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Recent New Results and Achievements of California South University (CSU) BioSpectroscopy Core Research Laboratory for COVID-19 or 2019-nCoV Treatment: Diagnosis and Treatment Methodologies of *"Coronavirus"*

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Abstract

Coronavirus nanoparticles show a strong peak of Plasmon absorption in ultraviolet–visible zone. A strong interaction exists between the surface of ***Coronavirus*** nanoparticles and Bcr–Abl tyrosine–kinase inhibitors (TKI) such as Imatinib (STI571), Nilotinib (AMN107), Dasatinib (BMS–345825), Bosutinib (SKI–606), Ponatinib (AP–24534) and Bafetinib (INNO–406). Bcr–Abl tyrosine–kinase inhibitors (TKI) such as Imatinib (STI571), Nilotinib (AMN107), Dasatinib (BMS–345825), Bosutinib (SKI–606), Ponatinib (AP–24534) and Bafetinib (INNO–406) cause to aggregation of ***Coronavirus*** nanoparticles linked to DNA/RNA and hence, lead to widening of peak Plasmon of ***Coronavirus*** nanoparticles surface at 550 (nm) and emerging a new peak at higher wavelength. In the current project, this optical characteristic of ***Coronavirus*** nanoparticles is used to time investigate of interaction between different Bcr–Abl tyrosine–kinase inhibitors (TKI) such as Imatinib (STI571), Nilotinib (AMN107), Dasatinib (BMS–345825), Bosutinib (SKI–606), Ponatinib (AP–24534) and Bafetinib (INNO–406) and ***Coronavirus*** nanoparticles. The results were shown that Bcr–Abl tyrosine–kinase inhibitors (TKI) such as Imatinib (STI571), Nilotinib (AMN107), Dasatinib (BMS–345825), Bosutinib (SKI–606), Ponatinib (AP–24534) and Bafetinib (INNO–406) with shorter chain length interact faster with ***Coronavirus*** nanoparticles. Therefore, a simple and fast method for identification of Bcr–Abl tyrosine–kinase inhibitors (TKI) such as Imatinib (STI571), Nilotinib (AMN107), Dasatinib (BMS–345825), Bosutinib (SKI–606), Ponatinib (AP–24534) and Bafetinib (INNO–406) with various chain length using red shift in surficial Plasmon absorption is presented.

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Keywords: Bcr–Abl Tyrosine–Kinase Inhibitors (TKI), Peak Plasmon Absorption, Aggregation, ***Coronavirus*** Nanoparticles, DNA/RNA, Imatinib (STI571), Nilotinib (AMN107), Dasatinib (BMS–345825), Bosutinib (SKI–606), Ponatinib (AP–24534), Bafetinib (INNO–406)

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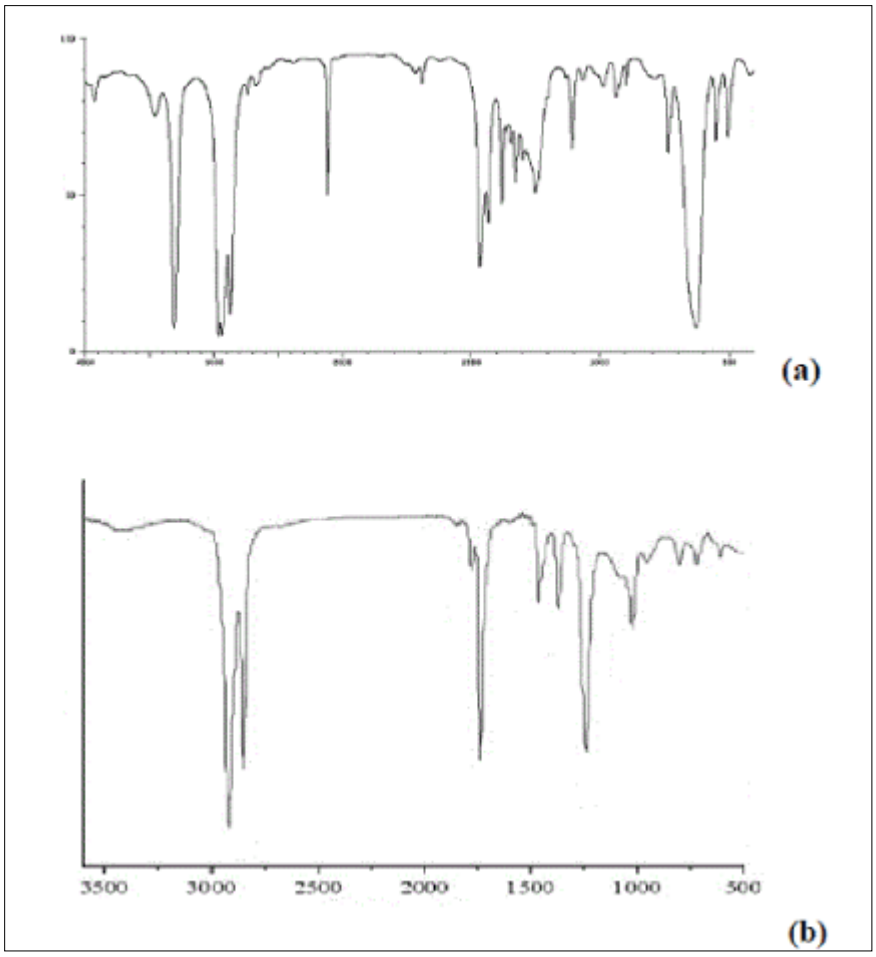
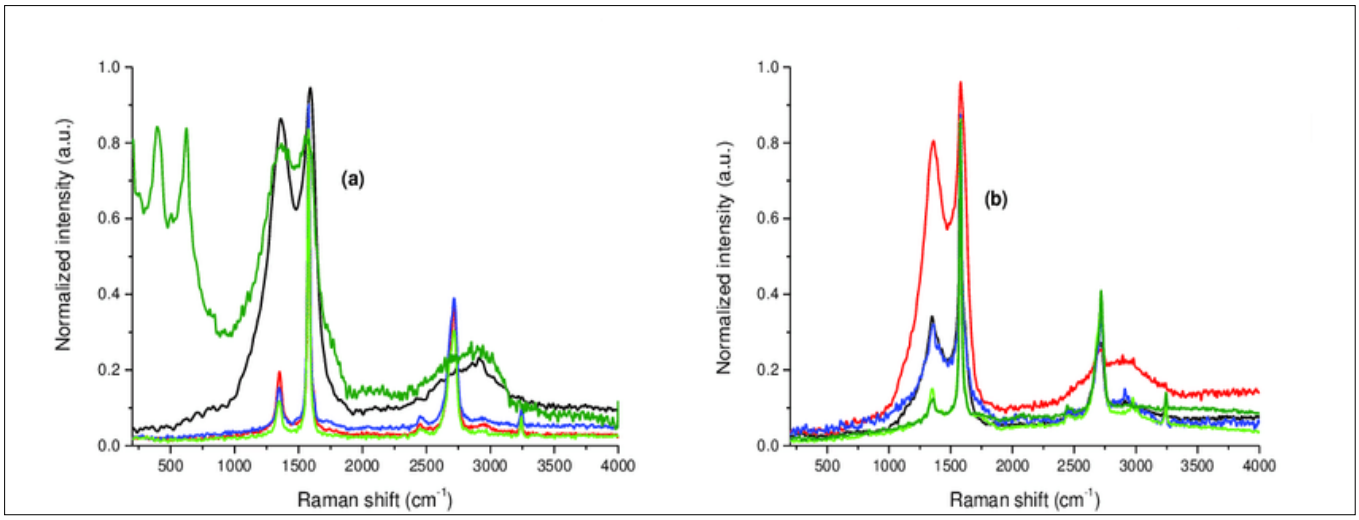
Concise Biography of Research Group Leader and Director of the Bio Spectroscopy Core Research Laboratory

