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Review Article

Medical Application of Graphene and its derivative

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ABSTRACT

Graphene is one of the most important compounds that possess a lot of very unique chemical properties. The importance of graphene and its diverse medical use in all directions has increased, making this matter the focus of attention and attention of scientists and medical specialists with regard to the early diagnosis of cancer and tumors, its clinical follow-up and treatment, especially in recent years. In this review, the medical and pharmacological applications and uses of graphene in the early diagnosis of different types of cancer and how to follow up on disease cases were discussed. The most important difficulties facing researchers in the applied medical field of graphene were also discussed. The important and exceptional feature of graphene composite was the influential point in the diversity of medical applications of graphene, including electronic superconductivity, very high surface area, thermal conductivity, mechanical strength, low economic cost, and possible development methods .A deep and comprehensive understanding of the interactions of graphene, which include organs and tissues, could lead to the production or formation of nano platforms such as graphene oxide that are more productive than graphene, Which has shown many important achievements regarding the applications of medical sensors that were in their initial stages.

Keywords: Drug delivery, graphene compound, medical application.

INTRODUCTION

The structure and engineering structure on the basis of two-dimensionality of the graphene compound made it one of the best composite composites for various uses in medical applications that owns sp_2 hybridization. Graphene possesses many unique thermal, mechanical, optical and electronic properties [1,2].

With the tremendous technological advances, the exceptional, excellent, and unique properties of graphene made it one of the best and most versatile compounds with various uses and applications [3], especially in the medical field. Many impressive achievements and results have been achieved [4], which include early detection of cancerous tumors, especially in its early stages, which are very difficult using traditional methods [5], and which also require uncomfortable uses for patients, such as the use of biopsy [6].

Modern design methods that depend on the formation and composition of superimposed sensors have the ability to achieve satisfactory results in medical applications [7]. Clinical applied studies and research have been conducted regarding the use of graphene and its compounds, especially graphene oxide is one of the best compounds in the field of drug delivery [8].The unique and pioneering qualities of these compounds, which include a very high surface area, strong mechanical and electronic properties, and strong durability, have made these compounds versatile in the medical field [9].

Advances in nanomaterial have received great value beside a major effect on sensers design technology due to the fascinating characteristic of nanostructure substances [10], that will be used in wide ranges of applications. The unique and unusual properties of graphene made it one of the most important compounds [11], used in the Medical field, which gives excellent results

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compared to others. The success and progress in this field has been the focus of attention and encouragement [12].

In the initial cases of the discovery of graphene and its derivatives, and because of the rare and unfamiliar features of this compound, such as the very high surface area, distinguished geometric structure, thermal, chemical and electronic properties, in addition to many other properties, these compounds made them the focus of attention and interests of many specialists in various medical applications.

Therefore, there is a need for a new approach that is consistent with the requirements of early detection through quick, sensitive and easy methods to apply towards reaching the point of correct diagnosis that helps to a very large extent in improving the clinical condition of the patient and reducing the economic burden caused by this pathology.

The results obtained using the proposed amperometric sensors depend on the composition: A mixture or mixture consisting of a graphite paste modified to use two active substances such as phthalo-cyanine-bodibe dye (Bodibe = boron dipyromethane) or olimide proves to be one of the best analytical results for the estimation of colon cancer biomarkers such as p53 (Figure 1) for a minimum detection limit of 3.8 femto- grams per ml, which is a very convenient and appropriate method for the initial diagnosis of colon tumors and cancer.

Biomedical analytical application and selectivity measurements, showed that the results obtained from the examinations demonstrated that the proposed sensor could be utilized to screen and estimate p53 from blood samples of patients with colon cancer. The accurate quantitative micro-assessment of vital indicators has taken a great deal of interest from scientists and researchers from all over the world because of its very great importance in the field of early detection of cancer, in addition to follow-up treatment as soon as possible, and accurate knowledge of any failures that the patient may experience, and most importantly, clinical follow-up of the patient.

Many scientists and international research centers have taken a great interest in estimating these vital indicators, for example, Zhang K [2] and Xuan Y [3]. They were concerned with the estimation process for these indicators, as well as Liu C [5] and Lu CH [6] and Qu LT [7] studied the effects of mutations caused by the action of these indicators, as well as Liu Z [8], Guo SJ [9], Hummers WS [10] studied the micro-estimation of cancer markers.But the method used for estimating vital signs and its more than excellent features and characteristics, especially compared with other methods.

