Egypt. J. Chem. Vol. 64, No. 9, pp. 5299 - 5313 (2021)

Egyptian Journal of Chemistry

http://ejchem.journals.ekb.eg/

Bioactive Phytoconstituents of Morus Plants exhibiting Numerous Therapeutic Activities

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Abstract

Morus is a plant genus of the family Moraceae, most of which is used as a decoction in traditional medicines for the treatment of cough, bronchitis, pulmonary diseases and reduces the plasma sugar level. Many studies in Morus phytochemistry have contributed to the discovery of Diels-Alder-type adducts, arylbenzofurans, and flavonoids with antioxidant, antihyperglycemic, antihypertensive, antihyperlipidemic, and anti-inflammatory activities. The purpose of this article was to offers an account of the updated knowledge on the phytochemicals and pharmacological activities of these compounds. This review will help to fully understanding the efficacy and pave the way for further explore the comprehensive use of Morus. We conclude that Morus needs further reports in the identification of bioactive constituents and strengthen the claim of folk medicines.

Keywords: Morus; Diels-Alder-type adducts; Arylbenzofurans; Flavonoids; Phytochemistry; Pharmacology.

1. Introduction

Traditional medicines show trust in phytoconstituents which are considered to be less toxic as compared to synthetic ones. Major interventions in the field of natural products focused on the identification of functional components that hold therapeutic potentials. *Morus* (Mulberry) is the main genus of the family Moraceae, distributed worldwide, having many therapeutic activities. Genus *Morus* consists of many species; *Morus alba* L., *M. nigra* L., *M. wittiorum* Hand.-Mazz., *M. mongolica* Schneid., and *M. australis* Poir., etc., where *M. alba* (white mulberry) is the dominant [1]. In European countries, mulberry is grown for its fruit, while in Japan its leaves are used as herbal tea. *M. alba* leaves are mainly used as silkworms feed [1]. *M. alba* leaves, fruits, and root barks are commonly used as traditional medicines in Asian countries [2]. Root barks of *M. alba* is a component of traditional Chinese medicine, Mori Cortex, where it is listed as a constituent in Chinese Pharmacopoeia for the treatment of cough, edema, and oliguria [3]. Many biological activities; antioxidant, antihyperglycemic, antibacterial, antihypertensive, antihyperlipidemic, anthelmintic, and antidiarrheal have been reported for *Morus* [4].

Several chemical and pharmacological reviews were published concerning *Morus* plants, however, no detailed reports discuss its mechanism of action. The current review focus on *Morus* bioactive compounds

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Receive Date: 26 May 2021, Revise Date: 01 June 2021, Accept Date: 01 June 2021
DOI: 10.21608/EJCHEM.2021.76688.3788

and their mechanisms to induce the reported pharmacological activities (from 1978 to 2020). Over 127 compounds; 2-Arylbenzofurans, Diels–Alder-type adducts, and flavonoids, with anti-inflammatory, antioxidant, antimicrobial, antidiabetic, antitumor, and other pharmacological activities were summarized. Our review will help us to fully understand how bioactive constituents of *Morus* work and lighten our way to a comprehensive study of *Morus* plants.

2. Traditional uses of Morus:

Medicinal plants are the major components of alternative medicines depending upon their phytoconstituents. *Morus* root is among the constituents of many Chinese traditional supplements; 'Sohaku hi', 'Jiang Qi Ding Chuan San' and 'Sang Bai Pi', which are used as a decoction for the treatment of cough, bronchitis, yellow sputum, nephritis, pulmonary diseases and reduces the plasma sugar level [4]. Owing to bitter acidic taste, root bark possesses cathartic and anthelmintic properties [2] and the leaves are diaphoretic, emollient, and prevent throat infections, and inflammations [2]. Aqueous extract of mulberry leaves exhibits significant hypolipidemic and hypoglycemic activities [5]. The mulberry fruit juice is used in diarrhea, cold, malaria, amoebiasis, and treat weakness, fatigue, and anemia [2].

3. Phytochemistry and Bioactive compounds of Morus

Morus plants are a rich source of natural isoprenoid substituted phenolics with a serious interest by many investigators [4]. Diels–Alder-type adducts are major compounds in *Morus*. It is formed by a Diels–Alder reaction between the *α, β*-olefinic moiety of a chalcone and an isoprene moiety (Figure 1, compounds **1-27**). *Morus* is rich in 2-arylbenzofurans, the most representative (Nearly 57) compounds, which are commonly different in cyclization or positions of prenyl and geranyl groups (Figure 2, compounds **28-79**). *Morus* is a rich source of phenolics; flavonoids and stilbenes with prenyl and geranyl substitutions. Diverse flavonoids have resulted from different positions of substituents and/or cyclization (Figure 3, compounds **80-127**).

4. Biological Activities

4.1. Antioxidant activity

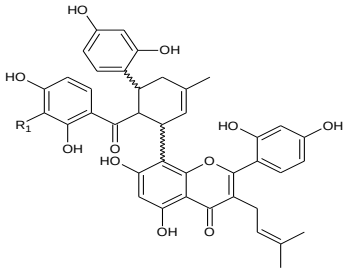
Morus plants are of great therapeutic value depending on their antioxidant activities. Functional antioxidant components enhancing the protective effect of mulberry supplementation. *Morus* root extracts showed a strong radical scavenging effect through different mechanisms include the inhibitory effect of xanthine oxidase and lipid peroxidation [29], DPPH scavenging activity [30 - 32], and ameliorating the level of blood glutathione, superoxide dismutase, and catalase [33], moreover, *in-vivo* antioxidant effects in $FeCl_2$–ascorbic acid-induced lipid peroxidation assays [34]. *M. alba* fruits have shown antioxidant activity, where phenolics and flavonoids count 181 and 29 mg/100 g as gallic acid, and quercetin equivalent respectively, moreover, ascorbic acid counts 100-300 mg/100 g [35]. Moracins identified from mulberry are scavengers of UV stress-generated free radicals [36] moreover inhibit malondialdehyde production [37].

