

Iris Species

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Contributor: Cecilia Faraloni

The genus *Iris* from the Iridaceae family consists of more than 262 recognized species. It is an ornamental and medicinal plant widely distributed in the Northern Hemisphere. *Iris* species convey a long history as valuable traditional drugs with a wide variety of applications in various cultures, having been recorded since medieval times.

genus Iris

ethnobotanical uses

phytochemistry

1. Introduction

For millennia, medicinal plants have long been recognized as a valuable wellspring of natural agents with high curative properties; they currently continue to be a precious resource for seeking new drug leads [1]. The dissemination of synthetic drugs has raised serious concerns regarding their quality, efficacy and safety [2]. In contrast, natural products are environmentally and biologically friendly since they are easily recognized by body cells, permitting their metabolism to be performed [3]. As a result, medicinal and aromatic plants that have historically been used by traditional practitioners (fortunetellers, midwives, herbalists) are gradually being exposed to scientific research to separate their active ingredients in order to use them in modern dispensing forms [4].

One such plant species is the *Iris* species (spp.) (**Figure 1**) (with 389 accepted species in the world according to (<http://www.theplantlist.org/tpl1.1/search?q=Iris>; accessed on 25 August 2021), a popular plant commonly used in landscaping due to its wide showy and colored flowers [5]. The plant draws its name from the Greek goddess of rainbows, referring to the wide range of bloom colors featured in *Iris* species [6]. The use of *Iris* species can be traced back to medieval painters and manuscript illuminators, by whom the plant's flowers were used to obtain "*Iris* green" and "*Iris* blue" pigments [7]. Likewise, the rhizomes of the plant were blended with other herbs, such as hyssop (*Hyssopus officinalis*), and used to treat skin conditions, whereas, during the nineteenth century, they were utilized to disguise tobacco smell and reduce bad-breath odors [8].



Figure 1. A collection of

pictures of various *Iris* spp. taken at “*Iris Garden*”, Florence, Italy. ©2022.

Currently, *Iris* species are still finding application in numerous sectors, including cosmetics, pharmaceuticals and the food industry. In Morocco, the rhizomes of *Iris* species, commonly known as Orris roots, are used as one of the many ingredients in *Ras el hanout*, a Moroccan spice blend [8]. Similarly, *I. germanica* L. rhizomes are peeled and used as a flavoring in ice cream, confectionery, baked products and alcoholic beverages [7][9]. In Southern Europe, *Iris* species are still grown for commercial purposes and are used in tooth powder, toothpaste and teething rings [10], while in the cosmetic field, some *Iris* spp., such as *I. florentina* L. and *I. germanica* L., are currently used in the manufacturing of high-priced luxury perfumes and lotions such as “*Iris Ganach*”©, Guerlain; “*Extravagance d’Amarige*”©, Givenchy; “*Chanel 19*”©; and “*So pretty*”©, Cartier [10][11][12][13].

Recently, phytochemical investigations of *Iris* species have resulted in the identification of various bioactive compounds belonging to different classes, including alkaloids [11], flavonoids and their derivatives [12][13][14], quinones, terpenes, steroids and simple phenolics [15]. Modern pharmacological studies have reported that these compounds exhibit significant effects on human health, such as cancer chemopreventive properties [16] and anticancer [17], antioxidant [18], antiplasmoidal [19], immunomodulatory and anti-inflammatory activities [20].

2. Botany (Taxonomy, Geographic Distribution and Edaphic Conditions)

The genus *Iris* (Table 1) is a well-reputed rhizomatous plant belonging to the Iridaceae, a family of herbaceous, perennial and bulbous plants [5]. This plant comprises over 260 species widely distributed in temperate regions across the Northern Hemisphere, occurring particularly across North America and Eurasia, with approximately four

species in northern Africa [21][22]. Although numerous *Iris* species have been found to be growing in mesic or wetland environments, the majority of *Iris* species thrives in montane, desert, semi-desert, or dry and rocky habitats [22]. Therefore, *Iris* species can withstand a wide variety of harsh environments, from cold areas where the hard grounds freeze to subtropical climates [10]. In terms of edaphic conditions, several *Iris* spp., such as *I. aucheri* (Baker) Sealy and *I. persica* L., prefer relatively acid soil, whilst the majority grows in slightly acid–alkaline soil, such as *I. danfordiae* (Baker) Boiss [5][10]. Some other species favor sunny borders with well-drained soil and full shade, whereas others thrive in dappled shade [10].

