

Flavonoids of the Genus *Iris* (Iridaceae)

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Abstract: Species of the genus *Iris* (Iridaceae) have a long history of traditional medicinal use in many places of the world, and they have been previously recognized as rich sources of secondary metabolites, in which flavonoids are found predominantly. During the last decade (1999-2008) over 90 flavonoid constituents have been discovered and characterized, including 38 new compounds, from 15 species of *Iris*. This review elucidates the structural features of these flavonoid constituents, and gives the details of their source, identification, biological activity and chemotaxonomy significance. At last, a checklist of the flavonoid compounds in *Iris* by species is given.

Keywords: *Iris*, Iridaceae, flavonoids, glycosides, isoflavones, chemotaxonomy, biological activity.

1. INTRODUCTION

The north temperate genus *Iris* consists of about 300 species of flowering plants [1], which is the largest and most complicated genus in the family Iridaceae. It is widely distributed throughout Eurasia and North America. Its differentiation center is in China, and spreads to the Middle East (Ancient Mediterranean area) [2]. There are more than 60 species found in China [1], 37 in Turkey [3], 16 in Pakistan [4,5], 12 in India [6], 3 in Egypt [7]. *Iris* species have been cultivated as decorative plants since the ancient times. These cultivated Irises have a wide variety of colors in their showy and usually perfumed blossoms [8]. In recent years, *Iris* species have gained a great popularity due to their sweet violet fragrance interested in the perfume and cosmetic industries [9]. Many members of the genus *Iris* have also been used as traditional folk medicine for the treatment of various diseases. The uses of underground parts of several *Iris* species in traditional European folk medicine have been well documented [10]. The rhizomes of some *Iris* species (*Iris germanica* and *Iris pseudacariis*) have been used as a diuretic, carminative and against constipation and stomachache in Anatolian folk medicine [11]. *Iris* species also have a long history of medicinal use in China. For example, The rhizomes of *Iris tectorum* were introduced in the first Chinese monograph on herbal medicine, “*Shen Nong Ben Cao Jing*” (also known as “The Divine Farmer’s Herb-Root Classic”) completed about 200 AD [12]. According to the latest edition of the Chinese Pharmacopoeia [13], *Iris tectorum* is referred to as “*Chuan She Gan*”, and is used to treat sore throat, to disperse phlegm, and for heat-clearing and detoxifying. Furthermore, *Iris* plants have been used in the treatment of cancer, inflammation, bacterial and viral infections [14], such as *Iris bungei* used in Mongolian traditional medicine [15].

Plants of the genus *Iris* have been recognized as rich sources of secondary metabolites. Previous phytochemical

investigations of the *Iris* plants have resulted in the isolation of a variety of compounds, including flavonoids and their glycosides, triterpenoids, benzoquinones and stilbene glycosides [16], in which flavonoids and their glycosides are found predominantly. The flavonoids are often biologically active secondary metabolites and about 2% of all the photosynthesized carbon is converted into flavonoids [17]. A number of flavonoids have been found to possess anti-protozoal, anti-inflammatory and antioxidant activities. Insecticidal, antifungal and antibacterial activities have also been reported for some isoflavonoids [18].

Iwashina *et al.* reviewed the flavonoids of the genus *Iris* in 1998, described their structures, distribution and function [19]. In the following decade the phytochemical studies and, to a lesser extent, pharmacological studies on *Iris* species have made further progress, and have not been reviewed subsequently. Thus the present review, which describes work published in this field from 1999 to 2008, seeks to fill this gap. There are about 94 flavonoid constituents discovered and characterized, including 38 new compounds, from 15 *Iris* species, including *Iris bungei*, *Iris cathayensis*, *Iris carthaliniae*, *Iris confusa*, *Iris germanica*, *Iris kumaonensis*, *Iris lactea*, *Iris leptophylla*, *Iris potaninii*, *Iris pseudopumila*, *Iris soforana*, *Iris songarica*, *Iris spuria*, *Iris tectorum*, *Iris tenuifolia*. The flavonoid constituents are all reported for the first time from each of the *Iris* species. Most of the flavonoids are characterized by their unique features, which may be of some chemotaxonomic significance, and many of the compounds also demonstrated potent biological activities. The large number of flavonoids characterised from *Iris* in this period bears witness to the continuing vitality of this area of natural products research.

2. CLASSIFICATION AND FEATURES OF FLAVONOID CONSTITUENTS OF *IRIS*

The normal flavonoid constituents of *Iris* reported during 1999-2008 can be classified, according to their skeletons, into five groups: isoflavones & their glycosides, flavones & their glycosides, flavonols & their glycosides, flavanones and dihydroflavonols. They constitute a relatively homogeneous group of compounds, almost all being derivatives

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from the basic tricyclic structure of isoflavone or flavone with simple patterns of *O*-substitution (e.g. hydroxy, methoxy and methylenedioxy) and glycosylation. They differ only in the nature of the substituent position of rings A and B. There are relatively common 5,7-di- or 5,6,7-tri-*O*-substitution pattern in the A-ring. Importantly, The most pronounced feature in this ring is 6,7-methylenedioxy substitution (32 out of 94 compounds possess the substitution pattern), which is less common in flavonoids obtained from other genus of Iridaceae. Furthermore, in the B-ring they often possess 2'- or 4'-*O*-substitution, 2',3'-, 3',4'- or 4',5'-di-*O*-substitution and 3',4',5'-tri-*O*-substitution, but it is noteworthy that 2'-*O*-substitution & 2',3'-di-*O*-substitution are rare in the aglycones of their glycosides. Finally, the majority of flavonoid glycosides characterized to date are either 6-, 7-, 3- or 4'- glycosides.

There are also classes of modified flavonoids found in *Iris* species, which in formal terms can be regarded as cyclized derivatives of the normal flavonoids mentioned above, namely peltogynoids, coumaronochromones and rotenoids. Similarly with the regular flavonoids, they possess simple patterns of *O*-substitution. The common feature of the compounds is that the substituent at C-2 or C-3 position is always found in the form of an oxygen-bearing ring fused with rings B and C.

As demonstrated previously by Iwashina *et al.* [19], isoflavones (mainly contained in the rhizomes) and glycosylflavones (mainly found from the leaves and flowers of almost *Iris* species), either C-glycosylflavones or *O*-

glycosylflavones, are major components of the genus *Iris*. We further find that *O*-glycosylisoflavones (mainly contained in the rhizomes) are also major components of *Iris* species. The residue flavones, flavonols & their glycosides, flavanones, dihydroflavonols, peltogynoids, coumaronochromones and rotenoids are all minor components. Importantly, Chondhary *et al.* first isolated five new peltogynoids from *Iris bungei* in 2001, and that was the first report of peltogynoid-type compounds found in the family of Iridaceae [20].

Summaries of the various classes of the regular, modified flavonoids are given in Figs. (1 and 2).

3. NATURALLY OCCURRING FLAVONOIDS OF *IRIS*

There have been a variety of flavonoid compounds isolated from *Iris* during 1999-2008. We present these compounds in the following six sections (isoflavones & their glycosides, flavones & their glycosides, flavonols & their glycosides, flavanones and flavanonols, peltogynoids, coumaronochromones and rotenoids), which follow a standard pattern so far as is practicable.

3.1. Isoflavones and their Glycosides

Isoflavones and their glycosides are the most important flavonoid compounds isolated from the genus *Iris*. In most reports they were found in the rhizomes, rare in the flowers and leaves. The number of the isoflavones and their glycosides described in the literature during the reporting period

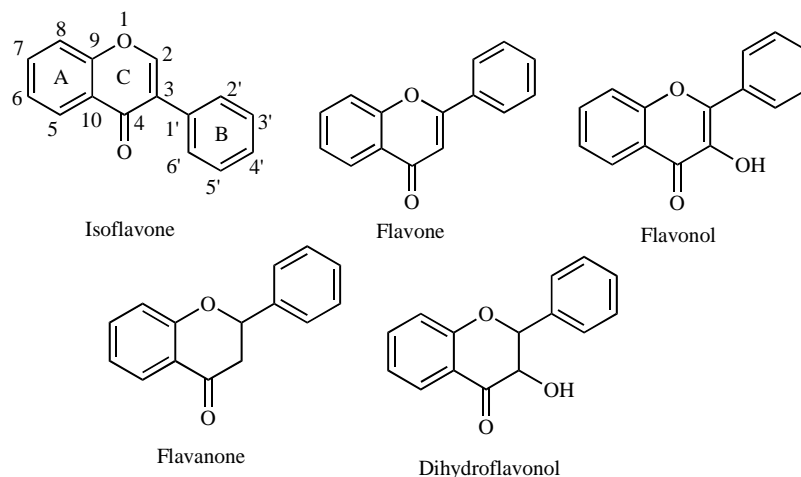


Fig. (1). Typical group of regular flavonoids in *Iris*.

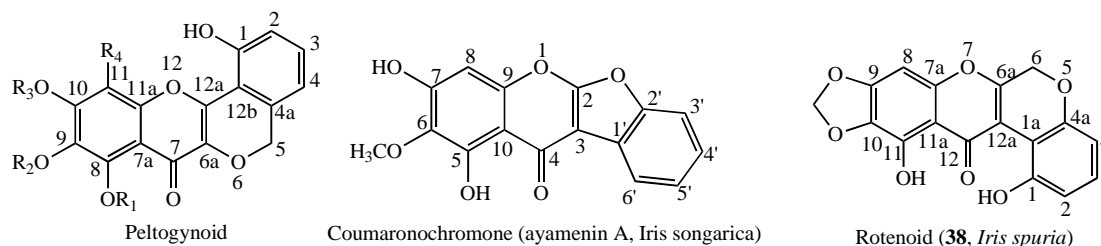


Fig. (2). Typical group of modified flavonoids in *Iris*.

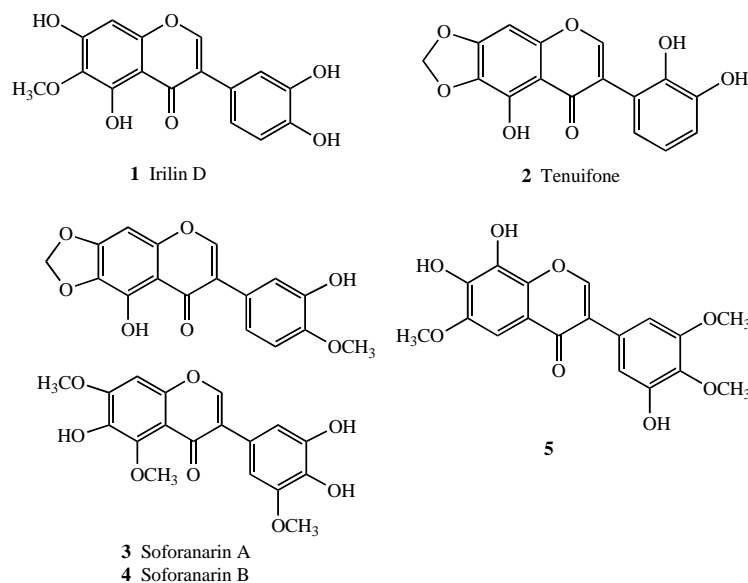


Fig. (3). Structures of new isoflavones (**1-5**) isolated from *Iris*.

exceeds that of any other subclass of flavonoids. All of the 56 compounds are listed in Table 1, which includes 20 new examples (5 isoflavones, 15 isoflavone glycosides).