4.2. Anti-inflammatory activity

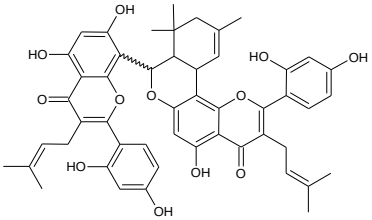
Morus root extracts showed inhibitory effects on COX isoenzymes [38]. Flavonoids and phenolics isolated from root barks of *M. alba* inhibit arachidonate metabolism in rat platelet homogenates [39, 40]. Arylbenzofurans; moracins and prenyl-flavonoids; kuwanons isolated from root barks of *M. alba* showed inhibitory effects on NO production in RAW264.7 cells [41]. Prenylated constituents; sanggenons isolated from *M. alba* and *M. nigra* inhibited TNF-α, IL-1β, and NF-κB activation [42].

4.3. Antitumor activity

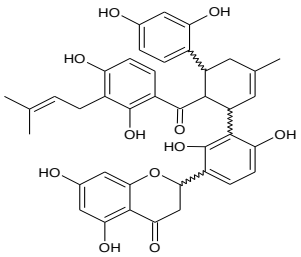
Morus root extracts showed cytotoxic activity against various cancer cell lines [4]. Water extract of Mori Cortex exhibited apoptosis and cytotoxic activity on human leukemia and mouse melanoma cells [43]. Compounds isolated from *M. alba* exhibit antitumor activities by different mechanisms, where kuwanons inhibit hypoxia-induced HIF-1α accumulation [44], and inhibit protein kinase C [45]. Sanggenons also inhibit hypoxia-induced HIF-1α accumulation [44], induce internucleosomal DNA fragmentation [46], induce cell cycle arrest at G0/G1 phase, and inhibit the chymotrypsin-like activity [47].



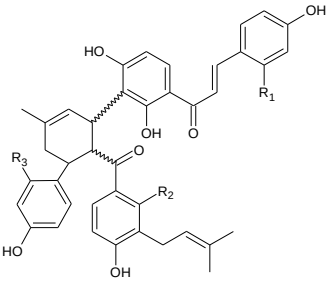
[1] Kuwanon G [6] R_1=H
[2] Kuwanon H [4] R_1=prenyl



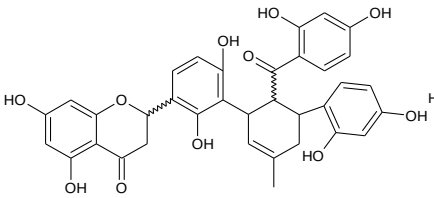
[3] Kuwanon M [4]



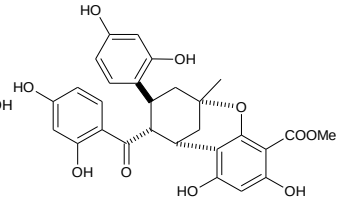
[4] Kuwanon O [4]



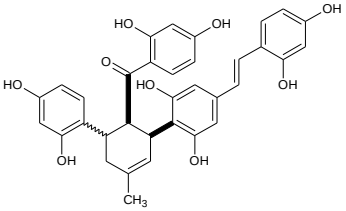
[6] Kuwanon J [8] R_1= R_2= R_3=OH
[7] Kuwanon R [8] R_1=H, R_2=R_3=OH
[8] Kuwanon V [8] R_1=H, R_2=OH, R_3=H
[9] Kuwanon Q [8] R_1=R_2=OH, R_3=H



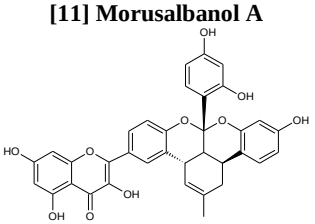
[5] Kuwanon L [4]



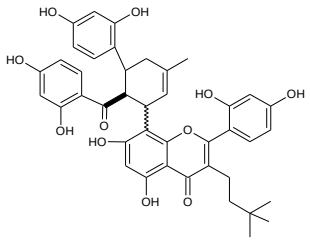
[11] Morusalbanol A



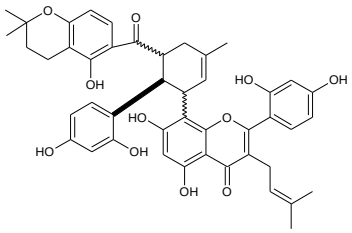
[10] Kuwanon Y [4]



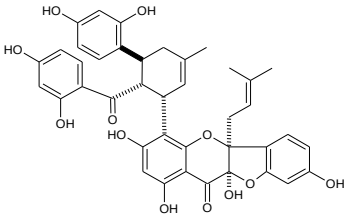
[12] Australisine A [7]



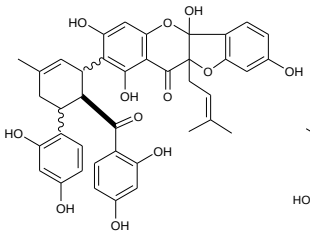
[13] Moracenin D [4]



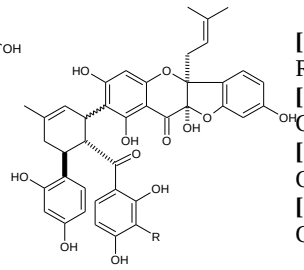
[14] Moracenin C [4]



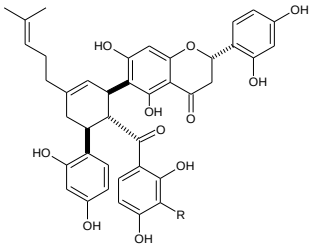
[15] Cathayanon A [4]



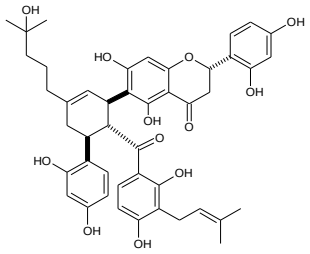
[16] Sanggenon D [4]



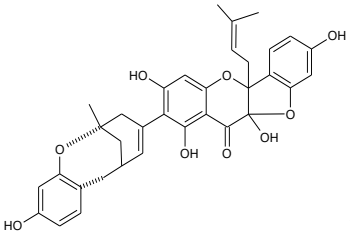
[17] Sanggenon E [4]
R=prenyl
[18] Sanggenon C [4] R=H, C2(R), C3(S), C3\(S)
[19] Sanggenon O [4] R=H C2(S), C3(R), C3\(S)
[20] Cathayanon B [4] R=H C2(S), C3(R), C3\(R)



