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Homoisoflavonoids from *Caesalpinia* spp.: A Closer Look at Chemical and Biological Aspects

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Abstract

Homoisoflavonoids are rare compounds distributed within a few families of plants including species from Fabaceae. The genus *Caesalpinia*, the main focus of this chapter, is a prolific source of these unique natural products. Homoisoflavonoids from *Caesalpinia* spp. are associated to ethnopharmacological uses for diverse purposes. In this sense, the following chapter sheds light on the occurrence, biosynthesis, isolation, synthesis, and structural analysis of these compounds from species of the genus *Caesalpinia* and their biological potential.

Keywords: *Caesalpinia*, Homoisoflavonoids, natural products, biological activities

1. Introduction

The genus *Caesalpinia* comprises more than 500 species around the world, existing essentially in tropical and subtropical zones. These species are correlated to ethnopharmacological uses due to their biological properties, which include analgesic, adaptogenic, antiangiogenic, antiulcer, anthelmintic, antibacterial, insecticidal, antifungal, anti-inflammatory, antipyretic, antioxidant, antiproliferative, antiviral, antimalarial, immunomodulatory, and immunosuppressive activities, as well as glutathione S-transferase (GST) inhibition, xanthine oxidase (XO) inhibition suppression of melanin synthesis, inhibition of viral neuraminidases, and other properties which will be further discussed ahead [1–5].

Associated to these biological properties, these plants are chemically composed by different classes of metabolites including steroids, organic acids, chromenes, diterpenes, triterpenes, polyphenols, tannins, anthraquinones, alkaloids, and flavonoids, which comprise the natural product diversity of this genus.

Besides these compounds, species from the genus *Caesalpinia* interestingly produce unusual compounds such as uncommon biflavonoids and a rare subclass of flavonoids, named homoisoflavonoids. The first group is more distributed within plants, while homoisoflavonoids are restrict only to some vegetal species including those from Fabaceae and Asparagaceae [6]. These compounds are also encountered, although less common, in other families as Gentianaceae, Polygonaceae, Portulacaceae, and Orchidaceae. There are two different work concerning about homoisoflavonoids, which relate the existence of approximately 240 naturally occurring compounds [6, 7].

In this sense, it is important to define the general characteristics of flavonoids, once they are the core subunits of biflavonoids and cover the rare class of homoisoflavonoids. In general, flavonoids are low molecular weight polyphenols, brightly colored due to their absorptions of UV light, and the most common structures are associated to antioxidant properties [8–10]. Flavonoids, classified as phytoalexins, are produced as a response to microbial infection in plants. They have a notorious participation into the scientific scenario due to the beneficial association to the humans' daily basis intake of nutrients as functional foods improving human health [8, 10].

The consumption of functional foods, or nutraceuticals, is strongly associated to these compounds. In addition, the ingestion of flavonoids from functional foods implicates in lowering blood triglycerides and homocysteine, decreasing blood pressure, acting against inflammatory, platelet antiaggregation processes, and the improvement of endothelial function [11]. These compounds are also associated to another range of biological properties lowering the incidence of cancer, including prostate, stomach, breast, and lung cancers [12]. In addition, various protective effects of flavonoids have demonstrated them as important multi-target agents [13, 14].

In that regard, the genus *Caesalpinia* is considered a rich source of common flavonoids. However, this genus is also associated to unique biflavonoids constituted by homoisoflavonoids subunits and a considerable amount of representatives from the class of naturally occurring homoisoflavonoids. Up to date, there are reports pointing to the existence of about 240 naturally occurring homoisoflavonoids [6, 7].

An interesting point is that homoisoflavonoids can also be found as dimers. Biflavonoids compounds are dimers of flavonoids assembled in diverse manners by different species. The number of possibilities for these structures (involving all classes of flavonoids) points to more than 20,000 different molecules. However, not all these have been encountered in nature so far, summing to 500 representatives [15]. From these, less than 10 are constituted by homoisoflavonoids subunits.

As homoisoflavonoids and their dimers from the genus *Caesalpinia* are unique compounds, this chapter proposes to gather the available data from the literature in a systematic overview associating them to biological properties aiming to demonstrate these compounds as notable representatives composing the chemical space associated to natural products.

