

# Sustained release of fungicide metalaxyl by mesoporous silica nanospheres

Harrison Wanyika

Received: 30 March 2013 / Accepted: 30 June 2013 / Published online: 10 July 2013  
© Springer Science+Business Media Dordrecht 2013

**Abstract** The use of nanomaterials for the controlled delivery of pesticides is nascent technology that has the potential to increase the efficiency of food production and decrease pollution. In this work, the prospect of mesoporous silica nanoparticles (MSN) for storage and controlled release of metalaxyl fungicide has been investigated. Mesoporous silica nanospheres with average particle diameters of 162 nm and average pore sizes of 3.2 nm were prepared by a sol–gel process. Metalaxyl molecules were loaded into MSN pores from an aqueous solution by a rotary evaporation method. The loaded amount of metalaxyl as evaluated by thermogravimetric analysis was about 14 wt%. Release of the fungicide entrapped in the MSN matrix revealed sustained release behavior. About 76 % of the free metalaxyl was released in soil within a period of 30 days while only 11.5 and 47 % of the metalaxyl contained in the MSN carrier was released in soil and water, respectively, within the same period. The study showed that MSN can be used to successfully store

metalaxyl molecules in its mesoporous framework and significantly delay their release in soil.

**Keywords** Mesoporous silica nanoparticles · Metalaxyl · Loading · Sustained release

## Introduction

Globally, only ~10 % of the applied pesticides realizes their intended purpose, otherwise, the rest is lost to the environment through various modes, such as, drift during application, as run-off, leaching, volatilization, and degradation by photolysis, hydrolysis and by microbial action (Ghormade et al. 2011). This has led to periodic application of the pesticides so as to achieve threshold concentration for effective crop protection. A direct and negative consequence of the prevailing phenomena is the unprecedented high cost of agricultural production and heavily polluted environment. Emerging pesticide application technologies need to be harnessed in order to improve efficacy, reduce the amounts applied, and provide better control of the agrichemicals, thus, make agriculture sustainable and the environment greener.

A successful pesticide formulation is one that possesses the following properties: remains potent for a significant period of time even in harsh environment, is pest/pathogen specific with less ecotoxicity, does not suffer pest resistance, is economically viable and is benign to plants and mammals (Nair et al. 2010).

---

Special Issue Editors: Mamadou Diallo, Neil Fromer, Myung S. Jhon

---

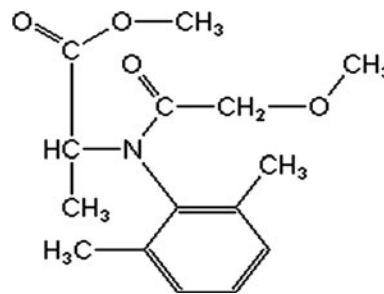
This article is part of the Topical Collection on Nanotechnology for Sustainable Development

---

H. Wanyika (✉)  
Department of Chemistry, Jomo Kenyatta University  
of Agriculture & Technology, P.O. Box 62000,  
Nairobi 00200, Kenya  
e-mail: hwanyika@gmail.com

Most of such requirements may be achieved by a state-of-the-art pesticide delivery system. In the last decade, scientists have put considerable efforts in studying suitable systems for the controlled release of drug molecules. Amongst the widely investigated techniques are the use of polymeric materials and liposomes. Zheng and co-worker suggested polymeric nanocapsules as vehicles for the pesticides ivermectin and acetamiprid (Zheng and Shang 2005). Liu et al. (2001) controllably released fungicides tebuconazole and chlorothalonil from polyvinylpyridine and polyvinylpyridine-*co*-styrene matrix. However, the commercialization of most reported potential pesticide carriers has not been realized due to low drug payload, scale-up difficulties, regulatory limitations and structural instability.

Recently, nanomaterials have been identified as potential targeted delivery carriers for pesticides. In particular, MSN attributes include well defined and tunable pore sizes (2–50 nm), large pore volumes, high surface areas, chemical stability, resistance to microbial attack, nanostructures that can be tailored, easily modified surface properties, biocompatibility, and aqueous degradability (Al-Kady et al. 2011; Ambrogio et al. 2011). In addition, MSN protect-loaded guest molecules against environmentally induced enzymatic degradation since no swelling or porosity changes occur in response to external stimuli, such as, pH and temperature (Yang 2011). Furthermore, MSN are excellent pesticide delivery carriers, as their structural properties can be modified to either enhance or slow down release kinetics (Ukmar et al. 2011). Arguably, MSN offers great promise for the fabrication of stimulus responsive and targeted pesticide delivery scaffolds. Indeed, various attempts have been made to study the suitability of siliceous materials for storage and sustained release (SR) of pesticides. Experimental results have shown that porous hollow silica nanoparticles (PHSNs) are excellent carriers for the SR of avermectin; an oil-soluble pesticide (Wen et al. 2005). Moreover, they can protect avermectin from photodegradation (Li et al. 2006). The pesticide molecules were loaded into PHSNs by simple immersion loading (SIL) and supercritical fluid loading (SFL) technologies, respectively. Liu et al. (2006) employed SFL method to entrap a different molecule, validamycin; a water-soluble pesticide into PHSNs, they observed a multi-stage release pattern from the nanocarrier.



