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Research Article

Physical Coating of Mesoporous Silica Nanoparticles with Poly (2-vinyl pyridine) and Polyvinylpyrrolidone for the adsorption and release of 5-Fluorouracil

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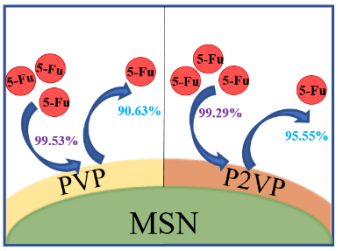
GRAPHICAL ABSTRACT



ABSTRACT

Nanotechnology is now being used in various application such as drug carrier, waste water treatment, internal air cleaner, catalyst, bio-catalyst etc. Currently, nanotechnology is widely used in medical application due to the disadvantage in conventional drug delivery which leaves side effects to the patient. Nanotechnology has the potential to improve the treatment methods. In this study, 5-fluorouracil (5-Fu) is used as model drug to evaluate the adsorption and release from drug carrier which is mesoporous silica nanoparticles (MSN). MSN is modified with pH-sensitive polymer which are poly (2-vinyl pyridine) (P2VP) and polivinylpyrrolidone (PVP). Modified MSN were characterized by using transmission electron microscopy (TEM), X-ray diffraction (XRD), Fourier transform infrared spectroscopy (FTIR) and field emission scanning electron microscopy (FESEM). Through the analysis, the results obtained prove that there is a cross-linkage between MSN molecules and polymers. Based on the result for drug loading, along 6 hours of experiment, the highest percentage of drug loading is at 80ºC which are 99.53%. and 99.29% for MSN-P2VP and MSN-PVP. Meanwhile, for drug release, the experiment was conducted at 37ºC for 72 hours. As a result, percentage of drug release for MSN-P2VP-5-Fu and MSN-PVP-5-Fu were 95.55% and 90.63%. It can be concluded that MSN-P2VP and MSN-PVP show slow release and could be recommended for further study in drug delivery.

Keywords: MSN; Poly (2-vinyl pyridine); Polyvinylpyrrolidone; 5-Fluorouracil; Adsorption; Drug release

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1. INTRODUCTION

A few decades ago, cancer therapy has improved and advancing, from the conventional injection and oral method to the intention of nanotechnology approach. However, new therapeutic methods are still needed as there are many studies proved that the treatment on conventional cytotoxic drugs for cancer patients will leave side effects [1]. Apart from anticancer medicines, other types of treatment also faced the same problem. Oral delivery system has disadvantages such as low stability in gastric, low solubility or bioavailability, and lack of permeability against intestinal membranes [2]. In addition, some types of medicines have low potential to achieve maximum therapeutic action through injection techniques [3]. Therefore, in order to overcome these problems, researchers have been looking forward for a more effective method in drug delivery. Nanotechnology that develops nano-structured particles is one of the major attractions by researchers. Nano particles are nano-sized substances that can transport drugs, imaging agents, and genes [4].

The strategic approach has been taken by researchers to design specific drug delivery system that can transport effective drug doses to targeted cells and tissues. A good drug delivery system should have biocompatible carrier, high drug loading, and ability to directly go to specific target cell or tissue, and control release of drugs with a proper releasing rates in order to achieve an effective local concentration [5]. There are several types of MSN that have been commercialized such as Mobil Composition Matter (MCM-41) and Santa Barbara Amorphous materials (SBA-15). MSN is now used in several applications including drug delivery, wastewater treatment, indoor air cleaning, catalyst, bio-catalyst and so on [6]. MSN has unique features such as

ordered pore structure, large pore volume and surface area, tuneable pore size, two functional surfaces and good biocompatibility [7]. Due to these unique features, MSN is anticipated in drug delivery application.

Studies have been conducted by researchers on drug delivery by using silica nanoparticle material. Drugs such as naproxen, a type of painkillers, has been loaded into the SBA-15 that has been modified. [8]. Thus, the adsorption and release of the drug is studied. Another study was conducted by Wang et al. (2014), by loading doxorubicin (DOX) drugs into the conjugated graphene oxide chlorotoxin (CTX-GO) to study the adsorption and release of drugs [9]. Both of these studies were released at different pH which are at pH 7.4 and 5.0. As a result, the release rate of the drug at pH 5.0 is higher than at pH 7.4. Therefore, the release of drugs can be controlled under certain pH conditions [10]. Nano particles with a responsive polymer coating has the ability to ensure good stability to MSN at pH 7.4. At this pH value, the polymer layer forms a cap, which is hydrophobic and impermeable to water, protein and salt around MSN. Moreover, the polymeric coating improves MSN stability at pH 5.0, where the cap is open and ready to release the drug. Comparison between MSN-polymer and uncoated MSN indicated that MSN-polymer showing less degradation [11].

