

Experimental study of anti-HIV medication azidothymidine (Azt) interactions with non-functionalized and functionalized nanotubes

Y. Hatami, M.M. Heravi*, A. Morsali, M.R. Bozorgmehr

Department of Chemistry, Mashhad Branch, Islamic Azad University, Mashhad, Iran.

Received: 10 May 2016; accepted: 13 September 2016

The current paper experimentally investigates Anti-HIV medication Azidothymidine (Zidovudine) interactions with Non-functionalized single-walled nanotube (5, 5) (NT) and functionalized nanotube NT-COOH. The computational results of bond interactions were studied through the NH, using pure Anti-HIV medication Azidothymidine (AZT) and its interaction with String and Ultrasonic methods with the nanotubes as well as taking advantage of FTIR and XRD spectroscopy methods. A comparison between FT-IR spectrum of Azidothymidine (AZT) and medication combination with sonicated functionalized nanotubes shows that the peak has reduced significantly at 3462cm^{-1} that may indicate the interaction between acidic factor and the combination of Azidothymidine N-H. Acidic functionalized nanotubes peak is clearly observed in FT-IR spectrum of medication combination with functionalized nanotubes in absence of waves that is overlapped with the combination of Azidothymidine N-H peak. In these circumstances, there was no possibility of interaction between medication combination and functionalized nanotubes. In XRD spectrum, Azidothymidine peaks have been sharp prior to being sonicated with carbon nanotubes, but peaks have been reduced in sharpness after interactions with carbon nanotubes in non-functionalized mode and functionalized nanotubes. Carbon nanotubes in non-functionalized mode Azidothymidine spectrum shows the minimum reduction in sharpness and differences with pure Azidothymidine, however the differences in peaks intensity is higher in Azidothymidine spectrum and functionalized carbon nanotubes that is as a result of higher interactions between the two and the evenly distributed medication.

Keywords: FTIR spectroscopy, XRD spectroscopy, HIV, Zidovudine, Azidothymidine, functionalized nanotubes, Carbon nanotubes in non-functionalized mode

INTRODUCTION

Medicine delivery is one of the most important branches of Nano medicine. It is predicted that 80 percent of the future global market for nano-medicine belongs to nano technology that 64 percent covers medicine delivery. Iran, according to the 20-year development visions has to allocate 10 percent of the global market of Nanotechnology in 2015, that close attention to the areas of medicine delivery is one of the approaches. Medicine delivery technology focused on delivering medicine to the correct location in the body at the right time with the right treatment effects. Conventional medicine delivery systems have virtually no control over time, place and there would be no medicine release, but in these medicine delivery systems medicine releases at a steady pace within the specified time.

In this method, the medicine's toxic effects reduces due to maintaining a constant medicine concentration released in the blood, while in the conventional medicine use, at first, medicine concentration is high (immediately after consumption) and after a period of time it is less than the effective level (extreme fluctuations in medicine concentration in the blood) that may lack necessary effectiveness [1].

Basically, a wide range of molecules can bind in nano-clusters and easily move toward cells. Generally nano-clusters do not have high toxicity and are harmless at low doses; however at high concentrations cause loss of cell and its effects in the body must be studied. Ruth Duncan, an England Cardiff University researcher, believes there are many reasons.

That indicate that nanoparticles may be useful in the pharmaceutical system but the mechanism to get into the cells is not clear; she adds, there have been unsuccessful researches to deliver spherical nano-carbon anti-cancer medicines and radiation nucleotides into the cell.

Moreover, cellular receptors can also be placed on carbon nanotubes for medicine delivery, which recognizes specific cells to effect on. Therefore, the healthy cells will not be exposed to these medicines. The medicine effectiveness increases because concentrates on defected cells as well as a large amount of medicine is placed on a small surface of carbon nanotubes [2].

Carbon nanotubes interaction with biologically living cells has become possible since the biocompatibility of carbon nanotubes with biological aquatic environment is provided. Experiments show that carbon nanotubes can interact with the membrane and penetrate into the

cytoplasm, without having to pass through the cellular pores. Studies showed that functionalized nanotubes can easily *intracellular* transport plasmid DNA [3].

