International Journal of Psychosocial Rehabilitation, Vol. 24, Issue 05, 2020
ISSN: 1475-7192

Synthesis and Characterisation of Magnetic Nanoparticles for Lung Cancer Detection and Therapy

T. Manikandan*, V. Nandalal, S. Joshua Kumaresan, J.L. Mazher Iqbal and A. Muruganandham

Abstract--- *Main cause for cancerous deaths in men is lung cancer. It has been reported that, smoking of cigarette/beedi is the major reason for lung cancer deaths (90%) in the world. The lung cancer also develops in non-smokers (people they do not smoke) but the chance is ten times lesser than the smoking people. Detecting the lung cancer in its initial stages are quite difficult. Treating the lung cancer in its advanced stages are surgical removal of the cancer affected portion of lung, chemotherapy and radiation therapy. To detect the cancer in early stage, nanotechnology is used. This paper focuses on the lung cancer detection by reaction of polymer coated magnetic nanoparticle with the cell line samples. The experimental results show that, the polymer coated magnetic nanoparticle can detect and treat the lung cancer.*

Keywords--- *Nanotechnology, Magnetic Nanoparticle, Lung Cancer, A549 and Cell Line.*

I. INTRODUCTION

The development of cancer in human lung is known as lung cancer and found to be main cause for cancerous deaths in men[1]. Every year it affects 100,000 Americans of the smoking population[2]. In India, a total of 51,000 lung cancerous deaths were reported in 2012, which accounts 41,000 men and 10,000 women deaths[3]. Detection of lung cancer in its initial stages may helpful to limit the danger[4-5]. However, detecting the lung cancer in its early stages are not easy[6]. In most of the patients (about 80%) lung cancer is diagnosed in middle or advanced stage[7]. In advanced stages, still five-year survival rate is low[8]. Identifying lung cancer in its early stage could improve the patient's chance for survival[9].

Nanotechnology have salient features that are quite attractive, which can be used in medical health care[10]. The growth of nanotechnology is revealed enormous enhancement in cancer detection and therapy with better accuracy. Nanomaterials have unique properties like penetration and binding with the cancerous cells, which can be very effective in bio sensing[11]. Some nanoparticles like silver, gold and carbon nanotubes have been developed recently to overcome the drawbacks of existing lung cancer detection techniques[12].

Magnetic nanoparticles have widespread applications in biosensors, magnetic cell sorting and drug delivery and targeting etc[13]. The magnetic nanoparticles with spinel ferrite structure can exhibit a variety of interesting properties and are ideal system for several practical applications[14]. Super paramagnetism is a distinctive property of magnetic

T. Manikandan, Professor, Department of ECE, Rajalakshmi Engineering College, Chennai. E-mail: manikandan.t@rajalakshmi.edu.in*
V. Nandalal, Professor, Department of ECE, Sri Krishna College of Engineering and Technology, Coimbatore.
S. Joshua Kumaresan., Associate Professor, Department of ECE, R.M.K Engineering College, Chennai.
J.L. Mazher Iqbal, Professor, Department of ECE, Veltech Rangarajan Dr. Sagunthala R&D Institute of Science and Technology, Chennai, India.
A. Muruganandham, Professor, Department of ECE, Rajarajeswari College of Engineering, Bengaluru.

DOI: 10.37200/IJPR/V24I5/PR201976
Received: 23 Feb 2020 | Revised: 18 Mar 2020 | Accepted: 30 Mar 2020

nanoparticles and has lot of fundamental interest and technological applications. This work focused on developing polymer coated magnetic nanoparticles for lung cancer detection and therapy via reaction with lung cancer (A549) cell line samples.

II. METHODOLOGY

The overall process involved in lung cancer detection using magnetic nanoparticles is shown in figure 1.