Table 1. Taxonomy of the genus *Iris* [23].

Taxonomic Hierarchy	Classification
Kingdom	Plantae
Subkingdom	Viridiplantae
Infrakingdom	Streptophyta
Superdivision	Embryophyta
Division	Tracheophyta
Subdivision	Spermatophytina
Class	Magnoliopsida
Superorder	Lilianae
Order	Asparagales
Family	Iridaceae
Genus	<i>Iris</i> L.— <i>Iris</i>

The genus *Iris* is identified by the basal fan of unifacial leaves, colorful perianth of three horizontal sepals and three upright petals that are basally fused into the tube and style branches that are fused at the base [24]. They are petaloid and distally expand beyond the tiny flap-like, transverse stigma as a bifid crest; they also have three stamens that are opposite to the sepals and are petaloid in style [22][24].

3. Pharmacological Properties of *Iris* spp.

3.1. Antioxidant Activity

Antioxidants are stable molecules that scavenge free radicals and maintain a lowered redox state inside cells to prevent or postpone cell damage [25]. The imbalance between free radicals and antioxidants leads to oxidative-stress-related diseases, such as diabetes, cancers, atherosclerosis, and inflammatory and neurodegenerative

diseases [26]. Recently, several synthetic antioxidants, such as butylated hydroxytoluene and butylated hydroxyanisole, were discovered to be harmful to human health [26]. As such, the quest for effective, non-toxic, natural substances with potent antioxidative effects has recently intensified.

Studies have shown that there is a substantial relationship between chemical composition and antioxidant activity. In particular, the contents of polyphenols, flavonoids and saponins are responsible for the antioxidant properties. Polyphenolic compounds act as antiradical activity, reducing agents, and complexes of pro-oxidant metals and quenchers of singlet oxygen, promoting the natural antioxidative defense mechanisms and protecting enzyme activity [27]. The genus *Iris* has been proven to contain substantial amounts of phenolic compounds, particularly flavonoids and their derivatives. Therefore, various extracts of this plant have been evaluated for their antioxidant potency.

Mahdinezhad et al. [28] investigated the in vivo protective effects of *I. germanica* L. hydroalcoholic extract at doses of 100 and 200 mg/kg on the liver and pancreas of a streptozotocin-induced diabetic rat model for 4 weeks. Accordingly, the repeated oral administration of the extract lowered the high level of aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP) compared with diabetic control rats. The extract also improved the liver antioxidant capacity (increase in thiol groups). The protective effect was ascribed to the significant amounts of flavonoids and anthocyanins in the hydroalcoholic extract. The authors supported the use of the plant as a natural antioxidant source to preserve the human body from free-radical-related disorders, especially diabetes mellitus and hepatic injury [28].

The in vitro antioxidant activity of *Iris* has been shown to be significantly correlated with the total content of phenolic compounds. The antioxidant activity of petroleum ether, chloroform and methanol crude extracts of fresh *I. suaveolens* Boiss & Reut rhizomes was tested using the β -carotene-linoleic acid and CUPRAC techniques; quercetin and butylated hydroxytoluene (BHT) served as positive controls [29]. The results disclosed that both petroleum ether and chloroform extracts exhibited pronounced antioxidant potency. Thirteen phenolic and flavonoid compounds were isolated from the petroleum ether and chloroform extracts and were screened in vitro for their antioxidant effects. Coniferaldehyde, a phenolic compound obtained from the chloroform extract, displayed the greatest activity among all the investigated compounds at 25 and 50 mg/mL in both β -carotene-bleaching and CUPRAC systems [29].

