Cumhuriyet Sci. J., 45(3) (2024) 465-470
DOI: https://doi.org/10.17776/csj.1519699

Cumhuriyet Science Journal

| csj.cumhuriyet.edu.tr | Founded: 2002 ISSN: 2587-2680 e-ISSN: 2587-246X Publisher: Sivas Cumhuriyet University

Examination of Biological Activity of *Passiflora edulis* (Çarkıfelek) Extract via Phytochemical Analysis

Tutku Tunç[1,a,*], Zeynep Sümer[2,b], Kerim Emre Öksüz[3,4,c]

[1]*Department of Pharmaceutical Microbiology, Faculty of Pharmacy, Cumhuriyet University, Sivas, Turkey*
[2]*Department of Medical Microbiology, Faculty of Medicine, Cumhuriyet University, Sivas, Turkey*
[3]*Department of Metallurgical & Materials Engineering, Faculty of Engineering, Cumhuriyet University, Sivas, Turkey*
[4]*Institute of Science and Technology, Department of Bioengineering, Sivas Cumhuriyet University, Sivas, Turkey*
**Corresponding author*

Research Article

History
Received: 20/07/2024
Accepted: 20/09/2024

ABSTRACT

In recent years, the use of medicinal plants as sources of drugs or herbal extracts has been of great importance. *Passiflora edulis* is nowadays widely studied for its antimicrobial, anticancer, and antioxidant potential. Therefore, this study aimed to determine the phytochemical structure of ethanol extract of *P. edulis* leaves and to investigate its biological properties such as antimicrobial and anticancer activities. The ethanol extract of *P. edulis* leaves was obtained and analyzed by GC-MS. The antimicrobial activity of *P. edulis* leaf extract was determined by MIC test. XTT method was used to determine the antiproliferative activity. In the phytochemical analysis of *P. edulis* extract, dodecanoic acid, tetradecanoic acid, and n-hexadecanoic acid were found the most. The antimicrobial effect of *P. edulis* leaf extract was found against pathogenic microorganisms. In addition, *P. edulis* leaf extract was found to have high anticancer activity against OvCar and MCF-7 cell lines, while it had the highest effect on the PC-3 cell line. It is thought that the effectiveness of this antiproliferative and antimicrobial activity is related to the secondary metabolites determined by GC-MS analysis.

Keywords: *Passiflora edulis,* Dodecanoic acid, Antimicrobial effect, Secondary metabolite, Antiproliferative effect.

[a] *tutkutunc58@hotmail.com* *https://orcid.org/0000-0002-8274-9386*
[b] *drzeynepsumer@gmail.com* *https://orcid.org/0000-0002-1520-3359*
[c] *emre.oksuz@cumhuriyet.edu.tr* *https://orcid.org/0000-0001-7424-5930*

Introduction

In recent years, the use of medicinal plants as sources of drugs or herbal extracts for various chemotherapeutic purposes has been of great importance in both developing and developed countries of the world. Furthermore, the use of plant-derived natural compounds as part of herbal preparations used as alternative sources of medicines continues to play important roles in human health and the treatment of diseases all over the world [1]. Throughout history, the use of plant-derived therapies in cancer treatment has been important due to their advantages in terms of efficiency, minimal side effects, easy accessibility, and improvement in quality of life. Several studies have identified various compounds with chemopreventive and/or chemotherapeutic potential in these medicinal plants, among which the polyphenol family has received much attention [2]. Advances in the field of biomedicine have allowed significant progress in the understanding of different antitumor mechanisms, which has helped in the development of cancer prevention strategies. One of these strategies is to promote the use of food phytochemicals that have the potential to inhibit, delay or reverse the process of carcinogenesis; many of these substances have been identified in fruits, vegetables and legumes [3].

Even with current treatment modalities, cancer causes more deaths than all coronary heart disease or strokes [4]. Breast cancer is the fifth leading cause of cancer deaths worldwide, with an estimated 2.3 million new cases, representing 11.7% of all cancer cases [5]. Although ovarian cancer is the third most common gynecologic cancer worldwide, it stands out for having the highest mortality rate among these cancers. This high mortality is associated with a tendency to progress without symptoms, leading to late diagnosis and a higher chance of recurrence [6]. Approximately one in six men is likely to develop prostate cancer, with most cases occurring after the age of 50 [7]. Various treatments are used to treat prostate cancer, including hormones, surgery, radiation and chemotherapy. However, all these treatments have limitations and in the majority of cases, relapse of the disease occurs [8].

