LIST OF FIGURES

Figure 1.1: Concept of biosensor. The biocatalyst (a) converts the substrate to product. This reaction is determined by the transducer (b) which converts it to a signal. The output from the transducer is amplified (c), processed (d) and displayed (e)…………………………………………………………… 4

Figure 1.2: Types of nanodevices based on their construction of nanostructures and functions……………………………………………………………………………………………………………………………………………………………. 5

Figure 1.3: Electrochemical nanobiosensor for monitoring drug-DNA interaction or enzyme inhibition/induction with drug………………………………… 9

Figure 1.4: Schematic representation of Optical nanobiosensor based on QDs……… 13

Figure 1.5: Schematic representation of Nanobiochip based on SERS and LEPR spectroscopy………………………………………………………………………………… 17

Figure 2.1: Schematic representation of MTX-DNA interaction development of nanobiosensor and monitoring of MTX-DNA interaction………………… 36

Figure 2.2: SEM image of SiO₂……………………………………………………………………………. 39

Figure 2.3: Particle size distribution of SiO₂……………………………………………………………… 40

Figure 2.4: MTX-DNA interaction in solution at various concentration of MTX… 42

Figure 2.5: Nanobiosensor monitoring MTX-DNA interaction at various concentration of MTX………………………………………………………………………………… 43

Figure 2.6: Potential difference between nanobiosensor and without nanobiosensor at various MTX concentration series……………………………………… 45

Figure 2.7: Calibration curves of MTX concentration versus the ΔE values………. 47

Figure 2.8: Validation of MTX-DNA adduct by UV-spectroscopy ………………… 50

Figure 2.9: Confirmation of MTX-DNA adduct by FT-IR spectroscopy (A: pure DNA, B: MTX, C: MTX DNA)…………………………………………………………… 51

Figure 2.10: Zeta-potential of DNA, MTX, and MTX-DNA adduct………………… 53

Figure 3.1: Schematic representation of development of Pt nanoparticles based nanobiosensor………………………………………………………………………………… 60

Figure 3.2: SEM image of Pt nanoparticles…………………………………………………………….. 64
List of Figures

Figure 3.3: Particle size distribution of Pt nanoparticles ................................. 65
Figure 3.4: Carboplatin-DNA interaction at various concentration of Carboplatin in solution (without nanobiosensor) ................................. 67
Figure 3.5: Carboplatin-DNA interaction at various concentration of Carboplatin determined by nanobiosensor ................................. 68
Figure 3.6: Potential difference between nanobiosensor and without nanobiosensor at various Carboplatin concentration series ...................... 70
Figure 3.7: Calibration curves of Carboplatin concentration versus the ΔE values. 72
Figure 3.8: Carboplatin-DNA adduct obtained at 100 ng/ml of Carboplatin by UV-spectroscopy .......................................................... 75
Figure 3.9: Carboplatin-DNA adduct obtained at 10 ng/ml of Carboplatin by UV-spectroscopy .......................................................... 75
Figure 4.1: Schematic representation of biosensor fabrication process and FRET phenomena. Binding of DNA to MTX, results in increase fluorescence intensity due to FRET. Solid and wavy arrows indicate the radiative and nonradiative processes, respectively. Hydrogen bonding in unreacted DNA is shown by dotted lines on lateral sides of the DNA... 81
Figure 4.2: SEM image of AuNPs ................................................................. 85
Figure 4.3: Average particle size distribution of AuNPs; (B) UV-visible spectra of AuNPs obtained at 527 nm, while the intensity peak decreased and shifted at 530 on binding with DNA. Also, peak of pure DNA is shifted from 260 to 256 on binding ........................................ 86
Figure 4.4: Fluorescence emission of DNA labeled AuNPs. (series 100 i.e., 100 µg/mL) Excitation(Ex) at 450 nm yield a fluorescence emission(Em) peak at 531 nm. [a: bare AuNPs, b: DNA-AuNPs, after addition of increasing amount of MTX to DNA-AuNPs, i.e., c:10µL, d:20µL, e:30µL, f:40µL, g:50µL] ......................................................... 88
Figure 4.5: Fluorescence emission of DNA labeled AuNPs. (Paracetamol at 100 µg/mL) Excitation(Ex) at 450 nm yield a fluorescence emission(Em) peak at 531 nm. [a: bare AuNPs, b: DNA-AuNPs, after addition of
increasing amount of Paracetamol to DNA-AuNPs, i.e., c:10µL, d:20µL, e:30µL, f:40µL, g:50µL]........................................................................................................ 89