Moreover, the aqueous and ethanol extracts of *I. germanica* L. were evaluated for their in vitro antioxidant activity using several testing systems, namely, free radical scavenging, reducing power, superoxide anion radical scavenging, metal chelating activities and hydrogen peroxide scavenging [30]. The results indicated that at concentrations of 15, 30 and 50 μ g/mL both aqueous and ethanol fractions exhibited excellent antioxidant properties, displaying 95.9, 88.4 and 79.9% and 90.5, 78.0 and 65.3% inhibition of peroxidation of linoleic acid emulsion, respectively. At concentrations of 20, 40 and 60 μ g/mL, both extracts showed remarkable reducing power, free radical scavenging, hydrogen peroxide scavenging, metal chelating and superoxide anion radical scavenging activities [30].

Similarly, the antioxidant activity of the ethanolic extracts *I. germanica* L. areal parts and rhizomes was assessed using free radical DPPH scavenging and β -carotene–linoleic acid assays [31]. The results showed that, in the DPPH system, the aerial part and rhizome extracts exhibited significant IC_{50} values of 5.38 and 12.3 mg/mL, respectively, while at the concentration of 3.15 mg/mL, the total antioxidant activity of the extracts was 98.7% and 97.4%, respectively [31].

In a recent study, the antioxidant activity of the petroleum ether, ethyl acetate and methanol extracts of *I. ensata* leaves was analyzed using various antioxidant assays such as the DPPH radical scavenging assay and FRAP (ferric ion reducing assay) [32]. Accordingly, all the extracts exhibited pronounced antioxidant potential. In addition, the research reported that the IC_{50} values decreased with the increase in polarity. In the ferric reducing assay, the IC_{50} values of the three extracts were found to be 226.66, 188.94 and 124.63 μ g/mL, respectively [32].

The genus *Iris* contains substantial amounts of glycosylated flavonoids and phenolic acids, which are, generally, water-soluble products and can be detected in great quantities in the bloodstream, thus exhibiting high oral bioavailability. Due to all these properties, polyphenols are involved in a wide range of biological effects, such as antibacterial, anti-inflammatory, antiallergic, hepatoprotective, antiviral, antithrombotic, anticarcinogenic, cardioprotective and vasodilatory effects.

3.2. Anticancer Activity

Recently, the use of anticancer drugs has been hampered by the emergence of several impediments, with these mostly being the cellular resistance to chemotherapy drugs and toxicities [33]. Therefore, the global trend is being shifted toward medicinal plants and plant-based compounds owing to their accessibility, affordability and effectiveness [33]. Several *Iris*-based compounds have been isolated from various extracts and tested in vitro (**Table 2**) for their cytotoxicity and chemopreventive activities (**Figure 2**).