3.1.1. Isoflavones

As many of the likely permutations of hydroxy, methoxy, and methylenedioxy substitutions have already been described, not surprisingly, the number of new isoflavones reported between 1999 and 2008 is relatively small. There are only five records (**1-5**) characterized.

5,7,3',4'-tetrahydroxy-6-methoxyisoflavone (irilin D, **1**) was isolated from the underground parts of *Iris bungei*, a species cited as a medicinal plant in Mongolian, along with four new flavonols, irisflavone A-D (**26-29**), and three known isoflavones, irilins A-B and tlatancuayin [15]. irilin D (**1**) had been earlier reported as a synthetic product [21], and that was the first time it was characterized as a new natural product. The whole plant of *Iris tenuifolia* yielded 5,2',3'-trihydroxy-6,7-methylenedioxyisoflavone (tenuifone, **2**) [8], which possesses the uncommon 6,7-methylenedioxy substitution in the A-ring. Another example with this substitution is 5,3'-dihydroxy-4'-methoxy-6,7-methylenedioxyisoflavone (Soforanarin A, **3**) from methanolic extracts of the rhizomes of *Iris soforana* of Turkish origin, which also yielded 6,3',4'-trihydroxy-5,7,5'-trimethoxyisoflavone (Soforanarin B, **4**) and other six known isoflavones [16]. To the best of our understanding, it was the first phytochemical work conducted on this species. Compounds (**1-4**) are examples exhibiting relatively common 5,6,7-tri-*O*-substitution pattern of the A-ring, but **7**, **8**, 5'-trihydroxy-6, 3', 4'-trimethoxyisoflavone (**5**) obtained from the underground parts of *Iris potaninii* [22] is unusual to some extent, which possesses 8-hydroxy substitution in the A-ring. This substitution is relatively uncommon in isoflavones [23].

3.1.2. Isoflavone Glycosides

Most of the saccharides found in isoflavone glycosides reported between 1999 and 2008 are monosaccharides or

disaccharides. The monosaccharides are normally β -D-glucopyranosides (β -D-Glcp), and similarly, the disaccharides are mainly β -D-Glcp-(1 \rightarrow 6)- β -D-Glcp. They usually form *O*-glycosides, with the sugar moiety often linked to C-7 or C-4' position of the known aglycones.

Among the new isoflavone glycosides isolated from the genus *Iris* during the reporting period, there are five containing monosaccharides, nine containing disaccharides and one containing trisaccharide. In the following part they are elucidated in detail.

Compounds (**6**) (*Iris Carthaliniae*) [24], (**7**) and (**8**) (*Iris germanica*) [25] are relatively common 7-*O*-, 4'-*O*- β -D-glucopyranosylisoflavones obtained from *Iris* species. Two unusual isoflavone monosaccharides are irisleptophyllidin (**9**) from rhizomes of *Iris leptophylla* [26] and 8,3',5'-trihydroxy-7,4'-dimethoxy-6-*O*- β -D-glucopyranosylisoflavone (**10**) from underground parts of *Iris potaninii* [22], which are 3'-*O*- and 6-*O*- β -D-glucopyranosylisoflavone, respectively. Similarly with **7**, **8**, 5'-trihydroxy-6, 3', 4'-trimethoxyisoflavone(**5**), the aglycone of compound (**10**) also possesses the uncommon 8-hydroxy substitution in the A-ring.

Compounds (**11**), (**15**), (**17**) (*Iris germanica*) [27], (**13**) (*Iris pseudopumila*) [28], (**12**), (**16**) (*Iris carthaliniae*) [24] contain relatively common 7-*O*-, 4'-*O*- β -D-Glcp-(1 \rightarrow 6)- β -D-Glcp. The uncommon disaccharide L-Rhap-(1 \rightarrow 2)-D-Glcp was reported in a 4'-*O*-glycoside of irilone (irilone-bioside, **14**) obtained from rhizomes of *Iris leptophylla* together with irisleptophyllidin (**9**) [26]. Compounds (**11-17**) are all linear disaccharides, but (**18**) (*Iris spuria*) [29] and (**19**) (*Iris germanica*) [27] are uncommon examples of two monosaccharides bound to different positions of the aglycones, respectively. The more noteworthy one is germanasim G (**19**), which is a 3',4'-di-*O*- β -D-glucopyranosylisoflavone with 2-methoxy-4-acetylphenyl group bound to the C-2 position of the 4'-glucopyranoside. The acylated phenyl derivative of a

Table 1. Isoflavones and their Glycosides Reported in the Period 1999-2008

No.	Class ^a	Compound ^b	Sub. ^c	Source	Tissue	Place	Year	Ref.
1	IF	5,7,4'-trihydroxyisoflavone(genistein)	5,7,4'	<i>Iris tectorum</i>	rhizomes	China	2008	[51]
2	IF	5,7,2'-trihydroxy-6-methoxyisoflavone(irilin B)	5,6,7,2'	<i>Iris bungei</i>	underground parts	Mongolia	2001	[15]
		5,7,2'-trihydroxy-6-methoxyisoflavone		<i>Iris tenuifolia</i>	whole plant	Pakistan	2008	[8]
		5,7,2'-trihydroxy-6-methoxyisoflavone		<i>Iris songarica</i>	rhizomes and roots	Iran	2008	[34]
		5,7,2'-trihydroxy-6-methoxyisoflavone		<i>Iris germanica</i>	rhizomes	Egypt	2006	[33]
3	IF	5,7-dihydroxy-6,2'-dimethoxyisoflavone		<i>Iris lactea</i>	underground parts	China	2005	[30]
		5,7-dihydroxy-6,2'-dimethoxyisoflavone		<i>Iris songarica</i>	leaves	China	2006	[31]
		5,7-dihydroxy-6,2'-dimethoxyisoflavone		<i>Iris songarica</i>	rhizomes and roots	Iran	2008	[34]
		5,7-dihydroxy-6,2'-dimethoxyisoflavone		<i>Iris tenuifolia</i>	whole plant	Pakistan	2008	[8]
4	IF	5,2'-dihydroxy-6,7-dimethoxyisoflavone(irilin A)		<i>Iris bungei</i>	underground parts	Mongolia	2001	[15]
		5,2'-dihydroxy-6,7-dimethoxyisoflavone		<i>Iris songarica</i>	rhizomes and roots	Iran	2004	[54]
		5,2'-dihydroxy-6,7-dimethoxyisoflavone		<i>Iris germanica</i>	rhizomes	Egypt	2006	[33]
5	IF	5,2'-dihydroxy-6,7-methylenedioxyisoflavone(irisone B)		<i>Iris songarica</i>	rhizomes and roots	Iran	2004	[54]
		5,2'-dihydroxy-6,7-methylenedioxyisoflavone		<i>Iris lactea</i>	underground parts	China	2005	[30]
		5,2'-dihydroxy-6,7-methylenedioxyisoflavone		<i>Iris tenuifolia</i>	whole plant	Pakistan	2008	[8]
6	IF	5-hydroxy-2'-methoxy-6,7-methylenedioxyisoflavone(irisone A)		<i>Iris tenuifolia</i>	whole plant	Pakistan	2008	[8]
7	IF	5,2'-dimethoxy-6,7-methylenedioxyisoflavone(tlatancuayin)		<i>Iris bungei</i>	underground parts	Mongolia	2001	[15]
8	IF	5,7,4'-trihydroxy-6-methoxyisoflavone(tectorigenin)	5,6,7,4'	<i>Iris kumaonensis</i>	rhizomes	India	2002	[55]
		5,7,4'-trihydroxy-6-methoxyisoflavone		<i>Iris confusa</i>	rhizomes and roots	China	2004	[53]
		5,7,4'-trihydroxy-6-methoxyisoflavone		<i>Iris spuria</i>	rhizomes	Egypt	2004	[29]
		5,7,4'-trihydroxy-6-methoxyisoflavone		<i>Iris lactea</i>	underground parts	China	2005	[30]
		5,7,4'-trihydroxy-6-methoxyisoflavone		<i>Iris cathayensis</i>	rhizomes and roots	China	2005	[36]
		5,7,4'-trihydroxy-6-methoxyisoflavone		<i>Iris songarica</i>	leaves	China	2006	[31]
9	IF	5,7-dihydroxy-6,4'-dimethoxyisoflavone(irisolidone)		<i>Iris pseudopumila</i>	rhizomes	Italy	2007	[28]
10	IF	5,4'-dihydroxy-6,7-dimethoxyisoflavone		<i>Iris lactea</i>	underground parts	China	2005	[30]
11	IF	5,4'-dihydroxy-6,7-methylenedioxyisoflavone(irilone)	'	<i>Iris germanica</i>	rhizomes	Germany	2003	[10]
		5,4'-dihydroxy-6,7-methylenedioxyisoflavone		<i>Iris leptophylla</i>	rhizomes	China	2003	[52]

(Table 1). Contd.....