Acquired immune deficiency syndrome (AIDS) is the biggest challenge of the 21st century. Human immunodeficiency virus (HIV) is a virus with low proliferation rate that is HIV disease agent. HIV is a virus that leads to immune deficiency by impairing and destruction of immune function of coordinator cells of the human body. It may take 6 months to 10 years or even more after the entry of HIV into the body to the incidence of the HIV, The person although seemingly healthy, but may spread the virus to others. HIV mainly transmitted through unprotected sexual intercourse, contaminated blood transfusion, infected needle stick, mother to child during pregnancy, childbirth or breastfeeding. Some body fluid such as saliva and tear are not able to transmit HIV. Prevention of HIV is carried out by safe sex and needle-exchange programs [4-7].

Zidovudine is a medicine that is widely used in the fighting against HIV. Its combination with nanotubes is a promising way to overcome the increasing cellular uptake and is internalized by functionalized carbon nanotubes, respectively. The aim of this experimental study was to study Anti-HIV medication Azidothymidine (AZT) interactions with non-functionalized and functionalized nanotubes [4].

MATERIALS AND METHODS

The materials used in this study include:

Non-functional chiral nanotube and carboxylic nanotube (Sigma-Aldrich Corporation), Zidovudine (Pars Darou Pharmaceutical Co.), Nano filter, and double distilled water.

Instruments used include:

1- FTIR Infrared Spectrometer: FT-IR5000 model, Galaxy- series models with wave length range 200-400cm⁻¹

2- X-ray Diffraction: PANNULYTICAL X ray model with $\lambda=1.5405$ Cu-kanm radiation in the area $2\theta=10-90$ with 0.03 degrees of accuracy

3- Heater stirrer model L-71

4- Ultrasonic bath model PARSONIC 7500S with a frequency of 28 ± 5 HZ and the ultrasonic power of 100 W 220VAC Max

PREPARATION OF SOLUTION METHOD

Zidovudine was provided from Pars Darou Pharmaceutical Co. by Kerman University of Medical Sciences. It is necessary to interact on the active ingredient so the purification of the medicine was firstly carried out. According to the Zidovudine solubility of 25mg/ml in water at 25°C first the

medicine was dissolved in an appropriate amount of distilled water with classical methods and then insoluble contents were separated and the solution was dried in vacuum oven.

FT-IR SPECTRUM

A FT-IR spectrum was obtained from the resulting dried solution (Fig. 1).