Passiflora edulis, the largest genus of the botanical family Passifloraceae, originates from tropical and subtropical regions of South America. *P. edulis* Sims (family Passifloraceae) is a strong climber. They cling to anything they can grab hold of. The leaves are evergreen and alternate, with three-lobed leaves when mature. They are fast growing and once established grow 15 - 20 feet a year. [1]. The plant is widely cultivated worldwide for the economic and medicinal value it adds to its fruits and derivatives. The sedative and tranquilizing activities of *P. edulis* are known and hence its leaves and fruits are widely

used as popular compounds in the treatment of alcoholism, anxiety, migraine, nervousness and insomnia [9]. Passion fruit is a characteristic fruit of tropical regions and is particularly prominent in the pharmaceutical industry due to its various medicinal properties in its extracts, leaves and flowers, as well as the antimicrobial and antioxidant potential presented in its pulp, leaves, seeds and bark. The leaves also contain the health-valuable cyanogenic glycosides β-D-allopyranose benzyl compounds [10].

The systematic screening of antimicrobial plant extracts represents a continuous effort to find new compounds with the potential to act against multidrug-resistant resistant pathogenic bacteria and fungi. The accumulation of phytochemicals in plant cell cultures has been studied for over three decades and the knowledge generated has helped realize the use of cell cultures to produce desired phytochemicals [11]. It is possible that phytochemicals derived from medicinal plants that exhibit antimicrobial activities have different structures from microbial-derived antibiotics and may have different modes of action [12].

In many studies, biological activities and possible therapeutic applications have been demonstrated using different organs of *P. edulis* [13]. Amaral et al. conducted a study for the first time on the cytotoxic potential of leaf extracts of 14 species of the genus *Passiflora* against cancer cell lines. Of these, only *Passiflora alata* leaf extract showed relevant cytotoxic potential. Based on these data, the hypothesis that other *Passiflora* species besides the 14 species tested may also exhibit anti-cancer activity is emphasized [14].

The search for more effective and selective compounds for use in cancer treatment is a challenging task and nature provides an alternative to this problem [15]. For these reasons, new strategies for cancer treatments are needed. Due to the increase in antibiotic resistance in recent years, it has become important to investigate the antimicrobial effects of phytochemicals in plants as alternative and supportive therapy in the treatment of infectious diseases.

In this study, the phytochemical structure and biological properties of the ethanol extract obtained from *P. edulis* leaves were investigated by antioxidant, antimicrobial and antiproliferative activity assays.

Materials and Methods

Collection and Identification of Plant Material

The leaves of *P. edulis* were collected from Dim Cave, situated in the Alanya district of Antalya, Türkiye in July 2023. The plant samples were identified by Dr. Hülya Özpınar. Dim Cave, located 11 kilometers from Alanya, is situated 232 meters above sea level on the western slope of Cebeli Reis Mountain. All parts of the plant were washed ten times with sterile distilled water. They were then air-dried at 25°C for ten days in the absence of sunlight. Subsequently, the dried plant material was coarsely ground using a blender. The powdered material was weighed, placed in an airtight container, and stored in a refrigerator at 4 °C for future use.

Sample Extractions

Approximately 50 grams of the finely ground plant material were carefully transferred into an extraction thimble. This thimble was then positioned within a Soxhlet apparatus, which was connected to a reflux condenser to facilitate the continuous extraction process. The extraction was performed using a series of solvents, specifically petroleum ether, chloroform, ethyl acetate, ethanol, and distilled water, each added sequentially to the extraction flask to ensure comprehensive extraction of the plant's constituents. The Soxhlet apparatus was operated for a total of 6 hours to ensure the thorough extraction and complete exhaustion of the *P. edulis* herbal material. Following this extraction period, the resulting extracts were collected and concentrated using a rotary evaporator, which allowed for the removal of solvents under reduced pressure. The concentrated plant material was subsequently subjected to vacuum drying at a temperature of 40°C for two hours to eliminate any residual solvents and moisture. After drying, the concentrated material was transferred into sterile glass bottles to prevent contamination and was stored at 4°C until it was required for further experimental procedures [16].

