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Adiantumpedatum as anticancer, anti-oxidant and antiinflammatory agent

*Abd EL-Aziz Diab ,**Samih Al-Dahmi,*Mansour Zahra,*Basant Hendawi *ZagazigUniersity ,Faculty of Science ,Zoology Department ** Zagazig University ,Faculty of Pharmacy, Pharmacology Department

ABSTRACT: Natural products are potential sources for the development of effective and safe anticancer substances. The emergence of therapeutic agents derived from natural products has reignited global interest and encouraged scientists to reconsider medicinal plant research as a viable scientific option for diseases treatment. The potential of natural compounds such as flavonoids, polyphenols, or terpenoids for cancer prevention has been widely investigated. Experimental evidences confirmed that Genus Adiantum (Pteridaceae) that is known as maidenhair ferns have been used medicinally in different parts of the world. They exhibit antidysenteric, antimicrobial, antitumor, antiviral and anti-inflammatory activities. Among these ferns, Adiantumpedatum was found to have antioxidant and anti-microbial activity.

KEYWORDS: Adiantum pedatum, anticancer, anti-oxidant and anti-inflammatory

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INTRODUCTION

Using medicinal plant extracts is potent for restoring healthy state in a number of diseases (**Bianchiet al., 2009**).Genus Adiantum (Pteridaceae) forms a significant dominant component of many plant communities especially in the tropical and temperate regions. These are commonly known as maidenhair ferns(**Chandrappa et al., 2011**). These ferns are one of the world's oldest and most basic vascular plant groupings, including leaves (called fronds), roots, and upright stems. They do not possess flowers or seeds, but instead reproduce by spores (**Ishaq et al., 2014**).Many of them have been used medicinally in different parts of the world. They exhibit antidysenteric, antiulcer, antimicrobial, antitumor and antiviral activities (**Rastogi et al., 2018**).More than 130 triterpenoids, flavanoids, phenyl propanoids, phenolics, coumarins, phytosterols, fatty acids, and other chemicals were discovered, including steroids, salicylic acids, lipids, and long-chain compounds (**Pan et al., 2011**).The genus Adiantum pedatum belongs to the Pteridaceae family, along with over 200 other species (**Chandrappa et al., 2011**).

Botanical classification of Adiantum pedatum: Division: Pteridophyta Class: Polypodiopsid Subfamily: Vittarioideae Genus:Adiantum Species: Adiantumpedatum This classification is according to (Rothfels and Schuettpelz, 2014and Irfan et al., 2021).

II. MATERIALS AND METHODS

Chemical composition of Adiantum pedatum:

Arachidonic acid (ARA) was found in several ferns, including *Adiantum pedatum* (Gellermanand Schlenk, 1964), it can be supplied from diet or from plant-rich essential fatty acid, linoleic acid, which may be generated

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in plants from oleic acid (Abediand Sahari, 2014). It is an important polyunsaturated fatty acid present as an essential constituent of cell membrane conferring it with fluidity and flexibility (Wang et al., 2019). Reports

from decades ago suggested that polyunsaturated fatty acids (PUFA), particularly free unesterified ARA, had tumoricidal potential in vitro and in vivo (Siegel et al., 1987).Undurti Das and colleagues, who proposed ARA as a possible anti-cancer therapy, provided the most important and consistent research showing the tumoricidal impact of PUFA, specifically ARA (Das, 1990), Thus, ARA has been shown to preferentially kill tumor cells in vitro (Das, 1991).

The presence of twelve different triterpenoids extracted from the dried leaves of this fern (Shiojima et al., 1993).Triterpenoids are naturally occurring and physiologically active chemicals derived from a variety of plants have anti-inflammatory, anticancer, and anti-oxidant activities. Triterpenoids such as ursolic acid (UA) and oleanolic acid (OA) are inhibitors of leukemia cell proliferation and inducers of apoptosis (Cipak et al., 2006).

Cardiac glycosides (Flavonols) (Lea et al., 2010), terpenoids, steroids, and phenols were abundant in A. pedatum. Various plant researches have revealed that cardiac glycosides have antioxidant and antibacterial effects (Chandrappaet al., 2011). Steroids have antioxidant properties as well (Savage et al., 2002). There are four organic solvent extracts of *Adiantum pedatum* present (acetone, ethyl acetate, ethanol, and hexane). The acetone and ethyl acetate extracts shows substantial antibacterial activity. The antibacterial activity of A. pedatum acetone extract is substantially greater than that of ethyl acetate. The ethyl acetate extracts of A. pedatum demonstrated stronger antioxidant activity than the acetone, ethyl alcohol, and hexane extracts; the extracts had proton donating capacity and may operate as free radical inhibitors or scavengers, perhaps serving as main antioxidants (Chandrappa et al., 2011).

