GEORGIAN BIOMEDICAL NEWS

ISSN (Online): 2720-8796 ISSN (Print): 2720-7994 VOLUME 1. ISSUE 1. JANUARY-MARCH 2023

Evaluation of Antioxidant and Cytotoxic Activity of Plants Allium Ponticum and Allium Saxatile, Growing in Georgia

Giorgi Jgerenaia[1], Olivier Bonnet[2], Carla Hamann[2], Tsiala Gviniashvili[3], Michel Frederich[2], Nathalie Augé[4], Lasha Mskhiladze[1*]

DOI: 10.52340/GBMN.2023.01.01.02

ABSTRACT

BACKGROUND.

Plants of the genus Allium have a long history of traditional use worldwide, dating back to the early ages, as food and medicine. The Allium genus has been recognized as a rich source of secondary metabolites with related health benefits. Allium species are widely used in Georgian traditional medicine against many diseases.

OBJECTIVES

In this research, we have evaluated the antioxidant and cytotoxic activity of Allium ponticum Miscz, Sect. Allium and Allium saxatile M. Bieb, Sect. Oreiprason F. Hern. Two Allium species growing in Georgia.

METHODS

Ethanol extracts from both plants were obtained, using an ultrasonic water bath. The dried ethanol extract was subjected to fractionation using column chromatography, with Water-Methanol as a mobile phase. The cytotoxic properties of all these extracts and fractions were evaluated against human melanoma cells (A2058). The antioxidant activity of fractions was evaluated using the TBARS assay on RAW 264.7 murine macrophages. The anti-inflammatory activity of extracts and fractions was studied using RT-qPCR, and the inflammation was induced with LPS (Lipopolysaccharide).

RESULTS

The crude extract of A. saxatile showed cytotoxic activity with IC50 value of 37.62 µg/ml, 100% methanolic fractions of A. saxatile and A. ponticum showed activity with IC50 4.04 µg/ml and 37.67 µg/ml respectively. Among the fractions, 50% methanolic fraction had better activity than others, IC50 _ 2.93 µg/ml and 14.78 µg/ml for A. saxatile F2 and A. ponticum F2, respectively, Doxorubicin 5 µM. The results of antioxidant activity were IC50_ 3.5 µg/ml and 58.48 µg/ml for crude extracts of A. saxatile and A. ponticum respectively. Extracts and fractions haven't expressed an anti-inflammatory activity.

CONCLUSIONS

Overall, these data confirm the therapeutic potential of Allium ponticum and Allium saxatile, and the need for the isolation of individual compounds, which are responsible for these biological activities.

KEYWORDS

Allium ponticum; Allium saxatile; Allium; antioxidant activity; cytotoxicity.

BACKGROUND

The genus Allium belongs to the family Alliaceae, they are an important herbaceous plant.[1] This genus involves up to 1233 species, mostly growing in the northern hemisphere (Allium L. in GBIF Secretariat (2021). Among them, 70 species grow in the Caucasus region and 35 species are described in Georgia, among which, 7 species are endemic to the Caucasus region and 5 species are endemic to Georgia.[2]

Plants of the genus Allium have a long history of traditional uses worldwide dating back to the early ages as food and medicine. The history of Allium cultivation dates to ancient Egypt, more than 4,000 years ago. It is cited in the Egyptian Codex Ebers, a 35-century-old document, as being useful in the treatment of heart disorders, tumors, worms, bites, and other illnesses.[3] These plants were also well-known in ancient Greece, the Roman Empire, India, China, Central Asia, the Middle East, etc.[4] Allium plants have been used to treat high blood pressure, worms, colds, inflammation, loss of appetite, fungal infections, intestine disorders, infertility, and diabetes.[5,6] Ayurvedic medicine claims that garlic (Allium sativum L.) maintains the fluidity of blood and strengthens the heart 6. Allium species are widely used in Georgian traditional medicine as antifungal, antiseptic, and antibacterial remedies.[7,8]

The Allium genus is a well-known source of secondary metabolites, including phenolic acids and their derivatives, flavonoids, flavonoid polymers, steroidal saponins, and organic sulfur compounds, with related health benefits.[9-11]

Species of Allium have shown important cytotoxic activity, such as Allium leucanthum K. Koch;[12] Allium gramineum K. Koch;[10] Allium flavum L;[13] Allium cepa L.[14]

Antioxidants play a significant role in health. They are also used to reduce disease risk and can protect the body against oxidative damage, which causes various diseases (diabetes, cancer, neurodegenerative disorders, etc.). Several reports have described that antioxidant supplementation may exert antiatherogenic properties via their ability to limit the early steps of atherogenesis associated with low-density lipoprotein (LDL) oxidation. Independently of their antioxidant activities, other features, such as defense against oxLDL-induced toxicity or anti-inflammatory action, have been reported.[15]

Research on antioxidant activity in Allium species has been widely reported. Antioxidant activity is found in A. cepa, A. sativum, and A. schoenoprasum with different testing methods.[16]

Studies on the different plants, in the genus Allium have shown that they have various interesting biological activities, which have already been well studied. This encouraged us to evaluate the cytotoxic, antioxidant, and anti-inflammatory activities of the plants of the genus Allium, Allium saxatile and Allium ponticum, growing in Georgia. Previous phytochemical or pharmacological studies on these plants have not been reported.

