Chapter 4

Isoflavonoids

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Additional information is available at the end of the chapter

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Abstract

Isoflavonoids are interesting class of natural products due to their positive effects on human health. Isoflavonoids include isoflavones, isoflavanones, isoflavans, rotenoids and pterocarpans. Although they are reported from many plant families, most isoflavonoids are produced by the subfamily *Papilionaceae* of the Fabaceae. Various chromatographic methods have been applied for the purification of isoflavonoids. Simple Ultra Violet (UV) absorption spectra as well as both One and two dimensional NMR (1D- and 2D-NMR) are critical for the identification of isoflavonoids. Each class of isoflavonoids has its unique feature in both ^{1}H- and ^{13}C-NMR that enable their proper characterization. High Resolution Mass Spectrometry (HRMS) is a substantial tool in such challenge. *In vitro* experiments indicated that isoflavonoids possess antioxidant, antimutagenic, antiproliferative as well as cancer preventive effects. Epidemiological studies provide support for some of these effects on human. Members of this class also are reported to have antimicrobial activity. In this chapter, isoflavones, isoflavanones, isoflavans, homoisoflavonoids and isoflavenes will be discussed in relation to their occurrence, methods of purification, spectral characters helpful in structure elucidation as well as their biological importance.

Keywords: isoflavones, isoflavanones, isoflavans, homoisoflavonoids, isoflavenes

1. Introduction

Genstin (**1**) was the first isolated isoflavone from *Genista tinctoria* known as Dyer's Brrom in 1899 [1]. Later in 1926 [2], the structure was identified. Genstin (**1**) was isolated from Soybeans in 1941 [3]. Although the main source of isoflavonoids is member of the Fabaceae [4], some were reported from other families such as Amaranthaceae [5, 6], Rosacease [7] and Poaceae [8]. Isoflavonoids were also reported from fungi [9] and Propolis [10]. The dietary consumption of isoflavonoid-rich sources is linked with health advantages toward osteoporosis, post-menopausal symptoms, cardiovascular diseases and chemo-prevention [11]. People from SE

Asia have much lower risk of developing prostate cancer compared to Americans due to high consumption of soy rich in isoflavonoids. Upon immigration to the USA and changing the dietary components, this difference rapidly disappears [12]. Isoflavonoids are also classified as dietary antioxidants [13]. These facts were the driving force behind the use of isoflavonoid-rich sources as nutraceutical and dietary supplements [14].

Isoflavonoids are a large subclass of the most common plant polyphenols containing 15 carbon atoms known as flavonoids [15]. In isoflavonoids (3-phenylchromans), the phenyl ring B is attached to heterocyclic ring C at position 3 rather than 2 in flavonoids [16]. Generally, flavonoids are biosynthesised via Shikimic acid pathway. Shikimic acid is also a precursor for the biosynthesis of phenylpropanoids and aromatic acids. At certain stages, the activity of the key enzyme chalcone isomerase (CHI) resulted in the formation of flavanones that converted to isoflavonoids under the influence of isoflavone synthase [17]. The biosynthesis of isoflavonoids, consequently, is considered as an offshoot from the flavonoids biosynthetic pathway [18]. Highest level of isoflavonoids occurs usually in roots, seedlings and seeds [18, 19].

Isoflavonoids are sub-classified into many subclasses based on the oxidation status of ring C as well as the formation of a forth ring 'D' by coupling between rings B and C. Subclasses free from ring D include isoflavones, isoflavanones, isoflavan-4-ol, homoisoflavonoids, isoflavans and isoflav-3-ene. Rotenoids, pterocarpans, coumaronochromones and coumaronochromene represent the subclasses with additional ring D formation [11].

This chapter will deal with the different aspects of the isoflavonoid subclasses keeping the original three-ring skeleton (**Figure 1**). Occurrence, isolation, key spectroscopic characters and biological activities will be covered starting from 2000 to date.

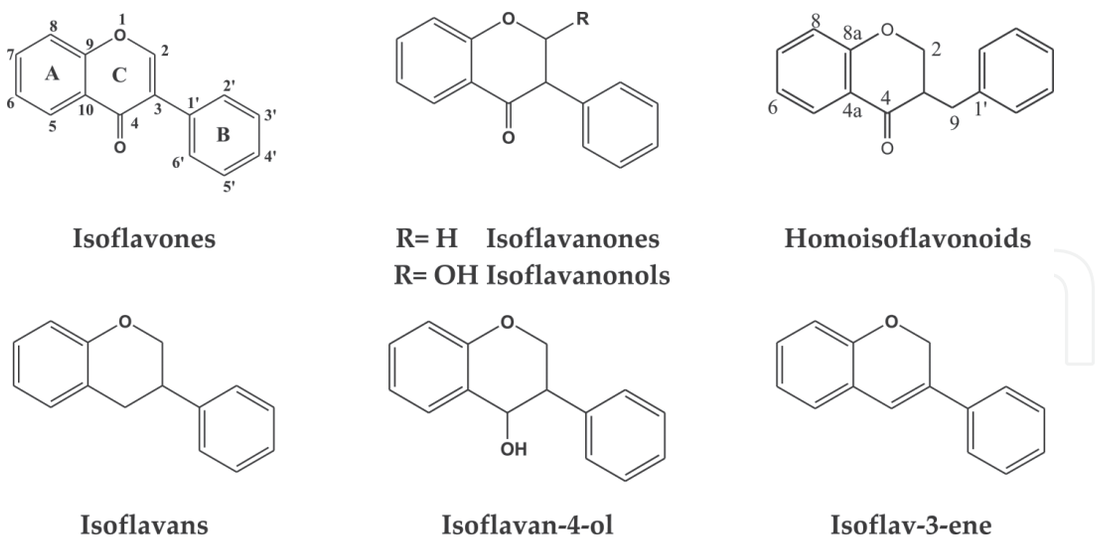


Figure 1. The skeletons of the isoflavonoids with three-ring structures.

2. Extraction and purification

The most popular method used for extraction of isoflavonoids is maceration with either MeOH or EtOH containing various percentages of H_2O at room temperature followed by liquid-liquid

fractionation using solvents with different polarities [6, 10, 19–32]. Another method of extraction used MeOH or EtOH under reflux or in soxhlet apparatus [5, 33–36]. Mixture of MeOH and $CHCl_3$ or CH_2Cl_2 (1:1) was also applied for extraction [37–41]. Other research groups extracted the plant materials with acetone [42–44], $CHCl_3$ [45, 46], CH_2Cl_2 [47–50] or diethyl ether [51] at room temperature. Successive extraction starting with petroleum ether or hexane, $CHCl_3$, EtOAc and MeOH using soxhelt apparatus [52–56] was also reported. The isoflavone contents of soybeans were extract using supercritical fluid extraction [57].

The majority of purification and isolation steps utilized silica gel in the form of column, Preparative Thin Layer Chromatography (PTLC) or Centrifugal Preparative Thin Layer Chromatography (CPTLC) [19, 21, 45]. Combination of silica gel and Sephadex LH-20 was also applied for isoflavonoid purification [6, 10, 54, 55]. In addition to silica gel, semi-preparative C_{18} High Performance Liquid Chromatography (HPLC) columns were used for final purification of isoflavonoids [23, 30, 31, 38, 48]. The polar *n*-butanol fraction of *Ononis serrata* was fractionated on C_{18} silica gel applying the Vacuum Liquid Chromatography (VLC) technique followed by normal silica gel column for purification of isoflavonoid glucosides [27]. Two isoflavenes were isolated from *Lespedeza homoloba* after chromatography on porous polymer gel Diaion followed by silica gel column. Final purification step was performed on preparative C_{18} HPLC column [36]. Isoflavonoids from *Iris germanica* were purified by silica gel VLC and CC, and final purification was achieved via LiChrolut EN/RP-18 solid phase extraction tubes [26]. High-speed counter-current chromatography (HSCCC) was applied for the purification of flavan glycoside and isoflavones from *Astragalus membranaceus*, the seeds of *Millettia pachycarpa* and soy flour [20, 58, 59]. Isolation and identification of isoflavanones, biflavanones and bisdihydrocoumarins were achieved using Liquid Chromatography- Mass Spectrometry (LC-MS), Liquid Chromatography- Solid Phase Extraction- Nuclear Magnetic Resonance (LC-SPE-NMR) and Electronic Circular Dichroism (ECD). In this method, MS of target compounds was measured directly in the LC effluent. For NMR analyses, the peaks were collected from 20 LC runs, loaded on SPE cartilages, dried with nitrogen gas and finally eluted with CD_3OD [32].

3. Spectroscopic identification

3.1. Infrared (IR) transmission spectra

Both phenolic hydroxyls and carbonyl groups are present in most of the isoflavonoid classes. However, the most characteristic feature of isoflavans and isoflavenes is the lack of carbonyl function bands. The absorption bands for the C-4 carbonyl in isoflavones and isoflavanones present in the range 1606–1694 cm^{-1} [9, 23–26]. Differentiation between isoflavones and isoflavanones from the position of C-4 carbonyl bands in the IR spectra is not achievable.

3.2. Ultra Violet (UV) absorption spectra

In spite of the tremendous advances in 2D-NMR and MS, the UV absorption spectra in MeOH and MeOH with shift reagent still can provide useful information for flavonoids identification. In all isoflavonoids except isoflavenes, ring B has no or little conjugation with the main chromophore composed of rings A and C. This fact is expressed as intense band II and diminished band I [60].

For isoflavones, band II shows absorption at λ_{max} 245–275 nm. Shift reagents can be used to detect hydroxylation at ring A. NaOAc induces 6–20 nm bathochromic shift as an indication of free 7-hydroxyl group. The 10–14 nm shift with $AlCl_3$/HCl is diagnostic for free 5-OH group. The absence of any shift with NaOMe is an evidence for the absence of free hydroxyls in ring A [19, 27, 28, 50, 60].

The UV spectra of about 28 published isoflavanone were reviewed. Band II absorption was found in the range 270–295 nm [5, 9, 23, 25, 29, 33, 39, 41, 43, 44, 47–50, 55, 61, 62]. Among these publications, only three used shift reagents with five isolated isoflavanones. Analysis of the obtained results revealed that $AlCl_3$ induced 17–23 nm bathochromic shift in band II due to the complex formed between C-4 carbonyl and C-OH groups. All the entitled compounds contain C-7 free hydroxyl groups, and NaOAc produced 34–37 nm bathochromic shift in band II [39, 47, 50]. However, more data are required to draw a solid conclusion.

The few available UV data of homoisoflavonoids showed band II absorption in the same range reported for isoflavanones [63].

Isoflavans UV spectra show one prominent maxima representing band II between 270 and 295 nm [21, 37, 38, 45]. The available UV data of isoflavenes indicated the presence of two bands at 235–245 and 320–337 nm along with a shoulder 287–300 nm [29, 30, 31, 35, 36].

3.3. Circular Dichroism (CD) Spectroscopy

Saturation of the double bond between C-2 and C-3 creates a new asymmetric center in the molecules. The orientation at these centers is in most cases determined from the CD spectra.

Isoflavanones show three absorption maxima at 200–240, 260–300 and 320–352 nm. Determination of the absolute configuration at C-3 is based on the n→π* carbonyl transition between 320 and 352 nm. The positive sign at this region is diagnostic for (3*R*) orientation with ring B having equatorial position. The coupling constant between the *trans*-diaxial $H2_\beta$ and H3 can confirm the equatorial orientation of ring B [64]. Optical inactivity of isoflavanones most probably is a result of racemization that can occur during extraction and purification [64]. The isolation of two racemic mixtures, 3*S*- and 3*R*-7-O-glucosyldiphysolones (**2, 3**) and (3*S*)- and (3*R*)-7,4′-di-O-glucosyldiphysolones (**4, 5**), from *Ormocarpum kirkii* was explained as result of isomerization in aqueous solution [32]. The same observation was reported in three isolated isoflavanones from *Platycelphium voënse* and *Desmodium canum* [41, 47]. Due to the positive cotton effect at 337 nm, the (3*R*) orientation was assigned to eryzerin B (**6**). However, eryzerin A (**7**) was reported in the same publication with undetermined absolute stereochemistry [44]. The (3*R*) orientation was also assigned to 2,3-dihydro-7-demethylrobustigenin (**8**) and saclenone (**9**) isolated from *Erythrina sacleuxii* based on the positive cotton effect at 320 and 334 nm, respectively [49].