Gas chromatography-mass spectroscopy (GC-MS) is a combined analytical technique used to determine and identify compounds present in a plant sample. GC-MS plays an essential role in the phytochemical analysis and chemotaxonomic studies of medicinal plants containing biologically active components (**Olivia et al.**, **2021**)such as flavonoids, tannins, saponins, alkaloids, and terpenoids which have several biological properties including antioxidant, anti-inflammatory, anti-diarrhea, anti-ulcer, and anticancer activities, among others(**Starlin et al.**, **2019**).

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Bioactive compounds	RT	Area%	MF	MW	Formula	Activity	Reference
à-D-GLUCOPYRANOSIDE, METHYL	21.36	1.68	739	331	C13H26BNO6Si	Anticancer	(Islam et al.,
						Antioxidant	2022) (Abdullah at
							(Abdullall et al., 2022)
5,8,11,14-Eicosatetraynoic acid,TMS derivative	21.36	9.68	707	368	C23H32O2Si	Anticancer	(Shahin <i>et al.</i> ,
							2022)
Dasycarpidan-1-methanol, acetate	21.36	12.68	713	326	C20H26N2O2	Anticancer	(Nasr <i>et al.</i> , 2023)
Traumatic acid, (E)-, 2TMS derivative	22.74	0.69	710	372	C18H36O4Si2	Anticancer	(Jabłońska-
						Antioxidant	Trypuć <i>et al.</i> , 2020)
Panaxydol, TMS	22.6	11.25	694	332	C20H32O2Si	Anticancer	(Kim <i>et al.</i> , 2016)
2-Oleoylglycerol, 2TMS derivative	22.88	0.36	731	500	C27H56O4Si2	Antioxidant	(Masek <i>et al.</i> , 2020)
MANNOFURANOSIDE, METHYL	23.31	8.56	772	482	C19H46O6Si4	Anticancer	(Al-Abdallah et
2,3,5,6-TETRAKIS-O-(TRIMETHY LSILYL)-,						Antimicrobial	al., 2022)
à-D- Uridina 2TMS darivativa	22.21	7.56	717	460	C19H26N2O6S;2	Antioxidant	(Khwaza at al
ondine, 5 nws derivative	23.31	7.50	/1/	400	C18H30N2O0313	Anticancer	(Kiiwaza et al., 2020)
á-D-GALACTOPYRANOSIDE, METHYL	23.07	15.38	734	362	C14H31BO6Si2	Anticancer	(Lyantagaye, 2013)
Methyl à-D-glucofuranoside, 4TMS derivative	24.43	2.5	836	482	C19H46O6Si4	Anticancer	(Abotaleb <i>et al.</i> , 2019)
D-(-)-Tagatofuranose,pentakis(trimethylsilyl) ether (isomer1)	24.77	8.77	765	540	C21H52O6Si5	Antioxidant	(Fatani <i>et al.</i> , 2022)
D-(-)-Fructofuranose, pentakis(trimethylsilyl)	24.82	8.91	782	540	C21H52O6Si5	Antioxidant	(Ragab et al.,
ether (isomer2)						Anti-	2021)
D-Psicofuranose, pentakis(trimethylsilyl) ether	24.82	10.91	777	540	C21H52O6Si5	Antioxidant	(Ragab <i>et al.</i> ,
(isomer1)						anticancer	2021)
1,5-Anhydrohexitol, 4TMS derivative	25.44	9.97	797	452	C18H44O5Si4	Antioxidant	(Spanou <i>et al.</i> , 2007)
á-DL-ARABINOPYRANOSE, 1,2,3,4-	25.44	8.97	807	438	C17H42O5Si4	Antioxidant	(Chen et al.,
TETRAKIS-O-(TRIMETHY LSILYL)-	26.2	()	729	100	C1911420(S:4	anticancer	2015)
(TRIMETHY LSILYL)- LACTONE	20.2	0.2	128	400	C18H4206S14	anticancer	(Youssel et al., 2023)
Dulcitol, 6TMS derivative	27.72	6.27	759	614	C24H62O6Si6	Anti-	(Suresh <i>et al.</i> ,
						inflammatory	2011)
	07.50	6.05	752	61.5	C2411(22.55) 5	Anticancer	
D-Sorbitol, 61MS derivative	27.72	6.27	752	614	C24H62O6S16	Antioxidant	(El Far and Taie, 2009)
BUTANAL, 2,3,4-	27.72	6.27	870	336	C13H32O4Si3	Antioxidant	(Bekhouche et
TRIS[(TRIMETHYLSILYL)O XY]-, (R*,R*)-	27.72	6.27	750	526	C21115405515	Antionidant	al., 2018)
L-FUCITOI, 5 I MIS DERIVATIVE	21.12	0.27	152	526	C21H3405815	anticancer	(r'ai <i>et al., 2022)</i>

