Available Online at

http://www.ijcpa.in

January-March 2017

DOI : http://dx.doi.org/10.21276/ijcpa

International Journal of CHEMICAL AND PHARMACEUTICAL ANALYSIS

eISSN: 2348-0726 ; pISSN : 2395-2466

Research Article | Volume-4 | Issue-2 | Article ID: 1271

SYNTHESIS AND CHARACTERIZATION OF SILVER NANOPARTICLES USING α- CYCLODEXTRIN AS A ENCAPPING AGENT AND DRUG DELIVERY

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Received: 9 March 2017 / Revised: 20 March 2017 / Accepted: 21 March 2017 / Available online: 31 March 2017

ABSTRACT

The present study deals with the synthesis of silver nanoparticles (AgNPs) using α- cyclodextrin (α- CD) as the reducing agent as well as capping agent and describe cost effective, novel and environment friendly synthesis of silver nanoparticles. This involves the synthesiszed nanoparticles by capping with different concentrations of α-cyclodextrin. The synthesiszed nanoparticles were characterized using Ultraviolet Visible Spectroscopy (UV-VIS), Fourier Transform Infra-Red (FT–IR) Spectroscopy, X-ray Diffraction studies (XRD) and Scanning Electron Microscope (SEM). UV-Vis Spectroscopy, FT-IR Spectroscopy and X-ray diffraction study confirmed the formation of nanoparticles. SEM studies reveal the existence of spherical shaped particles of nano dimension. α- CD capped AgNPs coated with Imatinib an anticancer drug achieves a strong effect than Imatinib. This reduces the dosing frequency and side effect. Capping with α-cyclodextrin showed much pronounced enhancement in antibacterial behaviour in silver nanoparticles.

***Keyword**: α-cyclodextrin . Nanoparticles, Sodium Hydroxide (NaOH), Imatinib, Antimicrobial activity.*

1. INTRODUCTION

The field of nanotechnology is one of the most active areas in science. Nanoparticles are now considered a viable alternative to antibiotics and seem to have a high potential to solve the problem of the emergence of bacterial multidrug resistance[1,2]. In particular, silver nanoparticles (AgNPs) have attracted much attention in the scientific field[3,4]. Nanoparticles are stable systems suitable to provide targeted drug delivery and to enhance the efficacy and bioavailability of poorly soluable drugs. CDs too induce nanoparticle assembly via host-guest interactions because of their relatively weak capping ability for metal nanoparticles . Although the hydroxylic groups are poor electron donar ligands to silver in relatively high concentrations, α-cyclodextrin is able to stabilize silver nanoparticles. The synthesis of silver nanoparticles was investigated by employing UV-visible spectrophotometry, FT-IR, XRD, SEM and antimicrobial activity were studied.

Imatinib (INN) , marketed by Novartis as Gleevec (Canada , South Africa and the USA) or Glivec (Australia , Europe and Latin America), investigational name STI – 571 , is a tyrosine - Kinase inhibitor used in the treatment of multiple cancers , most notably

Philadelpia chromosome positive (Ph^+) chronic mylogenous leukemia (CML)[4-16]. In healthy cells, these tyrosine kinase enzymes are turned on and off as needed . Imatinib is used to treat chronic myelogenous leukemia (CML), gastrointestinal stromal tumors (GISTs) and a number of other malignancies . The systematic IUPAC name is Methylpiperazin-1-yl)methyl]-*N*- (4-methyl-3-{[4-(pyridin-3-yl)pyrimidin-2-yl]amino}phenyl)benzamide. The molecular formula of Imatinib is $C_{29}H_{31}N_7O$ and molar mass is 493.603 g/mol.

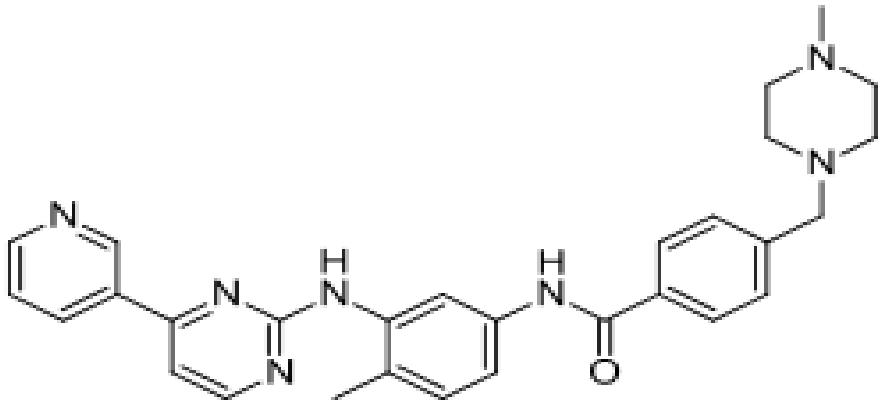

Fig.1: Chemical Structure of Imatinib

2. MATERIALS AND METHODS

2.1 Materials

Aqueous α- cyclodextrin solutions , $AgNO_3$, Sodium Hydroxide were purchased from Ponmani chemical agencies, Madurai. Double distilled water was used for the preparation of aqueous solutions . Imatinib is obtained from the Pharmaceutical company. All solvents used were of the highest grade commercially available .