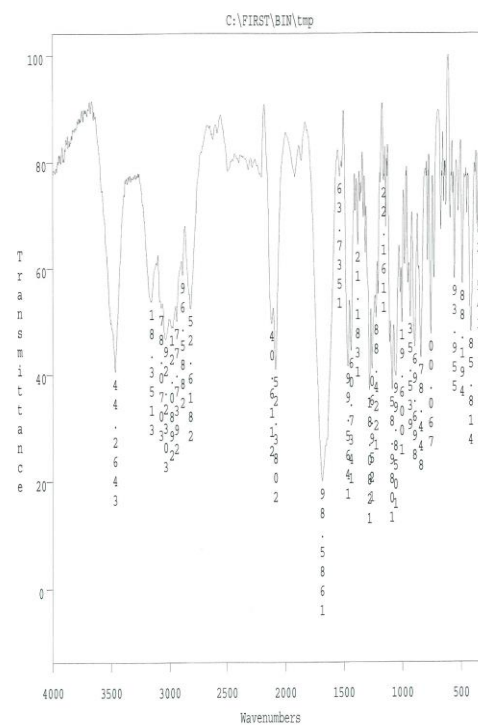


Fig. 1. Zidovudine FT-IR spectrum

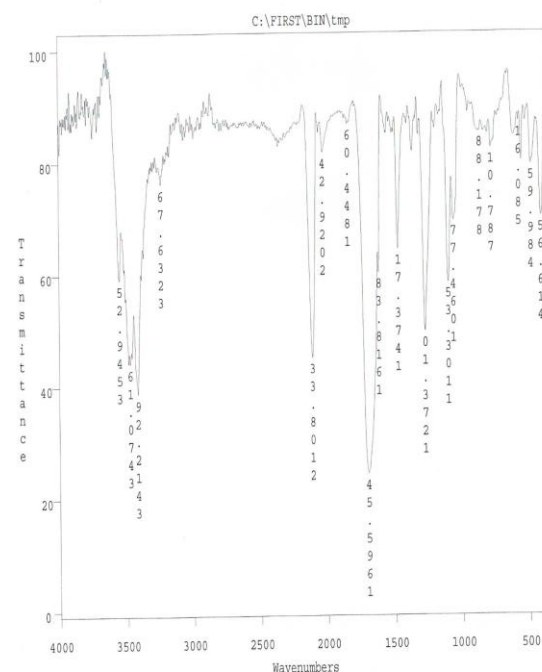


Fig. 2. Functionalized nanotubes with the stirrer Zidovudine FT-IR spectrum

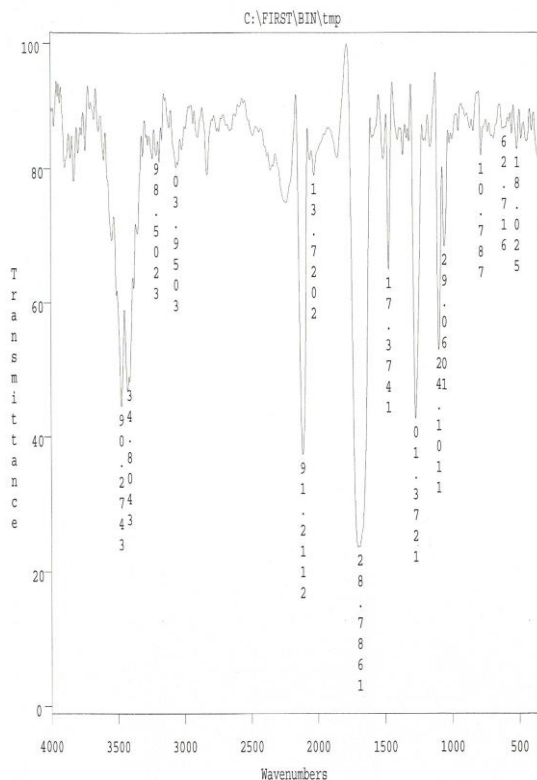


Fig. 3. Non-functionalized nanotubes with the stirrer Zidovudine FT-IR spectrum

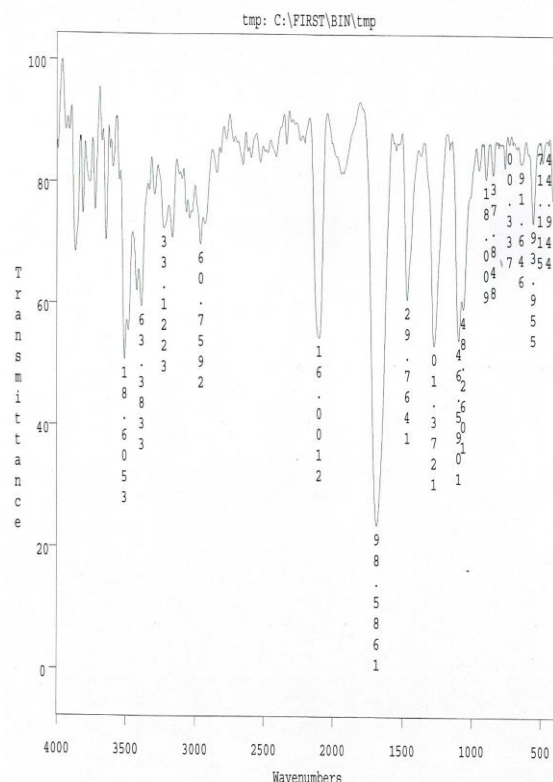


Fig. 4. Non-functionalized nanotubes with the sonicated Zidovudine FT-IR spectrum