Isoflavans configuration is much more complicated. The heterocyclic ring C is expected to have the half-chair form a fact that can be diagnosed from the vicinal coupling constants between H-2, H-3 and H-4 protons. Such *J* values along with the CD curves can then lead to determination of the absolute configuration [64]. (3*S*)-isoflavans with oxygenation at both the A and B rings display positive and negative cotton effects at 240 and 270–280 nm regions, respectively. The opposite was observed for the (3*R*)-enantiomers. The 7-deoxy (3*S*)-isoflavans

with mono- and di-oxygenation at ring B displayed negative cotton effects in both the 230–240 and 270–290 nm regions, and the opposite was observed for the (3*R*)-enantiomers [64]. The difficulty in assigning the absolute configuration of isofalvans was reflected by Bedane et al. [37]. The authors isolated two new isoflavans, erylivingstone J (**10**) and erylivingstone K (**11**). The measured CD spectrum showed negative cotton effect near 306 nm and a positive cotton effect near 240 nm supporting (*S*)-configuration. Three known compounds, 2′-methoxyphaseollinisoflavan (**12**), 7,4′-dihydroxy-2′,5-dimethoxy isoflavan (**13**) and 7,4′-dihydroxy-2′-methoxy-3′-(3-methylbut-2-enyl) isoflavan (**14**), with (*R*)-absolute configuration were isolated from the same source in this study. Suspicions about the purity of the new compounds and isolation of compounds with (*R*)-absolute configuration led the authors to report the new compounds without absolute configuration [37]. The enantiomer (3*S*) (+) 2′-*O*-methylphaseollidinisoflavan (**15**) was isolated from *Erythrina caffra* along with the (3*R*) (−) erythbidin A (**16**). The configuration was assigned based on ^{1}H-NMR *J* values, optical rotation and CD spectra. However, the reported CD data did not cover the lower range of the spectrum near 240 nm [45]. The absolute configuration of abruquinone L (**17**) was successfully assigned by combination of ^{1}H-NMR analyses of the *J* values between ring C protons and the CD spectrum which showed a strong positive cotton effect at 202 nm and two negative cotton effects at 212 and 233 nm [38]. Due to the positive cotton effect at 337 nm, the (3*R*) orientation was assigned to eryzerin C (**18**). However, eryzerin D (**19**) was reported with undetermined absolute stereochemistry [44].

In case of isoflavan-4-ol, C-4 becomes a new chiral center and 4 isomers could exist. Out of the possible isomers, two are *cis-* and two are *trans-*. Hata et al. synthesized and compared the CD spectra of four stereoisomers. The 3*R*, 4*S*-*trans*-isoflavan-4-ol stereoisomer showed negative cotton effect between 250 and 300 nm and positive cotton effect between 220 and 240 nm. The other 3*S*, 4*R*-*trans*-isoflavan-4-ol stereoisomer showed CD spectrum having cotton effect at the same ranges but with opposite sign. The 3*S*, 4*S cis*-isoflavan-4-ol stereoisomer expressed positive cotton effect between 245 and 300 nm, while the other enantiomer 3*R*, 4*R*-isoflavan-4-ol has a negative cotton effect at the same region [65].

3.4. Nuclear Magnetic Resonance (NMR) Spectroscopy

3.4.1. ^{1}H- and ^{13}C-NMR

^{1}H- and ^{13}C-NMR spectra provide key information for the identification of the isoflavonoids skeleton. The proton and carbon signals for positions 2–4 in ring C (**Table 1**) provide a unique feature for each class.

The simplest ring C spectrum is that of isoflavones as it shows only one downfield proton singlet for H-2. The oxygenated C-2 chemical shift is also characteristic for isoflavones. The wide range for C-4 carbonyl resulted from the effect of C-5 substitutions. The lack of C5 free hydroxyl resulted in the upfield shift of the C-4 carbonyl chemical shift to a value less than 175.0 ppm in most cases [27, 34]. With the presence of C-5 free hydroxyl and formation of hydrogen bond C-4 carbonyl, the carbonyl chemical shift value is usually above 180.0 ppm [19, 24, 28].

Saturation of the double bond between C-2 and C-3 of isoflavones leads to the formation of the isoflavanone skeleton. Such array contains a CH_2-O and CH-aryl and renders the

	Position 2		Position 3		Position 4	
	^{1}H	^{13}C	^{1}H	^{13}C	^{1}H	^{13}C
Isoflavones	7.82–8.45 s	150.9–155.0	–	121.5–125.5	–	173.9–181.5
Isoflavanones	4.46–4.76 (dd, ax) 4.34–4.63 (dd, eq)	69.6–72.3	3.93–4.32 (dd)	45.3–51.1	–	193.0–198.8
Homoisoflavonoids	4.06–4.32 (dd)	68.8–69.3	2.65–2.80 (m)	46.8–48.7	–	192.7–198.3
Isoflavans	4.33–3.83 (t, ddd, tdd, dt, dd)	69.2–71.2	3.36–3.55 (tdd, dd, dddd, m)	30.79–33.6	2.64–2.98 (dd, ddd)	26.1–31.9
Isoflavan-4-ol	4.21–3.60 (dd, t)	66.8–66.9	3.52–3.49 (ddd)	40.5–40.6	5.47–5.49 (d)	79.0–79.6
Isoflavenes	4.83–5.25 (s, d)	67.6–68.8	–	127.5–129.6	6.47–6.74 (s, d)	118.3–121.9

Table 1. Key ^{1}H- and ^{13}C-NMR spectral data for identification of isoflavonoid classes.

^{1}H-NMR signals of ring C more complex making an AMX spin system. The three protons appear as dd with different *J* values due to *ax-ax*, *ax-eq* and/or *eq-eq* splitting. In some cases, some signals may appear as *t* or interfere with other signals in the molecule [23, 41, 55, 61, 62]. Absolute configuration of isoflavanones was determined by a simple ^{1}H-NMR experiment in the presence of (*R*)- and (*S*)-binol as chiral solvating agent. The presence of (*R*)- or (*S*)-binol produces variable changes in the chemical shifts of the most downfield H-2 proton. Comparing these chemical shift changes enables the assignment of the absolute configuration [66].

No significant difference can be observed when the chemical shifts of positions 2–4 are compared in the ^{1}H-and ^{13}C-NMR spectra of isoflavanones and homoisoflavonoids. The splitting pattern of H-3 is expected to be much more complex. However, the additional C-9 in homoisoflavonoids provides the key evidence for their identification. The H-9 protons appear in the range of δ_H 2.62–3.13 (dd) as a result of coupling with H-3 proton. The C-9 methylene appears at δ_C 31.9–32.2 ppm [63, 67].

Isoflavans lacks the C-4 carbonyl present in isoflavanones with expected two more proton signals from ring C to form an ABMXZ spin system. Although the H-4 proton signals are more upfield compared to H-2 and H-3, the splitting pattern is more complex than the corresponding isoflavanones. This pattern along with the ^{13}C-NMR chemical shifts of C-2, C-3 and C-4 is the diagnostic feature for the isoflavan nucleus [20–22]. Isoflavan-4-ol is characterized by two oxygenated methines in both ^{1}H- and ^{13}C-NMR spectra.

Formation of double bond between C-3 and C-4 in isoflavans led to the emerging of the isoflav-3-ene class. The ring C ^{1}H-NMR signals of isoflavenes is simplified to two singlet for the 2H of C-2 and 1H of C-4. In some reports, a long-range coupling with small *J* value (1–2 Hz) was observed between H-2 and H-4 protons [35, 36, 43, 56].

3.4.2. 2D-NMR

^{1}H-NMR and different ^{13}C-NMR experiments like Distortionless Enhancement by Polarization Transfer (DEPT 45, DEPT 90 and DEPT 135) in most cases enable the identification of the

main skeleton of the isoflavonoids as well as the substitution pattern. Heteronuclear Single-Quantum Correlation (HSQC) experiment is applied to correlate protons and carbons through one bond. So, assignment of protons and carbons as CH_3, CH_2 and CH can be confirmed undoubtfully. ^{1}H-^{1}H-Correlation Spectroscopy (COSY) or similar experiments are applied to identify the spin systems in the compounds. These experiments identified protons separated by 3 bonds as well as different arrays present in the aromatic systems. The obtained COSY data allow the identification of the adjacent groups in the compounds and substitution pattern in the aromatic systems. Heteronuclear Multiple-Bond Correlation (HMBC) experiment acquired at different *J* values can identify correlation between protons and carbons through 2, 3 or sometimes 4 bonds especially in the aromatic systems. HMBC data play a key role in the determination of substituents location on the main skeleton. For example, the location of the furan ring in 4′-O-methylerythrinin C (**20**) at C-6 was assigned from HMBC correlations [28]. The location of the prenyl group at C-8 in erysubin F (**21**) was also assigned from correlations obtained from HMBC experiment [42].

Nuclear Overhauser Effect (NOE) is an effect observed between protons close to each other in space regardless to the number of bonds separating them [68]. The NOE effect can be clarified via One dimensional Nuclear Overhauser effect (1D-NOESY), Gradient-Enhanced Nuclear Overhauser Effect (GOESY) experiments or the now more favorable 2D-NOESY or Rotating Frame Nuclear Overhauser Effect (ROESY) experiments. The NOE effect is sometimes crucial for correct assignments of substitutions especially in the absence of significant UV data with shift reagents that can give information about OH group positions. The NOE effect in some situations is more decisive than HMBC due to the few number of correlations that can be observed and the fact that correlations are dependent on distance in space rather than direct bond correlations.

The positions of ring B substituents in lysisteisoflavanone (**22**) were assigned utilizing GOESY experiment where irradiation of the OCH_3 and H-1″ of the prenyl group resulted in enhancement in their neighboring protons [50]. The NOE enhancement experiment was utilized to determine the position of OCH_3 in olibergin B (**23**) [24]. Position of OCH_3 in platyisoflavanone B (**24**) [41], vestitol (**25**), lotisoflavan (**26**) [21], erypoegin D (**27**) [43] and eryzerin B (**6**) [44] was assigned based on NOESY experiment results. The NOESY experiment was also employed to determine the position of glucose in ormosinoside A (**28**) [25].

NOESY data were also utilized to analyse the relative stereochemistry of the isoflavanol pumilanol (**29**) ring C protons [46].