METHODS

Chemical reagents and cell lines

All reagents, solvents, and chemicals used in the experiments were of analytical grade. Methanol, dichloromethane, and ethyl acetate were acquired from VWR Chemicals (France). For column chromatography, Diaion HP-20 resin (Mitsubishi, Japan) was used. Tri-reagent RT and High-Capacity cDNA reverse transcription Kit with RNase Inhibitor were purchased from ThermoFisher Scientific (USA). RPMI medium supplemented with 10% fetal calf serum was obtained from “Thermo Fisher Scientific Inc.” USA (Gibco™). To extract total RNA from cells we used Tri-reagent RT obtained from Molecular Research Center, Inc. For retrotranscription_High-capacity cDNA Reverse Transcription Kit from Applied Biosystems® and for mRNA level measurement SsoFast™ EvaGreen® Supermix from BIO-RAD.

RAW 264.7 murine macrophages (RAW264.7 ATCC® TIB-71™) and A2058 human melanoma cells (A2058 ATCC® CRL-11147™) were obtained from American Type Culture Collection (Manassas, Virginia), and were cultured in RPMI medium supplemented with 10% fetal calf serum in a 37 °C humidified incubator containing 5% CO2. For the experiments, the cells were incubated in a serum-free RPMI-1640 medium. A2058 human melanoma cells were grown in Dulbecco’s modified Eagle’s medium (DMEM) supplemented with glucose (4.5 g/L), glutamine (2 mM), penicillin (50 IU/mL), streptomycin (0.5 mg/mL), sodium pyruvate (0.5 mM) and 10% fetal bovine serum (FBS). All the culture reagents were obtained from “ThermoFisher scientific”.

Plant Material

The aerial parts of Allium saxatile M. Bieb, Sect. Oreiprason F. Hern and Allium ponticum Miscz, Sect. Allium, was collected, respectively, in the Racha and Javakheti, regions of Georgia. They were collected and identified by Pr. Tsiala Ghviniashvili (Botanical Institute of Ilia State University).

Extraction and fractionation

Each plant was dried and milled to 1 mm particles. Powdered plants were extracted with 80% EtOH, using an ultrasonic water bath at 50 °C. Extracts were concentrated with a rotary evaporator.

Dried extracts of each plant were subjected to Diaion HP-20 column chromatography. The mobile phase was H2O-MeOH in gradient condition and EtOAc to give four enriched fractions of each plant. Biological studies were conducted on crude extracts of both plants and fractions including A. saxatile F1, A. saxatile F2, A. saxatile F3, A. ponticum F1, A. ponticum F2, and A. ponticum F3. The fractions A. saxatile F4 and A. ponticum F4 were not used for studies because the obtained amount was not enough for research; these fractions only contained lipophilic compounds with low solubility.

LDL Isolation and oxidation

Human LDLs (d 1.019–1.063) were isolated from pooled fresh sera, provided by the French organization, "établissement français du sang" by sequential ultracentrifugation, dialyzing, and sterilization by filtration as previously described by Augé et al.[17]

Cell viability assay (MTT assay)

The cell viability was evaluated on RAW 264.7 macrophages using the MTT (3-(4, 5 dimethylthiazol-2-yl)-2, 5 diphenyltetrazolium bromide) assay. Cells were exposed to the fractions, with different concentrations. Crude extracts with 0,5 µg/mL, 5 µg/mL, 50 µg/mL, and 100 µg/mL concentrations. Fractions with 0,1 µg/mL, 1 µg/mL, 10 µg/mL and 20 µg/mL concentrations. An untreated control was used as control.[17]

Antioxidant activity (TBARS assay)

For evaluation of cytotoxicity, extracts and fractions were assessed in 96-well microplates using the Prestoblue® colorimetric assay for cell viability based on the reduction of resazurin in resorufin dependent on the metabolic activity of cells. This color change was detected using fluorescence measurements (SpetraMax i3, Molecular Devices™) at 560 and 590 nm. Each dilution of the tested extract and fraction was assessed in triplicate. Doxorubicin was used as the positive control and cells with 1.5% DMSO was used as a negative control.[18]

Cytotoxicity assay

We decided to study the antioxidant activity of A. saxatile and A. ponticum in two diverse ways. Firstly, a non-cellular assay was performed in the culture medium, where we added LDL,

The Georgian Biomedical News
ISSN (Online): 2720-8796 ISSN (Print): 2720-7994

CuSO4, and extracts and fractions of the plants, with increasing concentration, dissolved in 0.1% DMSO. In this case, we wanted to see if the studied products would prevent LDL oxidation directly via biochemical pathways. Secondly in a cellular assay on RAW 264.7 cells, incubated with LDL, CuSO4, and extracts and fractions of the plants, with increasing concentration, were dissolved in DMSO and samples for 24 hours. After this period, the medium was removed, and the antioxidant activity was evaluated using the thiobarbituric acid reactive substances (TBARS) assay.[19]

The cells were seeded on a 24-well plate with a 500 µL serum-free RPMI 1640 culture medium and were treated with LDL (200 µg/mL) and samples. TBARS were evaluated exactly as previously described referring to a Malone di-aldehyde standard. The control was performed under the same conditions but with only 0.1% DMSO.[17]

Anti-Inflammatory activity

The anti-inflammatory activity of the samples was evaluated using RT-qPCR, according to the previously described method20. We treated cells with lipopolysaccharide (LPS), low-density lipoprotein (LDL), and oxidized low-density lipoprotein (oxLDL), then crude extracts and fractions of both plants at different concentrations were added.