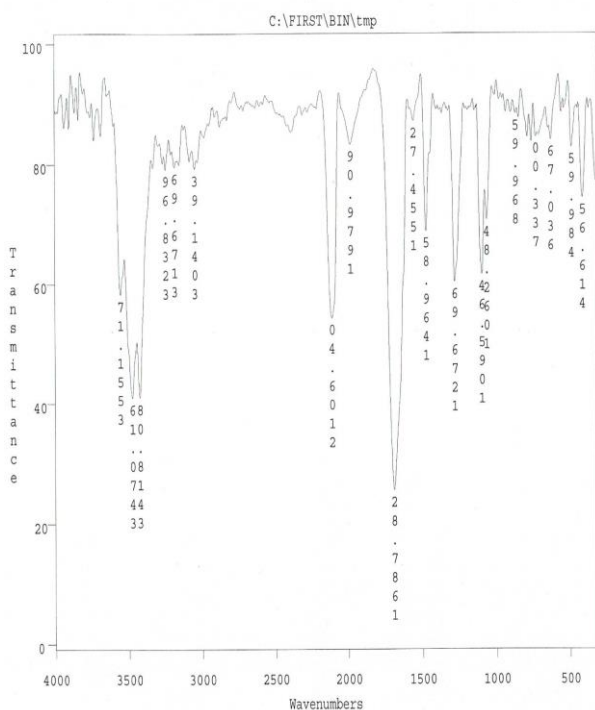


Fig. 5-Functionalized nanotubes with the sonicated Zidovudine FT-IR spectrum.

Compounds of medicine, nanotube, and water was prepared from purified medicine with optimized ratio of 5 to 1 with non-functionalized nanotubes and carboxylic functionalized nanotube in water solvent mixtures under the same conditions (temperature 25°C, ambient pressure) and dried control samples were made from each mixture after stirring with a stirrer and then FT-IR spectra were prepared (Fig. 2, 3). Samples were sonicated for an hour and a half. Then, the solvent was evaporated and FT-IR spectrums were taken of them Figure (4 and 5).FT-IR spectra was obtained from non-functionalized nanotubes and functionalized nanotube (Fig. 6, 7).

Compounds of medicine, nanotube, and water was prepared from purified medicine with optimized ratio of 5 to 1 with non-functionalized nanotubes and carboxylic functionalized nanotube in water solvent mixtures under the same conditions (temperature 25°C, ambient pressure) and dried control samples were made from each mixture after stirring with a stirrer and then FT-IR spectra were prepared (Fig. 2, 3). Samples were sonicated for an hour and a half. Then, the solvent was evaporated and FT-IR spectrums were taken of them Figure (4 and 5).FT-IR spectra was obtained from non-functionalized nanotubes and functionalized nanotube (Figs. 6, 7).