2. General classification and biosynthesis of flavonoids

The classification of flavonoids consists in two main groups, the 2-phenylchromans and the 3-phenylchromans. Compounds presenting the 2-phenylchroman core, in which the aromatic ring B is connected to C-2 atom, include flavonols, flavanones, flavan-3-ols, flavones, anthocyanins, and proanthocyanidins. On the other hand, compounds with the 3-phenylchroman group, in which the aromatic ring B is connected to C-3 atom, include isoflavonoids named isoflavones, isoflavans, and pterocarpanes. Another group, named neoflavonoids, in which the benzene ring B is connected to C-4 atom, is less common. There are cases in which the ring C occurs as an isomeric form presenting a five-membered ring, which is associated to the formation of aurones. Another class of phenolic compounds, named chalcones, is not considered true flavonoids due to their lack on the aromatic C ring but still considered members of the flavonoids family. In the same way, a closely related group compounds, the stilbenes, are important due to their biological potential [16]. A brief representation of each class of flavonoids and their sources is demonstrated in **Figure 1**.

Figure 1. Classification of flavonoids, general structures, examples, and biological sources.

These structures are important for the recognition and classification of biflavonoids moieties, once they could exist as complex structures presenting aurones, isoflavonoids, neoflavonoids, chalcones, and other moieties as well as dimers of homoisoflavonoids.

Flavonoids are products from the phenylpropanoid building block cinnamoyl-CoA, in which chain extension is provided by three units of malonyl-CoA [17]. Cinnamoyl-CoA is derived from the amino acids phenylalanine and tyrosine which are converted by phenylalanine and tyrosine ammonia lyases to cinnamic acid and *para*-hydroxycinnamic acid, respectively [18]. The aromatic polyketide formed from the union of cinnamoyl-CoA and three units of malonyl-CoA might form the benzo- γ -pyrone nucleus containing aromatic rings A, B, and a heterocyclic ring C, substituted or not. This nucleus is precursor of a great number of flavonoids. In this sense, flavonoids are characterized by the classic flavan nucleus presenting a C₆-C₃-C₆ skeleton. In addition, chalcones might undergo different cyclization with the addition of a single carbon, provided by S-methyl moiety of methionine, which lead to the formation of the homoisoflavonoid nucleus, which can be converted to the other classes of homoisoflavonoids (**Figure 2**).

Figure 2. Biosynthetic scheme for the formation of a flavonoid nucleus (monomeric structure of biflavonoids) and the formation of the existing types of homoisoflavonoid nucleus.

3. Occurrence of homoisoflavonoids in *Caesalpinia* spp.

Homoisoflavonoids have a general structure of 16 carbons containing two phenyl rings and one heterocyclic ring. Homoisoflavonoids are biosynthesized from cinnamic acid derivatives along with malonyl-CoA subunits. The resulting compound, an aromatic polyketide, is the precursor of chalcones. In the following step, the aromatic polyketide undergoes a Claisen and enolization reactions, which lead to the formation of the chalcone backbone. An additional carbon is added to the chalcone, provided by S-methyl moiety from methionine, creating the homoisoflavonoid skeleton containing 16 carbons. Thus, there is the formation of 3'-hydroxyl-chalcone as a precursor, which is transformed to 3-benzylchroman-4-one. Subsequently, different cyclization leads to the formation of other types of homoisoflavonoids (**Figure 2**).

The existence of these compounds is associated to the genus *Caesalpinia* involving species as *C. pulcherrima* [19, 20], *C. echinata* [1, 21, 22], *C. bonduc* [3], *C. sappan* [4, 23–28], *C. japonica* [29], and *C. milletti* [30]. However, the diversity of compounds (in number and structurally) is associated to *C. sappan*, a prolific source of homoisoflavonoids with important ethnopharmacological applications. The crude extract of *C. sappan*, named Sappan lignum, is widely studied and used for the treatment of diverse diseases [28].

The classification of homoisoflavonoids comprises five main groups named scillascillin, brazilin, caesalpin, protosappanin, and sappanins. Homoisoflavonoids from the class scillascillins exhibit a spiro ring with four members between rings C and D. However, species from the genus *Caesalpinia* do not produce scillascillins. These compounds are encountered only in the family Asparagaceae [7].