Gas Chromatography-Mass Spectroscopy (GC-MS) Analysis of Passiflora Edulis Extract

GC-MS analysis of the ethanolic extract of *P. edulis* leaves was conducted using the Shimadzu QP2010 SE Ultra Version. The instrument was equipped with a DB-35 MS Capillary Standard Non-polar column, with dimensions of 30 mts x 0.25 mm ID x 0.25 µm film thickness. Helium was used as the carrier gas, flowing at a rate of 1 mL/min. The injector temperature was set to 250°C, and the oven temperature was programmed to start at 60°C for 15 minutes, then gradually increased to 280°C and held for 3 minutes. Component identification was based on comparing their mass spectra with those in the Wiley and NBS libraries, as well as their retention indices [17].

Antimicrobial Activity

The antimicrobial activity of *P. edulis* leaf extract against gram-positive and gram-negative bacteria and yeast fungi was determined using the Minimum Inhibition Concentration (MIC) test [18]. *Staphylococcus aureus* (ATCC 29213), *Enterococcus faecalis* (ATCC 29212), *Bacillus cereus* (ATCC 11778), *Pseudomonas aeruginosa* (ATCC 27853), *Escherichia coli* (ATCC 25922), *Klebsiella pneumoniae* (ATCC 13883) and *Candida albicans* (ATCC 10231) standard strains were used for this test. 10 µL of the extracts prepared by dissolving in DMSO was added to the first well and serial dilutions were made with a total of 10 concentrations. The microorganisms cultured in blood agar were then transferred to Mueller Hinton Broth (Accumix® AM1072) and Saboraud Dextrose Broth (Himedia ME033) and the concentrations were adjusted

to 0.5 McFarland. 50 µL of microorganism culture was added to all wells. Microplates cultured with bacteria were incubated at 37°C and microplates cultured with yeast fungi were incubated at 35°C for 24 hours. The first well in which microorganism growth disappeared was considered as the MIC value. The analysis was performed in 3 replicates [19].

Antiproliferative Activity

Antiproliferative effects of plant extracts were tested on the human lung cancer cell line (A549, ATCC-CCL-185), human breast cancer cell line (MCF-7, ATCC-HTB-22), mouse glioma cell line (C6, ATCC-CCL-107) and human normal lung fibroblast (WI-38, ATCC-CCL-75) cell lines using XTT Assay method. Cells were first passaged and grown until they reached the appropriate density for the appropriate experiment. They were then seeded in microplates at 10.000 cells per well. The extracts were added to the cells in a total of 8 concentrations. DMSO was used as negative control and antineoplastic agents were used as positive control. Microplates were incubated for 24 hours at 37°C in an atmosphere with 5% CO_2. At the end of the incubation period, the medium was removed and 100 µL of XTT solution prepared according to the experimental procedure was added to each well. After 4 hours of incubation, optical density values were measured at 450 nm with a microplate reader (ELISA Reader) [20].

Statistical Analysis

One Way Anova test as well as Tukey test were used for statistical analysis of the findings. For this purpose, the SPSS 16.0 (SPSS, Chicago, IL, USA) statistical program was used and a $p<0.05$ value at 95% confidence interval was considered significant between groups.

Results and Discussion

Gas Chromatography-mass Spectroscopy (GC-MS) Analysis of Passiflora Edulis Extract

In the GC-MS analysis, 25 main bioactive compounds were identified in the ethanolic extract of *P. edulis* leaves extract and the results were given in Table 1. These compounds were identified based on their peak areas, molecular weights, and molecular formulas. The GC-MS spectrum indicated the presence of several long-chain hydrocarbons. As the number of carbon atoms in a molecule increases, its hydrophilicity decreases and its lipophilicity increases.

The extract of *P. edulis* extract contained 62.05 to 73.78 % of total linolenic and linoleic acids, comparable to safflower seeds. Monounsaturated fatty acids such as oleic acid and stearic acid have been shown to lower blood glucose levels when consumed as part of the diet [21]. Thus, the analysis indicates that the passiflora plant extract of *P. edulis* extract contains fatty acids with significant beneficial properties [22].