3.5. Mass Spectroscopy (MS)

Mass spectroscopy with different techniques and the great advances in instrumentation can provide accurately the molecular weight and the exact molecular formula. In addition, some common routes of fragmentation can provide additional evidences about the substitution pattern on both rings A and B. The mass fragments derived from a *retro*-Diels Alder (RDA) type cleavage give an idea about the substituent's on ring A and ring B as well (**Figure 2**). These MS fragments were used for the confirmation of ring A and ring B substitution pattern in the structure elucidation. Observation of MS ion fragments at *m*/*z* 177 and 153 as a result of *RDA* type cleavage followed by a hydrogen transfer indicated the location of two

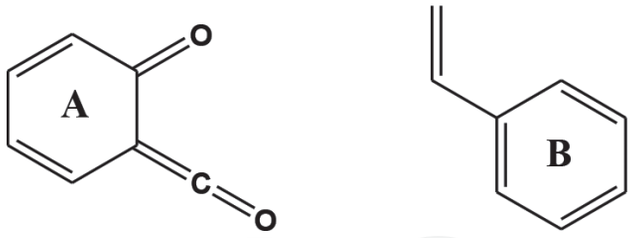


Figure 2. Main fragments of retro-diels–alder (RDA) type cleavage.

methoxyls and a hydroxyl group on the B ring of the isoflavone olibergin A (**30**) [24]. The placement of two hydroxyl group at ring A and methylenedioxy and one methoxyl at ring B in the structure of (±)5,7-dihydroxy-2′-methoxy-3′,4′-methylenedioxyisoflavanone (**31**) was confirmed by MS fragments [33]. (S)-Platyisoflavanone A (**32**) mass spectrum showed fragment at *m*/*z* 232 indicating two methoxyls and 3-methylbut-2-enyl group at ring B [41]. The base peak in the MS spectrum of uncinanone D (**33**) at *m*/*z* 194 [$C_{11}H_{14}O_3$] resulted from *retro*-Diels Alder (RDA) cleavage of ring C supported the presence of 3 methoxyl groups at ring B [48]. Similarly, the location of three methoxyl groups on ring B and two hydroxyl groups on ring A in the structure of the isoflavanone (±)5,7-Dihydroxy-2′,3′,4′-trimethoxy-isoflavanone (**34**) was supported by MS fragmentation [33]. The fragmentation of 5,7-Dihydroxy-2′,4′,5′-trimethoxyisoflavanone (**35**) generated mass fragments at *m*/*z* 153 corresponding with ring A with two hydroxyls and at *m*/*z* 194 for ring B with three methoxyls [39]. The location of the methyl group in desmodianone A (**36**), desmodianone B (**37**), desmodianone D (**38**), desmodianone E (**39**) and 6-methyltetrapterol A (**40**) at C-6 was confirmed from the MS fragment at *m*/*z* 167 for A-ring [47]. The MS fragments at *m*/*z* 346 [508−163+H]$^+$ and 194 indicated the presence of a sugar moiety in the A ring and three methoxyl groups in the B ring in the structure of 5,7-dihydroxy-2′,3′,4′-trimethoxy-isoflavanone 7-O-β-glucopyranoside (**41**) [33]. With a fragment 30 mass units less at *m*/*z* 164 in the spectrum of 5,7-Dihydroxy-2′,4′-dimethoxy-isoflavanone 7-O-β-glucopyranoside (**42**), only two methoxyls were assigned to ring B and sugar was placed on ring A [33].

In addition to providing the M+ at 328 *m*/*z* of 2-methoxyjudaicin (**43**) the fragment at *m*/*z* 297 due to loss of the two methoxyls was very supportive for the structure since the MS spectrum of judaicin (**44**) show only fragment due to loss of one methoxyl group at C-2′. The MS data of judaicin 7-*O*-glucoside (**45**) and judaicin 7-*O*-(6″-*O*-malonylglucoside) (**46**) showed common ion at *m*/*z* 298 corresponding to the aglycone part after the loss of the glycosyl moieties at C-7 [30, 31].

4. Isolated compounds update

The isolated isoflavonoids from natural sources are presented in **Tables 2–6**, and their structures are provided in **Figures 3–7**. Isoflavones, isoflavanones and isoflavans from 2000 to date are arranged according to publication date in **Tables 2–4**, respectively. Due to the limited number of isoflavenes, the current survey includes all isolated members available in the literature (**Table 5**). Synthetic compounds are not included in this chapter.

Name	Source	Ref.
2,3-Dehydrokievitone (**47**)	*Erythrina sacleuxii*	[49]
5′-Prenylpratensein (**48**)	*Erythrina latissima*	[39]
Erysubin F (**21**)	*Erythrina suberosa*	[42]
6″-*O*-Malonylgenistin (**49**)	*Glycine max*	[59]
Irisolone (**50**)	*Polygala stenopetala*	[69]
Isoerysenegalensein E (**51**), Alpinumisoflavone (**52**), Wighteone (**53**)	*Erythrina lysistemon*	[50]
2″,6″-O-Diacetyloninin (**54**)	*Glycine max*	[70]
Isoprunetin 7,4′-di-O-*β*-D-glucopyranoside (**55**) Genistein 7,4′-di-O-*β*-D-glucopyranoside (**56**)	*Genista morisii*	[54]
Genistein (**57**)	*Desmodium uncinatum*	[62]
Olibergin A (**30**), Olibergin B (**23**), Genistein (**57**), Formononetin (**58**) Biochanin A (**59**)	*Dalbergia oliveri*	[24]
Rothindin(**60**)	*Ononis serrata*	[27]
4′-*O*-Methylerythrinin C (**20**), 4′-*O*-Methylalpinumisoflavone (**61**) 4′-*O*-Methyl-2″-hydroxydihydroalpinumisoflavone (**62**) 7-O-Methylbiochanin A (**63**)	*Lotus polyphyllos*	[28]
Genistin (**1**), Genistein (**57**), Daidzein (**64**), Daidzin (**65**) Glycitein (**66**), Glycitin (**67**)	*Semen sojae praeparatum*	[71]
7-O-Geranylbiochanin A (**68**)	*Tephrosia tinctoria*	[72]
Olibergin B (**23**), Biochanin A (**59**), 8-C-Geranyl-7-O-methylbiochanin A (**69**)	*Dalbergia paniculata*	[73]
Biochanin A (**59**), 6-Hydroxy-7,4′-dimethoxyflavone (**70**) 6,7,4′-Trimethoxyflavone (**71**)	*Gynerium sagittatum*	[8]
4′-O-Methylderrone (**72**)	*Lotus polyphyllos*	[19]
4′,5′-Dimethoxy-6,6-dimethylpyranoisoflavone (**73**)	*Millettia pachycarpa*	[58]
Erypoegin D (**27**), Alpinumisoflavone (**52**), Wighteone (**53**) 5,4′-Dihydroxy-7-methoxy-3′-(3-methylbuten-2-yl)isoflavone (**74**) 5,2′,4′-Trihydroxy-7-methoxy-5′-(3-methylbuten-2-yl)isoflavone (**75**) 5,4′-Dihydroxy-7-methoxy-3′-(3-methyl-2-hydroxybuten-3-yl) isoflavone (**76**) 3′-Formyl-5,4′-dihydroxy-7-methoxyisoflavone (**77**) 5-Hydroxy-3″-hydroxy-2″,2″dimethyldihydropyrano[5″,6″:3′,4′] isoflavone (**78**) 3′-Isoprenylgenistein (**79**), Isolupabigenin (**80**)	*Erythrina poeppigiana*	[74]
Genistein (**57**), Formononetin (**58**), Biochanin A (**59**), Calycosin (**81**) Ononin (**82**), Sissotrin (**83**)	*Cicer arietinum*	[75]
Tlatlancuayin (2′,5-dimethoxy-6,7-methylenedioxyisoflavone) (**84**)	*Iresine herbstii*	[5]
2′-Hydroxygenistein (**85**), 3′-Omethylorobol (**86**) 7-O-Methyltectorigenin (**87**), Prunetin (**88**), Licoagroisoflavone (**89**) Cajanin (**90**), Lachnoisoflavone A (**91**)	*Crotalaria lachnophora*	[76]

Name	Source	Ref.
Pierreione A (**92**), Pierreione B (**93**), Pierreione C (**94**), Pierreione D(**95**)	*Antheroporum pierrei*	[77]
Genistein 5-*O*-*β*-glucopyranoside (**96**), Prunetin 5-*O*-*β*-glucopyranoside (**97**)	*Potentilla astracanica*	[7]
Erysubin F (**21**), Erythraddison I (**98**), Erythraddison II (**99**) Echrenone b10 (**100**)	*Erythrina addisoniae*	[23]
Ormosinosides A (**28**), Genistein (**57**), Biochanin A (**59**), Daidzein (**64**) Daidzin (**65**), Sissotrin (**83**), 7-O-Methylbiochanin A (**63**) Isoformononetin (**101**), 4′,7-Di-O-methyldaidzein (**102**), Isoprunetin (**103**) Sophoricoside (**104**), Isoprunetin-7-O-*β*-D-glucoside (**105**) 6″-*β*-D-Xylose-genistin (**106**)	*Ormosia henryi*	[25]
Genistein (**57**),Biochanin A (**59**), Daidzein (**64**) 3′-Hydroxydaidzein-7-O-glucopyranoside (**107**) Calycosin-7-O-glucopyranoside (**108**)	*Trifolium scabrum*	[78]
5,6-Dihydroxy-7,8,3′,5′-tetramethoxyisoflavone (**109**)	*Iris pseudacorus*	[79]
Formononetin (**58**), Ononin (**82**), Calycosin (**81**) Calycosin-7-O-glucopyranoside (**108**)	*Astragalus mongholicus*	[80]
Formononetin (**58**)	*Dalbergia oliveri*	[53]
Genistein (**57**), Biochanin A (**59**), Calycosin-7-O-glucopyranoside (**108**)	*Dalbergia odorifera*	[81]
Neobavaisoflavone (**110**)	*Erythrina excels*, *Erythrina senegalensis*	[40]
Biochanin A (**59**)	*Dothideomycetes fungus CMU-99*	[9]
Neoraudiol (**111**)	*Neorautanenia mitis*	[52]
Genistin (**1**), Daidzein (**64**), Daidzin (**65**), Puerarin (**112**)	*Pueraria lobata*	[34]
Formononetin (**58**), Ononin (**82**), 3-(4-(Glucopyranosyloxy)-5-hydroxy-2-methoxyphenyl)-7-hydroxy-4H-chromen-4-one (**113**)	*Ononis angustissima*	[82]
7,2′,5′-Trimethoxy-3′,4′-methylenedioxyisoflavone (**114**) 6,7-Dimethoxy-3′,4′-methylenedioxyisoflavone (**115**) 5,4′-Dihydroxy-7,2′,5′-trimethoxyisoflavone (**116**)	*Piscidia carthagenensis*	[83]
Isosideroxylin (**117**)	*Leiophyllum buxifolium*	[84]
Achyranthoside A (**118**), Achyranthoside B (**119**)	*Achyranthes bidentata*	[6]
Genistein (**57**), Biochanin A (**59**), Prunetin (**88**), Tectorigenin (**120**)	*Dalbergia odorifera*	[85]
8-Hydroxyirilone 5-methyl ether (**121**), 8-Hydroxyirilone (**122**) Irilone 4′-methyl ether (**123**), Irilone (**124**), Irisolidone (**125**) Irigenin S (**126**), Irigenin (**127**), Iridin S (**128**), Iridin (**129**) 4′-*O*-*β*-D-glucopyranoside (**130**)	*Iris germanica*	[26]

Table 2. Isolated isoflavones from natural sources since 2000 to date.