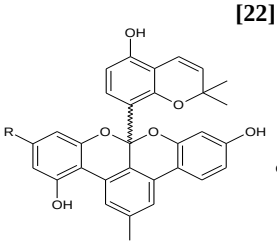
[21] Sanggenol M [4]
R=prenyl
[22] Sanggenon G [4] R=H



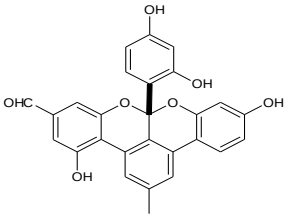
[23] Sanggenon T [4]



[24] Sanggenon B [4]

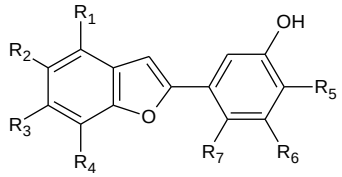


[25] Soroceal [4]
R=CHO
[26] Yunanensin A [9]
R=benzofuran

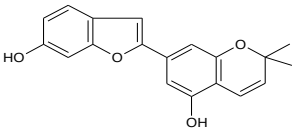


[27] Soroceal B [4]

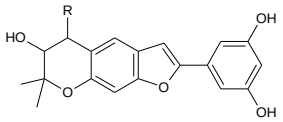
Figure 1: Isolated *Diels–Alder-type adducts* from genus *Morus*



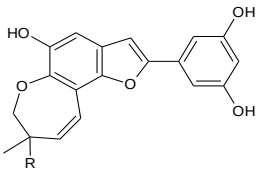
[28] Moracin C [10]**,** R_1=R_2=H, R_3=OH, R_4=H, R_5=prenyl, R_6=OH, R_7=H
[29] Moracin I, R_1=R_2=H, R_3=OH, R_4=R_5=H, R_6=OMe, R_7=prenyl
[30] Moracin M [10] **,** R_1=R_2=H, R_3=OH, R_4=R_5=H, R_6=OH, R_7=H
[31] Moracin M-3'-*O-β*-D-glucopyranoside [11]**,** R_1=R_2=R_4=R_5=R_7=H, R_3=OH, R_6=OGLu
[32] Moracin N [12]**,** R_1=H, R_2=prenyl, R_3=OH, R_4=R_5=H, R_6=OH, R_7=H
[33] Moracin S [13]**,** R_1=R_2=H, R_3=OH, R_4=prenyl, R_5=H, R_6=OH, R_7=H
[34] Moracin T [13]**,** R_1=prenyl, R_2=OMe, R_3=OH, R_4=R_5=H, R_6=OH, R_7=H
[35] Moracin Y [12]**,** R_1=H, R_2=CHO, R_3=OH, R_4=R_5=H, R_6=OH, R_7=H
[36] 4-Prenylmoracin, R_1=prenyl, R_2=H, R_3=OH, R_4=R_5=H, R_6=OH, R_7=H
[37] Mulberrofuran A, R_1=R_2=H, R_3=OH, R_4=R_5=H, R_6=OMe, R_7=geranyl
[38] Mulberrofuran D, R_1=R_2=H, R_3=OH, R_4=geranyl, R_5=H, R_6=OH, R_7=prenyl
[39] Mulberrofuran L, R_1=R_2=H, R_3=OH, R_4=geranyl, R_5=H, R_6=OH, R_7=H
[40] Mulberrofuran W, R_1=R_2=H, R_3=OH, R_4=R_5=H, R_6=OH, R_7=farnesyl
[41] Mulberrofuran Y, R_1=geranyl, R_2=OMe, R_3=OH, R_4=R_5=H, R_6=OH, R_7=H
[42] Mulberroside F, R_1=R_2=H, R_3=OGLu, R_4=R_5=H, R_6= OGLu, R_7=H
[43] Albafuran A, R_1=R_2=H, R_3=OH, R_4=R_5=H, R_6=OH, R_7=geranyl
[44] Albafuran B, R_1=R_2=H, R_3=OH, R_4=H, R_5=geranyl, R_6=OH, R_7=H
[45] Artoindonesianin O, R_1=R_2=H, R_3=OH, R_4=H, R_5=prenyl, R_6=OMe, R_7=H
[46] 3',5'-dihydroxy-6-methoxy-7-prenyl-2-arylbenzofuran,
R_1=R_2=H, R_3=OMe, R_4=prenyl, R_5=H, R_6=OH, R_7=H



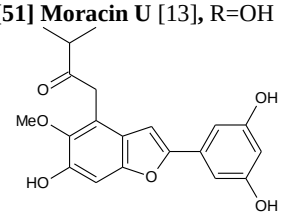
[47] Moracin D [14]



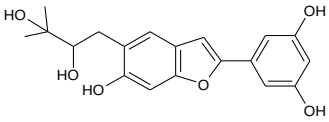
[48] Moracin P [12]**,** R=H
[49] Moracin V [12]**,** R=OH



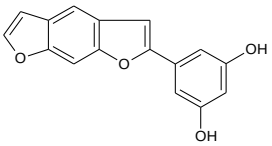
[50] Moracin L [15]**,** R=H
[51] Moracin U [13]**,** R=OH



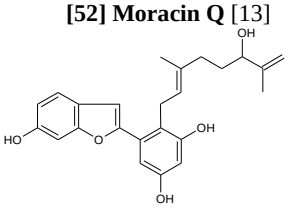
[52] Moracin Q [13]



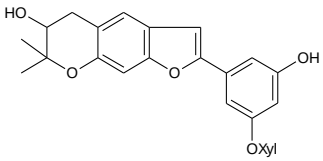
[53] Moracin R [13]



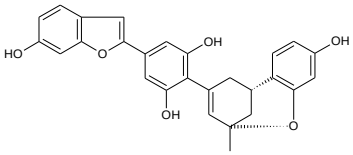
[54] Moracin X [12]



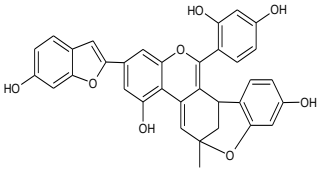
[55] Mornigrol D



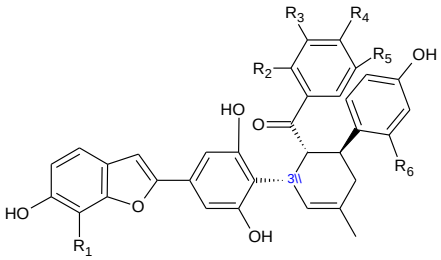
[56] Mulberroside C



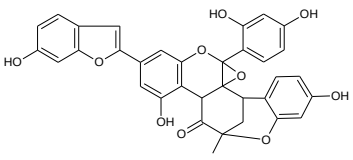
[57] Mulberrofuran H [14]