Table 1. Phytocompounds identified in the ethanolic extract of *Passiflora edulis* extract by GC-MS analysis

No	RT (min.)	Compound name	Molecular formula	Molecular weight
1	2.711	Benzhydrazide,N2-(2-methoxy-5nitrobenzylideno)-	$C_{15}H_{12}N_4O_6$	299.091
2	3.976	Styrene	$C_6H_5CH=CH_2$	104.063
3	4.356	Tetraethyl orthosilicate	$Si(OC_2H_5)_4$	208.113
4	6.543	1-Dodecene	$CH_3(CH_2)_9CH=CH_2$	168.188
5	8.146	9-Octadecene, (E)-	$C_{18}H_{36}$	252.282
6	10.153	7-Hexadecene, (Z)-	$C_{16}H_{32}$	224.25
7	12.209	cis-11-Hexadecenal	$C_{16}H_{30}O$	238.23
8	17.022	Oxacyclotetradecane-2,11-dione, 13-methyl-	$C_{14}H_{24}O_3$	240.173
9	17.622	n-Hexadecanoic acid	$C_{16}H_{32}O_2$	256.23
10	18.453	Palmitic acid	$C_{18}H_{36}O_2$	284.272
11	20.867	Linolelaidic acid	$C_{19}H_{34}O_2$	294.256
12	21.031	11-Octadecenoic acid, methyl ester, (Z)-	$C_{19}H_{36}O_2$	296.272
13	22.572	Ethyl Oleate	$C_{20}H_{38}O_2$	310.287
14	23.011	Ethyl Stearate	$C_{20}H_{40}O_2$	312.303
15	26.442	9, 12- Linoleic acid	$C_{18}H_{32}O_2$	280.24
16	27.355	Methyl nonyl acetaldehyde	$C_{12}H_{24}O$	184.183
17	27.711	Pregna-3,5-dien-20.alpha.-ol,O-trimethylsilyl	$C_{24}H_{40}Osi$	372.285
18	27.966	Heptadecane	$C_{17}H_{36}$	240.282
19	28.207	Palmitic acid β-monoglyceride	$C_{19}H_{38}O_4$	330.277
20	28.728	9,12-Tetradecadien-1-ol, (Z,E)-	$C_{14}H_{26}O$	210.198
21	30.122	4-(3,4,5,6-Tetrahydroxy-2-oxo-hexylamino)- benzonitrile	$C_{13}H_{16}N_2O_5$	280.106
22	30.439	9,17-Octadecadienal, (Z)-	$C_{18}H_{32}O$	264.245
23	30.90	15-Hydroxypentadecanoic acid	$C_{15}H_{30}O_3$	258.219
24	31.905	E-11-Hexadecenoic acid, ethyl ester	$C_{18}H_{34}O_2$	282.256
25	33.723	(R)-(-)-14-Methyl-8-hexadecyn-1-o	$C_{17}H_{32}O$	252.245

In this study, the GC-MS analysis of the ethanolic extract of *P. edulis* leaves revealed the presence of dodecanoic acid, tetradecanoic acid, n-hexadecanoic acid, 9,12-octadecadienoic acid (Z, Z), oleic acid, stearic acid, palmitic acid, and linolenic acid. Among these identified compounds, dodecanoic acid, tetradecanoic acid, and n-hexadecanoic acid possess antioxidant and antimicrobial properties. Additionally, n-hexadecanoic acid exhibits larvicidal effects, while 9,12-octadecadienoic acid (Z, Z) demonstrates anti-inflammatory and anti-arthritic activities [23].

Determination of the Antimicrobial Activity of Passiflora Edulis Extract

Antimicrobial Activity Results

In the determination of the antimicrobial activity of *P. edulis* leaf extracts, MIC values were determined by microdilution test. The results were compared with reference sources [27] and MIC values of standard antibiotics. Reference sources given as [Effective (MIC < 100 µg/mL), Moderate (100 < MIC ≤ 625 µg/mL), and Weak (MIC > 625 µg/mL)] were used. The MIC values of the extracts and antibiotics are given in the table below (Table 2).