**Fig. 1** Structure of metalaxyl

Metalaxyl, [methyl-*N*-(2,6-dimethylphenyl)-*N*-(2-methoxyacetyl)alaninate] (Fig. 1) is an acylanilide fungicide with residual and systemic activity against fungi of the order Peronosporales, which attack a wide range of crops. Its application may be foliar, soil incorporation, surface spraying (broadcast or band), drenching, sprinkler or drip irrigation, soil mix or seed treatment (Sukul and Spittler 2001).

In this study, MSN with honeycomb like structure were loaded with fungicide metalaxyl by rotar vapor method. Metalaxyl was chosen as a model pesticide molecule due to nature of its use. Sustained release profiles of metalaxyl–MSN composites (RMSN) were investigated in water and in soil. Our results epitomize a novel application of MSN as sustained release carrier for fungicides.

## Materials and methods

Cetyltrimethylammonium bromide (CTAB), tetraethylorthosilicate (TEOS), NaOH, Metalaxyl were purchased from Sigma-Aldrich Company. All chemicals used in this study were analytical grade. Nano pure water was used for the analysis.

### Synthesis of mesoporous silica nanoparticles

MSN were synthesized under basic conditions using CTAB as the structure-directing agent, and TEOS as the silica source. In summary, TEOS (24.0 mL) was slowly added into a homogeneous surfactant solution-containing 4.0 g CTAB/1920 mL water/14 mL NaOH (2.0 M) that had been heated to 80 °C at a stirring rate of 1,000 rpm. After stirring for 2 h, the resulting precipitate was filtered and washed with water, then, oven dried at 120 °C for 4 h and finally calcined at 550 °C for 5 h in air.

## Loading of metalaxyl into mesoporous silica nanoparticles

To entrap the pesticide into MSN, metalaxyl (14.0 mg) was homogeneously dissolved in 20.0 mL of water by sonication for 15 min. Then, 220 mg of MSN was added and suspended in the solution by magnetic stirring at RT for 12 h. The solvent was then slowly evaporated under reduced pressure (0.085 mPa) in water bath at 50 °C for 2 h using a rotary evaporator. The metalaxyl-loaded MSN denoted as RMSN was dried at RT for 24 h and used for further tests.

## Characterization

The crystallinity and structural properties of the MSN and RMSN samples were characterized with XRD diffractometer (LR 39487C XRD) using nickel filtered  $\text{CuK}\alpha$  ( $\lambda = 1.542 \text{ \AA}$ ) radiation operated at 40 kV/40 mA in the range  $0.5\text{--}10^\circ$  with a step size of  $0.002^\circ 2\theta$ .

The adsorption of metalaxyl was examined by Infrared (IR) spectroscopy. IR spectra were recorded on a FT-IR spectrophotometer (SPECTMM ONE B) using KBr discs in the range  $400\text{--}4,000 \text{ cm}^{-1}$ .

The morphology and size of MSN and RMSN were observed by a scanning electron microscope (SEM, Hitachi S4800) and transmission electron microscope (TEM, Tecnai G<sup>2</sup> 20 S-TWIN).

The quantification of the relative amount of the loaded metalaxyl was carried out by thermal analysis, that is, thermal gravimetric analysis (TGA), and differential thermal analysis (DTA) at a heating rate of  $3 \text{ min}^{-1}$  with  $\text{N}_2$  using thermal gravimetric analyzer (TGA-7) from RT to 800 °C. The nitrogen adsorption/desorption isotherms were collected on Micromeritics equipment (ASAP 2020). Specific surface areas and pore volumes were determined by standard BET and BJH methods, respectively, from adsorption branches of the isotherms.

## Sorption–desorption studies

Sorption isotherms were measured using a batch equilibration method. Triplicates of 20 mg of MSN were treated with 6 mL of solutions containing  $0.2\text{--}0.8 \text{ mg mL}^{-1}$  initial concentrations ( $C_i$ ) of metalaxyl in water. The suspensions were shaken at  $25 \pm 2 \text{ }^\circ\text{C}$  for 24 h and centrifuged at 10,000 rpm for

10 min. Supernatants were filtered through  $0.22 \text{ }\mu\text{m}$  diameter nylon filters and equilibrium concentrations ( $C_e$ ) determined by UV spectrophotometry scan in the range  $330\text{--}200 \text{ nm}$ . The UV absorption peak at 270 nm was used to monitor concentration changes. Standard concentrations of metalaxyl ranged from 0.05 to  $0.8 \text{ mg mL}^{-1}$ . The amount of fungicide adsorbed ( $C_s$ ) was calculated from the difference between the initial ( $C_i$ ) and the equilibrium ( $C_e$ ) solution concentrations. Adsorption isotherms were fitted to the logarithmic form of the Freundlich equation:

$$\log C_s = \log K_f + 1/n_f \log C_e$$

where  $C_s$  ( $\text{mg kg}^{-1}$ ) is the amount of herbicide adsorbed at the equilibrium concentration  $C_e$  ( $\text{mg l}^{-1}$ ) and  $K_f$  ( $\text{mg}^{1-n_f} \text{g}^{-1}$ ) and  $n_f$  (unitless) are the empirical Freundlich constants.