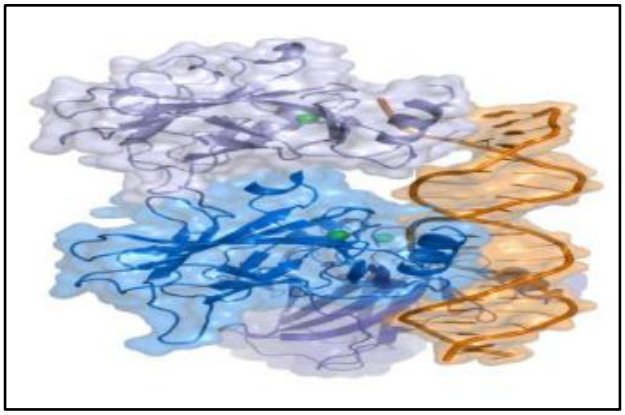

Figure 1. Structure of P53.

CANCER THERAPY

Drug Delivery

Graphene oxide is a compound produced by severe oxidation of graphene using Hammers method [13].The presence of some pioneering and unique qualities that include high surface area and mechanical and electronic strength have made some of the graphene derivatives, especially graphene oxide, one of the best means of transporting drugs [14], and the results in this field were impressive and wonderful.

In addition to the geometrical hybridization in the form of sp2 and by the chemical method called chemical coupling, the process of using nanocomposites in the form of tubes in drug delivery processes [15]. Dai (Non-Governmental Organization), [16] discovered graphene oxide as a very excellent conductor and carrier in drug delivery for some types techniques such as [17],method via π-stacking, polyethylene glycol bound with amines [18].

Gene Delivery

It has become clear that gene therapy is one of the most important new and promising methods for treating various diseases caused by genetic disorders, including cystic fibrosis, Parkinson's

disease and types of cancer [19]. One of the most important requirements for successful and effective gene therapy is the presence of the genetic medium that protects the DNA from nuclease degradation and helps in the process of cell uptake of DNA with high efficiency [20]. We can say that the shortage of effective and safe gene vectors is one of the main challenges that try to reduce the development stages of gene therapy [21].

Electrochemical sensors (Figure 2) it can be considered one of the most important and best modern medical techniques that are used for the purpose of primary detection of oncological diseases and cancer, especially colon tumors, through the impressive results of the performance of this technique [22].The great and remarkable development in nanomaterials technology and in the design of sensors has opened the door to the ultra-accurate [23] use of these technologies in various medical applications.

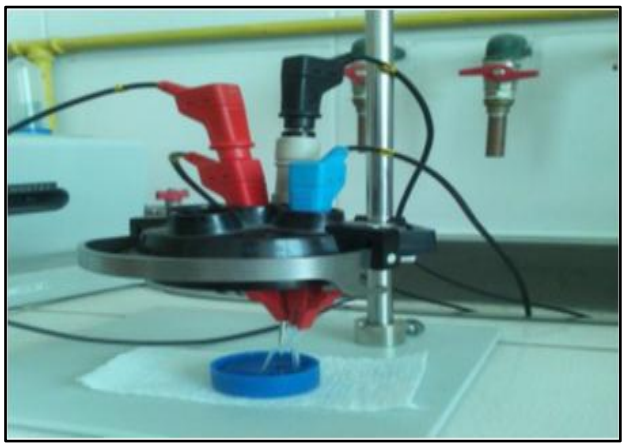

Figure 2. Electrochemical cell of sensor.

Cancer Therapy

The very effective method, which is used in the field of drug delivery effectively and effectively, was highly dependent on the exceptional and distinctive qualities of these compounds, which made it a pioneer in medical applications. The presence of some effective groups associated with oxygen will make these compounds [24], especially graphene oxide, one of the most important compounds in drug delivery and disease follow-up.

In a nutshell, the unique and remarkable features in terms of structural structure and ease of chemical[25], processing of graphene oxide have provided great possibilities for the delivery and loading of different and diverse groups of genes, chemotherapies and photosensitizers for the treatment and follow-up of pathological cases of cancerous tumors [26]. It has become clear that excellent and more effective results will be obtained in the field of clinical use [27], especially after the integration and coupling of research ideas and the addition of rare properties of the materials used [28].