Prof. Dr. Alireza Heidari, Ph.D., D.Sc. is a Full Distinguished Professor and Academic Tenure of Chemistry and also Enrico Fermi Distinguished Chair in Molecular Spectroscopy at California South University (CSU), Irvine, California, USA. He has got his Ph.D. and D.Sc. degrees from California South University (CSU), Irvine, California, USA. Furthermore, he has double postdocs in Project Management, Oncology, Human Cancer Tissues and Synchrotron Radiation from Monash University, Melbourne, Victoria, Australia and also in Nanochemistry and Modern Molecular Electronic–Structure Computations Theory from California South University (CSU), Irvine, California, USA. His research interests include Biophysical Chemistry, Biomolecular Spectroscopy, Quantum Chemistry, Nanochemistry, Modern Electronic Structure Computations, Theoretical Chemistry, Mathematical Chemistry, Computational Chemistry, Vibrational Spectroscopy, Molecular Modelling, Ab initio & Density Functional Methods, Molecular Structure, Biochemistry, Molecular Simulation, Pharmaceutical Chemistry, Medicinal Chemistry, Oncology, Synchrotron Radiation, Synchrocyclotron Radiation, LASER, Anti–Cancer Nano Drugs, Nano Drugs Delivery, ATR–FTIR Spectroscopy, Raman Spectroscopy, Intelligent Molecules, Molecular Dynamics, Biosensors, Biomarkers, Molecular Diagnostics, Numerical Chemistry, Nucleic Acids, DNA/RNA Monitoring, DNA/RNA Hypermethylation & Hypomethylation, Human Cancer Tissues, Human Cancer Cells, Tumors, Cancer Tissues, Cancer Cells, etc. He has participated at more than five hundred reputed international conferences, seminars, congresses, symposiums and forums around the world as yet. Also, he possesses many published articles in Science Citation Index (SCI)/ International Scientific Indexing (ISI), Medline/PubMed and Scopus Journals. It should be noted that he has visited many universities or scientific and academic research institutes in different countries such as United States, United Kingdom, Canada, Australia, New Zealand, Scotland, Ireland, Netherlands, Belgium, Denmark, Luxembourg, Romania, Greece, Russia, Estonia, Ukraine, Turkey, France, Swiss, Germany, Sweden, Norway, Italy, Austria, Czech Republic, Hungary, Poland, South Africa, Egypt, Brazil, Spain, Portugal, Mexico, Japan, Singapore, Malaysia, Indonesia, Thailand, Taiwan, Hong Kong, South Korea, China, India, Kingdom of Saudi Arabia, Jordan, Qatar, United Arab Emirates, etc. as research fellow, sabbatical and volunteer researcher or visitor and so on heretofore. He has a history of several years of teaching for college students and various disciplines and trends in different universities. Moreover, he has been a senior advisor in various industry and factories. He is expert in many computer programs and programming languages. Hitherto, he has authored more than twenty books and book chapters in different fields of Chemistry. Syne, he has been awarded more than one thousand reputed international awards, prizes, scholarships and honors. Heretofore, he has multiple editorial duties in many reputed international and peer–reviewed journals, books and publishers. Hitherward, he is a member of more than five hundred reputed international academic–scientific–research institutes around the world. It should be noted that he is currently the President of American International Standards Institute (AISI), Irvine, California, USA and also Director of the BioSpectroscopy Core Research Laboratory at California South University (CSU), Irvine, California, USA.



The Attenuated Total Reflectance–Fourier Transform Infrared (ATR–FTIR) spectra of DNA/RNA (a) before and (b) after aggregation linked to *Coronavirus* Nanoparticles.



Fourier Transform Raman (FT–Raman) spectra of DNA/RNA during hydration to dehydration transition (a) before and (b) after aggregation linked to *Coronavirus* Nanoparticles.

Introduction

Investigations about *Coronavirus* 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 [1–11]. *Coronavirus* nanoparticles show a strong absorption peak in ultraviolet–visible zone when interact with light. The maximum position of spectrum depends on size, form, inter–particle space and de–electric environment of nanoparticles [12–21].

There is a high affinity between Bcr–Abl tyrosine–kinase inhibitors (TKI) groups and *Coronavirus* nanoparticles which leads to aggregation of *Coronavirus* nanoparticles linked to DNA/RNA. As a result of this aggregation, the Plasmon absorption peak of *Coronavirus* nanoparticles widen at 550 (nm) and a new peak emerges at higher wavelength. Numerous researches have been performed about *Coronavirus* nanoparticles aggregation linked to DNA/RNA and application of this characteristic of *Coronavirus* nanoparticles for identification of target analytes and producing sensors [22–39]. In a research, chemical absorption of Bcr–Abl tyrosine–kinase inhibitors (TKI) such as Imatinib (STI571), Nilotinib (AMN107), Dasatinib (BMS–345825), Bosutinib (SKI–606), Ponatinib (AP–24534) and Bafetinib (INNO–406) on *Coronavirus* 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) such as Imatinib (STI571), Nilotinib (AMN107), Dasatinib (BMS–345825), Bosutinib (SKI–606), Ponatinib (AP–24534) and Bafetinib(INNO–406) chains [40–56]. At another research, the effective factors on controlling the optical characteristics of *Coronavirus* 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 *Coronavirus* 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 [57–69]. 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 [70–81].

Bcr–Abl tyrosine–kinase inhibitors (TKI) are important compounds in chemical synthesizes, environment, gas and petrochemical industries and biology [82–99]. In the current research, optical characteristic of *Coronavirus* nanoparticles is used to time identification of Bcr–Abl tyrosine–kinase inhibitors (TKI) such as Imatinib (STI571), Nilotinib (AMN107), Dasatinib (BMS–345825), Bosutinib (SKI–606), Ponatinib (AP–24534) and Bafetinib (INNO–406) with various chain length. 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 [100–163].

Materials and Experimental Methodology and Techniques

Preparing Coronavirus Nanoparticles and Description of Coronavirus Nanoparticles Aggregation Linked to DNA/RNA

All glass wears used in this test was 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 *Coronavirus* nanoparticles. A 0.05 (gr) of hydrogen tetra coloro–urate (H Bcr–Abl tyrosine–kinase inhibitors (TKI) Cl_4, $3H_2O$) was solved in 100 (ml) of water and then, was indirectly heated under 150 º C temperature and stirring rate of 500 (rpm) in a balloon connected to a cooler. When *Coronavirus* solution was boiled, 2.5 (ml) solution of sodium citrate of 0.05 (M) was added and the colloidal solution of *Coronavirus* was gradually produced with reduction of *Coronavirus* 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 *Coronavirus* nanoparticles was determined by DLS. In order to time

investigate the interaction of *Coronavirus* nanoparticles, Bcr–Abl tyrosine–kinase inhibitors (TKI) such as Imatinib (STI571), Nilotinib (AMN107), Dasatinib (BMS–345825), Bosutinib (SKI–606), Ponatinib (AP–24534) and Bafetinib (INNO–406) with various lengths were added to *Coronavirus* nanoparticles at room temperature [164–256].

