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Comparison of Buspirone adsorption by modification of carboxylated multi-walled carbon nanotube

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ABSTRACT: To overcome the problems of gene and drug delivery, nanotechnology has gained interest in recent years. Nanosystems with different compositions and biological properties have been extensively investigated for drug and gene delivery applications. Nanotechnology in drug delivery has been manifested into nanoparticles that can have unique properties both *in vitro* and *in vivo*, especially in targeted drug delivery to tumors. Carbon nanotubes hold tremendous potential as an effective drug delivery system. The carboxylated multi-walled carbon nanotube was modified by p-amino acetanilide and 5-aminoisophthalic acid. The modified multi-walled carbon nanotube was used to adsorption and determines the amount of Buspirone drug in the human urine. The synthesized adsorbent was characterized using Fourier transform infrared spectroscopy (FTIR), scanning electron microscopy (SEM), energy-dispersive X-ray spectroscopy (EDX) and Thermogravimetric analysis (TGA). The developed method was utilized for determination of Buspirone drug in pharmaceutical and human urine samples by high performance liquid chromatography (HPLC).

Keywords: *Buspirone, Carbon nanotube, Modification, Sorption*

INTRODUCTION

Nanotechnology is the study, design, creation, synthesis, manipulation, and application of materials, devices, and systems at the nanometer scale. Nanotechnology is expected to have a revolutionary impact on medicine. Nanoparticles can play a major role in medicine and especially in diagnosis and therapy of cancer, cardiovascular diseases and infectious diseases. To further the application of nanoparticles in pharmacy, it is important that the systems are stable, capable of being functionalized, biocompatible and directed to specific target sites in the body after systemic administration. Nanotechnology is on its way to make a big impact in Pharmaceutical and Medical diagnostics sciences. Nanotechnology is also opening up new opportunities in implantable delivery systems (Singh Suri and Fenniri, 2007, Saleh and Gupta, 2016, He, *et al.*, 2017, Doane and Burda, 2012). Pharmaceutical carriers are divided into organic and inorganic groups. These include: ceramic nanoparticles, metal nanoparticles, magnetic

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nanoparticles, carbon nanoparticles, liposomes, solid lipid nanoparticles, polymer nanoparticles, polymer micelles, dendrites, polymerases, hydrogel nanoparticles (Shi, *et al.*, 2013, Kang, *et al.*, 1996, Yang, *et al.*, 2016). There are several types of carbon, Graphene, Amorphous Carbon, Activated Carbon, Glassy, Carbon, Fullerene, Diamond (Yang, *et al.*, 2015, Kam, *et al.*, 2005, Tang, *et al.*, 2012, Zhang, *et al.*, 2006, Kong, *et al.*, 2000, Song, *et al.*, 2017).

There are two groups of carbon nanotubes: multi-walled carbon nanotubes (MWCNT) -and single-walled carbon nanotubes (SWCNT). Carbon nanotubes (CNTs) The unique chemical and physical properties of carbon nanotubes make them interesting nanomaterial for widespread applications i.e. as semiconductors in nanoscale devices, in energy related fields (batteries), and in drug delivery (Boyd, 2008, Mohammadi Nodeh and Rahemi Haghighi, 2018, Ahmad Panahi, *et al.*, 2010, Kukowska-Latallo, *et al.*, 2005, Neimark, *et al.*, 2009, Lee, *et al.*, 2006). In this article, carboxylated multi-walled carbon nanotubes were functionalized with cyanuric chloride then modified by p-amino acetanilide (MWCNT1) and In another part carboxylated multi-walled carbon nanotubes were functionalized with 1,4 dichlorobenzene then modified by Resorcinol (MWCNT2). MWCNT1 and MWCNT2 were used to measurement and determine the amount of Buspirone drug in human urine. Buspirone with $C_{21}H_{31}N_5O_2$ and 385.512 g/mol as molecular formula and molecular weight an anxiolytic agent and serotonin receptor agonist belonging to the azaspirodecanedione class of compounds. Schematic representation of the final synthesis of MWCNT1 and MWCNT2 is provided in (Fig. 1).