[58] Mulberrofuran I [16]



[60] Mulberrofuran C [16]**,** R_1=H, R_2=OH, R_3=H, R_4=OH, R_5=H, R_6=OH
[61] Mulberrofuran E [8]**,** R_1=H, R_2=OH, R_3=prenyl, R_4=OH, R_5=R_6=H
[62] Mulberrofuran T [17]**,** R_1=γ,γ dimethylallyl, R_2=H, R_3=R_5=R_6=OH, R_4=prenyl
[63] Mulberrofuran U [11]**,** R_1=prenyl, R_2=OH, R_3=H, R_4=OH, R_5=H, R_6=OH
[64] Chalcomoracin, 3\\ - β-H, **(Mongolicin F,** 3\\ - α-H) [7] R_1=R_2=H, R_3=OH, R_4=prenyl, R_5=R_6=OH



[59] Mulberrofuran Q

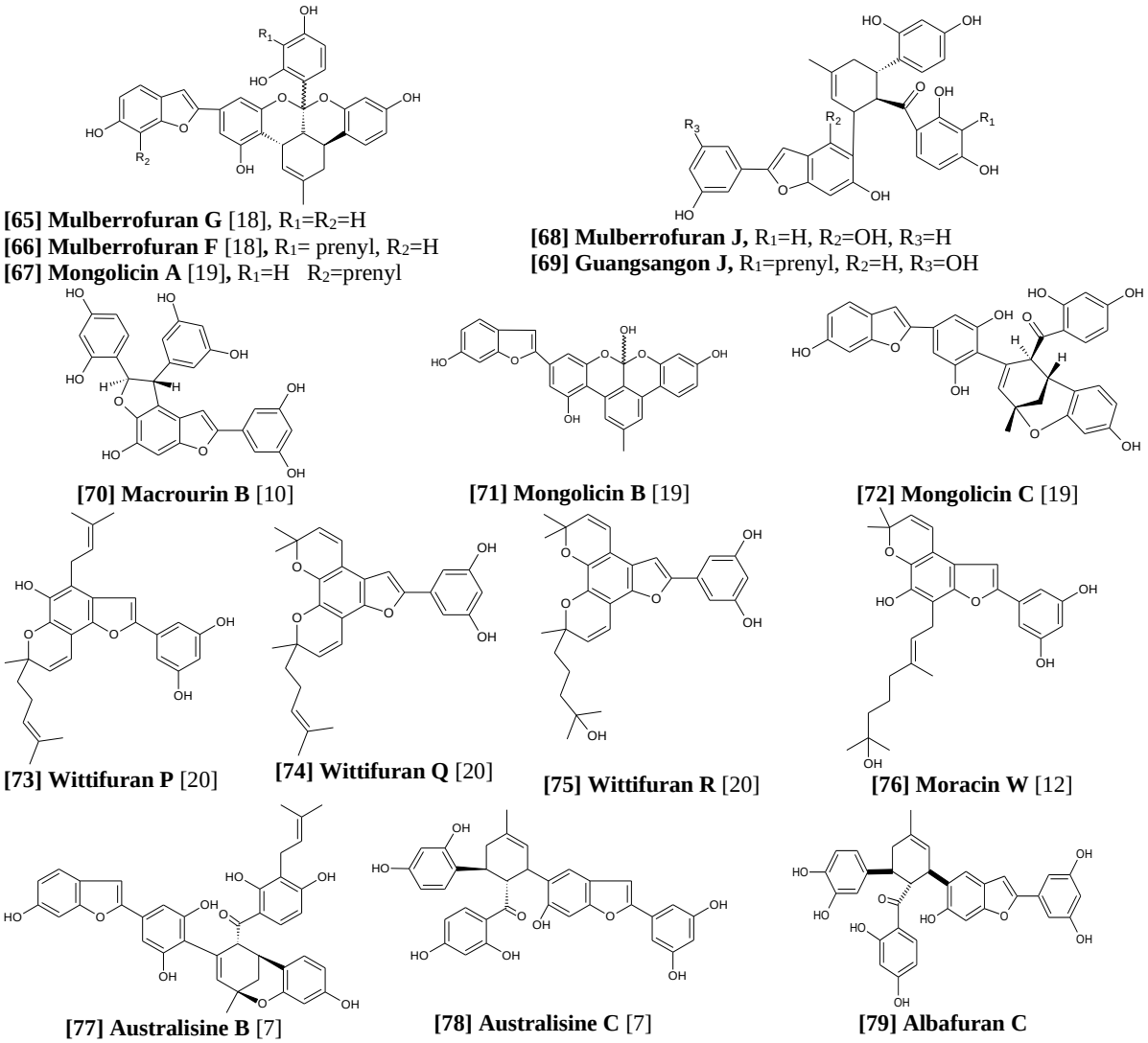


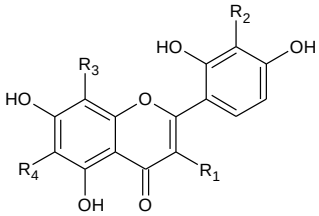
Figure 2: Isolated 2-Arylbenzofuran derivatives from genus *Morus*

4.4. Antidiabetic activity

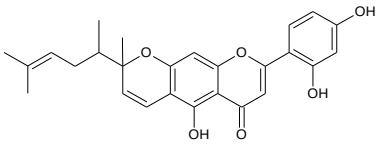
Mulberry leaves behind their use as insect feed, have been widely consumed in Japan, and Korea as antihyperglycemic functional foods. Mulberry leaves tea is common in Asian countries as an antidiabetic drink, it could inhibit the activities of α-glucosidases, sucrase, and maltase enzymes [43]. The root bark of *M. alba* also possesses a promising hypoglycemic activity as reduces the glucose amount, increases insulin production, protects the pancreatic *β*-cells, diminishes lipid peroxidation, and inhibits LDL [48] [49]. Mulberrofurans, kuwanons, and sanggenons showed an antihyperglycemic activity by inhibiting protein tyrosine phosphatase [50, 51]. Albafuran A and B also inhibit α-glucosidase and protein tyrosine phosphatase [52]. Moracins, morusin, cyclomorusin, and neocyclomorusin protect the pancreatic *β*-cells and diminish lipid peroxidation [49]