Statistical analysis

Each experiment was performed independently 3 to 6 times before statistical analysis. Results were expressed as mean ± SEM. All data passed a normality test followed by a normal Gaussian test repartition to verify whether there was equal variance or not (Minitab software), which orientates the statistical analysis test that was done using GraphPad Prism 6 for Windows (GraphPad Software). Results were considered significant at $p<0.05$. *: Untreated control used as reference (*: $p<0.05$; **: $p<0.01$; ***: $p<0.001$; ****: $p<0.0001$).

RESULTS

Extract yield

Extraction of 500 g of each plant yielded a crude extract of A. saxatile - 35.7 g and A. ponticum - 30.5 g. 15 g dried extracts of each plant were separated using column chromatography. The stationary phase was Diaion HP-29 and the mobile phase was H2O-MeOH in gradient condition (100:0; 50:50; 0:100 v/v) and finally EtOAc to give four enriched fractions of each plant. in total 8 fractions were obtained: A. saxatile F1; A. saxatile F2; A. saxatile F3; A. saxatile F4; A. ponticum F1; A. ponticum F2; A. ponticum F3 and A. ponticum F4. (Tab.1a and 1b)

TABLE 1a. Obtained fractions of A. saxatile after separation using column chromatography

Fraction	*Solvent for elution*	Yield (g)
A. saxatile F1(Fraction 1)	100% Water	8.1
A. saxatile F2 (Fraction 2)	50% water : 50% Methanol	1.7
A. saxatile F3 (Fraction 3)	100% Methanol	3.5
A. saxatile F4 (Fraction 4)	100% EtOAc	0.02

TABLE 1b. Obtained fractions of A. ponticum after separation using column chromatography

Fraction	*Solvent for elution*	Yield (g)
A. ponticum F1(Fraction 1)	100% Water	6.7
A. ponticum F2 (Fraction 2)	50% water : 50% Methanol	3.9
A. ponticum F3 (Fraction 3)	100% Methanol	2.3
A. ponticum F4 (Fraction 4)	100% EtOAc	0.2

Cytotoxic Activity

Cytotoxic activity of the fractions from Allium saxatile and Allium ponticum was assessed against human melanoma cells (A2058). Crude extract and 100% methanolic fraction (A. saxatile F3) of A. saxatile showed cytotoxic activity against melanoma cells, with IC50 values of 37.62 µg/mL and 4.04 µg/mL respectively. In the case of A. ponticum, only the methanol fraction (A. ponticum F3) showed cytotoxic activity with IC50_35.67 µg/mL. (Tab.2)

TABLE 2. in vitro cytotoxic activity of crude extract and fractions of Allium saxatile and Allium ponticum on A2058 cells. Doxorubicin was used as a reference

Sample	*IC_{50} µg/mL*
A. saxatile Crude extract	37.62
A. saxatile F1	>50
A. saxatile F2	>50
A. saxatile F3	4.04
A. ponticum Crude extract	>50
A. ponticum F1	>50
A. ponticum F2	>50
N=3	

Toxicity of crude extract and fractions and cytoprotective effect against oxLDL induced apoptosis

Toxicity of the crude extract and fractions were investigated on murine RAW264.7 macrophages. For A. Ponticum only methanol fraction (A. ponticum F3) showed low toxicity with 20% inhibition at 20 µg/mL in comparison with untreated control (Fig.1). A. Saxatile crude extract showed 45% inhibition and a methanolic fraction (A. saxatile F3) showed 55% inhibition at 20 µg/mL and 30% inhibition at 10 µg/mL. (Fig.2)

The toxic effect of oxLDL is quite dramatic and leads to cell death, either through apoptosis or necrosis.[21]

Our data has shown that the viability of cells incubated with an oxLDL-containing medium decreased by 50%.

In the case of incubation of cells with oxLDL and studying objects, we see that the viability of cells was increased up to 100% after incubation with crude extract of A. ponticum and fractions A. ponticum F1, A. ponticum F3 with 1 µg/mL and 0.1 µg/mL and fraction A. ponticum F2 with 1 µg/mL concentrations (Fig.3).

Crude extract and fractions A. saxatile F1 and A. saxatile F2 have increased cell viability with low concentrations, and fraction A. saxatile F3 with all concentrations showed protective effects against oxLDL-induced cell death (Fig.4).