2.2 Sample characterization

The UV-visible spectra were measured on a Systronics Smart 2203 UV – visible double beam spectrophotometer operating in the range of 200 – 800nm. FT-IR spectra were measured using SCHIMADZU FT-IR spectrophotometer affinity operating range 400 – 4000Cm-1 by KBr pelleting X-ray diffraction measurements were carried out using Bruker AXSD8 Advance. All measurements were performed at room temperature

2.3 Synthesis of Ag nanoparticles

Synthesis of α-CD capped AgNPs was simply achieved by the reduction of silver nitrate with α-CD in alkaline aqueous solution. Working solutions of silver nitrate with concentration 10^{-3}M was prepared from stock solution of 10^{-1}M in doubly distilled water. Aqueous α-CD solutions (5, 10 and 15mM) were stirred into equal volumes of 2mM $AgNO_3$ for 15minutes. Then ice cold NaOH solution was added and magnetically stirred continuously until silver ions were reduced to silver metal of nano dimensional range. During reduction process the temperature was kept at 30-35ºC and α-CD free control was similarly prepared.

2.4 Imatinib loading on α-CD capped AgNPs

A constant volume of imatinib dissolved in methanol which is added to 10mM capped AgNps at room temperature with constant stirring continuously until silver metal nanoparticles were formed. The reaction mixture showed colour change from yellowish brown which indicated the formation of silver nanoparicles.

2.5 Antimicrobial analysis

For the evaluation of antimicrobial activity, four bacterial strains were selected namely, *Klebsiella, Pseudomonas, Staphylococcus* and *Escherichia coli.*

3. RESULTS AND DISCUSSION

3.1 UV-Visible spectroscopic studies

Table 1: Absorption maxima of AgNPs , α- CD capped AgNPs , Imatinib and Imatinib capped AgNPs

α-CD Capped AgNPs	λmax	Absorbance
Uncapped AgNps	420.5	2.632
5mM capped AgNPs	417.0	1.321
10mM capped AgNPs	410.4	2.465
15mM capped AgNPs	407.4	2.909
Imatinib	290.3	1.116
Imatinib 10mM α-CD capped AgNPs	322.4	1.232

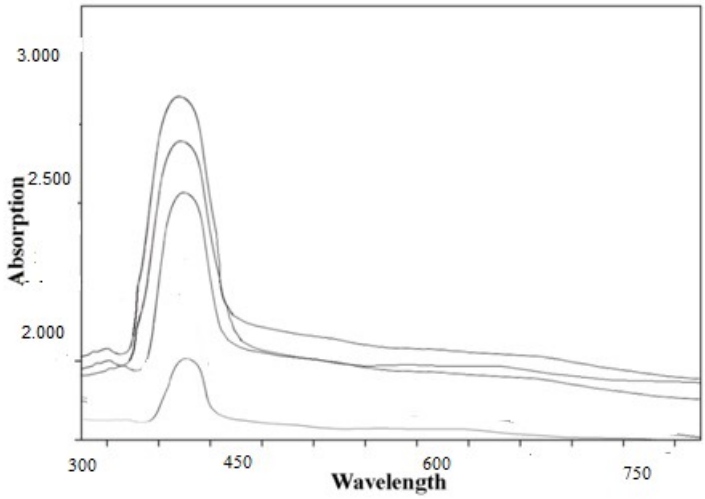

Fig .2(a): UV-Visible spectrum of AgNPs and α- CD capped AgNPs

UV – visible spectroscopy is one of the most widely used techniques for structural characterization of silver nanoparticles. The absorption spectrum of the pale yellow – brown silver colloid prepared by α- CD reduction showed a surface Plasmon absoption band with a maximum of 420.5nm indicating the presence of spherical or roughly spherical silver nanoparticles. The reaction mixture showed colour change from yellowish brown which indicated the formation of silver nanoparicles [6-8]. The absorption peak obtained in the visible range that is a clear evidence of formation of AgNPs from the metal nitrate solution.The absorption peak was blue shifted from 420.5nm- 407nm when it is capped with α-CD. The absorption intensity increased with increase in α-CD as shown in fig:2(a).The absorption spectra of Imatinib show an peak at 290.3nm. When the drug is loaded with α-CD capped AgNPs, the absorption maxima is bathochromically shifted to 322.4nm. The absorption intensity is also increases which is shown in fig.2(b).