4.5. Antihyperlipidemic and Hepatoprotective activities

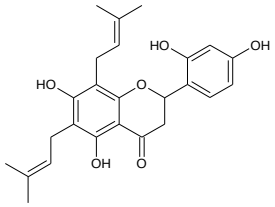
Butanol extract of mulberry leaves inhibits the oxidative modification of LDL and prevents atherosclerosis [2]. The root bark of *M. alba* possesses an antihyperlipidemic effect by inhibiting effect on the synthesis of fatty acids and lowering the plasma triglycerides level, also preventing liver damage in hyperlipidemic rats [48]. Oral administration of the bark extract results in alleviation of atherosclerotic state, LDL oxidation, aggregation, and retention [48]. Sanggenon, sanggenol, and cudraflavone B showed hepatoprotective activities by protective effects against glutamate-induced oxidative stress [53].



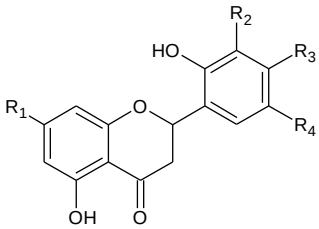
[80] Kuwanon C [10], R_1=prenyl, R_2=H, R_3=prenyl, R_4=H
[81] Kuwanon T, R_1=R_2=prenyl, R_3=R_4=H
[82] Artocarpesin [15], R_1=R_2=R_3=H, R_4=prenyl
[83] Norartocarpetin [21], R_1=R_2=R_3=R_4=H
[84] 5,7,2\,4\-tetrahydroxy-3-methoxyflavone [10], R_1=OMe, R_2=R_3=R_4=H
[85] 5,7,2′,4′-tetrahydroxy-3-geranylflavone [9], R_1=geranyl, R_2=R_3=R_4=H
[86] 3′-geranyl-3-prenyl-2′,4′,5,7-tetrahydroxyflavone [22], R_1=prenyl, R_2=geranyl, R_3=R_4=H



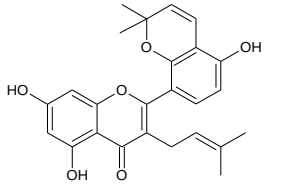
[87] Australone A [23]



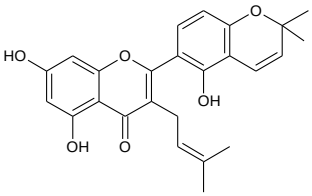
[88] Kushenol E [15]



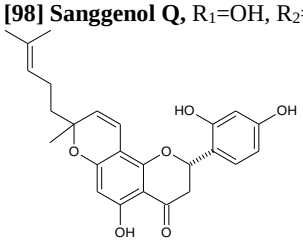
[91] Kuwanon E, R_1=OH, R_2=H, R_3=OH, R_4=geranyl
[92] Kuwanon U, R_1=OH, R_2=H, R_3=OMe, R_4=geranyl
[93] Norartocarpanone, R_1=OH, R_2=H, R_3=OH, R_4=H
[94] Steppogenin-7,4'-di-*O*-*β*-D-glucoside [24], R_1= OGlu, R_2=H, R_3= OGlu, R_4=H
[95] Steppogenin-4'-*O*-*β*-D-glucoside, R_1= OH, R_2=H, R_3= OGlu, R_4=H
[96] Steppogenin-7-*O*-*β*-D-glucoside, R_1= OGlu, R_2=H, R_3= OH, R_4=H
[97] Sanggenol A, R_1=OH, R_2=geranyl, R_3=OH, R_4=H
[98] Sanggenol Q, R_1=OH, R_2=prenyl, R_3=OH, R_4=prenyl



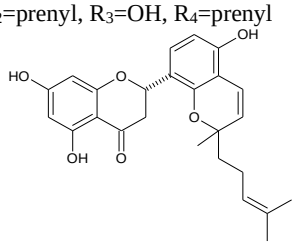
[89] Kuwanon A [25]



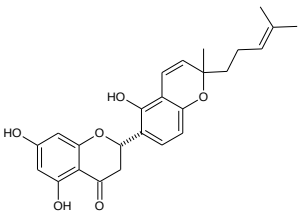
[90] Kuwanon B [25]



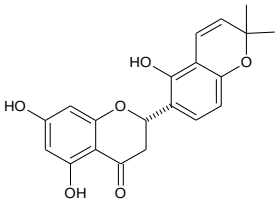
[99] Sanggenol L



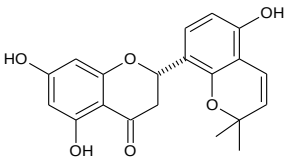
[100] Sanggenon I



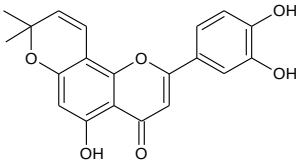
[101] Sanggenon N



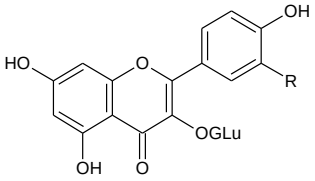
[102] Sanggenon F



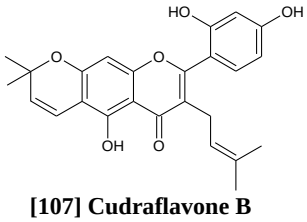
[103] Sanggenon H



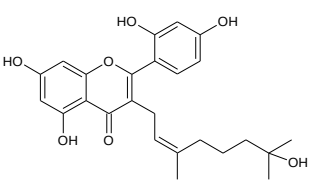
[104] Artochamin C [15]



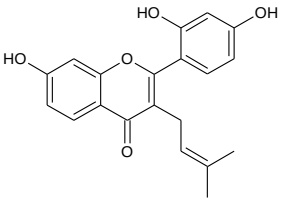
[105] Astragalin [26] R=H
[106] Isoquercitrin [26] R=OH



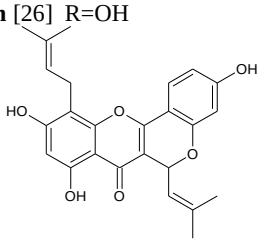
[107] Cudraflavone B



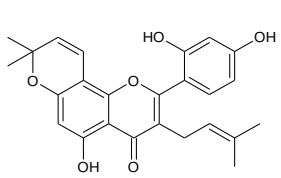
[108] Yunanensol A [9]