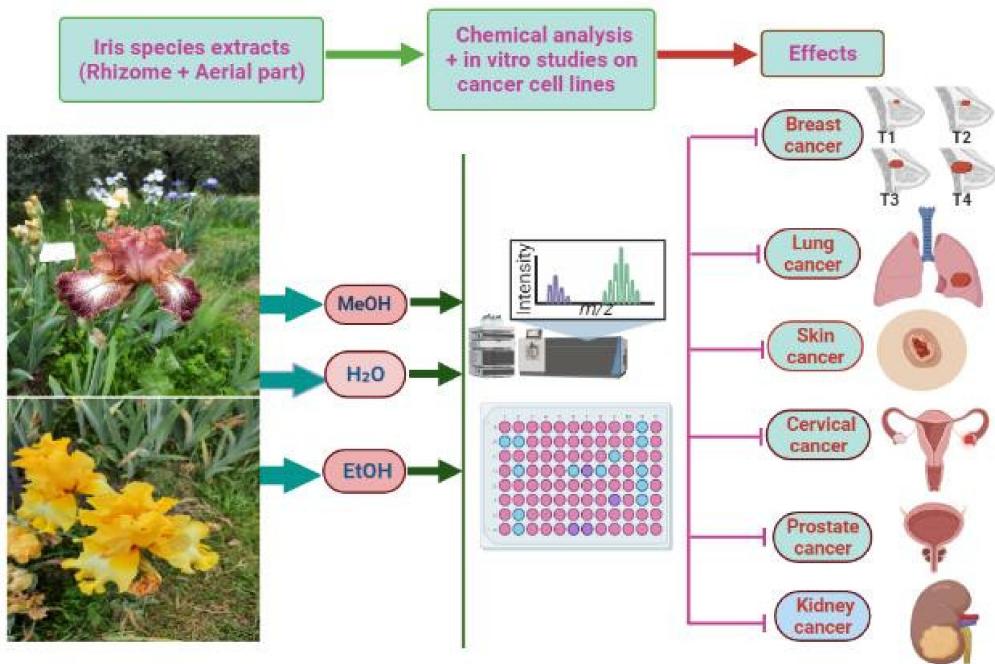


Figure 2. General approach

applying to assess the anticancer effect of *Iris* spp. in vitro.

Irilone, iriflogenin, genistein and iris kashmirianin are only a few of the flavonoids isolated from *I. germanica* L. that have been shown to exert chemopreventive benefits by reducing cytochrome P450 1A activity and enhancing NAD(P)H: quinone reductase (QR)activity [16].

Alam et al. [34] evaluated the cytotoxicity potential of glycosides and isoflavonoids newly isolated from the rhizomes of *I. kashmiriana* Baker against several cancer cell lines, namely, MCF-7 and MDA-MB-231 (breast cancer), HeLa (cervical cancer), PC-3 (prostate cancer) and A-549 (lung cancer), using the MTT cellular viability assay. Accordingly, the compounds 5,7,8-trihydroxy-3-(4-methoxyphenyl)-4H-chromen-4-one, 5,7,8-trihydroxy-3-(4-hydroxyphenyl)-4H-chromen-4-one, 5,7,8-triacetoxyoxy-3-(4-methoxyphenyl)-4H-chromen-4-one and 6,7-diacetoxyoxy-3-(4-methoxyphenyl)-4H-chromen-4-one showed prominent anticancer activity against all cell lines, with IC₅₀ values ranging from 3.8 to 5.6 mg/mL. These compounds were also found to induce cell-cycle block at the G2/M phase [34].

Similarly, Tantry et al. [35] studied the in vitro cytotoxicity activity of a new alkylated 1,4-benzoquinone derivative obtained from the chloroform extract of *I. nepalensis* rhizomes against various cancer cell lines using the MTT colorimetric assay. The compound revealed remarkable cytotoxicity against HCT116 (colon carcinoma), HL-60 (blood cancer) and ZR-75 (breast cancer), with IC₅₀ values of 10 ± 1.1002, 34 ± 1.1205 and 31 ± 1.1001, respectively. Likewise, the cytotoxicity potential of two flavonoids, 7-O-methylaromadendrin and tectorigenin, as well as four iridal-type triterpenes, iritectols A and B, isoiritidogermanal and iridobelamal A, isolated from the rhizomes of *I. tectorum* Maxim were assessed against four cancer cell lines using the SRB method (sulphorhodamine B) [36]. The results indicated that iritectorol B, isoiritidogermanal and iridobelamal A displayed identical cytotoxicity against both MCF-7 and C32 cell lines, with IC₅₀ values for a range of 11 µM and 23 µM. Moreover, they found that iritectorol B exhibited a dose-dependent apoptotic effect against COR-L23, while both 7-O-

methylaromadendrin and tectorigenin flavonoids were discovered to be capable of triggering cell-cycle arrest at the S and G2/M phases, respectively (**Table 2**). In vivo experiments based on animal models and molecular targets involved in the anticancer effects studies are mandatory to confirm the anticancer potential of *Iris* spp.

