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Sahibi:

Prof. Dr. Asuman BOZKIR
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06560, Yenimahalle, Ankara, Türkiye
Tel: +90 312 203 31 52
Faks: +90 312 213 10 81
e-posta: ctsengel@pharmacy.ankara.edu.tr
efd.editor@ankara.edu.tr

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Owner:

Prof. Dr. Asuman BOZKIR
Ankara University Faculty of Pharmacy, Department of Pharmaceutical Technology
06560 Yenimahalle, Ankara, Türkiye

Editor-in-Chief:

Prof. Dr. Ceyda Tuba ŞENGEL TÜRK
Ankara University Faculty of Pharmacy, Department of Pharmaceutical Technology
06560 Yenimahalle, Ankara, Türkiye
Phone: +90 312 203 31 52
Fax: +90 312 213 10 81
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e-mail: doganc@ankara.edu.tr

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e-mail: akarabay@ankara.edu.tr
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e-mail: belma.pehlivanovic@ffsa.unsa.ba
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Ankara University, Faculty of Pharmacy, Department of Analitical Chemistry
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ORIGINAL ARTICLE / ÖZGÜN MAKALE

CRITICAL POINTS OF INTERFERENCE AND PROBABLE INFLUENCE ON THE VALIDITY OF RESULTS OF A BIOCHEMICAL MEDICAL ANALYSIS: STATISTICAL APPROACH

BİYOKİMYASAL TIBBİ ANALİZ SONUÇLARININ GEÇERLİLİĞİ ÜZERİNDEKİ KRİTİK MÜDAHALE NOKTALARI VE OLASI ETKİLERİ: İSTATİSTİKSEL YAKLAŞIM

Habiba BERBAOUI[1,2]*, Abdenbi ASMA[1,2], Seghir ABDELHADI[1,2], Touati BOUMEDIENNE[1,2]

[1]Tahri Mohamed University, Faculty of Exact Sciences, Department of Matter Sciences 08000, Béchar, Algeria
[2]Energetic Laboratory in Arid Zones, Team of Solar Resource and Its Applications University Tahri Mohamed of Béchar, Algeria

ABSTRACT

Objective: *The manipulator must be aware that some results obtained by the various biochemical analysis methods may be erroneous and don't represent reality. For this, the biochemist is asked to identify the critical points responsible for the aberration of the results obtained and it is imperative that he be aware of all the factors that can induce the modification of the results obtained. The influencing factors listed are the results of long practical experience within a biochemical analysis laboratory supplemented by bibliographic research that we have brought together in an educational document in the form of a guide and of which the statistical study is reported by the present study.*
Material and Method: *Through this study, we used the Ichikawa diagram of Hazard Analysis Critical Control Point to list and organize all the factors of influence and probable interference on the results of a biochemical medical analysis, subsequently, we determined the influence rates of each factor as well as all the factors linked to it. The statistical study carried out relates to the pre-analytical, analytical and post-analytical stages of a biochemical analysis. The rates obtained represent the influence of an isolated factor or a common set of factors in relation to all the factors determined.*
Result and Discussion: *The critical points of interference and influence on the validity of the results obtained have been listed through all the steps of a biochemical analysis with variable rates of 60.26%, 28.75% and 07.84% respectively for the pre- analytical stage, analytical and post analytical stage; The highest rate for the pre--analytical stage was represented by factors related to patient with a rate of 35.29%,concerning the analytical stage, the materials used presented a rate of 11.11% for the post-analytical stage, factors that could interfere with the measurement presented a rate of 05.58%.*
Keywords: *Analysis, biochemical, HACCP, influence, interference*

* **Corresponding Author / Sorumlu Yazar:** Habiba Berbaoui
e-mail / e-posta: berbaoui.habiba@univ-bechar.dz, **Phone / Tel.:** +21358543904

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ÖZ

Amaç: *Manipülatör, çeşitli biyokimyasal analiz yöntemleriyle elde edilen bazı sonuçların hatalı olabileceğinin ve gerçeği temsil etmediğinin farkında olmalıdır. Bunun için, biyokimyacıdan elde edilen sonuçların sapmasından sorumlu kritik noktaları belirlemesi istenir ve elde edilen sonuçların değişmesine neden olabilecek tüm faktörlerin farkında olması zorunludur. Listelenen etkileyici faktörler, bir biyokimyasal analiz laboratuvarındaki uzun pratik deneyimin sonuçları olup, bir rehber şeklinde bir eğitim belgesinde bir araya getirdiğimiz ve istatistiksel çalışması bu çalışma tarafından rapor edilen bibliyografik araştırmalarla desteklenmiştir.*

Gereç ve Yöntem: *Bu çalışmada, bir biyokimyasal tıbbi analizin sonuçları üzerindeki tüm etki faktörlerini ve olası girişimleri listelemek ve düzenlemek için Tehlike Analizi Kritik Kontrol Noktasının Ichikawa diyagramını kullandık, ardından her bir faktörün etki oranlarını ve bununla bağlantılı tüm faktörleri belirledik. Yürütülen istatistiksel çalışma, bir biyokimyasal analizin analiz öncesi, analitik ve analitik sonrası aşamalarıyla ilgilidir. Elde edilen oranlar, belirlenen tüm faktörlerle ilişkili olarak izole bir faktörün veya ortak bir faktör kümesinin etkisini temsil etmektedir.*

Sonuç ve Tartışma: *Elde edilen sonuçların geçerliliği üzerindeki kritik müdahale ve etki noktaları, biyokimyasal bir analizin tüm aşamaları boyunca %60.26, %28.75 ve %07.84 gibi değişken oranlarla listelenmiştir. En yüksek oran analitik öncesi aşamada %35.29 ile hastaya ait faktörlerde, analitik aşamada kullanılan malzemeler %11.11 oranında, analiz sonrası aşama için ölçümü etkileyebilecek faktörler %05.58 oranında ortaya çıkmıştır.*

Anahtar Kelimeler: *Analiz, biyokimyasal, HACCP, girişim, etki*

INTRODUCTION

The human body is governed by a panoply of devices themselves made up of organs, which are structured by tissues and cells whose functioning is orchestrated by a set of chemical molecules participating in cellular anabolism and catabolism. These chemical molecules are found in the blood and other bodily fluids, with a remarkable divine balance expressing unequivocal homeostasis, with varying serum levels. The detection and measurement of the levels of these molecules are carried out by qualitative and quantitative biochemical analysis methods. The smooth running of the detection and measurement of the levels of these molecules is the major objective of the present study.

In order to provide correct results to patients, the biochemist is called upon to follow a panoply of recommendations and directives and to avoid prohibitions relating to factors and critical points that may interfere with or influence the validity of the result of the analysis at the level of the pre-analytical stage, the analytical stage, and the post-analytical stage.

Indeed, such simple gestures as bringing the reagent used to room temperature before implementing the "sample-reagent" reaction and handling the micropipette may involve a set of interfering and influencing factors that can induce the modification of results of the biochemical medical analysis.

The objectives of the present study are to list all the factors of interference and influence, realize a statistical study of the factors listed, and help the biochemist become aware of interfering and influencing factors in order to avoid them.

All the factors listed through the study conducted were exposed through a practical guide entitled "Critical points of interference and probable influence on the validity of the results of a biochemical analysis" [1], which we present in this follows the overall statistical study obtained.

MATERIAL AND METHOD

Means of Study

Through this study, we exposed all the factors that we have listed through the Ichikawa diagram, which allowed us to organize the factors revealed in the form of a multitude of axes, each consisting of several levels presenting certain correlations.

The Ishikawa diagram is a method of brainstorming that is used to find and represent the different causes of a problem. The Ishikawa diagram is particularly well suited to the risk management. We have adapted it to our study, in order to identify the problems encountered during a biochemical analysis.

The statistical study carried out relates to the pre-analytical, analytical and post-analytical stages of a biochemical analysis. The rates obtained represent the influence of an isolated factor or a common set of factors in relation to all the factors determined.

$$RIF\ (\%) = 100 / TNF$$

IRF = Rate of Influencing factor(S)
TNF= Total number of factors determined for a stage or all stages of a biochemical médical analysis.

Through this study we evaluated:
* Rate of interference and influence critical points relative to each stage
** Manipulator interference and influence critical point rate relative to each level.
*** Total rate of critical points of interference and influence relating to the manipulator compared to all the factors listed at the level of all the stages of the analysis.

Stages Investigated

We have investigated the three stages that constitute a biochemical medical analysis, which are: [1,2]

a] -pre-analytical stage

is a stage which concerns all the facts and acts which:
- precede the collection of the sample,
- during sampling
- and the processing of the sample in order to prepare a sample ready for the biochemical analysis to be carried out.

b] - analytical stage

The analytical stage concerns all the acts relating to the implementation of the analysis from a sample ready to be analyzed until the expected result is obtained.

c] - post-analytical stage

Concerns all the acts relating to the processing of the result obtained from the analysis carried out: case of an anomaly or inconsistent results, badreading or bad interpretation of the results obtained.

RESULT AND DISCUSSION

Listed Interfering and Influencing Factors

In this part of the study, we present all listed factors, or critical points, of interference and influence on the validity of the results of a biochemical medical analysis, through the pre-analytical stage, analytical stage and post-analytical stage.

Pre-Analytical Stage [1-12]

We have listed a number of 92 factors relating to the patient, including sampling, we have also listed the factors frequently encountered during a biochemical medical analysis.

a] - Patient Factors
b] - Sample Collection Factors
c] - Frequent factors

a] - Patient Factors

At this level, we have listed a fairly large number of factors that may be the cause of the probable modification of the results expected from the biochemical analysis.

Table 1 presents the results of the investigationof interfering and influencing factors relating to the patient.

A large number of factors relating to the patient have been listed, with a value of 54 factors, among which are age, physiological state, sex, weight and others, factors listed in this stage are mainly represented by factors related to the physiological state of the patient concerned.

b] - Sample Collection Factors

Table 2 presents the results of the investigation of interfering and influencing factors relating to

Sample Collection Factors.

Table 1. Probable interfering and influencing factors relating to the patient [1-12]

Interfering and influencing factors relating to the patient		
Age	New born	
	Teenager	
	Adult	
	Old	
Sex	Female	
	Male	
Weight	Obesity	
Physiological State	Fasting	Mandatory
		Preference
		Prolonged
		Not necessary
	Pregnancy	
	Menstrual cycle	
	Menopause	
	Nychthemeral cycle	
	Circadian rhythm	
	Seasons	Summer
		Winter
	Heat	Prolonged exposure to heat
		Fever
	Underlying disease	Infectious episode
		Diabetes
		Dialysis
		Severe hepatic impairment
	Specific diet	Malnutrition.
		High protein
		Rich in carbohydrates
		High in saturated fat
		High calorie
		Vegetarian diets
		Anorexia nervosa
		Fruit and liquorice
		Rich in iron
	Bad consumption Chronic	Alcohol
		Caffeine
		Tobacco
		Cocaine
Others	Physical exercise / cycling	
	Stress / Black skin color	
	Deficiency / Acidity of the sample	
	Ejaculation / Altitude.	

Table 2. Probable interfering and influencing factors relating to sampling [3-9]

Probable interfering and influencing factors relating to sampling		
Terms of Sampling	Moment	Inadequate
	Position	Standing during collection
		Prolonged standing position before sampling
		Bedridden

Table 2 (*continue*). Probable interfering and influencing factors relating to sampling [3-9]

Probable interfering and influencing factors relating to sampling			
Matérials Used	Vials	Cleanliness	
		Quantity	
	Tubing	Without Anticoagulant / clean	
		With Anticoagulant	Nature
			Quantity
		Additive	Nature
			Quantity
	Laidof gorrate	Extended	
		Prohibited	
	Syringe	Diameter	
		Transposition	Remove the needle
			Transpose slowly
	Catheter	Nature	
		Diameter	
Processing of the sample	Distribution	Order of tubes used	
		Quantity distributed	
	Moderate stir (manual turning 6 to 8 times)		
	Preservation	Séparationserum / plasma	
		Temperature	
		Duration	
	Transportation	Jerks	
		Correct tube position	

We have listed a number of 31 factors relating to sampling at the level of:

- terms of sampling,
- materials used,
- and processing of the sample.

c]- Frequent factors [13]

We have listed a number of 4 frequent factors represented by:

- haemolizedserum:increase/ decrease
- lipimicserum:increase/ decrease
- icteric serum:increase
- drugs: normal dose / high dose

Analytical Stage [1,2,5,14-17]

Regarding the analytical stage, we have listed 44 factors relating to:

- a] Materials used
- b] Technical sheet

a]- Materials used

The materials used for the realization of the biochemical medical analysis can present many critical points of inference and influence on the expected results, in particular if the latter is inadequate, badly used, or not controlled.

Table 3 presents the results of the investigationof interfering and influencing factors relating to the materials used.

The factors listed at this level were 17 factors equivalent to 11.11% relative to all the factors that we listed for the three stages of a biochemical analysis.

The manipulator must relate to the equipment used, because the latter is involved in several factors at this level of analysis.

Table 3. Probable interfering and influencing factors relating to the materials used

Probable interfering and influencing factors relating to the materials used			
Materials and equipment used	Measuring devices	*Starting up	
		Maintenance	
		*Programming	
		Specific reagent	
		*Accessories and consumables	
		Specific fuel	
		Agarose gel	
	Pipette and micropipette	Calibration	
		Tip	*Position
			Change*
		Handling	* 1st Stop
			*2nd Stop
	Tank	Quality	
		*State	
		Thickness	
		*Wear	
		*Insertion	

* Probable influence of the manipulator

b]- Technical sheet

The technical sheet presents all the information necessary to carry out the biochemical medical analysis, the latter may present a large number of critical points of interference and influence on the expected results.

Table 4 presents the results of the investigationof interfering and influencing factors relating to the technical sheet**.**

Table 4. Probable interfering and influencing factors relating to the data sheet

Probable interfering and influencing factors relating to the data sheet		
Method adopted	Understanding and applying guidelines	
	Chronological order	
Reagent used	Quantity	
	Bring the reagents to room temperature 25°C	
	Contamination	
	Stability of stored reagent	Duration
		Temperature
	Stability of reconstituted reagent	Duration
		Temperature
	Stability of reagent-Sample reaction,	Duration
		Temperature
	Incubation of reagent-Sample reaction,	Duration
		Temperature
Sample	Nature	
	Quantity	
	Preservation of samples	
Interfering / Influencing factors Manipulator: Behavioral habits		
Compliance with all the directives of the pré analytical / Analytical and post analytical stages		
Organization Labeling	Labeling	
Organization Labeling	Arrangement of materials	
Good gesture		
Chemicals on fingers		

It is essential for the manipulator to be able to understand and apply the directives given in the technical data sheet of the product used for the analysis because the latter is closely linked to all the factors relating to the technical data sheet.

The technical data sheet provides all the information and directives relating to:

- the reagent used,
- the analyzed sample,
-and the method adopted for carrying out the analysis.

The factors relating to the reagent are the most numerous concerning the technical data sheet, the latter presented a rate of 73.33% factors compared to the factors listed for the technical data sheet.

Post-Analytic Stage [18]

At this level, we have listed 12 factors from references and personal experiences:

- during the measurement and after measurement.

The Table 5 presents the results of the investigationof interfering and influencing factors relating to the post-analytic stage.

Table 5. Probable interfering and influencing factors relating to the post- analytical stage

Probable interfering and influencing factors relating to the post- analytical stage	
Errors occurred during measurement	Calibration
	Zero adjustment
	Wave length
	Programming
	Accuracy
	Maintenance
	Aberrant calculation formulas.
Errors occurred after measurement	Results interpretation
	Presentation of the results
	Calculations made
	Confusion between patient A and B
	Reference limit values

We noted that the rate, of critical points of interference and probable influence, at the level of the post-analytical stage, was relatively low compared to the rates highlighted at the level of the pre-analytical and analytical stage and factors listed at this stage of the biochemical analysis are split into factors relating to the measuring device used for the analysis and factors relating to the manipulator.

Results of the Statistical Approach Relating to the Critical Points Which Can Influence the Results of a Biochemical Analysis Manipulator

Regarding to results obtained and Statistical approach realized relating to the critical points that can influence the results of a biochemical analysis a great attention must be paid to the manipulator whose interference and influence factors presented a rate of 40.52% compared to all the factors listed through the present study.

Results of the Statistical Approach of Terfering and Influing Factors Relating to the Manipulator

The rates of interference and influence factors relating to the manipulator are listed in Table 6.

The manipulator is responsible for:

- 77.41% of the factors relating to the –sampling in the pre-analytical stage.
- 58.82% of the factors listed for the material used and 100% of the factors relating to the application of the directives of the technical sheet in the analytical stage.
- 66.66% of the factors that may occur during the measurement and 80% of those that may occur after the measurement in the post- analytical stage.