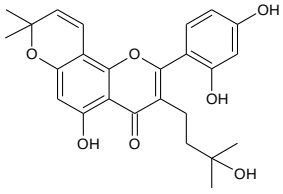
[109] Yunanensol B [9]



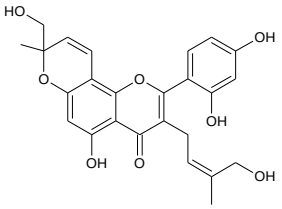
[110] Cyclomulberrin



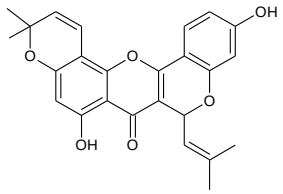
[111] Morusin [10]



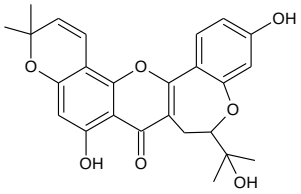
[112] Oxydihydromorusin [25]



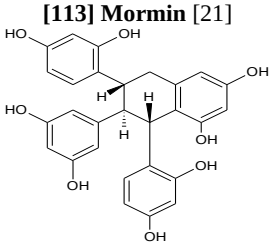
[113] Mormin [21]



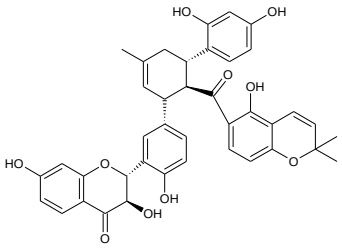
[114] Cyclomorusin [27]



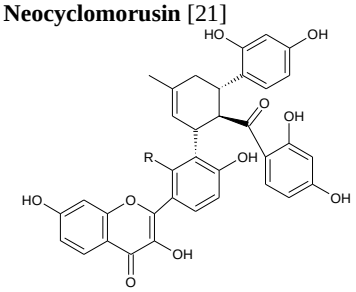
[115] Neocyclomorusin [21]



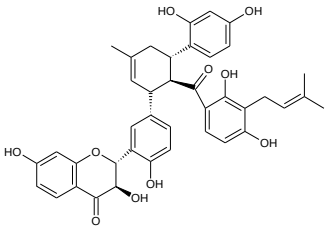
[116] Alboctalol [10]



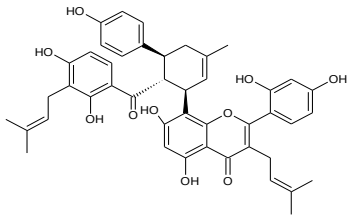
[117] Guangsangon F [28]



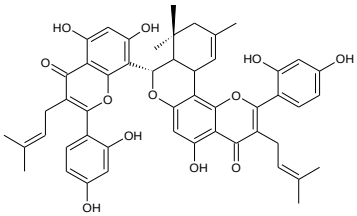
[118] Guangsangon G [28], R=H
[119] Guangsangon I [28], R=OH



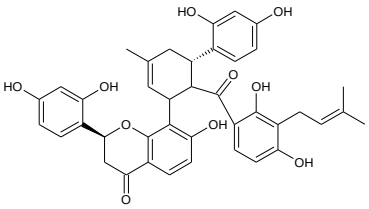
[120] Guangsangon H [28]



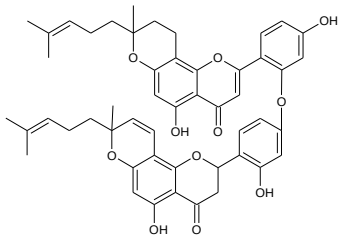
[121] Mongolicin D [19]



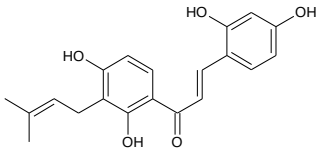
[122] Mongolicin E [19]



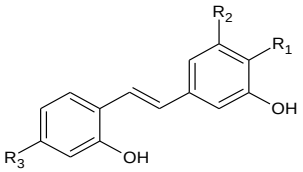
[123] Wittiorumin G [20]



[124] Australone B



[125] Morachalcone A [10]



[126] Mulberroside A R_1=H, R_2=R_3=OGLu
[127] Oxyresveratrol [10]**,** R_1=H, R_2=R_3=OH
4\-prenyl-oxyresveratrol [10]**,** R_1= prenyl, R_2=R_3=OH