Most of polymeric nanoparticles are biodegradable and biocompatible, and are most preferable method for nanomaterial drug delivery. Polymeric nanoparticles also show a great potential for surface modification through chemical transformation, providing excellent pharmacokinetic control, and are particularly suited for the adsorption and release of therapeutic agents [12]. The types of polymers used are poly (2-vinyl pyridine) (P2VP) and polyvinylpyrrolidone (PVP). P2VP is a weak poly-electrolyte base and pH-sensitive polymer. This can result in expanding the nanogel hence release the drug or vice versa [13]. On the other hand, PVP is one of the famous chemical inert polymers in physiological response. PVP has a strong hydrophilic component in pyrrolidone moiety and hydrophobic groups in alkyl groups. This makes it one of the best materials to modify MSN [14]. In this study, 5-Fu was used as the drug model and the adsorption and release rate of MSN modification with P2VP (MSN-P2VP) and PVP (MSN-PVP) were studied. The added polymer is expected to extend the release time of the drug.

2. EXPERIMENTS

2.1 Modification of MSN with P2VP and PVP

Polymeric coating of mesoporous silica nanoparticle is post-synthesized by using physical mixing method. MSN and PVP (99% purity) or P2VP (99% purity) were mashed up and grinded for an hour resulting in modified mesoporous silica nanoparticle with poly (2-vinyl pyridine) (MSN-P2VP) and modified mesoporous silica nanoparticle with polyvinylpyrrolidone (MSN-PVP).

2.2 Characterization of MSN-P2VP, MSN-PVP, MSN-P2VP-5-Fu and MSN-PVP-5-Fu

The crystallinity of synthesized MSN-P2VP and MSN-PVP are characterized by x-ray diffraction (XRD). Whereas the morphology and structure of the modified MSN are performed by transmission electron microscopy (TEM) and field emission scanning electron microscopy (FESEM). The presence of the functional group in the studied materials is confirmed by using the Fourier transform infrared spectroscopy (FTIR).

2.3 Adsorption of 5-Fu by MSN-P2VP and MSN-PVP

5-Fu solution in ethanol was prepared by dissolving 5-Fu powder into 250 mL of ethanol to produce a concentration of 50 ppm solution. Next, MSN-P2VP or MSN-PVP is added into the solution. The solution temperature is maintained at 25°C throughout the experiment. Then, at each interval of 10 minutes, 5 mL of the solution will be taken. Clear solution is tested by using ultra-violet spectrophotometer (UV-vis) at λ = 290 nm. The resulting MSN-P2VP-5-Fu and MSN-PVP-5-Fu will be washed by using ethanol and dried in the oven at 60°C for 24 hours. The procedure is repeated by using different temperature at 25, 50 and 80°C.

2.4 Release of 5-Fu from MSN-P2VP-5-Fu and MSN-PVP-5-Fu

The release of 5-Fu drug from MSN-P2VP and MSN-PVP were tested by taking MSN-P2VP-5-Fu and MSN-PVP-5-Fu powder resulting from previous experiment into incubator shaker with 250 ml of pH 5 phosphate buffered solution (PBS) at 37°C for 72 hours. The shaker is operated at 150 rpm for 72 hours. Then, at each interval of 10 minutes, 5 mL of the solution were taken and tested by using UV-vis spectrophotometer at λ=290 nm.

3. RESULTS AND DISCUSSION

3.1 Modification of MSN with P2VP and PVP

The existing MSN has been modified by physical mixture methods. Post synthesis is one of the effective ways to modify the outer surface of MSN. By implementing this method, MSN was combined with the polymer prior to the drug loading. The surfactant was removed before the post-synthesis process, theoretically, the polymer will stick on both internal and external surface of MSN. The MSN-P2VP and MSN-PVP in dry form is a kind of yellowish white or white powder with different particle size.