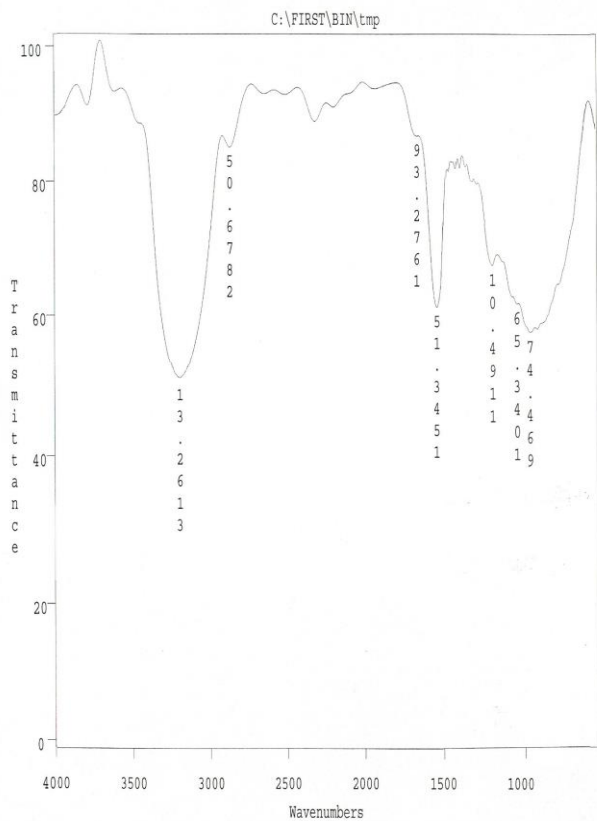


Fig. 6-Functionalized nanotubes FT-IR spectrum

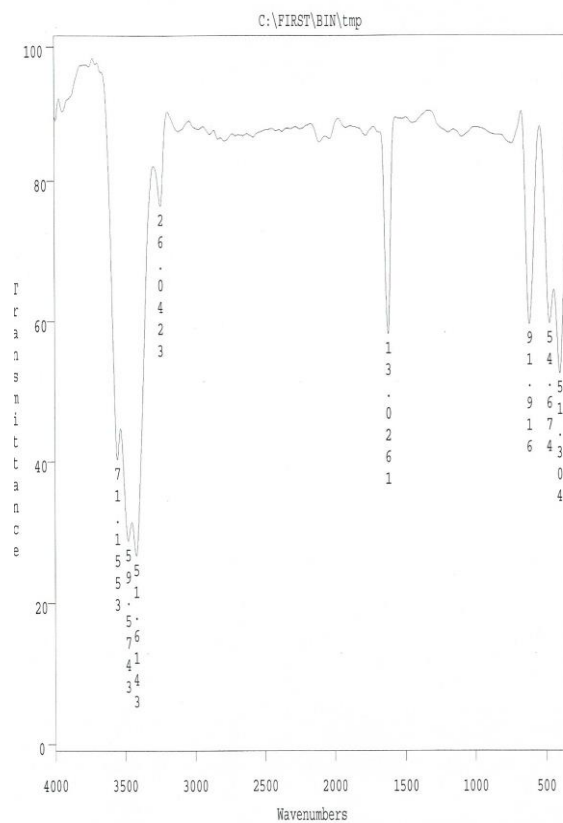


Fig. 7-Non-functionalized nanotubes FT-IR spectrum

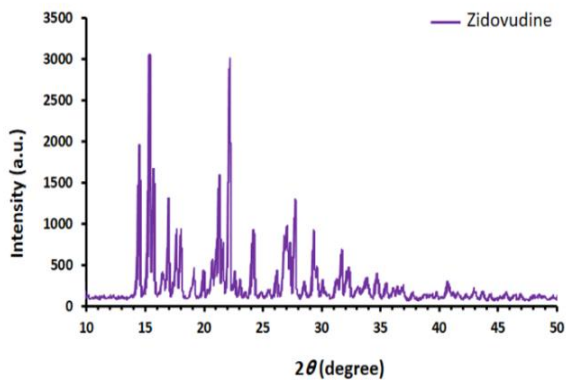


Fig. 8-Zidovudine XRD spectrum

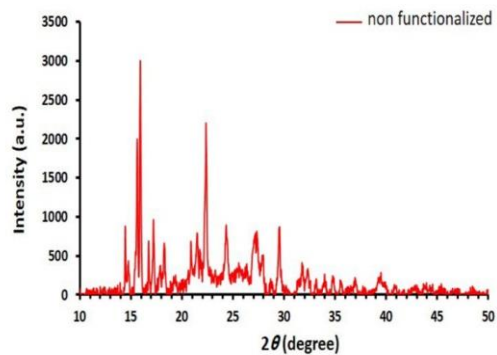


Fig. 9- Non-functionalized nanotubes with the sonicated Zidovudine XRD spectrum

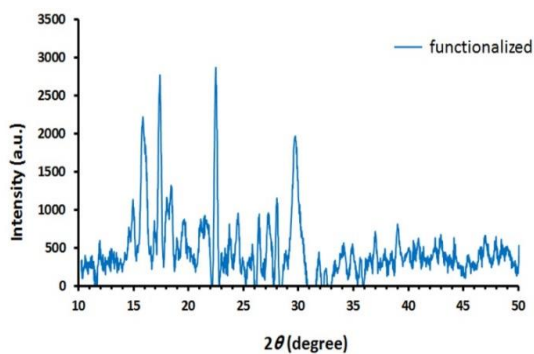


Fig. 10- Functionalized nanotubes with the sonicated Zidovudine XRD spectrum.