Cancer is considered one of the most important and complex pathological conditions, especially when the disease reaches its final stages, where treatment is difficult, economically burdensome, and psychologically inappropriate for the patient [29].

Therefore, it is important to reduce the death rate, and find a suitable method for detecting tumor diseases in the initial stages, and this purpose has begun to witness a remarkable development by improving and designing sensor systems based on nanomaterials, especially graphene and its compounds. It is very important to keep pace with development and improve it in order to comply with the requirements of early medical diagnosis of cancerous diseases and tumors, and patient follow-up and treatment [30].

Bio sensing and Bio imaging

Bio Sensing

Intensive studies of graphene and its derivatives included original grapheme, chemically reduced grapheme [31] and doped graphene due to the importance of medical applications of graphene, especially in the field of biological sensitivity [32] and the possibility of obtaining new molecules such as oligonucleotide [33], dopamine, amino acids [34] and thrombin [35].

It is important to realize that most patients with cancerous tumors do not show symptoms except in the final cases of the disease, and in this case the patient has reached the final stages and treatment is difficult. Therefore, early-stage colon cancer screening is clinically important to reduce mortality rates and improve outcomes for patients with this fatal disease. A variety of methods and methods have been used to detect this disease, but these techniques suffer from constraints and drawbacks that conflict with the means for early detection [36].

Previously, the methods used for the detection process depended on taking a part of the patient's tissue (biopsy) and then doing the necessary tests to detect the presence of cancer, including colon cancer, but this method has many caveats and obstacles such as that it causes pain to the patient and takes a long time to obtain results and most importantly It has a very big impact on the patient's will to complete the examination process [37].

Therefore, there is a need for a new approach that is consistent with the requirements of early detection through quick, sensitive and easy methods to apply towards reaching the point of correct diagnosis that helps to a very large extent in improving the clinical condition of the patient and reducing the economic burden caused by this pathology [38].

The desired mixture to prepare the graphene paste was as follows: The paraffin oil solution will be mixed from the graphene paste according to a certain percentage. In order to improve and increase the efficiency of the graphite sensor [39], a material with high electrical effectiveness will be added to increase the sensitivity, and a voltammetric cell will be formed that calculates the current intensity that is equivalent to the amount and concentration of the bioreagent to be estimated.

Bio Imaging

In recent years, the importance and usefulness of graphene and its derivatives began to crystallize, especially in the field of medical applications in the examination [40], diagnosis and early detection of cancerous tumors. For this reason, scientists and researchers have begun to prepare and produce graphene oxide in small sizes (approximately with measurements of 10 nanometers or less), which are usually called graphene quantum dots (GQDs), using the method of chemically oxidizing graphene, in a bottom-up manner, which can ideally be used For bioimaging purposes [41].

Estimation and evaluation of the p53 biomarker responsible for detecting tumors. The proposed paste for the design of the nanosensor for the measurement of amperometry is mainly dependent on the dye phthalocyanine-BODIPY (BODIPY = boron-dipyromethane) Figure 3.The results obtained using this paste prove to be tangible and decisive results in the quantification of a biomarker that is effective in early detection of cancerous tumors.

Different concentrations of the biomarker were prepared and used to measure the current intensity according to the differential [42] pulse voltmeter method. All solutions used in the method are for analytical purposes. Galvanostat was used for all amperometric measurements.

The amperometric cell consists of a three-electrode system, where the silver electrode is used as the auxiliary electrode and the platinum electrode is used as the counter electrode in addition to the working electrode. Differential pulse voltammetry method was used to measure different concentrations of KRAS solutions [43]. The scanning rate was 50 millivolts per second and the measurements were made at 25°C.

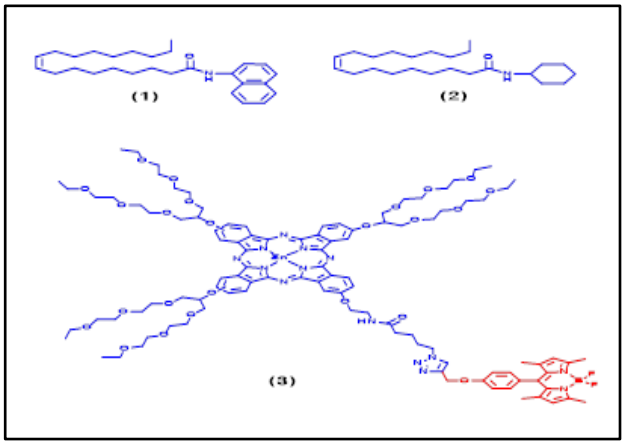

Figure 3. Structure of phthalocyanine-BODIPY dye.