Table 2. In vitro anticancer and cytotoxic activities of *Iris* spp. extracts against various cell lines.

Species	Parts	Extract	Cancer Type	Cell Line	Method	IC50	Results	References
<i>I.nertschinskia</i> Lodd.	Rhizomes	EtOH	Breast	MCF-7	TBE	-	Induced apoptosis; triggered cell cycle block at G1 phase; ↑ p53 phosphorylation in a dose-dependent fashion; ↑ Bax expression; induced caspase-7 cleavage.	[17]
<i>I.nertschinskia</i> Lodd.	Whole plant	EtOH	Breast	Hs578T MDA-MB-231	TBE	-	Triggered apoptosis hallmarked by cells accumulation in the sub-G 1 phase.	[37]
<i>I. pseudopumila</i> Tineo	Rhizomes	PET	Breast Skin	MCF-7 C32	SRB	96.79 µg/mL 57 ± 1.04 µg/mL	Induced potent cytotoxic effects against the three cell lines.	[38]
<i>I. variegata</i> L.	Rhizomes	H ₂ O	Skin Breast	IGR39 MDA-MB-231	MTT	0.53 mg/mL 0.33 mg/mL	Reduced significantly cell viability; the ethanolic extract was shown to be more efficient	[39]
<i>I. hungarica</i> Waldst. & Kit.		H ₂ O	Skin	IGR39		1.15 mg/mL		

Species	Parts	Extract	Cancer Type	Cell Line Method	IC50	Results	References	
<i>I. pseudopumila</i> Tineo	Rhizomes	70% EtOH	Breast	MDA-MB-231	0.57 mg/mL	against both cell lines.	[40]	
			Skin	IGR39	0.53 mg/mL			
		MeOH	Breast	MDA-MB-231	0.33 mg/mL			
			Lung	CORL-23	31.5 ± 2.6 µg/mL			
<i>I. Spuria</i> L.	Flowers	MeOH	Skin	C32	48.7 ± 2.6 µg/mL	Both extracts revealed strong antiproliferative effects towards both cell lines.	[40]	
			Lung	CORL-23	25.4 ± 2.6 µg/mL			
		MeOH	Skin	C32	50.9 ± 2.6 µg/mL			
			Lung	A549	123.04 µg/mL			
<i>I. kashmiriana</i> Baker	Rhizomes	MeOH	Colon	Caco-2	302.94 µg/mL	All extracts displayed a dose dependent inhibitory potential against both cell lines A549, and Caco-2.	[41]	
			Lung	A549	128.7 µg/mL			
		MeOH	Colon	Caco-2	237.76 µg/mL			
			Lung	A549	134.72 µg/mL			
<i>I. germanica</i> L.	Rhizomes	MeOH	Colon	Caco-2	230.82 µg/mL	All extracts displayed a dose dependent inhibitory potential against both cell lines A549, and Caco-2.	[41]	
			Lung	A549	149.80 µg/mL			
			Colon	Caco-2	368.88 µg/mL			
			Lung	A549	137.98 µg/mL			
<i>I. ensata</i> Thunb.		MeOH	Colon	Caco-2	358.81 µg/mL	The ethanol extract	[42]	
			Lung	A549	128.7 µg/mL			
<i>I. kashmiriana</i> Baker	Whole plant	MeOH	Lung	A549	MTT	128.7 µg/mL	The ethanol extract	[42]

Species	Parts	Extract	Cancer Type	Cell Line Method	IC50	Results	References
<i>I. hungarica</i>	Rhizomes	H_2O	Colon	Caco-2	237.76 μ g/mL	exhibited a dose-dependent selective antiproliferative effect on epithelial cancers.	amine B; say; Bax:
			Colon	HCT116	42.3 μ g/mL	Cell lines HCT116, HeLa, HL-60 were sensitive to the plant aqueous extract. The highest cytotoxicity was noticed against HL-60.	protective neurons prevented lying the Shp-2
			2 ² Cervical	HeLa	MTT	78.7 μ g/mL	[43]
<i>I. tenuifolia</i>	Leaves	H_2O	Leukemia	HL-60	3.6 μ g/mL		