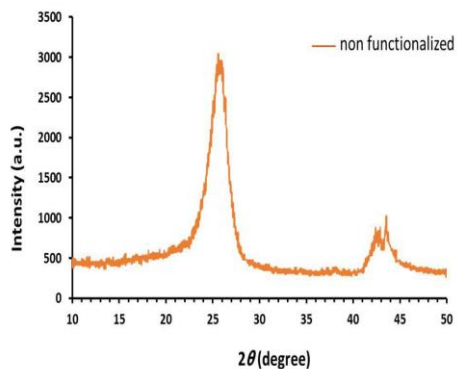


Fig. 11. Non-functionalized nanotubes XRD spectrum.

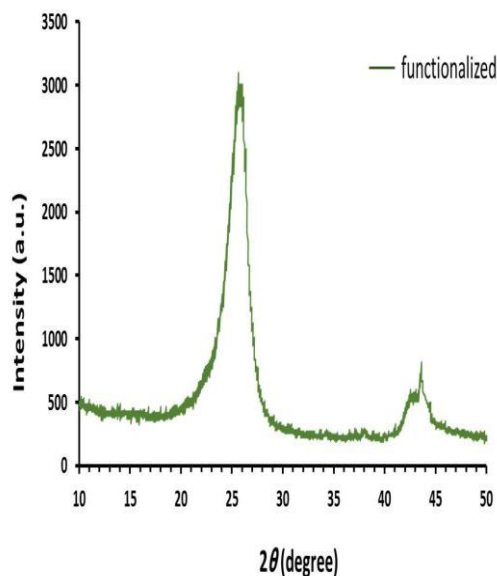


Fig. 12- Functionalized nanotubes XRD spectrum

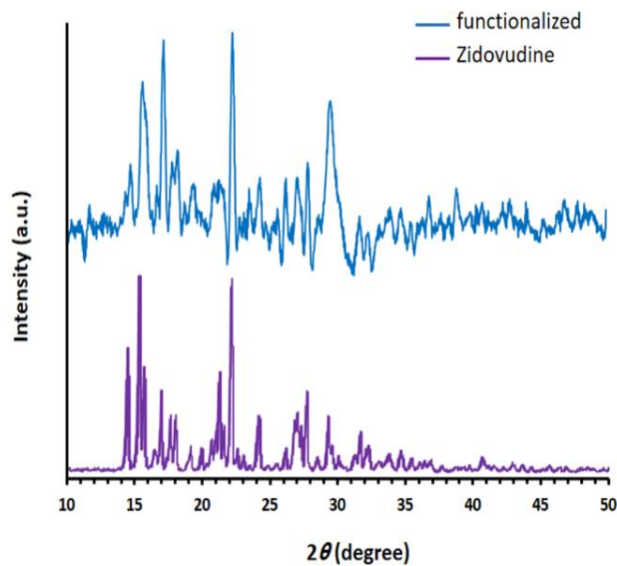


Fig. 13- Comparison between Zidovudine XRD spectrum and functionalized nanotubes sonicated with Zidovudine XRD spectrum

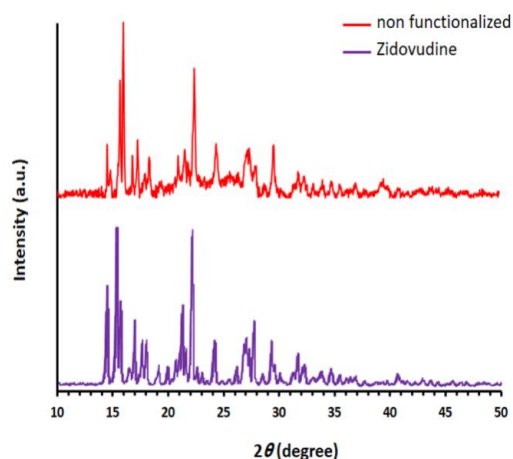


Fig. 14- Comparison between Zidovudine XRD spectrum and non- functionalized nanotubes sonicated with Zidovudine XRD spectrum

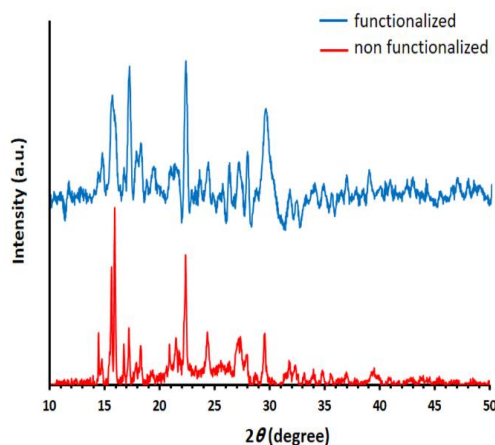


Fig. 15- Comparison between Zidovudine functionalized nanotubes XRD spectrum and sonicated with Zidovudine non-functionalized nanotubes XRD spectrum