Desorption was followed immediately after adsorption using the  $0.8 \text{ mg mL}^{-1}$  metalaxyl concentrations by replacing 3 mL of the supernatant with 3 mL of pure water. This desorption procedure was repeated three times for each sample. Desorption isotherms were also fitted to Freundlich equation and desorption coefficients calculated. A desorption hysteresis coefficient was calculated as the percentage of ratio between the sorption and desorption isotherms slopes (Fernandes et al. 2003):

$$H = \frac{n_{f_{\text{ads}}}}{n_{f_{\text{des}}}} \times 100$$

## Release measurements

### Batch release kinetics in water

The release of metalaxyl from RMSN was carried out by suspension of 4.0 mg of RMSN in 4.0 ml of water contained in glass bottles and sealed with screw caps for different time periods. Different experiments for the different periods of time were set up simultaneously. In all cases, the release kinetics was obtained in triplicate. After each time lapse, the bottles were hand-shaken, and centrifuged at 10,000 rpm for 10 min. The supernatant were filtered, and analyzed by high performance liquid chromatography (HPLC). The following HPLC conditions were used: detector, UV,  $\lambda = 220 \text{ nm}$ ; column, supelcosil LC-18  $5 \text{ }\mu\text{m}$ ,

250 × 4.6 mm<sup>2</sup>; temperature, 30 °C; mobile phase, acetonitrile/water (50/50 v/v); injection volume, 10 µL; flow rate 1.0 ml min<sup>-1</sup>; run time, 10 min.

### Release in soil

The controlled release characteristics of the RMSN were determined with soil-filled glass separating funnels with a volume of 25 cm<sup>3</sup>. Pure metalaxyl (7.0 mg) corresponding to the amount entrapped in the controlled release systems was used as control. The soil columns were settled by the addition of 20 ml of water, 50 mg of RMSN were placed on top of the soil column and 10 ml of pure water was applied on a 3 days interval for 1 month to the tubes. The elute was filtered through 0.22 µm syringe filters and analyzed for metalaxyl content by HPLC method previously described.

## Results and discussion

### Loading and characterization of samples

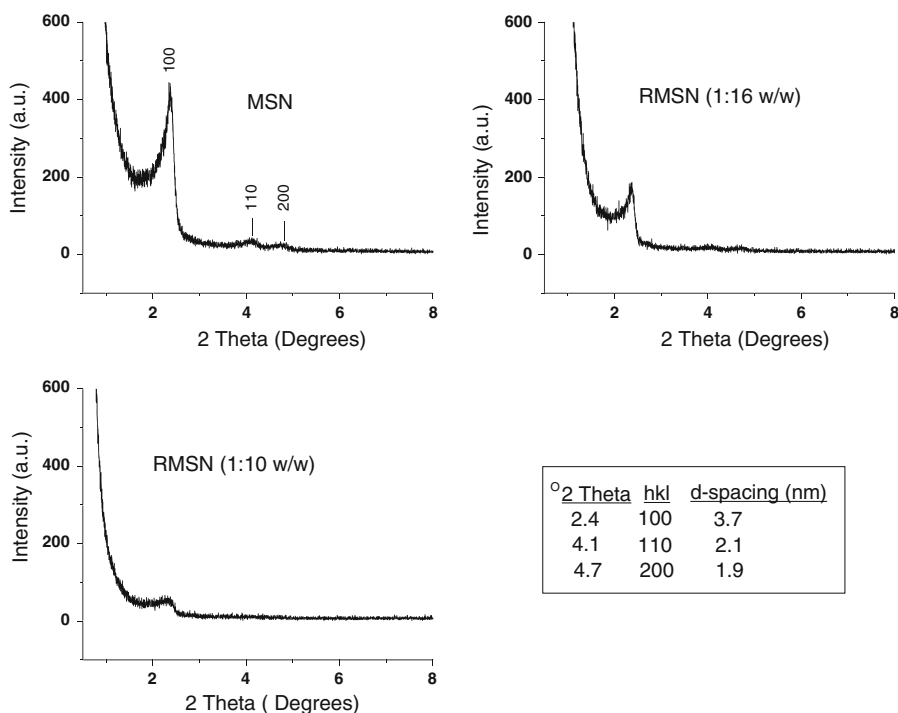
Rotavapor-loading method was employed, a driving concentration gradient was generated by evaporating