Discovery, Synthesis, Molecular Structure, Characteristics, Generation, Development and Resistance Anti–Coronavirus Drugs

Imatinib remains a standard frontline Bcr–Abl tyrosine–kinase inhibitors (TKI) such as Imatinib (STI571), Nilotinib (AMN107), Dasatinib (BMS–345825), Bosutinib (SKI–606), Ponatinib (AP–24534) and Bafetinib (INNO–406). Nilotinib and dasatinib are also approved by the FDA as frontline drugs, in June and October 2010, respectively (Figures 1–9). Four of these drugs, nilotinib, dasatinib, bosutinib and ponatinib are approved for the treatment of imatinib–resistant or intolerant CML. The first–line data for these compounds are encouraging and suggest that some or all of them may replace imatinib as a frontline standard Bcr–Abl tyrosine–kinase inhibitors (TKI) such as Imatinib (STI571), Nilotinib (AMN107), Dasatinib (BMS–345825), Bosutinib (SKI–606), Ponatinib (AP–24534) and Bafetinib (INNO–406) in the future (Table 1) [257–348]. Figures (1-9)

Results and Discussion

The absorption spectrum of *Coronavirus* nanoparticles was recorded in various times with Bcr–Abl tyrosine–kinase inhibitors (TKI) such as Imatinib (STI571), Nilotinib (AMN107), Dasatinib (BMS–345825), Bosutinib (SKI–606), Ponatinib (AP–24534) and Bafetinib (INNO–406) with various chain lengths as shown in Figures (10), (11) and (12). As can be seen in these figures, peak is decreased at 573 (nm) and a new peak is emerged 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 *Coronavirus* nanoparticles.

The results show that Bcr–Abl tyrosine–kinase inhibitors (TKI) such as Imatinib (STI571), Nilotinib (AMN107), Dasatinib (BMS–345825), Bosutinib (SKI–606), Ponatinib (AP–24534) and Bafetinib (INNO–406) with shorter chain length lead to faster aggregation of *Coronavirus* nanoparticles linked to DNA/RNA than ones with longer chain length. In other words, at shorter time, *Coronavirus* nanoparticles is aggregated with Bcr–Abl tyrosine–kinase inhibitors (TKI) such as Imatinib (STI571), Nilotinib (AMN107), Dasatinib (BMS–345825), Bosutinib (SKI–606), Ponatinib (AP–24534) and Bafetinib (INNO–406) with shorter chain length at higher wavelength compared to absorption spectrum of *Coronavirus* nanoparticles aggregated with Bcr–Abl tyrosine–kinase inhibitors (TKI) chains with longer chain length. As can be seen in Figure (13), during 90 (s), Bcr–Abl tyrosine–kinase inhibitors (TKI) 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.

The optical difference for aggregation of Bcr–Abl tyrosine–kinase inhibitors (TKI) such as Imatinib (STI571), Nilotinib (AMN107), Dasatinib (BMS–345825), Bosutinib (SKI–606), Ponatinib (AP–24534) and Bafetinib (INNO–406) connected to chains with various lengths to *Coronavirus* nanoparticles can be attributed to size of aggregation linked to DNA/RNA and inter–particle distance.

Conclusions, Useful Suggestions and Future Studies

In the current study, optical characteristics of peal Plasmon of absorption of *Coronavirus* nanoparticles was used to identify Bcr–Abl tyrosine–kinase inhibitors (TKI) with various chain length 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 *Coronavirus* nanoparticles in Bcr–Abl tyrosine–kinase inhibitors (TKI) such as Imatinib (STI571), Nilotinib (AMN107), Dasatinib (BMS–345825), Bosutinib (SKI–606), Ponatinib (AP–24534) and Bafetinib (INNO–406) with shorter chain length at shorter time duration observe at higher wavelength than Bcr–Abl tyrosine–kinase inhibitors (TKI) such as Imatinib (STI571), Nilotinib (AMN107), Dasatinib (BMS–345825), Bosutinib (SKI–606), Ponatinib

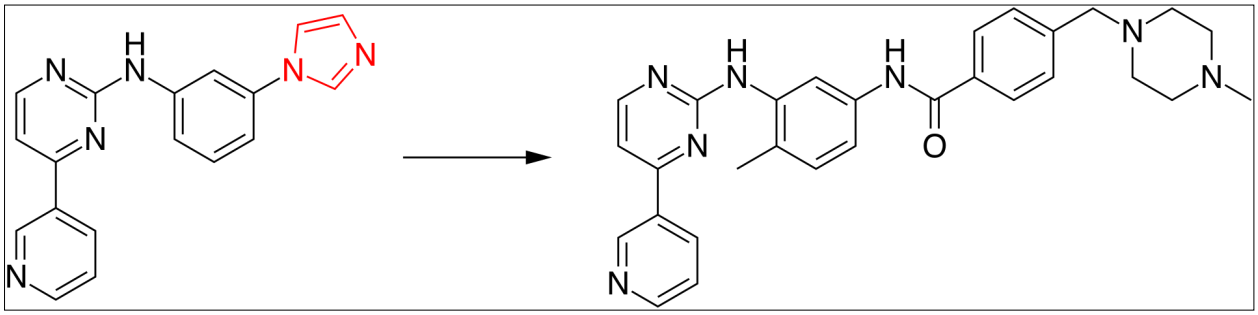


Figure 1. Evolution of Pyrimidin A to imatinib.

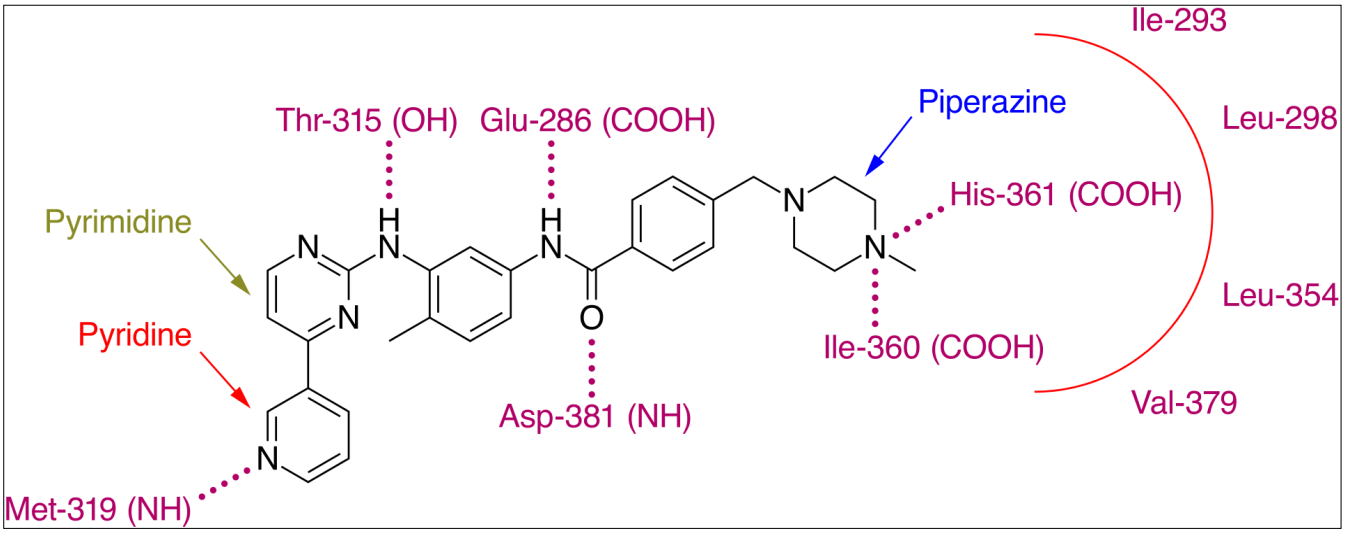


Figure 2. Imatinib in its binding site.