Application

The field of application of this study in hospitals and medical centers specialized in the detection, treatment and follow-up of cancer in general and colon cancer in particular. But the method used for estimating vital signs and its more than excellent features and characteristics, especially when compared with other methods [44].

Features of this method:

1. The above method has advantages such as simplicity, speed, low cost and high sensitivity.
2. It is not necessary to process the samples before the examination process.
3. Importantly,it contributes greatly to reducing death rates for colon cancer patients.

4. Follow-up of the disease, especially assessing the risk of future collapse of the diseased condition [45].
5. It will be considered the decisive factor in early detection and thus improving the pathological condition.
6. This method used for estimating vital indicators and its more than excellent features and characteristics, especially when compared with other methods [46].

The response properties, which include high sensitivity and excellent selectivity, gave these sensors the opportunity to confirm the possibility of their use in the field of early detection of colon cancer. This method used for estimating vital indicators and its more than excellent features and characteristics, especially when compared with other methods (Table 1) shows the superiority of this method over other methods.

Table 1. Comparisons of our method to others' methods.

Procedure	Concentration range (nmol/L)	Limit of Detection (pmol/L)
Fluorescent-dependent copper nanoparticles.	0.09-210	49
Electrochemical graphene oxide.	0.1-1.9	10
Sandwich graphene sensor.	0.1-1.9	110
The scarlet electrochemical reagent.	0.02-9	3.54
Novel Chemiluminescence (ECL).	0.1-150	0.2
Magnetic particles.	0.01-15	20
Functional composite nanofibers.	0.09-50	0.040
Electrochemical based on gold nano particles/ graphene oxide Novel (ECL).	0.02-0.9	2.6
Novel DNA zyme molecular beacon (MB zyme).	$3.6x10^{-109}$ - $3.65x10^{-6}$	0.034
Electrochemical based on gold nano particles/ graphene oxide (Au NPs/Go).	0.1-4	0.024
Graphene modified with Phthalo-cyanine BODIPY dye and Azulene.	3.24- 7.15	$0.783x10^{-4}$

CONCLUSION

In the initial cases of the discovery of graphene and its derivatives, and because of the rare and unfamiliar features of this compound, such as the very high surface area, distinguished geometric structure, thermal, chemical and electronic properties, in addition to many other properties, these compounds made them the focus of attention and interests of many specialists in various medical applications.

We can give a summary of the most important points that were touched upon in the field of medical uses of graphene and its derivatives. The unique and unusual properties of graphene made it one of the most important compounds used in the medical field, which gives excellent results compared to others. The success and progress in this field has been the focus of attention and encouragement. There are also challenges arising from a comprehensive and deep understanding of the interactions of graphene cells.

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Conflicts of Interest

We have no conflicts of interest to disclose.