Name	Source	Ref.
(*R*)-2,3-Dihydro-7-demethylrobustigenin (**8**), (*R*)-saclenone (**9**)	*Erythrina sacleuxii*	[49]
5,7-Dihydroxy-2′,4′,5′-trimethoxyisoflavanone (**35**)	*Erythrina latissima*	[39]
Bolusanthol B (**131**), Bolusanthol C (**132**) 5,7,3′-Trihydroxy-4′-methoxy-5′-γ,γ-dimethylallylisoflavanone (**133**) 5,7,2′-Trihydroxy-4′-methoxy-6,5′-di(γ,γ-dimethylallyl)isoflavanone (**134**) 5,7,2′,4′-Tetrahydroxy-8,3′-di(γ,γ-dimethylallyl)-isoflavanone (**135**)	*Bolusanthus speciosus*	[86]
Lysisteisoflavanone (**22**)	*Erythrina lysistemon*	[50]
Seputheisoflavone (**136**)	*Ptycholobium contortum*	[87]
Dihydrodaidzin (**137**), Dihydrogenistin (**138**)	*Glycine max*	[70]
Erypoegin C (**139**), Erypoegin D (**140**)	*Erythrina poeppigiana*	[43]
Eryzerin B (**6**), Eryzerin A (**7**)	*Erythrina zeyheri*	[44]
Erypoegin G (**141**)	*Erythrina poeppigiana*	[61]
Cajanol (**142**)	*Crotalaria lachnophora*	[76]
7,4′-Dihydroxy-2′-methoxy-6-geranylisoflavanone (**143**) 2′,4′-Dihydroxy-6″-methyl-6″-(4‴-methylpent-3-enyl) pyrano(3″,2″:6,7)-isoflavanone (**144**)	*Lespedeza bicolor*	[88]
Desmodianone A (**36**), Desmodianone B (**37**), Desmodianone D (**38**) Desmodianone E(**39**), 6-Methyltetrapterol A (**40**)	*Desmodium canum*	[47]
Uncinanone A (**145**), Uncinanone B (**146**), Uncinanone C (**147**)	*Desmodium uncinatum*	[62]
(±)5,7-Dihydroxy-2′-methoxy-3′,4′-methylenedioxyisoflavanone (**31**) (±)5,7-Dihydroxy-2′,3′,4′-trimethoxy-isoflavanone (**34**) 5,7-Dihydroxy-2′,3′,4′-trimethoxy-isoflavanone 7-O-*β*-glucopyranoside (**41**) 5,7-Dihydroxy-2′-methoxy-3′,4′-methylenedioxyisoflavanone 7-O-*β*-glucopyranoside (**148**) 5,7-Dihydroxy-2′,4′-dimethoxy-isoflavanone 7-O-*β*-glucopyranoside (**42**) 5,7,4′-Trihydroxy-2′,3′-dimethoxy-isoflavanone 7-O-*β*-glucopyranoside (**149**)	*Desmodium styracifolium*	[33]
Uncinanone D (**33**), Uncinanone E (**150**)	*Desmodium uncinatum*	[48]
Ferreirin (**151**), Dihydrocajanin (**152**), Dalbergioidin (**153**) Dihydrobiochanin A (**154**)	*Gynerium sagittatum*	[8]
5,7-Dihydroxy-2′-methoxy-3′,4′-methylenedioxyisoflavanone (**31**) Uncinanone A (**37**), Dalbergioidin (**153**) 4′,5-Dihydroxy-2′,3′-dimethoxy-7-(5-hydroxyoxychromen-7yl)-isoflavanone (**155**), Parvisoflavanone (**156**), Isoferreirin (**157**)	*Uraria picta*	[55]
Dalhorridin (**158**), Dalhorridinin (**159**)	*Dalbergia horrida*	[89]
5,3′-Dihydroxy-4′-methoxy-5′-(3-methyl-1,3-butadienyl)-2″,2″-dimethylpyrano[5, 6:6,7]isoflavanone (**160**) 5,3′-Dihydroxy-5′-(3-hydroxy-3-methyl-1-butenyl)-4′-methoxy-2″,2″-dimethylpyrano[5, 6:6,7]isoflavanone (**161**)	*Erythrina costaricensis*	[90]
Sophoronol A (**162**), Sophoronol B (**163**), Sophoronol C (**164**) Sophoronol D (**165**), Sophoronol E (**166**), Sophoronol F (**167**)	*Sophora mollis*	[91]

Name	Source	Ref.
3-Hydroxy-kenusanone B (**168**), Sophoraisoflavanone A (**169**) Kenusanone H (**170**)	*Echinosophora koreensis*	[92]
Desmodianone F (**171**), Desmodianone G (**172**)	*Desmodium canum*	[93]
5,7,3′-Trihydroxy-4′-methoxy-6,5′-di(γ, γ-dimethylallyl)-isoflavanone (**173**) 5,3′-Dihydroxy-4′-methoxy-5′-γ,γ-dimethylallyl-2″,2″-dimethylpyrano[5, 6: 6,7]isoflavanone (**174**) 5,3′-Dihydroxy-2″,2″-dimethylpyrano[5, 6: 6,7]-2‴,2‴-dimethylpyrano[5, 6: 5,4]isoflavanone (**175**)	*Erythrina costaricensis*	[94]
Glabraisoflavanone A (**176**), Glabraisoflavanone B **(177)**	*Glycyrrhiza glabra*	[95]
Isodarparvinol B (**178**), Dalparvin (**179**), (3*S*)-Sativanone (**180**)	*Dalbergia parviflora*	[96]
2′,2,5-Trimethoxy-6,7-methylenedioxyisoflavanone (**181**)	*Iresine herbstii*	[5]
Erythraddison III (**182**), Erythraddison IV (**183**)	*Erythrina addisoniae*	[23]
Dalbergioidin (**153**)	*Lespedeza cyrtobotrya*	[29]
3(*R*)-2′-Methoxyl-5,7,4′-trihydroxy-6-(3-methylbut-2-enyl)-isoflavanone (**184**) 3′-Geranyl-3,5,7,2′,4′-pentahydroxyflavonol (**185**)	*Campylotropis hirtella*	[97]
Triquetrumone E (**186**), Triquetrumone F (**187**)	*Tadehagi triquetrum*	[98]
Hirtellanine H (**188**), Hirtellanine I (**189**), Hirtellanine J (**190**)	*Campylotropis hirtella*	[99]
Ormosinol (**191**)	*Ormosia henryi*	[25]
7-O-Glucosyldiphysolone (**2, 3**), (3*R*)-7,4′-Di-O-glucosyldiphysolone (**4**) (3*S*)-7,4′-Di-O-glucosyldiphysolone (**5**), 4″-hydroxydiphysolone (**192**)	*Ormocarpum kirkii*	[32]
Platyisoflavanone B (**24**), Platyisoflavanone A) (**32**) Platyisoflavanone C (**193**), Platyisoflavanone D (**113**) Sophoraisoflavanone A (**169**), Glyasperin F (**194**)	*Platycelphium voënse*	[41]
(+)-Violanone (**195**)	*Dalbergia oliveri*	[53]
(3*S*)-2′,4′-Dimethoxy-3,7-dihydroxyisoflavanone (**196**) (3*S*)-2′,4′,5′-Trimethoxy-7-hydroxyisoflavanone (**197**) (3*R*)-4′-Methoxy-2′,3,7-trihydroxyisoflavanone (**198**) (3*R*)-Violanone (**199**), (3R)-3′-O-methylviolanone (**200**) (3*R*)-Sativanone (**201**)	*Dalbergia odorifera*	[100]
Dalbergioidin (**153**) (3*R*) 5,7,3′,4′-Tetrahydroxy-2′-methoxyisoflavanone (**202**) (3*R*) 5′,8-Di-(γ,γ-dimethylallyl)-2′,5-dihydroxyl-4′,7-dimethoxyl-isoflavanone (**203**) 5,7-Dihydroxy-2′,4′-dimethoxyisoflavanone (**204**)	*Uraria clarkei*	[101]
Uncinanone E (**150**) 5,7-dihydroxy-2′-methoxy-3′,4′-methylenedioxy isoavanone (**155**) (3*R*) 7,2′,4′-Trihydroxy-3′-methoxy-5-methoxycarbonylisoflavanone (**205**) (3*R*) 7,2′-Dihydroxy-3′,4′-dimethoxy-5-methoxycarbonylisoflavanone (**206**)	*Cassia siamea*	[102]
Sigmoidin H (**207**)	*Erythrina excels*, *Erythrina senegalensis*	[40]
6,3′-di(3-hydroxy-3-methylbutyl)-5,7,2′, 4′-tetrahydroxyisoflavanone (**208**) 3(R)-6,3′-di(3-hydroxy-3-methylbutyl)-2′-methoxyl-5,7,4′-trihydroxyisoflavanone (**209**)	*Campylotropis hirtella*	[103]

Name	Source	Ref.
Uncinanone D (**33**), Desmodianone E (**144**), Desmodianone F (**171**) Grabraisoflavanone A (**176**) (3*R*)-7-Hydroxy-4′-methoxy-5-methoxycarbonyl-isoflavanone (**210**) (3*R*)-8-Hydroxy-4′-methoxy-7-methoxycarbonyl-isoflavanone (**211**) (3*R*)-7,2′,4′-Trihydroxy-3′-methoxy-5-methoxycarbonyl-isoflavanone (**205**)	*Desmodium oxyphyllum*	[104]
Glycitein (**66**), Dihydrodaidzein (**133**), Dihydrogenistein (**134**) Dothideoisoflavanone (**212**), (3*S*)-3,4′,7-trihydroxyisoflavanone (**213**)	Dothideomycetes fungus CMU-99	[9]
Neotenone (**214**)	*Neorautanenia mitis*	[52]
Eryvarins Y (**215**), Eryvarins Z (**216**), Orientanol E (**217**) 2,3-Dihydroauriculatin (**218**)	*Erythrina variegata*	[105]

Table 3. Isolated isoflavonones from natural sources since 2000 to date.

Name	Source	Ref.
5,7-Dimethoxy-3-(4-hydroxybenzyl)-4-chromanone (**219**) 5,6-Dihydroxy-7-methoxy-3-(4-hydroxybenzyl)-4-chromanone (**220**) 7-*O*-Methyl-3,9-dihydropunctatin (221) 5,7-Dihydroxy-3-(4-hydroxybenzyl)-4-chromanone (222)	*Drimiopsis burkei* *Drimiopsis maculata*	[63]

Table 4. Isolated homoisoflavonoids from natural sources since 2000 to date.

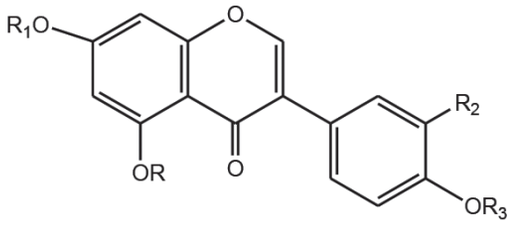
Name	Source	Ref.
Bolusanthol A (**223**)	*Bolusanthus speciosus*	[86]
Neocandenatone (**224**)	*Dalbergia congestiflora*	[22]
(3*R*)-(−)-7,2′-Dihydroxy-3′,4′-dimethylisoflavan-7-O-*β*-D-glucopyranoside (**225**)	*Astragalus membranaceus*	[20]
Eryzerin C (**18**), Eryzerin D (**19**)	*Erythrina zeyheri*	[44]
6-Desmethyldesmodian A (**226**), Desmodian A (**227**) Desmodian B (**228**), 6-Desmethylesmodian B (**229**) Desmodian C (**230**), 3′-Hydroxydesmodian B (**231**)	*Desmodium canum*	[106]
Pumilanol (**29**)	*Tephrosia pumila*	[46]
Salisoflavan (**232**)	*Salsola imbricata*	[107]
Desmodian A (**227**), Desmodian D (**233**)	*Desmodium canum*	[93]
3*S* (+) 2′-O-Methylphaseollidinisoflavan (**15**) 3*R*(-)Erythbidin A (**16**)	*Erythrina caffra*	[45]
Vestitol (**25**), Neovestitol (**234**)	Brazilian propolis	[10]
(3*S*,4*R*)-4′-Hydroxy-6,3′-dimethoxyisoflavan-4-ol (**235**)	*Taxus yunnanensis*	[108]
Cordifoliflavanes A (**236**), Cordifoliflavanes B (**237**)	*Codonopsis cordifolioidea*	[109]
Vestitol (**25**), Lotisoflavan (**26**)	*Lotus lalambensis*	[21]
Abruquinone A (**238**), Abruquinone D (**239**), Abruquinone J (**240**) Abruquinone K (**241**), Abruquinone L (**17**)	*Abrus precatorius*	[38]

Name	Source	Ref.
Erylivingstone J (**10**), Erylivingstone K (**11**) 2′-Methoxyphaseollinisoflavan (**12**) 7, 4′-Dihydroxy-2′,5′-dimethoxy isoflavan (**13**) 7,4′-Dihydroxy-2′-methoxy-3′-(3-methylbut-2-enyl) isoflavan (**14**)	*Erythrina livingstoniana*	[37]
Kotstrigoisoflavanol (**242**)	*Kotschya strigosa*	[110]

Table 5. Isolated isoflavans from natural sources since 2000 to date.