XRD is used in order to verify the crystallinity of modified MSN. The diffraction peak for MSN powder shows three different peaks as shown in Fig. 1 (A), which is in 2.5°, 4.1° and 4.5°. This proves that the MSN has a 2D hexagonal pore structure arrangement [15]. After being modified by physical mixture method, the intensity of diffraction peak decreases from three peaks to two peaks, which lies around 2.1° and 4.6°. In addition, the peak intensity in MSN samples modified by two different types of polymers has a lower intensity than the intensity diffraction peak in the MSN sample. In agreement to previous study, this shows that the presence of polymer coating on the external surface of slightly alter the MSN structure after cross-linking [16].

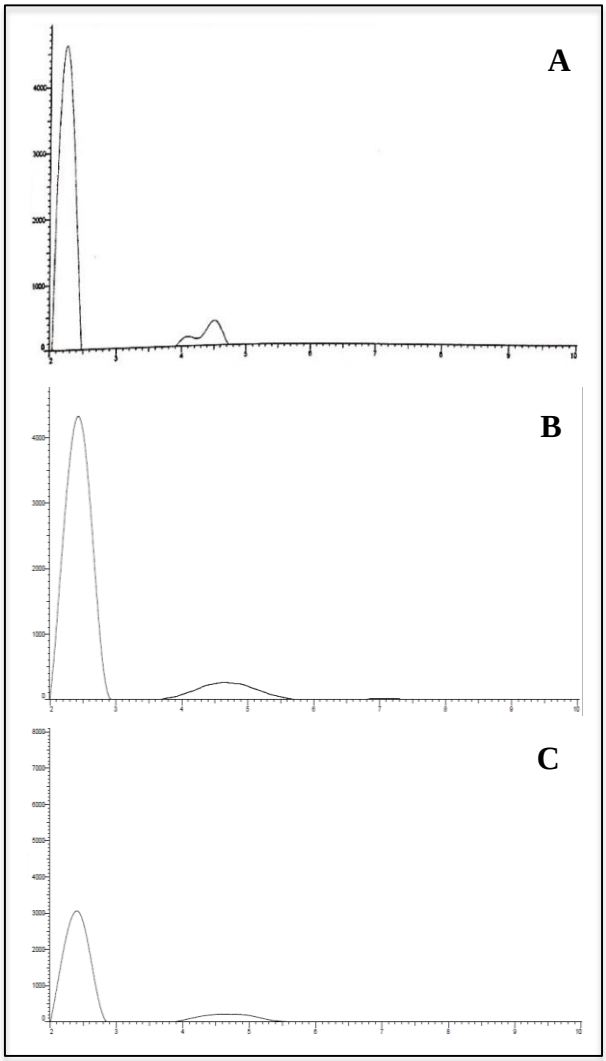

Fig. 1 XRD pattern of the MSN (A), MSN-P2VP (B) and MSN-PVP (C).

FESEM and TEM are used to capture the morphology and topology image of modified MSN. Fig. 2 (A) and (B) show FESEM image of MSN-P2VP and MSN-PVP.