XRD SPECTRA METHOD OF PREPARATION

First, XRD spectra were obtained from non-functionalized nanotubes and functionalized nanotube (Fig. 11, 12). XRD spectra were also obtained from solutions (medicine non-functionalized and water) and (functionalized medicine nanotubes and water) after sonicated (Fig. 9, 10)

DISCUSSION AND EXPERIMENTAL CONCLUSION

A comparison of FT-IR spectra of Zidovudine medicine (Fig. 1) and combination of medicine with sonicated functionalized nanotubes (Fig. 5)

shows that peak in 3462cm⁻¹ area decreased significantly, indicating interaction of acidic factor and N-H Zidovudine compound.

Flatten peaks in the spectral region between 3000 and 3400 cm⁻¹ confirmed the presence of the carboxylic acid functionalized nanotubes. The result confirms the interaction of Anti-HIV Zidovudine medicine and functionalized nanotubes using ultrasonic waves.

The FT-IR spectra in the combination of medicine and functionalized nanotubes stirred without the presence wave (Fig. 2). Functionalized nanotubes acidic peak is clearly seen overlapping with Zidovudine compound N-H peak that in these

circumstances there is no possibility of interacting between medicine and functionalized nanotubes.

A comparison of the FT-IR spectra of medicine combined with non-functionalized nanotubes in sonicated condition (Fig. 4) and normal stirring (Fig. 3) shows no changes in product range in both circumstances, and the presence of peak in 3200-3400 area due to the presence of Zidovudine N-H indicates no interaction.

XRD analysis of pure Zidovudine shows the crystal structure of the medicine (Fig. 8). XRD spectra of non-functionalized nanotubes in sonicated with Zidovudine and XRD spectra of functionalized nanotubes in sonicated with Zidovudine show a similar peak pattern with little change in intensity (Fig. 9, 10).

As can be seen in Zidovudine spectrum prior to sonication with carbon nanotubes peaks have been sharp prior to being sonicated with carbon nanotubes, but peaks have been reduced in sharpness after interactions with carbon nanotubes in non-functionalized mode and functionalized nanotubes. Carbon nanotubes in non-functionalized mode Zidovudine spectrum shows the minimum reduction in sharpness and differences with pure Zidovudine, however the differences in peaks intensity is higher in Zidovudine spectrum and functionalized carbon nanotubes that is a result of

higher interactions between the two and the evenly distributed medication.

Comparison between Zidovudine XRD spectrum and functionalized nanotubes sonicated with Zidovudine XRD spectrum, Zidovudine XRD spectrum and non-functionalized nanotubes sonicated with Zidovudine XRD spectrum, and Zidovudine functionalized nanotubes XRD spectrum and sonicated with Zidovudine non-functionalized nanotubes XRD spectrum were shown in fig. 13, 14 and 15, respectively.

REFERENCES

1. A. Bianco, M. Prato, *Advanced Materials*, **15**, 1765 (2003).
2. T.D. Burchell, *Carbon materials for advanced technologies*, Elsevier (1999), p.38.
3. D.C. Douek, M. Roedrer, R.A. Koup, *Ann. Rev. Med.*, 2009, pp. 471-484.
4. R. Pignatello, S. Guccione, S. Forte, C. Di Giacomo, V. Sorrenti, L. Vicari, G.U. Barretta, F. Balzano, G. Puglisi, *Bioorg. Medic. Chem.*, **12**, 2951 (2004).
5. N.W. Kam, S.M. O'Connell, J.A. Wisdom, H. Dai, H., *Proc. National Academy of Sciences of the U.S.A.*, **102**, 11600 (2005).
6. K.A Sepkowitz, *North. Engl. J. Med.*, **344**, 1764 (2001).
7. R.A. Weiss, *Science*, **42**, 1273 (1993).