Similarly, the *in vivo* neuroprotective potential of *I. tenuifolia* Pall ethanolic extract was evaluated for the first time in a middle cerebral artery occlusion model (MCAO) using C57BL/6J mice [45]. Accordingly, the applications of *I. tenuifolia* Pall ethanolic extract one hour before or immediately after the surgery outstandingly decreased the infarct size. However, treatment with the same extract less than one hour after surgery did not show any protective effect. The reduction in infarct volume is likely attributable to the richness of *I. tenuifolia* Pall in flavonoid compounds, which acted as protective agents in the MCAO model due to their significant antioxidant potential. The other factor that might be involved in the protective effect is the activation of both ERK1/2 stimulated by *I. tenuifolia* Pall flavonoids. The research likewise reported an increase in interleukin-6 concentration in blood plasma. However, the mechanism via which interleukin-6 exerted its protective effects was not determined.

In a similar approach, the *in vitro* neuroprotective activity of three iridals, namely, Spirioiridotectal A, Spirioiridotectal Band and Spirioiridotectal F, isolated from the ethanolic extract of the rhizomes of *I. tectorum* Maxim was evaluated at the concentration of 10 μ M against serum-deprivation-induced PC12 cell damage using the MTT method [46]. The results revealed that all the tested compounds exhibited moderate neuroprotective effects against serum-deprivation-induced PC12 cell damage. Despite some promising results in terms of neurological disease prevention, the neuroprotective activities of *Iris* species are still poorly investigated. *In vitro* and *in vivo* studies are still mandatory, especially against neurodegenerative diseases such as Alzheimer's disease.

3.4. Hepatoprotective Activity

The *in vivo* hepatoprotective activity of the methanolic extract of *I. spuria* rhizomes was evaluated against paracetamol-induced hepatotoxicity in Wistar rats at the two doses of 100 and 200 mg/kg [47]. The results revealed an increase in serum enzymes and bilirubin level as a sign of hepatic injury in intoxicated rats. Interestingly, the administration of paracetamol along with *I. spuria* L. methanolic extract was shown to exert a dose-dependent protective effect, bringing the levels of ALT, AST, ALP and total bilirubin to normal ranges as a consequence.

Furthermore, the research reported that the methanolic extract restored the serum levels of albumin and glutathione (GSH) and prevented both elevated triglyceride and lipid peroxidation [47].

Likewise, the in vitro hepatoprotective potential of three iridal metabolites, iridojaponal A, B and C, isolated from the ethanolic extract of *I. japonica* whole plant was assessed against *N*-acetyl-*p*-aminophenol (APAP)-induced toxicity in HepG2 cells [48]. Accordingly, iridojaponal A and B exhibited moderate hepatoprotective effects, with cell survival rates of 55.27 and 56.45%, respectively, while the positive control displayed a cell survival rate of 59.28%.

3.5. Anthelmintic Activity

Standard anthelmintic drugs are widely utilized against internal parasites and encompass several classes, such as benzimidazoles and avermectins. They are classified based on their chemical structure and mode of action [49]. Although synthetic anthelmintics have effectively been applied to control helminth infections, their usage has lately been hampered by nematode resistance; they may also affect the host itself and remain as residues in edible tissue [49]. These drawbacks have prompted researchers to look for alternate control strategies, such as using traditional medicinal herbs.