Table 2. MIC results of *Passiflora edulis* leaf extract (µg/mL)

Microorganisms (Bacteria and Yeasts)	Leaf extract MIC (µg/mL)	Antibiotics MIC (µg/mL)	Antibiotics
E. coli	50	8	Amoxicillin
K. pneumoniae	100	16	Piperacillin/Tazobactam
P. aeruginosa	25	4	Imipenem
S. aureus	50	2	Linezolid
E. faecalis	50	2	Linezolid
B. cereus	50	1	Linezolid
C. albicans	50	0.25	Fluconazole

P. edulis leaf extract showed effective antimicrobial activity on the tested microorganisms based on reference sources. When compared with the MIC values of standard antibiotics, it was observed that the antimicrobial activity was not at the targeted level. Ripa et al. showed that *P. edulis* leaf petroleum ether and chloroform extract moderately inhibited the growth of *B. megaterium, P. aeruginosa, S. dysenteriae* and *S. boydii* microorganisms [1]. Akanbi et al. reported that the leaf hexane extract of *P. edulis* showed high antimicrobial activity in a study with *S. aureus, Salmonella paratyphi, P. aeruginosa* and *K. pneumoniae* obtained from clinical isolates [12]. Ramaiya et al. and Kannan et al. found moderate antimicrobial activity (12.0 mm / 10 ± 1.03 mm) of *P. edulis* leaf methanol extract against *Bacillus subtilis* and *S. auerus* [24, 25]. Nugraha et al. showed that *P. edulis* ethanol extract has antimicrobial activity against *S. aureus* and *E. coli* bacteria [26]. According to the results of our study, *P. edulis* leaf extract was found to have antimicrobial activity considering the reference values. These results are in agreement with the literature studies mentioned here.

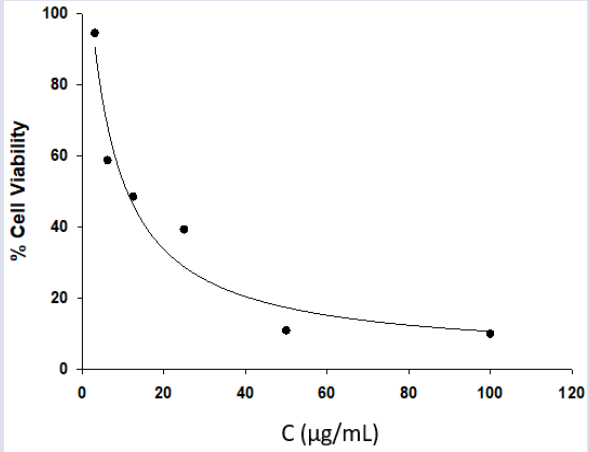
Determination of the Antiproliferative Activity of Passiflora Edulis Plant Extracts

The cytotoxicity of *P. edulis* leaf extract on three different tumor cell lines (PC-3, OvCar, MCF-7) was evaluated by XTT assay. Healthy WI-38 cell line was used as a positive control. Cell viability was determined as optical density. IC_{50} values were obtained by dose-response curve and the following tables and graphs were generated (Table 3, Figure 1).

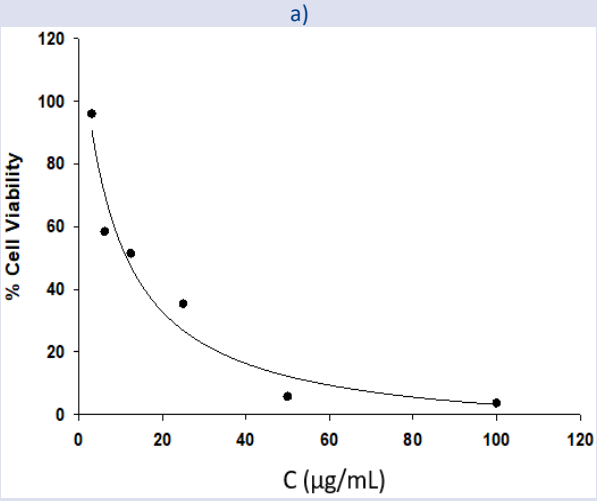
Table 3. IC_{50} values of *P. edulis* extract