Therefore, it is imperative for the technician to learn the good practices required for carrying out a biochemical analysis leading to valid results.

Table 6. Interference and influence factors relating to the manipulator [1]

Stages	% *	Manipulator interference level	%**	Total%***
Pre-analytical stage	60.13	Sampling	77.41	40.52
Analytical stage	28.75	Materials used	58.82	
		Data sheet.	100	
		Others	100	
Post-analytical stage	07.84	During measurement	66.66	
		After measurement	80	

* Rate of interference and influence critical points relative to each stage
** Manipulator interference and influence critical point rate relative to each level
*** Total rate of critical points of interference and influence relating to the manipulator compared to all the factors listed at the level of all the stages of the analysis

Results of the Statistical Approach Relating to All Critical Points Which Can Influence the Results of a Biochemical Analysis

The statistical study realized allowed us to evaluate the rates of factors listed using the Ishikawa diagram adopted for the realization of our study, which aims to draw the attention of the manipulator to the most relevant factors that can affect the results expected from a biochemical medical analysis.

The factors listed through our investigation and their rates are recorded in Table 7.

Table 7. Results of the statistical approach relating to the critical points which can influence the results of a biochemical analysis [1]

Stages of biochimical analysis	Critical points of interference/influence	Rate
Pre-analytical stage 92 Factors 60.13%	Patient	35.29%
	Sampling	20.26%
	Common interference factors	04.57%
Analytical stage 44 Factors 28.75%	Materials used	11.11%
	Technical sheet	09.80%
	Manipulator B.H*	03.26%
Post-analytical stage 12 Factors 07.84%%	During measurement	04.57%
	After measurment	03.26%

- The pre-analytical stage revealed a number of 92 points equivalent to a rate of 60.13% presented the highest rate for all the stages investigated.
- Patient-related factors presented the highest rate with a rate of 35.29%,

We have listed at the level of the analytical stage a number of 44 factors equivalent to a rate of 28.75%

- The highest rate was represented by the materials used.
- The post-analytical stage revealed a relatively low number of 12 factors with a value of 07.84%.

Conclusion

Through the Ichikawa diagram of HACCP, we listed all the factors of influence and probable interference on the results of a biochemical medical analysis.

It is very important to bear in mind that some results obtained by the various biochemical analysis methods may be erroneous and don't represent reality. For this, the biochemist is asked to identify the critical points responsible for the aberration of the results obtained and it is imperative that he be aware of all the factors that can induce the modification of the results obtained.

This fact constituted the main objective of the present study, through which we have attempted to list all the critical points from personal experiences and bibliographic datathat must be imperatively known by the manipulator of a biochemical medical analysis, who, alone, presented a rate of factors with a value of 40.52%.

We have the prospect of carrying out other studies and translating them into practice guides for students and technicians.

The educational purpose of these guides is to provide the student with a data base grouping the directives of gestures to follow or to avoid in order to carry out the practice of their specialty under the required conditions.

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AUTHOR CONTRIBUTIONS

Concept: H.B.; Design: S.A.; Control: H.B., T.B.; Sources; H.B.; Materials: H.B., A.A., S.A.; Data Collection and/or Processing: H.B.; Analysis and/or Interpretation: H.B.; Literature Review: A.A., T.B.; Manuscript Writing: H.B.; Critical Review: T.B.; Other: A.A., S.A.

CONFLICT OF INTEREST

The authors declare that there is no real, potential, or perceived conflict of interest for this article.

ETHICS COMMITTEE APROVAL

The authors declare that the ethics committee approval is not required for this study.

REFERENCES

1. Berbaoui, H. (2022). Guide de pratique Points critiques d'interférence et probable influence sur la validité des résultats d'une analyse médicale biochimique, Polycopié pédagogique Ref (n° 65), Université Tahri Mohamed, Bechar, Algérie, p.58.
2. Vaubourdolle, M. (2010). Recommandations pour l'accréditation des laboratoires de biologie médicale. Société Française de Biologie Clinique, Paris, 1-312.
3. Laboratoire Orbio conditions-pre-analytiques Web site (2004). Retrieved from https://www.orbio.fr/le-laboratoire-orbio/conditions-pre-analytiques/. Accessed date: 03.03.2024.
4. Dailymed Web Site. (2021). Retrieved from https://dailymed.nlm.nih.gov/dailymed/. Accessed date: 03.03.2024.
5. Ordre professionnel des technologistes médicaux du Québec et Ordre des chimistes du Québec. Guide de Collecte de Transport de Conservation et D'analyse des Urines Web site. (2024). Retrieved from https://www.optmq.org/. Accessed date: 03.03.2024.
6. World Health Organization. Diagnostic Imaging and Laboratory & Stability of blood, plasma and serum samples. Use of anticoagulants in diagnostic laboratory investigations. Web site (2024). Retrieved from https://iris.who.int/bitstream/handle/10665/65957/;jsessionid=309A516243D7A5468631D29F0C7D02D1?sequence=1. Accessed date: 03.03.2024.
7. Clark, S., Youngman, L.D., Palmer, A., Parish, S., Peto, R., Collins, R. (2003). Stability of plasma analytes after delayed separation of whole blood implications for epidemiological studies. International Journal of Epidemiology, 32(1), 125-130. [CrossRef]

8. D'Orazio, P., Toffaletti, J.G., Wandrup, J.H. (2001). C31-A2: Ionized calcium determinations: Precollection variables specimen choice, collection, and handling. Clinical and Laboratory Standards Institute, 15(20), from https://clsi.org/media/1363/c31a2-sample.pdf. Accessed date: 03.03.2024.
9. Barbier, F., Berkane Z., Dehorne, J., Desch, G., Dhondt, J., Drouillard, I. (2010). Recommandations pour la maîtrise de l'étape de prélèvement des échantillons biologiques. Annales de Biologie Clinique, 68(1), 69-104.
10. LeBlanc, R.M. (2007). Comment maîtriser les interférences des médicaments sur l'immuno-analyse, Option Bio, 0389, 15-16.
11. Ben Jdidia, I., Zribi, K., Boubeker, M., Brahem, A., Sayadi, M., Tlijavani, M., Cherif, Z.S.A. (2021). Les médicaments qui interfèrent avec les bilans biologiques. Revue de la littérature. Canadian Journal of Hospital Pharmacy, 74(4), 378-385. [CrossRef]
12. Simundic, A.M., Filipi, P., Vrtaric, A., Miler, M., Gabaj, N.N., Kocsis, A., Avram, S., Barhanovic, N.G., Bulo, A., Cadamuro, J., Dongen-Lases, E., Eker, P., Vital-e-Silva, A., Homsak, E., Ibarz, M., Labudovic, D., Nybo, M., Plvovarniková, H., Shmidt, I., Siodmiak, J., Sumarac, Z., Vitkus, D. (2019). Patient's knowledge and awareness about the effect of the over-the-counter (OTC) drugs and dietary supplements on laboratory test results a survey in 18 European countries. Clinical Chemistry and Laboratory Medicine, 57(2), 183-194. [CrossRef]
13. Damien, A. (2015). PhD Thesis. Interférence de l'hémolyse, de la lipémie et de l'ictère sur les dosages des principaux paramètres biochimiques. Faculté de Pharmacie, Université Angers, Angers, France.
14. Metais, P. (2000). Biochimie clinique, édlavoisier, p.356.
15. Bakerman, S., Bakerman, P., Strausbauch, P. (2002). ABC's of Interpretive Laboratory Data, 4th edition, Interpretive Laboratory Data Inc., Bloomington, Indiana, USA, p.580.
16. Mayo Medical Laboratory Website (1995). Retrieved from https://www.mayocliniclabs.com/. Accessed date: 03.03.2024.
17. Wu, A.H.B. (2006). Clinical guide to laboratory tests. 4th edition, Saunders Elsevier, p.1798.
18. D'Orazio, P., Ehrmeyer, S.S., Jacobs, E., Toffaletti, J.G., Wandrup, J.H. (2009). C46-A2: Approved Blood Gas and pH Analysis and Related Measurements. Clinical and Laboratory Standards Institute, 29(8), from https://clsi.org/media/1355/c46a2_sample.pdf. Accessed date: 03.03.2024.

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ORIGINAL ARTICLE / ÖZGÜN MAKALE

ANTIFUNGAL ACTIVITY OF METHYL GALLATE AND SYRINGIC ACID ISOLATED FROM *ASTERISCUS GRAVEOLENS* AGAINST *FUSARIUM OXYSPORUM* F. SP. *ALBEDINIS*

ASTERISCUS GRAVEOLENS'TEN İZOLE EDİLEN METİL GALAT VE SİRİNGİK ASİDİN FUSARIUM OXYSPORUM F. SP. ALBEDINIS'E KARŞI ANTİFUNGAL AKTİVİTESİ

Zeyneb BELHI[1]*, Zahira ROUCHAM[1], Noureddine BOULENOUAR[1,2], Abdelkrim CHERITI[1]

[1]Tahri Mohamed University, Phytochemistry and Organic Synthesis Laboratory, 08000, Bechar, Algeria
[2]Nour Bachir University Center, Biological Sciences Department, 32000, El-Bayadh, Algeria

ABSTRACT

Objective: *The objective of this study was to isolate and identify the compounds responsible for the antifungal activity against Fusarium oxysporum f. sp. albedinis (Foa) from Asteriscus graveolens aerial parts extract, and to evaluate the effects in vitro of selected compounds for control of Fusarium wilt.*
Material and Method: *We reveal the presence of the phenolic compounds in Asteriscus graveolens, from which the antifungal activities of aerial parts extracts were investigated for effects on the growth of mycelia against Fusarium oxysporum f. sp. albedinis (Foa) by direct bioautography. The antifungal compounds were isolated from A. graveolens extract using silica gel column chromatography and thin-layer chromatography. Structural identification of the antifungal compounds was conducted using NMR (^{1}H and ^{13}C) spectrophotometry and LC-MS.*
Result and Discussion: *The isolated compounds were identified as methyl gallate (MG) and syringic acid (SA) based on comparing their spectral and physical data with the literature.*
Keywords: *Asteriscus graveolents, Fusarium oxysporum f. sp. Albedinis, methyl gallate, syringic acid*

ÖZ

Amaç: *Bu çalışmanın amacı, Asteriscus graveolens toprak üstü kısımları ekstresinden Fusarium oxysporum f. sp. albedinis'e (Foa) karşı antifungal aktiviteden sorumlu bileşikleri izole etmek ve tanımlamak ve Fusarium solgunluğunun kontrolü için seçilen bileşiklerin in vitro etkilerini değerlendirmektir.*
Gereç ve Yöntem: *Asteriscus graveolens'te fenolik bileşiklerin varlığını ortaya koyduk ve bu bileşiklerden elde edilen toprak üstü kısım ekstrelerinin antifungal aktiviteleri doğrudan biyootografi ile Fusarium oxysporum f. sp. albedinis'e (Foa) karşı misel büyümesi üzerindeki etkileri açısından araştırıldı. Antifungal bileşikler silika jel kolon kromatografisi ve ince tabaka kromatografisi kullanılarak A. graveolens ekstresinden izole edilmiştir. Antifungal bileşiklerin*

* **Corresponding Author / Sorumlu Yazar:** Zeyneb Belhi
e-mail / e-posta: belhi.zeyneb@univ-bechar.dz, **Phone / Tel.:** +213664043808

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yapısal tanımlaması NMR (^{1}H ve ^{13}C) spektrofotometrisi[A1] ve LC-MS/MS[A2] kullanılarak yapılmıştır.
Sonuç ve Tartışma: *İzole edilen bileşikler, spektral ve fiziksel verilerinin literatürle karşılaştırılmasına dayanarak metil gallat (MG) ve siringik asit (SA) olarak tanımlanmıştır*.
Anahtar Kelimeler: *Asteriscus graveolents, Fusarium oxysporum f. sp. Albedinis, metil gallat, siringik asit*

INTRODUCTION

Date palm (*Phoenix dactylifera* L.) constitutes an important in the social and economic life of the Algerian Sahara. It represents the food, shade, garden, and refuge for the Saharan people [1]. This crop belongs to the Arecaceae family and is used in diet and traditional medicine due to its nutritive and pharmacological importance [2]. Besides, they provide a suitable microclimate for other crops (fruit, cereals, etc.) and they also protect them against the wind. For this, palm trees represent food and ecological security measures[3]. However, its culture is threatened by several pests and diseases such as *Fusarium* wilt caused by *Fusarium oxysporum* f. sp. *albedinis* [4].

Fusarium oxysporum is well-known as a plant pathogen causing severe damage in many crops, both in the field and during postharvest storage. Strains of *F. oxysporum* can grow under very low oxygen tensions and often have been detected as contaminants in ultrahigh-temperature processed fruit juices. Some strains are known to produce fumonisin mycotoxins [5]. The plant pathogenic strains are divided into special forms or *formae speciales* according to the plant species on which they cause disease [6,7]

Diseases caused by *F. oxysporum* are widespread in the world. They are harmful to many vegetables (tomato, cucurbit ...) and ornamental (carnation) plants, as well as to field crops such as cotton [8], chili [9], wheat [10], banana (Panama disease) [7,11], and date palm (Bayoud disease) [1,3].

Asteriscus graveolens, a member of the Asteraceae family, is the subject of research in numerous pharmacological and chemical studies. This plant mainly contains alkaloids, flavonoids, and terpenoids. These molecules exhibit various pharmacological benefits, such as anti-inflammatory, anticancer, and anti-viral effects, on the cardiovascular system.

The objective of this study was to isolate and identify the compounds responsible for the antifungal activity against *Fusarium oxysporum* f. sp. *albedinis* (Foa) from *Asteriscus graveolens* aerial parts extract, and to evaluate the effects *in vitro* of selected compounds for control of *Fusarium* wilt.

MATERIAL AND METHOD

Plant Materials

The aerial parts of *Asteriscus graveolens* (Figure 1) were collected from Bechar (road of Lahmer, Bechar, Algeria). The collected plants were identified, and voucher specimens were conserved at the herbarium of the Phytochemistry and Organic Synthesis Laboratory under accession No CA00/14. The aerial parts were air-dried at room temperature in a shady place and then ground in the blender. After grinding, the material was stored at room temperature.

Figure 1. General view of *Asteriscus graveolens*

Extraction and Bioguided Fractionation

The dried aerial part plants were extracted with 80% ethanol for 18 h using Soxhlet apparatus and then evaporated to dryness by a rotary evaporator (Büchi Rotavapor R-210) at 55°C under reduced pressure. This extract was suspended in distilled water and partitioned sequentially with n-hexane, dichloromethane, ethyl acetate, and n-butanol, respectively. This extract was suspended in distilled water and portioned sequentially with hexane, dichloromethane, ethyl acetate, and n-Butanol. The organic phase was evaporated to dryness under reduced pressure.

Thin-Layer Chromatography (TLC)

The extracts of each solvent were subjected to TLC. TLC was carried out on silica gel 60 F_{254} plates (Merck, Germany The used solvent system was ethyl acetate: heptane (75:25). Spots were detected on TLC under UV light. R_f values of evaluated spots were recorded.

Determination of the Total Phenolic Contents (TPC)

The total phenolic content (TPC) of the extracts was determined by the Folin–Ciocalteu method using a modified procedure of Sengul et al., 2009 [12] and [13].

Gallic acid was used as the standard phenolic compound. The calibration was plotted by mixing aliquots of 1000; 500; 250; 125; 62.5 and 31.25 ppm of gallic acid solutions with 5 ml of Folin Ciocalteu reagent and 5 ml of crude extract. After 3 min, a solution of sodium carbonate 10 % Na_2CO_3 was added and the mixture was allowed to stand for 1 h with intermittent shaking. The color was developed and absorbance was measured at 760 nm in a Shimadzu UV 1800 Spectrophotometer after 30 min using Gallic acid as a standard. The total phenolic content (TPC) was calculated from the calibration curve, and the results were expressed as µg of gallic acid equivalent per mg dry weight (mg GA/g).

Determination of the Total Flavonoid Contents (TFC)

The aluminum chloride colorimetric method was used for the determination of the total flavonoid content of the samples; quercetin was used to make the standard calibration curve [14].

Antifungal Screening by Direct Bioautography

To screen for and identify compounds with antifungal activity present in the plant extracts, direct bioautography was used as described by Boulenouar et al. [15]. This approach involves directly immersing and cultivating a suspension of fungal spores on a developed TLC chromatogram.

Fungal Strain

The phytopathogenic filamentous fungus (Foa) used in this work was obtained from The Technical Institute for Saharian Agronomy (TISA), Adrar, Algeria. The strain was identified, and a voucher specimen was stored at the Phytochemistry and Organic Synthesis Laboratory under N° POSL/2011/01.