No.	Class ^a	Compound ^b	Sub. ^c	Source	Tissue	Place	Year	Ref.
		5,4'-dihydroxy-6,7-methylenedioxyisoflavone		<i>Iris confusa</i>	rhizomes and roots	China	2004	[53]
		5,4'-dihydroxy-6,7-methylenedioxyisoflavone		<i>Iris soforana</i>	roots	Turkey	2004	[16]
		5,4'-dihydroxy-6,7-methylenedioxyisoflavone		<i>Iris cathayensis</i>	rhizomes and roots	China	2005	[36]
		5,4'-dihydroxy-6,7-methylenedioxyisoflavone		<i>Iris pseudopumila</i>	rhizomes	Italy	2007	[28]
12	IF	5-hydroxy-6,7,4'-trimethoxyisoflavone(dimethy-tectorigenin)		<i>Iris tectorum</i>	rhizomes	China	2008	[51]
13	IF	5-hydroxy-4'-methoxy-6,7-methylenedioxyisoflavone(4'-methoxy nigricin)		<i>Iris soforana</i>	roots	Turkey	2004	[16]
14	IF	4'-hydroxy-5-methoxy-6,7-methylenedioxyisoflavone(nigricin/irisolone)		<i>Iris potaninii</i>	underground parts	Mongolia	2002	[22]
		4'-hydroxy-5-methoxy-6,7-methylenedioxyisoflavone		<i>Iris soforana</i>	roots	Turkey	2004	[16]
		4'-hydroxy-5-methoxy-6,7-methylenedioxyisoflavone		<i>Iris songarica</i>	leaves	China	2006	[31]
15	IF	6'-hydroxy-5-methoxy-6,7-methylenedioxyisoflavone(betaulgarin)	5,6,7,6'	<i>Iris tenuifolia</i>	whole plant	Pakistan	2008	[8]
16	IF	5,2',3'-trihydroxy-6,7-methylenedioxyisoflavone (tenuifone,2*)	5,6,7,2',3'	<i>Iris tenuifolia</i>	whole plant	Pakistan	2008	[8]
17	IF	5,3'-dihydroxy-2'-methoxy-6,7-methylenedioxyisoflavone		<i>Iris lactea</i>	underground parts	China	2005	[30]
18	IF	5,7,3',4'-tetrahydroxy-6-methoxyisoflavone(irilin D,1 [*])	5,6,7,3',4'	<i>Iris bungei</i>	underground parts	Mongolia	2001	[15]
19	IF	5,7,3'-trihydroxy-6,4'-dimethoxyisoflavone		<i>Iris germanica</i>	rhizomes	Turkey	2003	[40]
20	IF	5,3'-dihydroxy-4'-methoxy-6,7-methylenedioxyisoflavone(soforanarin A,3*)		<i>Iris soforana</i>	roots	Turkey	2004	[16]
21	IF	5,4'-dihydroxy-3'-methoxy-6,7-methylenedioxyisoflavone(iriflogenin)		<i>Iris potaninii</i>	underground parts	Mongolia	2002	[22]
		5,4'-dihydroxy-3'-methoxy-6,7-methylenedioxyisoflavone		<i>Iris germanica</i>	rhizomes	Germamy	2003	[10]
22	IF	3'-hydroxy-5,4'-dimethoxy-6,7-methylenedioxyisoflavone		<i>Iris potaninii</i>	underground parts	Mongolia	2002	[22]
23	IF	4'-hydroxy-5,3'-dimethoxy-6,7-methylenedioxyisoflavone(nigricanin/iriskashmirianin)		<i>Iris germanica</i>	rhizomes	Germamy	2003	[10]
		4'-hydroxy-5,3'-dimethoxy-6,7-methylenedioxyisoflavone		<i>Iris soforana</i>	roots	Turkey	2004	[16]
		4'-hydroxy-5,3'-dimethoxy-6,7-methylenedioxyisoflavone		<i>Iris leptophylla</i>	rhizomes	China	2007	[26]
24	IF	5,3',4'-trimethoxy-6,7-methylenedioxyisoflavone(3'-O-methyl iriskumaonin)		<i>Iris soforana</i>	roots	Turkey	2004	[16]
		5,3',4'-trimethoxy-6,7-methylenedioxyisoflavone		<i>Iris leptophylla</i>	rhizomes	China	2007	[26]
25	IF	5,3'-dihydroxy-7,8,2'-trimethoxyisoflavone	5,7,8,2',3'	<i>Iris songarica</i>	rhizomes and roots	Iran	2008	[34]
26	IF	5,7,3'-trihydroxy-6,4',5'-trimethoxyisoflavone(irigenin)	5,6,7,3',4',5'	<i>Iris kumaonensis</i>	rhizomes	India	2002	[55]
		5,7,3'-trihydroxy-6,4',5'-trimethoxyisoflavone		<i>Iris soforana</i>	roots	Turkey	2004	[16]
		5,7,3'-trihydroxy-6,4',5'-trimethoxyisoflavone		<i>Iris leptophylla</i>	rhizomes	China	2007	[26]
		5,7,3'-trihydroxy-6,4',5'-trimethoxyisoflavone		<i>Iris pseudopumila</i>	rhizomes	Italy	2007	[28]

(Table 1). Contd.....

No.	Class ^a	Compound ^b	Sub. ^c	Source	Tissue	Place	Year	Ref.
27	IF	6,3',4'-trihydroxy-5,7,5'-trimethoxyisoflavone(soforanarin B,4*)		<i>Iris soforana</i>	roots	Turkey	2004	[16]
28	IF	5,5'-dihydroxy-3',4'-dimethoxy-6,7-methylenedioxyisoflavone		<i>Iris potaninii</i>	underground parts	Mongolia	2002	[22]
29	IF	5,3',4',5'-tetramethoxy-6,7-methylenedioxyisoflavone(irisforentin)		<i>Iris potaninii</i>	underground parts	Mongolia	2002	[22]
		5,3',4',5'-tetramethoxy-6,7-methylenedioxyisoflavone		<i>Iris leptophylla</i>	rhizomes	China	2003	[52]
30	IF	5,7,3'-trihydroxy-8,4',5'-trimethoxyisoflavone	5,7,8,3',4',5'	<i>Iris germanica</i>	rhizomes	Turkey	2003	[40]
31	IF	7, 8, 5'-trihydroxy-6, 3', 4'-trimethoxyisoflavone(5*)	6,7,8,3',4',5'	<i>Iris potaninii</i>	underground parts	Mongolia	2002	[22]
IFG (monosaccharides)								
		5,7,4'-trihydroxy-6-methoxyisoflavone(tectorigenin)	5,6,7,4'					
32	IFG	7-O-β-D-Glcp(tectoridin)		<i>Iris carthaliniae</i>	rhizomes	Egypt	1999	[24]
		7-O-β-D-Glcp		<i>Iris leptophylla</i>	rhizomes	China	2003	[52]
		7-O-β-D-Glcp		<i>Iris spuria</i>	rhizomes	Egypt	2004	[29]
		7-O-β-D-Glcp		<i>Iris confusa</i>	rhizomes and roots	China	2004	[53]
		7-O-β-D-Glcp		<i>Iris cathayensis</i>	rhizomes and roots	China	2005	[36]
		7-O-β-D-Glcp		<i>Iris songarica</i>	leaves	China	2006	[31]
33	IFG	4'-O-β-D-Glcp		<i>Iris carthaliniae</i>	rhizomes	Egypt	1999	[24]
		4'-O-β-D-Glcp		<i>Iris spuria</i>	rhizomes	Egypt	2004	[29]
		5,7-dihydroxy-6,4'-dimethoxyisoflavone(irisolidone)						
34	IFG	7-O-β-D-Glcp(6*)		<i>Iris carthaliniae</i>	rhizomes	Egypt	1999	[24]
35	IFG	7-O-α-D-Glcp		<i>Iris germanica</i>	rhizomes	Germany	2003	[10]
		5,4'-dihydroxy-6,7-dimethoxyisoflavone						
36	IFG	4'-O-β-D-Glcp		<i>Iris pseudopumila</i>	rhizomes	Italy	2007	[28]
		5,4'-dihydroxy-6,7-methylenedioxyisoflavone(irilone)						
37	IFG	4'-O-β-D-Glcp		<i>Iris germanica</i>	rhizomes	Turkey	2002	[25]
		4'-O-β-D-Glcp		<i>Iris leptophylla</i>	rhizomes	China	2003	[52]
		4'-O-β-D-Glcp		<i>Iris pseudopumila</i>	rhizomes	Italy	2007	[28]
		4'-hydroxy-5-methoxy-6,7-methylenedioxyisoflavone(nigracin/irisolone)						
38	IFG	4'-O-β-D-Glcp(germanasim B,7*)		<i>Iris germanica</i>	rhizomes	Turkey	2002	[25]
		4'-O-β-D-Glcp		<i>Iris pseudopumila</i>	rhizomes	Italy	2007	[28]
		5,7,3'-trihydroxy-6,4'-dimethoxyisoflavone	5,6,7,3',4'					
39	IFG	7-O-β-D-Glcp(iristectorin)		<i>Iris kumaonensis</i>	rhizomes	India	2002	[55]
		5,4'-dihydroxy-3'-methoxy-6,7-methylenedioxyisoflavone(iriflogenin)						

(Table 1). Contd.....

No.	Class ^a	Compound ^b	Sub. ^c	Source	Tissue	Place	Year	Ref.
40	IFG	4'-O-β-D-Glcp(irifloside)		<i>Iris leptophylla</i>	rhizomes	China	2007	[26]
		3'-hydroxy-5,4'-trimethoxy-6,7-methylenedioxyisoflavone						
41	IFG	3'-O-β-D-Glcp (irisleptophyllidin, 9*)		<i>Iris leptophylla</i>	rhizomes	China	2007	[26]
		4'-hydroxy-5,3'-dimethoxy-6,7-methylenedioxyisoflavone(nigricanin/iriskashmirianin)						
42	IFG	4'-O-β-D-Glcp(germanaism A, 8*)		<i>Iris germanica</i>	rhizomes	Turkey	2002	[25]
		4'-O-β-D-Glcp		<i>Iris leptophylla</i>	rhizomes	China	2007	[26]
		5,7,3'-trihydroxy-6,4',5'-trimethoxyisoflavone(irigenin)	5,6,7,3',4',5'					
43	IFG	7-O-β-D-Glcp(iridin)		<i>Iris leptophylla</i>	rhizomes	China	2003	[52]
		7-O-β-D-Glcp		<i>Iris confusa</i>	rhizomes and roots	China	2004	[53]
		7-O-β-D-Glcp		<i>Iris pseudopumila</i>	rhizomes	Italy	2007	[28]
		6,8,3',5'-tetrahydroxy-7,4'-dimethoxyisoflavone	6,7,8,3',4',5'					
44	IFG	6-O-β-D-Glcp(10*)		<i>Iris potaninii</i>	underground parts	Mongolia	2002	[22]
IFG (disaccharides)								
		5,6,7,4'-tetrahydroxyisoflavone(6-hydroxygenistein)	5,6,7,4'					
45	IFG	4'-O-β-D-Glcp-(1→6)-β-D-Glcp(germanasim D, 11*)		<i>Iris germanica</i>	rhizomes	Turkey	2003	[27]
		5,7,4'-trihydroxy-6-methoxyisoflavone(tectorigenin)						
46	IFG	4'-O-β-D-Glcp-(1→6)-β-D-Glcp(12*)		<i>Iris carthaliniae</i>	rhizomes	Egypt	1999	[24]
47	IFG	7-O-β-Glcp-(1→6)-β-Glcp		<i>Iris spuria</i>	rhizomes	Egypt	2004	[29]
		5,4'-dihydroxy-6,7-dimethoxyisoflavone(7-methyltectorigenin)						
48	IFG	4'-O-β-D-Glcp-(1→6)-β-D-Glcp		<i>Iris pseudopumila</i>	rhizomes	Italy	2007	[28]
		5,4'-dihydroxy-6,7-methylenedioxyisoflavone(irilone)						
49	IFG	4'-O-β-D-Glcp-(1→6)-β-D-Glcp(13*)		<i>Iris pseudopumila</i>	rhizomes	Italy	2007	[28]
50	IFG	4'-O-L-Rhap-(1→2)-D-Glcp (irilone-bioside, 14*)		<i>Iris leptophylla</i>	rhizomes	China	2007	[26]
		4'-hydroxy-5-methoxy-6,7-methylenedioxyisoflavone(nigricin/irisolone)						
51	IFG	4'-O-β-D-Glcp-(1→6)-β-D-Glcp(germanasim E, 15*)		<i>Iris germanica</i>	rhizomes	Turkey	2003	[27]
		4'-O-β-D-Glcp-(1→6)-β-D-Glcp		<i>Iris pseudopumila</i>	rhizomes	Italy	2007	[28]
		5,7,4'-trihydroxy-6,3'-dimethoxyisoflavone(iristectorigenin B)	5,6,7,3',4'					
52	IFG	7-O-β-D-Glcp-(1→6)-β-D-Glcp(16*)		<i>Iris carthaliniae</i>	rhizomes	Egypt	1999	[24]
		5,7,3'-trihydroxy-6,4',5'-trimethoxyisoflavone(irigenin)	5,6,7,3',4',5'					
53	IFG	7-O-β-D-Glcp-(1→6)-β-D-Glcp(germanasim C, 17*)		<i>Iris germanica</i>	rhizomes	Turkey	2003	[27]
		5,7,4'-trihydroxy-6-methoxyisoflavone(tectorigenin)	5,6,7,4'					
54	IFG	7-O-β-D-Glcp-4'-O-β-D-Glcp(18*)		<i>Iris spuria</i>	rhizomes	Egypt	2004	[29]
		7-O-β-D-Glcp-4'-O-β-D-Glcp		<i>Iris tectorum</i>	rhizome	China	2007	[41]
		3',4'-dihydroxy-5-methoxy-6,7-methylenedioxyisoflavone	5,6,7,3',4'					

(Table 1). Contd.....