The Georgian Biomedical News
ISSN (Online): 2720-8796 ISSN (Print): 2720-7994

FIGURE 1. Effect of crude extract and fractions on RAW 264.7 viability. Macrophages were incubated with A. ponticum Crude extract; A. ponticum F1; A. ponticum F2; A. ponticum F3 fractions, with different concentrations

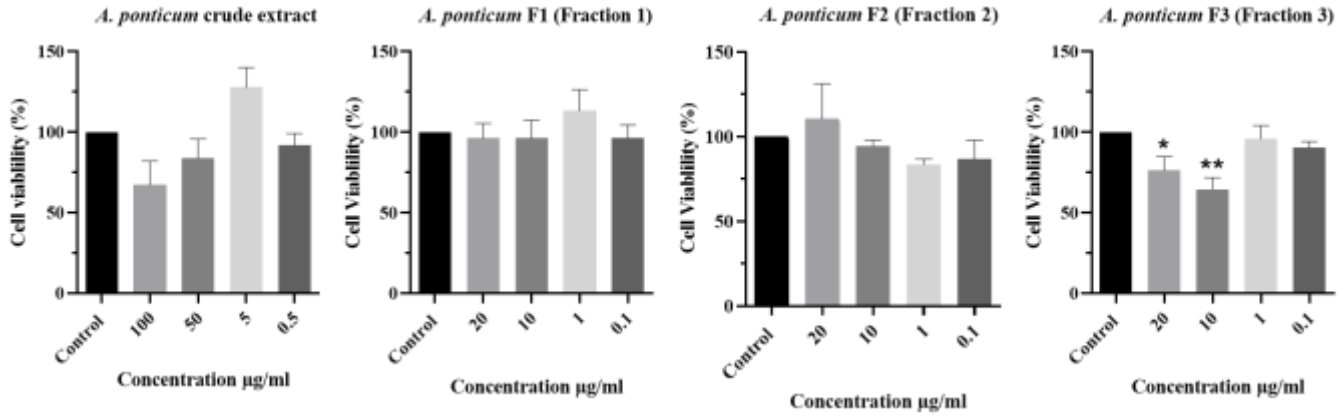


FIGURE 2. Effect of crude extract and fractions on RAW 264.7 viability. Macrophages were incubated with A. saxatile Crude extract; A. saxatile F1; A. saxatile F2; A. saxatile F3 fractions, with different concentrations

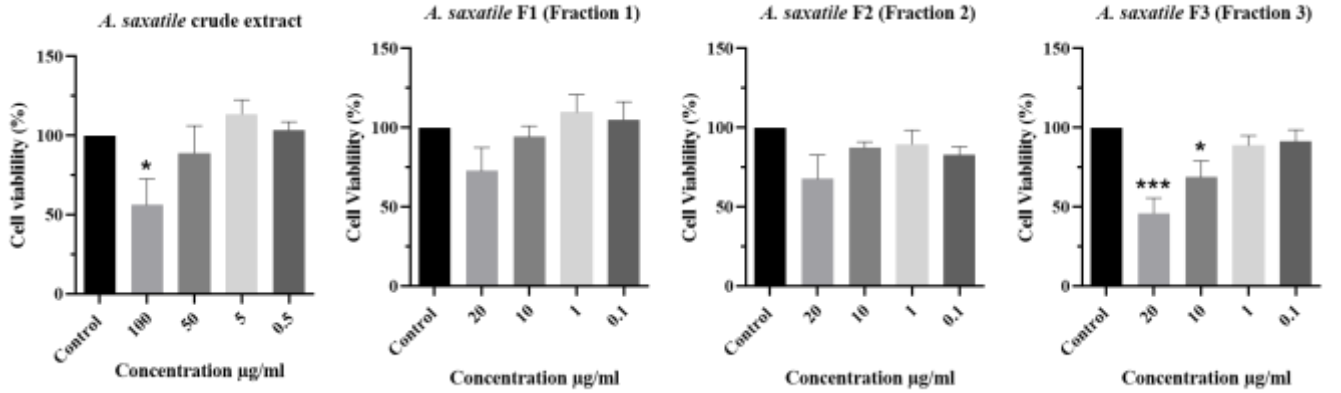
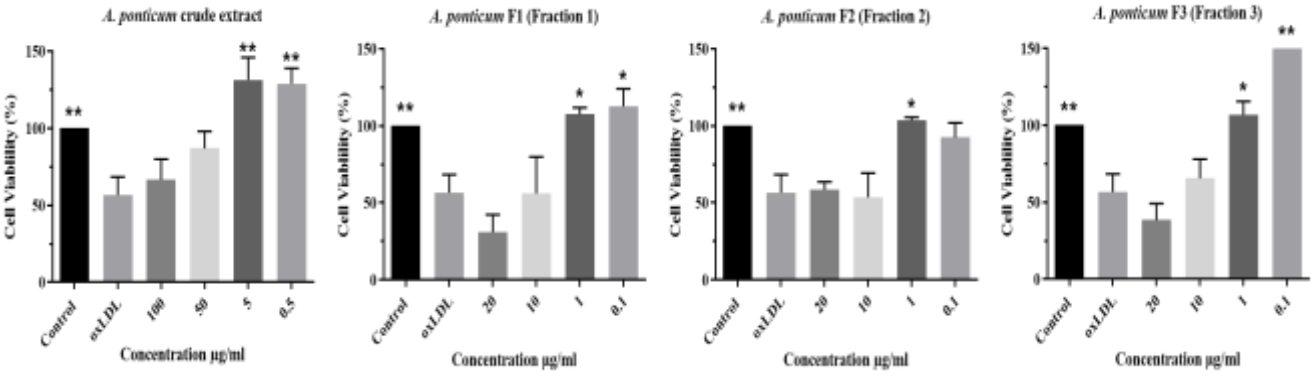
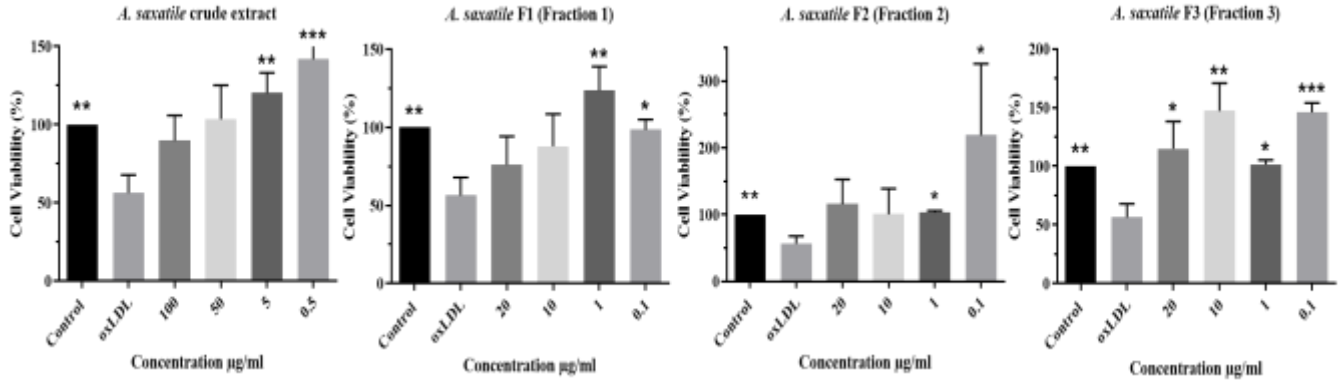