P. edulis	IC_{50}(µg/ml)			
	PC-3	OvCar	MCF-7	WI-38
Leaf Ethanol	10,11±0,17	12,97±0,62	11,31±0,34	>100

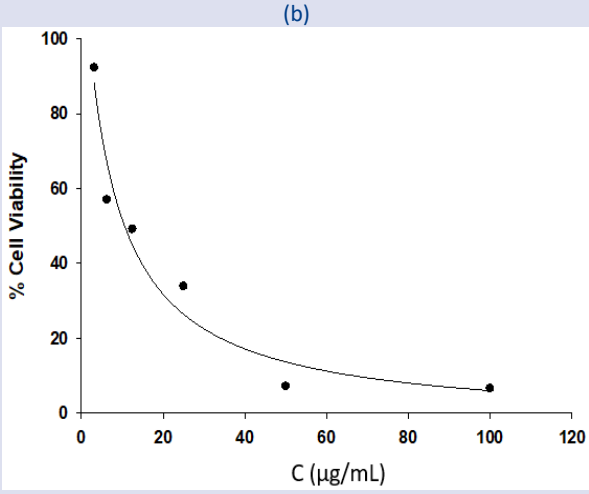
Significant p≤ 0.05 level of analysis of variance (One Way Anova Tukey)



a)



(b)



(c)

Figure 1. a, b, c; Cell viability of PC-3, OvCar and MCF-7

The IC_{50} values given in Table 3 (PC-3=10.11, OvCar=12.97, MCF-7=11.31) prove that effective anticancer activity was found even at low concentrations. When the anticancer activity of the three different cell lines was compared with each other, no statistically significant difference was found ($p \geq 0.05$).

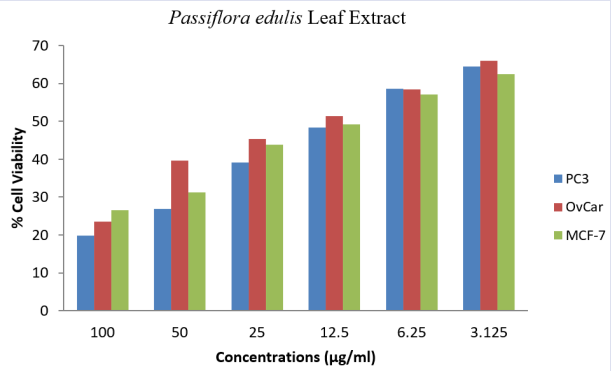


Figure 2. % Cell viability graphic of *P. edulis* extract.

P. edulis leaf extract showed high anticancer activity on cancer cells as shown in cell viability graphs (Figure 2). On healthy WI-38 cells, cell viability reached 100% even at high concentrations of the extract. This indicates that the toxic effect of *P. edulis* extract is almost negligible. Sari et al. and Kuete et al. showed antiproliferative activity on MCF-7 cells in a study with *P. edulis* extract [5, 27]. In an in vitro study conducted by Fotsing et al., *P. edulis* leaf extract showed significant inhibition in the growth of MCF-7 and MDA-MB 231 cells at 100 µg/mL [28]. An article examining the cytotoxic effect of *P. edulis* extracts on OvCar and PC-3 cells was not found in the literature. However, in a study conducted by Amaral et al. on 14 different *Passiflora* species, *P. alata* leaf extract was shown to have a high antiproliferative effect on OvCar cells [29]. In addition, da Silva et al. and Amaral et al. showed antiproliferative effects on PC-3 cells in their studies with *P. mucronate and P. alata* species [14, 30].

Conclusions

In this study, *P. edulis* leaves were extracted in ethanol and analyzed for phytochemical content. While looking at the biological activities, it was observed that antimicrobial activity and anticancer effect were high. In line with these data, more biological activities of *P. edulis* plant with high biological activity can be investigated. In addition, depending on the high antiproliferative activity, it may be recommended to investigate the apoptosis mechanisms of the cell lines examined.

Acknowledgments

The authors would like to thank Dr. Ceylan Hepokur for her aid and support and Dr. Hülya Özpınar for her aid in plant species identification.

Conflict of Interest

The authors declare that they have no conflicts of interest in the publication.

References

[1] Ripa F. A., Haque M., Nahar L., Islam M. M., Antibacterial, cytotoxic and antioxidant activity of Passiflora edulis Sims, *Eur. J. Sci. Res.*, 31(4) (2009) 592-598.