No.	Class ^a	Compound ^b	Sub. ^c	Source	Tissue	Place	Year	Ref.
55	IFG	3'-O-β-D-Glcp-4'-O-[2''-O-(2'''-methoxy-4'''-acetylphenyl)-β-D-Glcp](germanasim G, 19*)		<i>Iris germanica</i>	rhizomes	Turkey	2003	[27]
IFG (trisaccharides)								
		4'-hydroxy-5-methoxy-6,7-methylenedioxyisoflavone(nigrin/irisolone)	5,6,7,4'					
56	IFG	4'-O-β-D-Glcp-(1→2)-α-L-Rhap-(1→6)-β-D-Glcp(germanasim F, 20*)		<i>Iris germanica</i>	rhizomes	Turkey	2003	[27]

^aFlavonoid subclass codes: IF, isoflavone; IFG, isoflavone glycoside.

^bStandard three-letter codes for monosaccharids are used; *p* = pyranoside. For di- and trisaccharides *O*-linked to isoflavones, the last-listed sugar (primary) is that attached to the aglycone.

^cThe *O*-substitution pattern of the isoflavones and the aglycones of their glycosides are indicated. Compounds are presented in order of increasing *O*-substitution, with the A-ring substituents taking precedence over those of the B-ring (primed numbers).

*The new compound numbers refers to the main text.

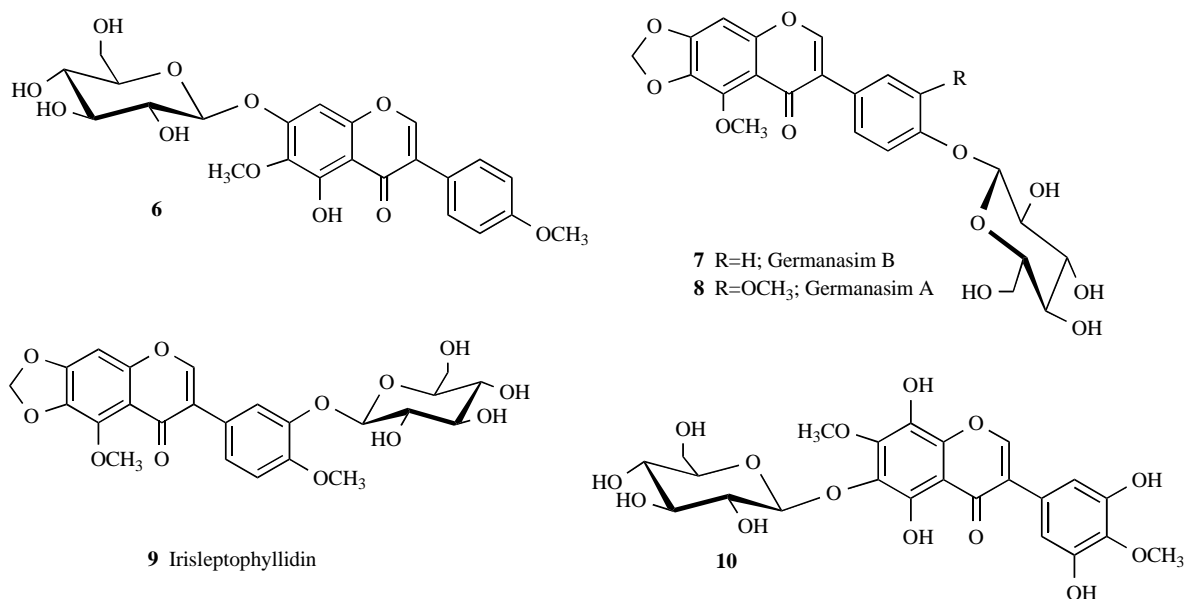


Fig. (4). Structures of new isoflavone monosaccharides (**6-10**) isolated from *Iris*.

glucose moiety is very rare among the isoflavone glycosides obtained from the genus *Iris*.

The unique example of new isoflavone glycoside containing a linear trisaccharide is germanasim F(**20**) isolated from rhizomes of *Iris germanica*, together with germanasim C-E and G (**11**, **15**, **17**, **19**). [27] The linear trisaccharide of germanasim F(**20**), β-D-Glcp-(1→2)-α-L-Rhap-(1→6)-β-D-Glcp, is characterized in a 4'-*O*-glycoside of nigrin (irisolone).

3.2. Flavones and Flavone Glycosides

Since flavones are less dominant components compared with their glycosides, the number of flavones reported from 1999 to 2008 is relatively smaller than their glycosides. There are only two known flavones reported, tectochrysin (*Iris lactea*, *Iris songarica*) [30,31] and wogonin (*Iris songarica*) [31]. As noted previously by Iwashina *et al.* [19], *C*-glycosylflavones (*e.g.* isovitexin, vitexin, orientin, isoorientin, swertisin, swertiajaponin) and *O*-glycosylflavones are major components of *Iris*, and are found from leaves and flowers of

almost species. During the reporting period, There are 11 flavone glycosides, either *C*-glycosylflavones or *O*-glycosylflavones, characterized in *Iris* species, four of which are new compounds. The sugar moiety is often linked to C-6 and C-7 position of the aglycone, which is different from the 7-, 4'-*O*-glycosylisoflavones. All of the 13 compounds are listed in Table 2, which also includes other flavonoids except isoflavones and their glycosides.

Compounds (**21**) (*Iris Carthaliniae*) [24] and (**22**) (*Iris pseudopumila*) [28] are relatively common 7-*O*-, 6-*C*-β-D-glucopyranosylflavones obtained from *Iris* species. Two of the most unusual examples, irisactin A (**23**) and irisactin B (**24**), are *O*-acetyl derivatives of *C*-glycosylflavones isolated from 70% ethanol extracts of the leaves of *Iris lactea* Pall. var. *chinensis*, a species which is widely distributed in the northeast and northwest of China [32]. The main difference of irisactin A (**23**) and irisactin B (**24**) is only in the substitution and glycosylation of C-6 and C-7 position of the A-ring. In irisactin A (**23**), an acylated linear disaccharide, 6-*O*-acetyl-α-L-Glcp-(1→2)-β-D-Glcp, is *O*-linked at C-6 and an

acylated monosaccharide, 2,4-di-*O*-acetyl- β -D-Rhap, is C-linked at C-7, respectively. In irislactin B (**24**), there is only an acylated linear disaccharide, 2,3-di-*O*-acetyl- α -L-Rhap-(1 \rightarrow 2)- β -D-Glcp, C-linked at C-6 with a methoxy group bound to the C-7 position of the A-ring.

3.3. Flavonols and their Glycosides

Seven flavonols and three flavonol glycosides have been reported from the genus *Iris* during the period, in which five flavonols are considered as new examples (four of them are

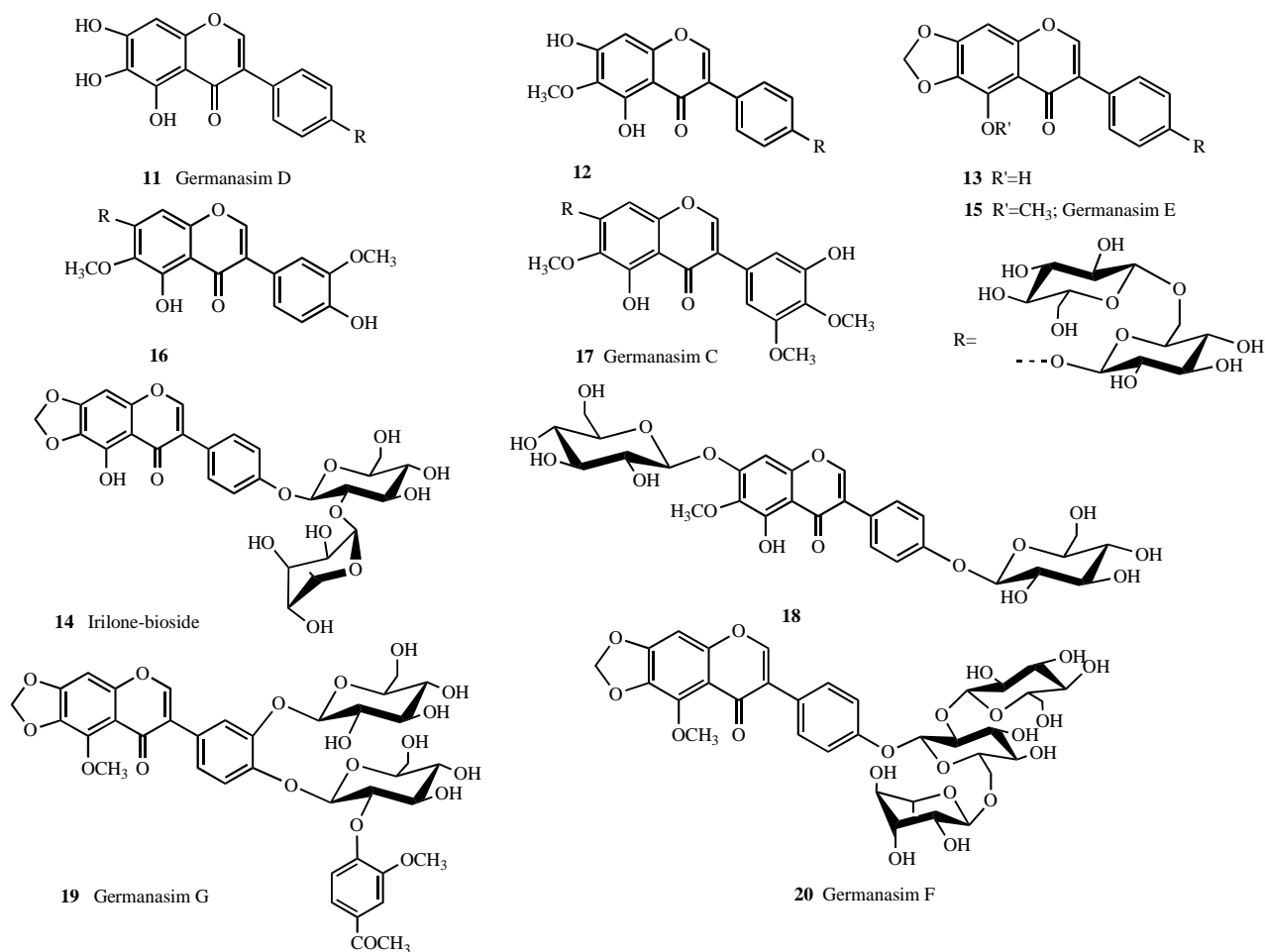


Fig. (5). Structures of new isoflavone disaccharides (**11-19**) and trisaccharide (**20**) isolated from *Iris*.