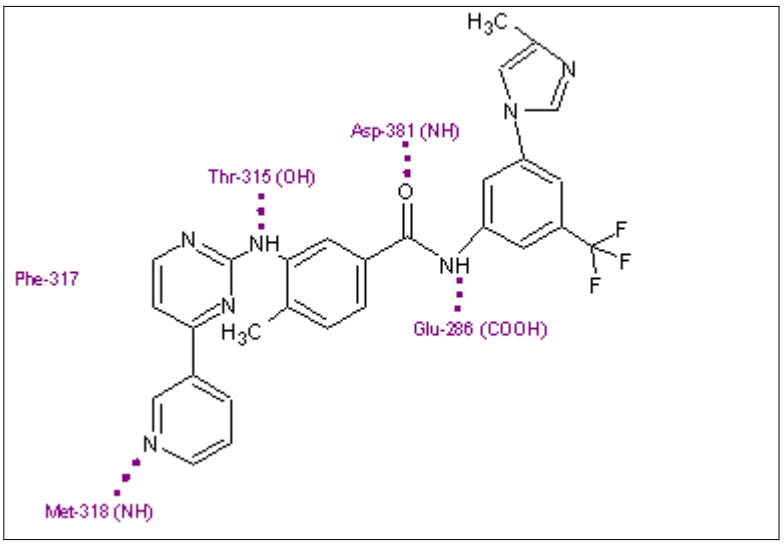


Figure 3. Nilotinib in its binding site.

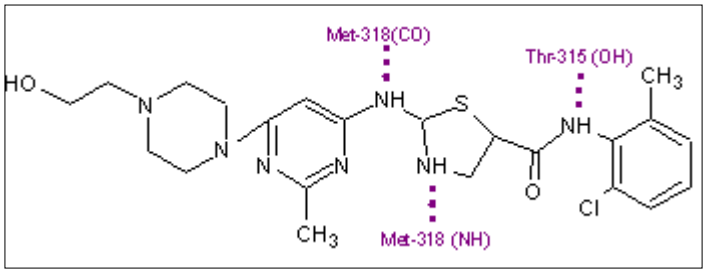


Figure 4. Dasatinib in its binding site.

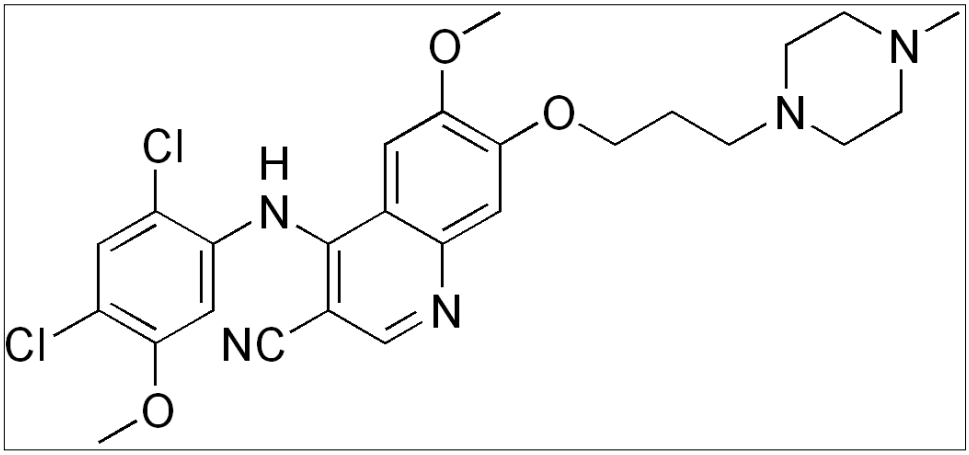
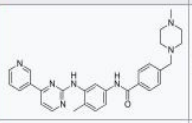
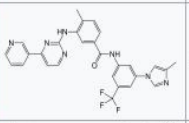
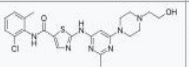
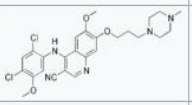
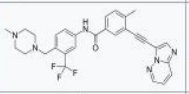
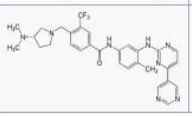


Figure 5. Bosutinib molecular structure.

Table 1. Bcr–Abl tyrosine–kinase inhibitors (TKI) characteristics.

Drug	Structure	H-bonds	H-bonding amino acids	Binding confirmation	Discovery	Status as of 2017
Imatinib (STI571)		6	Met-318, Thr-315, Glu-286, Asp-381, Ile-380, His-361	Inactive	Drug screening	Marketed as first line therapy
Nilotinib (AMN107)		4	Met-318, Thr-315, Glu-286, Asp-381	Inactive	Rational drug design	Marketed as second line therapy
Dasatinib (BMS-345825)		3	Met-318, Thr-315	Active	Rational drug design	Marketed as second line therapy
Bosutinib (SKI-606)		-	-	Inactive	Rational drug design	Marketed as second line therapy
Ponatinib (AP-24534)		5	Met-318, Asp-381, Glu-286, His-381, Ile-380	Inactive	Rational drug design	Marketed as second line therapy
Bafetinib (INNO-406)		6	Met-318, Thr-315, Glu-286, Asp-381, His-361, Ile-360	Inactive	Rational drug design	Marketed as second line therapy