The most common class of homoisoflavonoids in the genus *Caesalpinia* is the sappanin-type. This class presents a 3-benzyl chromanone unit. The diversity of these compounds is associated to a wide variation of substituents, such as hydroxyl, methoxyl, formyl, methyl groups, among others, which confer to sappanin-type the position of the most abundant. In this chapter, the sappanin-type homoisoflavonoids corresponded approximately to 70% of the compounds.

In this aspect, the species *C. pulcherrima*, which is a perennial large shrub, widely distributed in the tropical and subtropical areas of Americas, South India, Taiwan and South-East Asian countries [20, 31]. It is used in the folk medicine due to its medicinal properties for the treatment of skin diseases, tumors, and fevers, and association to antibacterial, antidiarrheal, cytotoxic, and antiulcer properties [32]. *C. pulcherrima* produces a large variety of sappanin-type homoisoflavonoids exhibiting a diverse pattern of substitution such as bonducellin (**1**), isobonducellin (**2**), 7-*O*-methylbonducellin (**3**), 2'-*O*-methylbonducellin (**4**), sappanone A (**5**), (3*E*)-3-(1,3-benzodioxol-5-ylmethylene)-2,3-dihydro-7-hydroxy-4*H*-1-benzopyran-4-one (**6**), (3*E*)-3-(1,3-benzodioxol-5-ylmethylene)-2,3-dihydro-7-methoxy-4*H*-1-benzopyran-4-one (**7**), (*E*)-3-(3-hydroxy-4-methoxybenzylidene)-6,7-dimethoxychroman-4-one (**8**), (3*E*)-2,3-dihydro-7-hydroxy-3-[(3-hydroxy-4-methoxyphenyl)methylene]-4*H*-1-benzopyran-4-one (**9**), (3*E*)-2,3-dihydro-3-[(3,4-dimethoxyphenyl)methylene]-7-methoxy-4*H*-1-benzopyran-4-one (**10**), (*E*)-7-methoxy-3-(4-methoxybenzylidene)chroman-4-one (**11**), (*E*)-7-hydroxy-3-(3,4,5-trimethoxybenzylidene)chroman-4-one (**12**) [19, 20, 31]. Some of these compounds were tested against Gram-positive microorganisms such as *Bacillus subtilis*, *Bacillus sphaericus*, and

Staphylococcus aureus exhibiting moderate antimicrobial activity. However, they were inactive or weakly active against Gram-negative microorganisms such as *Pseudomonas aeruginosa*, *Klebsiella aerogenes*, and *Chromobacterium violaceum*. Concerning the antifungal activity, these compounds presented moderate activity against *Aspergillus niger* and *Candida albicans* in comparison with standard compounds Clotrimazole (antifungal), Streptomycin (antibacterial), and Penicillin G (antibacterial) [19]. Compounds **5** and **6** presented moderate activity against *Staphylococcus aureus* (inhibition zone of 11–15 cm) at 100 µg/mL, while **6** and **10** presented moderate activity against *Klebsiella aerogenes* (inhibition zone of 11–15 cm) at 100 µg/mL. Streptomycin presented an inhibition zone of 21–25 cm at 100 µg/mL. Compounds **5**, **8**, and **9** exhibited moderated activity against *Aspergillus niger* (inhibition zone of 5–10 cm at 150 µg/mL). On the other hand, the compounds **4**, **8**, **7**, **9**, and **10** were moderately active against *Candida albicans* at 150 µg/mL (inhibition zone of 5–10 cm). To comparison, positive control clotrimazole was active against all strains at 100 µg/mL (inhibition zone 21–25 cm) [19].

Rao and collaborators tested the compound **2** against the inflammatory process and described that **2** inhibits the production of NO, TNF- α , and IL-12. In fact, **2** was the most active compound in the experiments at the concentration of 40 µM, reducing 92% of the NO production (IC_{50} = 20 µM) in mouse peritoneal macrophages induced by LPS + IFN- γ . The authors suggested that the mode of action of **2** probably affects the production of NO by the induction of LPS + IFN- γ in mouse peritoneal macrophages [20].