References

1. Novoselov KS, Geim AK, Morozov SV. Electric field effect in atomically thin carbon films. Science. 2018;306(5696):666–669.
2. Zhang K, Zhang LL, Zhao XS. Graphene-polyaniline nanofiber composites as supercapacitor electrodes. Chem Mater. 2019; 22(4) :1392–1401.
3. Xuan Y, Wu YQ, Shen T. Atomic-layer-deposited nanostructures for graphene-based nano electronics. Appl Phys Lett. 2018; 92 (1) :013101–3.
4. Yang XM, Tu YF, Li L. Well-dispersed chitosan/graphene oxide nanocomposites. ACS Appl Mater. Interfaces. 2019;2(6):1707–1713.
5. Liu C, Alwarappan S, Chen ZF. Membraneless enzymatic biofuel cells based on graphene nano sheets. Biosens Bioelectron.2020;25:1829–1833.
6. Lu CH, Yang HH, Zhu CL. A graphene platform for sensing biomolecules. Angew Chem Int Ed. 2019;121(26):4879–4881.
7. Qu LT, Liu Y, Baek JB. Nitrogen-doped graphene as efficient metal-free electrocatalyst for oxygen reduction in fuel cells. ACS Nano. 2019;4(3):1321–1326.
8. Liu Z, Robinson JT, Sun XM. PEGylated nanographene oxide for delivery of water-insoluble cancer drugs. J Am Chem Soc. 2018; 130(33):10876–10877.
9. Guo SJ, Dong SJ. Graphene nanosheet: synthesis, molecular engineering, thin film, hybrids, and energy and analytical applications. Chem Soc Rev. 2021; 40(5):2644–2672.
10. Hummers WS, Offeman RE. Preparation of Graphitic Oxide. J Am Chem Soc. 2017;80:1339–1339.
11. Dai HJ. Carbon nanotubes: opportunities and challenges. Surface Sci. 2002;500 :218–241.
12. Yang ZR, Wang HF, Zhao J. Recent developments in the use of adenoviruses and immunotoxins in cancer gene therapy. Cancer Gene Ther. 2017;14: 599–615.
13. Naldini L, Blömer U, Gallay P. In Vivo gene delivery and stable transduction of nondividing cells by a lentiviral vector. Science. 2016; 272: 263–267.
14. Mintzer MA, Simanek EE. Nonviral vectors for gene delivery. Chem Rev. 2019;109(2):259–302.
15. Yang K, Zhang S, Zhang GX. Graphene in mice: ultrahigh in vivo tumor uptake and efficient photothermal therapy. Nano Lett. 2020; 10(9): 3318 –3323.
16. Tang LH, Wang Y, Li YM. Preparation, structure and electrochemical properties of graphene modified electrode. Adv Funct Mater. 2019; 19(17):2782–2789.
17. Wang Y, Shao YY, Matson DW. Nitrogen-doped graphene and its application in electrochemical biosensing. ACS Nano. 2020; 4(4):1790–1798.
18. Chang HX, Tang LH, Wang Y. Graphene fluorescence resonance energy transfer aptasensor for the thrombin detection. Anal Chem. 2019; 82(6):2341–2346.
19. Wang Y, Li ZH, Hu DH. Aptamer/graphene oxide nanocomplex for in situ molecular probing in living cells. J Am Chem Soc. 2018; 132(27):9274–9276.
20. Tang LH, Wang Y, Liu Y. DNA-directed self-assembly of graphene oxide with applications to ultrasensitive oligonucleotide assay. ACS Nano. 2017;5 (5):3817–3822.
21. Dong XL, Cheng JS, Li JH. Graphene as a novel matrix for the analysis of small molecules by MALDI-TOF MS. Anal Chem. 2018; 82(14):6208–6214.
22. Wang Y, Li YM, Tang LH. Application of graphene modified electrode for selective detection of dopamine. Electrochem Commun . 2019; 11(4):889–892.
23. Peng C, Hu WB, Zhou YT. Intracellular imaging with a graphene-based fluorescent probe. Small. 2019 ; 6(15):1686–1692.
24. Pan DY, Zhang JC, Li Z. Hydrothermal route for cutting graphene sheets into blue-luminescent graphene quantum dots. Advan Mater. 2019; 22(6) : 734–738.
25. Takeda A, Oku T, Suzuki A, Akiyama T, Yamasaki Y. Fabrication and Characterization of Fullerene based Solar Cells Containing Phthalocyanine and Naphthalocyanine Dimers. Synthetic Metals. 2013; 177: 48–51.
26. Simon J, Sirlin C. Mesomorphic molecular materials for electronics, opto-electronics, iono-electronics: Octaalkyl- phthalocyanine derivatives. Pure Applied Chemistry.1989; 61: 1625–1629.
27. Guillaud G, Simon J, Germain JP. Metallo phthalo cyanines: Gas sensors, resistors and field effect transistors.Coordination Chemistry Reviews. 1998; 178:1433-1483.
28. Meunier B. "Metalloporphyrins as versatile catalysts for oxidation reactions and oxidative DNA cleavage". Chemistry Reviews.1992; 92: 1411–1456.
29. Sehlotho N, Nyokong T. Zinc Phthalocyanine photocatalyzed oxidation of cyclohexene., J Mol Catalysis A: Chemical.2004; 219: 201–207.
30. Tu W, Lei J, Zhang and H S, Ju H. Novel Graphene-Based Nanostructures Production, Functionalization, and Engineering., Chemistry. 2010;16: 10771-10777.
31. Stojek Z. Pulse voltammetry, in Electroanalytical Methods, Scholz, F. (Ed.), Springer, Berlin = Heidelberg=New York, 2001, chap. II.
32. Qiu S, LiX, XiongW,Xie L,Guo L,Lin Z,Qiu B, Chen G. A novel fluorescent sensor for mutational p53 DNA sequence detection based on click chemistry. Biosens Bioelectron.2013; 41: 403-408.
33. Du D, Wang L,ShaoY, Wang J, Engelhard MH, LinY. Functionalized graphene oxide as a nano carrier in a multienzyme labeling amplification strategy for ultrasensitive electrochemical