Figure 3: Isolated phenolics; flavonoids and stilbenes from genus *Morus*

Table 1: reported activities of isolated compounds from genus *Morus*

No.	Compound name	Biological activity	Mechanism of action	Ref.
	Diels–Alder-type adducts			
1	kuwanon G (moracenin B or albanin F)	Anti-inflammatory	inhibit IL-6 and NO production	[54]
			inhibit arachidonate metabolism	[39] [40]
		Antimicrobial	---	[55] [56]
		Antihypertensive	---	[6]
		Antitumor	Non-peptide bombesin receptor antagonist	[57]
2	kuwanon H (moracenin A or albanin G)	Antihypertensive	----	[58]
		Anti-inflammatory	inhibit arachidonate metabolism	[39] [40]
3	kuwanon M	Antihypertensive	---	[59]
4	Kuwanon O	Antimicrobial	---	[56]
5	Kuwanon L	Antimicrobial	---	[60]
		Antihyperglycemic	inhibit protein tyrosine phosphatase	[51]
6	kuwanon J	Antihyperglycemic	inhibit protein tyrosine phosphatase	[50]
		Antitumor	inhibit hypoxia-induced HIF-1α accumulation	[44]
7	kuwanon R	Antihyperglycemic	inhibit protein tyrosine phosphatase	[50]
		Anti-inflammatory	inhibit NF-κB activity	[61]
8	kuwanon V	Antihyperglycemic	inhibit protein tyrosine phosphatase	[50]
10	kuwanon Y	Antitumor	inhibit protein kinase C	[45]
11	Morusalbanol A	Neuroprotective	attenuate H_2O_2-induced cell damage	[62]
12	Australisine A	Antitumor	*In-vitro* cytotoxicity	[7]
13	Moracenin D	Antihypertensive	---	[63]
14	Moracenin C	Antihypertensive	---	[63]
15	Cathayanon A	Antitumor	inhibit adhesion of leukemia cell to bovine aortic endothelial cells	[64]
16	Sanggenon D	Anti-inflammatory	inhibit arachidonate metabolism	[39] [40]
			Anti-COX activity	[65] [66]
		Antihypertensive	---	[67]
		Antimicrobial	---	[60] [68]
17	Sanggenon E	Anti-inflammatory	Anti-COX activity	[38]
			inhibit TNF-α, IL-1β, and NF-κB	[42]
		Antimicrobial	---	[60]
18	Sanggenon C	Antimicrobial	---	[60]
		Anti-inflammatory	Anti-COX activity	[38]
		Antihyperglycemic	inhibit protein tyrosine phosphatase	[51]
		Antitumor	induce internucleosomal DNA fragmentation	[46]
			induce cell cycle arrest at G0/G1 phase and inhibit the chymotrypsin-like activity	[47]
		Antihypertensive	---	[6]
19	Sanggenon O	Antimicrobial	---	[60]
		Anti-inflammatory	Anti-COX activity	[38]
		Antitumor	inhibit hypoxia-induced HIF-1α accumulation	[44]
20	Cathayanon B	Antitumor	inhibit adhesion of leukemia cell to bovine aortic endothelial cells	[64]
21	Sanggenol M	Antitumor	induce internucleosomal DNA fragmentation	[46]
22	Sanggenon G	Antimicrobial	---	[60]
		Antihyperglycemic	inhibit protein tyrosine phosphatase	[51]
23	Sanggenon T	Depigmenting	tyrosinase inhibitory activity	[69]

24	Sanggenon B	Anti-inflammatory	Anti-COX activity	[66] [38]
		Antimicrobial	---	[68] [60]
25	Soroceal	Anti-inflammatory	inhibit TNF-α, IL-1β and NF-κB	[42]
27	Soroceal B	Antitumor	*In-vitro* cytotoxicity	[70]
	2-Arylbenzofurans			
28	Moracin C	Anti-inflammatory	inhibit NO production	[41]
			inhibit TNF-α, IL-1β, and NF-κB	[42]
		Antioxidant	Superoxide anion scavenging	[36]
			inhibit malondialdehyde production	[37]
		Antimicrobial	---	[71]
		Antitumor	*In-vitro* cytotoxicity	[10]
29	Moracin I	Antihyperglycemic	inhibit α-glucosidase and protein tyrosine phosphatase	[52]
30	Moracin M	Antioxidant	inhibit malondialdehyde production	[37]
			DPPH scavenging activity	[30][31][32]
		Antiviral	Anti-HCV	[72]
		Antimicrobial	---	[71] [30]
		Antihyperglycemic	protect the pancreatic *β*-cells and diminish lipid peroxidation	[49]
32	Moracin N	Antioxidant	Superoxide anion scavenging	[36]
		Depigmenting	tyrosinase inhibitory activity	[73]
37	Mulberrofuran A	Antimicrobial	---	[74]
		Anti-inflammatory	inhibit arachidonate metabolism	[39] [40]
		Antihyperglycemic	inhibit α-glucosidase and protein tyrosine phosphatase	[52]
38	Mulberrofuran D	Antihyperglycemic	inhibit protein tyrosine phosphatase	[50]
		Antitumor	inhibit hypoxia-induced HIF-1α accumulation	[44]
39	Mulberrofuran L	Anti-inflammatory	inhibit NO production	[41]
40	Mulberrofuran W	Antihyperglycemic	inhibit protein tyrosine phosphatase	[50]
		Antitumor	inhibit hypoxia-induced HIF-1α accumulation	[44]
41	Mulberrofuran Y	Anti-inflammatory	inhibit NO production	[41]
			inhibit TNF-α, IL-1β, and NF-κB	[42]
43	Albafuran A	Antitumor	inhibit hypoxia-induced HIF-1α accumulation	[44]
		Antihyperglycemic	inhibit α-glucosidase and protein tyrosine phosphatase	[50] [52]
		Anti-inflammatory	inhibit NO production	[41]
44	Albafuran B	Antihyperglycemic	inhibit α-glucosidase and protein tyrosine phosphatase	[52]
45	Artoindonesianin O	Anti-inflammatory	inhibit NO production	[41]
47	Moracin D	Anti-inflammatory	inhibit NO production	[41]
48	Moracin P	Anti-inflammatory	inhibit NO production	[41]
		Antitumor	inhibit hypoxia-induced HIF-1α accumulation	[44]
		Antiviral	Anti-HCV	[72]
52	Moracin Q	Antimicrobial	---	[71]
		Antitumor	inhibit hypoxia-induced HIF-1α accumulation	[44]
53	Moracin R	Anti-inflammatory	inhibit NO production	[41]
55	Mornigrol D	Anti-inflammatory	inhibit *β*-glucuronidase	[75]
56	Mulberroside C	Antiviral	Anti-HCV	[72]
57	Mulberrofuran H	Anti-inflammatory	inhibit TNF-α, IL-1β and NF-κB	[42]
		Antitumor	inhibit hypoxia-induced HIF-1α accumulation	[44]