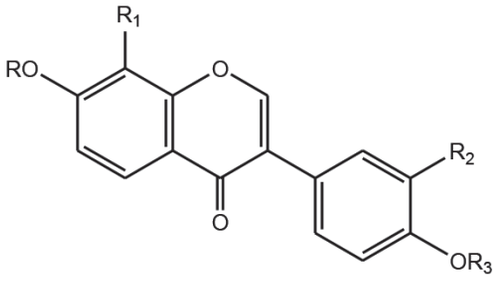
Name	Source	Ref.
Neorauflavene (**243**)	*Neorautanenia edulis*	[51]
Sepiol (**244**), 2′-O-Methylsepiol (**245**)	*Gliricidia speium*	[111]
Dimethoxytrihydroxyisoflavene (**246**)	*Baphia nitida*	[56]
Haginin A (**247**), Haginin B (**248**)	*Lespedeza cyrtobotrya*	[35]
7,3′,4′-Triacetoxy-6′-methoxyisoflav-3-ene (**249**) 7, 2′-Diacetoxy-4′-methoxyisoflav-3-ene (**250**)	*Millettia* sp.	[112]
2-Methoxyjudaicin (**43**)	*Cicer bijugum*	[30]
Judaicin (**44**), Judaicin 7-*O*-glucoside (**45**) Judaicin 7-*O*-(6″-*O*-malonylglucoside) (**46**)	*Cicer judaicum*	[31]
Haginin C (**251**), Haginin D (**252**)	*Lespedeza cyrtobotrya*	[113]
Haginin D (**253**), Haginin E (Phenoxodiol) (**254**)	*Lespedeza homoloba*	[36]
Erypoegin A (**255**), Erypoegin B (**256**)	*Erythrina poeppigiana*	[43]
Glabrene (**257**)	*Glycyrrhiza glabra*	[114]
Haginin A (**247**)	*Lespedeza cyrtobotrya*	[29]
Haginin E (Phenoxodiol) (**254**)	*Dothideomycetes* fungus CMU-99	[9]

Table 6. Isolated isoflavenes from natural sources.

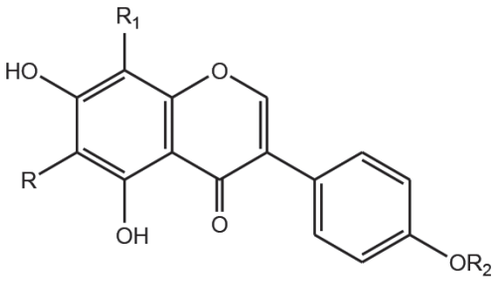


(1) R= R_2= R_3= H, R_1= Glucose
(28) R= Me, R_1= 6"-(β-D-Xylosyl)-glucopyranoside, R_2= R_3= H
(49) R= R_2= R_3= H, R_1= 6"-O-(Malonyl)-glucopyranoside
(55) R= Me, R_1= R_3= Glucose, R_2= H
(56) R= R_2= H, R_1= R_3= Glucose
(57) R= R_1= R_2= R_3= H
(59) R= R_1= R_2= H, R_3= Me
(63) R= R_2= H, R_1= R_3= Me
(68) R= R_2= H, R_1= Geranyl, R_3= Me
(74) R= R_3= H, R_1= Me, R_2 
(77) R= R_3= H, R_1= Me, R_2= Formyl
(79) R= R_1= R_3= H, R_2= Prenyl
(83) R= R_2= H, R_1= Glucose, R_3= Me
(86) R= R_1= R_3= H, R_2= OMe
(88) R= R_2= R_3= H, R_1= Me
(96) R= Glucose, R_1= R_2= R_3= H
(97) R= Glucose, R_1= Me, R_2= R_3= H
(103) R= Me, R_1= R_2= R_3= OH
(104) R= R_1= R_2= H, R_3= Glucose
(105) R= Me. R_1= Glucose, R_2= R_3= H
(106) R= R_2= R_3= H, R_1= 6"-(β-D-Xylosyl)-glucopyranoside

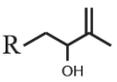
http://dx.doi.org/10.5772/intechopen.68701



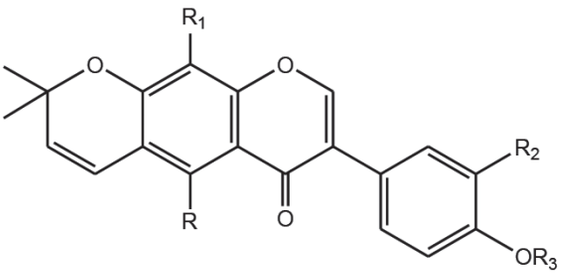
(**21**) R= R_3= H, R_1= R_2= Prenyl
(**69**) R= R_3= H, R_1= Geranyl, R_2= H
(**112**) R= R_2= R_3= H, R_1= Glucose



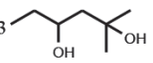
(**23**) R= H, R_1= Geranyl, R_2= Me

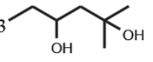
(**51**) R  , R_1= Prenyl, R_2= H

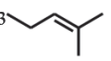
(**53**) R= Prenyl, R_1= R_2= H
(**120**) R= OMe, R_1= R_2= H

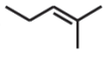


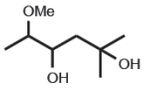
(**52**) R= OH, R_1= R_2= R_3= H
(**61**) R= OH, R_1= R_2= H, R_3= Me

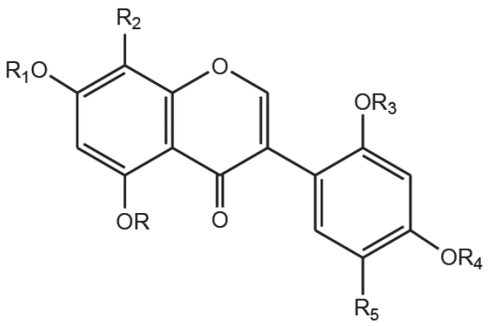
(**92**) R= R_2= OMe, R_1= H, R_3 

(**93**) R= R_1= H, R_2= OMe, R_3 

(**94**) R= R_2= OMe, R_1= H, R_3 

(**95**) R= R_1= H, R_2= OH, R_3 

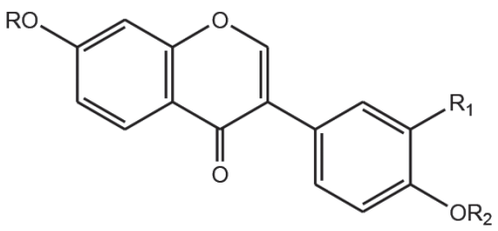
(**98**) R=OH, R_1  , R_2= R_3=H



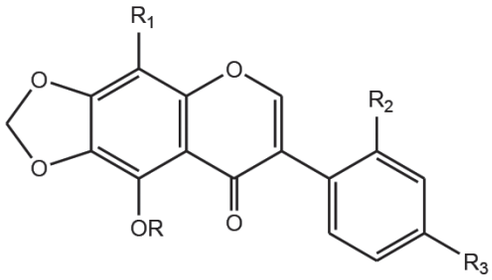
(**27**) R= R_2= R_4= H, R_1= R_3= Me, R_5= Prenyl
(**30**) R= R_1= R_2= R_4= H, R_3= Me, R_5= OMe
(**47**) R= R_1= R_3= R_4= R_5= H, R_2= Prenyl

(**75**) R= R_2= R_3= R_4= H, R_1= Me, , R_5 

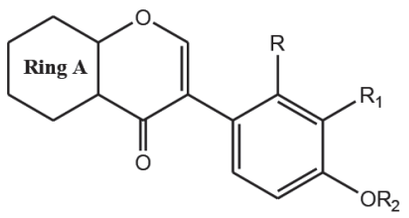
(**85**) R= R_1= R_2= R_3= R_4= R_5= H
(**109**) R= R_2= R_3= R_4= R_5= H R_1= Me
(**116**) R= R_2= R_4= H, R_1= R_3= Me, R_5= OMe



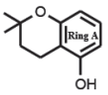
(**54**) R= 2", 6"-Diacetylglucoside, R_1= H, R_2= Me
(**58**) R= R_1= H, R_2= Me
(**64**) R= R_1= R_2= H,
(**65**) R= Glucose, R_1= R_2= H
(**81**) R= H, R_1= OH, R_2= Me
(**82**) R= Glucose, R_1= H, R_2= Me,
(**101**) R= Me, R_1= R_2= H
(**102**) R= R_2= Me, R_1= H
(**110**) R= R_2= H, R_1 



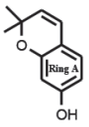
(**50**) R= Me, R_1= R_2= H, R_3= OH
(**84**) R= Me, R_1= R_3= H, R_2= OMe
(**121**) R= Me, R_1= R_3= OH, R_2= H
(**122**) R= R_2= H, R_1= R_3= OH,
(**123**) R= R_1= R_2= H, R_3= OMe
(**124**) R= R_1= R_2= H, R_3= OH
(**130**) R= R_1= R_2= H, R_3= O-Glucose



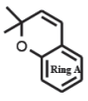
(**62**) R= R_1= H, R_2= Me



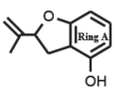
(**72**) R= R_1= H, R_2= Me



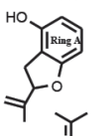
(**73**) R= H, R_1= OMe, R_2= Me



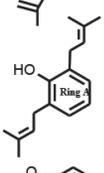
(**89**) R= R_1= R_2= H



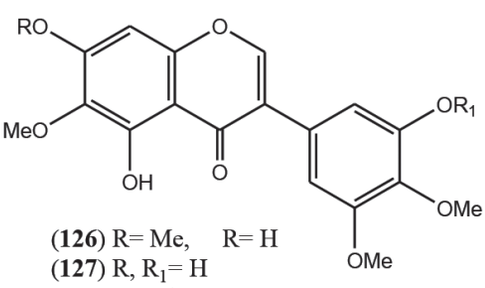
(**91**) R= OH, R_1= R_2= H



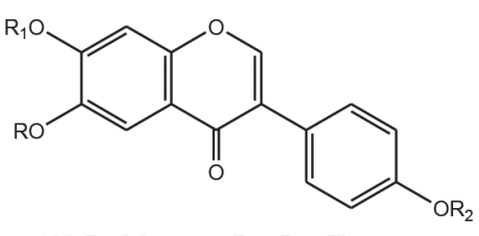
(**99**) R= OH, R_1= R_2= H



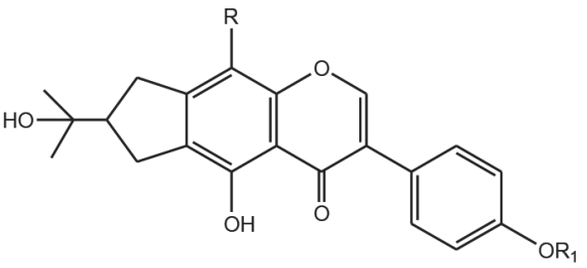
(**111**) R= R_2= H, R_1= OH



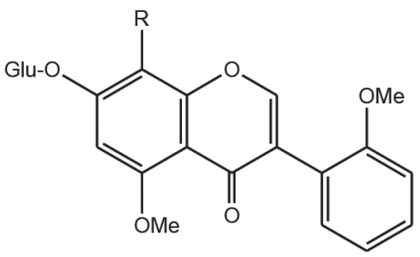
(**126**) R= Me, R= H
(**127**) R, R_1= H
(**128**) R= Glucose, R_1= Me
(**129**) R= Glucose, R_1= H



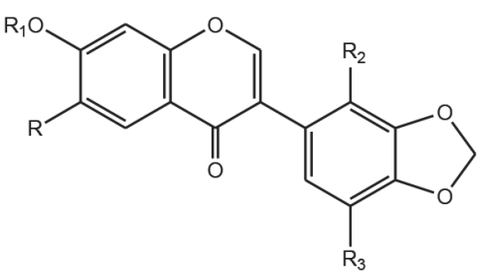
(**66**) R= Me, R_1= R_2= H
(**67**) R= Me, R_1= Glucose, R_2= H
(**70**) R= H, R_1= R_2= Me
(**71**) R= R_1= R_2= Me



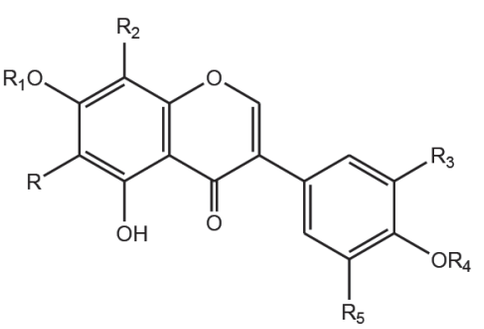
(**20**) R= H, R_1= Me
(**100**) R= Prenyl, R_1= H



(**118**) R= CH_2OMe
(**119**) R= OMe



(**60**) R= R_2= R_3 = H, R_1= Glucose
(**114**) R= H, R_1= Me, R_2= R_3 = OMe
(**115**) R= OMe, R_1= Me, R_2= R_3 = H



(**48**) R= R_1= R_2= R_4= H, R_3= Prenyl, R_5= OMe
(**80**) R= R_1= R_4= R_5= H, R_2= R_3= Prenyl
(**87**) R= OMe, R_1= Me, R_2= R_3= R_4= R_5= H
(**109**) R= OH, R_1= R_4= Me, R_2= R_3= OMe, R_5= H
(**117**) R= R_1= R_2= Me, R_3= R_4= R_5= H
(**125**) R= OMe, R_1= R_2= R_3= R_5= H, R_4= Me

Figure 3. Isolated isoflavones from natural sources since 2000 to date.