FIGURE 3. Effect of crude extract and fraction cell-oxidized LDL induced cell death. Cells were incubated with LDL and A. ponticum Crude extract; A. ponticum F1; A. ponticum F2; A. ponticum F3 fractions, with different concentrations



The Georgian Biomedical News
ISSN (Online): 2720-8796 ISSN (Print): 2720-7994

FIGURE 4. Effect of crude extract and fraction cell-oxidized LDL induced cell death. Cells were incubated with oxLDL and A. saxatile Crude extract; A. saxatile F1; A. saxatile F2; A. saxatile F3 fractions, with different concentrations



Antioxidant activity

According to the results obtained, the crude extract of plant A. Ponticum inhibited the oxidation of LDL. Concerning the fractions, A. ponticum F2 and A. ponticum F3 showed antioxidant activity in the non-cellular assay IC50 at 14.78 µg/mL and 24.53 µg/mL respectively. (Tab.3)

In the case of A. saxatile, the activity of the crude extract and fractions was higher than the crude extract and fractions of A. ponticum. All the fractions have expressed antioxidant activity, particularly, fraction A. saxatile F2 (eluted with 50% methanol) had better activity than others, with an IC50 value of 2.93 µg/mL (Table 3).

Regarding cellular assay, we tested the capacity of crude extract, and fractions of A. ponticum and A. saxatile to limit cell-induced LDL oxidation. According to the results, crude extract of A. ponticum and fraction A. ponticum F3 (eluted with 100% Methanol) have shown better activity than in non-cellular experiment IC50 42.16 µg/mL and 12.15 µg/mL respectively. (Tab.3)

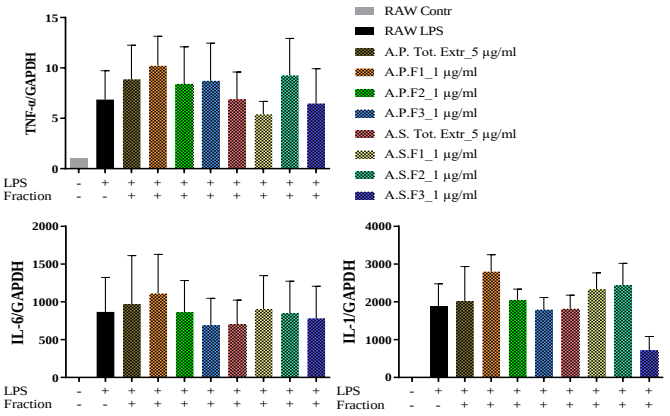
TABLE 3. Obtained fractions of A. ponticum after separation using column chromatography

Fraction	*Non cellular assay IC50 µg/mL*	Cellular assay IC50 µg/mL
A. saxatile (A.S.) crude extr.	3.5	40.13
A.S.F1	16.41	>50
A.S.F2	2.93	14.42
A.S.F3	8.2	14.13
A. ponticum (A.P.) crude extr.	58.48	42.16
A.P.F1	>50	>50
A.P.F2	14.78	>50
A.P.F3	24.53	12.15

Anti-inflammatory activity

The anti-inflammatory evaluation of the extracts and fractions of A. saxatile and A. ponticum did not show an inhibitory effect on the expression of pro-inflammatory cytokines induced by LPS.