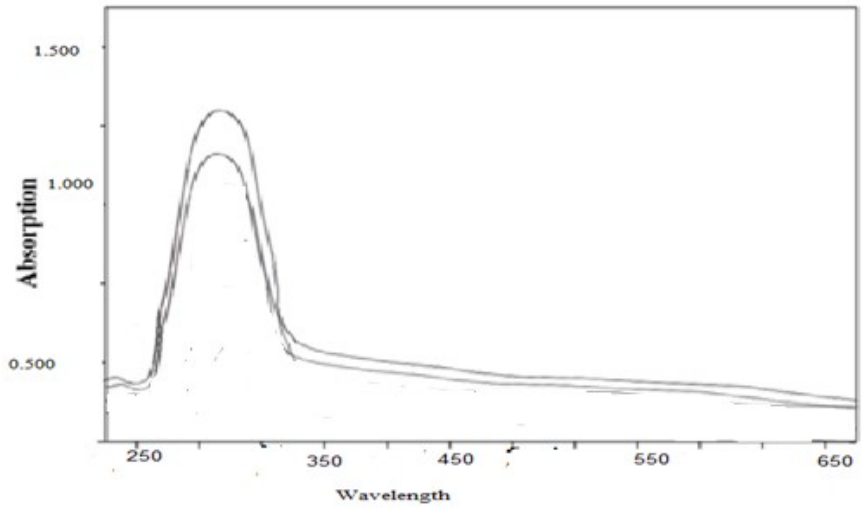

Fig. 2 (b): UV - Visible spectra of Imatinib and 10mM α-CD capped imatinib

3.2 FT-IR studies

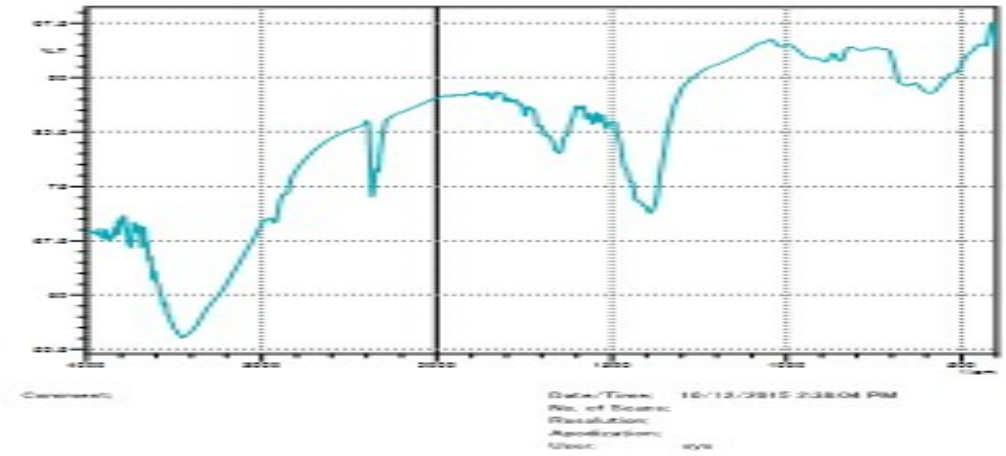

Fig.3 (a) : FT-IR spectrum of uncapped AgNPs

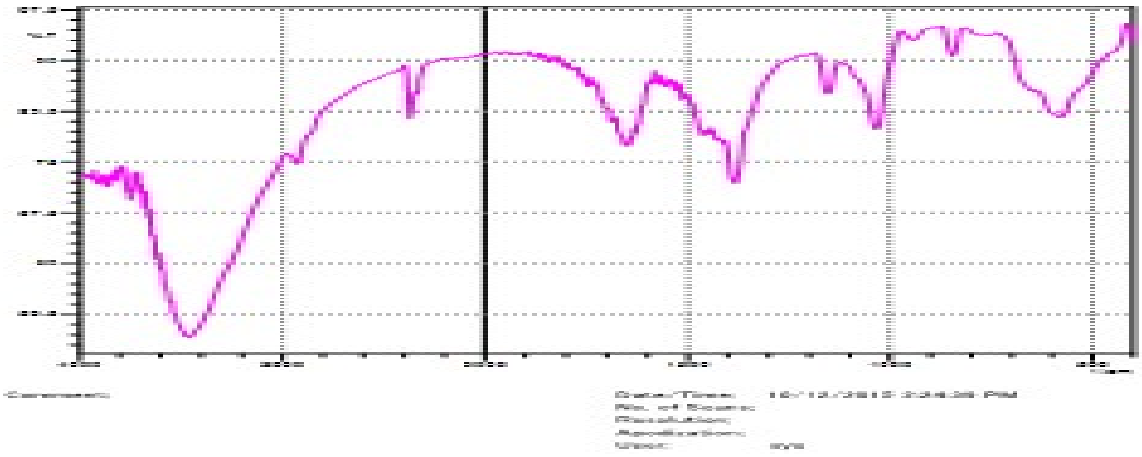

Fig.3 (b) : FT-IR spectrum of 5mM α-CD capped AgNPs

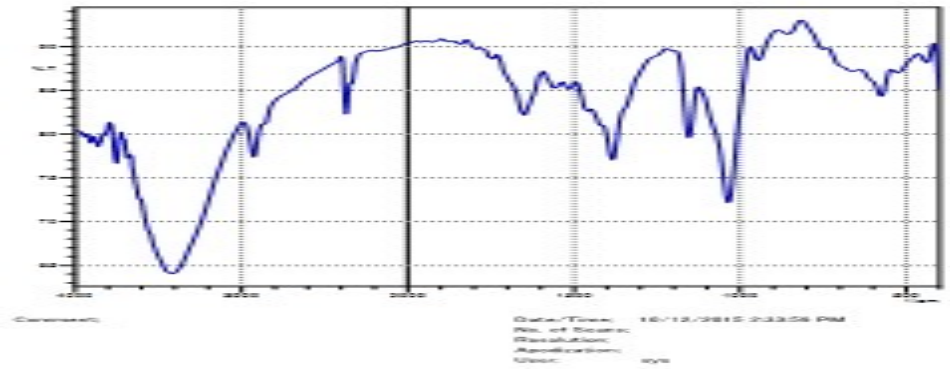

Fig. 3 (c) : FT-IR spectrum of 10mM α-CD capped AgNPs

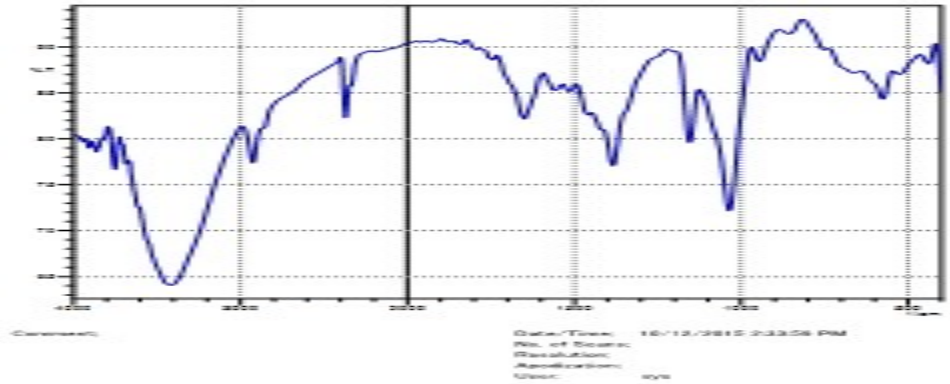

Fig.3 (d) : FT-IR spectrum of 15mM α-CD capped AgNPs

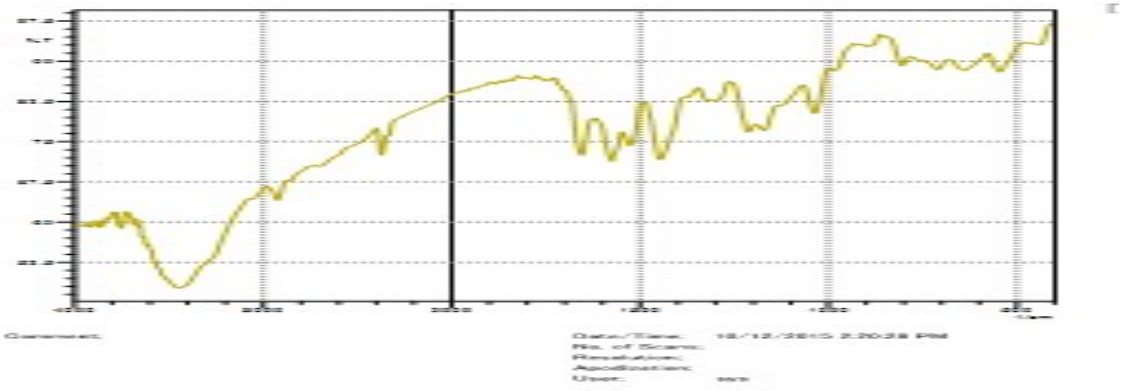

Fig.3 (e): FT-IR spectrum of matinib

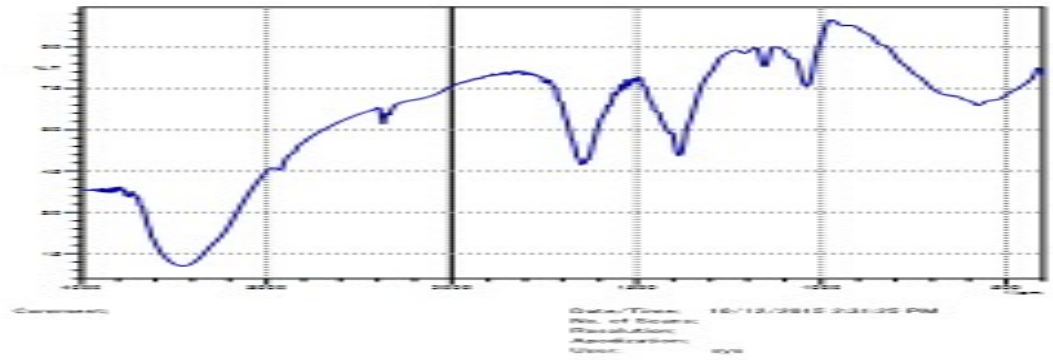

Fig.3 (f): FT-IR spectrum of Imatinib loaded α-CD capped AgNPs

Fig.3 (a)- (f) shows the FT-IR spectrum of uncapped AgNps, α-CD capped AgNPs via 5mM, 10mM, 15mM, Imatinib and Imatinib loaded α-CD capped AgNPs. Peak at 1600cm^{-1} indicates the presence of primary amine group in both imatinib and imatinib loaded AgNPs. It confirmed the binding of α-CD and drug to the AgNPs surface. The drug and drug loaded AgNPs showed a relative decrease in intensities of transmittance band and a suppression of the deprotonation of the hydroxyl groups at the rim of the α-CD cavity. The hydroxyl groups of α-CD act as the reducing species for the reduction of Ag+ into metallic Ag and they were self oxidized to carboxylic acid. The oxidation product of α-CD molecules bering a negative charge would provide a more efficient capping on the surface of AgNPs due to Ag-COO interactions.