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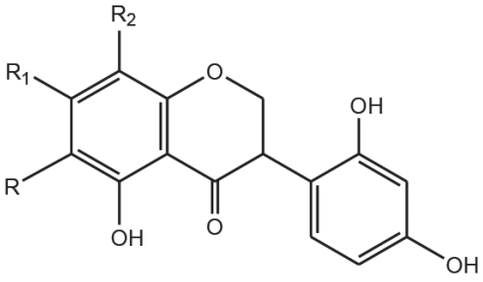
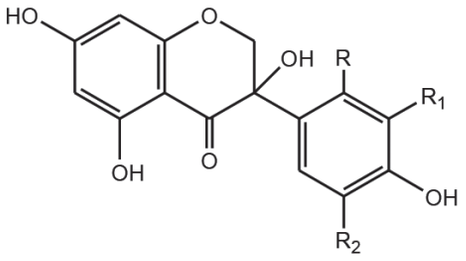
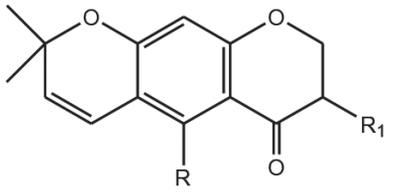
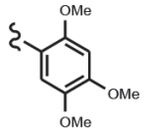


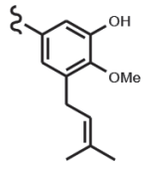
(**2,3**) R= Prenyl, R_1= O-Glucose, R_2 = H
(**145**) R= Prenyl, R_1= OH, R_2 = H
(**152**) R= R_2= H, R_1 = OMe
(**153**) R= R_2= H, R_1= OH
(**170**) R= H, R_1= OH, R_2 = Geranyl
(**184**) R= Prenyl, R_1= OH, R_2= H
(**192**) R= 4-Hydroxyprenyl, R_1= OH, R_2= H
(**217**) R= R_2= Prenyl, R_1= OH

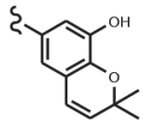


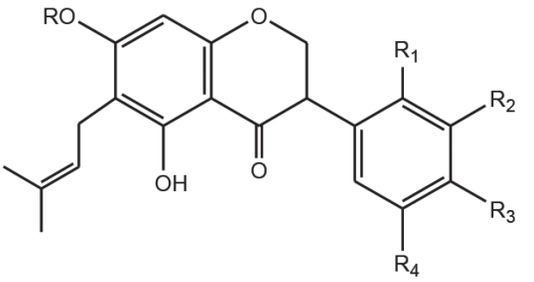
(**165**) R= OH, R_1= Prenyl, R_2= OH
(**185**) R= OH, R_1= Geranyl, R_2= H
(**212**) R= R_1= R_2= H



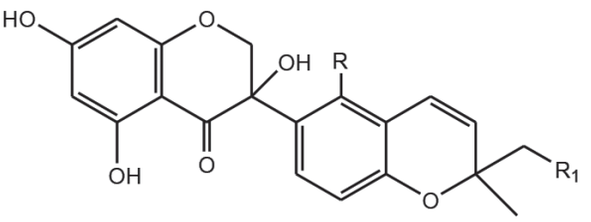
(**9**) R= OH, R_1 

(**174**) R= H, R_1 

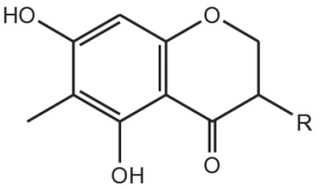
(**175**) R= H, R_1 

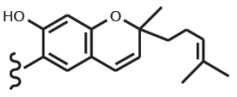


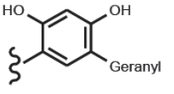
(**5**) R= Glucose, R_1= OH, R_2= R_4= H, R_3= O-Glucose
(**33**) R= R_4= H, R_1= R_2= R_3= OMe
(**132**) R= R_1=R_4= H, R_2= Prenyl, R_3= OH
(**134**) R= R_2= H, R_1= OH, R_3= OMe, R_4= Prenyl
(**135**) R= R_1= H, R_2= R_3=OH, R_4= Prenyl
(**173**) R= R_1= H, R_2= OH, R_3=OMe, R_4= Prenyl

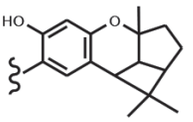


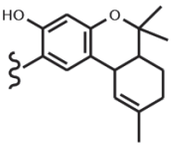
(**162**) R= R_1= H
(**163**) R= OOH, R_1= OH

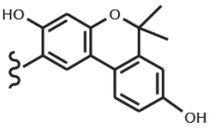


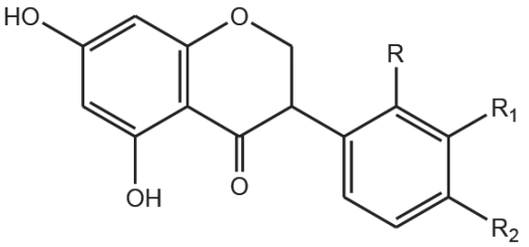
(**36**) R 

(**37**) R 

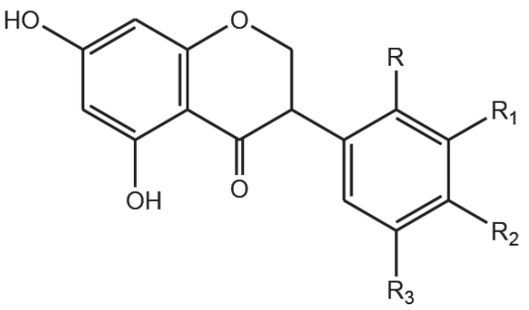
(**38**) R 

(**39**) R 

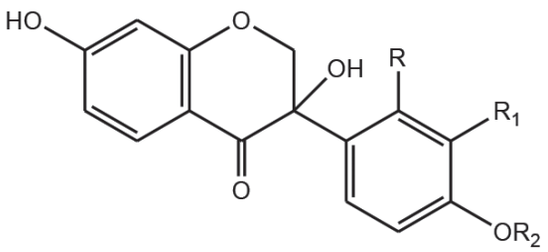
(**40**) R 



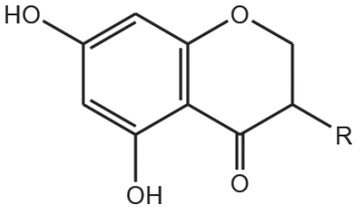
(31) R= OMe, R_1, R_2 = Methylenedioxy
(32) R= OMe, R_1= Prenyl, R_2= OMe
(24) R= OH, R_1= Prenyl, R_2= OMe
(34) R= R_1= R_2 = OMe
(137) R= R_1= H, R_2= OH
(151) R= OH, R_1= H, R_2= OMe
(154) R= R_1= H, R_2= OMe
(156) R= R_1= OMe, R_2= OH
(157) R= OMe, R_1= H, R_2= OH
(169) R= OMe, R_1= Prenyl, R_2= OH
(182) R= H, R_1= Prenyl, R_2= OMe
(202) R= OH, R_1= OMe, R_2= OH
(204) R= R_2= OMe, R_1= H

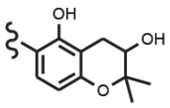


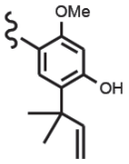
(8) R= R_2= R_3= OMe, R_1= H
(22) R= OH, R_1= H, R_2= OMe, R_3 = Prenyl
(123) R= H, R_1= Prenyl, R_2 = R_3= OH
(125) R= H, R_1= OH, R_2= OMe, R_3 = Prenyl
(131) R= OMe, R_1= H, R_2= OH, R_3 = Prenyl
(179) R= OMe, R_1= H, R_2= OMe, R_3= OH

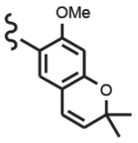


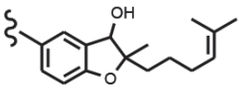
(178) R, R_1= OH, R_2= Me
(196) R= OMe, R_1= H, R_2= Me
(198) R= OH, R_1= H, R_2= Me
(213) R= R_1= R_2= H

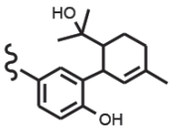


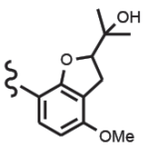
(113) R 

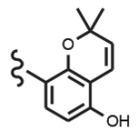
(136) R 

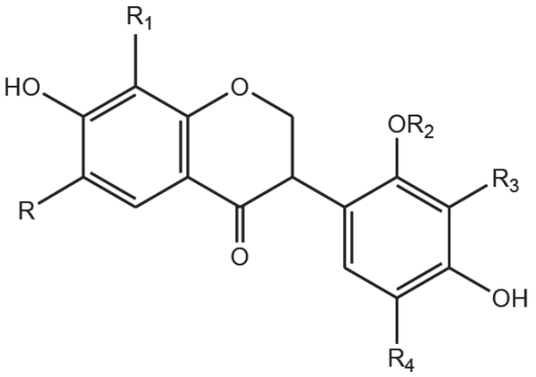
(183) R 

(188) R 

(190) R 

(193) R 

(194) R 



(6) R= R_1= Prenyl, R_2= R_3= R_4= H
(7) R= R_2= R_4= H, R_1= R_3= Prenyl
(191) R= R_1= R_4= Prenyl, R_2= R_3= H
(215) R= Prenyl, R_1= 2-Hydroxyprenyl, R_2= R_3= R_4= H
(216) R= 2-Hydroxyprenyl, R_1= Prenyl, R_2= R_3= R_4= H

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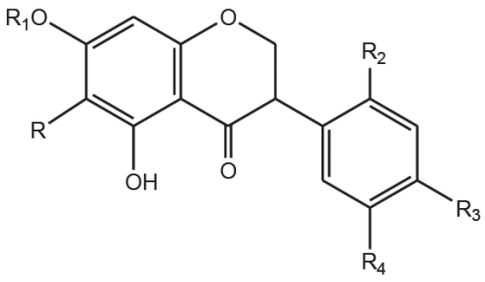
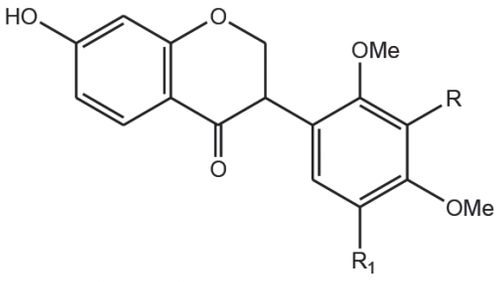
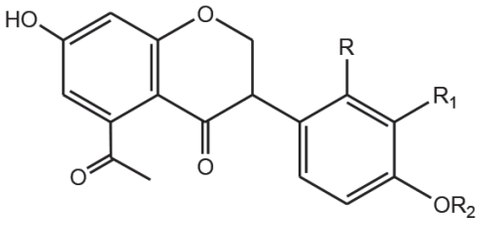


