A BIOSPECTROSCOPIC AND BIOIMAGING ANALYSIS OF IMATINIB NANOPARTICLES AGGREGATION LINKED TO DNA/RNA BY BCR–ABL TYROSINE–KINASE INHIBITORS (TKI) WITH VARIOUS CHAIN LENGTH

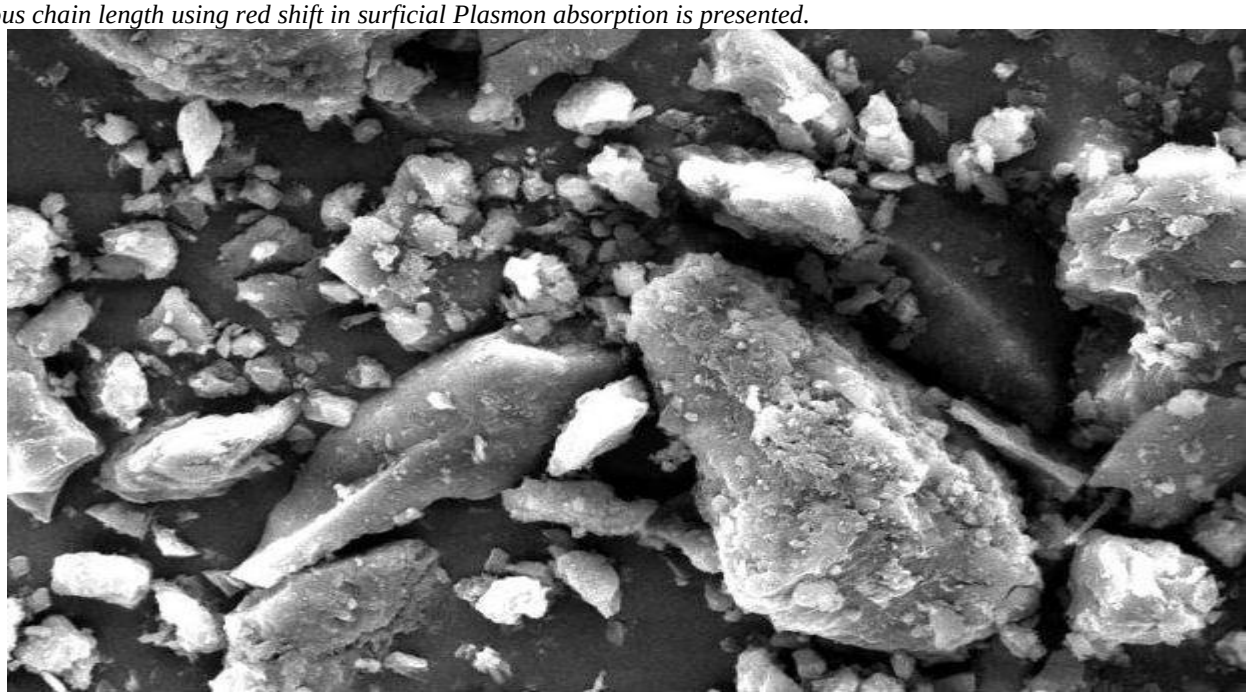
Alireza Heidari[1,2*]

[1]Faculty of Chemistry, California South University, 14731 Comet St. Irvine, CA 92604, USA

[2]American International Standards Institute, Irvine, CA 3800, USA

*Corresponding Author E–Mail Addresses: Scholar.Researcher.Scientist@gmail.com; Alireza.Heidari@calsu.us; Central@aisi-usa.org

GRAPHICAL ABSTRACT : *Imatinib nanoparticles show a strong peak of Plasmon absorption in ultraviolet–visible zone. A strong interaction exists between the surface of Imatinib nanoparticles and different Bcr–Abl tyrosine–kinase inhibitors (TKI) compounds.Different Bcr–Abl tyrosine–kinase inhibitors (TKI) compounds cause to aggregation of Imatinib nanoparticles linked to DNA/RNA and hence, lead to widening of peak Plasmon of Imatinib nanoparticles surface at 760 (nm) and emerging a new peak at higher wavelengths. In the current project, this optical characteristic of Imatinib nanoparticles is used to time investigate of interaction between different Bcr–Abl tyrosine–kinase inhibitors (TKI) and Imatinib nanoparticles. The results were shown that different Bcr–Abl tyrosine–kinase inhibitors (TKI) compounds with shorter chain length interact faster with Imatinib nanoparticles. Therefore, a simple and fast method for identification of Bcr–Abl tyrosine–kinase inhibitors (TKI) with various chain length using red shift in surficial Plasmon absorption is presented.*



Scanning Electron Microscope (SEM) image of Imatinib nanoparticles with 50000x zoom.