59	Mulberrofuran Q	Anti-inflammatory	inhibit arachidonate metabolism	[39] [40]
60	Mulberrofuran C	Antihypertensive	---	[76]
		Antihyperglycemic	inhibit protein tyrosine phosphatase	[51]
		Neuroprotective	Protective effects against glutamate-induced oxidative stress	[53]
64	Chalcomoracin	Antioxidant	Superoxide anion scavenging	[36]
		Antitumor	*In-vitro* cytotoxicity	[7]
65	Mulberrofuran G (albanol A)	Antihyperlipidemic	inhibit LDL atherogenic modifications and lipid peroxides formation	[48]
		Antioxidant	DPPH scavenging activity	[31] [32]
		Antimicrobial	---	[68]
		Antiviral	Anti-HBV	[77]
		Antitumor	inhibit hypoxia-induced HIF-1α accumulation	[44]
			induce apoptotic cell death	[78] [7]
		Antihypertensive	---	[79]
		Anti-inflammatory	inhibit arachidonate metabolism	[39] [40]
		Neuroprotective	Protective effects against glutamate-induced oxidative stress	[53]
		Depigmenting	tyrosinase inhibitory activity	[73]
66	Mulberrofuran F	Antihypertensive	---	[79]
68	Mulberrofuran J	Anti-inflammatory	inhibit arachidonate metabolism	[39] [40]
			inhibit NO production	[70]
72	Mongolicin C	Antitumor	*In-vitro* cytotoxicity	[7]
77	Australisine B	Antitumor	*In-vitro* cytotoxicity	[7]
78	Australisine C	Antitumor	*In-vitro* cytotoxicity	[7]
79	Albafuran C	Antioxidant	Inhibit the release of *β*-glucuronidase	[75]
	Phenolics; flavonoids and stilbenes			
80	kuwanon C	Anti-inflammatory	inhibit arachidonate metabolism	[39] [40]
			inhibit TNF-α, IL-1β, and NF-κB	[42]
			Anti-COX activity	[65] [66]
			inhibit NO production	[41]
		Antimicrobial	---	[30] [68]
		Antihyperlipidemic	inhibit the differentiation of 3T3-L1 adipocytes.	[41]
		Antiplatelet effect	inhibit thromboxane A2 formation	[23]
		Depigmenting	tyrosinase inhibitory activity	[80]
81	Kuwanon T	Antihyperlipidemic	inhibit the differentiation of 3T3-L1 adipocytes.	[41]
		Anti-inflammatory	inhibit NO production	
		Hepatoprotective	Protective effects against glutamate-induced oxidative stress	[53]
83	Norartocarpetin	Anti-inflammatory	inhibit the release of *β*- glucuronidase	[75]
89	kuwanon A	Anti-inflammatory	inhibit NO production	[41]
		Antihyperlipidemic	inhibit the differentiation of 3T3-L1 adipocytes.	
91	Kuwanon E	Anti-inflammatory	inhibit production of IL-6 and NO	[54]
			inhibit NO production	[41]
		Antihyperglycemic	protect the pancreatic *β*-cells and diminish lipid peroxidation	[49]
		Antitumor	inhibit G1/S transition in leukemia cells	[81]
92	Kuwanon U	Antitumor	inhibit G1/S transition in leukemia cells	[81]
93	Norartocarpanone	Anti-inflammatory	inhibit IL-6 and NO	[54]
94	Steppogenin-7,4\- di-*O*-*β*-D-glucoside	Antitumor	*In-vitro* cytotoxicity	[24]
95		Antihyperglycemic	prevent the atrophy of pancreatic *β*-cells	[82]

	Steppogenin-4\-O-*β*-D-glucoside	Depigmenting	tyrosinase inhibitory activity	[83]
98	Sanggenol Q	Hepatoprotective	Protective effects against glutamate-induced oxidative stress	[53]
99	Sanggenol L	Anti-inflammatory	inhibit NO production	[70]
		Antitumor	*In-vitro* cytotoxicity	[70]
101	Sanggenon N	Hepatoprotective	Protective effects against glutamate-induced oxidative stress	[53]
102	Sanggenon F	Anti-inflammatory	inhibit NO production	[41]
		Antihyperlipidemic	inhibit the differentiation of 3T3-L1 adipo-cytes.	[41]
103	sanggenon H	Anti-inflammatory	inhibit TNF-α, IL-1β and NF-κB	[42]
107	Cudraflavone B	Antitumor	inhibit G1/S transition in leukemia cells	[81]
		Anti-inflammatory	inhibit TNF-α gene expression	[84]
		Hepatoprotective	Protective effects against glutamate-induced oxidative stress	[53]
110	Cyclomulberrin	Antitumor	*In-vitro* cytotoxicity	[22]
111	Morusin	Anti-inflammatory	inhibit arachidonate metabolism	[39], [40]
			Anti-COX activity	[65], [66]
			inhibit NO production	[70]
		Antioxidant	Superoxide anion scavenging	[85]
			DPPH scavenging	[30]
		Antimicrobial	---	[30] [68]
		antihyperglycemic	protect the pancreatic *β*-cells and diminish lipid peroxidation	[49]
		Antihyperlipidemic	inhibit the differentiation of 3T3-L1 adipo-cytes.	[41]
		Antitumor	inhibit the induction of ornithine decarbox-ylase	[86]
		Anticholinesterase	---	[87]
		Antiplatelet effect	inhibit thromboxane A2 formation	[23]
112	Oxydihydromoru-sin (Morusinol)	Anti-inflammatory	inhibit arachidonate metabolism	[39] [40]
		Anti-inflammatory	inhibit TNF-α, IL-1β and NF-κB	[42]
		Antitumor	*In-vitro* cytotoxicity	[70]
		Anticholinesterase	---	[87]
114	Cyclomorusin	Antihyperglycemic	protect the pancreatic *β*-cells and diminish lipid peroxidation	[49]
		Antitumor	*In-vitro* cytotoxicity	[22]
		Anticholinesterase	---	[87]
115	Neocyclomorusin	Antihyperglycemic	protect pancreatic *β*-cells and diminish lipid peroxidation	[49]
124	Australone B	Antioxidant	Superoxide anion scavenging	[85]
126	Mulberroside A	Antihyperlipidemic	---	[88]
		Antihyperglycemic	hypoglycemic effects on alloxan-diabetic mice	[89]
127	Oxyresveratrol	Antitumor	inhibit protein kinase C	[45]
		Anti-inflammatory	inhibit iNOS expression	[90]
		Antioxidant	DPPH scavenging activity	[91]
			Superoxide anion scavenging	[92]
		Antimicrobial	---	[30]
		Antihyperlipidemic	---	[88]

5. Conclusion

Recently, *Morus* has been highlighted in various scientific investigations. Mulberry is used in traditional medicine as a kidney tonic, liver tonic, cardioprotective, skin whitening, antihyperglycemic, neuroprotective, and anti-ulcer agent. Mulberry is rich in phenolic compounds especially, 2-Arylbenzofurans, Diels–Alder-type adducts, and flavonoids. It holds free radical scavenging potential, cytotoxicity, anti-inflammatory, antidiabetic, antimicrobial, and improves the functionality of the cardiovascular system. This review will pay attention to the phytochemical and pharmacological features of *Morus* plants. *Morus* has been highlighted in various scientific investigations. Still, researchers should make effort in the identification of bioactive constituents and strengthen the claim of their use in folk medicines.

6. Conflict of interest:

The authors declare that they have no conflict of interest.

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