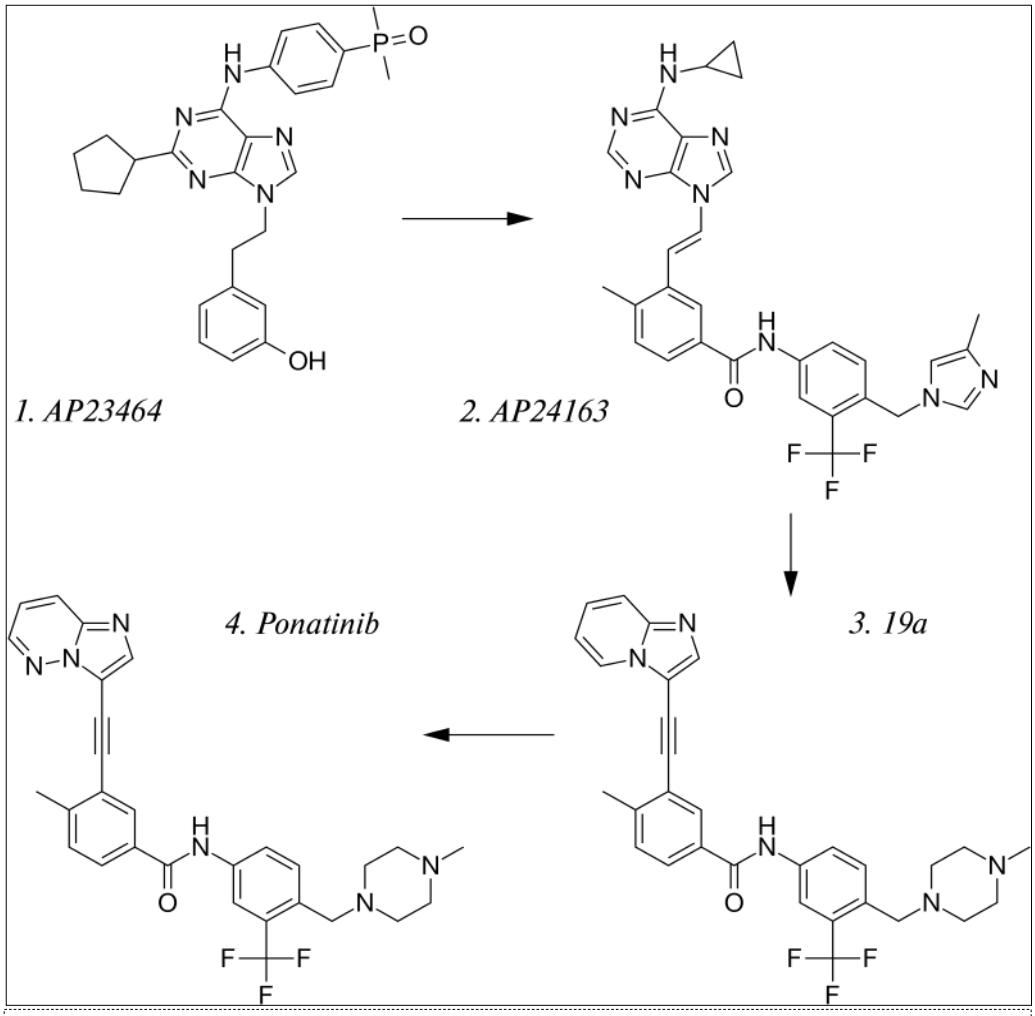


Figure 6. Ponatinib development history.

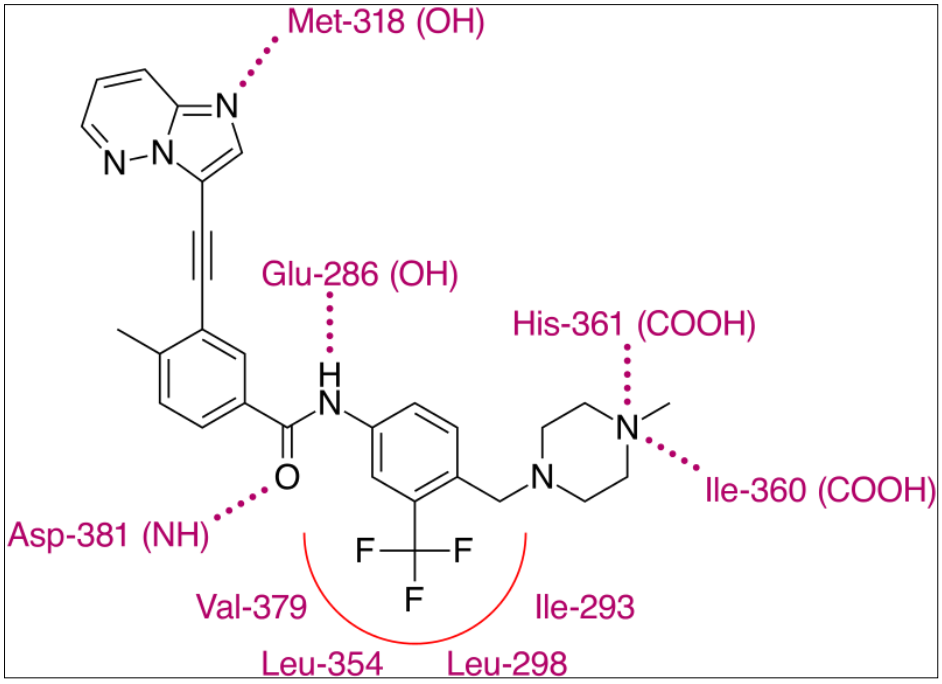


Figure 7. Ponatinib in its binding site.

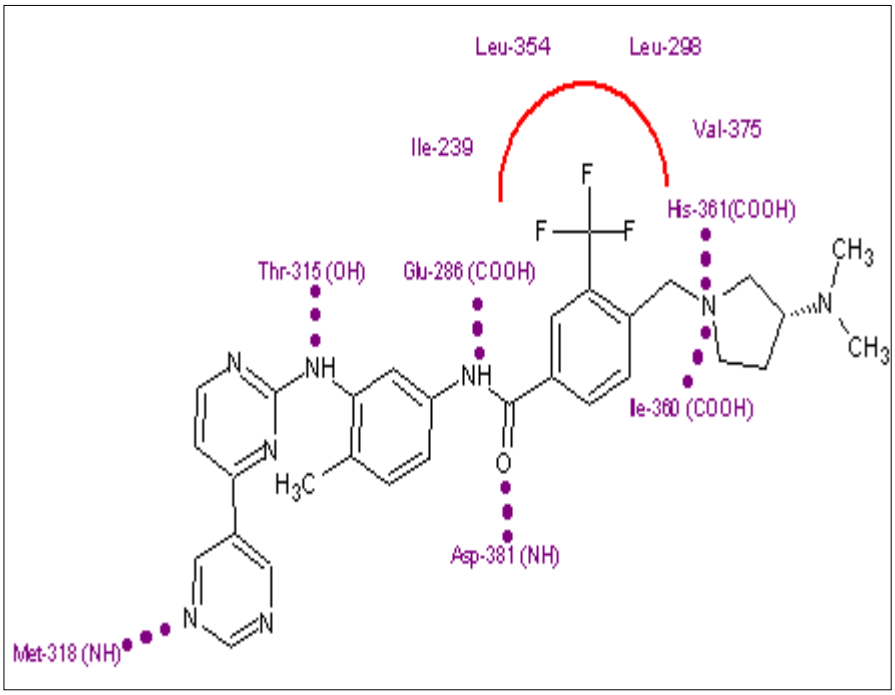


Figure 8. Bafetinib in its binding site.