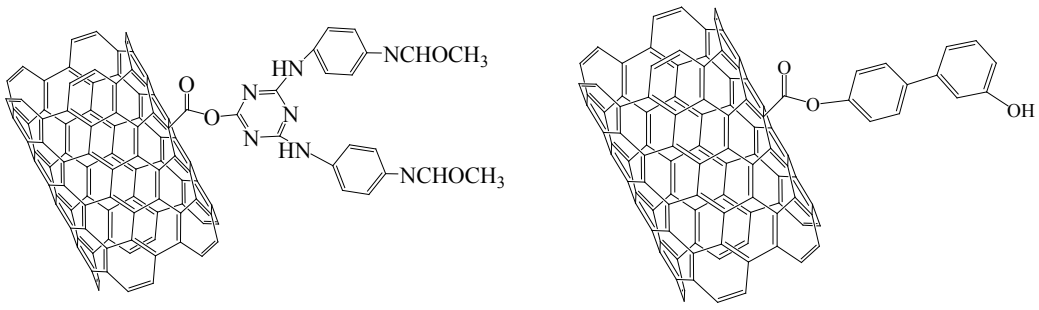
EXPERIMENTAL

Instruments

Infrared spectra were recorded on Fourier transform infrared spectroscopy (Spectrum100, PerkinElmer, Baesweiler, Germany). Thermo gravimetric analysis was carried out¬ using a TGA/SPTA851 (Metter Toledo, Germany). The scanning electron microscopy (SEM) micrographs were obtained on a MIRA3TESCAN of RMRC (USA) scanning electron microscopy. Elemental analysis was carried out on a Thermo-Finnegan model Flash EA elemental analyzer.

Reagents and solutions

MWCNT-COOH (purity >95 wt.%, inner diameter of 3–5 nm, outer diameter of 15–20 nm, length and ~50 μm carboxyl content of 1.56 wt.%), was obtained from US Research Nanomaterials, Houston, Texas , USA. Buspirone was purchased from Tehran drug co, Iran. In addition, cyanuric chloride, 1,4 dichlorobenzene, Resorcinol, p- amino acetanilide, 1,4-dioxane, methanol, Potassium di hydrogen phosphate, Xylene, acetic acid and all the inorganic acid and salt were products of Merck (Darmstadt, Germany). The Buspirone stock solution (1000 mg L^{-1}) was prepared in HPLC-grade H_2O. The stock solution of Buspirone was prepared in water (500 mg L^{-1}). All solutions were made by stock solution and their pH was adjusted by acetate buffer. The buffer solution (used as HPLC mobile phase) was prepared as follows; 10 mM of phosphate buffer solution (KH_2PO_4) was solved in distilled water, and then the solution's pH was adjusted 5.0 ± 0.01 using the concentrated phosphoric acid solution.



MWCNT1 MWCNT2

Fig. 1. Schematic of the final synthesis of MWCNT1 and MWCN.

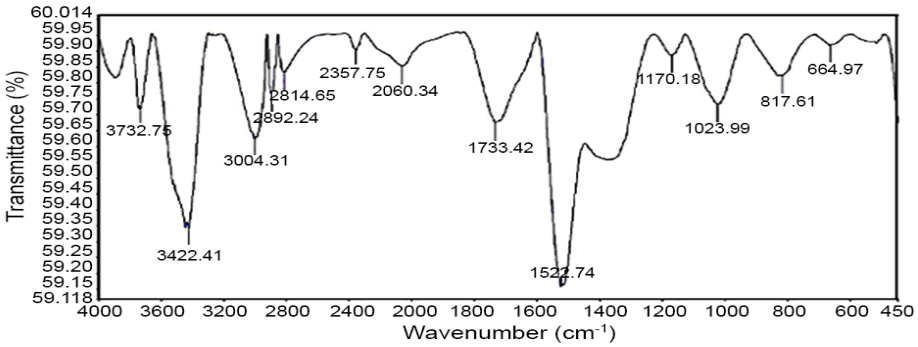


Fig. 2. FT-IR spectrum of the multi-walled carbon nanotube modified by P-amino acetanilide (MWCNT1)