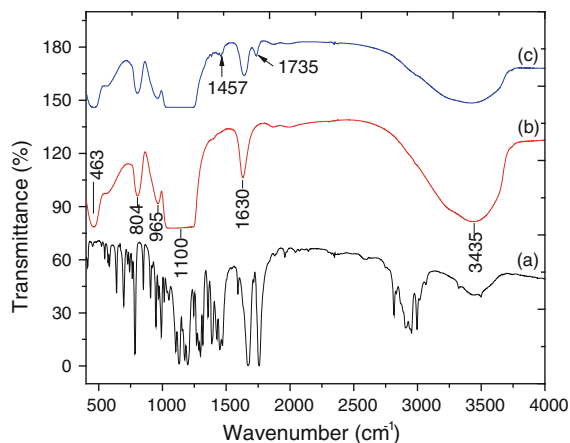
the solvent slowly but steadily. Metalaxyl was driven into the MSN pores in a fashion similar to immersion loading method which requires utilization of high drug concentration (Limnell et al. 2011).

Powder SAXRD patterns for MSN and RMSN samples are shown in Fig. 2. For MSN, three diffraction peaks at 2θ (2.4°, 4.1°, and 4.7°) were observed, which could be indexed as (100), (110), and (200) reflections based on the hexagonal unidirectional structure system. XRD of RMSN reveals a similar pattern with the intensity of the peaks greatly reduced, indicating reduced scattering contrast between the pore walls and pore space of silica due to successful loading of metalaxyl (Popovici et al. 2011). It is clear that loading efficiency was improved by increasing the metalaxyl: MSN particle ratio from 1:16 to 1:10 w/w. However, the presence of *d*<sub>100</sub> reflection suggests that the mesoporous structure of MSN was retained after loading with the fungicide molecules.

A comparison of Fourier transform-IR (FT-IR) spectra (Fig. 3) of free metalaxyl, MSN and RMSN reveals that the metalaxyl characteristic stretching frequencies of the di-substituted amide and carbonyl ester groups at 1,457 and 1,735 cm<sup>-1</sup>, respectively, are depicted in RMSN spectrum without any significant bond shift. This corroborates the XRD results. MSN

**Fig. 2** SAXRD patterns of MSN and RMSNs with different metalaxyl: MSN particle ratios



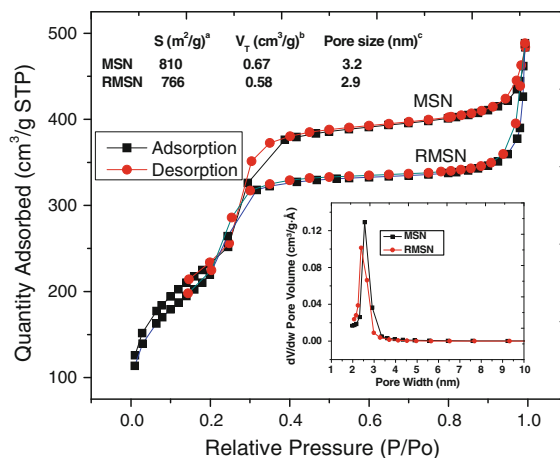


**Fig. 3** IR spectra of *a* metalaxyl, *b* MSN, and *c* RMSN

exhibits characteristic absorption bands corresponding to Si–OH<sub>Stretching</sub> (3,435 cm<sup>-1</sup>), SiO–H<sub>Bending</sub> (1,630 cm<sup>-1</sup>), Si–O–Si<sub>Stretching</sub> (1,100 cm<sup>-1</sup>), Si–OH<sub>Bending</sub> (965 cm<sup>-1</sup>), and SiO–H<sub>Stretching</sub> (804 cm<sup>-1</sup>).

Moreover, the absence of new peaks that cannot be ascribed to either metalaxyl or MSN in the RMSN spectrum suggests MSN–metalaxyl interactions through noncovalent bonding in the adsorption process. Weak van der Waals forces and hydrogen bonds describe the kind of host–guest chemistry observed in the entrapment of metalaxyl molecules into the MSN pores.

N<sub>2</sub> sorption studies resulted in type-IV isotherms (Fig. 4) typical of mesoporous materials according to the International Union of Pure and Applied Chemistry (IUPAC) convention. Both isotherms depicted a type H3 hysteresis loop in the high pressure region. This indicates existence of mesoporosity. A sharp inflection point at  $P/P_0 = 0.3$  is indicative of narrow pore-size distribution as confirmed by the inset figure. The amount of nitrogen adsorbed by RMSN was reduced while the shape of the hysteresis loop was not altered, which indicated that some adsorptive sites in MSN were already occupied by metalaxyl and the loading process had no significant effect on the pore shape. Single point surface area of MSN reduced from 810 to 766 m<sup>2</sup>g<sup>-1</sup> while total pore volume and adsorption average pore size reduced from 0.67 to 0.58 cm<sup>3</sup>g<sup>-1</sup> and 3.2 to 2.9 nm, respectively, after loading with metalaxyl (inset). The reduction in sorption parameters confirmed further the successful entrapment of the fungicide onto the nanocarrier.



