Fabrication of Porous Silicon Nanoparticles to Attach Clorgyline for Drug Delivery

Department of Biotechnology, Periyar Maniammai University, Vallam-613403, Tamilnadu, India

Kumaran.S
Department of Biotechnology, Periyar Maniammai University, Vallam, Thanjavur-613403, Tamil Nadu, India

Abstract—Maturity of nanomaterials shapes the field of nanomedicines, due to superior property of nanomaterials the controlled and multifunctional drug delivery systems are established. So, in the present study we fabricate Porous Silicon Nanoparticles (pSiNPs) and attached Clorgyline drug. Drug loaded pSiNPs play significant role as an attractive materials for controlled drug delivery systems, since pSiNPs are biocompatible, biodegradable and carry a drug payload that circulate in body, hold great potential to treat disease. Clorgyline, a Monoamine Oxidase inhibitor favors the synthesis of neurotransmitter dopamine treating neurodegenerative diseases like Parkinson’s, Alzheimer’s, and Central nervous disease(CNS) disorder. Synthesized and drug loaded nanoparticles are characterized by Atomic Force Microscopy (AFM). Surface topography of pSiNPs shows the average height in range of 0.09 nm to 1.9 nm whereas Clorgyline loaded pSiNPs shows an increased in average height ranges from 0.0487 µm to 0.0104 µm and the angle calculated for pSiNPs, drug, drug attached pSiNPs sample were 0.03°, 0.07° and 0.11° respectively, which confirms the attachment of drug molecules to pSiNPs

Keywords- Nanomedicine, pSiNPs, Drug delivery, Clorgyline, AFM

I. INTRODUCTION

Nanomaterials are at a cutting edge of rapid development in the area of Bionanotechnology. pSiNPs are a form of silica and a recent identification due to development in nanotechnology. Its applications are in variety of areas like drug delivery, imaging and biosensor.[1]. Porous silicon was accidentally discovered by Uhlir at Bell Laborites in the mid 1950s[2]. He was trying to develop a means to machine electrochemically silicon wafers for use in microelectronic circuits. Porous Silicon being investigated for application in microelectronics, optoelectronics, chemical[3] and biomedical devices[4]. Porous Si or porous SiO₂ (Prepared from porous Si by oxidation) has been employed to demonstrate in vitro release of the Steroid dexamethasone[5], ibuprofen[6], cis-platin[7], doxorubicin[8], and many other drugs[9]. The first report of drug delivery from porous Si across a cellular barrier was performed with insulin, delivered across monolayers of Caco-2 cells[9]. There are many possibilities of drug delivery using nanoparticles, we have chosen pSi due to its inherited advantages. An excellent review on potential use of porous Si in various drug delivery applications has recently appeared[9]. Clorgyline is an irreversible and selective inhibitor of monoamine oxidase A (MAO-A) that degrades amine neurotransmitters such as dopamine, norepinephrine, and serotonin leading to neurodegenerative processes and results many Neuro Degenerative Diseases (NDD) including Parkinson’s, Alzheimer’s and Huntington’s.

II. MATERIALS AND METHODS

P++ silicon wafer (resistivity 0.8-1.2 mΩ cm) was purchased from Vin Karola Instruments USA. All chemicals including Phosphate buffered saline (PBS), Bovine Serum Albumin (BSA), aqueous hydrofluoric acid (48%), drug...
clorgyline, hydrogen peroxide (H$_2$O$_2$), ethanol, methanol were purchased from Sigma Aldrich.

Fig 1 shows Schematic representation of pSi nanoparticle preparation and attachment of clorgyline drug to the synthesized nanoparticle. Silicon wafer is cleaned by SC1 process and pSiNPs is a product of electrochemical etching by using Teflon Etch cell with electrolyte solution of HF (48%) and Ethanol in ratio 3:1 by applying constant current density of 200mA/cm$^2$ for 150 s. A freestanding film of the porous silicon nanostructure were removed from crystalline silicon substrate by application of a current pulse of 4 mA/cm$^2$ for 250 s in a solution of 3.3% (by volume) 48% aqueous HF in ethanol. Freestanding hydrogen-terminated porous silicon film is fractured into multi-sized particles by sonicating in deionized water for overnight. Then the particles were filtered by 0.45 µm filtration membrane (Millipore).

0.1 µg/ml of clorgyline is taken in PBS and 500 µl solution of pSiNPs in DI water was added with 500 µl of clorgyline in PBS and it was incubated overnight at 37°C (pH 7.0). The surface morphology and roughness of pSiNPs, drug, drug attached pSiNPs sample were characterized by Atomic Force Microscopy (Innova, Veeco).