[2] Aguillón J., Arango S. S., Uribe D. F., Loango N., Cytotoxic and apoptotic activity of extracts from leaves and juice of Passiflora edulis, *J. Liver. Res. Disord. Ther.*, 4(2) (2018) 67-71.

[3] Ramírez V., Arango S. S., Uribe D., Maldonado M. E., Aguillón J., Effect of the ethanolic extract of Passiflora edulis F. Flavicarpa leaves on viability, cytotoxicity and apoptosis of colon cancer cell lines, *J. Chem. Pharm. Res.*, 9(6) (2017) 135-9.

[4] Antoni S., Soerjomataram I., Møller B., Bray F., Ferlay J., An assessment of GLOBOCAN methods for deriving national estimates of cancer incidence, *Bulletin of the World Health Organization*, 94(3) (2016) 174.

[5] Sari L. M., Sari D. K., Bustami A., Gazali A. D., Auerkari E. I., Cytotoxicity and apoptosis activities of passion fruit (Passiflora edulis Sims) seed extract on HSC-2, HSC-3, MCF-7, and HaCaT cell lines, *Journal of Pharmacy & Pharmacognosy Research*, 12(4) (2024) 659-672.

[6] Çoban H. Ş., Çil N., Önder E., Abban Mete G., Anti-cancer effects of alpha lipoic acid, cisplatin and paclitaxel combination in the OVCAR-3 ovarian adenocarcinoma cell line, *Molecular Biology Reports*, 51(1) (2024) 485.

[7] Eisermann K., Tandon S., Bazarov A., Brett A., Fraizer G., Piontkivska H., Evolutionary conservation of zinc finger transcription factor binding sites in promoters of genes co-expressed with WT1 in prostate cancer, *BMC Genomics*, 9 (2008) 1-15.

[8] Choi E. S., Kim J. S., Kwon K. H., Kim H. S., Cho N. P., Cho S. D., Methanol extract of Sanguisorba officinalis L. with cytotoxic activity against PC3 human prostate cancer cells, *Molecular Medicine Reports*, 6(3) (2012) 670-674.

[9] Li H., Zhou P., Yang Q., Shen Y., Deng J., Li L., Zhao D., Comparative studies on anxiolytic activities and flavonoid compositions of Passiflora edulis 'edulis' and Passiflora edulis 'flavicarpa', *Journal of Ethnopharmacology*, 133(3) (2011) 1085-1090.

[10] Oliveira H. M., Espinheira M. J. C. L., de Souza F. M., Duarte S. F. P., David I. R., Sousa B. R., Evaluation of the antimicrobial potential of essential oil of the leaf of Passiflora edulis, *Int. J. Adv. Eng. Res. Sci.* (IJAERS), 6(5) (2019) 390-395.

[11] Johnson M., Maridass M., Irudayaraj V., Preliminary phytochemical and anti-bacterial studies on Passiflora edulis, *Ethnobotanical Leaflets*, (1) (2008) 51.

[12] Akanbi B. O., Bodunrin O. D., Olayanju S., Phytochemical screening and antibacterial activity of Passiflora edulis, *Researcher*, 3(5) (2011) 9-12.

[13] de Sousa G. F., Santos D. K. D. D. N., da Silva R. S., Barros B. R. D. S., da Cruz-Filho I. J., Ramos B. D. A., Lagos de Melo C. M., Evaluation of cytotoxic, immunomodulatory effects, antimicrobial activities and phytochemical constituents from various extracts of Passiflora edulis F. flavicarpa (Passifloraceae), *Natural Product Research*, 35(24) (2021) 5862-5866.

[14] Amaral R. G., Gomes S. V., Andrade L. N., Dos Santos S. A., Severino P., de Albuquerque Júnior R. L., Carvalho A. A., Cytotoxic, antitumor and toxicological profile of Passiflora alata leaf extract, *Molecules*, 25(20) (2020) 4814.

[15] Dias D. A., Urban S., Roessner U., A historical overview of natural products in drug discovery, *Metabolites*, 2(2) (2012) 303-336.

[16] Bohórquez-Moreno C. D., Öksüz K. E., Dinçer E., Hepokur C., Şen L., Plant-inspired adhesive and injectable natural hydrogels: in vitro and in vivo studies, *Biotechnology Letters*, 45(9) (2023) 1209–1222.