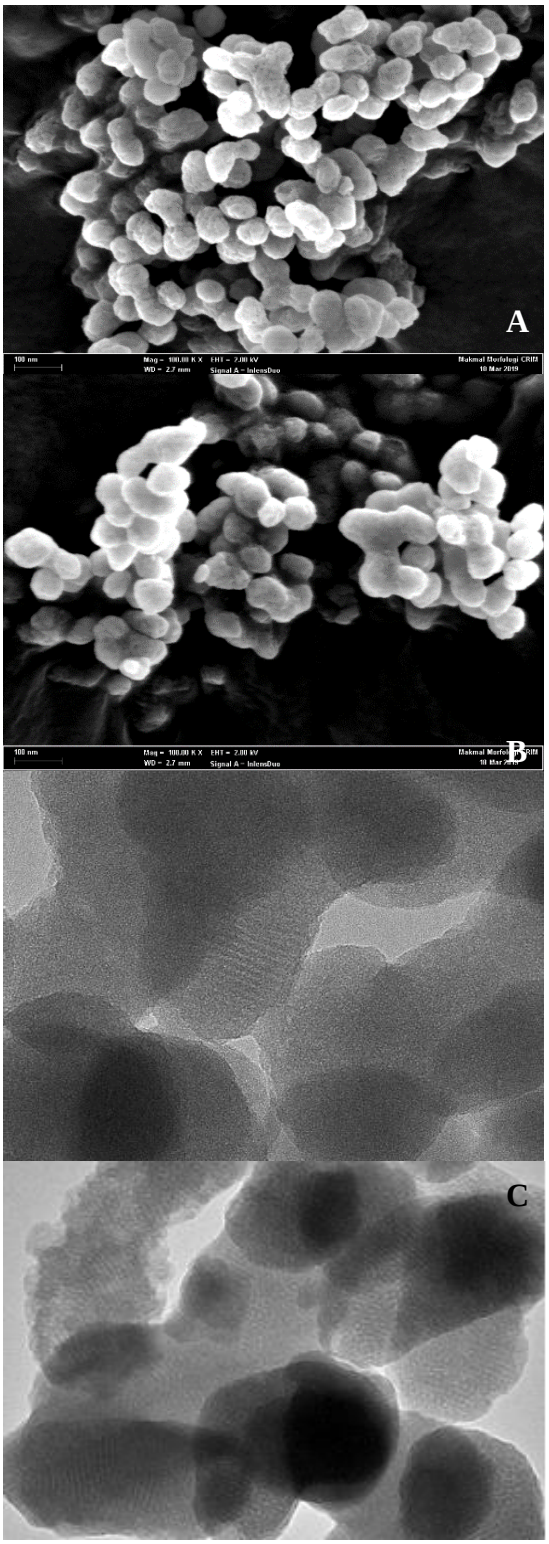

Fig. 2 FESEM image for MSN-P2VP (A) and MSN-PVP (B) and TEM image for MSN-P2VP (C) and MSN-PVP (D).

Based on the figure, it can be seen that the particles are attached to each other and produce non-uniform sphere shape forms. This is due to the polymeric coating on the surface of MSN causing MSN to lose its original shape which is uniform sphere [17]. Fig. 2 (C) and (D) confirmed that MSN modification with P2VP and PVP does not change the basic pore structure of MSN. This comparison is made based on our previous publication on MSN image before the modification [18]. Based on the observation, large domains show the unique properties of MSN, such as highly ordered hexagonal strip-like arrays. A good pore structure is very important to ensure the homogeneity of the drug distribution [19]. However, there are certain parts on MSN surfaces that have been probably enclosed by polymers since they have been modified. Thus, there is a pore structure that cannot be clearly seen on the figure.

3.2 Adsorption of 5-Fu

In this experiment, 5-Fu has been selected as a drug model to demonstrate the drug's adsorption over MSN at temperatures of 25, 50 and 80ºC. MSNs were modified by two types of amine-based polymer which are P2VP and PVP. The quantity of the drug being adsorbed is evaluated using UV-Vis at wavelength 290nm. Referring to Fig. 3, the highest percentage of adsorption of 5-Fu by MSN-P2VP for 6 hours is 80ºC which is 99.53% followed by 50ºC and 25ºC with its adsorption percentage value of 92.20% and 25.13%. The adsorption pattern at 50ºC increased dramatically during the first hour due to a sudden rise in temperature which could not be controlled.

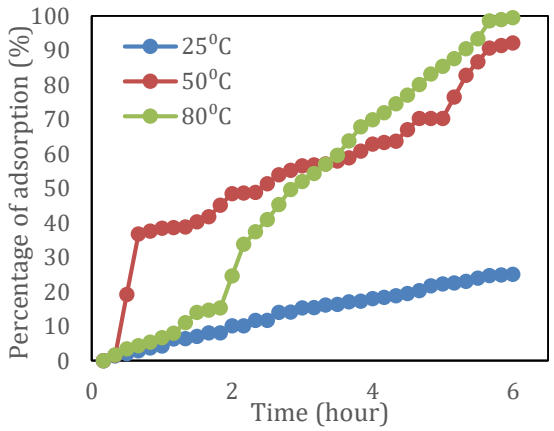

Fig. 3 The percentage of 5-Fu adsorption on MSN-P2VP at 25, 50 and 80ºC.