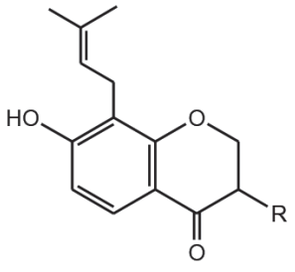
(**35**) R= R_1= H, R_2= R_3=R_4= OMe
(**138**) R= R_2= R_4= H, R_1= Glucose, R_3= OH
(**142**) R= R_4= H, R_1=Me, R_2= R_3= OMe
(**143**) R= Geranyl, R_1= R_4= H, R_2= OMe, R_3= OH
(**150**) R= R_1=Me, R_2= OMe, R_3=OH, R_4= H

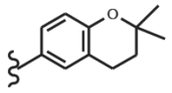


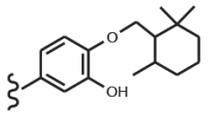
(**180, 201**) R= R_1= H
(**195, 199**) R= OH, R_1= OH
(**197**) R= H, R_1= OMe
(**200**) R= OMe, R_1= H

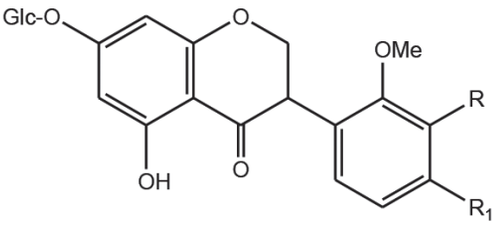


(**205**) R= OH, R_1= OMe, R_2= H
(**206**) R= OH, R_1= OMe, R_2= Me
(**210**) R= R_1= H, R_2= Me

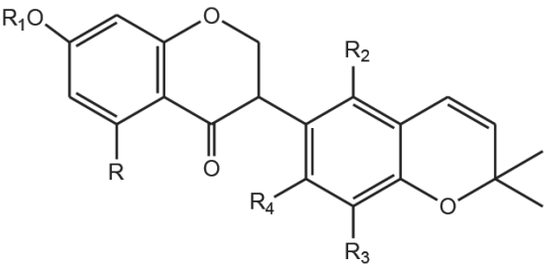


(**176**) R 

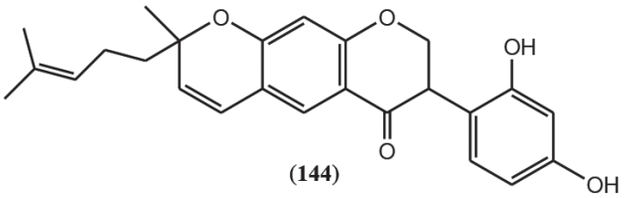
(**177**) R 



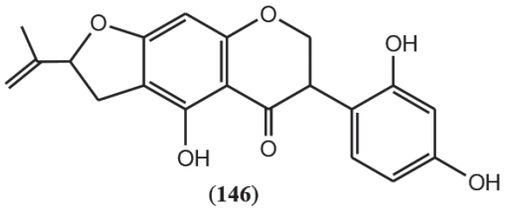
(**41**) R= R_1= OMe
(**42**) R= H, R_1= OMe
(**148**) R, R_1= Methylenedioxy
(**149**) R= OMe, R_1= OH



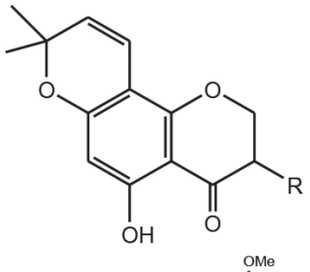
(**141**) R= OH, R_1= Me, R_2= R_3=H, R_4= OMe
(**189**) R= R_1= R_3= H, R_2= OMe, R_4= OH
(**207**) R= R_1=R_2=R_3= H, R_4= OMe

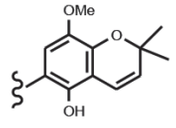


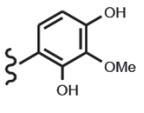
(**144**)



(**146**)



(**186**) R 

(**187**) R 

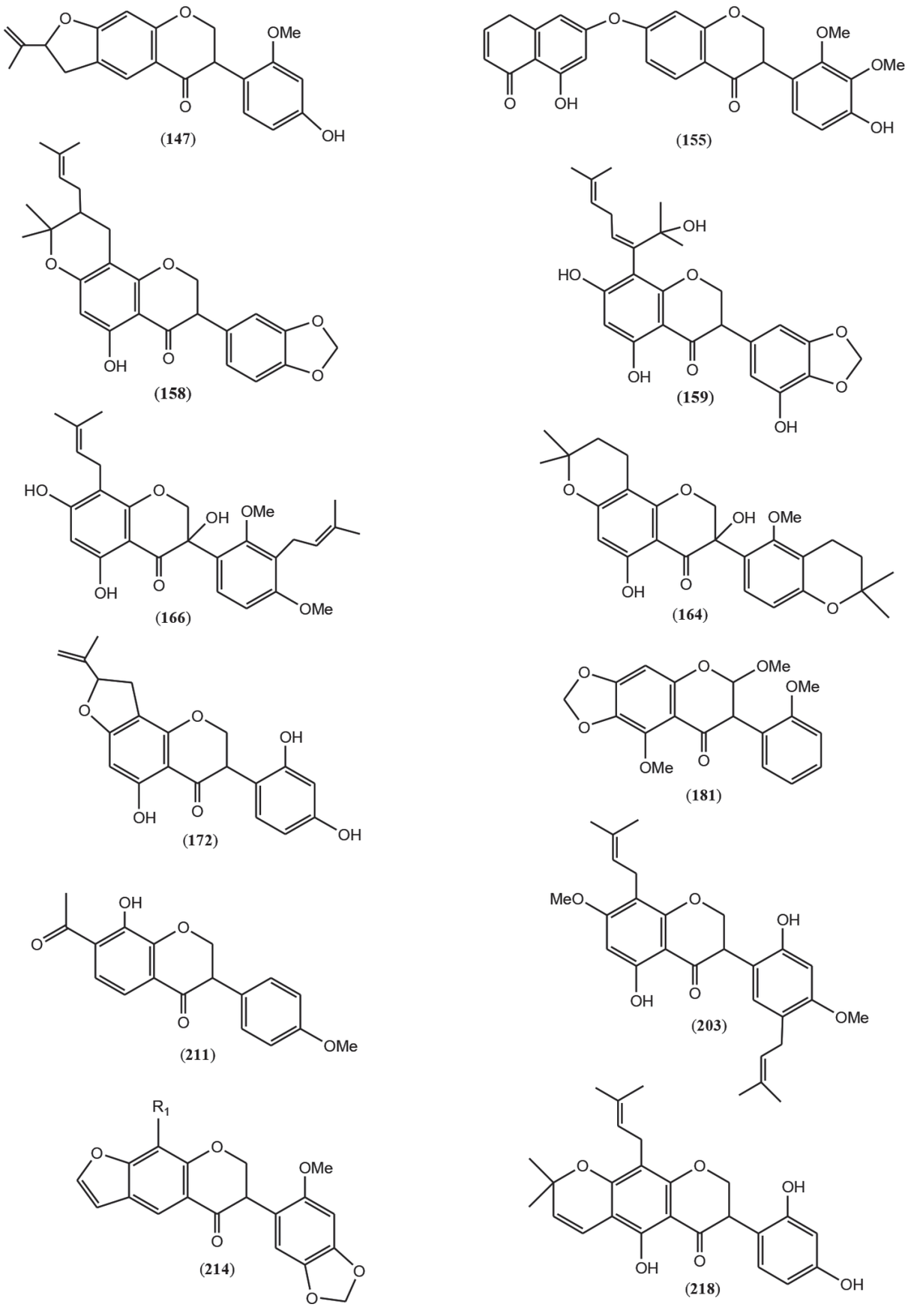
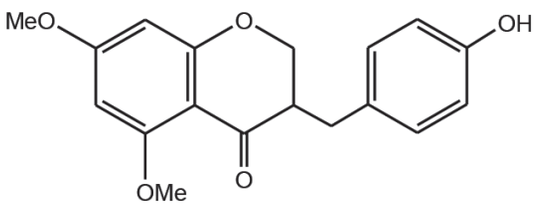
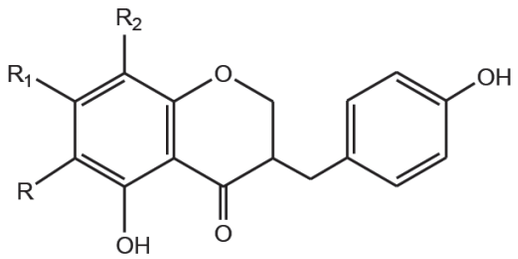


Figure 4. Isolated isoflavanones from natural sources since 2000 to date.

http://dx.doi.org/10.5772/intechopen.68701

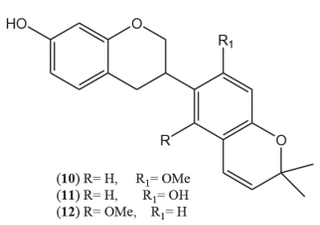


(**219**)

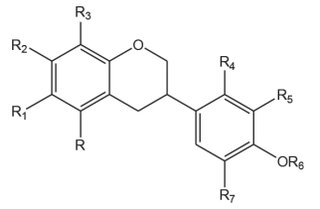


(**220**) R= OH, R_1= OMe, R_2= H
(**221**) R= H, R_1= R_2= OMe
(**222**) R= R_2=H, R_1= OH

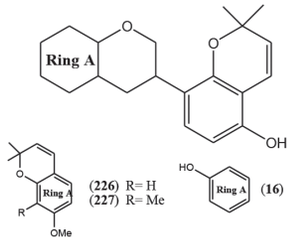
Figure 5. Isolated homoisoflavonoids from natural sources since 2000 to date.



(**10**) R= H, R_1= OMe
(**11**) R= H, R_1= OH
(**12**) R= OMe, R_1= H

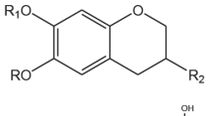


(**13**) R= R_1= R_3= R_5= R_6= H, R_2= OH, R_4= R_7= OMe
(**14**) R= R_1= R_3= R_6= R_7= H, R_2= OH, R_4= OMe, R_5= Prenyl
(**15**) R= R_1= R_3= R_6= R_7= H, R_2= OH, R_4= OMe, R_5= Prenyl
(**17**) R= R_3=H, R_1= R_5= OMe, R_2 = R_4= R_7= OH, R_6= Me
(**18**) R= R_5= R_6= R_7= H, R_1= R_3= Prenyl, R_2= R_4= OH
(**25**) R= R_1= R_2= R_3= R_5= R_7= H, R_4= OH, R_6= Me
(**26**) R_1= R_3= R_5= R_6= R_7= H, R= R_2 = OMe, R_4= OH
(**225**) R= R_1= R_3= R_7= H, R_2= R_4= OH, R_5= OMe, R_6= Me
(**234**) R= R_1= R_3= R_5= R_6= R_7= H, R_2= OMe, R_4= OH



(**226**) R= H
(**227**) R= Me

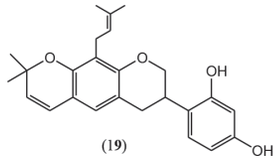
(**16**)



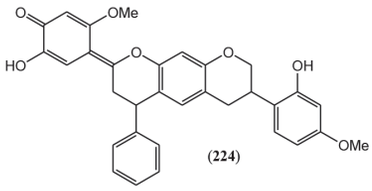
(**29**) R= Me R_1= H R_2

(**223**) R-R_1 = CH_2 R_2

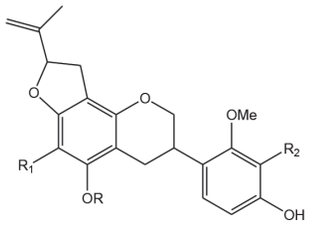
(**242**) R-R_1 = CH_2 R_2



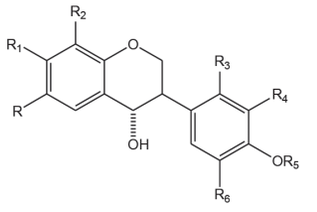
(**19**)



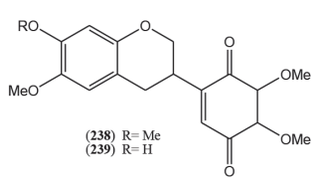
(**224**)



(**228**) R= R_1= Me, R_2= H
(**229**) R= R_2= H, R_1= Me
(**231**) R= R_1= Me, R_2= OH



(**232**) R= R_4= R_ R_5= R_6= H, R_1= OH, R_2= OMe
(**235**) R= OMe, R_1= R_2= R_3= R_5= R_6= H, R_4= OMe
(**236**) R= R_2= R_4= R_5= R_6= H, R_1= R_3= OMe
(**237**) R= OH, R_1= R_3= OMe, R_2= R_4= R_ R_6= H
(**240**) R= R_3= R_4= OH, R_1= OMe, R_2= R_6= H, R_5= Me
(**241**) R= R_4 = OMe, R_1= R_3= R_6= OH, R_2= H, R_5= Me



(**238**) R= Me
(**239**) R= H

Figure 6. Isolated isoflavans from natural sources since 2000 to date.