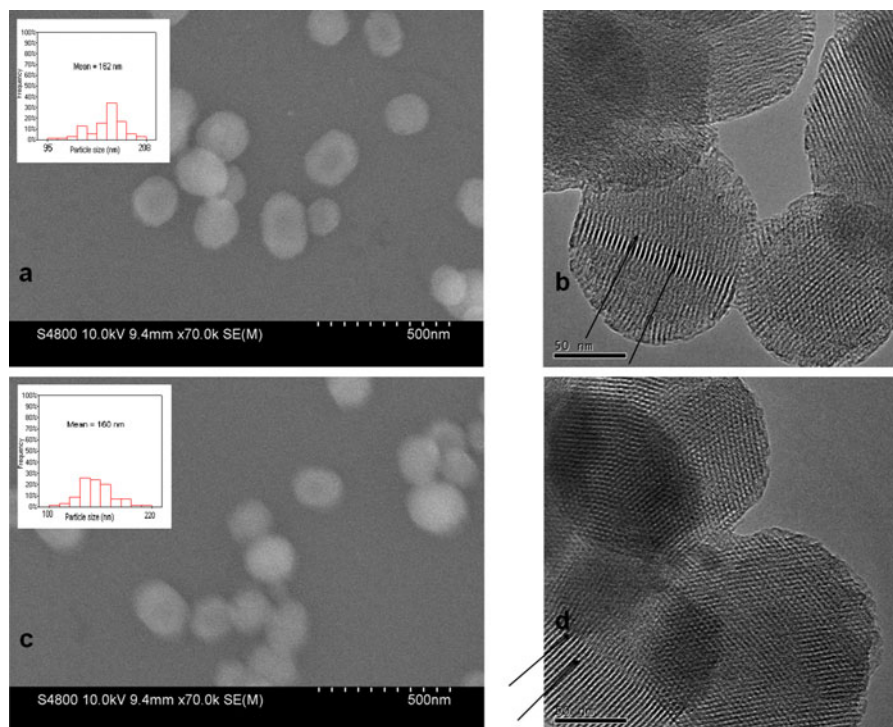
**Fig. 4** Nitrogen adsorption–desorption isotherms of MSN, RMSN and (inset) pore width distribution (figure) and physical parameters (table) of the samples

Electron microscopy was used to examine the effect of the entrapment of metalaxyl on physical and morphological characteristics of the MSN. The SEM and TEM images of MSN and RMSN are shown in Fig. 5. Particle diameters were estimated from SEM images using a nano measurer 1.2 software and an average of 70 randomly selected particles calculated. Respective particle sizes for MSN and RMSN are averaged at ~160 and ~162 nm with a narrow distribution (inset in Fig. 5a, c). Positions of mesopores on the TEM images are indicated by arrows. All materials show highly ordered honeycomb-like porous system typical of mesoporous silica. Evidently, the structural integrity of MSN was preserved after the loading process.

The amount of metalaxyl entrapped in MSN was estimated by thermogravimetry. TGA curves (Fig. 6) revealed that, MSN and RMSN showed a weight loss of 10 % (Fig. 6a) and 24 % (Fig. 6b), respectively, after heating to 800 °C. The difference of 14 wt% was taken to be the amount of metalaxyl loaded in MSN. The greatest weight loss happened at <300 °C since far beyond this temperature range, metalaxyl which has a melting point of ~73 °C and a boiling point of ~296 °C in pure state had decomposed. Adsorbed water and surface silanol groups contribute to extra weight loss at low and high temperature, respectively. The amount of fungicide loaded was considered significant cognisant to the fact that application of metalaxyl active ingredient is in very minute amounts, typically, in the range of 0.151–8.970 kg ha<sup>-1</sup> for



**Fig. 5** SEM and corresponding TEM images of MSN (a, b) and metalaxyl–MSN hybrid (c, d). Inset particle-size distributions



agricultural crops, 0.154–0.700 g kg<sup>-1</sup> for seed treatment, and 1.00–8.07 kg ha<sup>-1</sup> for ornamental trees and plants (Monkiedje et al. 2002). However, the amount of fungicide loaded in the MSN carrier matrix could be increased by increasing the concentration of the pesticide solution as demonstrated by XRD studies.