Preparation of MWCNT- COOH/ P-amino acetanilide

First, a sample of acetylated carboxylic carbon nanotube (CNT-COOH) was purchased and forwarded for FT-IR, TGA tests, (Figs. 2 and 5). MWCNT1 and MWCNT2 were synthesized via method (Saleh and Gupta, 2016). First, 3 g of cyanuric chloride (1,4 dichlorobenzene for MWCNT2) was solved in a 50:50 mixture of xylene/dioxane in a beaker at the ambient temperature. Then, 2 g of MWCNTs-COOH was added to the solution. The reaction continued for 24 hours in a closed chamber. In order to remove interferences, the resulted compound was filtered and washed with 20 mL of petroleum ether for several times. Afterwards, the product was oven dried at 40°C for 24 h. For the synthesis of the final MWCNTs-resorcinol, 250 mL of sodium acetate buffer was poured into an Erlenmeyer flask and 1 g of p- amino acetanilide (ligand) (Resorcinol for MWCNT2) was added under the temperature of 65°C through mixing. Lastly, the freshly prepared compound was added to the above solution and the reaction was continued for 10 h. The obtained product (MWCNTs-resorcinol) was washed with excess deionized water and sodium chloride (0.1 M) and dried at 40°C for 24 h.

Chromatographic conditions

In order to analyze the drug, HPLC apparatus equipped with a UV-VIS detector and the column C18 (250 mm × 4.6 mm id, 5 µm) was used. The Buffer used in the solution system 10 mM has been of the phosphate buffer (KH_2PO_4) which was arranged by the phosphoric acid solution with pH= 7.5. The mobile phase consisted of phosphate buffer solution of 10 mM with pH= 3 and Acetonitrile in the ratio (40:60) was used. Flow rate was 1 ml/min and the injection volume of 20 micro-liters well as the column temperature was set to 35 degrees Celsius. The Wavelength set for the detector equals to 238 nm.

Sorption of Buspirone Drug

Different concentrations of Buspirone (0.1 to 10 µg mL^{-1}) were prepared at pH= 5. Then, 0.01 g of the synthesized nanoadsorbent was added into 10 mL of Buspirone solutions followed by shaking for 20 min. The solvent was transferred into micro-tube, and after centrifugation the supernatant was filtered by a syringe filter (0.2 µm, nylon). Lastly, 20 µL of the filtered solvent was injected to HPLC-UV for determination of residual Buspirone.

RESULTS AND DISCUSSION

Characterization of structures

Review of spectrum (FT-IR)

In order to verify the structure of samples in each step, their IR spectrum was reviewed. Results of FT-IR, MWCNT- COOH/ P-amino acetanilide (MWCNT1) and MWCNT-COOH, MWCNT-COOH/ 1,4 dichlorobenzene, MWCNT- COOH/Resorcinol (MWCNT2) are observed in Figs. 2 and 3, respectively. In Fig. 2, the peak observed in the area 1733 cm^{-1} is related to carboxyl C=O existing in –COOH. Furthermore, the wide peak band observed in the area 3422 cm^{-1} is related to OH stretching vibration. In addition, stretching vibrations between C-H Stretching vibrations was observed. In Fig. 3 (a), the peak observed in the

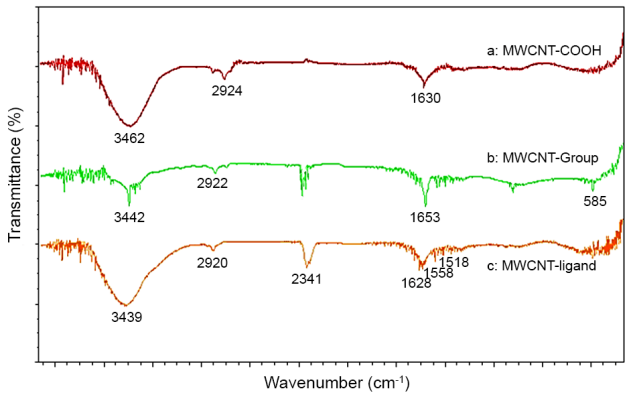


Fig. 3. FT-IR spectrum of a: MWCNT-COOH, b: MWCNT-COOH/ 1,4 dichlorobenzene, c: MWCNT- COOH/Resorcinol (MWCNT2)

area 1630 cm^{-1} is related to carboxyl C=O existing in –COOH. Furthermore, the wide peak band observed in the area 3462 cm^{-1} is related to OH stretching vibration. On the other hand, the band observed in the area 2924 cm^{-1} is related to C-H Stretching vibration. In the second step (b), IR spectrum was obtained from the nanostructure functionalized by MWCNT-COOH/ 1,4 dichlorobenzene.