Spore suspensions of plant pathogens (Foa) were used. The concentration of Foa spores was adjusted to approximately 10^7 spores/ ml by dilution and counting.

Antifungal Activity of the Plant Extracts

The antifungal potential of the plant extracts was assessed by applying 80 µg/µl of each extract onto silica gel 60 F_{254} TLC plates (7 × 1.5 cm). These chromatograms were then immediately transferred into Petri dishes containing 20 ml of a spore solution with a concentration of 2×10^7 spores/ml, and left for 10 seconds. The development of fungal growth was monitored periodically until the TLC plates were completely covered with mycelial growth. Control plates, spotted with the respective organic solvent, were concurrently processed [15]. For visualization of microbial growth, tetrazolium salts, particularly p-iodonitrotetrazolium violet (INT) solution at a concentration of 2 mg/ml, were sprayed onto the Bioautograms [16]. Following overnight reincubation at 21°C, clear white zones against a purple background on the TLC plate indicated the presence of antimicrobial activity in the sample [17]. To identify the active compound, the R_f values on the plates were compared with those of reference plates.

Fractions

Among all extracts and fractions, ethyl acetate fractions exhibited a great antifungal effect on Foa and have been further characterized by chemical methods (TPC, TFC, NMR, and LC-MS/MS analysis).

The ethyl acetate fractions were chromatographed over silica gel open Column chromatography (30 g) using a mobile phase: (ethyl acetate: heptane) with the report in the following volume: (75: 25). Column chromatography was performed over silica gel 60 (Merck, particle size 290-320 mesh).

The recovered fractions were analyzed again by TLC, and fractions with identical spots and R_f values were pooled together for the antifungal evaluation using the antimicrobial assays described below.

Characterization of Isolated Compounds

The extracted and purified bioactive compounds from *Asteriscus graveolens* were characterized by nuclear magnetic resonance (NMR) techniques: Routine ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Model Avance AMX spectrometer (^{1}H 400 MHz and ^{13}C 100 MHz respectively) in deuterated chloroform ($CDCl_3$) with tetramethylsilane (TMS) as an internal reference. Mass spectrometry detection was conducted using a Shimadzu LC-MS 8040 model triple quadrupole mass spectrometer equipped with an ESI source operating in both positive and negative ionization modes. Data were acquired by Lab Solutions software (Appendix C). Ethyl acetate fractions of *Asteriscus graveolens* were analyzed by the LCMS-8040 system (Shimadzu, Kyoto, Japan). The mobile phase consisted of 100% methanol (solvent A) and acetonitrile (solvent B) (1:1 v/v). The mobile phase flow rate was 0.3 ml/min. The column temperature was fixed at 40°C. Plant compounds were detected by a full scan mode ranging from m/z 100 - 1000 amu.

The LC-MS/MS, ^{13}C NMR, and ^{1}H NMR analyses were carried out in the laboratory of the "Catalysis Research and Application Center" of the University of İnönü, Malatya, Turkey.

Preliminary Evaluation of the Antifungal Activity

Preliminary analysis of the antifungal activity was performed using the agar-disc diffusion bioassay [19] and the agar-well diffusion bioassay [20] for the evaluation of ethyl acetate fractions.

For the disc diffusion bioassay, sterile discs (6 mm in diameter) of Whatman filter paper No.10 were impregnated with (20, 50, 80, and 100 µl) of each extract. The solvent was left to evaporate at room temperature, and the discs were placed on the surface of the plates previously seeded. Paper discs impregnated with ethyl acetate were used as controls.

For the well-diffusion bioassay, wells were made in the agar using an inverted sterile Pasteur pipette (6 mm in diameter), and (20, 50, 80, and 100 µl) of ethyl acetate extracts were deposited in the wells. Ethyl acetate was used as a control (all manipulations were done in sterile conditions). Plates were incubated at 21°C for 5 days.

Antimicrobial activity was detected by the presence of a growth inhibition zone surrounding the disc or well. The diameter of this zone was measured and recorded. The tests were realized in triplicate (the standard errors were less than 10%).

RESULT AND DISCUSSION

Phytochemical Study of the Bioactive Extracts/Fractions

Total Phenolic Contents

The crude extracts and ethyl acetate fractions of the investigated plant underwent phytochemical screening, revealing the presence of phenolics. Total phenolic contents were quantified utilizing the Folin-Ciocalteu method and expressed as Gallic acid equivalents (GAE) in µg GA/mg of the extract. The determination of total phenolic content was facilitated by reference to the graph depicted in Figure 1, and the standard curve equation was $y = 0.00146x + 0.02028$, where $R^2 = 0.99913$. The total phenolic contents (Gallic acid equivalents, µg GA/mg) in the samples were calculated to be 1144,879 and 366,052 µg GA/mg in *A. graveolens*,respectively (Table 1).

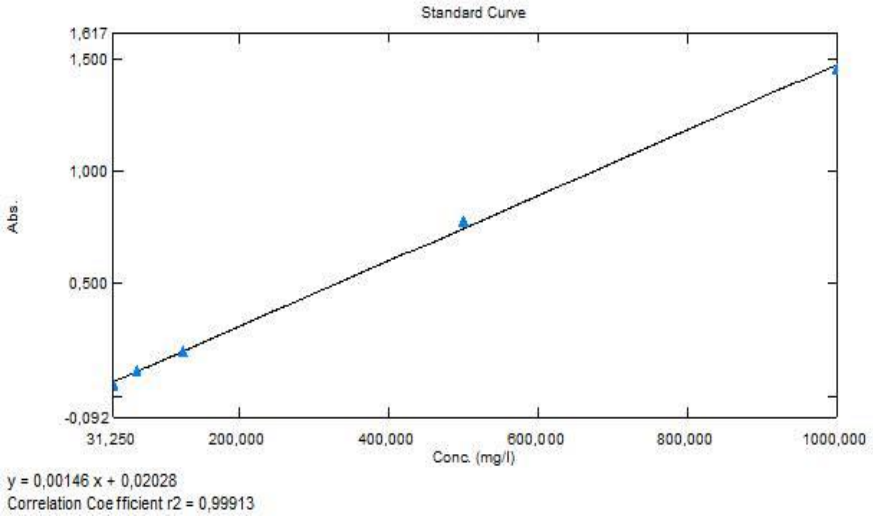

Figure 2. Standard curve of gallic acid

Figure 2 shows the total phenolic content in the samples of aerial parts of *A. graveolens* spontaneously grown in the southwest of Algeria.

The high amount of phenolic compounds from *A. graveolens* was reported by Ramdane et al. (2017). The variance in total phenolic content could be due to the chemical composition of the extract but also to the extreme conditions of growth and an arid ecosystem.

Total Flavonoid Contents

The concentration of total flavonoid contents in the test samples was calculated from the calibration plot (Y=0.00535 – 0.00381; R^2=0.99917) and expressed as µg quercetin equivalents per mg of dry extract (µg QE/mg). The total flavonoid contents in different extracts are shown in Figure 3.

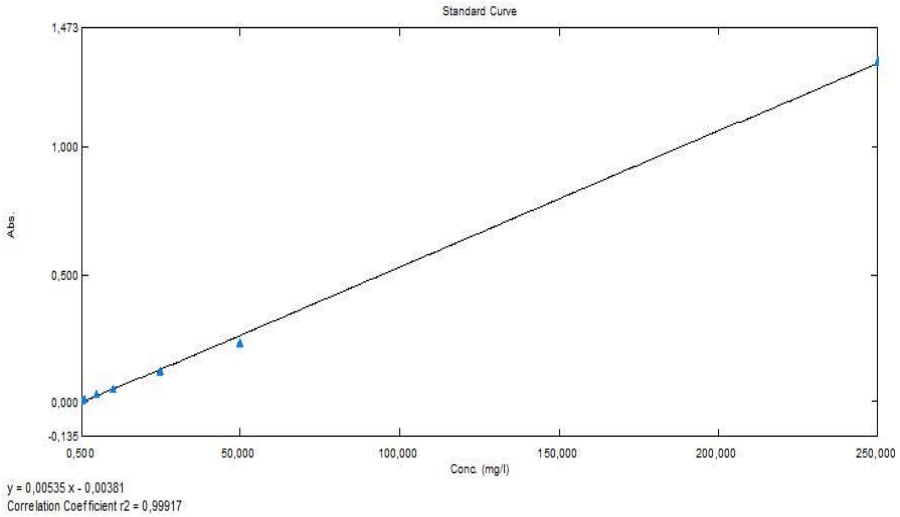

Figure 3. The total flavonoid content in the samples of aerial parts of *Asteriscus graveolens*

Many studies on the phytochemical composition of *A. graveolens* showed that this plant produced phenolic compounds including flavonoids:

Ahmed et al. (1991) have identified kaempferol 3-*O*-β-glucoside, kaempferol 3-*O*-β-galactoside, kaempferol 7-*O*-β-galactoside, quercetin 7-*O*-β-glucoside, luteolin 7-*O*-β-glucoside, and quercetin as major compounds in *A. graveolens* in Egypt.

Table 1. Total phenolic and flavonoid contents of crude extracts and ethyl acetate fractions of *A. graveolens*

Sample Code	TPC (mg GAE/gDry extract wt)	TFC (mg QE/g dry extract wt)
A graveolens Crude extract	1144.879	13.824
A graveolens EtOAc fraction	366.052	5.573

TPC: total phenol content; TFC: total flavonoid content; GAE: gallic acid equivalents; QE: quercetin equivalents; wt: weight; EtOH: ethanol; EtOAc: ethyl acetate [18]

The total phenolic content of the ethyl acetate fractions, calculated from the calibration curve (R^2 = 0.99913), was 366.052 µg GA/mg in *A. graveolens* and the total flavonoid content (R^2 = 0.99917) was 5.573 µg QE/mg in*A. graveolens* (Table 1).

A recent study on the phytochemical composition of *A. graveolens* [19] showed that ethyl acetate is the most suitable solvent for the extraction of bioactive compounds from this plant.

Direct Bioautography

Frequently, TLC-Direct Bioautography is used as a bio-guiding method to destine substances with biological activity that can be further analyzed by spectroscopic methods to obtain information on their structure [20].

The richness of natural substances reported by Cheriti *et al.* (2007) can explain the antifungal activity in certain extracts of *A. graveolens* (Table 2).

Table 2. Direct bioautography results of the extracts of *Asteriscus graveolens*

Specie	Eluent	Extraction Solvent	Antifungal Effect
Asteriscus graveolens	**EtOAc: Hep 75:25**	EtOH	++
		Hex	-
		DCM	++
		EtOAc	++
		n-But	+

Hep: heptane; EtOH: ethanol; Hex: hexane; DCM: dichloromethane; EtOAc: ethyl acetate; *n*-But: butanol

The absence of observed effects from testing an extract on a specific biological target does not necessarily negate the presence of active substances, as synergy between components may occur. Additionally, in some instances, the concentration of these substances may be sufficiently low that their activity can only be detected on TLC plates.

Characterization of Bioactive Compounds by NMR and LC-MS

LC-MS/MS analyses showed that plant extracts were decomposed topreviously known ones. The structures of compounds were elucidated by NMR techniques and mass spectroscopy. The compounds isolated from the ethyl acetate fractions of the species *Asteriscus graveolens* display a powerful antifungal effect.

The known compounds were identified as methyl gallate and syringic acid based on comparing their spectral and physical data with the literature (Figure 4). Effectively, the *m*/*z* values of 185 and 198 corresponded to their molecular weight of 184.15 and 198.17 g/mol respectively, thus validating the output of the mass spectrometer. Figure 4 shows the structure of the compounds isolated.

Identification of molecules by NMR (^{1}H and ^{13}C) spectrophotometry and LC-MS/MS showed the presence of methyl gallate and syringic acid in aerial parts of *A. graveolens*.

NMR spectra of methyl gallate ($C_8H_8O_5$): ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 3.95 (s, 3H, CH_3), 6.91 (s, 2H, C_6H_2), 8.73 (s, 3H, OH). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 52.08 (CH_3O), 110.8, 123.82, 137.57, and 146.65 (C_6H_2), 166.51 (CO). The molecular mass of isolated methyl gallate was determined as 185 using LC-MS/MS analysis. Results obtained with ^{1}H-NMR; ^{13}C-NMR and LC-mass spectroscopy were identical to published data [21].

NMR spectra of syringic acid ($C_8H_8O_5$): ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 3.82 (s, 6H, CH_3), 7.07 (s, 2H, C_6H_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 56.78 (CH_3O), 106.09, 121.39, 141.78 and 149.19 (C_6H_2), 167.49 (CO). The molecular mass of isolated syringic acid was determined as 198 using LC-MS/MSanalysis.

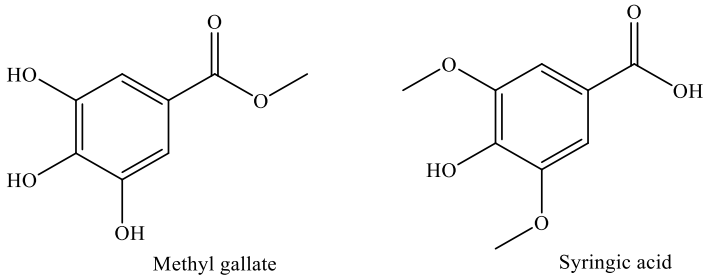

Figure 4. Compounds isolated and identified in aerial parts of *Asteriscus graveolens*

In this research, the assessment of *A. graveolens* extracts against the pathogen responsible for Bayoud disease, *Fusarium oxysporum* f. sp. *albedinis* (Foa), incorporated innovative principles into direct bioautography. Previous research conducted at the Phytochemistry and Organic Synthesis Laboratory (POSL, Bechar University, Algeria) has established that this plant contains secondary metabolites possessing various biological activities.

This medicinal plant has previously been investigated by our research group (POSL team) for its antibacterial and antifungal properties. They were chosen for initial testing based on a systematic review conducted on promising bioactive plants which highlighted the above species [1,22-24].

Plant extracts were selected for inclusion in this study because their ability to inhibit the respective enzymes and biological activities has already been established in studies published by others and in previous studies carried out by our research group [1,22-24].

Bioautography is notably significant to avoid the time-consuming isolation of inactive compounds [25]. TLC bioautographic methods combine chromatographic separation and in situ activity determination facilitating the localization and target-directed isolation of active constituents in a mixture [26]. The bioautography technique is inexpensive, so beneficial for screening large numbers of samples (particularly crude extracts). Although results are not completely quantitative, they can give information about how many and which substances in a mixture showed antifungal activity [27].

The phytochemical analysis aimed to identify the specific metabolite accountable for the observed antifungal activity. Based on TLC profiling results, it is conjectured that the inhibition may be attributed to flavonoids found in the ethyl acetate extracts derived from the aerial parts of *A. graveolens*, with R_f values of 0.24 and 0.88.

The number of active compounds in the plant extracts was determined using the bioautography method, those compounds were separated with CC and had similar R_f values of 0.24, and 0.88 in *A. graveolens* ethyl acetate fractions.

Apart from the advantages of rapidly detecting active compounds in mixtures and high sensitivity, the depicted bioautography also points to a potential disadvantage of this diffusion assay. Its applicability is limited to microorganisms that easily grow on TLC plates [28].

Recently, the fungicidal activities of plant extracts have been extensively reported [27]. Research investigating the fungicidal effects of *A. graveolens* extracts on the pathogen *F. oxysporum*, responsible for *Fusarium* wilt in date palms, remains limited. This disease presents a significant threat to date palm cultivation. However, the medicinal potential of *A. graveolens* is bolstered by the presence of phenolics and flavonoids, indicating promising therapeutic applications.

The effects of the extracts utilized were demonstrated by Boulenouar et al. (2014) using the disc diffusion technique. Results indicated detectable effects against Foa in at least two tests, thus confirming the presence of antifungal substances despite the variance in the techniques employed. The notable impact observed across different parts of the plant may be attributed to variations in the components present. This discrepancy could stem from differences in chemical composition or mechanism of action. It's noteworthy that certain substances exhibit antifungal activity against Foa but not against its toxins, highlighting the intricate nature of the pathogenic mechanism.

Indeed, Foa is known to produce multiple toxins, which play a crucial role in its pathogenicity. Consequently, previous research conducted against Foa has identified active substances that can influence one or more of these mycotoxins. This influence may occur through the modification of their metabolism or their effects, thereby affecting the pathogenic behavior of the fungus [24,29].