### Sorption studies

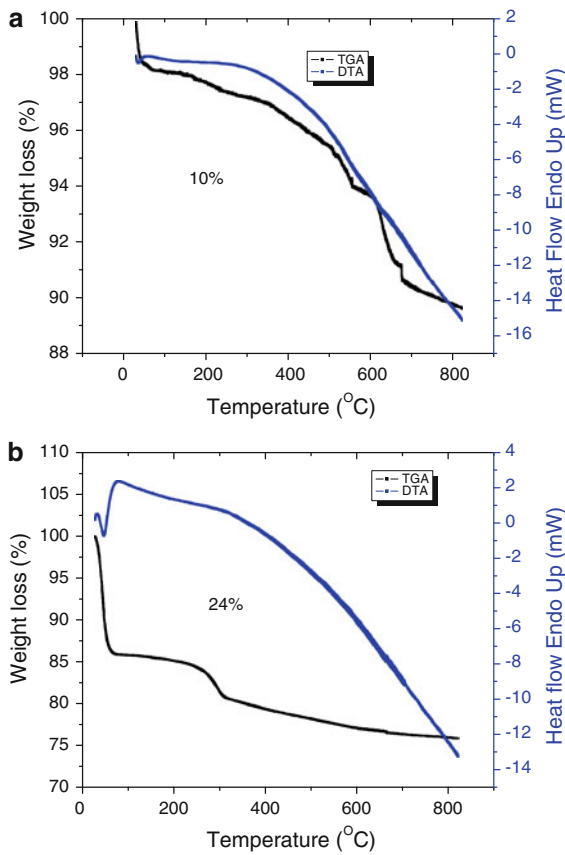
UV spectra of metalaxyl standard concentrations and corresponding calibration curve are exhibited in Fig. 7. The spectra express two distinct absorption peaks of equal intensity at 270 and 247 nm, the absorbance values of the peaks varied proportionally with concentration. The peaks were ascribed to the R- and S-enantiomers of metalaxyl which is a racemic mixture of the two. The absorbance values of the peak at 270 nm were used for quantification.  $R^2$  value ratified the analysis method.

Metalaxyl sorption isotherms and corresponding Freundlich curves are shown in Fig. 8. Type L-isotherms (Fig. 8a) according to Giles classification (Giles et al. 1960) are exhibited which suggested that sorption occurred by physical forces. The adsorption and desorption isotherms fitted the Freundlich sorption equation with  $R^2$  values of 0.99 and 0.93, respectively

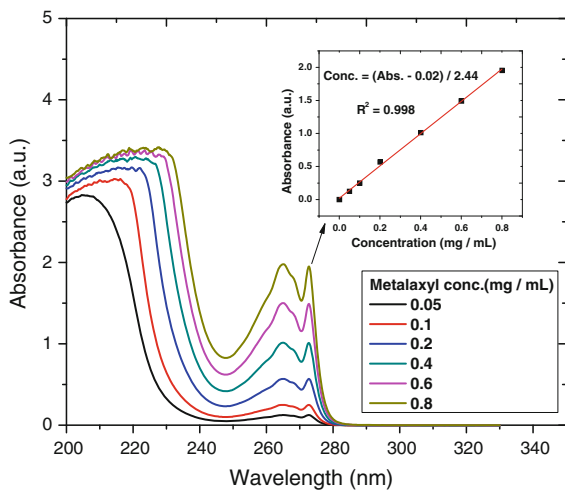
(Fig. 8b) which indicated a strong linear relationship between equilibrium concentration ( $C_e$ ) and amount sorbed ( $C_s$ ). Values of Freundlich adsorption–desorption coefficients are inset in Fig. 8b. Low value of  $K_f$  implied that the fungicide was adsorbed in low amounts while the low  $n_f$  value suggested broad distribution of adsorption site types on the MSN surface (Rodriguez-Cruz et al. 2008). Low fungicide payload was attributed to low metalaxyl concentration in the loading solution. The finding on availability of multiple adsorption sites on MSN resonated well with its structural nature of having outer and inner surfaces. A much lower  $K_{fd}$  than  $K_f$  value confirmed desorption. A  $n_{fd}$  value that approached zero implied desorption process involving multiple stages. Low value of the desorption hysteresis coefficient ( $H$ ) value verified reversibility of the sorption process. Reversibility is sine-qua-non for sustained release application of any carrier matrix.

### Fungicide release studies

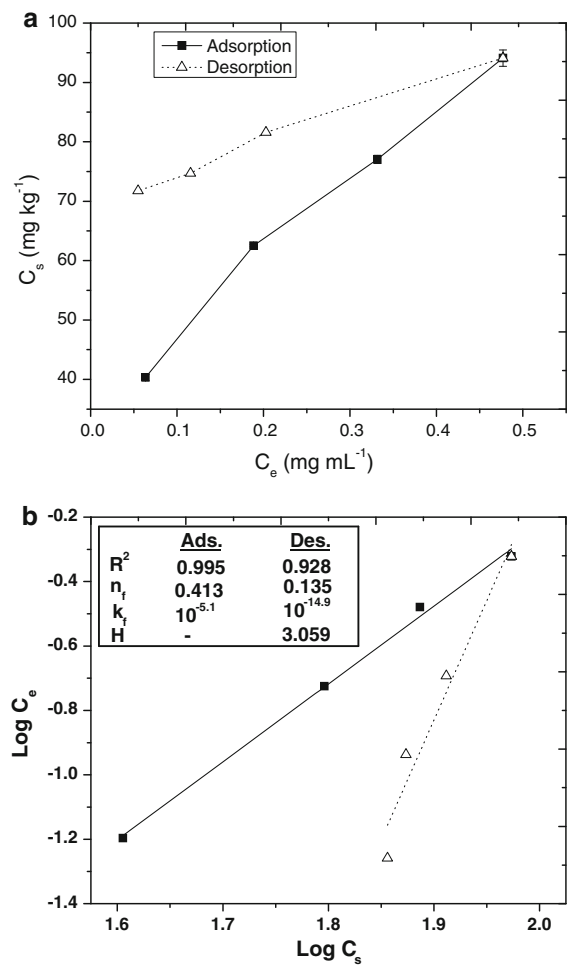
The amount of metalaxyl released from RMSN was determined using high performance liquid chromatography. The metalaxyl standards calibration curve and HPLC chromatogram are displayed in Fig. 9.