FIGURE 5. Anti-inflammatory activity. Inflammation induced by LPS. Cells were incubated with LPS and A. ponticum Crude extract; A. ponticum F1; A. ponticum F2; A. ponticum F3; A. saxatile Crude extract; A. saxatile F1; A. saxatile F2; A. saxatile F3 fractions



DISCUSSION

Natural phytochemicals are well known for their ability to aid in the treatment of a variety of diseases. During the research, 80% ethanolic extracts of plants, A. Saxatile and A. Ponticum representing the genus Allium, were subjected to fractionation, over Diaion HP-20, column chromatography. From each plant, four different fractions were obtained, and their different pharmacological activities were evaluated using in vitro analysis.

This study revealed that fractions obtained from A. saxatile and A. ponticum can inhibit the growth of melanoma cancer cells with an IC50 of 4.04 µg/ml and 35.67 µg/ml, respectively.

In vitro studies have revealed that some saponins extracted from the plant genus Allium have a cytotoxic effect on human and animal cancer cells. For example, Spirostanol saponins, extracted from Allium leucanthum, have a cytotoxic effect against adenocarcinoma (A549) and colorectal adenocarcinoma (DLD-1) cells.[12] Compounds identified in Allium gramineum have strongly inhibited the growth of breast

The Georgian Biomedical News
ISSN (Online): 2720-8796 ISSN (Print): 2720-7994

adenocarcinoma cell lines, with an IC50 of 4.5 ± 0.7µg/mL for MDAMB-231 and 4.8 ± 0.9µg/mL for MCF-7 cells10. Furostanol saponins, from Allium chinense, have induced apoptosis of HepG2 cells.[22] Biological research on steroidal saponins extracted from Allium flavum exhibited moderate cytotoxicity against a human colorectal cancer cell line (SW480)13. Steroidal glycoside from Allium macrostemon has also shown moderate cytotoxicity against A549 and SK-MEL-2 cells.[23]

Antioxidants are substances that protect cells from damage caused by free radicals. These free radicals can damage lipids, proteins, and DNA and can cause peroxidation of the cell membrane. The accumulation of free radicals has been implicated in many diseases including cancer, heart disease, stroke, etc. Antioxidants are also antiatherogenic, as they scavenge reactive oxygen species (ROS), inhibiting the LDL oxidation elicited by cultured vascular cells.[24]

The results of the studies show that, in the non-cellular assay, the crude extract of A. saxatile is more active than A. ponticum, concerning fractions, we see that, 50% methanolic fraction of both plants have better antioxidant activity than 100% methanolic fractions (Tab.3). This can signify that compound, responsible for the described activity is mostly concentrated in a 50% methanolic fraction.

In the case of the cellular assay, results show that crude extract and fractions of A. saxatile are more active than A. ponticum, but the activity of A.P.F3 fraction is increased in the cellular assay, which can mean that compounds in this fraction express their antioxidant activity with different pathway.

The free radical scavenging activity of the extract of Allium species is well known. Antioxidant activity is described in onion, garlic, and many other species of the genus Allium (A. roseum; A. subhirsutum; A. neapolitanum).[25-28] For example, ethanol extract from Allium saralicum can neutralize ROS in a dose-depending manner.[29] The antioxidant potential of Allium species is mostly associated with high amounts of polyphenols and flavonoids, found in these species, which are natural antioxidants.[30] The flavonoids extracted from Allium cepa have exhibited antioxidant activity.[31] The ethanol extract of A. ursinum leaves showed antioxidant activity of 77% with an EC50 value of 322 g/mL in the DPPH assay. The activity was influenced by the presence of phenolic compounds in extract.[32]

Flavonoids extracted from onion can protect against oxidative damage, and also can protect against LDL oxidation and lipid peroxidation.[33] Many proatherogenic factors, such as ox-LDL, ROS, and Ang II, induce endothelial cell apoptosis, while protective factors, such as antioxidants, which can reduce the effect of oxLDL, inhibit endothelial cell apoptosis. Therefore, endothelial cell apoptosis is closely related to the initiation of atherosclerosis and can be used as a target for the prevention and treatment of atherosclerosis.[34]

The samples did not decrease the expression of pro-inflammatory cytokines. Only the A. saxatile F3 fraction slightly decreased the expression of IL-1, but this result was not significant (Fig.5).

In the present study, we report new data on Allium species and interesting information about their biological activities. The results of the present study provided a basis for further development and isolation of the individual compounds which are responsible for the biological activities of A. saxatile and A. ponticum and increased the knowledge about these species as potential sources of medicinal agents.