Flavonoids represent a class of compounds known for their ability to inhibit various enzymes. Through phytochemical screening, our study identified a diverse array of phytoconstituents, with phenolic compounds being particularly abundant [30].While numerous investigations have explored the structure-activity relationship of various polyphenols and their antifungal properties, the precise relationship remains unclear despite the vast number of these compoundsclear [31]. Plants synthesize a wide range of metabolites to ensure their survival, growth, development, and defense against a broad spectrum of pathogens, including bacteria, fungi, and viruses. In our study, we isolated methyl gallate (MG) and syringic acid (SA) as major metabolites exhibiting antifungal activity from the aerial parts of *A. graveolens*.

The LC-MS/MSchromatogram data of the EtOAc extract revealed a group of peaks that were fractionated from one to seven by open silica column chromatography. The active compounds of fractions 5 and 6 were purified and identified as MG using NMR and LC-MS/MSanalysis. MG and SA are natural constituents isolated from different plants [21,32]. *In vitro* studies on the antifungal activity of SA were done by Chong et al. using concentrations ranging from 50 to 110 ml μg^{-1}, those typically recorded in oil palm roots. SA was found to be antifungal against *G. boninense* [33,34].

Phenylpropanoid metabolism produces an enormous array of secondary metabolites. The biosynthesis of GA and its derivative MG takes place via phenylpropanoid metabolism [35].

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AUTHOR CONTRIBUTIONS

Concept: Z.B., Z.R., N.B., A.C.; Design: Z.B., Z.R., N.B., A.C.; Control: Z.B., A.C.; Sources: Z.B., Z.R., N.B., A.C.; Materials: A.C.; Data Collection and/or Processing: Z.B., Z.R., N.B., A.C.; Analysis and/or Interpretation: Z.B., Z.R., N.B., A.C.; Literature Review: N.B., A.C; Manuscript Writing: Z.B.; Critical Review: Z.B., Z.R., N.B., A.C.; Other: -

CONFLICT OF INTEREST

The authors declare that there is no real, potential, or perceived conflict of interest for this article.

ETHICS COMMITTEE APPROVAL

The authors declare that ethics committee approval is not required for this study.

REFERENCES

1. Belhi, Z., Boulenouar, N., Cheriti, A., Marouf, A. (2020). Antifungal and anti-cellulases activity of Limoniastrum feei extracts to promote Bayoud disease treatment using bioautography. Cogent Food and Agriculture, 6(1), 1726083. [CrossRef]

2. Hussain, A., Aslam, B., Gilani, M.M., Khan, J.A., Anwar, M.W. (2019). Biochemical and histopathological investigations of hepatoprotective potential of Phoenix dactylifera against isoniazid induced toxicity in animal model. Pakistan Journal of Agricultural Sciences, 56(2), 489-493. [CrossRef]
3. El Hadrami, I., El Bellaj, M., El Idrissi, A., J'Aiti, F., El Jaafari, S., Daayf, F. (1998). Biotechnologies végétales et amélioration du palmier dattier (Phoenix dactylifera L.), pivot de l'agriculture oasienne marocaine. Cahiers Agricultures, 7(6), 463-468.
4. Ait Kettout, T., Rahmania, F. (2010). Identification par CG-SM de l'acide phénylacétique produit par *Fusarium oxysporum* f. sp. *albedinis*, agent causal du bayoud. Comptes Rendus Biologies, 333(11), 808-813. [CrossRef]
5. Thrane, U. (2014). Fusarium. In C.A. Batt and M.L. Tortorello (Eds.), Encyclopedia of Food Microbiology (Second Edition). Oxford: Academic Press, pp. 76-81.
6. Fourie, G., Steenkamp, E.T., Ploetz, R.C., Gordon, T.R., Viljoen, A. (2011). Current status of the taxonomic position of *Fusarium oxysporum* formae specialis *cubense* within the *Fusarium oxysporum* complex. Infection, Genetics and Evolution, 11(3), 533-542. [CrossRef]
7. Muhammad, A., Hussain, I., Khanzada, K.A., Kumar, L., Ali, M., Yasmin, T., Hyder, M.Z. (2017). Molecular characterization of *Fusarium oxysporum* f. sp. *cubense* (Foc) tropical race 4 causing Panama disease in Cavendish banana in Pakistan. Pakistan Journal of Agricultural Sciences, 54(1), 1-8.
8. Belhi, Z., Boulenouar, N., and Cheriti, A. (2020). The use of natural products against *Fusarium oxysporum*: A review. The Natural Products Journal, 10, 1-12. [CrossRef]
9. Bashir, M.R., Atiq, M., Sajid, M., Hussain, A., Mehmood, A. (2018). Impact of organic matter and soil types on the development of Fusarium wilt of chilli. Pakistan Journal of Agricultural Sciences, 55(4), 749-753.
10. Fatima, S.A., Huang, Q., Sarfaraz, Z., Luo, P. (2019). Effects of the interaction of Fusarium head blight and stripe rust on wheat yield parameters. Pakistan Journal of Agricultural Sciences, 56(2), 351-358.
11. Munusamy, U., Mohd-Yusuf, Y., Baharum, N.A., Zaidi, K., and Othman, R.Y. (2019). RT-qPCR profiling of pathogenesis related genes in *Musa acuminata* cv.'Berangan'seedlings challenged with *Fusarium oxysporum* f. sp. *cubense* tropical race 4. Pakistan Journal of Agricultural Sciences, 56(1), 37-42.
12. Slinkard, K., Singleton, V.L. (1977). Total phenol analysis: Automation and comparison with manual methods. American Journal of Enology and Viticulture, 28(1), 49-55.
13. Sengul, M., Yildiz, H., Gungor, N., Cetin, B., Eser, Z., Ercisli, S. (2009). Total phenolic content, antioxidant and antimicrobial activities of some medicinal plants. Pakistan Journal of Pharmaceutical Sciences, 22(1), 102-106.
14. Chandra, S., Khan, S., Avula, B., Lata, H., Yang, M.H., ElSohly, M.A., Khan, I.A. (2014). Assessment of total phenolic and flavonoid content, antioxidant properties, and yield of aeroponically and conventionally grown leafy vegetables and fruit crops: A comparative study. Evidence-based Complementary and Alternative Medicine, 2014(1), 253875.
15. Boulenouar, N., Marouf, A., Cheriti, A. (2011). Antifungal activity and phytochemical screening of extracts from *Phoenix dactylifera* L. *cultivars*. Natural Product Research, 25(20), 1999-2002. [CrossRef]
16. Rana, B., Singh, U., Taneja, V. (1996). A rapid method for detecting fungi-toxic substances. World Journal of Microbiology and Biotechnology, 12(3), 301-302.
17. Mahlo, S.M., Chauke, H.R., McGaw, L., Eloff, J. (2016). Antioxidant and antifungal activity of selected medicinal plant extracts against phytopathogenic fungi. African Journal of Traditional, Complementary and Alternative Medicines, 13(4), 216-222.
18. Saxena, G., Farmer, S., Towers, G., Hancock, R. (1995). Use of specific dyes in the detection of antimicrobial compounds from crude plant extracts using a thin layer chromatography agar overlay technique. Phytochemical Analysis, 6(3), 125-129. [CrossRef]
19. Boulenouar, N., Marouf, A., Cheriti, A. (2009). Effect of some poisonous plants extracts on *Fusarium oxysporum* f. sp. *albedinis*. Journal of Biological Sciences, 9(6), 594-600. [CrossRef]
20. Magaldi, S., Mata-Essayag, S., De Capriles, C.H., Perez, C., Colella, M., Olaizola, C., Ontiveros, Y. (2004). Well diffusion for antifungal susceptibility testing. International Journal of Infectious Diseases, 8(1), 39-45. [CrossRef]
21. Ramdane, F., Essid, R., Mkadmini, K., Hammami, M., Fares, N., Mahammed, M.H., Hadj, M.D.O. (2017). Phytochemical composition and biological activities of *Asteriscus graveolens* (Forssk) extracts. Process Biochemistry, 56, 186-192. [CrossRef]
22. Aryal, S., Baniya, M.K., Danekhu, K., Kunwar, P., Gurung, R., Koirala, N. (2019). Total phenolic content, flavonoid content and antioxidant potential of wild vegetables from western nepal. Plants, 8(4), 96. [CrossRef]
23. Choma, I., Jesionek, W. (2015). TLC-direct bioautography as a high throughput method for detection of

antimicrobials in plants. Chromatography, 2(2), 225-238. [CrossRef]
24. Kamatham, S., Kumar, N., Gudipalli, P. (2015). Isolation and characterization of gallic acid and methyl gallate from the seed coats of Givotia rottleriformis Griff. and their anti-proliferative effect on human epidermoid carcinoma A431 cells. Toxicology Reports, 2, 520-529. [CrossRef]
25. Boulenouar, N., Marouf, A., Cheriti, A., Belboukhari, N. (2012). Medicinal plants extracts as source of antifungal agents against *Fusarium oxysporum* f. sp. *albedinis*. Journal of Agricultural Science and Technology, 14, 659-669.
26. Ghazi, R., Boulenouar, N., Cheriti, A., Reddy, K., Govender, P. (2020). Bioguided fractionation of citrullus colocynthis extracts and antifungal activity against *Fusarium oxysporum* f.sp. *albedinis*. Current Bioactive Compounds, 16(3), 302-307. [CrossRef]
27. Dewanjee, S., Gangopadhyay, M., Bhattacharya, N., Khanra, R., Dua, T.K. (2015). Bioautography and its scope in the field of natural product chemistry. Journal of Pharmaceutical Analysis, 5(2), 75-84. [CrossRef]
28. Suleiman, M.M., McGaw, L., Naidoo, V., and Eloff, J. (2010). Detection of antimicrobial compounds by bioautography of different extracts of leaves of selected South African tree species. African Journal of Traditional, Complementary and Alternative Medicines, 7(1), 64-78.
29. Balouiri, M., Sadiki, M., and Ibnsouda, S.K. (2016). Methods for in vitro evaluating antimicrobial activity: A review. Journal of Pharmaceutical Analysis, 6(2), 71-79. [CrossRef]
30. Prieto, J.A., Patiño, O.J., Plazas, E.A., Pabón, L.C., Ávila, M.C., Guzmán, J.D., Cuca, L.E. (2013). Natural products from plants as potential source agents for controlling fusarium. Fungicides-Showcases of Integrated Plant Disease Management from Around the World. Croacia: Intech, 233-278.
31. El Hadrami, A., El Idrissi-Tourane, A., El Hassni, M., Daayf, F., and El Hadrami, I. (2005). Toxin-based *in-vitro* selection and its potential application to date palm for resistance to the bayoud Fusarium wilt. Comptes Rendus Biologies, 328(8), 732-744.
32. El Haci, I.A., Mazari, W., Atik-Bekkara, F., Hassani, F., Gherib, M. (2017). Assessment of the cytotoxic activity and the reduction power of Limoniastrum feei Girard (Batt.): A medicinal plant from Algerian Sahara. Oriental Pharmacy and Experimental Medicine, 17(2), 143-150.
33. Munari, C. (2006). Investigation phytochimique de plantes alpines: Etude d'espèces du genre Oxytropis (Fabaceae) et isolement de composés antifongiques et antiradicalaires à partir d'Oxytropis fetida (Vill.) DC., *Potentilla grandiflora* L. (Rosaceae) et *Vaccinium uliginosum* ssp., University of Geneva. Retrieved from https://nbn-resolving.org/urn:nbn:ch:unige-33548/. Accesed date: 20.02.2024.
34. Abou-Zaid, M.M., Lombardo, D.A., Nozzolillo, C. (2009). Methyl gallate is a natural constituent of maple (Genus Acer) leaves. Natural Product Research, 23(15), 1373-1377. [CrossRef]
35. Chong, K., Atong, M., Rossall, S. (2012). The role of syringic acid in the interaction between oil palm and Ganoderma boninense, the causal agent of basal stem rot. Plant Pathology, 61(5), 953-963. [CrossRef]
36. Chong, K.P., Rossall, S., and Atong, M. (2009). *In vitro* antimicrobial activity and fungitoxicity of syringic acid, caffeic acid and 4-hydroxybenzoic acid against *Ganoderma boninense*. Journal of Agricultural Science, 1(2), 15.
37. Vogt, T. (2010). Phenylpropanoid Biosynthesis. Molecular Plant, 3(1), 2-20. [CrossRef]

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ORIGINAL ARTICLE / ÖZGÜN MAKALE

TOTAL PHENOLIC AND FLAVONOIDS QUANTIFICATION AND ANTIOXIDANT ACTIVITY OF BIOACTIVE EXTRACTS FROM THE LEAVES OF *ATRIPLEX HALIMUS*

ATRIPLEX HALIMUS YAPRAKLARINDAN ELDE EDİLEN BİYOAKTİF EKSTRAKTLARIN TOPLAM FENOLİK VE FLAVONOİD ÖLÇÜMÜ VE ANTİOKSİDAN AKTİVİTESİ

Laid ZIANE[1], Abdelaziz BERREGHIOUA[1]*

[1]Tahri Mohammed University, Faculty of Exact Sciences, Chemistry and Science Environment Laboratory, BP 417, Bechar 08000, Algeria

ABSTRACT

Objective: *This study sought to identify potential sources for upcoming novel antioxidants in food and pharmaceutical formulations by screening various solvent extracts from the leaves of Atriplex halimus Lin. for their ability to exhibit strong antioxidant activity in vitro, as well as their total phenolic and flavonoid contents.*
Material and Method: *To determine the total amount of polyphenols and flavonoids in Atriplex halimus extracts, including ethyl ether, ethyl acetate, and n-butanol extracts, as well as their corresponding impact on this plant's antioxidant activity, were carried out using the conventional procedures.*
Result and Discussion: *In the current investigation, total phenolic and flavonoid contents in butanolic extract were found to be 68.20 mg gallic acid equivalent (GAE)/g dry extract) and 439 mg quercetin equivalent (QE)/g dry extract. The hydro-alcoholic extract was extracted by liquid/liquid partition with solvents of increasing polarity: ethyl ether, ethyl acetate and n-butanol) by the free radical DPPH removing garbage and HPTLC as well as their reduction kinetics. It was found that the extract of butanol and ethyl acetate had powerful uplifting power garbage DPPH with IC_{50} values of 2.1959 and 2.4234 mg/ml, respectively.*
Keywords: *Antioxidant activity, Atriplex halimus, bioactive extract, DPPH, phytochemical, quercetin*

ÖZ

Amaç: *Bu çalışmada, Atriplex halimus bitkisinin tamamının çeşitli solvent ekstrelerini, in vitro güçlü antioksidan aktivite sergileme yetenekleri ve ayrıca toplam fenolik ve flavonoid içerikleri açısından tarayarak, gıda ve farmasötik formülasyonlarda gelecek yeni antioksidanlar için potansiyel kaynakları belirleme amaçlandı.*
Gereç ve Yöntem: *Etil eter, etil asetat ve n-butanol ekstreleri dahil olmak üzere Atripleks halimus ekstrelerindeki polifenollerin ve flavonoidlerin toplam miktarının yanı sıra bunların bu bitkinin antioksidan aktivitesi üzerindeki karşılık gelen etkilerini belirlemek için geleneksel prosedürler kullanılarak gerçekleştirildi.*
Sonuç ve Tartışma: *Mevcut araştırmada, bütanolik ekstredeki toplam fenolik ve flavonoid içeriğinin 68.20 mg gallik asit eşdeğeri (GAE)/g kuru ekstrakt) ve 439 mg kersetin eşdeğeri (QE)/g kuru ekstre olduğu*

* **Corresponding Author / SorumluYazar:** Berreghioua Abdelaziz
e-mail / e-posta: berghioua.abdelaziz@univ-bechar.dz, **Phone / Tel.:** +213676973321

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bulunmuştur. Hidro-alkolik ekstresi, artan polariteye sahip solventler (etil eter, etil asetat ve n-butanol) ile sıvı/sıvı partitisyona tabi tutulmasıyla, serbest radikal DPPH'nin atıkları ve HPTLC'yi ve bunların indirgeme kinetiklerini ortadan kaldırmasıyla ekstre edildi. Butanol ve etil asetat ekstreleri sırasıyla 2.1959 ve 2.4234 mg/ml IC_{50} değerleriyle DPPH radikali süpürücü aktivitesine sahip olduğu bulundu.
Anahtar Kelimeler: *Antioksidan aktivite, Atriplex halimus, biyoaktif ekstre, DPPH, fitokimyasal, quercetin*

INTRODUCTION

Numerous plants, including aromatic, medicinal, and other types, have intriguing biological qualities that are used in a variety of contexts, including cosmetics, pharmacy, and medicine. However, assessing the antibacterial and antioxidant qualities of plant protection remains a highly intriguing issue when using whole particles for uncommon, or unknown plants in traditional medicine [1]. *Atriplex halimus* is a shrubby, succulent halophyte that is commonly found in semi-arid Mediterranean regions, particularly on high plateaus and along the littoral regions, where favorable conditions are regrouped with an intra- and interindividual polymorphism for a number of floral morphological characters, such as styles, ovule types and radicle orientation according to salinity [2,3]. *A. halimus* has up to 10% sodium chloride, according to a study of its chemical composition, and it also contains secondary metabolites such tannins, flavonoids, saponins, alkaloids, and resins [4,5].