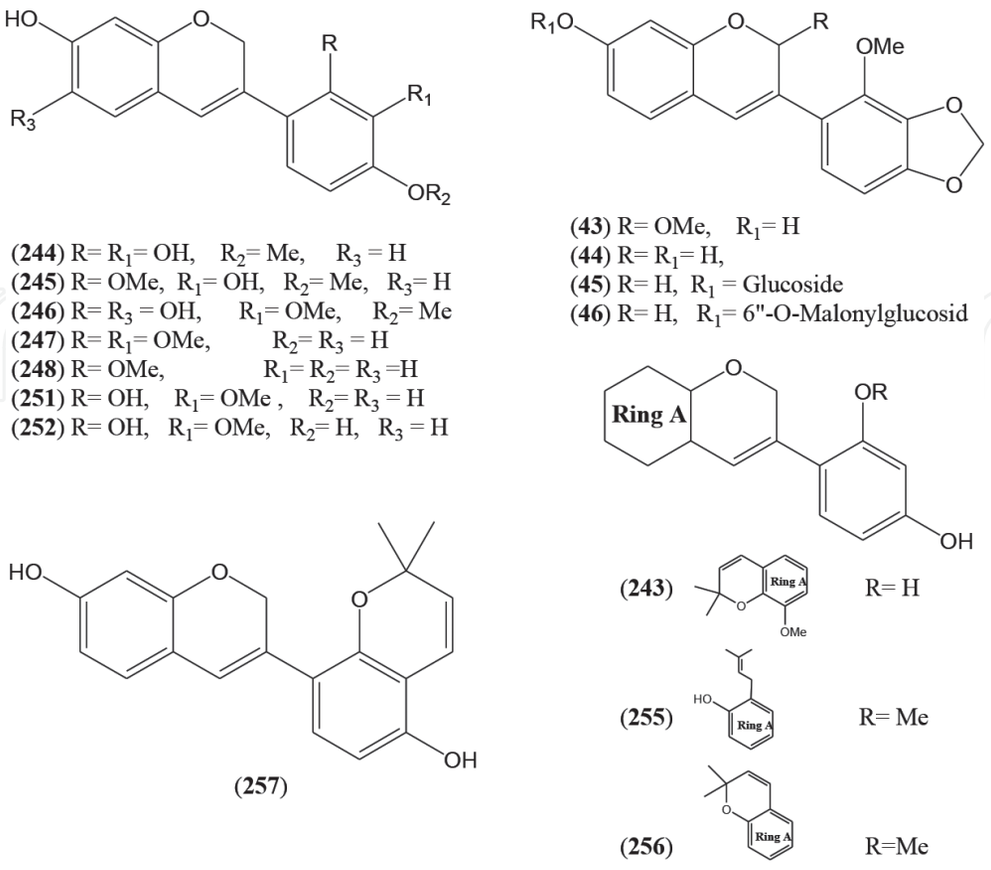


Figure 7. Isolated isoflavenes from natural sources since 2000 to date.

5. Biological activities

Isoflavonoids are reported to have a variety of bioprotective effects, including antioxidant, antimutagenic, anticarcinogenic and antiproliferative activities. Isoflavonoids may protect the body from hormone-related cancers, like breast, endometrial (uterine) and prostatic [115–119]. Isoflavonoids have gained a lot of public interest due to the possible correlation between their dietary consumption and health beneficial effects toward osteoporosis and post-menopausal symptoms [120, 121].

Among the isoflavonoids isolated from dothideomycetes fungus CMU-99, Biochanin A (**59**) showed weak cytotoxic activity against lung cancer cells (NCI-H137) and noncancerous Vero cells. Dothideoisoflavanone (**212**) exhibited cytotoxic effect against oral human carcinoma (KB) but was non-toxic against noncancerous Vero cells [9]. Among the isoflavonoids isolated from *Erythrina addisoniae*, Echrenone b10 (**100**) was found to be more than three times as potent as tamoxifen against MCF7/ADR and MDA-MB-231. Erythraddison III (**182**) was twice as potent as tamoxifen [23]. The isoflavanone Ormosinol (191) significantly inhibited adenocarcinomic human alveolar basal epithelial cells (A549) and human hepatic cell line (HepG2) [25]. Neobavaisoflavone (**110**) and Sigmoidin H (**207**) were selectively active *in vitro* against the resistant cancer cells 6/9, 4/9, CCRF-CEM, HCT116 (p53+/+),

MDA-MB-231-BCRP and U87MG [40]. Platyisoflavanone A (**32**) showed cytotoxic effect against noncancerous Vero cells [41]. 2″,6″-O-diacetyloninin (**54**) was active against human stomach carcinoma (Hs 740.T, Hs 756 T), breast adenocarcinoma (Hs 578 T, Hs 742.T) and prostate carcinoma (DU 145, LNCaP-FGC) cell lines [70]. Pierreione A (**79**) and Pierreione B (**93**) demonstrated selective toxicity to solid tumor cell lines with minimal cytotoxicity [77]. Isosideroxylin (**117**) was selectively active against the against ER^- MDA-MB-231 breast cancer cell line [84]. (3*R*) 5′,8-Di-(γ,γ-dimethylallyl)-2′,5-dihydroxyl-4′,7-dimethoxyl-isoflavanone (**203**) isolated from *Uraria clarkei* possessed good activity against the tested Hela, K562 and HL60 cell lines [101].

Haginin E (Phenoxodiol) (**254**) inhibits cell proliferation of a wide range of human cancer cell lines including leukemia, breast and prostate carcinomas, and is 5–20 times more potent than genistein [122]. Primary ovarian cancer cells resistant to conventional chemotherapy undergo apoptosis following Haginin E (Phenoxodiol) (**254**) treatment. Haginin E (Phenoxodiol) (**254**) is an efficient inducer of cell death in ovarian cancer cells and sensitizes the cancer cells to Fas-mediated apoptosis [123]. Haginin E (Phenoxodiol) (**254**) also exhibits significant ability to induce cell death in the prostate cancer cell lines LNCaP, DU145 and PC3 that utilize different signaling pathways than those reported in ovarian cancer studies [124]. Haginin E (Phenoxodiol) (**254**) development as an antitumor drug was based to a large extent on its low toxicity in normal tissues, but potent topoisomerase-II inhibitory effects in rapidly dividing tumor cells. This advantage led to its fast-track FDA approval for Phase II/III clinical trials [125].

Platyisoflavanone A (**32**) showed antibacterial activity against *Mycobacterium tuberculosis* (TB) in the microplate alamar blus assay (MABA) [41]. Isoflavonoids isolated from roots of *Erythrina zeyheri* were tested against methicillin-resistant *Staphylococcus aureus* (MRSA). Anti-MRSA potency of the isoflavan Eryzerin C (**18**) was the highest followed by Eryzerin D (**19**) [44]. 5,7,3′-Trihydroxy-4′-methoxy-6,5′-di(γ, γ-dimethylallyl)-isoflavanone (**173**) isolated from *Erythrina costaricensis* was also active on MRSA [94]. The two isoflavans 3*S* (+) 2′-O-Methylphaseollidinisoflavan (**15**) and 3*R*(-)Erythbidin A (**16**) isolated from *E. caffra* as well as the two isoflavanones 5,7-Dihydroxy-2′-methoxy-3′,4′-methylenedioxyisoflavanone (**31**) and 4′,5-Dihydroxy-2′,3′-dimethoxy-7-(5-hydroxyoxychromen-7yl)-isoflavanone (**155**) isolated from *Uraria picta* were active against *S. aureus* [45, 55]. The isoflavone Neoraudiol (**111**) displayed antimicrobial activity on *Bacillus subtilis, Salmonella typhii* and *Candida albicans* [52]. Lachnoisoflavone A (**91**) from *Crotalaria lachnophora* showed moderate inhibitory activities against *Escherichia coli* and *Klebsiella pneumonia* [76].

Isoflavanones from the Stem of *Cassia siamea* were evaluated for their anti-tobacco mosaic virus (Anti-TMV)activities[102].(3*R*)7,2′,4′-Trihydroxy-3′-methoxy-5-methoxycarbonylisoflavanone (**205**) was the most active among the tested compounds [102]. In addition to anti-TMV, cordifoliflavanes A (**236**) cordifoliflavanes B (**237**) expressed anti-HIV-1 activities [109].

As a part of plant phenolics, isoflavonoids are expected to have antioxidant activities. Ormosinol (**191**) showed significant antioxidant activity against DPPH radicals [25]. The isoflavene Haginin A (**247**) and the isoflavonones dalbergioidin (**153**) showed antioxidant properties in

both 2,2′-Azino-bis(3-ethylbenzthiazoline-6-sulfonic acid) (ABTS) and 1,1-Diphenyl-2-picryl-hydrazyl (DPPH) assays [29]. Seputheisoflavone (**132**) from *Ptycholobium contortum* was active in the ABTS assay [87]. Isoflavones from the *Astragalus mongholicus* were examined for antioxidant potential in DPPH assay. Results indicated that Calycosin (**81**) and Calycosin-7-O-glucopyranoside (**108**) are more active than Formononetin (**58**) [80].

The *in vitro* antiprotozoal activity of isoflavan quinines from *Abrus precatorius* was tested against *Plasmodium falciparum* (K1 strain), *Trypanosoma brucei rhodesiense* (STIB 900 strain), *Trypanosoma cruzi* (Tulahuen strain C2C4 w/LacZ) and *Leishmania donovani* (strain MHOM/ET/67/L82). Abruquinone D (**239**) and abruquinone K (**241**) were the most active against *T. brucei rhodesiense* [38]. Pumilanol (**29**), an isoflavan from *Tephrosia pumila*, exhibited significant antiprotozoal activities against *T. brucei rhodesiense, T. cruzi* and *L. donovani* [46]. Sophoronol C (**164**) and Sophoronol E (**166**) exhibited moderate anitplasmodial activity against the CQS D10 strain of *P. falciparum* [91].

Daidzein (**64**) and Daidzin (**65**) possess a vasorelaxant action through opening of K^+ channels and inhibition of Ca^{2+} influx in the vascular smooth muscle cells. This cerebral vasodilator activity may be beneficial to patients with obstructive cerebrovascular diseases [126].

Other studies reported on the effects of isoflavonoids on specific enzymes are presented in **Table 7**.

Compound name	Activity	Significance	Ref.
Tlatlancuayin (**84**) 2′,2,5-Trimethoxy-6,7-methylenedioxyisoflavanone (**181**)	a-glucosidase inhibitory	Weak	[5]
Achyranthoside A (**118**) Achyranthoside B (**119**)	Lipopolysaccharide (LPS)-induced nitric oxide (NO) production	Significant inhibition	[6]
Erysubin F (**21**), Erythraddison II (**99**) Echrenone b10 (**100**), Erythraddison III (**182**) Erythraddison IV (**183**)	Protein tyrosine phosphatase 1B (PTP1B)	Significant inhibition	[23]
Sophoraisoflavanone A (**169**) Kenusanone H (**170**)	Alcohol dehydrogenase (ADH) Aldehyde dehydrogenase (ALDH)	Significant activation	[92]
Glabrene (**257**)	Tyrosinase inhibition	Significant inhibition	[114]

Table 7. Effect of isoflavonoids on specific enzyme activities.

Dedication

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