AUTHOR AFFILIATION

1 Department of Pharmacognosy, Direction of Pharmacognosy and Pharmaceutical Botany, Faculty of Pharmacy, Tbilisi State Medical University, Tbilisi, Georgia;
2 Laboratory of Pharmacognosy, Department of Pharmacy, Centre Center for Interdisciplinary Research on Medicines-CIRM, University of Liège, Liège, Belgium;
3 Institute of Botany, Ilia State University, Tbilisi, Georgia;
4 INSERM U-1048, I2MC, Université Paul Sabatier, Toulouse, France;
*Corresponding author. E-mail: l.mskhiladze@tsmu.edu.

ACNOWLEDGMENTS

The authors wish to thank to Pauline Desdemoustier for technical help. This research was supported by ERASMUS+ scholarship program and “Campus France” scholarship for doctoral mobility.

REFERENCES

1. Allium L. in GBIF Secretariat (2021). GBIF Backbone Taxonomy. Checklist Dataset Https://Doi.Org/10.15468/39omei Accessed via GBIF.Org on 2022-06-01.
2. Gagnidze R. Vascular Plants of Georgia a Nomenclatural Checklist. Institute of Botany.; 2005.
3. Rahman K. Historical Perspective on Garlic and Cardiovascular Disease. J Nutr. 2001;131(3):977S-979S. doi:10.1093/jn/131.3.977S
4. Teshika JD, Zakariyyah AM, Zaynab T, et al. Traditional and modern uses of onion bulb (Allium cepa L.): a systematic review. Crit Rev Food Sci Nutr. 2019;59(sup1):S39-S70. doi:10.1080/10408398.2018.1499074
5. Uzun M, Kaya A. Ethnobotanical research of medicinal plants in Mihalgazi (Eskişehir, Turkey). Pharm Biol. 2016;54(12):2922-2932. doi:10.1080/13880209.2016.1194863
6. Ekşi G, Gençler Özkan AM, Koyuncu M. Garlic and onions: An eastern tale. J Ethnopharmacol. 2020;253:112675. doi:10.1016/j.jep.2020.112675
7. Panaskerteli-Tsitsishvili Z. Karabadini. Sabchota Sakartvelo; 1978.
8. Bagrationi D. Iadigar Daudi. Edition of Tbilisi University.; 1993.
9. Rezaee F, Zolfaghari B, Dinani M. Isolation of dioscin-related steroidal saponin from the bulbs of Allium paradoxum L. with leishmanicidal activity. Res Pharm Sci. 2018;13(5):469. doi:10.4103/1735-5362.236875
10. Mskhiladze L, Chincharadze D, Tits M, et al. IDENTIFICATION OF CYTOTOXIC AND ANTIOXIDANT COMPOUNDS FROM ALLIUM GRAMINEUM FLOWERS. Int J Pharm Sci Drug Res. 2015;7(1). Accessed October 14, 2021. https://ijpsdr.com/index.php/ijpsdr/article/view/382