In this work, we use a DPPH radical scavenging and reducing power test to examine the polyphenol content and antioxidant capacity in *A. halimus* leaves in methanolic extract. (The aqueous residue was then partitioned sequentially with ethyl ether, ethyl acetate and n-butanol) [6].

MATERIAL AND METHOD

Plant Material

Atriplix halimus was collected in march 2019 from Boukais (South Western Algeria) Algeria. It was identified by several herborists, a voucher specimen was deposited at the herbarium of the Chemistry and Science Environment Laboratory, South West of Algeria, University of Béchar.

Extraction

Using a soxhlet apparatus, 100 g of dried *Atriplex halimus* plant leaves were extracted with 400 ml of 80% MeOH; reflux was carried out for four hours.

The residue was evaporated in a vacuum device, and the natural product present in the bioactive extract was identified using the working principles of chemical screening [7-8]. The resulting product can be dissolved in 100 ml of distilled water to produce a brown-colored aqueous solution. This aqueous residue was divided using n-butanol, ethyl ether, and ethyl acetate in that order [9-10].

Total Phenolic Quantification

Standard process designed the procedure. For the quantification of total polyphenols, this method has been used. Each sample extract was transferred to a 25 ml volumetric flask containing 2.5 ml of 3.54 $g.l^{-1}$ Iron(III) chloridehexahydrate ($FeCl_3.6H_2O$) solution. The sample solution was then placed in a volumetric flask and kept at 80°C in a water bath for 20 min. Following that, 2.5 ml of acetate buffer (CH_3COOH/CH_3COOK) solution (pH 4.6), 5.0 ml of 3.28 $g.l^{-1}$ 1,10-phenanthrolinehydrate (1,10-phen), and 2.5 ml of 3.72 $g.l^{-1}$ Ethylene diaminetetraaceticaciddihydrate (EDTA) solutions were added, in that order. Finally, each flask was filled with distilled water to the specified level, chilled, and absorbance measurements were taken at 511 nm [11].

Total Flavonoid Quantification

The total flavonoid content of the plant extracts was determined by producing different aliquots of the extracts. 0.1 ml 10 percent aluminum chloride and 0.1 ml potassium acetate (1 M) were added to this method, and the final volume was increased to 3 ml by adding distilled water. The samples were then incubated at room temperature for 30 minutes.

The calibration curve was created by reading the absorbance at 415 nm and using quercetin as a reference. The total flavonoid content was quantified using the standard curve of quercetin and the results were represented in milligrams of quercetin equivalents (QE) per gram of dry extract (mg QE/g of dry extract) [12].

Determination of Free Radical Scavenging Activity by DPPH Method

The scavenging activity of the stable 1,1-diphenyl-2-picrylhydrazyl (DPPH) free radical was used to determine the antioxidant potential of the crude extracts of n-butanol, ethyl ether, and ethyl acetate. In summary, 1.9 ml of a DPPH (0.004%) methanol solution has been mixed with 100 µl of different extract concentrations in methanol. The mixture was first given a good shake before being let to stand at room temperature for half an hour in the dark. A double-beam UV–vis Camspec M550 spectrophotometer was used to test the mixture's absorbance at 517 nm. A mixture of 100 µl of methanol and 1.9 ml of DPPH is used as the control. Using the following formula, the scavenging activity on the DPPH radical was expressed as an inhibition percentage [13]:

$$\%\text{Inhibition} = [(A_B - A_S)/A_B] \times 100$$

Where A_S is the absorbance of the test compound and A_B is the absorbance of the control reaction, which is made up of all the reagents except the test compound. Antioxidant ascorbic acid has been utilized as a positive control or for comparison. There were three copies of each test run. The graph of the inhibition percentage plotted against the extract concentration (0.5; 0.25; 0.125; 0.0625; 0.0312; 0.0156; 0.0078 mg/ml) was used to determine the extract concentration producing 50% inhibition (IC_{50}). Quercetin was used as a standard to determine the calibration curve after the absorbance was measured at 415 nm. To measure the total flavonoid content using the quercetin standard curve, each test was run three times, and the findings were represented in milligrams of quercetin equivalents (QE) per gram of dry extract (mg QE/g of dry extract).

RESULT AND DISCUSSION

Using the Folin-Ciocalteu technique, the total phelolic content of all examined extracts was determined. The butanolic extract was shown to be the most active, with a total concentration of 68.20 ± 0.03 GAE mg/g in dry extract. However, ethyl acetate had 38.80 ± 0.11 mg GAE/g, but diethyl ether extract contained 26.40 ± 4.73 GAE mg/g, dry extract (Table 1).

The total flavonoid content of butanolic extract was 439 ± 2.77 mg QE/g of dry extract, indicating the presence of the most polyphenols in *Atriplix halimus*, followed by ethyl acetate extract with 411 ± 5.69 mg QE/g of dry extract (Table 1).

Phenolics compounds were extracted by Soxhlet method and analyzed by the Folin–Ciocalteu colorimetric method, while flavonoids were determined by aluminum trichloride assay. All tested extracts contain phenolic compounds, however the most significant amount of total phenolic and flavonoid contents was presented in butanolic extract (68.20 mg GAE/g, dry extract and 439 mg QE/g, dry extract) respectively.

Table 1. Total phenolic and flavonoid contents (mg/g) of the *Atriplex halimus*

Extraction Solvents	Total Polyphenol Content (mg GAE/g dry extract)	Flavonoids Content (mg QE/g dry extract)
Ethyl ether	26.40 ± 4.73	212 ± 4.15
Ethyl acetate	38.80 ± 0.11	411 ± 5.69
Butanol	68.20 ± 0.03	439 ± 2.77

Due to its additional electron, DPPH produces a potent absorption band in visual spectroscopy at 517 nm [14].

Using the thin layer chromatography (TLC) bioautography technique, we noted on the TLC plate the appearance of zones of antiradicalaire activity of pale yellow hue on purple bottom for the under-researched extracts as well as for the ascorbic acid [15].

Table 2. IC_{50} concentrations of DPPH scavenging capacity from bioactive extracts of *Atriplex halimus*

Bioactive Extracts	**IC_{50} (mg/ml)**
Ethyl ether	2.9382
Ethyl acetate	2.4234
Butanol	2.1959
Ascorbic acid (positive control)	0.0331

Table 2 shows that the scavenging effects of samples on DPPH radical and were in the following order: *n*-butanol extract > ethyl acetate extract > ethyl ether extract. The IC_{50} values of scavenging DPPH radicals for the n-butanol and ethyl acetate extracts were 2.1959 and 2.4234 mg/ml respectively. Previous findings have demonstrated a substantial correlation between the phenolic content and the antioxidant ability of fig leaves [16]. Researchers in the fields of food science, health, and medicine have recently shown a growing interest in antioxidant properties. A popular technique for assessing a sample's capacity to scavenge free radicals is the scavenging of the stable DPPH radical, which can be applied to plant extracts as well. This method was applied in this study to investigate the extracts of the Algerian species *Atriplex halimus* for their strong antioxidant content. Based on the findings, and by comparing the IC_{50} values of each extract to ascorbic acid, which is a genuine simple IC_{50} of 0.0331 mg/ml [17], the results showed that the Butanolic extract of *Atriplex halimus* had the activity with IC_{50} value of 2.1959 mg/ml. Generally, the antioxidant activity of polyphenol is related to their major compounds.

Conclusion

One theory is that *A. halimus*, like all halophyte plants, produces bioactive compounds like polyphenols that may have therapeutic use as well as serve as a natural food preserver. The distribution of these molecules was unequal in different parts of the plant; the leaves showed a higher phenolic content in comparison with the previous studies; however, the flavonoids in ethyl acetate and butanolic fractions possess potential antioxidant activity which explains the relation structure-activity; further isolation and identification of potential bioactive compounds, particularly flavonoids responsible for antioxidant activity, are needed. The results of the study showed that n-butanol and ethyl acetate extracts have significant antioxidant activity; these two fractions' high levels of observed antiradical capabilities may be related to the presence of phenolic chemicals, which include phenolic hydroxyls.

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AUTHOR CONTRIBUTIONS

Concept: L.Z., A.B.; Design: L.Z., A.B.; Control: L.Z., A.B.; Sources: L.Z., A.B.; Materials: L.Z., A.B.; Data Collection and/or Processing: L.Z., A.B.; Analysis and/or Interpretation: L.Z., A.B.; Literature Review: L.Z., A.B.; Manuscript Writing: L.Z.; Critical Review: A.B.; Other: L.Z., A.B.

CONFLICT OF INTEREST

The authors declare that there is no real, potential, or perceived conflict of interest for this article.

ETHICS COMMITTEE APPROVAL

The authors declare that the ethics committee approval is not required for this study.

REFERENCES

1. Slimani, A., Moussaoui, A., Laazouni, A., Hamadi, N. (2016). Phytochemical screening, contribution to the study of the antifungal effect of flavonoids from different parts of *Ziziphus lotus* of South-West Algeria. Asian Journal of Pharmaceutical and Clinical Research, 10(2), 20.
2. Lim, Y., Lim, T., Tee, J. (2007). Antioxidant properties of several tropical fruits: A comparative study. Food Chemistry, 103, 1003-1008. [CrossRef]
3. Ismail, A., Marjan, Z., Foong, C. (2004). Total antioxidant activity and phenolic content in selected vegetables. Food Chemistry, 87, 581-586. [CrossRef]
4. Benhammou, N., Bekkara, F.A., Panovska, T.K. (2009). Antioxidant activity of methanolic extracts and some bioactive compounds of *Atriplex halimus*. Comptes Rendus Chimie, 12, 1259-1266. [CrossRef]
5. Abd El-Rahman, H.H., Mohamed, M.I., Gehad, A.E.A., Awadallah, I.M. (2006). Ameliorating the anti-nutritional factors effect in *Atriplex halimus* on sheep and goats by ensiling or polyethylene glycol (PEG) supplementation. International Journal of Agriculture and Biology, 8, 766.
6. Ziane, L., Lazouni, H.A., Moussaoui, A., Namidi, N., Djellouli, M., Belabbes, A. (2015). Flavonoid from methanolic extract of *Limoniastrum feei* (girard) batt (*Plumbaginaceae*). Asian Journal of Pharmaceutical and Clinical Research, 8, 218-219.
7. King, M.B., Bott, T.R. (1993). Extraction of Natural Products Using Near- Critical Solvents. Chapman & Hall, Glasgow, p.325.
8. Kumar, G.P., Kumar, S.V., Kumar, A.S. (2017). Quantification of total phenolic and flavonoid contents, and evaluation of free radical scavenging potential of *Vernonia cinerea*. Asian Pacific Journal of Health Sciences. 4(3), 279-287. [CrossRef]
9. Rajappa, K.C., Sasidhar, B.S., Naika, M., Keri, R.S. (2018). Phytochemical composition of *Caesalpinia crista* extract as potential source for inhibiting cholinesterase and β-amyloid aggregation: Significance to Alzheimer's disease. Asian Pacific Journal of Tropical Biomedicine. 8(10), 500-512. [CrossRef]
10. Rydberg, J. (2004). Solvent Extraction Principles and Practice. CRC Press, Boca Raton, p.480.
11. Rosset, R., Jardy A., Caude, M. (1991). Chromatographie en phase liquide et supercitique, Masson, Paris, p.919.
12. Hostettman, K., Marston, A., Hostettman, M. (1998). Preparative chromatography techniques: Applications in natural product isolation, Springer: Berlin Heidelberg. p.240.
13. Blois, M.S. (1958). Antioxidant determinations by the use of a stable free radical. Nature, 181, 1199-1200. [CrossRef]
14. Molyneux, P. (2004). The use of the stable free radical diphenylpicrylhydrazyl (DPPH) for the antioxidant activity. Songklanakarin Journal of Sciences and Technology, 26, 211-219.
15. Raquibul Hasan, S.M., Mokarram Hossain, M., Raushanara, A., Mariam, J., Ehsanul Hoque, M., Shafiqur, R. (2009). DPPH free radical scavenging activity of some Bangladeshi medicinal plants. Journal of Medicinal Plants Research, 3(11), 875-879.
16. Mahmoudi, S., Khali, M., Benkhaled, A., Benamirouche, K., Baiti, I. (2016). Phenolic and flavonoid contents, antioxidant and antimicrobial activities of leaves extracts from ten Algerian *Ficus carica* L. varieties. Asian Pacific Journal of Tropical Biomedicine, 6, 239-245. [CrossRef]
17. Ziane, L., Djellouli, M., Berghioua, A. (2021). Short Communication: Chemical composition, antioxidant andantimicrobial activity of *Fagonia longispina* (*Zygophyllaceae*) of Algeria. Biodiversitas Journal of Biological Diversity, 22, 3448-3453. [CrossRef]

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9. Bütün tablo ve şekiller metin içindeki yerlerine yazım alanından taşmadan yerleştirilmiş olmalıdır.
10. Tablolar üstlerine, şekiller (formül, grafik, şema, spektrum, kromatogram, fotoğraf vb.) de altlarına arabik rakamlarla (**Şekil 1**., **Tablo 2**.,) numaralandırılmalı ve metin içinde yer verilmelidir. "Tablo", "Şekil" sözcükleri ile bunlara ait numaralar koyu yazılmalı ve 11 punto olmalıdır. Şekil/Resim (**JPEG formatında**) makale içinde yerleşmiş ve **resimler 300 dpi veya daha yüksek çözünürlükte** olmalıdır. Üzerinde oynanmış (parlaklık, kontrast, gama ayarı vb.) şekillerde şekil altı metninde yapılan ayarlar belirtilmelidir. **Yazarlar, önceki makalelerinden alıntılanmış olsalar bile, diğer kaynaklardan herhangi bir görüntüyü çoğaltmak için ilgili yayıncılardan yazılı izin almalıdır**.
11. **Tablo** başlıkları Tabloların üstüne ve iki yana yaslı ve bunların genişliğini aşmayacak şekilde 11 punto ve bir satır aralıkta yazılmalıdır. Tabloya ait açıklama varsa tablonun altına 9 punto ile yazılmalıdır. Tablo içindeki metin 8-11 punto arasında yazılabilir. **Şekil** başlıkları ise şekillerin altına birer satır aralıkla ortalı ve 11 punto yazılmalıdır. Şekil başlığı ve şekil arasında 6 nk aralık olmalıdır. Tablo ve Şekiller metin içine yerleştirilirken metin ile aralarında 18 nk aralık olmalıdır.

    Örnek tablolar için bakınız.
    - Tüm satır ve sütun çizgileri yer almalı.
    - Tablo tasarımı tüm makalede tek tip ve düz olmalı, herhangi bir renklendirme/gölgelendirme kullanılmamalıdır.
    - Tablo içinde yer alan başlıklar **bold/koyu** renkte yazılmalıdır. Tablo başlığı ve tablo arasında 6 nk aralık olmalıdır.

Tablo 1. Türlere ait morfolojik özellikler

Bitki kısmı*	***C. nummularia***	***C. integerrimus***
Yaprak	Genişçe eliptik-orbikular, 0.9-2.5-(4) x 0.5-2.5-(3-5) cm	Orbikulardan ovata kadar farklı şekillerde, 1.2-(4-5) x 0.9-3 cm
Tohum	3.5-4 x 1-2 mm, koyu kahverengi	3-4 x 1.5-2 mm, açık kahverengi

*Açıklama: 9 punto, 1 aralık olmalı.

Tablo 2. Hastaların özellikleri

Demografik bilgiler	**A grubu***	**B grubu**	**C grubu**
Erkek cinsiyet	10 (%30)	20 (%60)	10 (% 30)
Sigara kullanımı	20 (%60)	10 (%30)	20 (%60)

*Açıklama: 9 punto yazılmalıdır.