In Fig. 3b, the peak observed in the area 3442 cm^{-1} is highly reduced compared to the wide peak of 3462 cm^{-1} in the carboxylated carbon nanotube's spectrum, which shows the reduction of OH group in the carboxylic acid. On the other hand, the peak observed in the area 1653 cm^{-1} is related to C=O carboxyl group existing in the compound. In addition, the peak observed in the area 585 cm^{-1} is related to stretching vibrations between carbon and chlorine C-Cl. In the third step, IR spectrum was obtained from the nanostructure functionalized by the ligand (MWCNT2). In a spectrum provided in Fig. 3c, the peak observed in the area 3439 cm^{-1} is related to the stretching vibration between OH. The peak observed in the area 1628 cm^{-1} is related to carboxyl C=O.

Review of TGA

According to the spectrum provided in Fig. 4a, Fig. 5a

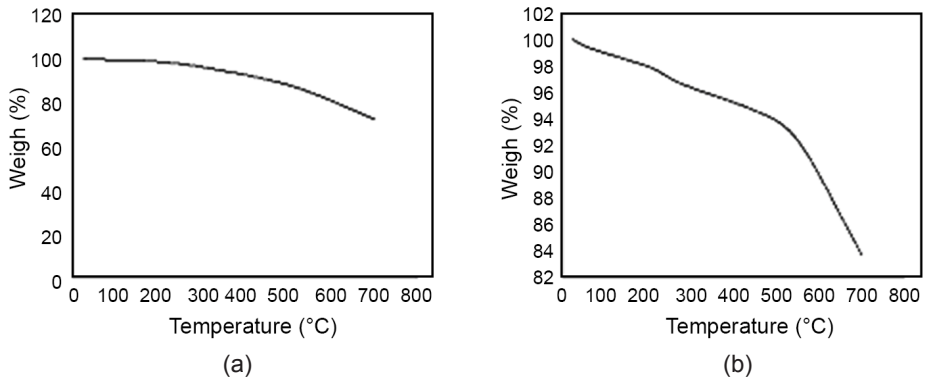


Fig. 4. Results obtained from TGA; a: The carboxylated multi-walled carbon nanotube (MWCNT-COOH), b: MWCNT1

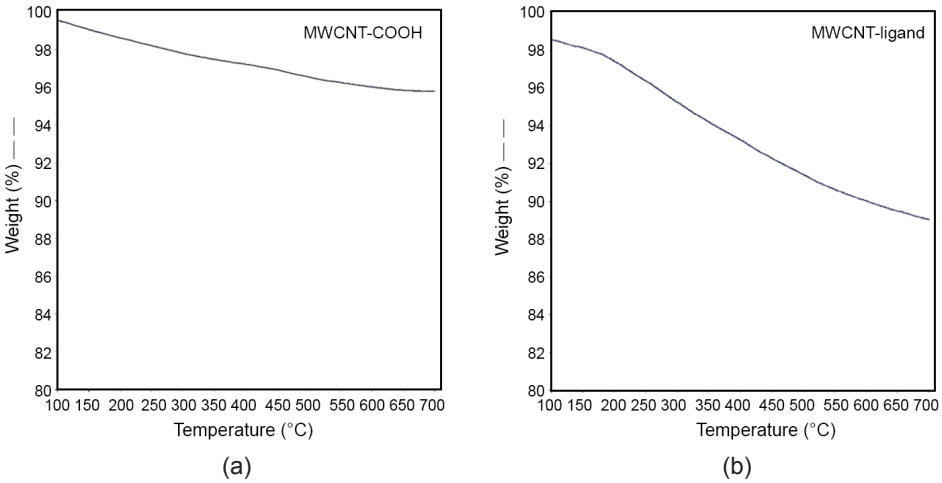


Fig. 5. Results obtained from TGA; a: The carboxylated multi-walled carbon nanotube (MWCNT-COOH), b: MWCNT2.