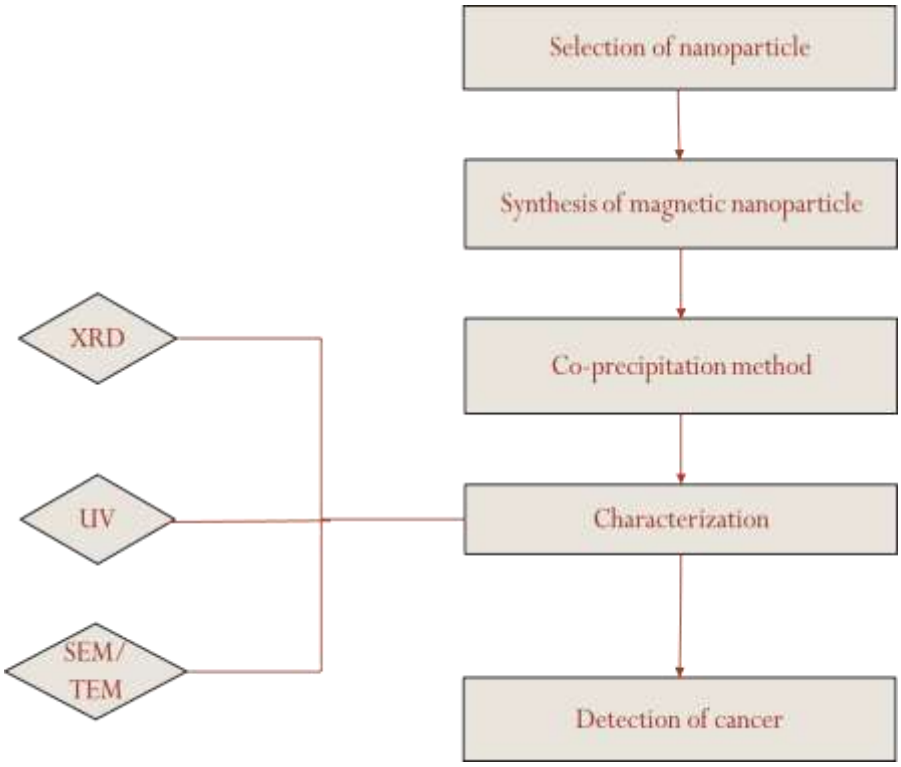

Figure 1: Outline of synthesis and charactierization of magnetic nanoparticle for lung cancer detection and treatment

2.1 Materials and Methods

The magnetic nanoparticles is chosen for the lung cancer detection and therapy, because, it has properties like cancer targeting and cancer fighting. Further, magnetic nanoparticles is of our great interest because, it is cheaper than silver and gold. Thus, this work involves rapid synthesis and characterisation of magnetic nanoparticles to detect and treat the lung cancer in its early stage.

2.2 Synthesis of Magnetic Nanoparticles (Fe_3O_4)

The magnetic nanoparticles (Fe_3O_4) were synthesized using chemical co-precipitation method. To prepare the magnetic nanoparticles ferrous chloride and ferric chlorides were taken in 0.15 M and 0.3 M each. They were taken 1:2 ration and about 15 minutes stirred well. After stirring, the sodium hydroxide (NaoH) was added at regular intervals to the mixture solution. After adding NaoH, the mixture solution was turned black, which is the indication of presence of magnetic nanoparticles. Stirring was continued about one hour then PVP about 0.2 M was added. The

DOI: 10.37200/IJPR/V24I5/PR201976
Received: 23 Feb 2020 | Revised: 18 Mar 2020 | Accepted: 30 Mar 2020

PVP added magnetic nanoparticles were centrifuged and washed with deionised water. Then the nanoparticles are powdered and used for further analysis. The entire reaction is given by the equation,

$$\underset{\text{(Ferrous chloride)}}{FeCl_2} + \underset{\text{(Ferric chloride)}}{FeCl_3} \longrightarrow \underset{\text{(Magnetite)}}{Fe_3O_4} \quad (1)$$

The following steps are involved in the preparation of magnetic nanoparticles:

1. Calculation of molar Concentration

The molar concentration is the method of expressing the concentration of solute in a solution. C is the molar concentration in Mol/L.

Molar concentration = Amount in moles/Volume in solution

The molecular weight of ferric chloride is 162.2

The molecular weight of ferrous chloride is 151.91

The molecular weight of NaOH is 39.997

The molecular weight of PVP is 2.5

Calculations are as follows for determining reagent's concentration

Ferric Chloride, Fe^{3+} = (0.3 * 162.2*100) / 1000 = 4.86 gm/mol.

Ferrous Chloride, Fe^{2+} = (0.15* 151.91*100) / 1000 = 2.3 gm/mol.

Sodium Hydroxide, NaoH = (0.25 * 39.997*100) / 1000 = 0.25gm/mol.

Poly Vinyl Pyrolidine, (PVP) = (0.3 * 162.2*100) / 1000 = 4.86 gm/mol.

2. 4.86 gram ferric chloride is weighed in a beaker and pour 100 ml of pure distilled water in it.

3. 2.3 gram ferrous chloride is weighed in a beaker and pour 100 ml of pure distilled water in it. Add this concentration to the ferric chloride solution to get the mixing solution.

4. The mixing solution is allowed to stir by using pellet. After 10 minutes, 0.25 gm of NaOH solution is added to this mixing solution at regular intervals by using dropper.

5. Stir and heat the solution at 60C.

6. After 1 hour, add the polymer Poly Vinyl Pyrolidine (PVP) to the heating solution and again heat the solution for 3 hours at 90C.

7. The PVP added magnetic nanoparticles washed with deionising water in order to remove the ionic impurities.

8. The water washed PVP added magnetic nanoparticles were added with acetone. The acetone added magnetic nanoparticles were dried about 2 days in inert atmosphere at 35°C. The acetone washed PVP added magnetic nanoparticles were powdered with has shown good purity.