III. RESULTS AND DISCUSSION

Topography of pSiNPs, Drug, Clorgyline attached pSiNPs by using AFM. In Fig 2(a) shows the topographical lattice 3D image of pSiNPs after cleaning process, it has an average height range from 0.93 nm to 1.9 nm. Fig 2(b) is the 3D view of clorgyline drug by using silicon as substrate which results an average height of 0.3 nm to 0.8 nm. Fig 2(c) shows Drug loaded pSiNPs with slight increase in the height of the pSiNPs in range from 0.01 µm to 0.04 µm [11]. We have tried to take images at different location by scanning over the region of 5µm to 20 µm. Vertical size analysis from the AFM images shows small particles with narrow distribution of well symmetrically structured particles [11].

![Figure 2](image)

**Figure 2.** Tapping mode AFM image of (a) pSiNPs (b) Drug clorgyline (c) Drug loaded pSiNPs

- **Line measurement:** Line measurement analysis function allows to do cross-sectional measurement along a particular line on the image to obtain few parameters such as line length and (X,Y,Z) position for both start and end points of the line. Then the difference among the points in (X,Y,Z) position were observed for all the three different images. Fig 3 represent line measurement profile and angle calculated for the pSiNPs, drug and drug attached pSiNPs.

- **Height measurement:** AFM was used to measure standard roughness of whole as well as the particular area of nanoparticle and drug loaded nanoparticle sample was measured. Then the roughness parameters such as roughness average (Ra), root mean square roughness (Rms), average height, maximum height are listed in table II. height measurement shows the exact particle diameter since the particles are spherical shaped [12].

<table>
<thead>
<tr>
<th>Name</th>
<th>pSiNPs</th>
<th>Drug</th>
<th>Drug attached pSiNPs</th>
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<tbody>
<tr>
<td>Average roughness(Ra)</td>
<td>0.4648nm</td>
<td>0.3673nm</td>
<td>0.0147µm</td>
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<tr>
<td>Root mean square roughness(RMS)</td>
<td>0.6722nm</td>
<td>0.5487nm</td>
<td>0.0215µm</td>
</tr>
<tr>
<td>Average Height</td>
<td>6.0328nm</td>
<td>2.3322nm</td>
<td>0.0335µm</td>
</tr>
<tr>
<td>Maximum height</td>
<td>5.0261µm</td>
<td>5.7824µm</td>
<td>0.1021µm</td>
</tr>
</tbody>
</table>

Table I shows the calculated angles on the three images were 0.03°, 0.07° and 0.11°, this angle variation between pSiNPs and drug load pSiNPs confirms the attachment of drug to pSiNPs.

**Table II. ROUGHNESS PARAMETERS**
Figure 4. Height profile of (a) pSiNPs (b) Drug clorgyline (c) Drug loaded pSiNPs

Fig 4 shows the height distribution profiles of surface roughness. It clarifies the surface with irregularities arrangement of the particles, this disturbance can be calibrated by the surface roughness (R_{rms}) values from the images. The pSiNPs surface has less (R_{rms}) roughness value than the drug modified pSiNPs.

Surface topography images of pSiNPs, drug, drug attached pSiNPs are several grains are found 509,486,249 grains are found in surface an average height of 5.65,2.27,26.8nm respectively.

This confirms that pSi nanoparticle can be produced and Clorgyline can be attached successfully using electrostatic attachment.

IV. CONCLUSION

In the present study of pSiNPs synthesized and clorgyline drug were attached to nanoparticles was well confirmed by AFM analysis. Since pSiNPs is biocompatible and excellent carrier of clorgyline across Blood Brain barrier and it can be taken to super nanomedicine for treating neurodegenerative diseases like Parkinson’s, Alzheimer’s.

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REFERENCES

<table>
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<tr>
<th>SAMPLE</th>
<th>pSiNPs</th>
<th>Drug</th>
<th>pSiNPs + Drug</th>
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<tr>
<td></td>
<td>$X_{(\mu m)}$</td>
<td>$Y_{(\mu m)}$</td>
<td>$Z_{(\mu m)}$</td>
</tr>
<tr>
<td>Point 1</td>
<td>0.582</td>
<td>0.168</td>
<td>-0.172</td>
</tr>
<tr>
<td>Point 2</td>
<td>0.136</td>
<td>0.168</td>
<td>0.050</td>
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<tr>
<td>Diff</td>
<td>-0.446</td>
<td>0.000</td>
<td>0.223</td>
</tr>
<tr>
<td>Length(\mu m)</td>
<td>0.446</td>
<td>0.434</td>
<td>3.563</td>
</tr>
<tr>
<td>Pt Angle</td>
<td>0.03</td>
<td>0.07</td>
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