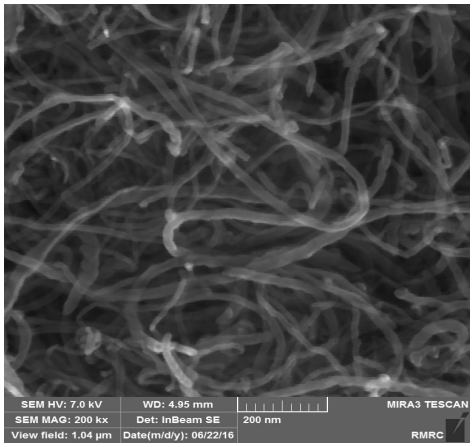


Fig. 6. SEM image of the final functionalized multi-walled carbon nanotube (MWCNT1).

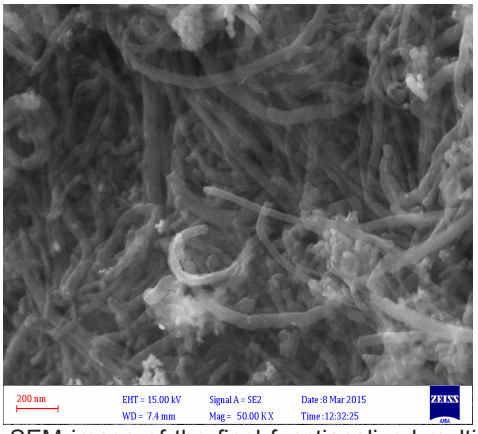


Fig. 7. SEM image of the final functionalized multi-walled carbon nanotube (MWCNT2).

the initial nanotube has a stable structure which maintains its structural skeleton to the temperature of 600 °C. Of course, there are impurities in the compound which are analyzed. On the other hand, Fig. 4b, Fig. 5b shows a structure with a modified surface indicates a reduction in the structure's resistance at high temperatures.

SEM microscopy

Figs. 6 and 7 are the SEM image in a 200 nm scale of the initial carboxylated carbon nanotube. The bumps surface and increase in the diameter is due to the several chemical reactions and the covalent bond (bonding) of the functional groups on the wall of nanotubes. It verifies the modification of the nanostructure's surface.

Determination of Optimum pH & mixing time

First, the maximum wavelength of Buspirone drug was determined (238 nm). Then, in the maximum wavelength, the drug's linear range is drawn between 1 and 30 µg mL^{-1} and the computation of drug's concentration in reviewing parameters is studied in this range. The method's validation parameters are listed in Table 1. The percentage of the drug adsorbed with the concentration of 20 µg mL^{-1} in different pH (3-8) was studied by HPLC which the best result of sorption was obtained in pH= 8. Its experimental results are shown in Fig. 8. Then, by adjusting pH= 8 in the solution as the optimum pH, the optimum time was determined in the same concentrations of the drug

Table 1. Validation parameters for standard solutions of Buspirone drug

Line equation	Correlation coefficient (R^2)	Linear range	RSD% (experimental)	LOD (ng mL^{-1})	LOQ (ng mL^{-1})
y=19001x + 3761.7	0.999	1-30	0.18	72	24

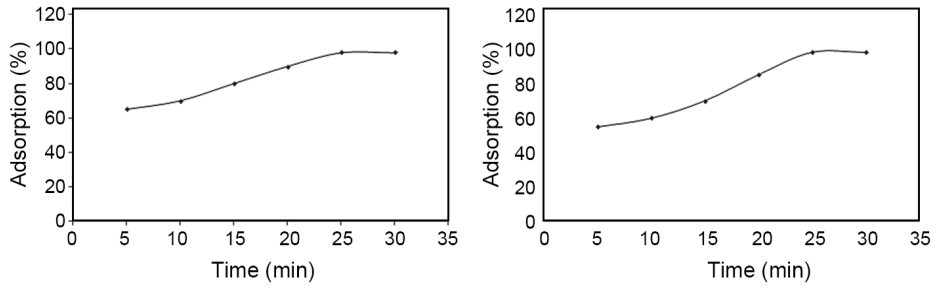


Fig. 8. The effect of time on the sorption of Buspirone drug by A: MWCNT1, B: MWCNT2.