Keywords*:* Bcr–Abl Tyrosine–Kinase Inhibitors (TKI), Peak Plasmon Absorption, Aggregation, Imatinib Nanoparticles, DNA/RNA

1. INTRODUCTION

Investigations about Imatinib nanoparticles are widely developed due to their considerable optical characteristics and potential application in optical devices, sensors and optical circuits specially in diagnostic and treating medical sciences [1–20]. Imatinib nanoparticles show a strong absorption peak in ultraviolet–visible zone when interact with light. The maximum position of the spectrum depends on size, form, inter–particle space and de–electric environment of nanoparticles [21–39].

There is a high affinity between Bcr–Abl tyrosine–kinase inhibitors (TKI) groups and Imatinib nanoparticles which leads to aggregation of Imatinib nanoparticles linked to DNA/RNA. As a result of this aggregation, the Plasmon absorption peak of Imatinib nanoparticles widens at 760 (nm) and a new peak emerges at higher wavelengths. Numerous researches have been performed about Imatinib nanoparticles aggregation linked to DNA/RNA and application of this characteristic of Imatinib nanoparticles for identification of target analytes and producing sensors [40–63]. In a research, chemical absorption of Bcr–Abl tyrosine–kinase inhibitors (TKI) on Imatinib colloid at the presence of sodium hydroxide was investigated; the results were shown that the largeness of these changes depends on pH, chain length and the end of Bcr–Abl tyrosine–kinase inhibitors (TKI) chain [64–85]. At another research, the effectiveness factors in controlling the optical characteristics of Imatinib nanoparticles aggregation linked to DNA/RNA including oligonucleotides linked with various lengths (72–24 pairs) were studied. This test was shown that optical characteristics of DNA/RNA aggregation linked to Imatinib nanoparticles are controlled with size of aggregation and ignoring the chain

length of oligonucleotides which is important for colorimetric identification based on nanoparticle, it was shown that optical effects are more dependent to size of aggregation which in turn, it is under kinetic control [86–99]. The rate of band change of surface Plasmon is conversely related to the length of DNA/RNA connections so that 24 chains systems (shortest) have shown the highest change in rate [100–111].

Bcr–Abl tyrosine–kinase inhibitors (TKI) are important compounds in chemical synthesizes, environment, gas and petrochemical industries and biology [112–129]. In the current research, optical characteristic of Imatinib nanoparticles is used for time identification of Bcr–Abl tyrosine–kinase inhibitors (TKI) with various chain lengths. In previously used methods for identification of Bcr–Abl tyrosine–kinase inhibitors (TKI) in petrochemical and oil industry, only total Bcr–Abl tyrosine–kinase inhibitors (TKI) could be identified; however, the current method can identify Bcr–Abl tyrosine–kinase inhibitors (TKI) with various chain lengths which is very important for making sensors of these compounds [130–163].

2. MATERIALS AND EXPERIMENTAL METHODOLOGY AND TECHNIQUES

2.1. Preparing Imatinib Nanoparticles and Description of Imatinib Nanoparticles Aggregation Linked to DNA/RNA

All glass wares used in this test were washed with a solution of HCl: HNO_3 with concentration ratio of 3:1 and then, with deionized water and acetone and afterwards, dried in air. In this project, Terkovic method was used for synthesizing the Imatinib nanoparticles. A 0.05 (gr) of hydrogen tetra coloro–urate ($HCdCl_4$, $3H_2O$) was solved in 100 (ml) of water and then, was indirectly heated under 150 ° C temperature and stirring rate of 500 (rpm) in a balloon connected to a cooler. When Imatinib solution was boiled, 2.5 (ml) solution of sodium citrate of 0.05 (M) was added and the colloidal solution of Imatinib was gradually produced with reduction of Imatinib ions (III). The color of initial solution was mellow yellow. The color of this solution was gradually changed to blue, violet and dark red. At the end of test, the color was dark red. The size of produced nanoparticles was 25 (nm). The size of Imatinib nanoparticles was determined by DLS. In order to timely investigate the interaction of Imatinib nanoparticles, Bcr–Abl tyrosine–kinase inhibitors (TKI) with various lengths were added to Imatinib nanoparticles at room temperature [164–227].