ISSN (Online): 2720-8796 ISSN (Print): 2720-7994

11. Zhou Y, Li C, Feng B, Chen B, Jin L, Shen Y. UPLC-ESI-MS/MS based identification and antioxidant, antibacterial, cytotoxic activities of aqueous extracts from storey onion (Allium cepa L. var. proliferum Regel). Food Res Int. 2020;130:108969. doi:10.1016/j.foodres.2019.108969
12. Mskhiladze L, Legault J, Lavoie S, et al. Cytotoxic Steroidal Saponins from the Flowers of Allium leucanthum. Molecules. 2008;13(12):2925-2934. doi:10.3390/molecules13122925
13. Rezgui A, Mitaine-Offer AC, Paululat T, Delemasure S, Dutartre P, Lacaille-Dubois MA. Cytotoxic steroidal glycosides from Allium flavum. Fitoterapia. 2014;93:121-125. doi:10.1016/j.fitote.2013.12.018
14. Li CJ, Yuan L, Ji TF, Yang JB, Wang AG, Su YL. Furostanol saponins from the seeds of Allium cepa L. Fitoterapia. 2014;99:56-63. doi:10.1016/j.fitote.2014.08.022
15. Jeong YJ, Choi YJ, Kwon HM, et al. Differential inhibition of oxidized LDL-induced apoptosis in human endothelial cells treated with different flavonoids. Br J Nutr. 2005;93(5):581-591. doi:10.1079/bjn20041397
16. Kurnia D, Ajiati D, Heliawati L, Sumiarsa D. Antioxidant Properties and Structure-Antioxidant Activity Relationship of Allium Species Leaves. Mol Basel Switz. 2021;26(23):7175. doi:10.3390/molecules26237175
17. Augé N, Pieraggi MT, Thiers JC, Nègre-Salvayre A, Salvayre R. Proliferative and cytotoxic effects of mildly oxidized low-density lipoproteins on vascular smooth-muscle cells. Biochem J. 1995;309(3):1015-1020. doi:10.1042/bj3091015
18. Kowa TK, Tchokouaha LRY, Nyemb JN, et al. Antipromastigote and cytotoxic activities of some chemical constituents of Hypericum lanceolatum Lam. (Guttifereae). J Appl Pharm Sci. 2020;10,(1):026-032. doi:10.7324/JAPS.2020.101004
19. Seo CS, Kim OS, Kim Y, Shin HK. Simultaneous quantification and inhibitory effect on LDL oxidation of the traditional Korean medicine, Leejung-tang. BMC Complement Altern Med. 2014;14(1):3. doi:10.1186/1472-6882-14-3
20. Maurent K, Vanucci-Bacqué C, Baltas M, Nègre-Salvayre A, Augé N, Bedos-Belval F. Synthesis and biological evaluation of diarylheptanoids as potential antioxidant and anti-inflammatory agents. Eur J Med Chem. 2018;144:289-299. doi:10.1016/j.ejmech.2017.12.033
21. Salvayre R, Auge N, Benoist H, Negre-Salvayre A. Oxidized low-density lipoprotein-induced apoptosis. Biochim Biophys Acta BBA - Mol Cell Biol Lipids. 2002;1585(2-3):213-221. doi:10.1016/S1388-1981(02)00343-8
22. Wang Y, Yi X, Xiang L, Huang Y, Wang Z, He X. Furostanol saponins from Chinese onion induce G2/M cell-cycle arrest and apoptosis through mitochondria-mediate pathway in HepG2 cells. Steroids. 2019;148:11-18. doi:10.1016/j.steroids.2019.04.003
23. Kim YS, Suh WS, Park KJ, Choi SU, Lee KR. Allimacrosides A–E, new steroidal glycosides from Allium macrostemon Bunge. Steroids. 2017;118:41-46. doi:10.1016/j.steroids.2016.12.002
24. Malekmohammad K, Sewell RDE, Rafieian-Kopaei M. Antioxidants and Atherosclerosis: Mechanistic Aspects. Biomolecules. 2019;9(8):301. doi:10.3390/biom9080301
25. Nencini C, Menchiari A, Franchi GG, Micheli L. In vitro Antioxidant Activity of Aged Extracts of some Italian Allium Species. Plant Foods Hum Nutr. 2011;66(1):11-16. doi:10.1007/s11130-010-0204-2
26. Gois Ruivo da Silva M, Skrt M, Komes D, Poklar Ulrih N, Pogačnik L. Enhanced Yield of Bioactivities from Onion (Allium cepa L.) Skin and Their Antioxidant and Anti-α-Amylase Activities. Int J Mol Sci. 2020;21(8):2909. doi:10.3390/ijms21082909
27. Capasso A. Antioxidant Action and Therapeutic Efficacy of Allium sativum L. Molecules. 2013;18(1):690-700. doi:10.3390/molecules18010690
28. Štajner D, Popovic BM, Čanadanović-Brunet J, Igić RS. Antioxidant and free-radical scavenging activities of Allium roseum and Allium subhirsutum. Phytother Res. 2008;22(11):1469-1471. doi:10.1002/ptr.2495
29. Jalalvand AR, Zhaleh M, Goorani S, et al. Chemical characterization and antioxidant, cytotoxic, antibacterial, and antifungal properties of ethanolic extract of Allium Saralicum R.M. Fritsch leaves rich in linolenic acid, methyl ester. J Photochem Photobiol B. 2019;192:103-112. doi:10.1016/j.jphotobiol.2019.01.017
30. Xu DP, Li Y, Meng X, et al. Natural Antioxidants in Foods and Medicinal Plants: Extraction, Assessment and Resources. Int J Mol Sci. 2017;18(1):96. doi:10.3390/ijms18010096
31. Li Q, Wang Y, Mai Y, et al. Health Benefits of the Flavonoids from Onion: Constituents and Their Pronounced Antioxidant and Anti-neuroinflammatory Capacities. J Agric Food Chem. 2020;68(3):799-807. doi:10.1021/acs.jafc.9b07418
32. Bârlă GF, Seriţan MP, Sănduleac (tudosi) E, Ciornei (ştefăroi) SE. Antioxidant Activity and Total Phenolic Content in Allium Ursinum And Ranunculus Ficaria. Food Environ Saf J. 2016;13(4). Accessed January16,2022. http://fens.usv.ro/index.php/FENS/article/view/123
33. Jaiswal N, Rizvi SI. Onion extract (Allium cepa L.), quercetin and catechin up-regulate paraoxonase 1 activity with concomitant protection against low-density lipoprotein oxidation in male Wistar rats subjected to oxidative stress: Up-regulation of PON1 activity and protection of LDL oxidation by onion extract and flavonoids. J Sci Food Agric. 2014;94(13):2752-2757. doi:10.1002/jsfa.6620
34. Duan H, Zhang Q, Liu J, et al. Suppression of apoptosis in vascular endothelial cell, the promising way for natural medicines to treat atherosclerosis. Pharmacol Res. 2021;168:105599. doi:10.1016/j.phrs.2021.105599

The Georgian Biomedical News
ISSN (Online): 2720-8796 ISSN (Print): 2720-7994