Molecular docking simulation of interaction between insulin and silica nanoparticle

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Abstract. Molecular docking simulation has been done in this research by using Hex version 8.0 software package, respectively, to explore the interaction between insulin and silica nanoparticle. Silica nanoparticle acts as receptor and insulin acts as ligand in this research. It was found that insulin form more stable interaction when it is in the pore of silica nanochannel than on the surface of silica nanosheet. Insulin prefer to interact with silica atoms than oxygen atoms in the pore of silica nanochannel

1. Introduction
Insulin is a hormone produced naturally by the pancreas. This hormone serves to help cells absorb glucose, thereby keeping blood sugar stable. However, in diabetics, the amount of insulin produced is insufficient or even non-existent. In these conditions, additional insulin is needed. Until now, the most common way to use insulin is through an injection or infusion. However, the use of insulin in this way has several disadvantages such as (1) fear of syringes, (2) lipodystrophy, peripheral hyperinsulinemia & other long-term injection side effects, (3) patient disobedience with treatment, (4) more treatment have expensive costs, (5) complexity of injection procedures, (6) special education needs for patients & / or their families, (7) sterility or hygiene must be maintained. One solution to overcome this problem is the use of insulin orally. In order for insulin to be administered orally, a drug carrier is needed to deliver insulin into the human body. One drug carrier material that is widely used by researchers is Mesoporous Silica Nanoparticle (MSN) [1-4]. In this research, in silico study has been carried out in the application of Mesoporous Silica Nanoparticle (MSN) as oral insulin delivery material by using Molecular Docking simulation to study the interaction between insulin and the surface and pore of MSN in silica nanosheet and silica nanochannel, respectively.

2. Methods
In this research we applied a computational method which is divided by three sections. First, construct the receptor and ligand molecule, and Second, molecular docking simulation.
2.1. Construct the receptor and ligand molecule

The receptor molecules are silica made in two form, as nanosheet and as nanochannel. The silica structure is cristobalite structure as. cif file downloaded from http://www.crystallography.net/ with ID 9001578. Cristobalite silica has been used as silica model in previous researches [5-7]. Then, the. cif file of cristobalite silica was modified to be nanosheet and nanochannel with the structure size of 198.88 Å x 24.86 Å x 6.92 Å. The nanochannel model of silica is made from rolled nanosheet silica. The structure of silica nanosheet and nanochannel is shown in Figure 1. In this research, we made two different structures of nanochannel, first, with Si-terminated surface in the cavity of silica nanochannel, and second, with O-terminated surface in the cavity of silica nanochannel, which is shown in Figure 1(b) and Figure 1(c).

![Figure 1](image)

**Figure 1.** The structure of (a) silica nanosheet, (b) silica nanochannel with Si-terminated surface in the cavity, (c) silica nanochannel with O-terminated surface in the cavity

The ligand used in this research is human insulin downloaded from http://www.rcsb.org with the code of 3i40.

2.2. Molecular docking simulation

In our previous research regarding to host-guest inclusion complex [8-11], we have carried out molecular docking simulation by using ArgusLab version 4.0.1 software package [12]. However,
ArgusLab cannot carry out molecular docking simulation with oxide material or inorganic solid state material as receptor. We also have tried another molecular docking software packages [13-17] and they also cannot carry out molecular docking simulation with such material as receptor. To overcome this limitation of ArgusLab and other molecular docking software packages, in this research, Hex version 8.0 software package has been used as tool for molecular docking simulation [18]. Hex version 8.0 has been used by some researchers as tool for molecular docking simulation with inorganic solid state material as receptor [19-25]. In this molecular docking simulation, the insulin was treated as ligand and silica material (silica nanosheet and silica nanochannel) were treated as receptor. This molecular docking simulation used varied correlation type as shown in Table 1, 3D FFT mode, range angels sampling method, OPLS and DARS minimisation post processing in pair with each of correlation type as shown in Table 1, grid dimension of 0.6, solutions of 2000, receptor range of 180 and step size of 7.5, ligand range of 180 and step size of 7.5, twist range of 360 and step size of 5.5, distance range of 40, box size of 10, translation step of 0.8, substeps of 0, score threshold of 0.0, steric scan of 18, and final search of 25. The use of varied correlation type and post processing method is to validate the molecular docking result. Table 2 show the notation of complex of receptor and ligand used in this research.

