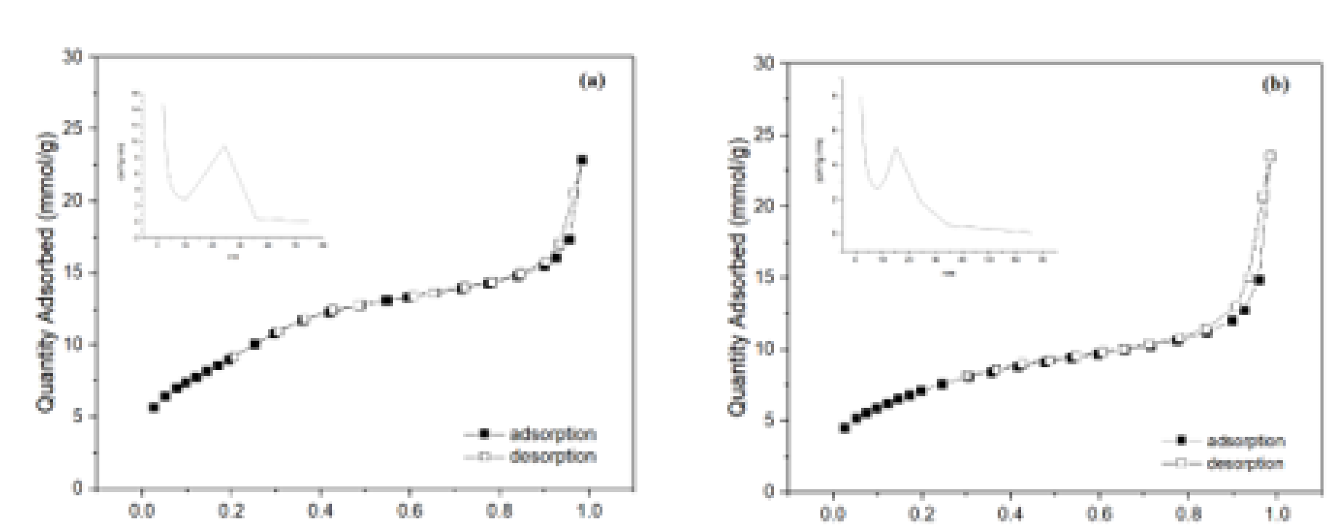


Figure 5. Nitrogen isotherms from MSiNP (a) and MSiNP-DTC (b).

Table 2: Textural properties of MSiNP: SBET (specific surface area,); Pv (pore volume, by BJH); PD (average pore diameter, by BJH).

Sample	SBET (m^2/g)	PV (cm^3/g)	PD (nm)
MSiNP	1021.05 ± 14.6	1.61 ± 0.04	6.29 ± 0.1
MSiNP-DTC	617.99 ± 15.3	1.01 ± 0.01	6.52 ± 0.1