Data have shown that *I. hookeriana* Linn and *I. kashmiriana* Linn exhibit significant in vitro and in vivo anthelmintic activities. To corroborate the ethnoveterinary use of *I. kashmiriana* Linn, Khan et al. [50] evaluated the in vitro anthelmintic activity of *I. kashmiriana* Linn aqueous and methanolic extracts against *Haemonchus contortus* nematodes using the motility inhibition test. The positive control was the standard treatment Levamisole 0.5 mg/mL, while the negative control was 0.95% (PBS solution). The worms were exposed to 50, 25 and 12.5 mg/mL crude extracts and their motility was examined 0, 1, 2, 5 and 8 h post-exposure. After 6 h of treatment, the authors observed that the aqueous extract of *I. kashmiriana* inhibited worm motility by 85.0% at 50 mg/mL, whereas the methanolic extract exhibited better anthelmintic activity, displaying a mean worm-motility inhibition of 100.0%. The anthelmintic effect was attributed to the presence of alcohol-soluble and water-soluble active molecules in the extracts.

Using the same method, Tariq et al. [51] tested the crude aqueous extract and crude ethanolic extract of *I. hookeriana* Linn rhizomes against *Trichuris ovis* worms to validate the ethnoveterinary uses of *I. hookeriana* Linn. They proved that both extracts had significant anthelmintic activity and the highest worm-motility inhibition was exhibited by the ethanolic extract (84.6%) at 25 mg/mL.

Likewise, *I. kashmiriana* aqueous extract at 2 g/kg body weight exhibited a maximum (70.27%) egg-count reduction in sheep naturally infected with mixed gastrointestinal nematodes after 15 days of treatment [51]. In the same way, *I. hookeriana* ethanolic extract at 2 g/kg displayed a maximum (45.62%) egg-count reduction in sheep naturally infected with mixed gastrointestinal nematodes after 10 days of treatment. The authors of both studies supported the application of *I. hookeriana* and *I. kashmiriana* as natural veterinary agents to control sheep gastrointestinal nematode parasites [50][51].

3.6. Antibacterial Activity

The ethanol/water extracts (70/30, v/v) of *I. haphylla* L. rhizomes at the concentration of 1% were tested in vitro against standard Gram-positive and Gram-negative bacterium strains. The optimal activity was noticed against the Gram-positive strains, *Basillus subtilis* ATCC 6633 and *Staphylococcus aureus* ATCC 25923, with diameters of growth inhibition of 16.00 and 15.60 nm, respectively. Meanwhile, Gram-negative strains were relatively resistant to the plant extracts [52].

The ethyl acetate fractions derived from 70% of ethanolic extract of *I. unguicularis* Poir rhizomes at concentrations of 25, 50 and 100 μ g/mL were investigated for their antibacterial activity against two Gram-positive and five Gram-negative bacterium strains using the disk diffusion method [18]. The best antibacterial activity was observed against *S. aureus* (11–23 mm zone of inhibition) followed by *B. subtilis* (8–13 mm zone of inhibition). The lowest activity was noticed against *M. Morganii* [18]. The antibacterial activity of the methanolic extract of *I. pseudopumila* Tineo rhizomes was assessed against four Gram-negative and nine Gram-positive strains using the broth dilution method [53]. The extract exhibited prominent inhibition against all the bacterial strains with minimum inhibitory concentrations (MIC) ranging between 7.8 and 250 μ g/mL. It is worth mentioning that the Gram-negative strains, especially *E. coli* and *E. aerogenes*, were more sensitive to the *Iris* species extract.

3.7. Antifungal Activity

The in vitro antifungal activity of *I. unguicularis* Poir methanolic extract was tested against the *Aspergillus Niger* 2CA936, *Aspergillus flavus* NRRL3357 and *Candida albicans* ATCC1024 fungal strains [54]. The results revealed that the methanolic extract exhibited potent antifungal properties, mainly against *Aspergillus Niger* 2CA936. *I. unguicularis* Poir antifungal activity was attributed to the lipophilic properties of the phenolic compounds. The essential oils of *I. persica* L. extracted from flowers, leaves and rhizomes were evaluated against three human pathogenic fungal strains, *Candida albicans*, *Trichophyton mentagrophytes* and *Microsporum canis*, using the broth microdilution assay. All the extracts exhibited moderate antifungal properties. The research also reported that the highest antifungal activity was detected for essential oils extracted from leaves and flowers.