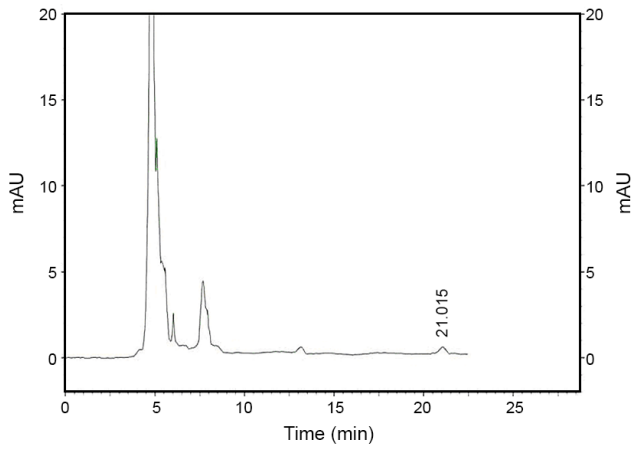


Fig. 9. HPLC results of sorption of drug in the urine MWCNT1

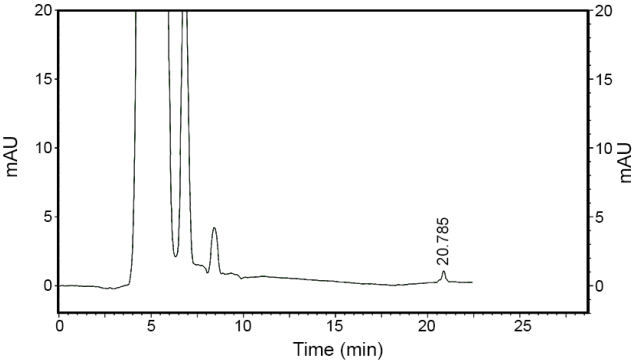


Fig. 10. HPLC results of sorption of drug in the urine MWCNT2

(20 μg mL^{-1}). Given Fig. 8, the maximum sorption was obtained in 20 min.

HPLC Results

After the determination of optimum conditions of sorption of Buspirone drug by the functionalized carbon nanotube (MWCN1, MWCNT2), a solution containing the drug was prepared in the urine and placed near the nanoadsorbent. Then, the supernatant was injected to the device. Based on the results of spectrums provided in Figs. 9 and 10 the sorption percentages were 98.9 (MWCNT1) and 97.7 (MWCNT2), respectively.

CONCLUSIONS

In this research adding functional group by covalent mechanism in multi membrane Nanotubes in order to make nanostructures capable of reacting with solute drug in urine was done. In general, by functionalizing the multi-walled carbon nanotube and studying the effect of different factors on the sorption of drug on the adsorbent, the best absorption was obtained in pH= 8 and 20 min. By applying optimum conditions, the efficiency of adsorbent in the adsorption was evaluated in the plasma. The maximum adsorption of drug by MWCNT1 and MWCNT2 were 98.9 and 97.7 respectively. For the determination of the drug sorption value in urine, high performance liquid chromatography (HPLC) was used. According to the results the presence of the rings by π-π interactions and the more functional group in the adsorbent structure led to increases the absorption efficiency between the adsorbent and drug.

REFERENCES

1.Singh Suri, S., Fenniri, H., (2007). Baljit Singh Nanotechnology-based drug delivery systems. J. Occup. Med. Toxicol., 2: 16.

2. Saleh, T.A., Gupta, V.K., (2016). Structural characterization of nanomaterial–polymer Membranes, first ed., T.A. Saleh, Nanomaterial and polymer membranes: synthesis, characterization, and applications. Elsevier, 67: 187-205.