### Table 1. Correlation type and post processing method used in this research.

| Correlation Type   | Post Processing Method | Notation |
|--------------------|------------------------|----------|
| Shape              | No minimisation        | S-NM     |
|                    | OPLS minimisation      | S-OM     |
|                    | DARS minimisation      | S-DM     |
| Shape + Electro    | No minimisation        | SE-NM    |
|                    | OPLS minimisation      | SE-OM    |
|                    | DARS minimisation      | SE-DM    |
| Shape + DARS       | No minimisation        | SD-NM    |
|                    | OPLS minimisation      | SD-OM    |
|                    | DARS minimisation      | SD-DM    |
| Shape + Electro + DARS | No minimisation   | SED-NM   |
|                    | OPLS minimisation      | SED-OM   |
|                    | DARS minimisation      | SED-DM   |

### Table 2. Notation of receptor and ligand complex used in this research.

| Complex of receptor and ligand                                           | Notation |
|------------------------------------------------------------------------|----------|
| Insulin and silica nanosheet with insulin-Si terminated surface interaction | I-SNSA   |
| Insulin and silica nanosheet with insulin-O terminated surface interaction | I-SNSB   |
| Insulin and silica nanochannel with insulin-Si terminated surface interaction | I-SNCA   |
| Insulin and silica nanochannel with insulin-O terminated surface interaction | I-SNCB   |

### 3. Results and discussion

The result of molecular docking simulation between insulin and silica nanoparticle (silica nanosheet and nanochannel) is shown in Table 3.
Table 3. $E_{\text{total}}$ of interaction between insulin and silica nanoparticle

| I-SNSA | $E_{\text{total}}$ (kJ/mol) |
|--------|-----------------------------|
| S-DM   | -179.4                      |
| SE-DM  | -216.7                      |
| SD-DM  | -163.5                      |

| I-SNSB | $E_{\text{total}}$ (kJ/mol) |
|--------|-----------------------------|
| S-NM   | -151.7                      |
| S-OM   | -179.4                      |
| SE-NM  | -216.7                      |
| SE-OM  | -216.6                      |
| SD-NM  | -163.5                      |
| SD-OM  | -143.8                      |
| SED-NM | -163.5                      |
| SED-OM | -143.8                      |
| SED-DM | -141.1                      |

| I-SNCA | $E_{\text{total}}$ (kJ/mol) |
|--------|-----------------------------|
| S-NM   | -422.5                      |
| S-OM   | -381.7                      |
| S-DM   | -422.5                      |
| SE-NM  | -422.5                      |
| SE-OM  | -381.7                      |
| SE-DM  | -422.5                      |
| SD-NM  | -422.5                      |
| SD-OM  | -381.7                      |
| SD-DM  | -422.5                      |
| SED-NM | -422.5                      |
| SED-OM | -381.7                      |
| SED-DM | -422.5                      |

| I-SNCB | $E_{\text{total}}$ (kJ/mol) |
|--------|-----------------------------|
| S-NM   | -542.5                      |
| S-OM   | -373.1                      |
| S-DM   | -530.8                      |
| SE-NM  | -542.5                      |
| SE-OM  | -373.1                      |
| SE-DM  | -530.8                      |
| SD-NM  | -542.5                      |
| SD-OM  | -373.1                      |
| SD-DM  | -530.8                      |
| SED-NM | -542.5                      |
| SED-OM | -373.1                      |
| SED-DM | -530.8                      |
From Table 3, we found that interaction between insulin and silica nanochannel have more negative value of $E_{\text{total}}$ than interaction between insulin and silica nanosheet for all of the docking parameter configuration.

4. Conclusion

From molecular docking simulation, it can be concluded that insulin form more stable interaction when it is in the pore of silica nanochannel than on the surface of silica nanosheet, with the lowest $E_{\text{total}}$ of $-542.5$ kJ/mol for docking parameter S-NM, SE-NM, SED-NM and interaction type I-SNCB where the insulin prefer to interact with silica atoms than oxygen atoms in the pore of silica nanochannel. However, this molecular docking simulation result must be validated by using higher and better theory level of computational method, such as DFT (Density Functional Theory), in order to get more accurate results, and also Molecular Dynamics to get the insight of interaction dynamics between insulin and silica nanoparticle, especially silica nanochannel.

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