Figure 4.6: Fluorescence emission of DNA labeled AuNPs. (series 50) Excitation(Ex) at 450 nm yield a fluorescence emission(Em) peak at 531 nm. [a: bare AuNPs, b: DNA-AuNPs, after addition of increasing amount of MTX to DNA-AuNPs, i.e., c:10µL, d:20µL, e:30µL, f:40µL, g:50µL]........................................................................................................ 90

Figure 4.7: Fluorescence emission of DNA labeled AuNPs. (series 10) Excitation(Ex) at 450 nm yield a fluorescence emission(Em) peak at 531 nm. [a: bare AuNPs, b: DNA-AuNPs, after addition of increasing amount of MTX to DNA-AuNPs, i.e., c:10µL, d:20µL, e:30µL, f:40µL, g:50µL]........................................................................................................ 91

Figure 4.8: Comparative study of MTX-DNA and Paracetamol-DNA interaction by optical nanobiosensor at 100 µg/mL....................................................... 92

Figure 4.9: Comparison of interacting behavior of MTX and Paracetamol with DNA........................................................................................................ 93

Figure 4.10: Comparative study of MTX-DNA interaction by optical nanobiosensor at 50 and 10 µg/mL................................................................. 93

Figure 4.11: Comparison of interacting behavior of different behavior of MTX with DNA................................................................................................. 94

Figure 4.12: Plots of the concentration of MTX versus the intensity of MTX-DNA interaction (100µg/mL)........................................................................... 92

Figure 4.13: Plots of the concentration of Paracetamol versus the intensity of Paracetamol-DNA interaction (100µg/mL).............................................. 95

Figure 4.14: Plots of the concentration of MTX versus the intensity of MTX-DNA interaction (50µg/mL)................................................................. 97

Figure 4.15: Plots of the concentration of MTX versus the intensity of MTX-DNA interaction (10µg/mL)................................................................. 98

Figure 5.1: Schematic representation of optical nanobiosensor. AuNPs were labeled with DNA and exposed to drug solution. Fluorescence
enhancement observed on binding of DNA to drug via FRET. Solid and wavy arrows indicate the radiative and nonradiative processes, respectively.

Figure 5.2: SEM image of AuNPs.

Figure 5.3: Average particle size distribution of AuNPs.

Figure 5.4: UV-visible spectra of AuNPs obtained at 527 nm, while the intensity peak decreased and shifted at 530 on binding with DNA.

Figure 5.5: Fluorescence emission of DNA labeled AuNPs. Excitation(Ex) at 450 nm yield a fluorescence emission(Em) peak at 531 nm. [a: bare AuNPs, b: DNA-AuNPs, after addition of increasing amount of Carboplatin to DNA-AuNPs, i.e., c:5µL, d:10µL, e:15µL, f:20µL, g:25µL].

Figure 5.6: Fluorescence emission of DNA labeled AuNPs. Excitation(Ex) at 450 nm yield a fluorescence emission(Em) peak at 531 nm. [a: bare AuNPs, b: DNA-AuNPs, after addition of increasing amount of Paracetamol to DNA-AuNPs, i.e., c:5µL, d:10µL, e:15µL, f:20µL, g:25µL].

Figure 5.7: Comparative study of Carboplatin-DNA and Paracetamol-DNA interaction by optical Nanobiosensor.