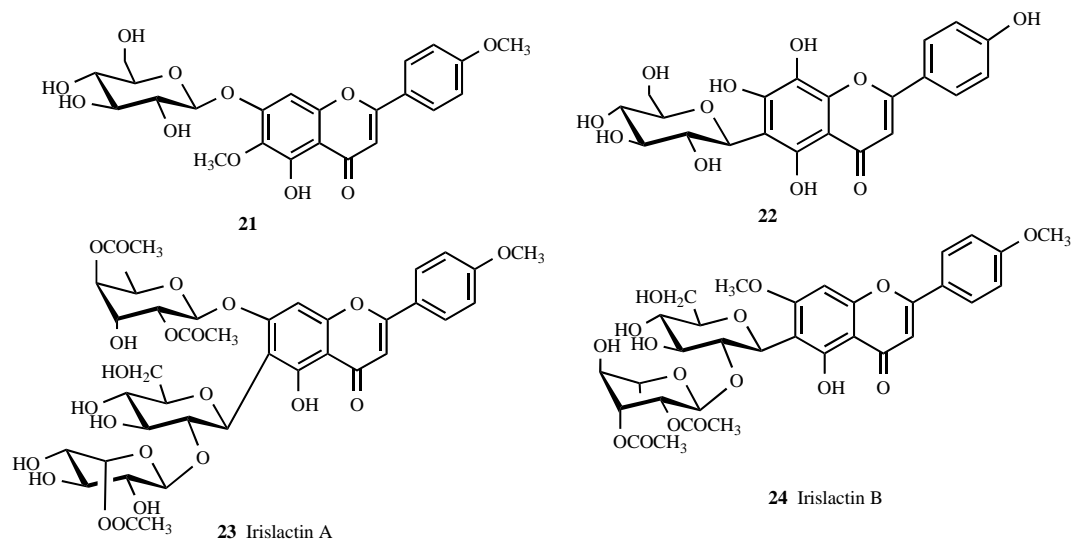


Fig. (6). Structures of new flavone glycosides (**21-24**) isolated from *Iris*.

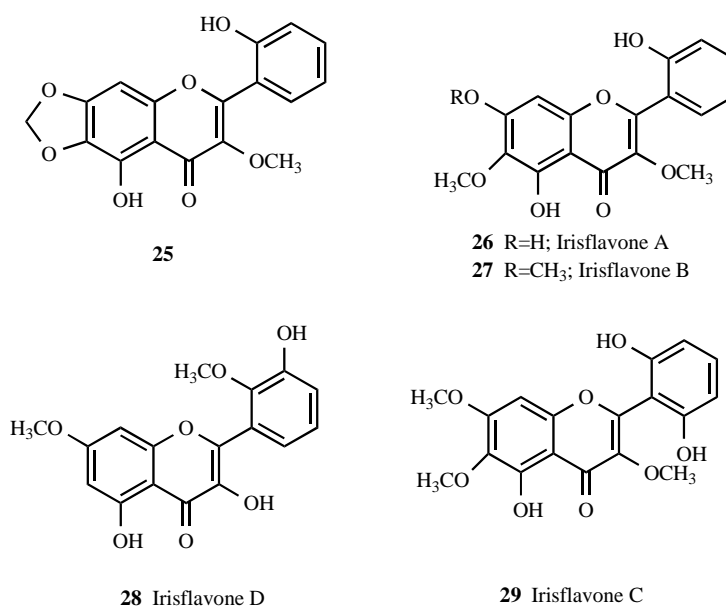


Fig. (7). Structures of new flavonols (25-29) isolated from *Iris*.

Table 2. Other Flavonoids Reported in the Period 1999-2008

No.	Class ^a	Compound ^b	Sub. ^c	Source	Tissue	Place	Year	Refs.
57	Fn	5-hydroxy-7-methoxyflavone(tectochrysin)	5,7	<i>Iris lactea</i>	underground parts	China	2005	[30]
		5-hydroxy-7-methoxyflavone		<i>Iris songarica</i>	leaves	China	2006	[31]
58	Fn	5,7-dihydroxy-8-methoxyflavone(wogonin)	5,7,8	<i>Iris songarica</i>	leaves	China	2006	[31]
		5,7,4'-trihydroxyflavone(apigenin)	5,7,4'					
59	FnG	6-C-β-D-Glcp		<i>Iris pseudopumila</i>	rhizomes	Italy	2007	[28]
		5,7-dihydroxy-4'-methoxyflavone(acacetin)	5,7,4'					
60	FnG	6-C-β-D-Glcp		<i>Iris pseudopumila</i>	rhizomes	Italy	2007	[28]
		5,6,7,4'-tetrahydroxyflavone(scutellarein)	5,6,7,4'					
61	FnG	6-O-β-D-Glcp		<i>Iris pseudopumila</i>	flowers	Italy	2008	[44]
		5,7-dihydroxy-6,4'-dimethoxyflavone	5,6,7,4'					
62	FnG	7-O-β-D-Glcp(21 [*])		<i>Iris carthaliniae</i>	rhizomes	Egypt	1999	[24]
		5,7,8,4'-tetrahydroxyflavone(isoscutellarein)	5,7,8,4'					
63	FnG	6-C-β-D-Glcp(22 [*])		<i>Iris pseudopumila</i>	rhizomes	Italy	2007	[28]
		5,6,7,4',5'-pentahydroxyflavone	5,6,7,4',5'					
64	FnG	6-O-β-D-Glcp		<i>Iris pseudopumila</i>	flowers	Italy	2008	[44]
		5,7-dihydroxy-4'-methoxyflavone(acacetin)	5,7,4'					

(Table 2). Contd.....

No.	Class ^a	Compound ^b	Sub. ^c	Source	Tissue	Place	Year	Refs.
65	FnG	7-O- α -L-Rhap-(1 \rightarrow 6)- β -D-Glcp		<i>Iris songarica</i>	leaves	China	2006	[31]
		5,6,7,4'-tetrahydroxyflavone(scutellarein)	5,6,7,4'					
66	FnG	6-O- β -D-Glcp-(1 \rightarrow 6)- β -D-Glcp		<i>Iris pseudopumila</i>	flowers	Italy	2008	[44]
		5,6,7-trihydroxy-4'-methoxyflavone	5,6,7,4'					
67	FnG	7-O-(2,4-di-O-acetyl- β -D-Rhap)-6-C-(6-O-acetyl- α -L-Glcp)-(1 \rightarrow 2)- β -D-Glcp(irislactin A, 23 *)		<i>Iris lactea</i>	leaves	China	2008	32
		5,6-dihydroxy-7,4'-dimethoxyflavone	5,6,7,4'					
68	FnG	6-C-(2,3-di-O-acetyl- α -L-Rhap)-(1 \rightarrow 2)- β -D-Glcp(irislactin B, 24 *)		<i>Iris lactea</i>	leaves	China	2008	[32]
		5,6,7,4',5'-pentahydroxyflavone	5,6,7,4',5'					
69	FnG	6-O- β -D-Glcp-(1 \rightarrow 6)- β -D-Glcp		<i>Iris pseudopumila</i>	flowers	Italy	2008	[44]
70	Fl	5-hydroxy-7-methoxyflavonol(izalpinin)	3,5,7	<i>Iris songarica</i>	leaves	China	2006	[31]
		5-hydroxy-7-methoxyflavonol		<i>Iris tenuifolia</i>	whole plant	Pakistan	2008	[8]
71	Fl	3,4',5-trihydroxy-7-methoxyflavone(rhamnocitrin)	3,5,7,4'	<i>Iris tectorum</i>	rhizomes	China	2007	[41]
72	Fl	5,2'-dihydroxy-3-methoxy-6,7-methylenedioxyflavone(25 *)	3,5,6,7,2'	<i>Iris germanica</i>	rhizomes	Egypt	2006	[33]
73	Fl	5,7,2'-trihydroxy-3,6-dimethoxyflavone(irisflavone A, 26 *)	3,5,6,7,2'	<i>Iris bungei</i>	underground parts	Mongolia	2001	[15]
		5,7,2'-trihydroxy-3,6-dimethoxyflavone		<i>Iris songarica</i>	rhizomes and roots	Iran	2008	[34]
74	Fl	5,2'-dihydroxy-3,6,7-trimethoxyflavone(irisflavone B, 27 *)	3,5,6,7,2'	<i>Iris bungei</i>	underground parts	Mongolia	2001	[15]
75	Fl	3,5,3'-trihydroxy-7,2'-methoxyflavone(irisflavone D, 28 *)	3,5,7,2',3'	<i>Iris bungei</i>	underground parts	Mongolia	2001	[15]
76	Fl	5,2',6'-trihydroxy-3,6,7-trimethoxyflavone(irisflavone C, 29 *)	3,5,6,7,2',6'	<i>Iris bungei</i>	underground parts	Mongolia	2001	[15]
		3,5,7,4'-tetrahydroxyflavone(kaempferol)	3,5,7,4'					
77	FIG	3-O- β -D-Glcp		<i>Iris pseudopumila</i>	rhizomes	Italy	2007	[28]
78	FIG	3-O- α -L-Rhap-(1 \rightarrow 6)- β -D-Glcp		<i>Iris pseudopumila</i>	rhizomes	Italy	2007	[28]
		3,5,7,4'-tetrahydroxy-3'-methoxyflavonol(isorhamnetin)	3,5,7,3',4'					
79	FIG	7-O- β -D-Glcp		<i>Iris songarica</i>	leaves	China	2006	[31]
80	Fa	(2S)-5,2'-dihydroxy-7-methoxyflavanone(dihydroechioidinin)	5,7,2'	<i>Iris cathayensis</i>	rhizomes and roots	China	2005	[36]
81	Fa	5,7,2'-trihydroxy-6-methoxyflavanone(30 *)	5,6,7,2'	<i>Iris germanica</i>	rhizomes	Egypt	2006	[33]

(Table 2). Contd.....