GC-MS ANALYSIS OF ADIANTUM PEDATUM ETHANOLIC EXTRACT:

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III.RESULTS

Oxidative stress and chronic inflammation in human carcinogenesis:

Tissue homeostasis is an equilibrium that involves cell proliferation and cell death, and any disruption in this balance has been associated to a variety of cancers (**Shin et al., 2019**). Cancer is thought to be a "disease of mutations" in the cell genome that disrupts the balance between cell division (proliferation) and resting or quiescence in favor of cell proliferation (**Hassanpour and Dehghani, 2017**).

One of the most significant characteristics of cancers is their capacity to avoid programmed cell death, often known as apoptosis (Hanahanand Weinberg, 2011). So, cancer cells continue to divide abnormally in an active state because they lack control over the homeostatic process of the cells. As a result, they produce oncogenic proteins that duplicate normal growth signals. Oncogenic proteins causes malignant cells to become independent of growth signals (gain autonomy), resulting in uncontrolled proliferation (Sever and Brugge, 2015).

Reactive oxygen species (ROS) that present as a result of oxidative stress can cause damage to proteins and nucleic acids, impairing their functions. Oxygen participates in numerous biochemical processes that generate harmful reactive intermediates that have the potential to damage DNA. Oxidative DNA damage leads to replication errors that can lead to mutations and chromosomal aberrations (**Cho et al., 2022**) and mutations are known to cause cancer (**Gupta et al., 2014**).

In recent years, evidence has been obtained that cellular oxidative stress play critical roles in the pathophysiology of inflammation (**Nathan and Cunningham-Bussel, 2013**). As the bimolecular damage caused by oxidative stress is greater than the body's ability to repair it, it may trigger cellular death and extracellular matrix breakdown. The leakage of normal intracellular enzymes into extracellular fluids from necrotic cells functions as "alarmins" inducing inflammatory cascades by activating innate immune defense mechanisms caused chemo taxis of neutrophils and other inflammatory cells to the site of damage (**Federico et al., 2007**, Chan **et al., 2012 and Lugrin et al., 2014**).

Medicinal uses of Adiantum pedatum:

As antioxidant: The inhibition of oxidative stress by natural antioxidant molecules has sparked the interest of researchers as a promising strategy to colorectal cancer prevention. Phenolic components have been shown to have antioxidant action as well as the ability to interfere with numerous carcinogenic signaling pathways (**Ramos et al., 2021**). Phenols were abundant in A. pedatum(**Chandrappaet al., 2011**).

As anti-inflammatory agent: Triterpenoids are found in *Adiantumpedatum*. Several triterpenoids have anticancer and anti-inflammatory activities. Triterpenoids are multifunctional chemicals with anticancer activity determined by their capacity to suppress nuclear factor-B activation, cause apoptosis, and inhibit signal transducers (**Petronelli et al., 2009**).

As anticancer: For the treatment of cancer, there are several specific procedures and medicinal compositions including plant extracts. It is presented a way of treating cancer by targeting two cellular proteases, metalloproteinase-9 (MMP-9) and cathepsin B (CB). A composition including one or more plant extracts is capable of suppressing one or more of neoplastic cell migration, endothelial cell migration, tumor development, tumor metastasis, and tumor-induced angiogenesis by inhibiting the activities of MMP-9 and CB at the same time (**Cyr**, 2009). Cellular proteases play a significant role in extracellular matrix (ECM) degradation, which contributes to tumor migration and metastasis (**Danø et al., 2005**). Targeting molecules implicated in metastasis, such as (MMP-9) and (CB) might be an effective cancer therapy (**Nalla et al., 2010**). The extraction from *Adiantum pedatum* plant is capable of Inhibiting MMP-9 (**Cyr, 2009**).

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