**Fig. 6** TGA and DTA curves for **a** MSN and **b** RMSN

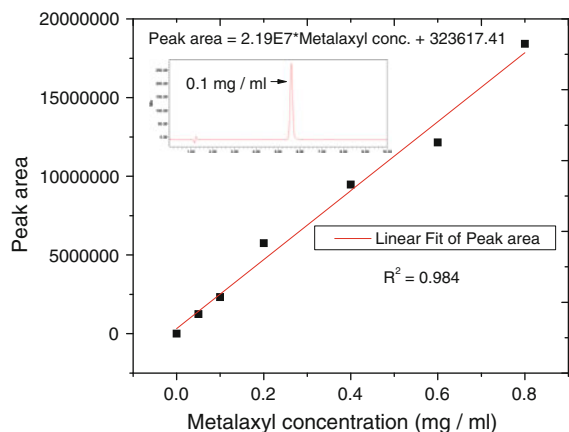


**Fig. 7** UV absorption spectra for metalaxyl calibration standards and (inset) calibration curve showing a linear relationship between the fungicide concentrations and UV absorbance

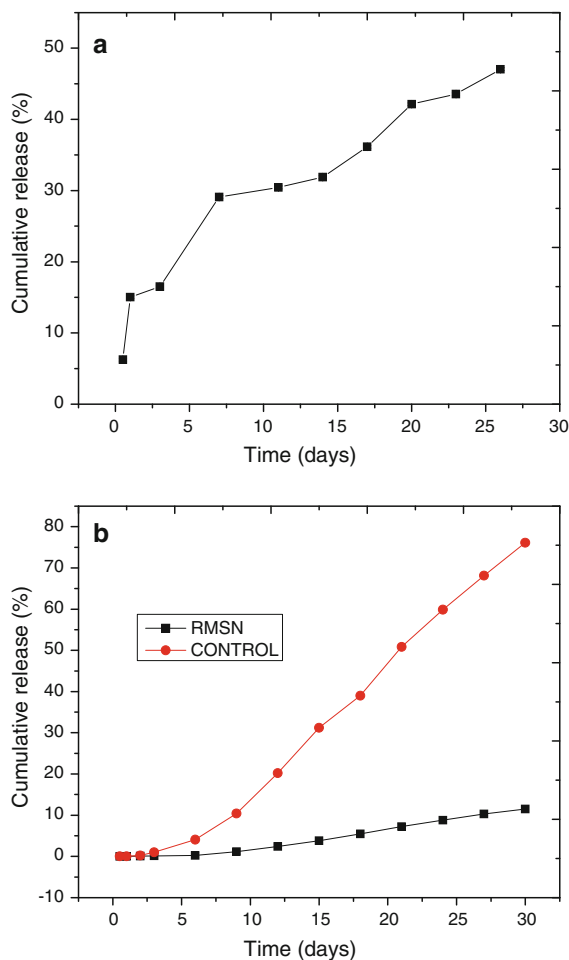


**Fig. 8** **a** Metalaxyl adsorption and desorption isotherms in MSN. **b** Freundlich curves and (inset) constants for the sorption process

Correlation coefficient ( $R^2$ ) value demonstrated linear relationship between peak areas and metalaxyl concentration. The release profiles are shown in Fig. 10. Slow and sustained release behavior was manifested with 47 and 11.5 % of the loaded metalaxyl been released in water (Fig. 10a) and soil (Fig. 10b), respectively, within a period of 30 days. Application of free metalaxyl in soil (control) resulted in 76 % release. The results demonstrated  $\sim 7$  times delay in the release of metalaxyl into the soil from the MSN matrix. This would facilitate long periods of soil protection and treatment using the same quantity of the fungicide. MSN are inorganic and water insoluble materials that do not leach in soil. However, their efficiency as fungicide carriers could also be improved



**Fig. 9** Curve of best fit for metalaxyl standard concentrations and (inset) HPLC chromatogram



**Fig. 10** Sustained release profiles for RMSN in **a** water and **b** soil

by functionalizing them with moieties that would make them “anchor” to the plant roots. Moreover, future studies should aim at determining the long term residual levels of various pesticide molecules loaded in the siliceous nanoscale delivery vehicles.