No.	Class ^a	Compound ^b	Sub. ^c	Source	Tissue	Place	Year	Refs.
82	Fa	5,2'-dihydroxy-6,7-methylenedioxyflavanone	5,6,7,2'	<i>Iris lactea</i>	underground parts	China	2005	[30]
		5,2'-dihydroxy-6,7-methylenedioxyflavanone		<i>Iris cathayensis</i>	rhizomes and roots	China	2005	[36]
		5,2'-dihydroxy-6,7-methylenedioxyflavanone		<i>Iris songarica</i>	leaves	China	2006	[31]
83	DF	5-hydroxy-7-methoxyflavanonol(alpinone)	3,5,7	<i>Iris tenuifolia</i>	whole plant	Pakistan	2008	[8]
84	DF	3,5,7-trihydroxy-4'-methoxyflavanone(dihydrokaempferide)	3,5,7,4'	<i>Iris tectorum</i>	rhizomes	China	2007	[41]
85	DF	3,5,4'-trihydroxy-7-methoxyflavanone(7-O-methylaromadendrin)	3,5,7,4'	<i>Iris tectorum</i>	rhizomes	China	2008	[43]
86	DF	(2R,3R)-5,3'-trihydroxy-7,4'-dimethoxyflavanonol(31 *)	3,5,7,3',4'	<i>Iris potaninii</i>	underground parts	Mongolia	2002	[22]
87	DF	(2R,3R)-5,2',3'-trihydroxy-6,7-methylenedioxyflavanonol(songaricol, 32 *)	3,5,6,7,2',3'	<i>Iris songarica</i>	rhizomes and roots	Iran	2008	[34]
88	PE	1,8,10-trihydroxy-9-methoxy-[1]benzopyrano-[3,2-c][2]-benzopyran-7(5H)-one(irisoid A, 33 *)	1,8,9,10	<i>Iris bungei</i>	underground parts	Mongolia	2001	[20]
		irisoid A		<i>Iris lactea</i>	underground parts	China	2005	[30]
		irisoid A		<i>Iris cathayensis</i>	rhizomes and roots	China	2005	[36]
		irisoid A		<i>Iris songarica</i>	leaves	China	2006	[31]
		irisoid A		<i>Iris songarica</i>	rhizomes and roots	Iran	2008	[34]
		irisoid A		<i>Iris tenuifolia</i>	whole plant	Pakistan	2008	[8]
89	PE	1,8-dihydroxy-9,10-dimethoxy-[1]benzopyrano-[3,2-c][2]-benzopyran-7(5H)-one(irisoid B, 34 *)	1,8,9,10	<i>Iris bungei</i>	underground parts	Mongolia	2001	[20]
		irisoid B		<i>Iris songarica</i>	leaves	China	2006	[31]
90	PE	1,10-dihydroxy-8,9-dimethoxy-[1]benzopyrano-[3,2-c][2]-benzopyran-7(5H)-one(irisoid C, 35 *)	1,8,9,10	<i>Iris bungei</i>	underground parts	Mongolia	2001	[20]
91	PE	1,8-dihydroxy-9,10-methylenedioxy-[1]benzopyrano-[3,2-c][2]-benzopyran-7(5H)-one(irisoid D, 36 *)	1,8,9,10	<i>Iris bungei</i>	underground parts	Mongolia	2001	[20]
		irisoid D		<i>Iris lactea</i>	underground parts	China	2005	[30]
		irisoid D		<i>Iris songarica</i>	leaves	China	2006	[31]
92	PE	1,8,11-trihydroxy-9,10-methylenedioxy-[1]benzopyrano-[3,2-c][2]-benzopyran-7(5H)-one(irisoid E, 37 *)	1,8,9,10,11	<i>Iris bungei</i>	underground parts	Mongolia	2001	[20]
93	RO	1,11-dihydroxy-9,10-methylenedioxy-12a-dehydrorotenoid(38 *)	1,9,10,11	<i>Iris spuria</i>	rhizomes	Egypt	2004	[29]
94	CC	5,7-dihydroxy-6-methoxycoumaronochromone(ayamenin A)	5,6,7	<i>Iris songarica</i>	rhizomes and roots	Iran	2008	[34]

^aFlavonoid subclass codes: Fn, flavone; FnG, flavone glycoside; Fl, flavonol; FIG, flavonol glycoside; Fa, flavanone; DF, dihydroflavanol; PE, peltogynoid; RO, rotenoid; CC, coumaronochromone.

^bStandard three-letter codes for monosaccharids are used; p = pyranoside. For di- or trisaccharides O-linked to isoflavones, the last-listed sugar (primary) is that attached to the aglycone.

^cThe O-substitution pattern of the flavonoids and the aglycones of their glycosides are indicated. Compounds are presented in order of increasing O-substitution, with the A-ring substituents taking precedence over those of the B-ring (primed numbers).

*The new compound numbers refers to the main text.

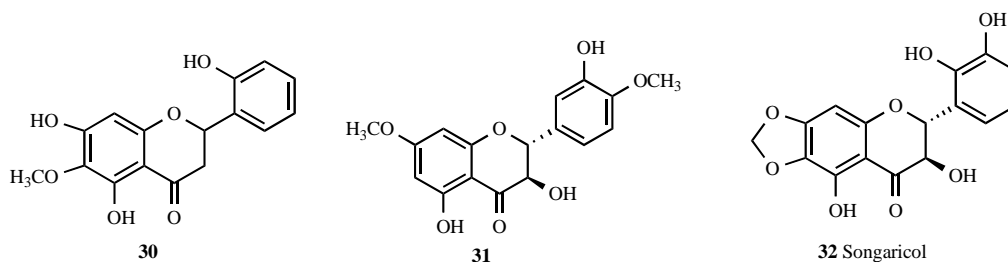


Fig. (8). Structures of new Flavanones and dihydroflavonols (**30-32**) isolated from *Iris*.

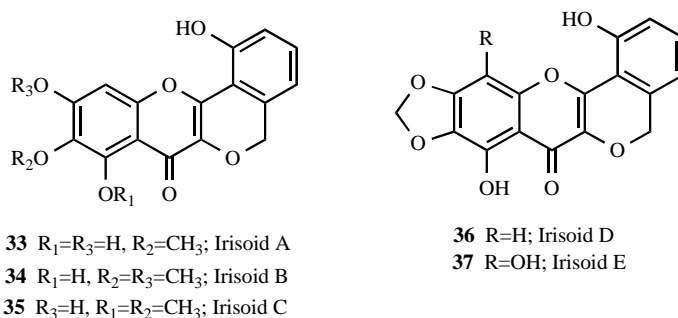


Fig. (9). Structures of new peltogynoids (**33-37**) isolated from *Iris*.

3-methyl ethers). It is noteworthy that all of the new flavonols possess 2'-*O*-substitution in the B ring, which is a characteristic feature of the *Iris* flavonoids. Evaluation of the rhizome extracts of *Iris germanica* for molluscicidal activity against the snail *Biomphalaria alexandrina* led to the isolation of 5,2'-dihydroxy-3-methoxy-6,7-methylenedioxyflavone (**25**), irilins A-B, and the flavanone, (**30**) [33]. Although obtained from an active fraction, the compounds were not tested individually. The other four new compounds, irisflavone A-D (**26-29**), were all obtained from the underground parts of *Iris bungei* [15]. The most unusual one may be irisflavone D (**25**) with 2',6'-di-*O*-substitution in the B-ring, which is rare in *Iris* flavonoids.

3.4. Flavanones and Dihydroflavonols

The number of flavanones and dihydroflavonols obtained from *Iris* species between 1999 and 2008 is relatively small, and only eight examples have been recorded, including one new flavanone, 5,7,2'-trihydroxy-6-methoxyflavanone (**30**, *Iris germanica*) [33], and two new dihydroflavonols, 5,3'-trihydroxy-7,4'-dimethoxyflavanonol (**31**, *Iris potaninii*) [22] and songaricol (**32**, *Iris songarica*) [34]. As reported previously, flavanones characterized by 2'-oxygenation in the B-ring have a relatively limited distribution, and are particularly associated with the genus *Andrographis* (Acanthaceae), other sources including Asteraceae, Iridaceae, Leguminosae and Moraceae [35]. Compound (**30**) is an example from Iridaceae corroborates this trend. The absolute configuration of the two new flavanonols (**31**) and (**32**) at C-2 and C-3 were all determined to be R configuration due to CD spectra and ¹H-NMR coupling constants. The *O*-substitution in the B-ring of compound (**31**) is uncommon to some extent, as the author argued that dihydroflavonols germanasim with a dihydroxy B-ring, 2',4'-dihydroxy, 3',4'-dihydroxy, 2',6'-dihydroxy, 3',5'-dihydroxy and 2',3'-dihydroxy, were known from their previous paper, but 3'-hydroxy-4'-methoxy sub-

stituents in the B-ring were very rare and had not been found in conjunction with a 5-hydroxy-7-methoxy A-ring.

3.5. Peltogynoids

There were five new peltogynoids, irisoid A-E (**33-37**), reported by Choudhary *et al.* in their study of the constituents of underground part extracts of *Iris bungei* in 2001 [20]. Although peltogynoids had been isolated from several genera of the family Leguminosae previously, that was the first report of the isolation of peltogynoids from the family Iridaceae and the first X-ray structure determination of peltogynoid-type compounds. After that, no new peltogynoids have ever been isolated from the genus *Iris*, but irisoid A, B and D have been obtained from some other species of *Iris* [8,30,31,34,36].

3.6. Coumaronochromones and Rotenoids

The rhizomes and roots of *Iris songarica* provided the only coumaronochromone constituent ayamenin A [34], which had been earlier produced by *Iris pseudacorus* leaves treated with cupric chloride [37].

The unique rotenoids characterized during the reporting period is a new 12a-dehydrorotenoid, 1,11-dihydroxy-9,10-methylenedioxy-12a-dehydrorotenoid (**38**), which was obtained from the rhizomes of *Iris spuria*, along with tectori-

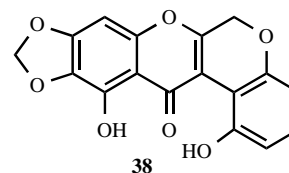


Fig. (10). Structure of the new rotenoid (**38**) isolated from *Iris spuria*.

Table 3. Distribution of Flavonoids in *Iris* Species

Class ^a	Name of compound	<i>I. bungei</i>	<i>I. cathayensis</i>	<i>I. carthagenica</i>	<i>I. confusa</i>	<i>I. germanica</i>	<i>I. kumaonensis</i>	<i>I. lactea</i>	<i>I. leptophylla</i>	<i>I. poluninii</i>	<i>I. pseudopuntica</i>	<i>I. soforana</i>	<i>I. songarica</i>	<i>I. spuria</i>	<i>I. tectorum</i>	<i>I. tenuifolia</i>
IF	irilin B (2)	X				X							X			X
IF	5,7-dihydroxy-6,2'-dimethoxyisoflavone (3)							X					X			X
IF	irilin A (4)	X				X							X			
IF	irison B (5)							X					X			X
IF	tectorigenin (8)		X		X		X	X			X	X		X		
IF	irilone (11)		X		X				X		X	X				
IF	nigrin/irisonone (14)										X	X				
IF	iriflogenin (21)					X				X						
IF	nigrinamin/iriskashmirianin (23)					X		X				X				
IF	3-O-methyl iriskumaonin (24)							X				X				
IF	ingenin (26)						X		X		X	X				
IF	iriforenin (29)								X	X						
IFG	tectoridin (32)		X		X				X				X	X		
IFG	tectorigenin-4'-O-β-D-Glcp (33)			X										X		
IFG	irilone-4'-O-β-D-Glcp (37)					X			X		X					
IFG	germanasim B (38)					X					X					
IFG	germanasim A (42)					X			X							
IFG	iridin (43)				X				X		X					
IFG	germanasim E (51)					X					X					
IFG	tectorigenin-7-O-β-D-Glcp-4'-O-β-D-Glcp (54)													X	X	
Fu	tectochrysin (57)							X					X			
Fl	izalpinin (70)												X			X
Fl	irisflavone A (73)	X											X			
Fa	5,2'-dihydroxy-6,7-methylenedioxyflavanone (82)		X					X					X			
PE	irisoid A (88)	X											X			X
PE	irisoid B (89)	X											X			
PE	irisoid D (91)	X						X					X			

^aFlavonoid subclass codes: IF, isoflavone; IFG, isoflavone glycoside; Fu, flavone; Fl, flavone; Fa, flavanone; PE, peltoglyonoid.