3. He, K., Ma, Y., Yang, B., Liang, C., Chen, X., Cai, C., (2017). The efficacy assessments of alkylating drugs induced by nano-Fe3O4 /CA for curing breast and hepatic cancer. Spectrochim. Acta, 173: 82–86

4. Doane, T.L., Burda, C., (2012). The unique role of nanoparticles in nanomedicine: imaging, drug delivery and therapy. Chem. Soc. Rev., 41: 2885–2911.

5. Shi, S., Fan, Y., Huang, Y., Facile low temperature hydrothermal synthesis of magnetic mesoporous carbon nanocomposite for adsorption removal of ciprofloxacin antibiotics, Ind. Eng. Chem. Res., 52: 2604-2612 (2013).

6. Kang, Y.S., Risbud, S., Rabolt, J.F., Stroeve, P., (1996). Synthesis and characterization of nanometer-size Fe3O4 and γ-Fe2O3 particles. Chem. Mat., 8: 2209-2211.

7. Yang, Z., Guo, R., Shi, X., Wang, C., Dai, L.M., (2016). Magnetite nanoparticles enable a rapid conversion of volatile fatty acids to methane. RSC Adv., 6: 25662-25668.
8. Yang, Z., Shi, X., Wang, C., Wang, L., Guo, R., (2015). Magnetite nanoparticles facilitate methane production from ethanol via acting as electron acceptors. Sci. Rep., 5: 16118.
9. Kam, N.W., O'Connell, M., Wisdom, J.A., Dai, H., (2005). Carbon nanotubes as multifunctional biological transporters and near-infrared agents for selective cancer cell destruction. Proc. Natl. Acad. Sci., 102(33): 11600-5.
10. Tang, F., Li, L., Chen, D., (2012). Mesoporous silica nanoparticles: synthesis, biocompatibility and drug delivery. Adv. Mater., 24: 1504-1534.
11. Zhang, Z., Yang, X., Zhang, Y., Zeng, B., Wang, S., Zhu, T., (2006). Delivery of telomerase reverse transcriptase small interfering RNA in complex with positively charged single-walled carbon nanotubes suppresses tumor growth. Clin. Cancer Res., 12(16): 4933-4939.
12. Kong, G., Braun, R.D., Dewhirst, M.W., (2000). Hyperthermia enables tumor-specific nanoparticle delivery: effect of particle size. Cancer Res. 60(16), 4440-4445.
13. Song, M.M., Xu, H.L., Liang, J.X., Xiang, H.H., Liu, R., Shen, Y.X., (2017). Lactoferrin modified graphene oxide iron oxide nanocomposite for glioma-targeted drug delivery. Mater. Sci. Eng. C, 77: 904–911.
14. Boyd, B.J., (2008). Past and future evolution in colloidal drug delivery systems. Exp. Opin. Drug Deliv., 5: 69–85.
15. Mohammadi Nodeh, M.H., Rahemi Haghighi, M., (2018). Release and extraction of letrozole in blood plasma using resorcinol functionalized multi-walled carbon nanotube coupled with high-performance liquid chromatography. J. Liq. Chromatogr. Relat. Technol., 41(5): 239-245.
16. Ahmad Panahi, H., Morshedian, H., Mehmandost, N., Moniri, E., Galaev, I.Y., (2010). Grafting of poly[1-(N,N-bis-carboxymethyl)amino-3-allylglycerol- odimethy- acrylamide] copolymer onto siliceous support for preconcentration and determination of lead (II) in human plasma and environmental samples. J. Chromatogr. A, 1217: 5165–5172.
17. Kukowska-Latallo, J.F., Candido, K.A., Cao, Z, Nigavekar, S.S., Majoros, I.J., and Thomas T.P., (2005). Nanoparticle targeting of anticancer drug improves therapeutic response in animal model of human epithelial cancer. Cancer Res., 65(12): 5317-5324.
18. Neimark, A.V., Lin, Y., Ravikovitch, P.I., Thommes, M., (2009). Quenched solid density functional theory and pore size analysis of micro–mesoporous carbons. Carbon, 47: 1617–1628.
19. Lee, J., Kim, J., Hyeon, T., (2006). Recent progress in the synthesis of porous carbon materials. Adv. Mater., 18: 2073–2094.

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