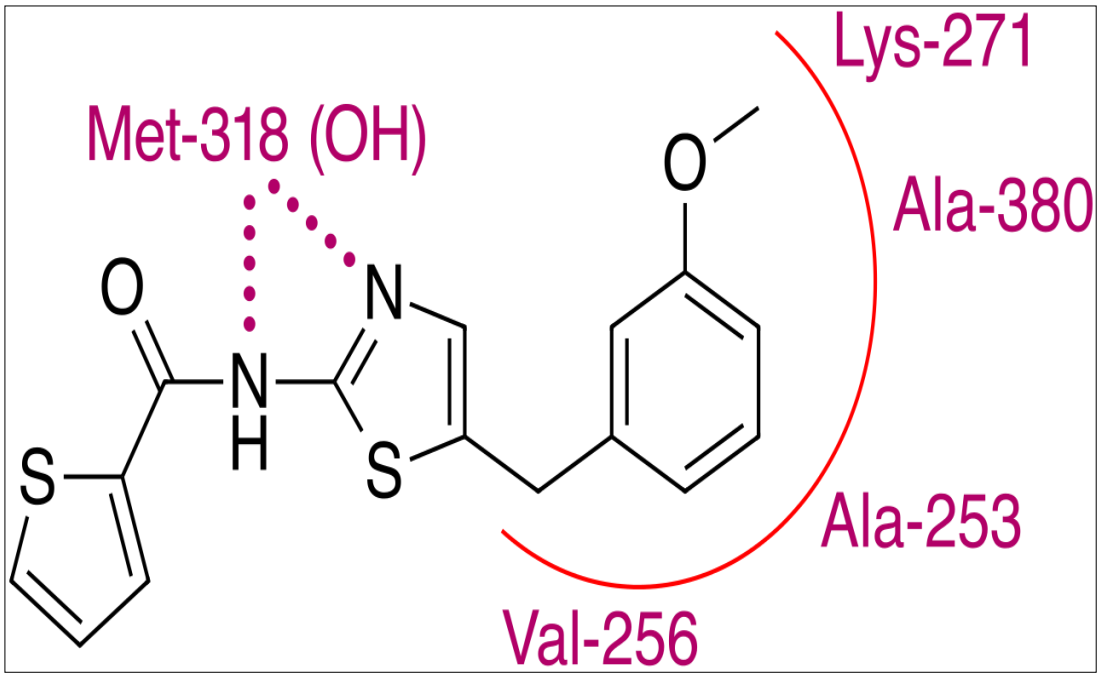
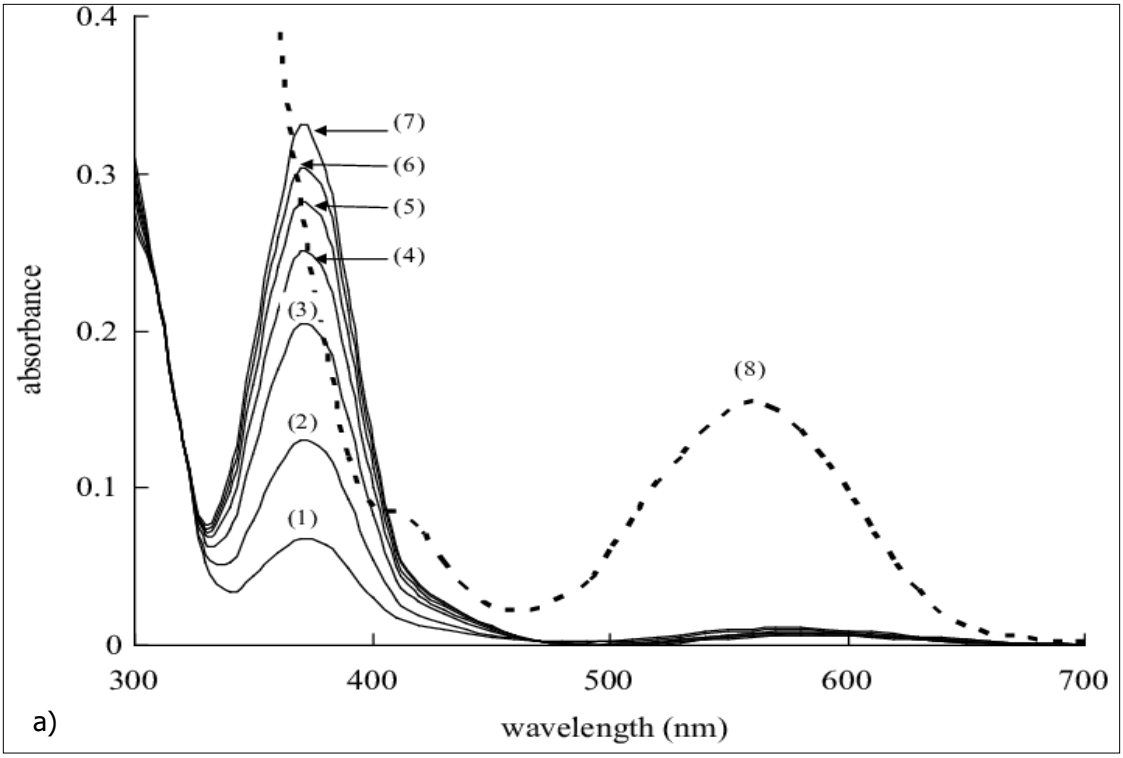


Figure 9. Proposed binding site interactions of substance.



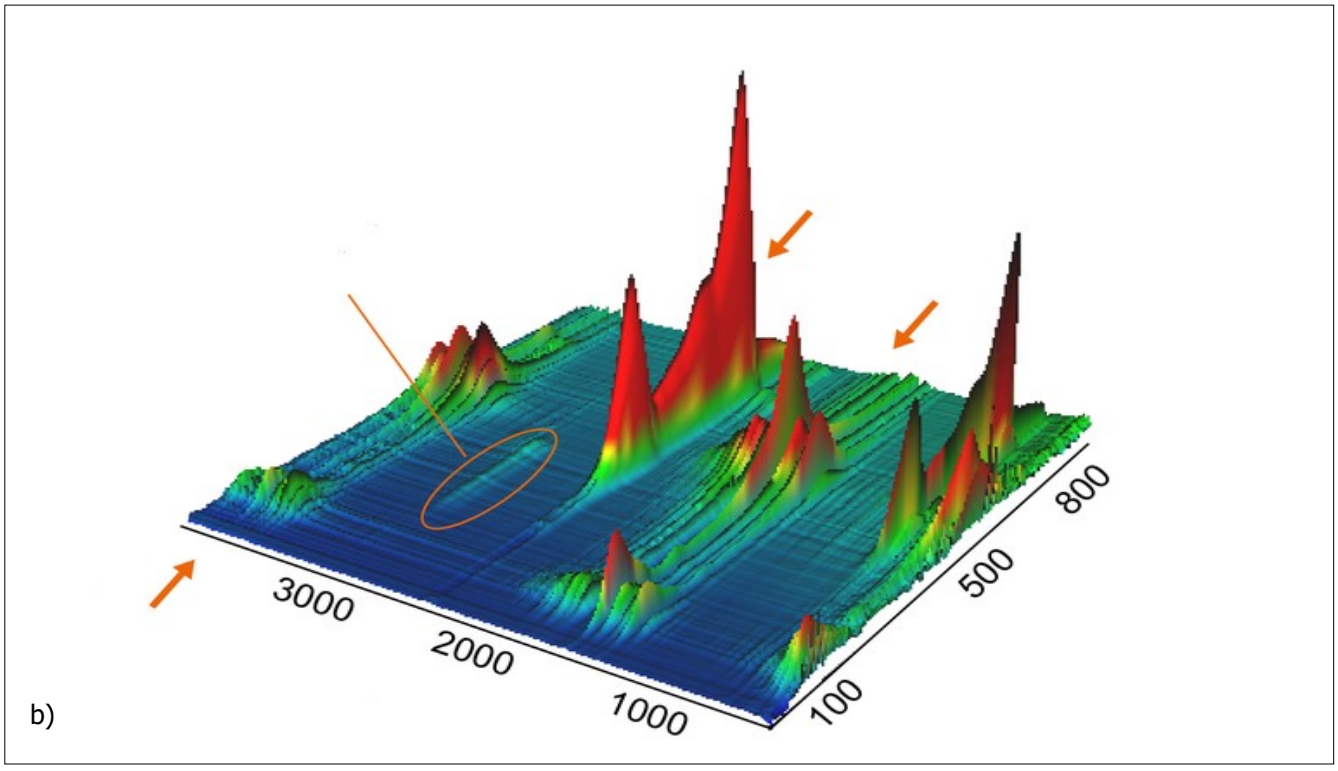


Figure 10. (a) Absorption spectrum of *Coronavirus* nanoparticles–Bcr–Abl tyrosine–kinase inhibitors (TKI) during 0–1200 (s). (b) Absorption curve against time for *Coronavirus* nanoparticles–Bcr–Abl tyrosine–kinase inhibitors (TKI) at maximum wavelength.