DOI: 10.37200/IJPR/V24I5/PR201976
Received: 23 Feb 2020 | Revised: 18 Mar 2020 | Accepted: 30 Mar 2020

The above steps are shown in figure 1.

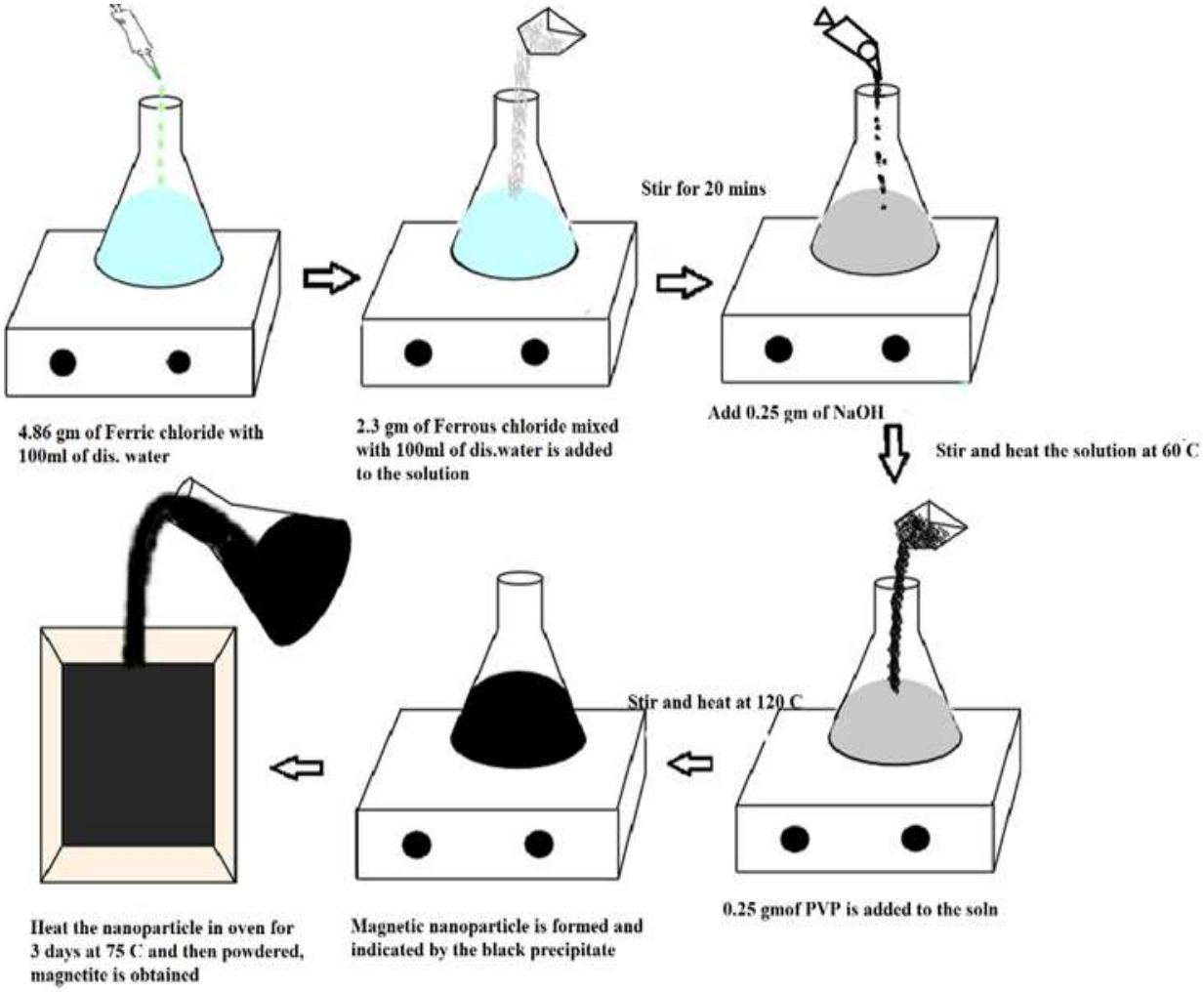

Figure 2: Synthesis of magnetite nanoparticle using co-precipitation method

The prepared PVC coated magnetic nanoparticles are characterised by X-ray diffraction technique (XRD), Ultraviolet visible spectroscopy (UV-vis), scanning electron microscopy (SEM) and transmission electron microscopy (TEM). The magnetite nanoparticles is further subjected to biomarker characterization to check the viability for cancer detection. Finally, synthesised magnetic nanoparticles are injected in the cell line for cancer detection and to check the viability of the nanoparticle.

III. Results And Discussions

The figure 2 gives series of steps involved in formation of black precipitate of magnetite nanoparticles, filtering of nanoparticle using centrifuge and poured in the beaker for heating. The series of steps involved in the formation of precipitate and the particle is confirmed via the magnet is given in figure 3. The magnetic nanoparticles are centrifuged and dried using microwave oven, which is shown in figure 4.