3.3 XRD studies

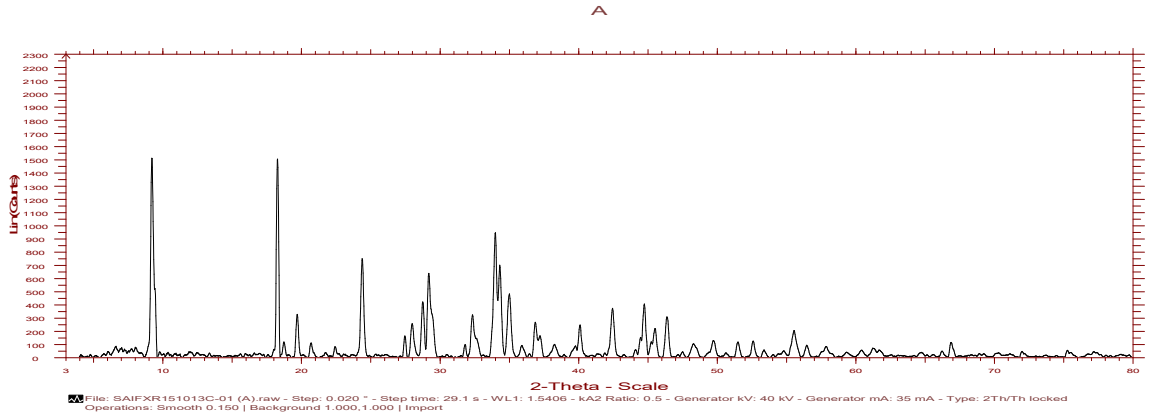

Fig. 4 (a): XRD spectrum of uncapped AgNPs

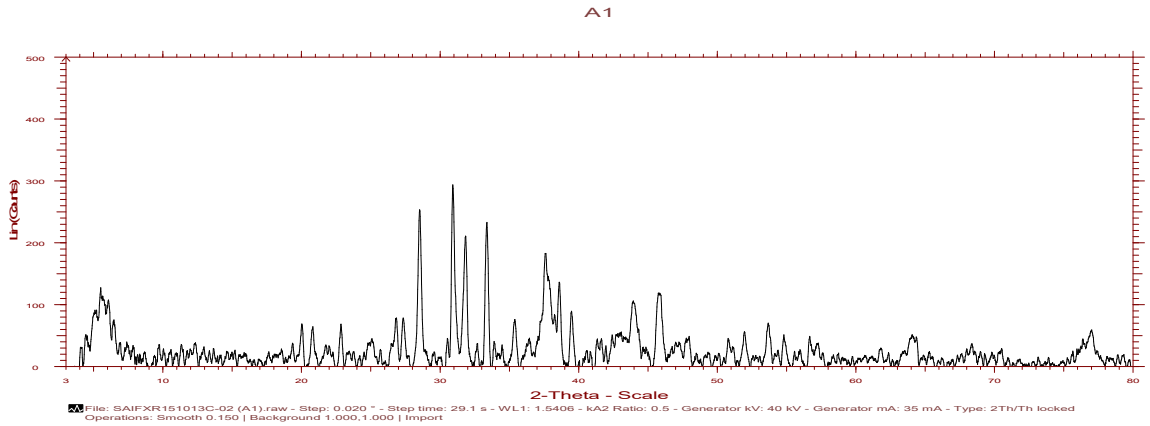

Fig.4 (b): XRD spectrum of 5mM α-CD capped AgNPs

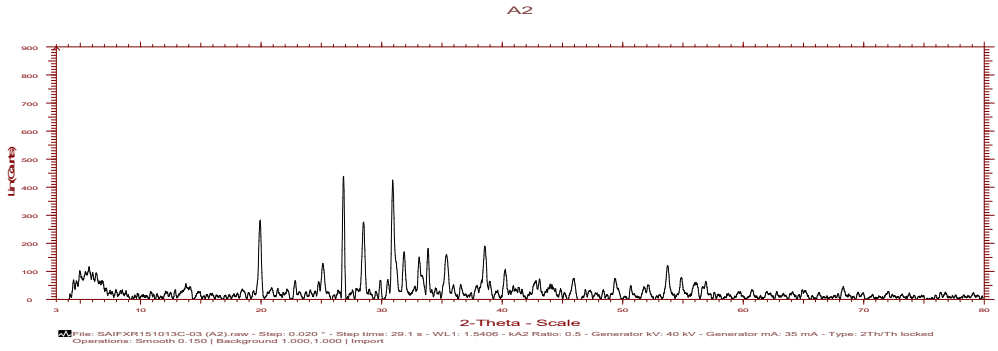

Fig. 4 (c): XRD spectrum of 10mM α-CD capped AgNPs

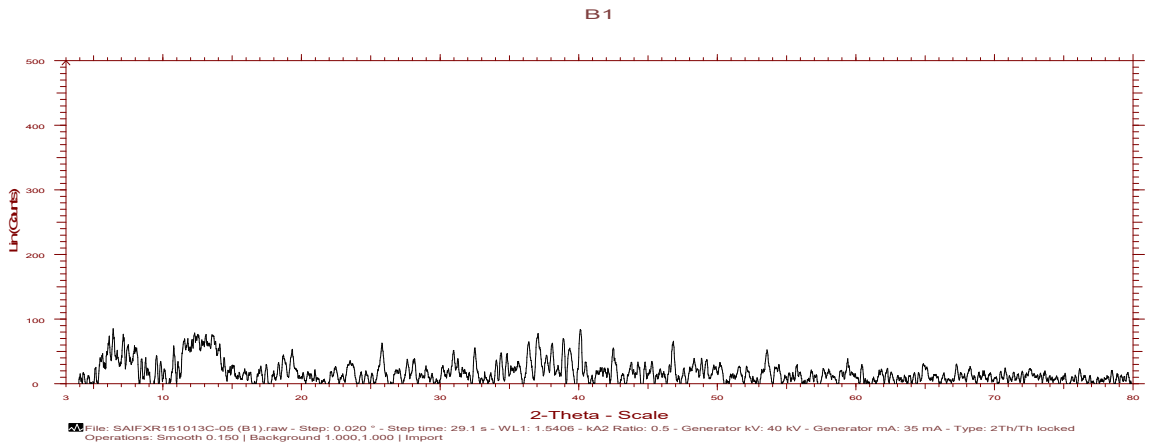

Fig.4 (d) : XRD spectrum of Imatinib

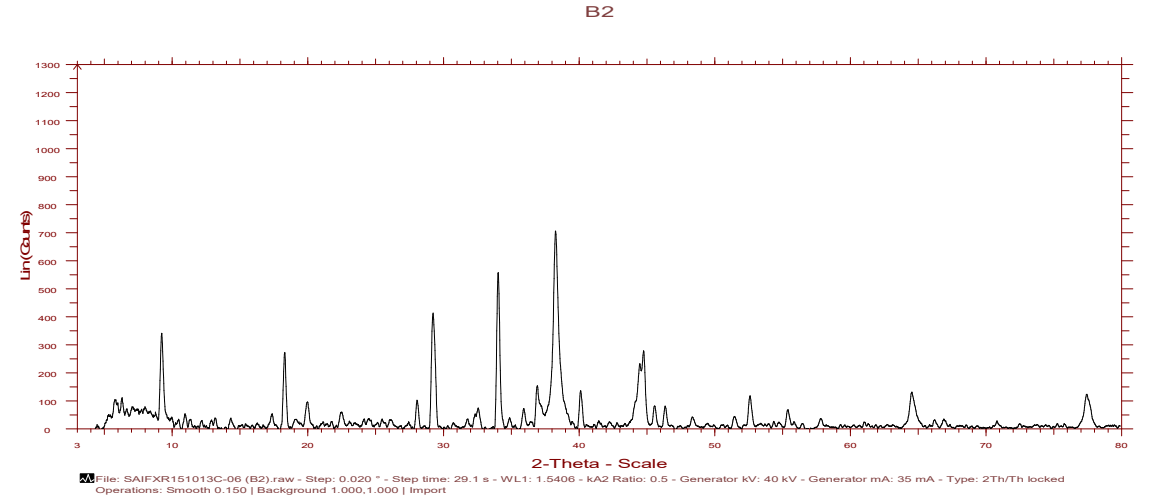

Fig.4(e) : XRD spectrum of Imatinib loaded capped AgNPs

Fig: 4 (a)-(e) shows the XRD spectrum of uncapped AgNPs, α-CD capped 5mM, 10mM, Imatinib and Imatinib loaded capped AgNPs. XRD is one of the most important characterization tools used in solid state chemistry. XRD is an easy tool to determine the size and the shape of the unit cell for any compound. The XRD pattern of the AgNPs are exhibited sharp peaks indicating that the nanoparticles are crystalline in nature. The peaks at 2θ= 24.316, 31.786, 30.865 in various concentration of α-CD and 19.161,18.207,18 236 in drug loaded AgNps revealed that it is a face centre cubic (FCC) crystalline structure. The average crystalline size (D) was calculated from the Full- width at half maximum (FWHM) of the most intense peak of the plane of AgNps using Debye – Scherrer formula

$$D=K\lambda/\beta\cos\theta$$

Where ,λ is the wavelength of X-ray (0.1541nm) , β is FWHM (Full Width at Half Maximum), θ is the diffraction angle and D is particle diameter size.

The calculated particle size of the AgNps is 50nm and the drug loaded α-CD capped AgNps is 20nm. These results shows that the particle size was less when compared to the drug loaded AgNPs.