Fig. 4 shows the percentage of drug adsorption by MSN-PVP for various temperatures which are 25, 50 and 80ºC are 21.91%, 76.46% and 99.29%. From the percentage of adsorption, it can be seen that the highest adsorption percentage is at 80ºC. During the third hour, the percentage of drug adsorption at 50ºC increased sharply. This is due to the error that occurred during the experiment. From Fig. 3 and Fig. 4, it can be concluded that the optimum temperature for both MSN-P2VP and MSN-PVP are at 80ºC and the percentage of adsorption is slightly different by 0.24% which can be neglected. This result is supported by Fathi et. al 2015, which stated that percentage of adsorption for two types of amine-based polymer are the same [8].

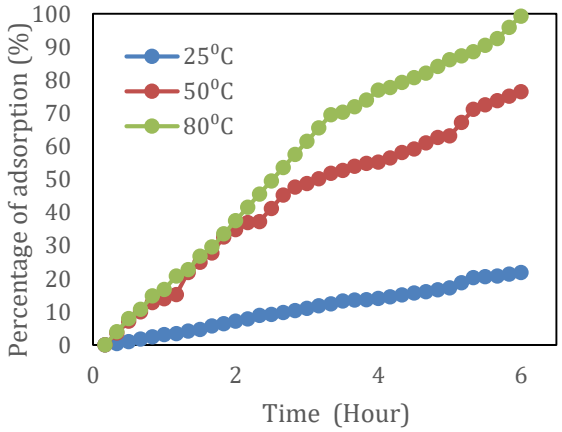

Fig. 4 The percentage of 5-Fu adsorption on MSN-PVP at 25, 50 and 80ºC.

The resulting MSN-PVP-5-Fu and MSN-P2VP-5-Fu powders were analysed by using FTIR to identify the functional groups that is present (Fig. 5). The FTIR for MSN was reported in our previous study while the FTIR for polymer-MSN is presented in this current study [18].

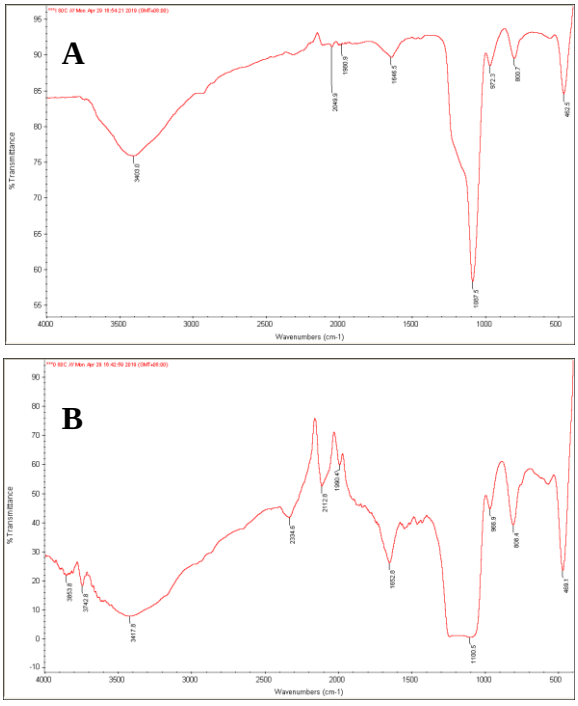

Fig. 5 FTIR spectra of the MSN-P2VP (A) and MSN-PVP (B).

Table 1 shows the FTIR data of both samples after drug adsorption. Some of the peak features corresponding to the drugs are found to overlap with peak characteristics corresponding to the polymer used. From the results obtained, it proves that 5-Fu and polymer molecules which are P2VP and PVP are not just attached on the MSN surface, nevertheless, it also forms hydrogen bonds with MSN. This is actually presumed from the reduced of the –OH region detected.

Table 1 Wavenumber frequency for MSN-P2VP-5Fu and MSN-PVP-5Fu [18, 20-22].