The species *C. echinata*, commonly known as *Pau-brasil* (brazilwood), is endemic from Brazil and played an important historical role in the country [1]. This species has been reported to contain a large range of polyphenols including the homoisoflavonoids brazilin (**13**) and braziliin (**14**). The compound **15** is a natural dye and is also abundant in the species *C. sappan* (from 8 to 22%). The species *C. echinata*, considered the first source of brazilin, is used for diverse purposes such as healing agent, oral analgesic, and tonics. The species *C. echinata* has also demonstrated antitumor effect *in vivo* against cells strains of Ehrlich Carcinoma and Sarcoma 180. In addition, an interesting antiangiogenic effect was noticed [21]. On the other hand, compound **14**, an oxidation product of brazilin, was considered effective against the inflammatory and cytotoxic processes [22]. Compound **14** displayed cytotoxic effects against human cancer cell lines, such as HepG2 and Hep3B (liver), MDA-MB-231 and MCF-7 (breast), A549 (pulmonary), and CA9-22 (gingival) [22].

Phytochemical studies on ethanolic extracts of *C. bonduc* yielded two sappanin-type homoisoflavonoids identified as caesalpinianone (**15**) and 6-*O*-methylcaesalpinianone (**16**), which exhibited different levels of GST inhibition and antifungal activities [3]. The IC_{50} values of compounds **15** and **16** were determined as 16.5 and 17.1 µM, respectively for GST inhibition. Ethacrynic acid, a standard substrate GST inhibitor, exhibited a IC_{50} = 17.6 µM, suggesting that homoisoflavonoids have significant inhibition of GST activity [3].

The species *C. sappan* is the most prolific source of homoisoflavonoids with many representatives involving brazilin-, caesalpin-, protosappanin- and sappanin-types. Extracts of *C. sappan*, known as sappan lignum, have been used as emmenagogue, hemostatic, anti-inflammatory and for treatment of thrombosis. There are also relates about its antimicrobial activity against *Staphylococcus*, *Diplococcus*, *Corynebacterium*, and *Shigella baydii* [24]. The species *C. sappan*

afforded brazilin- and sappanin-types homoisoflavonoids such as compounds **13**, **14**, caesalpin P (**17**), 3'-O-methylbrazilin (**18**), brazilide A (**19**), 3'-deoxy-4-O-methylsappanol (**20**), sappanol (**21**), 4-O-methylsappanol (**22**, **Figure 3**), in which compounds **13**, **14**, and **20**, and were active to the suppression of melanin synthesis [4]. Melanin is important to the protection of the skin from UV radiation, and its excessive synthesis could lead to melasma and lentigo. Compound **13** exhibited strong suppression of melanogenesis ($EC_{50} = 3.0 \mu M$) and cell viability around 95%. Furthermore, compound **20** also exhibited expressive activity ($EC_{50} = 4.6 \mu M$) with nonsignificant toxicity (cell viability around 92%). The other compounds displayed high cytotoxicity against HMV-II cells [4].

Species *C. sappan* constitute a source of sappanin-type homoisoflavonoids. Related compounds such as 4-(7-hydroxy-2,2-dimethyl-9 β H-1,3,5-trioxo-cyclopenta[α]naphthalene-3-lymethyl)-benzene-1,2-diol (**23**), 7,3',4'-trihydroxy-3-benzyl-2H-chromene (**24**) exhibited moderate activity as inhibitors of viral neuraminidases. Viral neuraminidases are considered essential to viral replication cycle and a valid therapeutic target for antiviral drugs. Compound **5** presented the best activity against H1N1 ($IC_{50} = 0.7 \mu M$); H3N2 ($IC_{50} = 1.1 \mu M$); and H9N2 ($IC_{50} = 1.0 \mu M$) [23].

Figure 3. Sappanin-type and brazilin-type homoisoflavonoids from *Caesalpinia* spp.

Other sappanin-type compounds such as (3*R*,4*S*)-3-(4'-hydroxybenzyl)-3,4-dihydro-2'',3''-dimethyl-3*H*-[1,3]dioxolo[4,5-*c*]chromen-7-ol (**25**), and (3*aR*,9*bS*)-3*a*-(4-hydroxy-3-methoxybenzyl)-2,2-dimethyl-4,9*b*-dihydro-3*aH*-[1,3]dioxolo[4,5-*c*]chromen-7-ol (**26**) are associated to the inhibition of NO production [27]; **21** and **22** associated to the inhibition of melanin synthesis [4]. Sappanol derivatives were also identified from *C. sappan* as in the case of 3'-*O*-methylsappanol (**27**), 3'-*O*-methylepisappanol (**28**), and a unique lactone-based homoisoflavonoid named caesalpiniaphenol B (**29**) [6]. In addition, the compound caesalpin J (**30**), one of the only seven caesalpin-type homoisoflavonoids reported in the literature, was isolated from *C. sappan*. Caesalpin J exhibited weak to moderate antimicrobial effects [25].