DOI: 10.37200/IJPR/V24I5/PR201976
Received: 23 Feb 2020 | Revised: 18 Mar 2020 | Accepted: 30 Mar 2020

Figure 2: Series of steps involved in synthesis of magnetic nanoparticle by co-precipitation method

Figure 3: The series of steps involved in the formation of precipitate and the particle is confirmed via the magnet.

Figure 4: The magnetic nanoparticles are centrifuged and dried using microwave oven

The figure 5 shows the XRD pattern of the synthesised magnetic nanoparticles. The crystalline nature of the magnetic nanoparticles shows the sharp peaks in XRD pattern, which confirms the cubic inverse spinel structure. The size of the magnetic nanoparticle was found to be 10.07nm from XRD pattern and estimated lattice parameters are found to be 8.366Å.

DOI: 10.37200/IJPR/V24I5/PR201976
Received: 23 Feb 2020 | Revised: 18 Mar 2020 | Accepted: 30 Mar 2020

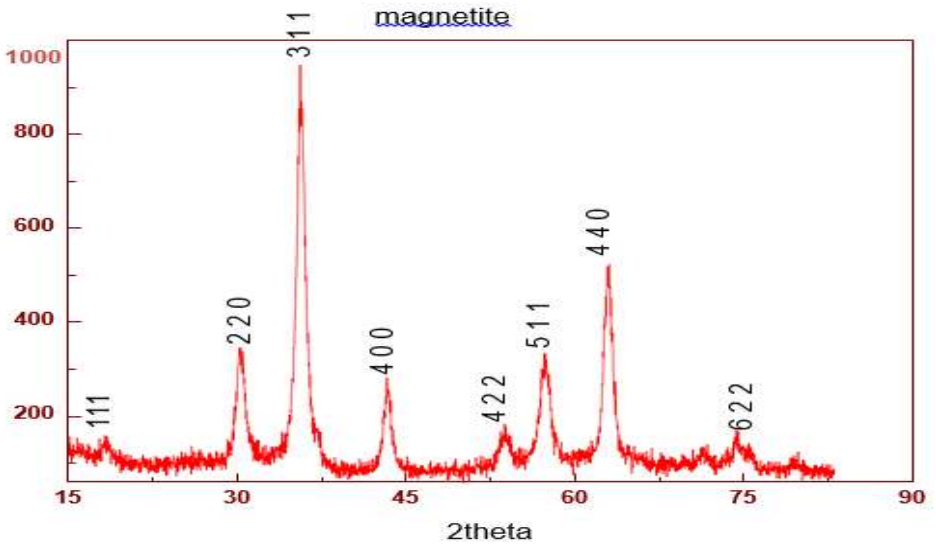

Figure 5: The XRD pattern of Fe3O4 nanoparticles

The ultraviolet visible spectroscopy (UV-vis) of synthesised nanoparticles is given in figure 6. This characterization describes the bonding of metal ions with polymer or surfactant compounds. In this case, maximum peaks at 303 nm is obtained and absorbance is found to be 0.104. Thus indicating that, metal ions is bonded with polymer-surfactant.

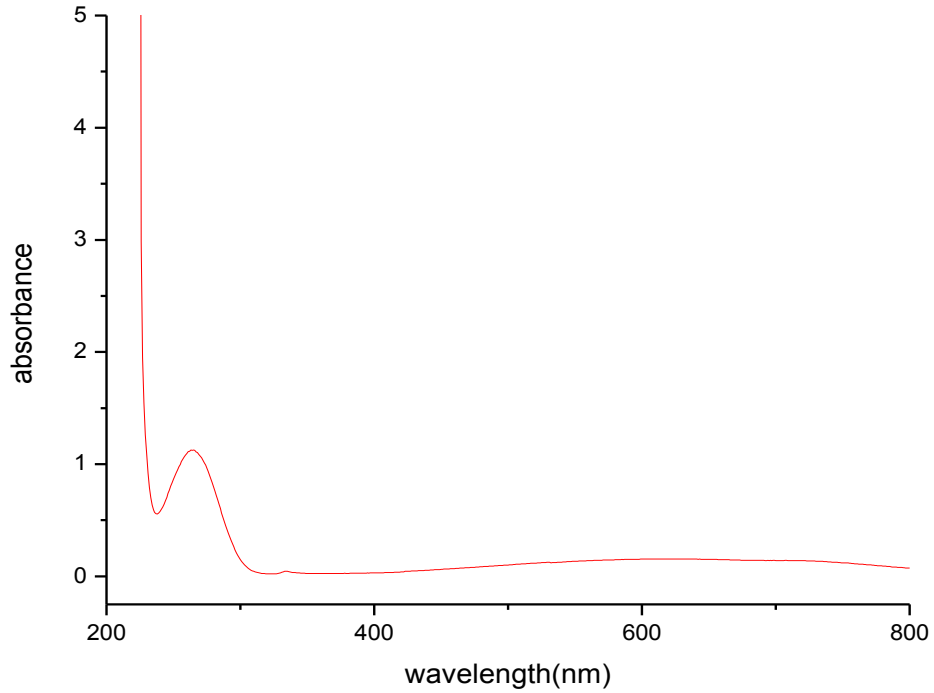

Figure 6: UV-vis spectroscopy peak

DOI: 10.37200/IJPR/V24I5/PR201976
Received: 23 Feb 2020 | Revised: 18 Mar 2020 | Accepted: 30 Mar 2020