immunoassay of phosphorylatedp53 (S392). Analytical Chemistry.2011; 83:746.
34. Xie Y,Chen A, Du D,Lin Y, Graphene-based immunosensor for electrochemical quantification of phosphorylated p53 (S15). Analytica chimica acta.2011; 699: 44.
35. Hamidi-Asl E, Raoof JB, Ojani R, Hejazi MS. Indigo carmine as new label in PNA biosensor for detection of short sequence of p53 tumor suppressor gene. Electro analysis.2013; 25: 2075.
36. Wang X, ZhangX, He P, FangY. Sensitive detection of p53 tumor suppressorgene using an enzyme-based solid-state electrochemilumine scence sensing platform. Biosensors and Bioelectronics .2011; 26: 3608.
37. Chen A, BaoY, GeX, ShimY, Du D, Lin Y. Magnetic particle-based immunoassay of phosphorylated p53 using protein cage templated lead phosphate and carbon nanospheres for signal amplification. Royal Society of Chemistry. 2012; 2:11029.
38. Wang X, Wang X, Wang X, Chen F, ZhuK, Xu Q, Tang M, Novel electrochemical biosensor based on functional composite nanofibers for sensitive detection of p53 tumor suppressor gene. Analytica Chimica Acta.2013;765: 63.
39. Chen X, HeC, Zhang Z, Wang J. Sensitive chemiluminescence detection of wild-type p53 protein captured by surface-confined consensus DNA duplexes. Biosensors and Bioelectronics. 2013; 47: 335.
40. Li H, Wu Z, QiuL, LiuJ,Wang C, Shen G, YuR. Ultrasensitive label-freeamplified colorimetric detection of p53 based on G-quadruplex MBzymes. Biosensors and Bioelectronics.2013; 50:180.
41. Hadi A, Balal K, Habib T, Mahmood M, Farzaneh N, Mohammad-Reza R. A sandwich type immunosensor for ultrasensitive electrochemical chemical quantification of p53 protein based on gold nano particles/ graphene oxide. Electro chimica Acta.2016;188:153-164.
42. Ahmed Jassim Muklive AL-ogaidi1, Aliaa A. Razzak, Mais Abdul Hakim Mohammed. Adsorption of Oils Pollutants by Using Nano Materials.NeuroQuantology.2021;19 (10): 8-1. doi: 10.14704/nq.2021.19.10.NQ21150
43. Ahmed Jassim Muklive Al-Ogaidi, Raluca-Ioana Stefan-Van Staden, Livia Alexandra Gugoasa, Jacobus Frederick Van Staden, Hülya Yanik, Meltem Göksel, Mahmut Durmuş. A new potentiometric sensor for the assay of p53 in blood samples.U.P.B. Sci. Bull. Series B. 2017;79 (2):113-120 doi: www. Connect journals. com/ bca.
44. Ahmed Jassim Muklive Al-Ogaidi, Raluca-Ioana Stefan-van Staden,Livia Alexandra Gugoasa, Marcela-Corina Rosu & Crina Socaci. Electrochemical determination of the KRAS genetic markers for colon cancer with modified graphete and graphene paste electrodes. Analytical Letters. 2018;51(17):2820–2832.Doi:http://www. tandfonline . com/ loi/ lanl20.
45. Mohammed MA, Al-Ogaidi AJM, Kamil GM.Micro determination of tyrosine by spectrophotometric techniques. International Journal of Medical Toxicology and Legal Medicine. 2021; 24 (3-4):308-311. Doi: 10. 5958/ 0974 -4614,2021,00099,1.
46. Ahmed Jassim Muklive Al-Ogaidi, Bashar Qasim, Daniah M Hamid, Aliaa A. Razzak Mohammed. Ultra higher assessment of tyrosine compounds by coupling for biological samples Annals of Tropical Medicine & Public Health.2020; 23 (19): SP232112 .http:// doi.org/ 10.36295/ASRO.2020.232112.

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