The species *C. japonica* is considered another source of biologically active homoisoflavonoids in which diverse homoisoflavonoids including **5**, **13**, **20**, **21**, **22**, protosappanin A-C (**31**–**33**), 4-*O*-methylepisappanol (**34**), episappanol (**35**), and sappanone B (**36**, **Figures 4–6**) have been isolated and characterized [29].

Figure 4. Sappanin-, casealpin-, and protosappanin-type structures of homoisoflavonoids from *Caesalpinia* spp.

Figure 5. Bihomoisoflavonoids from species of the genus *Caesalpinia*.

Figure 6. Scheme of synthesis of sappanin-type homoisoflavonoids obtained from *C. pulcherrima*. Reagent and conditions: (i) CH₃I, K₂CO₃, acetone, 2h, reflux, (91%); (ii) substituted benzaldehyde, piperidine, 2h (58–69%). Adapted from Ref. [19].

Homoisoflavonoids classified as protosappanins are commonly associated to the species *C. sappan* and *C. japonica*. These compounds are resulting from the connection of C-4 and C-4a atoms forming an eight-membered ring. There are only eleven protosappanins reported so far [26]. Compounds **31–33** did not show significant cytotoxicity against MCF7, A549, LN229 cell lines. In addition, compounds **32** and **33** were also tested against the inflammatory process exhibiting weak to moderate activity [27].

4. Biflavonoids containing homoisoflavonoids subunits in *Caesalpinia* spp.

Flavonoids can also exist as dimers, named biflavonoids, which represents flavonoids linked by C–C or C–O–C bond in order to form a flavonoid-flavonoid structure. The connection can occur in several modes in the three rings of the flavan nucleus. The ring A could be linked to the ring A', indicated as A-A. This could also occur between the rings A-C, B-B, C-B, among other possibilities that are enlarged by functional groups as OH, MeO, C=O, C=C. The occurrence of common biflavonoids in the genus *Caesalpinia* is known only to some species, such as *C. ferrea* [33], *C. pyramidalis* [34], *C. pluviosa* [35].

Furthermore, certain species from the *Caesalpinia*, mostly *C. sappan*, are associated to the production of biflavonoids containing homoisoflavonoids subunits such as protosappanin D (**37**), a biflavonoid which exhibit two subunits of **33**, and protosappanin E (**38**), which display **13** and **33** as subunits. Compounds **37** and **38** were tested against the inflammatory process associated to the inhibition of iNOS and PGE2 production, as well as the suppression of TNF- α and COX-2. Washiyama and collaborators suggested that the protosappanin skeleton and the functional group at C7 would be important to the activity of **37** and **38** [27]. The investigation of sappan lignum as a possible XO inhibitor leads to the isolation of diverse compounds including neoprotosappanin (**39**) and protosappanin E-2 (**40**, **Figure 5**). These two compounds presented IC₅₀ of 38.3 and 18.9 μ M, respectively, exhibiting a concentration-dependent behavior. In what extent their mode of inhibition, the biflavonoid **39** was considered a noncompetitive XO inhibitor while **40**, a competitive inhibitor [2]. The inhibition of XO is associated to improvements in cardiovascular health as well as, the reduction of ROS, and the amelioration of gout cases [36].

The presence of rare caesalpins is correlated to *C. sappan*. A dimer named neosappanone (**41**) was isolated from this species and evaluated against XO. The IC₅₀ of **41** was determined as 29.7 μ M and associated to a competitive inhibition of XO. Therefore, these results showed that the traditional use of *C. sappan* for rheumatism and inflammatory diseases could be attributed to its phenolic composition, specifically to dimers of homoisoflavonoids [2].

5. Isolation, synthesis, and structural analysis of homoisoflavonoids

Due to the intrinsic interest in homoisoflavonoids and their biological activities, several works have been discussing different structural aspects of homoisoflavan nucleus-bearing

organic compounds [6, 7]. The structural uniqueness of these compounds and their potent biological activities makes them a target of choice for studies in natural products research on the determination of absolute configurations, organic synthesis, isolation, and structural determination [7].