The size of the magnetite nanoparticles obtained through scanning electron microscopic (SEM) image, which is given in figure 7. The size is found to be within 100nm.

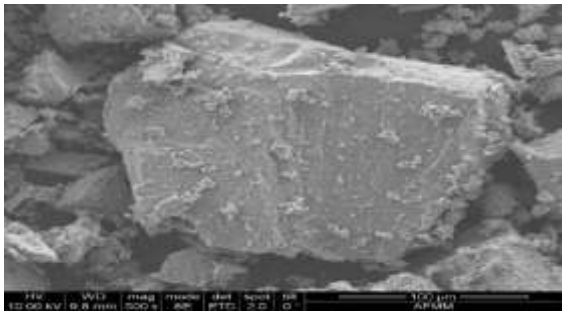

Figure 7: SEM image of synthesised magnetic nanoparticles

The figure 8 represents the transmission electron microscopic (TEM) image of synthesised magnetite nanoparticles. The TEM image shows the structure and texture of the magnetic nanoparticles in molecular level.

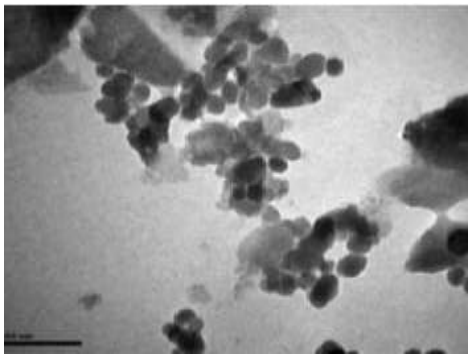

Figure 8: TEM image of synthesised magnetite nanoparticles

The synthesised magnetic nanoparticles are reacted with lung cancer cell line samples (A549) National centre for cell sciences Pune (NCCS) for its anticancer activity and cell viability. Table 1 gives the anticancer effect of magnetic nanoparticles with lung cancer (A549) cell line sample. It is clear from Table 1 that, as the concentration increases absorbance and cell viability are increases. Figure 9 presents cell viability of magnetic nanoparticles with lung cancer cell line sample. From figure 9 it is evident that 50% cell viability is achieved with concentration of 125 micro gram per milliliter.

Table 1: Anticancer effect of magnetic nanoparticles against A549 cell line sample

S.No.	Concentration (µg/ml)	Dilutions	Absorbance (O.D)	Cell Viability (%)
1.	1000	Neat	.217	40.18
2.	500	1:1	.238	44.07
3.	250	1:2	.257	47.59
4.	125	1:4	.274	50.74
5.	62.5	1:8	.294	54.44
6.	31.2	1:16	.326	60.37
7.	15.6	1:32	.348	64.44
8.	7.8	1:64	.361	66.85
9.	Cell control	-	.540	100

DOI: 10.37200/IJPR/V24I5/PR201976
Received: 23 Feb 2020 | Revised: 18 Mar 2020 | Accepted: 30 Mar 2020