[17] Li C., Xin M., Li L., He X., Yi P., Tang Y., Li J., Zheng F., Liu G., Sheng J., Li Z., Sun J., Characterization of the aromatic profile of purple passion fruit (Passiflora edulis Sims) during ripening by HS-SPME-GC/MS and RNA sequencing, *Food Chemistry*, 355 (2021) 129685.

[18] Rizwana H., Al Otibi F., Al-Malki N., Chemical composition, FTIR studies and antibacterial activity of Passiflora edulis f. edulis (Fruit), *J. Pure Appl. Microbiol.*, 13(4) (2019) 2489-2498.

[19] Hepokur C., Misir S., Tunç T., Tutar U., Hepokur A., Çiçek, M., In vitro antimicrobial, antioxidant, cytotoxic activities, and wound healing potential of Thymbra capitata ethanolic extract, *Turkish Journal of Biochemistry*, 45(6) (2020) 843-849.

[20] Gezegen H., Tutar U., Hepokur C., Ceylan M., Synthesis and biological evaluation of novel indenopyrazole derivatives, *Journal of Biochemical and Molecular Toxicology*, 33(5) (2019) e22285.

[21] Thomsen C., Rasmussen O., Lousen T., Holst J. J., Fenselau S., Schrezenmeir J., Hermansen K., Differential effects of saturated and monounsaturated fatty acids on postprandial lipemia and incretin responses in healthy subjects, *The American Journal of Clinical Nutrition*, 69 (6) (1999) 1135–1143.

[22] Calder P. C., Functional Roles of Fatty Acids and Their Effects on Human Health. JPEN, *Journal of Parenteral and Enteral Nutrition*, 39 (2015) (1S).

[23] Lalitharani S, Mohan VR, Regini GS., GC-MS analysis of ethanolic extract of Zanthoxylum rhetsa (roxb.) dc spines, *J. Herbal Med. Toxicol.* 4(1) (2010) 191-2.

[24] Ramaiya S. D., Bujang J. S., Zakaria M. H., Assessment of total phenolic, antioxidant, and antibacterial activities of Passiflora species, *The Scientific World Journal*, (1) (2014) 167309.

[25] Kannan S., Devi B. P., Jayakar B., Antibacterial evaluation of the methanolic extract of Passiflora edulis. *Hygeia - Journal for Drugs and Medicine*, 3(1) (2011) 46-49.

[26] Nugraha S. E., Achmad S., Sitompul E., Antibacterial activity of ethyl acetate fraction of passion fruit peel (Passiflora Edulis Sims) on Staphylococcus aureus and Escherichia coli, *Indonesian Journal of Pharmaceutical and Clinical Research*, 2(1) (2019) 07-12.

[27] Kuete V., Dzotam J. K., Voukeng I. K., Fankam A. G., Efferth T. Cytotoxicity of methanol extracts of Annona muricata, Passiflora edulis and nine other Cameroonian medicinal plants towards multi-factorial drug-resistant cancer cell lines, *Springerplus*, 5 (2016) 1-12.

[28] Fotsing S. I., Pambe J. C. N., Silihe K. K., Yembeau N. L., Choupo A., Njamen D., Zingue S., Breast cancer cell growth arrest and chemopreventive effects of Passiflora edulis Sims (Passifloraceae) ethanolic leaves extract on a rat model of mammary carcinoma, *Journal of Ethnopharmacology*, 311 (2023) 116408.

[29] Amaral R. G., Gome, S. V. F., Luciano M. C. D. S., Pessoa C. D. Ó., Andrade L. N., Severino P., Carvalho A. A., Cytotoxic potential of 14 Passiflora species against cancer cells, *Journal of Medicinal Plants Research*, 13(7) (2019) 157-166.

[30] da Silva I. C., Kaluđerović G. N., de Oliveira P. F., Guimarães D. O., Quaresma C. H., Porzel A., Leal I. C., Apoptosis caused by triterpenes and phytosterols and antioxidant activity of an enriched flavonoid extract from Passiflora mucronata, *Anti-Cancer Agents in Medicinal Chemistry*, 18(10) (2018) 1405-1416.