^bStandard three-letter codes for monosaccharids are used; p = pyranoside.

genin-7-*O*- β -glucosyl-4'-*O*- β -glucoside(18) and some other known isoflavones and glucosylisoflavones by Singab *et al.* [29] It is noteworthy that they also isolated seven known iridal glycosides from the same species, which were obtained from the family Iridaceae for the first time [38].

4. CHEMOTAXONOMY OF *IRIS*

Despite the wide variety of natural flavonoids, the present work has shown that the majority of flavonoids isolated from *Iris* species, in which the regular examples (seen in Table 1 and Table 2) are all derivatives from the basic tricyclic structure of isoflavone or flavone with simple patterns of *O*-substitution and glycosylation, have some principal features. There are relatively common 5,7-di- or 5,6,7-tri-*O*-substitution pattern in the A-ring. Apparently, The most pronounced feature in this ring is 6,7-methylenedioxy substitution. Furthermore, in the B-ring they often possess 2'- or 4'-*O*-substitution, 2',3'-, 3',4'- or 4',5'-di-*O*-substitution and 3',4',5'-tri-*O*-substitution. These features may be of some chemotaxonomic significance, and the restricted occurrence of some of the compounds may be proposed as a taxonomic marker in the classification of *Iris* species. Table 3 summarizes the distribution of these chemical characters found in the isoflavone, isoflavone glycoside, flavone, flavonol, flavanone type compounds, in all members of *Iris* reported from 1999 to 2008. It can be concluded that isoflavones and their glycosides are the characteristic constituents of *Iris*, the most representative compounds including irilin B, tectorigenin, irilone, irigenin and tectoridin. Furthermore, according to Qin *et al.* in their study on the distribution pattern of isoflavones in rhizomes of *Iris* from China, most of the species containing isoflavone aglycones but not isoflavone glycosides belong to the subgenus *Limniris* [39]. This trend is corroborated by the present survey, with the subgenus *Limniris* species *Iris bungei*, *Iris lactea* and *Iris tenuifolia* containing isoflavone aglycones only.

Table 3 also gives data on the distribution of the modified flavonoids, peltogynoids, in the genus *Iris*. It shows the restricted occurrence of peltogynoids in the subgenus *Limniris* species, *Iris bungei*, *Iris cathayensis*, *Iris lactea*, *Iris songarica* and *Iris tenuifolia*, which may be proposed as a taxonomic marker. As peltogynoids are biologically more advanced group of metabolites, we also indicate that these species are relatively more advanced species than the other ones listed in Table 3.

Besides, 10 known flavonoids have been obtained from *Iris* for the first time during the reporting period, namely 5,3'-dihydroxy-2'-methoxy-6,7-methylenedioxyisoflavone (isoflavone) [30], 5,7,3'-trihydroxy-4',5',8-trimethoxyisoflavone(isoflavone) [40], acacetin-7-*O*- α -L-rhamnopyranosyl-(1 \rightarrow 6)- β -D-glucopyranoside(flavone glycoside) [31], rhamnocitrin(flavonol) [41], isorhamnetin-7-*O*- β -D-glucopyranoside(flavonol glycoside) [31], kaempferol-3-*O*- β -D-glucopyranoside(flavonol glycoside) [28], dihydroechinidin(flavanone) [36], 5,2'-dihydroxy-6,7-methylenedioxy-flavanone (flavanone) [30], 7-*O*-methylaromadendrin (dihydroflavonol) [43] and alpinone (dihydroflavonol) [8]. They also may be of some chemotaxonomic significance in the relationship between the genus *Iris* and other genera of the family Iridaceae.

5. BIOLOGICAL ACTIVITY OF *IRIS*

Plants produce a wide range of structurally complex bioactive molecules, allowing them rich sources of different types of medicine. Herbal medicine is still the primary health care for the most of the world population, mainly in the developing countries [42]. Many of the *Iris* species are used as traditional folk medicine, their crude extracts and individual phenolic metabolites have been searched to identify their biological activities between 1999 and 2008, which range from cytotoxicity to antibacterial, virucidal activities.

5.1. Cancer Chemotherapy and Chemopreventive Activities

In the course of searching for novel cytotoxic compounds which can be used in chemotherapy, Fang *et al.* screened several Traditional Chinese Medicine (TCM). Extracts of the rhizomes of *Iris tectorum* led to the isolation of two known flavonoids, 7-*O*-methylaromadendrin and tectorigenin, and four iridal-type triterpenes by bioassay-guided fractionation and isolation. The effects of these compounds on human cancer cell lines were evaluated [43].

The cytotoxicities of the isolated compounds against four human cancer cell lines (COR-L23, C32, MCF-7, HepG2) were evaluated by the sulphorhodamine B (SRB) assay, with genistein and luteolin as positive controls. In the present study Luteolin (a well-known cytotoxic flavonoid) was found to be the most cytotoxic compound with IG_{50s} of 11 μ M and 9.4 μ M against COR-L23 and HepG2, respectively. Broadly, the order of cytotoxicity for the four tested flavonoids was luteolin > 7-*O*-methylaromadendrin > genistein > tectorigenin. Of the six isolated compounds, tectorigenin was relatively non-cytotoxic with IG_{50s} higher than 100 μ M against various cancer cell lines. Genistein and tectorigenin are both isoflavonoids with low molecular weight (270 and 300, respectively)—they differ from each other only by the presence of one extra methoxyl group in tectorigenin. However, the cytotoxicity of genistein was around 200% higher than that of tectorigenin against various cancer cell lines. Therefore, the 6-methoxyl group in the A-ring is important to reduce the cytotoxicity in this series.

Cell cycle-specific inhibition and apoptosis induced by the isolated compounds were determined using flow cytometry with two sets of co-labelling systems: annexin V-FITC/propidium iodide and fluorescein diacetate/propidium iodide. After exposure to 7-*O*-methylaromadendrin, COR-L23 cells were significantly ($p < 0.001$) arrested in S phase at 60 μ M and 100 μ M, and it also showed dose-dependent apoptosis against COR-L23 cells. On the other hand, the percentage of cells in G₂/M phase gradually increased with the dose of tectorigenin from 50 μ M to 400 μ M. The accumulation of cells in G₂/M phase at 400 μ M of tectorigenin was significant ($p < 0.001$), but it did not demonstrate apoptotic effect against COR-L23 cells up to 1mM.

Wollenweber *et al.* isolated six known isoflavones, irisolidone, irisolidone 7-*O*- α -D-glucoside, irigenin, irilone, iriflogenin and iriskashmirianin, in their study of the constituents of rhizome extracts of *Iris germanica*, and the cancer chemopreventive potential of these compounds were also examined [10]. They were shown to be potent inhibitors of

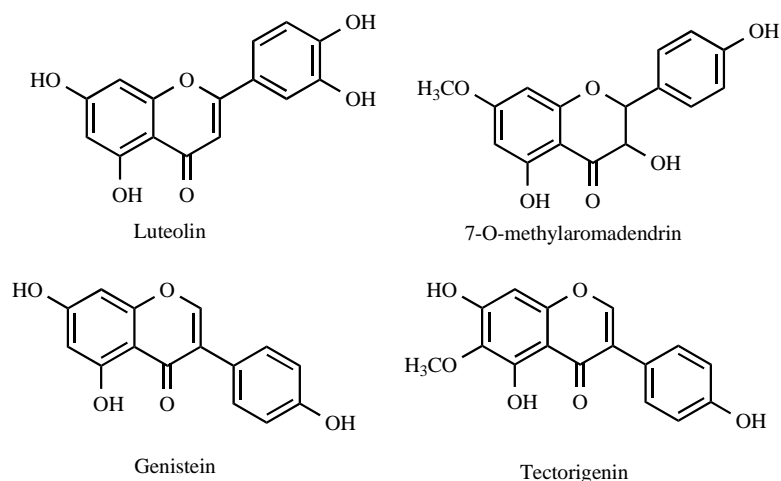


Fig. (11). Structures of the flavonoids tested on cytotoxicities in Section 5.1.

cytochrome P450 1A with IC_{50} values in the range 0.25–4.9 μ M. The isoflavones irigenin, irilone, and iriskashmirianin displayed moderate activity as inducers of NAD(P)H: quinone reductase (QR) in cultured mouse Hepa 1c1c7 cells, with CD values (concentration required to double the specific activity of QR) of 3.5–16.7 μ M, whereas weak activity was observed with iriflogenin and iriskashmirianin in the radical (DPPH) scavenging bioassay (IC_{50} values of 89.6 μ M and 120.3 μ M, respectively). With respect to anti-tumor promoting potential based on anti-inflammatory mechanisms, none of the compounds demonstrated significant activity in the concentration range tested.

5.2. Anti-Inflammatory and Anti-Neurodegenerative Activities

The anti-inflammatory activity of nine isoflavonoids isolated from an important folkloric medicinal plant *Iris germanica* was determined by a spectrophotometric assay using the activated human neutrophils [40]. It was important to note that the anti-inflammatory activities of compounds 5',5,7-trihydroxy-3',4',8-trimethoxyisoflavone, 5,7,3'-trihydroxy-6,4',5'-trimethoxyisoflavone, 5-hydroxy-4'-methoxy-6,7-methylenedioxyisoflavone, 5-methoxy-4'-hydroxy-6,7-methylenedioxyisoflavone, 5',5,7-trihydroxy-4',6-dimethoxyisoflavone, and 5,7,5'-trihydroxy-6,4'-dimethoxyisoflavone were significant when compared with aspirin and indomethacin, clinically used anti-inflammatory drugs. These active members of this group adds into the growing number of non-steroidal anti-inflammatory agents.

Conforti *et al.* described for the first time the *in vitro* properties (anti-neurodegenerative activity) of *Iris pseudopumila* flower and rhizome extracts and their constituents [44]. Methanolic extracts of the rhizomes showed significant anti-inflammatory activity through inhibition of NO production in the murine monocytic macrophage cell line RAW 264.7. Among the isolated compounds, those which most effectively inhibited LPS-induced NO production were irisolidone and 7-methyl-tectorigenin-4'-*O*-[β -D-glucopyranosyl-(1 \rightarrow 6)- β -D-glucopyranoside], with IC_{50} values of 23.6 μ M and 29.4 μ M respectively. Isoorientin and isovitexin exhibited the most promising activity against acetylcholine

esterase (AChE) with IC_{50} values of 26.8 μ M and 36.4 μ M, respectively. The same compounds also exhibited higher activity against butyrylcholinesterase (BChE) than other isolated compounds with IC_{50} values of 31.5 μ M and 54.8 μ M, respectively. The authors concluded that isoorientin was the most potent inhibitor of both AChE and BChE.