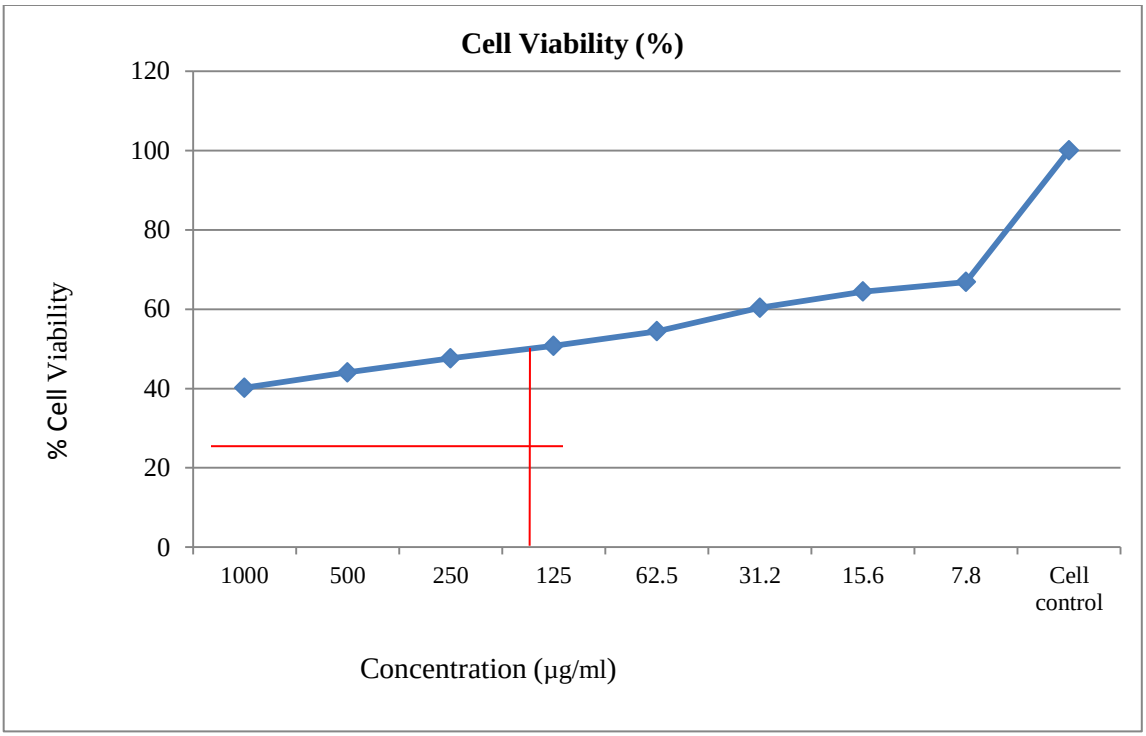

Figure 9: Cell viability of magnetic nanoparticles against A549 cell line sample

Table 2 gives the anticancer effect of PVP treated magnetic nanoparticles against A549 cell line sample. It is clear from Table 2 that, as the concentration increases absorbance and cell viability are increases. Figure 10 presents cell viability of PVP treated magnetic nanoparticles against A549 lung cancer cell line sample. From figure 10, it is evident that approximately 50% cell viability is achieved with the concentration of 62.5 micro gram per milliliter. However, 50% cell viability is achieved with magnetic nanoparticles without PVP coating is 125 micro gram per milliliter concentration. Thus, the PVP coated magnetic nanoparticles has the better anticancer effects even with reduced concentration. The Biomarker images of PVP treated magnetic nanoparticles against lung cancer cell line samples are given in figure 11. It is evident from figure 11 that, the number of live lung cancer cells are much higher in A549 cell line sample. Also it is clear that, as the toxicity increases number of live lung cancer cells decreases as a result of anticancer effect present in PVP coated magnetic nanoparticles.

Table 2: Anticancer effect of PVP coated magnetic nanoparticles against A549 cell line sample

S.No.	Concentration (µg/ml)	Dilutions	Absorbance (O.D)	Cell Viability (%)
1.	1000	Neat	.148	27.40
2.	500	1:1	.176	32.59
3.	250	1:2	.190	35.18
4.	125	1:4	.227	42.03
5.	62.5	1:8	.261	48.33
6.	31.2	1:16	.294	54.44
7.	15.6	1:32	.321	59.44
8.	7.8	1:64	.347	64.25
9.	Cell control	-	.540	100

DOI: 10.37200/IJPR/V24I5/PR201976
Received: 23 Feb 2020 | Revised: 18 Mar 2020 | Accepted: 30 Mar 2020