Örnek şekil;

Şekil 1. *C. nummularia*'nın genel görünüşü (Yazı karakteri "Times New Roman" ve 11 punto, "1" aralık, ortalı)

12. Makalelerin bölümleri **BAŞLIK** (Türkçe ve İngilizce), **ÖZ**, **ABSTRACT**, **GİRİŞ, GEREÇ VE YÖNTEM, SONUÇ VE TARTIŞMA, TEŞEKKÜR** (varsa eklenmeli), **YAZAR KATKILARI**, **ÇIKAR ÇATIŞMASI**, **ETİK KURUL ONAYI** (varsa eklenmeli) ve **KAYNAKLAR** sırasına uygun olarak hazırlanmalıdır. Bu bölümleri ifade eden başlıklar (Makalenin ilk başlığı hariç) **12 punto ile koyu olarak büyük harflerle ve sayfanın solundan başlanarak** yazılmalıdır. **GİRİŞ**'ten önce ve sonra sırasıyla 18 nk ve 6 nk aralık bırakılmalıdır. Diğer ana başlıklardan önce ve sonra sırasıyla 12 nk ve 6 nk aralık olmalıdır. Bölüm başlıkları ile metin arasında belirtilenin dışında ayrıca aralık **bırakılmamalıdır.**

- **BAŞLIK:** Türkçe ve İngilizce olarak büyük harf ve **ilk başlık** (Türkçe makalelerde Türkçe başlık, İngilizce makalelerde İngilizce başlık ilk başlıktır) **14 punto, koyu** ve ikinci başlık 12 punto, *italik* olarak yazılmalıdır. Başlık metine uygun, kısa, çalışmayı tanıtıcı ve açık ifadeli olmalıdır.

- **ÖZ** ve **ABSTRACT:** Türkçe (**ÖZ**) ve İngilizce (**ABSTRACT**) olarak makalelerin başında **200**'er kelimeyi geçmeyecek şekilde 10 punto ile *italik* olarak yazılmalıdır. Yabancı dilde yazılmış makalelerde önce **ABSTRACT** daha sonra mutlaka Türkçe olarak **ÖZ** bulunmalıdır. **ÖZ** ve **ABSTRACT** başlıkları 12 punto ve koyu yazılıp kendi içlerinde alt başlıklar (aşağıda görüldüğü gibi) halinde makalenin özeti sunulmalıdır. Her bir alt başlık 10 punto, koyu, normal yazılmalıdır. Alt başlıkların içeriğindeki metinler *italik* yazılmalıdır. **ÖZ ve ABSTRACT metni blok halinde sağdan ve soldan 1 cm boşluk bırakılarak yazılmalıdır.**

Özgün makalelerde;

ÖZ için kullanılacak alt başlıklar:
Amaç: *Metin italik yazılmalıdır.*
Gereç ve Yöntem: *Metin italik yazılmalıdır.*
Sonuç ve Tartışma: *Metin italik yazılmalıdır.*
Anahtar Kelimeler: *Metin italik yazılmalıdır, alfabetik sıralama gözetilmelidir*

ABSTRACT için kullanılacak alt başlıklar:
Objective: *Metin italik yazılmalıdır.*
Material and Method: *Metin italik yazılmalıdır.*
Result and Discussion: *Metin italik yazılmalıdır.*
Keywords: *Metin italik yazılmalıdır, alfabetik sıralama gözetilmelidir*

Derleme makalelerde;

ÖZ için kullanılacak alt başlıklar:
Amaç: *Metin italik yazılmalıdır.*
Sonuç ve Tartışma: *Metin italik yazılmalıdır.*
Anahtar Kelimeler: *Metin italik yazılmalıdır, alfabetik sıralama gözetilmelidir*

ABSTRACT için kullanılacak alt başlıklar:
Objective: *Metin italik yazılmalıdır.*
Result and Discussion: *Metin italik yazılmalıdır.*
Keywords: *Metin italik yazılmalıdır, alfabetik sıralama gözetilmelidir*

- **Anahtar Kelimeler (Keywords):** En az 3 sözcükten oluşmalı, ilgili dilde alfabetik, *italik* olarak, yalnızca ilk anahtar sözcüğün ilk harfi büyük olacak şekilde (büyük harf kullanılarak yapılan kısaltmalar hariç) aralara virgül konularak yazılmalı son anahtar sözcükten sonra ise bir imla işareti **kullanılmamalıdır.**

- **METİN:** Orijinal Türkçe makalede metin kısmı **GİRİŞ, GEREÇ VE YÖNTEM, SONUÇ VE TARTIŞMA** olmak üzere 3 ana başlıktan oluşmalıdır. Bu ana başlıkların tamamı 12 punto, **büyük harflerle** ve koyu olacak şekilde yazılmalıdır. Derleme makalelerde ise **GİRİŞ** ile **SONUÇ VE TARTIŞMA ana başlıkları olmalı,** diğer başlıklar yazarın belirleyeceği şekilde **her kelimenin ilk harfi büyük diğerleri küçük ve koyu** olacak şekilde yazılmalıdır. Alt başlıklar 11 punto, 1satır aralık, **bold/koyu** yazılmalı ve sola dayalı olmalıdır Alt başlıklarda numaralandırma sistemi **kullanılmamalıdır**. Alt başlıklardan önce ve sonra 6 nk aralık olmalıdır.

- **GİRİŞ:** Araştırmanın amacı ve konuyla ilgili çalışmaların yer aldığı bölüm olmalıdır.

- **GEREÇ VE YÖNTEM**: Kullanılan gereç belirtilerek, uygulanan yöntem hakkında gerekli bilgiler açıkça ifade edilmelidir. **Bileşiklerin karakterizasyonu** ayrı bir paragraf ile gösterilmeli ve yeni bileşiklerin saflıkları ve yapı aydınlatılmaları sağlanmalıdır. Eğer çalışmada hayvan ya da insan örnekleri/gönüllüler kullanılıyorsa, araştırıcılar tüm işlemlerin ilgili kanun ve kurumsal kılavuzlara uygun şekilde gerçekleştirildiğine ve uygun idari kurul tarafından bu işlemlerin onaylandığına ve Etik Kurul onayı alındığına dair ifadenin çalışma içinde yer almasını sağlamalıdırlar. Etik Kurul onayının zorunlu olduğu çalışmalarda, etik kurul onayı alınan kurumun adı ve etik kurul onay numarası, gereç ve yöntem kısmında belirtilmelidir. Ayrıca, kullanılan protokol ve prosedürlerin etik olarak gözden geçirildiği ve onaylandığı, makalenin gereç ve yöntem bölümüne eklenmelidir. Detaylı bilgi için lütfen http://journal.pharmacy.ankara.edu.tr/en/ethical-principles-and-publication-policy/ web sayfasını ziyaret ediniz.

- **SONUÇ VE TARTIŞMA:** Bulguların verilerek değerlendirildiği bölümdür.
  - Dileyen yazar, RESULT AND DISCUSSION bölümünün son paragrafı olarak "Conclusion" başlığı oluşturabilir. Ancak 11 punto Times New Roman karakterinde İlk harfi büyük diğer harfleri küçük olmalıdır.

- **TEŞEKKÜR:** Varsa araştırmayı destekleyen kuruluşa ve katkısı olan kişilere Yazarların Katkısından önce yer alan bu bölümde kısaca teşekkür edilebilir.

- **YAZAR KATKILARI:** Makalede yer alan yazarların katkısı yazarlar tarafından imzalanan Telif Hakkı Devir Sözleşmesi (*Copyright Transfer Agreement*) uyarınca, çıkar çatışması bildiriminden hemen önce, makalede yer alan isim sırası gözetilerek yazılmalıdır. Lütfen bu bildirim için açık ad ve soyad yerine aşağıdaki örnekte olduğu gibi yazarların baş harflerini kullanınız. Yazar katkısı belirtilmeyecek alanlar için "-" işareti konulmalıdır.

  Örnek:

  YAZAR KATKILARI

  Kavram: İ.Y., M.M.H., C.H., K.B.; Tasarım: İ.Y., C.H., I.Ö.G., Ö.Ü.; Denetim: C.H., I.Ö.G., M.M.H., K.B.; Kaynaklar: Ö.Ü., Z.K., K.B., M.M.H., A.K., İ.A., G.A.G., B.G., B.K.; Malzemeler: I.Ö.G., B.E., G.A.G., B.K., D.Ç.P.; Veri Toplama ve/veya İşleme: A.K., Ö.Ü., M.K., A.S., D.Ç.P., T.C.Ş.T.; Analiz ve/veya Yorumlama: Ö.Ü., B.G., T.C.Ş.T., E.K.S.; Literatür Taraması: B.K., D.Ç.P, B.G., B.E.; Makalenin Yazılması: A.K., İ.A., T.C.Ş.T.; Kritik İnceleme: İ.Y., B.G., Ö.Ü., İ.A.; Diğer: -

- **ÇIKAR ÇATIŞMASI BEYANI**

  Çıkar çatışması varsa ne şekilde olduğu açıkça beyan edilmelidir. Eğer yok ise "Yazarlar bu makale için gerçek, potansiyel veya algılanan çıkar çatışması olmadığını beyan ederler." ifadesini kullanmalıdırlar.

- **ETİK KURUL ONAYI**

  Çalışmanın sonunda kaynaklardan önce etik kurul onayı alınmışsa hangi kurumdan ve ne zaman alındığı onay numarası ile mutlaka belirtilmeli ve Etik Kurul Onayını makale gönderim sırasında yüklemelidir. Etik kurul onayına gerek olmayan çalışmalarda aşağıdaki cümle yazılmalıdır.

  "Yazarlar bu çalışma için etik kurul onayının zorunlu olmadığını beyan etmektedir."

- **KAYNAKLAR:** Kaynak yazım stili Amerikan Psikoloji Derneği'ne (APA) göredir. Yazı karakteri "Times New Roman" ve 10 punto, "1" aralık, iki yana yaslı. Metinde, geçiş sırasına göre köşeli parantez içinde, örneğin: [1,6,9], [5-7] gibi numaralandırılmalı ve metin sonunda bu numaralara göre sıralanmalıdır. Alt başlıkların yanına kaynak belirtilmemelidir. Tablo içinde kaynak bildirilmesi gerekiyorsa metin içinde verildiği gibi belirtilmelidir.

  - **Makale için:** Yazarın soyadı, adının baş harfleri (Birden fazla adı olan yazarın her bir isminin baş harfinden sonra nokta konmalı ve arada boşluk bırakılmamalıdır. Birden fazla yazarların arasında virgül yer almalıdır. **Son yazar ile bir önceki yazar arasında "ve" kelimesi veya "&" sembolü <u>kullanılmamalıdır</u>**.), makalenin tam başlığı, derginin adı, cilt no, varsa sayı no (parantez içinde), başlangıç ve bitiş sayfa numarası (veya makale numarası), yıl yazar isimlerinden sonra (parantez içinde) yazılmalıdır. **Birden fazla yazar varsa hepsi yazılmalıdır.** Makalenin adı yazılırken ilk kelimenin ilk harfi büyük diğer kelimelerin ilk harfi küçük yazılmalıdır. Kaynaklarda verilen **dergi adları kısaltma yapılmadan açık olarak yazılmalıdır.**

Her bir referansın sonuna [CrossRef] **ekleyerek aşağıdaki formatta DOI numarasını köprü olarak giriniz. Lütfen https://www.crossref.org/'da yer almayan makaleleri** [CrossRef] şeklinde **belirtmeyiniz.**
https://doi.org/10.1016/0006-2952(89)90403-6

Örnekler:

1. Martinez, M.J.A., Del Olmo, L.M.B., Benito, P.B. (2005). Antiviral activities of polysaccharides from natural sources. Studies in Natural Products Chemistry, 30, 393-418. [CrossRef]
2. Bahiense, J.B., Marques, F.M., Figueira, M.M., Vargasa, T.S., Kondratyuk, T.P., Endringer, D.C., Scherer, R., Fronzaa, M. (2017). Potential anti-inflammatory, antioxidant and antimicrobial activities of *Sambucus australis*. Pharmaceutical Biology, 55(1), 991-997. [CrossRef]

- **Elektronik Makale için:**

Örnek:
Perneger, T.V., Giner, F. (1998). Randomized trial of heroin maintenance programme for adults who fail in convential drug treatments. British Medical Journal, 317, from http://www.bmj.com/cgi/content/full/317/7150/ Erişim tarihi: 14.03.2021

- **Web sitesi için:**

Örnek:
Clinical Pharmacology Web site. (2001). Erişim adresi http://cpip.gsm.com/ Erişim tarihi: 14.03.2021.

- **Kitap için:** Yazarın soyadı, adının baş harfleri, kitabın adı, cilt no (varsa), kitabevi, yayınlandığı şehir, sayfa no, basıldığı yıl (parantez içinde) yazılmalıdır.

Örnek:
Franke, R. (1984). Theoretical Drug Design Methods, Elsevier, Amsterdam, p.130.

- **Kitap bölümü için:** Yazarın soyadı, adının baş harfleri, bölümün başlığı, editör/editörlerin soyadı, adının baş harfleri, (Ed./Eds.) ibaresi, kitabın adı, varsa cilt no, kitabevi, yayınlandığı şehir, sayfa no, basıldığı yıl (parantez içinde) yazılmalıdır.

Örnek:
Weinberg, E.D. (1979). Antifungal Agents. In: M.E. Wolff and S.E. Smith (Eds.), Burger's Medicinal Chemistry, (pp. 531-537). New York: John Wiley and Sons.

- **Tez için:** Yazarın soyadı, adının baş harfleri, yıl yazar isimlerinden sonra (parantez içinde) yazılıp nokta işareti konmalıdır. Ne tür tez olduğu belirtildikten sonra tezin başlığı, nerde yapıldığı yazılmalıdır.

Örnek:
Ahmed, J. (2008). PhD Thesis. Pharmaceutical Botany investigations on *Prangos* Lindl. (Umbelliferae) growing in Konya province. Department of Pharmaceutical Botany, Faculty of Pharmacy, Ankara University, Ankara, Turkey.

- **Patent için:** Yazarın soyadı, adının baş harfleri, yıl yazar isimlerinden sonra (parantez içinde) yazılıp nokta işareti konmalıdır. Patent başlığı ve patent numarası yazılmalıdır.

Örnek:
Mahoney, S., Molz, L., Narayan, S., Saiah, E. (2018). Heteroaryl RHEB Inhibitors and Uses Thereof. WO 2018/191146 A1.

ETİK İLKELER VE YAYIN POLİTİKASI

Ankara Üniversitesi Eczacılık Fakültesi Dergisi, açık erişimli, hakemli bir dergi olup Türkçe veya İngilizce olarak farmasötik bilimler alanındaki önemli gelişmeleri içeren orijinal araştırmalar, derlemeler ve kısa bildiriler için bir yayım ortamıdır. Ankara Üniversitesi Eczacılık Fakültesi Dergisi'nin makale yayın ücreti (APC) veya abonelik ücreti yoktur.

Yayın kurulu olarak dergi kapsamında önemli katkı sağlayan kaliteli yeni çalışmaların yayınlanması amaçlanmaktadır. Bu amaca ulaşmak için gönderilen makaleler, dergide yayınlanmak için bilimsel ve biçimsel gerekli kriterleri karşıladıklarından emin olmak adına baş editör ve/veya editör yardımcıları tarafından ilk değerlendirmeye tabi tutulur. Yalnızca bu ön değerlendirme sürecini geçen çalışmalar, daha ileri değerlendirme için diğer aşamalara devam ettirilir.

Ön Değerlendirme

- Çalışmanın bilimsel kalitesi ve yeniliği dergide yayınlanmak için yeterli olmalıdır.
- Dergiye gönderilen çalışmalar derginin amaç ve kapsamına uygun olmalıdır.
- Metin İngilizce veya Türkçe olarak dilbilgisi kurallarına uygun ve bilimsel olarak iyi yazılmış olmalıdır.
- Dergiye gönderilen çalışmaların benzerlik oranı %20'i geçmemelidir.
- Çalışmalar derginin yazım kurallarına ve şablonuna uygun olacak şekilde düzenlenmelidir.
- Telif hakkı devir formu, etik kurul onay belgesi, yazar katkı formu mutlaka yüklenmeli ve imzalı olmalıdır.
- Çalışmalar elektronik online başvuru sistemi aracılığı ile dergiye gönderilmiş olmalıdır.

Bu yeterlikleri taşımayan çalışmaların ileri değerlendirme süreci başlatılamaz.

Dergi yayınlanma sürecinde dergi editörleri, hakemler ve yazarlara bazı sorumluluklar düşmektedir. Bu sorumluluklar aşağıdaki şekilde açıklanmıştır.

1. Editörün Görevleri ve Etik Sorumlulukları

Editör, dergiye gönderilen makalelerden hangilerinin yayınlanması gerektiğine bağımsız olarak tek başına karar verebileceği gibi editör kurulunun üyelerine veya hakemlere de danışabilir. Derginin etik ilkeleri ve yayın politikası çerçevesinde, çalışmaların ön değerlendirme, hakem değerlendirmesi ve yayınlanma aşamalarının tarafsız, denetlenebilir, adil, çıkar ilişkisinden bağımsız ve gizlilik ilkelerine uygun şekilde yürütülmesinden sorumludur. Yayın politikası ve etik ilkeleri açısından ihlal yoksa derginin amacına ve kapsamına uygun çalışmaları, ön değerlendirme aşamasına almalıdır.