3. RESULTS AND DISCUSSION

The absorption spectrum of Imatinib nanoparticles was recorded in various times with Bcr–Abl tyrosine–kinase inhibitors (TKI) with various chain lengths as shown in Figures (1), (2) and (3). As can be seen in these figures, peak is decreased at 573 (nm) and a new peak is emerging at higher wavelength which gradually increased with time and after reaching to the maximum, the absorption decreases, which is due to complete aggregation linked to DNA/RNA and instability of the produced Imatinib nanoparticles [228–272].

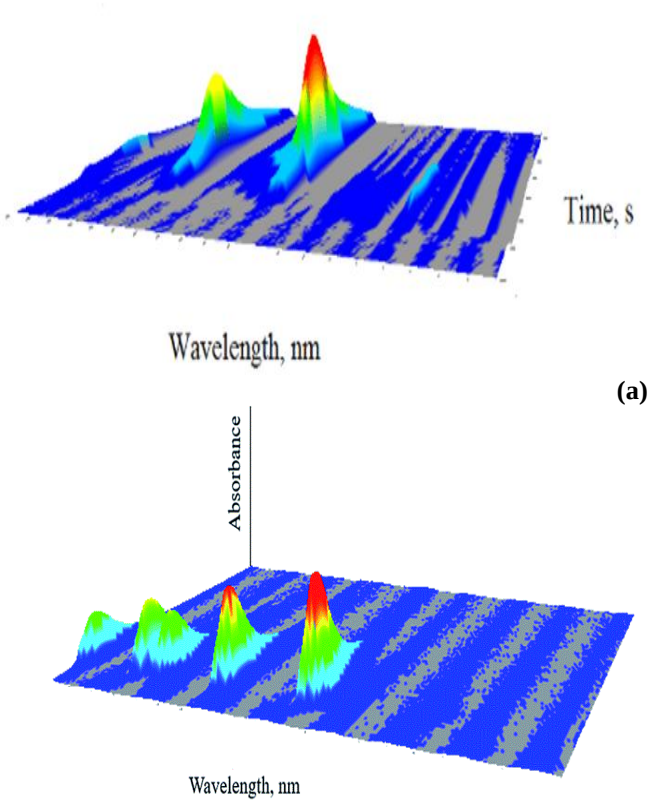


Figure (1): (a) Absorption spectrum of Imatinib nanoparticles–Bcr–Abl tyrosine–kinase inhibitors (TKI) during 0–1200 (s). (b) Absorption curve against time for Imatinib nanoparticles– Bcr–Abl tyrosine–kinase inhibitors (TKI) at maximum wavelength.

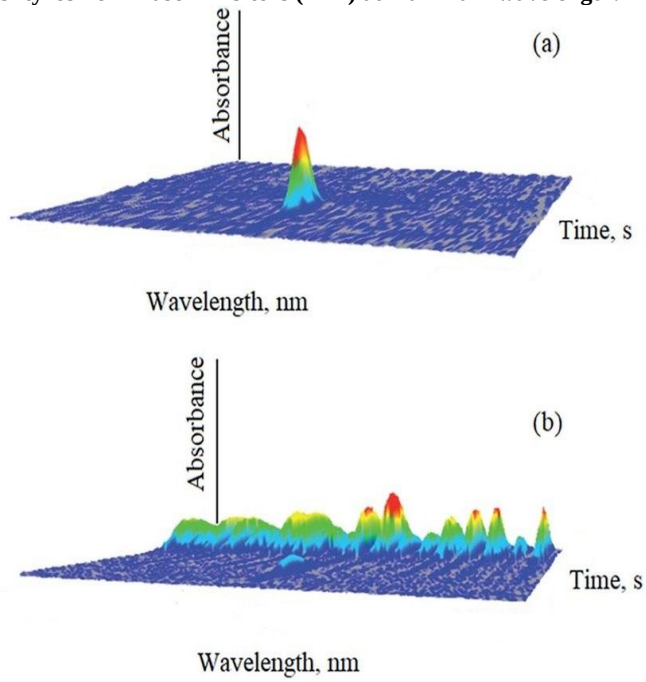


Figure (2): (a) Absorption spectrum of Imatinib nanoparticles–Bcr–Abl tyrosine–kinase inhibitors (TKI) during 0–1200 (s). (b) Absorption curve against time for Imatinib nanoparticles– Bcr–Abl tyrosine–kinase inhibitors (TKI) at maximum

wavelength.