Component	Functional group	Wavenumber frequencies (cm^{-1})	
		MSN-P2VP-5Fu	MSN-PVP-5Fu
MSN	Si-O-Si	1087.5	1100.5
	Si-OH	972.3	966.9
	OH vibration	3403	3417.8
PVP	C-CH_2 bending (alkane)	-	1485-1445
	C-H stretching (alkane)	-	2954
	C-H bending (aromatic)		808.4
	C-N vibration	-	1580
	N-C=O stretching (carbonyl)	-	1652.8
P2VP	C-H stretching (alkane)	2925	-
	C-CH_2 bending (alkane)	1470	-
	C=C or C=N stretching	1590	-
	C-C stretching	1087.5	-
5-Fu	CO-NH-CO	1646.5	1652.8

3.3 Release of 5-Fu

5-Fu drug release from MSN-P2VP-5-Fu and MSN-PVP-5-Fu were performed at a constant temperature of 37ºC and pH 5 for 72 hours. MSN-P2VP-5-Fu and MSN-PVP-5-Fu were placed into a phosphate buffer solution and placed in an incubator shaker for continuous shaking purposes at 150 rpm. In a certain time interval, 5 mL of samples were taken (Fig. 6). As a result of the study, Fig. 6 shows that the percentage of drug release by MSN-P2VP-5-Fu at 72 hours is 95.55% while for MSN-PVP-5-Fu is 90.63%. This phenomenon occurs because at pH 5.0, polymer coating is open and ready to release drug. Previous study reported that the assistance of polyvinyl pyridine to the polystyrene block had resulted to the significantly slow release of cucurbit[7]urils [23]. The MSN-PVP-5Fu graph pattern is more consistent than MSN-P2VP-5Fu proving MSN-PVP-5Fu releasing the drugs gradually. Therefore, the concentration of drugs in the body at one time is not too high and the cytotoxicity of the drug can be reduced. Throughout the experiment, it can be proven that the drug is released effectively in a prolonged period [24-28].

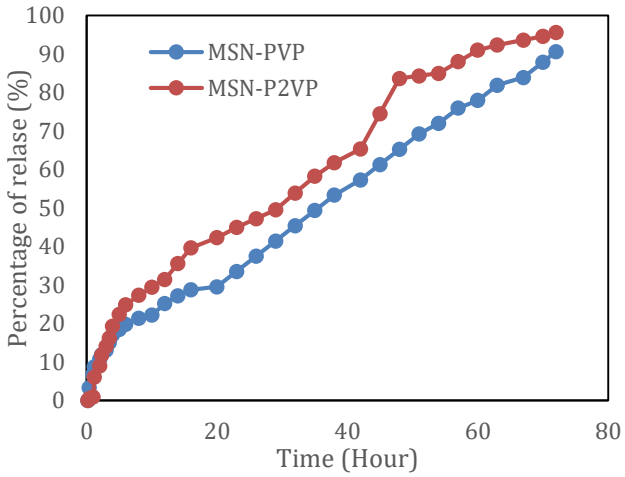

Fig. 6 Percentage of 5-Fu release for MSN-P2VP-5-Fu and MSN-PVP-5-Fu at 37ºC.

4. CONCLUSION

Through this study, differences in adsorption rates for MSN-P2VP and MSN-PVP on 5-Fu anti-cancer drugs were compared. Based on the results obtained, MSN-P2VP and MSN-PVP have been successfully synthesized. The physical properties exhibited were white-colored powder with different particle size. According to XRD analysis, decreasing in the diffraction peak from three peaks to two peaks proving the presence of a polymer layer. In addition, the TEM and FESEM results prove that the morphology of MSN-P2VP and MSN-PVP were transformed into non-uniform forms and the particles attached to each other. This is because of the polymeric coating on the surface of MSN causing MSN to lose its original. 5-Fu adsorption by MSN-P2VP and MSN-PVP were performed at different temperatures which are 25, 50 and 80ºC for 6 hours. The findings of both MSN modifications were at 80ºC, adsorption rate the highest with 99.53% for MSN-P2VP and 99.29% for MSN-PVP. According to the study conducted, percentage of drug release by MSN-P2VP was higher than MSN-PVP with a difference of 5%. Both types of polymer are sensitive to pH and stable at pH 5 resulting in prolonged period of drug release. It can be concluded that MSN-P2VP and MSN-PVP release drug effectively in a prolonged period. Holistically, all the objectives that are targeted have been achieved.