3.4 Scanning Electron Spectroscopy

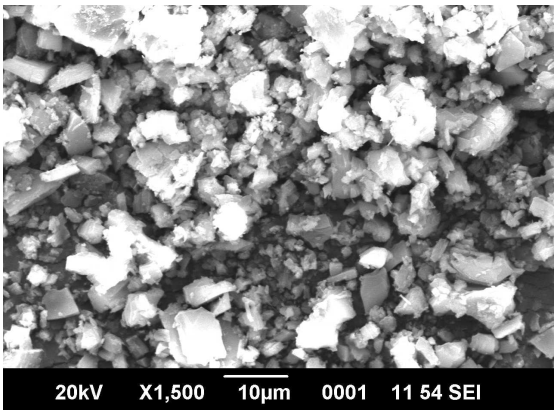

Fig.5 (a) : Image of uncapped AgNPs

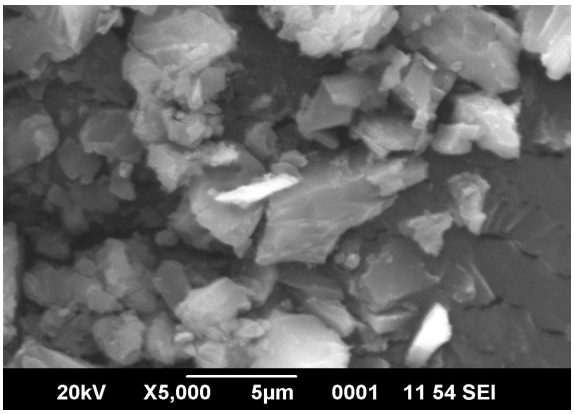

Fig.5(b) : Image of 5mM α-CD capped AgNPs

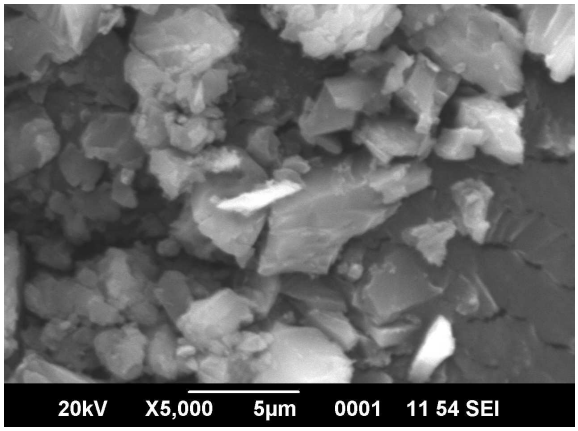

Fig.5(c): Image of 10mM α-CD capped AgNPs

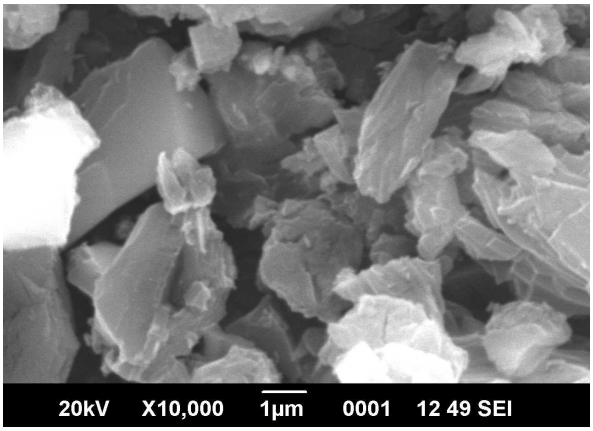

Fig.5(d) : Image of 5mM α-CD capped AgNPs

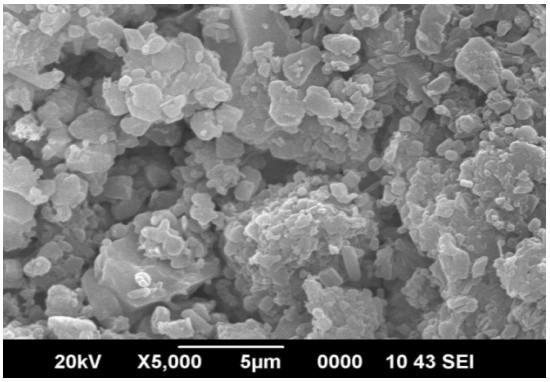

Fig. 5(e) : Image of Imatinib

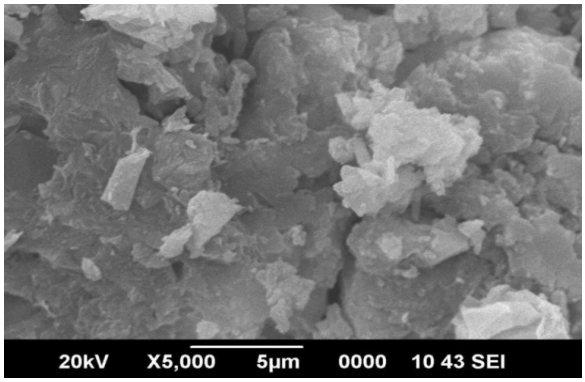

Fig.5(f) : Image of Imatinib loaded capped AgNPs

A SEM employed to analyze the morphology and size details of the silver nanoparticles that were formed. From Fig.5(a)-(f) it was showed that the silver nanoparticles formed were almost spherical in shape, and uniformly distributed silver nanoparticles on the surface of the cells were observed. A similar phenomenon has been reported[9-12].Thus the interactions between silver nitrate and cyclodextrin are important factors responsible for the production of weakily agglomerated and uniformly dispersed silver nanoparticles[13-14]. When imatinib is loaded with AgNPs the morphological changes occurred. These result suggest that the drug molecule is included in the capped AgNPs.