Baş editörün, editör yardımcılarının, alan editörlerinin ve editoryal danışma kurulunun görevleri ve tanımları aşağıdaki gibidir:

Baş Editör: Dergi içeriğinin yayınlanması konusunda tam yetkiye sahip kişidir. Editör yardımcıları, alan editörleri ve editöryal danışma kurulu ile birlikte çalışır.
Editör Yardımcıları: Dergi ilgili sorulara cevap vermek, dergi hakem ve kuruluna önerilerde bulunmak, makale yayın sürecinde baş editöre yardımcı olan kişilerdir.
Alan Editörleri: Çift kör hakem atamalarının gerçekleşmesi ve dergi ile ilgili sorulara cevap vermek konusunda yazarlara yardımcı olan kişilerdir.
Editoryal Danışma Kurulu: Editoryal Danışma Kurulu, Ankara Üniversitesi Eczacılık Fakültesi Dergisinin, amacına uygun ve kaliteli yayın üretilmesine ilişkin konularda Baş Editör ve Editör Yardımcılarına kılavuzluk eder.

1.1. Yayın Politikası

- Baş editör, dergiye gönderilen makalelerden hangilerinin yayımlanması gerektiği kararından tek başına sorumludur. Editörün kararı, derginin editör kurulunun prensipleri doğrultusunda olabileceği gibi, onur kırıcı yayım yapmak, telif hakkı ihlali ve intihal gibi konularla ilgili olarak yürürlükte olan yasal gereklilikler ile sınırlandırılmıştır.
- Baş editör, makale yayımlanmadan önce yazarların yayımcıya makalenin “Copyright Transfer Form” unu, doldurarak telif hakkını gönderdiğinden emin olmaktadır.
- Baş editör, yazarların makale yayımlanmadan önce "Conflict of Interest Form”unu ve “Author Contribution Form” unu doldurduğundan emin olmaktadır.
- Baş Editör, dergiye gönderilen makalelerin biçimsel olarak incelenmesi için editör yardımcılarını görevlendirmektedir. Ankara Üniversitesi Eczacılık Fakültesi Dergisinin kurallarını sağlamayan makaleler kesinlikle değerlendirmeye alınmadan reddedilmektedir.

1.2. Yayın Değerlendirmesi

- Baş editör, yayın değerlendirme sürecinin adil, tarafsız ve zamanına uygun şekilde gerçekleşmesini sağlamaktan sorumludur.
- Editör, tüm makaleleri genel olarak dışardan ve bağımsız en az iki hakem ile değerlendirilmesini sağlamaktadır. Gerek olması durumunda editör üçüncü bir hakemden ek görüş istemektedir.
- Editör, hakem seçimini makale kapsamına uygun olan uzmanları değerlendirerek yapar.
- Editör, olası çıkar çatışmaları için yapılan açıklamaları, hakemler tarafından yapılan “self-citation” önerilerini ve herhangi bir taraflılık olasılığını değerlendirmek ve karar vermek için dikkatli bir şekilde yayın sürecini gözden geçirmektedir.
- Baş editör/editörler, hakem değerlendirmesi veya değerlendirme/yayım sürecinin herhangi bir noktasında bir benzerlik tespit yazılımı (iThenticate) tarafından taratılmasını yazardan istemektedir veya kendisi yapmaktadır. Bu anlamda ifadelerin veya cümlelerin yazarın/yazarların kendileri olsa dahi metin daha önce yayınlanmış verilerle kabul edilemez bir benzerliğe sahip olmamalıdır.
- Baş editör, bir makaledeki hataları yayımlanmadan önce tespit ederse düzeltmektedir. Eğer daha sonra tespit ederse bu durumda düzeltmeleri yayımlamak zorundadır. Tüm düzeltme veya geri çekme bildirimlerini dergide belirgin bir şekilde yayımlamalıdır. Ayrıca içindekiler sayfasında listelemelidir.
- Ankara Üniversitesi Eczacılık Fakültesi Dergisinin editörleri, Yayın Etiği Komitesi (Committee on Publication Ethics (COPE)) tarafından yayınlanan "COPE Code of Conduct and Best Practice Guidelines for Journal Editors" ve "COPE Best Practice Guidelines for Journal Editors" kılavuzlarına uyarak çalışmalarını sürdürür.

1.3. Adil Değerlendirme

- Baş editör/editörler, makaleleri yazarların ırk, cinsiyet, cinsel eğilim, inanç, etnik köken, vatandaşlık ya da politik görüşlerine bakmaksızın bilimsel içeriklerine göre değerlendirmektedir. Derginin editoryal prensipleri şeffaf ve tümüyle dürüst değerlendirmeyi desteklemektedir.
- Editör, hakemlerin ve yazarların kendilerinden bekleneni tam olarak anladıklarından emin olmalıdır.
- Editör, dergi ile ilgili tüm iletişimini derginin elektronik başvuru sisteminden yapar ve kararlarında itirazlar olması halinde şeffaf ve hakkaniyetli bir yol izler.

1.4. Gizlilik İlkesi

- Baş editör/editör, dergiye yapılan başvurudaki tüm materyallerin ve hakemlerle yapılan tüm iletişimin gizliliğini (ilgili yazar ve hakemlerle aksi onaylanmadığı sürece) korumakla yükümlüdür.

- Baş editör/editör, hakemlerin isimlerinin açıklanmasını kabul etmediği sürece, hakemlerin kimliklerini ve haklarını korumakla sorumludur.
- Başvurusu tamamlanmış bir makaleye ait basılmamış materyaller, yazarın yazılı onayı alınmadan editörün kendi çalışmaları/araştırmaları için kullanılmamalıdır.
- Baş editör/editör, makale değerlendirme sürecinde edinilen tüm bilgileri veya fikirleri gizli tutmalı ve kişisel amaçlar için kullanmamalıdır.

2. Hakemlerin Görevleri ve Etik Sorumlulukları

Ankara Üniversitesi Eczacılık Fakültesi Dergisi'nin makale değerlendirme süreci çift taraflı kör hakemlik ilkesiyle yürütülmektedir. Dolayısıyla hakemler yazar/yazarlarla iletişim kuramazlar, değerlendirmeler dergipark yönetim sistemi üzerinden paylaşılır. Değerlendirme sürecinde tam metinlere ilişkin değerlendirme formları hakem yorumları editör aracılığı ile sorumlu yazara iletilir. Hakemler, değerlendirme süreci boyunca tarafsızlık, gizlilik, nesnellik, bilimsel yönden inceleme ilkelerine uygun hareket etmelidir. İlgili alanda uzman ve yetkinliğe sahip olmalıdır. Değerlendirmesine sunulan çalışmaya ilişkin raporunu belirtilen zaman aralığı içinde bitirmelidir. Zamanında sunulamayacak raporlar için gecikmeden editör ile iletişime geçilmelidir. Etik ilkeleri, telif hakkı ihlali, olası çıkar çatışması ve intihal yapıldığının fark edilmesi durumlarında editör kurulunu bilgilendirmelidir.

Ankara Üniversitesi Eczacılık Fakültesi Dergisi için makaleleri değerlendiren hakemlerin aşağıda belirtilen görevlere ve etik sorumluluklara uyması beklenmektedir.

2.1. Editöryal Kararlara Katkı

- Hakemler, yazarların sundukları çalışmaları yapıcı ve uygun şekilde değerlendirmelidirler.
- Hakemler, makalede yer alan araştırmayı değerlendirmeye yetkin olmadığını düşünüyorsa veya yeterli sürede tamamlayamayacaksa editöre durumu bildirmelidirler.
- Hakemler, yazarlara yönelik sert ve kişisel eleştirilerde bulunmamalıdırlar.
- Hakemler, makale değerlendirmesi için davet aldığında eğer kendilerini makalede çalışılan konu hakkında yetersiz hissederlerse makaleyi değerlendirmeyi reddetmelidirler.
- Hakemler, makale değerlendirmesini verilen süre içinde yapmalıdırlar.
- Hakemler, sadece çalışmanın içeriğine ilişkin değerlendirmeyi objektif olarak yapmalıdırlar.

2.2. Gizlilik

- Hakemler, değerlendirmeyi tarafsızlık ve gizlilik içerisinde yapmalıdırlar.
- Hakemler, makale hakkındaki değerlendirmelerini ya da bilgilerini üçüncü kişilerle paylaşmamalıdırlar.
- Hakemler, makale değerlendirme sürecinde edinilen bilgileri, fikirleri ve basılmamış materyal veya çalışmaları gizli tutmalı ve kişisel amaçlar için kullanmamalıdırlar.
- Hakemler, makalenin bir kopyasını elinde bulundurmamalı veya çoğaltmamalıdırlar.

2.3. Etik Sorunları Fark Etme

- Hakemler, makalede yer alan etik sorunları fark etmeli ve editörün dikkatine sunmalıdırlar.
- Hakemler, makalenin daha önce başka bir yerde basıldığını veya basılmış önceki bir makale ile önemli ölçüde benzerlik ya da örtüşme tespit ederse editöre bildirmelidirler. Daha önce yayımlanmış olan herhangi bir gözlem ve/veya argüman, ilgili referans ile birlikte verilmelidir.

2.4. Tarafsızlık ve Rekabet Standartları

- Hakemler, tarafsız olarak değerlendirmelerini yapmalı ve önyargıdan uzak şekilde değerlendirmelidirler. Yazarın kişi olarak eleştirilmesi uygun değildir. Hakemler, görüşlerini destekleyici argümanlarla ifade etmelidirler.

- Hakemler, makale değerlendirmeyi kabul etmeden önce olası çıkar çatışmasını kontrol etmelidirler. Eğer çıkar çatışmasıyla karşı karşıya olduğunu düşünüyorsa makaleyi incelemeyi reddetmeli ve editörü bilgilendirmelidirler.
- Hakemler, yazar tarafından hakemin (ya da hakemle çalışan kişilerin) çalışmalarının kaynak olarak alındığını ileri sürerse, gerçek bilimsel gerekçeler sunmalılar, bu durumun hakemin kaynak gösterilme sayısını ya da çalışmalarının görünürlüğünü artırmaya yönelik bir girişim olmamasına özen göstermelidirler.
- Hakemler, değerlendirmelerini yaparken bilimsel gerçeklikten uzaklaşmamalı ve gerekirse kaynak gösterme yoluna başvurmalıdırlar.

3. Yazarların Görevleri ve Etik Sorumlulukları

Ankara Üniversitesi Eczacılık Fakültesi Dergisi'ne gönderilen makaleler, daha önce herhangi bir yayın organında yayımlanmamış olmalıdır veya yayımlanmak üzere aynı zaman diliminde başka bir yayın organına gönderilmiş olmamalıdır. Çalışmalarda yararlanılan araştırmaların ve yayınların, alıntılarının veya atıflarının bilimsel araştırma ilkelerine uygun olarak eksiksiz yapılması ve kaynakların belirtilmesi zorunludur. Çalışmada yer alan yazar sayısı birden fazla ise, yazarların çalışmaya bilimsel ve akademik olarak somut ve yeterli düzeyde katkı sağlaması beklenir. Çalışmaya ait tüm finansal destek kaynakları açıklamalıdır. Olası çıkar çatışması durumlarını yayın kuruluna bildirmelidir.

Ankara Üniversitesi Eczacılık Fakültesi Dergisi'ne makale gönderen yazar/yazarların aşağıda belirtilen görevlere ve etik sorumluluklara uymalıdır.

3.1. Bildirim Standartları

- Yazar(lar)ın gönderdiği makale (araştırma, derleme veya kısa bildiri) özgün olmalıdır.
- Yazar(lar), çalışmanın önemine ilişkin tarafsız bir tartışma ile gerçekleştirilen araştırmayı net bir şekilde sunmalıdır.
- Yazar(lar), makalede verileri açık bir şekilde sunmalıdır.
- Yazar(lar)ın başka çalışmalardan faydalanması halinde tam ve doğru bir şekilde alıntı yapmalıdır.
- Makale, diğer araştırmacıların çalışmayı tekrar edebilmesine olanak verecek şekilde yeterli detay ve kaynak içermelidir.
- Yazar(lar), etik dışı davranarak yanıltıcı ya da net olmayan ifadeleri makalelerinde kullanmamalıdır.
- Yazar(lar), dergi kurallarına uymadıkları ve belirtilen sürede aksiyon almadıkları sürece makalelerinin dergi tarafından yayımlanmayacağını bilerek hareket etmelidir.

3.2. Veri Ulaşımı ve Saklama

- Yazarlardan editöryal değerlendirme için makalelerini destekleyici araştırma verisi istenebilir.
- Yazarlar, değerlendirme sürecinde makalelerine ilişkin ham verilerin veya makalelerini destekleyecek verilerin talep edilmesi durumunda belirtilen verileri yayın kuruluna sunmaya hazır bulunmalıdırlar.

3.3. Orijinallik, İntihal ve Kaynakların Belirtilmesi

- İntihal, yazarın başka bir makaleyi kendi çalışması olarak göstermesi, kaynak göstermeden başka birine ait çalışmanın belli bölümlerinin kopyalanması ya da başka sözcüklerle anlatılması veya başkaları tarafından yapılan çalışmanın sonuçlarının alınarak sunulması şeklinde olabilir. İntihalin her biçimi etik olmayan davranıştır ve kesinlikle kabul edilmemektedir. Yazarlar intihalden uzak durmalıdır. İntihal tanımı için buraya bakınız.
- Yazarlar çalışmalarının tümüyle orijinal olduğunu garanti etmelidirler. Yazarlar, başkalarının fikirlerini veya metinlerini kullanıyorlarsa mutlaka uygun şekilde kaynak ya da alıntı

göstermeliler ve gerekliyse izin almalıdırlar.

- Yazarlar kendilerine ait olan çalışmayı etkileyen ve çalışmaya ait uygun içeriğin oluşturulmasında katkısı olan tüm yayınları veya eserleri kaynak olarak göstermelidirler. Özel olarak (görüşme, yazışma ya da üçüncü taraflar ile tartışma) ile elde edilen bilgiler kullanılmamalı ya da kullanılacaksa izin alınarak bildirilmelidir.
- Yazarlar, Ankara Üniversitesi Eczacılık Fakültesi Dergisi'ne yayımlanmak üzere gönderdikleri makalelerini intihal tarama programları (iThenticate) ile taramalı ve dergipark sisteminde çevrim içi makale gönderim sırasında makalelerinin intihal içermediğine dair raporu yüklemek zorundadırlar.

3.4. Çoklu, Gereksiz ve Tekrar Yayınlama

- Aynı makale ile birden fazla dergiye başvuruda bulunmak etik olmayan bir davranıştır ve asla kabul edilmemektedir. Genel olarak, yazar daha önce basılmış bir yayını, özet formunda ya da yayınlanmış bir ders, akademik tez ya da elektronik ön baskının bir parçası olması dışında, değerlendirme için başka bir dergiye göndermemelidir.
- Yazarlar başvuru sırasında makaleyi başka bir dergiye daha aynı anda göndermediklerini garanti etmelidirler.
- Yazarlar, gönderilen yazının değerlendirme aşamasında olmadığını veya başka bir yerde yayımlanmak üzere kabul edilmediğini ve eğer kabul edilirse, aynı biçimde, başka bir dilde, elektronik ortam da dahil olmak üzere, yazarın yazılı izni olmaksızın başka bir yerde yayımlanmayacağını garanti etmelidir.

3.5. Yazar Katkıları

- Yazar katkıları, çalışmanın konseptine, tasarımına, gerçekleştirilmesine ya da yorumlanmasına önemli katkı sağlayan kişiler ile sınırlandırılmalıdır.
- Yazarlar, çalışmaya katkı veren yazarların listesini dikkatli bir şekilde hazırlamalıdır. Bazı durumlar eşyazar (co-author) olmayı bazı durumlar ise çalışmanın "Teşekkür" (Acknowledgement) bölümünde yer almasını hak edebilir.
- Sorumlu yazar, tüm eşyazarların çalışmada uygun şekilde yer aldığına, tüm eşyazarların çalışmayı görüp onayladıklarına ve yayınlanmak üzere başvuru yapılmasına dair verdikleri onaya ilişkin sorumluluğu üstlenmelidir.
- Sorumlu yazar, makaledeki tüm yazarların yazar sıralaması, çalışmanın kesinliği ve bütünlüğü gibi konularda fikir birliğinin sağlanmasından sorumludur ve orijinal başvuru sırasında kesin bir yazar listesi sunmalıdır.
- Çalışmanın başvurusu tamamlandıktan sonra, sadece istisna durumlarda, editör yazar listesinde ekleme, silme ya da yeniden düzenleme yapabilir. Tüm yazarlar bu şekilde yapılacak ekleme, silme ve yeniden düzenleme konusunda fikir birliği içinde olmalıdırlar. Tüm yazarlar çalışmanın ortak sorumluluğunu aldıklarını kabul ederler. Her yazar, uygun şekilde araştırılan ve karara bağlanan çalışmanın kesinliği ve bütünlüğü ile ilişkili sorulardan sorumludur.
- Sorumlu yazar, editör ile iletişime geçen kişi olarak Ankara Üniversitesi Eczacılık Fakültesi Dergisi'ne makale ile birlikte "Yazar Katkı Formu"nun da doldurulup gönderilmesinden sorumludur.