Moreover, the antifungal activity of iridal, a triterpenoid compound isolated from the rhizomes of *I. germanica* L., was performed against *Plasmodium falciparum* chloroquine-resistant and -sensitive strains. Iridal was less effective against both fungal strains, with minimal inhibitory concentration values exceeding 50 mg/mL from 24 to 48 h of incubation [19]. Furthermore, the ethanolic extract of *I. hungarica* rhizomes was evaluated in vitro against *Candida albicans* ATCC 653/885 at the concentration of 1%. The fungal strain was interestingly sensitive to the ethanolic extract, with 16.30 nm as a diameter of growth inhibition [52].

3.8. Antiviral Activity

The aqueous and ethanolic extracts of *I. sibirica* L. were evaluated against herpes simplex virus type 1. Accordingly, the rhizome ethanolic extract was the most effective on the herpes simplex virus when compared with the aqueous extract [55].

3.9. Antidiabetic Activity

Standard antidiabetic drugs, especially α -amylase and α -glucosidase inhibitors, have recently been linked to a number of serious side effects in humans, including diarrhea, bloating and abdominal pain [56]. Thus, researchers have switched their attention to a plethora of medicinal plants that have been exploited by indigenous people worldwide, which has led to a rich know-how related to diabetes treatment. Researchers have lent credence to their ethnomedicinal uses and identified many bioactive compounds endowed with substantial antidiabetic activity, primarily flavonoids and phenolic acids [57].

Although there are more than 260 accepted species of the genus *Iris* worldwide, data have shown that the only *Iris* spp. that have been evaluated for their antidiabetic activity are *I. germanica* L. and *I. ensata* Thunb. In this sense, Mahdinezhad et al. [28] studied the hypoglycemic effect of the hydroalcoholic extract of *I. germanica* L. rhizomes on streptozotocin-induced diabetic rats. The repeated oral administration of the doses of 100 and 200 mg/kg for 4 weeks significantly decreased the levels of glucose, triglycerides and oxidative stress markers levels such as ALT (alanine aminotransferase), AST (aspartate aminotransferase) and ALP (alkaline phosphatase). The authors stated that the antihyperglycemic and antihypertriglyceridemic effects of *I. germanica* L. could be attributed to the abundance of phenolic constituents in the hydroalcoholic extract, especially anthocyanins.

Furthermore, Suresh et al. [58] used normal, glucose-loaded and streptozotocin-induced diabetic rats to evaluate the hyperglycemic effect of *I. Ensata* Thunb dried root extract for 21 days. The authors reported that the oral administration of the extract reduced blood glucose in both normal and streptozotocin-diabetic rats. They associated the observed effect with the capacity of the extract to lower the intestinal uptake of glucose (digestive-enzyme inhibition), increase the glucose absorption at the tissue level (sensitize the cells) and enhance the activity of the β -cells of the pancreas.

On the other hand, the increase in blood glucose levels is mainly ascribed to the degradation of carbohydrates in the intestine, which is under the control of α -amylase, β -amylase and α -glucosidase [59]. Inhibiting or slowing down the activity of these key enzymes might be an effective therapeutic approach for preventing glucose from entering the bloodstream [56].

Therefore, Ibrahim et al. [60] identified eight known isoflavonoids, as well as two novel isoflavonoids, 8-hydroxyirilone 5-methyl ether and 8-hydroxyirilone, from the methanolic extract of *I. germanica* L. powdered rhizomes. Using acarbose as a reference, they assessed the in vitro α -amylase inhibitory potency of these compounds. They reported that, among all the tested components, 8-hydroxyirilone 5-methyl ether, 8-hydroxyirilone, irilone and irisolidone exhibited prominent α -amylase inhibitory capacity at the concentration of 250 μ g/mL with inhibition rates of 66.1, 78.3, 67.3 and 70.1%, respectively. They indicated that the α -amylase inhibitory potency increased with the presence of C-7 hydroxyl and C-5 hydroxyl or with the methylation of the hydroxyl groups in the A and B rings of isoflavonoids.

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