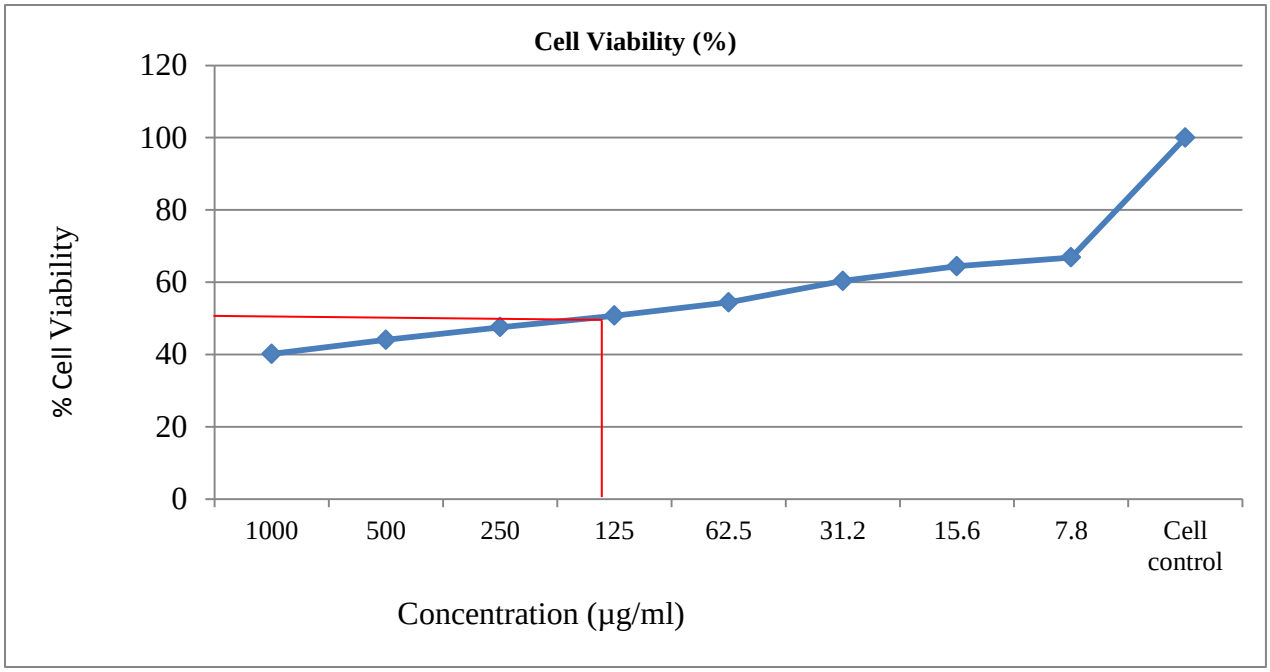

Figure 10: Cell viability of PVP coated magnetic nanoparticles against A549 cell line sample

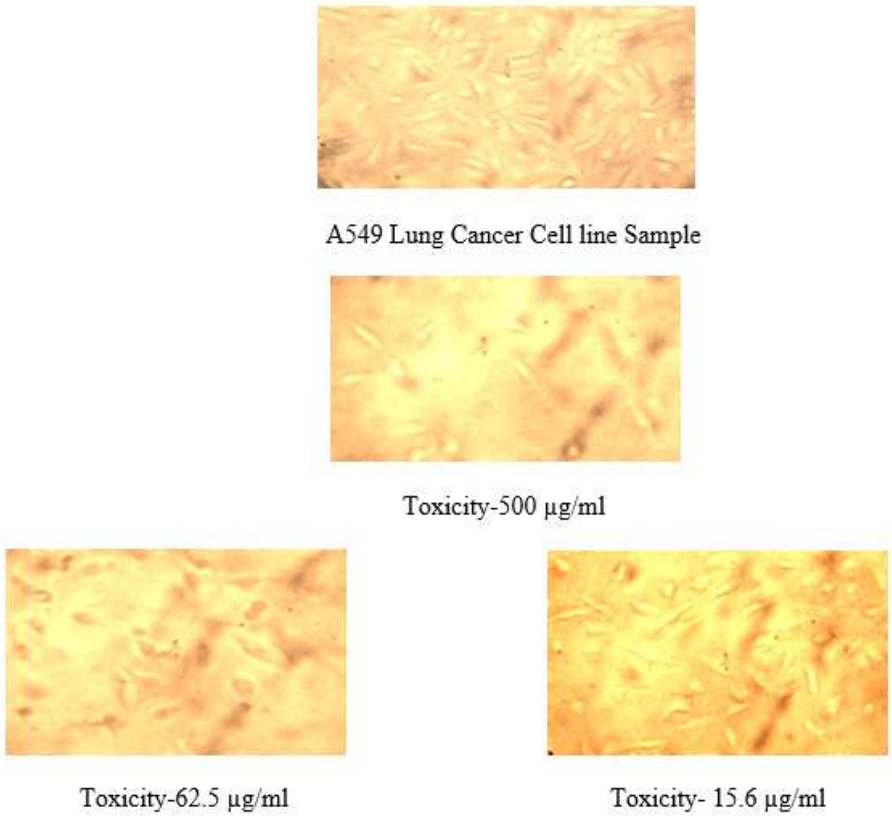

Figure 11: Biomarker images of PVP coated magnetic nanoparticles against A549 cell line sample

DOI: 10.37200/IJPR/V24I5/PR201976
Received: 23 Feb 2020 | Revised: 18 Mar 2020 | Accepted: 30 Mar 2020

IV. CONCLUSION

The Magnetic nanoparticles have been prepared using co-precipitation technique using alkali like NaOH and characterized by XRD, UV-vis, SEM and TEM. The average crystallite size of magnetite are found to be 10.07 nm. The XRD analysis shows that the crystal structure of magnetic nanoparticles which is found to be spinel cubic structure. The lattice parameters of magnetite was found to be 8.366 Å. The UV-vis analysis shows that the maximum peaks is at 303 nm and absorbance is found to be 0.104. The maximum peak and the absorbance shows that the metal ions is bonded with polymer-surfactant. The SEM image describes the size of the magnetite nanoparticles. The size is found to be within 100 nm. The TEM analysis gives structure and texture of the magnetic nanoparticles in molecular level. Finally, the reaction of synthesised magnetic nanoparticles with lung cancer (A549) cell line sample is used detect the lung cancer and to check the viability of the nanoparticles to the treatment of cancer cells. The experimental result shows that the PVP coated magnetic nanoparticles has the viability to detect and treat the lung cancer cells.