3.6. Çıkar Çatışması Beyanı

- Yazarlar, çalışmalarını uygunsuz bir şekilde etkileyebilecek olarak gördükleri diğer kişi veya organizasyonlarla çıkar çatışması oluşturabilecek her türlü durum ve ilişkileri beyan etmelidirler.
- Sorumlu yazar, editör ile iletişime geçen kişi olarak Ankara Üniversitesi Eczacılık Fakültesi Dergisi'ne makale ile birlikte "Çıkar Çatışması Beyanı Formu"nun da doldurulup gönderilmesinden sorumludur.

- Yazarlar çıkar çatışmalarının olduğu durumları mutlaka açıklamalıdırlar.

3.7. Temel Hataların Bildirimi

- Yazarlar, yayımlanmış, erken görünüm veya değerlendirme sürecinde olan bir çalışmasında önemli bir hata ya da eksiklik fark ettiğinde, acil olarak dergi baş editörüne/yayınevine veya ilgili editöre bildirmek ve editör tarafından gerekli görülmesi durumunda makaleyi geri çekmek veya düzeltmek için editörle işbirliği yapmak ile yükümlüdür.
- Editör/yayınevi yayımlanmış olan makalenin bir hata içerdiğini üçüncü bir taraftan öğrenirse, editör ile işbirliği yapmak ve gerektiğinde destekleyici kanıt sağlamak yazarın yükümlülüğüdür.

3.8. Olası Riskler ve İnsan veya Hayvan Konuları

- Yazarlar, kullanımları sırasında olağan dışı risk yaratan kimyasallar, işlemler ya da malzemeler ile çalışmışlarsa açıkça belirtmelidirler.
- Eğer çalışmada hayvan ya da insan örnekleri/gönüllüler kullanılıyorsa, araştırmacılar tüm işlemlerin ilgili kanun ve kurumsal kılavuzlara uygun şekilde gerçekleştirildiğine ve uygun idari kurul tarafından bu işlemlerin onaylandığına ve Etik Kurul Onayı alındığına dair ifadenin makale içinde yer alması sağlamalıdırlar.
- Yazarlar, Etik Kurul Onayının zorunlu olduğu çalışmalarda, etik kurul onayı alınan kurumun adı ve etik kurul onay numarasını, gereç ve yöntem kısmında ve Etik Kurul Onay bölümünde belirtmelidirler. Ayrıca, kullanılan protokol ve prosedürlerin etik olarak gözden geçirildiğini ve onaylandığını, makalenin gereç ve yöntem bölümüne eklemelidirler.
- Etik kurul raporu alınması gerektiği halde, etik kurul raporu olmayan çalışmalar reddedilecektir.
- İnsanlar veya insandan elde edilen örnekler üzerinde yapılan klinik araştırmalarda bilgilendirilmiş onam formu mutlaka alınmış olmalıdır ve gereç ve yöntem kısmında belirtilmelidir. İnsan gönüllüleri ile yapılan araştırmalar için araştırma protokolüne uygun olarak hazırlanmış yazılı bilgilendirilmiş gönüllü onam formu alınmalıdır.
- Yazarlar, çalışmalarında, hayvan ya da insan örnekleri/gönüllüler kullanmışsa gerekli etik kurul izinlerini aldığından emin olmalıdır. Etik kurul izin ifadesini makalede mutlaka belirtmelidir.
- Bu anlamda yazarlar aşağıda sıralanmış olan kılavuzlara uyarak çalışmalarını gerçekleştirmiş olmalıdırlar:
  İnsanlar üzerinde gerçekleştirilen tüm araştırmalar Helsinki Bildirgesi ilkelerine göre yapılmalıdır (World Medical Association (WMA) Helsinki Declaration for Medical Research in Human Subject). İnsan gönüllülerinden bilgilendirilmiş onam formu alınmış olmalıdır. Tüm hayvan çalışmaları ARRIVE kılavuzuna uygun olmalı (Animal Research: Reporting of In Vivo Experiments (ARRIVE) Guidelines) ve "Bilimsel Amaçlı Kullanılan Hayvanların Korunmasına İlişkin Konsey Direktifi"ne (EU Directive 2010/63/EU for animal experiments), "Birleşik Krallık Hayvan Yasası"na (The U.K. Animals (Scientific Procedures) Act 1986) ve/veya "U.S. İnsan Bakımı ve Laboratuvar Hayvanlarının Kullanımına İlişkin Halk Sağlığı Hizmeti Politikası" rehberine (U.S. Public Health Service Policy on Humane Care and Use of Laboratory Animals) uygun şekilde yürütülmelidir. Bitkiler ile ilgili tüm deneysel araştırmalar, uluslararası yönergelere uygun olmalıdır.

4. Ücret Politikası

- Hiçbir ad altında yazar veya kurumundan ücret alınmaz.
- Dergi ile işleme ve yayınlama ücretsizdir. Gönderilen veya kabul edilen makaleler için makale işleme ücreti veya gönderim ücreti yoktur.

Publication Terms

1. The Journal of Faculty of Pharmacy of Ankara University (J. Fac. Pharm. Ankara) is an open-access, peer reviewed journal and is published three times (January-May-September) a year.

2. The Journal of Faculty of Pharmacy of Ankara University publishes articles in every field of Pharmaceutical Sciences. The manuscript to the journal should not be published previously as a whole or in part and not be submitted elsewhere. Manuscript should be written in Turkish or in English. The experiments used have to be adhered to the Declaration of Helsinki for humans and European Community Guidlines for animals. In studies where Ethics Committee Approval is mandatory, the name of the institution from which ethics committee approval was obtained and the ethics committee approval number should be stated in the material and method section and the Ethics Committee Approval section, and the relevant document should be uploaded during article submission.

3. All manuscripts will be submitted to a review process by the editors and by qualified at least 2 outside reviewers. The article evaluation process of Journal of Faculty of Pharmacy of Ankara University is carried out on the principle of double-blind refereeing.

4. Manuscripts are published in order of final acceptance after review and revision.

5. If a manuscript returned to the authors for revision is not received back to the editor within 3 months it will be treated as a new article. When the article is published, authors must send the copyright of the article to the Publisher by filling out the "Copyright Transfer Form".

6. Manuscript will be controlled using plagiarism checker. Articles sent to Journal of Faculty of Pharmacy of Ankara University for publication must be scanned with plagiarism scanning programs (iThenticate) and a report stating that the articles do not contain plagiarism must be uploaded during online article submission.

7. Journal of Faculty of Pharmacy of Ankara University does not have an article publication fee (APC) or subscription fee.

8. The following types of articles are accepted in the Journal Faculty of Pharmacy of Ankara University:

    a) **Original articles**: Articles written in English or Turkish in scientific format presenting original research. Articles should be printed on A4 size papers not exceeding 25 pages (including tables and figures). Research articles are expected to be innovative and contributing to science. Articles must have the main headings specified in the writing rules and must be prepared using a Windows compatible program.
    b) **Review articles:** An updated comprehensive review of scientific works on a particular subject. Articles written in English or Turkish should be printed on A4 size papers not exceeding 30 pages (including tables and figures). Articles must have the main headings specified in the writing rules and must be prepared using a Windows compatible program.
    c) **Short communications:** Rapid announcement of the results of a continuing research written in English or Turkish, no longer than 5, A4 size pages. Articles must have the main headings specified in the writing rules and must be prepared using a Windows compatible program.

Preparation of Manuscript

1. Texts must be written in A4 norm (21 x 29.7 cm).
2. Texts should be written with 1 line spacing, with 2.5 cm margins on the left and right sides of the A4 norm page, 3 cm margins each from the top and bottom edges (3 line spacing from the top on the first page). Articles accepted for publication will be directly uploaded to the system as a "Microsoft Word" file (online submission). The main text font should be **"Times New Roman"** and **11 pt**.
3. Page numbers **should not be specified** in the article.
4. Paragraph headings must **begin 1 cm inside**. Additional spaces should not be left between paragraphs.
5. On the title page, the title of the manuscript the name/s, the full address/es and ORCID no of the author/s, and the full address, telephone number, e-mail address of the corresponding author should be written and all should be centered in the text. It should be indicated by placing (*) above the surname of the corresponding author. Name, surname, full address, telephone number and e-mail address of this person should be specified at the bottom of the title page.
6. **Author's Name** (**first letter capital, others lowercase**) and **SURNAME** (**all capital letters**) should be written in bold, three lines spaced under the title, and without a title underneath. If there is more than one author, they should be written by separating them with a comma and leaving a space. The numbers to be placed on the surnames of the authors and the institution names and postal addresses (For example: Ankara University Faculty of Pharmacy, Department of Pharmaceutical Chemistry, 06560, Ankara, Turkey) should be clearly written on the line just below the names.
   - **ORCID ID number must be declared for all authors**. ORCID IDs of the authors should be created by creating a hyperlink to the relevant logo and adding URL links.
7. International abbreviations may be used. ml for milliliter in the text; min. for minutes It should be written as specified.
8. Units should be expressed using the metric system.
9. All tables and figures should be placed in their places in the text without exceeding the writing area.
10. Tables should be numbered on the top, figures (formula, graph, chart, spectrum, chromatogram, photograph, etc.) should be numbered below with Arabic numbers (**Figure 1., Table 2.)** and should be included in the text. The words "Table", "Figure" and their numbers should be written in bold and in 11 pt. Figure/Picture (**in JPEG format**) must be placed in the article and pictures must be at least **300 dpi or in higher resolution**. Authors must obtain written permission to reproduce any images from other sources.
11. **Table** titles should be written in 11 font size justified on the top of the tables and not exceeding their width. If there is an explanation for the table, it should be written in 9 font size at the bottom of the table. The text in the table can be written between 8-11 points. **Figure titles** should be written at the bottom of the figures with a line spacing, centered and 11 pt. There must be **6 nk** space between the figure and figure title. There should be **18 nk** space between the text and title of figure and/or table.

    See for below examples for tables:
    - All row and column lines should be included.
    - Table design should be uniform and straight throughout the article, no coloring / shading should be used.
    - Headings in the table should be written in **bold**. There must be **6 nk** space between the table and table title.

Table 1. Morphological characteristics of the species

Plant part*	***C. nummularia***	***C. integerrimus***
Leaf	Broadly elliptical-orbicular, 0.9-2.5-(4) x 0.5-2.5-(3-5) cm	From orbicular to ovate, 1.2-(4-5) x 0.9-3 cm,
Seed	3.5-4 x 1-2 mm, dark brown	3-4 x 1.5-2 mm, light brown

* Explanation should be 9 font size, 1 range.

Table 2. Patient demographics

Demographics	**Group A***	**Group B**	**Group C**
Male gender	10 (%30)	20 (%60)	10 (% 30)
Cigarette consumption	20 (%60)	10 (%30)	20 (%60)

* Explanation should be 9 font size, 1 range.

Example for figure:

Figure 1. General view of *C. Nummularia* (The font size must be 11 pt with 1 line spacing and "Times New Roman" font, and must be centered in the text)

12. The sections of the articles should be prepared in accordance with the **TITLE** (Turkish and English), **ABSTRACT, INTRODUCTION, MATERIAL AND METHOD, RESULT AND DISCUSSION, ACKNOWLEDGEMENTS** (if available), **AUTHOR CONTRIBUTIONS, CONFLICT OF INTEREST, ETHICS COMMITTEE APPROVAL** (if available) and **REFERENCES**. Titles expressing these sections (except the first title of the article) should be written in **12 pt**, **bold capital letters and starting from the left of the page**. **There should be 18 nk space before and 6 nk space after the INTRODUCTION.** For, there should be 12 nk space before and 6 nk space after the other titles. Between the chapter titles and the text, a separate space **should not be left** other than the specified in this document.

- **TITLE:** Capital letters and **first title** in Turkish and English (Turkish title is the first title in Turkish articles, English title is the first title in English articles), **14 pt, bold** and the second title should be written in 12 pt, *italic*. The title should be appropriate to the text, short, introducing the work and clearly worded.

- **ABSTRACT** and **ÖZ:** It should be written in English (**ABSTRACT**) and Turkish (**ÖZ**) at the beginning of the articles, not exceeding 200 words, 10 pt, *italic* and within a frame. In articles written in a foreign language, first **ABSTRACT** and then **ÖZ** in Turkish. **ABSTRACT** and **ÖZ** titles should be written in 12 pt. And bold and the summary of the article should be presented as subheadings. Each subtitle should be written in 10 pt, bold, normal and 1 cm indented. **ABSTRACT** and **ÖZ** should be written in blocks with 1 cm margins from the right and left.

For original articles;

Subheadings to be used for **ABSTRACT**:

Objective: *Text should be written in italic.*
Material and Method: *Text should be written in italic.*
Result and Discussion: *Text should be written in italic.*
Keywords:

Subheadings to be used for **ÖZ**:

Amaç: *Text should be written in italic.*
Gereç ve Yöntem: *Text should be written in italic.*
Sonuç ve Tartışma: *Text should be written in italic.*
Anahtar Kelimeler: *Text should be written in italic.*

For review articles;

Subheadings to be used for **ABSTRACT**:

Objective: *Text should be written in italic.*
Result and Discussion: *Text should be written in italic.*
Keywords:

Subheadings to be used for **ÖZ**:

Amaç: *Text should be written in italic.*
Sonuç ve Tartışma: *Text should be written in italic.*
Anahtar Kelimeler:

- **Keywords (Anahtar Kelimeler)**: It should consist of a minimum of 3 words, should be written alphabetically, italic in the relevant language, with only the first letter of the first keyword capitalized (except for abbreviations using capital letters) with commas between them and a spelling mark **should not be** used after the last keyword.

- **TEXT:** The text part of the original Turkish article should consist of 3 main headings: **INTRODUCTION, MATERIAL AND METHOD, RESULT AND DISCUSSION**. All of these main headings should be written in 12 pt, **capital letters** and bold. In review articles, there should be the main headings of **INTRODUCTION** and **RESULT AND DISCUSSION**, other titles should be written with the first letter of each word capital, the others in lowercase and bold, as determined by the author. Subheadings should be written in 11 font size, 1.5 line spacing, **bold** and aligned to the left. Numbering system **should not be** used in subheadings.

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  - If the author wishes, "Conclusion" can be added as the last paragraph of the RESULT AND DISCUSSION section. The font size must be 11 pt with 1 line spacing and “Times New Roman” font and the first letter must be uppercase and the other letters must be lowercase.

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  Example:

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  Concept: İ.Y., M.M.H., C.H., K.B.; Design: İ.Y., C.H., I.Ö.G., Ö.Ü.; Control: C.H., I.Ö.G., M.M.H., K.B.; Sources: Ö.Ü., Z.K., K.B., M.M.H., A.K., İ.A., G.A.G., B.G., B.K.; Materials: I.Ö.G., B.E., G.A.G., B.K., D.Ç.P.; Data Collection and/or Processing: A.K., Ö.Ü., M.K., A.S., D.Ç.P., T.C.Ş.T.; Analysis and/or Interpretation: Ö.Ü., B.G., T.C.Ş.T., E.K.S.; Literature Review: B.K., D.Ç.P, B.G., B.E.; Manuscript Writing: A.K., İ.A., T.C.Ş.T.; Critical Review: İ.Y., B.G., Ö.Ü., İ.A.; Other: -

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Examples:

1. Martinez, M.J.A., Del Olmo, L.M.B., Benito, P.B. (2005). Antiviral activities of polysaccharides from natural sources. Studies in Natural Products Chemistry, 30, 393-418. [CrossRef]
2. Bahiense, J.B., Marques, F.M., Figueira, M.M., Vargasa, T.S., Kondratyuk, T.P., Endringer, D.C., Scherer, R., Fronzaa, M. (2017). Potential anti-inflammatory, antioxidant and antimicrobial activities of *Sambucus australis*. Pharmaceutical Biology, 55(1), 991-997. [CrossRef]

- **Online articles:**

Example:
Perneger, T.V., Giner, F. (1998). Randomized trial of heroin maintenance programme for adults who fail in convential drug treatments. British Medical Journal, 317. Retrieved August 12, 2005, from ttp://www.bmj.com/cgi/content/full/317/7150/

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