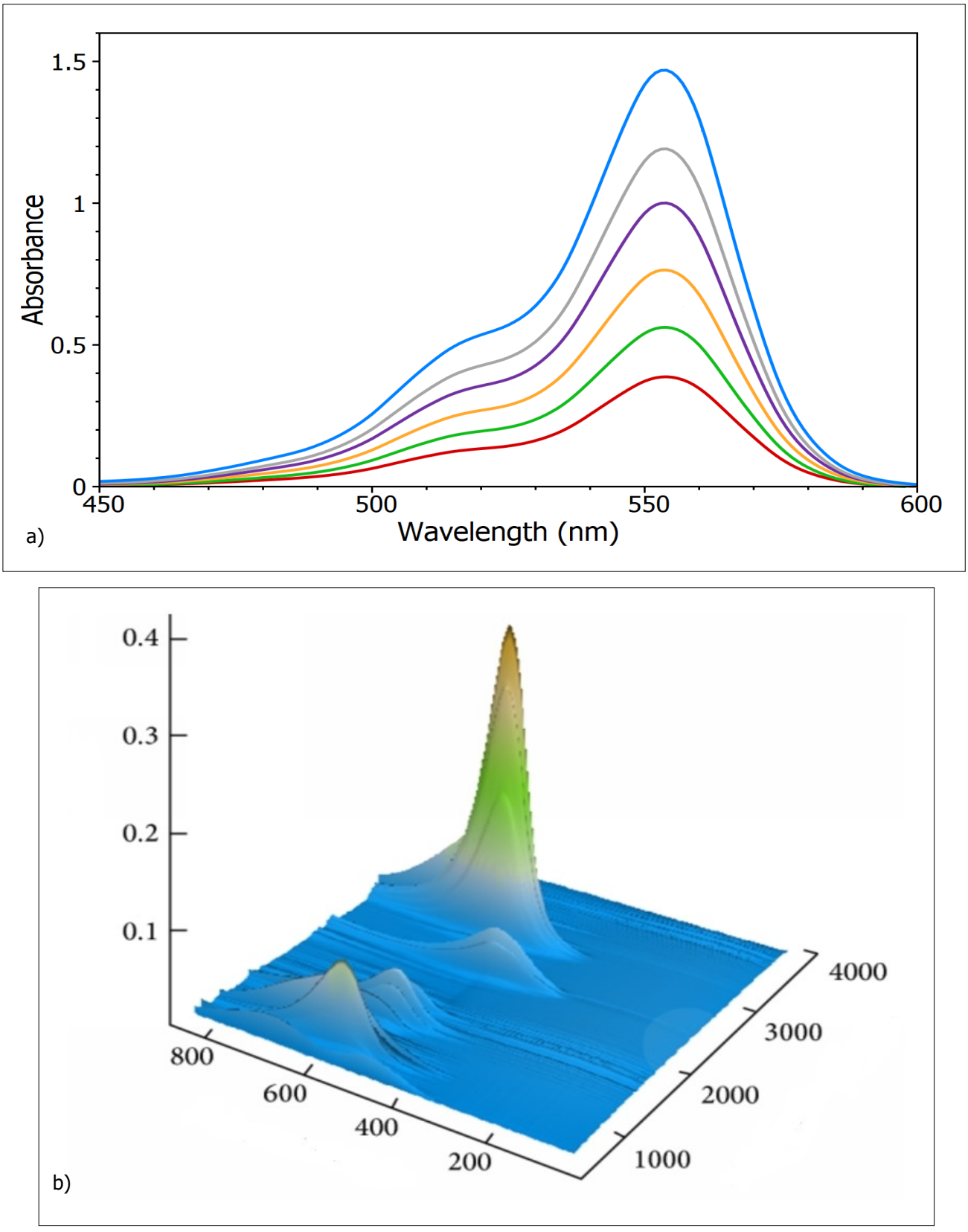
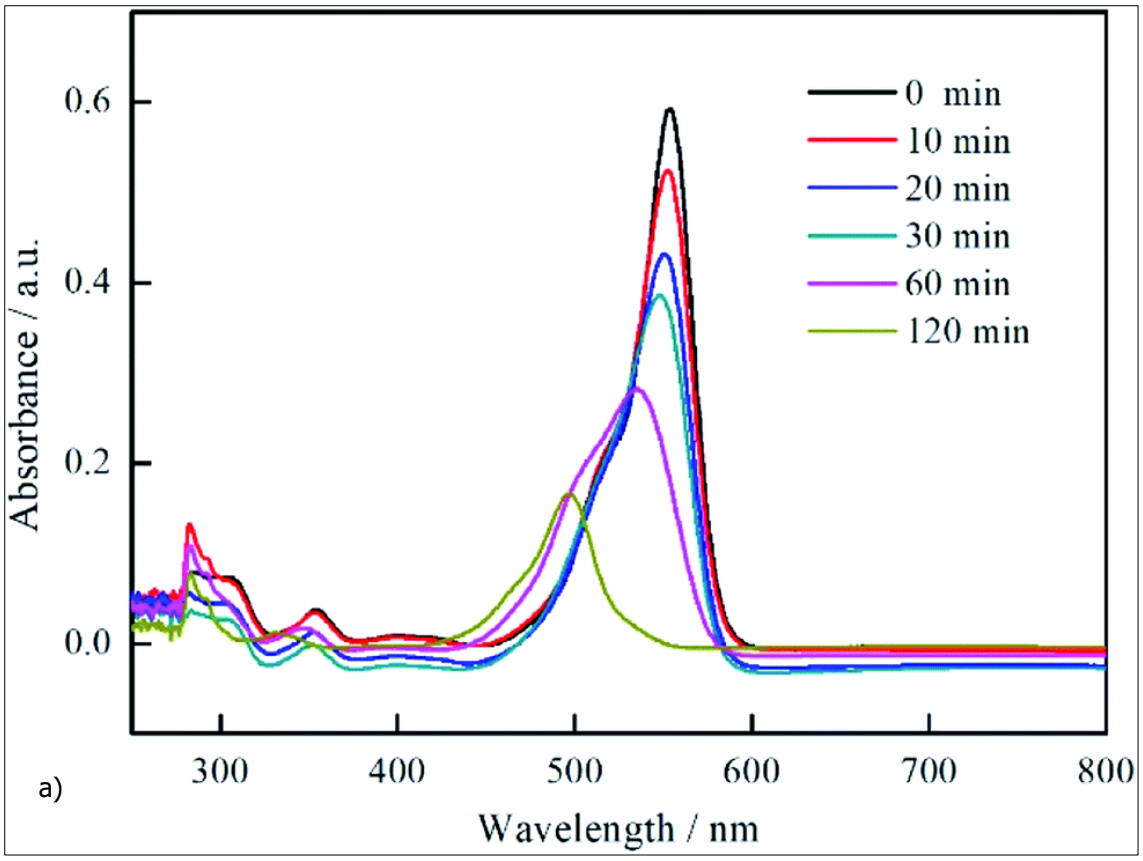


Figure 11. (a) Absorption spectrum of *Coronavirus* nanoparticles–Bcr–Abl tyrosine–kinase inhibitors (TKI) during 0–1200 (s). (b) Absorption curve against time for *Coronavirus* nanoparticles–Bcr–Abl tyrosine–kinase inhibitors (TKI) at maximum wavelength.