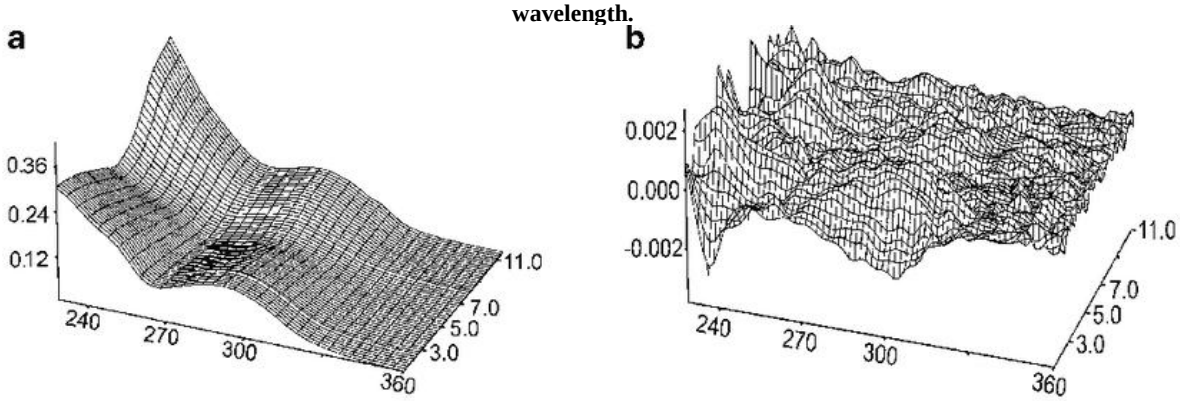


Figure (3): (a) Absorption spectrum of Imatinib nanoparticles–Bcr–Abl tyrosine–kinase inhibitors (TKI) during 0–1200 (s). (b) Absorption curve against time for Imatinib nanoparticles– Bcr–Abl tyrosine–kinase inhibitors (TKI) at maximum wavelength.

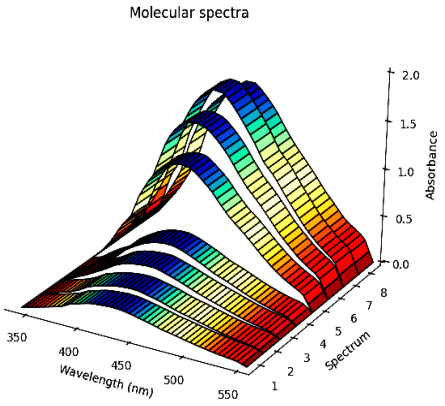


Figure (4): Absorption spectra of Imatinib nanoparticles with various Bcr–Abl tyrosine–kinase inhibitors (TKI) during 90 (s) (concentration of CdNPs is equal to 250 ppm and 2.5 ml used, Bcr–Abl tyrosine–kinase inhibitors (TKI) 60 nmol, Bcr–Abl tyrosine–kinase inhibitors (TKI) 45.5 nmol and Bcr–Abl tyrosine–kinase inhibitors (TKI) 55.5 nmol).

The results show that Bcr–Abl tyrosine–kinase inhibitors (TKI) with shorter chain length lead to faster aggregation of Imatinib nanoparticles linked to DNA/RNA than ones with longer chain length. In other words, at a shorter time, Imatinib nanoparticles is aggregated with Bcr–Abl tyrosine–kinase inhibitors (TKI) with shorter chain length at higher wavelength compared to the absorption spectrum of Imatinib nanoparticles aggregated with Bcr–Abl tyrosine–kinase inhibitors (TKI) chains with longer chain length. As can be seen in Figure (4), during 90 (s), Bcr–Abl tyrosine–kinase inhibitors (TKI) is emerged at higher wavelength (812.49 nm) than phenyl (777.91 nm) and Bcr–Abl tyrosine–kinase inhibitors (TKI) (a wide peak between 500–760 nm) and hence, Bcr–Abl tyrosine–kinase inhibitors (TKI) chains with various chain length can be identified through controlling the aggregation time [273–303].

4. CONCLUSION

In the current study, the optical characteristics of peal Plasmon of absorption of Imatinib nanoparticles were used to identify Bcr–Abl tyrosine–kinase inhibitors (TKI) with various chain lengths and through time controlling, they were identified successfully. It was observed that the second peak at wavelength between 500–760 (nm) induced by interaction of Bcr–Abl tyrosine–kinase inhibitors (TKI) with Imatinib nanoparticles in Bcr–Abl tyrosine–kinase inhibitors (TKI) with shorter chain length at shorter time duration observe at higher wavelength than Bcr–Abl tyrosine–kinase inhibitors (TKI) with longer wavelength.

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