The isolation of homoisoflavonoids involves different chromatographic techniques. Homoisoflavonoids are generally separated after treatment of the organic extract (MeOH, CHCl₃) with several chromatographic phases. The use of column chromatography steps (using silica gel and/or Sephadex LH-20), preparative thin layer chromatography, as well as high performance liquid chromatography (HPLC) methods (semi-preparative and preparative) have been used to purification [7]. In addition, there are other methods used to the isolation of flavonoids, such as counter current chromatography [37] can be adopted for the isolation of homoisoflavonoids and flavonoids.

Besides the isolation of naturally occurring homoisoflavonoids from the species *C. pulcherrima*, a synthetic approach of the isolated homoisoflavonoids **1**, **3**, **4**, **5**, **6**, **7**, **9**, and **10** employed the piperidine catalyzed condensation as key steps in this synthesis of these structures (**Figure 6**). This procedure afforded products reaching around 60% yielding following conditions exhibited in **Figure 3** [19].

The structures of homoisoflavonoids have been unambiguously established by analysis of spectroscopic NMR data supported by analysis of UV and MS spectra. These analyses confirm the presence of the 15-carbon backbone related to classic flavonoids, and the 16-carbon skeleton with two phenyl rings (A and C) and one heterocyclic ring (B) separated by an additional carbon, forming the homoisoflavonoids skeleton [24, 29, 31].

Analysis of the ¹H and ¹³C NMR spectra indicates the presence of carbonyl groups at δ_C 170.7–220.0 as well as those assigned to carbons/hydrogens of aromatic ring at δ_C 100.0–170.0/ δ_H 6.00–8.50 and hydroxyl derivate group as characteristic signs. The homoisoflavonoids, when existing as dimers, exhibited their ¹³C and ¹H NMR spectra typically duplicate and superposed when presenting the same subunits.

The extra carbon existing in homoisoflavonoids compared to ordinary flavonoids can be aliphatic displaying ¹³C and ¹H NMR signs at δ_C 30.0–35.0/ δ_H 2.60–3.00; or olefinic at δ_C 100.0–140.0/ δ_H 5.30–6.00, respectively. Correlations in the HMBC, HSQC and COSY spectrum resolve all ambiguities to the structure of these compounds.

The compounds **17**, **19**, **29**, **37**, **38** are homoisoflavonoids derived from the auto-oxidation of precursors or present differentiated biosynthesis. These compounds present uncommon chemical structures with ¹H, and ¹³C NMR spectra relativity complex, in some cases, exhibiting signs that indicate the presence of lactone and others characteristic group.

Homoisoflavonoids present signals of absorptions in the UV spectrum at λ_{max} 222–230, 270–280, and 300–310 nm, depending on the presence of conjugated double bonds on their structures. The MS spectrum present [M+H]⁺ ions between m/z 250–350 to homoisoflavonoids and [M+H]⁺ ions between m/z 500–600 to dimers of homoisoflavonoids with some minor compounds with $m/z > 600$ [24, 29, 31].

The absolute stereochemistry can be established by circular dichroism analysis by comparison to models with known stereochemistry. The compound **28**, isolated from *C. sappan*, had its absolute stereochemistry determined by this method compared with data from 3-deoxysappanol. The result suggested that **28** has the absolute stereochemistry at the C-3 and C-4 positions to be (3*R*,4*S*) [24].

6. Conclusion

The chemical space related to natural products is associated to important scientific findings in what to extent the discovery of important new chemical entities. In this sense, the genus *Caesalpinia* is a prolific source of secondary metabolites which also biosynthesize homoisoflavonoids. In addition, only a few species are reported to produce dimers of homoisoflavonoids as secondary metabolites. Homoisoflavonoids and its dimers are classified as unusual natural products with strict occurrence in nature present the most diverse types of biological activities. These compounds are isolated through HPLC methods and identified by different techniques as NMR, UV, MS based on the biosynthesis of chalcones with an additional carbon provided by *S*-methyl from methionine. It is important to highlight that these phenolic compounds are part of ethnopharmacological applications by people whose access and use the biodiversity for the improvement of health conditions are made for centuries. Furthermore, the investigation of this class of phenolic compounds provides chemosystematics data for classification and discovery of pharmacologically efficient compounds from species of *Caesalpinia* spp.

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Conflict of interests

The authors declare no conflict of interests.

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