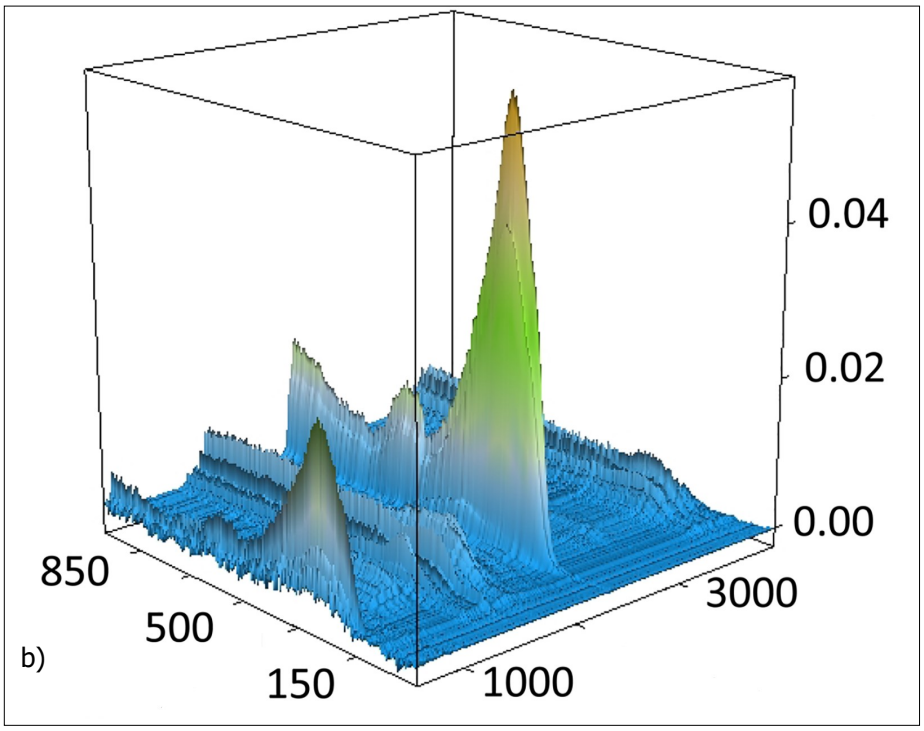


Figure 12. (a) Absorption spectrum of *Coronavirus* nanoparticles– Bcr–Abl tyrosine–kinase inhibitors (TKI) during 0–1200 (s). (b) Absorption curve against time for *Coronavirus* nanoparticles– Bcr–Abl tyrosine–kinase inhibitors (TKI) at maximum wavelength.

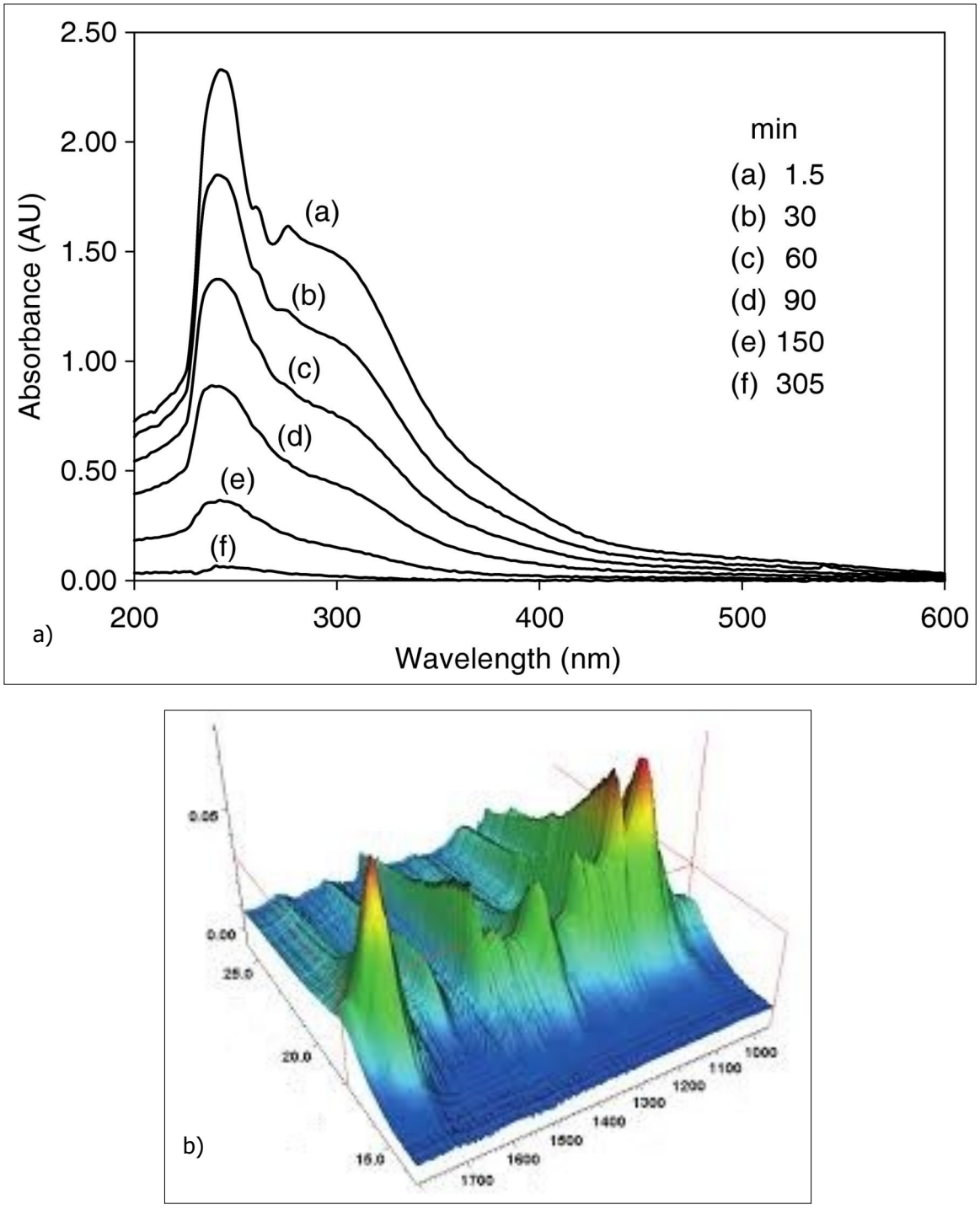


Figure 13. (a) Absorption spectrum of *Coronavirus* nanoparticles with various Bcr–Abl tyrosine–kinase inhibitors (TKI) such as Imatinib (STI571), Nilotinib (AMN107), Dasatinib (BMS–345825), Bosutinib (SKI–606), Ponatinib (AP–24534) and Bafetinib (INNO–406) during 90 (s) (concentration of Bcr–Abl tyrosine–kinase inhibitors (TKI) NPs 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). (b) Absorption curve against time for *Coronavirus* nanoparticles– Bcr–Abl tyrosine–kinase inhibitors (TKI) at optimum wavelength.

(AP–24534) and Bafetinib (INNO–406) with longer wavelength.

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