5.3. Antioxidant and Antiradical Activities

A new flavanone, songaricol (**32**) and seven known flavonoids were isolated from rhizomes and roots of *Iris songarica*. Compounds songaricol (**32**), irilin B and irisoid A showed antioxidant activity, which inhibited the generation of reactive oxygen species (ROS) in PMA-induced HL-60 cells with IC_{50} values of 21, 9.25 and 3.75 μ g/mL, respectively [34]. The authors also determined the specificity of the antioxidant effect, with their cytotoxicity to HL-60 cells tested. No cytotoxicity of songaricol (**32**) was showed up to 31.25 μ g/mL; cytotoxicity was observed for irilin B and irisoid A at much higher concentrations than the concentration responsible for their antioxidant effect (IC_{50} = 31 and 32 μ g/mL irilin B and irisoid A, respectively), indicating that the antioxidant effect of irilin B and irisoid A was not due to their cytotoxic effect.

Chromatographic separation of methanolic extracts from *Iris pseudopumila* rhizomes led to the isolation of a new natural isoflavone glycoside (**13**) and a new flavone glycoside (**22**), along with other 13 known flavonoids. Isolated compounds were evaluated for their antioxidant activity on circulating human polymorphonuclear using the luminol-dependent chemiluminescence assay, with quercetin as a positive control [28]. The known compounds irilone 4'-*O*- β -D-glucopyranoside and kaempferol 3-*O*-[α -L-rhamnopyranosyl-(1 \rightarrow 6)- β -D-glucopyranoside] both inhibited whole blood chemiluminescence emission at all used concentrations (0.1–100 μ g/mL), which showed more significant antioxidant activity than the other isolated flavonoids and comparable, in the highest concentration (100 μ g/mL), to quercetin, a known antioxidant.

Choudhary *et al.* obtained a new benzil tenuifodione, a new isoflavone tenuifone (**2**), and 12 known compounds from the whole plant of *Iris tenuifolia*. Among the isolated

compounds, izalpinin, 5,7-dihydroxy-2',6-dimethoxyisoflavone and tenuifone (**2**) showed antiradical activity by reducing the stable DPPH radicals to the yellow colored diphenylpicrylhydrazine derivative, with IC_{50} values of 159.153 ± 4.492 , 293.939 ± 17.984 and $418.727 \pm 10.219 \mu M$, respectively [8]. The author also discussed the structure-activity relationship of these compounds. Flavonoids are known to possess antiradical activity by acting as hydrogen donor or chelating metals. The activity of flavonoids with polyhydroxylated substitution is based on the location of the hydroxyl substitution on the ring B. Hydroxyl substitution on the ortho position in the ring B yielded a lower activity as in irisone B, however additional hydroxylation on meta position of ring B enhanced the activity many fold (e.g. tenuifone, **2**). In case of irilin B and 5,7-dihydroxy-2',6-dimethoxy isoflavone, it was observed that a methoxy group at ortho position of ring B yielded a higher activity than hydroxylation at the same position as in irilin B. With methylenedioxy group in ring A, irisone B showed low activity. In addition, it was also observed that compound with conjugated double bond in ring C, as in izalpinin, had a higher antiradical activity than non-conjugated double bond at ring C as in alpinone.

5.4. Estrogenic Activity

The rhizomes and roots of *Iris songarica* yielded a new flavanonol, songaricol (**32**) and seven known flavonoids, which have been discussed in section 3.3 for their antioxidant activity. The author also tested the estrogenic activity of these compounds [34]. Ayamenin A, irilin B and the previously isolated irisone B were able to show estrogenic response (EC_{50} values of 305.5, 159.7 and 322.0 $\mu g/mL$) in yeast cells expressing human estrogen receptor (ER- α). The estrogenic activity of ayamenin A, irilin B and irisone B was much weaker compared to that of 17β -estradiol, with a % maximal 17β -estradiol response of 35.6%, 19.3% and 10.8% observed. The activities of the isolates were compared in the same assay with those of other flavonoids which have been reported as phytoestrogens [45]. The estrogenic activities of ayamenin A, irilin B and irisone B were comparable to those of kaempferol ($EC_{50} = 200.5 \mu g/mL$) and apigenin ($EC_{50} = 116.6 \mu g/mL$), but were weaker than the activities of narin-

genin, daidzein and genestein which produced a% maximal 17β -estradiol responses of 90.7%, 43.3% and 109.3%, respectively. In general, phytoestrogens are known to produce weak estrogenic responses in comparison to the synthetic estrogen 17β -estradiol but are considered beneficial for women's health [45]. The popularity of phytoestrogens as dietary supplements has been increasing and they have been the focus of research in recent years.

5.5. Cardiovascular Disease and Diabetes Chemotherapy Activities

Ethanollic extracts of *Iris germanica* rhizomes was investigated for hypolipidemic activity [46]. Two groups of Wistar rats were fed with high-fat diet, and ethanollic extracts of *Iris germanica* were administered orally in one group of rats, while the other received saline for 10 weeks. Results indicated that ethanollic extracts of *Iris germanica* significantly lowered the lipid components, especially the cholesterol and triglycerides. The author also tested cytotoxicity of the crude extracts by using human neutrophils-cell viability assay to assess its acceptability level in living system. And it was shown to be minimal at low doses.

α -glucosidase inhibitory activity of the compounds isolated from underground parts of *Iris bungei* was determined spectrophotometrically. A novel peltogynoid type compound named iris-6 was found to be active, and its IC_{50} value was $0.226 mM \pm 0.0059$, where standard (deoxynojirimycin) showed IC_{50} value of 0.3 mM [47]. The data suggest that iris-6 needs further investigation as a potential drug delaying glucose absorption in the gastrointestinal tract (GIT) which is an attractive mode of treatment for diabetes mellitus.

5.6. Virucidal, Antibacterial and Allelopathic Activities

Rajtar *et al.* evaluated the virucidal activity of the extracts from underground parts of *Iris flavissimal* [48]. The methanolic and methanol/H₂O extracts were found to be non-toxic to GMK cells at the concentration of 1 mg/ml and 2 mg/ml, respectively. Human enterovirus ECHO 9 was used for the evaluation of the virucidal activity of the extracts at the concentrations non-toxic to GMK cell cultures. The titre of the virus was estimated according to the Reed-Muench method [49]. The methanolic extracts decreased ECHO 9

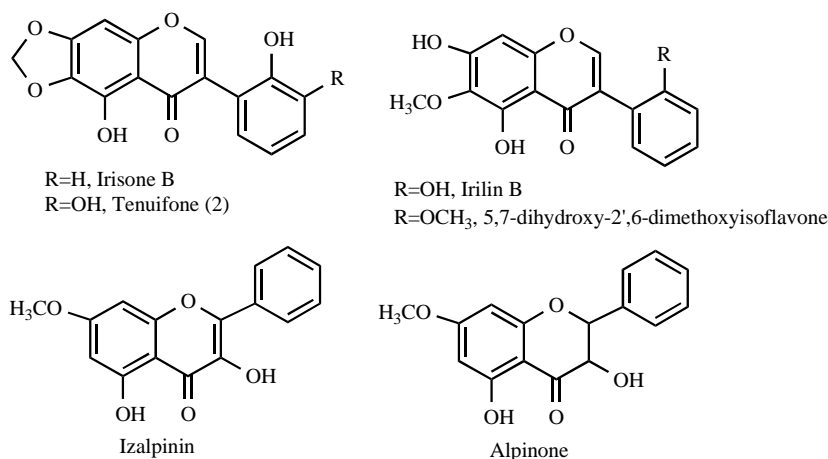


Fig. (12). Structures of the flavonoids tested on antiradical activities in Section 5.3.

Table 4. Species Checklist for Iris Flavonoids Reported from 1999-2008

Species	Tissue	Flavonoids ^a	Ref.
<i>I. bungei</i>	underground parts	IF 2, 4, 7, 18; F1 73-76; PE 88-92	[15, 20]
<i>I. cathayensis</i>	rhizomes and roots	IF 8, 11; IFG 32; FA 80, 82; PE 88	[36]
<i>I. carthaliniae</i>	rhizomes	IFG 32-34, 46, 52; FnG 62	[24]
<i>I. confusa</i>	rhizomes and roots	IF 8, 11; IFG 32, 43	[52]
<i>I. germanica</i>	rhizomes	IF 2, 4, 11, 19, 21, 23, 30; IFG 35, 37, 38, 42, 45, 51, 53, 55, 56, F1 72; Fa 81	[10, 25, 27, 33, 40]
<i>I. kumaonensis</i>	rhizomes	IF 8, 26; IFG 39	[55]
<i>I. lactea</i>	leaves	FnG 67, 68	[32]
	underground parts	IF 3, 5, 8, 10, 17; Fn 57; Fa 82; PE 88, 91	[30]
<i>I. leptophylla</i>	rhizomes	IF 11, 23, 24, 26, 29; IFG 32, 37, 40-43, 50	[26, 52]
<i>I. potaninii</i>	underground parts	IF 14, 21, 22, 28, 29, 31; IFG 44; DF 86	[22]
<i>I. pseudopumila</i>	flowers	FnG 61, 64, 66, 69	[44]
	rhizomes	IF 9, 11, 26; IFG 36-38, 43, 48, 49, 51; FnG 59, 60, 63, 77, 78	[28]
<i>I. soforana</i>	roots	IF 11, 13, 14, 20, 23, 24, 26, 27	[16]
<i>I. songarica</i>	leaves	IF 3, 8, 14; IFG 32; Fn 57, 58; FnG 65; F1 70; FIG 79; Fa 82; PE 88, 89, 91	[31]
	rhizomes and roots	IF 2-5, 25; F1 73; DF 87; PE 88; CC 94	[34, 54]
<i>I. spuria</i>	rhizomes	IF 8; IFG 32, 33, 47, 54; RO 93	[29]
<i>I. tectorum</i>	rhizomes	IF 1, 12; IFG 54; F1 71; DF 84, 85	[41, 43, 51]
<i>I. tenuifolia</i>	whole plant	IF 2, 3, 5, 6, 15, 16; F1 70; DF 83; PE 88	[8]

^aFlavonoid subclass codes: IF, isoflavone; IFG, isoflavone glycoside; Fn, flavone; FnG, flavone glycoside; F1, flavonol; FIG, flavonol glycoside; Fa, flavanone; DF, dihydroflavonol; PE, peltogynoid; RO, rotenoid; CC, coumaronochromone.

replication by 1.46 log, and methanol/H₂O extracts by 2.08log.

The methanolic extracts of rhizomes of *Iris pseudopumila* were tested for antibacterial and allelopathic activities [50]. The methanolic extracts of *Iris pseudopumila* showed good inhibition against all the bacterial strains tested (MIC between 7.8 and 250µg/ml), with the exception of *Staphylococcus aureus* that showed a MIC of 512µg/ml. The Gram(+) bacteria were not very sensitive to the extracts, and had the highest MICs; The Gram(-) bacteria were more sensitive, and in particular *Enterobacter aerogenes* and *Escherichia coli* showed greater sensitivity to the extracts. The allelopathic effect was tested against *Raphanus sativus* seed germination. A decrease in the percentage of seed germination and root and epicotyl growth was caused by the extracts, which was also dose dependently affected.

6. SPECIES CHECKLIST

Table 4 contains a checklist arranged by species for all *Iris* flavonoids reported from 1999 to 2008.

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