V. ACKNOWLEDGEMENTS

The authors would like to thank the members of UGC (MRP-6626/16-SERO/UGC) for providing the necessary infrastructure to complete this work. Further, the authors would like thank Dr. Swaminathan, Director, Sasham Biological Pvt. Ltd., Chennai for providing cell line sample and other biological tests.

REFERENCES

[1] American cancer society, "Cancer facts & figures 2014", *American Cancer Society, Atlanta,* 2014.
[2] Manikandan. T and Bharathi. N, "Lung cancer detection using fuzzy auto-seed cluster means morphological segmentation and SVM classifier", *In journal of medical systems,* vol. 40(7), pp. 1-9, 2016.
[3] Manikandan. T and Bharathi. N, "Hybrid neuro-fuzzy system for prediction of stages of lung cancer based on the observed symptom values", *In biomedical research (India),* vol. 28(2), pp. 588-593, 2017.
[4] Wook-Jin. C and Tae-Sun. C, "Genetic programming-based feature transform and classification for the automatic detection of pulmonary nodules on computed tomography images", *In information sciences,* vol.212, pp.57–78, 2012.
[5] Manikandan. T and Bharathi. N, "Lung cancer detection by automatic region growing with morphological masking and neural network classifier', *In Asian journal of information technology,* vol. 15 (21), pp. 4189-4194, 2016.
[6] Manikandan. T, Devi. B and Helanvidhya. T, "A Computer-aided diagnosis system for lung cancer detection with automatic region growing, multistage feature selection and neural network classifier", *In international journal of innovative technology and exploring Engineering,* vol. 9 (1S), pp. 409-413, 2019.
[7] Wook-Jin. C and Tae-Sun. C, "Automated pulmonary nodule detection system in computed tomography images: A hierarchical block classification approach", *In entropy.* vol. 15, pp.507–523, 2013.
[8] Manikandan. T and Bharathi. N, "A novel semi-automated 3-D CAD visualization system as an aid for surgical planning of lung cancer", *In ARPN journal of Engineering and applied sciences,* vol. 10(4), pp. 1872-1878, 2015.
[9] Sousa. J.R.F.D.S, Silva. A.C, Paiva. A.C.D and Nunes. R.A, "Methodology for automatic detection of lung nodules in computerized tomography images", *In computer methods and programs in biomedicine,* vol. 98, pp.1–14, 2010.
[10] Ozekes. S, Osman. O and Ucan. O.N, "Nodule detection in a lung region that's segmented with using genetic cellular neural networks and 3-D template matching with fuzzy rule based thresholding", *In Korean journal of radiology,* vol.9, pp.1–9, 2008.
[11] Manikandan. T and Bharhathi. N, "Lung cancer diagnosis from CT images using fuzzy inference system", *In communications in computer and information science,* vol.250 CCIS, pp.642-647, 2011.

DOI: 10.37200/IJPR/V24I5/PR201976
Received: 23 Feb 2020 | Revised: 18 Mar 2020 | Accepted: 30 Mar 2020

[12] Kouser.R, Manikandan. T and Kumar. V, "Heart disease prediction system using artificial neural network, radial basis function and case based reasoning", *In journal of computational and theoretical nanoscience,* vol. 15, pp. 2810-2817, 2018.

[13] Bharathi Raj. M, Ewins Pon Pushpa. S and Vaithiyanathan. D, "Performance analysis of 7-nm node negative capacitance - MoS2 nanotube transistor based SRAM", *In proceedings of International Workshop on Nano/Micro 2D-3D Fabrication, Manufacturing of Electronic - Biomedical Devices & Applications at Indian Institute of Technology (IIT),* Mandi, India, Oct. 31 - Nov. 02, 2018.

[14] Bharathi Raj. M, Ewins Pon Pushpa. S and Vaithiyanathan. D, "Investigation of negative capacitance - MoS2 based nanotube transistor sandwiched with polyvinylidence fluoride as ferroelectric gating material", *In proceedings of International Workshop on Nano/Micro 2D-3D Fabrication, Manufacturing of Electronic - Biomedical Devices & Applications at Indian Institute of Technology(IIT),* Mandi, India, Oct. 31 - Nov. 02, 2018.

[15] Mosmann.T, "Rapid colorimetric assay for cellular growth and survival: application to proliferation and cytotoxicity assays", *In journal of immunological methods,* vol. 65, pp.55-63, 1983.

DOI: 10.37200/IJPR/V24I5/PR201976
Received: 23 Feb 2020 | Revised: 18 Mar 2020 | Accepted: 30 Mar 2020