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REFERENCES

[1]. Aslan, B., Ozpolat, B., Sood, A. K., Lopez-Berestein, G. J. Drug Target. 21(10) (2013) 904.
[2]. Pawar, V. K., Meher, J. G., Singh, Y., Chaurasia, M.S., Reddy, B. & Chourasia, M. K.Hubbell. J. Control Rel. 196 (2014) 168.
[3]. Dikmen, G., Genç, L. & Guney, G. J. Mater. Sci. Eng. 5 (2011) 468.
[4]. Farokhzad, O. C., Langer, R. ACS Nano 3(1) (2009) 16.
[5]. Vallet-Regí, M., Colilla, M., Izquierdo-Barba, I. & Manzano, M. Molecules 23(1) (2018) 1.
[6]. Slowing, I. I., Vivero-Escoto, J. L., Wu, C. W. & Lin, V. S. Y. Adv. Drug Del. Rev. 60(11) (2008) 1278.
[7]. Watermann A. Nanomaterials 7(7) (2017) 189.
[8]. Fathi V., Ziarani, G., Badiei, A. 2015. RSC Adv. 5(111) (2015) 91686.
[9]. Wang, H., Gu, W., Xiao, N., Ye, L. & Xu, Q. Int. J. Nanomed. 9(1) (2014) 1433.
[10]. Zhang, L., Xia, J., Zhao, Q., Liu, L. & Zhang, Z. Small 6(4) (2010) 537–544.
[11]. Niedermayer, S., Weiss, V., Herrmann, A., Schmidt, A., Datz, S., Müller, K., Wagner, E. Nanoscale 7(17) (2015) 7953.
[12]. Faraji, A. H. & Wipf, P. Bioorg. Med. Chem. 17(8) (2009) 2950.
[13]. Zha, L., Banik, B. & Alexis, F. Soft Matt. 7(13) (2011) 5908.
[14]. Koczkur, K. M., Mourdikoudis, S., Polavarapu, L., Skrabalak, S. E., Dalton Trans. 44(41) (2015) 17883-905.
[15]. Kamarudin, N.H.N., Jalil, A.A., Triwahyono, S., Salleh, N.F.M., Karim, A.H., Mukti, R.R., B.H. Hameed. Micropor. Mesopor. Mater. 180 (2013) 235.
[16]. Ahmad A., Li, H., Yu, H., Zhu, C., Hu, J., Du, M., Zhang, F., Yang, D. RSC Adv. 6 (96) (2016) 94160.
[17]. Özbek, B. & Ünal, Ş. Kor. J. Chem. Eng. 34(7) (2017) 1992.
[18]. Kamarudin, N. H. N., Jalil, A. A., Triwahyono, S., Artika, V., Salleh, N. F. M., Karim, A. H., Jaafar, N. F. Journal of Colloid and Interface Science 421 (2014) 6.
[19]. Niu, X., Wan, L., Hou, Z., Wang, T., Sun, C., Sun, J., Zhao, P. Int. J. Pharm. 452 (1–2) (2013) 382.
[20]. Bieg, K. W. & Ottesen, D. K. Div. Polym. Chem. 19(2) (1978) 471–476.
[21]. Rajabalaya R., David S.R.N., Khanam J., Nanda A. J. Excip. Food Chem. 1(2) (2010) 3.
[22]. Gao, Y., Huo, X., Dong, L., Sun, X., Sai, H., Wei, G., Xu, Y. Molec. Med. Rep. 11(4) (2015) 2585.
[23]. Moosa, B.A., Mashat, A., Li, W., Fhayli, K., Khashab, N.M. J. Nanomater. (2014) 719168.
[24]. Azali, N.S., Kamarudin N.H.N., Rahim A.R.A., Nasir, N.S.J., Timmiati S.N., Jaafar N.F. Mater. Today Proceed. 19 (2019) 1722.
[25]. Rahim A.R.A., Kamarudin N.H.N., Timmiati S.N., Jusoh R., Salleh, N.F.M. Mater. Today Proceed. 19 (2019) 1673.
[26]. Jaafar J.A., Kamarudin N.H.N., Setiabudi H.D., Timmiati S.N., Teh L.P. Mater. Today Proceed. 19 (2019) 1420.
[27]. Kamarudin, N.H.N., Jalil, A.A., Triwahyono, S.T., Timmiati, S.N. Malay. J. Analyt. Sci. 20 (2016) 1382.
[28]. Sajab, M.S., Mohan, D., Santanaraj, J., Chia, C.H., Kaco, H., Harun, S., Kamarudin. N.H.N. Sci. Reports 9 (2019) 11703.