3.5 Anti-Microbial studies

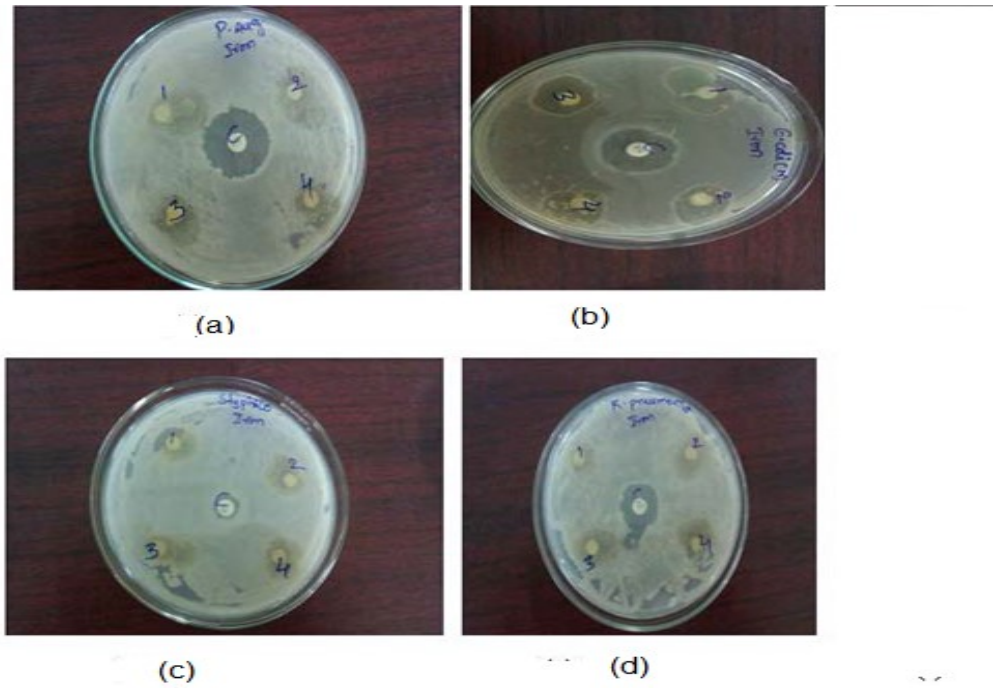

Fig.6 : Antimicrobial activity of α-CD capped AgNPs

Organisms	**Sample's antimicrobial activity(mm)**				**Positive control (Amikacin)**
	AgNPs	5mM	10mM	15mM	
E.Coli	10mm	10mm	10mm	10mm	23mm
Klebsiella	10mm	10mm	10mm	13mm	21mm
Pseudomonas	10mm	9mm	12mm	10mm	21mm
Staphylococcus	NZ	NZ	NZ	NZ	22mm

The above figures Fig:6 (a) – (d) shows the anti-microbial activity of uncapped and capped AgNPs . In the present investigation the antimicrobial effect of synthesized AgNPs is studied on different types of bacteria such as *Klebsiella, Pseudomonas* (gram negative), *E.Coli, Staphylococcus* (gram positive). The antimicrobial activities of three different concentration of α-CD capped AgNPs with four microorganisms were studied. AgNPs had the highest antimicrobial activity against *Klebsiella > E.Coli > Pseudomonas.* No zone of inhibition is formed by AgNPs with *Staphylococcus*. While the concentration of α-CD was increased antimicrobial activity of AgNPs with 15mM concentration was found to be pronounced against *Klebsiella* and 10mM concentration againat *Pseudomonas*. These results clearly indicated that silver nanoparticles could provide a safer alternative to conventional antimicrobial agents.The nanoparticles are too small in size , they can come in contact with antibiotics , there by either it can inhibit peptidoglycan synthesis or AgNPs antibiotics complex can react with DNA leading to the damage of the bacterial cells.

4. CONCLUSION

Well dispersed silver nanoparticles were synthesized by reducing $AgNO_3$ with α-CD. NaOH is used to enhance the reaction velocity. The synthesis of cyclodextrin capped silver nanoparticles by this method is eco-friendly, of low cost and capable of producing AgNPs at room temperature. Here α-CD acts as both capping agent and reducing agent. The AgNPs were characterized by UV-Vis, FT-IR, XRD and SEM analysis. The antimicrobial activity increased as the concentration of α-CD increased. The obtained uniform AgNPs functionalized by α-CD molecules would find a wide range of biomedical application by virtue of biologically compatible characteristic as well as the special inclusion ability of the α-CD molecules. α-CD are proved to be the good alternatives for polymers which are the commonly used capping agents in nanoparticle synthesis.

The size of the nanoparticles was determined to below 50nm. From the results that anticancer drugs were successfully incorporated into the α-CD - AgNPs. Complexation with cyclodextrins, (polysaccharides) increases the solubility of pharmacons and allows reducing significantly the effective dose avoiding, at the same time some unwanted side effects. Thus a new perspective is opening of obtaining highly effective and safe drugs and new ways of drug delivery.

5. ACKNOWLEDGEMENT

The author is thankful to the Research department of Chemistry, Scott Christian College, Nagercoil for providing necessary facilities.

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