## Conclusion

Metalaxyl was successfully loaded into MSN mesoporous framework; payload was significant at 14 % w/w. A slower and more sustained release of metalaxyl was realized from the nanoscale carrier compared with free fungicide. It is demonstrated that MSN can provide an efficient means to deliver pesticides in a controlled fashion thus reducing wastage and environmental hazard. We envisage that, in future, MSN will find application in smart pesticide delivery systems not only for slow release but also capable of detecting an early stress or infection and offer targeted treatment.

**Acknowledgments** This research was supported by the German Academic Exchange Service (DAAD) and Jomo Kenyatta University of Agriculture and Technology (JKUAT).

## References

- Al-Kady AS, Gaber M, Hussein MM, Ebeid EM (2011) Nanostructure-loaded mesoporous silica for controlled release of coumarin derivatives: a novel testing of the hyperthermia effect. *Eur J Pharm Biopharm* 77:66–74
- Ambrogio MW, Thomas CR, Zhao Y-L, Zink JJ, Stoddart JF (2011) Mechanized silica nanoparticles: a new frontier in theranostic nanomedicine. *Acc Chem Res* 44(10):903–913. doi:10.1021/ar200018x
- Fernandes MC, Cox L, Hermosin MC, Cornejo J (2003) Adsorption-desorption of metalaxyl as affecting dissipation and leaching in soil role of mineral and organic components. *Pest Manag Sci* 59:545–552
- Ghormade V, Deshpande MV, Paknikar KM (2011) Perspectives for nano-biotechnology enabled protection and nutrition of plants. *Biotechnol Adv* 29:792–803
- Giles CH, Mac Ewan TH, Nakhwa SN, Smith D (1960) Studies in adsorption. Part XI. A system of classification of solution adsorption isotherms, and its use in diagnosis of adsorption mechanisms and in measurement of specific surface areas of solids. *J Chem Soc* 111:3973–3993
- Li Z-Z, Xu S-A, Wen L-X, Liu F, Liu A-Q, Wang Q, Sun H-Y, Yu W, Chen J-F (2006) Controlled release of avermectin from porous hollow silica nanoparticles: influence of shell thickness on loading efficiency, UV-shielding property and release. *J Controlled Release* 111:81–88



- Limnell T, Santos HA, Makila E, Heikkila T, Salonen J, Murzin DY, Kumar N, Laaksonen T, Peltonen L, Hirvonen J (2011) Drug delivery formulations of ordered mesoporous silica: comparison of three drug loading methods. *J Pharm Sci* 100(8):3294–3306. doi:[10.1002/jps.22577](https://doi.org/10.1002/jps.22577)
- Liu Y, Yan I, Heiden P, Laks P (2001) Use of nanoparticles for controlled release of biocides in solid wood. *J Appl Polym Sci* 79:458–465
- Liu F, Wen L-X, Li Z-Z, Yu W, Sun H-Y, Chen J-F (2006) Porous hollow silica nanoparticles as controlled delivery system for water-soluble pesticide. *Mater Res Bull* 41:2268–2275
- Monkiedje A, Ilori MO, Spiteller M (2002) Soil quality changes resulting from the application of the fungicides mefenoxam and metalaxyl to a sandy loam soil. *Soil Biol Biochem* 34:1939–1948
- Nair R, Varghese SH, Nair BG, Maekawa T, Yoshida Y, Kumar DS (2010) Nanoparticulate material delivery to plants. *J Plant Sci* 179:154–163
- Popovici RF, Seftel EM, Mihai GD, Popovici E, Voicu VA (2011) Controlled drug delivery system based on ordered mesoporous silica matrices of captopril as angiotensin-converting enzyme inhibitor drug. *J Pharm Sci* 100(2):704–714
- Rodriguez-Cruz MS, Andrades MS, Sanchez-Martín MJ (2008) Significance of the long-chain organic cation structure in the sorption of the penconazole and metalaxyl fungicides by organo clays. *J Hazard Mater* 160:200–207
- Sukul P, Spiteller M (2001) Influence of biotic and abiotic factors on dissipating metalaxyl in soil. *Chemosphere* 45:941–947
- Ukmar T, Maver U, Planinsek O, Kaucic V, Gaberscek M, Godec A (2011) Understanding controlled drug release from mesoporous silicates: theory and experiment. *J Controlled Release* 155:409–417
- Wen L-X, Li Z-Z, Zou H-K, Liu A-Q, Chen J-F (2005) Controlled release of avermectin from porous hollow silica nanoparticles. *Pest Manag Sci* 61:583–590
- Yang Y-W (2011) Towards biocompatible nanovalves based on mesoporous silica nanoparticles. *Med Chem Commun* 2:1033–1049. doi:[10.1039/c1md00158b](https://doi.org/10.1039/c1md00158b)
- Zheng H, Shang Q (2005) Water suspension acetamidiprid nanocapsule preparation and its repairing method. *Chem. Abs.* 143:73729