Figure 5.8: Comparison of interacting behaviour of Carboplatin and Paracetamol with DNA.

Figure 5.9: Plots of the concentration of Carboplatin versus the intensity of Carboplatin-DNA interaction.

Figure 5.10: Plots of the concentration of Paracetamol versus the intensity of Paracetamol-DNA interaction.
# LIST OF TABLE

Table 1.1: List of drugs that interact with DNA and produce cytotoxicity ........ 7
Table 1.2: List of few drugs can induce and inhibit the P-450 enzyme ........... 11
Table 2.1 Time dependent changes of MTX-DNA interaction determined in solution (without Nanobiosensor) ................................................. 41
Table 2.2: Time dependent changes of MTX-DNA interaction determined by Nanobiosensor ................................................................. 44
Table 2.3: Potential difference at various concentration series ....................... 46
Table 2.4: Comparison of the analytical parameters for nanobiosensor and without Nanobiosensor ......................................................... 46
Table 2.5: Comparison of the analytical performance for nanobiosensor and without nanobiosensor ................................................. 48
Table 2.6: Statistical Comparison between two methods ............................... 49
Table 2.7: Wavenumbers (in cm⁻¹) of DNA, MTX and MTX-DNA interaction. 52
Table 3.1: Time dependent changes of Carboplatin-DNA interaction determined in solution (Without nanobiosensor) ......................... 66
Table 3.2: Time dependent changes of Carboplatin-DNA interaction performed by nanobiosensor ......................................................... 68
Table 3.3: Potential difference at various concentration series ....................... 71
Table 3.4: Comparison of the analytical parameters for nanobiosensor and without Nanobiosensor ......................................................... 71
Table 3.5: Comparison of the analytical performance for nanobiosensor and without nanobiosensor ......................................................... 73
Table 3.6: Statistical Comparison between two methods ............................... 74
Table 4.1: Comparison of the analytical performance for determination of MTX-DNA and paracetamol-DNA interaction for series 100 .......... 96
Table 5.1: Comparison of the analytical performance for determination of carboplatin-DNA and paracetamol-DNA interaction ................. 116
ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>AuNPs</td>
<td>Gold nanoparticles</td>
</tr>
<tr>
<td>DNA</td>
<td>Deoxyribonucleic acid</td>
</tr>
<tr>
<td>dsDNA</td>
<td>double stranded Deoxyribonucleic acid</td>
</tr>
<tr>
<td>EMF</td>
<td>Electromotive Force</td>
</tr>
<tr>
<td>FRET</td>
<td>Fluorescence Resonance Energy Transfer</td>
</tr>
<tr>
<td>FT-IR</td>
<td>Fourier-transformed Infrared</td>
</tr>
<tr>
<td>HCl</td>
<td>Hydrochloric acid</td>
</tr>
<tr>
<td>LOD</td>
<td>Limit of detection</td>
</tr>
<tr>
<td>LOQ</td>
<td>Limit of quantification</td>
</tr>
<tr>
<td>µg/mL</td>
<td>Microgram per millilitre</td>
</tr>
<tr>
<td>mV</td>
<td>Mili-Volt</td>
</tr>
<tr>
<td>MTX</td>
<td>Mitoxantrone</td>
</tr>
<tr>
<td>NH₄OH</td>
<td>Ammonium Hydroxide</td>
</tr>
<tr>
<td>ng/ml</td>
<td>nanogram per millilitre</td>
</tr>
<tr>
<td>Pt</td>
<td>Platinum</td>
</tr>
<tr>
<td>SEM</td>
<td>Scanning Electron Microscope</td>
</tr>
<tr>
<td>SiO₂</td>
<td>Silicon dioxide</td>
</tr>
<tr>
<td>TEOS</td>
<td>Tetraethylorthosilicate</td>
</tr>
<tr>
<td>UV-visible</td>
<td>ultraviolet and visible</td>
</tr>
</tbody>
</table>